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Chemical Transformation of Terpenoids. II.[1] Acid Treatment of (3*S*)-1-Vinyl-, (3*S*)-1-Hydroxypropenyl-, and (3*S*)-1-Epoxyethyl-1,2,2-trimethylcyclopentane Derivatives: Ring Enlargement Reactions and Successive Migrations of Methyl Residues

Isao Kitagawa,* Hirotaka Shibuya, Hiromichi Fujioka, Akiharu Kajiwara, Yoshio Yamamoto, Shinji Tsujii, and Kazuya Murakawa

Faculty of Pharmaceutical Sciences, Osaka University, 1-6, Yamada-oka, Suita, Osaka 565, Japan

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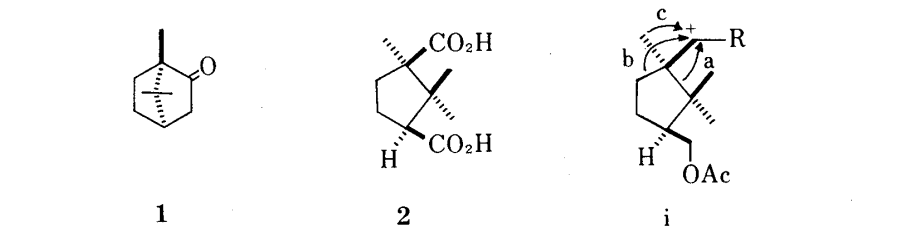
Four 1,2,2-trimethylcyclopentane derivatives, (+)-(1*S*,3*S*)-3-acetoxymethyl-1,2,2-trimethyl-1-vinylcyclopentane (**3**), (+)-(1*S*,3*S*)-3-acetoxymethyl-1-(3′-hydroxypropenyl)-1,2,2-trimethylcyclopentane (**4**), (+)-(1*R*,3*S*,1′*S*)-3-acetoxymethyl-1-(1′,2′-epoxyethyl)-1,2,2-trimethylcyclopentane (**5**), and (+)-(1*R*,3*S*,1′*R*)-3-acetoxymethyl-1-(1′,2′-epoxyethyl)-1,2,2-trimethylcyclopentane (**6**), which were synthesized from *d*-camphor (**1**), were subjected to acid treatment. It was found that i) treatment of **3** with 2,4,4,6-tetrabromocyclohexa-2,5-dienone yielded a cyclohexane derivative (**7**) which was formed *via* a ring-enlargement reaction sequence, ii) BF_3-etherate treatment of **5** furnished three cyclopentane derivatives (**14**, **15**, **16**), among which **14** and **15** possess a 2-oxa-bicyclo[3.3.0]-octane skeleton produced through successive migrations of methyl groups, and iii) BF_3-etherate or titanium tetrachloride treatment of **6** resulted in a ring-enlargement reaction giving **19** and **20**, or **21**.

Keywords——acid treatment; 2,4,4,6-tetrabromocyclohexa-2,5-dienone; ring-enlargement reaction; successive methyl migration; 2-oxa-bicyclo[3.3.0]octane derivative

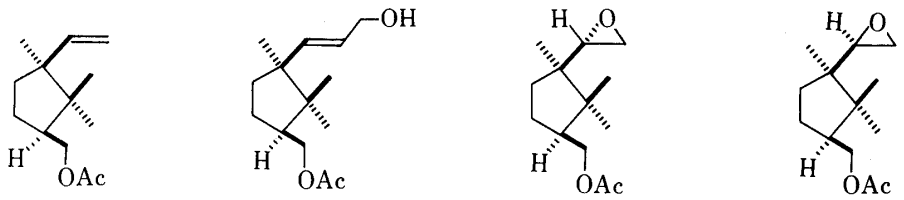
In the preceding paper,[1] we reported syntheses of four optically active 1,2,2-trimethylcyclopentane derivatives, (+)-(3*S*)-vinylcyclopentane (**3**), (+)-(3*S*)-hydroxypropenylcyclopentane (**4**), (+)-(3*S*)-(1′*S*,2′)-epoxyethylcyclopentane (**5**), and (+)-(3*S*)-(1′*R*,2′)-epoxyethylcyclopentane (**6**), from *d*-camphor (**1**) *via* *d*-camphoric acid (**2**). Under acidic conditions, all these cyclopentane derivatives (**3**, **4**, **5**, **6**) were expected to undergo conversions through a presumed carbonium cation i (*via* path a, b, or c).

The present paper deals in detail with the results of acidic treatments of these 1,2,2-trimethylcyclopentane derivatives (**3**, **4**, **5**, **6**): i) treatment of (+)-(3*S*)-vinylcyclopentane (**3**) with 2,4,4,6-tetrabromocyclohexa-2,5-dienone (TBCO)[2] effected a ring-enlargement reaction (*via* path b) to yield a monobromocyclohexane derivative (**7**),[3] ii) boron trifluoride (BF_3)-etherate treatment of (+)-(3*S*)-(1′*S*,2′)-epoxyethylcyclopentane derivative (**5**) was found to effect successive migrations of methyl groups (*via* path c) to yield two 2-oxa-bicyclo[3.3.0]-octane derivatives (**14**, **15**) and a cyclopentane derivative (**16**),[4] and iii) both BF_3-etherate and titanium tetrachloride ($TiCl_4$) treatments of **6** were found to effect a ring-enlargement reaction (*via* path b) to yield three cyclohexane derivatives (**19**, **20**, **21**).

After examination of acidic treatments of (+)-(3*S*)-vinylcyclopentane (**3**) under various conditions, it was found that heating of **3** under reflux with 1.5 molar equivalent of TBCO in tetrahydrofuran for 30 min furnished a bromine-containing product (**7**, 20%) together with a complex mixture. Since the mixture was presumed to contain a dibromide (**8**) and/or tribromide (**9**) as judged from the proton nuclear magnetic resonance (^1H NMR) spectrum, the whole reaction mixture obtained after TBCO treatment was successively treated with zinc and acetic acid at 60°C for one hour to furnish **7** in improved yield (63%) with a 24% recovery of the starting compound (**3**). A similar result could be obtained by treatment of **3** with TBCO in nitromethane followed by heating with zinc and acetic acid.

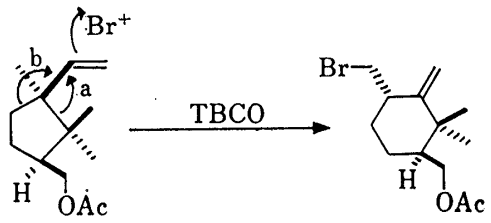


1 2 i

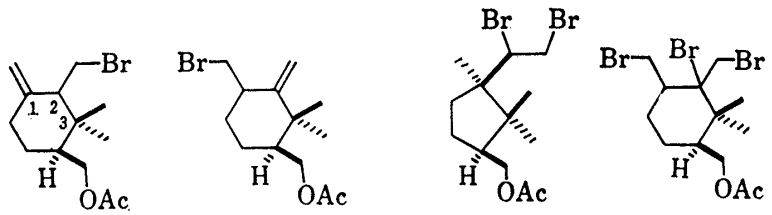


3 4 5 6

Chart 1



3 7



7a 7b 8 9

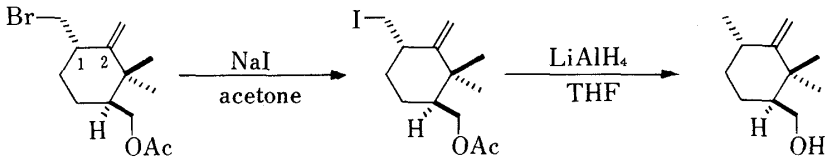
Chart 2

The brominated product (7), $C_{13}H_{21}BrO_2$, showed a positive Beilstein test. The infrared (IR) spectrum of 7 shows the presence of a terminal methylene moiety (3080, 1633 cm^{-1}) and an acetoxyl group (1750 cm^{-1}), while the ^1H NMR spectrum shows signals due to two tertiary methyl groups (δ 1.10, 1.22), one acetoxymethyl group attached to a tertiary carbon (δ 2.00, 3H, s; δ 3.8—4.2, 2H, AB in ABX), a bromomethyl group attached to another tertiary carbon (δ 3.2—3.8, 2H, AB in ABX), and a terminal methylene moiety (δ 4.58 and 4.86, 1H each, both br. s.).

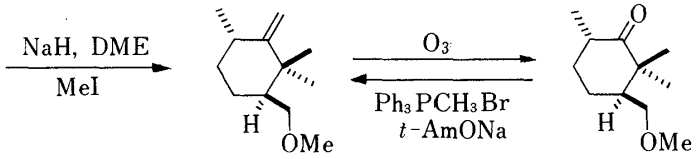
Based on these data, the monobromo derivative (7) was presumed to be either **7a** or **7b**, which may be formed from 3 *via* an initial attack of a bromonium cation on the vinyl group followed by a C–C bond migration (path a or b). The structure 7 (formed *via* path b), including the C–1 configuration, is supported by the following experiments.

Treatment of **7** with sodium iodide in acetone quantitatively yielded an iodo-acetate (**10**), which, by reduction with lithium aluminum hydride, was converted quantitatively to an alcohol (**11**): IR, 3400 cm^{-1}. The ^1H NMR spectrum of **11** lacks signals due to methylene protons attached to carbons bearing an iodine and an acetoxyl group, but shows signals ascribable to a newly formed secondary methyl group at δ 1.03 (3H, d, J=6 Hz) and a hydroxymethyl group at δ 3.2—3.8 (2H, AB in ABX) together with two broad singlets at δ 4.59 and 4.73 due to a terminal methylene moiety. Methylation of **11** with methyl iodide and sodium hydride in dimethoxyethane (DME) afforded a methyl ether (**12**): no OH (IR) and 3H, s, at δ 3.22 (^1H NMR). Ozonolysis of **12** in methanol at −72°C furnished in 65% yeld a six-membered ring ketone (**13**), whose IR spectrum shows an absorption band at 1700 cm^{-1}. The ^1H NMR spectrum lacks signals due to a terminal methylene moiety. In the spin-decoupling experiments with **13**, irradiation of a signal due to a secondary methyl group (δ 0.93, d, J=6 Hz) changed a signal (δ 2.55, m) due to a methine proton attached to a ring-carbon into a pair of doublets (J=10, 6 Hz). The monobromocyclohexane (**7**) was thus proved to be a **7b**-type compound rather than a **7a**-type one. During ozonolysis of **12**, retention of the secondary methyl configuration was confirmed by regeneration in high yield of **12** from **13** by methylenation with methyltriphenylphosphonium bromide and sodium tertiary amylate.[5]

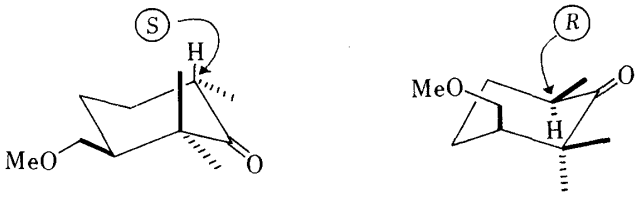
The large coupling constant (10 Hz) between a proton geminal to a secondary methyl group and one of the neighboring methylene protons in **13**, led us to consider two possible chair-like conformations (**13** and **13a**) for **13**, in which the secondary methyl group must be in an equatorial orientation. The predominance of **13** over **13a** is indicated by the circular dichroism (CD) spectrum of **13**, which shows a positive maximum of $[\theta]_{292}$ +4500 due to an



7 **10** **11**



12 **13**



13 **13a**

Chart 3

n→π^* transition of the carbonyl.[6] The structure **13** having a 1*S* configuration is thus proved and consequently the structure **7** is determined for the monobromocyclohexane which was obtained by the TBCO reaction of **3**.

Treatment of (+)-(3*S*)-hydroxypropenylcyclopentane (**4**), a second substrate for our transformation studies, under various conditions (*p*-TsOH·H_2O, CF_3COOH, BF_3-etherate, $TiCl_4$, *etc.*) resulted in the formation of complex mixtures and no promising compound has yet been isolated.

In the case of (+)-(3*S*)-(1′*S*,2′)-epoxyethylcyclopentane (**5**), treatment with excess BF_3-etherate in benzene at room temperature afforded three isomeric products, $C_{13}H_{22}O_3$: **14** (38%), **15** (13%), and **16** (42%).

The retention of an acetoxymethyl group in **14** was shown by the IR absorption band (1738 cm^{-1}) and the ^1H NMR signals (δ 1.93, 3H, s, and δ 3.6—4.3, 2H, AB in ABX). Further, the ^1H NMR spectrum of **14** shows signals due to two tertiary methyl groups (δ 0.96, 1.09), one secondary methyl group (δ 0.90, d, J=7 Hz) and two methylene protons involved in a five-membered ring and adjacent to an ether oxygen (δ 3.15, 1H, d.d, J=8, 12 Hz and δ 3.85, 1H, d.d, J=8, 8 Hz).[7]

A second isomer (**15**) also retains an acetoxymethyl group as shown by its IR and ^1H NMR spectra (as described above for **14**). Here again, the ^1H NMR spectrum of **15** shows signals due to two tertiary methyl groups (δ 0.87, 1.02), one secondary methyl group (δ 0.88, d, J=7 Hz), and two methylene protons located in a chemical environment similar to that in **14** (δ 3.27, 1H, d.d, J=8, 9 Hz; δ 3.83, 1H, d.d, J=8, 6 Hz).[7] These properties are very similar to those of **14**.

Based on these properties, **14** and **15** were presumed to be 2-oxa-bicyclo[3.3.0]octane derivatives having one acetoxymethyl group, one secondary methyl group at C–4, and two angular methyl groups.

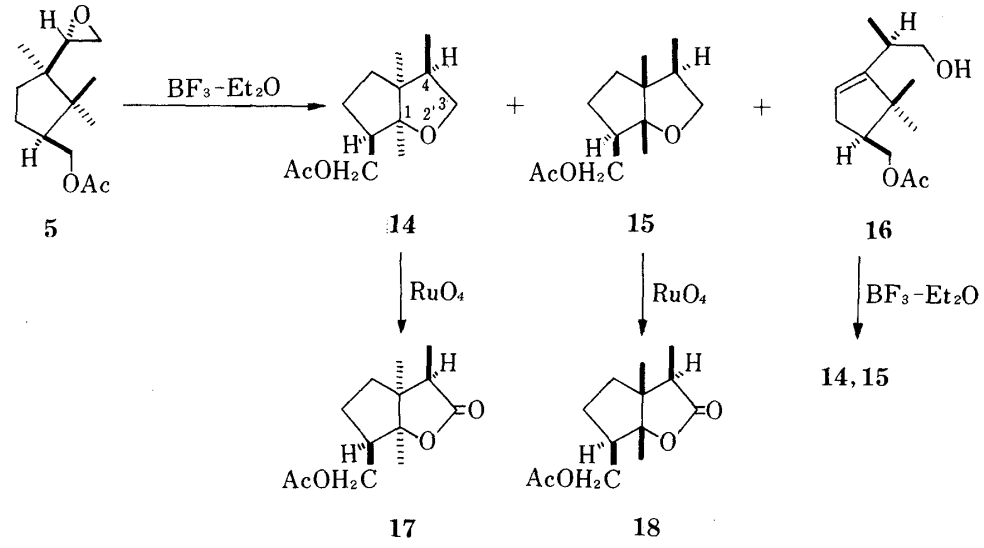
When both **14** and **15** were oxidized with ruthenium tetroxide,[8] corresponding γ-lactones, **17** (IR: 1776 cm^{-1}) and **18** (IR: 1771 cm^{-1}), were obtained. The CD spectra of both γ-lactones (**17**, **18**) show a negative maximum due to an n→π^* transition of a γ-lactone carbonyl[9]: $[\theta]_{217}$ −6800 for **17** and $[\theta]_{223}$ −2500 for **18**. Thus the 4*R* configuration for both **17** and **18** is proved and **14** and **15** are presumed to be isomeric in regard to their angular methyl configurations. Finally, the whole structures of **14** and **15** were established by X-ray analysis of **17** by the direct method, as reported in our previous communication.[4]

With regard to the reaction pathway from **5** to **14** and **15**, a successive migration process of methyl groups seems to be plausible. Thus, a presumed carbonium cation (ii), which may be formed by epoxide-ring opening (from **5**), would suffer a 1,2-shift of a methyl residue at C–2 either *via* path a or *via* path b and a resulting carbonium cation at C–2 would be attacked by a primary hydroxyl group (path c), finally constructing an oxolane ring to yield **14** and **15**.

A third isomer (**16**) shows hydroxyl and acetoxyl absorption bands in its IR spectrum (3400(br), 1732 cm^{-1}). The ^1H NMR spectrum of **16** shows signals ascribable to two tertiary methyl groups (δ 0.88, 1.11), one secondary methyl group (δ 1.07, d, J=7 Hz), and one acetoxymethyl residue (δ 2.00, 3H, s; δ 4.07, 2H, m). Characteristic signals in the ^1H NMR spectrum of **16** are those ascribable to a hydroxymethyl residue (δ 3.1—3.6, 2H, AB in ABX) and an olefinic proton in a five-membered ring (δ 5.29, 1H, narrow m, $W_{h/2}$=5 Hz). Based on these data and mechanistic considerations, the structure **16**, which may be derivable from the above-mentioned carbonium cation (ii) *via* a deprotonation (path d), is proposed. This proposal is substantiated by the result of further treatment of **16** with BF_3-etherate in benzene for 24 h, to furnish **14** (51%) and **15** (9%) with a 33% recovery of **16**.

Finally, (+)-(3*S*)-(1′*R*,2′)-epoxyethylcyclopentane (**6**) was treated with BF_3-etherate in dichloromethane at −78°C to afford two products: **19** (10%) and **20** (63%).

The IR and ^1H NMR spectra of the minor product **19** show the presence of a hydroxy-



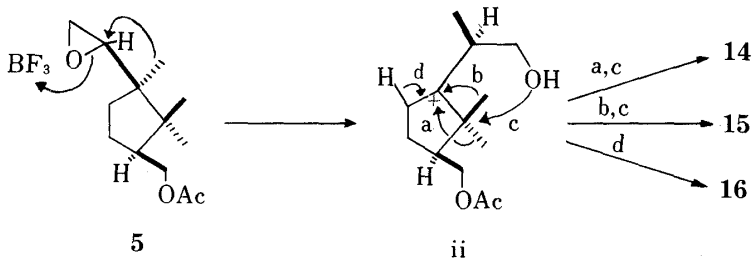


Chart 4

methyl group and an acetoxymethyl group (3640, 1750 cm^{-1}; δ 3.3—4.4, 4H, m; δ 1.96, 3H, s), a terminal methylene function (3120, 1636 cm^{-1}; δ 4.56, 4.82, both 1H, br.s), and two tertiary methyl groups (δ 1.01, 1.20). These properties suggest close similarity of the structure of **19** and that of the above-mentioned bromocyclohexane derivative (**7**). This suggestion was verified by conversion of **19** to **7** with triphenylphosphine and carbon tetrabromide.[10]

The major product (**20**) contains a fluorine atom. A significant difference in the structures of **19** and **20** is that **19** possesses a terminal methylene function whereas **20** comprises a methyl group attached to a ring-carbon bearing a fluorine atom (δ 1.22, 3H, d, J=23 Hz). The retention of a hydroxymethyl group, an acetoxymethyl group and two tertiary methyl groups in **20**, as in **19**, is shown by the IR and ^{1}H NMR spectra. The structure **20** was assigned on the basis of these results and mechanistic considerations. As shown in iii, if a presumed carbonium cation, which is produced by an epoxide-ring opening followed by a C–C bond migration, is terminated by deprotonation (path a), an exo-methylene compound (**19**) may be formed. If a fluorine anion attacks (path b) the intermediary carbonium cation, the major product (**20**) may be obtained.

On the other hand, when **6** was treated with $TiCl_4$ in benzene at room temperature, a chlorine-containing product (**21**) was formed as the major product (83%). The IR and ^{1}H NMR spectra of **21** indicate structural resemblance of **21** and **20** (see "Experimental"). Among signals due to three tertiary methyl groups in **21**, a singlet at δ 1.52 is assigned to a methyl group attached to a ring-carbon bearing a chlorine atom (*cf.* δ 1.22, d, J=23 Hz for **20**). Acetylation of **21** with acetic anhydride and pyridine furnished a diacetate (**22**), which, on treatment with 1,5-diazabicyclo[5.4.0]undecene-5 (DBU) at 120°C, yielded a dehydrochlorinated product. This product (**23**) was found to be identical with an acetylation product

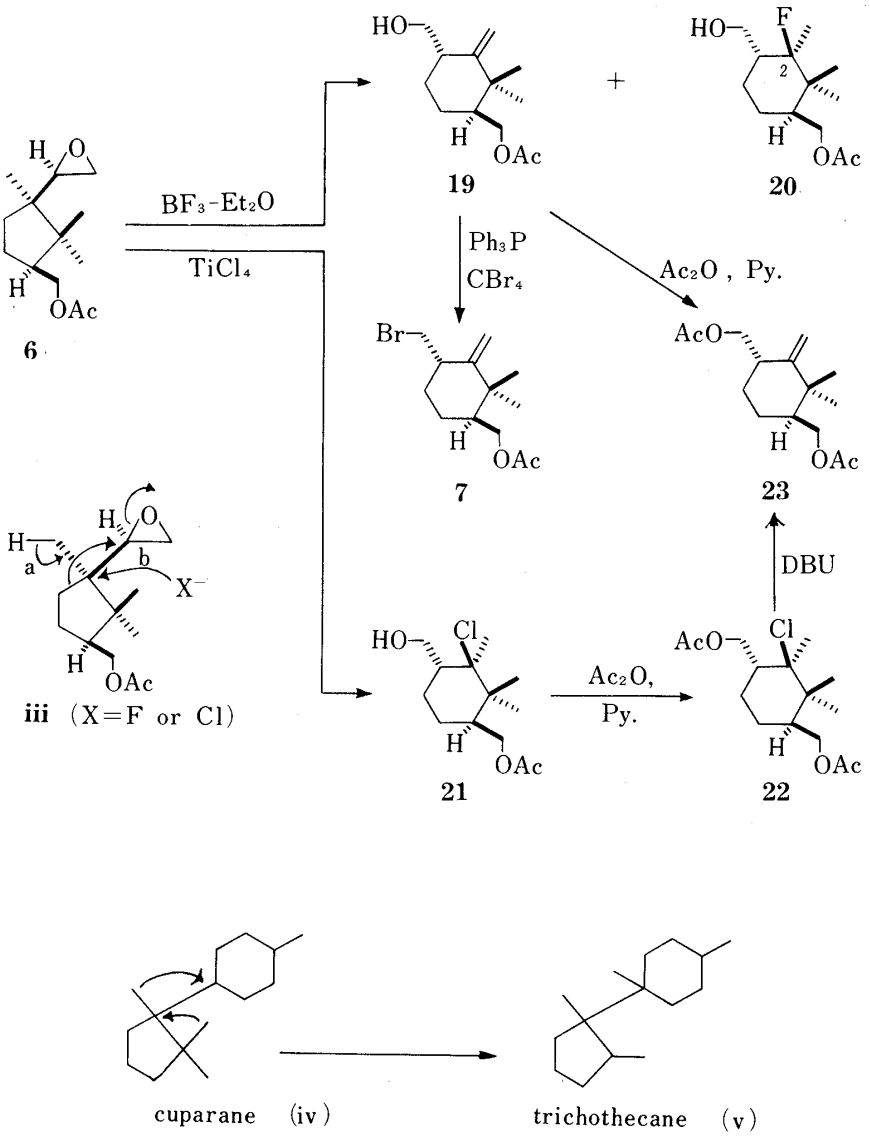


Chart 5

of **19**, and thus the structure **21** was corroborated. The 2*R* configuration (2*β*-Cl) in **21** is supported by mechanistic considerations as mentioned for **20** and by the fact that the DBU treatment of **22** predominantly afforded **23**, which suggested a *cis* relationship of 1-H and 2-Cl in **22**.

As described above, it has been found that i) on acid treatment (with TBCO, BF_3-etherate, or $TiCl_4$) of a 1,2,2-trimethyl-1-vinylcyclopentane derivative (**3**) or a (1′*R*)-1-epoxyethyl-1,2,2-trimethylcyclopentane derivative (**6**), ring-enlargement reactions occur to afford cyclohexane derivatives (**7**, or **19**, **20**, **21**), and ii) on acid treatment (with BF_3-etherate) of a (1′*S*)-1-epoxyethyl-1,2,2-trimethylcyclopentane derivative (**5**), a successive migration of methyl groups occurs to furnish two 2-oxa-bicyclo[3.3.0]octane derivatives (**14**, **15**) in addition to a cyclopentane derivative (**16**). Among these reactions, the conversions from **5** to **14** and **15** are interesting since they are reminiscent of a transformation pathway from a cuparane-type sesquiterpenoid (iv) to a trichothecane-type sesquiterpenoid (v).

Experimental

The instruments used for obtaining physical data and the experimental conditions for chromatography were the same as described in the preceding paper.[1)]

TBCO Treatment of (+)-(3*S*)-Vinylcyclopentane (3) followed by Zn-AcOH Treatment——a) TBCO in THF: A solution of 3 (20.8 g, 98 mmol) in THF (470 ml) was treated with TBCO (60.3 g, 147 mmol) and heated under reflux for 30 min. The reaction mixture was cooled, then AcOH (20 ml) and Zn powder (20 g, 310 mmol) were added and the whole was heated at 60°C for 1 h. After dilution with ether (500 ml), the whole mixture was filtered to remove Zn and the filtrate was successively washed with aq. 5% NaOH, aq. 5% HCl, aq. sat. $NaHCO_3$, and sat. saline, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product (29 g) which was purified by column chromatography (SiO_2 300 g, *n*-hexane–EtOAc=50: 1) to furnish 7 (17.8 g, 63%) and 3 (4.9 g, 24% recovered).

b) TBCO in CH_3NO_2: A solution of 3 (2.08 g, 9.8 mmol) in CH_3NO_2 (30 ml) was treated with TBCO (6.03 g, 14.7 mmol) and the mixture was stirred at 30°C for 2 h, then poured into ice-water. The whole mixture was extracted with *n*-hexane. The *n*-hexane extract was successively washed with aq. 5% NaOH, aq. 5% HCl, aq. sat. $NaHCO_3$, and sat. saline, then dried over $MgSO_4$. The product (3.5 g) obtained by removal of the solvent under reduced pressure was dissolved in AcOH (8 ml) and treated with Zn powder (4 g, 62 mmol). After heating at 60°C for 1 h, the whole mixture was diluted with ether (100 ml) and filtered to remove Zn. The filtrate was successively washed with aq. sat. $NaHCO_3$ and sat. saline, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product (2.7 g). Purification of the product by column chromatography (SiO_2 30 g, *n*-hexane–EtOAc=50: 1) furnished 7 (1.37 g, 50%) and 3 (0.53 g, 27% recovered). 7, colorless oil, $[\alpha]_D^{18}$ +62° (*c*=0.37, $CHCl_3$). *Anal.* Calcd for $C_{13}H_{21}BrO_2$: C, 53.99; H, 7.32; Br, 27.63. Found: C, 54.00; H, 7.39; Br, 27.36. IR ν_{max}^{film} cm^{-1}: 3100, 1750, 1633. ^1H NMR (CCl_4, δ): 1.01, 1.22 (3H each, both s, *tert.* $CH_3\times2$), 2.00 (3H, s, OAc), 3.2—3.8 (2H, m, $-C\underline{H}_2Br$), 3.8—4.2 (2H, AB in ABX, $-C\underline{H}_2OAc$), 4.58, 4.86 (1H each, both br.s, $>C=C\underline{H}_2$). MS *m/z*(%): 290 (1, $C_{13}H_{21}{}^{81}BrO_2$, 288 (1, $C_{13}H_{21}{}^{79}BrO_2$), 149 (100).

NaI Treatment of 7 giving the Iodo-acetate (10)——A solution of 7 (2.6 g, 9 mmol) in dry acetone (30 ml) was treated with NaI (8.0 g, 53 mmol) and heated under reflux for 5 h. After cooling, the solvent was evaporated off under reduced pressure to give a residue, which was extracted with EtOAc. The EtOAc extract was then washed with aq. 5% $Na_2S_2O_3$ and sat. saline and dried over $MgSO_4$. Removal of the solvent under reduced pressure furnished 10 (3.0 g, quant.), colorless oil, $[\alpha]_D^{20}$ +33° (*c*=3.0, $CHCl_3$). *Anal.* Calcd for $C_{13}H_{21}IO_2$: C, 46.43; H, 6.31; I, 37.74. Found: C, 46.18; H, 6.22; I, 38.15. IR ν_{max}^{film} cm^{-1}: 3100, 1740, 1635. ^1H NMR (CCl_4, δ): 0.99, 1.20 (3H each, both s), 1.95 (3H, s), 3.0—3.5 (2H, AB in ABX, $-C\underline{H}_2I$), 3.8—4.2 (2H, AB in ABX, $-C\underline{H}_2OAc$), 4.63, 4.88 (1H each, both br.s). MS *m/z*(%): 336 (1, M^+), 149 (100).

$LiAlH_4$ Reduction of 10 giving the Alcohol (11)——A solution of 10 (2.8 g, 8.3 mmol) in THF (20 ml) was added dropwise to a suspension of $LiAlH_4$ (1.0 g, 2.6 mmol) in THF (6 ml) and the whole was stirred at room temperature for 6 h. After decomposition of the excess reagent with EtOAc, the whole mixture was acidified with aq. 5% H_2SO_4 and extracted with EtOAc. Work-up of the EtOAc extract in the usual manner and removal of the solvent under reduced pressure furnished 11 (1.4 g, quant.), colorless oil, $[\alpha]_D^{18}$ +100° (*c*=0.7, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400, 3095, 1633. ^1H NMR (CCl_4, δ): 0.94, 1.19 (3H each, both s), 1.03 (3H, d, *J*=6 Hz), 3.2—3.8 (2H, AB in ABX, $-C\underline{H}_2OH$), 4.59, 4.73 (1H each, both br.s). High resolution MS (*m/z*): Calcd for $C_{11}H_{20}O$: 168.152. Found: 168.152. MS *m/z*(%): 168 (20, M^+), 81 (100).

Methylation of 11 giving the Methyl Ether (12)——A solution of 11 (1.42 g, 8.4 mmol) in DME (15 ml) was added to a suspension of NaH (400 mg, 60% in oil, 10 mmol, washed with *n*-pentane beforehand) in DME (8 ml) and the mixture was heated under reflux for 50 min. After cooling, the reaction mixture was treated with MeI (0.7 ml, 11 mmol) at 0°C and the whole was stirred at room temperature for 1 h. The reaction mixture was poured into ice-water and extracted with EtOAc. The EtOAc extract was washed with aq. 10% $Na_2S_2O_3$ and sat. saline, then dried over $MgSO_4$. Removal of the solvent under reduced pressure furnished 12 (1.4 g, 92%), colorless oil, $[\alpha]_D^{16}$ +99° (*c*=2.0, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.77; H, 11.99. IR ν_{max}^{film} cm^{-1}: 3085, 1622. ^1H NMR (CCl_4, δ): 0.93, 1.15 (3H each, both s), 1.02 (3H, d, *J*=6 Hz), 3.22 (3H, s), 3.0—3.5 (2H, AB in ABX, $-C\underline{H}_2OMe$), 4.58, 4.72 (1H each, both br.s). MS *m/z*(%): 182 (6, M^+), 135 (100).

Ozonolysis of 12 giving the Ketone (13)——A solution of 12 (1.15 g, 6.3 mmol) in MeOH (60 ml) was cooled to −72°C and bubbled through with a stream of ozonized oxygen for 70 min (12 ml/min). Excess ozone was flushed out with a nitrogen stream and the whole mixture was gradually allowed to come to room temperature. Removal of the solvent by evaporation under reduced pressure gave a product (1.28 g) which was purified by column chromatography (SiO_2 40 g, *n*-hexane–EtOAc=10: 1) to furnish 13 (0.75 g, 65%), colorless oil, $[\alpha]_D^{15}$ +129° (*c*=1.9, $CHCl_3$). *Anal.* Calcd for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 71.62; H, 10.86. IR ν_{max}^{film} cm^{-1}: 1700. ^1H NMR (CCl_4, δ): 0.93 (3H, d, *J*=6 Hz), 1.00, 1.07 (3H each, both s), 2.55 (1H, m, on irr. at δ 0.93 changed to d.d, *J*=10, 6 Hz, $-C\underline{H}-CH_3$), 3.24 (3H, s), 3.1—3.5 (2H, AB in ABX). CD (*c*=0.37, MeOH) $[\theta]^{18}$ (nm): +4900 (292) (pos. max.). CD (*c*=0.35, CCl_4) $[\theta]^{17}$ (nm): +4500 (292) (pos. max.). MS *m/z*(%): 184 (20, M^+), 69 (100).

Methylenation of 13 giving 12——A mixture of NaH (40 mg, 60% in oil, 1.0 mmol, pre-washed with *n*-pentane) in benzene (2 ml), diisopropyl ether (2 ml), and *tert*-AmOH (0.15 ml, 1.3 mmol) was stirred at room temperature for 30 min, and then treated with methyltriphenylphosphonium bromide (500 mg, 1.4 mmol). The whole was stirred at room temperature for 1.5 h, then a solution of 13 (50 mg, 0.27 mmol) in benzene (0.25 ml) and diisopropyl ether (0.25 ml) was added. The mixture was stirred at room tempera-

ture for a further 10 h, then poured into ice-water and extracted with EtOAc. The EtOAc extract was successively washed with aq. 5% HCl, aq. sat. $NaHCO_3$, and sat. saline, and dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product (55 mg) which was purified by column chromatography (SiO_2 10 g, benzene) to furnish **12** (37 mg, 74%). The product obtained here was identical with **12** described above as judged by TLC, GLC (SE-30), $[\alpha]_D$ ($CHCl_3$), IR (film), and ^1H NMR (CCl_4) comparisons.

BF_3-etherate Treatment of (+)-(3*S*)-(1′*S*,2′)-Epoxyethylcyclopentane (5)——A solution of **5** (200 mg, 0.88 mmol) in benzene (40 ml) was treated with BF_3-etherate (1 ml, 8.1 mmol) and the mixture was stirred at room temperature for 50 min. After addition of aq. sat. $NaHCO_3$ (5 ml), the whole was extracted with EtOAc. The EtOAc extract was washed with sat. saline and dried over $MgSO_4$. The product (195 mg) obtained by removal of the solvent under reduced pressure was purified by column chromatography (SiO_2 20 g, *n*-hexane–EtOAc=3: 1) to furnish **14** (75 mg, 38%), **15** (26 mg, 13%), and **16** (83 mg, 43%).

14, colorless oil, $[\alpha]_D^{15}$ +12° (c=1.4, $CHCl_3$). *Anal.* Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.85; H, 9.86. IR ν_{max}^{film} cm^{-1}: 1738. ^1H NMR (CCl_4, δ): 0.90 (3H, d, J=7 Hz), 0.96, 1.09 (3H each, both s), 1.93 (3H, s), 3.15 (1H, d.d, J=8, 12 Hz, 3-H_A), 3.85 (1H, d.d, J=8, 8 Hz, 3-H_B), 3.6—4.3 (2H, AB in ABX, -C<u>H</u>$_2$OAc). MS m/z(%): 183 (2, M^+-43), 112 (100).

15, colorless oil, $[\alpha]_D^{15}$ +37° (c=1.0, $CHCl_3$). *Anal.* Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.24; H, 9.82. IR ν_{max}^{film} cm^{-1}: 1738. ^1H NMR (CCl_4, δ): 0.87, 1.02 (3H each, both s), 0.88 (3H, d, J=7 Hz), 1.96 (3H, s), 3.27 (1H, d.d, J=8, 9 Hz, 3-H_A), 3.83 (1H, d.d, J=8, 6 Hz, 3-H_B), 3.6—4.2 (2H, AB in ABX, -C<u>H</u>$_2$OAc). MS m/z(%): 226 (1, M^+), 43 (100).

16, colorless oil, $[\alpha]_D^{15}$ +9° (c=1.3, $CHCl_3$). *Anal.* Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.29; H, 9.94. IR ν_{max}^{film} cm^{-1}: 3400, 1732. ^1H NMR (CCl_4, δ): 0.88, 1.11 (3H each, both s), 1.07 (3H, d, J=7 Hz), 2.00 (3H, s), 3.1—3.6 (2H, AB in ABX, -C<u>H</u>$_2$OH), 4.07 (2H, m, -C<u>H</u>$_2$OAc), 5.29 (1H, narrow m, $W_{h/2}$=5 Hz). MS m/z(%): 226 (1, M^+), 43 (100).

RuO_4 Oxidation of 14 giving the γ-Lactone (17)——a) RuO_4–CCl_4 Reagent: A suspension of $RuO_2 \cdot xH_2O$ (500 mg) in CCl_4 (50 ml) was mixed with a solution of $NaIO_4$ (4 g) in water (30 ml) and stirred at room temperature for 1 h. The yellow CCl_4 phase was used as the oxidation reagent.

b) A mixture of **14** (61 mg, 0.27 mmol) in RuO_4–CCl_4 reagent (6 ml) was stirred at room temperature for 30 min then treated with 99% EtOH (1 ml). After the removal of insoluble substance by filtration, the solvent was evaporated off under reduced pressure to furnish **17** (63 mg, 96%). **17**, mp 80—81°C (transparent prisms from *n*-hexane), $[\alpha]_D^{25}$ −42° (c=0.77, $CHCl_3$). *Anal.* Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.73; H, 8.56. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1776, 1747. ^1H NMR (CCl_4, δ): 1.11, 1.37 (3H each, both s), 1.15 (3H, d, J=9 Hz), 2.04 (3H, s), 3.9—4.4 (2H, AB in ABX). CD (c=0.55, MeOH) $[\theta]^{22}$ (nm): −6800 (217) (neg. max.). MS m/z(%): 240 (3, M^+), 43 (100).

RuO_4 Oxidation of 15 giving the γ-Lactone (18)——A solution of **15** (20 mg, 0.09 mmol) in RuO_4–CCl_4 reagent (2 ml) was stirred at room temperature for 30 min then treated with 99% EtOH (1 ml). After filtration, work-up of the filtrate as described above furnished **18** (19 mg, 90%), colorless oil. $[\alpha]_D^{25}$ +27° (c=0.63, $CHCl_3$). *Anal.* Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.93; H, 8.51. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1771, 1748. ^1H NMR (CCl_4, δ): 0.96, 1.26 (3H each, both s), 1.09 (3H, d, J=9 Hz), 2.00 (3H, s), 4.03 (2H, d, J=6 Hz). CD (c=0.37, dioxane) $[\theta]^{22}$ (nm): −2500 (223) (neg. max.). MS m/z(%): 240 (5, M^+), 43 (100).

BF_3-etherate Treatment of 16 giving 14 and 15——A solution of **16** (197 mg, 0.87 mmol) in benzene (40 ml) was treated with BF_3-etherate (4 ml, 32.4 mmol) and stirred at room temperature for 24 h. Then aq. sat. $NaHCO_3$ (5 ml) was added and the whole was extracted with EtOAc. Work-up of the EtOAc extract and removal of the solvent under reduced pressure yielded a product (190 mg), which was purified by column chromatography (SiO_2 20 g, *n*-hexane–EtOAc=3: 1) to furnish **14** (101 mg, 51%), **15** (17 mg, 9%), and **16** (65 mg, 33% recovered). **14** and **15** obtained here were identical with the above-described authentic compounds as judged by TLC, IR (film), $[\alpha]_D$ ($CHCl_3$), and ^1H NMR (CCl_4) comparisons.

BF_3-etherate Treatment of (+)-(3*S*)-(1′*R*,2′)-Epoxyethylcyclopentane (6)——A solution of **6** (520 mg, 2.3 mmol) in CH_2Cl_2 (100 ml) was treated at −78°C with a 1% BF_3-etherate–CH_2Cl_2 solution (143 ml, 11.6 mmol) and the mixture was stirred at the same temperature for 4 h. Then aq. sat. $NaHCO_3$ (10 ml) was added and the whole was extracted with EtOAc. Work-up of the EtOAc extract as described above gave a product (565 mg) which was purified by column chromatography (SiO_2 90 g, *n*-hexane–EtOAc=5: 1) to furnish **19** (50 mg, 10%) and **20** (356 mg, 63%). **19**, colorless oil, $[\alpha]_D^{19}$ +74° (c=0.5, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3640, 3120, 1750, 1636. ^1H NMR (CCl_4, δ): 1.01, 1.20 (3H each, both s), 1.96 (3H, s), 3.3—4.4 (4H, m, -C<u>H</u>$_2$OH, -C<u>H</u>$_2$OAc), 4.56, 4.82 (1H each, both br.s, >C=C<u>H</u>$_2$). High resolution MS (m/z): Calcd for $C_{13}H_{22}O_3$: 226.157. Found: 226.156. MS m/z(%): 226 (0.3, M^+), 148 (100). **20**, colorless oil, $[\alpha]_D^{15}$ +46° (c=5.4, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 1748. ^1H NMR (CCl_4, δ): 0.98, 1.06 (3H each, both s), 1.22 (3H, d, J=23 Hz, -C<u>H</u>F-C<u>H</u>$_3$), 1.94 (3H, s), 3.1—4.2 (4H, m, -C<u>H</u>$_2$OH, -C<u>H</u>$_2$OAc). High resolution MS (m/z): Calcd for $C_{13}H_{23}FO_3$: 246.163. Found: 246.163. MS m/z(%): 246 (9, M^+), 171 (100).

Bromination of 19 giving 7——A solution of **19** (10 mg, 0.044 mmol) in ether (0.2 ml) was treated with triphenylphosphine (24.1 mg, 0.09 mmol) and CBr_4 (30.5 mg, 0.09 mmol) and stirred at room temperature for 4 h. The whole mixture was poured into ice-water and extracted with EtOAc. The EtOAc extract was washed with aq. sat. $NaHCO_3$ and sat. saline, then dried over $MgSO_4$. Evaporation of the solvent

under reduced pressure gave a product (37 mg) which was purified by column chromatography (SiO_2 3 g, *n*-hexane–EtOAc=20: 1) to furnish **7** (9 mg, 70%), identical with the above-described authentic compound as judged by TLC, $[\alpha]_D$ ($CHCl_3$), and ^1H NMR (CCl_4) comparisons.

$TiCl_4$ Treatment of 6 giving 21——A solution of **6** (120 mg, 0.53 mmol) in benzene (0.25 ml) was treated with a 1% $TiCl_4$–benzene solution (2 ml, 0.18 mmol) and the mixture was stirred at room temperature for 2 h. Then aq. sat. $NaHCO_3$ (1 ml) was added and the whole was extracted with EtOAc. Work-up of the EtOAc extract in the usual manner and removal of the solvent under reduced pressure yielded a product (124 mg). Purification of the product by column chromatography (SiO_2 7 g, *n*-hexane–EtOAc=3: 1) furnished **21** (115 mg, 83%), colorless oil, $[\alpha]_D^{18}$ +56° (*c*=3.0, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3630, 1742. ^1H NMR ($CDCl_3$, δ): 1.11, 1.16, 1.48 (3H each, all s), 2.03 (3H, s), 3.3—4.4 (4H, m, $-C\underline{H}_2OH$, $-C\underline{H}_2OAc$). High resolution MS (*m/z*): Calcd for $C_{13}H_{23}ClO_3$: 262.134. Found: 262.135. MS *m/z*(%): 262 (2, M^+), 187 (100).

Acetylation of 21 giving 22——A solution of **21** (33 mg, 0.125 mmol) in pyridine (0.5 ml) was treated with Ac_2O (0.5 ml, 5 mmol) and left to stand at room temperature for 1 h. The reaction mixture was poured into ice-water and extracted with EtOAc. Work-up of the EtOAc extract in the usual manner gave **22** (38 mg, 99%), colorless oil, $[\alpha]_D^{20}$ +57° (*c*=0.55, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740. ^1H NMR (CCl_4, δ): 1.12, 1.19, 1.50 (3H each, all s), 1.97, 1.99 (3H each, both s), 3.5—4.5 (4H, m, $-C\underline{H}_2OAc\times2$). High resolution MS (*m/z*): Calcd for $C_{15}H_{25}{}^{35}ClO_4$: 304.144. Found: 304.145. MS *m/z*(%): 304 (36, M^+), 184 (100).

Acetylation of 19 giving 23——Acetylation of **19** (20 mg, 0.088 mmol) with Ac_2O (0.5 ml, 5 mmol) and pyridine (0.5 ml) followed by work-up as described for **21** furnished **23** (23 mg, 98%), colorless oil, $[\alpha]_D^{20}$ +77° (*c*=1.8, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1620. ^1H NMR (CCl_4, δ): 1.00, 1.20 (3H each, both s), 1.94, 1.96 (3H, each, both s), 3.7—4.4 (4H, m, $-C\underline{H}_2OAc\times2$), 4.53, 4.82 (1H each, both br.s). High resolution MS (*m/z*): Calcd for $C_{15}H_{24}O_4$: 268.167. Found: 268.165. MS *m/z*(%): 268 (4, M^+), 165 (100).

DBU Treatment of 22 giving 23——A solution of **22** (27 mg, 0.089 mmol) in DBU (0.3 ml, 2 mmol) was heated at 120°C for 15.5 h. After cooling, the reaction mixture was treated with Ac_2O (0.15 ml, 1.5 mmol) and pyridine (0.07 ml) and left to stand at room temperature for 1 h. The whole mixture was poured into ice-water and extracted with EtOAc. The EtOAc extract was washed successively with aq. 5% HCl, aq. sat. $NaHCO_3$, and sat. saline, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product (20 mg), which was purified by column chromatography (SiO_2 2 g, *n*-hexane–EtOAc=5: 1). The diacetate (19 mg, 78%) thus obtained was identical with the above-described **23** as judged by TLC, IR (CCl_4), and ^1H NMR (CCl_4) comparisons.

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