Pergamon

SCIENCE DIRECT®

Tetrahedron: *Asymmetry* 14 (2003) 2195–2199

TETRAHEDRON: *ASYMMETRY*

Highly stereoselective synthesis of a seven-membered carbasugar via triisobutylaluminium promoted Claisen rearrangement

Cai Jia,[a] Yongmin Zhang[b] and Lihe Zhang[a,*]

[a]*National Research Laboratory of Natural and Biomimetic Drugs, School of Pharmaceutical Sciences, Peking University, 38 Xueyuan Road, Beijing 100083, PR China*

[b]*Ecole Normale Supérieure, Département de Chimie, UMR CNRS 8642, 24 rue Lhomond, 75231 Paris, Cedex 05, France*

Received 6 May 2003; accepted 12 June 2003

Abstract—2-Methylene-5-vinyl-tetrahydrofuran derivative **6** was obtained from α-D-glucose. Treatment of **6** with triisobutylaluminium (TIBAL) induced Claisen expansion reaction to give the seven-membered carbasugar derivative **7**, which represents a new type of chiral building blocks. The rearrangement reaction has been proved to be highly stereoselective.

1. Introduction

Carbocyclic sugars are important analogues of sugars. Owing to the replacement of their endocyclic oxygen atom by a methylene group, they have the advantage of being hydrolytically stable. When incorporated into biologically active molecules, such as nucleosides[1] and oligosaccharides,[2] this kind of analogue has a variety of remarkable biological behaviors, including antiviral, antitumor and antibiotic activities. For quite a long time, effort in the synthetic study of the carbasugars has been focused on five-membered[3] and six-membered[4] carbocyclic sugars. Compounds containing a seven-membered-ring carbocycle are widely present as a structural motif in natural products,[5] some of which have interesting biological activities.[6] However, the synthesis of medium-sized rings, notably seven and eight-membered ring systems, has been a challenge for synthetic chemists. Several synthetic methods have been reported for the asymmetric synthesis of seven-membered carbocyclic frameworks.[7]

Among the different synthetic approaches for carbocycles, the conversion of a carbohydrate into a target compound is an attractive methodology. The Claisen rearrangement of allyl vinyl ethers is commonly used for the stereoselective carbon–carbon bond formation and organoaluminum reagents have been widely investigated as reagents.[8] Paquette et al. developed an elegant TIBAL-promoted Claisen rearrangement of 2-methylene-6-vinyl-tetrahydropyrans to afford cyclooctane derivatives.[9] A full account of the same arrangement in a glucopyranoside derivative has also been given, offering a new alternative to conventional carbohydrates.[10] Herein we report the TIBAL-promoted sigmatropic rearrangement of 3,4-*O*-dibenzyl-2-methylene-5-vinyl-tetrahydrofuran, which provides a practical way to prepare seven-membered carbasugars, a new type of chiral building blocks.

2. Results and discussion

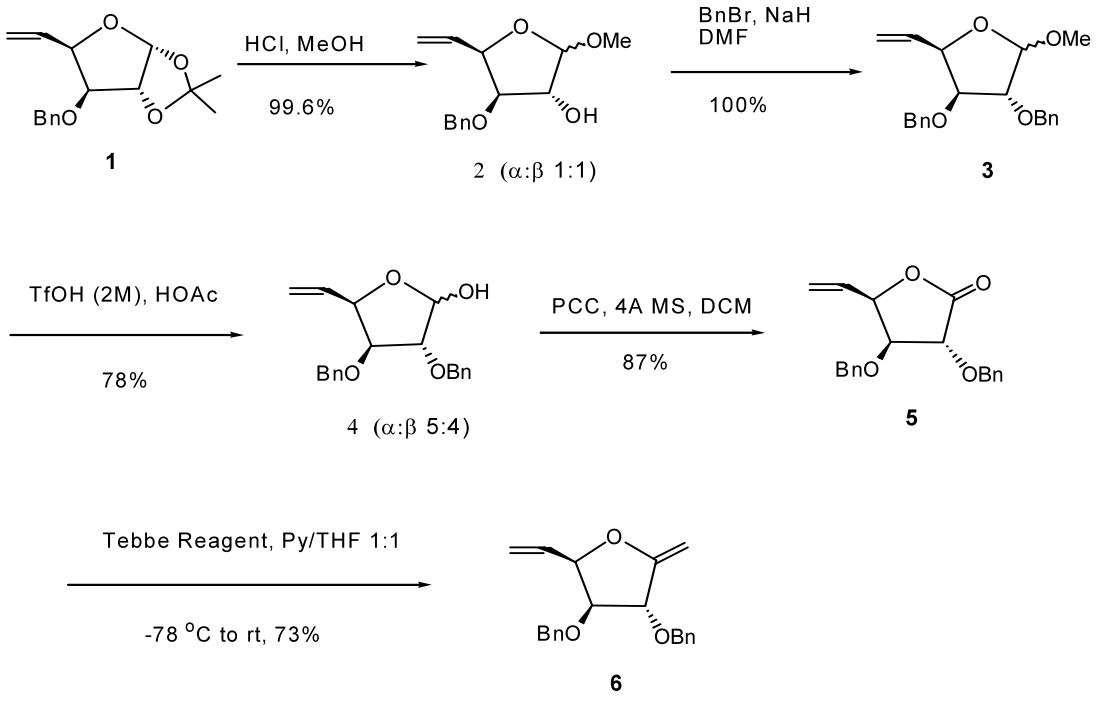
Compound **1**, 1,2-*O*-isopropylidene-3-*O*-benzyl-4-vinyl-hydrofuranose, was easily obtained from α-D-glucose in a five-step sequence, which we have described.[11] Compound **1** was treated with a methanol solution of hydrochloride to give **2**, as a mixture of α-and β-isomers. Benzylation of **2** followed by demethylation generated the intermediate **4**, also as a mixture of α- and β-isomers. This mixture of **4** was then used for the next step. Oxidation of **4** with PCC, in the presence of 4 Å molecular sieves, in dichloromethane afforded the lactone **5**. Subsequent treatment of **5** with Tebbe's Reagent, $[Cp_2Ti(\mu\text{-}Cl)(\mu\text{-}CH_2)AlMe_2]$, gave 73% yield of the key intermediate 3,4-*O*-dibenzyl-2-methylene-5-vinyl tetrahydrofuran **6**. As compound **6** is unstable in acidic conditions, purification was carried out through a silica gel column eluting with petroleum ether:ethyl

* Corresponding author. Tel.: 86-10-6209-1700; fax: 86-10-6209-2724; e-mail: zdszlh@tree.bjmu.edu.cn

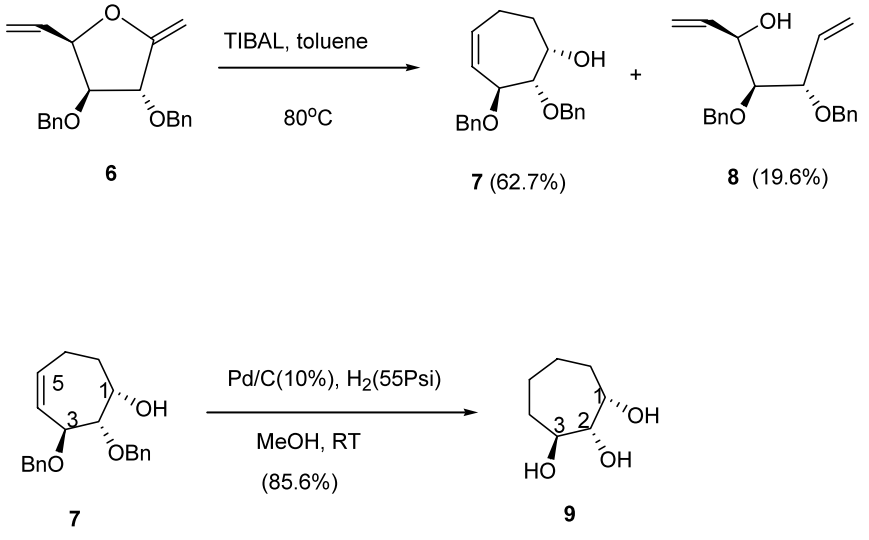
0957-4166/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0957-4166(03)00490-7

acetate (100:1), modulated by 0.03% of Et_3N. The ^{13}C NMR of **6** showed the new carbon signal in 85.85 (C-1) and the molecular weight was identified with the designed compound (Scheme 1).

First we tried a Claisen-rearrangement reaction of compound **6** in boiling xylene but with no result. However, the rearrangement reaction was promoted by triisopropylaluminium (TIBAL). After optimizing the reaction conditions, TIBAL (10 equiv.) was added at room temperature to a solution of compound **6** (0.122 g, 0.38 mmol) in anhydrous toluene (15 ml) under argon. The reaction was then heated to 80°C. When TLC indicated the disappearance of the starting material, the reaction was completed. The reaction mixture was purified by a silica gel column to afford the product **7**, in a yield of 62.7%. ^{13}C NMR of compound **7** showed that the signals of the terminal double bonds at C-1 (85.85 ppm) and C-7 (118.57 ppm) disappeared and that a new double bond between C-4 (81.48 ppm) and C-5 (70.91 ppm) in the seven membered ring was formed. The coupling constant of H-4 and H-5 ($J=3.0$ Hz) in the ^1H NMR indicated the existence of a *cis*-double bond. From the reaction mixture, compound **8** was obtained in a yield of 19.6%. When comparing the molecular weights and NMR spectra of compounds **8** (325.1824) and **6** (323.1613), it was suggested that compound **8** was formed from compound **6** by ring-open and reduction (Scheme 2).

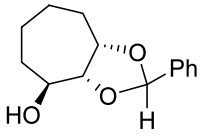


Scheme 1.



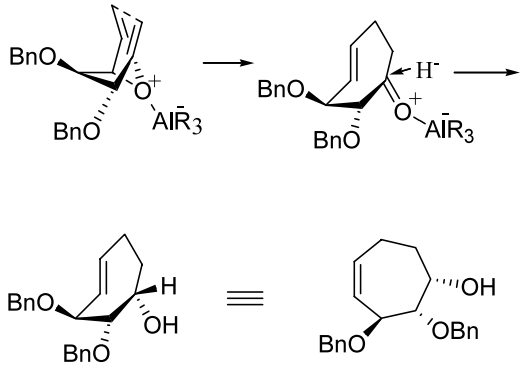
Scheme 2.

Compound **7** contains three stereogenic centers. The configurations of C-2 and C-3 are the same as compound **6** and the coupling constants of $J_{3,4}=4.0$ Hz and $J_{2,3}=8.5$ Hz in ^{1}H NMR of compound **6** indicate no change of configuration at these two carbons during this rearrangement. Only C-1 is formed from the reaction. There are two possibilities of the configuration of C-1 in compound **7**. However, compound **7** was hydrogenated over Pd/C to give compound **9** (Scheme 2). The $[\alpha]_D^{20}$ of compound **9** was +10.8 (*c* 0.315, MeOH) and showed an asymmetric structure. If the hydroxyl group at C-1 is *trans* to the C-2 OH group and *cis* to the C-3 OH group, then compound **9** would be a symmetric structure and thus an optically inactive substance. ^{1}H NMR of compound **9** also showed $J_{1,2}=2.8$ Hz and $J_{2,3}=7.2$ Hz to identify the existence of 1,2-*cis* OH and 2,3-*trans* OH. Compound **9** reacted with benzaldehyde dimethyl acetal under acidic conditions to give compound **10**. The ^{1}H and ^{13}C NMR indicate that compound **10** is an acetal formed from the two *cis*-hydroxyl groups of compound **9**. All data considered, the configuration of C-1 is (*S*) with the two hydroxyl groups at C-1and C-2 located on the same side of the seven-membered ring. The mechanism of this Claisen rearrangement reaction was suggested as follows (Scheme 3). The chair form of the transition state favors the H^- attack to form the *cis* C-1 OH compound.



10

In conclusion, we have developed a novel and highly stereoselective access to substituted seven-membered carbasugars starting from α-D-glucose. Due to the growing number of natural products containing seven-membered rings with biological activity, this synthetic method will be useful for a variety of rational designs directed toward the synthesis of some molecules with potential therapeutic interest. This approach also provides new types of chiral building blocks for the synthesis of natural products.



Scheme 3.

3. Experimental

3.1. General

TLC: silica-gel-GF-254 (Qing Dao Chemical Company, China) plate with detection by UV. NMR Spectra: Varian VXR-300, Bruker DPX-400 or Varian INOVA-500; δ in ppm rel. to $SiMe_4$ as an internal standard, *J* in Hz. MS: VG-ZAB-Hs, KYKY-ZHP-5 and APEX II FTICR in *m*/*z*.

3.2. 1-*O*-Methyl-3-*O*-benzyl-5,6-dideoxy-5-ene-D-glucofuranose 2

Compound **1** (4.8 g, 17.4 mmol) was dissolved in a solution of HCl in methanol (1% mol/V) and stirred. When TLC showed the absence of the material **1**, the solution was neutralized with NaOH and filtered. The filtrate was concentrated and then extracted with $CHCl_3$ and H_2O. The organic layers were combined and concentrated. The residue was purified through a silica gel column to give the product as a colorless oil (4.3 g, 90%). The product was a mixture of two isomers with α- and β-configuration (α:β = 1:1).

2 (α-configuration), ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.46 (s, 3H, OCH_3), 3.95 (dd, $J=4.2$ Hz, $J=5.7$ Hz, 1H, H_3), 4.23 (br.S, 1H, H_2), 4.58, 4.61 (2d, $J=12.3$ Hz, 2H, $PhCH_2$), 4.61 (m, 1H, H_4), 4.95 (d, $J_{1,2}=4.8$ Hz, 1H, H_1), 5.26 (d, $J_{5,6a}=10.5$ Hz, 1H, H_{6a}), 5.38 (d, $J_{5,6b}=17.4$ Hz, 1H, H_{6b}), 6.00 (m, 1H, H_5), 7.23–7.32 (m, 5H, aromatic H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 55.55 (OCH_3), 71.65 ($PhCH_2$), 76.51 (C_4), 79.55 (C_3), 84.28 (C_2), 101.49 (C_1), 118.26 (C_6), 127.34∼128.16 (5C, aromatic C), 133.68 (C_5), 137.72 (C-*ipso*). HRFAM-MS (*m*/*z*): calcd for $C_{14}H_{18}O_4Na$ $[M+Na]^+$ 273.1097, found 273.1099.

2 (β-configuration), ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.41 (s, 3H, OCH_3), 3.91 (dd, $J_{2,3}=3.6$ Hz, $J_{3,4}=6.3$ Hz, 1H, H_3), 4.20 (br.S, 1H, H_2), 4.56 (s, 2H, $PhCH_2$), 4.64 (t, $J=6.9$ Hz, 1H, H_4), 4.77 (d, $J_{1,2}=2.4$ Hz, 1H, H_1), 5.25 (d, $J_{5,6a}=10.2$ Hz, 1H, H_{6a}), 5.31 (d, $J_{5,6b}=17.4$ Hz, 1H, H_{6b}), 6.06 (m, 1H, H_5). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 55.68 (OCH_3), 72.06 ($PhCH_2$), 79.46 (C_4), 82.08 (C_3), 83.81 (C_2), 108.90 (C_1), 118.32 (C_6), 127.68∼128.34 (5C, aromatic C), 134.77 (C_5), 137.59 (C-*ipso*). HRFAB-MS (*m*/*z*): calcd for $C_{14}H_{18}O_4Na$ $[M+Na]^+$ 273.1097, found 273.1100.

3.3. 1-*O*-Methyl-2,3-di-*O*-benzyl-5,6-dideoxy-5-ene-D-glucofuranose 3

NaH (80%, 1.20 g, 62.5 mmol) was suspended in dried DMF with compound **2** (3.93 g, 15.7 mmol). BnBr (3.70 ml, 30.51 mmol) was dropped in the solution. The mixture was stirred and when TLC showed the absence of compound **2**, DMF was removed under vacuum. The residue was dissolved with EtOAc, dried, concentrated and purified through a silica gel column. The column was eluted by petroleum ether and ethyl acetate (30:1). The product was an oily mixture of α- and β-configuration (5.01 g, 94.5%).

3 (β configuration) ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.42 (s, 3H, OCH_3), 4.03 (m, 2H, H_2, H_3), 4.53 (m, 4H, $2PhCH_2$), 4.64 (m, 1H, H_4), 4.91 (d, $J_{1,2}=1.5$ Hz, 1H, H_1), 5.26 (d, $J_{5,6a}=10.2$ Hz, 1H, H_{6a}), 5.38 (d, $J_{5,6b}=17.4$ Hz, 1H, H_{6b}), 6.11 (m, 1H, H_5), 7.24–7.36 (m, 10H, aromatic H). ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 55.62 (OCH_3), 71.97, 72.01 ($2PhCH_2$), 82.32 (C_4), 82.47 (C_3), 87.10 (C_2), 107.92 (C_1), 118.37 (C_6), 127.69–128.40 (10C, aromatic C), 134.88 (C_5), 137.54, 137.72 (2C-*ipso*). HRFAB-MS (*m*/*z*): calcd for $C_{21}H_{24}O_4Na$ $[M+Na]^+$ 363.1567, found 363.1565.

3 (α-configuration), ^{1}H NMR (300 MHz, $CDCl_3$): δ ppm 3.41 (s, 3H, OCH_3), 4.01 (dd, $J_{1,2}=4.5$ Hz, $J_{2,3}=6.0$ Hz, 1H, H_2), 4.29 (t, $J=6.0$ Hz, 1H, H_3), 4.53, 4.55 (2d, 2H, $PhCH_2$), 4.63 (m, 2H, $PhCH_2$), 4.64 (m, 1H, H_4), 4.80 (d, $J_{1,2}=4.2$ Hz, 1H, H_1), 5.27 (d, $J_{5,6a}=10.2$ Hz, 1H, H_{6a}), 5.33 (d, $J_{5,6b}=17.1$ Hz, 1H, H_{6b}), 5.99 (m, 1H, H_5), 7.25–7.36 (m, 5H, aromatic H) ^{13}C NMR (75 MHz, $CDCl_3$): δ ppm 55.23 (OCH_3), 72.25, 72.59 ($PhCH_2$), 78.57 (C_4), 82.40 (C_3), 83.58 (C_2), 100.51 (C_1), 118.63 (C_6), 127.64∼128.37 (10C, aromatic C), 134.16 (C_5), 137.69, 137.93 (2C-*ipso*). HRFAB-MS (*m*/*z*): calcd for $C_{21}H_{24}O_4Na$ $[M+Na]^+$ 363.1567, found 363.1567.

3.4. 2,3-Di-*O*-benzyl-5,6-dideoxy-5-ene-D-glucofuranose 4

Compound **3** (0.251 g, 0.74 mmol) was dissolved in a solution of AcOH (7.4 ml) and TfOH (2 M, 1.48 ml) and heated at 80°C. When TLC showed the absence of the material, the reaction mixture was cooled down to rt, added to CH_2Cl_2 (10 ml) and neutralized with saturated solution of $NaHCO_3$ at 4°C. The mixture was extracted with CH_2Cl_2 (2×30 ml). The organic layer was separated, then concentrated and purified through a silica gel column eluting with petroleum ether and ethyl acetate to obtain a colorless oily mixture (0.188 g, 78.4%, α:β = 5:4).

3.5. 1-Dehydro-2,3-di-*O*-benzyl-5,6-dideoxy-5-ene-D-glucofuranose 5

PCC (0.55 g, 2.55 mmol) and 4 Å MS (0.30 g) were mixed in CH_2Cl_2 (20 ml) under argon. The solution of compound **4** (0.165 g, 5.06 mmol) in CH_2Cl_2 was then cooled to 0°C and stirred at rt. When TLC showed the absence of the material of compound **4**, the reaction mixture was purified on a silica gel column eluting by petroleum ether and ethyl acetate (10:1) to give a colorless oil (0.136 g, 83.0%).

5: $[\alpha]_D^{20}=+108.9$ (*c* 2.2, MeOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 4.22 (d, $J_{2,3}=6.4$ Hz, 1H, H_2), 4.27 (t, $J=6.4$ Hz, 1H, H_3), 4.56, 4.59 (2d, $J=12$ Hz, 2H, $PhCH_2$), 4.72, 4.97 (2d, $J=12$ Hz, 2H, $PhCH_2$), 5.00 (m, $J_{3,4}=6.4$ Hz, $J_{4,5}=6.2$ Hz, $J_{4,6}=1.2$ Hz, 1H, H_4), 5.36, 5.39 (2t, $J_{5,6a}=10.4$ Hz, $J_{4,6}=1.2$ Hz, 1H, H_{6a}), 5.41, 5.45 (2t, $J_{5,6b}=17.2$ Hz, $J_{4,6}=1.2$ Hz, 1H, H_{6b}), 5.99 (m, $J_{4,5}=6.2$ Hz, $J_{5,6a}=10.4$ Hz, $J_{5,6b}=17.2$ Hz, 1H, H_5, 7.26∼7.37 (m, 10H, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 72.44, 72.59 ($2PhCH_2$), 76.74 (C_3), 79.67 (C_5), 79.89 (C_4), 119.70 (C_7), 127.76–128.58 (10C, aromatic C), 131.28 (C_6), 136.84, 136.97 (2C-*ipso*), 172.53 (C_2). HRFAB-MS (*m*/*z*): calcd for $C_{20}H_{20}O_4Na$ $[M+Na]^+$ 347.1254, found 347.1252.

3.6. 1,5,6-Trideoxy-1-methylidene-3,4-di-*O*-benzyl-5-ene-D-glucofuranose 6

When the solution of compound **5** (0.208 g, 0.64 mmol) in THF/Py (20 ml/20 ml) was cooled down to −78°C, Tebbe's reagent (0.5 mol/l, 2.7 ml) was dropped into the solution. The reaction mixture was stirred from −78°C to rt. When TLC showed the absence of material **5**, the mixture was cooled with ice water bath and quenched with NaOH solution of water (10%, 0.88 ml) and then filtered. The filtrate was concentrated and the residue was purified with a silica gel column eluting by petroleum ether and ethyl acetate (100:1) with 0.03% Et_3N (V/V). The product **6** was colorless oil (0.151 g, 73.0%). $[\alpha]_D^{20}=+2.9$ (*c* 1.2, MeOH), ^{1}H NMR: δ ppm 3.95 (dd, $J_{3,4}=3.9$ Hz, $J_{3,1}=1.8$ Hz, 1H, H_3), 4.28, 4.88 (2d, 2H, H_1), 4.30, 4.34 (2d, $J=12.1$ Hz, 2H, $PhCH_2$), 4.37 (s, 1H, H_5), 4.43, 4.69 (2d, $J=11.6$ Hz, 2H, $PHCH_2$), 4.98 (q, $J_{4,3}=3.9$ Hz, $J_{4,5}=7.5$ Hz, 1H, H_4), 5.18 (d, $J_{6,7a}=10.8$ Hz, 1H, H_{7a}), 5.35 (d, $J_{6,7b}=17.2$ Hz, 1H, H_{7b}), 6.24 (m, 1H, H_6), 7.17-7.36 (m, 10H, aromatic H). ^{13}C NMR (100 MHz, Benzene-d^6): δ ppm 70.01, 71.80 ($2PhCH_2$), 80.90 (C_5), 83.39 (C_3), 84.19 (C_4), 85.85 (C_1), 118.57 (C_7), 127.39–128.36 (10C-aromatic), 133.30 (C_6), 138.02, 138.19 (2C-*ipso*), 159.97 (C_2). HRFAB-MS (*m*/*z*): calcd for $C_{21}H_{23}O_3$ $[M+H]^+$ 323.1647, found 323.1613.

3.7. (1S,6S,7S)-2,3-Dibenzyloxycyclohepta-4-en-1-ol 7

TIBAL (1 mol/l, 3.90 ml) in toluene was added to a solution of compound **6** (0.122 g, 0.38 mmol) in toluene (15 ml) at rt under argon. The mixture was heated to 80°C and stirred. When TLC showed the absence of compound **6**, the reaction solution was cooled down to 0°C and quenched with ice water (8 ml). The mixture was filtered and the filtrate extracted with EtOAc. The organic layers were combined, dried and concentrated. The residue was purified on a silica gel column eluting by petroleum and ethyl acetate (30:1). Two products **7** (colorless oil, 77 mg, 62.7%) and **8** (colorless oil, 24 mg, 19.6%) were obtained.

7: $[\alpha]_D^{20}=-300.2$ (*c* 0.5, $CHCl_3$), ^{1}H NMR (500 MHz, $CDCl_3$): δ ppm 1.67–1.73, 1.76–1.85 (2m, 2H, H_7), 1.94–2.01, 2.28–2.34 (2m, 2H, H_6), 3.61 (dd, $J_{2,3}=8.5$ Hz, $J_{1,2}=3.0$ Hz, 1H, H_2), 4.16 (m, $J_{1,2}=3.0$ Hz, $J_{1,7a}=3.8$ Hz, $J_{1,7b}=7.5$ Hz, 1H, H_1), 4.47 (dd, $J_{3,4}=4.0$ Hz, $J_{3,2}=8.5$ Hz, $J_{3,5}=1.5$ Hz, 1H, H_3), 4.63, 4.66 (2d, $J=12$ Hz, 2H, $PhCH_2$), 4.64, 4.83 (2d, $J=12$ Hz, 2H, $PhCH_2$), 5.70 (dd, $J_{4,5}=11.5$ Hz, $J_{3,4}=4.0$ Hz, 1H, H_4), 5.93 (m, $J_{4,5}=11.5$ Hz, $J_{5,6}=6.0$ Hz, $J_{3,5}=1.5$ Hz, 1H, H_5), 7.25∼7.34 (m, 10H, aromatic H). ^{13}C NMR (125 MHz, $CDCl_3$): δ ppm 21.73 (C_6), 30.68 (C_7), 70.91 (C_1), 72.21, 73.67 (2C, $2PhCH_2$), 75.56 (C_3), 81.48 (C_2), 127.43–128.39 (10C, aromatic C), 131.57 (C_4), 133.10 (C_5), 138.53, 138.71 (2C-*ipso*). HRFAB-MS (*m*/*z*): calcd for $C_{21}H_{24}O_3Na$ $[M+Na]^+$ 347.1618, found

347.1619. **8** ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 3.43 (dd, $J_{3,4}=3.6$ Hz, $J_{4,5}=6$ Hz, 1H, H_4), 4.07 (m, $J_{4,5}=6$ Hz, 1H, H_5), 4.27 (br.s, 1H, H_3), 4.40, 4.63 (2d, $J=11.6$ Hz, 2H, $PhCH_2$), 4.63, 4.82 (2d, $J=11.2$ Hz, 2H, $PhCH_2$), 5.16 (2t, $J_{2,1a}=10.5$ Hz, 1H, H_{1a}), 5.30 (2t, $J_{2,1b}=17.2$ Hz, 1H, H_{1b}), 5.36 (2br.t, 1H, H_{7a}), 5.41 (2br.t, 1H, H_{7b}), 5.87 (m, 1H, H_2), 5.91 (m, 1H, H_2), 7.26–7.33 (m, 10H, aromatic H). ^{13}C NMR (100 MHz, $CDCl_3$): δ ppm 70.71, 75.23 (2C, $2PhCH_2$), 72.04 (C_3), 81.77 (C_5), 83.93 (C_4), 115.78 (C_1), 119,45 (C_7), 127.59–128.36 (10C, aromatic C), 135.42 (C_6), 138.24, 138.28 (2C-*ipso*), 138.33 (C_2). HRFAB-MS (m/z): calcd for $C_{21}H_{25}O_3$ $[M+H]^+$ 325.1804, found 325.1824.

3.8. (1*S*,2*R*,3*S*)-2,3-*O*-Benzylidene cycloheptanol 10

Compound **7** (14.0 mg, 0.043 mmol) was dissolved in dried MeOH (14.0 ml) containing Pd/C (10%, 6 mg). The hydrogenation was carried on at rt under 55 Psi of H_2. When TLC showed the absence of the starting compound, the mixture was filtered. The filtrate was concentrated to give a colorless oil of compound **9** (5.6 mg, 86%), $[\alpha]_D^{20}=+10.8$ (c 0.315, MeOH). ^{1}H NMR (400 MHz, D_2O): δ ppm 1.38 (m, 2H, $1H_5$, $1H_6$), 1.5 (m, 4H, $1H_4$, $1H_7$, $1H_5$, $1H_6$), 1.70 (m, 2H, $1H_4$, $1H_7$), 3.56 (dd, $J_{1,2}=2.8$ Hz, $J_{2,3}=7.2$ Hz, 1H, H_2), 3.63 (dt, $J_{3,4}=3.2$ Hz, $J_{2,3}=7.2$ Hz, $J_{3,4'}=7.2$ Hz, 1H, H_3), 3.92 (dt, $J_{1,2}=2.8$ Hz, $J_{1,7}=8.8$ Hz, $J_{1,7'}=2.0$ Hz, 1H, H_1). ^{13}C NMR (100 MHz, D_2O): δ ppm 23.33 (C_6), 23.91 (C_5), 30.21(C_7), 32.78 (C_4), 72.55 (C_1), 74.57 (C_3), 79.39 (C_2). HRFAB-MS (m/z): calcd for $C_7H_{14}O_3Na$ $[M+Na]^+$ 169.0841, found 169.0828.

Compound **9** (3.1 mg, 0.021 mmol) was dissolved into acetonitrile (2.0 ml) and reacted with benzaldehyde dimethyl acetal (4 μl) and DL-10 camphorsulfonic acid (0.4 mg) at rt under argon overnight. The reaction mixture was neutralized using triethylamine and concentrated. The residue was purified on silica gel column eluting with petroleum and ethyl acetate to give compound **10** (2.8 mg) as two diastereoisomers (1: 0.7) in 56% yield. **10**: ^{1}H NMR (400 MHz, acetone-d^6): δ ppm 1.27–2.08 (m, 13.6H, $4CH_2$), 3.82 (dd, $J=2.8$ Hz, $J=9.0$ Hz, H_2), 3.86 (m, 1H, $H_{3'}$), 4.10 (t, $J=8.0$ Hz, 1H, $H_{2'}$), 4.23 (m, 0.7H, H_3), 4.28 (m, 1H, $H_{1'}$), 4.42 (m, 0.7H, H_1), 5.73 (s, 1H, PhCH′), 5.91 (s, 0.7H, PhCH), 7.36–7.51 (m, 8.5H, aromatic H); ^{13}C NMR (100 MHz, acetone-d^6): δ ppm 21.24, 24.82, 25.87, 27.70, 31.42, 34.62, 34.82, 34.87, 66.89 (C_3), 72.35 ($C_{3'}$), 76.29 (C_1), 79.14 ($C_{1'}$), 84.59 (C_2), 85.41 ($C_{2'}$), 103.56, 104.77, 127.49, 127.82, 128.80, 128.84, 129.62, 129.92, 138.75, 140.16. HRFAB-MS (m/z): calcd for $C_{14}H_{19}O_3$ $[M+H]^+$ 235.1329, found 235.1331.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (20128002).

References

1. (a) Crimmins, M. T. *Tetrahedron* **1998**, *54*, 9229–9272; (b) Zhu, X. F. *Nucleosides, Nucleotides & Nucleic Acid* **2000**, *19*, 651–690.
2. (a) Angelaud, R.; Landais, Y.; Parra-Rapado, L. *Tetrahedron Lett*. **1997**, *38*, 8845–8848; (b) Ferrito, R.; Vogel, P. *Tetrahedron Lett*. **1995**, *36*, 3517–3518.
3. (a) Bodenteich, M.; Marquez, V. E. *Tetrahedron* **1992**, *48*, 5961–5968; (b) Désiré, J.; Prandi, J. *Tetrahedron Lett*. **1997**, *38*, 6189–6192; (c) Yakura, Y.; Ueki, A.; Kitamura, T.; Tanaka, K.; Nameki, M.; Ikeda, M. *Tetrahedron* **1999**, *55*, 7461–7470; (d) Horneman, A. M.; Lundt, I.; Inge, L. *Tetrahedron* **1997**, *53*, 6879–6892; (e) Marschner, C.; Baumgartner, J.; Griengl, H. *J. Org. Chem*. **1995**, *60*, 5224–5235.
4. (a) Arjona, O.; Iradier, F.; Medel, R.; Plumet, J. *Tetrahedron: Asymmetry* **1999**, *10*, 3431–3442; (b) Das, S. K.; Mallet, J. M.; Sinaÿ, P. *Angew. Chem., Int. Ed. Engl*. **1997**, *36*, 493–496.
5. (a) Wender, P. A.; Rice, K. D.; Schnute, M. E. *J. Am. Chem. Soc*. **1997**, *119*, 7897–7898; (b) Malpass, J. R.; Wallis, A. L. *Tetrahedron* **1998**, *54*, 3631–3644; (c) Wender, P. A.; Husfeld, C. O.; Langkopf, E.; Love, J. A. *J. Am. Chem. Soc*. **1998**, *120*, 1940–1941; (d) Molander, G. A. *Acc. Chem. Res*. **1998**, *31*, 603–609; (e) Winkler, J. D.; Rouse, M. B.; Greaney, M. F.; Harrison, S. J.; Jeon, Y. T. *J. Am. Chem. Soc*. **2002**, *124*, 9726–9728; (f) Tanino, K.; Onuki, K.; Asano, K.; Miyashita, M.; Nakamura, T.; Takahashi, Y.; Kuwajima, Y. *J. Am. Chem. Soc*. **2003**, *125*, 1498–1500.
6. Goldmann, A; Milat, M. L.; Ducrot, P. H.; Lallemand, J. Y.; Maille, M.; Lepingle, A.; Charpin, I.; Tepfer, D. *Phytochemistry* **1990**, *29*, 2125–2127.
7. (a) Fatig, T.; Soulié, J.; Lallemand, J. Y.; Ricard, L. *Tetrahedron: Asymmetry* **1999**, *10*, 2165–2174; (b) Barco, A.; Benetti, S.; De Risi, C.; Marchetti, P.; Pollini, G. P.; Zanirato, V. *Tetrahedron* **1999**, *55*, 5923–5930; (c) Lautens, M.; Rovis, T. *J. Am. Chem. Soc*. **1997**, *119*, 11090–11091; (d) Yoshizaki, H.; Yoshioka, K.; Sato, Y.; Mori, M. *Tetrahedron* **1997**, *53*, 5433–5454.
8. (a) Mori, I.; Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron* **1984**, *40*, 4013–4018; (b) Nonoshita, K.; Banno, H.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc*. **1990**, *112*, 316–322; (c) Maruoka, K.; Saito, S.; Yamamoto, H. *J. Am. Chem. Soc*. **1995**, *117*, 1165–1166; (d) Maeda, K.; Shinokubo, K.; Oshima, K.; Utimoto, K. *J. Org. Chem*. **1996**, *61*, 2262–2263.
9. Paquette, L. A.; Philippo, C. M. G.; Vo, N. H. *Can. J. Chem*. **1992**, *70*, 1356–1365.
10. Wang, W.; Zhang, Y.; Zhou, H.; Blériot, Y.; Sinaÿ, P. *Eur. J. Org. Chem*. **2001**, 1053–1059.
11. Tian, X. B.; Min, J. M.; Zhang, L. H. *Tetrahedron: Asymmetry* **2000**, *11*, 1877–1889.