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Facile approach towards the synthesis of homochiral functionalised alcohols from 4-*O*-[(*tert*)-butyldimethylsilyl]-2,3-*O*-cyclohexylidene-L-threose of (L)-(+)-tartaric acid origin

Angshuman Chattopadhyay * and Bhaskar Dhotare

Bio-Organic Division, Bhabha Atomic Research Centre, Mumbai-400085, India

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Abstract

(L)-(+)-Diethyl tartarate **2** has been transformed into the aldehyde **6**. Grignard additions to **6** take place with moderate diastereoselectivity giving predominant formation of the *anti* products **8a–e**. However, in each case the diastereoalcohols are easily separable by column chromatography giving rise to the formation of a series of functionalised homochiral alcohols **7** and **8**. On the other hand Zn mediated allylation and propargylation of **6** in the presence of water proceeded efficiently with almost absolute (>99%) stereoselective formation of versatile functionalised homoallylic **8d** and homopropargylic **8e** alcohols respectively.

1. Introduction

Recent years have witnessed a tremendous upsurge in the synthesis of optically active compounds of biological relevance. In this endeavour, the chiron approach[1] which deals with the exploitation of suitably functionalised chiral building blocks, has drawn considerable attention. These chirons on careful functional and stereochemical manipulation generate the basic structural units that are present in the target molecules. For such operations a major prerequisite is the availability of suitably functionalised chirons in enantiomerically pure form. Any polyfunctional chiron is said to have good synthetic potential if its functional groups are amenable for chemical as well as stereochemical manipulation independently of each other. One convenient approach to prepare such chiral intermediates bearing contiguous stereocentres, is based on the stereodifferentiating addition[2–4] of simple or functionalised organometallics to α- and/or β-alkoxy[3a–j] or other heterosubstituted[3k–m] acyclic carbonyls. Consequently, there has been a considerable amount of recent interest in understanding the acyclic stereochemistry involved during such

* Corresponding author.

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organometallations.[2–4] The advantage for choosing acyclic carbonyls lies with the possible stereochemical flexibility for the addition of a given nucleophile which can be achieved by changing metal, solvent or other additives. However, from a synthetic viewpoint an organometallation which is associated with a very high stereoselectivity is always desirable. In the case of poor or moderately selective addition each of the resulting diastereoalcohols needs to be isolated in pure form from the product mixture without being derivatised as this may not be compatible with the subsequent reactions. Usually for a polyhydroxylated carbonyl substrate, choosing the right combination of *O*-protecting groups, means that each of the hydroxyl functionalities of the resulting diastereoalcohols after organometallation become amenable for selective manipulation. In view of these facts, there is always scope for the development of an operationally simple procedure for the preparation of polyoxygenated chirons with hydroxyls versatilely and stably protected.

During our ongoing programme on the synthesis of bioactive compounds, we have developed[5] a convenient synthesis of a chemically stable (*R*)-2,3-cyclohexylideneglyceraldehyde **1** of (D)-mannitol origin. Subsequently **1** has been treated with several Grignard reagents[5] under anhydrous conditions and also subjected to Barbier type allylation, crotylation and propargylation[6] in the presence of water, following Luche's procedure,[7] to synthesise a series of homochiral functionalised alcohols which have good potential as functionalised chirons. We observed that the presence of stable cyclohexylidene functionality generates hydrophobicity in **1** and the product alcohols giving rise to an operational advantage during the organometallations of **1** in the presence of water and also allowing acid treatment which is required to facilitate the work up after the reactions in some cases. We have subsequently utilised three of these addition products of **1** as useful chirons to develop facile routes for the synthesis of coriolic acid,[5] LTB_4[6] and 2,3-dideoxy-3-substituted sugar modified nucleosides[8] which have significant biological importance.

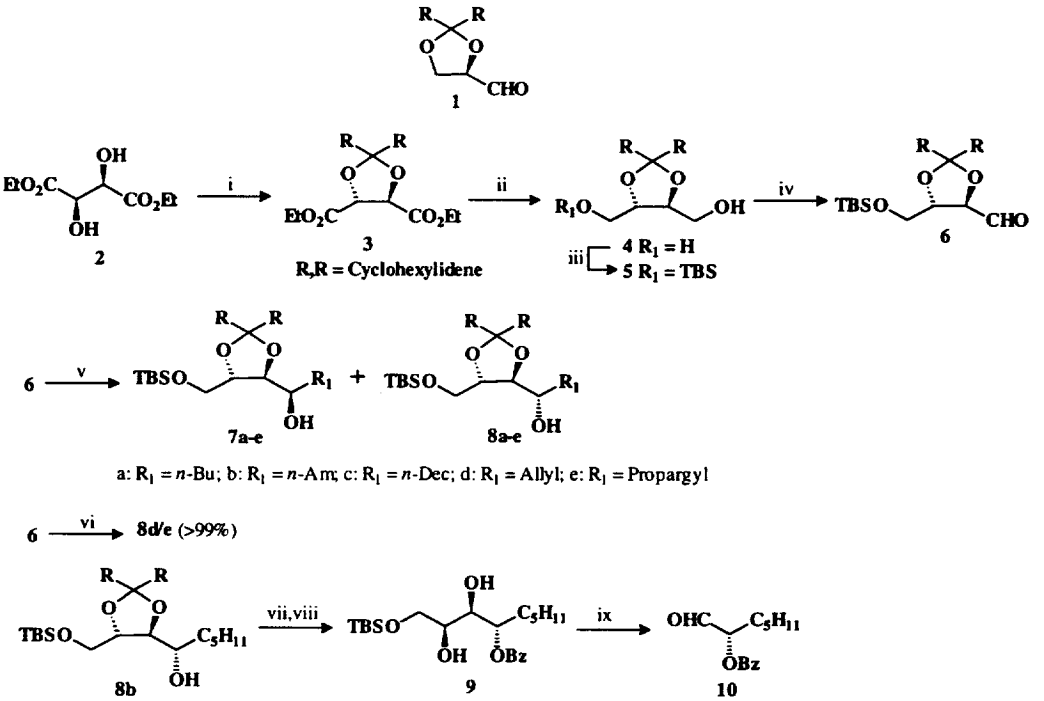
We report here the synthesis of another useful aldehyde **6** which has been prepared from commercially available (L)-(+)-diethyl tartarate **2** and discuss our study on some simple organometallations of **6**. This has been initiated with a view to developing an easy approach for the synthesis of a series of homochiral alcohols bearing additional stereogenic centres compared to those generally preparable from **1**. Incidentally, several reports[9–11] are available regarding the organometallation of several other aldehydes similar to **6** originating from **2** bearing different *O*-protecting groups. We also present here a comparative survey of our investigation with those done by others.

2. Results and discussion

To obtain **6**, **2** was first ketalised on treatment with cyclohexanone following a standard procedure, to give **3** in high yield. Compound **3**, without being purified further by chromatography, was directly treated with $LiAlH_4$ to afford the diol **4**. Monosilylation of the C_2-symmetric diol **4** has been performed easily to give **5** in good yield. Oxidation of the purified alcohol **5** has been found to be effected smoothly using a recently reported method[12] to give the aldehyde **6**. The formation of **6** was confirmed by IR and ^{1}H-NMR spectra of the residue after usual extraction and solvent removal of the oxidation product. Though not very stable, the aldehyde **6** was sufficiently pure (TLC) and could be used for further reaction without any purification.

Compound **6** was subjected to a number of Grignard additions (as shown in Scheme 1). In all cases, the reaction proceeded smoothly producing the desired products with good yield. In each case the reaction was associated with the formation of a major amount of *anti* alcohols **8** and a minor but appreciable amount of the *syn* alcohols **7** of the diastereoisomers which were easily separable by column

chromatography (SiO_2). The ^{1}H-NMR spectra chemical shifts of the CHO and CH_2O of the alcohols show two distinguishable patterns of multiplets with a broad one in the region of δ 3.5–4.25 for all the *syn* products **7a–e** and a compact one in the region of δ 3.6–4.0 for the *anti* products **8a–e** for five protons. However in order to establish the absolute configuration of the stereogenic centre, formed by the organometallation, **8b**, one of the *anti* products was chosen as a representative example. This was sequentially subjected to benzoylation and then deketalization (CF_3COOH/water) at low temperature. Finally $NaIO_4$ cleavage of the resulting diol **9** afforded **10**, the coriolic acid synthon whose spectral and optical data were in accordance with those already reported by us.[5]



i) Cyclohexanone/PTS, ii) LAH/THF, iii) TBSCl/imidazole/CH_2Cl_2, iv) P_2O_5/DMSO/TEA, v) R_1MgX, vi) Allyl or Propargyl Bromide/Zn/THF-H_2O, vii) PhCOCl/py, viii) CF_3CO_2H/H_2O, ix) $NaIO_4/CH_3CN$-H_2O

Scheme 1.

The advantages of this approach are the operational simplicity during the preparation of **6** and its good reactivity towards the practically viable Grignard additions, which are followed by easy isolation and separability of the diastereoalcohols **7** and **8**. Here, the moderate selectivity of the Grignard additions has been exploited to make both the diastereoalcohols **7** and **8** available on a preparative scale with high enantiopurity (see Table 1). As in the case for **1** and its addition products,[5,6] the poor water solubility and relative functional stability of **6**, **7** and **8** due to the presence of cyclohexylidene moiety, also add advantages to the entire operation. Reports are available[10] for Grignard addition to the corresponding 1-*O*-benzyl-2,3-bis-(methoxymethyl) derivative which gives predominantly the *syn* product. In their case the addition is associated with an α-chelate model[4b] whereas in our case the predomonancy of the *anti* products suggests that the addition takes place in accordance with the Felkin–Anh model.[4h,i] It is generally observed that Grignard addition to α-OMOM-carbonyls gives rise to *syn* products[4b] However this requires handling of highly toxic MOMCl which is unwarranted for practical purposes. Similar to

Table 1
Organometallation of **6**

Entry	Organometallic	Solvent	*anti* **8** (%) /*syn* **7** (%)
a	*n*-BuMgBr	THF	69.5/30.5
b	*n*-AmMgBr	THF	71.4/28.6
c	*n*-DecMgBr	THF	75.4/24.6
d	i) AllylMgBr	Ether	73.0/27.0
	ii)AllylBr, Zn	THF/Water	>99
e	i) PropargylMgBr	Ether	81.3/18.7
	ii) PropargylBr, Zn	THF/ Water	>99

our case, the *anti* selectivity of Grignard addition was reported for a 2,3-*O*-isopropylidene derivative[11] corresponding to **6**. Hence it can be concluded that the stereochemical flexibility during the Grignard additions of (L)-threose can be achieved by changing the *O*-protecting groups.

The efficacy of our approach is further established by the possible isolation of both the diastereomers of the homoallylic **7d** and **8d** and homopropargylic **7e** and **8e** alcohols which are rich with diverse functionalities. It should be recalled that Mukaiyama's group[9] have investigated varied types of organometallation of a 2,3-*O*-isopropylidene derivative of DET origin. Allylation of their aldehyde with diallyltin in anhydrous medium afforded the homoallylated alcohols with a *syn*:*anti* ratio of 1:9 which were then separated by flash chromatography. They subsequently utilised the purified *anti* isomer as a useful building block for stereoselective synthesis of a number of diversely functionalized monosaccharides. However, in the two cases[9,11] the presence of the isopropylidene moiety in the aldehydes is likely to restrict their use under all conditions due to its greater affinity to be hydrolysed in a mild acidic environment during a reaction or work up causing difficulty in selective manipulation of the hydroxyl groups of their products.

The enormous synthetic potential of versatilely functionalised allylated[9] and propargylated products (entries d and e) led us to explore the viability of a more practical approach for their preparation. In view of this, **6** was subjected to Barbier type allylation and propargylation in the presence of water using Luche's procedure.[7] Both the reactions were carried out following similar experimental conditions as reported by us earlier in the case of **1**.[6] To our satisfaction, in both the cases using excess Zn and bromide, compound **6** was found to be reacted completely producing the desired homoallylic (entry d ii) and homopropargylic alcohols (entry e ii) in appreciable yield. The isolation of the product was facilitated during work up by treating the filtrate with acid to dissolve the suspended turbid material without affecting the stable cyclohexylidene moiety. The reactions were associated with a high improvement of stereoselectivity showing almost total formation (>99%) of *anti* products **8d** and **8e**. This was evident from the TLC and the spectral pattern in the region of δ 3.5–4.0 in the ^{1}H-NMR of the crude residue after the usual extraction and solvent removal under reduced pressure. Furthermore, any *syn* isomer could not be isolated by us after column chromatography. In this case the propargylation proceeded with the formation of a negligible amount (<1.5%) of the allene compound which was also evident from the ^{1}H-NMR spectrum of the residue (entry e ii).

In conclusion, **6** can be considered to be an easily accessible and effective precursor for the practical synthesis of a variety of functionalised diastereoalcohols whose contiguous stereocentres make them useful chiral building blocks for the synthesis of bioactive molecules. Moreover considering all the operational advantages associated with **6** *viz.* its relatively easy preparation without handling any toxic materials, functional stability, sufficiently good reactivity even in the presence of water, separability of

the diastereoisomers of its organometallated products by simple means like column chromatography etc., it has apparently an edge over the other reported aldehydes[9–11] of the same origin **2** from a practical viewpoint. Using the same reaction protocol with the commercially available enantiomer of **2**, the enantiomeric series of polyoxygenated chirons can be achieved with equal ease.

3. Experimental section

Chemicals used as starting materials are commercially available and were used without further purification unless otherwise mentioned. The IR spectra were recorded with a Perkin–Elmer spectrophotometer model 837. The PMR spectra were scanned with a Brucker AC-200 (200 MHz) instrument in $CDCl_3$. The optical rotations were measured with a Jasco DIP-360 polarimeter. The organic extracts were desiccated over Na_2SO_4.

3.1. (2S,3S)-2,3-Cyclohexylidene-butan-1,2,3,4-tetrol **4**

A solution of diethyl (L)-tartarate **2** (30.9 g, 0.15 mol), cyclohexanone (16 g, 0.16 mol) and PTS (~100 mg) in benzene (200 ml) was refluxed in a Dean–Stark apparatus for 6 h with continuous removal of water. The reaction was monitored with TLC and stopped when the starting material had been consumed. The solution was washed with 10% aqueous Na_2CO_3 and water and dried. Solvent removal under reduced pressure afforded the residue containing diester **3** in almost quantitative yield. It was taken in THF (100 ml). The solution was added dropwise to a cooled suspension of $LiAlH_4$ (8 g, 0.21 mol) in THF (100 ml) over a period of 2 h. The mixture was refluxed for another 2 h. Saturated aqueous solution of Na_2SO_4 was added dropwise to decompose the excess hydride. The mixture was filtered and the precipitate was washed with $CHCl_3$. Solvent removal under reduced pressure and column chromatography of the residue (silica gel, 0–5% MeOH in $CHCl_3$) afforded the diol **4**. Yield: 23.5 g (77.5%); $[\alpha]_D^{20}$ −5.27 (*c* 2.2, $CHCl_3$); IR (film): 3462, 1466, 1363, 1064, 837; ^{1}H-NMR ($CDCl_3$) δ 1.5–1.6 (m, 10H), 2.7 (bs, D_2O exchangeable, 2H), 3.6–4.2 (m, 6H). Anal. calcd For $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.19; H, 9.18.

3.2. (2S,3S)-2,3-Cyclohexylidene-4-silyloxybutane-1,2,3-triol **5**

To a stirred mixture of **4** (10.1 g, 0.05 mol) and imidazole (5.1 g, 0.075 mol) in CH_2Cl_2 (100 ml) was added *tert*-butyldimethylsilyl chloride (7.53 g, 0.05 mole) in portions over a period of 1.5 h. It was stirred for 2 h more and poured into water. After the usual extraction and solvent removal, the residue was chromatographed over SiO_2 column (0–20% EtOAc in petroleum ether) to afford **5**. Yield: 11.8 g (74.7%); $[\alpha]_D^{20}$ +3.54 (*c* 3.9, $CHCl_3$); IR (film) 3484, 2855, 1474, 1369, 1256, 1011, 950, 845; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0.88 (s, 9H), 1.5–1.6 (m, 10H), 2.9 (bs, D_2O exchangeable, 1H), 3.6–4.2 (m, 6H). Anal. calcd for $C_{16}H_{32}O_4Si$: C, 60.71; H, 10.19. Found: C, 60.87; H, 10.28.

*3.3. 4-O-[(*tert*)-Butyldimethylsilyl]-2,3-O-cyclohexylidene-*L*-threose* **6**

A mixture of **5** (3.16 g, 0.01 mol), DMSO (1.8 ml, 0.025 mol) and P_2O_5 (3.5 g, 0.025 mol) in CH_2Cl_2 (25 ml) was stirred at room temperature for 4 h. Triethylamine (5.6 ml, 0.04 mol) was added to it. The mixture was stirred for 2 h more, cooled with ice–water and treated with 5% aqueous HCl (15 ml). The organic layer was washed successively with water and brine and dried. Solvent removal under reduced

pressure gave the residue (2.7 g, 84.6%) containing the aldehyde **6**. As the aldehyde was found to be sufficiently pure but unstable on long standing, it was immediately used as such for the next step without being purified further. IR (film): 2855, 2720, 1735, 1474, 1369, 1256, 1120, 1011, 950, 845, 800; the pertinent signals and their relative intensity in ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0.88 (s, 9H), 1.5–1.6 (m, 10H), 3.7–4.4 (m, 4H), 9.8 (d, J=1.5 Hz, 1H).

3.4. *General procedure for the preparation of 7 and 8*

To a stirred solution of Grignard reagent at −50°C, prepared by treating halide (0.025 mol) with a suspension of Mg (720 mg, 0.03 g equiv.) in the required solvent (60 ml) (as shown in Table 1), was added **6** (3.14 g, 0.01 mol) in THF (30 ml) over a period of 1 h. The mixture was stirred at −50°C for 3 h and at room temperature overnight to ensure completion of the reaction. Saturated aqueous NH_4Cl was added followed by extraction with ether. The organic layer was washed with water and brine, dried, and evaporated under reduced pressure with 0–20% ethyl acetate in hexane resulting in the separation of pure **7** and **8**. In all the cases the minor *syn* isomer **7** was eluted first followed by the major *anti* isomer **8**. The R_f values on the TLC (16 cm plate) of all the isomers have been indicated.

3.5. *1-[(tert-Butyldimethylsilyl)oxy]-2,3-O-cyclohexylidene-octane-2,3,4-triol* **7a** *and* **8a**

3.5.1. *Minor (2S,3S,4R)-isomer* **7a**

Yield 901 mg (25.5%); R_f 0.63 (20% EtOAC/hexane); $[\alpha]_D^{20}$ −3.33 (*c* 0.9, $CHCl_3$); IR (film) 3461, 2857, 1463, 1363, 1254, 837; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0. 87 (s, 9H overlapped with a t, J=6 Hz, 3H), 1.24 (bs, 1H, D_2O exchangeable), 1.3–1.4 (m, 6H), 1.5–1.6 (m, 10H), 3.5–4.25 (m, 5H). Anal. calcd for $C_{20}H_{40}O_4Si$: C, 64.46; H, 10.82. Found: C, 64.57; H, 10.62.

3.5.2. *Major (2S,3S,4S)-isomer* **8a**

Yield 2.16 mg (57.9%); R_f 0.53 (20% EtOAC/hexane); $[\alpha]_D^{20}$ −1.17 (*c* 1.08, $CHCl_3$); IR (film) 3455, 2858, 1463, 1363, 1253, 837; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0. 87 (s, 9H overlapped with a t, J=6 Hz, 3H), 1.3–1.4 (m, 6H), 1.5–1.6 (m, 10H), 3.06 (bs, 1H, D_2O exchangeable), 3.6–4.0 (m, 5H). Anal. calcd for $C_{20}H_{40}O_4S$: C, 64.46; H, 10.82. Found: C, 64.63; H, 10.59.

3.6. *1-[(tert-Butyldimethylsilyl)oxy]-2,3-O-cyclohexylidene-nonane-2,3,4-triol* **7b** *and* **8b**

3.6.1. *Minor (2S,3S,4R)-isomer* **7b**

Yield 877 mg (22.7%); R_f 0.66 (20% EtOAC/hexane); $[\alpha]_D^{20}$ −5.79 (*c* 1.06, $CHCl_3$); IR (film) 3464, 2857, 1464, 1365, 1256, 837; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0.87 (s, 9H overlapped with a t, J=6 Hz, 3H), 1.3–1.4 (m, 8H), 1.5–1.6 (m, 10H), 2.35 (bs, 1H, D_2O exchangeable), 3.5–4.25 (m, 5H). Anal. calcd for $C_{21}H_{42}O_4Si$: C, 65.23; H, 10.95. Found: C, 65.34; H, 10.72.

3.6.2. *Major (2S,3S,4S)-isomer* **8b**

Yield 2.18 mg (56.7%); R_f 0.57 (20% EtOAC/hexane); $[\alpha]_D^{20}$ −1.15 (*c* 1.06, $CHCl_3$); IR (film) 3464, 2858, 1463, 1366, 1256, 837; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0. 87 (s, 9H overlapped with a t, J=6 Hz, 3H), 1.3–1.4 (m, 8H), 1.5–1.6 (m, 10H), 3.06 (bs, 1H, D_2O exchangeable), 3.6–4.0 (m, 5H). Anal. calcd for $C_{21}H_{42}O_4Si$: C, 65.23; H, 10.95. Found: C, 65.37; H, 10.89.

3.7. 1-[(tert-Butyldimethylsilyl)oxy]-2,3-O-cyclohexylidene-tetradecane-2,3,4-triol **7c** and **8c**

3.7.1. Minor (2S,3S,4R)-isomer **7c**

Yield 865 mg (18.9%); R_f 0.71 (20% ether/hexane); $[\alpha]_D^{20}$ +2.46 (*c* 3.6, $CHCl_3$); IR (film) 3464, 2857, 1464, 1365, 1256, 837; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0.9 (s, 9H overlapped with a t, *J*=6 Hz, 3H), 1.3–1.4 (m, 18H), 1.5–1.6 (m, 10H), 2.5 (bs, 1H, D_2O exchangeable), 3.5–4.25 (m, 5H). Anal. calcd for $C_{26}H_{52}O_4Si$: C, 68.36; H, 11.48. Found: C, 68.57; H, 11.62

3.8. Major (2S,3S,4S)-isomer **8c**

Yield 2.64 mg (57.9%); R_f 0.64 (20% ether/hexane); $[\alpha]_D^{20}$ +14.07 (*c* 2.6, $CHCl_3$); IR (film) 3464, 2858, 1463, 1366, 1256, 837; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0. 9 (s, 9H overlapped with a t, *J*=6 Hz, 3H), 1.3–1.4 (m, 18H), 1.5–1.6 (m, 10H), 3.06 (bs, 1H, D_2O exchangeable), 3.6–4.0 (m, 5H). Anal. calcd for $C_{26}H_{52}O_4Si$: C, 68.36; H, 11.48. Found: C, 68.63; H, 11.69.

3.9. 1-[(tert-Butyldimethylsilyl)oxy]-2,3-O-cyclohexylidene-6-heptene-2,3,4-triol **7d** and **8d**

3.9.1. Minor (2S,3S,4R)-isomer **7d**

Yield 807 mg (22.6%); R_f 0.72 (20% EtOAc/hexane); $[\alpha]_D^{20}$ −5.14 (*c* 1.56, $CHCl_3$); IR (film) 3453, 3082, 2857, 1640, 1364, 1254, 1004, 941, 911, 837; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0.88 (s, 9H), 1.5–1.6 (m, 10H), 2.2–2.5 (m, 2H), 2.9 (bs, 1H, D_2O exchangeable), 3.5–4.25 (m, 5H), 5.0–5.1 (m, 2H), 5.7–5.9 (m, 1H). Anal. calcd for $C_{19}H_{36}O_4Si$: C, 64.0; H, 10.18. Found: C, 63.89; H, 10.26.

3.9.2. Major (2S,3S,4S)-isomer **8d**

Yield 2.17 mg (60.9%); R_f 0.65 (20% EtOAc/hexane); $[\alpha]_D^{20}$ +9.09 (*c* 1.68, $CHCl_3$); IR (film) 3455, 3074, 2857, 1640, 1471, 1365, 1253, 1004, 941, 911, 837; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0.88 (s, 9H), 1.5–1.6 (m, 10H), 2.2–2.5 (m, 2H), 2.75 (bs, 1H, D_2O exchangeable), 3.6–4.0 (m, 5H) 5.0–5.1 (m, 2H), 5.7–5.9 (m, 1H). Anal. calcd for $C_{19}H_{36}O_4Si$: C, 64.0; H, 10.18. Found: C, 63.77; H, 10.19.

3.10. 1-[(tert-Butyldimethylsilyl)oxy]-2,3-O-cyclohexylidene-6-heptyne-2,3,4-triol **7e** and **8e**

3.10.1. Minor (2S,3S,4R)-isomer **7e**

Yield 522 mg (14.7%); R_f 0.63 (20% EtOAc/hexane); $[\alpha]_D^{20}$ −3.7 (*c* 3.06, $CHCl_3$); IR (film) 3440, 3310, 2857, 1369, 1254, 950, 845; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0.90 (s, 9H), 1.5–1.6 (m, 10H), 2.05 (t, *J*=1.5 Hz, 1H), 2.4–2.6 (m, 2H), 3.05 (bs, 1H, D_2O exchangeable), 3.5–4.25 (m, 5H). Anal. calcd for $C_{19}H_{34}O_4Si$: C, 64.36; H, 9.66. Found: C, 64.56; H, 9.82.

3.10.2. Major (2S,3S,4S)-isomer **8e**

Yield 2.26 mg (63.9%); R_f 0.57 (20% EtOAc/hexane); $[\alpha]_D^{20}$ +3.57 (*c* 1.06, $CHCl_3$); IR (film) 3445, 3300, 2857, 1471, 1365, 1253, 847; ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6H), 0. 88 (s, 9H), 1.5–1.6 (m, 10H), 2.05 (t, *J*=1.5 Hz, 1H), 2.4–2.6 (m, 2H), 2.9 (bs, 1H, D_2O exchangeable), 3.6–4.0 (m, 5H). Anal. calcd for $C_{19}H_{34}O_4Si$: C, 64.36; H, 9.66. Found: C, 64.27; H, 9.51.

3.11. General procedure for allylation and propargylation of 6

To a cooled (10°C) and well-stirred mixture of **6** (4.7 g, 0.015 mol), Zn dust (2 g, 0.03 mol for allylation; 3.4 g, 0.052 mol for propargylation) and bromide (3.63 g for allylation, 0.03 mol; 5.4 g for propargylation, 0.045 mol) in THF (50 ml) was added a saturated aqueous solution of NH_4Cl (1 ml) in portions over a period of 0.5 h. The reaction started vigorously soon after the addition of the first portion of the salt solution. The mixture was stirred for 4 h more for allylation or 6 h more for propargylation till the complete disappearance of the aldehyde (TLC). The mixture was filtered and washed with EtOAc. The organic layer was washed with 5% HCl to dissolve the suspended turbid material, then successively with 10% $NaHCO_3$, water and dried. Solvent removal under reduced pressure and column chromatography of the residue (silica gel, 0–20% EtOAc in petroleum ether) afforded **8d** (3.9 g, 73.8%) for allylation and **8e** (3.8 g, 71.7%) for propargylation.

3.12. (2S)-2-Benzoyloxyheptanal 10

To a solution of **8b** (965 mg, 0.0025 mol) in THF (15 ml) containing pyridine (3 ml) at 0°C was added benzoyl chloride (0.9 ml, 0.0075 mol) dropwise over a period of 30 min. After stirring the mixture for 2 h at 0°C and 2 h more at room temperature, it was poured into water and extracted with ether. The usual work up and solvent removal under reduced pressure afforded the residue benzoate. This was mixed with 90% aqueous trifluoroacetic acid (10 ml), stirred for 3 h at −70°C, and diluted with $CHCl_3$ and water. The aqueous layer was extracted with $CHCl_3$. The combined organic layer was washed successively with 2% $NaHCO_3$ and water until neutral. Solvent removal under reduced pressure gave the residue diol **9**. To a stirred solution of this diol in 60% aqueous acetonitrile (15 ml), was added $NaIO_4$ (1.0 g). The white precipitate started separating, then the mixture was stirred for 30 min more and filtered. The precipitate was washed with $CHCl_3$. The combined organic layer was washed with water and brine, and dried. Solvent removal under reduced pressure afforded the residue which was chromatographed (silica gel, 0–10% EtOAc in hexane) to furnish pure **10** (306 mg, 53.1%). Its spectral and optical data $[\alpha]_D^{20}$ −31.2 (*c* 1.44, CH_2Cl_2); were found to be identical with those previously reported[5] by us $[\alpha]_D^{20}$ −31.1 (*c* 1.41, CH_2Cl_2).

References

1. (a) Hanessian, S. *Total Synthesis of Natural Products: The Chiron Approach*, 1986 , Pegamon Press Ltd and references cited therein. (b) Mori, K. *The Total Synthesis of Natural Products*, ApSimon, J., Ed., John Wiley & Sons, 1992, Vol. 9 and references cited therein. (c) Hanessian, S. *Pure Appl. Chem.* **1993**, *65*, 1189.
2. (a) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 3. (b) Stephenson, G. R., *Advanced Asymmetric Synthesis*; Chapman & Hall, 1996. (c) Van Dranne, N. A.; Arsenayadis, S.; Crimnins, M. T.; Heathcock, C. H. *J. Org. Chem.*, **1991**, *56*, 2499. (d) Mulzer, J.; Altenbach, H. J.; Braun, M.; Krohn, K.; Reissig, H. U. *Organic Synthesis Highlights*; VCH: Weinheim, 1991; pp. 1–118. (e) *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983–85; Vol. 1–5. (f) Mukaiyama, T. *Org. React.* **1982**, *28*, 103. (g) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31 and references cited therein. (h) Hoffman, R. W. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 489. (i) Heathcock, C. H., In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, pp. 181–238. (j) Elliel, E. L.; Otsuka, S. *Asymmetric Reactions and Processes in Chemistry, ACS Symposium Series* 185, 1982. (k) Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.
3. (a) Li, C. *Chem. Rev.* **1993**, *93*, 2023. (b) Buse, C. T.; Heathcock, C. H. *Tetrahedron Lett.* **1978**, *19*, 1685. (c) Marshall, J. A.; Jabionowski, J. A.; Luke, J. P. *J. Org. Chem.* **1994**, *59*, 7825. (d) Yamammoto, Y.; Assao, N. *Chem. Rev.* **1993**, *93*, 2207. (e) Roush, W.; Banfi, L. *J. Am. Chem. Soc.* **1988**, *110*, 3979. (f) Brown, H. C.; Rana, R. S.; Bhat, K. S.; Zaidelwitcz, M.; Racheria, V. S. *J. Am. Chem. Soc.* **1990**, *112*, 2389. (g) Marshall, J. A.; Hinkle, K. H. *J. Org. Chem.* **1995**, *60*, 1912.

(h) Keck, G. E.; Savin, K. A.; Cressman, E. K.; Abbott, D. E. *J. Org. Chem.* **1994**, *59*, 7889. (i) Dondoni, A.; Orduna, J.; Merino, P. *Synthesis* **1992**, 201. (j) Carda, M.; Gonzalez, F.; Rodriguez, S.; Marco, J. A. *Tetrahedron: Asymmetry* **1992**, *3*, 1511. (k) Reetz, M. K.; Rotfling, K.; Griebenow, N. *Tetrahedron lett.* **1994**, *35*, 1969 and references cited therein. (l) Marco, J. L.; Martin, G.; Martinez-Grau, A.; Cano, F. H. *Tetrahedron* **1993**, *49*, 7133. (m) Sjechner, B.; Achmatowich, O.; Caldecki, Z. *Tetrahedron* **1994**, *50*, 7611.

4. (a) Heathcock, C. H.; Pirrung, M. C; Montegomery, S. H.; Lampe, J. *Tetrahedron*, **1981**, *37*, 4095. (b) Still, W. C.; McDonald, J. H. *Tetrahedron Lett.* **1980**, *21*, 1031. (c) Still, W. C.; Schneider, J. A. *Tetrahedron Lett.* **1980**, *21*, 1035. (d) Mulzer, J.; Angermann, A. *Tetrahedron lett.* **1983**, *24*, 2843. (e) Springer, J. B.; DeBoard, J.; Corcoran, R. C. *Tetrahedron Lett.* **1995**, *36*, 8733. (f) Fleischer, J. M.; Gushurst, A. J.; Jorgensen, W. L. *J. Org. Chem.* **1995**, *60*, 490. (g) Eliel, E. *Asymmetric Synthesis*; Morrison, J. D., Ed; Academic Press: Orlando; Vol. 2, pp. 125–155. (h) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron lett.* **1968**, 2199. (i) Anh, N. T. *Top. Crr. Chem.* **1980**, *88*, 145. (j) Evans, D. A.; Dart, M. J.; Duffy, J. L. *Tetrahedron lett.* **1994**, 8541.
5. Chattopadhyay, A.; Mamdapur, V. R. *J. Org. Chem.* **1995**, *60*, 585.
6. Chattopadhyay, A. *J. Org. Chem.* **1996**, *61*, 6104.
7. (a) Petrier, C.; Luche, J. L. *J. Org. Chem.* **1985**, *50*, 910. (b) Einhorn, C.; Luche, J. L. *J. Organomet. Chem.* **1987**, *322*, 177.
8. Chattopadhyay, A. *Tetrahedron: Asymmetry* **1997**, *8*, 2727.
9. Mukaiyama, T.; Suzuki, K.; Yamada, T.; Tabusa, F. *Tetrahedron* **1990**, *46*, 265 and references cited therein.
10. Iida, H.; Yamazaki, N.; Kibayashi, C. *J. Org. Chem.* **1986**, *51*, 3769.
11. Achmatowicz, B.; Wicha, J. *Liebigs. Ann. Chem.* **1988**, 1135.
12. Taber, D. F.; Amedio Jr., J. C.; Jung, K. Y. *J. Org. Chem.* **1987**, *52*, 5621.