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The absolute configuration of eudesmane-type sesquiterpenoids found in the Japanese liverwort *Chiloscyphus polyanthos*

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Abstract

The ether extract of the liverwort *Chiloscyphus polyanthos* afforded sesquiterpenoids which are enantiomeric to those found in another liverwort *Lepidozia vitrea*. The absolute configurations of the sesquiterpenoids found in the title species were determined by spectroscopic evidence, chemical derivatization and /or X-ray crystallographic analysis. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Hepaticae; Liverwort; *Chiloscyphus polyanthos*; *Lepidozia vitrea*; Absolute configuration; Sesquiterpenoids; Eudesmane-type

1. Introduction

Liverworts are an interesting group in plant kingdom phytochemically, some species of which elaborate unusual natural products in high yield (Asakawa, 1995). Many of these compounds have novel carbon skeletons and opposite configuration to those found in higher plants (Asakawa, 1995).

The distribution of enantiomeric sesquiterpenoids in liverworts as compared to those found in higher plants has been reported (Asakawa, 1995; Huneck & Klein, 1967, Matsuo et al., 1973; Andersen et al., 1973, 1978; Matsuo et al., 1974; Ohta et al, 1977). The isolation of (−)-longifolene and (−)-longiborneol from the liverwort *Scapania undulata* was the first example (Huneck et al., 1967). Recent work of the enantiomeric composition of sesquiterpenoids in liverworts is progressing after the introduction of a chiral capillary column with high separation efficiency (König et al., 1994, 1996; Fricke et al, 1995). The first report of a precise determination of the enantiomeric composition of sesquiterpenoids has been performed using the chiral capillary gas chromatography (König, 1994).

The previous work of *Chiloscyphus polyanthos* (L.) Corda collected in Germany led to the isolation of (−)-α-selinene (Andersen et al., 1973) enantiomeric to that found in higher plants. Our previous work led to the isolation of β-barbatene, β-chamigrene, (−)-5-hydroxycalamene and *ent*-eudesmane-type sesquiterpene lactones from French *C. polyanthos* (Asakawa et al., 1979, 1983). We report here the isolation and elucidation of the absolute configuration of four eudesmane-type sesquiterpenoids from the Japanese *C. polyanthos*.

2. Results and discussion

The ether extract of *C. polyanthos* was repeatedly chromatographed on silica gel and Sephadex LH-20 to give four eudesmane-type sesquiterpenoids **1**, **5**, **11** and **14**, in addition to known sesquiterpenoids, (−)-chiloscyphone (**15**) (Connolly et al., 1982; Tori et al., 1991) and (+)-chiloscypholone (**16**) (Connolly et al., 1982; Tori et al., 1991).

The ^{1}H NMR spectrum of **1** was identical to that of eudesm-3-en-7α-ol isolated from the Japanese liverwort *Lepidozia vitrea* (Toyota et al., 1996), although the optical rotation of **1**, $[\alpha]_D$ −23.2° ($CHCl_3$; *c*2.59)

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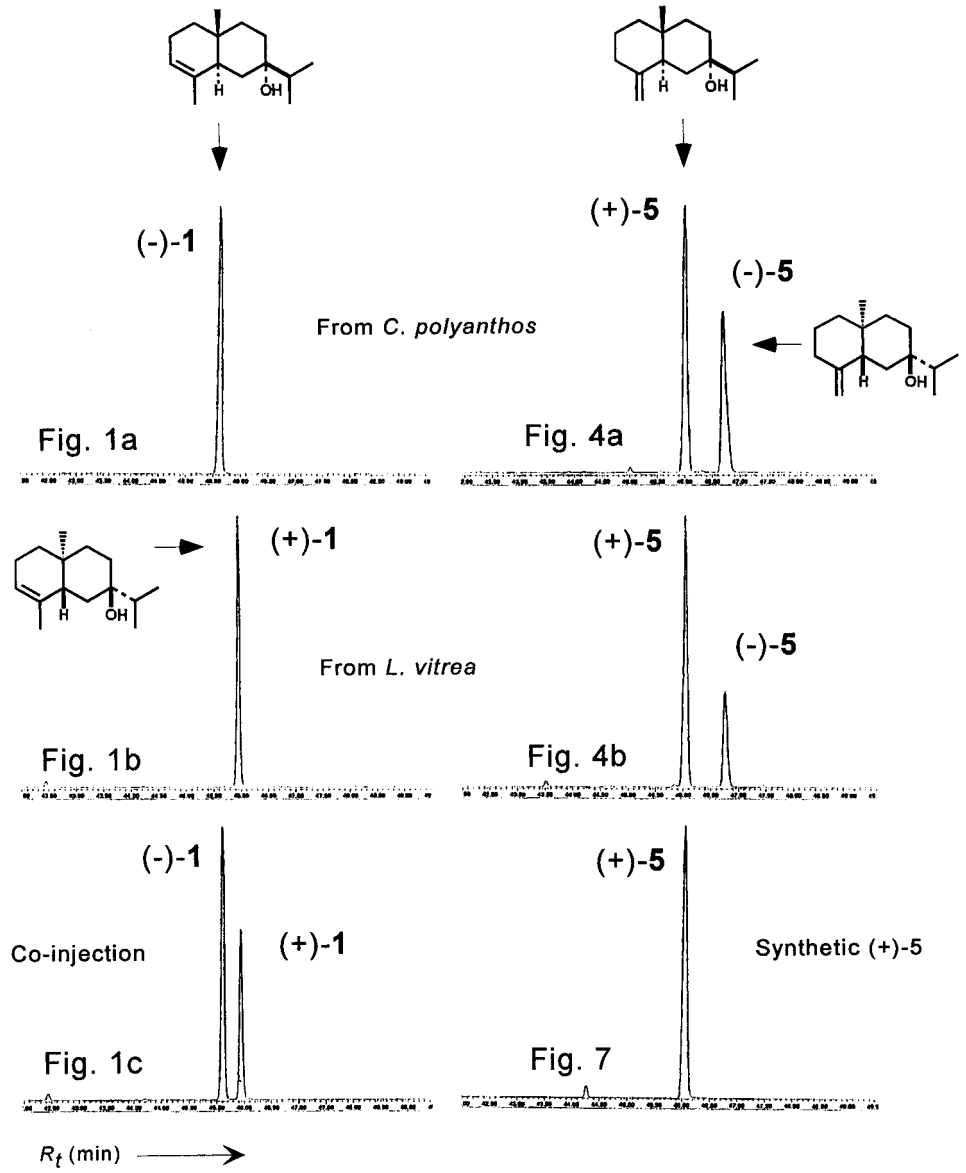


Figs. 1, 4 and 7. Total ion chromatograms (TICs) of the chiral GC–mass analysis for compounds **1** and **5**.

{from *L. vitrea*; $[\alpha]_D$ +27.7° ($CHCl_3$; *c* 2.41)} showed opposite sign to that found in *L. vitrea*. In the our previous work, the absolute configuration of eudesm-3-en-7α-ol has been tentatively assigned as (5R*,7 S*,10R*)-eudesm-3-en-7-ol (**1**), since (5R,7R,10R)-6α-acetoxy-eudesm-3-en-7-ol (**2**) has coexisted within *L. vitrea* (Toyota et al., 1996). Furthermore, the absolute configuration of **2** has been established as follows. The CD spectrum [$\Delta\varepsilon_{302\ nm}$ +25.6 in CCl_4 employing Eu $(FOD)_3$ as the complexing reagent] of the vicinal glycol derivative obtained by lithium alminium hydride reduction of **2** revealed 6*R*-configuration.

It was strongly suggested that the absolute configuration of **1** opposite to that from *L. vitrea*. Actually, the GC–MS analysis on a chiral capillary column of both compounds showed different retention time as shown in Fig. 1a and 1b, respectively. Further analysis with co-injection gave two peaks on a TIC in Fig. 1c. The above evidence apparently indicated that **1** isolated from *C. ployanthos* was enantiomeric to that from *L. vitrea*.

In order to confirm the absolute configuration of **1**, further experiments were performed as follows. Catalytic asymmetric dihydroxylation (Sharpless et al., 1992) of **1** afforded a triol **3**. The X-ray analysis of the triol **3** not only revealed the presence of an equatorial hydroxyl group at C-3, but also showed the relative stereochemistry of the triol (Fig. 2). Esterification of the hydroxyl group at C-3 by *R*(+)- and *S*(−)-α-methoxy-α-trifluoromethylphenyl acetic acid (MTPA) to give MTPA esters **4a** and **4b**, respectively. The 2D NMR experiments of **4a** and **4b** involving the determi-

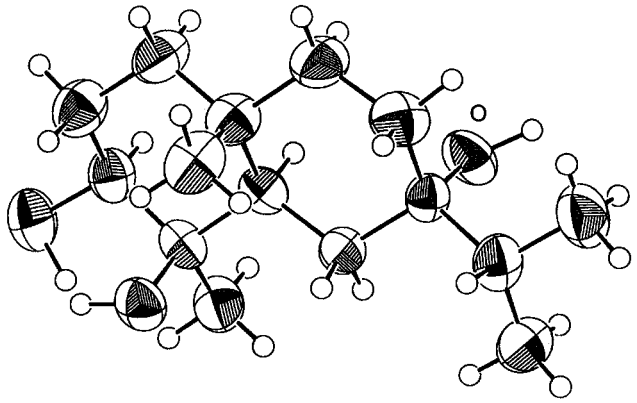


Fig. 2. The ORTEP drawing of compound **3**.

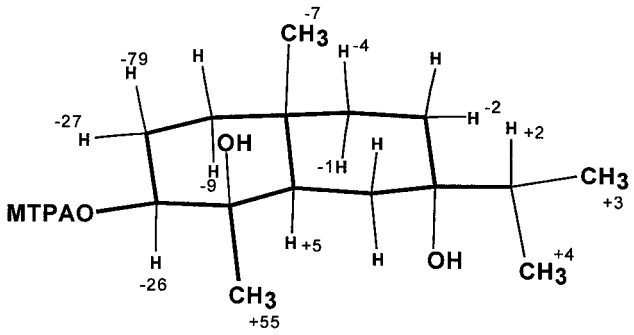


Fig. 3. The $\delta\Delta$ values in (Hz) of MTPA esters between **4a** and **4b** are displayed.

nation of ^1H–^1H COSY and HMQC spectra were effective for assignment of the protons, although some of which were not able to assigned by the overlapping proton signals. Fig. 3 shows that the $\delta\Delta$ values of the ester revealed the absolute configuration of **3** (Kusumi et al., 1988).

As described earlier, the chiral GC–mass analysis of **1** isolated from *C. polyanthos* and *L. vitrea* indicated that both sesquiterpenoids were enantioisomeric paired with each other. The above determination of the absolute configuration of **3** resulted in the elucidation of the absolute configuration of **1** as (−)-(5R, 7S,10R)-eudesm-3-en-7-ol from *C. polyanthos*. This indicates that the absolute configuration of (+)-eudesm-3-en-7-ol from *L. vitrea* should be an opposite configuration.

Compound **5** was identical to that found in the liverwort *L. vitrea*, except for the sign of the optical rotation (Toyota et al., 1996). The chiral GC–mass analysis of eudesm-4(15)-en-7α-ol (**5**) found in both species demonstrated a mixture of enantiomeric isomers as shown in Fig. 4a (56:44 area %; from *C. p*) and 4b (72:28 *L. v*). The earlier eluted peak area was in excess on the both TIC, although the sign of the optical rotation of **5** showed opposite to that found in *L. vitrea*. To distinguish between (+) and (−)-enantiomeric isomer, (+)-eudesm-4(15)-en-7α-ol (**5**) was prepared from (+)-β-eudesmol (**6**). (+)-β-Eudesmol (**6**), $[\alpha]_D$ +57.7° ($CHCl_3$; *c* 1.32) {literature value; $[\alpha]_D$ +58.0° ($CHCl_3$) (Varma & Bathacharyya, 1964)} was isolated from the ether extract of *Atractylodes lancea* rhizome. In order to confirm the absolute configuration of **6**, it was attempted to obtain a suitable crystal derivative for an X-ray crystallographic analysis. The crystal *m*-bromobenzoate **8** was obtained from the esterification of a triol **7** which was derived from (+)-

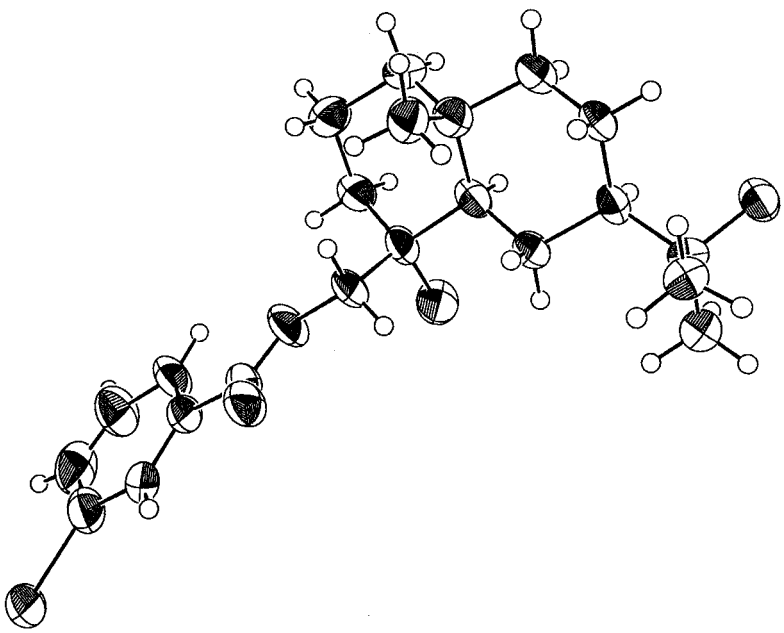


Fig. 5. The ORTEP drawing of compound **8**.

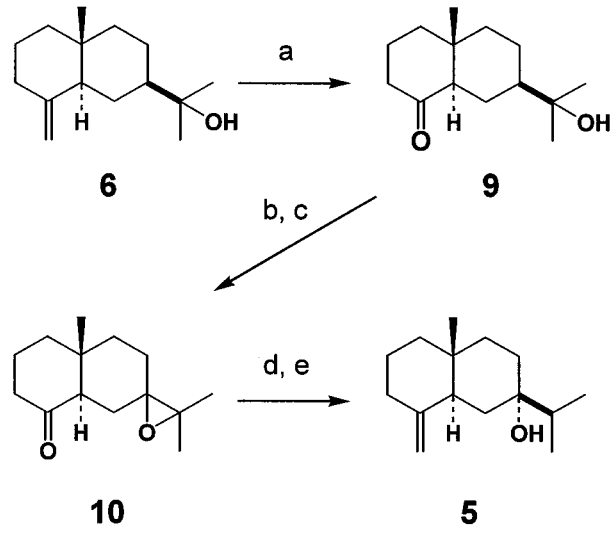


Fig. 6. The partial analysis of **5** from (+)-*β*-eudesmol (**6**).

β-eudesmol by catalytic asymmetric dihydroxylation. The X-ray analysis of **8** established the absolute configuration as shown in the ORTEP drawing (Fig. 5). This is the first example for the elucidation of the absolute configuration of (+)-*β*-eudesmol (**6**) by X-ray crystallographic analysis, whereas it was established by chemical means (Riniker et al., 1954; Mash & Fryling, 1987). (+)-Eudesm-4(15)-en-7α-ol (**5**), $[\alpha]_D$ +36.0° ($CHCl_3$; *c* 4.55) was prepared from (+)-*β*-eudesmol (**6**) by a five-step derivatization as shown in Fig. 6. The retention time of synthetic (+)-**5** (Fig. 7) corresponding to the earlier eluted peak was confirmed by co-injection experiment in the chiral GC–mass analysis of **5** found in both species. Accordingly, the optical purity of (+)-eudesm-4(15)-en-7α-ol (**5**) was demonstrated as 12% ee from *C. polyanthos* and 44% ee from *L. vitrea*, respectively. The optical rotation of **5** found in both species gave the opposite sign with each other, it might be resulted from the low concentration of **5** in the measurement of the optical rotation.

The spectral data of **11** were identical to those found in the Scottish liverwort *C. pallescens* (Connolly et al., 1982). The chiral GC–mass analysis of **11** gave a single peak on the TIC. Since the absolute configuration of **11** has not been established yet, further experiments were performed as follows. Esterification of the equatorial hydroxyl group at C-6 by R-(+)- and S-(−)-MTPA gave esters **12a** and **12b**, respectively. The modified Mosher's method applied to the esters and the calculated $\delta\Delta$ values are displayed in Fig. 8. Accordingly, the absolute configuration of **11** was established as 6*R*-configuration. Further evidence for this absolute configuration was provided by X-ray analysis of *m*-bromobenzoate **13** derived from the esterification of **11** by *m*-bromobenzoic acid. It resulted in the confirmation of the absolute configuration of (+)-eudesm-4(15)-ene-6α,7α-diol (**11**) as shown in Fig. 9.

Chetty et al., (1968) reported the synthesis of (−)-eudesm-7(11)-en-4α-ol (**14**) (Chetty et al., 1968). The spectral data of **14** isolated from the present species were identical to those of the synthetic **14**. As there was no description for the magnitude of the optical rotation in the literature, compound **14** was synthesized according to the same manner. (−)-Eudesm-7(11)-en-4α-ol (**14**) was obtained by derivatization from (+)-*β*-eudesmol (**6**) whose absolute configuration was confirmed by X-ray as described earlier. The chiral GC–mass analysis of both **14** not only showed a single peak, but also exhibited a single peak on the TIC in its co-injection, respectively. This indicated that the absolute configuration of **14** found in *C. polyanthos* was identical to that of synthetic **14**. The magnitude of synthetic **14**, $[\alpha]_D$ −6.0° ($CHCl_3$; *c* 2.45) was slightly different from naturally occurred **14**, $[\alpha]_D$ −3.0° ($CHCl_3$; *c* 2.41), whereas the chiral GC–mass analysis did not show the presence of an enantiomeric isomer.

It is noteworthy that only compound **5** found in both species of *C. polyanthos* and *L. vitrea* was shown to be a mixture of enantiomers in the GC–mass analysis using a chiral capillary column, although compounds **1**, **11** and **14** were obtained as optically pure state.

Connolly et al. (1982) reported the isolation of (+)-eudesm-4(15)-ene-6α,7α-diol (**11**) which was inferred to be a biogenetically precursor of (−)-chiloscyphone (**15**) and (+)-chiloscypholone (**16**). On the other hand, our previous work showed the absolute configuration of **15**

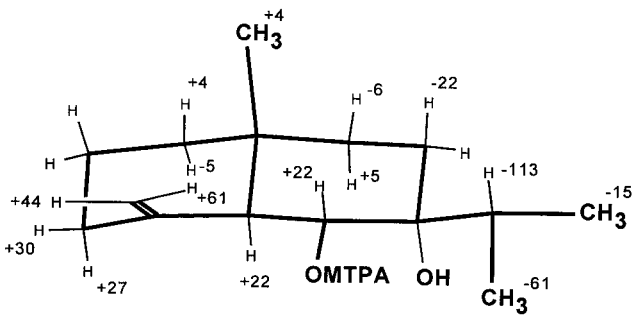
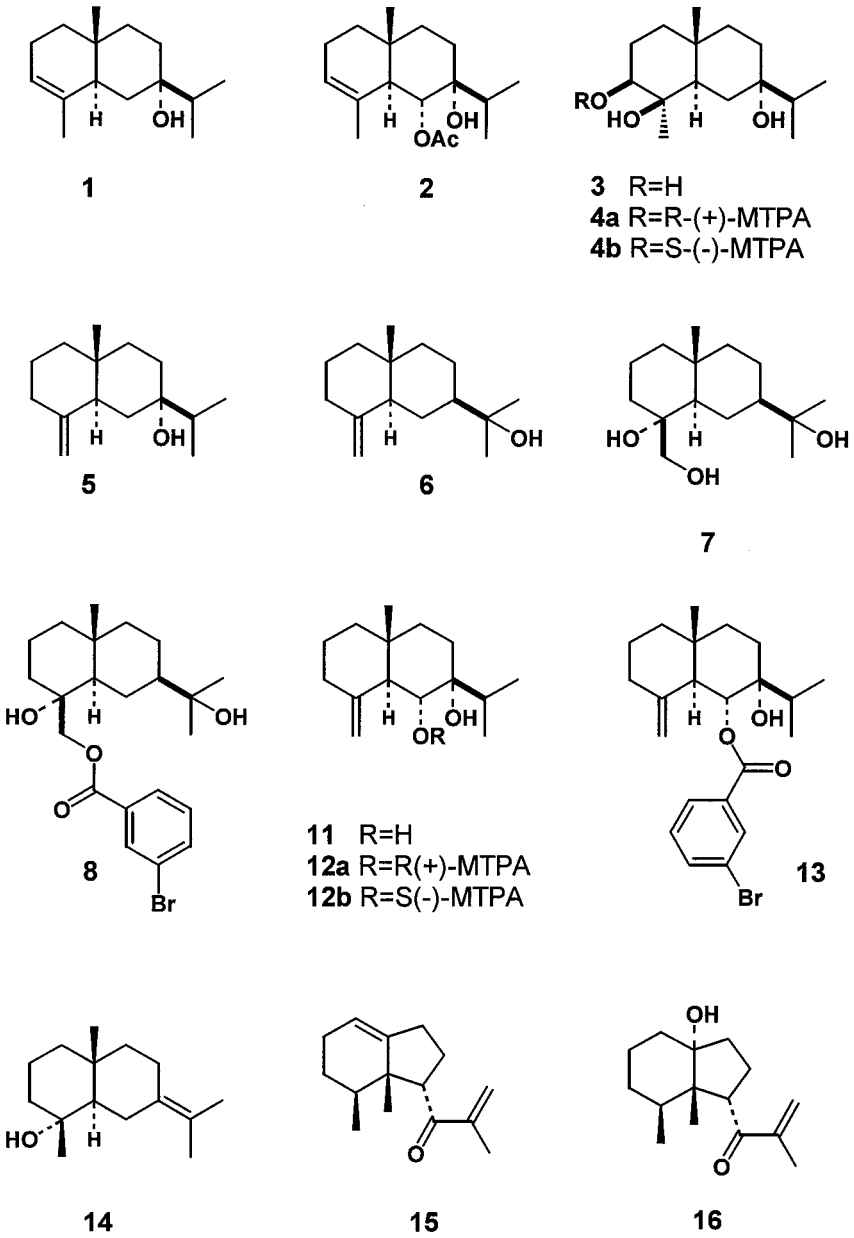


Fig. 8. $\delta\Delta$ values (in Hz) of MTPA esters between **12a** and **12b** are displayed.



and **16** as shown below (Tori et al., 1991). The present work resulted in the elucidation of the absolute configuration of **11** corresponding to those of **15** and **16**. This proves further evidence for the presence of the biogenetic pathway from **11** to **15** and **16** with ring contraction and methyl migration process.

Andersen et al. (1973) reported the isolation of *ent*-(−)-selinene, which was optically antipodal structure to the present eudesmane-type sesquiterpenoids, even the material plants were the same species of *C. polyanthos*. It seems reasonable to conclude from the present result that the German and Japanese species possess a different set of enzyme acting in the cyclization process of germacradiene intermediate to produce eudesmanes.

3. Experimental

3.1. General

TLC was carried out on silica gel precoated glass plates with *n*-hexane–EtOAc (1:1 and 4:1). Detection was with Godin reagent (Godin, 1954). For normal phase column chromatography (CC), silica gel 60 (40–63 μm) was used. The mixture of CH_2Cl_2-MeOH (1:1) was used for CC on Sephadex LH-20 as solvent.

3.2. Spectral data

NMR spectra were recorded at 150 or 100 MHz for ^{13}C and 600 or 400 MHz for ^{1}H. EIMS were measured

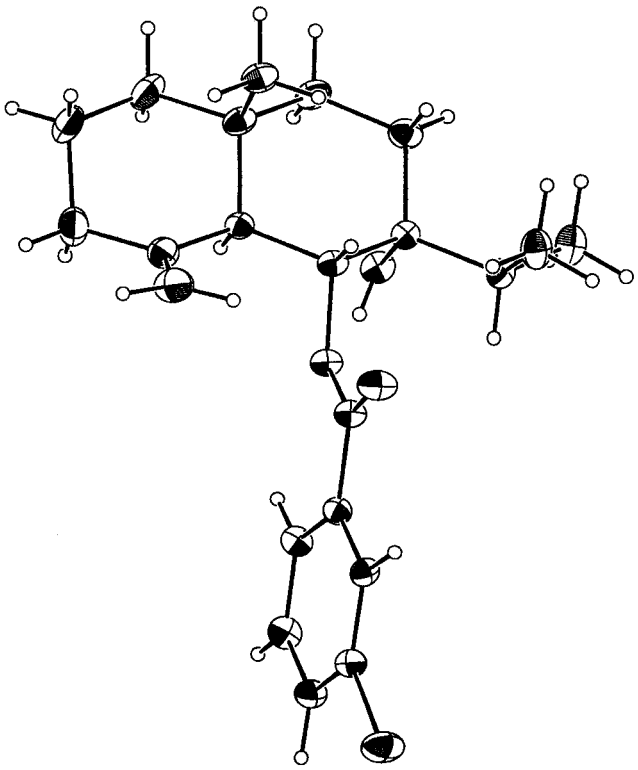


Fig. 9. The ORTEP drawing of *m-bromobenzoate* **13**.

at 70 eV. The temperature programming of chiral GC–mass analysis performed from 50° isothermal for 3 min, then 50-230° at 3o min-1, and finally isothermal at 230o for 5 min. Injection temp was 250°. A fused silica column coated with β-DEX 120 (30 m × 0.25 mm i.d., film thickness 0.25 μm) was used. Helium was used as carrier gas (1 ml min^{-1}).

3.3. X-ray crystallographic analysis

Refraction data were measured with a Mac Science MXC18 diffractometer using copper radiation Cu Kα (λ = 1.54178 Å). All diagrams and calculations were performed using CRYSTAN SIR92.

3.4. Plant material

C. polyanthos (L.) Corda. (Herbarium specimen No. 96067; dry wt 136.4 g) was collected in May 1996 at Tsushima, Nagasaki, Japan. Voucher specimens are deposited at the Faculty of Pharmaceutical Sciences, Tokushima Bunri University.

3.5. Extraction and isolation

C. polyanthos was gently washed with water, impurities removed and ground, then extracted with Et_2O for 2 weeks. The ether extract (4.4 g) was chromatographed on silica gel to divide into 8 frs (fr. I–VIII). The fr. II was rechromatographed on Sephadex LH-20 to give (−)-chiloscyphone (**15**) (789.9 mg; 18% of total extract). Fr. III was rechromatographed on Sephadex LH-20 and silica gel followed by pre.-HPLC to give (−)-(5*R*, 7*S*, 10*R*)-eudesm-3-en-7-ol (**1**) (52.5 mg; 1.2%), eudesm-4(15)-en-7α-ol (**5**) (3.6 mg; 0.08 %), (−)-eudesm-7(11)-en-4α-ol (**14**) (48.1 mg; 1.1%) and (+)-chiloscypholone (**16**) (624.0 mg; 14.2%). Further purification of fr. IV with Sephadex LH-20, silica gel column chromatography and then prep.-HPLC gave (+)-eudesm-4(15)-ene-6α, 7α-diol (**11**) (116.9 mg; 2.7%).

3.6. Asymmetric dihydroxylation of (-)-(5R, 7S, 10R)-eudesm-3-en-7α-ol (*1*)

To a mix of *t*-BuOH (1.25 ml) and H_2O (1.25 ml), AD-mix-α (350 mg), $CH_3SO_2NH_2$ (24 mg) and **1** (52.5 mg) were added and the reaction mix was stirred for 32 h at 0°C. A diol **3** (44.1 mg) was obtained after purification of the mix.

3.7. (−)-Eudesm-3β,4β,7α-triol (*3*)

mp 153°; $[\alpha]_D$ −7.1 ($CHCl_3$; *c* 2.10), EI–MS *m*/*z* (rel. int.): 256 $[M]^+$ (1), 220(73), 195(100), 177(91), 159(52), 135(60), 93(59), 81(53). FT–IR (neat) ν_{max} cm^{-1}: 3391 (–OH), 2973, 2240, 1456, 1377, 1184, 1061, 959, 918, 766.

3.8. Crystal data for (−)-eudesm-3β,4β,7α-triol (*3*)

Crystal dimension = 0.5 × 0.5 × 0.1 mm, Monoclinic space group $P2_1$, a = 12.484 (7) Å, b = 11.200 (7) Å, c = 11.127 (6) Å, V = 1531.359985 (1) $Å^3$; Z = 4, D_{calc} = 1.110. 1955 observed reflections, S = 1.617, final residuals R and Rw with 0.068, 0.089.

3.9. Esterification of (−)-eudesm-3β,4α,7α-triol (*3*) by R(+) and S(−)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA)

To a soln of **3** (6.1 mg) in dry CH_2Cl_2 (0.7 ml), *R*(+)-MTPA (29 mg), DCC (29 mg) and DMAP (10 mg) were added and the reaction mixture was stirred for 5 h. To the mix, H_2O was added and the soln was washed with 1N HCl, saturated $NaHCO_3$ and NaCl. After evaporation, the CH_2Cl_2 layer was purified by prep.-HPLC to give a mono *R*(+)-MTPA ester **4a** (8.8 mg). *S*(−)-MTPA ester (7.8 mg) of **3** (5.9 mg) was obtained by *S*(−)-MTPA **4b** with in the same manner as above.

3.10. R(+)-MTPA ester **4a**

Oil; ^{1}H-NMR (600 MHz; $CDCl_3$): δ 1.33 (H-1ax.), 2.03 (H-2ax.), 1.86 (H-2eq.), 4.83 (H-3), 1.50 (H-5), 1.37 (H-8eq.), 1.43 (H-9ax.), 1.19 (H-9eq.), 1.61 (H-11), 0.94 (Me-12), 0.94 (Me-13), 1.00 (Me-14), 1.01 (Me-15).

3.11. S(+)-MTPA ester **4b**

Oil; ^{1}H-NMR (600 MHz; $CDCl_3$): δ 1.31 (H-1ax.), 1.90 (H-2ax.), 1.81 (H-2eq.), 4.78 (H-3), 1.51 (H-5), 1.37 (H-8eq.), 1.43 (H-9ax.), 1.18 (H-9eq.), 1.61 (H-11), 0.94 (Me-12), 0.95 (Me-13), 0.99 (Me-14), 1.10 (Me-15).

3.12. Crystal data for m-bromobenzoate **8**

Crystal dimension $=0.5\times0.3\times0.1$ mm, Monoclinic, Space group $P2_1$, $a=6.561$ (5) Å, $b=11.207$ (2) Å, $c=28.663$ (8) Å, $V=2107.500000$ (8) Å^3, $Z=4$, CuKα($\lambda=1.54178$ Å), final residuals R and Rw with 0.0963, 0.1435. Eta = 0.901.

3.13. Synthesis of (+)- eudesm-(4)15-en-7-ol (**5**)

Ozone was bubbled into the soln of (+)-β-eudesmol (**6**) (1.3 g) in MeOH (10 ml) at −78° for 1 h. The reaction product was dissolved in pyridine (10 ml) and $POCl_3$ (2 ml) was added at 0°. The reaction mix was stirred for 3 h, then poured into ice water and extracted with ether. After evaporation, the resulted mix was dissolved in dry CH_2Cl_2 (40 ml) and *m*-chloroperoxybenzoic acid (820 mg) was added, then the mix was stirred for 2 h. The usual work-up afforded **10**. NaH (320 mg) in DMSO (8 ml) was stirred for 45 min at 75–80° under nitrogen. The resulting soln was cooled in ice water bath and methyltriphenylphosphonium bromide (4.8 g) in DMSO (10 ml) was added, then the mix was stirred for 10 min. To the mix was added **10** (320 mg) in DMSO (8 ml) and the reaction mix was stirred at 50–60° for 30 h. After the usual work-up afforded the resulting mix. To $LiAlH_4$ (120 mg) in dry Et_2O (10 ml), the mix in dry ether (2 ml) was added and stirred for 3 days at room temp. The usual work-up afforded (+)-eudesm-4(15)-en-7-ol (**5**) {96.2 mg, $[\alpha]_D$ +36.00 ($CHCl_3$; *c* 4.55), $R_t=46.7$ min on the chiral GC–mass analysis}. The spectral data of **5** were identical to those found in *C. polyanthos* [naturally occurred **5**: $R_t=46.1$ and 46.7 min on the chiral GC–mass analysis; peak area ratio of (−)-form: (+)-form = 56:44].

3.14. Esterification of (+)-eudesm-4(15)-ene-6α,7α-diol (**11**) by R(+) and S(−)-MTPA

To a soln of **11** (10 mg) in dry CH_2Cl_2 (0.7 ml), *R*(+)-MTPA (60 mg), DCC (60 mg) and DMAP (20 mg) were added and the reaction mixture was stirred for 48 h. After evaporation, the CH_2Cl_2 layer was purified by prep.-HPLC to give a mono *R*(+)-MTPA ester **12a** (9.7 mg). S(−)-MTPA ester **12b** (8.9 mg) from **11** (6.1 mg) was obtained by S(−)-MTPA with in the same manner as above.

3.15. R(+)-MTPA ester **12a**

Oil; ^{1}H-NMR (600 MHz; $CDCl_3$): δ 1.40 (H-1ax.), 1.43 (H-1eq.), 1.89 (H-3ax.), 2.24 (H-3eq.), 2.52 (H-5), 5.44 (H-6), 1.53 (H-8ax.), 1.65 (H-9ax.), 1.25 (H-9eq.), 1.38 (H-11), 0.84 (Me-12), 0.97 (Me-13), 0.77 (Me-14), 4.73 (H-15α), 4.54 (H-15β).

3.16. S(+)-MTPA ester **12b**

Oil; ^{1}H-NMR (600 MHz; $CDCl_3$): δ 1.40 (H-1ax.), 1.44 (H-1eq.), 1.94 (H-3ax.), 2.29 (H-3eq.), 2.56 (H-5), 5.47 (H-6), 1.49 (H-8ax.), 1.66 (H-9ax.), 1.24 (H-9eq.), 1.19 (H-11), 0.74 (Me-12), 0.94 (Me-13), 0.78 (Me-14), 4.80 (H-15α), 4.64 (H-15β).

3.17. Esterification of (+)-eudesm-4(15)-ene-6α,7α-diol (**11**) by m-bromobenzoic acid

To a soln of **11** (10 mg) in CH_2Cl_2 (2 ml), m-bromobenzoic acid (60 mg), DCC (60 mg) and DMAP (20 mg) were added and stirred for 3 days at room temp. The usual work-up and purification gave *m*-bromobenzoate **13** (7.6 mg).

3.18. m-Bromobenzoate **13**

mp 170°. $[\alpha]_D$ −24.8 ($CHCl_3$; *c* 0.76). EI-MS *m*/*z* (rel. int.): 420 $[M]^+$(1), 149(100).

3.19. Crystal data for m-bromobenzoate **13**

Crystal dimension = 0.5 × 0.2 × 0.2 mm, orthorhombic, space group $P2_12_12_1$, $a=18.149$ (6) Å, $b=18.869$ (6) Å, $c=6.015$ (3) Å, $V=2059.899902$ (1) Å^3, $Z=4$, $D_{calc}=1.354$, 1790 observed reflections, Cu Kα ($\lambda=1.54178$ Å), $S=1.667$, final residuals *R* and *Rw* with 0.054, 0.071. Eta = 1.394.

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References

Andersen, N. H., Shunk, B., & Costin (1973). *C. R. Experientia*, *29*, 645.

Andersen, N. H., Tseng, C-L. W., Moore, A., & Ohta, Y. (1978). *Tetrahedron*, *34*, 47.

Asakawa, Y., Toyota, M., Takemoto, T., & Suire, C. (1979). *Phytochemistry*, *18*, 1007.

Asakawa, Y., Matsuda, R., Toyota, M., Takemoto, T., Connolly, J. D., & Phillips, W. R. (1983). *Phytochemistry*, *22*, 961.

Asakawa Y. (1995). Herz W., Kirby G.W., Moore R.E., Steglich W., Tamm Ch (Ed.), *Progress in the chemistry of organic natural products* (65, pp. 1–562).

Chetty, G. L., Zalkow, V. B., & Zalkow, L. H. (1968). *Tetrahedron Letters*, *28*, 3223.

Connolly J.D., Harrison L.J., Rycroft D.S. (1982). *Journal of Organic Chemistry, Chemical Communication* 1236.

Fricke, C., Rieck, A., Hardt, I. H., König, W. A., & Muhle, H. (1995). *Phytochemistry*, *39*, 1119.

Godin, P. (1954). *Nature*, *174*, 134.

Huneck, S., & Klein, E. (1967). *Phytochemistry*, *6*, 383.

König, W. A., Rieck, A., Hardt, I., Gehrcke, B., Kubeczka, K. H., & Muhle, H. (1994). *Journal of High Resolution Chromatography*, *17*, 315.

König, W. A., Bülow, N., Fricke, C., Melching, S., Rieck, A., & Muhle, H. (1996). *Phytochemistry*, *43*, 629.

Kusumi, T., Ohtani, I., Inouye, Y., & Kakisawa, H. (1988). *Tetrahedron Letters*, *29*, 4731.

Mash, E. A., & Fryling, J. A. (1987). *Journal Organic Chemistry*, *52*, 3000.

Matsuo A., Nakayama M., Hayashi S. (1973). *Chemistry Letters* 769.

Matsuo, A., Nakayama, M., Sato, S., Nakamoto, T., Uto, S., & Hayashi, S. (1974). *Experientia*, *30*, 321.

Ohta, Y., Andersen, N. H., & Liu, C-B. (1977). *Tetrahedron*, *33*, 617.

Riniker, B., Kalvoda, J., Arigoni, D., Fürst, A., Jeger, O., Gold, A. M., & Woodward, R. B. (1954). *Journal of American Chemical Society*, *76*, 313.

Sharpless, K. B., Amberg, W., Bennani, Y. L., Crispino, G. A., Hartung, J., Jeong, K. S., Kwong, H. L., Morikawa, K., Wang, Z. M., Xu, D., & Zhang, X. L. (1992). *Journal of Organic Chemistry*, *57*, 2768.

Tori, M., Hasebe, T., & Asakawa, Y. (1991). *Bulletin of the Chemical Society of Japan*, *64*, 2303.

Toyota, M., Nakaishi, E., & Asakawa, Y. (1996). *Phytochemistry*, *41*, 833.

Varma, K. R., & Bathacharyya, S. C. (1964). *Tetrahedron 1964*, *20*, 2927.