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# Stereoselective synthesis of a novel natural carbasugar and analogues from hydroxymethylated cycloalkenone scaffolds

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ABSTRACT

Novel carbasugars from *Streptomyces lincolnensis* have been synthesized from an enantiomerically pure 5-hydroxymethyl-cyclohex-2-enone scaffold via a stereoselective approach. Several structural analogues of those carbasugars have also been synthesized in a stereoselective manner from hydroxymethylated cycloalkenone derivatives.

## 1. Introduction

Nature has been a great source of therapeutic agents for many decades and continues to be a rich supplier of novel chemotypes and pharmacophores. With only 5–15% of the approximately 250,000 species of higher plants thoroughly investigated,[1] and the potential of the marine environment scarcely tapped, these areas remain an essential resource for the discovery of new bioactive compounds. Less than 1% of bacterial and 5% of fungal species have been explored, and the probability of finding novel microbial sources, predominantly in extreme environments, seems limitless.[2] It is thus obvious that Nature can offer novel multifunctional chemical scaffolds for synthetic manipulation by combinatorial approaches (chemical and biochemical), leading to agents that have been optimized on the basis of their pharmacological activities.[3] The proven natural product guided drug discovery programme, coupled with the enduring threat to biodiversity through the destruction of terrestrial and marine ecosystems and the current low number of new chemical entities in pharmaceutical industry pipelines, provides undeniable argument in favor of expanded multidisciplinary and international collaboration in the exploration of nature as a source of new lead molecules for the development of drugs and other precious medicinally active ingredients.

*Streptomyces lincolnensis* is well known to produce antibiotics and other secondary metabolites under normal cultivation conditions.[4] Recently novel carbasugars (hydroxy skipped at the 4-position; **1** and **2**; Fig. 1) have although isolated from *S. lincolnensis*.[5] Simple carbasugars are usually not abundant in Nature, however they are often present as a subunit of natural products exhibiting a wide array of biological activities.[6] In our recent work in the area of SOS (scaffold oriented synthesis), we have identified hydroxymethylated cycloalkenone derivatives as potential multifunctional scaffolds, which can be successfully applied for the asymmetric synthesis of natural products[7] and designed cyclitols.[8] Herein we report the synthesis of two carbasugars isolated from *S. lincolnensis* **1** and **2** and a few of its structural analogues. We have also synthesized novel carbasugars based on a cyclopentane framework from 5-hydroxymethyl-2-cyclopentenone and some cyclopropane based carbasugars in a stereoselective manner. The main highlight of our synthetic strategy was the stereoselective reduction of the carbonyl functionality of the core hydroxymethylated cycloalkenone scaffolds, substrate directed asymmetric epoxidation/cyclopropanation, and stereoselctive dihydroxylation (Scheme 1).

## 2. Results and discussion

### 2.1. Synthesis of natural carbasugars 1 and 2, their analogues and related cyclopropane carbasugars from 5-hydroxymethylated cyclohex-2-enone

The parent scaffold was synthesized by adopting a known literature procedure.[9] However, we found that the procedure was ineffective in terms of chemical yield. Hence we decided to adopt a new strategy for synthesizing both the scaffolds (cyclopentane and cyclohexane based) from the same starting material. We started by using 2-allyl-1,3-propane diol. Selective monoprotection with NaH and TBDPS-Cl afforded the mono TBDPS protected alcohol **7** in 90% yield. Enzymatic kinetic resolution (EKR) of **7** with lipase PS-D and vinyl acetate as acyl donor afforded (*R*)-acetate **8** and (*S*)-alcohol **9** with excellent enantioselectivity. Compound **9** was oxidized under Swern's conditions[10] to afford aldehyde **10** in 92% yield. Vinylmagnesium bromide addition onto aldehyde **10** at −78 °C afforded alcohol **11** in 78% yield as a diastereomeric mixture. The alcohol functionality in **11** was oxidized to compound **12** in 88% yield. The ring closing metathesis (RCM) reaction of compound **12** with G-I catalyst[11] in DCM as the solvent afforded the

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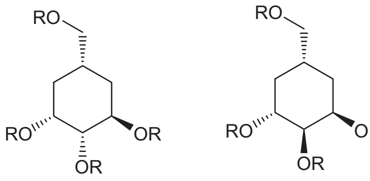


**1** R = H **2**

**Figure 1.** Novel carbasugars from *S. lincolnensis*.

5-hydroxymethyl-2-cyclopentenone scaffold **13** in 76% yield. The other enantiomer of compound **13** can easily be synthesized by applying the same procedure starting from acetate **8**.

For the synthesis of 5-hydroxymethyl-2-cyclohexenone, we started with(*R*)-acetate **8**, which was transformed into the corresponding mesylate **14** in 93% yield by deacetylation followed by treatment with methanesulfonyl chloride (MsCl) and triethyl amine. Treatment of compound **14** with NaCN in refluxing DMSO as a solvent afforded compound **15** in 90% yield. Compound **15** on DIBAL-H reduction at −78 °C afforded the aldehyde **16** in 82% yield.[12] Vinylmagnesium bromide addition onto aldehyde **16** yielded compound **17** in 80% yield. After Swern oxidation of compound **17**, respective ketone **18** was obtained in 90% yield. The RCM with compound **18** with the G-I catalyst afforded the parent cyclohexane based scaffold **19** in 90% yield. The other enantiomer of **19** can also be synthesized by adopting a similar strategy starting from alcohol **9** (Scheme 2).

After the successful synthesis of both scaffolds **13** and **19** (in both enantiomeric forms) we turned our attention toward the synthesis of natural carbasugars **1** and **2** and their analogues. The synthetic route for the cyclohexane based carbasugars **1** and **2** has started from compound **19**. Reduction of the carbonyl functionality with an $NaBH_4{\cdot}CeCl_3$ reagent system[13] afforded compound **20** as a single diastereomer in 82% yield. Dihydroxylation of **20** with $OsO_4$ followed by deprotection with TBAF/THF at room temperature afforded the carbasugar **2** in 60% overall yield (in two steps). A similar type of stereoselective hydroxylation has already been demonstrated in our earlier work. The substrate directed epoxidation[14] of compound **20**, with *m*CPBA (*meta*-chloro per-benzoic acid) afforded epoxide **21** as the major diastereomer (20:1 in favor of **21**) in 75% yield. The acid catalyzed epoxide ring opening of **21** furnished compound **22** as a single product in 65% yield. Deprotection of the TBDPS group with TBAF–THF afforded carbasugar **1** in 83% yield (overall yield = 33% from **19**; Scheme 3).

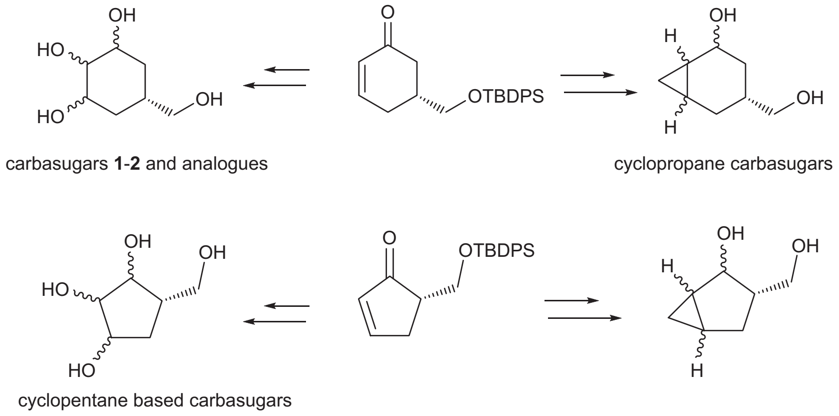
Compound **20**, when treated with a Zn–Cu couple[15] and $CH_2Br_2$, afforded the cyclopropane derivative **23** as a single diastereomer in 68% yield. Deprotection of the TBDPS group was achieved as before to afford the cyclopropane based carbasugar **4** in 80% yield (overall yield = 44% from **19**; Scheme 3).

Compound **19** upon reduction with L-selectride[16] at −78 °C afforded compound **24** as a single product in 72% yield. The substrate directed cyclopropanation afforded compound **25** in 80% yield as a single diastereomer. Deprotection of the TBDPS group with TBAF·THF afforded cyclopropane carbasugar **5** in 88% yield (overall yield = 50% from **19**). The substrate directed epoxidation of **24** with *m*CPBA afforded epoxide **26** as a single diastereomer in 78% yield. The ring opening of epoxide[17] **26** was achieved with 0.2 M $H_2SO_4$ to afford triol **27** (71% yield), which upon deprotection of the TBDPS group afforded carbasugar **3** in 84% yield (overall yield = 33% from **19**; Scheme 3).

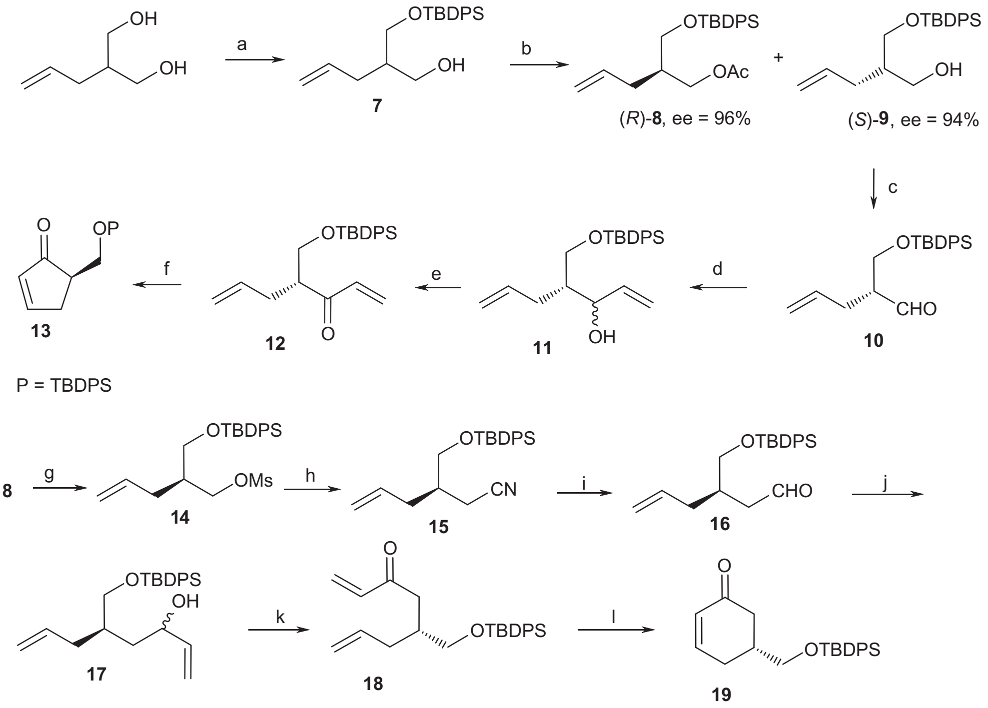
For the synthesis of carbasugar analogue **6**, the secondary hydroxyl group in **20** was protected as its TBS ether by treatment of TBS·Cl in the presence of imidazole to afford compound **28** in 82% yield. Epoxidation of compound **28** was achieved with *m*CPBA to yield the epoxide **29** as the sole product in 79% yield. The reaction outcome in favor of the formation of **29**, was attributed mainly due to the steric parameters imposed by the TBDPS and TBS groups. The selective deprotection of the TBS group was achieved with PPTS/MeOH to afford the epoxy alcohol **30** in 76% yield. The epoxide opening of compound **30** was achieved by applying similar condition as described earlier to afford triol **31** in 70% yield. Finally removal of the TBDPS group afforded the carbasugar **6** in 87% yield (overall yield = 25% from **19**; Scheme 3).

### 2.2. Synthesis of carbasugar analogues and related cyclopropane carbasugars from 5-hydroxymethylated cyclopent-2-enone

For the synthesis of carbasugars based on the cyclopentane scaffolds, we started from the parent 5-hydroxymethyl-2-cyclopentenone **13**. Reduction with $NaBH_4{\cdot}CeCl_3$ afforded compounds **32** and **33** in equimolar ratio and they could be separated by chromatography. At this point we are unsure about the absolute configurations of **32** and **33**, hence both compounds were subjected to next round of reaction. The substrate directed epoxidation of *syn*-diastereomer **32** with *m*CPBA afforded two epoxides **34** (substrate directed) and **35** (directed by steric factors) in a 4:1 ratio. The epoxidation of **33** under similar conditions afforded epoxide **36** as a single product. The formation of the single epoxide diastereomer **36** from **35** can be attributed to the combined effort of the directed reaction as well as the steric effects caused by the bulky OTBDPS groups on the cyclopentane ring that indirectly correlates to the fact that **33** is an *anti*-diastereomer. Epoxides **34** and **35**



**Scheme 1.** 5-Hydroxymethyl-cycloalkenones as starting materials for carbasugar synthesis.



**Scheme 2.** Reagents and conditions: (a) NaH, TBDPS-Cl, THF, rt, 90%; (b) Lipase PS-D; vinyl acetate, DIPE; (c) $(COCl)_2$, $Me_2SO$, $Et_3N$, −78 °C, 92%; (d) $CH_2{=}CHMgBr$, THF, −78 °C, 78%; (e) same as c, 88%; (f) G-I, DCM, rt, 90%; (g) (i) $K_2CO_3$, MeOH, rt, (ii) $Et_3N$, Ms-Cl, DCM, rt, 93%; (h) NaCN, DMSO, reflux, 90%; (i) DIBAL-H, −78 °C, 82%; (j) same as conditions d; 80%; (k) same as conditions c, 90%; (l) same as conditions f; 78%.

were treated separately with 0.2 M $H_2SO_4$ in dioxane to afford the epoxide cleaved triol products **37** and **38**. Cleavage of the OTBDPS groups under standard conditions afforded the cyclopentane based carbasugars **40** and **41**. A similar reaction sequence was performed with epoxide **36** to give carbasugar **42** (overall yield = 27% from **13**, Scheme 4).

Compound **32** was subjected to a cyclopropanation reaction under standard Simmon–Smith conditions to afford cyclopropane derivatives **43** and **44** in a 6:1 ratio, which could be separated by chromatography. Deprotection of the OTBDPS group with TBAF·THF afforded cyclopropane based carbasugars **45** and **46**. A similar reaction sequence was performed with **33** to afford cyclopropane based carbasugars **48** (Scheme 4, overall yield = 57% from **13**).

## 3. Conclusion

In conclusion, we have described stereoselective synthetic strategies for the synthesis of a few natural cyclohexane based carbasugars **1** and **2** isolated from *Streptomyces lincolnensis*. The synthetic strategy described herein is a unified and general one, and was successfully applied to the synthesis of several carbasugar analogues based on cyclohexane and cyclopentane scaffolds.

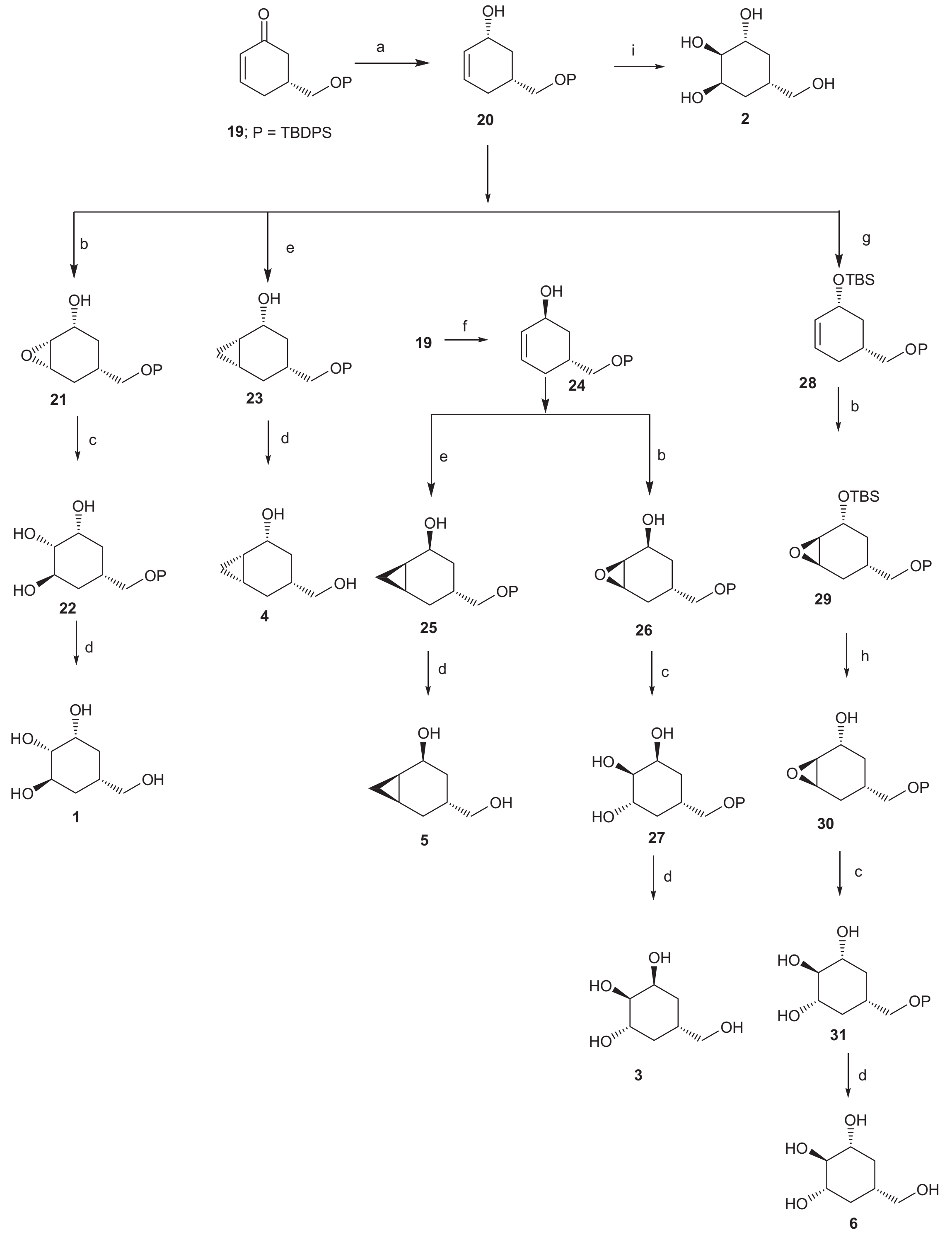
## 4. Experimental

### 4.1. General

Unless otherwise stated, materials were obtained from commercial suppliers and used without further purification. THF and diethylether were distilled from sodium benzophenone ketyl. Dichloromethane (DCM), dimethylformamide (DMF) and dimethylsulfoxide (DMSO) were distilled from calcium hydride. Diisopropyl ether (DIPE) was refluxed over $P_2O_5$ and distilled prior to use. Lipase PS-D (*Burkholderia cepacia*, immobilized on diatomite), was purchased from Amano, Japan. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates (Merck) with UV light, ethanolic anisaldehyde and phosphomolybdic acid/heat as developing agents. Silica gel 100–200 mesh was used for column chromatography. Concentrations were performed on a Buchi rotary evaporator at a temperature below 40 °C. Yields refer to chromatographically and spectroscopically homogeneous materials unless otherwise stated. NMR spectra were recorded on Bruker 200 and 400 MHz spectrometers at 25 °C in $CDCl_3$ using TMS as the internal standard. Chemical shifts are shown in $\delta$. $^{13}C$ NMR spectra were recorded with a complete proton decoupling environment. The chemical shift value is listed as $\delta_H$ and $\delta_C$ for $^1H$ and $^{13}C$, respectively. For NMR spectra in deuterated solvents, the solvent peak was used as the reference ($CDCl_3$: $\delta = 7.26$ for $^1H$, 76.93 for $^{13}C$). Optical rotations were measured on a JASCO P-1020 digital polarimeter. Mass spectroscopic analysis was performed at IACS-Kolkata. Chiral HPLC was performed using Chiral OJ-H and OD-H column (0.46 × 25 cm, Daicel industries) with a Shimadzu Prominence LC-20AT chromatograph coupled with a UV–Vis detector (254 nm). Eluting solvent used had different ratios of hexane and 2-propanol.

#### 4.1.1. 2-(*tert*-Butyldiphenylsilanyloxymethyl)-pent-4-en-1-ol 7

At first, NaH (60% dispersion in mineral oil, 0.45 g, 11.2 mmol) was taken in 50 mL of dry THF. Then, 2-allyl-1,3-propane diol (1.3 g, 11.2 mmol) was added to it portionwise at 0 °C. The reaction mixture was stirred at 0 °C for 1 h. Next, TBDPS·Cl (2.9 mL, 11.2 mmol) was added to the reaction mixture. The reaction mixture was stirred overnight at room temperature. Water was added carefully to the reaction mixture to quench any excess NaH. The reaction mixture was then extracted with a large volume of diethyl ether. The organic solution was washed with water and brine. Evaporation and purification by means of silica gel chromatogra-

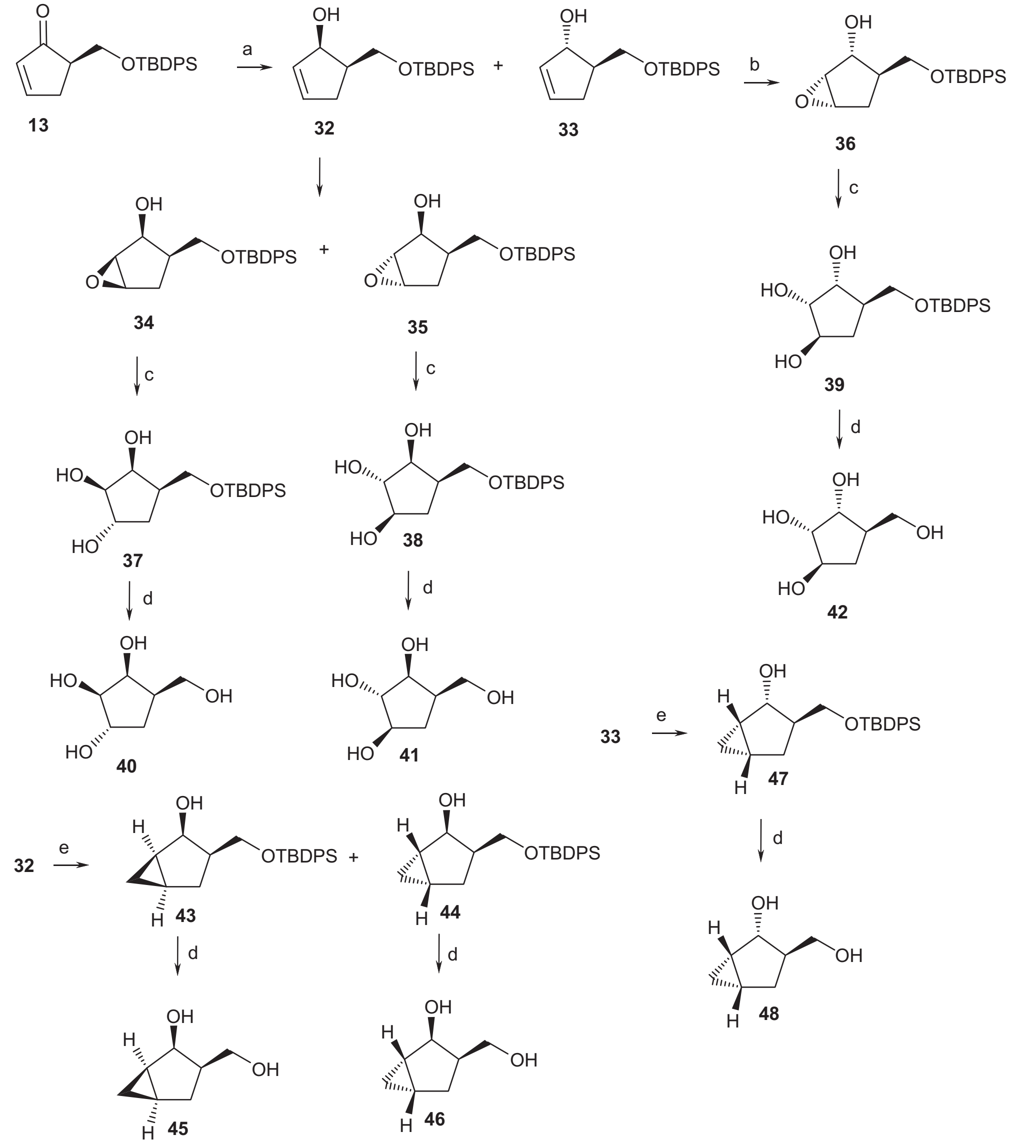


**Scheme 3.** Stereoselective synthesis of cyclohexane based carbasugars; Reagents and conditions: (a) $CeCl_3{\cdot}7H_2O$, $NaBH_4$, MeOH, 0 °C to rt, 3 h; (b) *m*CPBA, $NaHCO_3$, DCM, 0 °C to rt, 2 h; (c) 0.2 M $H_2SO_4$/dioxan (1:1), rt, 6 h; (d) TBAF, THF, 0 °C, rt, 5 h; (e) $CH_2Br_2$, Zn–Cu couple, diethylether, 30 h, reflux; (f) L-selectride, −78 °C, THF, 2 h; (g) TBS-Cl, imidazole, DCM, rt, 6 h; (h) PPTS, MeOH, rt, 4 h; (i) AD mix-β, $MeSo_2NH_2$, TBAF, THF.

phy (50:1, petroleum ether/EtOAc) afforded the compound **7** in 90% yield. $\delta_H$ (200 MHz, $CDCl_3$): 7.75–7.71 (m, 4H), 7.45–7.43 (m, 6H), 5.86–5.65 (m, 1H), 5.9–4.99 (m, 2H), 3.87–3.67 (m,4H), 3.01 (broad s,1H), 2.15–2.08 (t, 2H, *J* = 6.8 Hz), 1.96–1.91 (m, 1H), 1.12 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 136.4, 135.6, 133.2, 129.9, 127.8, 116.4, 66.1, 65.0, 42.3, 32.4, 26.9, 19.3.

#### 4.1.2. (*R*)-Acetic acid 2-diphenylsilanyloxymethyl-pent-4-enyl ester 8

Compound **7** (2.7 g, 7.3 mmol) was taken in 50 mL of dry anhydrous diisopropyl ether (DIPE) on 4 Å molecular sieves. Then lipase-AK enzyme (1 g) was added to it followed by the addition of vinyl acetate (1.4 mL, 15 mmol) to the reaction mixture at



**Scheme 4.** Reagents and conditions: (a) $CeCl_3{\cdot}7H_2O$, $NaBH_4$, MeOH, 0 °C to rt, 3 h; (b) *m*CPBA, $NaHCO_3$, DCM, 0 °C to rt, 19 h; (c) 0.2 M $H_2SO_4$/dioxane (1:1); rt, 6 h; (d) TBAF, THF, rt; (e) $CH_2Br_2$, Zn–Cu couple, diethylether, 30 h, reflux.

25 °C. The reaction mixture was stirred at 25 °C for 3 h. The reaction mixture was then filtered on a Celite pad. Evaporation and purification by means of silica gel chromatography (20:1, petroleum ether/EtOAc) afforded acetate **8** (1.34 gm) and alcohol **9** (1.264 g) in 95% yield. $\delta_H$ (200 MHz, $CDCl_3$): 7.68–7.64 (m, 4H), 7.41–7.36 (m, 6H), 5.84–5.64 (m, 1H), 5.08–4.99 (m, 2H), 4.4 (d, *J* = 6.0 Hz, 2H), 3.66–3.63 (m, 2H), 2.24–2.08 (m, 2H), 2.08 (s, 3H), 2.0–1.92 (m, 1H), 1.06 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 171.1, 135.9, 135.6, 133.6, 129.6, 127.6, 116.7, 64.2, 62.9, 40.1, 26.8, 20.9, 19.3. $[\alpha]_D^{28} = +12.4$ (*c* 1.0, $CHCl_3$).

### 4.1.3. (*R*)-2-Diphenylsilanyloxymethyl-pent-4-enal 10

Oxalyl chloride (0.47 mL, 5.4 mmol) was taken in anhydrous DCM (25 mL). Then DMSO (0.8 mL, 10.7 mmol) was added to the solution and kept at −78 °C. After 15 min, alcohol **9** (1.264 g, 3.6 mmol) was added, and the solution was stirred at the same temperature for a further 45 min. After this time $Et_3N$ (3 mL, 21.4 mmol) was added slowly to the reaction mixture at the same temperature. The reaction mixture was allowed to return to room temperature. Water was then added to the solution, and the mixture was extracted with DCM. The organic extract was washed with water, $NaHCO_3$ solution, and brine. The organic layer was dried ($MgSO_4$) and evaporated. Purification by silica gel chromatography afforded aldehyde **10** in 92% yield. $\delta_H$ (200 MHz, $CDCl_3$): 9.77–9.75 (d, 1H, *J* = 1.4 Hz), 7.66–7.62 (m, 4H), 7.45–7.36 (m, 6H), 5.81–5.61 (m, 1H), 5.23–5.0 (m, 2H), 3.99–3.83 (m, 2H), 2.54–2.44 (m, 2H), 2.44–2.23 (m, 1H), 1.07 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 203.7, 135.6, 134.9, 133.1, 129.9, 127.8, 117.2, 62.0, 53.6, 29.6, 26.8, 19.3. $[\alpha]_D^{28} = +18.45$ (*c* 1.0, $CHCl_3$).

### 4.1.4. 4-Diphenylsilanyloxymethyl-hepta-1,6-dien-3-ol 11

Aldehyde **10** (0.6 g, 1.7 mmol) was taken in 10 mL of dry THF. A freshly prepared solution of vinyl magnesium bromide (3.8 mmol) in dry THF was then added to it at −78 °C. The reaction mixture was stirred for a further 2 h at room temperature, after which a saturated $NH_4Cl$ solution was added to it. The solution was extracted with diethyl ether, and the organic layer was washed with water and brine. The organic layer was dried ($MgSO_4$) and evaporated, purification by silica gel chromatography (20:1, petroleum ether/EtOAc) afforded alcohol **11** in 78% yield. $\delta_H$ (200 MHz, $CDCl_3$, mixture of diastereomers): 7.72–7.67 (m, 4H), 7.49–7.38 (m, 6H), 5.96–5.84 (m, 1H), 5.83–5.64 (m, 1H), 5.42–5.33 (m, 1H), 5.29–5.20 (m, 1H), 5.05–4.93 (m, 2H), 4.84–4.78 (m, 1H), 4.46–4.42 (m, 0.5H), 4.38–4.31 (m, 0.5H), 3.97–3.91 (m, 0.5H), 3.76–3.63 (m, 2H), 3.51–3.41 (m, 1H), 2.32–1.67 (m, 3H), 1.08 (s, 9H). $\delta_C$ (50 MHz, CDCl$_{3,}$ mixture of diastereomer): 139.9, 138.4, 136.7, 136.5, 135.6, 135.4, 132.7, 129.9, 127.8, 116.6, 116.4, 115.5, 75.4, 74.7, 65.3, 64.8, 44.7, 32.6, 30.4, 26.9, 19.1.

### 4.1.5. (*R*)-4-Diphenylsilanyloxymethyl-hepta-1,6-dien-3-one 12

Oxalyl chloride (0.16 mL, 1.8 mmol) was taken in anhydrous DCM (10 mL). Then DMSO (0.3 mL, 3.6 mmol) was added to the solution and kept at −78 °C. After 15 min, alcohol **11** (0.45 g, 1.183 mmol) was added to it, and the solution was stirred at the same temperature for a further 45 min. After this time, Et$_3$N (1 mL, 7.1 mmol) was added slowly to the reaction mixture at the same temperature. The reaction mixture was allowed to return to room temperature. Water was then added to the solution, and the mixture was extracted with DCM. The organic extract was washed with water, NaHCO$_3$ solution, and brine. The organic layer was dried (MgSO$_4$) and evaporated. Purification by silica gel chromatography yielded ketone **12** (0.385 g) in 88% yield. $\delta_H$ (200 MHz, CDCl$_3$): 7.66–7.62 (m, 4H), 7.44–7.28 (m, 6H), 6.54–6.40 (m, 1H), 6.29–6.18 (m, 1H), 5.83–5.56 (m, 2H), 5.03–4.94 (m, 2H), 3.92–3.71 (m, 2H), 3.22–3.08 (m, 1H), 2.48–2.09 (m, 2H), 1.02 (s, 9H). $\delta_C$ (50 MHz, CDCl$_3$): 202.2, 136.7, 135.7, 135.3, 133.3, 129.9, 128.3, 127.8, 116.9, 64.7, 51.1, 32.5, 26.9, 19.3. $[\alpha]_D^{28} = +31.9$ (*c* 1.0, CHCl$_3$).

### 4.1.6. (*R*)-5-Diphenylsilanyloxymethyl-cyclopent-2-enone 13

Ketone **12** (0.1 g, 0.2643 mmol) was taken in 50 mL of dry DCM. A small amount of 1st generation Grubbs' catalyst was then added to it. The reaction mixture was stirred overnight at room temperature. After that time, the organic solvent was evaporated and the crude reaction product was purified by silica gel chromatography (10:1, petroleum ether/EtOAc) to afford compound **13** (0.085 g) in 90% yield. $\delta_H$ (200 MHz, CDCl$_3$): 7.78–7.76 (m, 1H), 7.66–7.63 (m, 4H), 7.42–7.40 (m, 6H), 6.26–6.22 (m, 1H), 4.09–4.02 (dd, *J* = 9.8, 4.8 Hz, 1H), 3.88–3.76 (dd, *J* = 9.8, 3.6 Hz, 1H), 2.82–2.8 (m, 2H), 2.51–2.31 (m, 1H), 1.01 (s, 9H). $\delta_C$ (50 MHz, CDCl$_3$): 210.4, 135.6, 134.4, 133.5, 133.1, 129.7, 127.7, 63.0, 47.1, 32.9, 26.8, 19.3. $[\alpha]_D^{28} = +22.8$ (*c* 1.0, CHCl$_3$).

### 4.1.7. (*S*)-Methanesulfonic acid 2-diphenylsilanyloxymethyl-pent-4-enyl ester 14

Alcohol *ent*-**9** (1 g, 2.7 mmol) was taken in 20 mL dry DCM. Then, Et$_3$N (0.6 mL, 4.12 mmol) was added to it portionwise at 0 °C. Next, a small portion of DMAP was added. Then MsCl (0.3 mL, 3.3 mmol) was added slowly to the reaction mixture at the same temperature. The reaction mixture was stirred for a 2 h at room temperature. The reaction mixture was extracted with a large volume of diethyl ether. The organic solution was washed with water and brine. Evaporation and purification by means of silica gel chromatography (20:1, petroleum ether/EtOAc) afforded compound **14** in 93% yield. $\delta_H$ (200 MHz, CDCl$_3$): 7.72–7.68 (m, 4H), 7.49–7.39 (m, 6H), 5.84–5.64 (m, 1H), 5.13–5.05 (m, 2H), 4.32 (d, *J* = 9.8 Hz, 2H,), 3.79–3.63 (m, 2H), 2.98 (s, 3H), 2.25–2.18 (t, *J* = 6.7 Hz, 2 H), 2.14–1.98 (m, 1H), 1.11 (s, 9H). $\delta_C$ (50 MHz, CDCl$_3$): 135.6, 135.1, 133.2, 129.8, 127.7, 117.4, 69.4, 62.3, 40.5, 37.0, 31.9, 26.9, 19.3. $[\alpha]_D^{28} = -6.7$ (*c* 1.0, CHCl$_3$).

### 4.1.8. (*R*)-3-Diphenylsilanyloxymethyl-hex-5-enenitrile 15

Compound **14** (1.07 g, 2.5 mmol) was taken in 30 mL dry DMSO. Then NaCN (0.5 g, 8.5 mmol) was added and reaction mixture was stirred overnight at room temperature. The reaction mixture was extracted with a large volume of diethyl ether. The organic solution was washed with water and brine. Evaporation and purification by means of silica gel chromatography (20:1, petroleum ether/EtOAc) afforded compound **15** in 90% yield. $\delta_H$ (200 MHz, CDCl$_3$): 7.72–7.68 (m, 4H), 7.52–7.31 (m, 6H), 5.79–5.59 (m, 1H), 5.16–5.07 (m, 2H), 3.79–3.59 (m, 2H), 2.56–2.46 (d, *J* = 6.0 Hz, 2H), 2.31–2.11 (m, 2H), 2.11–1.97 (m, 1H), 1.12 (s, 9H). $\delta_C$ (50 MHz, CDCl$_3$): 135.6, 134.6, 133.1, 129.0, 127.8, 118.6, 118.0, 64.7, 37.9, 34.5, 26.9, 19.3, 18.7. $[\alpha]_D^{28} = -11.25$ (*c* 1.0, CHCl$_3$).

### 4.1.9. (*R*)-3-Diphenylsilanyloxymethyl-hex-5-enal 16

Compound **15** (0.7 g, 1.93 mmol) was taken in 80 mL of dry DCM and cooled to −78 °C. Then 4 mL of 1 M DIBAL-H solution was added slowly to the reaction mixture at the same temperature. The reaction mixture was stirred for 2 h at −78 °C. A saturated solution of Na$_2$SO$_4$ was then added dropwise to the reaction mixture to precipitate aluminum hydroxide. The reaction mixture was then filtered on a Celite pad. The organic solution was washed with water and brine. Evaporation and purification by means of silica gel chromatography (20:1, petroleum ether/EtOAc) afforded compound **16** in 82% yield. $\delta_H$ (200 MHz, CDCl$_3$): 9.78 (1H), 7.67–7.64 (m, 4H), 7.49–7.40 (m, 6H), 5.80–5.59 (m, 1H), 5.05–4.99 (d, *J* = 12.6 Hz, 2H), 3.69–3.50 (m, 2H), 2.52–2.46 (m, 1H), 2.37–2.01 (m, 4H), 1.07 (s, 9H). $\delta_C$ (50 MHz, CDCl$_3$): 202.5, 136.0, 135.7, 133.5, 129.9, 127.8, 117.3, 66.2, 45.9, 36.1, 35.7, 29.8, 27.0, 19.4. $[\alpha]_D^{28} = -4.6$ (*c* 1.0, CHCl$_3$).

### 4.1.10. 5-Diphenylsilanyloxymethyl-octa-1,7-dien-3-ol 17

Aldehyde **16** (0.5 g, 1.4 mmol) was taken in 10 mL of dry THF. A freshly prepared solution of vinyl magnesium bromide (2.8 mmol) in dry THF was then added to it at −78 °C. The reaction mixture was stirred for a further 2 h at room temperature, after which a saturated NH$_4$Cl solution was added to it. The solution was extracted with diethyl ether, and the organic layer was washed with water and brine. The organic layer was dried (MgSO$_4$) and evaporated; purification by silica gel chromatography (20:1, petroleum ether/EtOAc) afforded alcohol **17** in 80% yield. $\delta_H$ (200 MHz, CDCl$_3$, mixture of diastereomers): 7.69–7.67 (m, 4H), 7.52–7.27 (m, 6H), 5.93–5.59 (m, 2H), 5.29–4.93 (m, 4H), 4.17–4.15 (m, 1H), 3.63–3.54 (m, 2H), 2.36–2.25 (m, 2H), 1.90–1.65 (m, 1H), 1.58–1.54 (m, 2H), 1.07 (s, 9H). $\delta_C$ (50 MHz, CDCl$_3$, mixture of diastereomers): 141.7, 136.9, 136.7, 135.9, 133.6, 129.9, 127.9, 116.6, 114.4, 71.9, 70.9, 67.2, 66.5, 40.0, 39.2, 38.2, 37.0, 36.5, 27.1, 19.5.

### 4.1.11. (*R*)-5-Diphenylsilanyloxymethyl-octa-1,7-dien-3-one 18

Oxalyl chloride (0.12 mL, 1.33 mmol) was taken in anhydrous DCM (10 mL). Then DMSO (0.2 mL, 2.67 mmol) was added to the solution and kept at −78 °C. After 15 min, alcohol **17** (0.35 g, 0.9 mmol) was added to it, and the solution was stirred at the same temperature for a further 45 min. After this time, Et$_3$N (0.7 mL, 5.3 mmol) was added slowly to the reaction mixture at the same temperature. The reaction mixture was then allowed to return to room temperature. Water was added to the solution, and the mixture was extracted with DCM. The organic extract was washed with water, NaHCO$_3$ solution and brine. The organic layer was dried (MgSO$_4$) and evaporated. Purification by silica gel chromatography yielded ketone **18** in 90% yield. $\delta_H$ (200 MHz, CDCl$_3$): 7.66–7.62 (m, 4H), 7.46–7.25 (m, 6H), 6.32–6.14 (m, 2H), 5.81–5.76 (m, 2H), 5.03–4.95 (m, 2H), 3.60–3.57 (m, 2H), 2.82–2.71 (dd, *J* = 16.6, 6.4 Hz, 1H), 2.57–2.46 (dd, *J* = 16.6, 6.0 Hz, 1H), 2.33–2.05 (m, 3H), 1.05 (s, 9H). $\delta_C$ (50 MHz, CDCl$_3$): 200.2, 136.9, 136.3, 135.6, 133.6, 129.6, 127.6, 116.7, 65.6, 40.7, 36.5, 35.5, 26.9, 19.3. $[\alpha]_D^{28} = -44.2$ (*c* 0.8, CHCl$_3$).

### 4.1.12. (*R*)-5-Diphenylsilanyloxymethyl-cyclohex-2-enone 19

Ketone, compound **18** (0.1 g, 0.2643 mmol) was taken in 50 mL of dry DCM. A small amount of 1st generation Grubbs' catalyst

(0.027 mmol) was then added to it. The reaction mixture was stirred overnight at room temperature. Evaporation and purification by means of silica gel chromatography (10:1, petroleum ether/EtOAc) afforded compound **19** in 78% yield. The spectroscopic data were similar to those reported earlier.[8]

### 4.1.13. General procedure for the $NaBH_4/CeCl_3$ reduction

To a cooled (0 °C) solution of enones (0.1 mmol) in MeOH, $CeCl_3\cdot7H_20$ (0.12 mmol) was added. The mixture was stirred at 0 °C for 10 min, and then $NaBH_4$ was added. The resulting mixture was stirred for 3 h at ambient temperature until the reaction was complete (monitored by TLC). The solution was diluted with EtOAc (20 mL), washed with brine (2 mL), dried over $Na_2SO_4$, and concentrated in vacuo to give the crude product. The residue was purified by flash column chromatography (1:5, hexane/EtOAc) to afford the alcohols in 95% yield.

### 4.1.14. General procedure for the substrate directed epoxidation with *m*CPBA

Unsaturated alcohols (0.31 mmol) were dissolved in dichloromethane (5 mL) along with sodium hydrogencarbonate (52 mg, 0.62 mmol). To the stirred suspension, *meta*-chloroperoxybenzoic acid (108 mg, 0.62 mmol) was added at room temperature. The resulting suspension was stirred vigorously for 19 h. Next a 20% aqueous solution of sodium sulfite (10 mL) was added and the resulting two-phase mixture was stirred vigorously for 15 min. The two layers were separated and the aqueous layer was extracted with dichloromethane (30 mL). The combined organic layers were washed with a 20% aqueous solution of sodium sulfite (10 mL) and a 5% aqueous solution of sodium hydrogencarbonate (5 mL), dried ($Na_2SO_4$) and evaporated under reduced pressure. The residue was purified by flash column chromatography (1:3, hexane/EtOAc) to afford the compound in 88–90% yield.

### 4.1.15. General procedure for the acid induced epoxide ring opening

Epoxide compounds (0.085 mmol) were added to a 1:1 mixture of 0.2 M sulfuric acid/1,4-dioxane (5 mL) and the reaction mixture was stirred at room temperature for 0.5 h. The reaction was then diluted with a saturated solution of sodium hydrogencarbonate (5 mL) and extracted with ethyl acetate (30 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash column chromatography (1:1, hexane/EtOAc) to afford the diols in 80% yield.

### 4.1.16. General procedure for the cyclopropanation reaction

To a hot, rapidly stirred solution of (126 mg, 0.7 mmol) cupric acetate monohydrate in 1 mL of glacial acetic acid was added zinc dust (800 mg, 12 mmol). After about 0.5 min, all of the copper had deposited on the zinc. The couple was allowed to settle for 10 min, then the acetic acid was decanted while taking care to not lose the silt-like couple. The dark reddish gray couple was then washed with one portion (2 mL) of acetic acid followed by three portions (10 mL) of ether. The moist couple was then ready for use.

Methylene bromide (124 mg, 72 mmol) and iodine (0.15 g, 0.06 mmol) in anhydrous ether (5 mL) were added to the mixture of zinc–copper couple. The iodine color disappeared immediately; the initial gray-colored mixture was then refluxed for 30 min. During this period the mixture turned darker; the color change was accompanied by a gentle exothermic reaction. External heating was discontinued and the compound (60 mg, 18 mmol, in anhydrous ether 2 mL) was added dropwise over 30 min. During the addition, the mixture continued to reflux. Heating was resumed and the mixture refluxed for 30 h. The reaction mixture was cooled and filtered. The ether solution was extracted with hydrochloric acid (3 mL) to remove the dissolved zinc iodide, aqueous sodium bicarbonate (5 mL) and saturated aqueous sodium chloride. The combined ether extract was evaporated. The product was purified by flash chromatography (1:5; hexane/EtOAc) to afford the compounds in 75% yield.

### 4.1.17. (1*R*,5*R*)-5-(*tert*-Butyldiphenylsilyloxymethyl)-cyclohex-2-enol 20

$\delta_H$ (200 MHz, $CDCl_3$): 7.70–7.65 (m, 4H), 7.48–7.32 (m, 6H), 5.82–5.66 (m, 2H), 4.3 (br, 1H), 3.57 (d, *J* = 5.6 Hz, 2H), 2.23–1.91 (m, 3H), 1.34–1.23 (m, 2H), 1.1 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 135.6, 133.8, 131.0, 129.6, 128.4, 127.7, 68.2, 67.8, 35.9, 35.8, 28.3, 26.9, 19.3. $[\alpha]_D^{28} = -19.5$ (*c* 0.6, $CHCl_3$).

### 4.1.18. (1*R*,2*R*,3*R*,5*R*)-5-(Hydroxymethyl)cyclohexane-1,2,3-triol 2

At first, *t*BuOH (2 mL), $H_2O$ (2 mL) and AD-mix β (550 mg) were mixed and the mixture was stirred for 15 min. Methane sulfonamide (28 mg, 0.3 mmol) was then added and the stirring was continued for a further 15 min. Compound **20** (100 mg, 0.3 mmol) was then added in one portion. The slurry was stirred vigorously at 20 °C for 24 h. After that time, sodium sulfite (750 mg) was added and stirring was continued for a further 1 h. The reaction mixture was extracted with EtOAc (4 × 10 mL). The organic layer was dried ($Na_2SO_4$) and evaporated in vacuo. The diol was purified by flash chromatography (1:1; hexane/EtOAc) followed by TBDPS deprotection by TBAF in THF to afford compound **2** in 75% yield. $\delta_H$ (200 MHz, $CDCl_3$): 4.19–4.12 (m, 1H), 3.98–3.86 (m, 1H), 3.43 (d, *J* = 5.6 Hz, 2H), 3.41–3.37 (m, 1H), 2.16–2.10 (m, 2H), 1.98–1.91 (m, 1H), 1.5–1.42 (m, 2H). $\delta_C$ (50 MHz, $CDCl_3$): 76.6, 70.2, 70.0, 68.1, 35.9, 33.9, 33.1. $[\alpha]_D^{28} = +17.0$ (*c* 1.0, $H_2O$). HRMS (ESI) calculated for $C_7H_{14}O_4Na$: 185.0790; observed: 185.0796.

### 4.1.19. (1*R*,2*R*,4*S*,6*S*)-4-(*tert*-Butyldiphenylsilyloxymethyl)-7-oxa-bicyclo[4.1.0]heptan-2-ol 21

$\delta_H$ (200 MHz, $CDCl_3$): 7.65–7.51 (m, 4H), 7.47–7.38 (m, 6H), 4.06–3.98 (m, 1H), 3.43 (d, *J* = 5.6 Hz, 2H), 3.37–3.31 (m, 2H), 2.01–1.49 (m, 5H), 1.09 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 135.7, 133.8, 129.8, 127.8, 69.3, 67.8, 56.4, 54.8, 36.4, 31.0, 27.0, 26.2, 19.4. $[\alpha]_D^{28} = +4.4$ (*c* 0.5, $CHCl_3$).

### 4.1.20. (1*R*,2*S*,3*R*,5*S*)-5-(*tert*-Butyldiphenylsilyloxymethyl)cyclohexane-1,2,3-triol 22

$\delta_H$ (200 MHz, $CDCl_3$): 7.75–7.68 (m, 4H), 7.50–7.36 (m, 6H), 4.09 (br, 2H), 3.81 (br, 1H), 3.55 (d, *J* = 5.4 Hz, 2H), 2.92 (br, 3H, –OH), 2.06–1.50 (m, 5H), 1.15 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 135.6, 133.6, 129.7, 127.7, 73.4, 69.7, 68.6, 68.3, 33.5, 31.6, 30.9, 26.9, 19.3.

### 4.1.21. (1*R*,2*S*,3*R*,5*S*)-5-(Hydroxymethyl)cyclohexane-1,2,3-triol 1

$\delta_H$ (200 MHz, $CDCl_3$): 4.1–4.01 (br, 2H), 3.8–3.73 (br, 1H), 3.51 (d, *J* = 5.6 Hz, 2H), 2.90–2.2 (br, 3H, –OH), 2.06–1.48 (m, 5H). $\delta_C$ (50 MHz, $CDCl_3$): 71.4, 70.1, 67.8, 66.6, 32.5, 30.6, 29.4. $[\alpha]_D^{28} = -8.8$ (*c* 1.0, $H_2O$). HRMS (ESI) calculated for $C_7H_{14}O_4Na$: 185.0790; observed: 185.0796.

### 4.1.22. (1*S*,2*R*,4*R*,6*R*)-4-(*tert*-Butyldiphenylsilyloxymethyl)bicyclo[4.1.0]heptan-2-ol 23

$\delta_H$ (400 MHz, $CDCl_3$): 7.67–7.65 (m, 4H), 7.46–7.38 (m, 6H), 4.26–4.24 (m, 1H), 3.43–3.40 (m, 2H), 2.02–2.0 (m, 1H), 1.9–1.87 (m, 1H), 1.59–1.54 (m, 2H), 1.3–1.24 (m, 2H), 1.1 (s, 9H), 0.78–0.7 (m, 2H), 0.28 (m, 1H). $\delta_C$ (50 MHz, $CDCl_3$): 135.6, 133.8, 129.6, 127.6, 68.7, 68.0, 37.9, 32.2, 26.8, 26.5, 19.3, 18.5, 12.3, 8.5. $[\alpha]_D^{28} = -22.1$ (*c* 0.6, $CHCl_3$).

### 4.1.23. (1*S*,2*R*,4*R*,6*R*)-4-(Hydroxymethyl)bicyclo[4.1.0]heptan-2-ol 4

$\delta_H$ (200 MHz, $CDCl_3$): 4.26–4.15 (m, 1H), 3.38–3.34 (m, 2H), 2.06–1.98 (m, 1H), 1.92–1.5 (m, 4H), 1.1–1.0 (m, 1H), 0.6–0.5 (m, 2H), 0.3–0.25 (m, 1H). $\delta_C$ (50 MHz, $CDCl_3$): 68.7, 67.5, 38.1, 32.2, 26.6, 18.5, 12.4, 8.8. $[\alpha]_D^{28} = -12.5$ (*c* 1.0, $CHCl_3$). HRMS (ESI) calculated for $C_8H_{14}O_2Na$: 165.0891; observed: 165.0894.

### 4.1.24. (1*S*,5*R*)-5-(*tert*-Butyldiphenylsilyloxymethyl)cyclohex-2-enol 24

$\delta_H$ (200 MHz, $CDCl_3$): 7.70–7.66 (m, 4H), 7.42–7.36 (m, 6H), 5.96–5.72 (m, 2H), 4.23 (br, 1H), 3.63–3.57 (m, 2H), 2.37–1.42 (m, 5H), 1.1 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 135.8, 134.0, 131.1, 129.8, 128.4, 127.8, 68.3, 64.3, 34.4, 31.6, 28.8, 27.1, 19.5. $[\alpha]_D^{28} = -18.8$ (*c* 0.3, $CHCl_3$).

### 4.1.25. (1*S*,2*S*,4*S*,6*R*)-4-(*tert*-Butyldiphenylsilyloxymethyl)-7-oxa-bicyclo[4.1.0]heptan-2-ol 26

$\delta_H$ (200 MHz, $CDCl_3$): 7.69–7.59 (m, 4H), 7.48–7.35 (m, 6H), 4.15–4.08 (m, 1H), 3.46 (d, J = 5.4 Hz, 2H), 3.38–3.32 (m, 2H), 2.26–1.34 (m, 5H), 1.09 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 135.7, 133.8, 129.8, 127.8, 67.8, 64.0, 55.8, 54.4, 33.7, 28.8, 27.4, 27.0, 19.4. $[\alpha]_D^{28} = -17.3$ (*c* 1.0, $CHCl_3$).

### 4.1.26. (1*S*,2*S*,3*S*,5*S*)-5-(*tert*-Butyldiphenylsilyloxymethyl)cyclohexane-1,2,3-triol 27

$\delta_H$ (200 MHz, $CDCl_3$): 7.65–7.63 (m, 4H), 7.44–7.35 (m, 6H), 4.14 (br, 1H), 3.87–3.83 (m, 1H), 3.56–3.50 (m, 2H), 3.48–3.46 (m, 1H), 2.12–1.89 (m, 3H), 1.42–1.28 (m, 2H), 1.08 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 135.7, 133.7, 129.9, 127.9, 77.4, 70.4, 69.8, 67.9, 35.8, 33.8, 33.1, 27.0, 19.5.

### 4.1.27. (1*S*,2*S*,3*S*,5*S*)-5-(Hydroxymethyl)cyclohexane-1,2,3-triol 3

$\delta_H$ (200 MHz, $CDCl_3$): 4.14–4.1 (br, 2H), 3.87–3.83 (m, 1H), 3.56–3.50 (m, 2H), 2.82 (br, 4H, –OH), 1.8–1.4 (m, 5H). $\delta_C$ (50 MHz, $CDCl_3$): 76.4, 70.1, 69.6, 66.2, 35.4, 33.5, 32.4. $[\alpha]_D^{28} = -6.2$ (*c* 0.5, $CHCl_3$).

HRMS (ESI) calculated for $C_7H_{14}O_4Na$: 185.0790; observed: 185.0796.

### 4.1.28. (1*R*,2*S*,4*R*,6*S*)-4-(*tert*-Butyldiphenylsilyloxymethyl)bicyclo[4.1.0]heptan-2-ol 25

$\delta_H$ (200 MHz, $CDCl_3$): 7.70–7.64 (m, 4H), 7.44–7.27 (m, 6H), 4.51–4.37 (m, 1H), 3.48 (d, *J* = 5.8 Hz, 2H), 1.89–1.45 (m, 7H), 1.1 (s, 9H), 0.55–0.38 (m, 2H). $\delta_C$ (50 MHz, $CDCl_3$): 135.8, 134.1, 129.7, 127.8, 68.2, 64.3, 34.3, 30.4, 27.1, 26.1, 19.5, 17.1, 12.6, 5.0. $[\alpha]_D^{28} = -34.2$ (*c* 1.0, $CHCl_3$).

### 4.1.29. (1*R*,2*S*,4*R*,6*S*)-4-(Hydroxymethyl)bicyclo[4.1.0]heptan-2-ol 5

$\delta_H$ (200 MHz, $CDCl_3$): 4.44–4.37 (m, 1H), 3.48 (d, *J* = 5.8 Hz, 2H), 1.92–1.43 (m, 7H), 0.50–0.38 (m, 2H). $\delta_C$ (50 MHz, $CDCl_3$): 68.7, 64.8, 34.2, 30.8, 27.1, 17.1, 12.6, 5.0. $[\alpha]_D^{28} = -9.8$ (*c* 1.0, $CHCl_3$). HRMS (ESI) calculated for $C_8H_{14}O_2Na$: 165.0891; observed: 165.0894.

### 4.1.30. (3*R*,5*R*)-3-*tert*-Butyldimethylsilyloxy-5-(*tert*-butyldiphenylsilyloxymethyl)cyclohex-1-ene 28

$\delta_H$ (200 MHz, $CDCl_3$): 7.74–7.71 (m, 4H), 7.52–7.44 (m, 6H), 5.8–5.62 (m, 2H), 4.4 (br, 1H), 3.61 (d, *J* = 5.2 Hz, 2H), 2.15–1.42 (m, 5H), 1.15 (s, 9H), 1.02 (s, 9H), 0.2 (s, 6H). $\delta_C$ (50 MHz, $CDCl_3$): 135.6, 133.9, 132.3, 129.6, 127.7, 127.4, 68.6, 68.3, 36.1, 36.0, 28.3, 26.9, 26.0, 19.4, 18.3, −4.4, −4.6. $[\alpha]_D^{28} = -44.2$ (*c* 1.0, $CHCl_3$).

### 4.1.31. (1*S*,2*R*,4*S*,6*R*)-2-Methoxy-4-(methoxymethyl)-7-oxa-bicyclo[4.1.0]heptanes 29

$\delta_H$ (200 MHz, $CDCl_3$): 7.67–7.63 (m, 4H), 7.43–7.35 (m, 6H), 3.97–3.89 (m, 1H), 3.51–3.47 (m, 2H), 3.3 (br, 1H), 3.06 (d, *J* = 6.8 Hz, 1H), 2.17–2.11 (m, 1H), 1.93–1.83 (m, 1H), 1.61–1.3 (m, 3H), 1.1 (s, 9H), 0.95 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H). $\delta_C$ (50 MHz, $CDCl_3$): 135.6, 133.7, 129.6, 127.7, 67.9, 67.5, 57.7, 54.1, 35.0, 29.7, 28.0, 26.8, 25.8, 19.3, 18.2, −4.6, −4.8. $[\alpha]_D^{28} = -31.9$ (*c* 1.0, $CHCl_3$).

### 4.1.32. (1*S*,2*R*,3*R*,5*R*)-5-(Hydroxymethyl)cyclohexane-1,2,3-triol 6

$\delta_H$ (200 MHz, $CDCl_3$): 4.18–4.12 (m, 1H), 4.0–3.95 (m, 1H), 3.57–3.53 (m, 2H), 3.44–3.40 (m, 1H), 1.94–1.42 (m, 5H). $\delta_C$ (50 MHz, $CDCl_3$): 82.9, 71.1, 70.6, 68.5, 33.4, 32.8, 30.2. $[\alpha]_D^{28} = +7.4$ (*c* 1.0, $H_2O$). HRMS (ESI) calculated for $C_7H_{14}O_4Na$: 185.0790; observed: 185.0796.

### 4.1.33. (1*R*,5*R*)-5-(*tert*-Butyldiphenylsilyloxymethyl)cyclopent-2-enol 32

$\delta_H$ (200 MHz, $CDCl_3$): 7.71–7.65 (m, 4H), 7.48–7.38 (m, 6H), 5.98–5.87 (m, 2H), 4.95 (br, 1H), 3.90 (d, J = 6.4 Hz, 2H), 2.79–2.38 (m, 3H), 1.15 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 135.5, 135.4, 134.3, 133.1, 133.0, 132.8, 129.8, 129.7, 127.7, 127.6, 76.6, 64.1, 42.6, 33.7, 26.6, 19.1. $[\alpha]_D^{28} = +2.25$ (*c* 1.0, $CHCl_3$).

### 4.1.34. (1*S*,5*R*)-5-(*tert*-Butyldiphenylsilyloxymethyl)cyclopent-2-enol 33

$\delta_H$ (200 MHz, $CDCl_3$): 7.70–7.65 (m, 4H), 7.48–7.38 (m, 6H), 5.89–5.75 (m, 2H), 4.80 (br, 1H), 3.82–3.63 (m, 2H), 2.6–2.38 (m, 2H), 2.0–1.88 (m, 1H), 1.15 (s, 9H). $\delta_C$ (50 MHz, $CDCl_3$): 135.6, 133.6, 133.4, 132.8, 129.7, 127.7, 80.8, 66.0, 50.4, 34.0, 26.9, 19.2. $[\alpha]_D^{28} = +5.3$ (*c* 1.0, $CHCl_3$).

### 4.1.35. (1*S*,2*S*,3*R*,5*R*)-3-(*tert*-Butyldiphenylsilyloxymethyl)-6-oxa-bicyclo[3.1.0]hexan-2-ol 34

$\delta_H$ (400 MHz, $CDCl_3$): 7.67–7.64 (m, 4H), 7.46–7.37 (m, 6H), 4.54–4.52 (m, 1H), 4.15–4.10 (m, 1H), 4.02 (m, 1H), 3.61 (br, 1H), 3.52–3.49 (m, 1H), 3.40 (br, 1H), 2.39–2.35 (m, 1H), 1.91–1.85 (m, 1H), 1.4 (m, 1H), 1.05 (s, 9H). $\delta_C$ (100 MHz, $CDCl_3$): 135.4, 132.9, 129.8, 127.7, 74.9, 67.2, 60.8, 55.4, 38.2, 29.5, 26.7, 18.9. $[\alpha]_D^{28} = +12.3$ (*c* 1.0, $CHCl_3$).

### 4.1.36. (1*R*,2*S*,3*R*,5*S*)-3-(*tert*-Butyldiphenylsilyloxymethyl)-6-oxa-bicyclo[3.1.0]hexan-2-ol 35

$\delta_H$ (400 MHz, $CDCl_3$): 7.68–7.64 (m, 4H), 7.47–7.40 (m, 6H), 4.45 (br, 1H), 3.99–3.96 (m, 1H), 3.80–3.75 (m, 1H), 3.55 (br, 1H), 3.49 (br, 1H), 2.08–2.0 (m, 1H), 1.97–1.85 (m, 1H), 1.7–1.6 (m, 1H), 0.99 (s, 9H). $\delta_C$ (100 MHz, CDCl3): 135.4, 132.7, 129.9, 127.8, 72.6, 62.8, 58.3, 56.7, 40.0, 27.6, 26.7, 19.0. $[\alpha]_D^{28} = +22.1$ (c 1.0, $CHCl_3$).

### 4.1.37. (1*R*,2*R*,3*R*,5*S*)-3-(*tert*-Butyldiphenylsilyloxymethyl)-6-oxa-bicyclo[3.1.0]hexan-2-ol 36

$\delta_H$ (400 MHz, $CDCl_3$): 7.65–7.63 (m, 4H), 7.46–7.37 (m, 6H), 4.17 (t, J = 6.4 Hz, 1H), 3.81–3.77 (m, 1H), 3.65–3.63 (m, 1H), 3.54 (1H), 3.46 (1H), 2.14–2.09 (m, 2H), 1.80–1.6 (m, 1H), 1.09 (s, 9H). $\delta_C$ (100 MHz, $CDCl_3$): 135.5, 133.1, 129.8, 127.7, 76.4, 64.3, 58.4, 54.5, 41.8, 31.8, 29.6, 26.8. $[\alpha]_D^{28} = +22.0$ (*c* 1.0, $CHCl_3$).

### 4.1.38. (1*S*,2*R*,3*S*,4*R*)-4-(Hydroxymethyl)cyclopentane-1,2,3-triol 40

$\delta_H$ (400 MHz, $CDCl_3$): 4.48–4.14 (m, 3H), 3.52–3.44 (m, 2H), 3.40–2.92 (br, 4H, –OH), 1.91–1.45 (m, 3H). $\delta_C$ (100 MHz, $CDCl_3$): 77.2, 72.3, 71.9, 68.4, 38.2, 33.5. $[\alpha]_D^{28} = +8.35$ (*c* 1.0, $H_2O$). HRMS (ESI) calculated for $C_6H_{12}O_4Na$: 171.0633; observed: 171.0628.

### 4.1.39. (1*R*,2*S*,3*S*,4*R*)-4-(Hydroxymethyl)cyclopentane-1,2,3-triol 41

$\delta_H$ (400 MHz, $CDCl_3$): 4.42–4.08 (m, 3H), 3.46–3.40 (m, 2H), 3.20–2.92 (br, 4H, –OH), 1.88–1.40 (m, 3H). $\delta_C$ (100 MHz, $CDCl_3$): 77.6, 72.7, 71.5, 67.2, 38.7, 32.5. $[\alpha]_D^{28} = +12.1$ (*c* 1.0, $H_2O$). HRMS (ESI) calculated for $C_6H_{12}O_4Na$: 171.0633; observed: 171.0628.

### 4.1.40. (1*R*,2*S*,3*R*,4*R*)-4-(Hydroxymethyl)cyclopentane-1,2,3-triol 42

$\delta_H$ (400 MHz, $CDCl_3$): 4.52–4.34 (m, 1H), 4.26–4.20 (m, 1H), 4.12–4.06 (m, 1H), 3.48–3.42 (m, 2H), 3.12–2.90 (br, 4H, –OH), 1.80–1.45 (m, 3H). $\delta_C$ (100 MHz, $CDCl_3$): 77.7, 72.3, 70.9, 66.4, 37.3, 30.8. $[\alpha]_D^{28} = -6.9$ (*c* 1.0, $H_2O$). HRMS (ESI) calculated for $C_6H_{12}O_4Na$: 171.0633; observed: 171.0628.

### 4.1.41. (1*R*,2*R*,3*R*,5*R*)-3-(*tert*-Butyldiphenylsilyloxymethyl)bicyclo[3.1.0]hexan-2-ol 43

$\delta_H$ (200 MHz, $CDCl_3$): 7.68–7.63 (m, 4H), 7.45–7.36 (m, 6H), 4.88–4.79 (m, 1H), 3.76–3.53 (m, 2H), 2.59–2.49 (m, 1H), 2.12–2.0 (m, 1H), 1.67–1.60 (m, 1H), 1.44–1.38 (m, 2H), 1.1 (s, 9H), 0.63–0.60 (m, 2H). $\delta_C$ (50 MHz, $CDCl_3$): 135.4, 133.6, 129.7, 127.7, 75.5, 65.3, 46.0, 30.9, 26.7, 26.1, 19.0, 17.5, 9.8.

### 4.1.42. (1*S*,2*R*,3*R*,5*S*)-3-(*tert*-Butyldiphenylsilyloxymethyl)bicyclo[3.1.0]hexan-2-ol 44

$\delta_H$ (200 MHz, $CDCl_3$): 7.69–7.61 (m, 4H), 7.47–7.38 (m, 6H), 4.80–4.72 (m, 1H), 3.81–3.67 (m, 2H), 2.50–2.44 (m, 1H), 2.09–2.0 (m, 1H), 1.64–1.57 (m, 1H), 1.40–1.28 (m, 2H), 1.09 (s, 9H), 0.60–0.55 (m, 2H). $\delta_C$ (50 MHz, $CDCl_3$): 135.6, 133.2, 129.9, 127.4, 75.9, 65.8, 46.6, 31.5, 26.8, 26.4, 19.8, 17.6, 9.2.

### 4.1.43. (1*R*,2*R*,3*R*,5*R*)-3-(hydroxymethyl)bicyclo[3.1.0]hexan-2-ol 45

$\delta_H$ (200 MHz, $CDCl_3$): 4.84–4.79 (m, 1H), 3.70–3.58 (m, 2H), 2.9 (br, 2H, –OH), 2.56–2.48 (m, 1H), 2.04–2.0 (m, 1H), 1.6–1.38 (m, 3H), 0.55–0.50 (m, 2H). $\delta_C$ (50 MHz, $CDCl_3$): 76.8, 67.4, 44.8, 31.5, 26.8, 17.5, 9.2. $[\alpha]_D^{28} = -2.3$ (*c* 1.0, $CHCl_3$). HRMS (ESI) calculated for $C_7H_{12}O_2Na$: 151.0735; observed: 151.0739.

### 4.1.44. (1*S*,2*R*,3*R*,5*S*)-3-(Hydroxymethyl)bicyclo[3.1.0]hexan-2-ol 46

$\delta_H$ (200 MHz, $CDCl_3$): 4.72–4.64 (m, 1H), 3.65–3.52 (m, 2H), 2.94 (br, 2H, –OH), 2.50–2.36 (m, 1H), 2.0–1.92 (m, 1H), 1.64–1.45 (m, 3H), 0.48–0.42 (m, 2H). $\delta_C$ (50 MHz, $CDCl_3$): 77.1, 68.2, 43.9, 32.3, 27.4, 18.2, 8.8. $[\alpha]_D^{28} = -8.2$ (*c* 1.0, $CHCl_3$). HRMS (ESI) calculated for $C_7H_{12}O_2Na$: 151.0735; observed: 151.0739.

### 4.1.45. (1*S*,2*S*,3*R*,5*S*)-3-(*tert*-Butyldiphenylsilyloxymethyl)bicyclo[3.1.0]hexan-2-ol 47

$\delta_H$ (200 MHz, $CDCl_3$): 7.68–7.60 (m, 4H), 7.44–7.35 (m, 6H), 4.84–4.76 (m, 1H), 3.83–3.69 (m, 2H), 2.52–2.48 (m, 1H), 2.12–2.05 (m, 1H), 1.64–1.57 (m, 1H), 1.42–1.32 (m, 2H), 1.09 (s, 9H), 0.62–0.55 (m, 2H). $\delta_C$ (50 MHz, $CDCl_3$): 135.7, 133.5, 129.3, 127.6, 75.5, 66.2, 46.1, 31.7, 26.7, 26.1, 19.5, 17.3, 9.1.

### 4.1.46. (1*S*,2*S*,3*R*,5*S*)-3-(Hydroxymethyl)bicyclo[3.1.0]hexan-2-ol 48

$\delta_H$ (200 MHz, $CDCl_3$): 4.67–4.61 (m, 1H), 3.68–3.59 (m, 2H), 2.90–2.8 (br, 2H, –OH), 2.42–2.31 (m, 1H), 2.04–1.92 (m, 1H), 1.67–1.49 (m, 3H), 0.45–0.41 (m, 2H). $\delta_C$ (50 MHz, $CDCl_3$): 77.3, 68.5, 43.3, 32.8, 27.6, 18.7, 8.9. $[\alpha]_D^{28} = +1.2$ (*c* 1.0, $CHCl_3$). HRMS (ESI) calculated for $C_7H_{12}O_2Na$: 151.0735; observed: 151.0739.

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