Pheromone Synthesis, CXC[◇]

Synthesis of Stegobiol and Its Oxidation to Stegobinone, the Components of the Female-Produced Sex Pheromone of the Drugstore Beetle

Kenji Mori*[a], Satoshi Sano[a], Yusuke Yokoyama[a], Masahiko Bando[b], and Masaru Kido[b]

Department of Chemistry, Faculty of Science, Science University of Tokyo[a],
Kagurazaka 1-3, Shinjuku-ku, Tokyo 162-8601, Japan
Fax: (internat.) +81-3-3235-2214

Second Tokushima Institute of New Drug Research, Otsuka Pharmaceutical Co, Ltd.[b],
Kawauchi, Tokushima 771-01, Japan
Fax: (internat.) +81-886-65-6031

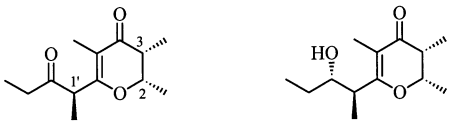
Received January 5, 1998

Keywords: Heterocycles / Lipases / Oxidations / Pheromones /Stegobinone / *Stegobium paniceum*

Crystalline (–)-stegobinone [(2*S*,3*R*,1′*R*)]-2,3-dihydro-2,3,5-trimethyl-6-(1′-methyl-2′-oxobutyl)-4*H*-pyran-4-one (**1**)], the major component of the female-produced sex pheromone of the drugstore beetle (*Stegobium paniceum* L.), was synthesized by oxidation of crystalline and the minor component (–)-stegobiol [(2*S*,3*R*,1′*S*,2′*S*)-2,3-dihydro-2,3,5-trimethyl-6-(2′-hydroxy-1′-methylbutyl)-4*H*-pyran-4-one (**2**)] under the appropriate conditions using Jones's chromic acid, Dess-Martin's periodinane or Ley's ruthenium reagent. The latter (**2**) was synthesized by employing lipase and the Sharpless epoxidation for the introduction of the proper chiral centers. The streostructure of **1** was comfirmed by X-ray analysis.

Drugstore beetle (*Stegobium paniceum* L.) is a serious pest of a wide variety of commodities and stored products. In 1978 Y. Kuwahara et al. proposed the structure of stegobinone, the major and crystalline component of the female-produced sex pheromone of *S. paniceum*, as 2,3-*cis*-dihydro-2,3,5-trimethyl-6-(1′-methyl-2′-oxobutyl)-4H-pyran-4-one (**1**, Scheme 1)[1]. The minor component of the pheromone was later shown to be stegobiol [2,3-*cis*-dihydro-2,3,5-trimethyl-6-(2′-hydroxy-1′-methylbutyl)-4H-pyran-4-one (**2**)] by Kodama et al. in 1987[2].

Scheme 1. Structures of the pheromone components of the female drugstore beetle



Stegobinone (2*S*,3*R*,1′*R*)-**1**

Stegobiol (2*S*,3*R*,1′*S*,2′*S*)-**2**

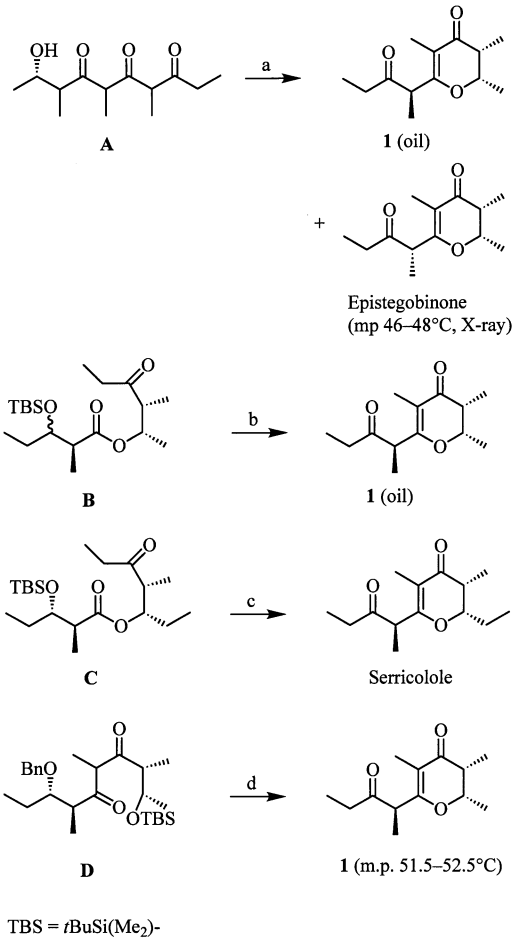
The unique structure of stegobinone (**1**) with unkown stereochemistry evoked much interest among synthetic chemists, and the first synthesis of (±)-**1** as a mixture of diastereomers at C-1′ by cyclization of (±)-**A** (Scheme 2) was reported simultaneously by Mori[3], Hassner[4] and their respective coworkers in 1979. Subsequently in 1981 Hoffmann et al. cyclized optically active **A** and separated the resulting mixture of products by HPLC to give stegobinone (**1**) and epistegobinone[5], the latter of which was crystalline and its structure was solved by X-ray analysis. The absolute configuration of stegobinone was therfore assigned as depicted [(2*S*,3*R*,1′*R*)-**1**], although their synthetic **2** was oily[5]. We then synthesized stegobinone (**1**) also as an oil by employing base-catalyzed cyclization of **B** as the key step[6]. Stegobiol (**2**) was prepared as an oil by cyclization followed by desilylation of (*S*)-*tert*-butyldimethylsilyloxy (TBSO-) keto ester (**B**). It should be added that the natural **2** was also reported to be oily[2]. Unfortunately our base-catalyzed cyclization of **B** was capricious and difficult to reproduce. Oppolzer and Rodriguez therefore developed a more reliable titanium tetrachloride-catalyzed condensation[8][9][10], and synthesized serricolole by cyclization of **C**. A totally new approach leading to **1** was reported in 1993 by Matteson et al.[11][12][13]. They prepared **D** by their stereodirected use of organoboranes, and **D** afforded both stegobiol (**2**) and stegobinone (**1**) as crystals. In order to obtain crystalline products, we started a new project to prepare both **1** and **2** as crystals.

Scheme 3 shows our retrosynthetic analysis of stegobinone (**1**). In order to secure pure and crystalline **1**, crystalline stegobiol (**2**) must be synthesized from **E**. We adhered to our previous idea of using ester **E** as the intermediate. The ester **E** can be obtained by acylation of **F** with **G**. For the preparation of **F**, lipase-catalyzed kinetic resolution of (±)-**F** may be useful, while the Sharpless epoxidation is to be employed for the preparation of **G**.

[◇] Part CLXXXIX: H. Takikawa, H. Tamagawa, K. Mori, *J. Indian Chem. Soc.* **1997**, *74*, 863–865.

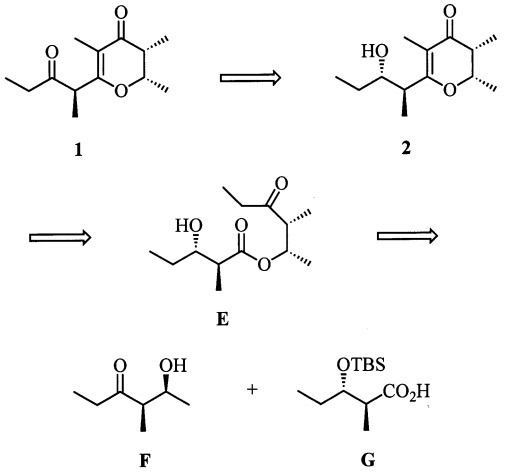
  1434–193X/98/0606–1135 $ 17.50+.50/0

Scheme 2. Previous syntheses of stegobinone and serricolole



Reagents: (a) i) H_2SO_4, MeOH; ii) HPLC separation. – (b) i) $LiN(TMS)_2$, THF, TMEDA; ii) $ClCH_2CO_2H$, THF, H_2O; iii) HF, MeCN, H_2O; iv) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2 (14%). – (c) i) 5 equiv. $TiCl_4$, 8 equiv. iPr_2NEt, CH_2Cl_2; ii) HF, MeCN, H_2O (78%). – (d) i) CF_3CO_2H, $CHCl_3$; ii) cyclohexane, $Pd(OH)_2$; iii) Pr_4NRuO_4, NMO, CH_2Cl_2 (77%).

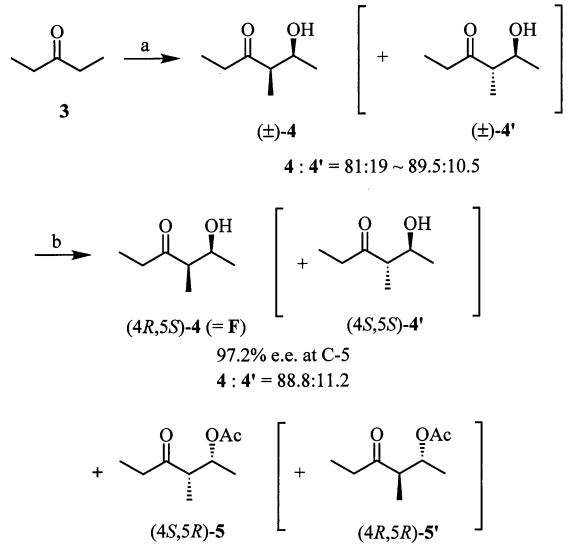
Scheme 3. Retrosynthetic analysis of **1**



The synthesis of (4*R*,5*S*)-5-hydroxy-4-methyl-3-hexanone (**4** = building block **F**) was executed as shown in Scheme 4.

The boron enolate of diethyl ketone (**3**) was prepared by treatment of **3** with dibutylboryl trifluoromethanesulfonate (Bu_2BOTf) in the presence of ethyldiisopropylamine[14], and was treated with acetaldehyde to give the *syn*-aldol [(±)-**4**] as the major product with varying ratio of **4**/**4**′ = 81:19 – 89.5:10.5. Instead of carrying out the asymmetric version of this aldol reaction we adopted the enzymatic resolution of (±)-**4** with lipase[15][16], because the enzymatic reaction was known to be practically easier to execute. To find out a suitable enzyme for acetylation of **4** with vinyl acetate, the following enzymes were examined with the criteria of high enantioselectivity and reasonable reaction rate: Amano′s Lipase AK, Lipase PS, and Lipase AH-S, Meito′s Lipase OF, Aldrich′s pig liver esterase (PLE) and pig pancreatic lipase (PPL), Toyobo′s lipase and Novo Nordisk′s Novozyme 435. Among them Lipase AH-S, Toyobo′s lipase and Novozyme 435 were good candidates. For the preparative-scale experiment, Novozyme 435 was employed because of its higher reaction rate at room temperature. The enzymatic acetylation followed by chromatographic separation afforded (4*R*,5*S*)-(−)-**4**[6] and (+)-**5**. The resulting crude (4*R*,5*S*)-**4** was treated once more with vinyl acetate and Novozyme 435 to give a mixture of (4*R*,5*S*)-**4** (= **F**) and (4*S*,5*S*)-**4**′ (88.8:11.2) with 97.2% e.e. at C-5 as estimated by GC analysis on a chiral stationary phase (Chirasil-DEX® CB). The present preparation of (4*R*,5*S*)-**4** proceeded in 17% overall yield based on **3** after only two steps, while the previous synthesis[8] furnished it in the same 17% overall yield after twelve steps starting from ethyl (*R*)-3-hydroxybutanoate[6]. The enzymatic method could thus simplify the synthesis of (4*R*,5*S*)-**4** (= building block **F**).

Scheme 4. Synthesis of **4**

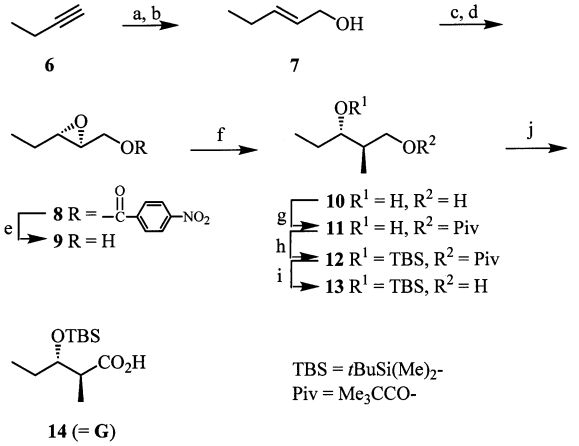


Reagents: (a) Bu_2BOTf, iPr_2NEt, Et_2O then MeCHO, −78°C (51%). – (b) Novozyme 435, $CH_2C{=}CHOAc$, molecular sieves (4 Å), hexane, (twice), (33%).

The second building block **G** (= 1**4**) was prepared as summarized in Scheme 5. 1-Butyne (**6**) was converted to (*E*)-2-penten-1-ol (**7**) in the usual manner[17]. Sharpless′s asymmetric epoxidation[18] of **7** yielded crude (2*R*,3*S*)-2,3-

epoxypentan-1-ol (**9**), which was purified as its crystalline *p*-nitrobenzoate (**8**) to give **8** of >99% e.e. as determined by HPLC analysis on Chiralcel® OD. Alkaline hydrolysis of **8** afforded pure **9** in 42% yield based on **7**. Treatment of **7** with lithium dimethylcuprate[19] gave the methylated 1,3-glycol **10** together with undesired 3-methylated 1,2-glycol. The latter could be destroyed by treatment with sodium periodate. To convert **10** into the acid **14**, the primary hydroxy group of **10** was tentatively protected as the pivalate **11**. The free hydroxy group of **11** was then protected as *tert*-butyldimethylsilyl (TBS) ether to give **12**. After removing the pivaloyl group of **13** under basic condition, the resulting alcohol **13** was oxidized with ruthenium tetroxide-catalyzed conditions[6][20] to give the desired acid **14** (= **G**). The overall yield of **14** was 5.4% based on **6** (10 steps) or 10.4% based on **7** (8 steps). In our previous synthesis of **14**[7], it was prepared from octyl (*S*)-3-hydroxypentanoate in 5.4% overall yield (6 steps). Octyl (*S*)-3-hydroxypentanoate (97% e.e.) was obtained by the reduction of octyl 3-oxopentanoate with baker's yeast in 64% yield[21]. Since octyl 3-oxopentanoate was prepared from cyanoacetic acid in 70% yield (2 steps), the overall yield of **14** was 2.4% based on cyanoacetic acid (9 steps). In the case of synthesis of **14**, use of asymmetric epoxidation eventually afforded **14** in better yield than the previous route employing the yeast reduction.

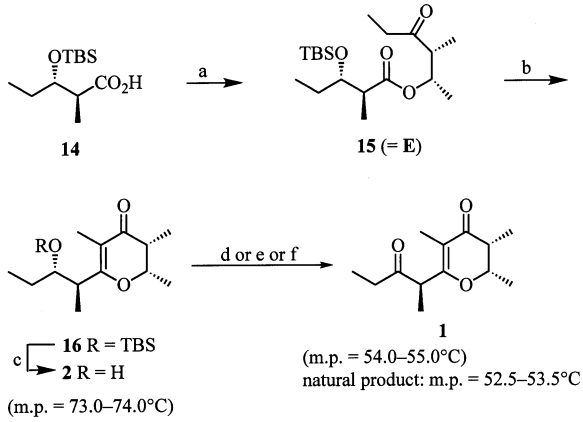
Scheme 5. Synthesis of **14**



Reagents: (a) BuLi, $(CH_2O)_n$, Et_2O (63%). – (b) $LiAlH_4$, Et_2O (82%). – (c) $Ti(OiPr)_4$, *t*BuOOH, (+)-diethyl tartrate, molecular sieves (3 Å), CH_2Cl_2. – (d) *p*-$O_2NC_6H_4COCl$, C_5H_5N, CH_2Cl_2 (2 steps, 63%); recrystallization (76%). – (e) NaOH, MeOH, H_2O (87%). – (f) i) Me_2CuLi, Et_2O; ii) $NaIO_4$, H_2O (41%). – (g) PivCl, C_5H_5N, CH_2Cl_2 (91%). – (h) TBSCl, imidazole, DMF (quant.). – (i) KOH, MeOH, reflux (80%). – (j) $RuCl_3$, $NaIO_4$, CCl_4, MeCN, pH 7 buffer (84%).

With two necessary building blocks **4** and **14** in hand, we proceeded to the final stage of our work as shown in Scheme 6. According to the reported procedure[6][7] **4** and **14** were coupled to give the known ester **15** (= **E**)[7]. Cyclization of **15** to stegobiol TBS ether was executed previously by employing lithium hexamethyldisilazide[7]. As criticized by Oppolzer[8], however, this procedure was very difficult to be reproduced. Oppolzer's procedure[8][9] was then exactly followed by using 5 equiv. of titanium tetrachloride and 8 equiv. of ethyldiisopropylamine. This reaction was also capricious in our hands. Nevertheless, twice per three trials, we could secure **16** in 66% yield. When the TBS protective group of **16** was deprotected by treatment with hydrofluoric acid in acetonitrile, stegobiol (**2**) was obtained in 47% yield. Pure stegobiol was indeed crystalline as reported by Matteson et al.[11][12][13], although Kodama et al.[2] and also ourselves[7] reported it to be oily. Finally we carefully examined the oxidation of stegobiol (**2**) to stegobinone (**1**) so as to find out the proper conditions to obtain **1** as crystals. We first oxidized **2** with tetrapropylammonium perruthenate (TPAP)[22] as reported by Matteson et al, and obtained crystalline **1** in 89% yield. When **2** was oxidized under the conventional Swern conditions[23] as employed by us previously[6], the resulting **1** was oily. Very recently Dondoni et al. reported a modification of the Swern oxidation to replace triethylamine with ethyldiisopropylamine to avoid racemization in the course of the reaction[24]. Even under these modified conditions only oily **1** resulted. We then oxidized **2** with Dess-Martin periodinane[25]. This reagent gave crystalline **1** quantitatively. Jones's chromic acid[26] was also successful to give crystalline **1** in 96% yield. However, 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO)[27] gave no crystalline **1**. Our experiments showed that the Dess-Martin periodinane was the mildest oxidant to avoid epimerization at C′-1. Jones's chromic acid and TPAP were also satisfactory, but TEMPO and Swern oxidation were found to cause deterioration presumably due to the presence of bases to give epistegobinone and other impurities.

Scheme 6. Synthesis of **1** and **2**

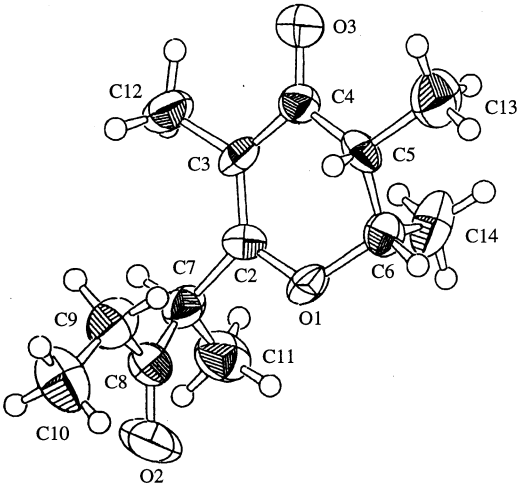


Reagents: (a) i) 2,6-$Cl_2C_6H_3COCl$, Et_3N, THF; ii) **4**, DMAP, C_6H_6 (90%). – (b) 5 equiv. $TiCl_4$, 8 equiv. iPr_2NEt, CH_2Cl_2 , –78°C, 3 h, then –10 to –20°C, 2 d (66%). – (c) HF, MeCN, H_2O (47%). – (d) Pr_4NRuO_4, NMO, CH_2Cl_2 (89%). – (f) Dess-Martin periodinane, C_5H_5N, CH_2Cl_2 (quant.). – (f) Jones CrO_3, Me_2CO (96%).

In conclusion, crystalline (2*S*,3*R*,1′*R*)-(–)-stegobinone (**1**) was obtained from **14** in 28% yield based on **14** (4 steps). The CD spectrum of synthetic **1** was in good agreement with the reported value[1][6]. The stereostructure of our synthetic stegobinone (**1**) could be confirmed by its X-ray analysis. Its computer-generated perspective view is shown in Figure 1. (–)-Stegobinone is thus (2*S*,3*R*,1′*R*)-2,3-dihydro-2,3,5-trimethyl-6-(1′-methyl-2′-oxobutyl)-4H-pyran-4-one

(**1**). Finally, it should be added that pure and crystalline **1** is stable as reported by Matteson et al.[11][12][13], and does not epimerize to (2*S*,3*R*,1′*S*)-epistegobinone, which is known to inhibit the action of **1**[28].

Figure 1. Perspective view of stegobinone



Financial support of this work by a Grant-in-Aid for Scientific Research (No. 09680576), *Japanese Ministry of Education, Science, Sports and Culture*, is gratefully acknowledged.

Experimental Section

General: Boiling points and melting points: Uncorrected values. − IR: Jasco IRA-102 and Hitachi Perkin Elmer 1640. − ^{1}H NMR: Jeol JNM-EX 90A (90 MHz), Bruker DPX 300 (300 MHz), (TMS at δ_H = 0.00 or $CHCl_3$ at δ_H = 7.26 as an internal standard). − ^{13}C NMR: Bruker DPX 300 (75.5 MHz), ($CDCl_3$ at δ_C = 77.0 as an internal standard). − MS: Jeol JMS-SX 102A and Hitachi M-80B. − Optical rotation: Jasco DIP-1000. − CC: Merck Kieselgel 60 Art 1.07734. − CD spectrum: Jasco J-720 spectropolarimeter. − M.p.: Yanaco MP-S3. − TLC: 0.25 mm Merck silica gel plates (60F-254). − PTLC: 0.5 mm Merck silica gel plates (60F-254).

(±)-5-Hydroxy-4-methylhexan-3-one [(±)-**4**]: To a solution of diethyl ketone **3** (14.5 ml, 12.4 g, 144 mmol) in dry ether (280 ml) was added dropwise Bu_2BOTf (43.4 g, 158 mmol) and *N*,*N*-diisopropylethylamine (30.1 ml, 22.9 g, 173 mmol) successively at 0°C under argon. Then to the mixture was added dropwise acetaldehyde (12.2 ml, 9.52 g, 215 mmol) at −78°C, and the mixture was stirred at −78°C for 1 h and at 0°C for 1 h. To the reaction mixture was added aqueous phosphate buffer (pH = 7, 150 ml), diluted with diethyl ether, and the layers were separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with a satd. aqueous sodium hydrogen carbonate solution, dried with sodium sulfate and concentrated in vacuo. The residue was chromatographed on silica gel (200 g, hexane/diethyl ether, 20:1) to give 9.60 g (51%) of (±)-**4** as a colorless oil. An analytical sample was purified by distillation, b.p. 44−45°C/1 Torr, n_D^{23} = 1.4365. − IR (film): $\tilde{\nu}_{max}$ = 3445 cm^{-1} (s, br. O−H), 1705 (s, C=O), 1095 (m, C−O), 1020 (m, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 1.06 (t, 3 H, *J* = 7.3 Hz, 1-H_3), 1.15 (d, 6 H, *J* = 6.4 Hz, 4-CH_3, 6-H_3), 1.56 (s, 1 H, -OH), 2.38−2.74 (m, 3 H, 2-H_2, 4-H), 3.98−4.25 (m, 1 H, 5-H).

Determination of the Diastereomeric Purity of (±)-**4**: GLC (column: Chirasil-DEX® CB, 0.25 mm × 25 m, 110°C constant; carrier gas: He, press 110 kPa). t_R = 7.50 min and 7.74 min (86.5%, *syn*-**4**), t_R = 8.00 min and 8.98 min (13.5%, *anti*-**4**). The diastereomeric purity of (±)-**4** was estimated to be 73%.

(4R,5S)-5-Hydroxy-4-methylhexan-3-one (**4**): To a solution of (±)-**4** (1.04 g, 7.99 mmol, *syn*/*anti*, 81:19) in hexane (100 ml) were added powdered molecular sieves (4 Å) (1 g), vinyl acetate (2.5 ml, 2.3 g, 27 mmol) and Novozyme 435 (100 mg). The suspension was stirred at room temp. for 21 h, and then the insoluble material was filtered off through Celite. The filtrate was concentrated in vacuo, and the residue was chromatographed on silica gel (10 g, hexane/diethyl ether, 20:1) to give **4** (559 mg, 54%) and acetate **5** (446 mg, 34%). This alcohol **4** was subjected again to the lipase-catalyzed acylation in the same manner as described above. To a solution of **4** (559 mg, 4.29 mmol) in hexane (50 ml) were added powdered molecular sieves (4 Å) (540 mg), vinyl acetate (1.3 ml, 1.2 g, 14 mmol) and Novozyme 435 (55 mg). The suspension was stirred at room temp. for 52 h, and then the insoluble materials were filtered off through Celite. The filtrate was concentrated in vacuo, and the residue was chromatographed on silica gel (5 g, hexane/diethyl ether, 20:1) to give (4*R*,5*S*)-**4** (305 mg, 55%) and acetate **5** (222 mg, 30%). An analytical sample was purified by distillation, b.p. 60°C/3 Torr, n_D^{24} = 1.4351. − $[\alpha]_D^{26}$ = −18.2 (*c* = 1.02, $CHCl_3$). − The IR and ^{1}H NMR spectra were identical with those of (±)-**4**.

Determination of the Enantiomeric Purity of (4R,5S)-**4**: GLC (column: Chirasil-DEX® CB, 0.25 mm × 25 m, 80°C constant; carrier gas: He, press 110 kPa). t_R = 30.3 min [98.6%, (4*R*,5*S*)-**4**], t_R = 34.0 min [1.4%, (4*S*,5*R*)-**4**]. The enantiomeric purity at C-5 of (−)-(4*R*,5*S*)-**4** was estimated to be 97.2%. t_R = 30.3 min and 34.0 min (88.8%, *syn*-**4**), t_R = 36.8 min and 47.4 min (11.2%, *anti*-**4′**). The diastereomeric purity of (4*R*,5*S*)-**4** was estimated to be 77.6%.

(2′S,3′S)-Epoxypentyl p-Nitrobenzoate (**8**): To a suspension of activated and powdered molecular sieves (3 Å) (6.4 g) in dry CH_2Cl_2 (700 ml) were added at −20°C a solution of (+)-diethyl tartrate (2.62 g, 12.7 mmol) in dry CH_2Cl_2 (10 ml) and Ti(O*i*Pr)$_4$ (3.13 ml, 3.04 g, 10.6 mmol). Then a solution of *t*BuOOH (3.40 M in isooctane, 125 ml, 424 mmol) was added dropwise over 10 min. The resulting mixture was stirred for 30 min at −20°C, and a solution of **7** (18.3 g, 212 mmol) in dry CH_2Cl_2 (100 ml) was added dropwise over 40 min with vigorous stirring. After stirring for 5 h at −20°C, the reaction mixture was warmed to 0°C and poured into a mixture of $FeSO_4 \cdot H_2O$ (66 g) and tartaric acid (20 g) in deionized water (100 ml) at 0°C. After stirring for 10 min, organic layer was separated and aqueous layer was extracted with diethyl ether (60 ml). The combined organic layers were cooled to 0°C and to this was added 30% NaOH in saturated brine (20 ml). After stirring vigorously at 0°C for 1h, this mixture was diluted with water (100 ml), the organic layer was separated, and the aqueous layer was extracted twice with diethyl ether (100 ml). The combined organic layers were dried with sodium sulfate and concentrated in vacuo. The residue was dissolved into CH_2Cl_2 (300 ml). To this was added pyridine (72.2 ml, 954 mmol) and *p*-nitrobenzoyl chloride (59.0 g, 318 mmol) at 0°C. After stirring at 0°C for 2h, to the reaction mixture was added water and this was further stirred for 1h. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with a saturated aqueous $CuSO_4$ solution (twice), water, a satd. aqueous sodium hydrogen carbonate solution and brine, dried with sodium sulfate and concentrated in vacuo. The residue was chromatographed on silica gel (500 g, hexane/ethyl acetate, 30:1) to give 33.7 g (63%) of **8** as a solid. This was recrystallized several times from hexane/diethyl ether (5:1) to give 24.2 g (73%) of yellow needles, m.p. 60−61°C. − $[\alpha]_D^{22}$ = −44.7 (*c* = 1.14, $CHCl_3$). −

IR (KBr): $\tilde{\nu}_{max}$ = 3110 cm^{-1} (m, aromatic), 3080 (w, aromatic), 3055 (w, aromatic), 1725 (s, C=O), 1610 (m, arom. C=C), 890 (s). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 1.03 (t, *J* = 6.8 Hz, 3 H, 5′-H_3), 1.48−1.87 (m, 2 H, 4′-H_2), 2.94 (br. dt, 1 H, *J* = 2.3, *J′* = 5.4 Hz, 3′-CH), 3.06−3.24 (m, 1 H, 2′-CH), 4.20 (br. dd, 1 H, *J* = 12.2, *J′* = 6.5 Hz, 1′-H_a), 4.71 (br. dd, 1 H, *J* = 12.2, *J′* = 3.1 Hz, 1′-CH_b), 8.27 (br. s, 4 H, Ar). − $C_{12}H_{13}NO_5$ (251.2): calcd. C 57.53, H 5.22, N 5.58; found C 57.07, H 5.09, N 5.59.

Determination of the Enantiomeric Purity of (2′S,3′S)-**8**: HPLC [column: Chiralcel® OD, 4.6 mm × 25 cm; solvent: hexane/*i*PrOH (3/1), flow rate: 0.5 ml/min; detector: 254 nm]: t_R = 18.3 min [0.30%, (2′*R*,3′*R*)-**8**], t_R = 19.4 min [99.7%, (2′*S*,3′*S*)-**8**]. The enantiomeric purity of (2′*S*,3′*S*)-**8** was estimated to be 99.4%.

(2S,3S)-Epoxypentan-1-ol (**9**): To **8** (19.2 g, 76.3 mmol) was added a solution of 1.0 M NaOH methanol/water (1:1, 152 ml, 152 mmol) at 0°C. After stirring at room temp. for 1 h, the reaction mixture was saturated with sodium chloride and extracted with diethyl ether. The combined organic layers were dried with anhydrous sodium sulfate and concentrated in vacuo at 0−10°C. The residue (ca. 55 g containing methanol) was filtered through silica gel (100 g). Elution with hexane/diethyl ether (1:1) and subsequent evaporation of the eluents gave an oily residue, which was distilled to give 6.79 g (87%) of **9** as a colorless oil; b.p. 75−76°C/13 Torr, n_D^{22} = 1.4297. − $[\alpha]_D^{22}$ = −45.6 (*c* = 1.31, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 3415 cm^{-1} (s, br. O−H), 1055 (s, C−O), 1025 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 1.00 (t, *J* = 7.2 Hz, 3 H, 5-H_3), 1.45−1.80 (m, 2 H, 4-H_2), 1.93 (t, *J* = 7.2 Hz, 1 H, OH), 2.86−3.02 (m, 2 H, 2-, 3-H), 3.63 (ddd, 1 H, *J* = 12.6, *J′* = 7.2, *J″* = 4.5 Hz, 1-H_a), 3.90 (ddd, 1 H, *J* = 12.6, *J′* = 5.9, *J″* = 2.1 Hz, 1-H_b). This was so volatile that no correct combustion analytical data could be obtained.

(2R,3S)-2-Methyl-1,3-pentanediol (**10**): To a vigorously stirred suspension of CuI (24.4 g, 128 mmol) in dry diethyl ether (180 ml) was added dropwise MeLi (1.03 M in diethyl ether, 249 ml, 256 mmol) at 0°C. After stirring at 0°C for 15 min, to the resulting solution was added dropwise a solution of **9** (5.69 g, 55.7 mmol) in diethyl ether (15 ml) at 0°C. After stirring at 0°C for 4.5 h, to the reaction mixture was added a satd. aqueous NH_4Cl. The mixture was filtered through Celite and the filter cake was washed several times with diethyl ether. The combined filtrate and washings were washed with a satd. aqueous sodium thiosulfate solution (three times) and brine. The combined aqueous layers were saturated with sodium chloride and extracted four times with ethyl acetate. The combined organic layers were concentrated in vacuo. To the residue (7.7 g) was added water (50 ml) and $NaIO_4$ (5.97 g, 27.9 mmol) and the resulting mixture was stirred vigorously at room temp. for 16 h. Then this was saturated with sodium chloride and extracted four times with ethyl acetate. The combined organic layers were concentrated in vacuo and the residue was chromatographed on silica gel (40 g, hexane/diethyl ether, 3:1) to give 2.71 g (41%) of **10** as a colorless oil. An analytical sample was purified by distillation, b.p. 82−83°C/1.5 Torr, n_D^{22} = 1.4483. − $[\alpha]_D^{24}$ = −22.6 (*c* = 1.22, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 3345 cm^{-1} (s, br. O−H), 1075 (s, C−O), 1030 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.90 (d, 3 H, *J* = 6.8 Hz, 2-CH_3), 0.97 (t, 3 H, *J* = 6.8 Hz, 5-H_3), 1.19−1.89 (m, 3 H, 2-H, 4-H_2), 2.25−2.45 (m, 2 H, 1-OH, 3-OH), 3.46−3.90 (m, 3 H, 1-H_2, 3-H). − $C_6H_{14}O_2$ (118.18) calcd. C 60.98, H 11.94, found C, 60.56, H 11.94.

Bis(3,5-dinitrobenzoate) of **10**: M.p. 130.5−132°C (recrystallized from hexane/ethyl acetate, 1:1). − $C_{20}H_{18}N_4O_{12}$ (506.4) calcd. C 47.44, H 3.58, N 11.06, found C, 47.37, H 3.59, N 11.07.

(2′R,3′R)-3′-Hydroxy-2′-methylpentyl 2,2-Dimethylpropanoate (**11**): To a solution of **10** (558 mg, 4.72 mmol) and pyridine (3.0 ml, 37.1 mmol) in CH_2Cl_2 (30 ml) was added PivCl (1.16 ml, 1.15 g, 9.44 mmol) at 0°C. After stirring at 0°C for 3.5 h, to the reaction mixture was added water and this mixture was stirred for 1h. This was poured into water and extracted with ethyl acetate. The combined organic layers were washed with dil. hydrochloric acid, water, a satd. aqueous sodium hydrogen carbonate solution and brine, dried with sodium sulfate and concentrated in vacuo. The residue was chromatographed on silica gel (25 g, hexane/ethyl acetate, 100:1) to give 867 mg (91%) of **11** as a colorless oil. A part of **11** was further purified by distillation, b.p. 80−82°C/1.5 Torr, n_D^{24} = 1.4335. − $[\alpha]_D^{24}$ = −11.9 (*c* = 1.08, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 3320 cm^{-1} (s, br. O−H), 1730 (s, C=O), 1710 (s, C=O), 1170 (s, C−O), 1030 (s, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.93 (d, 3 H, *J* = 6.8 Hz, 2′-CH_3), 0.97 (t, 3 H, *J* = 6.8 Hz, 5′-H_3), 1.20 (s, 9 H, *t*Bu), 1.28−1.72 (m, 1 H, 2′-H), 3.22−3.48 (m, 1 H, 3′-H), 4.08 (dd, 1 H, *J* = 5.4, *J′* = 11.1 Hz, 1′-H_a), 4.20 (dd, 1 H, *J* = 5.9, *J′* = 11.1 Hz, 1′-H_b). This was directly employed for the next step.

(2′R,3′S)-3′-tert-Butyldimethylsilyloxy-2′-methylpentyl 2,2-Dimethylpropanoate (**12**): A solution of **11** (1.96 g, 9.69 mmol) in dry DMF (100 ml) was added imidazole (3.96 g, 58.2 mmol) and TBSCl (4.38 g, 29.1 mmol). The solution was stirred at room temp. for 14h. The mixture was diluted with water, stirred for 1h and extracted with diethyl ether. The organic layer was washed with water, brine, dried with magnesium sulfate and concentrated in vacuo. The residue was chromatographed on silica gel (40 g, hexane/ethyl acetate, 200:1) to give 2.69 g (quant.) of **12** as a colorless oil. An analytical sample was purified by distillation, b.p. 93−95°C/1.5 Torr, n_D^{22} = 1.4539. − $[\alpha]_D^{23}$ = +17.0 (*c* = 1.07, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1730 cm^{-1} (s, C−O), 1285 (m, Si−Me). 1255 (m, Si−Me), 1160 (m, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.05 [s, 6 H, $Si(CH_3)_2$], 0.78−0.99 (m, 3 H, 5′-H_3), 0.88 [s, 9 H, $SiC(CH_3)_3$], 0.90 (d, 1 H, *J* = 6.6 Hz, 2′-CH_3), 1.30−1.64 (m, 2 H, 4′-H_2), 1.80−2.15 (m, 1 H, 2′-H), 3.59 (q, 1 H, *J* = 5.4 Hz, 3′-H), 3.90 (dd, 1 H, *J* = 11.7, *J′* = 6.6 Hz, 1′-H_a), 4.13 (dd, 1 H, *J* = 11.7, *J′* = 6.2 Hz, 1′-H_b). − $C_{17}H_{36}O_3Si$ (316.56) calcd. C 64.50, H 11.46, found C 64.56, H 11.67.

(2R,3S)-3-tert-Butyldimethylsilyloxy-2-methylpentan-1-ol (**13**): To **12** (178 mg, 0.562 mmol) was added 10% KOH in MeOH (5 ml) and the mixture was stirred under reflux for 5 h. To the reaction mixture was added a satd. NH_4Cl solution at room temp. and the mixture was saturated with sodium chloride. The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with water, a satd. aqueous sodium hydrogen carbonate solution, brine, dried with magnesium sulfate and concentrated in vacuo. The residue was chromatographed on silica gel (5 g, hexane/ethyl acetate, 50:1) to give 105 mg (80%) of **13** as a colorless oil. An analytical sample was purified by distillation, b.p. 83°C/1.5 Torr, n_D^{22} = 1.4439. − $[\alpha]_D^{24}$ = +17.4 (*c* = 1.19, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 3360 cm^{-1} (m, O−H), 1285 (m, Si−Me), 1255 (m, Si−Me), 1015 (m, C−O). − ^{1}H NMR (90 MHz, $CDCl_3$): δ = 0.05 [s, 6 H, $Si(CH_3)_2$], 0.87 (t, 3 H, *J* = 7.7 Hz, 5-H_3), 0.90 [s, 9 H, $SiC(CH_3)_3$], 0.98 (d, 3 H, *J* = 7.0 Hz, 2-CH_3), 1.40−1.87 (m, 3 H, 2-H, 4-H_2), 2.72 (br. t, 1 H, *J* = 5.8 Hz, OH), 3.40−3.90 (m, 3 H, 1-H_2 and 3-CH). These spectral data were in good accord with those reported previously[29].

(2S,3S)-3-tert-Butyldimethylsilyloxy-2-methylpentanoic Acid (**14**): To a biphasic solution of **13** (436 mg, 1.88 mmol) in CCl_4 (6 ml), MeCN (6 ml) and phosphate buffer (pH = 7, 0.4 M, 9 ml) was added $NaIO_4$ (1.20 g, 5.63 mmol) at room temp.. After stirring for 5 min, to the resulting mixture was added $RuCl_3 \cdot n\ H_2O$ (40 mg).

This was stirred vigorously at room temp. for 10 h and then diluted with CH_2Cl_2. The organic layer was separated and aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried with magnesium sulfate and concentrated in vacuo. The residue was diluted with diethyl ether, filtered through Celite and concentrated in vacuo. The residue was chromatographed on silica gel (15 g, hexane/diethyl ether, 20:1) to give 386 mg (84%) of **14** as a colorless oil. This was immediately used in the next step without further purification, $n_D^{23} = 1.4422$. − $[\alpha]_D^{24} = +10.0$ (c = 1.11, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 3000 cm^{-1} (m, br. CO_2H), 1710 (s, C=O), 1055 (m, C−O), 1015 (m, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.05 [s, 6 H, $Si(CH_3)_2$], 0.87 (m, 3 H, 5-H_3), 0.90 [s, 9 H, $SiC(CH_3)_3$], 1.20 (d, 3 H, J = 7.6 Hz, 2-CH_3), 1.58 (br. quint., 2 H, J = 6.9 Hz, 4-H_2), 2.68 (dq, 1 H, J = 4.8, J' = 7.6 Hz, 2-H), 3.80 (q, 1 H, J = 4.8, J' = 6.2 Hz, 3-H).

(1′S,2′R,2S,3S)-1′,2′-Dimethyl-3′-oxopentyl 3-tert-Butyldimethylsilyloxy-2-methylpentanoate (**15**): 2,6-Dichlorobenzoyl chloride (230 mg, 1.10 mmol) was added to a mixture of **14** (270 mg, 1.10 mmol) and triethylamine (122 mg, 1.21 mmol) in dry THF (7 ml) under argon. The mixture was stirred for 11 h at room temp.. After the removal of $Et_3N{\cdot}HCl$ by filtration, the filtrate was concentrated under N_2, and the residue was dissolved in dry benzene (15 ml). To this solution were added a solution of **4** (186 mg, 1.43 mmol) in dry benzene (1 ml) and DMAP (148 mg, 1.21 mmol) in dry benzene (1 ml) at 0°C under argon. The resulting mixture was stirred for 3 h at 0°C, then diluted with diethyl ether, washed with dil. hydrochrolic acid, water, a satd. aqueous sodium hydrogen carbonate solution, brine, dried with magnesium sulfate and concentrated in vacuo. The residue was purified by chromatography on silica gel (10 g, hexane/diethyl ether, 40:1) to give (357 mg, 90%) of **15** as a colorless oil. This was immediately used in the next step without further purification, $n_D^{24} = 1.4455$. − $[\alpha]_D^{24} = +1.50$ (c = 1.10, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1735 cm^{-1} (s, C=O), 1720 (s, C=O), 1050 (m, C−O), 1015 (m, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = 0.05 [br. s, 6 H, $Si(CH_3)_2$], 0.63−1.60 (m, 17 H, 2-, 1′-, 2′-CH_3, 4-H_2, 5-,5′-H_3), 0.87 [s, 9 H, $SiC(CH_3)_3$], 2.35−2.90 (m, 3 H, 2, 2′-CH_3), 2.50 (quint., 2 H, J = 6.7 Hz, 4′-H_2), 3.90 (q, 1 H, J = 5.1 Hz, 3-H), 5.13 (quint., 1 H, J = 6.2 Hz, 1′-CH). These spectral data were in good accord with those reported in ref.[7].

(2S,3R,1′S,2′S)-2,3-Dihydro-6-[1′-methyl-2-(tert-butyldimethylsilyloxybutyl]-4H-pyran-4-one (**16**): A 0.5 M solution of $TiCl_4$ in CH_2Cl_2 (21.5 ml, 10.8 mmol) was added dropwise at −78°C to a solution of **15** (770 mg, 2.15 mmol) and ethyldiisopropylamine (2.68 ml, 17.2 mmol) in CH_2Cl_2 (92 ml). The mixture was stirred at −78°C for 3 h, then allowed to warm up to −10°C over 2 h and stirred between −10°C and −20°C for 2 d. Then to the mixture was added a satd. aqueous NH_4Cl solution, diluted with diethyl ether, and the organic layer was separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with water (twice), a satd. aqueous sodium hydrogen carbonate solution, brine, dried with magnesium sulfate and concentrated in vacuo. The residue was purified by chromatography on silica gel (20 g, hexane/diethyl ether, 30:1) to give 480 mg (66%) of **16** as an oil. This was immediately used in the next step without further purification, $n_D^{24} = 1.4805$. − $[\alpha]_D^{24} = +66.3$ (c = 1.10, $CHCl_3$). − IR (film): $\tilde{\nu}_{max}$ = 1665 cm^{-1} (vs, C=O), 1605 (s, C=C), 1140 (m, Si−Me), 1115 (m, Si−Me), 1030 (m, C−O). − ^1H NMR (90 MHz, $CDCl_3$): δ = −0.2 (s, 3 H, Si-CH_3), 0.2 (s, 3 H, Si-CH_3), 0.82 [s, 9 H, $SiC(CH_3)]_3$, 0.76−1.1 (m, 6 H, 1′-, 4′-CH), 1.1 (d, 3 H, J = 7.5 Hz, 3-CH_3), 1.33 (d, 3 H, J = 7.2 Hz, 2-CH_3), 1.38−1.64 (m, 2 H, 3′-H_2), 1.75 (s, 3 H, 5-CH_3) 2.38 (dq, 1 H, J = 3.2, J' = 7.2 Hz, 1′-H), 2.86 (m, 1 H, 3-H), 3.74−4.00 (m, 1H, 2′-H), 4.49 (dq, 1 H, J = 4.0, J' = 6.4 Hz, 2-H).

(2S,3R,1′S,2′S)-2,3-Dihydro-6-[2-hydroxy-1-methybutyl]-2,3,5-trimethyl-4H-pyran-4-one (**2**) (Stegobiol): To a solution of **16** (480 mg, 1.39 mmol) in CH_3CN was added 46% hydrofluoric acid (152 µl, 3.48 mmol) at 0°C. The mixture was stirred at 0−4°C for 14 h, then diluted with diethyl ether, and a satd. aqueous sodium hydrogen carbonate solution, and separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with a satd. sodium hydrogen carbonate solution, brine dried with magnesium sulfate and concentrated in vacuo. The residue was purified by preparative TLC to give 150 mg (47%) of stegobiol **2** as an oil and a mixture of its stereoisomer (61 mg, 19%) which could not be identified. The oily stegobiol **2** crystallized when left to stand in a refrigerator (0−4°C). The crude crystalline stegobiol was recrysytallized from pentane/diethyl ether (1:1) to give pure crystalline stegobiol **2** (117 mg) as prisms, m.p. 73.0−74.0°C [ref.[12] m.p. 73−74.2°C]. − $[\alpha]_D^{24} = -108.2$ (c = 0.09, $CHCl_3$) [ref.[7] $[\alpha]_D^{19} = -110\pm6$ (c = 0.42, $CHCl_3$), ref.[12] $[\alpha]_D^{25} = -118.7\pm7$ (c = 0.107, $CHCl_3$)]. − IR (KBr): $\tilde{\nu}_{max}$ = 3500 cm^{-1} (m, −OH), 3000 (m), 2950 (m), 2900 (m), 1640 (s, C=O), 1610 (s, C=O), 1460 (w), 1450(w), 1395 (m), 1380 (m), 1360 (m), 1340 (m), 1320 (w), 1300 (w), 1285 (w), 1240 (w), 1200 (m), 1150 (m), 1135 (w), 1112 (m), 1110 (w), 1080 (w), 1040 (w), 1030 (w), 1005 (w), 1000 (w), 980 (w), 970 (w), 940 (w), 920 (w), 870 (w), 840 (w), 830 (w), 780 (w), 710 (w). − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, 3 H, J = 7.4 Hz, 4′-H_3), 1.04 (d, 3 H, J = 7.4 Hz, 1′-CH_3), 1.18 (d, 3 H, J = 7.1 Hz, 3-CH_3), 1.33 (d, 3 H, J = 6.6 Hz, 2-CH_3), 1.37−1.48 (m, 1 H, 3′-H_a), 1.52−1.64 (m, 1 H, 3′-H_b), 1.75 (s, 3 H, 5−CH_3), 1.91 (d, 1 H, J = 7.4 Hz, 2′-OH), 2.38 (dq, 1 H, J = 3.5, J' = 7.3 Hz, 1′-H), 2.86 (dq, 1 H, J = 6.9, J' = 7.0 Hz, 3-H), 3.53−3.63 (m, 1 H, 2′-H), 4.49 (dq, 1 H, J = 6.5, J' = 3.6 Hz, 2-H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 9.2, 9.4, 10.1, 14.7, 15.9, 28.3, 40.8, 43.7, 75.3, 76.6, 109.3, 172.7, 197.1. These spectral data were in good accord with those reported in refs[7][12]. − $C_{13}H_{22}O_3$ (226.32) calcd. C 68.99, H 9.80, found C 68.74, H 9.57.

(2S,3R,1′R)-2,3-Dihydro-6-[1-methyl-2-oxobutyl]-2,3,5-trimethyl-4H-pyran-4-one (**1**) (Stegobinone). − (i) *Dess-Martin Oxidation*: Preparation of pyridine-buffered Dess-Martin periodinane stock solution: Dess-Martin periodinane (140 mg, 0.331 mmol) was added to an argon-purged flask (glove bag). The solid was taken up in CH_2Cl_2 (5.4 ml) and pyridine (160 µl, 1.98 mmol) was added. This stock solution was employed in the oxidation immediately. To a solution of stegobiol **2** (14 mg, 0.062 mmol) in CH_2Cl_2 (1 ml) was added freshly prepared periodinane stock solution (2.0 ml) in one portion. After 25 min, this solution was diluted with diethyl ether and quenched by introducing a satd. aqueous sodium hydrogen carbonate solution/sodium bisulfate (1:1, 5 ml), and the resulting mixture was stirred for 5 min. Upon further dilution with diethyl ether, the mixture was washed with a satd. sodium hydrogen carbonate solution, brine, dried with magnesium sulfate and concentrated in vacuo. The residue was purified by chromatography on silica gel (1g, pentane/diethyl ether, 5:1) to give 14 mg (quant.) of (2*S*,3*R*,1′*R*)-stegobinone (**1**) as an oil, which crystallized under −78°C in a freezer. This was recrystallized from pentane as described in ref.[12] to give pure crystalline stegobinone as prisms.

(ii) *TPAP−NMO:* To a solution of stegobiol **2** (10 mg, 0.044 mmol) in CH_2Cl_2 (0.6 ml) was added tetrapropylammoinum perruthenate (TPAP) (84.7 mg, 0.013 mmol), *N*-methylmorpholine *N*-oxide (21 mg, 0.18 mmol) and powdered molecular sieves (4 Å) (0.1 g). The mixture was stirred at room temp. for 28 h, diluted with diethyl ether, and purified by preparative TLC to give the recovered **2** (2 mg, 20%) and 7 mg (89% based on the comsumed **2**) of stegobinone **1** as an oil. This was also recrystallized in the same manner as described above.

(iii) *Jones' Oxidation:* Jones' reagent (2.69 N, 0.027 mmol) was added slowly to a stirred and cooled solution of **2** (14 mg, 0.062 mmol) in acetone (1 ml) at 0°C over 30 s, then the mixture was diluted with diethyl ether and a satd. sodium thiosulfate, and the organic layer was separated. The aqueous layer was extracted with diethyl ether. The combined organic layers were washed with water, a satd. sodium hydrogen carbonate solution, brine, dried with magnesium sulfate and concentrated in vacuo. The residue was purified by chromatography on silica gel (1 g, pentane/diethyl ether, 5:1) to give 13.6 mg (96%) of stegobinone **1** as an oil. This was also recrystallized in the same manner as described above, m.p. 54.0−55.0°C [ref.[1] m.p. 52.5−53.5°C, ref.[12] m.p 51.5−52.5°C]. − $[\alpha]_D^{24} = -283$ (c = 0.07, $CHCl_3$) [ref.[6] $[\alpha]_D^{23} = -282\pm10$ (c = 0.11, $CHCl_3$)]. − CD (c = 0.00098, hexane) $\Delta\varepsilon$ (λ, nm) = −0.88 (347), −16.7 (289), +12.7 (263.4) [ref.[1] −0.42 (360), −0.87 (345), −13.0 (290), +9.0 (262)]. − IR (KBr): $\tilde{\nu}_{max}$ = 3000 cm^{-1} (s), 2950 (m), 2925 (w), 2880 (w), 1720 (s, C=O), 1660 (s, C=O), 1610 (s, C=C), 1450 (m), 1390 (m), 1380 (m), 1360 (m), 1340 (w), 1300 (w), 1280 (w), 1240 (w), 1195 (m), 1150 (m), 1130 (m), 1110 (w), 1095 (w), 1070 (m), 1050 (m), 1020 (w), 1000 (m), 960 (w), 920 (w), 860 (w), 835 (w), 805 (w), 780 (w), 705 (w), 690 (w). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.04 (d, 3 H, J = 7.3 Hz, 1′-CH_3), 1.06 (t, 3 H, J = 7.3 Hz, 4′-H_3), 1.29 (d, 3 H, J = 6.5 Hz, 3-CH_3), 1.31 (d, 3 H, J = 6.9 Hz, 2-CH_3), 1.79 (s, 3 H, 5−CH_3), 2.35−2.53 (m, 3 H, 3′-H_2, 3-H), 3.63 (q, 1 H, J = 6.9 Hz, 1′-H), 4.46 (dq, 1 H, J = 6.9, J' = 3.6 Hz, 2-H). − ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 7.9, 9.39, 9.41, 12.8, 15.7, 33.9, 43.7, 49.2, 77.2, 109.4, 168.9, 197.1, 207.6. − These spectral data were in good accord with those reported in ref[6][12]. − $C_{13}H_{20}O_2$ (224.30) calcd. C 69.61, H 8.99, found C 69.7, H 8.96. − $C_{13}H_{20}O_2$: calcd. 224.1413; found 224.1409 (HRMS).

X-ray Analysis of **1**: Crystal size, 0.5 × 0.3 × 0.1 mm. All data were obtained on a Rigaku AFC-5S automated four circle diffractometer with graphite-monochromated Mo-K_α radiation. Final lattice parameter were obtained from a least-squares refinement using 25 reflections. Crystal data: $C_{13}H_{20}O_3$, Mr = 224.30, triclinic, space group $P2_12_12_1$, a = 9.355(4), b = 19.830(4), c = 7.014(5) Å, V = 1301(1) Å^3, Z = 4.0, Dx = 1.145 g/cm^3, F(000) = 488 and μ(Mo-K_α) = 0.796 cm^{-1}. The intensities were measured using ω/2θ scan up to 45°. Three standard reflections were monitored every 150 measurements. The data were corrected for Lorentz and polarization factors. Absorption correction was applied and decay correction was not applied. Of the 1043 independent reflections which collected, 609 reflections with $I > 3.0\sigma(I)$ were used for structure determination and refinement. The structure was solved by direct method using TEXSAN crystallographic software package[30]. All non-H atoms were found in Fourier map. All H atoms were calculated at geometrical positions and not refined. The refinement of atomic parameters were carried out by the full matrix least-squares refinement, using anisotoropically temperature factors for all non-H atoms. The final refinement converged with R = 0.057 and Rw = 0.080 for 145 parameters. The minimum and maximum peaks in the final difference Fourier map were −0.18 and 0.21 eÅ^{-3}. Atomic scattering factors were taken from "International Tables for X-ray Crystallography"[31]. The supplementary material includes the lists of atomic coordinates for the non-H atoms, the bond lengths and angles of **1** with their e.s.d.'s in parentheses[32].

[1] Y. Kuwahara, H. Fukami, R. Howard, S. Ishii, F. Matsumura, W. E. Burkholder, *Tetrahedron* **1978**, *34*, 1769−1774.
[2] H. Kodama, M. Ono, M. Kohno, A. Ohnishi, *J. Chem. Ecol.* **1987**, *13*, 1871−1879.
[3] M. Sakakibara, K. Mori, *Tetrahedron Lett*. **1979**, 2401−2402.
[4] J. M. Ansell, A. Hassner, *Tetrahedron Lett.* **1979**, 2497−2498.
[5] R. W. Hoffmann, W. Ladner, K. Steinbach, W. Massa, R. Schmidt, G. Snatzke, *Chem. Ber.* **1981**, *114*, 2786−2801.
[6] K. Mori, T. Ebata, *Tetrahedron* **1986**, *42*, 4413−4420.
[7] K. Mori, T. Ebata, *Tetrahedron* **1986**, *42*, 4685−4689.
[8] W. Oppolzer, I. Rodriguez, *Helv. Chim. Acta*, **1993**, *76*, 1275−1281.
[9] W. Oppolzer, I. Rodriguez, *Helv. Chim. Acta*, **1993**, *76*, 1282−1291.
[10] J. Morris, D. G. Wishka, G. P. Luke, T. M. Judge, R. B. Gammill, *Tetrahedron* **1997**, *53*, 11211−11222.
[11] D. S. Matteson, H. -W. Man, *J. Org. Chem.*, **1993**, *58*, 6545−6547.
[12] D. S. Matteson, H. -W. Man, O. C. Ho, *J. Am. Chem. Soc*. **1996**, *118*, 4560−4566.
[13] D. S. Matteson, *Stereodirected Synthesis with Organoboranes*, Springer, Berlin, **1995**, pp. 207−209.
[14] T. Inoue, T. Mukaiyama, *Bull. Chem. Soc. Jpn*. **1980**, *53*, 174−178.
[15] Review: F. Theil, *Chem. Rev.* **1995**, *95*, 2203−2227.
[16] Review: K. Mori, *Synlett* **1995**, 1097−1109.
[17] E. J. Corey, A. Marfat, G. Goto, *J. Am. Chem. Soc*. **1980**, *102*, 6607−6608.
[18] Review: T. Katsuki, V. S. Martin. *Org. React*. **1996**, *48*, 3−299.
[19] K. Mori, M. Itou, *Liebigs Ann.Chem*. **1992** 87−93.
[20] P. H. J. Carlsen, T. Katsuki, V. S. Martin, K. B. Sharpless. *J. Org. Chem*. **1981**, *46*, 3936−3938.
[21] K. Mori, H. Mori, T. Sugai, *Tetrahedron* **1985**, *41*, 919−925.
[22] Review: S. V. Ley, J. Norman, W. P. Griffith, S. P. Massden, *Synthesis* **1994**, 639− 666.
[23] A. J. Mancuso, S-L. Huang, D. Swern, *J. Org. Chem*. **1978**, *43*, 2480−2482.
[24] A. Dondoni, D. Perrone, *Synthesis* **1997**, 527−529.
[25] D. B. Dess, J. C. Martin, *J. Org. Chem.*, **1983**, *48*, 4155−4156.
[26] A. Bowess, T. G. Halsall, E. R. H. Jones, A. J. Lemin, *J. Chem, Soc.* **1953**, 2548− 2560.
[27] P. L. Anelli, C. Biffi, F. Montanari, S. Quici, *J. Org. Chem.*, **1987**, *52*, 2559−2562.
[28] H. Kodama, K. Mochizuki, M. Kohno, A. Ohnishi, Y. Kuwahara, *J. Chem. Ecol*. **1987**, *13*, 1859−1869.
[29] T. Chuman, M. Kohno, K. Kato, M. Noguchi, H. Nomi, K. Mori, *Agric. Biol. Chem*. **1981**, *45*, 2019−2023.
[30] *TEXSAN, TEXRAY Structure Analysis Package*, **1985**, Molecular Structure Corporation, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
[31] *International Tables for X-ray Crystallography*, vol IV, Table 2.2A, **1964**, Kynoch, Birmingham, UK.
[32] Further details of the crystal structure investigation are deposited to the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100771. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: int. code + 44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk].

[98005]