

A new and efficient route to derivatives of (*R*)-4-hydroxycyclohex-2-enone

Libing Yu, Ruzhou Zhang*† and Zhiqin Wang

Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

Received (in Cambridge, UK) 7th August 2001, Accepted 26th September 2001

First published as an Advance Article on the web 30th October 2001

A new and efficient route has been developed to four derivatives of (*R*)-4-hydroxycyclohex-2-enone (**7–10**) from one intermediate, **6**. These derivatives are useful chiral building blocks in the synthesis of natural products and in asymmetric reactions. The key step is a stereoselective intramolecular ene reaction with 4 Å MS as the Lewis acid and catalyst.

Introduction

Since polyoxygenated carbocyclic fragments are abundant in a variety of natural products, there is a constant need for the development of a general method for the stereoselective synthesis of these compounds with a view to natural product total synthesis and the development of efficient routes to new pharmaceuticals. The title compounds are considered to be very useful chiral starting materials and are found to be structural units in many natural products with biological activity, such as ML-236A,¹ compactin,¹ FK-506,² koniginin³ and rapamycin,⁴ *etc.* (Fig. 1). Furthermore, the compounds (*R*)- and (*S*)-4-hydroxycyclohex-2-enone can be used with excellent diastereoselectivity in Diels–Alder reactions as the dienophile and in 1,2- or 1,4-conjugate additions as the Michael acceptor. This has encouraged organic chemists to develop syntheses of (*R*)- and (*S*)-4-hydroxycyclohex-2-enone and their derivatives.

Winterfeldt and co-workers developed a simple approach to (*S*)-4-hydroxycyclohex-2-enone by using the reversibility of the Diels–Alder reaction with the configurationally well-defined cyclopentadiene as a chiral template.⁵ To complete their synthesis of (*R*)- and (*S*)-4-hydroxycyclohex-2-enone, Solladié and co-workers applied a chiral sulfoxide as the auxiliary, which was eliminated in the final step to form the conjugated double bond.⁶ Danishefsky and co-workers developed a multistep procedure starting from (–)-quinic acid in the total synthesis of FK-506,⁷ and emphasised the importance of the configuration of 4-hydroxycyclohex-2-enone because “all stereochemistry is introduced by communication from the single stereogenic center at C-4 of this compound” in the syntheses of ML-236A and compactin with racemic 4-hydroxycyclohex-2-enone as the starting material.¹ Yamamoto and co-workers reported a cyclization approach to this kind of compound, which involved a stereocontrolled intramolecular ene reaction with methylaluminum bis(4-bromo-2,6-di-*tert*-butylphenoxide) (MABR) as the Lewis acid.⁸ In the present paper, we describe an economical and stereospecific route to the synthesis of derivatives of (*R*)- and (*S*)-4-hydroxycyclohex-2-enone; the key step is a stereocontrolled intramolecular ene reaction.

Results and discussion

The synthesis started with (2*R*,3*R*,4*R*,5*R*)-1,2:5,6-dianhydro-3,4-isopropylidene-D-mannitol **1**, which had been obtained in

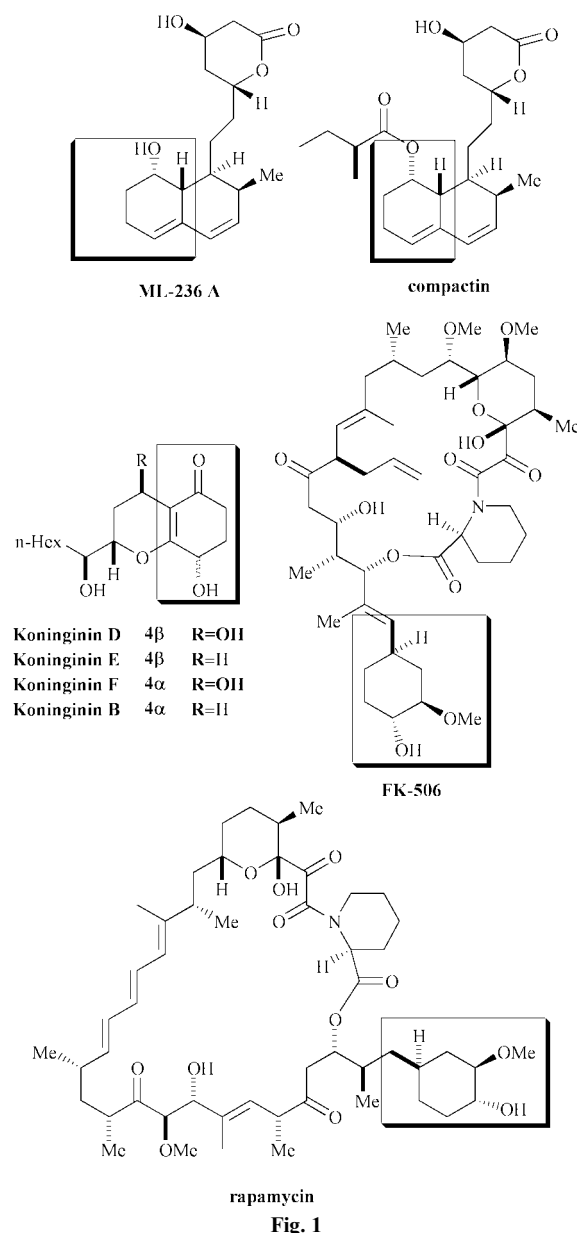
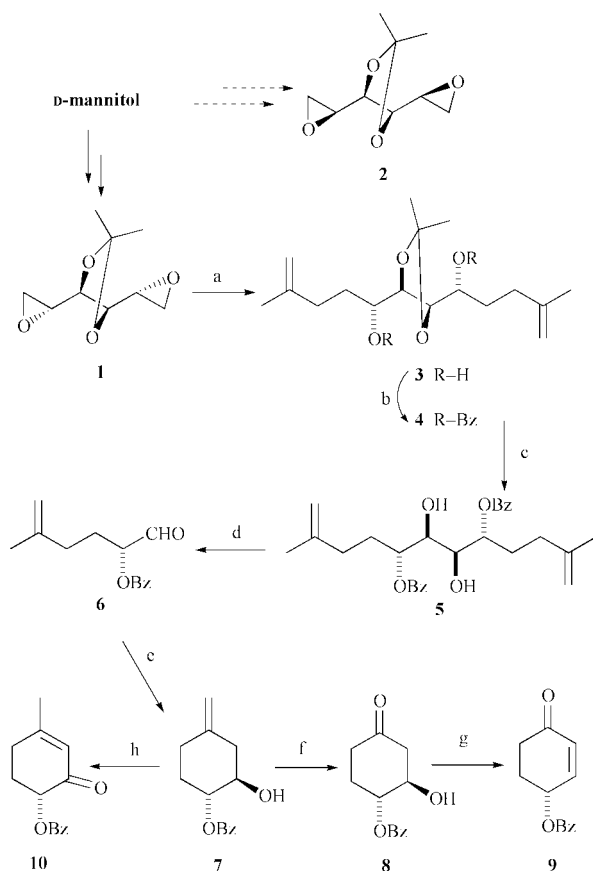


Fig. 1

four easy steps from D-mannitol by known procedures.⁹ After the carbon chain had been extended at both terminals of **1** by treatment of **1** with 2-methylallylmagnesium chloride to give **3**

† Present address: LEDSS 3—Chimie Recherches, Université Joseph Fourier, B. P. 53X—38041 Grenoble Cedex, France; E-mail: zhangrz_1999@yahoo.com; Fax: 00 33 4 76635754; Tel: 00 33 4 76514688.

in 83% yield, both hydroxy groups of **3** were protected with benzoyl chloride to afford benzoate **4** (97% yield).¹⁰ Treatment of **4** with a catalytic amount of toluene-*p*-sulfonic acid (PTSA) in methanol resulted in deprotection furnishing **5** (81%), which, upon oxidation with lead tetraacetate in CH₂Cl₂, afforded **6** in 91% yield (Scheme 1).



Scheme 1 Reagents and conditions: (a) 2-methylallylmagnesium chloride, 83%; (b) BzCl-Py, 97%; (c) PTSA (cat.)-MeOH, reflux, 81%; (d) Pb(CH₃COO)₄-CH₂Cl₂, 91%; (e) method A: ZnBr₂-4 Å MS, 81%; method B: 4 Å MS, 95%; (f) method A: O₃-Me₂S, 95%; method B: OsO₄-NaIO₄, 91%; (g) PTSA (cat.)-benzene, 91%; (h) Jones reagent, 80%.

The next step was a stereocontrolled cyclization of **6** by an intramolecular ene reaction, which is the key step in this work. ZnBr₂ was chosen as the Lewis acid for the reaction of **6** in anhydrous CH₂Cl₂, but a ¹H NMR spectrum showed that the product was a mixture of **7** and the species obtained by a shift of the double bond to the ring. The reason for this maybe that the reaction system was not absolutely anhydrous and H⁺ is produced by hydrolysis of ZnBr₂. When 4 Å MS were added to the reaction system (a widely used dehydrating agent and co-catalyst in asymmetric reactions),¹¹ compound **7** was obtained in 81% yield and no products of the double bond shift were found. When 4 Å MS and a catalytic amount of ZnBr₂ were used, similar results were obtained to those using equivalent amounts of ZnBr₂.¹² It was interesting that compound **7** could be obtained in 95% yield when only 4 Å MS were used in this ene reaction, which demonstrated that the 4 Å MS acted not only as a dehydrating agent, but also as a catalyst. The absolute configuration of the new chiral center in the structure of **7** was determined by the CD exciton chirality method to be that shown in Scheme 1, after transformation of **7** to **8**. The hydroxy group at C-3 of compound **8** was protected as a benzoyloxy group by treatment with benzoyl chloride. The CD spectrum of this benzoate shows negative chirality. According to the CD exciton chirality method, only when both vicinal groups are in the *anti* conformation in the six-membered ring is negative chirality obtained.¹³ As the absolute configuration

at C-4 comes from D-mannitol and is (*R*), so the new chiral center at C-3 of **7** should also possess the (*R*)-configuration. The *O*-benzyl compound **7** has already been synthesized by an intramolecular ene reaction with MABR as the Lewis acid, which was then transformed to a chiral building block of FK-506.⁸

With **7** in hand, the next transformation was easily accomplished with O₃ or OsO₄ (cat.)-NaIO₄ as the oxidizing agent to give **8** in excellent yield. Subsequent dehydration of **8** catalyzed by PTSA in benzene gave (*R*)-4-benzoyloxycyclohex-2-enone **9** ([α]_D²⁰ = +201 (*c* = 0.85, CHCl₃); lit. [α]_D = -197 (*c* = 1.9, CH₂Cl₂) for (*S*)-**9**¹⁴) in 91% yield. The other important compound (*R*)-6-benzoyloxy-4-methylcyclohex-2-enone **10** was synthesized from **7** in one step by oxidation with Jones reagent (80% yield). Since (2*S*,3*R*,4*R*,5*S*)-1,2:5,6-dianhydro-3,4-isopropylidene-D-mannitol **2** may be easily prepared from D-mannitol⁹ and subjected to the same reaction sequences, this route potentially also provides access to the enantiomers of compounds **7**–**10**.

In conclusion, we have presented a new and efficient route to four derivatives of (*R*)-4-hydroxycyclohex-2-enone, **7**–**10**, from one intermediate, **6**, using the simple, readily available D-mannitol as the chiral starting material. Such compounds are useful chiral building blocks that are widely used in the total synthesis of natural products and in asymmetric reactions.

Experimental

Mps were determined on an X4 micro-melting point instrument and are uncorrected. IR spectra were obtained on Shimadzu IR-440 and Perkin-Elmer 983 spectrometers. NMR spectra were recorded on an XL-300 spectrometer (300 MHz for ¹H) in CDCl₃ solution using TMS as the internal reference. MS were recorded on Finnigan-4921 and HP-5989 instruments. Optical rotations were obtained on Perkin-Elmer 241C and are reported in units of 10⁻¹ deg cm² g⁻¹. All reactions were monitored by TLC with Huanghai 60F₂₅₄ silica-gel-coated plates. Flash column chromatography was carried out with 300–400 mesh silica gel.

(5*R*,6*R*,7*R*,8*R*)-2,11-Dimethyl-5,8-dihydroxy-6,7-isopropylidenedioxydodeca-1,11-diene **3**

To a stirred solution of 2-methylallylmagnesium chloride [84 mmol in dry THF (30 mL), prepared from 3-chloro-2-methylpropene (84 mmol, 8.2 mL), magnesium ribbon (2.2 g, 6.6 equiv.), and dry THF (30 mL)] was added a solution of **1** (2.6 g, 37 mmol) in dry THF (10 mL) dropwise at 0 °C. The resulting mixture was then allowed to warm to room temperature. Stirring was continued for 1 h at this temperature. The mixture was quenched with MeOH (5 mL), and then poured into H₂O (200 mL) and extracted with EtOAc (150 mL). The combined organic solution was washed with H₂O and brine, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (20% acetone in hexane) to give **3** (3.68 g, 83%) as a white solid. Mp 51–52 °C; [α]_D²⁰ = +27.3 (*c* = 1.50, CHCl₃); ν_{max}(KBr)/cm⁻¹ 3300, 2920, 1650, 1450, 1380, 1230, 1070; δ_H 4.14 (4H, s, 2 × =CH₂), 3.80–3.50 (4H, m, 4CH), 2.35–1.93 (8H, m, 4CH₂), 1.76 (6H, s, 2CH₃), 1.30 (6H, s, 2 CH₃); *m/z* 299 (M⁺ + 1), 283 (M⁺ - 15), 59 (100%) (Found: C, 68.67; H, 10.36. C₁₇H₃₀O₄ requires C, 68.46; H, 10.07%).

(5*R*,6*R*,7*R*,8*R*)-2,11-Dimethyl-5,8-bis(benzoyloxy)-6,7-isopropylidenedioxydodeca-1,11-diene **4**

Benzoyl chloride (23.4 mmol, 2.7 mL) was added slowly to a solution of **3** (3.0 g, 10.0 mmol) in dry pyridine (30 mL) at 0 °C and then stirred overnight at room temperature. The reaction mixture was poured into H₂O (300 mL) and extracted with diethyl ether (200 mL). The combined organic layer was washed

fully with saturated CuSO_4 and then with H_2O and brine, respectively. The resulting solution was dried over Na_2SO_4 , concentrated under reduced pressure and purified by flash column chromatography on silica gel (10% ethyl acetate in hexane) to provide **4** (5.2 g, 97%). $[\alpha]_{\text{D}}^{20} = +22.0$ ($c = 1.5$, CHCl_3); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2960, 1725, 1650, 1600, 1580, 1450, 1380, 1270; δ_{H} 7.60–7.37 (4H, m), 7.30–7.00 (6H, m), 5.45–5.30 (2H, m, 2CH), 4.66 (2H, s, $=\text{CH}_2$), 4.61 (2H, s, $=\text{CH}_2$), 4.41–4.30 (2H, m, 2CH), 2.20–1.95 (8H, m, 4 CH_2), 1.66 (6H, s, 2 CH_3), 1.39 (6H, s, 2 CH_3); m/z 507 ($\text{M}^+ + 1$), 106 (100%) (Found: C, 73.13; H, 7.42. $\text{C}_{31}\text{H}_{38}\text{O}_6$ requires C, 73.52; H, 7.51%).

(5R,6R,7R,8R)-2,11-Dimethyl-5,8-bis(benzoyloxy)-6,7-dihydroxydodeca-1,11-diene 5

To a stirred solution of **4** (470 mg, 0.93 mmol) in methanol (20 mL), PTSA (50 mg) was added and then the reaction mixture was refluxed for 8 h. After removal of the solvent under reduced pressure, the residue was diluted with diethyl ether (20 mL) and washed with NaHCO_3 (aq.), H_2O and brine. The organic solution was dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (20% acetone in hexane) to afford **5** (260 mg, 81% yield and 74% conversion of **4**). $[\alpha]_{\text{D}}^{20} = +62.2$ ($c = 1.06$, CHCl_3); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3400, 2930, 1710, 1650, 1600, 1580, 1450, 1270; δ_{H} 8.10–7.97 (4H, m), 7.65–7.50 (2H, m), 7.50–7.40 (4H, m), 5.20–5.05 (2H, m, 2CH), 4.66 (2H, s, $\text{CH}_2=$), 4.62 (2H, s, $\text{CH}_2=$), 3.61 (2H, d, J 8 Hz, 2CH), 3.30 (OH, s), 2.20–1.90 (8H, m, 4 CH_2), 1.69 (6H, s, 2 CH_3); m/z 467 ($\text{M}^+ + 1$), 449 ($\text{M}^+ - 18$) (Found: C, 72.34; H, 7.53. $\text{C}_{28}\text{H}_{34}\text{O}_6$ requires C, 72.10; H, 7.30%).

(2R)-2-Benzoyloxy-5-methylhex-5-enal 6

A solution of lead tetraacetate (190 mg) in CH_2Cl_2 (10 mL) was cooled to -20°C and diol **5** (115 mg, 0.50 mmol) was added. After stirring for 1 h at this temperature, the reaction mixture was warmed to room temperature and quenched with ethylene glycol (0.5 mL). The upper phase was separated and the residue was washed with CH_2Cl_2 . The combined organic solution was washed with water and brine, and dried over Na_2SO_4 . The solvent was removed under reduced pressure and then purified by flash column chromatography on silica gel (5% ethyl acetate in hexane) to give **6** (105 mg) in 91% yield. $[\alpha]_{\text{D}}^{20} = +57.4$ ($c = 0.63$, CHCl_3); $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 2930, 1725, 1650, 1600, 1580, 1270, 1120, 859, 710; δ_{H} 9.65 (1H, s, CHO), 8.13–8.00 (2H, m, aromatic H), 7.65–7.50 (1H, m, aromatic H), 7.53–7.37 (2H, m, aromatic H), 5.22 (1H, dd, J 7.7, 4.7 Hz, CH-OBz), 4.79 (1H, s, $\text{CH}_2=$), 4.74 (1H, s, $\text{CH}_2=$), 2.35–2.05 (4H, m, 2 CH_2), 1.76 (3H, s, CH_3); m/z 233 ($\text{M}^+ + 1$) (Found: C, 72.50; H, 6.93. $\text{C}_{14}\text{H}_{16}\text{O}_3$ requires C, 72.39; H, 6.94%).

(1R,2R)-2-Benzoyloxy-5-methylenecyclohexanol 7

Method A. To a stirred solution of ZnBr_2 (65 mg, 0.26 mmol) in CH_2Cl_2 (5 mL), 4 Å MS (500 mg) were added. After stirring for 0.5 h, compound **6** (54 mg, 0.24 mmol) was added and stirring was continued for another hour. The solid was removed by filtration through Celite. The filtrate was washed with saturated NaHCO_3 , H_2O and brine, and dried over Na_2SO_4 . After evaporation of solution, the residue was purified by flash column chromatography on silica gel (5% acetone in hexane). Compound **7** was obtained in 81% yield (44 mg).

Method B. To a solution of **6** (1.0 g, 4.31 mmol) in CH_2Cl_2 (20 mL), 4 Å MS (1.0 g) were added and stirred for two days. After filtration through Celite, the residue was washed with CH_2Cl_2 . The combined organic solution was concentrated *in vacuo* and then purified by flash column chromatography on silica gel to provide **7** (950 mg) in 95% yield. $[\alpha]_{\text{D}}^{20} = -40.6$ ($c = 1.31$, CHCl_3); $\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 3600, 1710, 1650, 1600, 1580, 1458, 1280, 1070, 950, 720; δ_{H} 8.10–7.97 (2H, m), 7.43–7.30

(1H, m), 7.30–7.15 (2H, m), 5.02 (1H, td, J 8.1, 4.2 Hz), 4.93 (1H, s), 3.86 (1H, td, J 8.1, 4.0 Hz), 2.75 (1H, dd, J 14, 5.5 Hz), 2.30–1.60 (7H, m); m/z 233 ($\text{M}^+ + 1$) (Found: C, 72.27; H, 6.81. $\text{C}_{14}\text{H}_{16}\text{O}_3$ requires C, 72.39; H, 6.94%).

(3R,4R)-3-Hydroxy-4-benzoyloxycyclohexanone 8

Method A. A solution of **7** (125 mg, 0.54 mmol) in CH_2Cl_2 (5 mL) and methanol (3 mL) was cooled to -78°C in dry ice–acetone and then ozone was introduced to the reaction mixture. After the solution had turned blue, the flow of ozone was ceased and nitrogen was introduced to drive away the ozone dissolved in CH_2Cl_2 . Me_2S (0.5 mL) was added to the reaction mixture and stirred for 1 h at -78°C , and then overnight at room temperature. The solution was concentrated *in vacuo* and purified by flash column chromatography on silica gel (5% acetone in hexane) to afford **8** (120 mg, 95% yield).

Method B. OsO_4 (1.3 mg) and NaIO_4 (350 mg) were dissolved in 1,4-dioxane– H_2O (5 mL, v/v, 3 : 1). After stirring for 0.5 h, compound **7** (100 mg, 0.43 mmol) was added and the reaction mixture was stirred overnight. Na_2SO_3 (500 mg) was added to the reaction mixture and stirred for 15 min at room temperature. The solution was diluted with H_2O (20 mL) and then extracted with diethyl ether. The combined organic solution was washed with water and brine, and dried over Na_2SO_4 . The solvent was removed under reduced pressure and purified by flash column chromatography on silica gel to afford **8** (92 mg, 91% yield). $[\alpha]_{\text{D}}^{20} = -21.3$ ($c = 0.55$, CHCl_3); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3450, 2950, 1710, 1600, 1580, 1280, 1110, 930, 710; δ_{H} 8.13–8.00 (2H, m), 7.67–7.55 (1H, m), 7.55–7.43 (2H, m), 5.33–5.20 (1H, m), 4.40–4.27 (1H, m), 2.90 (1H, dd, J 15, 4 Hz), 2.65–2.43 (5H, m), 2.15–1.93 (2H, m); m/z , 235 ($\text{M}^+ + 1$) (Found: C, 66.24; H, 5.70. $\text{C}_{13}\text{H}_{14}\text{O}_4$ requires C, 66.60; H, 5.98%).

(R)-4-Benzoyloxycyclohex-2-enone 9

PTSA (5 mg) was added to a solution of **8** (46 mg, 0.20 mmol) in benzene (5 mL) and then refluxed for 20 min. After evaporation of the solution, the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in hexane) to give **9** (39 mg) in 91% yield. $[\alpha]_{\text{D}}^{20} = +201$ ($c = 0.85$, CHCl_3); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2960, 1715, 1690, 1600, 1580, 1270; δ_{H} 8.15–7.97 (2H, m), 7.42 (1H, br), 7.38 (2H, br), 7.00 (1H, dd, J 10, 4 Hz), 6.14 (1H, d, J 10 Hz), 5.90–5.80 (1H, m), 2.80–2.20 (4H, m); m/z 216 (M^+) (Found: C, 72.06; H, 5.62. $\text{C}_{13}\text{H}_{11}\text{O}_3$ requires C, 72.22; H, 5.56%).

Preparation of (R)-3-methyl-6-benzoyloxycyclohex-2-enone 10

Jones reagent (0.12 mL) was added dropwise to a solution of **7** (100 mg, 0.43 mmol) in freshly distilled acetone (10 mL). The reaction mixture was stirred for 2 h at room temperature and then quenched with H_2O (50 mL). After extraction with EtOAc, the combined organic solution was washed with brine and dried. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in hexane) to afford **10** as a white solid (80 mg, 80% yield). $[\alpha]_{\text{D}}^{20} = +86.4$ ($c = 0.78$, CHCl_3); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1735, 1690, 1640, 1280, 1215; δ_{H} 8.20–8.05 (2H, m), 7.65–7.50 (1H, m), 7.50–7.37 (2H, m), 5.98 (1H, s), 5.90 (1H, dd, J 10, 6 Hz), 2.70–2.20 (4H, m), 2.02 (3H, s); m/z 231 ($\text{M}^+ + 1$) (Found: C, 72.60; H, 5.94. $\text{C}_{14}\text{H}_{14}\text{O}_3$ requires C, 73.04; H, 6.09%).

References

- 1 S. Danishefsky and B. Simoneau, *J. Am. Chem. Soc.*, 1989, **111**, 2599.
- 2 (a) T. Kino, H. Hatanaka, M. Hashimoto, M. Nishiyama, T. Goto, M. Okuhara, M. Kohsaka, H. Aoki and H. Imanaka, *J. Antibiot.*, 1987, **40**, 1249; (b) H. Tanaka, A. Kuroda, H. Marusawa, H. Hatanaka, T. Kino, T. Goto, M. Hashimoto and T. Taga, *J. Am. Chem. Soc.*, 1987, **109**, 5031.

- 3 (a) R. Dunlop, A. Simon, K. Sivasithamparam and E. Ghisalberti, *J. Nat. Prod.*, 1989, **52**, 67; (b) E. Ghisalberti and C. Rowland, *J. Nat. Prod.*, 1993, **56**, 1799; (c) S. Parker, H. Cutler and P. Schreiner, *Biosci. Biotechnol. Biochem.*, 1995, **59**, 1747; (d) G. Liu and Z. Q. Wang, *Synthesis*, 2001, 119.
- 4 (a) C. Vezina, A. Kudelski and S. N. Sehgal, *J. Antibiot.*, 1975, **28**, 721; (b) S. N. Sehgal, H. Baker and C. Vezina, *J. Antibiot.*, 1975, **28**, 727; (c) D. Swindells, P. White and J. Findlay, *Can. J. Chem.*, 1978, **56**, 2491; (d) J. Findlay and L. Radics, *Can. J. Chem.*, 1980, **58**, 579; (e) K. C. Nicolaou, T. Chakraborty, A. D. Piscopio, N. Minowa and P. Bertinato, *J. Am. Chem. Soc.*, 1993, **115**, 4419.
- 5 R. Brünjes, U. Tilstam and E. Winterfeldt, *Chem. Ber.*, 1991, **124**, 1677.
- 6 M. Carreño, J. Ruano, M. Garrido, M. Ruiz and G. Solladié, *Tetrahedron Lett.*, 1990, **31**, 6653.
- 7 (a) A. Jones, M. Yamaguchi, A. Patten, S. Danishefsky, J. Ragan, D. Smith and S. Schreiber, *J. Org. Chem.*, 1989, **54**, 17; (b) J. Audia, L. Boisvert, A. Patten, A. Villalobos and S. Danishefsky, *J. Org. Chem.*, 1989, **54**, 3738; (c) S. Danishefsky and B. Simoneau, *Pure Appl. Chem.*, 1988, **60**, 1555.
- 8 Keiji Maruoka, Susumu Saito, Takashi Ooi and Hisashi Yamamoto, *Synlett*, 1991, 579.
- 9 Y. Merrer, C. Dureault, C. Gravier, D. Languin and J. Depezay, *Tetrahedron Lett.*, 1985, **26**, 319.
- 10 Wang *et al.* have reported the transformation of **1** to **4** in the synthesis of (2*R*,2'*R*,3*R*,3'*R*)-3,3'-dihydroxy-6,6,6',6'-tetramethyl-3,3',4,4',5,5',6,6'-octahydro-2,2'-bi(2*H*-pyran) as a letter: L. Yu, L. Xu and Z. Wang, *Chin. Chem. Lett.*, 1997, **8**, 653.
- 11 (a) *Catalytic Asymmetric Synthesis*, ed. I. Ojima, Wiley-VCH, 2000; (b) H. Kolb, M. VanNieuwenhze and K. B. Sharpless, *Chem. Rev.*, 1994, **94**, 2483.
- 12 Libing Yu, Dissertation, Shanghai Institute of Organic Chemistry, 1994.
- 13 (a) B. Ying, G. Qin and R. Xu, *Chin. J. Org. Chem.*, 1987, **3**, 165; (b) N. Harada and K. Nakanishi, *J. Am. Chem. Soc.*, 1969, **91**, 3989.
- 14 Kazlauskas *et al.* have reported the synthesis of (*S*)-4-benzoyloxycyclohex-2-enone, $[\alpha]_{\text{D}} = -197$ ($c = 1.9$, CH_2Cl_2), which was obtained from (*S*)-4-acetoxycyclohex-2-enone (98% ee) in two steps: R. J. Kazlauskas, A. N. E. Weissfloch, A. T. Rappaport and L. A. Cuccia, *J. Org. Chem.*, 1991, **56**, 2656.