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Enantioselective Synthesis and Stereochemical Revision of Communiols A–C, Antibacterial 2,4-Disubstituted Tetrahydrofurans from the Coprophilous Fungus *Podospora communis*

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The enantioselective synthesis of the originally proposed structure of communiol C, an antibacterial 2,4-disubstituted tetrahydrofuran natural product from the coprophilous fungus *Podospora communis*, and its epimer *via* the Sharpless asymmetric dihydroxylation as the source of chirality led us to propose that the genuine stereochemistry of communiol C should be 3*R*, 5*R*, and 6*S*. The synthesis of the (3*R*,5*R*,6*S*)-isomer of communiol C and its good accordance with natural communiol C in every respect enabled us to confirm the newly proposed (3*R*,5*R*,6*S*)-stereochemistry for communiol C. The stereochemistries of structurally-related natural products (communiols A and B) of the same microbial origin were also revised through their total synthesis.

Key words: communiol; antibacterial; enantioselective synthesis; asymmetric dihydroxylation; stereochemical revision

In the course of screening for bioactive natural products from coprophilous (dung-colonizing) fungi, Gloer and coworkers isolated three novel tetrahydrofuranyl carboxylic acids from the culture broth of *Podospora communis* as substances exhibiting significant antibacterial activity against *Bacillus subtilis* and *Staphylococcus aureus*, and named them communiols A, B, and C (Fig. 1).[1] They also isolated five new structurally-related compounds (communiols D–H), apparently of the same biosynthetic origin, from the culture broth of *P. communis*.[1,2] The structures of communiols A–C were proposed to be (5*R*,7*S*,8*S*)-**1**, (5*R*,7*S*,8*S*)-**2** and (3*S*,5*S*,6*S*)-**3**, respectively, based mainly on NMR analyses including Mosher's MTPA methodology.[3] The 2,4-disubstituted tetrahydrofuran substructure incorporated in communiols A–C is relatively rare as a structural unit of natural products,[1] displaying a clear difference in substitution pattern from 2,5-disubstituted tetrahydrofurans which are frequently found in annonaceous acetogenins or ionophores.[4,5] The structural uniqueness of communiols A–C coupled with their interesting biological activity prompted our efforts to synthesize communiols A–C, which recently culminated in our new proposal on the stereochemistries of communiols A–C and the confirmation of the newly proposed stereochemistries by total synthesis,[6] as well as the enantioselective synthesis of communiols D–F and H with revised stereochemistries.[7,8] Herein, we describe the full details of our synthetic studies on communiols A–C, which led to the revision of their stereochemistries.[6]

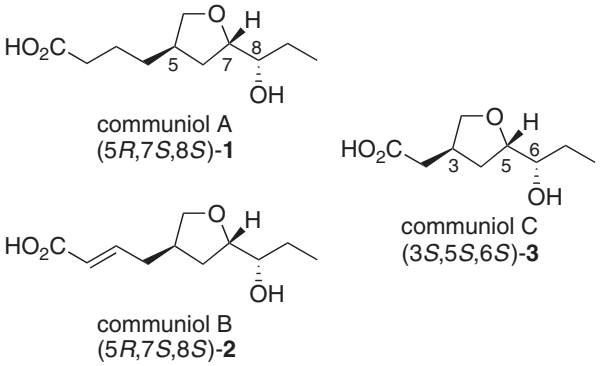

Fig. 1. Structures of Communiols A–C Proposed by Gloer *et al.*

Results and Discussion

Our retrosynthetic analysis of the originally proposed structure of communiol C [(3*S*,5*S*,6*S*)-**3**)], chosen as our first synthetic target due to its structural simplicity, is shown in Scheme 1. Bearing in mind that the 5,6-*threo*

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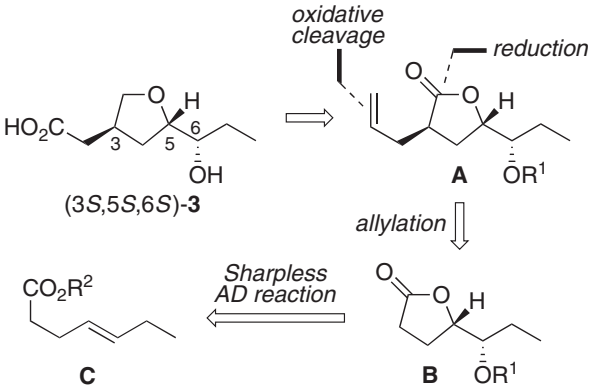
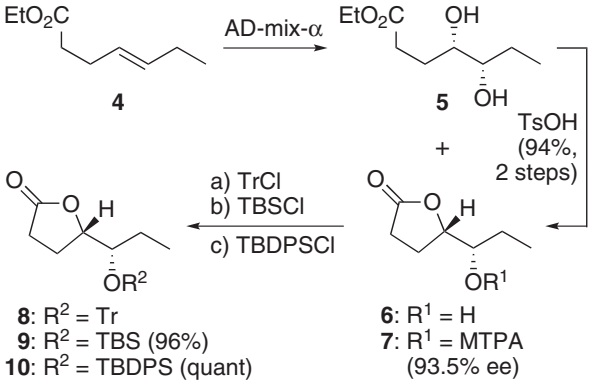
Abbreviations: DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; DEAD, diethyl azodicarboxylate; DIBAL, diisobutylaluminum hydride; DMAP, 4-(dimethylamino)pyridine; LDA, lithium diisopropylamide; MTPA, α-methoxy-α-(trifluoromethyl)phenylacetate; PNB, *p*-nitrobenzoate; TBAF, tetrabutylammonium fluoride; TBDPSCl, *tert*-butyldiphenylsilyl chloride; TBSCl, *tert*-butyldimethylsilyl chloride



Scheme 1. Retrosynthetic Analysis of (3*S*,5*S*,6*S*)-**3**.

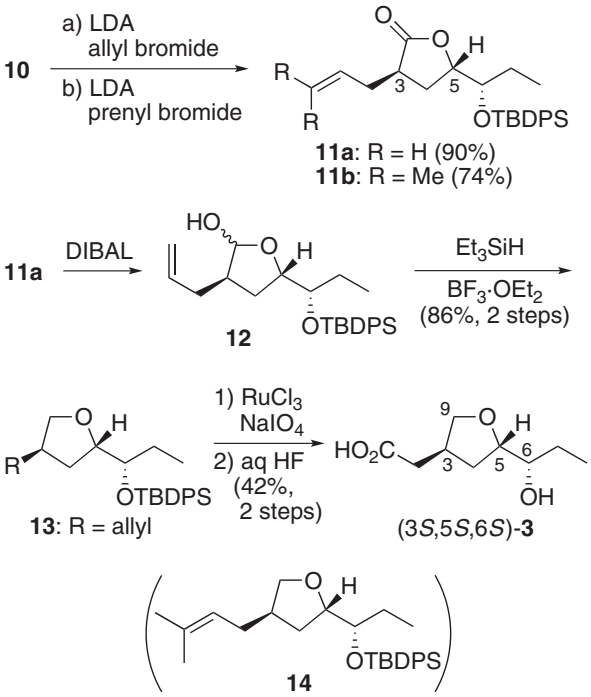


Scheme 2. Preparation of Protected Lactone Intermediates **8**–**10**.

stereochemistry of (3*S*,5*S*,6*S*)-**3** would readily be installed using the Sharpless asymmetric dihydroxylation (AD) reaction,[9,10] we planned to synthesize the target molecule from lactone intermediate **A**, which possesses an allyl substituent with the desired stereochemistry at the C3 position, *via* reduction of the lactone ring to the tetrahydrofuran ring followed by oxidative cleavage of the double bond. The lactone (**A**) with 3,5-*trans* relative stereochemistry could be prepared by applying the well-documented *trans*-selective alkylation of γ-substituted γ-lactones to **B**,[11,12] which in turn should be derivable from olefinic ester **C** by the Sharpless AD reaction and subsequent lactonization.

Our synthesis of (3*S*,5*S*,6*S*)-**3** began with the exposure of known olefinic ester **4**[13,14] to the AD reaction conditions using AD-mix-α as the chiral catalyst to give a mixture of dihydroxy ester **5** and monohydroxy lactone **6** (Scheme 2).[9,10] Treatment of the mixture with *p*-toluenesulfonic acid cleanly transformed **5** into **6**, whose ^{1}H-NMR spectrum was in good agreement with that reported for an authentic sample of **6** previously prepared from L-glutamic acid.[15] The absolute stereochemistry of **6** was confirmed by comparing its specific rotation ($[\alpha]^{22}_D$ +40.3 (*c* 2.25, CH_2Cl_2)) with the literature value ($[\alpha]^{22}_D$ +46.0 (*c* 2.0, CH_2Cl_2)),[15] and the enantiomeric excess (ee) of **6** was determined to be 93.5% by converting the alcohol into the corresponding (*R*)- and (*S*)-MTPA esters (**7**) and analyzing their ^{1}H-NMR spectra.[7] Prior to the introduction of an allyl substituent to the lactone, the protection of the hydroxyl group of **6** was attempted by treating **6** with trityl chloride (TrCl) and DBU in dichloromethane at room temperature,[16] in the hope that the very bulky protective group (trityl) of product **8** would effectively hamper the approach of the allylating agent from the bottom face of the lactone ring and thereby help enhance the *trans*-selectivity in the allylation step (**B** $\rightarrow$ **A**, Scheme 1). Unexpectedly, however, the protection did not proceed at all, resulting in the recovery of **6**, although the tritylation conditions (TrCl, DBU, CH_2Cl_2) have been known to effectively protect a variety of secondary alcohols. Other reaction conditions (TrCl, Et_3N, DMAP, CH_2Cl_2, room temperature to 40 °C; and TrCl, DBU, DMAP, DMF, 100 °C) brought about the formation of complex mixtures. On the other hand, silylation of the hydroxyl group using TBSCl or TBDPSCl as silylating agents gave the corresponding TBS- or TBDPS-protected products (**9** or **10**, respectively) in almost quantitative yields. Quite fortunately, the TBDPS-protected lactone (**10**) was obtained as a crystalline solid, which suggested the possibility that lactone **10** might be enantiomerically enriched by recrystallization from an appropriate solvent (*vide infra*). The good crystallinity of **10** coupled with the bulkier nature of TBDPS as compared to TBS led us to select **10** as the substrate for the next allylation step.

Allylation of the lithium enolate of **10** prepared by treating TBDPS-protected lactone **10** with LDA gave a 8.3:1 mixture of **11a** and its C3-epimer in 90% yield favoring the desired 3,5-*trans*-isomer **11a**, while the corresponding prenylation with prenyl bromide exhibited a slightly better *trans*-selectivity of 10:1 (74% combined yield) (Scheme 3).[11,12] When the allylation and prenylation were conducted using the TBS-ether (**9**) (see Scheme 2), the *trans*/*cis* ratio was 2.3:1 for the allylation and 4.2:1 for the prenylation. After careful purification of **11a** by silica gel column chromatography, the *trans*-allylation product isolated in 64% yield was reduced with DIBAL to give lactol **12** as a 3:1 anomeric mixture, which was further reduced with triethylsilane in the presence of $BF_3 \cdot OEt_2$ to afford tetrahydrofuran derivative **13**.[17,18] The prenylation product (**11b**) was also converted into tetrahydrofuran derivative **14** by the same two-step sequence of reactions. Oxidative cleavage of the double bond of **13** was performed using $RuCl_3$ and $NaIO_4$,[19] and the resulting carboxylic acid intermediate was deprotected with aqueous HF to afford (3*S*,5*S*,6*S*)-**3**, the structure proposed by Gloer for communiol C, while the prenylated derivative **14** gave a complex mixture when subjected to the same oxidative cleavage conditions ($RuCl_3/NaIO_4$). Unexpectedly, direct comparison of the ^{1}H-NMR spectrum of (3*S*,5*S*,6*S*)-**3** with that of natural communiol C revealed several clear differences, especially in the chemical shifts for 5-H, 6-H, and 9-H_2. In



Scheme 3. Synthesis of (3*S*,5*S*,6*S*)-**3**.

the synthetic sample, the signals for 5-H, 6-H, and 9-H_2 appeared at δ 3.85, 3.34, and 4.06/3.49, respectively, while the corresponding signals for natural communiol C were observed at δ 3.90, 3.68, and 4.09/3.41. In their report on the structural determination of communiols A–D, Gloer *et al.* determined the *trans*-relative stereochemistry between the C3 and C5-substituents of communiol C by observing several clear diagnostic NOESY correlations, and assigned the absolute configuration at the C6 chiral center to be *S* by analogy with the *S*-absolute configuration of communiol A (**1**), which in turn was established unambiguously by the modified Mosher method.[1,3] On the other hand, the *threo*-relative stereochemistry between C5 and C6 was proposed based only on Born's empirical rule, which has been employed to determine the relative stereochemistry between the C2 and C1′ stereogenic centers of 2-(1′-hydroxyalkyl)-tetrahydrofurans including those bearing an additional C5-alkyl substituent (Fig. 2).[20–22] According to the rule, the 1′-C signal is observed at *ca.* 74 ppm in ^{13}C-NMR

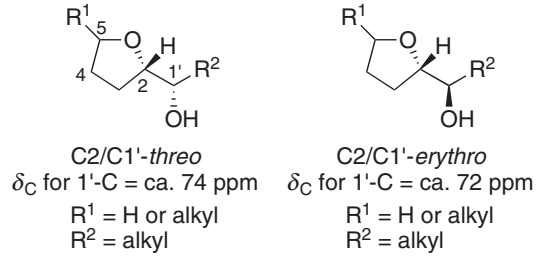
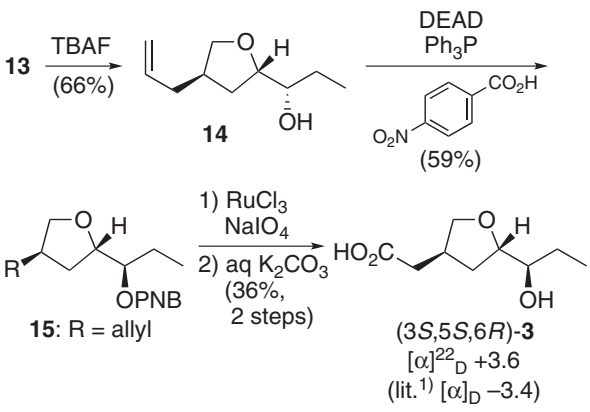


Fig. 2. Born's Rule for the Assignment of Relative Stereochemistry.

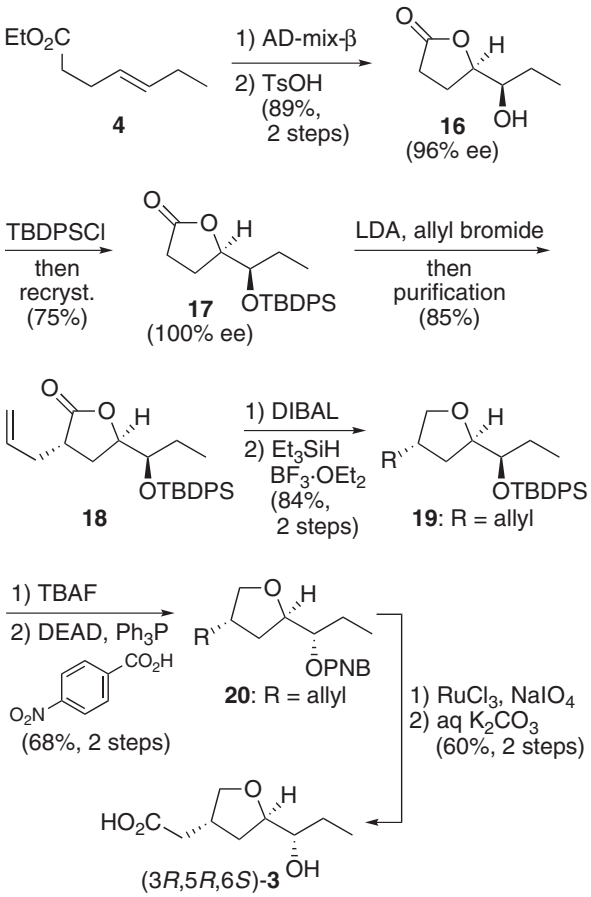
when the C2/C1′-relative stereochemistry is *threo*, while that of the corresponding *erythro*-isomer appears at *ca.* 72 ppm. The observed chemical shift (73.7 ppm) for the C6 carbon of natural communiol C led Gloer *et al.* to propose its 5,6-relative stereochemistry to be *threo* as shown in Fig. 1. To the best of our knowledge, however, Born's rule has never been applied to the determination of the C2/C1′-relative stereochemistry of 2,4-disubstituted tetrahydrofurans like communiol C. This led us to presume that the genuine 5,6-relative stereochemistry of communiol C might not be *threo*, but *erythro*, judging from the fact that the 3,5-*trans*-stereochemistry was determined by the well-established NOESY methodology.[1)]

According to our presumption that the genuine 5,6-relative stereochemistry of cmmuniol C might be *erythro*, we set about the synthesis of (3*S*,5*S*,6*R*)-**3** possessing 3,5-*trans*-5,6-*erythro* stereochemistry from intermediate **13** used in the synthesis of (3*S*,5*S*,6*S*)-**3** (Scheme 4). Deprotection of the TBDPS-ether gave alcohol **14**, which was then exposed to the Mitsunobu inversion conditions to afford PNB-ester **15** with inversion of the absolute configuration at the C6 position.[23,24)] Oxidative cleavage of the double bond of **15** gave a carboxylic acid intermediate, the PNB-ester group of which was deprotected by alkaline hydrolysis to furnish (3*S*,5*S*,6*R*)-**3**. As expected, the ^{1}H-NMR spectrum of (3*S*,5*S*,6*R*)-**3** was exactly the same as that of natural communiol C, which enabled us to establish the relative stereochemistry of communiol C as 3,5-*trans* and 5,6-*erythro*. Comparison of the specific rotation of (3*S*,5*S*,6*R*)-**3** ($[\alpha]^{22}_D$ +3.6 (*c* 0.24, CH_2Cl_2)) with that of natural communiol C ($[\alpha]_D$ −3.4 (*c* 0.142, CH_2Cl_2)) as well as the newly established relative stereochemistry of communiol C led us to conclude that the genuine structure of communiol C should be revised to (3*R*,5*R*,6*S*)-**3**, the enantiomer of (3*S*,5*S*,6*R*)-**3** depicted in Scheme 4.

Based on our new proposal for the stereochemistry of communiol C, we embarked on the synthesis of (3*R*,5*R*,6*S*)-**3** (Scheme 5). By following the same two-

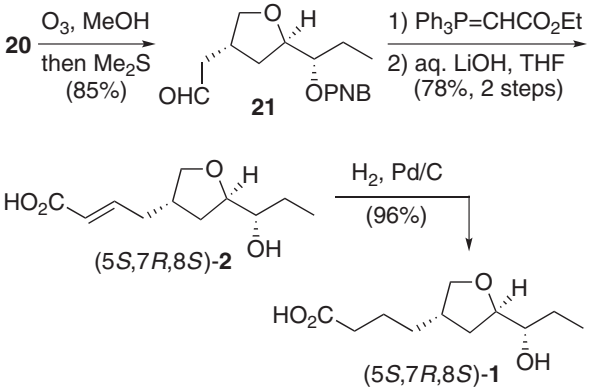


Scheme 4. Synthesis of (3*S*,5*S*,6*R*)-**3**.



Scheme 5. Synthesis of (3*R*,5*R*,6*S*)-**3**.

step sequence of reactions as employed for the preparation of **6** except that AD-mix-β, instead of AD-mix-α, was used in the asymmetric dihydroxylation step,[9,10] olefinic ester **4** was converted into hydroxy lactone **16**, whose enantiomeric excess was determined to be 96% by the same MTPA method as used for **6**. Protection of its hydroxyl group as a TBDPS ether gave rise to **17** as a white crystalline solid. Fortunately, and expectedly as well, a single recrystallization of the solid from hexane/EtOAc yielded enantiomerically pure **17** as colorless prisms (mp 62.5–63.0 °C), whose optical integrity was checked by deprotecting the TBDPS group with TBAF into the corresponding alcohol (*i.e.*, **16**) and analyzing the alcoholic product by the MTPA method.[7] Lactone **17** was transformed in 3 steps, *via* allylated intermediate **18**, into tetrahydrofuran derivative **19**, the TBDPS protecting group of which was then removed with TBAF to give an alcoholic intermediate. The inversion of the absolute configuration of the hydroxyl-bearing chiral center of the alcohol by the Mitsunobu reaction afforded **20**, which was then converted into (3*R*,5*R*,6*S*)-**3** *via* oxidative cleavage followed by hydrolysis. The ^{1}H- and ^{13}C-NMR spectra of the synthetic product were identical with those of natural communiol C, and its specific rotation ($[\alpha]^{22}_D$ −2.7 (*c* 1.16, CH_2Cl_2)) was in fairly good agreement with that of natural communiol C



Scheme 6. Synthesis of (5*S*,7*R*,8*S*)-**1** and (5*S*,7*R*,8*S*)-**2**.

($[\alpha]_D$ −3.4 (*c* 0.142, CH_2Cl_2)). Based on these results, we concluded that the genuine structure of communiol C is (3*R*,5*R*,6*S*)-**3** as depicted in Scheme 5. The same conclusion was reported by Murga and coworkers based on their synthesis of (3*S*,5*S*,6*R*)-**3** just after our preliminary communication.[25]

Assuming that the structurally-related tetrahydrofuran derivatives (communiols A and B) of the same microbial origin should have the same stereochemical arrangement as communiol C, we supposed that the correct structures of communiols A and B would be (5*S*,7*R*,8*S*)-**1** and (5*S*,7*R*,8*S*)-**2**, respectively, and set about their synthesis from **20**, the synthetic intermediate for (3*R*,5*R*,6*S*)-**3** (Scheme 6). Exposure of **20** to ozonolysis conditions gave aldehyde intermediate **21**, the chain elongation of which by the Wittig reaction afforded (5*S*,7*R*,8*S*)-**2** after hydrolysis of the PNB ester group. Finally, catalytic hydrogenation of (5*S*,7*R*,8*S*)-**2** afforded (5*S*,7*R*,8*S*)-**1**. The ^{1}H- and ^{13}C-NMR spectra of (5*S*,7*R*,8*S*)-**1** and (5*S*,7*R*,8*S*)-**2** were exactly the same as those of natural communiols A and B, respectively, which confirmed the 5,7-*trans*-7,8-*erythro* stereochemistry of natural communiols A and B, as expected. To confirm the absolute stereochemistry of communiols A and B, we next compared the specific rotations of synthetic and natural communiols A and B. Curiously, the specific rotations of (5*S*,7*R*,8*S*)-**1** ($[\alpha]^{22}_D$ +1.4 (*c* 1.17, CH_2Cl_2)) and (5*S*,7*R*,8*S*)-**2** ($[\alpha]^{22}_D$ +4.7 (*c* 1.00, CH_2Cl_2)) were inconsistent with reported data for communiols A and B, $[\alpha]_D$ −1.6 (*c* 0.25, CH_2Cl_2) and $[\alpha]_D$ −95 (*c* 0.075, CH_2Cl_2), respectively. Similar discrepancies were also reported by Murga *et al.*;[25] they attributed the discrepancies to concentration-dependency in specific rotation of chiral carboxylic acids. We believe that such big differences in optical rotation might be brought about also by the presence of small quantities of impurities in the synthetic and/or natural samples of communiols A and B; a recent report on the synthesis of communiol A by Trost and Zhang mentioned concentration- and impurity-dependency in the specific rotation of communiol A.[26] Despite this ambiguity, the complete agreement in ^{1}H- and ^{13}C-NMR data between (5*S*,7*R*,8*S*)-**1**

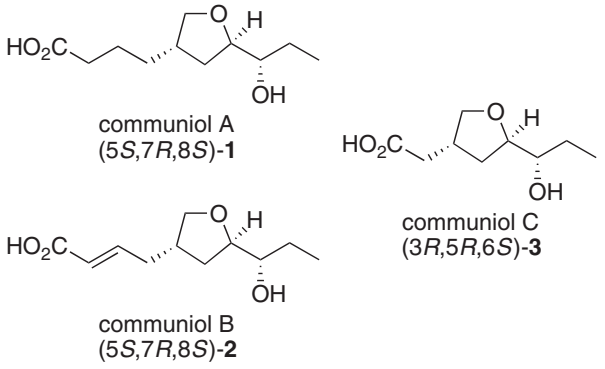


Fig. 3. Revised Stereochemistries for Communiols A–C.

and natural communiol A, and between (5*S*,7*R*,8*S*)-**2** and natural communiol B, together with the unambiguous determination of the absolute configuration of the C8 hydroxy-bearing stereogenic center as *S* by the well-established modified Mosher's MTPA method[3] strongly supported that the genuine structures of communiols A and B should be (5*S*,7*R*,8*S*)-**1** and (5*S*,7*R*,8*S*)-**2**, respectively.

In conclusion, the enantioselective synthesis of the originally proposed structure of communiol C, (3*S*,5*S*,6*S*)-**3**, was accomplished in 8 steps from known olefinic ester **4** using the Sharpless asymmetric dihydroxylation as the source of chirality. Clear differences in ^{1}H-NMR between (3*S*,5*S*,6*S*)-**3** and natural communiol C as well as good agreement of natural communiol C with the synthetic C6-epimer of (3*S*,5*S*,6*S*)-**3** in every respect except for the sign of specific rotation led us to propose that the genuine stereochemistry of communiol C should be 3*R*, 5*R*, and 6*S*. The synthesis of (3*R*,5*R*,6*S*)-**3** and its good accordance with natural communiol C in every respect confirmed the new proposal for the stereochemistry of communiol C (Fig. 3). Based on this stereochemical revision for communiol C, (5*S*,7*R*,8*S*)-**1** and (5*S*,7*R*,8*S*)-**2** were also synthesized as the most probable candidates for the genuine structures of communiols A and B, respectively. The ^{1}H- and ^{13}C-NMR of the synthetic products were identical with those of the corresponding natural products, which, coupled with the unambiguous determination of the (8*S*)-absolute stereochemistry by Gloer *et al.*, strongly supported the genuine structures of communiols A and B should be (5*S*,7*R*,8*S*)-**1** and (5*S*,7*R*,8*S*)-**2**, respectively (Fig. 3), although some ambiguities in their optical rotations have yet to be settled.

Experimental

IR spectra were recorded as films by a Jasco IR Report-100 spectrometer. ^{1}H NMR spectra (300, 500 or 600 MHz) and ^{13}C NMR spectra (125 or 150 MHz) were recorded with TMS as an internal standard in $CDCl_3$ by a Varian Gemini 2000 spectrometer, a Varian UNITY plus-500 spectrometer or a Varian UNITY plus-600 spectrometer. Optical rotation values were measured with a Horiba Septa-300 polarimeter, and mass spectra were obtained with a Jeol JMS-700 spectrometer. Merck silica gel 60 (70–230 mesh) was used for silica gel column chromatography.

*(2S,4R,5R)-2-Allyl-5-(tert-butyldiphenylsilyloxy)-4-heptanolide (**18**).* To a stirred solution of LDA, prepared by treating a solution of diisopropylamine (1.26 ml, 9.02 mmol) and hexamethylphosphoramide (1.50 ml, 8.63 mmol) in THF (30 ml) with butyllithium (1.6 M in hexane, 5.39 ml, 8.63 mmol) at −15 °C, was added dropwise a solution of **17** (3.00 g, 7.84 mmol) in THF (30 ml) at −78 °C. After 25 min, a solution of allyl bromide (0.747 ml, 8.63 mmol) in THF (10 ml) was added, and the resulting mixture was stirred for 15 min at −78 °C. After the addition of sat. NH_4Cl aq. (*ca.* 20 ml), the mixture was extracted with ether. The extract was successively washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was repeatedly chromatographed over SiO_2 (hexane/EtOAc, 30:1) to give 2.82 g (85%) of **18** as a colorless oil: $[\alpha]_D^{22}$ −10.9 (*c* 1.00, $CHCl_3$); IR ν_{max} cm^{-1}: 3080 (w), 3050 (w), 1770 (s), 1110 (s), 705 (s); ^{1}H-NMR (300 MHz) δ 0.70 (3H, t, $J = 7.5$ Hz), 1.04 (9H, s), 1.39 (1H, ddq, $J = 13.8$, 5.4, 7.5 Hz), 1.59–1.74 (1H, m), 1.94 (1H, dt, $J = 13.2$, 8.1 Hz), 2.16–2.33 (2H, m), 2.51–2.61 (1H, m), 2.78–2.89 (1H, m), 3.63 (1H, ddd, $J = 7.8$, 5.1, 3.3 Hz), 4.48 (1H, ddd, $J = 8.1$, 3.9, 3.3 Hz), 5.10 (1H, br d, $J = 11.1$ Hz), 5.11 (1H, dm, $J = 15.9$ Hz), 5.67–5.81 (1H, m), 7.35–7.48 (6H, m), 7.65–7.72 (4H, m); ^{13}C-NMR (150 MHz) δ 9.6, 19.5, 25.7, 27.0, 28.9, 35.5, 39.1, 76.6, 78.4, 117.7, 127.5 (2C), 127.7 (2C), 129.7, 129.9, 133.1, 133.9, 134.5, 135.81 (2C), 135.83 (2C), 179.1; HRMS (FAB) *m/z* calcd for $C_{26}H_{35}O_3Si$ ($[M + H]^+$) 423.2355, found 423.2358.

*(2R,4S)-4-Allyl-2-[(R)-1-(tert-butyldiphenylsilyloxy)-propyl]tetrahydrofuran (**19**).* To a stirred solution of **18** (0.603 g, 1.43 mmol) in CH_2Cl_2 (6 ml) was added dropwise DIBAL (0.94 M in hexane, 1.67 ml, 1.57 mmol) at −75 °C. After 20 min, the reaction was quenched with a saturated aqueous solution of Rochelle's salt, and the mixture was gradually warmed to room temperature over 1 h. The mixture was extracted with EtOAc, and the extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to give 0.627 g of an oil containing (2*R*/*S*,3*S*,5*R*)-3-allyl-5-[(*R*)-1-(*tert*-butyldiphenylsilyloxy)propyl]tetrahydrofuran-2-ol, which was then dissolved in CH_2Cl_2 (6.0 ml). To the solution was added dropwise Et_3SiH (0.251 ml, 1.57 mmol) at −78 °C, and the mixture was stirred for 5 min. $BF_3 \cdot OEt_2$ (0.198 ml, 1.57 mmol) was then added, and the mixture was gradually warmed to −5 °C while being stirred overnight. The reaction was quenched with a suspension of $NaHCO_3$ in MeOH, and the mixture was diluted with water and extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated *in*

vacuo. The residue was chromatographed over SiO_2 (hexane/EtOAc, 10:1) to give 0.490 g (84%) of **19** as a colorless oil: $[\alpha]_D^{22}$ +18.0 (*c* 1.00, $CHCl_3$); IR ν_{max} cm^{-1}: 3080 (w), 3050 (w), 1430 (m), 1110 (s), 700 (s); ^{1}H-NMR (300 MHz) δ 0.75 (3H, t, $J = 7.5$ Hz), 1.04 (9H, s), 1.28–1.42 (1H, m), 1.47–1.63 (2H, m), 1.97 (1H, ddd, $J = 12.3$, 7.8, 6.3 Hz), 2.07 (2H, t, $J = 7.2$ Hz), 2.14–2.30 (1H, m), 3.33 (1H, dd, $J = 8.4$, 6.3 Hz), 3.59 (1H, dt, $J = 5.5$, 5.1 Hz), 3.83 (1H, dd, $J = 6.3$, 8.4 Hz), 4.00 (1H, ddd, $J = 7.8$, 6.6, 5.1 Hz), 4.98 (1H, dm, $J = 10.2$ Hz), 5.01 (1H, dm, $J = 17.1$ Hz), 7.33–7.46 (6H, m), 7.68–7.75 (4H, m); ^{13}C-NMR (150 MHz) δ 10.0, 19.5, 25.5, 27.1, 32.7, 37.5, 38.8, 73.0, 76.6, 79.9, 115.7, 127.32 (2C), 127.35 (2C), 129.3, 129.4, 134.2, 134.7, 135.96, 135.98, 137.0; HRMS (FAB) *m/z* calcd for $C_{26}H_{36}O_2SiNa$ ($[M + Na]^+$) 431.2382, found 431.2390.

*(S)-1-[(2R,4S)-4-Allyltetrahydrofuran-2-yl]propyl p-nitrobenzoate (**20**).* To a stirred solution of **19** (0.941 g, 2.30 mmol) in THF (2 ml) was added TBAF (1 M in THF, 11.5 ml, 11.5 mmol) at room temperature. After 3 d, the reaction was quenched with water, and the mixture was extracted with EtOAc. The extract was successively washed with water and brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (hexane/ethyl acetate, 10:1) to give 0.386 g (99%) of (*S*)-1-[(2*R*,4*S*)-4-allyltetrahydrofuran-2-yl]-1-propanol as a colorless oil: $[\alpha]_D^{22}$ −1.59 (*c* 1.00, $CHCl_3$) ; IR ν_{max} cm^{-1}: 3460 (m), 3070 (w), 1640 (m); ^{1}H-NMR (300 MHz) δ 1.00 (3H, t, $J = 7.4$ Hz), 1.34–1.57 (2H, m), 1.66 (1H, ddd, $J =$ 12.9, 7.5, 5.7 Hz), 2.13 (2H, t, $J = 6.5$ Hz), 2.25–2.38 (1H, m), 2.38 (1H, d, $J = 4.2$ Hz, OH), 3.27–3.36 (1H, m), 3.45 (1H, dd, $J = 8.4$, 6.3 Hz), 3.82 (1H, q, $J = 6.9$ Hz), 3.95 (1H, dd, $J = 8.4$, 6.3 Hz), 5.02 (1H, dm, $J = 10.2$ Hz), 5.05 (1H, dm, $J = 17.1$ Hz), 5.77 (1H, ddd, $J = 17.1$, 10.2, 6.5 Hz); ^{13}C-NMR (150 MHz) δ 10.1, 26.5, 33.8, 37.4, 38.9, 72.9, 75.4, 81.4, 116.0, 136.6; HRMS (EI) *m/z* calcd for $C_{10}H_{18}O_2$ (M^+) 170.1306, found 170.1313. To a stirred solution of the alcohol (0.117 g, 0.684 mmol) in THF (4 ml) was successively added Ph_3P (0.718 g, 2.74 mmol), *p*-nitrobenzoic acid (0.457 g, 2.74 mmol), and DEAD (0.499 ml, 2.74 mmol) at 0 °C, and the mixture was stirred for 2 d at room temperature. The reaction was quenched with sat. $NaHCO_3$ aq., and the mixture was extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (hexane/EtOAc/$CHCl_3$, 20:1:2) to give 0.150 g (69%) of **20** as a colorless oil: $[\alpha]_D^{22}$ −1.88 (*c* 1.00, $CHCl_3$); IR ν_{max} cm^{-1}: 3070 (w), 1720 (s), 1515 (s), 1270 (s); ^{1}H-NMR (300 MHz) δ 0.98 (3H, t, $J = 7.4$ Hz), 1.66–1.84 (3H, m), 2.00 (1H, ddd, $J = 12.6$, 7.8, 6.3 Hz), 2.14 (2H, t, $J = 7.0$ Hz), 2.26–2.40 (1H, m), 3.43 (1H, dd, $J = 8.4$, 6.6 Hz), 3.95 (1H, dd, $J = 8.4$, 6.6 Hz), 4.16 (1H, ddd, $J = 7.5$, 6.3, 5.1 Hz), 5.02 (1H, dm, $J = 10.2$ Hz), 5.05 (1H, dm, $J = 17.1$ Hz), 5.19 (1H, ddd, $J = 7.8$, 5.1, 4.8 Hz), 5.76 (1H, ddt, $J = 17.1$, 10.2, 7.0 Hz), 8.20–8.25 (2H, m), 8.28–8.33 (2H, m); ^{13}C-NMR (150 MHz) δ 9.8, 23.8, 33.1, 37.1, 38.4, 73.4, 78.1, 79.0, 116.2, 123.5, 130.7, 135.8, 136.4, 150.5, 164.3; HRMS (FAB) *m/z* calcd for $C_{17}H_{22}O_5N$ ($[M + H]^+$) 320.1498, found 320.1498.

*{(3R,5R)-5-[(S)-1-Hydroxypropyl]tetrahydrofuran-3-yl}acetic acid [(3R,5R,6S)-**3**].* To a stirred solution of **20** (70.0 mg, 0.219 mmol) in $H_2O/CH_3CN/CCl_4$ (3:2:2, 2.8 ml) was successively added $NaIO_4$ (0.192 mg, 0.899 mmol) and a catalytic amount of $RuCl_3(H_2O)_n$ at 0 °C. After 2.5 h, the reaction was quenched with 2-propanol, and the mixture was extracted with CH_2Cl_2. The extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 ($CHCl_3$/MeOH, 75:1) to give 52.0 mg (70%) of {(3*R*,5*R*)-5-[(*S*)-1-(*p*-nitrobenzoyloxy)propyl]-tetrahydrofuran-3-yl}acetic acid as a colorless crystalline solid (mp 100.0–100.2 °C): $[\alpha]_D^{22}$ −5.14 (*c* 2.60, $CHCl_3$); IR ν_{max} cm^{-1}: ~3000 (br m), 1720 (vs), 1600 (w), 1510 (s), 1275 (s), 1100 (s); ^{1}H-NMR (300 MHz) δ 0.98 (3H, s, $J = 7.5$ Hz), 1.68–1.86 (3H, m), 2.18 (1H, ddd, $J = 12.9$, 7.8, 6.3 Hz), 2.47 (2H, d, $J = 7.5$ Hz), 2.61–2.76 (1H, m), 3.46 (1H, dd, $J = 8.7$, 6.6 Hz), 4.04 (1H, dd, $J = 8.7$, 6.6 Hz), 4.21 (1H, ddd, $J = 7.8$, 6.3, 5.1 Hz), 5.22 (1H, dt, $J = 7.8$, 4.8 Hz), 8.21–8.26 (2H, m), 8.28–8.33 (2H, m); ^{13}C-NMR (150 MHz) δ 9.8, 23.9, 33.0, 35.1, 36.9, 73.2, 77.8, 78.9, 123.5, 130.7, 135.6, 150.5, 164.3, 178.1; HRMS (FAB) *m/z* calcd for $C_{16}H_{20}O_7N$ ($[M + H]^+$) 338.1240, found 338.1243. To a stirred solution of the carboxylic acid (48.3 mg, 0.143 mmol) in THF (1 ml) was added 1 M K_2CO_3 aq. (1 ml) at room temperature. After 3 d, the mixture was acidified with 2 M HCl aq., and extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 [$CHCl_3$/MeOH (50:1) containing a trace amount of AcOH] to give 23.0 mg (86%) of [(3*R*,5*R*,6*S*)-**3** as a colorless oil: $[\alpha]_D^{22}$ −2.7 (*c* 1.16, CH_2Cl_2); IR ν_{max} cm^{-1}: 3350 (m), ~3000 (m), 1710 (s), 1460 (w), 1410 (m), 1235 (m), 1080 (m), 975 (m), 760 (m); ^{1}H-NMR (300 MHz) δ 0.99 (3H, t, $J = 7.4$ Hz), 1.38–1.50 (2H, m), 1.56 (1H, ddd, $J = 12.6$, 7.7, 6.0 Hz), 2.15 (1H, ddd, $J = 12.6$, 8.5, 7.4 Hz), 2.42 (1H, dd, $J = 16.1$, 8.0 Hz), 2.48 (1H, dd, $J = 16.1$, 6.9 Hz), 2.58–2.73 (1H, m), 3.44 (1H, dd, $J = 8.8$, 6.6 Hz), 3.72 (1H, ddd, $J = 8.0$, 5.2, 3.6 Hz), 3.95 (1H, dt, $J = 3.6$, 7.5 Hz), 4.12 (1H, dd, $J = 8.5$, 6.6 Hz); ^{13}C-NMR (125 MHz) δ 10.3, 25.6, 30.7, 35.5, 37.3, 73.3, 73.7, 81.3, 177.4; HRMS (FAB) *m/z* calcd for $C_9H_{17}O_4$ ($[M + H]^+$) 189.1127, found 189.1128.

*^{1}H- and ^{13}C-NMR data for (3S,5S,6S)-**3**, the originally proposed structure for communiol C.* ^{1}H-NMR (500 MHz) δ 1.00 (3H, t, $J = 7.6$ Hz), 1.37–1.54 (2H, m), 1.70 (1H, ddd, $J = 12.7$, 7.3, 5.9 Hz), 1.94 (1H, ddd,

$J = 12.7$, 7.8, 7.3 Hz), 2.46 (2H, d, $J = 7.3$ Hz), 2.68 (1H, sep, $J = 6.8$ Hz), 3.32–3.37 (1H, m), 3.49 (1H, dd, $J = 8.3$, 6.3 Hz), 3.85 (1H, q, $J = 6.8$ Hz), 4.06 (1H, dd, $J = 8.3$, 6.8 Hz); ^{13}C-NMR (125 MHz) δ 10.1, 26.5, 33.9, 35.6, 37.2, 72.8, 75.2, 81.3, 177.1.

*(S)-1-[(2R,4R)-4-(2-Oxoethyl)tetrahydrofuran-2-yl]-propyl p-nitrobenzoate (**21**).* Ozone was bubbled into a stirred solution of **20** (0.200 g, 0.626 mmol) in MeOH (2 ml) at $-78\,^{\circ}$C until the disappearance of **20** was observed by TLC monitoring. Me_2S (0.4 ml) was then added, and the mixture was gradually warmed to room temperature and then concentrated *in vacuo*. The residue was chromatographed over SiO_2 (hexane/EtOAc, 2:1) to give 0.171 g (85%) of **21** as a colorless oil: $[\alpha]_D^{22}$ -3.8 (*c* 0.510, $CHCl_3$); IR ν_{max} cm^{-1}: 2725 (w), 1720 (vs), 1605 (m), 1525 (s), 1275 (s); ^{1}H-NMR (300 MHz) δ 0.98 (3H, t, $J = 7.5$ Hz), 1.63–1.88 (3H, m), 2.18 (1H, ddd, $J = 12.9$, 7.8, 6.3 Hz), 2.60 (2H, d, $J = 6.8$ Hz), 2.65–2.80 (1H, m), 3.39 (1H, dd, $J = 8.7$, 6.6 Hz), 4.05 (1H, dd, $J = 8.7$, 6.6 Hz), 4.17 (1H, ddd, $J = 7.5$, 6.3, 4.8 Hz), 5.22 (1H, dt, $J = 7.8$, 3.9 Hz), 8.20–8.26 (2H, m), 8.28–8.34 (2H, m), 9.79 (1H, s); ^{13}C-NMR (125 MHz) δ 9.8, 23.9, 32.9, 33.2, 47.1, 73.3, 77.9, 78.9, 123.6, 130.7, 135.7, 150.5, 164.3, 200.6; HRMS (FAB) *m/z* calcd for $C_{16}H_{20}O_6N$ ($[M + H]^+$) 322.1290, found 322.1293.

*4-{(3S,5R)-5-[(S)-1-(p-Nitrobenzoyloxy)propyl]tetrahydrofuran-3-yl}-2-butenoic acid [(5S,7R,8S)-**2**].* A mixture of **21** (0.170 g, 0.530 mmol) and $Ph_3P{=}CHCO_2$-Et (0.203 g, 0.583 mmol) in CH_2Cl_2 (2.5 ml) was stirred for 9 h at room temperature. The mixture was diluted with water and extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 (hexane/EtOAc, 10:1) to give 0.170 g (82%) of ethyl 4-{(3*S*,5*R*)-5-[(*S*)-1-(*p*-nitrobenzoyloxy)propyl]tetrahydrofuran-3-yl}-2-butenoate as a colorless oil: $[\alpha]_D^{22}$ -1.9 (*c* 0.810, $CHCl_3$); IR ν_{max} cm^{-1}: 1720 (vs), 1650 (m), 1605 (w), 1530 (s), 1280 (s); ^{1}H-NMR (300 MHz) δ 0.98 (3H, t, $J = 7.4$ Hz), 1.29 (3H, t, $J = 7.1$ Hz), 1.67–1.86 (3H, m), 2.05 (1H, ddd, $J = 12.9$, 7.8, 6.3 Hz), 2.29 (1H, br t, $J = 7.0$ Hz), 2.34–2.46 (1H, m), 3.44 (1H, dd, $J = 8.7$, 6.3 Hz), 3.97 (1H, dd, $J = 8.7$, 6.3 Hz), 4.15–4.24 (1H, m), 4.18 (2H, q, $J = 7.1$ Hz), 5.20 (1H, dt, $J = 8.1$, 4.8 Hz), 5.85 (1H, dt, $J = 15.6$, 1.4 Hz), 6.89 (1H, dt, $J = 15.6$, 7.0 Hz), 8.19–8.25 (2H, m), 8.28–8.34 (2H, m); ^{13}C-NMR (125 MHz) δ 9.8, 14.2, 23.9, 33.1, 35.4, 37.8, 60.4, 73.3, 77.9, 79.0, 122.8, 123.6, 130.7, 135.7, 146.3, 150.5, 164.3, 166.3; HRMS (FAB) *m/z* calcd for $C_{20}H_{26}O_7N$ ($[M + H]^+$) 392.1709, found 392.1709. The ethyl ester (0.143 g, 0.364 mmol) was dissolved in THF (2.5 ml) and mixed with 1 M LiOH aq. (2 ml), and the mixture was stirred at room temperature for 20 h. The mixture was acidified with 2 M HCl aq. and extracted with EtOAc. The extract was washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed over SiO_2 [$CHCl_3$/MeOH (70:1) containing a trace amount of AcOH] to give 0.074 g (95%) of (5*S*,7*R*,8*S*)-**2** as a colorless oil: $[\alpha]_D^{22}$ $+4.7$ (*c* 1.00, CH_2Cl_2); IR ν_{max} cm^{-1}: 3400 (m), $\sim$3000 (m, broad), 1700 (s), 1655 (m), 1250 (m), 1085 (w), 980 (m), 885 (w), 760 (m); ^{1}H-NMR (300 MHz) δ 0.99 (3H, t, $J = 7.4$ Hz), 1.38–1.49 (2H, m), 1.52 (1H, ddd, $J = 12.6$, 7.4, 5.2 Hz), 2.09 (1H, dt, $J = 12.6$, 7.8 Hz), 2.32 (2H, br t, $J = 7.1$ Hz), 2.32–2.46 (1H, m), 3.42 (1H, dd, $J = 8.5$, 6.6 Hz), 3.71 (1H, ddd, $J = 7.7$, 5.5, 3.6 Hz), 3.93 (1H, dt, $J = 3.6$, 7.7 Hz), 4.05 (1H, dd, $J = 8.5$, 6.6 Hz), 5.87 (1H, br d, $J = 15.7$ Hz), 7.01 (1H, dt, $J = 15.7$, 7.1 Hz); ^{13}C-NMR (150 MHz) δ 10.3, 25.7, 30.5, 35.7, 38.2, 73.2, 73.6, 81.4, 122.0, 149.3, 170.7; HRMS (FAB) *m/z* calcd for $C_{11}H_{19}O_4$ ($[M + H]^+$) 215.1283, found 215.1286.

*4-{(3S,5R)-5-[(S)-1-Hydroxypropyl]tetrahydrofuran-3-yl}butanoic acid [(5S,7R,8S)-**1**].* A mixture of (5*S*,7*R*,8*S*)-**2** (0.025 g, 0.117 mmol) and 10% Pd-C (2.5 mg) in ethanol (0.25 ml) was stirred at room temperature for 1.5 h under hydrogen at atmospheric pressure. The mixture was filtered through a pad of Celite, and the filter cake was washed with EtOAc. The combined filtrates were concentrated *in vacuo*, and the residue was chromatographed over SiO_2 [$CHCl_3$/MeOH (70:1) containing a trace amount of AcOH] to give 0.024 g (96%) of (5*S*,7*R*,8*S*)-**1** as a colorless oil: $[\alpha]_D^{22}$ $+1.4$ (*c* 1.17, CH_2Cl_2); IR ν_{max} cm^{-1}: 3400 (m), $\sim$3000 (m, broad), 1710 (s), 1460 (m), 1260 (m), 1070 (m), 975 (w); ^{1}H-NMR (300 MHz) δ 0.97 (3H, t, $J = 7.4$ Hz), 1.37–1.51 (5H, m), 1.56–1.73 (2H, m), 2.06 (1H, ddd, $J = 12.4$, 8.8, 6.9 Hz), 2.12–2.27 (1H, m), 2.36 (2H, t, $J = 7.4$ Hz), 3.35 (1H, dd, $J = 8.2$, 7.7 Hz), 3.69 (1H, ddd, $J = 7.7$, 5.5, 3.3 Hz), 3.91 (1H, ddd, $J = 7.7$, 6.7, 3.6 Hz), 4.04 (1H, dd, $J = 8.2$, 6.6 Hz); ^{13}C-NMR (150 MHz) δ 10.4, 23.5, 25.7, 30.9, 32.5, 34.0, 39.3, 73.69, 73.74, 81.5, 178.7; HRMS (FAB) *m/z* calcd for $C_{11}H_{21}O_4$ ($[M + H]^+$) 271.1440, found 271.1442.

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References

1) Che, Y., Gloer, J. B., Scott, J. A., and Malloch, D., Communiols A–D: new mono- and bis-tetrahydrofuran derivatives from the coprophilous fungus *Podospora communis*. *Tetrahedron Lett.*, **45**, 6891–6894 (2004).
2) Che, Y., Araujo, A. R., Gloer, J. B., Scott, J. A., and

Malloch, D., Communiols E–H: new polyketide metabolites from the coprophilous fungus *Podospora communis*. *J. Nat. Prod.*, **68**, 435–438 (2005).
3) Ohtani, I., Kusumi, T., Kashman, Y., and Kakisawa, H., High-field FT NMR application of Mosher's method. The absolute configurations of marine terpenoids. *J. Am. Chem. Soc.*, **113**, 4092–4096 (1991).
4) Bermejo, A., Figadère, B., Zafra-Polo, M.-C., Barrachina, I., Estornell, E., and Cortes, D., Acetogenins from Annonaceae: recent progress in isolation, synthesis and mechanisms of action. *Nat. Prod. Rep.*, **22**, 269–303 (2005).
5) Wierenga, W., The total synthesis of ionophores. In "The Total Synthesis of Natural Products" Vol. 4, ed. ApSimon, J., Wiley, New York, pp. 263–351 (1981).
6) Kuwahara, S., and Enomoto, M., Enantioselective synthesis and stereochemical revision of communiols A–C. *Tetrahedron Lett.*, **46**, 6297–6300 (2005).
7) Enomoto, M., Nakahata, T., and Kuwahara, S., Stereochemical revision of communiols D and H through synthesis. *Tetrahedron*, **62**, 1102–1109 (2006).
8) Enomoto, M., and Kuwahara, S., Enantioselective total synthesis and stereochemical revision of communiols E and F. *J. Org. Chem.*, **71**, 6287–6290 (2006).
9) Kolb, H. C., VanNieuwenhze, M. S., and Sharpless, K. B., Catalytic asymmetric dihydroxylation. *Chem. Rev.*, **94**, 2483–2547 (1994).
10) Avedissian, H., Sinha, S. C., Yazbak, A., Sinha, A., Neogi, P., Sinha, S., and Keinan, E., Total synthesis of asimicin and bullatacin. *J. Org. Chem.*, **65**, 6035–6051 (2000).
11) Sells, T. B., and Nair, V., Synthetic approaches to novel cis and trans dideoxynucleosides of the apiose family. *Tetrahedron*, **50**, 117–138 (1994).
12) Bouchard, H., Soulié, J., and Lallemand, J. Y., Towards the total synthesis of clerodin. Part II. *Tetrahedron Lett.*, **32**, 5957–5958 (1991).
13) Odinokov, V. N., Vakhidov, R. R., Shakhmaev, R. N., and Zorin, V. V., Insect pheromones and their analogs. LIV. Synthesis of (*E*)-dodec-9-en-1-ol and its acetate, components of the sex pheromone of *Sparganothis pilleriana*. *Khim. Prir. Soedin.*, 936–939 (1996).
14) Bruyère, D., Bouyssi, D., and Balme, G., A study on the regio-and stereoselectivity in palladium-catalyzed cyclizations of alkenes and alkynes bearing bromoaryl and nucleophilic groups. *Tetrahedron*, **60**, 4007–4017 (2004).
15) Larchevêque, M., and Lalande, J., Les aminoacides précurseurs de synthons chiraux (IV) synthèse diastéréosélective d'α-diols énantiomériquement purs; préparation de la (+)-exobrévicomine. *Bull. Soc. Chim. Fr.*, 116–122 (1987).
16) Colin-Messager, S., Girard, J.-P., and Rossi, J.-C., Convenient method for the preparation of trityl ethers from secondary alcohols. *Tetrahedron Lett.*, **33**, 2689–2692 (1992).
17) Kraus, G. A., Frazier, K. A., Roth, B. D., Taschner, M. J., and Neuenschwander, K., Conversion of lactones into ethers. *J. Org. Chem.*, **46**, 2417–2419 (1981).
18) Brückner, C., Holzinger, H., and Reissig, H.-U., Diastereoselective syntheses of highly substituted methyl tetrahydrofuran-3-carboxylates by reactions of γ-lactols with silylated nucleophiles. *J. Org. Chem.*, **53**, 2450–2456 (1988).
19) Carlsen, P. H. J., Katsuki, T., Martin, V. S., and Sharpless, K. B., A greatly improved procedure for ruthenium tetraoxide catalyzed oxidations of organic compounds. *J. Org. Chem.*, **46**, 3936–3938 (1981).
20) Born, L., Lieb, F., Lorentzen, J. P., Moeschler, H., Nonfon, M., Söllner, R., and Wendisch, D., The relative configuration of acetogenins isolated from *Annona squamosa*; annonin I (squamocin) and annonin VI. *Planta Med.*, **56**, 312–316 (1990).
21) Chávez, D., Acevedo, L. A., and Mata, R., Jimenezin, a novel annonaceous acetogenin from the seeds of *Rollinia mucosa* containing adjacent tetrahydrofuran–tetrahydropyran ring systems. *J. Nat. Prod.*, **61**, 419–421 (1998).
22) Fujimoto, Y., Murasaki, C., Shimada, H., Nishioka, S., Kakinuma, K., Singh, S., Singh, M., Gupta, Y. K., and Sahai, M., Annonaceous acetogenins from the seeds of *Annona squamosa*. Non-adjacent bis-tetrahydrofuranic acetogenins. *Chem. Pharm. Bull.*, **42**, 1175–1184 (1994).
23) Mitsunobu, O., The use of diethyl azodicarboxylate and triphenylphosphine in synthesis and transformation of natural products. *Synthesis*, 1–28 (1981).
24) Martin, S. F., and Dodge, J. A., Efficacious modification of the Mitsunobu reaction for inversions of sterically hindered secondary alcohols. *Tetrahedron Lett.*, **32**, 3017–3020 (1991).
25) Murga, J., Falomir, E., Carda, M., and Marco, J. A., Stereoselective synthesis of *ent*-communiols A–C. *Tetrahedron Lett.*, **46**, 8199–8202 (2005).
26) Trost, B. M., and Zhang, T., Asymmetric synthesis of α-substituted aldehydes by Pd-catalyzed asymmetric allylic alkylation–alkene isomerization–Claisen rearrangement. *Org. Lett.*, **8**, 6007–6010 (2006).