Boron Trifluoride Etherate-Catalyzed Backbone Rearrangement of 3β,4β-Epoxyshionane and the Synthesis of Dihydrobaccharis Oxide

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3β,4β-Epoxyshionane (**15**) was treated with boron trifluoride etherate in ether at −30 °C to give dihydrobaccharis oxide (**4**; yield 17%), 4α-fluoroshionan-3β-ol (**17**; 10%), D: B-friedo-bacchar-5-en-3β-ol (**18**; 18%), D: B-friedo-bacchar-5(10)-en-3β-ol (**20**; 15%), and D: C-friedo-bacchar-7-en-3β-ol (**21**; 15%). The reaction in benzene, toluene, cyclohexane, or in hexane at −5 °C or at room temperature yielded bacchar-12-en-3β-ol (**5**), D: C-friedo-bacchar-8-en-3β-ol (**25**), **18**, **20**, and **21**. The reaction product ratios in the same reaction in various solvents are listed in Table 1.

Baccharis oxide (**1**)[2] is a triterpene oxide isolated from *Baccharis halimifolia* L. and shionone (**2**)[3] is a tetracyclic triterpene ketone contained in *Aster tataricus* L. These two triterpenes are biogenetically considered to be derived from a common intermediate (**3**) (or its equivalent species) and closely related to each other.[2,3] Baccharis oxide (**1**) may be formed from **3** by an attack of an oxygen atom on C-3 to the cationic center at C-10.

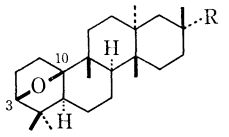
It has been reported that a boron trifluoride etherate-catalyzed rearrangement of dihydrobaccharis oxide (**4**) gives bacchar-12-en-3β-ol (**5**).[2b,4] In view of a correlation between compounds with shionane (D: A-friedobaccharane) and baccharane skeletons, we previously investigated[5] a backbone rearrangement of 3α,4α-epoxyshionane (**6**)[5] to afford bacchar-12-en-3α-ol (**7**) and D: B-friedo-bacchar-5(10)-en-3α-ol (**8**). We also reported[6] a transformation of friedelin (**9**) into dendropanoxide (**10**).[7] 3β,4β-Epoxyfriedelane (**11**) prepared from **9** was treated, according to Halsall's procedures,[8] with boron trifluoride etherate to give **10** together with D: B-friedo-olean-5(10)-en-3β-ol (**12**), D: B-friedo-olean-5-en-3β-ol (**13**), and β-amyrin (**14**).[6]

Backbone rearrangements in the steroid and terpenoid fields are well documented.[9] Intracyclic tension in the rigid polycyclic ring provokes of backbone rearrangements to give the products less constrained. Electronic effects resulting from the presence of functional groups and kinetic effects due to the nature of reagents can modify the development of rearrangement.[10] The shionane skeleton is considered to be 3α-(4-methylpentyl)-3β,5α,8β,17aβ-tetramethyl-D-homoandrostane, in which there exists an intracyclic tension due to 1,3-diaxial interactions among the alkyl substituents. The backbone rearrangements in **6** were shown to proceed from ring A towards ring D;[5] a 1,3-diaxial interaction between the side chain and the 13α-methyl group is released in **7**. The present paper deals with a reaction of 3β,4β-epoxyshionane (**15**) with boron trifluoride etherate and a preparation of dihydrobaccharis oxide (**4**).[2] Solvent effects on this reaction were also examined.

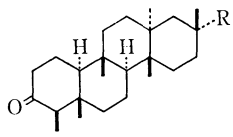
Shionone (**2**) was converted *via* shionan-3-one (**16**),[3b,c] shionan-3β-ol,[3b,c] and shion-3-ene,[3c] into 3β,4β-epoxyshionane (**15**)[5] by known procedures. Treatment of the β-epoxide (**15**) with boron trifluoride etherate in anhydrous ether at −30 °C for 1 h gave a complex mixture which was separated by column chromatography over silica gel, recrystallization, preparative thin-layer chromatography (TLC), column chromatography on silica gel impregnated with silver nitrate, and by high performance liquid chromatography (HPLC) (*cf.* Experimental).

The reaction mixture was separated into five components (**a**—**e**; designated in an order of the elution) by column chromatography (Column I). The least polar component **a** (yield: *ca.* 17%) was shown to be identical with dihydrobaccharis oxide (**4**),[2] mp 127—128.5 °C, by direct comparison with an authentic specimen, which was prepared by hydrogenation of baccharis oxide (**1**) over palladium charcoal.[2b] The second component **b** (y: *ca.* 1%) was found to be the starting β-epoxide (**15**).

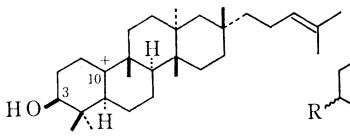
The third component **c** (**17**; y: *ca.* 10%), $C_{30}H_{53}OF$, mp 174—175 °C, was suggested to be a fluoro alcohol based on the spectral data and elemental analysis. The IR spectrum showed a band attributable to a hydroxyl group and the PMR spectrum showed a quintet centered at δ 3.70 due to a proton on a carbon atom ($C_{(3)}$) bearing the hydroxyl group. In the PMR



1 R = $(CH_2)_2CH=C(CH_3)_2$
4 R = $(CH_2)_3CH(CH_3)_2$



2 R = $(CH_2)_2CH=C(CH_3)_2$
16 R = $(CH_2)_3CH(CH_3)_2$



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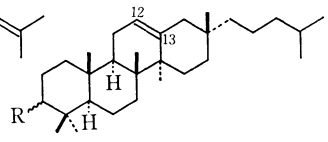
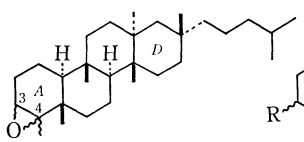
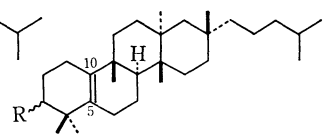


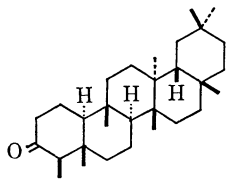
5 R = β-OH
7 R = α-OH



6 3α,4α-epoxide
15 3β,4β-epoxide



8 R = α-OH
20 R = β-OH



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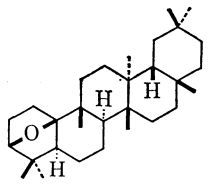

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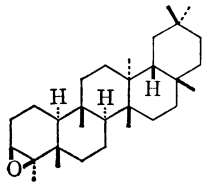

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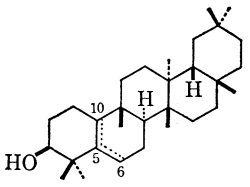
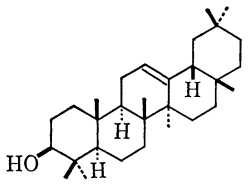


12 5(10)-ene

13 5-ene



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measurement using Eu(fod)$_3$-d_{27} as a shift reagent, signals due to a methyl group on a carbon atom bearing a fluorine atom ($C\underline{H}_3$–C(–F)) suffered a considerable downfield shift and were observed as a doublet (J=23 Hz). The fluoro alcohol (**17**) was treated with potassium hydroxide in methanol under reflux to generate the starting 3β,4β-epoxide (**15**). The reaction of an epoxide with boron trifluoride etherate to give a fluorohydrin is often encountered.[11] These observations together with the mechanistic consideration[11] led to the conclusion that the fluoro alcohol should be formulated as 4α-fluoroshionan-3β-ol (**17**).

The presence of a secondary hydroxyl group [IR 3450 cm^{-1}; PMR δ 3.47 (1H, t-like; $C_{(3)}$–H)] and a trisubstituted double bond [IR 820 cm^{-1}; PMR δ 5.62 (1H, m; $C_{(6)}$–H)] was shown for the fourth component **d** (**18**; y: *ca.* 18%), $C_{30}H_{52}O$, mp 124—125 °C, by its IR and PMR spectra. The appearance of peaks at *m/e* 276 and *m/e* 152 due to a retro-Diels-Alder fragmentation[12] in the mass spectrum showed the presence of the double bond between C-5 and C-6. Thus the structure of D: B-friedo-bacchar-5-en-3β-ol (**18**) was proposed for the fourth component **d**. This was substantiated by the following transformation. The unsaturated alcohol (**18**) was converted by a usual procedure into a corresponding acetate. Oxidation of the acetate with selenium dioxide in acetic acid under reflux gave a diene identical with a known D: B-friedo-bacchara-1(10),5-dien-3β-yl acetate (**19**).[5]

The fifth component **e** was found to be a mixture of two compounds (**20** and **21**) containing a small amount of **17** and **18** by HPLC examination. The component **e** was chromatographed on silica gel impregnated with silver nitrate (Column II) to give a mixture of two compounds (**20** and **21**). This mixture could not be separated into pure compounds by repeated column and thin layer chromatography and by recrystallization. Application of HPLC however gave a satisfactory separation: D: B-friedo-bacchar-5(10)-en-3β-ol (**20**; y: 15%) and D: C-friedo-bacchar-7-en-3β-ol (**21**; y: 15%) were obtained. Their structures were characterized as follows.

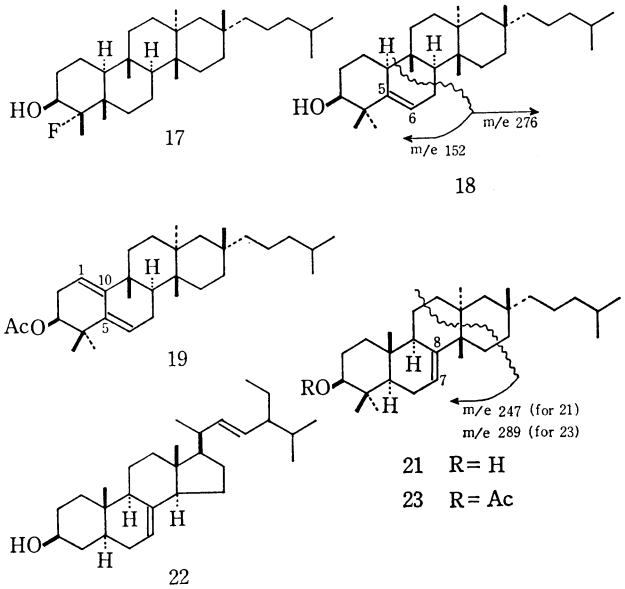
The former compound (**20**), mp 142—143 °C, showed the same spectral data and melting point (and mixed mp) as those of an authentic D: B-friedo-bacchar-5(10)-en-3β-ol (**20**)[13] prepared from shionanone (**16**) *via* D: B-friedo-bacchara-1,5(10)-dien-3-one.[13]

The latter compound was inferred to be **21** by the following evidence. The compound (**21**) had mp 136.5—137.5 °C and a molecular formula $C_{30}H_{52}O$. The presence of a secondary hydroxyl group [IR 3350 cm^{-1}; PMR δ 3.26 (1H, dd, $J_{2\beta,3\alpha}$=8 and $J_{2\alpha,3\alpha}$=5 Hz; $C_{(3\alpha)}$–H)] and a trisubstituted double bond [IR 820 cm^{-1}; PMR δ 5.39 (1H, quartet, $J_{6\beta,7}$=3, $J_{6\alpha,7}$=3, and $J_{7,9\alpha}$=3 Hz; $C_{(7)}$–H)] was indicated by the IR and PMR spectra. In the PMR spectrum using Eu(fod)$_3$-d_{27} as a shift reagent, signals due to the olefinic and allylic protons and the methyl protons at C-10 shifted to downfield and were easily assignable (Fig. 1). The magnitude and tendency of the shift of these protons were found to be similar to those (Fig. 2) of α-spinasterol (**22**).[14] The position of the trisubstituted double bond between C-7 and C-8 was supported by fragment ion peaks at *m/e* 247 and *m/e* 229. The peak at *m/e* 247 is characteristic for Δ^7- and Δ^8-triterpenoids[15] and the latter peak at *m/e* 229 is corresponding to the dehydration peak of the former ion. It is therefore concluded that the compound (**21**) should be formulated as D: C-friedo-bacchar-7-en-3β-ol. The proposed structure was further supported by the following transformations (a and b).

a) The compound (**21**) was acetylated in a usual manner to give an acetate (**23**), $C_{32}H_{54}O_2$, which also showed a characteristic fragment ion peak at *m/e* 289 due to a retro-Diels-Alder fragmentation of Δ^7- and Δ^8-triterpenoids[15] accompanied with a peak at *m/e* 229 due to loss of acetic acid from the ion at *m/e* 289. In the PMR and IR spectra, the presence of an acetoxyl group and an olefinic proton [PMR δ 5.39 (1H, quartet, $J_{6\beta,7}$=3, $J_{6\alpha,7}$=3, and $J_{7,9\alpha}$=3 Hz; $C_{(7)}$–H)] was observed. On allylic oxidation with *t*-butyl chromate,[16] the acetate (**23**) afforded an enone acetate (**24**), $C_{32}H_{52}O_3$, as an oil. Its IR, UV [λ_{max} 248 nm (ε 12000)], and PMR [δ 2.17 (s, $C_{(5)}$–H) and 5.81 (d, $J_{7,9\alpha}$=2.4 Hz; $C_{(7)}$–H)] spectral data may best be interpreted by a structure of D: C-friedo-bacchar-7-en-6-on-3β-yl acetate (**24**).[17]

b) Treatment of the acetate (**23**) with hydrogen chloride in chloroform, followed by alkaline hydrolysis and purification by HPLC, gave an isomerized product (**25**), $C_{30}H_{52}O$, as an oil. The presence of a hydroxyl group and the absence of olefinic proton in **25** were shown by the IR and PMR spectra. Prominent peaks at *m/e* 247 and 229 characteristic for Δ^7- and Δ^8-triterpenoids[15] were observed in the mass spectrum. When **23** was treated with hydrochloric acid in acetic acid at

60 °C and then subjected to alkaline hydrolysis, the 12-ene (**5**)[2b,4] was formed together with **25**. These observations suggest the structure of D: C-friedo-bacchar-8-en-3β-ol for the isomerized alcohol (**25**) and



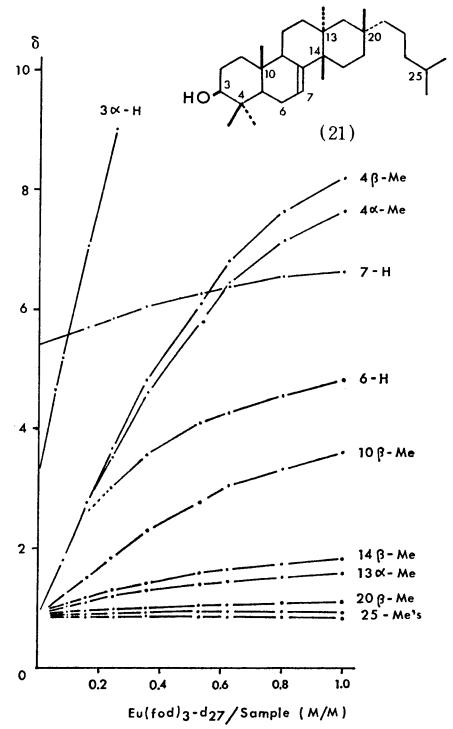


Fig. 1. Induced paramagnetic shifts for D: C-friedo-bacchar-7-en-3β-ol (**21**) in a 3% (w/v) solution in $CDCl_3$.

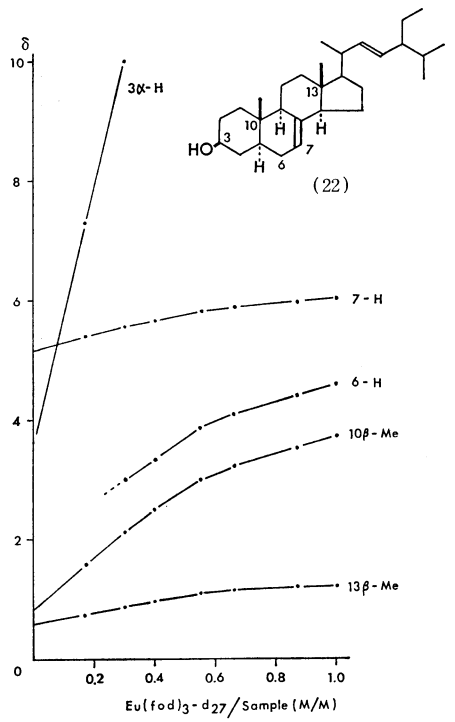


Fig. 2. Induced paramagnetic shifts for α-spinasterol (**22**) in a 3% (w/v) solution in $CDCl_3$.

that of D: C-friedo-bacchar-7-en-3β-ol for the alcohol (**21**).

Solvent effects on the formation of these reaction products were then investigated. The small scale reaction using 1—3 mg of the 3β,4β-epoxide (**15**) and boron trifluoride etherate (2 drops) in a solvent (2—10 ml) was carried out at room temperature or at —5 °C. The reaction mixture, after the usual treatment, was extracted with ether to give a residue. This residue was dissolved in 10% ether–hexane and the identification of each component and the determination of its relative amount were carried out by HPLC (Table 1).

In the reaction conditions listed in Table 1, five alcohols were detected besides dihydrobaccharis oxide (**4**) and the fluorohydrin (**17**), and four of the alcohols were identified to be **18**, **20**, **21**, and **25** by HPLC. The fifth alcohol was found to be bacchar-12-en-3β-ol (**5**) by direct comparison (IR, mass spectrum, TLC, and HPLC) with an authentic specimen[2b] prepared by the acid-catalyzed rearrangement of dihydrobaccharis oxide (**4**).

In the rearrangement of the 3β,4β-epoxide (**15**), the cationic center at C-4 was initially formed by boron trifluoride etherate-attack to an oxygen atom of the epoxide. A sequence of 1,2-shifts of methyl group(s) and hydrogen atom(s) were then followed. From the derived cations in various rearranged stages, the rearranged alcohols (**5**, **18**, **20**, **21**, and **25**) would be produced after deprotonation in the last step.[18]

It is obvious that the rearrangement in solvents with low nucleophilicity *e.g.* such as nitromethane, proceeds up to C/D rings because the cationic centers survive longer in these solvents and spread over the whole skeleton; therefore the formation of bacchar-12-en-3β-ol

Table 1. Relative amount ratios of the products in the reaction of **15** with boron trifluoride etherate[a)]

Solvents	Temp (°C)	Time (min)	**17**	**4**	**18** (5-ene)	**20** [5(10)-ene]	**25** (8-ene)	**21** (7-ene)	**5** (12-ene)
CH_3NO_2	r.t.[b)]	5	0	0	0	0	30	0	70
CH_2Cl_2	r.t.	5	0	0	20	trace	25	trace	55
Benzene	r.t.	5	0	0	15	20	20	15	30
Toluene	r.t.	5	0	0	10	15	25	15	35
Cyclohexane	r.t.	5	0	0	15	25	25	15	20
Hexane	r.t.	5	0	0	25	25	20	5	25
CH_3CN	r.t.	5	0	0	15	35	25	15	10
Ether	r.t.	5	40	25	5	15	0	15	trace
DME	r.t.	5	0	15	30	40	0	15	0
THF	r.t.	5	0	0	45	50	0	5	0
CH_3NO_2	−5	15	0	0	trace	0	35	30	35
CH_2Cl_2	−5	10	0	0	10	20	25	10	35
Toluene	−5	15	0	0	10	10	25	20	35
Hexane	−5	5	0	0	25	25	15	25	10
CH_3CN	−5	10	0	0	15	50	20	15	trace
Ether	−5	50	30	25	10	20	0	15	trace
DME	−5	20	0	15	30	30	0	25	0
THF[c)]	−5	5	0	0	10	10	0	0	0
Ether	−30	60	10	25	20	15	0	30	0
Ether[d,e)]	−30	60	10	17	18	15	0	15	0

a) Relative yields were determined by HPLC. Measurements were carried out at room temperature using a Liquid Chromatograph Model ALC/GPC 202/401 (Waters Assoc.) with an RI detector; column: μ-PORASIL 1/8 (inch) × 1 (foot); solvent system: 1 or 10% ether–hexane; flow rate: 1.0 or 1.2 ml/min; pressure: *ca.* 500 psi. Under the conditions (1% ether–hexane; 1.0 ml/min), retention time for **17**, **4**, **18**, **20**, and **21** was shown to be 54.7, 8.3, 51.7, 69.7, and 81.7 min, respectively. Under the other conditions (10% ether–hexane; 1.2 ml/min), retention time for **18**, **20**, **25**, **21**, and **5** was found to be 11.0, 14.6, 17.0, 15.6, and 18.3 min, respectively. b) Room temperature (r.t.) refers to a temperature range between 20 and 28 °C. c) The epoxide (**15**) was recovered in about 80% yield. d) Yields in this line are expressed as isolated yields (in %). e) A small quantity (*ca.* 1%) of the starting material (**15**) was recovered.

(**5**), derived from a species with a cationic center at C-13, was observed. On the contrary, in a solvent apt to coordinate with a cation such as dimethoxyethane (DME), tetrahydrofuran, or ether, the rearrangement reaction was interrupted in early stages; *e.g.* the D: B-friedo-type alcohols (**18** and **20**) were formed preferentially in the rearrangement in the former two solvents (DME and THF) (*vide infra* for the reaction in ether).

In the reaction of the 3β,4β-epoxide (**15**) in ether or in dimethoxyethane, dihydrobaccharis oxide (**4**) was formed together with the other reaction products, while no **4** was produced in the reaction in nitromethane, dichloromethane, benzene, toluene, cyclohexane, hexane, acetonitrile, and in tetrahydrofuran.

Dihydrobaccharis oxide (**4**) was then treated with boron trifluoride etherate in ether at various temperatures. No reaction occurred at a temperature range between −40 and 0 °C; this shows that the intermediacy of the oxide (**4**) for the formation of the rearranged alcohols (**18**, **20**, and **21**) from 3β,4β-epoxyshionane (**15**) under the similar conditions (at −30 and at −5 °C) is improbable. The reaction of **4** in ether at room temperature for 1 h gave **18** (relative yield determined by HPLC: 10%), **20** (8%), and **21** (2%), besides the starting material (**4**; 80%).

According to Anthonsen's procedure,[2b)] dihydrobaccharis oxide (**4**) was treated with boron trifluoride etherate in benzene at room temperature for 10 min. An examination of the reaction mixture by HPLC showed that bacchar-12-en-3β-ol (**5**; 50%) was the main product and that minor products were **18** (10%), **20** (10%), **21** (10%), and **25** (20%).

The conversion of shionone (**2**) into dihydrobaccharis oxide (**4**) *via* the 3β,4β-epoxide (**15**) was thus shown. As the total synthesis of shionone (**2**) was recently achieved,[19)] the present report constitutes formally the total synthesis of dihydrobaccharis oxide (**4**).

Experimental

Melting points were measured on a Mel-temp capillary melting point apparatus (Laboratory Devices) and were uncorrected. IR and UV spectra were determined on a Hitachi EPI-G2 and EPS-2 spectrometer, respectively. Mass spectra were taken on a Hitachi RMU-6-Tokugata mass spectrometer and high resolution mass spectra on a Hitachi RMH-2 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-20B (60 MHz), or a JEOL JNM FX-60 (Fourier Transform) spectrometer in deuteriochloroform. Measurements of optical rotations were carried out using a JASCO polarimeter DIP-SL. Thin layer chromatography (TLC) was carried out on Kieselgel PF_{254} (E. Merck) in 0.25 or 0.5 mm thickness or Wako Alumina B-10F (Wako). Wakogel C-200 (Wako) was used for column chromatography.

*Reaction of 3β,4β-Epoxyshionane (**15**) with Boron Trifluoride Etherate in Ether.* To a solution of 3β,4β-epoxyshionane (**15**; 384 mg)[5)] in ether (30 ml, distilled from sodium wire) at −30 °C was added boron trifluoride etherate (1.0 ml) with stirring. After 1 h the starting material mostly disappeared and several spots were observed on TLC. The reaction was stopped by addition of 5% methanolic potassium hydroxide (10 ml) kept at the same temperature. The reaction products were extracted with ether twice (each 50 ml) and the organic layer was washed with water (50 ml) and brine, dried over magnesium sulfate, and evaporated to give a colorless oil (384 mg).

The resulting oil was dissolved in petroleum ether–ether (10: 1), absorbed on silica gel (200 g), and eluted with the following solvent system (each fraction 100 ml; Column I): frs. 1—6, petroleum ether–ether (10: 1); frs. 7—12, (5: 1); frs. 13—35, (10: 3).

From frs. 5—8 was obtained dihydrobaccharis oxide (**4**; 42 mg)[2)] after purification by preparative TLC and crystallization from ethyl acetate–methanol, mp 127—128.5 °C (lit, 127—128 °C)[2b)]; IR (KBr) 1000 and 910 cm^{-1}; PMR δ 3.73 (1H, d, $J_{2\beta,3\alpha}$=5 Hz; $C_{(3\alpha)}$-H); mass spectrum *m/e* (relative intensity %) 428 (23; M^+), 413 (73), and 137 (base peak); $[\alpha]_D$ +45 ° (*c* 1.7, chloroform) [lit, +44 ° (*c* 2.30)][2b)]; Found: C, 84.00; H, 12.31%. Calcd for $C_{30}H_{52}O$: C, 84.02; H, 12.23%.

Fr. 9 gave the starting material (**15**; 4 mg).

From frs. 10—12 was obtained a mixture of dihydrobaccharis oxide (**4**) and 4α-fluoroshionan-3β-ol (**17**), which was further separated by preparative TLC to give **17** (35 mg), mp 174—175 °C (crystallized from methanol); IR (KBr) 3450 cm^{-1}; PMR δ 3.70 (1H, quintet, $J_{2\beta,3\alpha}=3$, $J_{2\alpha,3\alpha}=3$, and $J_{3\alpha,F}=6$ Hz; $C_{(3\alpha)}$–H); mass spectrum *m/e* 448 (11; M^+), 433 (8), 428 [18; $(M-HF)^+$], 413 (11), 343 (46), 275 (33), 247 (33), 229 (28), 220 (31), and 95 (base peak); Found: C, 80.29; H, 11.87%. Calcd for $C_{30}H_{53}OF$: C, 80.30; H, 11.90%.

From frs. 13—15 was obtained a mixture of 4α-fluoroshionan-3β-ol (**17**) and D: B-friedo-bacchar-5-en-3β-ol (**18**), which was passed through a short column of silica gel (4 g) impregnated with silver nitrate (20%, 1 g) and eluted with benzene to afford **17** (0.5 mg) and **18** (63 mg), mp 124—125 °C (crystallized from acetone); IR (KBr) 3450, 1630, 1100, 830, and 820 cm^{-1}; PMR δ 3.47 (1H, t-like, $W_{1/2}$ 6 Hz; $C_{(3\alpha)}$–H and 5.62 (1H, m, $C_{(6)}$–H); mass spectrum *m/e* 428 (8; M^+), 413 (10), 410 (5), 395 (8), 276 (39), 261 (base peak), 152 (21), and 134 (79); Found: C, 84.07; H, 12.62%. Calcd for $C_{30}H_{52}O$: C, 84.04; H, 12.23%.

Fractions 16—22 gave a mixture (194 mg) of D: B-friedo-bacchar-5(10)-on-3β-ol (**20**) and D: C-friedo-bacchar-7-en-3β-ol (**21**) containing a small amount of **17** and **18**. This mixture was dissolved in benzene, absorbed on silica gel (34 g) impregnated with silver nitrate (20%, 8 g), and eluted with the same solvent (Column II, each 100 ml). Frs. 1 and 2 gave **17** (4 mg), while **18** (6 mg) was obtained from frs. 13—18. Since frs. 3—12 afforded a mixture of **20** and **21** in a various ratio, these fractions were combined and subjected to separation by HPLC (*vide infra*).

Frs. 23—35 afforded a mixture of **20** and **21**, which was also subjected to HPLC separation (*vide infra*).

*Separation of D: B-Friedo-bacchar-5(10)-en-3β-ol (**20**) and D: C-Friedo-bacchar-7-en-3β-ol (**21**) by High Performance Liquid Chromatography (HPLC).* The above fractions (Column I, frs. 23—35 and Column II, frs. 3—12) were subjected to separation by HPLC to give D: B-friedo-bacchar-5(10)-en-3β-ol (**20**) and D: C-friedo-bacchar-7-en-3β-ol (**21**). Each compound was collected by repeating the procedure to afford **20** (59 mg), mp 142—143 °C (crystallized from acetone) (lit, 141.5—142 °C)[13]; IR (KBr) 3350 cm^{-1}: PMR δ 3.48 (1H, dd, $J_{2\beta,3\alpha}=10$ and $J_{2\alpha,3\alpha}=4$ Hz, $C_{(3\alpha)}$–H); mass spectrum *m/e* 428 (17; M^+) and 135 (base peak), and **21** (59 mg), mp 136.5—137.5 °C (crystallized from petroleum ether); IR (liquid) 3350, 1630, 1035, and 820 cm^{-1}; PMR δ 3.26 (1H, dd, $J_{2\beta,3\alpha}=8$ and $J_{2\alpha,3\alpha}=5$ Hz, $C_{(3\alpha)}$–H) and 5.39 (1H, quartet, $J_{6\beta,7}=3$, $J_{6\alpha,7}=3$, and $J_{7,9\alpha}=3$ Hz, $C_{(7)}$–H); mass spectrum *m/e* 428 (25, M^+), 413 (base peak), 395 (51), 247 (14), 229 (28), and 135 (46); high resolution mass spectrum, Found: 428.4000. Calcd for $C_{30}H_{52}O$: 428.4015. Found: 247.2045. Calcd for $C_{17}H_{27}O$: 247.2060. Found: 229.1928. Calcd for $C_{17}H_{25}$: 229.1954.

*Base Treatment of 4α-Fluoroshionan-3β-ol (**17**).* 4α-Fluoroshionan-3β-ol (**17**; 64 mg) was treated with 5% methanolic potassium hydroxide (15 ml) for 21 h under reflux temperature. The reaction mixture was extracted with chloroform followed by the usual work-up to give a residue (62 mg), which was crystallized from acetone to afford 3β,4β-epoxyshionane (**15**; 34 mg) as white needles, mp 152.5—153.5 °C (lit, 154—155 °C)[5]; IR, PMR, and mass spectrum were superimposable with those of an authentic specimen.

*D: B-Friedo-bacchara-1(10),5-dien-3β-yl Acetate (**19**).*

D: B-Friedo-bacchar-5-en-3β-ol (**18**; 23 mg) was treated with acetic anhydride (1.5 ml) in pyridine (2 ml) at room temperature and was allowed to stand overnight. After usual work-up, the corresponding acetate (24 mg) was obtained. A mixture of this acetate (11 mg) in acetic acid (3 ml) and selenium dioxide (11 mg) in water (0.5 ml) was heated under reflux for 5 h. After the similar work-up according to Ref. 5b, an oil was obtained. The dehydrogenation reaction of the acetate (5 mg) was repeated once more and the resulting oil was combined and passed through a short column of silica gel to afford a residue (16 mg). Purification by preparative TLC and crystallization from methanol gave white crystalline D: B-friedo-bacchara-1(10),5-dien-3β-yl acetate (**19**; 7 mg), mp 123—124 °C (lit, 123—123.5 °C).[5]

*Acetylation of D: C-Friedo-bacchar-7-en-3β-ol (**21**).* A solution of D: C-friedo-bacchar-7-en-3β-ol (**21**; 32 mg) in pyridine (2 ml) and acetic anhydride (1 ml) was allowed to stand overnight at room temperature. Methanol was added and the reaction mixture was poured into water and extracted with ether three times. On usual work-up, a colorless gum (**23**; 31 mg) was obtained. IR (liquid) 1730, 1240, 1030, 820, and 760 cm^{-1}; PMR δ 2.04 (3H, s, $-OCOCH_3$), 4.51 (1H, dd, $J_{2\beta,3\alpha}=9$ and $J_{2\alpha,3\alpha}=5$ Hz; $C_{(3\alpha)}$–H), and 5.39 (1H, quartet, $J_{6\beta,7}=3$, $J_{6\alpha,7}=3$, and $J_{7,9\alpha}=3$ Hz; $C_{(7)}$–H); mass spectrum *m/e* 470 (36; M^+), 455 (base peak), 395 (57), 289 (7), and 229 (28); molecular weight (by high resolution mass spectrometry), Found: 470.4121. Calcd for $C_{32}H_{54}O_2$: 470.4121.

*Allylic Oxidation of D: C-Friedo-bacchar-7-en-3β-yl Acetate (**23**).* A solution of D: C-friedo-bacchar-7-en-3β-yl acetate (**23**; 19 mg) in benzene (1 ml) was treated with *t*-butyl chromate in benzene [0.1 ml; prepared from *t*-butyl alcohol (24.6 g), chromium trioxide (11.1 g), and benzene (50 ml)] and was allowed to stand overnight at room temperature. Saturated aqueous formic acid solution was added and the reaction mixture was poured into water and extracted with ether three times. On usual work-up, a pale yellow oil was obtained, which was separated by TLC to give D: C-friedo-bacchar-7-en-6-on-3β-yl acetate (**24**; 0.5 mg) and the starting material (**23**; 14 mg). This procedure was repeated twice and the enone-acetate fractions were combined (1.8 mg), and purified by silica gel TLC, alumina TLC, and then by HPLC. D: C-Friedo-bacchar-7-en-6-on-3β-yl acetate (**24**; *ca.* 1.5 mg) was obtained as an oil, IR (liquid) 1730, 1660, 1610, and 1245 cm^{-1}; UV λ_{max}^{EtOH} 248 nm (ε 12000); PMR δ 2.17 (s, $C_{(5\alpha)}$–H) and 5.81 (d, $J_{7,9\alpha}=2.4$ Hz, $C_{(7)}$–H); mass spectrum *m/e* 484 (13; M^+), 469 (4), 424 (23), 409 (17), 302 (43), 277 (9), 243 (9), 217 (25), 196 (50), and 121 (base peak); molecular weight (by high resolution mass spectrometry), Found: 484.3902. Calcd for $C_{32}H_{52}O_3$: 484.3913.

*Isomerization of D: C-Friedo-bacchar-7-en-3β-yl Acetate (**23**).*

a) Hydrogen chloride was bubbled for 5 min through a solution of D: C-friedo-bacchar-7-en-3β-yl acetate (**23**; 7 mg) in chloroform (3 ml) at 0 °C. The solution was kept for 10 min at the same temperature, poured into water, extracted with chloroform, washed with 10% aqueous sodium carbonate, and brine, and then evaporated. A resulting residue was treated with 5% methanolic potassium hydroxide (10 ml) at 60 °C for 2 h. The reaction mixture was diluted with water and extracted with ether. After usual work-up and purification by preparative TLC, D: C-friedo-bacchar-8-en-3β-ol (**25**; 1.8 mg) was obtained as an oil, which was subjected to examination by HPLC and proved to be pure. IR (liquid) 3400 cm^{-1}; PMR δ 3.28 (1H, m, $C_{(3\alpha)}$–H), no olefinic proton was observed; mass spectrum *m/e* 428 (29; M^+), 413 (base peak), 395 (50), 247 (13), and 229 (40); high resolution mass spectrum, Found: 428.4018. Calcd for $C_{30}H_{52}O$: 428.4015, Found: 247.2056. Calcd for $C_{17}H_{27}O$: 247.2059. Found: 229.1929. Calcd for $C_{17}H_{25}$: 229.1954.

b) To a solution of D: C-friedo-bacchar-7-en-3β-yl acetate (**23**; 1.5 mg) in acetic acid (2 ml) was added concd hydro-

chloric acid (0.2 ml) and the mixture was heated at 60 °C for 19 h. The reaction mixture, after usual treatment, was extracted with ether to give a residue, which was treated with 5% methanolic potassium hydroxide (2 ml) at room temperature overnight. The usual work-up gave an oil, which was subjected to examination by HPLC and was found to be a mixture of the 7-ene (**21**), the 8-ene (**25**), and the 12-ene (**5**)[2b,4] in a ratio of 6: 9: 5.

Reaction of Dihydrobaccharis Oxide (4) with Boron Trifluoride Etherate in Ether and in Benzene. Boron trifluoride etherate (4 drops) was added to a solution of dihydrobaccharis oxide (**4**; 5 mg)[2] in ether (1 ml), and the solution was kept at room temperature for 1 h. The reaction mixture was treated as usual to give a residue. An examination of this residue by HPLC showed that it consisted of the 5-ene (**18**; relative amount ratio 10%), the 5(10)-ene (**20**; 8%), the 7-ene (**21**; 2%), and of the oxide (**4**; 80%).

The small scale reaction of **4** (9 mg) with boron trifluoride etherate (5 drops) in benzene[2b] (2 ml) was effected at room temperature for 10 min. The product was found to be a mixture of the 12-ene (**5**; relative amount ratio 10%), **18** (10%), **20** (10%), **21** (10%), and the 8-ene (**25**; 20%), by HPLC examination.

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References

1) Preliminary accounts of this paper: K. Tachibana and T. Takahashi, *Tetrahedron Lett.*, **1975**, 1857; M. Tori, K. Tachibana, Y. Moriyama, T. Tsuyuki, and T. Takahashi, *Chem. Lett.*, **1976**, 1359.

2) a) F. Mo, T. Anthonsen, and T. Bruun, *Acta Chem. Scand.*, **26**, 1287 (1972); b) T. Anthonsen, T. Bruun, E. Hemmer, D. Holme, A. Lamvik, E. Sunde, and N. A. Sφrensen, *ibid.*, **24**, 2479 (1970).

3) a) Y. Moriyama, Y. Tanahashi, T. Takahashi, and G. Ourisson, *Bull. Soc. Chim. Fr.*, **1968**, 2890; T. Tsuyuki, T. Hoshino, M. Ito, and T. Takahashi, *ibid.*, **1968**, 2895. And references cited therein; b) M. Takahashi, W. Kamisako, S. Ishimasa, and K. Miyamura, *Yakugaku Zasshi*, **79**, 1281 (1959); W. Kamisako and M. Takahashi, *ibid.*, **84**, 318 (1964); c) Y. Tanahashi, T. Takahashi, F. Patil, and G. Ourisson, *Bull. Soc. Chim. Fr.*, **1964**, 584.

4) E. Suokas and T. Hase, *Acta Chem. Scand.*, **25**, 2359 (1971).

5) S. Yamada, S. Yamada, K. Tachibana, Y. Moriyama, Y. Tanahashi, T. Tsuyuki, and T. Takahashi, *Bull. Chem. Soc. Jpn.*, **49**, 1134 (1976). And references cited therein.

6) T. Torii, K. Tachibana, S. Yamada, T. Tsuyuki, and T. Takahashi, *Tetrahedron Lett.*, **1975**, 2283; M. Tori, T. Torii, K. Tachibana, S. Yamada, T. Tsuyuki, and T. Takahashi, *Bull. Chem. Soc. Jpn.*, **50**, 469 (1977).

7) a) J. D. White, J. Fayos, and J. Clardy, *J. Chem. Soc., Chem. Commun.*, **1973**, 357; b) G. H. Constantine, Jr. and J. H. Block, *Phytochemistry*, **9**, 1659 (1970); c) J. H. Block and G. H. Constantine, Jr., *ibid.*, **11**, 3279 (1972). And references cited therein.

8) M. S. Hadley and T. G. Halsall, *J. Chem. Soc., Perkin Trans. 1*, **1974**, 1334.

9) *E.g.*, D. N. Kirk and M. P. Hartshorn, "Steroid Reaction Mechanism," Elsevier Publishing Company, Amsterdam (1968), pp. 290, 353; P. de Mayo, "Molecular Rearrangements," Vol. 2, John Wiley & Sons, Inc., New York (1964), p. 821; D. N. Kirk and P. M. Shaw, *Chem. Commun.*, **1971**, 948.

10) *E.g.*, J. Bascoul, B. Cocton, and A. Crastes de Paulet, *Tetrahedron Lett.*, **1969**, 2401; J. Bascoul, E. Noyer, and A. Crastes de Paulet, *Bull. Soc. Chim. Fr.*, **1972**, 2744; J. C. Jacquesy, J. Levisalles, and J. Wagnon, *ibid.*, **1970**, 670.

11) *E.g.*, L. H. Knox, J. A. Zderic, J. P. Ruelas, C. Djerassi, and H. J. Ringold, *J. Am. Chem. Soc.*, **82**, 1230 (1960); J. M. Coxon, M. P. Hartshorn, and D. N. Kirk, *Tetrahedron*, **20**, 2547 (1964); J. W. Blunt, M. P. Hartshorn, and D. N. Kirk, *ibid.*, **21**, 559 (1965); J. M. Coxon, M. P. Hartshorn, and D. N. Kirk, *ibid.*, **21**, 2489 (1965); J. R. Bull, *Tetrahedron Lett.*, **1968**, 5959; P. A. Diassi and J. Fried, U. S. P. 3 364 204 (1964), *Chem. Abstr.*, **69**, 27638a (1968).

12) In the mass spectrum of the 5-ene (**13**), a peak at *m/e* 274 due to a retro-Diels-Alder fragmentation was observed as a base peak.

13) K. Tachibana, S. Yamada, S. Yamada, T. Tsuyuki, and T. Takahashi, *Bull. Chem. Soc. Jpn.*, **48**, 3425 (1975).

14) L. F. Fieser and M. Fieser, "Steroids," Reinhold, New York (1959), p. 352; J. W. Clark-Lewis and I. Dainis, *Aust. J. Chem.*, **20**, 1961 (1967); M. Tada, T. Takahashi, and H. Koyama, *Phytochemistry*, **13**, 670 (1974).

15) H. Budzikiewicz, J. M. Wilson, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 3688 (1963).

16) K. Fujita, *Nippon Kagaku Zasshi*, **78**, 1112 (1957).

17) A proton at C-7 of 3β-acetoxybauer-7-en-6-one resonated at δ 5.72 as a doublet ($J_{7,9\alpha}$=3 Hz), while the corresponding proton ($C_{(7)}$-H) of 3β-acetoxy-9βH-bauer-7-en-6-one at δ 5.57 as a singlet: M. Fukuoka and S. Natori, *Chem. Pharm. Bull.*, **20**, 974 (1972). This provided support for the 9αH configuration of **24** (and of **21**).

18) *Cf.*, A. Eschenmoser, L. Ruzicka, O. Jeger, and D. Arigoni, *Helv. Chim. Acta*, **38**, 1890 (1955).

19) R. E. Ireland, C. A. Lipinski, C. J. Kowalski, J. W. Tilley, and D. M. Walba, *J. Am. Chem. Soc.*, **96**, 3333 (1974); R. E. Ireland, M. I. Dawson, C. J. Kowalski, C. A. Lipinski, D. R. Marshall, J. W. Tilley, J. Bordner, and B. L. Trus, *J. Org. Chem.*, **40**, 973 (1975); R. E. Ireland, C. J. Kowalski, J. W. Tilley, and D. M. Walba, *ibid.*, **40**, 990 (1975).