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Chemical Transformation of Terpenoids. IV.[1] Acid Treatment of (3*R*)-1-Vinyl-, (3*R*)-1-Hydroxypropenyl-, and (3*R*)-1-Epoxyethyl-5-methoxy-1,2,2-trimethylcyclopentane Derivatives: Ring Enlargement Reactions and Successive Migrations of Methyl Residues

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Three 5-methoxy-1,2,2-trimethylcyclopentane derivatives, *i.e.*, (+)-(1*R*,3*R*,5*S*)-3-acetoxymethyl-5-methoxy-1,2,2-trimethyl-1-vinylcyclopentane (**3**), (+)-(1*R*,3*R*,5*S*)-3-acetoxymethyl-1-(3′-hydroxypropenyl)-5-methoxy-1,2,2-trimethylcyclopentane (**4**), and (−)-(1*R*,3*R*,5*S*,1′*R*)-3-acetoxymethyl-1-(1′,2′-epoxyethyl)-5-methoxy-1,2,2-trimethylcyclopentane (**5**), which were synthesized from *d*-camphor (**1**) *via* 5-oxo-*d*-bornyl acetate (**2**), were subjected to acid treatment. It was found that i) treatment of **3** with 2,4,4,6-tetrabromocyclohexa-2,5-dienone yielded a 4-bromo-2-oxabicyclo[3.3.0]octane derivative (**8**), ii) BF_3-etherate treatment of **4** resulted in a ring-enlargement reaction giving two cyclohexane derivatives (**13**, **14**), and iii) BF_3-etherate treatment of **5** furnished a 2-oxabicyclo[3.3.0]octane derivative (**15**) which was derivable through successive migrations of the methyl residues.

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

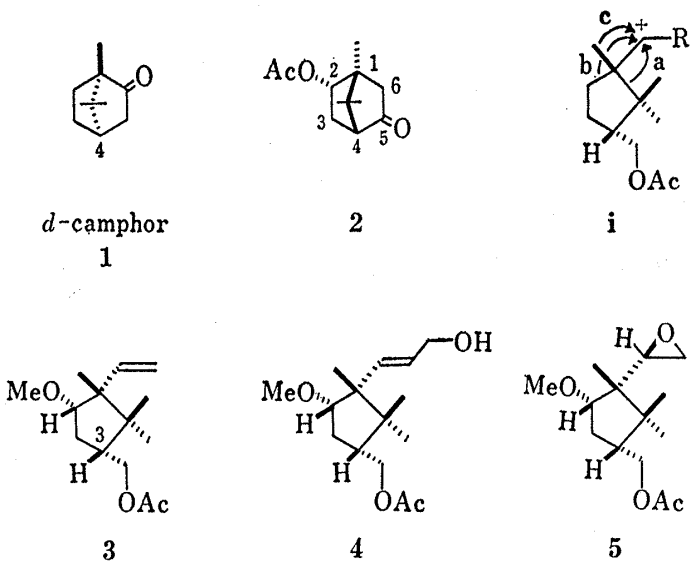
In the preceding paper,[1] we described syntheses of three optically active 5-methoxy-1,2,2-trimethylcyclopentane derivatives, *i.e.*, (+)-(3*R*)-vinylcyclopentane (**3**), (+)-(3*R*)-hydroxypropenylcyclopentane (**4**), and (−)-(3*R*)-(1′*R*, 2′)-epoxyethylcyclopentane (**5**), from *d*-camphor (**1**) *via* 5-keto-*d*-bornyl acetate (**2**). Each 1,2,2-trimethylcyclopentane derivative possesses the (5*S*)-methoxyl moiety. The 3*R* configuration of each arises from C-4 of *d*-camphor (**1**) in the turned-over manner.

As a continuation of our studies on the chemical behavior of (3*S*)-1,2,2-trimethylcyclopentane derivatives with similar acid-labile functions at C-1 (as in **3**, **4**, and **5**) but with inverted C-3 configuration and lacking the 5-methoxyl moiety,[2,3] we investigated the chemical behavior of (3*R*)-5-methoxy-1,2,2-trimethylcyclopentane derivatives (**3**—**5**)[1] upon acid treatment under various conditions.

This paper deals with the results, which include the findings that i) treatment of **4** with boron trifluoride (BF_3)-etherate effects a ring-enlargement reaction (path b in **i**) to afford the cyclohexane derivatives (**13**, **14**) and ii) a similar BF_3-etherate treatment of **5** yields the 2-oxabicyclo[3.3.0]octane derivative (**15**) which is derivable *via* initial methyl migration (path c in **i**) followed by another methyl migration and oxolane ring formation (paths a and c in **vi**).

Acid treatment of (+)-(3*R*)-vinylcyclopentane (**3**)[1] under various conditions resulted in the formation of a complex mixture, while heating of **3** under reflux with 1.5 molar equivalent of 2,4,4,6-tetrabromocyclohexa-2,5-dienone (TBCO)[4] for 20 min yielded three bromine-containing products, **6** (30%), **7** (46%), and **8** (6%). When the TBCO treatment was carried out in nitromethane, **7** (40%) and **8** (13%) were formed with a trace amount of **6**.

The one dibrominated product (**6**), $C_{14}H_{24}O_3Br_2$, showed a positive Beilstein test. The infrared (IR) spectrum of **6** lacks the olefinic absorption band, while the proton nuclear magnetic resonance (^1H NMR) spectrum shows signals due to three tertiary methyl residues,



d-camphor
1

2

i

3

4

5

Chart 1

one acetoxymethyl group attached to a tetriary carbon (δ 1.98, 3H, s; δ 3.4—4.1, m), and a methoxyl group on a tertiary carbon (δ 3.26, 3H, s; δ 3.30, 1H, m). The multiplet signals observed between δ 3.4 and 4.1 are equivalent to four-proton intensity, of which two-proton intensity is due to the methylene protons of the acetoxymethyl moiety and the remaining two-proton signals are ascribable to a methylene bearing a bromine. A one-proton signal observed at δ 4.75 (dd, J=*ca.* 2, 10 Hz) is assigned to a methine bearing a bromine.

The other dibrominated product (**7**), $C_{14}H_{24}Br_2O_3$, also showed a positive Beilstein test and is an isomer of **6**. The IR and ^{1}H NMR spectra show the structural similarity of **7** and **6**. The ^{1}H NMR spectrum of **7** shows signals due to three tertiary methyl groups and one acetoxyl group, five-proton multiplets between δ 3.3 and 4.3, and a one-proton signal at δ 4.50 (dd, J=*ca.* 2, 9 Hz) which is assignable to a methine bearing a bromine as described above.

Further, on treatment of **6** and **7** with zinc powder in acetic acid at 0°C, both reverted to the parent vinyl compound (**3**) in high yield. Based on these findings, the structures of **6** and **7**, which are formed by bromination of **3**, become clear. Both dibromides are isomeric with regard to the C-1′ configuration. We have not yet been able to identify the individual configurations.[5]

The minor product (**8**), $C_{13}H_{21}BrO_3$, also showed a positive Beilstein test. The IR spectrum of **8** shows the loss of the vinyl group in **3**, while the ^{1}H NMR spectrum shows signals due to three tertiary methyl groups, one acetoxymethyl group, a methine-proton geminal to a bromine, and three protons attached to two carbons adjacent to an oxygen atom. The loss of the methoxyl group was shown in the ^{1}H NMR spectrum of **8**. Thus, during the conversion from **3** to **8**, participation of the methoxyl moiety seemed probable.

Reduction of **8** with lithium aluminum hydride ($LiAlH_4$) gave a debrominated alcohol (**9**), which was acetylated in the usual manner to yield the monoacetate (**10**). Oxidation of **10** with ruthenium tetroxide (RuO_4)[3,6] at room temperature provided the γ-lactone monoacetate (**11**, IR: 1777, 1740 cm^{-1}) in excellent yield. Thus, the presence of an oxolane ring in **10** and **8** was proved. On the other hand, direct oxidation of **8** with RuO_4 yielded only a complex mixture of products. Of **6** and **7**, only **7** could be partly converted to **8** on treatment with alumina in benzene at room temperature.

Based on the above-described physicochemical and chemical evidence together with mechanistic considerations, the structures of **6**, **7**, and **8** were substantiated.[7] It has become clear that i) bromination on the vinyl residue of **3** occurs predominantly on TBCO treatment,

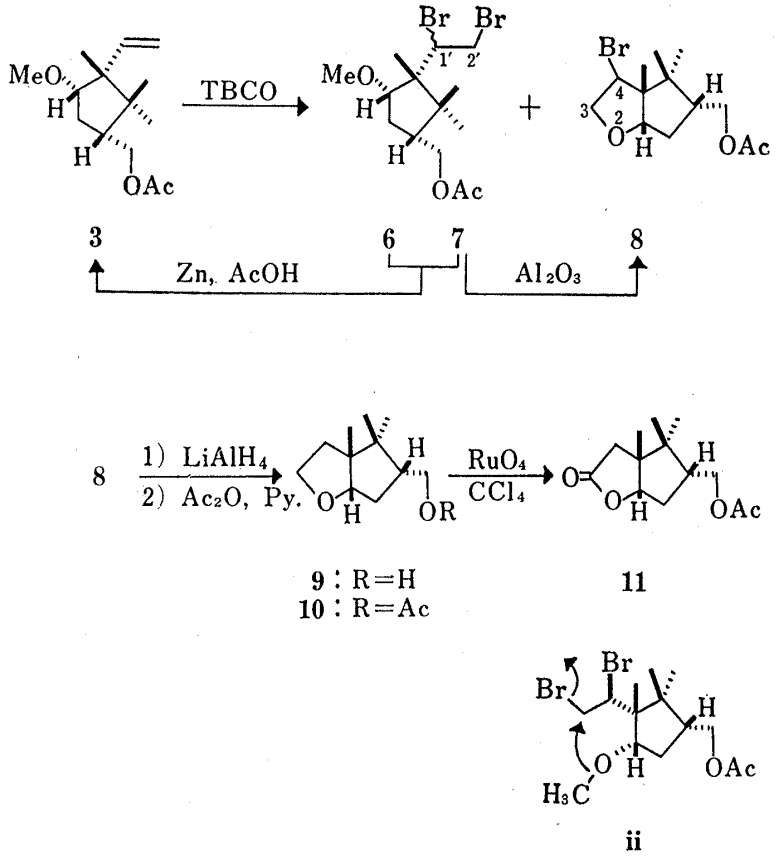


Chart 2

ii) one of the dibrominated products (**7**) may be converted to the 2-oxabicyclo[3.3.0]octane derivative (**8**) by participation of the methoxyl group (*cf.* **ii**), and iii) no product which may be formed *via* C–C bond migration as shown in path a, b, or c in **i** is obtained under the present reaction conditions.

As was found in the case of the 3*S*-counterpart [=(+)-(1*S*, 3*S*)-3-acetoxymethyl-1-(3′-hydroxypropenyl)-1,2,2-trimethylcyclopentane],[3] treatment of (+)-(3*R*)-hydroxypropenylcyclopentane (**4**), a second substrate in this study, under various acidic conditions (HCOOH, aq. H_2SO_4, *p*.TsOH·H_2O, *etc.*) resulted in the formation of a complex mixture. However, the following two acidic treatments gave some results.

Treatment of **4** with BF_3-etherate in benzene at room temperature furnished a phenylated product (**12**), $C_{21}H_{30}O_3$, in moderate yield. The IR spectrum of **12** shows the absence of hydroxyl group, while the UV spectrum shows the presence of a phenyl ring. The ^1H NMR spectrum exhibits signals due to three tertiary methyl residues, one acetoxyl group, one methoxyl group, two *E*-olefinic and two methylene protons in an allyl moiety (ABX_2 system) attached to the benzene ring (δ 3.40, 2H, X; δ 5.52, 1H, B; δ 5.90, 1H, A; J_{AB}=16 Hz, J_{AX}=0 Hz, J_{BX}=6 Hz), and five aromatic protons. The adjacency of the B-proton and X-protons in the allyl moiety was confirmed by decoupling experiments. Consequently, the structure **12** was rationalized. The product is presumed to be formed *via* a Friedel-Crafts type reaction between the allyl alcohol (**4**) and benzene.

We next carried out the BF_3-etherate treatment of **4** in dimethoxyethane (DME) in the presence of molecular sieves. Column chromatography of the reaction mixture furnished two ring-enlarged products, **13** (8%) and **14** (55%).

The minor product (**13**), $C_{14}H_{20}O_2$, shows a negative specific rotation and is a conjugated unsaturated compound as shown by its UV maximum at 243 nm. The IR spectrum of **13** lacks the hydroxyl absorption band but shows absorption bands due to the olefinic moieties.

The ^1H NMR spectrum shows the loss of the methoxyl group and shows signals ascribable to two tertiary methyls and one acetoxymethyl residue attached to a tertiary carbon. The olefinic proton region (6H) in the ^1H NMR spectrum suggests the presence of a vinyl group, a terminal methylene moiety, and an olefinic proton (δ 5.71, 1H, t-like, J=*ca.* 4 Hz). Based on these properties, the structure of the minor product was formulated as **13**, which was derivable *via* a hypothetical cation **iii** and path b and by final elimination of methanol from **ivb**, rather than **va**, which may be formed from **iii** (path a) and **iva** (then elimination of methanol).

The major product (**14**), $C_{15}H_{24}O_3$, also shows a negative specific rotation. The IR spectrum of **14** shows the loss of hydroxyl group but exhibits the olefinic absorption bands, while the ^1H-NMR spectrum indicates the retention of the methoxyl moiety attached to a tertiary carbon (δ 3.22, 3H, s; δ 3.34, 1H, m, 6-H). The latter spectrum also shows signals due to a vinyl residue (δ 4.8—5.1, 2H; δ 6.04, 1H, ABC system) attached to a tertiary carbon (δ 2.87, 1H, br d-like, 1-H), a terminal methylene moiety (δ 4.58, 1H, d, J=1 Hz; δ 4.85, 1H, br s), two tertiary methyl groups, and one acetoxymethyl group attached to a tertiary carbon (δ 3.7—4.3, 2H, AB in ABX). Based on these findings, the structure of the major product was initially assumed to be expressed as either **ivb** (formed from **iii** *via* path b) or **iva** (*via* path a). Further treatment of the major product with BF_3-etherate in dioxane at 100°C furnished **13**, together with an unidentified product in a ratio of 2: 1,[8] and thus the structure **14** became more reasonable. Finally, detailed decoupling experiments with **14** substantiated

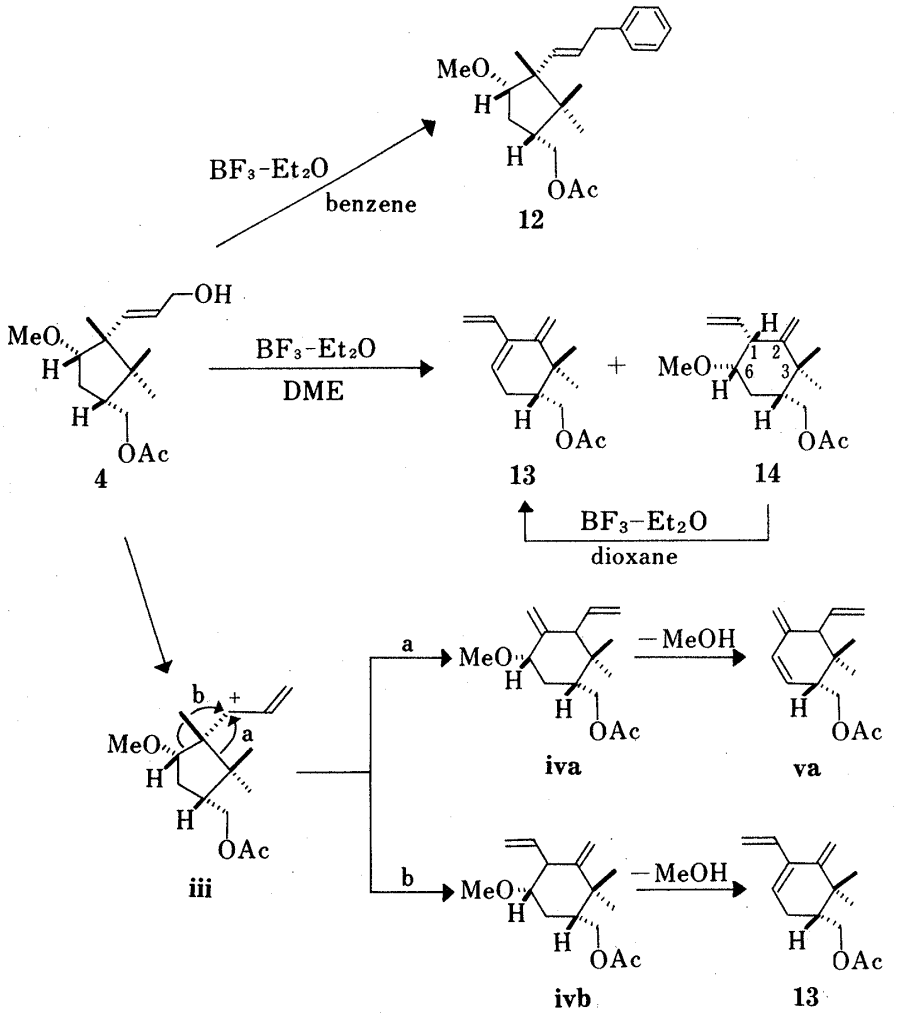


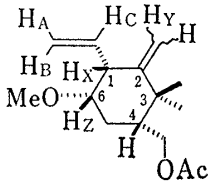
Chart 3

the structure including the configuration (Table I). It was clarified that the proton (1-H) geminal to the vinyl moiety in **14** couples with the proton (6-H) geminal to the methoxyl group with $J=3$ Hz, and thus the C-1 configuration was proved to be *R*.

Two products, **13** and **14**, are derived from **4** *via* the ring-enlargement reaction (*cf.* path b in **iii**), and this result is significantly different from that obtained upon acidic treatment of the 3*S*-counterpart, *i.e.*, (+)-(1*S*,3*S*)-3-acetoxymethyl-1-(3′-hydroxypropenyl)-1,2,2-trimethylcyclopentane,[3] which yielded a complex mixture of products. The behavior of **4** on acidic treatment was found to be rather similar to that of (+)-(1*S*, 3*S*)-3-acetoxymethyl-1,2,2-trimethyl-1-vinylcyclopentane.[3]

Table I. Spin Decoupling Experiments on **14** (δ, Hz)

Decoupled proton (δ)	Irradiated at δ		
	2.87 (H_X)	4.58 (H_Y)	6.04 (H_C)
2.87 (br d-like, H_X)	—	dd, $J=8$, 3	br s, $W_{h/2}=6$
4.58 (d, $J=1$, H_Y)	s	—	Unchanged
6.04 (C in ABCX, H_C)	dd, $J=16$, 10	Unchanged	—



$J_{AC}=10$ Hz
$J_{BC}=16$ Hz
$J_{XY}=1$ Hz
$J_{CX}=8$ Hz
$J_{XZ}=3$ Hz

Finally, (−)-(3*R*)-(1′*R*, 2′)-epoxyethylcyclopentane (**5**) was treated with BF_3-etherate in various kinds of solvents (*n*-hexane, benzene, methylene chloride, *etc*). The reaction in *n*-hexane gave the most promising result, although the yield (27%) of the product was unsatisfactory.

The product (**15**), $C_{14}H_{24}O_4$, shows a positive specific rotation. The IR and ^1H NMR spectra of **15** indicate retention of the acetoxyl and methoxyl residues during the reaction. The ^1H NMR spectrum also shows signals due to two tertiary methyl groups and one secondary methyl group (δ 1.05, d, $J=6$ Hz). The low-field region of the spectrum shows signals ascribable to a methine proton geminal to the methyl group, two methylene protons in the acetoxymethyl group, and the other two methylene protons (H_A, H_B) on a carbon connected to an ether oxygen (δ 3.37, 1H, dd, $J=8$, 8 Hz, H_A; δ 3.8—4.2, 4H, m, >C<u>H</u>–OMe, –C<u>H</u>$_2$–OAc, H_B).

Oxidation of **15** with RuO_4 gave the γ-lactone monoacetate (**16**), IR: 1780, 1750 cm^{-1}, whose ^1H NMR spectrum lacks signals due to the methylene protons (H_A and H_B). Thus, the ether oxygen of **15** was shown to be in an oxolane ring and the 2-oxabicyclo[3.3.0]octane skeleton, which is derivable from a hypothetical intermediate **vi** through successive migrations of methyl groups, was suggested for **15**. A similar type of successive methyl migrations was already observed in our previous study on the acidic treatment of (+)-(1*R*, 3*S*, 1′*S*)-3-acetoxymethyl-1-(1′,2′-epoxyethyl)-1,2,2-trimethylcyclopentane.[3]

Since the circular dichroism (CD) spectrum of **16** shows a positive maximum, $[\theta]_{218}$ +2300, due to the n—π^* transition of the lactone carbonyl,[9] the C-4 configuration was proved to be *S*. Finally, the total stereostructure of **15** was substantiated by the following conversion. Thus, treatment of **15** with di-*n*-propyl sulfide and ferric chloride at 0°C in methylene chloride[10] furnished the demethylation product (**17**), whose structure was supported by its physical properties. The acetoxyl group in **15** was retained under these reaction conditions. Successive treatments of **17** to accomplish the reductive elimination of the 6-hydroxyl group, *i.e.*, mesylation, iodination, and reduction with $LiAlH_4$ followed by re-acetylation, gave a monoacetate

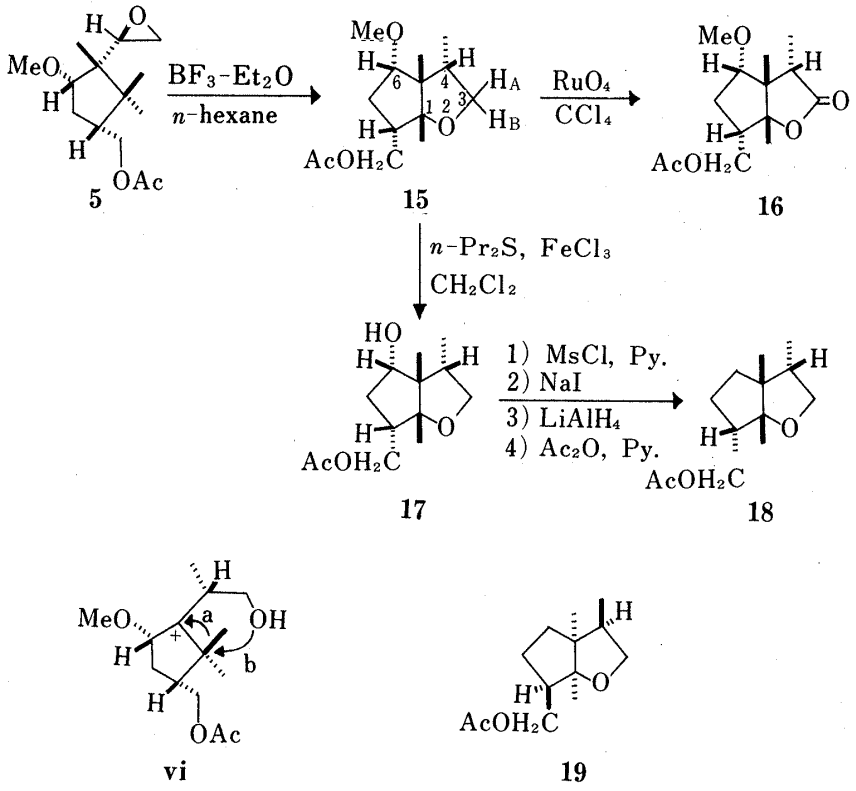


Chart 4

(**18**) in 40% yield from **17**. The finally obtained monoacetate (**18**) was found to be identical with **19**, which was obtained previously from the above-mentioned (+)-(1*R*, 3*S*, 1′*S*)-3-acetoxymethyl-1-(1′,2′-epoxyethyl)-1,2,2-trimethylcyclopentane by BF_3-etherate treatment,[3] in many respects (thin-layer chromatography (TLC), IR, ^1H NMR) except for the sign of the specific rotation, **18**: $[\alpha]_D$ −12°; 19:[3] $[\alpha]_D$ +12° (in chloroform).

It should be mentioned here that the 1′*R*,2′-epoxyethyl derivative (**5**) in the present (3*R*)-5-methoxy-1,2,2-trimethylcyclopentane series yields a 2-oxabicyclo[3.3.0]octane derivative (**15**) on acid treatment, however, the 1′*R*,2′-epoxyethyl derivative in the previous (3*S*)-1,2,2-trimethylcyclopentane series yields the ring-enlargement reaction products while the 1′*S*,2′-epoxyethyl derivative gives the 2-oxabicyclo[3.3.0]octane derivatives on a similar acidic treatment.[3] The reason for these different behaviors is not clear.

Detailed product analyses of the acid treatment of three optically active derivatives, *i.e.*, (+)-(3*R*)-vinylcyclopentane (**3**), (+)-(3*R*)-hydroxypropenylcyclopentane (**4**), and (−)-(3*R*)-(1′*R*,2′)-epoxyethylcyclopentane (**5**), showed that i) the ring-enlargement reactions occur from **4** to furnish the cyclohexane derivatives (**13**, **14**), ii) successive migrations of methyl groups occur from **5** to yield the 2-oxabicyclo[3.3.0]octane derivative (**15**), and iii) the TBCO treatment of **3** gives two brominated products (**6**, **7**) together with another type of 2-oxabicyclo-[3.3.0]octane derivative (**8**) which is formed by participation of the methoxyl group in the oxolane ring formation.

Experimental

The instruments used to obtain physical data and the experimental conditions for chromatography were the same as described in our previous paper.[2]

TBCO Treatment of (+)-(3*R*)-Vinylcyclopentane (**3**)——a) TBCO in THF: A solution of **3** (300 mg, 1.25 mmol) in THF (6 ml) was treated with TBCO (770 mg, 1.88 mmol) and heated under reflux for 20 min. The reaction mixture was cooled and poured into ice-water. The whole mixture was extracted with *n*-hexane and the extract was successively washed with aq. 4% NaOH and aq. sat. NaCl, then dried over

$MgSO_4$. Removal of the solvent under reduced pressure gave a product (550 mg) which was purified by repeated column chromatography (SiO_2, 50 g, *n*-hexane–EtOAc=10: 1, and then SiO_2, 30 g, benzene–acetone=50: 1) to furnish **6** (150 mg, 30%), **7** (230 mg, 46%), and **8** (23 mg, 6%).

b) TBCO in CH_3NO_2: A solution of **3** (900 mg, 3.75 mmol) in CH_3NO_2 (20 ml) was treated with TBCO (2.3 g, 5.63 mmol) and the mixture was stirred at room temperature for 6 h, then poured into ice-water. The whole mixture was extracted with *n*-hexane. The *n*-hexane extract was successively washed with aq. 4% NaOH and aq. sat. NaCl, then dried over $MgSO_4$. The product (1.5 g) obtained by removal of the solvent under reduced pressure was purified by repeated column chromatography (SiO_2, 100 g, *n*-hexane–acetone=20: 1, and then SiO_2, 50 g, benzene–acetone=20: 1) to furnish **7** (600 mg, 40%) and **8** (150 mg, 13%). **6**, colorless oil, $[\alpha]_D^{20}$ −33° (*c*=1.1, $CHCl_3$). *Anal.* Calcd for $C_{14}H_{24}Br_2O_3$: C, 42.02; H, 6.05; Br, 39.94. Found: C, 42.32; H, 6.10; Br, 39.47. IR ν_{max}^{film} cm^{-1}: 1745. ^1H NMR (CCl_4, δ): 1.08 (6H, s, *tert.* $CH_3\times2$), 1.16 (3H, s, *tert.* CH_3), 1.98 (3H, s, OAc), 3.26 (3H, s, OMe), 3.30 (1H, m, –C<u>H</u>–OMe), 3.4—4.1 (4H, m, –C<u>H</u>$_2$Br, –C<u>H</u>$_2$–OAc), 4.75 (1H, dd, *J*=*ca.* 2, 10 Hz, –C<u>H</u>Br–CH_2Br). MS *m/z* (%): 402 (21, $C_{14}H_{24}{}^{81}Br_2O_3$), 400 (45, $C_{14}H_{24}{}^{81}Br^{79}BrO_3$), 398 (26, $C_{14}H_{24}{}^{79}Br_2O_3$), 341 (100). **7**, mp 50—51°C, colorless needles (ether), $[\alpha]_D^{26}$ +22° (*c*=2.3, $CHCl_3$). *Anal.* Calcd for $C_{14}H_{24}Br_2O_3$: C, 42.02; H, 6.05; Br, 39.94. Found: C, 41.92; H, 6.03; Br, 39.90. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740. ^1H NMR (CCl_4, δ): 0.97, 1.00, 1.16 (3H each, all s, *tert.* $CH_3\times3$), 1.95 (3H, s, OAc), 3.23 (3H, s, OMe), 3.3—4.3 (5H, m, –C<u>H</u>–OMe, –C<u>H</u>$_2$–OAc, –C<u>H</u>$_2$Br), 4.50 (1H, dd, *J*=*ca.* 2, 9 Hz, –C<u>H</u>Br–CH_2Br). MS *m/z* (%): 402 (0.6, $C_{14}H_{24}{}^{81}Br_2O_3$), 400 (1.2, $C_{14}H_{24}{}^{81}Br^{79}BrO_3$), 398 (0.6, $C_{14}H_{24}{}^{79}Br_2O_3$), 227 (100). **8**, colorless oil, $[\alpha]_D^{25}$ −72° (*c*=2.3, $CHCl_3$). *Anal.* Calcd for $C_{13}H_{21}BrO_3$: C, 51.16; H, 6.94; Br, 26.18. Found: C, 51.11; H, 6.96; Br, 26.17. IR ν_{max}^{film} cm^{-1}: 1745. ^1H NMR (CCl_4, δ): 0.99 (6H, s, *tert.* $CH_3\times2$), 1.12 (3H, s, *tert.* CH_3), 1.95 (3H, s, OAc), 3.6—4.5 (6H, m, –C<u>H</u>$_2$–OAc, –C<u>H</u>Br, –C<u>H</u>–O–C<u>H</u>$_2$–). MS *m/z* (%): 306 (1, $C_{13}H_{21}{}^{81}BrO_3$), 304 (1, $C_{13}H_{21}{}^{79}BrO_3$), 225 (100).

Zn-AcOH Treatment of 6 giving 3——An ice-cooled (0°C) solution of **6** (30 mg, 0.075 mmol) in ether (1 ml) was treated with AcOH (0.1 ml) and Zn powder (10 mg, 0.16 mmol) and the whole mixture was stirred at room temperature for 10 h. After dilution with ether (5 ml), the whole mixture was filtered and the filtrate was successively washed with aq. 5% $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent gave the product (15 mg, 84%), which was identical with **3** as judged by TLC, GLC (SE-30), IR ($CHCl_3$), $[\alpha]_D$ ($CHCl_3$), and ^1H NMR (CCl_4) comparisons.

Zn-AcOH Treatment of 7 giving 3——An ice-cooled (0°C) solution of **7** (40 mg, 0.10 mmol) in ether (1 ml) was treated with AcOH (0.1 ml) and Zn powder (13 mg, 0.21 mmol) and the whole mixture was stirred at room temperature for 10 h. Work-up of the reaction mixture as described above yielded **3** (22 mg, 92%) which was identified as described above.

Al_2O_3 Treatment of 7——A solution of **7** (80 mg, 0.2 mmol) in benzene (4 ml) was treated with Al_2O_3 (160 mg, basic) and the whole mixture was vigorously stirred at room temperature for 2 d. After the removal of Al_2O_3 by filtration, the solvent was evaporated off under reduced pressure to yield a product (75 mg), which was purified by column chromatography (SiO_2, 4 g, benzene–acetone=20: 1) to furnish **8** (10 mg, 15%) and **7** (50 mg, 63%, recovered). Identification of **8** was made by TLC and ^1H-NMR (CCl_4) comparisons.

$LiAlH_4$ Reduction of 8 giving the Debrominated Alcohol (9)——A solution of **8** (20 mg, 0.06 mmol) in THF (1 ml) was treated with $LiAlH_4$ (12 mg, 0.31 mmol) and the whole was heated under reflux for 6 h. The reaction mixture was cooled and the excess reagent was decomposed with EtOAc. The whole mixture was acidified with aq. 5% H_2SO_4, then extracted with EtOAc. The EtOAc extract was successively washed with aq. sat. $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave the product (13 mg), which was purified by column chromatography (SiO_2, 2 g, *n*-hexane–acetone=5: 1) to furnish **9** (10 mg, 78%). **9**, colorless oil, $[\alpha]_D^{18}$ −53° (*c*=2.4, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400 (br). ^1H NMR (CCl_4, δ): 0.91, 0.93, 1.05 (3H each, all s, *tert.* $CH_3\times3$), 3.5—4.1 (5H, m, –C<u>H</u>$_2$–OH, –C<u>H</u>$_2$–O–C<u>H</u>–). High resolution MS (*m/z*): Calcd for $C_{11}H_{20}O_2$: 184.146. Found: 184.146. MS *m/z* (%): 184 (9, M^+), 98 (100).

Acetylation of 9 giving the Monoacetate (10)——A solution of **9** (20 mg, 0.11 mmol) in pyridine (1 ml) was treated with Ac_2O (0.5 ml, 5 mmol) and the whole was left to stand at room temperature for 2 h. The reaction mixture was poured into ice-water and extracted with EtOAc. Work-up of the EtOAc extract in the usual manner furnished **10** (25 mg, 98%), colorless oil, $[\alpha]_D^{18}$ −45° (*c*=2.7, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1737. ^1H NMR (CCl_4, δ): 0.92 (6H, s), 1.03 (3H, s) (*tert.* $CH_3\times3$), 1.97 (3H, s, OAc), 3.4—4.3 (5H, m, –C<u>H</u>$_2$–OAc, –C<u>H</u>$_2$–O–C<u>H</u>–). High resolution MS (*m/z*): Calcd for $C_{13}H_{22}O_3$: 226.157. Found: 226.157. MS *m/z* (%): 226 (5, M^+), 122 (100).

RuO_4 Oxidation of 10 giving the γ-Lactone (11)——A mixture of **10** (15 mg, 0.066 mmol) in RuO_4–CCl_4 reagent (2 ml)[3,6] was stirred at room temperature for 1 h, then treated with 99% EtOH (0.5 ml). After the removal of insoluble material by filtration, the filtrate was evaporated off under reduced pressure to furnish **11** (15 mg, 95%). **11**, colorless oil, $[\alpha]_D^{18}$ −70° (*c*=0.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1777 (γ-lactone), 1740 (OAc). ^1H NMR (CCl_4, δ): 0.83, 0.90, 1.08 (3H each, all s, *tert.* $CH_3\times3$), 1.98 (3H, s, OAc), 3.8—4.5 (3H, m, –C<u>H</u>$_2$–OAc, –C(=O)–O–C<u>H</u>–). High resolutions MS (*m/z*): Calcd for $C_{13}H_{20}O_4$: 240.136. Found: 240.135. MS *m/z* (%): 240 (25, M^+), 121 (100).

BF_3-etherate Treatment of (+)-(3*R*)-Hydroxypropenylcyclopentane (4) in Benzene——A solution of **4** (48 mg, 0.18 mmol) in benzene (10 ml) was treated with BF_3-etherate (1.0 ml, 8.1 mmol) and the mixture was stirred at room temperature for 1.5 h. Then aq. sat. $NaHCO_3$ (5 ml) was added and the whole was extracted with EtOAc. The EtOAc extract was washed with aq. sat. NaCl and dried over $MgSO_4$. The product (50 mg) obtained by removal of the solvent under reduced pressure was purified by column chromatography (SiO_2, 10 g, *n*-hexane–EtOAc=5:1) to furnish **12** (30 mg, 51%). **12**, colorless oil, $[\alpha]_D^{13}$ −8° (c=0.8, $CHCl_3$). UV λ_{max}^{MeOH} nm (ε): 247 (690), 253 (730), 259 (680). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3025, 1745, 1601, 1498. ^{1}H-NMR (CCl_4, δ): 0.81, 0.89, 0.92 (3H each, all s, *tert.* $CH_3\times3$), 1.94 (3H, s, OAc), 3.21 (3H, s, OMe), 3.40 (2H, X in ABX_2, J_{AX}=0 Hz, J_{BX}=6 Hz), 5.52 (1H, B in ABX_2, J_{AB}=16 Hz, J_{BX}=6 Hz), 5.90 (1H, A in ABX_2, J_{AB}=16 Hz, J_{AX}=0 Hz) ($-CH_A{=}CH_B{-}CH_{X_2}{-}Ph$), 7.0—7.2 (5H, m, aromatic protons). High resolution MS (m/z): Calcd for $C_{21}H_{30}O_3$: 330.219. Found: 330.219. MS m/z (%): 330 (0.7, M^+), 184 (100).

BF_3-etherate Treatment of 4 in DME——A solution of **4** (570 mg, 2.1 mmol) in DME (30 ml) was treated with molecular sieves 4A (20 g) and BF_3-etherate (25 g, 180 mmol) and the mixture was stirred at room temperature for 10 h. After the removal of the molecular sieves by filtration, the filtrate was neutralized with aq. sat. $NaHCO_3$ and the whole was extracted with EtOAc. Work-up of the EtOAc extract as described above gave the product (570 mg), which was purified by column chromatography (SiO_2, 60 g, benzene–EtOAc=10:1) to furnish **13** (40 mg, 8%) and **14** (290 mg, 55%). **13**, colorless oil, $[\alpha]_D^{20}$ −47° (c=0.45, $CHCl_3$). UV λ_{max}^{MeOH} nm (ε): 243 (3700). IR ν_{max}^{film} cm^{-1}: 3095, 3080, 1746, 1620, 1598. ^{1}H NMR (CCl_4 δ): 1.13 (6H, s, *tert.* $CH_3\times2$), 1.94 (3H, s, OAc), 3.62 (1H, dd, J=12, 8 Hz, $-\dot{C}H-C\underline{H}_A H_B-OAc$), 4.12 (1H, dd, J=12, 4 Hz, $-\dot{C}H-CH_A\underline{H}_B-OAc$), 4.9—5.5 (4H, m, $>C{=}C\underline{H}_2$, $=\dot{C}-CH-C\underline{H}_2$), 5.71 (1H, t-like, J=*ca.* 4 Hz, 6-H), 6.29 (1H, m, $=\dot{C}-C\underline{H}{=}CH_2$). High resolution MS ($m/z$): Calcd for $C_{14}H_{20}O_2$: 220.146. Found: 220.145. MS m/z (%): 220 (2, M^+), 117 (100). **14**, colorless oil, $[\alpha]_D^{15}$ −102° (c=0.80, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3080, 1745, 1638, 918, 907. ^{1}H NMR (CCl_4, δ): 1.01, 1.21 (3H, each, both s, *tert.* $CH_3\times2$). 1.97 (3H, s, OAc), 2.87 (1H, br d-like, 1-H), 3.22 (3H, s, OMe), 3.34 (1H, m, $-\dot{C}\underline{H}-OMe$), 3.7—4.3 (2H, AB in ABX, $-\dot{C}H-C\underline{H}_2-OAc$), 4.58 (1H, d, J=1 Hz), 4.85 (1H, br s), 4.8—5.1 (2H, AB in ABCX, $-\dot{C}H-CH{=}C\underline{H}_2$), 6.04 (1H, C in ABCX, $-\dot{C}H-C\underline{H}{=}CH_2$). High resolution MS ($m/z$): Calcd for $C_{15}H_{24}O_3$: 252.172. Found: 252.171. MS m/z (%): 252 (1, M^+), 43 (100).

BF_3-etherate Treatment of 14 in Hot Dioxane Giving 13——A solution of **14** (210 mg, 0.80 mmol) in dioxane (40 ml) was treated with BF_3-etherate (10 ml, 80 mmol) and the whole mixture was heated at 100°C for 80 min. The reaction mixture was cooled and diluted with EtOAc (300 ml). The whole was successively washed with aq. sat. $NaHCO_3$ and aq. sat. NaCl, then dried over $MgSO_4$. The product (180 mg) obtained by removal of the solvent under reduced pressure was purified by column chromatography (SiO_2, 20 g, benzene–EtOAc=10:1) and then HPLC (*n*-hexane–EtOAc=40:1, flow rate 3.0 ml/min) to furnish **13** (70 mg, 40%) and **14** (63 mg, 30%, recovered). Identification of **13** was made by TLC, $[\alpha]_D$ ($CHCl_3$), IR (CCl_4), and ^{1}H NMR (CCl_4) comparisons.

BF_3-etherate Treatment of (−)-(3*R*)-(1′*R*,2′)-Epoxyethylcyclopentane (5)——A solution of **5** (1.0 g, 3.9 mmol) in *n*-hexane (20 ml) was treated with 1% BF_3-etherate–*n*-hexane solution (20 ml, 1.6 mmol) and the mixture was stirred at 35°C for 30 min. After addition of aq. sat. $NaHCO_3$ (10 ml), the whole was extracted with EtOAc. The EtOAc extract was washed with aq. sat. NaCl and dried over $MgSO_4$. The product (900 mg) obtained by removal of the solvent under reduced pressure was purified by column chromatography (SiO_2, 50 g, *n*-hexane–EtOAc=5:1) to furnish **15** (270 mg, 27%). **15**, colorless oil, $[\alpha]_D^{20}$ +10° (c=2.0, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1738. ^{1}H NMR (CCl_4, δ): 0.83, 1.06 (3H each, both s, *tert.* $CH_3\times2$), 1.05 (3H, d, J=6 Hz, *sec.* CH_3), 1.95 (3H, s, OAc), 3.12 (3H, s, OMe), 3.37 (1H, dd, J=8, 8 Hz, 3-H_A), 3.8—4.2 (4H, m, $-\dot{C}\underline{H}-OMe$, $-C\underline{H}_2-OAc$, 3-H_B). High resolution MS (m/z): Calcd for $C_{14}H_{24}O_4$: 256.168. Found: 256.170. MS m/z (%): 256 (1, M^+), 225 (100).

RuO_4 Oxidation of 15 giving the γ-Lactone (16)——A solution of **15** (21 mg, 0.08 mmol) in CCl_4 (5 ml) was treated with $RuO_2\cdot xH_2O$ (50 mg) and aq. sat. $NaIO_4$ (5 ml). The whole mixture was stirred at 40°C for 48 h, then treated with 99% EtOH (0.5 ml). After the removal of insoluble material by filtration, the filtrate was diluted with EtOAc (100 ml). The whole was successively washed with aq. sat. Na_2SO_3 and aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure furnished **16** (21 mg, 99%). **16**, colorless oil, $[\alpha]_D^{20}$ −30° (c=1.2, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1750 (OAc). ^{1}H NMR (CCl_4, δ): 0.79, 1.10 (3H each, both s, *tert.* $CH_3\times2$), 1.32 (3H, d, J=7 Hz, *sec.* CH_3), 1.98 (3H, s, OAc), 3.36 (3H, s, OMe), 3.6—4.2 (3H, m, $-\dot{C}\underline{H}-OMe$, $-C\underline{H}_2-OAc$). CD (c=0.94, MeOH) $[\theta]^{20}$ (nm): +2300 (218) (pos. max.). High resolution MS (m/z): Calcd for $C_{14}H_{22}O_5$: 270.147. Found: 270.145. MS m/z (%): 270 (0.6, M^+), 83 (100).

Demethylation of 15 giving the Diol-monoacetate (17)——An ice-cooled (0°C) solution of **15** (80 mg, 0.31 mmol) in CH_2Cl_2 (10 ml) was treated with di-*n*-propyl sulfide (0.1 ml, 0.69 mmol) and $FeCl_3$ (100 mg, 0.62 mmol) and the whole mixture was stirred for 2 h. Then aq. 5% $NaHCO_3$ (5 ml) was added and the whole was extracted with EtOAc. The EtOAc extract was washed with aq. sat. NaCl, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product (80 mg), which was purified by column chromatography (SiO_2, 4 g, *n*-hexane–EtOAc=4:1) to furnish **17** (26 mg, 35%) and **15** (35 mg, 44%, recovered). **17**, colorless oil, $[\alpha]_D^{22}$ −39° (c=1.7, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (br), 1734. ^{1}H NMR (CCl_4, δ): 0.86, 1.11

(3H each, both s, *tert.* $CH_3 \times 2$), 1.08 (3H, d, $J=6$ Hz, *sec.* CH_3), 2.02 (3H, s, OAc), 3.5—4.3 (5H, m, $-\underline{C}\underline{H}-OH$, $-C\underline{H}_2-OAc$, $-C\underline{H}_2-O-\underline{C}-$). High resolution MS (*m/z*): Calcd for $C_{13}H_{22}O_4$: 242.152. Found: 242.151. MS MS *m/z* (%): 242 (5, M^+), 225 (100).

Conversion of 17 leading to 18——A solution of **17** (28 mg) in pyridine (0.2 ml) was treated with MsCl (0.1 ml) at 0°C and the whole mixture was left to stand at 0°C for 1 h. Work-up of the reaction mixture in the usual manner gave a product (36 mg). The product was dissolved in dry acetone (2 ml) and treated with NaI (85 mg), and the whole mixture was heated under reflux for 1 h. Work-up of the reaction mixture in the usual manner gave a product (40 mg), which was dissolved in THF (1 ml), then treated with $LiAlH_4$ (20 mg). The whole mixture was stirred at 60°C for 1 h and cooled. After decomposition of the excess reagent with EtOAc (0.2 ml), the mixture was treated with pyridine (0.5 ml) and Ac_2O (0.5 ml) and the whole was left to stand at 20°C for 1 h. The product (18 mg) obtained by work-up in the usual manner was purified by column chromatography (SiO_2, 1 g, *n*-hexane–EtOAc=5 : 1) to furnish **18** (11 mg, 40%), $[\alpha]_D^{19}$ −12° ($c=0.9$, $CHCl_3$). **18** obtained here was identical with **19**,[3] except for the sign of the specific rotation, **19**: $[\alpha]_D^{15}$ +12° ($c=1.4$, $CHCl_3$),[3] as judged by IR (film) and ^{1}H-NMR (CCl_4) comparisons.

References and Notes

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5) If the TBCO bromination of the vinyl moiety in **3** is initiated by attack of the bromonium cation from the same side of the double bond as in the peracid epoxidation of **3** (giving **5**[1]), the C-1′ configuration in the major dibromide (**7**) can be assumed to be *S* and that in the minor (**6**) to be *R*.
6) P.D. Hobbs and P.D. Magnus, *J. Am. Chem. Soc.*, **98**, 4594 (1976).
7) The C-4 configuration of **8** may be assigned as *S*, if the above assumption[5] on the C-1′ configuration of **7** is valid (*cf.* **ii**).
8) Further acidic treatment in DME did not affect **14** any more, but resulted in recovery of the starting material.
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10) M. Node, K. Nishide, M. Sai, K. Ichikawa, T. Kawabata, K. Fuji, and E. Fujita, The 6th Symposium on Progress in Organic Reactions and Syntheses (Nov., 1979, Tokyo), Abstract Papers, p. 56. We found that ferric chloride gave a better result than aluminum chloride[10] as the Lewis acid in the present case.