Backbone Rearrangements of 3α,4α-Epoxyshionane into Bacchar-12-en-3α-ol and D : B-Friedo-bacchar-5(10)-en-3α-ol[1]

Shûzô YAMADA, Sachiko YAMADA, Kazuo TACHIBANA, Yoshihiko MORIYAMA, Yoshiaki TANAHASHI, Takahiko TSUYUKI, and Takeyoshi TAKAHASHI

Department of Chemistry, Faculty of Science, The University of Tokyo, Bunkyo-ku, Tokyo 113

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Upon treatment with boron trifluoride etherate, 3α,4α-epoxyshionane (**7**) rearranged into bacchar-12-en-3α-ol (**9**) and D : B-friedo-bacchar-5(10)-en-3α-ol (**10**), and their structures have been determined. Revision of the structure for the latter product from previously reported D : C-friedo-bacchar-8-en-3α-ol (**20**) to **10** was described.

A structure of baccharis oxide,[2] obtained from dried roots of *Baccharis halimifolia* L., has been proposed as **1b**[2,3] and then revised to **1a** by X-ray study.[4] Dihydrobaccharis oxide was shown to rearrange into bacchar-12-en-3β-ol (**2**) by treatment with boron trifluoride etherate.[2]

Being interested in close biogenetic relationship between baccharis oxide (**1a**) and shionone (**3**)[5,6] and in their acid-catalyzed backbone rearrangements, we examined a backbone rearrangement reaction of 3α,4α-epoxyshionane (**7**) catalyzed by boron trifluoride etherate.

Shion-3-ene (**6**),[7] prepared from shionone (**3**) *via* shionan-3-one (**4**) and shionan-3β-ol (**5**), was subjected to epoxidation with *m*-chloroperbenzoic acid in benzene at room temperature. The reaction mixture was separated by silica gel chromatography to give two epoxides in a ratio of *ca.* 7 : 3. Assignment of the epoxide group was easily accomplished by PMR measurement using Eu(fod)$_3$-d_{27} as a shift reagent.

The signals due to all methyl groups of the minor epoxide suffered downfield shifts (Fig. 1), while in the case of the major epoxide the signals due to four methyl groups suffered downfield shifts and the signals due to other four methyl groups caused upfield shifts (Fig. 2). Assuming that the shift reagent is associated with the epoxide oxygen atom as shown in Figs. 1 and 2, the fact that the signals due to the four methyl groups caused upfield shifts would be explicable only in the case of 3α,4α-epoxyshionane (**7**) and these four methyl groups could be assigned to 13α-, 20β-, and the side chain two methyl groups which would be placed outside of a cone area suffered an upfield shift (Fig. 2). The epoxide ring of the major epoxide (**7**) was thus shown to be in an α-configuration. The 3β,4β-epoxide structure (**8**) follows for the minor isomer.

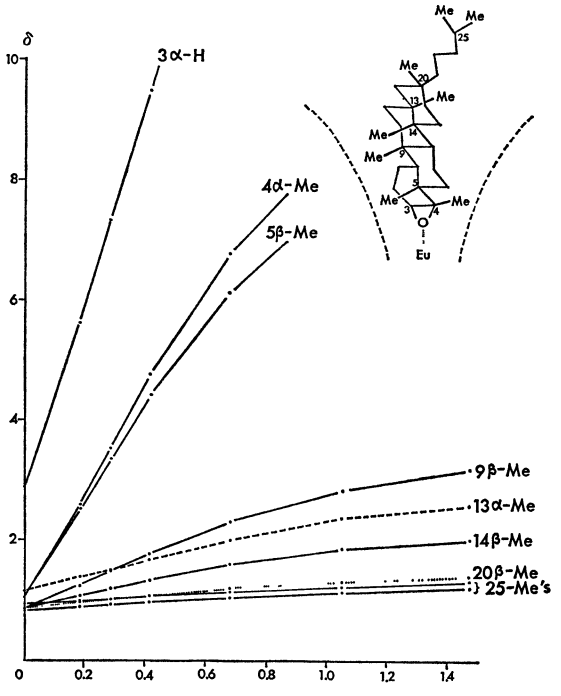


Fig. 1. Induced paramagnetic shifts for the 3β,4β-epoxide (**8**). [Eu(fod)$_3$-d_{27} was added to a 4% (w/v) solution of **8** in $CDCl_3$].

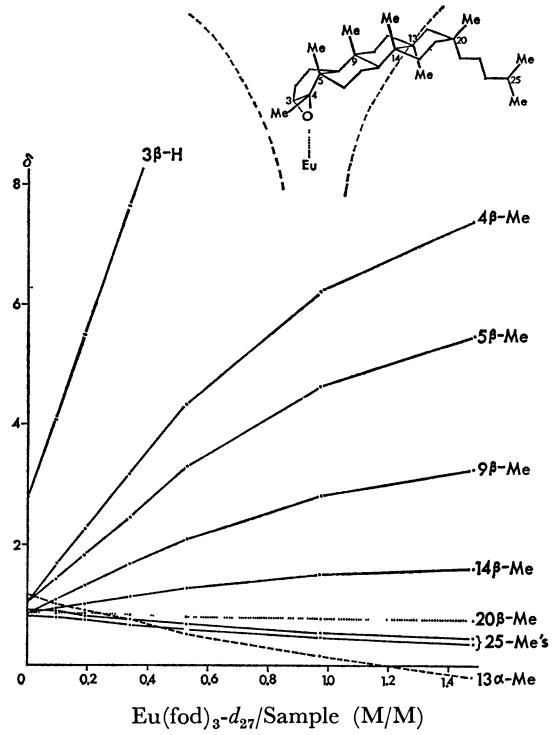
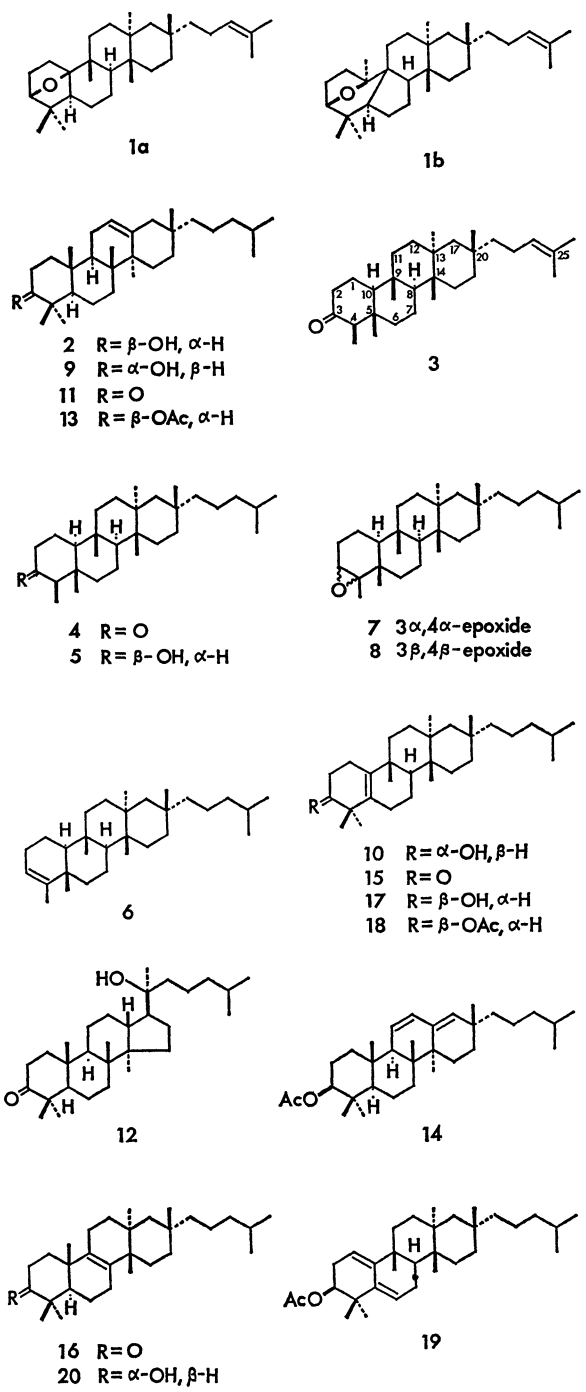


Fig. 2. Induced paramagnetic shifts for the 3α,4α-epoxide (**7**). [Eu(fod)$_3$-d_{27} was added to a 4% (w/v) solution of **7** in $CDCl_3$].

3α,4α-Epoxyshionane (**7**) in dry benzene was treated with boron trifluoride etherate at room temperature. Examination by thin layer chromatography (TLC) showed that the starting material was consumed within 10 min and that a complex mixture was formed. The resulting mixture was separated by column chro-



matography to give a mixture, which was later shown to be a mixture of bacchar-12-en-3α-ol (**9**) and D : B-friedo-bacchar-5(10)-en-3α-ol (**10**).

The mixture (**9** and **10**) without further separation was then subjected to the Collins oxidation to give after column chromatographic separation two unsaturated ketones (**11** and **15**).

A more polar ketone, crystallized from methanol, showed mp 111—112 °C (previously reported 102—102.5 °C[1]); IR (Nujol) 1710 and 815 cm^{-1}, and was shown to be bacchar-12-en-3-one (**11**) by the following evidence and derivation. The enone (**11**) showed PMR signals at δ 2.43 (2H, m) and 5.27 (1H, t-like, J=*ca.* 2 Hz). The former signal due to α-methylene protons to the carbonyl group is similar to those of triterpenes bearing 3-oxo-4,4,10-trimethyl moiety such as β-amyrone and lupenone. The latter signal is due to an olefinic proton. The CD data of **11** ($[\theta]_{290}$+2600, $[\theta]_{325}$−90 in methanol) was almost the same as those of dipterocarpol (**12**).[8] The A/B/C ring junctures were therefore suggested to be the same as those of **12**.

Reduction of bacchar-12-en-3-one (**11**) with sodium borohydride gave an alcohol. On column chromatographic separation followed by crystallization from methanol, there obtained pure bacchar-12-en-3β-ol [**2**; mp 143.5—144 °C (lit,[2] 147—148 °C); M^+ at *m/e* 428 (lit,[2] 428.403); $[\alpha]_D$ +55° (lit,[2] +39°)]. The PMR signals due to an axial proton at C-3 bearing an equatorial hydroxyl group were observed at δ 3.23 as double doublets (J=5 and 8 Hz) and an olefinic proton at C-12 resonated at δ 5.11 as a multiplet. On acetylation with acetic anhydride and pyridine, bacchar-12-en-3β-ol (**2**) afforded an acetate (**13**; mp 177—178 °C. lit,[2] 181—182 °C).

The acetate (**13**) was treated with selenium dioxide in acetic acid at 85 °C for 4 h to give bacchara-11,13-(17)-dien-3β-yl acetate[6] [(**14**; UV λ_{max}^{EtOH} 250 nm (ε 12500), 241 (19400), and 234 (17000); M^+ at *m/e* 468]. The PMR, UV, and mass spectral data were completely identical with those of the authentic sample[2] which was kindly donated from Dr. T. Bruun.

A less polar ketone (**15**) was previously reported as D : C-friedo-bacchar-8-en-3-one (**16**) on the basis of the following evidence. The ketone showed no signals due to olefinic proton and the molecular formula was shown to be $C_{30}H_{50}O$ by the elemental analysis and the mass spectrometry. These findings suggested that the ketone must contain a tetrasubstituted double bond and could be formulated as either D : C-friedo-bacchar-8-en-3-one (**16**) or D : B-friedo-bacchar-5(10)-en-3-one (**15**). The previously reported melting point, 174.5—177.5 °C[1] was not coincident with that of D : B-friedo-bacchar-5(10)-en-3-one (mp 78—80 °C[9]), which was prepared from shionan-3-one (**4**). These facts led to the conclusion that the ketone was not D : B-friedo-bacchar-5(10)-en-3-one (**15**), but was, instead, D : C-friedo-bacchar-8-en-3-one (**16**).

However, on reinvestigation of the less polar ketone, it was found that the melting point was 84—84.5 °C and the previously reported melting point (174.5—177.5 °C) was that of the decomposition product. The misinterpretation seemed to be mainly due to a fragility of the ketone. Thus, it is shown that the previous assignment (**16**) must be withdrawn and the ketone should be represented by D : B-friedo-bacchar-5(10)-en-3-one (**15**). The conclusion was supported by a direct comparison (mp, mixed mp (84—84.5 °C), TLC, IR and PMR spectra) with D : B-friedo-bacchar-5(10)-en-3-one (**15**; 84—84.5 °C), prepared from shionan-3-one (**4**) *via* D : B-friedo-bacchara-1,5(10)-dien-3-one.[10]

The ketone (**15**) was reduced with sodium borohydride to give D : B-friedo-bacchar-5(10)-en-3β-ol (**17**), mp 140.5—141 °C (lit, mp 135—136 °C[1]; 140.5—141 °C[9]; 141.5—142 °C[10]). The PMR signals due to 3α-(axial) proton were observed at δ 3.42 as double doublets (J=5 and 10 Hz).

The alcohol (**17**) was converted by a usual procedure into an acetate (**18**), mp 147—148 °C. Oxidation of the acetate (**18**) with selenium dioxide in acetic acid under reflux gave D : B-friedo-bacchara-1(10),5-dien-3β-yl acetate (**19**), mp 123—123.5 °C, which showed characteristic ultraviolet absorption bands due to heteroannular transoid dienone at 248 (sh. ε 12100), 238 (20900), and 231 nm (19400).[11]

The formation of the alcohols (**9** and **10**) from the α-epoxide (**7**) by boron trifluoride etherate-catalyzed rearrangement was thus shown. The structure of D : C-friedo-bacchar-8-en-3α-ol (**20**)[1] previously given for the latter product (**10**) should be revised to **10**.

Experimental

IR and UV spectra were measured on a Hitachi EPI-G2 and EPS-2 spectrometers, respectively. Mass spectra were taken on a Hitachi RMU-6-Tokugata mass spectrometer operating at 70 eV with a direct inlet system. PMR spectra were measured using a JEOL JNM PS-100 (100 MHz), a Hitachi R-20 (60 MHz) or a Hitachi R-24 (60 MHz) spectrometer. Chemical shifts were expressed in ppm downfield from TMS as an internal standard (δ value) and coupling constants in Hz. ORD and CD measurements were carried out on a JASCO ORD/UV-5 spectrometer. Measurements of optical rotation were carried out using a JASCO polarimeter DIP-SL. Thin layer chromatography (TLC) was carried out on Kieselgel G or PF_{254} (E. Merck) in 0.25 mm thickness. Wakogel C-200 (Wako Pure Chemical Ind.) was used for column chromatography. All melting points were determined on a hot block and reported uncorrected.

*3α,4α-Epoxyshionane (**7**).* A solution of *m*-chloroperbenzoic acid (516 mg) in benzene (12 ml) was added to shion-3-ene[7] (**6**; 1.00 g) in benzene (10 ml) at room temperature. The reaction mixture was allowed to stand for 1.5 h, and washed with a saturated sodium hydrogencarbonate solution and then with brine. After usual work-up, a residue (1.04 g), which gave two spots on TLC, was subjected to silica gel chromatographic separation quickly. 3α,4α-Epoxyshionane (**7**; 0.70 g) was eluted with benzene and crystallized from acetone to give colorless needles, mp 147—148 °C; PMR (100 MHz, $CDCl_3$) δ 0.86 (s; 3×*t*-CH_3), 0.87 (d, J=5.5 Hz; 2×*s*-CH_3), 1.04 (s; 2×*t*-CH_3), 1.17 (s; *t*-CH_3), and 2.83 (t, J=3 Hz; $C_{(3)}$–H); mass spectrum *m/e* 428 (M^+); Found: C, 84.12; H, 12.37%. Calcd for $C_{30}H_{52}O$: C, 84.04; H, 12.21%.

Further elution with the same eluent afforded 3β,4β-epoxyshionane (**8**; 0.28 g) mp 154—155 °C; PMR (100 MHz, $CDCl_3$) δ 0.86 (s: 3×*t*-CH_3), 0.88 (d, J=5 Hz; 2×*s*-CH_3), 1.05, 1.06, 1.16 (each s; *t*-CH_3), and 2.89 (t, J=*ca.* 1 Hz; $C_{(3)}$–H); mass spectrum *m/e* 428 (M^+); Found: C, 84.00; H, 12.14%. Calcd for $C_{30}H_{52}O$: C, 84.04; H, 12.21%.

The PMR spectral data using Eu(fod)$_3$-d_{27} as a shift reagent were given in Figs. 1 and 2.

*Reaction of 3α,4α-Epoxyshionane (**7**) with Boron Trifluoride Etherate.* To a solution of 3α,4α-epoxyshionane (**7**; 1.00 g) in benzene (40 ml, dried over sodium), freshly distilled boron trifluoride etherate (1.0 ml) was added with swirling. The reaction was monitored by TLC examination. After 10 min, the starting material completely disappeared and two new major spots were observed on TLC. The reaction was stopped by addition of a saturated sodium hydrogencarbonate solution, and the organic layer was washed with brine, dried over sodium sulfate, and evaporated to give a colorless oil (1.13 g).

The resulting oil was dissolved in benzene, passed through a column of silica gel (200 g), and eluted with the following solvents (each fraction 100 ml): frs 1—15, benzene; frs 16—19, benzene–ether (97 : 3). From fractions 6—9, a mixture of alcohols (**9** and **10**; 598 mg) was obtained.

*Collins Oxidation of the Alcohol Mixture (**9** and **10**).* The alcohol mixture (**9** and **10**; 596 mg), without further separation, was dissolved in dichloromethane (11 ml) and added to the Collins reagent (prepared from chromium trioxide (0.844 g), dry pyridine (1.4 ml), and dichloromethane (10 ml, dried over Zeolite)). After the solution was kept at room temperature for 2 h, the reaction mixture was passed through a short column of silica gel and eluted with ether. The eluates were combined and evaporated to yield a yellow oil (437 mg), which was dissolved in benzene, passed through a dry column of silica gel (300 g), and eluted with benzene (each fraction 100 ml). Fractions 5—8 gave D : B-friedo-bacchar-5(10)-en-3-one (**15**; 289 mg), fraction 9 gave a mixture (45 mg) of **15** and **11**, and fractions 10—16 gave bacchar-12-en-3-one (**11**; 69 mg).

D : B-Friedo-bacchar-5(10)-en-3-one (**15**) was crystallized from methanol to give colorless fine needles, mp 84—84.5 °C; IR (Nujol) 1715 cm^{-1}; PMR: no signal due to olefinic proton; mass spectrum *m/e* 426 (M^+); $[\alpha]_D$ −103° (*c* 0.10, methanol); ORD *a*=−66 (*c* 0.10, methanol); Found; C, 84.51; H, 11.51%. Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81%.

Bacchar-12-en-3-one (**11**) was crystallized from methanol and gave mp 111—112 °C; IR (neat) 1710 and 815 cm^{-1}; PMR (100 MHz, $CDCl_3$) δ 2.43 (m; 2×$C_{(2)}$–H) and 5.27 (t-like, J=2 Hz; $C_{(12)}$–H); ORD *a*=+33 (*c* 0.10, methanol); CD $[\theta]_{290}$+2600, $[\theta]_{325}$−90 (*c* 0.10, methanol); Found: C, 84.57; H, 11.97%. Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81%.

*Reduction of Bacchar-12-en-3-one (**11**) with Sodium Borohydride.* To a solution of bacchar-12-en-3-one (**11**; 47 mg) in methanol (10 ml), sodium borohydride (52 mg) was added and the reaction mixture was allowed to stand overnight at room temperature. After addition of dilute hydrochloric acid and removal of the solvent under reduced pressure, the reaction products were extracted with ether three times. On usual work-up, a residue (45 mg) was obtained, which was subjected to separation by silica gel (25 g) dry column chromatography. Elution with benzene (270 ml) afforded an oily product (4 mg) and successive elution with the same solvent (410 ml) gave bacchar-12-en-3β-ol (**2**; 36 mg), mp 143.5—144 °C (crystallized from methanol); IR (neat) 3400, 1045, and 820 cm^{-1}; PMR (100 MHz, $CDCl_3$) δ 3.23 (dd, J=5 and 6 Hz; $C_{(3)}$–H) and 5.11 (m; $C_{(12)}$–H); $[\alpha]_D$+55° (*c* 0.49, methanol); mass spectrum *m/e* 428 (M^+). (lit,[2] mp 147—148 °C; $[\alpha]_D$+39° (*c* 1.82); mass spectrum *m/e* 428.403).

*Acetylation of Bacchar-12-en-3β-ol (**2**).* A solution of bacchar-12-en-3β-ol (**2**; 17 mg) in pyridine (0.3 ml) was treated with acetic anhydride (0.2 ml) and was allowed to stand overnight at room temperature. Methanol was added and the reaction mixture was poured into water and extracted with ether twice. On usual work-up, a pale yellow crystal (18 mg) was obtained, which was recrystallized from methanol to give bacchar-12-en-3β-yl acetate (**13**; 8 mg) as colorless crystals, mp 177—178 °C; IR (neat) 1735, 1280, 1030, and 815 cm^{-1} (lit,[2] mp 181—182 °C; $[\alpha]_D$+21° (*c* 1.58); mass spectrum *m/e* 470.411).

*Bacchara-11,13(17)-dien-3β-yl Acetate (**14**).*[6] A mixture of bacchar-12-en-3β-yl acetate (**13**; 14 mg) in acetic acid (1 ml) and selenium dioxide (15 mg) in 96% aqueous

acetic acid solution (0.2 ml) was heated at 85 °C for 4 h. Extraction with ether and usual work-up gave a yellow solid (14 mg), which was subjected to separation by silica gel chromatography to afford bacchara-11,13(17)-dien-3β-yl acetate (**14**; 6.5 mg) as a pale red solid; IR (Nujol) 1735, 1280, 1245, and 875 cm^{-1}; UV λ_{max}^{EtOH} 250 nm (ε 12500), 241 (19400), and 234 (17000); PMR (100 MHz, $CDCl_3$) δ 2.03 (s; $-OCOCH_3$), 4.53 (dd, J=7 and 9 Hz; $C_{(3)}$–H), 5.23 (br. s; $C_{(17)}$–H), 5.55 (dd, $J_{11,12}$=10 Hz, $J_{9,12}$=1 Hz; $C_{(12)}$–H), and 5.92 (dd, $J_{11,12}$=10 Hz, $J_{9,11}$=3 Hz; $C_{(11)}$–H); mass spectrum *m/e* 468 (M^+) [lit,[2] mp 152—153 °C; PMR (60 MHz, $CDCl_3$) δ 5.16 (br. s; $C_{(17)}$–H), 5.40 (dd, $J_{11,12}$=10.5 Hz, $J_{9,12}$= 1 Hz; $C_{(12)}$–H), and 5.82 (dd, $J_{11,12}$=10.5 Hz, $J_{9,11}$=3 Hz; $C_{(11)}$–H); mass spectrum *m/e* 468.397 (M^+)].

The PMR, UV, and mass spectra of Bruun's authentic sample were measured under the same conditions as mentioned above. These spectral data were shown to be completely superimposable with ours.

*Reduction of D : B-Friedo-bacchar-5(10)-en-3-one (**15**) with Sodium Borohydride.* D : B-Friedo-bacchar-5(10)-en-3-one (**15**; 246 mg) in methanol (50 ml) was treated with sodium borohydride (200 mg) as the same procedure as described for bacchar-12-en-3-one (**11**) to afford a residue (239 mg), which gave two spots on TLC (a more polar spot was predominant). This was dissolved in benzene and passed through a dry column of silica gel (100 g). A minor component was eluted first with 600 ml of benzene, and successive elution with the same solvent (750 ml) afforded D : B-friedo-bacchar-5(10)-en-3β-ol (**17**; 176 mg), which was crystallized from methanol to give fine needles, mp 140.5—141 °C; IR (Nujol) 3350, 1175, 1120, 1070, 1040, 1030, and 980 cm^{-1}; PMR (100 MHz, $CDCl_3$) δ 3.42 (dd, J=10 and 5 Hz; $C_{(3)}$–H); Found: C, 83.90; H, 12.53%. Calcd for $C_{30}H_{52}O$: C, 84.04; H, 12.21%.

*Acetylation of D : B-Friedo-bacchar-5(10)-en-3β-ol (**17**).* Acetic anhydride (2 ml) was added to a solution of D : B-friedo-bacchar-5(10)-en-3β-ol (**17**: 123 mg) in pyridine (3 ml), and the solution was kept at room temperature for 2 h and then at 70 °C for 2 h. After addition of methanol to decompose excess of the reagent, the solution was poured into water and extracted with ether twice. Usual treatment gave a residue (162 mg), which was crystallized from methanol to give D : B-friedo-bacchar-5(10)-en-3β-yl acetate (**18**), mp 147—148 °C; IR (Nujol) 1725, 1250, 1025, and 970 cm^{-1}; PMR (100 MHz, $CDCl_3$) δ 2.03 (s; $-OCOCH_3$) and 4.64 (dd, J=10 and 5 Hz; $C_{(3)}$–H).

*D : B-Friedo-bacchara-1(10),5-dien-3β-yl Acetate (**19**).* A mixture of D : B-friedo-bacchar-5(10)-en-3β-yl acetate (**18**; 90 mg) in acetic acid (10 ml) and selenium dioxide (158 mg) in water (2 ml) was heated under reflux (bath temperature 100—130 °C) for 4.5 h. After addition of a cold aqueous potassium hydroxide solution, the mixture was extracted with ether twice, washed with a potassium hydroxide solution and then with brine. The ethereal layer was dried over sodium sulfate and evaporated. On standing for 2 days, the residue crystallized. The product was subjected to separation by silica gel (20 g) dry column chromatography using benzene as an eluent (each fraction 30 ml). Fractions 1 and 2, showing two spots on TLC, were combined and further separated by preparative TLC (2 plates (20×20 cm), SiO_2 0.5 mm in thickness; detection: I_2) to give D : B-friedo-bacchara-1(10),5-dien-3β-yl acetate (**19**; 43 mg), mp 123—123.5 °C; UV λ_{max}^{EtOH} 248 nm (sh. ε 12100), 238 (20900), and 231 (19400); PMR (100 MHz, $CDCl_3$) δ 2.04 (s; $-OCOCH_3$), 4.72 (dd, J=6 and 10 Hz; $C_{(3)}$–H), 5.28, and 5.68 (each m; $C_{(1)}$–H and $C_{(6)}$–H); mass spectrum *m/e* 468 (M^+).

The authors wish to thank Dr. T. Bruun for the generous gifts of the authentic bacchara-11,13(17)-dien-3β-yl acetate and of the IR and PMR spectra of bacchar-12-en-3β-ol and its acetate.

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11) The discrepancy, stated in the footnote 11 in the previous paper,[1] was found to be due to the impurity of the 3β-acetoxy-1(10),5-diene[1] which had been prepared from the less polar ketone by the same procedures now reinvestigated in the present paper.