A Versatile Intermediate for the Systematic Synthesis of All Regioisomers of *myo*-Inositol Phosphates

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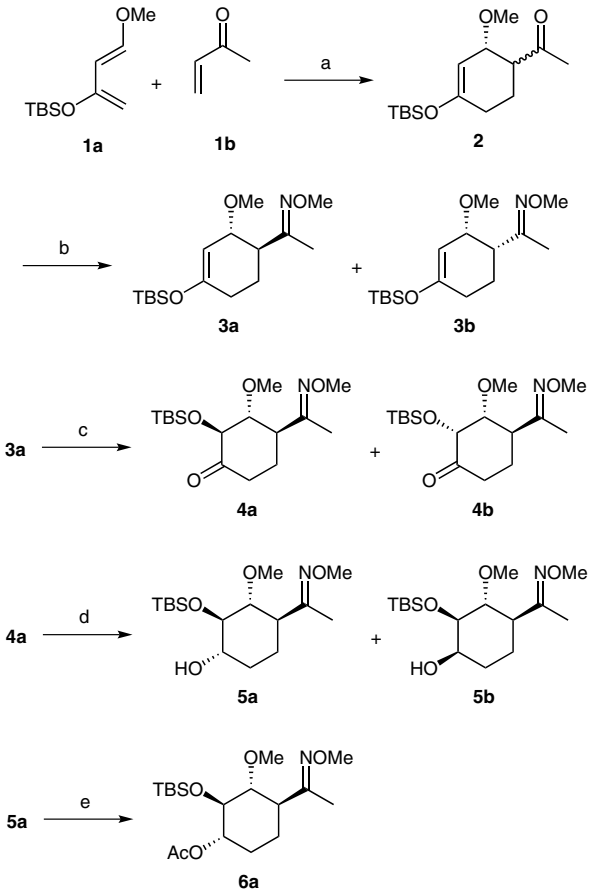
Abstract: Inositol phosphate derivatives are usually synthesized by repeated protection-deprotection procedures, necessitating development of an independent synthetic route for each inositol derivative. Herein, a synthetic precursor for all regioisomers of inositol phosphate is reported. A cycloadduct obtained by the Diels–Alder reaction of *trans*-1-methoxy-3-trimethylsilyloxybuta-1,3-diene and methyl vinyl ketone was converted into an inositol derivative by sequential introduction and immediate protection of hydroxy groups. Thus, the six hydroxy groups of the obtained inositol derivative are differentiated by different protective groups that are cleavable under independent conditions. This would enable us to prepare all regioisomers of inositol phosphate derivative.

Key words: inositol phosphate, Diels–Alder reaction, oxidative rearrangement, asymmetric dihydroxylation, monoacylation

There have been many reports on naturally occurring and synthetic inositol phosphates ($InsP_n$)[1,2] ranging from $InsP_1$ to $InsP_6$ that are often closely related to cell function; for example, D-*myo*-inositol 1,4,5-triphosphate [Ins(1,4,5)P_3], a crucial messenger to link the extracellular information to calcium mobilization.[3] We have previously reported the synthesis of biotinylated $InsP_n$s for the $InsP_n$-binding study of phospholipase A_2,[4] Grp1 Pleckstrin homology domain,[5] and HIV-1 Gag[6] proteins. However, our syntheses of $InsP_n$ derivatives were based on the repeated protection–deprotection of *myo*-inositol and hence we needed to develop an independent synthetic route for each $InsP_n$ derivative[4–6] as the other research groups did.[1,7] The present study was aimed at a 'total synthesis' of an inositol derivative equipped with six different protective groups that are cleavable under independent conditions. Our approach is featured by the Diels–Alder reaction and subsequent sequential introduction of hydroxy groups.

The Diels–Alder reaction of *trans*-1-methoxy-3-trimethylsilyloxybuta-1,3-diene (**1a**) affords a six-membered ring with oxygen substituents that are convertible into various natural products as pioneered by Danishefsky.[8] We intended to make use of the Danishefsky's diene for the synthesis of inositol derivatives. Thus, siloxy diene **1a** and methyl vinyl ketone (**1b**) were reacted in the presence of $Eu(fod)_3$ to give the cycloadduct **2** as a diastereomeric mixture in 86% yield. The ketone **2** was converted into methoximes **3a** and **3b**, which were separated by silica gel chromatography in 62% and 7% yield, respectively.[9] The compound **3a** was then subjected to a modification of the Paquette rearrangement,[10] affording siloxy ketone **4a** (56% yield) and **4b** (1% yield).[11] Ketone **4a** was reduced according to the procedure of Acena[12] using $NaBH_4$ to give alcohol **5a** and **5b** in 72% and 14% yield, respectively.[13] The alcohol **5a** was protected by an acetyl group[14] to give acetate **6a** quantitatively (Scheme 1).



Scheme 1 Synthesis of methoxime **6a**. *Reagents and conditions*: a) $Eu(fod)_3$, CH_2Cl_2, r.t.; b) $NH_2OMe{\cdot}HCl$, MeOH, pyridine; c) MCPBA, CH_2Cl_2, MS 4 Å; d) $NaBH_4$, MeOH; e) pyridine–Ac_2O (2:1).

The deprotection of the methoxyimino group of **6a** was not straightforward. The first attempt was done with [hydroxy(tosyloxy)iodo]benzene (HTIB)[15] by treating com-

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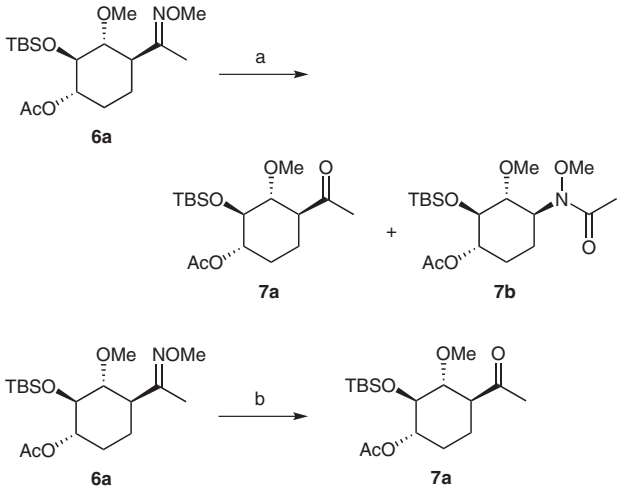
pound **6a** with HTIB in CH_2Cl_2 containing 1% water. Although ketone **7a** was obtained in 30% yield, the major product of this reaction was found to be the rearranged product **7b** (50% yield). The methoxime of **6a** was eventually removed by the Corey's procedure[16] using $TiCl_3$·3THF-DIBAL to give ketone **7a** in 83% yield (Scheme 2).

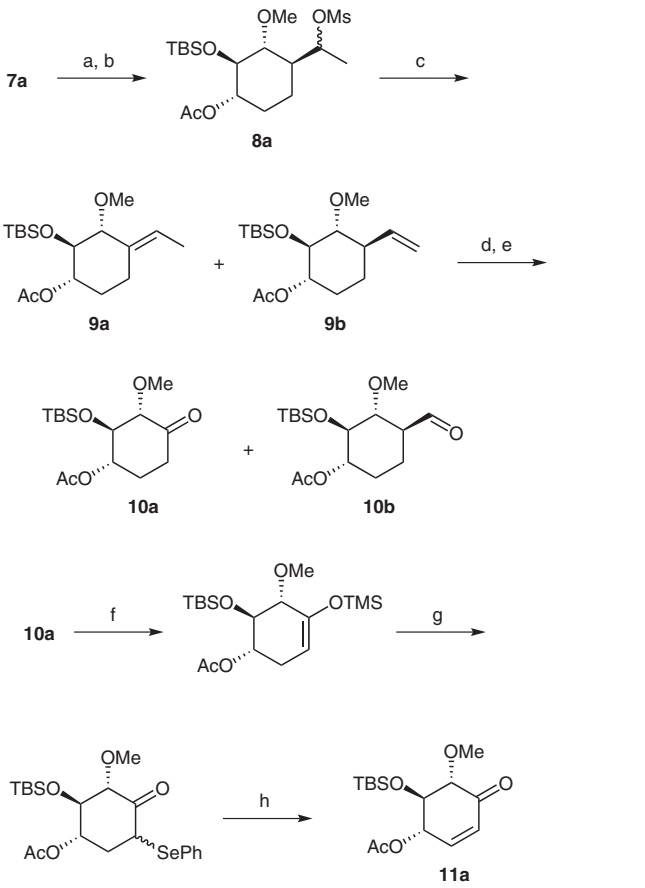


Scheme 2 Synthesis of methyl ketone **7a**. *Reagents and conditions*: a) HTIB, CH_2Cl_2 (1% H_2O); b) $TiCl_3$·3THF-DIBAL, toluene.

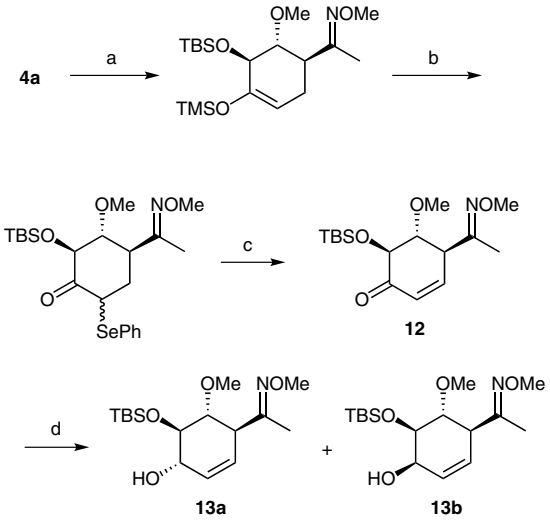
As the Baeyer–Villiger oxidation of the methyl ketone **7a** did not work well, it was transformed as follows. The ketone **7a** was converted into mesylate **8a** that was treated with DBU to give olefin **9a** and **9b** (**9a**/**9b** = 2:1). Ozonolysis of the mixture **9a** and **9b** afforded cyclohexanone **10a** and aldehyde **10b** in 25% and 11% overall yield based on **7a**, respectively. Cyclohexanone **10a** was converted into the TMS enolate by treatment with LiHMDS and TMSCl and further transformed to phenylselenyl ketone by treatment with PhSeCl. The subsequent oxidative elimination using H_2O_2 gave the desired cyclohexenone **11a** in 18% overall yield based on **10a** (Scheme 3). As the acetyl group of **11a** was unexpectedly found to be labile producing a deacetylated by-product, another synthetic route was explored.

The alternate approach was as follows. Cyclohexanone **4a** was converted into cyclohexenone **12** in 55% overall yield by treatment with a) LiHMDS, then TMSCl, b) PhSeCl, and c) 30% H_2O_2, $NaHCO_3$. The carbonyl group of **12** was reduced with $NaBH_4$ to give allyl alcohols **13a** and **13b** in 84% and 8% yield, respectively (Scheme 4). The stereochemistry of compound **13a** and **13b** was determined by converting **13a** into **5a** (Scheme 5) whose stereochemistry has already been established.

In this approach, the alcohol of **13a** was protected by MOM group (MOMCl, DIPEA) to afford the MOM derivative **14** in 92% yield. The olefin **14** was converted into *cis*-diols **15a** and **15b** in 65% and 29% yield, respectively, by the application of the Armstrong's modification of the Sharpless asymmetric dihydroxylation.[17,18] The diol **15a**

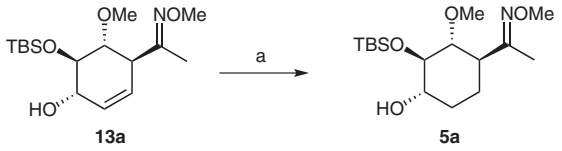


Scheme 3 Synthesis of cyclohexenone **11a**. *Reagents and conditions*: a) $NaBH_4$, MeOH–CH_2Cl_2; b) MsCl, Et_3N, CH_2Cl_2; c) DBU, toluene, Δ; d) O_3, CH_2Cl_2–MeOH; e) Me_2S; f) LiHMDS, TMSCl, THF; g) PhSeCl, CH_2Cl_2; h) $NaHCO_3$, 30% H_2O_2, THF.

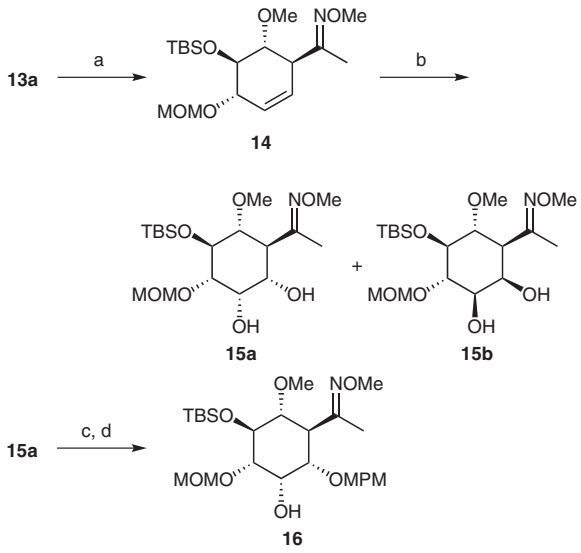


Scheme 4 Synthesis of allyl alcohol **13a**. *Reagents and conditions*: a) LiHMDS, THF, then TMSCl; b) PhSeCl, CH_2Cl_2; c) 30% H_2O_2, $NaHCO_3$, THF; d) $NaBH_4$, MeOH.

was converted into mono-MPM derivative **16** in 52% yield by the Nagashima–Ohno procedure using Bu_2SnO/CsF[19] (Scheme 6). Unfortunately, deprotection of the



Scheme 5 Stereochemical assignment of compound **13a**. *Reagents and conditions*: H_2, Pd/C, CH_2Cl_2.



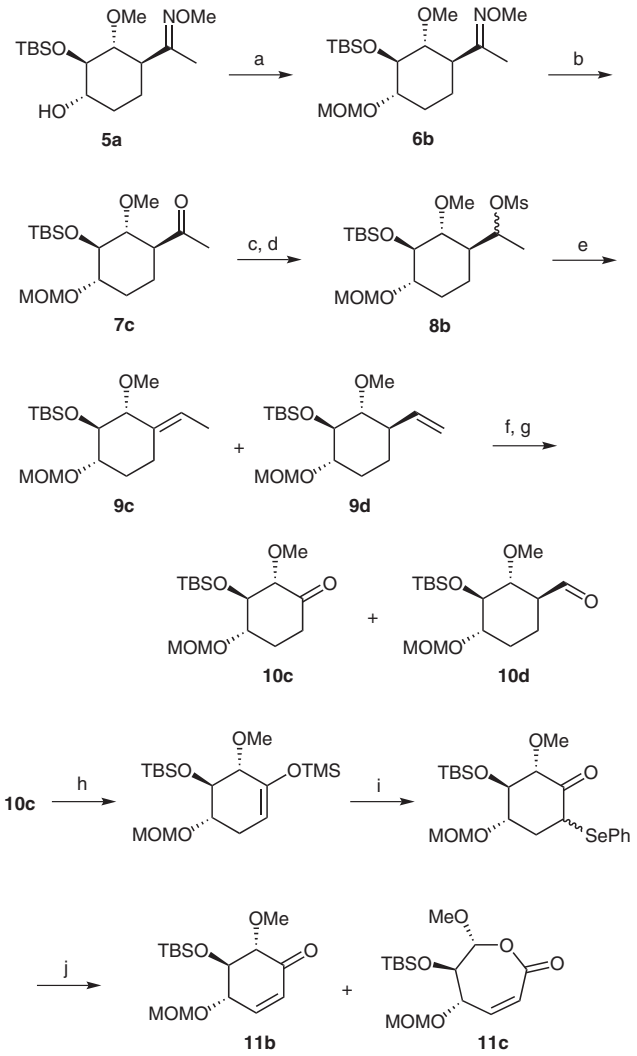
Scheme 6 Synthesis of mono-MPM derivative **16**. *Reagents and conditions*: a) MOMCl, DIPEA, CH_2Cl_2; b) AD-mix-β, OsO_4, $(DHQD)_2PHAL$, $MeSO_2NH_2$, *t*-BuOH–H_2O–CH_2Cl_2; c) Bu_2SnO, toluene; d) CsF, MPMCl, DMF.

methoxyimino group of compound **16** by the $TiCl_3$·3THF-DIBAL[16] procedure did not work.

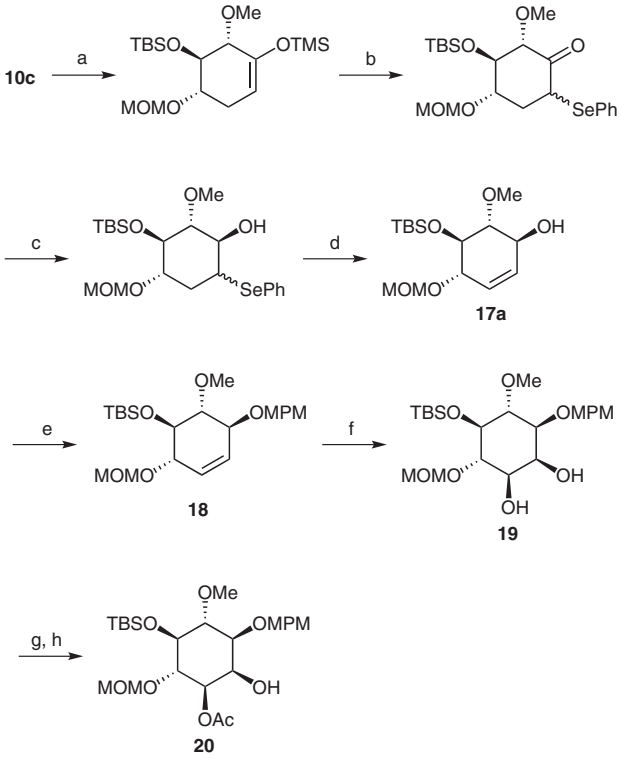
Thus, the synthetic route was revised as follows. Cyclohexanol **5a** was protected by a MOM group to give compound **6b** in 92% yield. The methoxyimino group of **6b** was smoothly removed with $TiCl_3$·3THF-DIBAL[16] to give methyl ketone **7c** in 85% yield. Methyl ketone **7c** was converted into mesylate **8b** by treatment with $NaBH_4$ followed by MsCl. Compound **8b** was further treated with DBU to give olefin **9c** and **9d**. Ozonolysis of the mixture **9c** and **9d** gave cyclohexanone **10c** in 24% yield based on **7c** and aldehyde **10d** (crude). Compound **10c** was converted into cyclohexenone **11b** in 34% yield via the TMS enolate and the phenylselenyl ketone intermediates by the above mentioned procedure. Unexpectedly, H_2O_2 treatment of the phenylselenyl ketone was accompanied by lactone **11c**, the Baeyer–Villiger product, in 23% yield (Scheme 7).

Thus, phenylselenyl ketone obtained from **10c** was converted into the corresponding phenylselenyl alcohol by treatment with $NaBH_4$ and subsequent treatment with 30% H_2O_2/$NaHCO_3$ gave allyl alcohol **17a** in 51% overall yield based on **10c**.[20] The hydroxy group of **17a** was protected by MPM group by treatment with NaH/MPMCl/TBAI in the presence of molecular sieves and compound **18** was obtained in 40% yield. Olefin dihydroxylation of compound **18** was achieved by the Armstrong procedure[17] to give *myo*-inositol derivative **19** in 59% yield. Diol **19** was converted into the desired monoacetate **20** in 39% yield by the Nagashima–Ohno procedure[19] (Scheme 8).

In summary, the Diels–Alder product **2** having two oxygen substituents on the cyclohexane ring was subjected to the Paquette's oxidative rearrangement to introduce the third oxygen substituent. Compound **5a** thus obtained was converted into cyclohexanone **10c** where the fourth oxygen group was introduced by ozonolytic cleavage of the carbon appendage. The fifth and sixth hydroxy groups were constructed and differentiated by the asymmetric dihydroxylation and the subsequent Nagashima–Ohno monoacylation. Thus, the six hydroxy groups of compound **20** are differentiated by protective groups that are cleavable under independent conditions. This would enable us to prepare not only all $InsP_n$ but also other inositol derivatives.



Scheme 7 Synthesis of cyclohexanone **11b**. *Reagents and conditions*: a) MOMCl, DIPEA, CH_2Cl_2; b) $TiCl_3$·3THF-DIBAL, toluene; c) $NaBH_4$, MeOH–CH_2Cl_2; d) MsCl, Et_3N, CH_2Cl_2; e) DBU, toluene, Δ; f) O_3, Et_3N, CH_2Cl_2–MeOH; g) Me_2S; h) LiHMDS, TMSCl, THF; i) PhSeCl, CH_2Cl_2; j) $NaHCO_3$, 30% H_2O_2.



Scheme 8 Synthesis of protected inositol **20**. *Reagents and conditions*: a) LiHMDS, TMSCl; b) PhSeCl, CH_2Cl_2; c) $NaBH_4$, MeOH; d) $NaHCO_3$, 30% H_2O_2, THF; e) NaH, MPMCl, TBAI, THF, MS 4 Å; f) AD-mix-β, OsO_4, $(DHQD)_2PHAL$, $MeSO_2NH_2$, *t*-BuOH–H_2O/CH_2Cl_2; g) Bu_2SnO, toluene; h) AcCl, CH_2Cl_2.

Reagents and solvents were purified by standard techniques. TLC was performed using silica gel 60 F_{254} (Merck) and visualized by 10% solution of phosphomolybdic acid in EtOH or 0.5% solution of $KMnO_4$ in 1 M aq NaOH. Column chromatography was carried out with silica gel 60 N (spherical neutral) (Kanto Chemical Co.). ^1H NMR and ^{13}C NMR spectra were recorded on JNM- AL300 with respect to internal standard TMS and *J* values are given in Hz. Mass spectra [MS (FAB)] and high-resolution mass spectra (HRMS) were recorded on Jeol JMS-DX303HF mass spectrometer. IR spectra were recorded on Jasco FT/IR-410. Elemental analyses were performed with Yanaco MT-5S.

(*S)-1-[4-(*tert*-Butyldimethylsilyloxy)-2-methoxycyclohex-3-enyl]ethanone (2)**

$Eu(fod)_3$ (0.72 g, 0.70 mmol) and methyl vinyl ketone (**1b**; 2.3 mL, 28 mmol) were successively dissolved in CH_2Cl_2 (6 mL). To the solution was added *trans*-3-(*tert*-butyldimethylsiloxy)-1-methoxybuta-1,3-diene (**1a**; 3.0 g, 14 mmol) and the resulting solution was stirred at r.t. for 7 h. The solution was concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 7:1) to give **2** as a mixture of diastereomers; yield: 3.4 g (86%); yellow oil.

1-[(1*S,2*S**)-4-(*tert*-Butyldimethylsilyloxy)-2-methoxycyclohex-3-enyl]ethanone *O*-Methyl Oxime (3a) and 1-[(1*R**,2*S**)-4-(*tert*-Butyldimethylsilyloxy)-2-methoxycyclohex-3-enyl]ethanone *O*-Methyl Oxime (3b)**

$NH_2OMe{\cdot}HCl$ (3.4 g, 40 mmol) was dissolved in MeOH (6.1 mL) under ice cooling. Pyridine (2.5 mL, 31 mmol) was added to the solution. The mixture was stirred for 10 min and was added to crude **2** (4.1 g, crude) under ice cooling. The solution was stirred for 45 min under ice cooling and then concentrated in vacuo at r.t. for 45 min. The residue was roughly purified by silica gel chromatography (silica gel 10 g, hexane–EtOAc, 20:1) and further purified by successive silica gel chromatography (hexane–EtOAc, 20:1) to give **3a** (2.8 g, 62%) and **3b** (0.31 g, 7%) as colorless oils.

3a

IR (film): 1665 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.15 (s, 6 H, 2 × $SiCH_3$), 0.92 [s, 9 H, $C(CH_3)_3$], 1.63–1.90 (m, 5 H, 2 × CH, CH_3), 1.94–2.05 (ddt, *J* = 4.95, 9.89, 17.2 Hz, 1 H, CH), 2.09–2.21 (m, 1 H, CH), 2.39–2.46 (ddd, *J* = 3.66, 7.88, 11.0 Hz, 1 H, CH), 3.25–3.32 (t, *J* = 11.9 Hz, 3 H, OCH_3), 3.80–3.87 (t, *J* = 11.9 Hz, 3 H, OCH_3), 4.07–4.13 (m, 1 H, CH), 4.97 (s, 1 H, =CH).

^{13}C NMR ($CDCl_3$): δ = –4.50 ($SiCH_3$), –4.41 ($SiCH_3$), 12.2 (CH_3), 18.0 (SiC), 24.6 (CH_2), 25.6 (CH_3), 29.1 (CH_2), 45.0 (CH), 54.8 (OCH_3), 61.2 (=$NOCH_3$), 76.4 (CH), 104 (=CH), 153 (=C), 158 (C=N).

MS (FAB): *m*/*z* = 314 $(M + H)^+$.

Anal. Calcd for $C_{16}H_{31}NO_3Si$: C, 61.30; H, 9.97; N, 4.47. Found: C, 61.03; H, 9.97; N, 4.52.

3b

IR (film): 1660 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.15 (s, 3 H, $SiCH_3$), 0.17 (s, 3 H, $SiCH_3$), 0.92 [s, 9 H, $C(CH_3)_3$], 1.72–1.80 (m, 1 H, CH), 1.87 (s, 3 H, CH_3), 1.89–2.12 (m, 3 H, 3 × CH), 2.39–2.46 (ddd, *J* = 3.30, 3.48, 12.1 Hz, 1 H, CH), 3.27 (s, 3 H, OCH_3), 3.80–3.88 (m, 4 H, CH, OCH_3), 5.15–5.17 (d, *J* = 3.30 Hz, 1 H, =CH).

^{13}C NMR ($CDCl_3$): δ = –4.56 ($SiCH_3$), –4.38 ($SiCH_3$), 12.9 (CH_3), 18.0 (SiC), 20.4 (CH_2), 25.6 (CH_3), 30.2 (CH_2), 44.8 (CH), 56.0 (OCH_3), 61.1 (=$NOCH_3$), 75.3 (CH), 103 (=CH), 156 (=C), 159 (C=N).

MS (FAB): *m*/*z* = 314 $(M + H)^+$.

Anal. Calcd for $C_{16}H_{31}NO_3Si$: C, 61.30; H, 9.97; N, 4.47. Found: C, 61.03; H, 9.99; N, 4.65.

(2*S,3*R**,4*R**)-2-(*tert*-Butyldimethylsilyloxy)-3-methoxy-4-[1-(methoxyimino)ethyl]cyclohexanone (4a) and (2*R**,3*R**,4*R**)-2-(*tert*-Butyldimethylsilyloxy)-3-methoxy-4-[1-(methoxyimino)ethyl]cyclohexanone (4b)**

Under ice cooling, **3a** (0.11 g, 0.34 mmol) was dissolved in CH_2Cl_2 (12 mL) and molecular sieves 4 Å (500 mg) were added. After stirring for 10 min, a solution of MCPBA (92 mg, 3.7 mmol) in CH_2Cl_2 (2.0 mL) was slowly added. The solution was stirred for 3 h under ice cooling and for 24 h at r.t. The reaction mixture was roughly purified by chromatography [silica gel (10 g), hexane–EtOAc, 8:1) and further purified by successive silica gel chromatography (hexane–EtOAc, 5:1) to give **4a** (63 mg, 56%) and **4b** (1.3 mg, 1%) as colorless oils.

4a

IR (film): 1732 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.05 (s, 3 H, $SiCH_3$), 0.13 (s, 3 H, $SiCH_3$), 0.95 [s, 9 H, $C(CH_3)_3$], 1.52–1.65 (ddd, *J* = 4.58, 13.6, 26.6 Hz, 1 H, CH), 1.84–1.95 (m, 4 H, CH_3, CH), 2.29–2.40 (m, 1 H, CH), 2.41–2.48 (ddd, *J* = 2.93, 4.76, 13.7 Hz, 1 H, CH), 2.63–2.72 (ddd, *J* = 3.85, 10.6, 12.7 Hz, 1 H, CH), 3.34–3.41 (dd, *J* = 9.16, 10.6 Hz, 1 H, –CH), 3.49 (s, 3 H, OCH_3), 3.87 (s, 3 H, =$NOCH_3$), 4.18–4.21 (dd, *J* = 0.92, 9.16 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –5.35 ($SiCH_3$), –4.75 ($SiCH_3$), 12.4 (CH_3), 18.5 (SiC), 25.3 (CH_3), 25.9 (CH_2), 38.5 (CH_2), 48.5 (CH), 60.9 (OCH_3), 61.4 (=$NOCH_3$), 82.6 (CH), 85.5 (CH), 156 (C=N), 206 (C=O).

MS (FAB): *m*/*z* = 330 $(M + H)^{+\cdot}$

Anal. Calcd for $C_{16}H_{31}NO_4Si$: C, 58.32; H, 9.48; N, 4.25. Found: C, 58.09; H, 9.58; N, 4.23.

4b

IR (film): 1733 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$), 0.92 [s, 9 H, $C(CH_3)_3$], 1.56–1.87 (m, 5 H, 2 × CH, CH_3), 2.02–2.12 (m, 1 H, CH), 2.56–2.65 (ddd, *J* = 5.50, 8.24, 13.7 Hz, 1 H, CH), 2.88–2.95 (td, *J* = 4.95, 6.96 Hz, 1 H, CH), 3.37 (s, 3 H, OCH_3), 3.63–3.66 (dd, *J* = 2.93, 6.96 Hz, 1 H, CH), 3.85–3.90 (m, 3 H, OCH_3), 4.58–4.59 (dd, *J* = 0.92, 2.93 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –5.15 ($SiCH_3$), –4.87($SiCH_3$), 13.1 (CH_3), 18.3 (SiC), 24.7 (CH_3), 25.8 (CH_2), 36.4 (CH_2), 43.6 (CH), 58.5 (OCH_3), 61.5 (=$NOCH_3$), 76.6 (CH), 84.3 (CH), 157(C=N), 209 (C=O).

HRMS (FAB): *m*/*z* calcd for $C_{16}H_{33}NO_4Si$ $(M + H)^+$: 330.2101; found: 330.2162.

1-[(1*S,2*R**,3*R**,4*S**)-3-(*tert*-Butyldimethylsilyloxy)-4-hydroxy-2-methoxycyclohexyl]ethanone *O*-Methyl Oxime (5a) and 1-[(1*S**,2*R**,3*R**,4*R**)-3-(*tert*-Butyldimethylsilyloxy)-4-hydroxy-2-methoxycyclohexyl]ethanone *O*-Methyl Oxime (5b)**

Under ice cooling, compound **4a** (0.44 g, 1.3 mmol) was dissolved in MeOH (5.0 mL) and $NaBH_4$ (0.20 g, 5.3 mmol) was added. The solution was stirred for 30 min under ice cooling. The solution was diluted with EtOAc (50 mL), washed with H_2O (50 mL) and brine (50 mL), and dried (Na_2SO_4). The solution was concentrated in vacuo. The solution was purified by silica gel chromatography (hexane–EtOAc, 3:1) to give **5a** as white crystals (0.32 g, 72%) and **5b** as a colorless oil (59 mg, 14%).

5a

Mp 56–62 °C.

IR (KBr): 3417, 1639 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.13 (s, 3 H, $SiCH_3$), 0.15 (s, 3 H, $SiCH_3$), 0.93 [s, 9 H, $C(CH_3)_3$], 1.23–1.48 (m, 2 H, CH, CH), 1.62–1.70 (m, 1 H, CH), 1.84 (s, 3 H, CH_3), 1.91–1.99 (m, 1 H, CH), 2.25–2.33 (m, 4 H, OH, CH), 3.05–3.11 (dd, *J* = 8.61, 10.6 Hz, 1 H, CH), 3.28–3.34 (t, *J* = 8.61 Hz, 1 H, –CH), 3.35 (s, 3 H, OCH_3), 3.37–3.48 (m, 1 H, CH), 3.85 (s, 3 H, OCH_3).

^{13}C NMR ($CDCl_3$): δ = –4.61 ($SiCH_3$), –4.10 ($SiCH_3$), 12.5 (CH_3), 18.2 (SiC), 25.2 (CH_3), 26.0 (CH_2), 30.1 (CH_2), 48.9 (CH), 60.1 (OCH_3), 61.3 (=$NOCH_3$), 73.8 (CH), 80.7 (CH), 83.6 (CH), 158 (C=N).

MS (FAB): *m*/*z* = 332 $(M + H)^+$.

Anal. Calcd for $C_{16}H_{33}NO_4Si$: C, 57.97; H, 10.03; N, 4.22. Found: C, 57.72; H, 10.04; N, 4.14.

5b

IR (film): 1741 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.10 (s, 3 H, $SiCH_3$), 0.14 (s, 3 H, $SiCH_3$), 0.93 [s, 9 H, $C(CH_3)_3$], 1.39–1.49 (m, 2 H, 2 × CH), 1.81–1.99 (m, 5 H, CH_3, 2 × CH), 2.17–2.26 (ddd, *J* = 3.11, 10.6, 12.6 Hz, 1 H, CH), 2.60–2.61 (d, *J* = 1.83 Hz, 1 H, OH), 3.35–3.41 (dd, *J* = 8.61, 10.6 Hz, 1 H, CH), 3.39 (s, 3 H, OCH_3), 3.50–3.54 (dd, *J* = 3.11, 8.61 Hz, 1 H, CH), 3.85 (s, 3 H, OCH_3), 3.89–3.90 (d, *J* = 2.75 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –4.92 ($SiCH_3$), –4.63 ($SiCH_3$), 11.8 (CH_3), 17.9 (SiC), 23.0 (CH_2), 25.8 (CH_3), 28.6 (CH_2), 48.9 (CH), 60.5 (OCH_3), 61.2 (=$NOCH_3$), 70.8 (CH), 77.6 (CH), 80.8 (CH), 158 (C=N).

HRMS (FAB): *m*/*z* calcd for $C_{16}H_{34}NO_4Si$ $(M + H)^+$: 332.2257; found: 332.2254.

(1*S,2*R**,3*R**,4*R**)-2-(*tert*-Butyldimethylsilyloxy)-3-methoxy-4-[1-(methoxyimino)ethyl]cyclohexyl Acetate (6a)**

Compound **5a** (1.0 g, 3.1 mmol) was dissolved in a solution of pyridine and Ac_2O (6.0 mL, pyridine–Ac_2O, 2: 1). The solution was stirred overnight at 40 °C. The reaction solution was concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 3:1) to give **6a** as a colorless oil; yield: 1.2 g (quant).

IR (film): 1741 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.09 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.88 [s, 9 H, $C(CH_3)_3$], 1.22–1.35 (m, 1 H, CH), 1.39–1.53 (m, 1 H, CH), 1.61–1.69 (qd, *J* = 3.66, 13.4 Hz, 1 H, CH), 1.84 (s, 3 H, CH_3), 1.99–2.05 (m, 1 H, CH), 2.05 (s, 3 H, CH_3), 2.23–2.32 (ddd, *J* = 3.85, 10.6, 12.5 Hz, 1 H, CH), 3.09–3.15 (dd, *J* = 8.61, 10.7 Hz, 1 H, CH), 3.37 (s, 3 H, OCH_3), 3.51–3.57 (dd, *J* = 8.79, 9.16 Hz, 1 H, CH), 3.85 (s, 3 H, =$NOCH_3$), 4.59–4.68 (ddd, *J* = 4.76, 9.34, 11.4 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –4.63 ($SiCH_3$), –4.16 ($SiCH_3$), 12.3 (CH_2), 18.0 (SiC), 21.4 (CH_3), 24.9 (CH_3), 25.8 (CH_3), 28.7 (CH_2), 48.7 (CH), 60.5 (OCH_3), 61.3 (=$NOCH_3$) 75.6 (CH), 77.0 (CH), 84.3 (CH), 157 (C=N), 170 (OC=O).

HRMS (FAB): *m*/*z* calcd for $C_{18}H_{36}NO_5Si$ $(M + H)^+$: 374.2363; found: 374.2367.

(1*S,2*R**,3*R**,4*S**)-4-Acetyl-2-(*tert*-butyldimethylsilyloxy)-3-methoxycyclohexyl Acetate (7a)**

Compound **6a** (0.16 g, 0.42 mmol) was dissolved in toluene (20 mL) under argon atmosphere and ice cooling. A 0.25 M solution of $TiCl_3$·3THF-DIBAL in toluene (2.1 mL, 0.53 mmol) was added. The solution was stirred for 20 min at r.t. A solution of $TiCl_3$·3THF-DIBAL in toluene (2.1 mL, 0.53 mmol) was added additionally and the solution was stirred for 20 min. Finally a solution of $TiCl_3$·3THF-DIBAL in toluene (2.1 mL, 0.53 mmol) was added again and the solution was stirred for 40 min at r.t. The reaction was terminated by the addition of sat. aq NaOAc (20 mL) and the pH of the solution was adjusted to 3.0 by aq citric acid. The solution was extracted with CH_2Cl_2 (4 × 30 mL) and dried (Na_2SO_4) and the solvent was evaporated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 5:1) to give **7a** as white crystals; yield: 0.12 g (83%); mp 68–70 °C.

IR (KBr): 1737, 1714 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.09 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.88 [s, 9 H, $C(CH_3)_3$], 1.19–1.32 (m, 1 H, CH), 1.34–1.48 (dq, *J* = 3.66, 12.1 Hz, 1 H, CH), 1.68–1.76 (qd, *J* = 3.66, 13.6 Hz, 1 H, CH), 2.01–2.10 (m, 1 H, CH), 2.05 (s, 3 H, CH_3), 2.23 (s, 3 H, CH_3), 2.55–2.64 (ddd, *J* = 3.66, 10.3, 12.1 Hz, 1 H, CH), 3.28–3.34 (dd, *J* = 8.80, 10.3 Hz, 1 H, CH), 3.38 (s, 3 H, OCH_3), 3.50–3.56 (dd, *J* = 8.80, 9.17 Hz, 3 H, CH), 4.57–4.65 (ddd, *J* = 4.77, 9.53, 11.0 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –4.58 ($SiCH_3$), –4.18 ($SiCH_3$), 18.0 (SiC), 21.4 (CH_3), 23.7 (CH_2), 25.7 (CH_3), 28.7 (CH_2), 31.1 (CH_3), 55.0 (CH), 61.4 (OCH_3), 75.3 (CH), 77.0 (CH), 84.2 (CH), 170 (OC=O), 210 (C=O).

HRMS (FAB): *m*/*z* calcd for $C_{17}H_{33}O_5Si$ $(M + H)^+$: 345.2097; found: 345.2102.

(1*S,2*R**,3*R**,4*S**)-2-(*tert*-Butyldimethylsilyloxy)-3-methoxy-4-[1-(methylsulfonyloxy)ethyl]cyclohexyl Acetate (8a)**

Under ice cooling, compound **7a** (0.34 g, 0.99 mmol) was dissolved in a mixture of MeOH (3.0 mL) and CH_2Cl_2 (2.0 mL). $NaBH_4$ (0.19 g, 4.9 mmol) was added and the resulting solution was stirred for 30

min. The solution was diluted with EtOAc (50 mL) and washed with H_2O (50 mL) and brine (50 mL), and dried (Na_2SO_4). The solution was concentrated in vacuo to give a colorless oil. The obtained crude alcohol (0.35 g) was dissolved in CH_2Cl_2 (19 mL) under argon atmosphere and ice cooling. Et_3N (1.4 mL, 10 mmol) and MsCl (0.56 mL, 7.2 mmol) were added and the resulting solution was stirred for 1.5 h and treated with sat. aq $NaHCO_3$ (20 mL). The solution was extracted with CH_2Cl_2 (3 × 40 mL), the combined organic layers were dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 3:1) to give white crystals of **8a** as a mixture of diastereomers.

(1*S,2*R**,3*R**,*E*)-2-(*tert*-Butyldimethylsilyloxy)-4-ethylidene-3-methoxycyclohexyl Acetate (9a) and (1*S**,2*R**,3*R**,4*R**)-2-(*tert*-Butyldimethylsilyloxy)-3-methoxy-4-vinylcyclohexyl Acetate (9b)**

Compound **8a** (0.35 g, 0.83 mmol) was dissolved in toluene (10 mL) and DBU (0.93 mL, 6.2 mmol) was added. The solution was heated at reflux for 48 h. Sat. aq NH_4Cl (15 mL) was added and the solution was extracted with CH_2Cl_2 (3 × 20 mL). The organic layers were combined and washed with brine (45 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 20:1) to give a mixture of **9a**,**b** (2:1) as a colorless oil.

(1*S,2*R**,3*S**)-2-(*tert*-Butyldimethylsilyloxy)-3-methoxy-4-oxocyclohexyl Acetate (10a) and (1*S**,2*R**,3*R**,4*S**)-2-(*tert*-Butyldimethylsilyloxy)-4-formyl-3-methoxycyclohexyl Acetate (10b)**

The crude mixture of **9a**,**b** (0.14 g) was dissolved in a mixture of CH_2Cl_2 (30 mL) and MeOH (6.0 mL). Et_3N (0.30 mL, 1% v/v) was added and the solution was stirred at –78 °C. O_3 was bubbled until the blue color persisted. O_2 was bubbled through the reaction solution for 30 min at –78 °C. Me_2S (0.22 mL, 3.1 mmol) was added and the resulting solution was stirred for 30 min, then further stirred at r.t. for 2 h. The reaction was terminated by the addition of sat. aq $NaHCO_3$ (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 5:1) to give **10a** (79 mg, 25% over 3 steps) and **10b** as white crystals (34 mg, 11% over 3 steps).

10a

Mp 77–81 °C.

IR (KBr): 1753, 1729 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.10 (s, 3 H, $SiCH_3$), 0.88 [s, 9 H, $C(CH_3)_3$], 1.46–1.54 (m, 1 H, CH), 2.08 (s, 3 H, CH_3), 2.18–2.27 (qd, *J* = 4.40, 13.2 Hz, 1 H, CH), 2.41–2.46 (m, 2 H, 2 × CH), 3.47 (s, 3 H, OCH_3), 3.61–3.64 (d, *J* = 9.16 Hz, 1 H, CH), 3.70–3.76 (t, *J* = 8.80 Hz, 1 H, CH), 4.97–5.05 (ddd, *J* = 4.40, 8.80, 11.0 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –4.64 ($SiCH_3$), –4.42 ($SiCH_3$), 18.1 (SiC), 21.2 (CH_3), 25.5 (CH_2), 25.7 (CH_3), 35.6 (CH_2), 59.6 (OCH_3), 74.0 (CH), 76.3 (CH), 88.2 (CH), 170 (OC=O), 206 (C=O).

HRMS (FAB): *m*/*z* calcd for $C_{15}H_{29}O_5Si$ $(M + H)^+$: 317.1784; found: 317.1782.

10b

Mp 155–164 °C.

IR (KBr): 1733, 1706 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.11 (s, 3 H, $SiCH_3$), 0.13 (s, 3 H, $SiCH_3$), 0.89 [s, 9 H, $C(CH_3)_3$], 1.26–1.54 (m, 2 H, 2 × CH), 1.77–1.86 (qd, *J* = 4.03, 13.6 Hz, 1 H, CH), 2.03–2.12 (m, 4 H, 2 × CH), 2.41–2.46 (m, 2 H, CH_3, CH), 2.41–2.52 (m, 1 H, CH), 3.29–3.35 (dd, *J* = 8.07, 9.53 Hz, 1 H, CH), 3.45 (s, 3 H, OCH_3), 3.62–3.68 (dd, *J* = 8.07, 8.43 Hz, 1 H, CH), 4.58–4.66 (ddd, *J* = 4.03, 8.43, 9.90 Hz, 1 H, CH), 9.77–9.78 (d, *J* = 2.20 Hz, 1 H, CHO).

^{13}C NMR ($CDCl_3$): δ = –4.64 ($SiCH_3$), –4.31 ($SiCH_3$), 18.0 (SiC), 20.1 (CH_2), 21.4 (CH_3), 25.7 (CH_3), 27.4 (CH_2), 54.4 (CH), 60.7 (OCH_3), 74.6 (CH), 75.6 (CH), 82.7 (CH), 170 (OC=O), 202 (COH).

MS (FAB): *m*/*z* = 331 $(M + H)^+$.

(1*S,5*S**,6*R**)-6-(*tert*-Butyldimethylsilyloxy)-5-methoxy-4-oxocyclohex-2-enyl Acetate (11a)**

Compound **10a** (66 mg, 0.21 mmol) was dissolved in THF (6.5 mL) under an argon atmosphere at –78 °C. A THF solution of LiHMDS (1.6 M, 0.20 mL, 0.32 mmol) was added and the solution was stirred for 1 h at –78 °C. TMSCl (51 μL, 0.40 mmol) was then added and the solution was stirred for 45 min at –78 °C and for 1 h at r.t. The solution was concentrated in vacuo and the residue was dissolved in anhyd *n*-pentane (20 mL) and filtered through Celite. The filtrate was concentrated in vacuo to give the crude intermediate TMS enolate as a colorless oil. The crude colorless oil was dissolved in CH_2Cl_2 (6.0 mL) under argon atmosphere at –78 °C. A solution of PhSeCl (45 mg, 0.23 mmol) in CH_2Cl_2 (6.0 mL) was added and the solution was stirred for 45 min at –78 °C and for 15 min at r.t. The solution was concentrated in vacuo to give the crude intermediate phenylselenyl ketone as a yellow oil. The crude yellow oil was dissolved in THF (6.5 mL) under argon atmosphere and ice cooling. $NaHCO_3$ (52 mg, 0.62 mmol) and 30% H_2O_2 (61 μL, 0.63 mmol) were successively added and the solution was stirred for 15 min at the same temperature, then for 2 h at r.t. H_2O (30 mL) was added and the mixture was extracted with Et_2O (3 × 40 mL). The combined organic layers were washed with brine (60 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 5:1) to give **11a** as white crystals; yield: 12 mg (18% over 3 steps); mp 62–68 °C.

IR (KBr): 1744, 1701, 1624 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.09 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.89 [s, 9 H, $C(CH_3)_3$], 2.14 (s, 3 H, CH_3), 3.63–3.67 (d, *J* = 10.3 Hz, 1 H, CH), 3.64 (s, 3 H, OCH_3), 3.98–4.04 (dd, *J* = 8.43, 10.3 Hz, 1 H, –CH), 5.58–5.62 (td, *J* = 2.20, 8.43 Hz, 1 H, CH), 6.06–6.10 (dd, *J* = 2.20, 10.6 Hz, 1 H, =CH), 6.63–6.67 (dd, *J* = 2.20, 10.6 Hz, 1 H, =CH).

^{13}C NMR ($CDCl_3$): δ = –5.09 ($SiCH_3$), –4.39 ($SiCH_3$), 18.1 (SiC), 21.0 (CH_3), 25.6 (CH_3), 60.9 (OCH_3), 74.3 (CH), 75.4 (CH), 86.2 (CH), 129 (=CH), 146 (=CH), 170 (OC=O), 197 (C=O).

HRMS (FAB): *m*/*z* calcd for $C_{15}H_{26}O_5Si$ + Na $(M + Na)^+$: 334.1447; found: 337.1463.

(4*R,5*R**,6*S**)-6-(*tert*-Butyldimethylsilyloxy)-5-methoxy-4-[1-(methoxyimino)ethyl]cyclohex-2-enone (12)**

Compound **4a** (1.7 g, 5.0 mmol) was dissolved in THF (16 mL) under argon atmosphere at –78 °C. A THF solution of LiHMDS (1.6 M, 7.5 mL, 12 mmol) was added and the solution was stirred for 1 h at –78 °C. TMSCl (0.95 mL, 7.5 mmol) was added and the solution was stirred for 45 min at –78 °C and for 1 h at r.t. The solution was concentrated in vacuo and the residue was dissolved in anhyd pentane (20 mL) and filtered through Celite. The filtrate was concentrated in vacuo to give the crude intermediate TMS enolate as a yellow oil. The crude yellow oil was dissolved in CH_2Cl_2 (50 mL) under argon atmosphere at –78 °C. A solution of PhSeCl (1.1 g, 5.6 mmol) in CH_2Cl_2 (10 mL) was added and the solution was stirred for 45 min at –78 °C and for 15 min at r.t. The solution was concentrated in vacuo to give the crude intermediate phenylselenyl ketone as a yellow oil. The yellow oil was dissolved in THF (40 mL) under argon atmosphere and ice cooling. $NaHCO_3$ (1.2 g, 15 mmol) and 30% H_2O_2 (1.4 mL, 15 mmol) were successively added and the so-

lution was stirred for 15 min at the same temperature, then for 2 h at r.t. H_2O (60 mL) was added and the mixture was extracted with Et_2O (3 × 80 mL). The combined organic layers were washed with brine (120 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 5:1) to give **12** as a colorless oil; yield: 0.91 g (55% over 3 steps).

IR (film): 1702, 1620, 1471, 1443 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.11 (s, 3 H, $SiCH_3$), 0.20 (s, 3 H, $SiCH_3$), 0.97 [s, 9 H, $C(CH_3)_3$], 1.91 (s, 3 H, CH_3), 3.35–3.40 (ddd, *J* = 2.20, 3.11, 9.52 Hz, 1 H, CH), 3.51 (s, 3 H, OCH_3), 3.56–3.63 (dd, *J* = 9.52, 10.3 Hz, 1 H, CH), 4.01 (s, 3 H, $=NOCH_3$), 4.19–4.23 (d, *J* = 10.3 Hz, 1 H, CH), 6.07–6.11 (dd, *J* = 3.11, 10.3 Hz, 1 H, =CH), 6.62–6.66 (dd, *J* = 2.20, 10.3 Hz, 1 H, =CH).

^{13}C NMR ($CDCl_3$): δ = –5.30 ($SiCH_3$), –4.59 ($SiCH_3$), 13.3 (CH_3), 18.6 (SiC), 25.8 (CH_3), 50.4 (CH), 61.0 (OCH_3), 61.7 ($=NOCH_3$), 80.3 (CH), 84.1 (CH), 129 (=CH), 146 (=CH), 155 (C=N), 198 (C=O).

HRMS (FAB): *m*/*z* calcd for $C_{16}H_{30}NO_4Si$ (M + H)$^+$: 328.1944; found: 328.1921.

1-[(1*S,4*S**,5*R**,6*R**)-5-(*tert*-Butyldimethylsilyloxy)-4-hydroxy-6-methoxycyclohex-2-enyl]ethanone *O*-Methyl Oxime (13a) and 1-[(1*S**,4*R**,5*R**,6*R**)-5-(*tert*-Butyldimethylsilyloxy)-4-hydroxy-6-methoxycyclohex-2-enyl]ethanone *O*-Methyl Oxime (13b)**

Compound **12** (85 mg, 0.26 mmol) was dissolved in a mixture of MeOH (1.0 mL) and CH_2Cl_2 (1.0 mL) under ice cooling. $NaBH_4$ (49 mg, 1.3 mmol) was added and the solution was stirred for 30 min and the solution was diluted with EtOAc (50 mL). The organic layer was washed with H_2O (50 mL) and brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 3:1) to give **13a** as a colorless oil (72 mg, 84%) and **13b** as a yellow oil (7.0 mg, 8%).

13a

IR (film): 3444, 1655, 1472 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.14 (s, 6 H, 2 × $SiCH_3$), 0.93 [s, 9 H, $C(CH_3)_3$], 1.81 (s, 3 H, CH_3), 2.06–2.08 (d, *J* = 4.40 Hz, 1 H, OH), 3.11–3.17 (dq, *J* = 2.57, 11.4 Hz, 1 H, CH), 3.28–3.34 (d, *J* = 9.17 Hz, 1 H, CH), 3.41 (s, 3 H, OCH_3), 3.61–3.66 (dd, *J* = 7.70, 9.17 Hz, 1 H, CH), 3.87 (s, 3 H, $=NOCH_3$), 4.17–4.19 (m, 1 H, CH), 5.39–5.44 (dd, *J* = 2.57, 10.3 Hz, 1 H, =CH), 5.68–5.73 (dd, *J* = 2.57, 10.3 Hz, 1 H, =CH).

^{13}C NMR ($CDCl_3$): δ = –4.67 ($SiCH_3$), –4.21 ($SiCH_3$), 12.4 (CH_3), 18.2 (SiC), 26.0 (CH_3), 50.2 (CH), 60.4 (OCH_3), 61.4 ($=NOCH_3$), 73.5 (CH), 78.1 (CH), 81.2 (CH), 127 (=CH), 130 (=CH), 157 (C=N).

HRMS (FAB): *m*/*z* calcd for $C_{16}H_{32}NO_4Si$ (M + H)$^+$: 330.2101; found: 330.2087.

13b

IR (film): 3550, 1701, 1471 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.13 (s, 3 H, $SiCH_3$), 0.16 (s, 3 H, $SiCH_3$), 0.94 [s, 9 H, $C(CH_3)_3$], 1.83 (s, 3 H, CH_3), 2.92 (s, 1 H, OH), 3.02–3.06 (m, 1 H, CH), 3.42 (s, 3 H, OCH_3), 3.44–3.50 (dd, *J* = 9.16, 9.53 Hz, 1 H, CH), 3.68–3.73 (dd, *J* = 4.40, 9.53 Hz, 1 H, CH), 3.88 (s, 3 H, $=NOCH_3$), 4.11–4.14 (dd, *J* = 4.40, 4.77 Hz, 1 H, CH), 5.53–5.57 (dd, *J* = 2.20, 9.90 Hz, 1 H, =CH), 5.89–5.95 (ddd, *J* = 2.57, 5.13, 9.90 Hz, 1 H, =CH).

^{13}C NMR ($CDCl_3$): δ = –5.00 ($SiCH_3$), –4.48 ($SiCH_3$), 11.9 (CH_3), 18.0 (SiC), 25.9 (CH_3), 50.5 (CH), 60.7 (OCH_3), 61.5 ($=NOCH_3$), 67.8 (CH), 74.6 (CH), 77.5 (CH), 128 (=CH), 130 (=CH), 156 (C=N).

HRMS (FAB): *m*/*z* calcd for $C_{16}H_{31}NO_4Si$ + Na (M + Na)$^+$: 352.1920; found: 352.1919.

Catalytic Hydrogenation of 1-[(1*S,4*S**,5*R**,6*R**)-5-(*tert*-Butyldimethylsilyloxy)-4-hydroxy-6-methoxycyclohex-2-enyl]ethanone *O*-Methyl Oxime (13a) to 1-[(1*S**,2*R**,3*R**,4*S**)-3-(*tert*-Butyldimethylsilyloxy)-4-hydroxy-2-methoxycyclohexyl]ethanone *O*-Methyl Oxime (5a)**

To a solution of compound **13a** (55 mg, 0.17 mmol) in CH_2Cl_2 (10 mL) was added 10% Pd/C (18 mg, 17 μmol). The mixture was stirred for 2 h under H_2 atmosphere at r.t. The solution was filtered to remove the Pd/C, which was washed with CH_2Cl_2 (20 mL) and the combined filtrates were concentrated in vacuo to give white crystals of **5a**, yield: 48 mg (87%). The NMR data of **5a** thus obtained were identical to that of the above described **5a**.

1-[(1*S,4*S**,5*S**,6*R**)-5-(*tert*-Butyldimethylsilyloxy)-6-methoxy-4-(methoxymethoxy)cyclohex-2-enyl]ethanone *O*-Methyl Oxime (14)**

Compound **13a** (58 mg, 0.18 mmol) was dissolved in CH_2Cl_2 (4.0 mL) under argon atmosphere with ice cooling. DIPEA (0.74 mL, 4.4 mmol) was added and the solution was stirred for 15 min with ice cooling. MOMCl (0.26 mL, 3.4 mmol) was added and the solution was stirred for 24 h at r.t. The reaction was terminated by the addition of sat. aq NH_4Cl (2.0 mL) and sat. aq $NaHCO_3$ (2.0 mL). After 10 min of hydrolysis, the aqueous layer was extracted with CH_2Cl_2 (2 × 4.0 mL), the combined organic layers were dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 10:1) to give **14** as a colorless oil; yield: 61 mg (92%).

IR (film): 1631 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.09 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.91 [s, 9 H, $C(CH_3)_3$], 1.81 (s, 3 H, CH_3), 3.08–3.14 (dddd, *J* = 2.20, 3.11, 3.30, 9.16 Hz, 1 H, CH), 3.22–3.29 (dd, *J* = 9.34, 9.52 Hz, 1 H, CH), 3.40 (s, 6 H, 2 × OCH_3), 3.67–3.74 (dd, *J* = 7.69, 9.52 Hz, 1 H, CH), 3.87 (s, 3 H, $=NOCH_3$), 4.02–4.07 (dddd, *J* = 2.02, 2.20, 3.30, 7.69 Hz, 1 H, CH), 4.68–4.71 (d, *J* = 6.78 Hz, 1 H, CH), 4.80–4.82 (d, *J* = 6.78 Hz, 1 H, CH), 5.35–5.40 (ddd, *J* = 2.02, 2.20, 10.3 Hz, 1 H, =CH), 5.71–5.76 (ddd, *J* = 2.20, 2.75, 10.3 Hz, 1 H, =CH).

^{13}C NMR ($CDCl_3$): δ = –4.53 ($SiCH_3$), –4.26 ($SiCH_3$), 12.2 (CH_3), 18.1 (SiC), 26.0 (CH_3), 50.1 (CH), 55.4 (OCH_3), 60.7 (OCH_3), 61.4 ($=NOCH_3$), 76.7 (CH), 81.6 (CH), 81.7 (CH), 98.5 (OCH_2), 126 (=CH), 130 (=CH), 157 (C=N).

HRMS (FAB): *m*/*z* calcd for $C_{18}H_{35}NO_5Si$ + Na (M + Na)$^+$: 396.2182; found: 396.2196.

1-[(1*S,2*R**,3*S**,4*S**,5*S**,6*S**)-3-(*tert*-Butyldimethylsilyloxy)-5,6-dihydroxy-2-methoxy-4-(methoxymethoxy)cyclohexyl]ethanone *O*-Methyl Oxime (15a) and 1-[(1*S**,2*R**,3*S**,4*S**,5*R**,6*R**)-3-(*tert*-Butyldimethylsilyloxy)-5,6-dihydroxy-2-methoxy-4-(methoxymethoxy)cyclohexyl]ethanone *O*-Methyl Oxime (15b)**

AD-mix-β (1.3 g), OsO_4 (2.3 mg, 9.4 μmol), and $(DHQD)_2$-PHAL (66 mg, 84 μmol) were dissolved in a mixture of H_2O (5.0 mL) and *t*-BuOH (5.0 mL) and the solution was stirred for 15 min. To this solution were added $MeSO_2NH_2$ (89 mg, 0.94 mmol) and a solution of compound **14** (0.18 g, 0.47 mmol) in CH_2Cl_2 (10 mL), and the resulting solution was stirred for 2 weeks. Subsequently Na_2SO_3 (0.50 g, 0.41 mmol) was added and the solution was stirred for 1 h. The aqueous layer and the organic layer were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 1:1) to give **15a** as a colorless amorphous solid (0.12 g, 65%) and **15b** as white crystals (55 mg, 29%).

15a

IR (film): 1631, 3200 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$), 0.90 [s, 9 H, $C(CH_3)_3$], 1.92 (s, 3 H, CH_3), 2.58–2.61 (d, *J* = 7.88 Hz, 1 H, OH), 2.74–2.81 (dd, *J* = 10.6, 11.2 Hz, 1 H, CH), 2.75 (s, 1 H, OH), 3.01–3.08 (dd, *J* = 8.79, 11.0 Hz, 1 H, CH), 3.31–3.35 (dd, *J* = 2.75, 9.52 Hz, 1 H, CH), 3.35 (s, 3 H, OCH_3), 3.41 (s, 3 H, OCH_3), 3.68–3.75 (ddd, *J* = 2.75, 8.06, 11.0 Hz, 1 H, CH), 3.83–3.89 (dd, *J* = 8.97, 9.16 Hz, 1 H, CH), 3.88 (s, 3 H, $=NOCH_3$), 4.19–4.21 (m, 1 H, CH), 4.68–4.71 (d, *J* = 6.59 Hz, 1 H, CH), 4.76–4.80 (d, *J* = 6.59 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –4.38 ($SiCH_3$), –4.21 ($SiCH_3$), 13.5 (CH_3), 18.0 (SiC), 26.0 (CH_3), 49.6 (CH), 55.7 (OCH_3), 60.4 (OCH_3), 61.5 ($=NOCH_3$), 68.9 (CH), 72.1 (CH), 73.9 (CH), 80.0 (CH), 82.3 (CH), 98.0 (OCH_2), 156 (C=N).

HRMS (FAB): *m*/*z* calcd for $C_{18}H_{38}NO_7Si$ $(M + H)^+$: 408.2418; found: 408.2410.

15b

Mp 63–70 °C.

IR (film): 1624, 3450 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.91 [s, 9 H, $C(CH_3)_3$], 2.00 (s, 3 H, CH_3), 2.23–2.28 (dd, *J* = 1.83, 11.4 Hz, 1 H, CH), 3.36–3.40 (ddd, *J* = 1.47, 2.93, 8.80 Hz, 1 H, CH), 3.41 (s, 3 H, OCH_3), 3.44–3.50 (dd, *J* = 8.43, 8.80 Hz, 1 H, CH), 3.45 (s, 1 H, OH), 3.45 (s, 3 H, OCH_3), 3.54–3.60 (t, *J* = 8.80 Hz, 1 H, CH), 3.62–3.68 (dd, *J* = 8.43, 11.0 Hz, 1 H, CH), 3.88 (s, 3 H, $=NOCH_3$), 4.07–4.08 (dd, *J* = 2.20, 2.57 Hz, 1 H, CH), 4.44 (d, *J* = 1.47 Hz, 1 H, OH), 4.65–4.67 (d, *J* = 6.23 Hz, 1 H, CH), 4.73–4.75 (d, *J* = 6.60 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –4.28 ($SiCH_3$), –4.20 ($SiCH_3$), 15.6 (CH_3), 18.0 (SiC), 25.9 (CH_3), 49.3 (CH), 55.8 (OCH_3), 60.9 (OCH_3), 61.6 ($=NOCH_3$), 70.6 (CH), 72.7 (CH), 76.6 (CH), 81.4 (CH), 86.5 (CH), 99.3 (OCH_2), 158 (C=N).

HRMS (FAB): *m*/*z* calcd for $C_{18}H_{38}NO_7Si$ $(M + H)^+$: 408.2418; found: 408.2417.

1-[(1*R,2*R**,3*S**,4*S**,5*S**,6*S**)-3-(*tert*-Butyldimethylsilyloxy)-5-hydroxy-2-methoxy-6-(4-methoxybenzyloxy)-4-(methoxymethoxy)cyclohexyl]ethanone *O*-Methyl Oxime (16)**

Compound **15a** (0.70 g, 0.17 mmol) was dissolved in toluene (80 mL) and Bu_2SnO (0.50 g, 2.0 mmol) was added. The solution was heated at reflux for 3 h while the H_2O formed was removed by using the Dean–Stark apparatus. The solvent was removed by evaporation. To the residue was added CsF (0.30 g, 2.0 mmol). The resulting material was dried for 1 h in vacuo and dissolved in DMF (30 mL). At –41 °C, MPMCl (0.27 mL, 2.0 mmol) was added and the solution was stirred for 24 h. The solution was concentrated in vacuo and then dried for 24 h in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 3:1) to give **16** as a colorless oil; yield: 0.47 g (52%).

IR (film): 1613, 3477 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.10 (s, 3 H, $SiCH_3$), 0.89 [s, 9 H, $C(CH_3)_3$], 1.81 (s, 3 H, CH_3), 2.31 (s, 1 H, OH), 2.78–2.85 (t, *J* = 11.2 Hz, 1 H, CH), 3.06–3.13 (dd, *J* = 8.79, 11.0 Hz, 1 H, CH), 3.24–3.28 (dd, *J* = 2.57, 9.34 Hz, 1 H, CH), 3.35 (s, 3 H, OCH_3), 3.41 (s, 3 H, OCH_3), 3.49–3.53 (dd, *J* = 2.56, 11.2 Hz, 1 H, CH), 3.80 (s, 3 H, OCH_3), 3.86 (s, 3 H, $=NOCH_3$), 3.86–3.92 (dd, *J* = 8.97, 9.34 Hz, 1 H, CH), 4.22–4.24 (dd, *J* = 2.56, 2.56 Hz, 1 H, CH), 4.39–4.42 (d, *J* = 11.5 Hz, 1 H, CH), 4.53–4.56 (d, *J* = 11.5 Hz, 1 H, CH), 4.70–4.73 (d, *J* = 6.78 Hz, 1 H, CH), 4.76–4.79 (d, *J* = 6.78 Hz, 1 H, CH), 6.85–6.88 (d, *J* = 8.61 Hz, 2 H_{arom}), 7.19–7.22 (d, *J* = 8.61 Hz, 2 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = –4.41 ($SiCH_3$), –4.16 ($SiCH_3$), 15.3 (CH_3), 18.0 (SiC), 26.0 (CH_3), 48.4 (CH), 55.3 (OCH_3), 55.6 (OCH_3), 60.7 (OCH_3), 61.4 ($=NOCH_3$), 68.9 (CH), 71.4 (OCH_2), 73.8 (CH), 76.9 (CH), 79.2 (CH), 83.2 (CH), 98.0 (OCH_2), 114 (Ar), 130 (Ar), 130 (Ar), 156 (Ar), 159 (C=N).

HRMS (FAB): *m*/*z* calcd for $C_{26}H_{46}NO_8Si$ $(M + H)^+$: 528.2993, found: 528.2994.

1-[(1*S,2*R**,3*R**,4*S**)-3-(*tert*-Butyldimethylsilyloxy)-2-methoxy-4-(methoxymethoxy)cyclohexyl]ethanone *O*-Methyl Oxime (6b)**

Compound **5a** (1.3 g, 3.9 mmol) was dissolved in CH_2Cl_2 (120 mL) under argon atmosphere and ice cooling. DIPEA (17 mL, 98 mmol) was added and the solution was stirred for 15 min with ice cooling. MOMCl (5.9 mL, 78 mmol) was added and the solution was stirred for 24 h at r.t. The reaction was terminated by the addition of sat. aq NH_4Cl (60 mL) and sat. aq $NaHCO_3$ (60 mL). After 10 min of hydrolysis, the aqueous layer was extracted with CH_2Cl_2 (2 × 120 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 10:1) to give **6b** as a colorless oil; yield: 1.4 g (92%).

IR (film): 1613 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$), 0.91 [s, 9 H, $C(CH_3)_3$], 1.33–1.40 (m, 2 H, 2 × CH), 1.60–1.67 (m, 1 H, CH), 1.83 (s, 3 H, CH_3), 2.03–2.09 (m, 1 H, CH), 2.20–2.29 (ddd, *J* = 3.66, 10.6, 12.3 Hz, 1 H, CH), 3.04–3.10 (dd, *J* = 8.43, 10.6 Hz, 1 H, CH), 3.24–3.45 (m, 2 H, 2 × CH), 3.36 (s, 3 H, OCH_3), 3.38 (s, 3 H, OCH_3), 3.85 (s, 3 H, $=NOCH_3$), 4.63–4.66 (d, *J* = 6.78 Hz, 1 H, CH_2), 4.74–4.76 (d, *J* = 6.78 Hz, 1 H, CH_2).

^{13}C NMR ($CDCl_3$): δ = –4.33 ($SiCH_3$), –4.16 ($SiCH_3$), 12.3 (CH_3), 18.1 (SiC), 25.2 (CH_2), 26.0 (CH_3), 30.5 (CH_2), 48.7 (CH), 55.3 (OCH_3), 60.4 (OCH_3), 61.3 ($=NOCH_3$), 79.1 (CH), 80.7 (CH), 81.0 (CH), 97.7 (OCH_2), 158 (C=N).

HRMS (FAB): *m*/*z* calcd for $C_{18}H_{38}NO_5Si$ $(M + H)^+$: 376.2519; found: 376.2536.

1-[(1*S,2*R**,3*R**,4*S**)-3-(*tert*-Butyldimethylsilyloxy)-2-methoxy-4-(methoxymethoxy)cyclohexyl]ethanone (7c)**

Compound **6b** (1.0 g, 2.7 mmol) was dissolved in toluene (50 mL) under argon atmosphere and ice cooling. A 0.25 M solution of $TiCl_3$·3THF-DIBAL in toluene (14 mL, 3.5 mmol) was added. The solution was stirred for 20 min at r.t. A solution of $TiCl_3$·3THF-DIBAL in toluene (14 mL, 3.5 mmol) was added additionally and the solution was stirred for 20 min. Finally a solution of $TiCl_3$·3THF-DIBAL in toluene (14 mL, 3.5 mmol) was added again and the solution was stirred for 40 min at r.t. The reaction was terminated by the addition of sat. aq NaOAc (50 mL) and the pH of the solution was adjusted to 3.0 by aq citric acid. The solution was extracted with CH_2Cl_2 (4 × 75 mL), the combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 5:1) to give **7c** as a colorless oil; yield: 1.6 g (85%).

IR (film): 1717 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$), 0.91 [s, 9 H, $C(CH_3)_3$], 1.26–1.40 (m, 2 H, CH, CH), 1.67–1.73 (m, 1 H, CH), 2.06–2.12 (m, 1 H, CH), 2.22 (s, 3 H, CH_3), 2.53–2.62 (ddd, *J* = 3.66, 11.7, 13.6 Hz, 1 H, CH), 3.22–3.31 (m, 2 H, 2 × CH), 3.35–3.42 (dd, *J* = 6.23, 9.16 Hz, 1 H, CH), 3.35 (s, 3 H, OCH_3), 3.38 (s, 3 H, OCH_3), 4.62–4.65 (d, *J* = 6.97 Hz, 1 H, CH), 4.72–4.75 (d, *J* = 6.60 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –4.38 ($SiCH_3$), –4.13 ($SiCH_3$), 18.1 (SiC), 24.0 (CH_2), 26.0 (CH_3), 30.6 (CH_2), 31.2 (CH_3), 55.1 (CH), 55.3

(OCH_3), 61.2 (OCH_3), 79.1 (CH), 80.8 (CH), 84.3 (CH), 97.7 (OCH_2), 211 (C=O).

HRMS (FAB): *m*/*z* calcd for $C_{17}H_{35}O_5Si$ (M + H)$^+$: 347.2254; found: 347.2243.

1-[(1*S,2*R**,3*R**,4*S**)-3-(*tert*-Butyldimethylsilyloxy)-2-methoxy-4-(methoxymethoxy)cyclohexyl]ethyl Methanesulfonate (8b)**

Under ice cooling, compound **7c** (1.8 g, 5.1 mmol) was dissolved in a mixture of MeOH (16 mL) and CH_2Cl_2 (16 mL). $NaBH_4$ (0.58 g, 15 mmol) was added and the solution was stirred for 30 min with ice cooling. The solution was diluted with EtOAc (50 mL), washed with H_2O (50 mL), brine (50 mL), dried (Na_2SO_4), and concentrated to give the intermediate alcohol as a colorless oil. Under argon atmosphere and ice cooling, the crude colorless oil was dissolved in CH_2Cl_2 (32 mL). Et_3N (7.1 mL, 50mmol) and MsCl (2.9 mL, 37 mmol) were added and the resulting solution was stirred for 1.5 h. To the solution was added sat. aq $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (3 × 40 mL). The combined extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was subjected to silica gel chromatography (hexane–EtOAc, 3:1) to give crude **8b** (1.7 g) as white crystals.

***tert*-Butyl[(1*R**,2*R**,6*S**,*E*)-3-ethylidene-2-methoxy-6-(methoxymethoxy)cyclohexyloxy]dimethylsilane (9c) and *tert*-Butyl[(1*R**,2*R**,3*R**,6*S**)-2-methoxy-6-(methoxymethoxy)-3-vinylcyclohexyloxy]dimethylsilane (9d)**

Compound **8b** (1.7 g, crude) was dissolved in toluene (50 mL) and DBU (4.4 mL, 29 mmol) was added. The solution was heated at reflux for 48 h. To the solution was added sat. aq NH_4Cl (75 mL) and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were washed with brine (200 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was subjected to silica gel chromatography (hexane–EtOAc, 20:1) to give crude **9c**,**d** (0.74 g) as a colorless oil.

(2*S,3*R**,4*S**)-3-(*tert*-Butyldimethylsilyloxy)-2-methoxy-4-(methoxymethoxy)cyclohexanone (10c) and (1*S**,2*R**,3*R**,4*S**)-3-(*tert*-Butyldimethylsilyloxy)-2-methoxy-4-(methoxymethoxy)cyclohexanecarbaldehyde (10d)**

Crude compound **9c**,**d** (0.74 g) was dissolved in a mixture of CH_2Cl_2 (30 mL) and MeOH (6.0 mL). Et_3N (0.30 mL, 1% v/v) was added and the solution was stirred at –78 °C. O_3 was bubbled until the blue color persisted. O_2 was bubbled through the reaction solution 30 min at –78 °C. Me_2S (1.2 mL, 17 mmol) was added and the resulting solution was stirred for 30 min and then stirred further at r.t. for 2 h. The reaction was terminated by the addition of sat. aq $NaHCO_3$ (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 5:1) to give **10c** (0.39 g, 24% over 3 steps) and **10d** (0.16 g, crude) as colorless oils.

10c

IR (film): 1731 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.09 (s, 3 H, $SiCH_3$), 0.90 [s, 9 H, $C(CH_3)_3$], 1.55–1.65 (ddd, *J* = 5.49, 10.6, 12.8 Hz, 1 H, CH), 2.21–2.30 (m, 1 H, CH), 2.34–2.45 (m, 2 H, 2 × CH), 3.39 (s, 3 H, OCH_3), 3.46 (s, 3 H, OCH_3), 3.56–3.59 (dd, *J* = 0.73, 8.79 Hz, 1 H, CH), 3.70–3.76 (dd, *J* = 7.33, 8.79 Hz, 1 H, CH), 3.68–3.75 (m, 1 H, CH), 4.67–4.70 (d, *J* = 6.78 Hz, 1 H, CH), 4.81–4.83 (d, *J* = 6.78 Hz, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = –4.58 (2 × $SiCH_3$), 18.2 (SiC), 25.8 (CH_3), 27.1 (CH_2), 35.9 (CH_2), 55.4 (OCH_3), 59.5 (OCH_3), 78.2 (CH), 79.2 (CH), 88.4 (CH), 97.5 (OCH_2), 206 (C=O).

HRMS (FAB): *m*/*z* calcd for $C_{15}H_{30}O_5Si$ + Na (M + Na)$^+$: 341.1760; found: 341.1770.

(1*S,4*S**,5*R**,6*R**)-5-(*tert*-Butyldimethylsilyloxy)-6-methoxy-4-(methoxymethoxy)cyclohex-2-enol (17a)**

Compound **10c** (61 mg, 0.19 mmol) was dissolved in THF (1.0 mL) under argon atmosphere at –78 °C. A THF solution of LiHMDS (1.6 M, 0.28 mL, 0.45 mmol) was added and the solution was stirred for 1 h at –78 °C. TMSCl (36 μL, 0.29 mmol) was then added and the solution was stirred for 45 min at –78 °C and for 1 h at r.t., and concentrated in vacuo. The residue was dissolved in anhyd pentane (20 mL) and filtered through Celite. The filtrate was concentrated in vacuo to give the crude intermediate TMS enolate as a colorless oil. The crude colorless oil was dissolved in CH_2Cl_2 (2.0 mL) under argon atmosphere at –78 °C. A solution of PhSeCl (40 mg, 0.21 mmol) in CH_2Cl_2 (1.0 mL) was added and the solution was stirred for 45 min at –78 °C and for 15 min at r.t. The solution was concentrated in vacuo to give the crude intermediate phenylselenyl ketone as a yellow oil. At –78 °C, the crude yellow oil was dissolved in MeOH (2.0 mL) and $NaBH_4$ (14 mg, 0.38 mmol) were added and the solution was stirred for 30 min. The solution was diluted with EtOAc (59 mL), the organic layer was washed with H_2O (50 mL) and brine (50 mL), dried (Na_2SO_4) and concentrated in vacuo to give the crude intermediate phenylselenyl alcohol as a yellow oil. The crude yellow oil was dissolved in THF (3.3 mL) under argon atmosphere and ice cooling. $NaHCO_3$ (49 mg, 0.58 mmol) and 30% H_2O_2 (47 μL, 0.49 mmol) were successively added and the solution was stirred for 15 min at the same temperature, then for 2 h at r.t. H_2O (30 mL) was added and the mixture was extracted with Et_2O (3 × 40 mL). The combined organic layers were washed with brine (60 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 5:1) to give **17a** as a colorless oil (31 mg, 51% over 4 steps).

IR (film): 3246 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.10 (s, 3 H, $SiCH_3$), 0.14 (s, 3 H, $SiCH_3$), 0.92 [s, 9 H, $C(CH_3)_3$], 2.35–2.37 (d, *J* = 5.13 Hz, 1 H, OH), 3.12–3.17 (dd, *J* = 6.96, 9.16 Hz, 1 H, CH), 3.40 (s, 3 H, OCH_3), 3.59 (s, 3 H, OCH_3), 3.72–3.77 (dd, *J* = 6.60, 9.16 Hz, 1 H, CH), 4.01–4.04 (dd, *J* = 1.83, 6.60 Hz, 1 H, –CH), 4.15–4.22 (m, 1 H, CH), 4.68–4.70 (d, *J* = 6.96 Hz, 1 H, CH), 4.77–4.79 (d, *J* = 6.97 Hz, 1 H, CH), 5.66–5.71 (dd, *J* = 1.47, 11.0 Hz, 1 H, =CH), 5.71–5.75 (dd, *J* = 1.47, 11.7 Hz, 1 H, =CH).

^{13}C NMR ($CDCl_3$): δ = –4.64 ($SiCH_3$), –4.49 ($SiCH_3$), 18.0 (SiC), 25.9 (CH_3), 55.5 (OCH_3), 61.3 (OCH_3), 71.3 (CH), 75.0 (CH), 80.6 (CH), 85.6 (CH), 98.0 (OCH_2), 128 (=CH), 129 (=CH).

HRMS (FAB); *m*/*z* calcd for $C_{15}H_{30}O_5Si$ + Na (M + Na)$^+$: 341.1760; found: 341.1767.

***tert*-Butyl[(1*R**,2*S**,5*S**,6*R**)-6-methoxy-5-(4-methoxybenzyloxy)-2-(methoxymethoxy)cyclohex-3-enyloxy]dimethylsilane (18)**

Under argon atmosphere and ice cooling, compound **17a** (55 mg, 0.17 mmol) was dissolved in THF (3.4 mL). NaH (42 mg, 1.0 mmol) and molecular sieves 4 Å (0.10 g) were added and the mixture was warmed to r.t. and stirred for 2 h at the same temperature. The solution was cooled to 0 °C and TBAI (6.4 mg, 17 μmol) and MPMCl (26 μL, 0.19 mmol) were added. The solution was warmed to r.t. and stirred for 2 d at the same temperature. To the solution wad added H_2O (5mL) and extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine (15 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 20:1) to give **18** as a colorless oil; yield: 30 mg (40%).

IR (film): 1613 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.12 (s, 3 H, $SiCH_3$), 0.92 [s, 9 H, $C(CH_3)_3$], 3.19–3.25 (dd, *J* = 7.69, 10.3Hz, 1 H, CH), 3.38 (s, 3 H, OCH_3), 3.58–3.64 (dd, *J* = 7.69, 10.3 Hz, 1 H, CH), 3.60 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.96–4.05 (m, 2 H, 2 × CH), 4.56–4.60 (d, *J* = 11.2 Hz, 1 H, CH), 4.62–4.65 (d, *J* = 11.0 Hz, 1 H, CH), 4.66–4.69 (d, *J* = 6.78 Hz, 1 H, CH), 4.77–4.80 (d, *J* = 6.78 Hz, 1 H, CH), 5.60–5.64 (d, *J* = 10.4 Hz, 1 H, =CH), 5.66–5.70 (d, *J* = 10.4 Hz, 1 H, =CH), 6.86–6.89 (dd, *J* = 1.83, 8.61 Hz, 2 H_{arom}), 7.27–7.30 (dd, *J* = 2.01, 8.61 Hz, 2 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = –4.58 ($SiCH_3$), –4.28 ($SiCH_3$), 18.2 (SiC), 26.0 (CH_3), 55.3 (OCH_3), 55.5 (OCH_3), 61.3 (OCH_3), 71.9 (OCH_2), 75.9 (CH), 80.4 (CH), 81.6 (CH), 85.2 (CH), 98.5 (OCH_2), 114 (Ar), 127 (=CH), 129 (=CH), 129 (Ar), 131 (Ar), 159 (Ar).

HRMS (FAB): *m*/*z* calcd for $C_{23}H_{38}O_6Si$ + Na $(M + Na)^+$: 461.2335; found: 461.2332.

(1*S,2*R**,3*S**,4*S**,5*R**,6*S**)-4-(*tert*-Butyldimethylsilyloxy)-5-methoxy-6-(4-methoxybenzyloxy)-3-(methoxymethoxy)cyclohexane-1,2-diol (19)**

AD-mix-β (0.10 g), OsO_4 (1.0 mg, 4.3 μmol), and $(DHQD)_2$-PHAL (22 mg, 28 μmol) were dissolved in a mixture of H_2O (1.5 mL) and *t*-BuOH (1.5 mL) and the solution was stirred for 15 min. To this solution, $MeSO_2NH_2$ (14 mg, 0.14 mmol) and a solution of compound **18** (31 mg, 71 μmol) in CH_2Cl_2 (3.0 mL) were added and the resulting solution was stirred for 2 weeks. Subsequently, Na_2SO_3 (76 mg, 0.60 mmol) was added and the solution was stirred for 1 h. The aqueous layer and the organic layer were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 3 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 1:1) to give **19** as a colorless oil; yield: 20 mg (59%).

IR (film): 3450 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.09 (s, 3 H, $SiCH_3$), 0.14 (s, 3 H, $SiCH_3$), 0.91 [s, 9 H, $C(CH_3)_3$], 2.35–2.36 (d, *J* = 4.03 Hz, 1 H, OH), 2.45 (s, 1 H, OH), 2.92–2.98 (dd, *J* = 9.16, 9.34 Hz, 1 H, CH), 3.29–3.33 (dd, *J* = 2.93, 9.52 Hz, 1 H, CH), 3.40 (s, 3 H, OCH_3), 3.45–3.51 (td, *J* = 3.30, 9.71 Hz, 1 H, CH), 3.60 (s, 3 H, OCH_3), 3.62–3.69 (t, *J* = 9.52 Hz, 1 H, CH), 3.80 (s, 3 H, OCH_3), 3.84–3.90 (t, *J* = 9.16 Hz, 1 H, CH), 4.18 (br s, 1 H, CH), 4.63–4.67 (d, *J* = 10.8 Hz, 1 H, CH), 4.68–4.70 (d, *J* = 6.78 Hz, 1 H, CH), 4.77–4.79 (d, *J* = 6.78 Hz, 1 H, CH), 4.86–4.90 (d, *J* = 11.0 Hz, 1 H, CH), 6.88–6.91 (dd, *J* = 2.02, 8.61 Hz, 2 H_{arom}), 7.29–7.33 (dd, *J* = 2.93, 8.61 Hz, 2 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = –4.36 ($SiCH_3$), –4.26 ($SiCH_3$), 18.1 (SiC), 26.0 (CH_3), 55.3 (OCH_3), 55.7 (OCH_3), 61.5 (OCH_3), 71.1 (CH), 71.5 (CH), 73.2 (CH), 75.0 (OCH_2), 79.9 (CH), 81.3 (CH), 85.6 (CH), 98.0 (OCH_2), 114 (Ar), 130 (Ar), 131 (Ar), 159 (Ar).

HRMS (FAB): *m*/*z* calcd for $C_{23}H_{40}O_8Si$ + Na $(M + Na)^+$: 495.2390; found: 495.2428.

(1*R,2*S**,3*S**,4*R**,5*S**,6*R**)-3-(*tert*-Butyldimethylsilyloxy)-6-hydroxy-4-methoxy-5-(4-methoxybenzyloxy)-2-(methoxymethoxy)cyclohexyl Acetate (20)**

Compound **19** (20 mg, 42 μmol) was dissolved in toluene (12 mL) and Bu_2SnO (13 mg, 51 μmol) was added. The solution was heated at reflux for 3 h while the water formed was removed by using the Dean–Stark apparatus. The solvent was then removed by evaporation. The residue was dissolved in CH_2Cl_2 (2.0 mL) under argon atmosphere and AcCl (4.6 μL, 63 μmol) was added at –41 °C, and the solution was stirred for 24 h. The solution was concentrated in vacuo and then dried for 24 h in vacuo. The residue was purified by silica gel chromatography (hexane–EtOAc, 3:1) to give **20** as a yellow oil; yield: 8.6 mg (39%).

IR (film): 1746, 3391 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.08 (s, 3 H, $SiCH_3$), 0.14 (s, 3 H, $SiCH_3$), 0.91 [s, 9 H, $C(CH_3)_3$], 2.06 (s, 3 H, CH_3), 2.33 (s, 1 H, OH), 2.98–3.04 (dd, *J* = 9.16, 9.34 Hz, 1 H, CH), 3.35–3.39 (dd, *J* = 2.93, 9.16 Hz, 1 H, CH), 3.38 (s, 3 H, OCH_3), 3.57 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 3.82–3.87 (dd, *J* = 7.51, 9.16 Hz, 1 H, CH), 3.87–3.90 (dd, *J* = 7.88, 9.52 Hz, 1 H, CH), 4.18–4.20 (dd, *J* = 2.56, 2.75 Hz, 1 H, CH), 4.60–4.63 (d, *J* = 11.0 Hz, 1 H, CH), 4.67–4.69 (d, *J* = 6.78 Hz, 1 H, CH), 4.73–4.77 (d, *J* = 10.8 Hz, 1 H, CH), 4.76–4.78 (d, *J* = 6.59 Hz, 1 H, CH), 4.85–4.90 (dd, *J* = 2.75, 10.4 Hz, 1 H, CH), 6.85–6.88 (dd, *J* = 2.75, 8.79 Hz, 2 H_{arom}), 7.21–7.24 (dd, *J* = 2.75, 8.61 Hz, 2 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = –4.35 ($SiCH_3$), –4.28 ($SiCH_3$), 18.1 (SiC), 21.1(CH_3), 25.9 (CH_3), 55.3 (OCH_3), 55.8 (OCH_3), 61.7 (OCH_3), 70.1 (CH), 72.9 (CH), 72.9 (CH), 75.0 (OCH_2), 79.2 (CH), 79.9 (CH), 85.3 (CH), 98.0 (OCH_2), 114 (Ar), 129 (Ar), 131 (Ar), 159 (Ar), 170 (OC=O).

HRMS (FAB): *m*/*z* calcd for $C_{25}H_{42}O_9Si$ + Na $(M + Na)^+$: 537.2496; found: 537.2527.

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