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Stereo- and Regioselectivity in an Intramolecular Nitrone–Alkene Cycloaddition of Hept-6-enoses with a *trans*-Acetonide Blocking Group

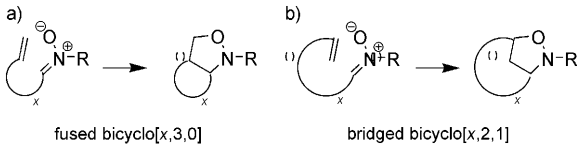
Tony K. M. Shing,*[a] Wai F. Wong,[a] Taketo Ikeno,[b] and Tohru Yamada*[b]

Abstract: The positional effect of the *trans*-acetonide blocking group and the effect of the stereochemistry of the substituents on the regio- and stereoselectivity in intramolecular nitrone–alkene cycloaddition (INAC) reactions of hept-6-enoses are reported. Hept-6-enoses with a 2,3-*trans*-acetonide group were reacted with *N*-alkyl hydroxylamine to give a mixture of *exo* and *endo* cycloadducts (cyclohexanols and cycloheptanols, respectively). Complete formation of *endo* cycloadducts (cycloheptanols) was realized for the INAC reaction of hept-6-enoses containing a 3,4-*trans*-*O*-isopropylidene ring. Similarly, reaction of a hept-6-enose possessing a 4,5-*trans*-acetonide group surprisingly afforded *exo* cycloadducts (cyclohexanols) exclusively. The regio- and stereochemical outcomes of these reactions were rationalized on the basis of transition-state energies obtained by computation.

Keywords: alkenes · carbohydrates · cycloaddition · cycloheptanes · nitrones

Introduction

Intramolecular nitrone–alkene cycloaddition (INAC) constitutes a versatile and efficient synthetic protocol for the construction of polyhydroxylated carbocycles from carbohydrates.[1] The *exo* or the *endo* mode of INAC cyclization affords a fused or a bridged isoxazolidine, respectively (Scheme 1).[2]



Scheme 1. The a) *exo* and b) *endo* modes of INAC cyclization.

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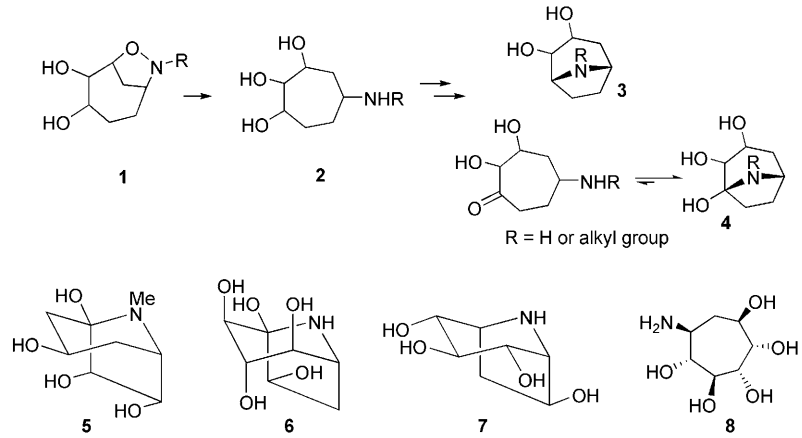
There are only two examples[3] of the synthesis of a bridged bicyclo[4.2.1] system, that is, a cycloheptane skeleton, from branched sugars, however, there are many examples[1] of unbranched hept-6-enose derivatives being used to form the fused bicyclo[4.3.0] system, that is, a cyclohexane skeleton. However, the regio- and diastereoselectivity of these INAC reactions have not been studied.

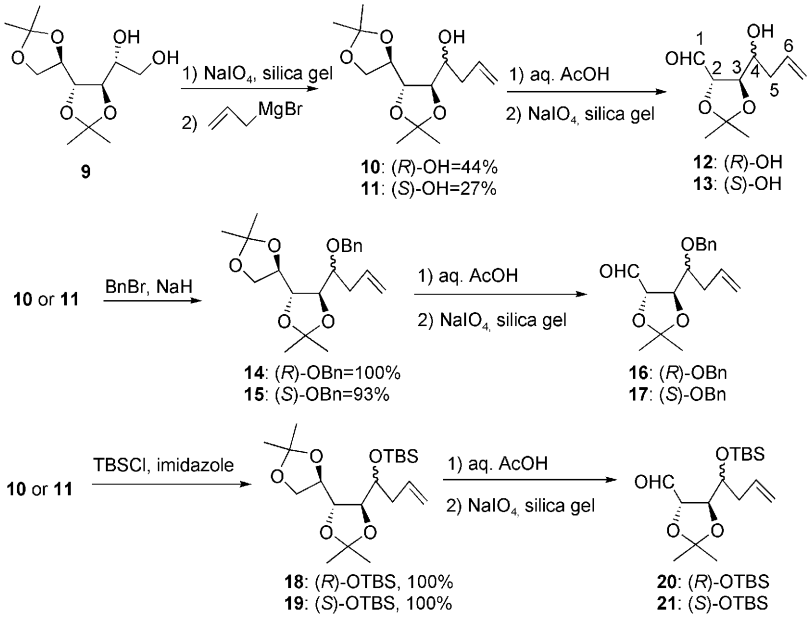
Both the fused and bridged isoxazolidines are key intermediates in the syntheses of natural products or analogues with biological importance.[1] Upon hydrogenolysis of the N–O bond, bridged bicyclo[4.2.1]isoxazolidine **1** provides the skeleton of aminocycloheptanol **2**, which is a new class of glycosidase inhibitor.[4] Further transformation of **2** could give alkaloid tropane **3**[5] and calystegine **4**[6] that exhibits specific glycosidase inhibition (Scheme 2).[7] Recently, we have successfully developed a method for the facile conversion of the bridged bicyclo[4.2.1] systems into two calystegines **5** and **6**, one tropane **7**, and one hydroxylated aminocycloheptane **8**.[8]

Our previous studies[9] have shown that *exo*-INAC cyclization is the preferred pathway for hept-6-enoses containing a *cis*-acetonide (*erythro*-diol-acetonide) to give fused isoxazolidines exclusively, whereas hept-6-enoses with a 2,3-*O*-*trans*-diacetal give a mixture of fused (cyclohexane) and bridged (cycloheptane) isoxazolidines. High yielding and exclusive *endo*-INAC reactions of hept-6-enoses have recently been realized with a 3,4-*O*-*trans*-acetonide to give bridged bicyclo[4.2.1]isoxazolidines for the first time.[8] In the present article, the positional effect of a *trans*-acetonide (*threo*-



Scheme 2. Transformation of isoxazolidine **1**.

diol-acetonide) blocking group on the stereo- and regioselectivity of INAC reactions of hept-6-enoses derived from carbohydrates is reported. Hept-6-enoses with a *trans*-acetonide group placed in different positions (2,3-, 3,4-, or 4,5-position) were synthesized from sugars and then subjected to INAC reactions to give cycloadducts. Theoretical analysis was carried out and the transition state (TS) energies of all the possible cycloadducts were computed. The present findings on the stereochemical outcome of the INAC reactions should assist synthetic chemists in their routes towards the preparation of calystegines, tropanes, and hydroxylated aminocycloheptanes.



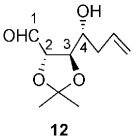
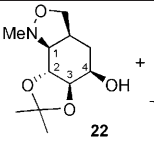
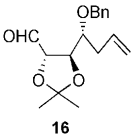
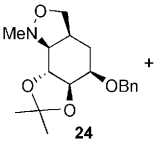
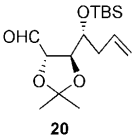
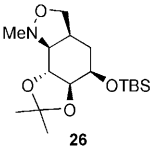
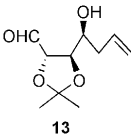
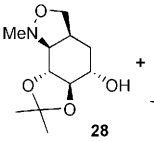
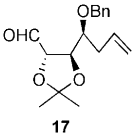
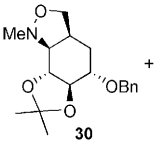
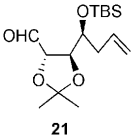
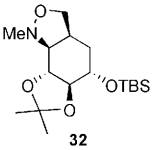
Scheme 3. Preparation of hept-6-enoses **12**, **13**, **16**, **17**, **20**, and **2** (Bn = benzyl; TBS = *tert*-butylsilyl).

Results and Discussion

Hept-6-enoses with a 2,3-*trans*-acetonide group: Diol **9**, synthesized from D-mannitol according to the literature,[10] underwent oxidative cleavage of glycol[11] and then allylation to afford alkenes **10** and **11** in 44 and 27% overall yields, respectively (Scheme 3). Both alkenes **10** and **11** were transformed into aldehydes **12** and **13**, respectively, upon regioselective terminal hydrolysis with aqueous acetic acid (AcOH) and subsequent glycol oxidative cleavage. Aldehydes **16** and **17** were obtained from alkenes **10** and **11**, respectively, through a synthetic sequence of benzylation, acid hydrolysis, and glycol-cleavage oxidation. With the same starting alkenes **10** and **11**, replacing benzylation with silylation and following the latter sequence gave aldehydes **20** and **21**, respectively, in good yields.

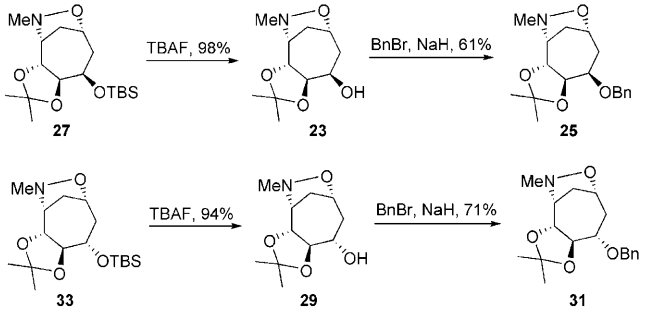
Individual aldehydes **12**, **13**, **16**, **17**, **20**, and **21** underwent an INAC reaction with MeNHOH smoothly to give one *exo* and one *endo* cycloadduct. The results are summarized in Table 1. The INAC reactions of heptenoses **12**, **16**, or **20** proceeded with excellent yields and cycloheptanes (*endo* product) **23**, **25**, or **27**, respectively, were obtained as the major cycloadducts (entries 1–3). As the size of the OR4 group increases from OH to OTBS, the *endo* selectivity increases from 86:14 (entry 1) to 92:8 (entry 3). The *endo* selectivity appears to be controlled by the OR group at C3 and the new C–N bond is always *anti* to OR3 in all entries. In cases in which the OR4 stereochemistry is synergetic, the *endo* cycloadduct was the major product (entries 1–3), otherwise (entries 4–6) the *endo* selectivity is poor and further diminishes as the size of the OR4 group increases. The structures of cycloheptanes **25** and **29**, and cyclohexane **28** were confirmed by X-ray crystallography analyses.[12] Desilylation of **27** gave alcohol **23**, which was benzylated to give cycloheptane **25** (Scheme 4). The constitutions of cycloheptanes **23** and **27** were therefore confirmed. Similar synthetic transformation on cycloheptanes **33** and **29** verified their structures.

Table 1. INAC reactions of hept-6-enoses with 2,3-*trans*-acetonide.

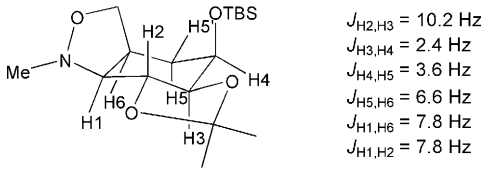
Entry	Aldehyde[a]	Cycloadducts	Yield[b] [%]
1	 **12**	 **22** + **23**	94 **22**/**23** 14:86
2	 **16**	 **24** + **25**	95 **24**/**25** 11:89
3	 **20**	 **26** + **27**	94 **26**/**27** 8:92
4	 **13**	 **28** + **29**	94 **28**/**29** 33:67
5	 **17**	 **30** + **31**	92 **30**/**31** 47:53
6	 **21**	 **32** + **33**	86 **32**/**33** 48:52

[a] Not characterized. [b] Overall isolated yield from the corresponding diol.

The stereochemistry of the cyclohexanes was established with the evidence from 1D ^{1}H NMR spectroscopy coupling data, and 2D COSY and NOESY analysis. The assignment of the stereochemistry of cyclohexane **26** is illustrated in Scheme 5. The quasi-diaxial arrangement of H2 and H3 was supported by the large coupling constant ($J_{H2,H3}$ = 10.2 Hz). The small coupling constants of H3 with H4 ($J_{H3,H4}$ = 2.4 Hz) and H4 with H5 ($J_{H4,H5}$ = 3.6 Hz) suggested a quasi-equatorial positioning of H4. The quasi-axial–axial coupling of H1 with H2 ($J_{H1,H2}$ = 7.8 Hz) and quasi-axial–equatorial coupling of H5 with H6 ($J_{H5,H6}$ = 6.6 Hz) demonstrated that the isoxazolidine ring was bending to the β face as shown in Scheme 5. The large coupling constant ($J_{H1,H6}$ = 7.8 Hz) between H1 and H6 verified an eclipsed conformational arrangement that hinted at a distorted-chair conformation for the cycloadduct **26**. The heterocyclic ring was in a *cis* arrangement and *anti* to the C–O bond at C2.



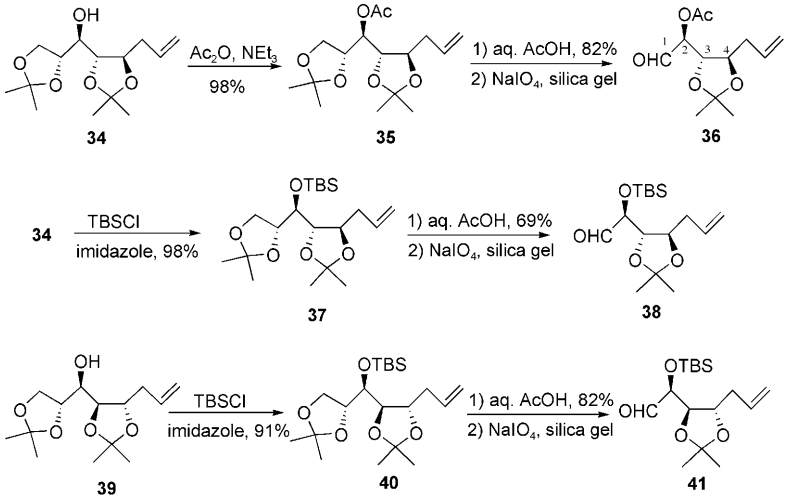
Scheme 4. Structural confirmation of cycloheptanes **23**, **27**, **31**, and **33**.



Scheme 5. Conformation of cyclohexane **26**.

Hept-6-enoses with a 3,4-*trans*-acetonide group: Diacetonide **34**, synthesized from D-ribose,[8] was acetylated to give acetate **35** (Scheme 6). Regioselective acid hydrolysis of acetate **35** gave a diol that was subjected to oxidative glycol cleavage to furnish hept-6-enose **36** as an INAC precursor with a 3,4-*trans*-isopropylidene blocking group.

The C2 hydroxyl group was protected in advance to obtain the desired hept-6-enose **36** instead of a hex-5-enose by further glycol-cleavage oxidation. The C2 substituent effect on the INAC reaction was then studied by converting diacetonide **34** into hept-6-enose **38** with a *tert*-butylsilyl (TBS) group by a reaction sequence involving silylation,



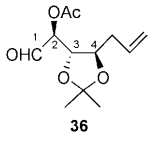
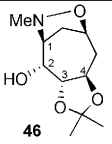
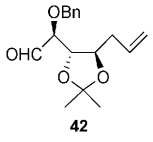
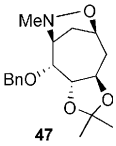
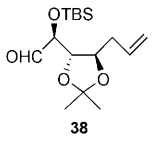
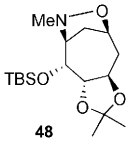
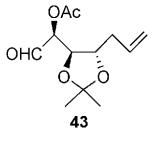
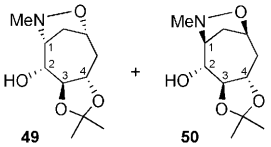
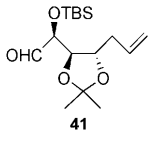
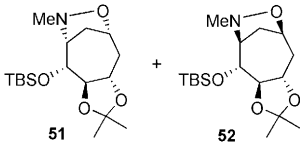
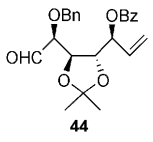
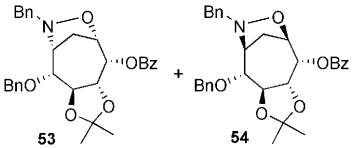
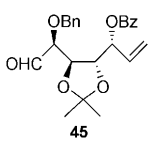
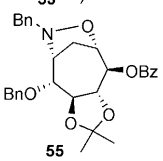
Scheme 6. Preparation of hept-6-enoses **36**, **38**, and **41** (Ac_2O = acetic anhydride).

acid hydrolysis, and glycol oxidative cleavage. Performing the same manipulation as with hept-6-enose **38**, hept-6-enose **41** was synthesized from the known diacetonide **39**.[8] Hept-6-enoses **42**, **43**, **44** (Bz = benzoyl), and **45** shown in Table 2 were synthesized from sugars by following the method detailed in our previous communication.[8]

Complete formation of the cycloheptanes was realized by means of the *endo* mode of the INAC reaction in excellent yields. The stereochemistry of the only/major heterocycle seems to be controlled by the OR group at C3. The new C–N bond is always *anti* to OR3 in all entries. In cases in which the OR2 stereochemistry is synergetic only one cycloadduct is formed (entries 1–3), otherwise the diastereoselectivity is analogously reduced (entries 4 and 5). Different C2 substituents in aldehydes **36**, **42**, and **38** result in the same regio- and stereochemical outcome. The amount of the major diastereomer **51** (entry 5) decreases as the size of the C2 substituent increases from a -OH group in aldehyde **43** (entry 4) to a -OTBS group in aldehyde **41**, which is in line with the stereochemistry mismatch at C2. The major cycloadduct **53** further decreases in entry 6 as there is an additional mismatched stereochemistry at C5, whereas only cycloadduct **55** was obtained with a synergetic C5 stereochemistry (entry 7).

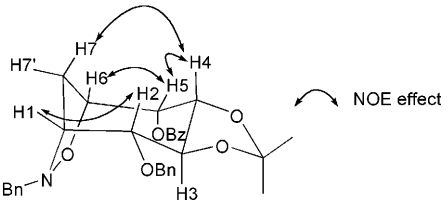
The structures of cycloheptanes **48** and **49** were confirmed by X-ray crystallography analyses.[13] Single crystals of a debenzoylated derivative of **55** confirmed its constitution by X-ray crystallography analyses.[14] The stereochemistry of cycloheptanes **46**, **47**, and **51** was assigned by protective-group transformation of the C2 substituent as described before. For cycloheptane **53**,[15] strong NOE correlations of H4 with H7 and H1 with H2 indicate that the bridgehead is pointing to the β face (Scheme 7). The NOE correlations of H4 with H5 and H5 with H6 demonstrate that the benzoyl group is at the α face. The isoxazolidine ring of cycloheptane **53** is *syn* to the C2 substituent and that of another cycloadduct **54** is *anti* to the C2 substituent by exclusion.

Table 2. INAC reactions of hept-6-enoses with 3,4-*trans*-acetonide.

Entry	Aldehyde[a]	Cycloadduct(s)	Yield[b] [%]
1	 **36**	 **46**	89
2	 **42**	 **47**	97
3	 **38**	 **48**	99
4	 **43**	 **49** **50**	93 **49**/**50** 91:9
5	 **41**	 **51** **52**	100 **51**/**52** 88:12
6	 **44**	 **53** **54**	85 **53**/**54** 66:34
7	 **45**	 **55**	93

[a] Not characterized. [b] Overall isolated yield from the corresponding diol or alcohol.

Hept-6-enoses with a 4,5-*trans*-acetonide group: Enoate **56** was synthesized from D-xylose by means of a Wittig reaction and acetylation according to the literature (Scheme 8).[16] The double bond in enoate **56** was saturated by palladium-catalyzed hydrogenation to give an ester that underwent acid hydrolysis to afford diol **57**. The terminal alkene functionality in alkene **58** was obtained in a high yield from diol **57** on treatment with triphenylphosphine, iodine, and imidazole.[17] Reduction of alkene **58** with diisobutylaluminum hydride (DIBAL-H) afforded alcohol **59** in a quantitative yield. 2-Iodoxybenzoic acid (IBX) oxidation[18] of alcohol **59** gave hept-6-enose **60**, which was subjected to the INAC reaction. Unexpected results of three cyclohexanes **61**, **62**, and **63** were generated in a moderate overall yield (67%). The structure of cyclohexane **61** was confirmed by X-ray crystallography[19] analyses and those of cyclohexanes **62** and **63** were established with the evidence from 1D ^{1}H NMR spectroscopy coupling data and 2D COSY and NOESY analysis. Strong NOE correlations of H1 with H6 and H4 with H6 of cyclohexane **62** illustrate a *cis*-fused

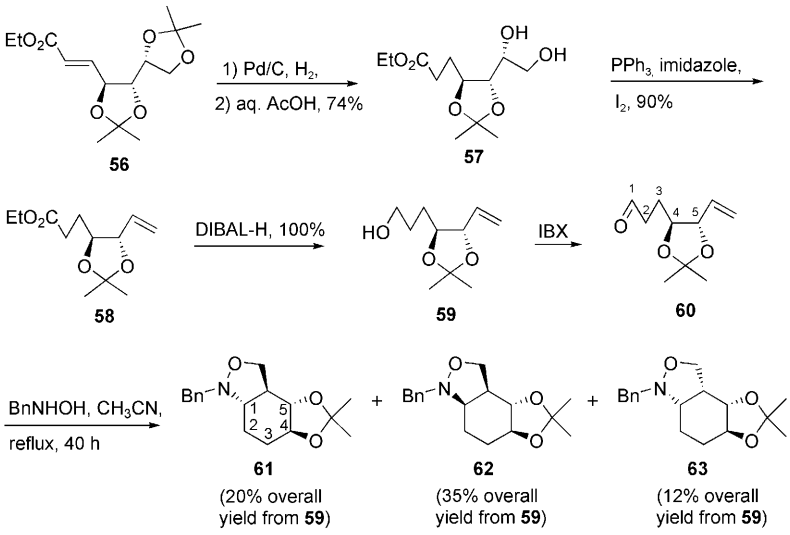


Scheme 7. Conformation of cycloheptane **53** (Bn = benzyl, Bz = benzoyl).

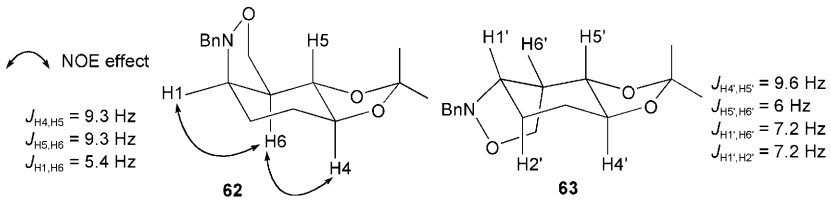
heterocyclic ring bending to the β face as shown in Scheme 9. From the ^{1}H NMR spectrum of **62**, the coupling constant between H1 and H6 ($J_{H1,H6}$ = 5.4 Hz) fell into the range of axial–equatorial coupling. Together with the axial–axial coupling of H4 with H5 ($J_{H4,H5}$ = 9.3 Hz) and H5 with H6 ($J_{H5,H6}$ = 9.3 Hz), it is suggested that a chair conformation is adopted by cyclohexane **62**. In the ^{1}H NMR spectrum of **63**, the large coupling constant between H4 and H5 ($J_{H4,H5}$ = 9.6 Hz) demonstrated a quasi-diaxial arrangement and the smaller one of H5 with H6 ($J_{H5,H6}$ = 6.0 Hz) fell into the range of quasi-axial–equatorial coupling. The coupling constants of H1 with H6 and H1 with H2 were both 7.2 Hz which suggested a distorted-chair conformation with the isoxazolidine ring bending to the α face.

Theoretical analysis: The ground-state structures were calculated with molecular mechanics by using the CONFLEX program for conformational search.[20] Many conformers were obtained and the relatively stable conformers (within 10 kcal mol^{-1} compared with the most stable one) were selected for further analysis. The ground states and all the transition states based on the ground-state structures were calculated by using B3LYP/6-31G* with Gaussian 98.[21,22] The obtained TS energies were compared with each other. The obtained structures were similar to those in previous reports[23,24] and the imaginary frequencies were checked to ensure that the vectors were directed toward the reaction pathway. Intrinsic reaction coordinate (IRC) calculations were performed for the most stable TSs. Only the concerted pathway was calculated as this was reported to be more favorable than the biradical pathway.[23]

The results of nitrone **64** derived from hept-6-enose **12** with a 2,3-*trans*-diacetonide are shown in Table 3. The calculated results suggested that cycloheptanol **23** (experimental

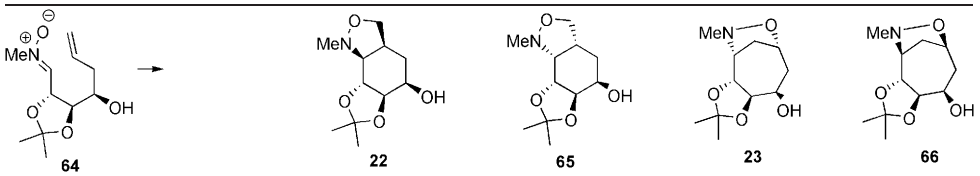


Scheme 8. Preparation of hept-6-enose **60**.



Scheme 9. Conformation of **62** and **63**.

Table 3. Theoretical analysis of INAC of nitrone **64**.[a]



ground state ΔE [kcal mol^{-1}]	3.07	4.62	0	2.90
bond length in TS [Å][b]				
C–C	2.25	2.22	2.17	2.08
C–O	2.07	2.07	2.21	2.33
experimental ratio [%]	14	0	86	0
TS ΔE [kcal mol^{-1}]	2.05	4.94	0	1.66
TS ΔG (100 °C) [kcal mol^{-1}]	1.27	4.84	0	2.14

[a] B3LYP/6-31G* calculations were performed. Relative energies are shown. [b] The new bonds formed in the INAC reaction.

ratio 86%) is the major isomer because it had the lowest Gibbs TS energy. The energy difference between the TSs of **23** and **22** was relatively smaller (1.27 kcal mol^{-1}) than that between **23** and **65** (4.84 kcal mol^{-1}), and **23** and **66** (2.14 kcal mol^{-1}). Therefore, cyclohexanol **22** (experimental ratio 14%) was obtained in low yields. The theoretical analysis is consistent with the experimental results.

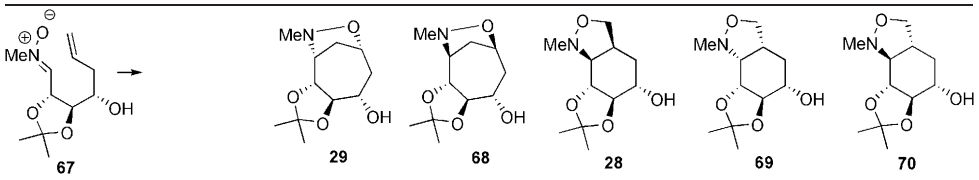
The results of nitrone **67** derived from hept-6-enose **13** are shown in Table 4. The TS leading to cycloheptane **29** is the lowest, which implies that **29** should be formed as the major cycloadduct and is in accord with the experimental results. The even smaller energy difference (0.69 kcal mol^{-1}) between the TSs of **29** and **28** suggested that cyclohexanol **28** (experimental ratio 34%) was obtained in an appreciable yield.

The results of nitrones **71** and **76**, derived from hept-6-enoses **36** and **43**, respectively, with a 3,4-*trans*-diacetonide are shown in Tables 5 and 6, respectively. The energy of the TS leading to cycloheptanol **46** is significantly lower than those of the rest of the TSs. Consequently, the *endo* cycloadduct **46** was the exclusive product. For nitrone **76**, the energy of the TS leading to *endo* cycloadducts **49** and **50** is also appreciably lower than those of the rest of the TSs.

The benzyl group of the nitrone derived from hept-6-enose **60** was replaced with a methyl moiety in the calculation for simplicity.[9] The calculation results for *N*-methyl nitrone **80** are illustrated in Table 7. Since the energies of the TSs leading to cyclohexanols **61**–**63** are relatively lower and the differences are not larger than 0.8 kcal mol^{-1}, we would expect the formation of all of them.

The conformation of the most stable TSs leading to the cycloadducts are showed in Figure 1. Only the skeleton atoms are shown for simplicity.

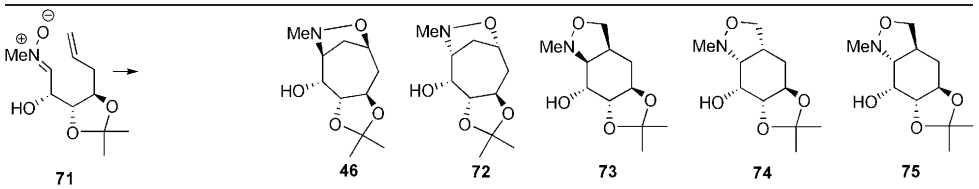
Table 4. Theoretical analysis of INAC of nitrone **67**.[a]



ground state ΔE [kcal mol^{-1}]	0	1.86	2.38	2.78	4.43
bond length in TS [Å][b]					
C–C	2.17	2.12	2.26	2.20	2.15
C–O	2.19	2.27	2.05	2.07	2.14
experimental ratio [%]	67	0	33	0	0
TS ΔE [kcal mol^{-1}]	0	3.27	1.80	4.79	4.66
TS ΔG (80 °C) [kcal mol^{-1}]	0	3.03	0.69	4.92	3.92

[a] B3LYP/6-31G* calculations were performed. Relative energies are shown. [b] The new bonds formed in the INAC reaction.

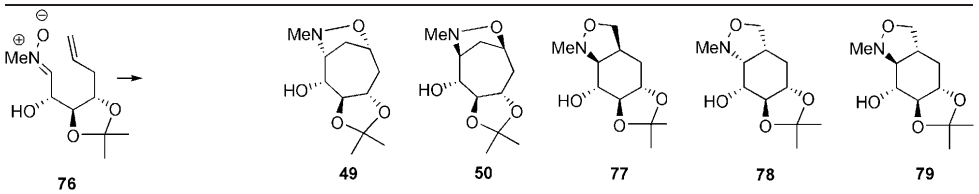
Table 5. Theoretical analysis of INAC of nitrone **71**.[a]



ground state ΔE [kcal mol^{-1}]	0	3.15	5.84	6.73	9.36
bond length in TS [Å][b]					
C–C	2.15	2.06	2.23	2.23	2.16
C–O	2.27	2.33	2.05	2.12	2.14
experimental ratio [%]	100	0	0	0	0
TS ΔE [kcal mol^{-1}]	0	5.46	4.54	5.01	6.33
TS ΔG (80 °C) [kcal mol^{-1}]	0	5.81	4.18	4.45	5.83

[a] B3LYP/6-31G* calculations were performed. Relative energies are shown. [b] The new bonds formed in the INAC reaction.

Table 6. Theoretical analysis of INAC of nitrone **76**.[a]

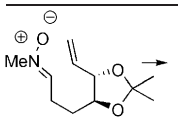
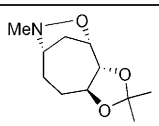
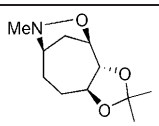
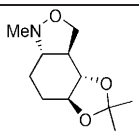
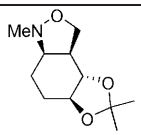
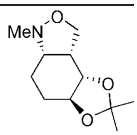


ground state ΔE [kcal mol^{-1}]	0	1.02	5.78	4.79	7.47
bond length in TS [Å][b]					
C–C	2.17	2.11	2.29	2.22	2.16
C–O	2.21	2.28	2.03	2.01	2.12
experimental ratio [%]	91	9	0	0	0
TS ΔE [kcal mol^{-1}]	0	1.52	4.01	4.12	6.06
TS ΔG (80 °C) [kcal mol^{-1}]	0	1.55	3.36	4.30	5.60

[a] B3LYP/6-31G* calculations were performed. Relative energies are shown. [b] The new bonds formed in the INAC reaction.

With the 2,3-*trans*-diequatorial acetonide, the TS leading to cyclohexanes **22** (TS-**22a**) and **28** (TS-**28a**) adopts a chair conformation that results in less efficient bonding orbital overlap as shown in TS-**22b** and TS-**28b**, respectively. Focusing on the *trans*-fused C2 and C3 carbon atoms of TS-**22a** and TS-**28a** revealed torsional strains, which is common in a

Table 7. Theoretical analysis of INAC of nitrone **80**.[a]

	 80	 81	 82	 83	 84	 85
ground state ΔE [kcal mol^{-1}]	0	0.88	3.07	0.22	1.66
bond length in TS [Å][b]					
C–C	2.09	2.14	2.19	2.24	2.24
C–O	2.30	2.23	2.10	2.03	2.07
experimental ratio [%][c]	0	0	20	35	12
TS ΔE [kcal mol^{-1}]	6.91	3.02	0.95	0	1.38
TS ΔG (80 °C) [kcal mol^{-1}]	6.84	3.40	0.32	0	0.80

[a] B3LYP/6-31G* calculations were performed. Relative energies are shown. [b] The new bonds formed in the INAC reaction. [c] Yield for the *N*-benzyl group.

trans-hydrindane system. On the other hand, the twist-chair conformation of TS-**23a** and TS-**29a** allows the orientation of bonding orbitals to be aligned on the same plane in space and lowers the TS energy. The torsional strain of substituents on the *trans*-fused C2 and C3 carbon atoms in TS-**23a** and TS-**29a** is relieved probably due to the twist-chair conformation of the cycloheptane and the torsional energy involved becomes smaller when compared to that in TS-**22a** and TS-**28a**. Cycloheptanes **23** and **29** were therefore formed as the major cycloadduct. Moreover, TS-**22a** is destabilized by a pseudo-1,3-diaxial interaction between the C4 hydroxyl group and the developing isoxazolidine ring; cycloheptane **23** was therefore harvested in a high relative composition of 86%. The (*R*)-C4-OH group in TS-**22a** is situated at the axial position. When the size of the (*R*)-C4-OR group increases from OH to OTBS, the *endo* selectivity increases from 86:14 to 92:8, respectively, as cyclohexanes **22**, **24**, and **26** (*exo* product) are destabilized by the 1,3-diaxial interaction. For the (*S*)-C4-OR group in TS-**29a** at the equatorial position, the *endo* cycloadducts **29**, **31**, and **33** might be destabilized by the steric repulsion between the isoxazolidine ring and the OR group at the same side. Consequently, the *endo* selectivity decreased as the size of the (*S*)-C4-OR group increased.

For nitrone **76**, both the twist-chair and chair conformation of TS-**49b** and TS-**50b**, respectively, result in efficient bonding orbital overlap. Among other *exo* cycloadducts, cyclohexane **77** has the lowest TS energy. To relieve the torsional strain imposed by the 3,4-*trans*-isopropylidene ring, TS-**77a**, which leads to cyclohexane **77**, adopts a conformation in which the bonding orbitals are oriented in different planes in space as shown in TS-**77b**. The less efficient orbital overlap increases the TS energy, which may explain the absence of cyclohexane **77** experimentally. The twist-chair and chair conformation of TSs leading to cycloheptane **49** and **50** are more easily observed from another angle of vision as shown in TS-**49a** and TS-**50a**, respectively. The twist-chair conformation of a seven-membered carbocycle is more stable than the chair conformation with an energy difference of 2.16 kcal mol^{-1}.[25] Such difference in the conformation of the TS may account for the formation of cycloheptane **49** (relative composition 91%) as the major diastereomer.

With nitrone **71**, the C2 substituent of TS-**46a** and TS-**72a** is situated at the axial position. The electronic and steric repulsion between the oxygen atom of the C2 hydroxyl group and that of the nitrone functionality in TS-**72a** is highly unfavorable and increases the TS energy. Cycloheptane **46**, with the heterocyclic ring *anti* to the C2 substituent, was therefore obtained exclusively.

Apart from the *trans*-isopropylidene blocking group, there are no other functional groups on the carbon chain of the TSs leading to cyclohexanes **83**, **84**, and **85**. The *trans*-acetonide in the C4 and C5 position allows the unsubstituted carbon chain to effect a conformation in which the bonding orbitals of the nitrone and the alkene were aligned on the same plane, to have efficient bonding orbital overlap. The torsional strain on TS-**82a** imposed by the 4,5-*trans*-isopropylidene ring is relieved by adopting a boatlike conformation, which has a relatively higher energy than the chair conformation. Moreover, the bonding orbitals are not oriented closely on the same plane as shown in TS-**82b** and the orbital overlap is inefficient.

Concerning stereoselectivity, the cyclohexane cycloadducts were usually *cis*-fused as in the case of nitrones **64**, **67**, and **80** because of more efficient overlap of bonding orbitals.

Conclusion

A series of hept-6-enoses was synthesized from sugars to investigate the positional effect of the *trans*-acetonide blocking group and the stereochemistry of the substituents on the regio- and stereoselectivity in INAC reactions. Hept-6-enoses with a 2,3-*trans*-acetonide gave a mixture of *exo* and *endo* cycloadducts. Complete formation of *endo* cycloadducts (cycloheptanes) was realized with a 3,4-*trans*-isopropylidene ring. However, hept-6-enoses possessing a 4,5-*trans*-acetonide, surprisingly, afforded *exo* cycloadducts (cyclohexanes) exclusively. The regio- and stereochemical outcomes of these reactions were rationalized on the basis of transition-state energies obtained by computation.

By studying the transition state leading to the cycloadducts obtained by computation, the regioselectivity was found to be controlled by the blocking groups that affect the conformation of the transition states. The torsional strain imposed by the *trans*-acetonide significantly affects the con-

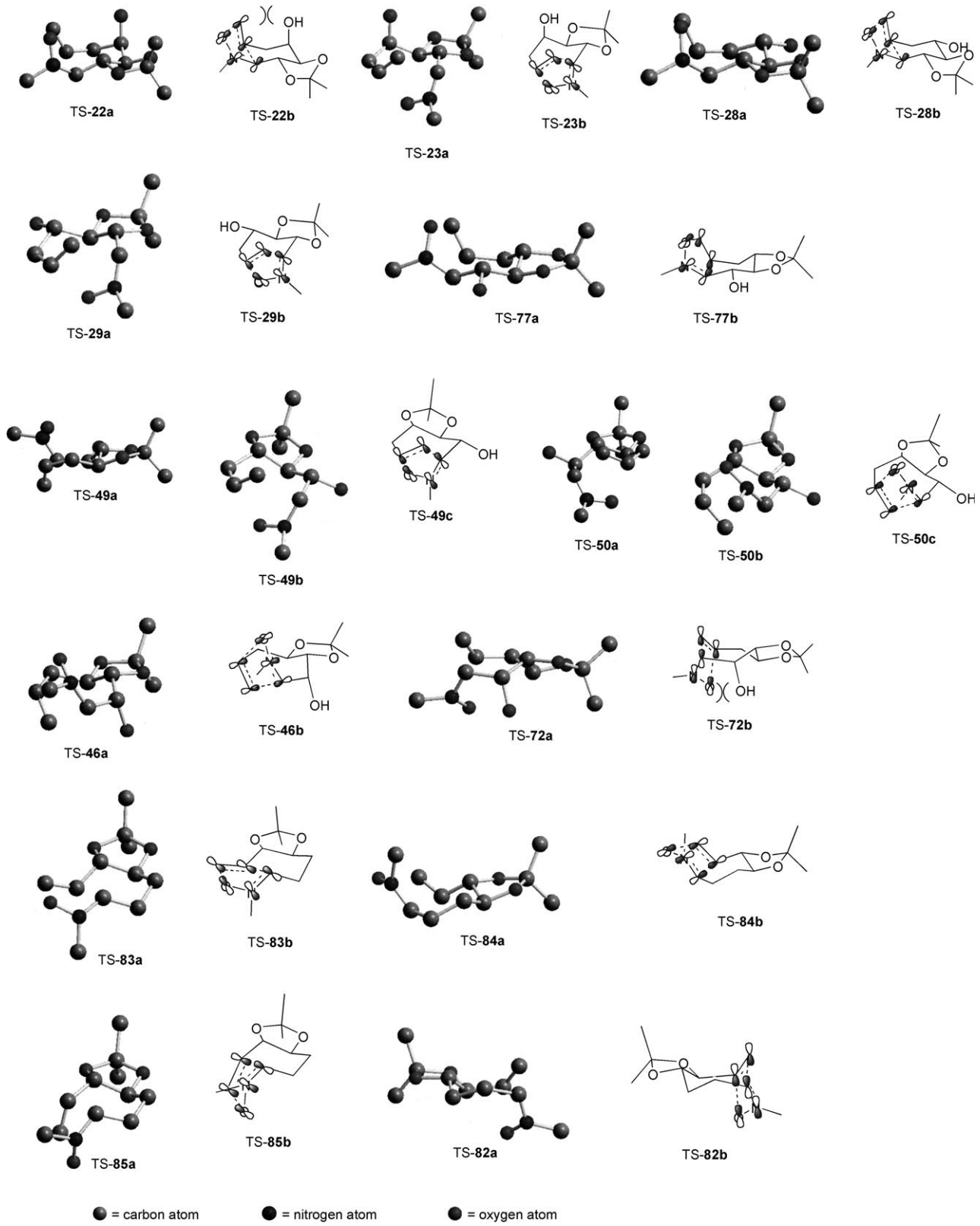


Figure 1. Transition states of the cycloadducts.

formation of the TSs and therefore the extent of the overlap of bonding orbitals.

A cycloheptane TS is more flexible and can exist in more conformations than a cyclohexane TS. It is proposed that

the TSs leading to the cycloheptanes can better accommodate the 2,3- or 3,4-*trans*-isopropylidene group and the torsional strain imposed by that blocking group is relieved. The bonding orbitals of the TSs leading to the cycloheptanes are oriented on the same plane in space, which results in more efficient orbital overlap and lower TS energy. With a 3,4-*trans*-diacetonide, *endo* cycloadducts (cycloheptane) were synthesized exclusively and in excellent yield.

The stereochemistry of the isoxazolidine ring was correlated to the C3 substituent. The cyclohexanes obtained are usually *cis*-fused. In the case of the cycloheptanes, the major isoxazolidine ring is always *anti* to the C3 substituent.

With this novel blocking-group strategy, polyhydroxylated cyclohexanes and cycloheptanes with a nitrogen functionality can be constructed regio- and stereoselectively from sugars by means of the INAC approach.

Experimental Section

NMR spectra were measured at 300.13 (^{1}H) or 75.47 MHz (^{13}C) in $CDCl_3$, unless stated otherwise. All chemical shifts were recorded in ppm relative to tetramethylsilane ($\delta = 0.0$ ppm).

General procedure for the glycol-cleavage reaction: $NaIO_4$ (3 equiv) was dissolved in a minimum amount of hot water (≈80 °C). Silica gel (230–400 mesh, 10 × weight of diol) was added to this solution with vigorous swirling and shaking. The mixture was suspended in CH_2Cl_2 and then a solution of diol (1 equiv) in CH_2Cl_2 was added. After vigorous stirring at room temperature for 1 h, the mixture was filtered. The filtrate was concentrated under reduced pressure to give the aldehyde product.

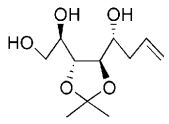
General procedure for selective deprotection with aqueous acetic acid: A solution of diol (1.0 mmol) in 80% aqueous AcOH (8 mL) was stirred at room temperature. The solvent was removed under reduced pressure and the residue was purified by using flash chromatography.

1,2,3-Trideoxy-5,6:7,8-di-*O*-isopropylidene-D-*manno*-oct-1-enitol (10) and 1,2,3-trideoxy-5,6:7,8-di-*O*-isopropylidene-D-*gluco*-oct-1-enitol (11): Diol **9** (1.48 g, 5.63 mmol) was converted into an aldehyde by following the glycol-cleavage procedure. A 1 M solution of allylmagnesium bromide in Et_2O (16.9 mL, 16.9 mmol) was added dropwise to a stirred solution of the aldehyde in Et_2O (50 mL) at −78 °C under N_2 over 30 min. After stirring at −78 °C for a further 1 h and then at room temperature for 12 h, the mixture was quenched with saturated NH_4Cl solution and the aqueous phase was extracted with Et_2O (2 × 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by using flash chromatography (hexane/CH_2Cl_2/EtOAc 10:1:2) to afford firstly alkene **10** (668 mg, 44% overall yield from **9**) and secondly alkene **11** (408 mg, 27% overall yield from **9**) as colorless oils.

*Data for **10***: $R_f = 0.35$ (hexane/$CHCl_3$/EtOAc 5:1:1); $[\alpha]_D^{20} = +6.20$ ($c = 1.75$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.36$–1.38 (2s, 9H), 1.44 (s, 3H), 2.25 (dt, $J = 15.3$, 7.5 Hz, 1H), 2.53 (dd, $J = 14.4$, 5.4 Hz, 1H), 3.44 (s, 1H), 3.68–3.75 (m, 3H), 4.00 (dd, $J = 9.0$, 5.1 Hz, 1H), 4.04–4.08 (m, 1H), 4.19 (dd, $J = 8.1$, 5.7 Hz, 1H), 5.10–5.21 (m, 2H), 5.94 ppm (dddd, $J = 16.8$, 9.9, 7.5, 6.3 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): $\delta = 1.36$–1.38 (2s, 9H), 1.44 (s, 3H), 2.25 (dt, $J = 15.3$, 7.5 Hz, 1H), 2.53 (dddd, $J = 15.6$, 6.3, 3.0, 1.5 Hz, 1H), 3.66–3.74 (m, 3H), 4.00 (dd, $J = 7.8$, 5.1 Hz, 1H), 4.05–4.10 (m, 1H), 4.19 (dd, $J = 7.8$, 5.7 Hz, 1H), 5.10–5.20 (m, 2H), 5.94 ppm (dddd, $J = 17.1$, 10.2, 7.5, 6.6 Hz, 1H); ^{13}C NMR: $\delta = 25.5$, 26.8, 27.2, 27.3, 38.5, 68.3, 72.1, 76.8, 81.4, 83.2, 109.7, 110.6, 117.9, 135.1 ppm; IR (thin film): $\tilde{\nu} = 3473$, 2987, 2936, 1372, 1215, 1070, 844, 512 cm^{-1}; MS (CI): *m*/*z* (%): 273 (26) $[M+H]^+$, 85 (56), 71 (89), 69 (100), 67 (70); HRMS (CI): *m*/*z* calcd for $C_{14}H_{24}O_5$ $[M+H]^+$: 273.1697; found: 273.1695.

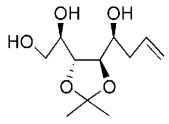
*Data for **11***: $R_f = 0.26$ (hexane/$CHCl_3$/EtOAc 5:1:1); $[\alpha]_D^{20} = -2.77$ ($c = 1.44$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.34$ (s, 3H), 1.38 (s, 3H), 1.41–1.42 (2s, 6H), 2.15 (d, $J = 9.0$ Hz, 1H), 2.27–2.44 (m, 2H), 3.76 (q, $J = 7.8$ Hz, 1H), 3.89–4.00 (m, 3H), 4.05 (ddd, $J = 8.1$, 5.7, 4.5 Hz, 1H), 4.14 (dd, $J = 8.1$, 6.0 Hz, 1H), 5.10–5.18 (m, 2H), 5.89 ppm (ddt, $J = 17.4$, 10.2, 7.2 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): $\delta = 1.34$ (s, 3H), 1.38 (s, 3H), 1.41–1.42 (2s, 6H), 2.27–2.41 (m, 2H), 3.76 (t, $J = 6.3$ Hz, 1H), 3.89–4.00 (m, 3H), 4.05 (dt, $J = 7.8$, 4.8 Hz, 1H), 4.14 (dd, $J = 8.1$, 5.7 Hz, 1H), 5.10–5.17 (m, 2H), 5.89 ppm (ddt, $J = 17.1$, 10.2, 6.9 Hz, 1H); ^{13}C NMR: $\delta = 25.7$, 27.1, 27.5, 27.6, 39.7, 68.2, 69.9, 77.6, 82.7, 109.8, 110.2, 117.9, 135.2 ppm; IR (thin film): $\tilde{\nu} = 2496$, 2986, 1371, 1214, 1067, 845, 511 cm^{-1}; MS (CI): *m*/*z* (%): 273 (78) $[M+H]^+$, 257 (18) $[M-OCH_3]^+$, 215 (76), 157 (100), 139 (57); HRMS (CI): *m*/*z* calcd for $C_{14}H_{24}O_5$ $[M+H]^+$: 273.1697; found: 273.1703.

Triol 10a: By following the aqueous acetic acid deprotection procedure and purification by using flash chromatography (hexane/EtOAc 5:1 to 1:3), alkene **10** (139 mg, 0.510 mmol) gave firstly starting material **10** (6.90 mg, 5%) and secondly triol **10a** (108 mg, 96% based on recovering starting material) as a colorless oil. Data for **10a**: $R_f = 0.19$ (hexane/EtOAc 1:2); $[\alpha]_D^{20} = +5.33$ ($c = 1.32$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.37$ (s, 6H), 2.22 (dt, $J = 14.4$, 8.1 Hz, 1H), 2.63 (dddd, $J = 14.4$, 6.3, 2.7, 1.5 Hz, 1H), 3.07 (br s, 1H), 3.61–3.89 (m, 7H), 5.16–5.22 (m, 2H), 5.87 ppm (dddd, $J = 18.3$, 10.5, 8.1, 6.3 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): $\delta = 1.37$ (s, 6H), 2.22 (dt, $J = 14.4$, 8.1 Hz, 1H), 2.62 (dddd, $J = 12.9$, 6.3, 3.1, 1.5 Hz, 1H), 3.61–3.86 (m, 6H), 5.16–5.22 (m, 2H), 5.87 ppm (dddd, $J = 18.3$, 10.5, 8.1, 6.3 Hz, 1H); ^{13}C NMR: $\delta = 27.2$, 27.3, 39.2, 64.2, 72.3, 73.0, 80.8, 82.5, 109.7, 119.2, 134.3 ppm; IR (thin film): $\tilde{\nu} = 3339$, 2986, 2935, 1372, 1214, 1071, 872 cm^{-1}; MS (FAB): *m*/*z* (%): 233 (28) $[M+H]^+$, 185 (100), 93 (85); HRMS (FAB): *m*/*z* calcd for $C_{11}H_{20}O_5$ $[M+H]^+$: 233.1384; found: 233.1386.



10a

Triol 11a: By following the aqueous acetic acid deprotection procedure and purification by using flash chromatography (hexane/EtOAc 5:1 to 1:3), alkene **11** (200 mg, 0.734 mmol) gave firstly starting material **11** (33.2 mg, 17%) and secondly triol **11a** (136 mg, 95% based on recovering starting material) as a colorless oil. Data for **11a**: $R_f = 0.16$ (hexane/EtOAc 1:2); $[\alpha]_D^{20} = -8.06$ ($c = 1.60$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.39$ (s, 3H), 1.42 (s, 3H), 2.30 (ddd, $J = 14.4$, 8.7, 7.5 Hz, 1H), 2.47 (dt, $J = 14.1$, 6.0 Hz, 1H), 2.57–2.64 (m, 2H), 3.36 (br s, 1H), 3.69–3.72 (m, 2H), 3.81–3.84 (m, 2H), 3.97 (t, $J = 6.6$ Hz, 1H), 4.03 (dd, $J = 7.8$, 2.4 Hz, 1H), 5.12–5.19 (m, 2H), 5.87 ppm (ddt, $J = 17.1$, 10.2, 7.2 Hz, 1H); ^{13}C NMR: $\delta = 27.4$, 27.5, 38.9, 64.2, 69.8, 73.1, 81.7, 109.8, 118.5, 135.0 ppm; IR (thin film): $\tilde{\nu} = 3387$, 2986, 1373, 1215, 1068, 872 cm^{-1}; MS (FAB): *m*/*z* (%): 233 (35) $[M+H]^+$, 185 (85), 93 (100); HRMS (FAB): *m*/*z* calcd for $C_{11}H_{20}O_5$ $[M+H]^+$: 233.1384; found: 233.138806.

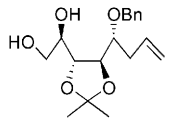


11a

4-*O*-Benzyl-1,2,3-trideoxy-5,6:7,8-di-*O*-isopropylidene-D-*manno*-oct-1-enitol (14): Sodium hydride (80%, 1.76 g, 43.2 mmol) was suspended in dry THF (50 mL) under nitrogen at 0 °C. A solution of alkene **10** (2.31 g, 8.47 mmol) in THF (100 mL) was added dropwise over 1 h at 0 °C, and then the mixture was stirred for 1 h at 0 °C. Benzyl bromide (2.56 mL, 21.6 mmol) was added dropwise over 20 min and tetra-*n*-butylammonium iodide (319 mg, 0.863 mmol) was added. The reaction mixture was stirred at room temperature for 12 h. Water was then added slowly at 0 °C to destroy the excess of hydride, and this was followed by the addition of saturated NH_4Cl solution. The aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered. Concentration of the filtrate followed by purification using flash chromatography (hexane/Et_2O 3:1) gave benzyl ether **14** (3.07 g, 100%) as a colorless oil. $R_f = 0.53$ (hexane/Et_2O 3:1); $[\alpha]_D^{20} = +11.7$ ($c = 2.27$ in $CHCl_3$); ^{1}H NMR: $\delta = 1.33$–1.40 (4s, 12H), 2.44 (t, $J = 6.0$ Hz, 2H), 3.65 (q, $J = 6.0$ Hz, 1H), 3.92–4.00 (m, 2H), 4.03–4.17

(m, 3H), 4.64 (2d, J=11.7, 11.7 Hz, 2H), 5.07 (dd, J=9.9, 1.5 Hz, 1H), 5.14 (dd, J=17.4, 1.8 Hz, 1H), 5.88 (ddt, J=17.1, 9.9, 6.9 Hz, 1H), 7.26–7.37 ppm (m, 5H); ^{13}C NMR: δ=25.8, 26.9, 27.8, 35.1, 67.3, 72.6, 77.4, 79.1, 79.4, 81.1, 109.9, 110.2, 117.7, 128.0, 128.4, 128.7, 135.3, 138.7 ppm; IR (thin film): $\tilde{\nu}$=2986, 1371, 1213, 1069, 848, 698 cm^{-1}; MS (EI): m/z (%): 347 (32) $[M-OCH_3]^+$, 143 (100), 91 (100); HRMS (EI): m/z calcd for $C_{21}H_{30}O_5$ $[M-OCH_3]^+$: 347.1853; found: 347.1850.

Diol 14a: By following the aqueous acetic acid deprotection procedure and purification by using flash chromatography (hexane/EtOAc 10:1 to 3:1), benzyl ether **14** (1.02 g, 2.81 mmol) gave firstly starting material **14** (51.2 mg, 5%) and secondly diol **14a** (821 mg, 95% based on recovering starting material) as a colorless oil.

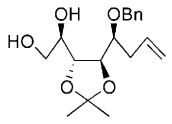


14a

Data for **14a**: R_f=0.52 (hexane/EtOAc 1:2); $[\alpha]_D^{20}$=−49.6 (c=2.34 in $CHCl_3$); ^{1}H NMR: δ=1.35–1.36 (2s, 6H), 2.27 (brs, 1H), 2.49 (ddd, J=15.0, 7.8, 4.2 Hz, 1H), 2.71 (ddd, J=15.0, 6.0, 4.5 Hz, 1H), 3.54–3.62 (m, 3H), 3.70–3.74 (m, 2H), 3.82 (t, J=7.2 Hz, 1H), 3.92 (dd, J=8.4, 7.2 Hz, 1H), 4.47 (d, J=11.1 Hz, 1H), 4.76 (d, J=11.1 Hz, 1H), 5.15–5.29 (m, 2H), 5.93 ppm (dddd, J=16.8, 10.2, 7.8, 6.6 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ=1.35–1.36 (2s, 6H), 2.49 (ddd, J=14.7, 7.8, 3.9 Hz, 1H), 2.71 (ddd, J=15.0, 6.3, 4.8 Hz, 1H), 3.55–3.66 (m, 3H), 3.71 (dd, J=11.1, 3.9 Hz, 1H), 3.82 (t, J=7.5 Hz, 1H), 3.92 (dd, J=8.4, 7.2 Hz, 1H), 4.47 (d, J=11.1 Hz, 1H), 4.76 (d, J=11.1 Hz, 1H), 5.15–5.25 (m, 2H), 5.93 ppm (dddd, J=17.1, 10.2, 7.8, 6.6 Hz, 1H); ^{13}C NMR: δ=27.1, 27.2, 34.8, 64.3, 72.0, 73.3, 79.8, 79.9, 80.9, 109.8, 118.8, 128.8, 128.9, 129.0, 133.3, 136.9 ppm; IR (thin film): $\tilde{\nu}$=3408, 2986, 1381, 1213, 1076, 872, 699 cm^{-1}; MS (FAB): m/z (%): 323 (67) $[M+H]^+$, 265 (21), 185 (39), 91 (100); HRMS (FAB): m/z calcd for $C_{18}H_{26}O_5$ $[M+H]^+$: 323.1853; found: 323.1858.

4-*O*-Benzyl-1,2,3-trideoxy-5,6:7,8-di-*O*-isopropylidene-D-*gluco*-oct-1-enitol (15): By following the same procedure for benzylation of alkene **10** to give benzyl ether **14**, alkene **11** (763 mg, 2.80 mmol) was converted into benzyl ether **15** (945 mg, 93%) as a colorless oil. R_f=0.37 (hexane/Et_2O 3:1); $[\alpha]_D^{20}$=+12.0 (c=3.84 in $CHCl_3$); ^{1}H NMR: δ=1.34 (s, 3H), 1.34 (s, 3H), 1.37 (s, 6H), 1.42 (s, 3H), 2.41–2.58 (m, 2H), 3.60 (td, J=6.9, 2.4 Hz, 1H), 3.89 (dd, J=7.2, 4.2 Hz, 1H), 3.98–4.13 (m, 4H), 4.56 (d, J=11.7 Hz, 1H), 4.70 (d, J=11.7 Hz, 1H), 5.08 (ddd, J=10.2, 2.1, 0.9 Hz, 1H), 5.16 (ddd, J=17.1, 3.0, 1.2 Hz, 1H), 5.88 (ddt, J=17.1, 10.2, 7.2 Hz, 1H), 7.26–7.35 ppm (m, 5H); ^{13}C NMR: δ=25.6, 26.9, 27.3, 36.2, 67.9, 72.8, 77.6, 77.6, 77.9, 82.0, 109.7, 109.9, 117.8, 127.9, 128.0, 128.7, 135.2, 138.9 ppm; IR (thin film): $\tilde{\nu}$=2987, 1371, 1214, 1070, 848, 698, 512 cm^{-1}; MS (EI): m/z (%): 363 (38) $[M+H]^+$, 362 (100) $[M]^+$, 347 (50) $[M-OCH_3]^+$, 143 (100), 101 (55), 91 (99), 43 (64); HRMS (EI): m/z calcd for $C_{21}H_{30}O_5$ $[M]^+$: 362.3088; found: 362.2085.

Diol 15a: By following the aqueous acetic acid deprotection procedure and purification by using flash chromatography (hexane/EtOAc 10:1 to 3:1), benzyl ether **15** (187 mg, 0.512 mmol) gave firstly starting material **15** (19.7 mg, 11%) and secondly diol **15a** (144 mg, 96% based on recovering starting material) as a colorless oil.

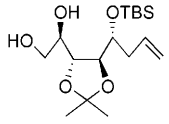


15a

Data for **15a**: R_f=0.59 (hexane/EtOAc 1:2); $[\alpha]_D^{20}$=+3.17 (c=2.42 in $CHCl_3$); ^{1}H NMR: δ=1.36 (s, 3H), 1.40 (s, 3H), 2.19 (t, J=6.0 Hz, 1H), 2.40 (dt, J=14.4, 8.1 Hz, 1H), 2.54 (dddt, J=14.4, 6.6, 4.2, 1.5 Hz, 1H), 3.59–3.67 (m, 3H), 3.73–3.82 (m, 2H), 3.92 (t, J=7.2 Hz, 1H), 4.00 (dd, J=8.1, 3.3 Hz, 1H), 4.59 (d, J=11.4 Hz, 1H), 4.73 (d, J=11.4 Hz, 1H), 5.10 (ddt, J=9.9, 1.8, 0.9 Hz, 1H), 5.18 (dq, J=17.1, 1.5 Hz, 1H), 5.87 (ddt, J=17.1, 10.2, 7.2 Hz, 1H), 7.31–7.37 ppm (m, 5H); ^{1}H NMR ($CDCl_3$–D_2O): δ=1.36 (s, 3H), 1.40 (s, 3H), 2.40 (dt, J=14.4, 7.5 Hz, 1H), 2.54 (dddt, J=14.4, 6.6, 4.5, 1.5 Hz, 1H), 3.56–3.67 (m, 2H), 3.92 (t, J=7.5 Hz, 1H), 4.00 (dd, J=8.1, 3.3 Hz, 1H), 4.59 (d, J=11.4 Hz, 1H), 4.73 (d, J=11.4 Hz, 1H), 5.10 (ddt, J=9.9, 1.8, 0.9 Hz, 1H), 5.18 (dq, J=17.1, 1.5 Hz, 1H), 5.87 (ddt, J=17.1, 10.2, 7.2 Hz, 1H), 7.31–7.37 ppm (m, 5H); ^{13}C NMR: δ=27.3, 27.3, 35.1, 64.4, 73.0, 73.8, 77.0, 77.7, 80.8, 109.5, 118.0, 128.6, 129.0, 135.2, 137.5 ppm; IR (thin film): $\tilde{\nu}$=3407, 2986, 1371, 1213, 1071, 871, 698 cm^{-1}; MS (FAB): m/z (%): 323 (56) $[M+H]^+$, 185 (27), 93 (32), 91 (100); HRMS (FAB): m/z calcd for $C_{18}H_{26}O_5$ $[M+H]^+$: 323.1853; found: 323.1859.

1,2,3-Trideoxy-5,6:7,8-di-*O*-isopropylidene-4-*O*-silyl-D-*manno*-oct-1-enitol (18): A solution of alkene **10** (105 mg, 0.387 mmol), imidazole (78.9 mg, 1.16 mmol), and TBSCl (117 mg, 0.773 mmol) in dry DMF (1 mL) was stirred at room temperature for 15 h. The mixture was quenched with saturated $NaHCO_3$ solution and the aqueous phase was extracted with Et_2O (2×20 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by using flash chromatography (hexane/Et_2O 1:5) to afford silyl ether **18** (150 mg, 100%) as a colorless oil. R_f=0.70 (hexane/Et_2O 2:1); $[\alpha]_D^{20}$=+4.81 (c=1.53 in $CHCl_3$); ^{1}H NMR: δ=0.08–0.09 (2s, 6H), 0.91 (s, 9H), 1.34–1.36 (2s, 6H), 1.39 (s, 3H), 1.41 (s, 3H), 2.35–2.39 (m, 2H), 3.86–4.00 (m, 4H), 4.06–4.17 (m, 2H), 5.05–5.13 (m, 2H), 5.85 ppm (ddt, J=17.1, 9.9, 7.2 Hz, 1H); ^{13}C NMR: δ=−4.3, −4.2, 18.2, 25.4, 26.0, 26.6, 27.2, 27.5, 37.7, 66.8, 72.5, 76.7, 77.1, 82.2, 109.5, 117.5, 134.8 ppm; IR (thin film): $\tilde{\nu}$=2987, 2933, 2858, 1371, 1256, 1066, 837, 776 cm^{-1}; MS (FAB): m/z (%): 387 (24) $[M+H]^+$, 185 (50), 101 (64), 73 (100); HRMS (FAB): m/z calcd for $C_{20}H_{38}O_5Si$ $[M+H]^+$: 387.2561; found: 387.2573.

Diol 18a: By following the aqueous acetic acid deprotection procedure and purification by using flash chromatography (hexane/EtOAc 10:1 to 3:1), silyl ether **18** (120 mg, 0.311 mmol) gave firstly starting material **18** (40.1 mg, 33%) and secondly diol **18a** (48.7 mg, 68% based on recovering starting material) as a colorless oil.

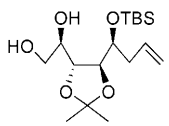


18a

Data for **18a**: R_f=0.22 (hexane/Et_2O 1:1); $[\alpha]_D^{20}$=−25.3 (c=1.13 in $CHCl_3$); ^{1}H NMR: δ=0.14–0.15 (2s, 6H), 0.92 (s, 9H), 1.37–1.38 (2s, 6H), 2.23 (brs, 1H), 2.44–2.48 (m, 2H), 3.21 (d, J=3.6 Hz, 1H), 3.65–3.85 (m, 4H), 3.91–3.97 (m, 2H), 5.11–5.17 (m, 2H), 5.88 ppm (ddt, J=18.0, 9.6, 7.2 Hz, 1H); ^{13}C NMR: δ=−3.9, −3.7, 18.5, 26.3, 27.3, 27.4, 38.7, 64.3, 73.5, 74.2, 80.0, 80.9, 110.0, 118.8, 133.3 ppm; IR (thin film): $\tilde{\nu}$=3407, 2930, 1254, 1079, 836, 776 cm^{-1}; MS (FAB): m/z (%): 347 (50) $[M+H]^+$, 185 (82), 93 (64), 75 (67); HRMS (FAB): m/z calcd for $C_{17}H_{34}O_5Si$ $[M+H]^+$: 347.2248; found: 347.2248.

1,2,3-Trideoxy-5,6:7,8-di-*O*-isopropylidene-4-*O*-silyl-D-*gluco*-oct-1-enitol (19): By following the same procedure for silylation of alkene **10** to give silyl ether **18**, alkene **11** (730 mg, 2.68 mmol) was converted into silyl ether **19** (708 mg, 100%) as a colorless oil. R_f=0.56 (hexane/Et_2O 4:1); $[\alpha]_D^{20}$=+23.9 (c=3.46 in $CHCl_3$); ^{1}H NMR: δ=0.08 (s, 6H), 0.90 (s, 9H), 1.34 (s, 3H), 1.41 (s, 6H), 2.30 (dddt, J=13.8, 7.2, 6.0, 1.2 Hz, 1H), 2.48 (ddt, J=13.8, 7.2, 1.2 Hz, 1H), 3.80 (ddd, J=7.5, 6.3, 3.0 Hz, 1H), 3.85–3.92 (m, 2H), 3.99 (t, J=7.2 Hz, 1H), 4.04–4.14 (m, 2H), 5.04–5.15 (m, 2H), 2.83 ppm (ddt, J=17.1, 10.2, 7.2 Hz, 1H); ^{13}C NMR: δ=−3.9, −3.7, 18.6, 25.7, 26.3, 26.9, 27.4, 27.8, 39.3, 67.9, 72.0, 77.6, 77.6, 82.2, 109.8, 109.9, 117.8, 135.2 ppm; IR (thin film): $\tilde{\nu}$=2933, 1371, 1254, 1073, 836, 776 cm^{-1}; MS (EI): m/z (%): 371 (30) $[M-OCH_3]^+$, 287 (62), 271 (83), 185 (83), 143 (83), 101 (96), 73 (100); HRMS (EI): m/z calcd for $C_{20}H_{38}O_5Si_2$ $[M-OCH_3]^+$: 371.2248; found: 371.2251.

Diol 19a: By following the aqueous acetic acid deprotection procedure and purification by using flash chromatography (hexane/EtOAc 10:1 to 3:1), silyl ether **19** (458 mg, 1.18 mmol) gave firstly starting material **19** (90.2 mg, 20%) and secondly diol **19a** (206 mg, 63% based on recovering starting material) as a colorless oil.



19a

Data for **19a**: R_f=0.27 (hexane/Et_2O 1:2); $[\alpha]_D^{20}$=−11.9 (c=1.50 in $CHCl_3$); ^{1}H NMR: δ=0.11–0.13 (2s, 6H), 0.90 (s, 9H), 1.37 (s, 3H), 1.39 (s, 3H), 2.21–2.31 (brs, 1H; dt, J=14.1, 7.8 Hz, 1H), 2.52 (ddd, J=14.1, 6.3, 4.5 Hz,

1H), 3.62 (dtd, J=8.4, 5.4, 1.5 Hz, 1H), 3.69–3.73 (m, 1H), 3.81–3.85 (brs, 1H; dd, J=8.4, 3.3 Hz, 1H), 3.93 (t, J=8.1 Hz, 1H), 3.99 (d, J=1.5 Hz, 1H), 4.04 (dt, J=7.8, 3.9 Hz, 1H), 5.06–5.12 (m, 2H), 5.80 ppm (dddd, J=17.1, 10.2, 7.8, 6.6 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ=0.11–0.13 (2s, 6H), 0.90 (s, 9H), 1.37 (s, 3H), 1.39 (s, 3H), 2.26 (dt, J=14.4, 8.1 Hz, 1H), 2.52 (dddt, J=14.1, 5.7, 4.2, 1.5 Hz, 1H), 3.61 (dt, J=8.1, 3.9 Hz, 1H), 3.71 (dd, J=11.1, 4.5 Hz, 1H), 3.81–3.85 (dd, J=6.3, 3.9 Hz, 1H; dd, J=6.6, 3.0 Hz, 1H), 3.93 (t, J=8.1 Hz, 1H), 4.04 (dt, J=7.8, 3.9 Hz, 1H), 5.06–5.15 (m, 2H), 5.80 ppm (dddd, J=16.8, 10.2, 7.8, 6.6 Hz, 1H); ^{13}C NMR: δ=−4.1, −4.0, 18.5, 26.2, 27.3, 27.4, 37.5, 64.3, 71.9, 72.4, 76.9, 83.2, 109.2, 118.3, 135.3 ppm; IR (thin film): $\tilde{\nu}$=3403, 2931, 1463, 1253, 1074, 836, 776 cm^{-1}; MS (FAB): m/z (%): 347 (100) $[M+H]^+$, 185 (57), 75 (40), 73 (49); HRMS (FAB): m/z calcd for $C_{17}H_{34}O_5Si$ $[M+H]^+$: 347.2248; found: 347.2256.

Isoxazolidines 22 and 23: By following the glycol-cleavage procedure, triol **10a** (66.5 mg, 0.286 mmol) was converted into aldehyde **12** as a colorless oil. *N*-Methylhydroxylamine hydrochloride (71.7 mg, 0.859 mmol) and $NaHCO_3$ (120 mg, 1.43 mmol) were added to a solution of aldehyde **12** in CH_3CN (15 mL). The reaction mixture was stirred at room temperature for 30 min until the disappearance of the starting material as shown by using TLC analysis. The mixture was then heated under reflux for 24 h. After cooling, the mixture was partitioned between EtOAc (20 mL) and water (20 mL). The aqueous layer was extracted with EtOAc (2× 20 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate followed by using flash chromatography (CH_3Cl/MeOH 40:1) gave firstly cycloheptane **23** (53.5 mg, 81% overall yield from **10a**) as a white solid and secondly cyclohexane **22** (8.50 mg, 13% overall yield from **10a**) as a white solid.

*Data for **23***: R_f=0.26 (EtOAc); m.p. 113–114 °C; $[\alpha]_D^{20}$=+24.6 (c=1.61 in $CHCl_3$); ^{1}H NMR: δ=1.42 (s, 3H), 1.48 (s, 3H), 1.80 (dd, J=16.2, 3.0 Hz, 1H), 2.05–2.15 (m, 2H), 2.21 (d, J=12.9 Hz, 1H), 2.56–2.65 (m, 4H), 3.54 (dd, J=7.2, 2.1 Hz, 1H), 3.92 (dd, J=8.7, 2.1 Hz, 1H), 4.24–4.30 (m, 2H), 4.56 ppm (dt, J=9.3, 2.7 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ=1.42 (s, 3H), 1.48 (s, 3H), 1.79 (dd, J=15.9, 3 Hz, 1H), 2.09 (ddd, J=16.2, 6.9, 2.7 Hz, 1H), 2.22 (d, J=12.6 Hz, 1H), 2.56–2.65 (m, 4H), 3.54 (dd, J=7.2, 1.8 Hz, 1H), 3.93 (dd, J=9.0, 2.1 Hz, 1H), 4.25–2.29 (m, 2H), 4.56 ppm (dt, J=9.3, 2.7 Hz, 1H); ^{13}C NMR: δ=27.3 (CH_3), 27.4 (CH_3), 31.4 (CH_2), 38.8 (CH_2), 47.3 (CH_3), 63.9 (CH), 65.7 (CH), 75.4 (CH), 76.3 (CH), 78.3 (CH), 108.6 ppm (C); IR (thin film): $\tilde{\nu}$=3468, 2984, 2929, 1379, 1230, 1073, 856, 754 cm^{-1}; MS (ESI): m/z (%): 230 (100) $[M+H]^+$; HRMS (ESI): m/z calcd for $C_{11}H_{19}O_4N$ $[M+H]^+$: 230.1387; found: 230.1386; elemental analysis calcd (%) for $C_{11}H_{19}O_4$: C 57.63, H 8.35, N 6.11; found: C 57.51, H 8.40, N 6.08.

*Data for **22***: R_f=0.17 (EtOAc); m.p. 87–88 °C; $[\alpha]_D^{20}$=−51.7 (c=1.42 in $CHCl_3$); ^{1}H NMR: δ=1.44–1.45 (2s, 6H), 1.89–2.05 (dt, J=15.0, 5.4 Hz, 1H; dt, J=15.3, 4.5 Hz, 1H), 2.36 (brs, 1H), 2.70 (s, 3H), 3.03–3.05 (m, 2H), 3.45 (dd, J=10.2, 3.3 Hz, 1H), 3.71 (m, 1H), 4.04 (t, J=9.0 Hz, 1H), 4.15 (t, J=8.4 Hz, 1H), 4.32 ppm (q, J=3.9 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ=1.44–1.45 (2s, 6H), 1.87–2.05 (dt, J=15.6, 5.7 Hz, 1H; dt, J=15.3, 4.8 Hz, 1H), 2.70 (s, 3H), 2.92–3.06 (m, 2H), 3.42 (dd, J=10.2, 3.3 Hz, 1H), 3.71 (t, J=8.1 Hz, 1H), 4.04 (t, J=9.6 Hz, 1H), 4.15 (t, J=8.4 Hz, 1H), 4.30 ppm (q, J=3.6 Hz, 1H); ^{1}H NMR ($CDCl_3$/C_6D_6 5:1): δ=1.41–1.42 (2s, 6H), 1.78–1.83 (m, 1H), 1.93 (dt, J=15.3, 3.9 Hz, 1H), 2.30 (brs, 1H), 2.66 (s, 3H), 2.87–2.96 (m, 2H), 3.37 (dd, J=10.2, 3.0 Hz), 3.66 (brs, 1H), 3.99–4.12 (dd, J=9.6, 7.8 Hz, 1H; m, 1H), 4.25 ppm (q, J=3.3 Hz, 1H); ^{1}H NMR ($CDCl_3$/C_6D_6 (5:1)–D_2O): δ=1.41–1.42 (2s, 6H), 1.80 (dt, J=15.0, 5.7 Hz, 1H), 1.93 (ddd, J=15.3, 4.8, 3.9 Hz, 1H), 2.66 (s, 3H), 2.85–2.97 (m, 2H), 3.36 (dd, J=10.2, 3.0 Hz, 1H), 3.66 (t, J=7.8 Hz, 1H), 3.99–4.10 (m, 2H), 4.23 ppm (q, J=3.6 Hz, 1H); ^{13}C NMR: δ=27.1 (CH_3), 27.6 (CH_3), 30.3 (CH_2), 38.9 (CH), 45.0 (CH_3), 65.3 (CH), 70.5 (CH), 71.6 (CH_2), 73.2 (CH), 79.2 (CH), 111.3 ppm (C); MS (FAB): m/z (%): 230 (20) $[M+H]^+$, 186 (87), 185 (74), 93 (100); IR (thin film): $\tilde{\nu}$=3430, 2984, 2932, 1439, 1372, 1229, 1095, 1031, 845, 789 cm^{-1}; HRMS (FAB): m/z calcd for $C_{11}H_{19}O_4N$ $[M+H]^+$: 230.1387; found: 230.1390; elemental analysis calcd (%) for $C_{11}H_{19}O_4$: C 57.63, H 8.35, N 6.11; found: C 57.55, H 8.39, N 6.06.

Cycloheptane 23 from 27: A 1 M solution of TBAF in THF (0.29 mL, 0.288 mmol) was added to a solution of silyl ether **27** (66.0 mg, 0.192 mmol) in THF (6 mL). The reaction mixture was stirred at room temperature for 5 d and the solvent was removed under reduced pressure. Flash chromatography of the residue ($CHCl_3$/MeOH 40:1) afforded cycloheptane **23** (43.0 mg, 98%) as a white solid.

Isoxazolidines 24 and 25: By following the glycol-cleavage procedure, diol **14a** (1.04 g, 3.24 mmol) was converted into aldehyde **16** as a colorless oil. By following the cyclization procedure of aldehyde **12** and purification by using flash chromatography (hexane/EtOAc 1:1), aldehyde **16** gave firstly cycloheptane **25** (784 mg, 76% overall yield from **14a**) as a white solid and secondly cyclohexane **24** (193 mg, 19% overall yield from **14a**) as a colorless oil.

*Data for **25***: R_f=0.33 (hexane/EtOAc 1:2); m.p. 53–54 °C; $[\alpha]_D^{20}$=+7.06 (c=1.52 in $CHCl_3$); ^{1}H NMR: δ=1.47 (s, 3H), 1.49 (s, 3H), 1.90 (ddd, J=15.6, 3.3, 1.2 Hz, 1H), 2.00 (ddd, J=15.9, 5.7, 2.1 Hz, 1H), 2.34 (d, J=12.6 Hz, 1H), 2.56 (ddd, J=12.6, 9.3, 7.5 Hz, 1H), 2.64 (s, 3H), 3.55 (dd, J=7.5, 2.1 Hz, 1H), 4.06–4.12 (d, J=5.7 Hz, 1H; dd, J=9.0, 2.1 Hz, 1H), 4.32 (d, J=9.0 Hz, 1H), 4.56–4.62 (d, J=11.7 Hz, 1H; m, 1H), 4.79 (d, J=11.7 Hz, 1H), 7.26–7.34 ppm (m, 5H); ^{1}H NMR ($CDCl_3$/C_6D_6 2:1): δ=1.37 (s, 3H), 1.42 (s, 3H), 1.65 (ddd, J=15.9, 3.6, 1.2 Hz, 1H), 1.80 (ddd, J=15.9, 6.0, 2.1 Hz, 1H), 2.11 (d, J=12.6 Hz, 1H), 2.26 (ddd, J=12.6, 9.3, 7.2 Hz, 1H), 2.45 (s, 3H), 3.33 (dd, J=7.2, 2.1 Hz, 1H), 3.91 (d, J=5.7 Hz, 1H), 3.97 (dd, J=6.0, 2.4 Hz, 1H), 4.28 (d, J=9.0 Hz, 1H), 4.33 (d, J=9.3 Hz, 1H), 4.44 (d, J=12.0 Hz, 1H), 4.66 (d, J=12.0 Hz, 1H), 7.09–7.24 ppm (m, 6H); ^{13}C NMR: δ=27.3 (CH_3), 27.4 (CH_3), 31.1 (CH_2), 38.2 (CH_2), 47.4 (CH_3), 64.1 (CH), 73.4 (CH_2), 73.5 (CH), 75.6 (CH), 76.7 (CH), 78.3 (CH), 108.8 (C), 127.6 (CH), 127.8 (CH), 128.7 (CH), 139.3 ppm (C); MS (EI): m/z (%): 320 (6) $[M+H]^+$, 319 (22) $[M]^+$, 154 (28), 91 (100), 84 (45); IR (thin film): $\tilde{\nu}$=3983, 2922, 1368, 1236, 1236, 1075, 756 cm^{-1}; HRMS (EI): m/z calcd for $C_{18}H_{25}O_4N$ $[M]^+$: 319.1778; found: 319.1774; elemental analysis calcd (%) for $C_{18}H_{25}O_4N$: C 67.69, H 7.89, N 4.38; found: C 67.38, H 7.90, N 4.19.

*Data for **24***: R_f=0.26 (hexane/EtOAc 1:2); $[\alpha]_D^{20}$=−16.3 (c=2.67 in $CHCl_3$); ^{1}H NMR: δ=1.45–1.46 (2s, 6H), 1.81 (ddd, J=15.3, 6.3, 4.5 Hz, 1H), 2.13 (d, J=15.6 Hz, 1H), 2.70 (s, 3H), 2.98–2.31 (m, 1H), 3.16 (t, J=8.1 Hz, 1H), 3.51 (dd, J=10.2, 2.5 Hz, 1H), 3.85 (t, J=8.7 Hz, 1H), 4.12–4.22 (m, 3H), 4.57 (d, J=12.0 Hz, 1H), 4.90 (d, J=12.0 Hz, 1H), 7.26–7.33 ppm (m, 5H); ^{13}C NMR: δ=27.1 (CH_3), 27.6 (CH_3), 29.1 (CH_2), 38.4 (CH), 45.2 (CH_3), 70.4 (CH), 71.1 (CH_2), 73.2 (CH_2), 73.3 (CH), 80.2 (CH), 110.6 (C), 127.4 (CH), 127.7 (CH), 128.7 (CH), 139.2 ppm (C); IR (thin film): $\tilde{\nu}$=2984, 2929, 1369, 1227, 1101, 846, 736, 698 cm^{-1}; MS (EI): m/z (%): 320 (30) $[M+H]^+$, 319 (100) $[M]^+$, 91 (100); HRMS (EI): m/z calcd for $C_{18}H_{25}O_4N$ $[M]^+$: 319.1778; found: 319.1775.

Cycloheptane 25 from 23: By following the same procedure for benzylation of alkene **10** to give benzyl ether **14**, cycloheptane **23** (11.6 mg, 0.051 mmol) was converted into cycloheptane **25** (9.90 mg, 61%) as a white solid.

Isoxazolidines 26 and 27: By following the glycol-cleavage procedure, diol **18a** (25.8 mg, 0.0745 mmol) was converted into aldehyde **20** as a colorless oil. By following the cyclization procedure of aldehyde **12** and purification by using flash chromatography (hexane/Et_2O 2:3), aldehyde **20** gave firstly cycloheptane **27** (22.2 mg, 87% overall yield from **18a**) and secondly cyclohexane **26** (2.00 mg, 7% overall yield from **18a**) as white solids.

*Data for **27***: R_f=0.44 (hexane/EtOAc 1:1); m.p. 50–51 °C; $[\alpha]_D^{20}$=−2.80 (c=3.84 in $CHCl_3$); ^{1}H NMR: δ=0.05 (s, 3H), 0.09 (s, 3H), 0.89 (s, 9H), 1.39 (s, 3H), 1.46 (s, 3H), 1.62–1.69 (m, 3H), 2.00 (ddd, J=15.6, 5.7, 2.1 Hz, 1H), 2.36 (d, J=12.6 Hz, 1H), 2.54 (ddd, J=12.3, 9.0, 7.2 Hz, 1H), 2.63 (s, 3H), 3.53 (dd, J=7.2, 2.1 Hz, 1H), 3.97 (dd, J=9.0, 2.4 Hz, 1H), 4.18 (d, J=9.0 Hz, 1H), 4.24 (d, J=5.4 Hz, 1H), 4.56 ppm (d, J=9.6 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ=0.05 (s, 3H), 0.08 (s, 3H), 0.89 (s, 9H), 1.39 (s, 3H), 1.46 (s, 3H), 1.65 (ddd, J=15.6, 3.6, 1.2 Hz, 1H), 2.00 (ddd, J=15.6, 5.4, 2.1 Hz, 1H), 2.37 (d, J=12.6 Hz, 1H), 2.54 (ddd, J=12.6, 9.3, 7.5 Hz, 1H), 2.63 (s, 3H), 3.53 (dd, J=7.2, 2.1 Hz, 1H), 3.97 (dd, J=8.7, 2.1 Hz, 1H), 4.18 (d, J=9.0 Hz, 1H), 4.24 (d, J=5.1 Hz, 1H), 4.56 ppm (d, J=9.3 Hz, 1H); ^{13}C NMR: δ=−4.7, −4.2, 18.4, 26.2, 27.4, 27.4, 30.8, 41.1, 47.5, 64.1, 66.7, 75.6, 76.4, 77.9, 108.7 ppm; IR (thin film):

$\tilde{\nu}$ = 2955, 2930, 2857, 1238, 1118, 1077, 990, 837, 776 cm^{-1}; MS (FAB): *m/z* (%): 344 (24) $[M+H]^+$, 343 (35) $[M]^+$, 99 (69), 75 (56), 73 (100); HRMS (FAB): *m/z* calcd for $C_{17}H_{33}O_4NSi$ $[M+H]^+$: 344.2252; found: 344.2252.

Data for ***26***: R_f = 0.30 (hexane/EtOAc 1:1); m.p. 69–70 °C; $[\alpha]_D^{20} = -50.6$ (c = 1.61 in $CHCl_3$); ^{1}H NMR ($CDCl_3/C_6D_6$ 1:5): δ = 0.05 (s, 3H), 0.09 (s, 3H), 0.89 (s, 9H), 1.41–1.43 (2s, 6H), 1.57 (ddd, J = 15.3, 6.9, 3.9 Hz, 1H), 1.82 (d, J = 14.7 Hz, 1H), 2.61 (s, 3H), 2.79–2.86 (m, 1H), 3.00 (brs, 1H), 3.21 (dd, J = 9.9, 2.1 Hz, 1H), 3.85 (dd, J = 9.3, 6.9 Hz, 1H), 4.01 (dd, J = 9.3, 7.2 Hz, 1H), 4.10 (brs, 1H), 4.21 ppm (q, J = 2.7 Hz, 1H); ^{13}C NMR: δ = −4.8, −4.2, 18.5, 26.1, 27.2, 27.7, 31.3, 38.4, 45.4, 67.3, 70.4, 71.0, 72.5, 79.8, 110.3 ppm; IR (thin film): $\tilde{\nu}$ = 2930, 2857, 1229, 1102, 1052, 838, 777 cm^{-1}; MS (FAB): *m/z* (%): 344 (42) $[M+H]^+$, 185 (66), 93 (90), 73 (100), 57 (52); HRMS (FAB): *m/z* calcd for $C_{17}H_{33}O_4NSi$ $[M+H]^+$: 344.2252; found: 344.2256.

Isoxazolidines 28 and 29: By following the glycol-cleavage procedure, triol **11a** (108 mg, 0.463 mmol) was converted into aldehyde **13** as a colorless oil. By following the cyclization procedure of aldehyde **12** and purification by using flash chromatography (CH_3Cl/MeOH 40:1), aldehyde **13** gave firstly cyclohexane **28** (32.9 mg, 31% overall yield from **11a**) and secondly cycloheptane **29** (66.8 mg, 63% overall yield from **11a**) as white solids.

Data for ***28***: R_f = 0.26 (EtOAc); m.p. 107–108 °C; $[\alpha]_D^{20} = -32.8$ (c = 2.78 in $CHCl_3$); ^{1}H NMR: δ = 1.43–1.44 (2s, 6H), 1.61–1.70 (m, 4H), 2.14 (dt, J = 14.7, 6.0 Hz, 1H), 2.35 (brs, 1H), 2.72 (s, 3H), 3.04 (m, 1H), 3.17 (dtd, J = 15.3, 7.8, 6.0 Hz, 1H), 3.39–3.55 (t, 2m, J = 8.1 Hz, 3H), 4.05 (q, J = 6.6 Hz, 1H), 4.19 ppm (t, J = 8.7 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ = 1.43–1.44 (2s, 6H), 1.65 (ddd, J = 14.7, 6.6, 6.3 Hz, 1H), 2.14 (dt, J = 14.4, 6.0 Hz, 1H), 2.72 (s, 3H), 3.05 (t, J = 7.2 Hz, 1H), 3.17 (dtd, J = 15.6, 7.8, 6.0 Hz, 1H), 3.39–3.54 (t, J = 8.1 Hz, 3H), 4.05 (q, J = 6.6 Hz, 1H), 4.20 ppm (t, 2m, J = 8.4 Hz, 1H); ^{1}H NMR ($CDCl_3/C_6D_6$ 4:1): δ = 1.41–1.53 (s, dt, J = 14.1, 6.3 Hz, 7H), 1.97–2.04 (m, 2H), 2.66 (s, 3H), 2.89–2.92 (m, 2H), 3.35–3.40 (m, 2H), 3.52 (t, J = 9.6 Hz, 1H), 3.89 (brs, 1H), 4.05 ppm (t, J = 8.4 Hz, 1H); ^{1}H NMR ($CDCl_3/C_6D_6$ (4:1)–D_2O): δ = 1.41–1.53 (2s, dt, J = 14.4, 6.3 Hz, 7H), 1.97 (dt, J = 15.0, 6.0 Hz, 1H), 2.65 (s, 3H), 2.92–2.99 (m, 2H), 3.29 (t, J = 7.8 Hz, 1H), 3.37–3.40 (brs, 1H), 3.45 (t, J = 8.7 Hz, 1H), 3.89 (q, J = 6.6 Hz, 1H), 4.04 ppm (t, J = 8.1 Hz, 1H); ^{13}C NMR: δ = 27.4 (CH_3), 32.8 (CH_2), 39.3 (CH), 44.9 (CH_3), 68.8 (CH), 69.8 (CH), 70.7 (CH_2), 82.6 (CH), 111.8 ppm (C); IR (thin film): $\tilde{\nu}$ = 3370, 2931, 1455, 1231, 1078, 1018, 843, 754, 509 cm^{-1}; MS (FAB): *m/z* (%): 230 (24) $[M+H]^+$, 185 (100), 93 (76); HRMS (FAB): *m/z* calcd for $C_{11}H_{19}O_4N$ $[M+H]^+$: 230.1387; found: 230.1387; elemental analysis calcd (%) for $C_{11}H_{19}O_4N$: C 57.63, H 8.35, N 6.11; found: C 57.35, H 8.36, N 6.08.

Data for ***29***: R_f = 0.22 (EtOAc); m.p. 137–138 °C; $[\alpha]_D^{20} = +62.1$ (c = 3.73 in $CHCl_3$); ^{1}H NMR: δ = 1.42 (s, 3H), 1.48 (s, 3H), 1.71 (d, J = 13.2 Hz, 1H), 1.80 (ddd, J = 15.0, 8.4, 2.4 Hz, 1H), 2.13 (ddd, J = 15.0, 7.2, 3.6 Hz, 1H), 2.27 (brs, 1H), 2.59–2.69 (m, 4H), 3.35 (dd, J = 8.7, 2.1 Hz, 1H), 3.51 (dd, J = 7.2, 1.8 Hz, 1H), 3.82 (q, J = 8.4 Hz, 1H), 4.17 (dd, J = 10.2, 9.0 Hz, 1H), 4.59 ppm (dt, J = 9.6, 2.7 Hz, 1H); ^{13}C NMR: δ = 27.1 (CH_3), 27.5 (CH_3), 32.1 (CH_2), 39.9 (CH_2), 47.2 (CH_3), 63.3 (CH), 68.2 (CH), 74.6 (CH), 78.8 (CH), 81.4 (CH), 109.8 ppm (C); IR (thin film): $\tilde{\nu}$ = 3455, 2980, 2940, 1370, 1232, 1076, 946, 808, 773, 576 cm^{-1}; MS (FAB): *m/z* (%): 230 (41) $[M+H]^+$, 186 (64), 185 (100), 93 (75); HRMS (FAB): *m/z* calcd for $C_{11}H_{19}O_4N$ $[M+H]^+$: 230.1387; found: 230.1390; elemental analysis calcd (%) for $C_{11}H_{19}O_4N$: C 57.63, H 8.35, N 6.11; found: C 57.26, H 8.35, N 6.01.

Cyclohexane 28 from 32: By following the desilylation procedure of cycloheptane **27** to give cycloheptane **23**, silyl ether **32** (69.1 mg, 0.201 mmol) was converted into cyclohexane **28** (43.7 mg, 95%) as a white solid.

Cycloheptane 29 from 33: By following the desilylation procedure of cycloheptane **27** to give cycloheptane **23**, silyl ether **33** (38.3 mg, 0.112 mmol) was converted into cycloheptane **29** (24.1 mg, 94%) as a white solid.

Isoxazolidines 164 and 165: By following the glycol-cleavage procedure, diol **15a** (103 mg, 0.319 mmol) was converted into aldehyde **17** as a colorless oil. By following the cyclization procedure of aldehyde **12** and purification by using flash chromatography (hexane/EtOAc 2:1) aldehyde **17** gave firstly cyclohexane **30** (44.2 mg, 44% overall yield from **15a**) as a colorless oil and secondly cycloheptane **31** (49.4 mg, 49% overall yield from **15a**) as a white solid.

Data for ***30***: R_f = 0.48 (hexane/EtOAc 1:1); $[\alpha]_D^{20} = -54.0$ (c = 2.48 in $CHCl_3$); ^{1}H NMR: δ = 1.43 (s, 3H), 1.45 (s, 3H), 1.75 (ddd, J = 15.0, 5.4, 3.9 Hz, 1H), 2.01 (ddd, J = 14.7, 9.9, 6.3 Hz, 1H), 2.75 (s, 3H), 2.84 (t, J = 9.6 Hz, 1H), 3.03–3.16 (m, 1H), 3.38 (t, J = 7.5 Hz, 1H), 3.54–3.69 (dd, J = 10.2, 8.4 Hz, 1H; dd, J = 10.5, 7.2 Hz, 1H), 3.87 (td, J = 6.6, 3.6 Hz, 1H), 4.15 (t, J = 8.4 Hz, 1H), 4.58 (d, J = 11.7 Hz, 1H), 4.74 (d, J = 12.0 Hz, 1H), 7.26–7.36 ppm (m, 5H); ^{13}C NMR: δ = 27.5 (CH_3), 27.6 (CH_3), 31.3 (CH_2), 39.9 (CH), 44.7 (CH_3), 70.3 (CH), 71.3 (CH_2), 71.5 (CH_2), 75.9 (CH), 77.3 (CH), 82.5 (CH), 111.9 (C), 128.0 (CH), 128.1 (CH), 128.7 (CH), 138.6 ppm (C); IR (thin film): $\tilde{\nu}$ = 2870, 1371, 1232, 1096, 842, 737, 698 cm^{-1}; MS (EI): *m/z* (%): 319 (15) $[M]^+$, 97 (33), 91 (100), 71 (55), 57 (72); HRMS (EI): *m/z* calcd for $C_{18}H_{25}O_4N$ $[M]^+$: 319.1778; found: 319.1777; elemental analysis calcd (%) for $C_{18}H_{25}O_4N$: C 67.69, H 7.89, N 4.38; found: C 67.14, H 7.86, N 4.03.

Data for ***31***: R_f = 0.26 (hexane/EtOAc 1:1); m.p. 79–80 °C; $[\alpha]_D^{20} = +12.1$ (c = 3.41 in $CHCl_3$); ^{1}H NMR: δ = 1.46 (s, 3H), 1.51 (s, 3H), 1.63 (d, J = 12.9 Hz, 1H), 1.88 (ddd, J = 15, 8.7, 2.4 Hz, 1H), 2.02 (ddd, J = 15.0, 7.2, 3.6 Hz, 1H), 2.53–2.61 (m, 1H), 2.63 (s, 3H), 3.32 (dd, J = 8.4, 1.8 Hz, 1H), 3.48 (dd, J = 7.2, 1.5 Hz, 1H), 3.55 (q, J = 8.4 Hz, 1H), 4.33 (dd, J = 9.9, 8.7 Hz, 1H), 4.54 (dt, J = 9.3, 2.7 Hz, 1H), 4.66 (d, J = 12.6 Hz, 1H), 4.81 (d, J = 12.6 Hz, 1H), 7.26–7.38 ppm (m, 5H); ^{13}C NMR: δ = 27.1 (CH_3), 27.6 (CH_3), 31.9 (CH_2), 39.1 (CH_2), 47.2 (CH_3), 63.3 (CH), 72.0 (CH_2), 74.5 (CH), 74.5 (CH), 78.7 (CH), 82.0 (CH), 109.4 (C), 127.8 (CH), 128.0 (CH), 128.6 (CH), 139.3 ppm (C); IR (thin film): $\tilde{\nu}$ = 2928, 1368, 1235, 1073, 737, 698 cm^{-1}; MS (EI): *m/z* (%): 320 (5) $[M+H]^+$, 319 (13) $[M]^+$, 304 (100) $[M-OCH_3]^+$, 153 (46), 91 (100); HRMS (EI): *m/z* calcd for $C_{18}H_{25}O_4N$ $[M-OCH_3]^+$: 304.1543; found: 304.1546.

Cycloheptane 31 from 29: By following the same procedure for benzylation of alkene **10** to give benzyl ether **14**, cycloheptane **29** (13.4 mg, 0.058 mmol) was converted into cycloheptane **31** (13.3 mg, 71%) as a white solid.

Isoxazolidines 32 and 33: By following the glycol-cleavage procedure, diol **19a** (76.1 mg, 0.220 mmol) was converted into aldehyde **21** as a colorless oil. By following the cyclization procedure of aldehyde **12** and purification by using flash chromatography (hexane/Et_2O 3:2), aldehyde **21** gave firstly cyclohexane **32** (30.9 mg, 41% overall yield from **19a**) as a colorless oil and secondly cycloheptane **33** (33.9 mg, 45% overall yield from **19a**) as a white solid.

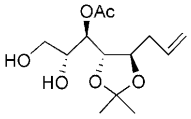
Data for ***32***: R_f = 0.38 (hexane/Et_2O 1:1); $[\alpha]_D^{20} = -20.8$ (c = 2.21 in $CHCl_3$); ^{1}H NMR: δ = 0.08–0.09 (2s, 6H), 0.88 (s, 9H), 1.38–1.39 (2s, 6H), 1.58 (dt, J = 14.7, 5.4 Hz, 1H), 1.99 (ddd, J = 14.1, 7.8, 6.0 Hz, 1H), 2.72 (s, 3H), 2.87–2.94 (m, 1H), 3.09 (dtd, J = 15.9, 7.8, 6.0 Hz, 1H), 3.35–3.50 (t, 2m, J = 7.8 Hz, 3H), 3.98 (q, J = 6.0 Hz, 1H), 4.16 ppm (t, J = 8.7 Hz, 1H); ^{13}C NMR: δ = −4.5 (CH_3), −4.1 (CH_3), 18.7 (C), 26.3 (CH_3), 27.5 (CH_3), 27.6 (CH_3), 34.7 (CH_2), 39.6 (CH), 44.9 (CH_3), 69.9 (CH), 70.4 (CH), 71.3 (CH_2), 77.0 (CH), 83.2 (CH), 111.4 ppm (C); IR (thin film): $\tilde{\nu}$ = 2933, 2858, 1462, 1233, 1099, 1061, 831, 778 cm^{-1}; MS (EI): *m/z* (%): 344 (15) $[M+H]^+$, 343 (71) $[M]^+$, 228 (100), 198 (90), 98 (100), 75 (92); HRMS (EI): *m/z* calcd for $C_{17}H_{33}O_4NSi$ $[M]^+$: 343.2173; found: 343.2178.

Data for ***33***: R_f = 0.21 (hexane/Et_2O 1:1); m.p. 90–91 °C; $[\alpha]_D^{20} = +54.9$ (c = 2.20 in $CHCl_3$); ^{1}H NMR: δ = 0.05–0.06 (2s, 6H), 0.86 (s, 9H), 1.38 (s, 3H), 1.44 (s, 3H), 1.68 (d, J = 12.9 Hz, 1H), 1.82 (ddd, J = 15.0, 7.2, 3.6 Hz, 1H), 2.54–2.64 (m, 4H), 3.28 (dd, J = 8.7, 2.1 Hz, 1H), 3.47 (dd, J = 7.2, 1.5 Hz, 1H), 3.76 (dt, J = 9.9, 8.1 Hz, 1H), 4.12 (dd, J = 9.6, 8.7 Hz, 1H), 4.52 ppm (dt, J = 9.3, 2.7 Hz, 1H); ^{13}C NMR: δ = −4.6, −3.9, 18.8, 26.2, 27.1, 27.6, 32.0, 42.3, 47.3, 63.4, 69.4, 74.8, 78.7, 81.8, 109.0 ppm; IR (thin film): $\tilde{\nu}$ = 2928, 2856, 1368, 1245, 1105, 1076, 837, 780 cm^{-1}; MS (EI): *m/z* (%): 343 (8) $[M]^+$, 228 (70), 84 (100), 75 (67); HRMS (EI): *m/z* calcd for $C_{17}H_{33}O_4NSi$ $[M]^+$: 343.2173; found: 343.2166.

6-*O*-Acetyl-1,2,3-trideoxy-4,5:7,8-di-*O*-isopropylidene-D-*altro*-oct-1-enitol (35): Acetic anhydride (4.21 mL, 44.6 mmol), triethylamine (8.48 mL, 60.8 mmol), and 4-dimethylaminopyridine (DMAP; 248 mg, 4.46 mmol) were added to a stirred solution of alkene **34** (11.0 g, 40.6 mmol) in CH_2Cl_2 (150 mL) at room temperature. The reaction mixture was stirred

for 12 h and quenched with saturated $NaHCO_3$ solution. The aqueous phase was extracted with Et_2O (2×100 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by using flash chromatography (hexane/Et_2O 7:2) to afford acetate **35** (12.5 g, 98%) as a colorless oil. R_f=0.39 (hexane/Et_2O 2:1); $[\alpha]_D^{20}$=+38.1 (c=1.90 in $CHCl_3$); ^{1}H NMR: δ=1.35 (s, 3H), 1.38 (s, 9H), 2.11 (s, 3H), 2.33 (dt, J=14.1, 6.9 Hz, 1H), 2.45 (dt, J=14.4, 5.4 Hz, 1H), 3.80 (dd, J=8.1, 4.5 Hz, 1H), 3.93 (dd, J=8.1, 6.9 Hz, 1H), 4.04–4.10 (m, 2H), 4.34 (td, J=6.9, 4.8 Hz, 1H), 5.11–5.18 (m, 2H), 5.21 (t, J=4.8 Hz, 1H), 5.86 ppm (ddt, J=17.1, 10.5, 7.2 Hz, 1H); ^{13}C NMR: δ=21.3, 25.7, 26.7, 27.2, 27.6, 37.9, 66.1, 72.4, 74.5, 77.7, 79.7, 109.6, 109.8, 118.3, 133.9, 170.3 ppm; IR (thin film): $\tilde{\nu}$=2987, 1751, 1371, 1227, 1060, 847, 512 cm^{-1}; MS (EI): m/z (%): 299 (41) $[M-OCH_3]^+$, 215 (42), 101 (42); HRMS (EI): m/z calcd for $C_{16}H_{26}O_6$ $[M-OCH_3]^+$: 299.1489; found: 299.1482.

Diol 35a: By following the aqueous acetic acid deprotection procedure and purification by using flash chromatography (hexane/EtOAc 5:1 to 1:2), acetate **35** (341 mg, 1.08 mmol) gave firstly starting material **35** (59.4 mg, 17%) and secondly diol **35a** (200 mg, 82% based on recovering starting material) as a colorless oil.

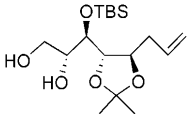


35a

Data for **35a**: R_f=0.19 (hexane/EtOAc 1:1); $[\alpha]_D^{20}$=+30.1 (c=0.82 in $CHCl_3$); ^{1}H NMR: δ=1.40–1.42 (2s, 6H), 2.12 (s, 3H), 2.31 (dt, J=14.4, 7.2 Hz, 1H), 2.45 (dt, J=14.7, 5.1 Hz, 1H), 2.56 (s, 1H), 3.05 (d, J=5.1 Hz, 1H), 3.61–3.75 (m, 2H), 3.87 (dt, J=9.6, 5.4 Hz, 1H), 3.99 (t, J=6.9 Hz, 1H), 4.09 (td, J=7.2, 3.6 Hz, 1H), 4.97 (t, J=6.3 Hz, 1H), 5.11–5.16 (m, 2H), 5.86 ppm (ddt, J=17.4, 10.7, 6.9 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ=1.40–1.42 (2s, 6H), 2.12 (s, 3H), 2.31 (dt, J=14.4, 7.2 Hz, 1H), 2.45 (dt, J=14.7, 5.1 Hz, 1H), 3.62 (dd, J=12.0, 4.2 Hz, 1H), 3.70 (dd, J=12.0, 3.6 Hz, 1H), 3.86 (dt, J=6.0, 4.2 Hz, 1H), 3.99 (t, J=6.9 Hz, 1H), 4.09 (td, J=7.2, 3.6 Hz, 1H), 4.97 (t, J=6.3 Hz, 1H), 5.10–5.16 (m, 2H), 5.86 ppm (ddt, J=17.4, 10.5, 6.9 Hz, 1H); ^{13}C NMR: δ=21.3, 27.2, 27.6, 38.2, 62.7, 71.8, 74.2, 78.6, 78.8, 110.1, 118.2, 134.0, 171.0 ppm; IR (thin film): $\tilde{\nu}$=3436, 2984, 2934, 1738, 1372, 1234, 1046 cm^{-1}; MS (FAB): m/z (%): 275 (74) $[M+H]^+$, 217 (100), 185 (47), 92 (47); HRMS (FAB): m/z calcd for $C_{13}H_{22}O_6$ $[M+H]^+$: 275.1489; found: 275.1493.

1,2,3-Trideoxy-4,5:7,8-di-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-D-*altro*-oct-1-enitol (37): By following the same procedure for silylation of alkene **10** to give silyl ether **18**, alkene **34** (251 mg, 0.922 mmol) was converted into silyl ether **37** (324 mg, 98%) as a colorless oil. R_f=0.50 (hexane/Et_2O 3:1); $[\alpha]_D^{20}$=+34.1 (c=1.16 in $CHCl_3$); ^{1}H NMR: δ=0.10–0.11 (2s, 6H), 0.90 (s, 9H), 1.34 (s, 3H), 1.38–1.42 (3s, 9H), 2.32 (dt, J=14.7, 7.2 Hz, 1H), 2.45 (dddd, J=14.4, 5.4, 3.9, 1.2 Hz, 1H), 3.73 (dd, J=8.1, 3.9 Hz, 1H), 3.90 (t, J=7.8 Hz, 1H), 3.95 (t, J=4.2 Hz, 1H), 3.99–4.16 (dd, J=7.8, 6.6 Hz, 1H; td, J=7.8, 4.2 Hz, 1H), 4.17 (ddd, J=7.5, 6.3, 4.8 Hz, 1H), 5.10–5.17 (m, 2H), 5.88 ppm (ddt, J=17.1, 10.2, 6.66 Hz, 1H); ^{13}C NMR: δ=−3.8, −3.5, 18.5, 25.7, 26.4, 26.9, 27.5, 38.6, 66.4, 72.7, 76.3, 77.2, 82.1, 109.1, 109.1, 117.8, 134.6 ppm; IR (thin film): $\tilde{\nu}$=2986, 2933, 2859, 1371, 1254, 1077, 837, 778 cm^{-1}; MS (EI): m/z (%): 371 (27) $[M-OCH_3]^+$, 271 (55), 213 (100), 141 (50), 101 (97), 73 (50); HRMS (EI): m/z calcd for $C_{20}H_{38}O_5Si$ $[M-OCH_3]^+$: 371.2248; found: 371.2240.

Diol 37a: By following the aqueous acetic acid deprotection procedure and purification by using flash chromatography (hexane/Et_2O 10:1 to 1:2), silyl ether **37** (324 mg, 0.839 mmol) gave firstly starting material **37** (79.4 mg, 25%) and secondly diol **37a** (151 mg, 69% based on recovering starting material) as a colorless oil.

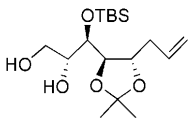


37a

Data for **37a**: R_f=0.24 (hexane/Et_2O 1:1); $[\alpha]_D^{20}$=+13.6 (c=0.91 in $CHCl_3$); ^{1}H NMR: δ=0.12–0.15 (2s, 6H), 0.91 (s, 9H), 1.39–1.40 (2s, 6H), 2.25–2.35 (m, 3H), 2.54 (dddd, J=14.7, 6.3, 3.0, 1.5 Hz, 1H), 3.73–3.89 (m, 5H), 4.04 (td, J=8.1, 3.3 Hz, 1H), 5.10–5.16 (m, 2H), 5.88 ppm (ddt, J=17.1, 10.5, 6.9 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ=0.12–0.15 (2s, 6H), 0.91 (s, 9H), 1.386–1.394 (2s, 6H), 2.30 (dt, J=15.0, 7.2 Hz, 1H), 2.54 (dddd, J=14.7, 6.6, 3.0, 1.5 Hz, 1H), 3.67–3.85 (m, 5H), 4.04 (td, J=7.8, 3.3 Hz, 1H), 5.10–5.16 (m, 2H), 5.89 ppm (ddt, J=16.8, 10.2, 6.6 Hz, 1H); ^{13}C NMR: δ=−3.9, −3.8, 18.5, 26.3, 27.5, 27.7, 38.8, 63.0, 73.8, 75.9, 78.9, 79.3, 109.6, 117.8, 134.6 ppm; IR (thin film): $\tilde{\nu}$=2429, 2932, 2858, 1371, 1255, 1063, 837, 778 cm^{-1}; MS (FAB): m/z (%): 347 (32) $[M+H]^+$, 289 (100) $[M-C_4H_9]^+$, 189 (54), 93 (64), 73 (80); HRMS (FAB): m/z calcd for $C_{17}H_{34}O_5Si$ $[M+H]^+$: 347.2248; found: 347.2247.

1,2,3-Trideoxy-4,5:7,8-di-*O*-isopropylidene-6-*O*-*tert*-butyldimethylsilyl-D-*gluco*-oct-1-enitol (40): By following the same procedure for silylation of alkene **10** to give silyl ether **18**, alkene **39** (424 mg, 1.56 mmol) was converted into silyl ether **40** (568 mg, 95%) as a colorless oil. R_f=0.67 (hexane/Et_2O 2:1); $[\alpha]_D^{20}$=+0.619 (c=1.72 in $CHCl_3$); ^{1}H NMR: δ=0.09 (s, 3H), 0.12 (s, 3H), 0.90 (s, 9H), 1.33 (s, 3H), 1.37 (s, 6H), 1.41 (s, 3H), 2.31 (dt, J=14.4, 7.2 Hz, 1H), 2.40–2.48 (m, 1H), 3.68 (dd, J=8.1, 3.6 Hz, 1H), 3.85 (t, J=3.6 Hz, 1H), 3.90 (t, J=7.8 Hz, 1H), 4.02 (dd, J=8.1, 6.3 Hz, 1H; td, J=7.8, 4.2 Hz, 1H), 4.12 (ddd, J=7.2, 6.3, 4.5 Hz, 1H), 5.09–5.16 (m, 2H), 5.87 ppm (ddt, J=17.1, 10.2, 6.9 Hz, 1H); ^{13}C NMR: δ=−3.7, −3.5, 18.7, 25.5, 26.4, 26.9, 27.3, 27.7, 37.9, 66.4, 72.3, 76.1, 77.4, 82.6, 108.8, 117.9, 134.5 ppm; IR (thin film): $\tilde{\nu}$=2986, 2933, 2859, 1370, 1254, 1077, 837, 777 cm^{-1}; MS (ESI): m/z (%): 409 (100) $[M+Na]^+$; HRMS (ESI): m/z calcd for $C_{20}H_{38}O_5Si$ $[M+Na]^+$: 409.2381; found: 409.2383.

Diol 40a: By following the aqueous acetic acid deprotection procedure and purification by using flash chromatography (hexane/Et_2O 10:1 to 1:2), silyl ether **40** (259 mg, 0.670 mmol) gave firstly starting material **40** (60.2 mg, 23%) and secondly diol **40a** (145 mg, 82% based on recovering starting material) as a colorless oil.



40a

Data for **40a**: R_f=0.25 (hexane/Et_2O 1:1); $[\alpha]_D^{20}$=−10.6 (c=0.84 in $CHCl_3$); ^{1}H NMR: δ=0.10 (s, 3H), 0.14 (s, 3H), 0.92 (s, 9H), 1.40–1.42 (2s, 6H), 2.30 (dt, J=15.6, 7.5 Hz, 1H; brs, 1H), 2.42 (m, 1H), 3.19 (d, J=4.8 Hz, 1H), 3.69–3.74 (m, 2H), 3.77–3.82 (m, 2H), 3.87 (dd, J=4.8, 3.0 Hz, 1H), 4.15 (td, J=7.8, 4.2 Hz, 1H), 5.10–5.17 (m, 2H), 5.87 ppm (ddt, J=17.1, 10.5, 6.9 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ=0.10 (s, 3H), 0.14 (s, 3H), 0.92 (s, 9H), 1.39–1.42 (2s, 6H), 2.30 (dt, J=14.4, 7.2 Hz, 1H), 2.42 (m, 1H), 3.65–3.74 (m, 2H), 3.75–3.82 (m, 2H), 3.87 (dd, J=5.1, 3.3 Hz, 1H), 4.15 (td, J=8.1, 4.2 Hz, 1H), 5.10–5.17 (m, 2H), 5.87 ppm (ddt, J=17.1, 10.2, 6.9 Hz, 1H); ^{13}C NMR: δ=−4.2, −3.9, 18.6, 26.3, 27.2, 27.6, 37.8, 63.8, 71.3, 74.1, 76.3, 81.9, 109.2, 118.61, 134.2 ppm; IR (thin film): $\tilde{\nu}$=3423, 2931, 2858, 1379, 1253, 1090, 835, 776 cm^{-1}; MS (ESI): m/z (%): 369 (100) $[M+Na]^+$; HRMS (ESI): m/z calcd for $C_{17}H_{34}O_5Si$ $[M+Na]^+$: 369.2068; found: 369.2069.

Cycloheptane 46: By following the glycol-cleavage procedure, diol **35a** (64.5 mg, 0.235 mmol) was converted into aldehyde **36** as a colorless oil. By following the cyclization procedure of aldehyde **12** and purification by using flash chromatography ($CHCl_3$/MeOH 40:1), aldehyde **36** was converted into cycloheptane **46** (47.9 mg, 89% overall yield from **35a**) as a white solid. R_f=0.23 (EtOAc); m.p. 97–98 °C; $[\alpha]_D^{20}$=−163.0 (c=2.21 in $CHCl_3$); ^{1}H NMR: δ=1.40 (s, 6H), 1.65 (dd, J=14.1, 9.9 Hz, 1H), 2.13 (ddd, J=14.1, 6.3, 4.2 Hz, 1H), 2.26 (d, J=13.5 Hz, 1H), 2.37–2.49 (m, 2H), 2.65 (s, 3H), 3.47 (t, J=5.7 Hz, 1H), 4.01 (dd, J=9.3, 2.7 Hz, 1H), 4.08–4.20 (m, 2H), 4.65 ppm (dd, J=9.3, 1.5 Hz, 1H); ^{1}H NMR ($CDCl_3$–D_2O): δ=1.398–1.401 (2s, 6H), 1.65 (ddd, J=14.1, 9.9, 1.2 Hz, 1H), 2.13 (ddd, J=13.8, 6.3, 3.9 Hz, 1H), 2.26 (d, J=13.5 Hz, 1H), 2.42 (ddd, J=13.5, 9.3, 6.9 Hz, 1H), 2.65 (s, 3H), 3.47 (dd, J=6.9, 5.1 Hz, 1H), 4.01 (dd, J=9.3, 2.7 Hz, 1H), 4.08–4.20 (m, 2H), 4.65 ppm (dd, J=9.3, 1.5 Hz, 1H); ^{13}C NMR: δ=27.2 (CH_3), 27.6 (CH_3), 28.2 (CH_2), 34.7 (CH_2), 46.9 (CH_3), 67.6 (CH), 68.1 (CH), 70.9 (CH), 74.7 (CH), 79.2 (CH), 108.6 ppm (C); IR (thin film): $\tilde{\nu}$=3467, 2985, 2930, 1370, 1240, 1071, 1013, 824, 799 cm^{-1}; MS (FAB): m/z (%): 230 (7) $[M+H]^+$, 185 (100), 93 (74); HRMS (FAB): m/z calcd for $C_{11}H_{19}O_4$ $[M+H]^+$: 230.1387; found: 230.1384; elemental analysis calcd (%) for $C_{11}H_{19}O_4$: C 57.63, H 8.35, N 6.11; found: C 57.64, H 8.39, N 6.10.

Cycloheptane 48: By following the glycol-cleavage procedure, diol **37a** (41.0 mg, 0.118 mmol) was converted into aldehyde **38** as a colorless oil. By following the cyclization procedure of aldehyde **12** and purification by using flash chromatography (hexane/Et_2O 2:1), aldehyde **38** was converted into cycloheptane **48** (40.3 mg, 99% overall yield from **37a**) as a white solid. R_f=0.45 (hexane/Et_2O 1:1); m.p. 71–72°C; $[\alpha]_D^{20}=-120.8$ (c=1.26 in $CHCl_3$); ^{1}H NMR: δ=0.08–0.11 (2s, 6H), 0.90 (s, 9H), 1.36 (s, 6H), 1.62 (dd, J=14.1, 9.6 Hz, 1H), 2.11 (ddd, J=14.1, 6.3, 4.2 Hz, 1H), 2.27–2.42 (m, 2H), 2.64 (s, 3H), 3.18 (t, J=5.7 Hz, 1H), 4.01 (dd, J=9.6, 2.4 Hz, 1H), 4.09–4.18 (m, 2H), 4.62 ppm (ddd, J=8.7, 4.2, 2.1 Hz, 1H); ^{13}C NMR: δ=−4.7 (CH_3), −3.9 (CH_3), 18.5 (C), 26.3 (CH_3), 27.5 (CH_3), 27.7 (CH_3), 28.3 (CH_2), 35.7 (CH_2), 47.4 (CH_3), 68.9 (CH), 69.7 (CH), 71.0 (CH), 75.0 (CH), 78.5 (CH), 108.5 ppm (C); IR (thin film): $\tilde{\nu}$=2930, 2856, 1367, 1251, 1123, 1073, 983, 894, 835, 778, 667 cm^{-1}; MS (FAB): m/z (%): 344 (80) $[M+H]^+$, 343 (10) $[M]^+$, 185 (100), 93 (83); HRMS (FAB): m/z calcd for $C_{17}H_{33}O_4NSi$ $[M+H]^+$: 344.2252; found: 344.226228.

Cycloheptanes 51 and 52: By following the glycol-cleavage procedure, diol **40a** (65.8 mg, 0.190 mmol) was converted into aldehyde **41** as a colorless oil. By following the cyclization procedure of aldehyde **12** and purification by using flash chromatography (hexane/Et_2O 3:1 to 1:2), aldehyde **41** gave firstly cycloheptane **52** (7.70 mg, 12% overall yield from **40a**) and secondly cycloheptane **51** (57.8 mg, 88% overall yield from **40a**) as white solids.

*Data for **51***: R_f=0.31 (hexane/Et_2O 3:2); m.p. 93–94°C; $[\alpha]_D^{20}=+56.3$ (c=2.60 in $CHCl_3$); ^{1}H NMR: δ=0.10–0.11 (2s, 6H), 0.89 (s, 9H), 1.34–1.36 (2s, 6H), 1.71 (dd, J=13.8, 10.2 Hz, 1H), 1.86 (d, J=13.2 Hz, 1H), 2.11 (ddd, J=14.1, 6.3, 4.5 Hz, 1H), 2.50 (dt, J=13.8, 8.7 Hz, 1H), 2.66 (s, 3H), 3.19 (d, J=5.4 Hz, 1H), 3.51 (dd, J=8.7, 2.7 Hz, 1H), 3.66 (td, J=9.6, 6.3 Hz, 1H), 4.03 (t, J=9.0 Hz, 1H), 4.61 ppm (dd, J=9.0, 3.9 Hz, 1H); ^{13}C NMR: δ=−4.7 (CH_3), −3.7 (CH_3), 18.7 (C), 26.3 (CH_3), 27.3 (CH_3), 27.6 (CH_3), 30.1 (CH_2), 35.6 (CH_2), 47.7 (CH_3), 70.5 (CH), 73.4 (CH), 74.4 (CH), 76.0 (CH), 80.3 (CH), 108.2 ppm (C); IR (thin film): $\tilde{\nu}$=2985, 2932, 2855, 1366, 1249, 1108, 857, 779, 671, 509 cm^{-1}; MS (ESI): m/z (%): 366 (55) $[M+Na]^+$, 344 (100) $[M+H]^+$; HRMS (ESI): m/z calcd for $C_{17}H_{33}O_4NSi$ $[M+H]^+$: 344.2252; found: 344.2245.

*Data for **52***: R_f=0.51 (hexane/Et_2O 3:2); m.p. 70–71°C; $[\alpha]_D^{20}=-47.8$ (c=2.48 in $CHCl_3$); ^{1}H NMR (C_6D_6): δ=0.18 (s, 3H), 0.26 (s, 3H), 1.04 (s, 9H), 1.12 (td, J=12.9, 1.2 Hz, 1H), 1.36–1.39 (2s, 6H), 1.78 (d, J=12.9 Hz, 1H), 1.90 (dt, J=12.9, 8.1 Hz, 1H), 2.33 (dt, J=13.2, 4.5 Hz, 1H), 2.52 (s, 3H), 2.85 (d, J=8.7 Hz, 1H), 3.60 (dd, J=9.6, 6.9 Hz, 1H), 3.96 (d, J=7.2 Hz, 1H), 4.10 (t, J=5.7 Hz, 1H), 4.59 ppm (td, J=10.5, 4.2 Hz, 1H); ^{13}C NMR: δ=−4.5, −4.1, 18.6, 26.2, 27.5, 27.6, 32.9, 37.5, 48.6, 72.3, 72.7, 75.6, 84.7, 108.5 ppm; IR (thin film): $\tilde{\nu}$=2929, 2856, 1248, 1095, 838, 778 cm^{-1}; MS (ESI): m/z (%): 344 (100) $[M+H]^+$; HRMS (ESI): m/z calcd for $C_{17}H_{33}O_4NSi$ $[M+H]^+$: 344.2252; found: 344.2250.

Cycloheptane 49 from 51: By following the desilylation procedure of cycloheptane **27** to give cycloheptane **23**, silyl ether **51** (24.8 mg, 0.072 mmol) was converted into cycloheptane **49** (15.1 mg, 91%) as a white solid.

Diol 57: 10% Pd on charcoal (148 mg, 0.139 mmol) was added to a solution of enoate **56** (1.39 g, 4.63 mmol) in EtOH (40 mL) and the mixture was stirred under an atmosphere of H_2 (balloon). After stirring at room temperature under H_2 for 1 h, the mixture was filtered and the filtrate was concentrated to give an ester. A solution of the ester in 80% aqueous AcOH (30 mL) was stirred at room temperature for 5 h. The solvent was removed under reduced pressure and the residue was purified by using flash chromatography (hexane/EtOAc 1:2) to afford diol **57** (903 mg, 74%) as a colorless oil. R_f=0.30 (hexane/EtOAc 1:2); $[\alpha]_D^{20}=-32.2$ (c=1.49 in $CHCl_3$); ^{1}H NMR: δ=1.26 (t, J=7.2 Hz, 3H), 1.39 (s, 6H), 1.81 (dtd, J=14.4, 8.4, 6.0 Hz, 1H), 1.97 (dddd, J=14.1, 9.0, 7.2, 3.3 Hz, 1H), 2.38–2.60 (ddd, J=16.5, 8.4, 7.2 Hz, 1H; ddd, J=16.5, 9.0, 6.0 Hz, 1H), 3.62–3.73 (m, 4H), 4.05 (td, J=8.1, 3.0 Hz, 1H), 4.13 (d, J=7.2 Hz, 1H), 4.16 ppm (d, J=7.2 Hz, 1H); ^{13}C NMR: δ=14.6, 27.2, 27.7, 28.1, 31.0, 60.9, 65.2, 70.2, 76.5, 81.9, 109.6, 173.7 ppm; IR (thin film): $\tilde{\nu}$=3445, 2986, 1732, 1373, 1216, 1082, 880 cm^{-1}; MS (ESI): m/z (%): 285 (100) $[M+Na]^+$; HRMS (ESI): m/z calcd for $C_{12}H_{22}O_6$ $[M+Na]^+$: 285.1309; found: 285.1312.

Ester 58: Triphenylphosphine (2.59 g, 9.87 mmol) was added in one portion to a stirred solution of iodine (1.90 g, 7.40 mmol) and imidazole (672 mg, 9.87 mmol) in dry toluene/acetonitrile (1:1, 20 mL). Diol **57** (645 mg, 2.47 mmol) dissolved in toluene (10 mL) was added to the resulting yellow suspension with stirring. The reaction mixture was then heated at 70°C under N_2 for 1 h and then filtered. The filtrate was washed with saturated $Na_2S_2O_3$ solution and then with saturated $NaHCO_3$ solution. The organic layer was concentrated under reduced pressure and flash chromatography of the residue (hexane/Et_2O 4:1) afforded ester **58** (505 mg, 90%) as a colorless oil. R_f=0.33 (hexane/Et_2O 4:1); $[\alpha]_D^{20}=-2.61$ (c=1.60 in $CHCl_3$) (ref. [26]: $[\alpha]_D^{22}=0$ (c=0.9 in $CHCl_3$)); ^{1}H NMR: δ=1.24 (t, J=7.2 Hz, 3H), 1.389–1.391 (2s, 6H), 1.80 (dtd, J=14.4, 8.4, 6.3 Hz, 1H), 1.95 (dddd, J=13.8, 9.3, 6.6, 3.6 Hz, 1H), 2.34–2.55 (ddd, J=16.2, 8.7, 6.6 Hz, 1H; ddd, J=16.2, 9.0, 6.0 Hz, 1H), 3.69 (td, J=8.4, 3.9 Hz, 1H), 3.99 (t, J=7.8 Hz, 1H), 4.09–4.16 (d, J=7.2 Hz, 1H; d, J=7.2 Hz, 1H), 5.25 (dt, J=10.2, 0.6 Hz, 1H), 5.37 (d, J=17.1 Hz, 1H), 5.79 ppm (ddd, J=17.1, 10.2, 7.2 Hz, 1H); ^{13}C NMR: δ=14.6, 27.2, 27.3, 27.6, 31.1, 60.8, 79.9, 82.8, 109.2, 119.6, 135.4, 173.5 ppm; IR (thin film): $\tilde{\nu}$=2986, 1736, 1371, 1242, 1167, 1070, 875 cm^{-1}; MS (ESI): m/z (%): 251 (100) $[M+Na]^+$; HRMS (ESI): m/z calcd for $C_{12}H_{20}O_4$ $[M+Na]^+$: 251.1254; found: 251.1256.

Alcohol 59: A solution of DIBAL-H (26.9 mL, 26.9 mmol) was added dropwise over 30 min to a solution of ester **58** (2.05 g, 8.96 mmol) in dry THF (80 mL) at −78°C. The temperature of the resultant solution was allowed to rise to 0°C and was stirred for 3 h. It was then quenched with saturated NH_4Cl solution and filtered through a pad of Celite. The residue was washed with EtOAc. Concentration of the filtrate followed by purification using flash chromatography (hexane/Et_2O 1:1) gave alcohol **59** (1.65 g, 100%) as a colorless oil. R_f=0.26 (hexane/Et_2O 1:2); $[\alpha]_D^{20}=+2.48$ (c=1.61 in $CHCl_3$) (ref. [27]: $[\alpha]_D^{22}=-3.06$ (c=0.49 in $CHCl_3$)); ^{1}H NMR: δ=1.40–1.41 (2s, 6H), 1.55–1.62 (m, 1H), 1.66–1.78 (m, 3H), 2.11 (brs, 1H), 3.64–3.72 (m, 3H), 3.98 (dd, J=8.1, 7.8 Hz, 1H), 5.25 (dt, J=10.2, 0.6 Hz, 1H), 5.36 (dt, J=17.1, 0.9 Hz, 1H), 5.79 ppm (ddd, J=17.4, 10.2, 7.5 Hz, 1H); ^{13}C NMR: δ=27.3, 27.6, 28.8, 29.8, 62.9, 81.0, 83.2, 109.1, 119.6, 135.4 ppm; IR (thin film): $\tilde{\nu}$=3418, 2987, 2937, 1371, 1241, 1050 cm^{-1}; MS (ESI): m/z (%): 209 (100) $[M+Na]^+$, 111 (10); HRMS (ESI): m/z calcd for $C_{10}H_{18}O_3$ $[M+Na]^+$: 209.1148; found: 209.1152.

Cyclohexanes 61, 62, and 63: IBX (458 mg, 1.63 mmol) was added to a solution of alcohol **59** (102 mg, 0.545 mmol) in CH_2Cl_2/DMSO (1:1, 6 mL) and the mixture was stirred at room temperature for 8 h. The mixture was partitioned between Et_2O (30 mL) and water (30 mL). The aqueous layer was extracted with Et_2O (2×30 mL) and the combined organic extracts were concentrated under reduced pressure to give aldehyde **60** as a colorless oil. BnNHOH (73.8 mg, 0.600 mmol) was added to a solution of aldehyde **60** in CH_3CN (8 mL) and the mixture was stirred at room temperature for 30 min and then heated under reflux for 40 h. The reaction mixture was partitioned between EtOAc (20 mL) and water (20 mL). The aqueous layer was extracted with EtOAc (2×20 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate followed by purification using flash chromatography (hexane/CH_2Cl_2/Et_2O 2:1:1) gave firstly cyclohexane **62** (51.0 mg, 32% overall yield from **59**) as a colorless oil, secondly cyclohexane **63** (18.3 mg, 12% overall yield from **59**) as a colorless oil, and cyclohexane **61** (32.1 mg, 20% overall yield from **59**) as a white solid.

*Data for **61***: R_f=0.27 (hexane/Et_2O/CH_2Cl_2 1:1:1); m.p. 94–95°C; $[\alpha]_D^{20}=+68.3$ (c=1.56 in $CHCl_3$); ^{1}H NMR: δ=0.43–1.52 (m, 8H), 1.81–1.83 (m, 1H), 2.15–2.21 (m, 1H), 2.44–2.63 (m, 2H), 3.37 (dd, J=9.9, 8.4 Hz, 1H), 3.48 (ddd, J=12.3, 8.7, 4.2 Hz, 1H), 3.77 (dd, J=9.3, 7.2 Hz, 1H), 3.89 (d, J=13.5 Hz, 1H), 4.06 (d, J=13.5 Hz, 1H), 4.15 (t, J=6.3 Hz, 1H), 7.26–7.39 ppm (m, 5H); ^{13}C NMR: δ=25.8 (CH_2), 26.0 (CH_2), 27.2 (CH_3), 51.1 (CH), 63.1 (CH_2), 68.0 (CH_2), 70.2 (CH), 80.3 (CH), 81.1 (CH), 111.1 (C), 127.8 (CH), 128.8 (CH), 129.4 (CH), 137.2 ppm (C); MS (ESI): m/z (%): 290 (100) $[M+H]^+$; IR (thin film): $\tilde{\nu}$=2936, 2871, 1454, 1371, 1229, 1179, 1113, 1078, 835, 700 cm^{-1}; HRMS (ESI): m/z calcd for $C_{17}H_{23}O_3N$ $[M+H]^+$: 290.1751; found: 290.1751.

Data for ***62***: R_f=0.50 (hexane/Et_2O/CH_2Cl_2 1:1:1); $[\alpha]_D^{20}=-143.4$ (c=2.15 in $CHCl_3$); ^{1}H NMR: δ=1.43 (s, 6H), 1.64–1.80 (m, 2H), 1.83–1.88 (m, 1H), 1.94–1.98 (m, 1H), 2.66 (ddd, J=10.5, 6.6, 1.8 Hz, 1H), 3.07–3.09 (m, 1H), 3.43 (ddd, J=10.8, 9.3, 3.9 Hz, 1H), 3.73 (dd, J=10.2, 9.6 Hz, 1H), 3.82 (d, J=13.5 Hz, 1H), 3.97–4.07 (m, 3H), 7.23–7.39 ppm (m, 5H); ^{1}H NMR (C_6D_6): δ=1.02–1.15 (m, 1H), 1.34–1.40 (m, 7H), 1.65–1.79 (m, 2H), 2.16 (dtd, J=10.8, 5.4, 1.5 Hz, 1H), 2.44 (ddd, J=6.9, 5.1, 2.1 Hz, 1H), 3.19 (td, J=9.3, 5.1 Hz, 1H), 3.57 (d, J=14.1 Hz, 1H), 3.65–3.73 (d, J=14.1 Hz, 1H; dd, J=7.8, 5.4 Hz, 1H), 3.84 (dd, J=10.2, 9.3 Hz, 1H), 3.92 (dd, J=7.5, 0.9 Hz, 1H), 7.03–7.18 (m, 4H), 7.34–7.37 ppm (m, 2H); ^{13}C NMR: δ=24.9 (CH_2), 25.0 (CH_2), 27.4 (CH_3), 27.4 (CH_3), 48.3 (CH), 62.0 (CH_2), 65.2 (CH), 68.4 (CH_2), 78.9 (CH), 79.7 (CH), 109.8 (C), 127.7 (CH), 128.7 (CH), 129.4 (CH), 137.7 ppm (C); IR (thin film): $\tilde{\nu}$=2983, 2943, 2875, 1370, 1236, 1131, 1091, 700 cm^{-1}; MS (ESI): m/z (%): 290 (100) $[M+H]^+$; HRMS (ESI): m/z calcd for $C_{17}H_{23}O_3N$ $[M+H]^+$: 290.1751; found: 290.1758.

Data for ***63***: R_f=0.43 (hexane/Et_2O/CH_2Cl_2 1:1:1); $[\alpha]_D^{20}=+39.0$ (c=1.06 in $CHCl_3$); ^{1}H NMR: δ=1.41–1.51 (m, 7H), 1.53–1.64 (m, 1H), 1.96 (dt, J=14.7, 5.4 Hz, 1H), 2.08 (ddd, J=11.7, 9.3, 4.5 Hz, 1H), 3.27 (q, J=7.2 Hz, 1H), 3.47 (pentet, J=7.2 Hz, 1H), 3.66 (dd, J=9.0, 6.6 Hz, 1H), 3.78–3.83 (m, 2H), 3.91 (t, J=8.1 Hz, 1H), 3.99 (d, J=13.2 Hz, 1H), 4.17 (t, J=8.7 Hz, 1H), 7.27–7.39 ppm (m, 5H); ^{13}C NMR: δ=25.3 (CH_2), 27.3 (CH_3), 27.4 (CH_3), 60.4 (CH_2), 64.3 (CH), 66.3 (CH_2), 73.6 (CH), 79.0 (CH), 110.1 (C), 127.9 (CH), 128.9 (CH), 129.3 (CH), 137.5 ppm (C); IR (thin film): $\tilde{\nu}$=2945, 1455, 1369, 1236, 1166, 1131, 1089, 730, 699 cm^{-1}; MS (ESI): m/z (%): 290 (100) $[M+H]^+$; HRMS (ESI): m/z calcd for $C_{17}H_{23}O_3N$ $[M+H]^+$: 290.1751; found: 290.1751.

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[1] a) A. E. Koumbis, J. K. Gallos, *Curr. Org. Chem.* **2003**, *7*, 585–628; b) B. von Bernet, A. Vasella, *Helv. Chim. Acta* **1979**, *62*, 1990–2016; c) T. K. M. Shing, D. A. Elsley, J. G. Gillhouley, *J. Chem. Soc. Chem. Commun.* **1989**, 1280–1282.

[2] J. J. Tufariello in *1,3-Dipolar Cycloaddition Chemistry, Vol. 2* (Ed.: A. Padwa), Wiley, New York, **1984**, pp. 83–168.

[3] a) A. Roy, K. Chakrabarty, P. K. Dutta, N. C. Bar, N. Basu, B. Achari, S. B. Mandal, *J. Org. Chem.* **1999**, *64*, 2304–2309; b) R. Patra, N. C. Bar, A. Roy, B. Achari, N. Ghoshal, S. B. Mandal, *Tetrahedron* **1996**, *52*, 11265–11272.

[4] C. Gravier-Pelletier, W. Maton, T. Dintinger, C. Tellier, Y. L. Merrer, *Tetrahedron* **2003**, *59*, 8705–8720.

[5] For recent syntheses, see: a) Y. Zhang, L. S. Liebeskind, *J. Am. Chem. Soc.* **2006**, *128*, 465–472; b) D. M. Mans, W. H. Pearson, *Org. Lett.* **2004**, *6*, 3305–3308.

[6] For recent syntheses, see: a) P. R. Skaanderup, R. Madsen, *J. Org. Chem.* **2003**, *68*, 2115–2122; b) J. Marco-Contelles, E. de Opazo, *J. Org. Chem.* **2002**, *67*, 3705–3717.

[7] a) B. Dräger, *Nat. Prod. Rep.* **2004**, *21*, 211–223; b) N. Asano, *Curr. Top. Med. Chem.* **2003**, *3*, 471–484.

[8] T. K. M. Shing, W. F. Wong, T. Ikeno, T. Yamada, *Org. Lett.* **2007**, *9*, 207–209.

[9] T. K. M. Shing, A. W. F. Wong, T. Ikeno, T. Yamada, *J. Org. Chem.* **2006**, *71*, 3253–3263.

[10] T. Gracza, T. Hasenöhrl, U. Stahl, V. Jäger, *Synthesis* **1991**, 1108–1118.

[11] Y. L. Zhong, T. K. M. Shing, *J. Org. Chem.* **1997**, *62*, 2622–2624.

[12] CCDC-242454, CCDC-614145, and CCDC-245397 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[13] CCDC-261413 and CCDC-262043 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[14] CCDC-614146 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Ref. [8] contains the experimental procedure for the debenzoylation and the relevant spectroscopic data.

[15] Ref. [8] contains the spectroscopic data of cycloheptane **53**.

[16] J. S. Yadav, D. K. Barma, *Tetrahedron* **1996**, *52*, 4457–4466.

[17] F. A. Luzzio, M. E. Menes, *J. Org. Chem.* **1994**, *59*, 7267–7272.

[18] M. Frigerio, M Santagostino, S. Sputore, G. Palmisano, *J. Org. Chem.* **1995**, *60*, 7272–7276.

[19] CCDC-607154 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[20] CONFLEX, Version 4.0.2 (Revision T), Conflex Corporation, Tokyo (Japan), **2000**.[20a,b] Although it is well established that the force field approach is useful for the TS search of flexible molecules[20c] and was successfully applied to 1,3-diplar cycloaddition,[23e] because CONFLEX does not support the TS molecular mechanics (MM) model and the tricyclic structures investigated in this paper are relatively rigid, TSs were calculated based on the ground-state conformers: a) H. Goto, E. Osawa, *J. Am. Chem. Soc.* **1989**, *111*, 8950–8951; b) H. Goto, E. Osawa, *J. Chem. Soc. Perkin Trans. 2* **1993**, 187–198; c) K. N. Houk, M. N. Paddon-row, N. G. Rondan, Y.-D. Wu, F. K. Brown, D. C. Spellmeyer, J. T. Mets, Y. Li, R. J. Loncharich, *Science* **1986**, *231*, 1108–1117.

[21] a) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648; b) C. T. Lee, W. T. Yang, R. G. Parr, *Phys. Rev. B* **1988**, 37, 785.

[22] Gaussian 98 (Revision A.11), M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, P. Salvador, J. J. Dannenberg, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh PA, **2001**.

[23] a) F. K. Brown, U. C. Singh, P. A. Kollman, L. Raimondi, K. N. Houk, C. W. Bock, *J. Org. Chem.* **1992**, *57*, 4862–4869; b) M. Carda, R. Portolés, J. Murga, S. Ureil, J. A. Marco, L. R. Domingo, R. J. Zaragozá, H. Röper, *J. Org. Chem.* **2000**, *65*, 7000–7009; c) J. Liu, S. Niwayama, Y. You, K. N. Houk, *J. Org. Chem.* **1998**, *63*, 1064–1073; d) E. C. Magnuson, J. Pranata, *J. Comput. Chem.* **1998**, *19*, 1795–1804; e) R. Annunziata, M. Benaglia, M. Cinquini, F. Cozzi, L. Raimondi, *Eur. J. Org. Chem.* **1998**, 1823–1832.

[24] C. D. Valentin, M. Freccero, R. Gandolfi, A. Rastelli, *J. Org. Chem.* **2000**, *65*, 6112–6120.

[25] J. B. Hendrickson, *J. Am. Chem. Soc.* **1961**, *83*, 4537–4547.

[26] D. Batty, D. Crich, *J. Chem. Soc. Perkin Trans. 1* **1992**, 3193–3204.

[27] L. Zhu, D. R. Mootoo, *Org. Lett.* **2003**, *5*, 3475–3478.

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