Pergamon

Tetrahedron 57 (2001) 2147–2153

TETRAHEDRON

Total synthesis of four diastereoisomers of Goniofufurone from D-(−)- or L-(+)-tartaric acid

Yong-Li Su, Chun-Song Yang, Shang-Jun Teng, Gang Zhao* and Yu Ding*

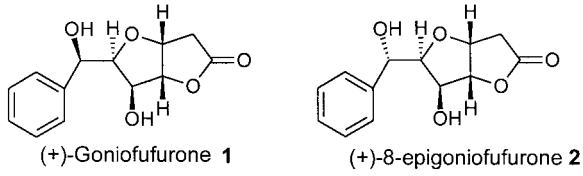
Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences, Academia Sinica, 354 Fenglin Lu, Shanghai 20032, People's Republic of China

Received 2 June 2000; revised 13 December 2000; accepted 4 January 2001

Abstract—(+) and (−)-Goniofufurones, (+) and (−)-8-*epi*-goniofufurones have been synthesized from D-(−) and L-(+)-tartaric acids by the addition of ethyl lithiopropiolate to a chiral aldehyde intermediate as a key step, in which LDA is the best base compared to *n*-BuLi plus Lewis acid YCl_3 (cat.). © 2001 Elsevier Science Ltd. All rights reserved.

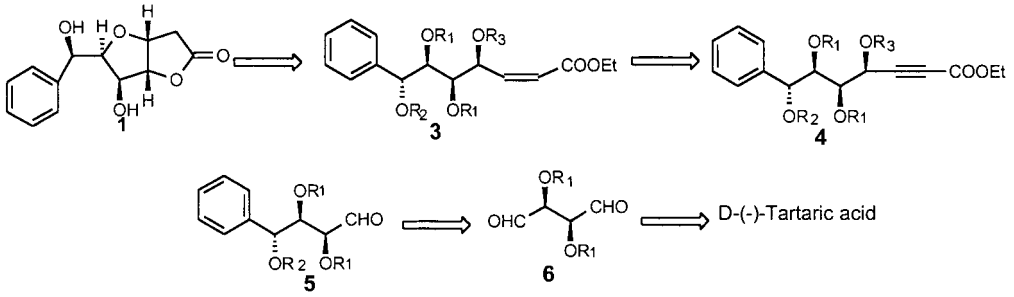
1. Introduction

Since the first styryl lactone goniothalamin was found from the trees of genus Goniothalamus in 1972[1] a variety of styryl lactones have been isolated and identified within the family Annonaceae.[2,3] The styryl lactones have been categorized as 10 types based on their skeleton structure and are reported to show cytotoxic, antitumour, pesticidal, teratogenic and embryotoxic activities.[4] Goniofufurones contain a furanofurone bicyclic structure and show significant cytotoxic activities against several human tumour cell lines. Herein, we would like to report our study on the synthesis of four diastereoisomers of Goniofufurone from commercially available tartaric acids.



Scheme 1.

Due to the unique structural features and significant bioactivity, (+)-goniofufurone, (+)-8-*epi*-goniofufurone and their stereoisomers have been synthesized by many groups from different starting materials. Most of them started from D-glucose[5] and D-mannose.[6] Shing et al. completed the first successful synthesis of these styryl lactones[7] starting from D-glycero-D-glyco-heptono-γ-lactone. Introduction of the desired chiral centers by asymmetric epoxidation and dihydroxylation of cinnamyl alcohol has been successfully used in their total syntheses.[8] Recently, Koll et al. reported an interesting route starting from a D-glucose derivative and reaction with Meldrum's acid.[9] Tsubuki et al. reported the syntheses of **1** from 2,3-O-isopropylidene-D-glyceraldehyde.[10] A synthesis of (+)-Goniofufurone by highly diastereoselective allenylation of D-glucurono-6,3-lactone was completed by Chao-jun Li.[11] Surivet et al. used mandelic acid as the starting material.[12] Roberts et al. synthesized **1** from furyl styryl ketone, which was oxidized



Scheme 2.

Keywords: lactones; alkynes; lithium and compounds; biologically active compounds.
* Corresponding authors. Tel.: +86-21-64163300; fax: +86-21-64166128; e-mail: dingyu@pub.sioc.ac.cn

PII: S0040-4020(01)00050-3

Table 1. Addition of ethyl lithiopropiolate to **11a**

Entry	Base	Lewis acid	Yield (%)
1	*n*-BuLi	–	Very low
2	*n*-BuLi	YCl_3 (0.1 equiv.)	60.0
3	LDA	–	78.9

Table 2. Addition of ethyl lithiopropiolate to **11b**

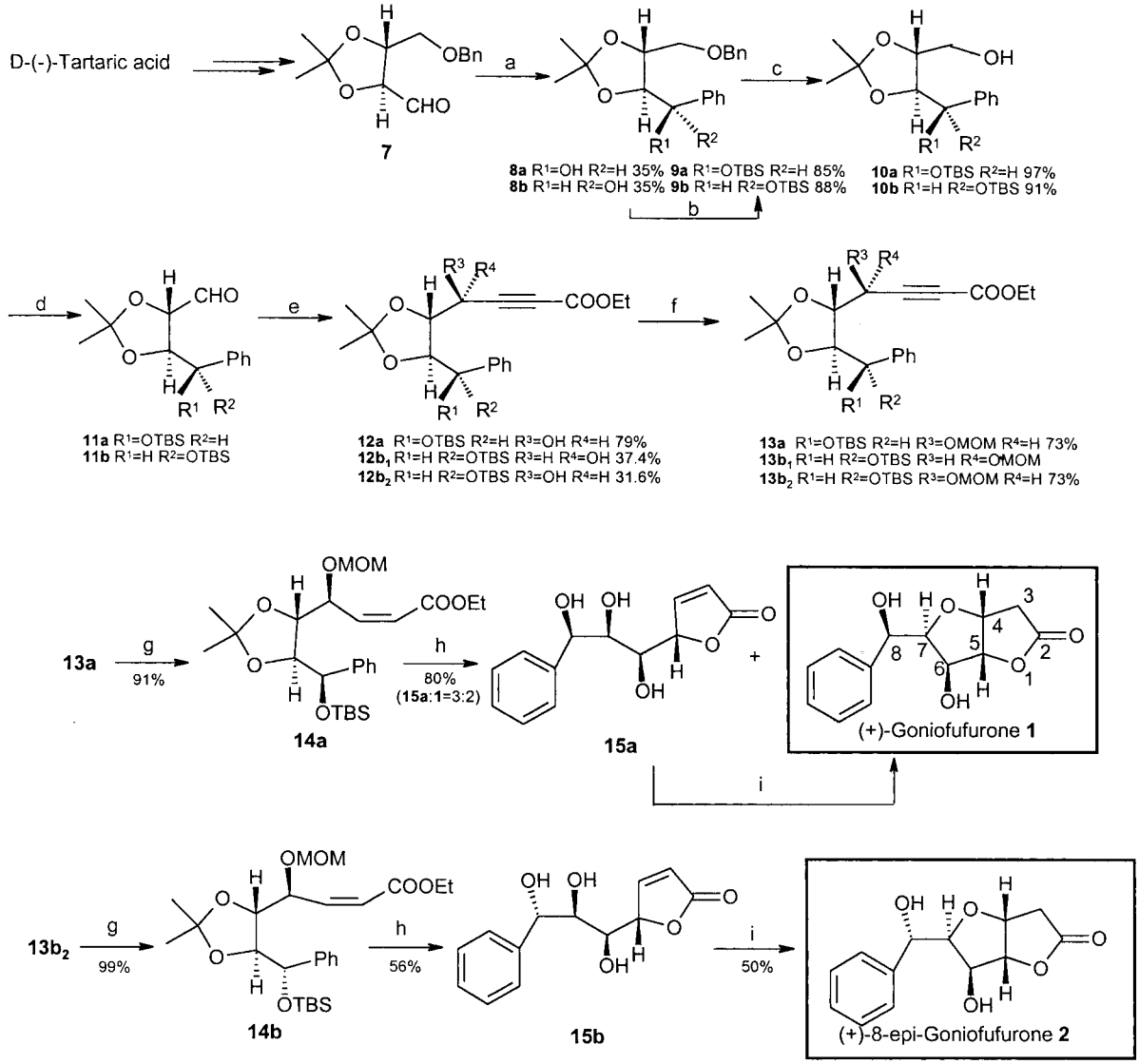
Entry	Base	Lewis acid	$\mathbf{12b_1}+\mathbf{12b_2}$ (%)	$\mathbf{12b_1}$:$\mathbf{12b_2}$
1	*n*-BuLi	Ycl_3 (0.1 equiv.)	40	1:1
2	LDA	–	69	1.2:1

stereoselectivity using urea hydrogen peroxide with polyleucine as the catalyst to give a chiral epoxide.[13] Here we would like to report in detail the synthesis of four isomers of Goniofufurone (Scheme 1).

2. Results and discussion

Retrosynthetic analysis of (+)-Goniofufurone **1** (Scheme 2) showed that intermediate **3** could be the precursor of **1** which will be obtained by intramolecular Michael addition and then lactonization. Compound **4** is the key intermediate and could be obtained by the addition of ethyl lithiopropiolate to aldehyde **5** which is easily prepared from D-(−)-tartaric acid.

Aldehyde **7**, readily available from (−)-tartaric acid in five steps according to a known procedure,[14] reacted with phenylmagnesium bromide without any purification to yield the addition product diastereoisomers **8a** and **8b** (ratio of **8a**/**8b**=1:1), which could be separated by column chromatography. The absolute configurations of newly formed stereogenic centers were assigned after being transformed, respectively, to target compounds later on. Monosilylation of **8a** and **8b**, and then hydrogenation on



Scheme 3. *Reagents and conditions*: (a) PhMgBr/THF, −78°C, 2 h, then rt 12 h; (b) TBSCl, imidazole/DMF, rt 1 day; (c) H_2, Pd–C/ethyl acetate, 45°C, 6 h; (d) Dess–Martin periodanane/CH_2Cl_2 1 h; (e) ethyl propiolate, 2 M BuLi, $^iPr_2NH$THF, −78°C, 12 h; (f) MOMCl, $(^iPr)_2NEt/CH_2Cl_2$, 40°C, 24 h; (g) H_2, Lindlar cat./ethyl acetate, 30°C, 3 days; (h) 1 M HCl/MeOH, reflux, 12 h; (i) DBU/THF, rt, 1 day.

Pd–C, followed by Dess–Martin oxidation, gave the key intermediate aldehydes **11a** and **11b**.[15]

Without further purification the aldehydes were treated, respectively, with ethyl lithiopropiolate[16] immediately to give addition products **12a**[17] and **12b$_1$**+**12b$_2$**, respectively. The results in Table 1 show that **12a** was obtained in very low yield when ethyl lithiopropiolate was used. But when a mixture of Lewis acid YCl_3 and aldehyde **11a** was added into the ethyl lithiopropiolate at −78°C dropwise, 60% yield could be given in two steps. When LDA instead of *n*-BuLi was used as a base in the absence of YCl_3, **12a** could be obtained in 79% in two steps.

In contrast with **11a** the addition reaction to **11b** generated a pair of diastereoisomers **12b$_1$** and **12b$_2$** with poor stereoselectivity. Once again LDA was the most effective base with 69% yield of **12b** in two steps, **12b$_1$/12b$_2$**=1.2:1 (Table 2).

Methoxymethylation of the secondary alcohol **12a** and **12b$_2$** followed by hydrogenation on Lindlar catalyst afforded **14a** and **14b**, respectively.

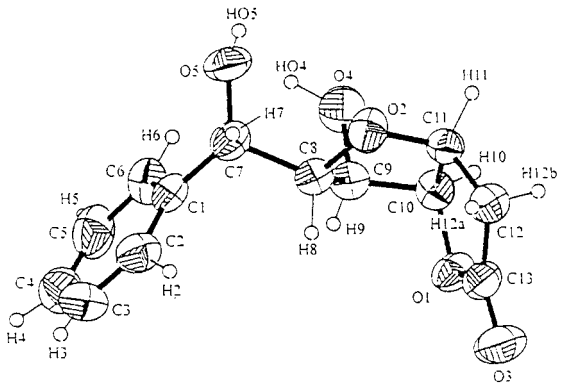
Exposure of **14b** to 1 M HCl[7] yielded a crystalline product, trihydroxybutenolide **15b**, which underwent an intramolecular Michael-type cyclization induced by DBU to form (+)-7-*epi*-Goniofufurone **2** as colorless plates. It is interesting that when treatment of **14a** with 1 M HCl **15a**, which could also be converted to **1** with DBU, and (+)-Goniofufurone **1** could be obtained simultaneously (ratio of **15a**:**1**=3:2) (Scheme 3). All spectroscopic data of **1** and **2** are in accord with those of the natural compound including the sign of the optical rotation[2b]: **1** $[\alpha]^{25}_D$=+9.0 (C 0.2 EtOH),{**1** lit. $[\alpha]^{22}_D$=+9.0 (C 0.5 EtOH)}; **2** $[\alpha]^{25}_D$=+106 (C 0.1 EtOH), {**2** lit. $[\alpha]^{22}_D$=+103 (C 1.0 EtOH)}.

Using the same strategy we have also obtained (−)-Goniofufurone **ent-1** and (−)-7-*epi*-Goniofufurone **ent-2** from L-(+)-tartaric acid (Scheme 3). The spectroscopic data of **ent-1** and **ent-2** are in accord with **1** and **2**. The H–H COSY spectrum of **ent-1** showed that the coupling constant $J_{4/5}$ is 4.2 Hz indicating that 3-H and 4-H must be *cis* to each other. Similarly, 7-H and 8-H ($J_{7/8}$=2.7 Hz) are *cis* to each other. Finally, the above structural elucidation of **ent-1** and **ent-2** were confirmed by X-ray crystallographic analysis (Fig. 1).[18]

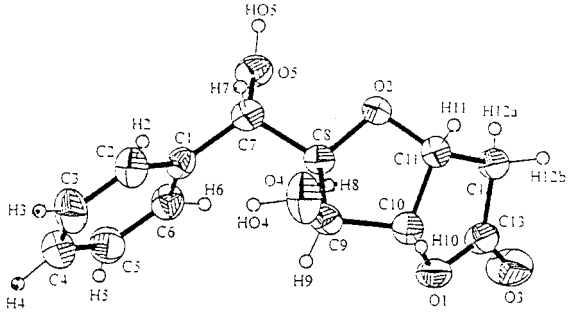
The optical rotation: **ent-1** $[\alpha]^{25}_D$=−10.2 (C 1.67 EtOH). {**1** lit. $[\alpha]^{22}_D$=+9.0 (C 0.5 EtOH)}; **ent-2** $[\alpha]^{25}_D$=−106 (C 0.3 EtOH) {**2** lit. $[\alpha]^{22}_D$=+103 (C 1.0 EtOH)}.

3. Conclusion

In summary, (+)-Goniofufurone **1** and (+)-7-*epi*-Goniofufurone **2** were synthesized from aldehyde **7** in nine steps with an overall 11% yield. The unnatural enantiomers of these styryl lactones can also be prepared from natural L-(+)-tartaric acid for biological evaluation.



ent-1



ent-2

Figure 1.

4. Experimental

4.1. General

All reactions were followed by TLC on precoated silica gel plate HSGF254 (Yantai chemical) developed with petroleum ether (PE)/ethyl acetate (EA). Column chromatography was performed on silica gel 300–400 μ (Yantai chemical). All solvents were refluxed and distilled under N_2 from sodium benzophenone ketyl (THF, Et_2O) or CaH_2 (CH_2Cl_2, $^iPr_2NH$).

Optical rotations were taken with a Perkin–Elmer 241 Autopol Polarimeter. IR spectra were measured on Digital FTIR spectrophotometer and reported in wave numbers (cm^{-1}). ^1H NMR spectra were obtained on Bruker AMX-300 or DRX-400 machines and reported in δ units from internal TMS. Mass spectra were measured with a Finnigan MAT-95 spectrometer. Elemental analyses were performed on Carlo-ERBA 1106.

Procedures for the syntheses of target compounds **1** and **2** from D-(−)-tartaric acid are described in detail as follows. Their enantiomers **ent-1** and **ent-2** were synthesized from L-(+)-tartaric acid using the same procedures.

4.1.1. 4-Hydroxy-4-phenyl-2*S*,3*S*-*O*-isopropylidene-butyl benzyl ether 8a(4*R*), 8b(4*S*). The Grignard reagent PhMgBr (1 M, 36 ml) was added to a solution of compound **7** (8.0 g, 32 mmol) in THF (30 ml) at −78°C. The mixture was stirred at −78°C for 2 h and left to stand overnight at room temperature to ensure reaction completion. Saturated aqueous NH_4Cl (30 ml) was added, the reaction mixture was extracted with ether, washed with water and brine, the combined organic layer was washed with brine and dried, before being concentrated. The residue was purified by flash column chromatography (PE/EA=5:1) to afford **8a** and **8b**, **8a/8b**=1:1 (7.36 g, 70%).

8a 3.16 g, yield 35%, colorless needles, mp 56.2±0.3°C; (Found: C, 73.19; H, 7.49. $C_{20}H_{24}O_4$ requires C, 73.14; H, 7.38%); $[\alpha]^{25}_D$=−7.49 (C 4.1 $CHCl_3$); ν_{max} (KBr): 3420, 3025, 2985, 2893, 1601, 1493, 1384, 1373, 1103, 1038 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.40 (3H, s, Me_2C), 1.44 (3H, s, Me_2C), 2.96 (1H, d, *J*=2.0 Hz, O*H*), 3.08 (2H, d, *J*=4.7 Hz, CH_2OBn), 4.03 (1H, dd, *J*=8.1, 5.0 Hz, C*H*O^{i}Pr), 4.22 (1H, dt, *J*=4.7, 8.1 Hz, C*H*O^{i}Pr), 4.39 (2H, s, CH_2OCH_2Ph), 4.92 (1H, d, *J*=3.6 Hz, PhC*H*OH), 7.23–7.36 (10H, m, 2×*Ph*); *m*/*z* (%): 313 (M^+-CH_3, 0.79), 221 (M^+-OCH_2Ph, 8.65), 107 (6.40), 91 (100).

8b 3.20 g, yield 35%, colorless oil. R_f (PE/EA=5:1) 0.55; (Found: C,72.95; H, 7.52. $C_{20}H_{24}O_4$ requires C, 73.14; H, 7.38%); $[\alpha]^{25}_D$=−23.6 (C 4.5 $CHCl_3$); ν_{max} (liquid film) 3453, 3032, 2988, 2870, 1604, 1496, 1381, 1371, 1086, 1048 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 1.44 (6H, s, Me_2C), 2.91 (1H, d, *J*=4.6 Hz, O*H*), 3.02–3.05 (2H, m, CH_aH_bOBn), 3.12–3.16 (1H, m, CH_aH_bOBn), 4.02–4.06 (2H, m, 2×C*H*O^{i}Pr), 4.39 (2H, s, CH_2OCH_2Ph), 4.66–4.68 (1H, m, PhC*H*OH), 7.20–7.34 (10H, m, 2×*Ph*); *m*/*z* (%): 313 (M^+-CH_3, 1.43), 221 (M^+-OCH_2Ph, 13.78), 107 (6.02), 91 (100).

4.1.2. 4-*t*-Butyldimethylsiloxy-4-phenyl-2*S*,3*S*-*O*-isopropylidene-butyl benzyl ether 9a(4*R*), 9b(4*S*). Compound **8a** (2.0 g, 6.1 mmol), imidazole (1.4 g, 22 mmol) and *t*-$BuMe_2SiCl$ (1.4 g, 9.3 mmol) in DMF (15 ml) were stirred for 1 day, then poured into water (30 ml), extracted with ether, washed with brine, dried, and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA=10:1) to afford **9a** (2.31 g, 85.4%).

9a colorless oil; R_f (PE/EA=10:1) 0.87; (Found: C, 70.66; H, 8.87. $C_{26}H_{38}O_4Si$ requires C, 70.54; H, 8.67%); $[\alpha]^{25}_D$=−18 (C 4.6 $CHCl_3$); ν_{max} (liquid film): 3033, 2931, 2858, 1604, 1496, 1379, 1369, 1095, 1069 cm^{-1}; δ_H (300 MHz, $CDCl_3$) −0.16 (3H, s, *t*BuSiMe_2O), 0.05 (3H, s, *t*BuSiMe_2O), 0.88 (9H, s, *tBu*SiMe$_2$O), 1.34 (3H, s, Me_2C), 1.43 (3H, s, Me_2C), 3.17 (1H, dd, *J*=3.7, 10.3 Hz, CH_aH_bO), 3.25 (1H, dd, *J*=2.3, 10.3 Hz, CH_aH_bO), 3.85 (1H, dd, *J*=5.2, 7.8 Hz, C*H*O^{i}Pr), 4.32–4.38 (1H, m, C*H*O^{i}Pr), 4.39 (1H, d, *J*=12.4 Hz, PhCH_aH_bO), 4.46 (1H, d, *J*=12.4 Hz, PhCH_aH_bO), 4.81 (1H, d, *J*=5.2 Hz, PhC*H*OTBS), 7.22–7.34 (10H, m, 2×*Ph*); *m*/*z* (%): 428 (M^+-CH_3, 0.56), 221 (PhCHOTBS, 38.04), 91 (100), 73 (23.75).

9b 4.31 g, yield 88%, colorless oil; R_f (PE/EA=10:1) 0.75; (Found: C, 70.45; H, 8.63. $C_{26}H_{38}O_4Si$ requires C, 70.54; H, 8.67%); $[\alpha]^{25}_D$=+38 (C 5.9 $CHCl_3$); ν_{max} (liquid film): 3032, 2931, 2859, 1604, 1496, 1379, 1369, 1087 cm^{-1}; δ_H (300 MHz, $CDCl_3$) −0.08 (3H, s, *t*BuSiMe_2O), 0.03 (3H, s, *t*BuSiMe_2O), 0.83 (9H, s, *tBu*SiMe$_2$O), 1.20 (3H, s, Me_2C), 1.44 (3H, s, Me_2C), 3.22 (2H, d, *J*=4.5 Hz, CH_2OBn), 3.89 (1H, dd, *J*=5.4, 8.4 Hz, C*H*O^{i}Pr), 3.97 (1H, dt, *J*=4.5, 8.4 Hz, C*H*O^{i}Pr), 4.40 (1H, d, *J*=12.4 Hz, PhCH_aH_bO), 4.50 (1H, d, *J*=12.4 Hz, PhCH_aH_bO), 4.79 (1H, d, *J*=5.4 Hz, PhC*H*OTBS), 7.21–7.36 (10H, m, 2×*Ph*); *m*/*z* (%): 428 (M^+-CH_3, 0.54), 221 (PhCHOTBS, 44.05), 115 (6.37), 91 (100), 73 (24.95).

4.1.3. 4-*t*-Butyldimethlsiloxy-4-phenyl-2*S*, 3*S*-*O*-isopropylidene-butanol 10a(4*R*), 10b(4*S*). Compound **9a** (1.92 g, 4.33 mmol), 5% Pd–C (600 mg) in ethyl acetate (100 ml) was stirred under a H_2 atmosphere (1 atm) at 45°C for 6 h. The reaction mixture was filtered over celite, and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA=10:1) to afford **10a** (1.480 g, 97%).

10a colorless oil; R_f (PE/EA=12:1) 0.3; (Found: C, 64.50; H, 9.23. $C_{19}H_{32}O_4Si$ requires C, 64.72; H, 9.17%); $[\alpha]^{25}_D$=−20.4 (C 0.9 $CHCl_3$); ν_{max} (liquid film): 3481, 3033, 2932, 2859, 1604, 1496, 1380,, 1371, 1080, 1070, 1031 cm^{-1}; δ_H (300 MHz, $CDCl_3$) −0.15 (3H, s, *t*BuSiMe_2O), 0.07 (3H, s, *t*BuSiMe_2O), 0.90 (9H, s, *tBu*SiMe$_2$O), 1.36 (3H, s, Me_2C), 1.44 (3H, s, Me_2C), 2.14 (1H, br, OH), 3.19–3.23 (1H, m, CH_aH_bOH), 3.45–3.49 (1H, m, CH_aH_bOH), 3.93 (1H, dd, *J*=5.5, 7.7 Hz, C*H*O^{i}Pr), 4.23 (1H, ddd, *J*=2.9, 5.0, 7.7 Hz, C*H*O^{i}Pr), 4.82 (1H, d, *J*=5.5 Hz, PhC*H*OTBS), 7.24–7.33 (5H, m, 2×*Ph*); *m*/*z* (%): 352 (M^+, 0.34), 337 (M^+-CH_3, 1.74), 221 (PhCHOTBS, 100), 131 (41.11), 91 (24.29).

10b 4.11g, 91%, colorless oil; R_f (PE/EA=7:1) 0.24; (Found: C, 64.49; H, 9.35. $C_{19}H_{32}O_4Si$ requires C, 64.72; H, 9.17%); $[\alpha]^{25}_D$=+45 (C 3.1 $CHCl_3$); ν_{max} (liquid film): 3472, 3034, 2931, 2859, 1604, 1496, 1380, 1371, 1098, 1068 cm^{-1}; δ_H ($CDCl_3$) −0.05 (3H, s, *t*BuSiMe_2O), 0.08 (3H, s, *t*BuSiMe_2O), 0.89 (9H, s, *tBu*SiMe$_2$O), 1.08 (3H, s, Me_2C), 1.38 (3H, s, Me_2C), 3.38 (1H, dd, *J*=4.7, 11.5 Hz, CH_aH_bOH), 3.60 (1H, dd, *J*=4.7, 11.5 Hz, CH_aH_bOH), 3.78 (1H, dt, *J*=4.7, 8.3 Hz, C*H*O^{i}Pr), 3.98 (1H, dd, *J*=5.3, 8.3 Hz, C*H*O^{i}Pr), 4.90 (1H, d, *J*=5.3 Hz, PhC*H*OTBS), 7.24–7.35 (5H, m, 2×*Ph*); *m*/*z* (%): 352 (M^+, 0.21), 337 (M^+-CH_3, 1.61), 221 (PhCHOTBS, 100), 131 (44.72), 91 (19.47).

4.1.4. Ethyl 7-*t*-butyldimethlsiloxy-7-phenyl-5*S*, 6*S*-*O*-isopropylidene-4-hydroxy-heptyn-2-oate 12a(7*R*, 4*S*), 12b$_1$(7*S*, 4*R*), 12b$_2$(7*S*, 4*S*). Compound **10a** (600 mg, 1.7 mmol) and Dess–Martin reagent (1.5 g, 3.5 mmol) in CH_2Cl_2 (75 ml) were stirred for 1 h. Saturated aqueous $Na_2S_2O_3$ and $NaHCO_3$ were added, followed by extraction with ether, dried, and concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA=10:1) to afford crude aldehyde **11a**.

A reaction flask was charged with THF (2 ml) and ^{i}Pr$_2$NH (0.13 ml). The solution was cooled to 0°C, and 2 M *n*-BuLi (0.44 ml) was added and stirred for 0.5 h at rt. The solution was cooled to −78°C and ethyl propiolate (0.06 ml,

0.58 mmol) was added. After 1 h at −78°C, aldehyde **11a** (100 mg, 0.29 mmol) was added. After 12 h at −78°C the reaction was stopped with sat. NH_4Cl, then extracted with ethyl acetate. The combined organic layer was washed with brine, dried with Na_2SO_4, before being concentrated in vacuo. The residue was purified by flash column chromatography (PE/EA=10:1) to afford **12a** (81 mg, 79%).

12a yellow oil; R_f (PE/EA=6:1) 0.4; (Found: C, 64.40; H, 8.57. $C_{24}H_{36}O_6Si$: C, 64.25; H, 8.10%); ν_{max} (liquid film): 3458, 2933, 2859, 2241, 1717, 1496, 1382, 1371, 1087, 1066, 1030 cm^{-1}; δ_H (300 MHz, $CDCl_3$) −0.13 (3H, s, *t*BuSi*Me*$_2$O), 0.09 (3H, s, *t*BuSi*Me*$_2$O), 0.92 (9H, s, *tBu*SiMe$_2$O), 1.30 (3H, t, *J*=7.1 Hz, OCH$_2$C*H*$_3$), 1.41 (3H, s, *Me*$_2$C), 1.48 (3H, s, *Me*$_2$C), 3.97 (1H, d, *J*=10 Hz, C*H*OH), 4.14 (1H, dd, *J*=5.6, 7.6 Hz, C*H*O^{i}Pr), 4.23 (2H, q, *J*=7.1 Hz, OC*H*$_2$CH$_3$), 4.27–4.33 (1H, m, C*H*O^{i}Pr), 4.83 (1H, d, *J*=5.6 Hz, PhC*H*OTBS), 7.26–7.39 (5H, m, 2×*Ph*); *m*/*z* (%): 448 (M^+, 0.98), 434 (M^++1-CH_3, 1.98), 221 (PhCHOTBS, 100), 115 (9.05), 91 (9.79), 73 (41.79).

12b$_1$ 32 mg, yield 37.4%, yellow oil. R_f (PE/EA=10:1) 0.42; $[\alpha]^{25}_D$=+43.7 (C 1.5 $CHCl_3$); ν_{max} (liquid film): 3404, 3034, 2933, 2859, 2241, 1717, 1604, 1496, 1381, 1371, 1088, 1067 cm^{-1}; δ_H (300 MHz, $CDCl_3$) −0.01 (3H, s, *t*BuSi*Me*$_2$O), 0.11 (3H, s, *t*BuSi*Me*$_2$O), 0.91 (9H, s, *tBu*SiMe$_2$O), 1.06 (3H, s, *Me*$_2$C), 1.30 (3H, t, *J*=7.1 Hz, OCH$_2$C*H*$_3$), 1.41 (3H, s, *Me*$_2$C), 3.81 (1H, dd, *J*=3.4, 8.3 Hz, C*H*O^{i}Pr), 3.98 (1H, d, *J*=10.7 Hz, CHO*H*), 4.23 (2H, q, *J*=7.1 Hz, OC*H*$_2$CH$_3$), 4.35 (1H, dd, *J*=4.6, 8.3 Hz, C*H*O^{i}Pr), 4.42 (1H, dd, *J*=3.4, 10.7 Hz, C*H*OH), 5.06 (1H, d, *J*=4.6 Hz, PhC*H*OTBS), 7.26–7.39 (5H, m, 2×*Ph*); *m*/*z* (%): 434 (M^++1-CH_3, 0.90), 221 (PhCHOTBS, 100), 115 (11.73), 91 (9.01), 73 (53.59).

12b$_2$ 27 mg, 31.6%, yellow oil. R_f (PE/EA=10:1) 0.27; ν_{max} (liquid film): 3424, 3034, 2933, 2859, 2243, 1717, 1495, 1381, 1371, 1085, 1069, 1031 cm^{-1}; δ_H (300 MHz, $CDCl_3$) −0.04 (3H, s, *t*BuSi*Me*$_2$O), 0.08 (3H, s, *t*BuSi*Me*$_2$O), 0.90 (9H, s, *tBu*SiMe$_2$O), 1.14 (3H, s, *Me*$_2$C), 1.24 (3H, t, *J*=7.1 Hz, OCH$_2$C*H*$_3$), 1.42 (3H, s, *Me*$_2$C), 3.30 (1H, d, *J*=6.4 Hz, CHO*H*), 3.90 (1H, dd, *J*=4.8, 8.2 Hz, C*H*O^{i}Pr), 4.13 (1H, dd, *J*=4.8, 8.2 Hz, C*H*O^{i}Pr), 4.20–4.27 (3H, buried m, OC*H*$_2$CH$_3$ and C*H*OH), 4.95 (1H, d, *J*=4.8 Hz, PhC*H*OTBS), 7.1–7.5 (5H, m, *Ph*); *m*/*z* (%): 448(M^+, 2.91), 434 (M^++1-CH_3, 2.59), 221 (PhCHOTBS, 100), 115 (5.31), 91 (5.02), 73(18.86).

4.1.5. Ethyl 7-*t*-butyldimethlsiloxy-7-phenyl-5*S*, 6*S*-*O*-isopropylidene-4-*O*-methoxymethyl-heptyn-2-oate 13a(7*R*, 4*S*), 13b(7*S*, 4*S*). To stirred solution of **12a** (1.1 g, 2.45 mmol) in CH_2Cl_2 (15 ml) were added ^{i}Pr$_2$NEt (0.8 ml, 4.9 mmol) and MOMCl (0.35 ml, 4.4 mmol) at 0°C. The reaction mixture was stirred for 24 h at 40°C. After addition of a saturated aqueous solution of NH_4Cl it was extracted with CH_2Cl_2 (100 ml). The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue, which was purified by column chromatography (PE/EA=10:1) to give **13a**.

13a 882 mg, yield 73%, colorless oil, R_f (PE/EA=10:1) 0.47; (Found: C, 63.39; H, 8.34. $C_{26}H_{40}O_7Si$ requires C, 63.38; H, 8.20%); $[\alpha]^{25}_D$=+22.9 (C 1.5 $CHCl_3$); ν_{max} (liquid film): 3033, 2933, 2240, 1717, 1604, 1496, 1381, 1370, 1065, 1029 cm^{-1}; δ_H ($CDCl_3$) −0.16 (3H, s, *t*BuSi*Me*$_2$O), 0.1 (3H, s, *t*BuSi*Me*$_2$O), 0.89 (9H, s, *tBu*SiMe$_2$O), 1.26 (3H, t, *J*=7.1 Hz, OCH$_2$C*H*$_3$), 1.39 (3H, s, *Me*$_2$C), 1.41 (3H, s, *Me*$_2$C), 3.27 (3H, s, OCH$_2$OC*H*$_3$), 4.14 (1H, d, *J*=3.4 Hz, C*H*OMOM), 4.14–4.46 (4H, buried m, OC*H*$_2$CH$_3$ and C*H*O^{i}Pr), 4.34 (1H, dd, *J*=3.4, 6.7 Hz, C*H*O^{i}Pr),4.45 (1H, d, *J*=6.7 Hz, PhC*H*OTBS), 4.80–4.89 (2H, m, OC*H*$_2$OCH$_3$), 7.25–7.36 (5H, m, *Ph*); *m*/*z* (%): 477 (M^+-CH_3, 1.09), 271 (M^+-PhCH$_2$OTBS, 3.56), 221 (100), 73 (73.79).

13b yield 73%, colorless oil. R_f (PE/EA=10:1) 0.35; (Found: C, 63.59; H, 8.36. $C_{26}H_{40}O_7Si$ requires C, 63.38; H, 8.20%); $[\alpha]^{25}_D$=−33.3 (C 1.8 $CHCl_3$); ν_{max} (liquid film): 2933, 2859, 2243, 1718, 1604, 1494, 1380, 1370, 1097, 1068, 1032 cm^{-1}; δ_H (300 MHz, $CDCl_3$) −0.1 (3H, s, *t*BuSi*Me*$_2$O), 0.1 (3H, s, *t*BuSi*Me*$_2$O), 0.9 (9H, s, *tBu*SiMe$_2$O), 1.22 (3H, s, *Me*$_2$C), 1.27 (3H, t, *J*=7.1 Hz, OCH$_2$C*H*$_3$), 1.45 (3H, s, *Me*$_2$C), 3.29 (3H, s, OCH$_2$OC*H*$_3$), 3.98 (1H, dd, *J*=2.5, 8.3 Hz, C*H*O^{i}Pr), 4.14–4.26 (3H, buried m, OC*H*$_2$CH$_3$ and C*H*O^{i}Pr), 4.18 (1H, d, *J*=2.5 Hz, C*H*OMOM), 4.51 (1H, d, *J*=6.9 Hz, PhC*H*OTBS), 4.82–4.89 (2H, m, OC*H*$_2$OCH$_3$), 7.29–7.34 (5H, m, *Ph*); *m*/*z* (%): 477 (M^+-CH_3, 0.95), 436 (M^++1-MOM, 3.17), 271 (M^+-PhCH$_2$OTBS, 2.46), 221 (100), 115 (13.92), 91 (87.83), 73 (64.57).

4.1.6. Ethyl 7-*t*-butyldimethlsiloxy-7-phenyl-5*S*, 6*S*-*O*-isopropylidene-4-*O*-methoxymethyl-hepten-2*Z*-oate 14a(7*R*, 4*S*), 14b(7*S*, 4*S*). A suspension of Lindlar catalyst (18 mg) in a solution of **13a** (339 mg, 0.69 mmol) and quinoline (3.4 μl) in ethyl acetate (4.5 ml) were stirred under H_2 atmosphere (1 atm) at 30°C for 3 days. The mixture was filtered over celite and concentrated in vacuo. The crude product was purified by column chromatography (PE/EA=10:1) to give **14a** (319 mg, 91%).

14a colorless oil, R_f (PE/EA=10:1) 0.42; $[\alpha]^{25}_D$=+20.1 (C 1.8 $CHCl_3$); ν_{max} (liquid film): 3030, 2933, 2859, 1720, 1651, 1496, 1380, 1370, 1089, 1064, 1031 cm^{-1}; δ_H (300 MHz, $CDCl_3$) −0.15 (3H, s, *t*BuSi*Me*$_2$O), 0.06 (3H, s, *t*BuSi*Me*$_2$O), 0.89 (9H, s, *tBu*SiMe$_2$O), 1.27 (3H, t, *J*=7.1 Hz, OCH$_2$C*H*$_3$), 1.62 (3H, s, *Me*$_2$C), 1.66 (3H, s, *Me*$_2$C), 3.24 (3H, s, OCH$_2$OC*H*$_3$), 4.10–4.23 (3H, m, OC*H*$_2$CH$_3$ and C*H*O^{i}Pr), 4.30 (1H, d, *J*=6.6 Hz, OC*H*$_a$H$_b$OCH$_3$), 4.34 (1H, t, *J*=5.8 Hz, C*H*O^{i}Pr), 4.47 (1H, d, *J*=6.6 Hz, OCH$_a$*H*$_b$OCH$_3$), 4.85 (1H,d, *J*=3.6 Hz, PhC*H*OTBS), 5.09 (1H, dd, *J*=5.8, 9.0 Hz, C*H*OMOM), 5.59 (1H, d, *J*=11.7 Hz, =C*H*CO$_2$Et), 5.71 (1H, dd, *J*=9.0, 11.7 Hz, C*H*=CHCO$_2$Et), 7.23–7.35 (5H, m, *Ph*); *m*/*z* (%): 479 (M^+-CH_3, 0.96), 378 (M^++1-OTBS, 1.19), 221 (75.97), 91 (11.39), 73 (71.49).

14b 200 mg, yield 99%, colorless oil, R_f (PE/EA=9:1) 0.50; $[\alpha]^{25}_D$=−9.7 (C 1.8 $CHCl_3$); ν_{max} (liquid film): 3030, 2956, 2933, 1719, 1652, 1494, 1380, 1369, 1099, 1032 cm^{-1}; δ_H (300 MHz, $CDCl_3$) −0.16 (3H, s, *t*BuSi*Me*$_2$O), 0.05 (3H, s, *t*BuSi*Me*$_2$O), 0.90 (9H, s, *tBu*SiMe$_2$O), 1.29 (3H, t, *J*=7.2 Hz, OCH$_2$C*H*$_3$), 1.34 (3H, s, *Me*$_2$C), 1.42 (3H, s, *Me*$_2$C), 3.35 (3H, s, OCH$_2$OC*H*$_3$), 3.92 (1H, dd, *J*=3.3, 7.8 Hz), 4.15–4.25 (2H, m), 4.35 (1H, dd, *J*=2.8, 7.8 Hz), 4.60 (1H, d, *J*=6.7 Hz, OC*H*$_a$H$_b$OCH$_3$), 4.66 (1H, d,

J=6.7 Hz, $OCH_aH_bOCH_3$), 4.76 (1H, d, J=3.3 Hz, PhC*H*OTBS), 5.34 (1H, ddd, J=0.8, 2.8, 9.0 Hz, C*H*OMOM), 5.93 (1H, dd, J=0.8, 11.7 Hz, =C*H*CO_2Et), 6.15 (1H, dd, J=9.0, 11.7 Hz, C*H*=CHCO_2Et), 7.22–7.37 (5H, m, *Ph*); δ_c (75 MHz, $CDCl_3$) −5.02, −4.60, 14.23, 18.30, 25.82, 25.90, 27.13, 27.29, 55.73, 60.38, 71.70, 74.54, 79.16, 82.02, 95.32, 109.80, 123.26, 127.23, 127.44, 127.54, 127.88, 128.10, 141.71, 144.48, 165.49; *m/z* (%): 479 (M^+-CH_3, 1.51), 221 (67.56), 91 (11.84), 73 (55.94).

4.1.7. 7*R*-Pheny-5*S*, 6*S*, 7*R*-trihydroxy-hept-2-enono-γ-lactone 15a, (+)-goniofufurone 1, 7*S*-pheny-5*S*, 6*S*, 7*S*-trihydroxy-hept-2-enono-γ-lactone 15b. A solution of the **14a** (50 mg) in 1 M HCl (0.4 ml) and MeOH (1 ml) was stirred at 60°C for 1 day. The mixture was diluted with ethyl acetate and washed with water and brine, dried with Na_2SO_4, concentrated in vacuo to leave a residue, which was purified by column chromatography (PE/EA=1:1) and then gave **1** (8 mg), **15a** (12 mg), total yield 80%.

15a white solid; R_f (PE/EA=1:3) 0.17; ν_{max} (KBr): 3420, 3100, 1735, 1600, 1496, 1179, 1108, 1040, 1050 cm^{-1}; δ_H (300 MHz, CD_3COCD_3+D_2O) 3.69 (1H, dd, J=2.0, 7.9 Hz, C*H*OH), 4.09 (1H, dd, J=2.0, 5.6 Hz, C*H*OH), 4.79 (1H, d, J=7.9 Hz, PhC*H*OH), 5.26 (1H, dt, J=1.7, 5.6 Hz, =C*H*OC=O), 6.14 (1H, dd, J=2.0, 5.7 Hz, =C*H*CO_2), 7.22–7.46 (5H, m, *Ph*), 7.81 (1H, dd, J=1.7, 5.7 Hz, =C*H*); *m/z* (%): 251(M^+H, 0.23), 215 (M^+H-2H_2O, 4.79), 126 (29.18), 107 (100), 97 (17.68), 79 (58.02). HRMS calcd for $C_{13}H_{13}O_4$ (M^+H–H_2O) 233.0814, Found: 233.0798.

1 white solid, mp 152–154°C. R_f (PE/EA=3:1) 0.23; $[\alpha]^{25}_D$=+9.0 (C 0.2 $CHCl_3$); ν_{max} (KBr): 3411, 3344, 3030, 3004, 2866, 1758, 1606, 1497, 1452, 1351, 1270, 1193, 1160, 1068, 1049, 1037 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.69 (1H, d, J=18.8 Hz, CH_aH_bC=O), 2.75 (1H, dd, J=5.4, 18.8 Hz CH$_aH_b$C=O), 2.88 (1H, d, J=3.1 Hz, CHO*H*), 4.07 (1H, dd, J=2.8, 4.8 Hz, C*H*CHOHPh), 4.17 (1H, d, J=2.9 Hz, PhCHO*H*), 4.40 (1H, br. s, C*H*OH-CHOC=O), 4.86 (1H, d, J=4.2 Hz, C*H*OC=O), 5.09–5.13 (1H, m, C*H*CH_aH_b), 5.18 (1H, dd, J=2.8, 4.5 Hz, PhC*H*OH), 7.3–7.5 (5H,m, *Ph*); δ_c (75 MHz, CD_3COCD_3) 36.13, 71.47, 74.04, 77.64, 84.68, 88.27, 127.36, 127.72, 128.40, 143.23, 176.18; *m/z* (%): 251(M^+H, 0.51), 233 (M^+H–H_2O, 5.54), 126 (48.76), 107 (93.56), 97 (12.07), 79 (100).

15b, yield 56.0%. ν_{max} (liquid film): 3541, 3443, 3225, 2913, 1793, 1750, 1596, 1494, 1161, 1106, 1074, 1034 cm^{-1}; δ_H (300 MHz, CD_3COCD_3+D_2O) 3.43 (1H, dd, J=1.5, 6.5 Hz, C*H*OH), 4.02 (1H, dd, J=1.5, 7.9 Hz, C*H*OH), 4.95 (1H, d, J=7.9 Hz, PhC*H*OH), 5.35 (1H,dt, J=1.7, 6.5 Hz, =C*H*OC=O), 6.31 (1H, dd, J=2.0, 5.8 Hz, =C*H*CO_2), 7.20–7.49 (5H, m, *Ph*), 8.03 (1H, dd, J=1.7, 5.8 Hz, =C*H*); *m/z* (%): 233 (M^+H–H_2O, 0.65), 215 (M^+H–2H_2O, 2.44), 126 (39.13.40), 107 (100), 97 (9.15), 79 (73.49). HRMS calcd for $C_{13}H_{13}O_4$ (M^+H–H_2O) 233.0814, Found: 233.0800.

4.1.8. (+)-8-*epi*-Goniofufurone 2. A solution of the unsaturated lactone **15b** (8 mg, 0.032 mmol) in dry 18 ml THF containing 0.05% (v/v) DBU was stirred at room temperature for 24 h. The solution was diluted with ethyl acetate and washed with water, dried with Na_2SO_4, concentrated in vacuo, the residue was purified by flash column chromatography (PE/EA=1:1) to give **2** (4 mg, 50%).

2 white solid, mp 197.5±0.3°C. R_f (PE/EA=3:1) 0.39; $[\alpha]^{25}_D$=+106 (C 0.1 EtOH). ν_{max} (KBr): 3450, 3380, 3300, 3032, 2926, 2850, 1759, 1640, 1496, 1455, 1351, 1255, 1200, 1151, 1064, 1045, 1030 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.67–2.83 (2H, m, CH_aH_bC=O), 4.24 (1H, t, J=3.5 Hz, C*H*CHOHPh), 4.43 (1H, d, J=3.2 Hz, C*H*OH), 4.90 (1H, d, J=4.4 Hz, C*H*OC=O), 5.08 (1H, d, J=3.8 Hz, PhC*H*OH), 5.10–5.14 (1H, m, C*H*CH_aH_b), 7.33–7.45 (5H, m, *Ph*); *m/z* (%): 251 (M^+, 1.53), 233 (M^+H–H_2O, 40.01), 215 (M^+H–2H_2O, 8.24), 126 (39.14), 107 (89.99), 97 (12.70), 73 (100). HRMS calcd for $C_{13}H_{14}O_5$(M^+): 250.0841, Found: 250.0812.

References

1. Jewers, K.; Davis, J. B.; Dougan, J.; Manchanda, A. H.; Blunden, G.; Kyi, A.; Wetchapinan, S. *Phytochemistry* **1972**, *11*, 2025.
2. (a) Fang, X. P.; Anderson, J. E.; Chang, C. J.; Mclaughlin, J. L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1655. (b) Fang, X. P.; Anderson, J. E.; Chang, C. J.; Mclaughlin, J. L. *J. Nat. Prod.* **1991**, *54*, 1034. (c) EI-Iayat, A. L.; Ferrigini, N. R.; Mclaud, T. G.; Mckenzie, A. T.; Byrn, S. R.; Cassady, J. M.; Chang, C. G.; Mclaughlin, J. L. *Tetrahedron Lett.* **1985**, *26*, 955. (d) Alkofahi, A.; Ma, W. W.; Mekenzie, M. T.; Byrn, S. R.; Mclaughlin, J. L. *J. Nat. Prod.* **1989**, *52*, 1371.
3. (a) Bermejo, A.; Blazquez, M. A.; Rao, K. S.; Cores, D. *Phytochemistry* **1998**, *47*, 1375. (b) Cao, Sh. G.; Wu, X. H.; Sim, K. Y.; Tan, B. K. H.; Pereira, J. T.; Goh, S.-H. *Tetrahedron* **1998**, *54*, 2143.
4. Blazquez, M. A.; Bermijo, A.; Zafra-Polo, M. C.; Cortes, D. *Phytochem. Anal.* **1999**, *10*, 161.
5. (a) Gracza, T.; Jäger, V. *Synthesis* **1994**, 1359. (b) Cagnolini, C.; Ferri, M.; Jones, P. R.; Murphy, P. J.; Ayres, B.; Cox, B. *Tetrahedron* **1997**, *53*, 4815. (c) Prakash, K. R. C.; Rao, S. P. *Tetrahedron* **1993**, *49*, 6695.
6. (a) Mereyala, H. B.; Gadikota, R. R.; Maju, J.; Arora, S. K.; Dastida, S. G.; Agarwal, S. *Bioorg. Med. Chem.* **1999**, *7*, 2095. (b) Shing, T. K. M.; Tsui, H. J.; Zhou, Z. H. *Tetrahedron* **1992**, *48*, 8659.
7. Shing, T. K. M.; Tsui, H.-C.; Zhou, Z.-H. *J. Org. Chem.* **1995**, *60*, 3121.
8. Zhi-Cai, Yang; Wei-Shai, Zhou *Heterocycles* **1997**, *45*, 367.
9. Bruns, R.; Wernicke, A.; Koll, P. *Tetrahedron* **1999**, *55*, 9793.
10. Tsubuki, M.; Kanai, K.; Nagase, H.; Honda, T. *Tetrahedron* **1999**, *55*, 2493.
11. Yi, X.-H.; Meng, Y.; Hui, X. G.; Li *J. Org. Chem.* **1998**, *63*, 7472.
12. Surivet, J. P.; Vatele, J. M. *Tetrahedron* **1999**, *55*, 13011.
13. Chen, W. P.; Roberts, S. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 103.
14. (a) Hungerbühler, E.; Seebach, D. *Helv. Chim. Acta* **1981**, *64*, 687. (b) Mukaiyama, T.; Suzuki, K.; Yamada, T.; Tabusa, F. *Tetrahedron* **1990**, *46*, 265.
15. Dess, D.; Martin, J. *J. Org. Chem.* **1983**, *48*, 4155.

16. (a) Bachmann, W. E.; Raunio, E. K. *J. Am Chem. Soc.* **1950**, *72*, 2533. (b) Herrmann, J. L.; Berger, M. H.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1979**, *101*, 1544. (c) Midland, M. M.; Tramontano, A.; Cable, J. R. *J. Org. Chem.* **1980**, *50*, 28.
17. There is small amount of its diastereoisomer in isolated **12a** based on its ^{1}H NMR spectrum at δ_H 1.30 (t, J=7.1 Hz) and 4.24 (q, J=7.1 Hz), which is hard to separate by column chromatography.
18. The crystallographic data (excluding structure factors) for the structures of compounds **ent**-**1** and **ent**-**2** reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 150288 and CCDC 150287, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).