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SOLVENT EFFECT ON THE BACKBONE REARRANGEMENT OF 3β,4β-EPOXYSHIONANE CATALYZED BY BORON TRIFLUORIDE ETHERATE

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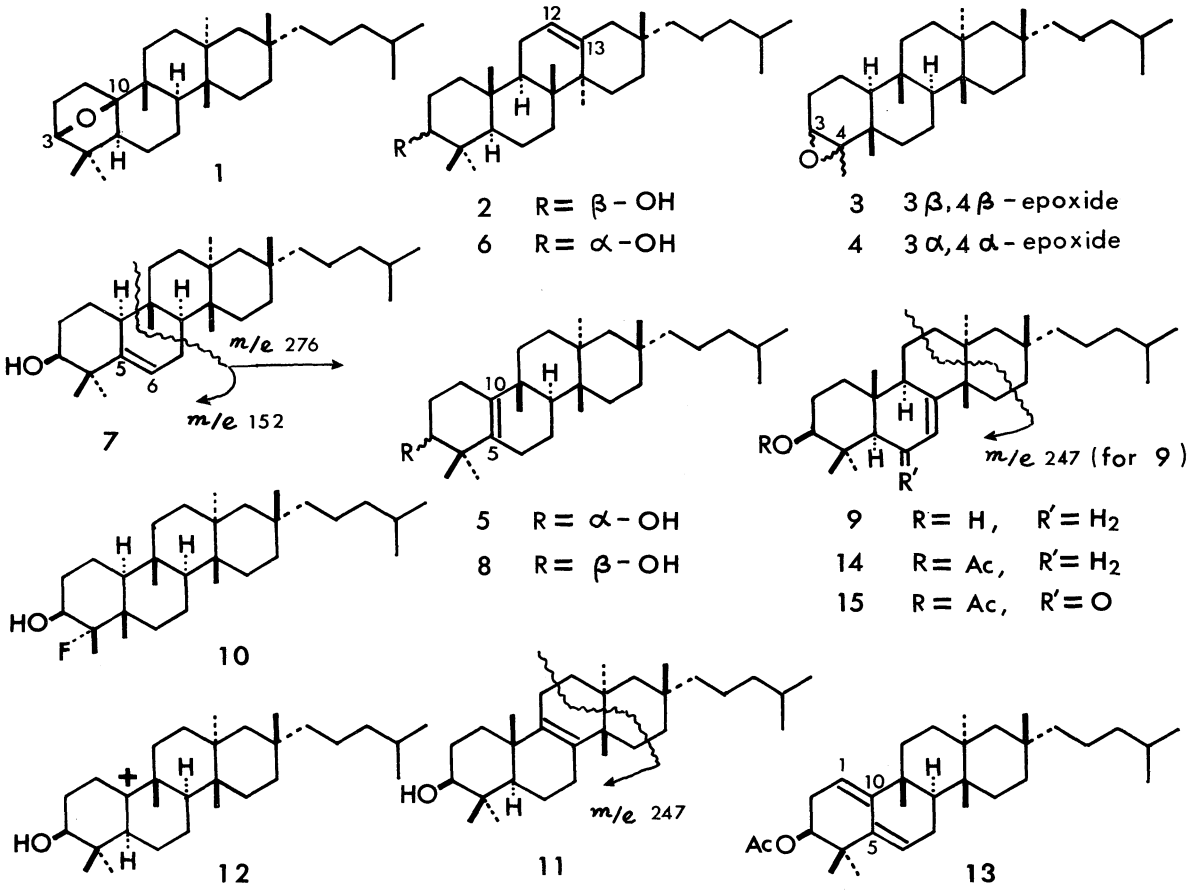
3β,4β-Epoxyshionane (3) was treated with BF_3-Et_2O in ether to give D:B-friedo-bacchar-5-en-3β-ol (7), D:B-friedo-bacchar-5(10)-en-3β-ol (8), D:C-friedo-bacchar-7-en-3β-ol (9), and 4α-fluoroshionan-3β-ol (10), besides previously reported dihydrobaccharis oxide (1), while the reaction in the solvents such as nitromethane, benzene, toluene, hexane, and acetonitrile gave no 1. In the reaction in THF at room temperature, the D:B-friedo-type products (7 and 8) were formed predominantly. The rearrangement in solvents with low nucleophilicity proceeded up to C/D rings; e.g. the reaction in nitromethane at room temperature yielded bacchar-12-en-3β-ol (2) and D:C-friedo-bacchar-8-en-3β-ol (11). The reaction product ratio in the same reaction in various solvents are listed in TABLE.

It has been reported that dihydrobaccharis oxide (1)[1] suffers rearrangement to give bacchar-12-en-3β-ol (2)[1b] on treatment with BF_3-Et_2O in benzene at room temperature.[1b] We previously described a conversion of 3β,4β-epoxyshionane (3) into 1 and 2 (trace amount) by treatment with BF_3-Et_2O in ether at - 15 °C.[2,3] The same treatment of 3α,4α-epoxyshionane (4) in benzene at room temperature yielded D:B-friedo-bacchar-5(10)-en-3α-ol (5) and bacchar-12-en-3α-ol (6);[4] this correlates a shionane skeleton with a baccharane framework. We wish to report solvent effect on a rearrangement of 3.

3β,4β-Epoxyshionane (3)[2,4] was treated with BF_3-Et_2O in ether at - 30 °C. A mixture of products was separated by silica gel column and thin layer chromatography, and by high performance liquid chromatography (HPLC) to give dihydrobaccharis oxide (1)[1b] and four products, which were now shown to be D:B-friedo-bacchar-5-en-3β-ol (7), D:B-friedo-bacchar-5(10)-en-3β-ol (8), D:C-friedo-bacchar-7-en-3β-ol (9), and 4α-fluoroshionan-3β-ol (10) (*vide infra* for characterizations of the latter compounds (7-10)); under these conditions 2 was not detected.

Solvent effect on the backbone rearrangement of 3 was then examined. 3β,4β-Epoxyshionane (3; 1-3 mg) dissolved in a solvent (2-10 ml) was treated with BF_3-Et_2O (2 drops) at room temperature or at - 5 °C. After the usual treatment, the reaction mixture was extracted with ether to give a residue, which was subjected to examination by HPLC. The results are summarized in TABLE. The formation of



D:B-friedo-bacchar-8-en-3β-ol (11)(vide infra) and bacchar-12-en-3β-ol (2),[1b] besides the products (7-10, and 1) described above, was observed.

An attack of BF_3-Et_2O to an oxygen atom of 3 gives rise to the cationic center at C-4. The subsequent 1,2-shifts of methyl group(s) and hydrogen atom(s) lead to cations in various rearrangement stages, which after deprotonation afford the rearranged alcohols (2, 7-9, and 11). Dihydrobaccharis oxide (1) can be derived from a cation (12) by an attack of an oxygen atom at C-3 to the cationic center at C-10. It was shown that the rearrangement in solvents such as ether, THF, and dimethoxyethane (DME), which are able to coordinate with a cation, was interrupted in early stages; e.g. D:B-friedo-type alcohols (7 and 8) were formed preferentially in the rearrangement in THF and DME (vide infra for the reaction in ether). The rearrangement in the solvents with low nucleophilicity was effected up to C/D rings to yield bacchar-12-en-3β-ol (2), as the cationic center survives longer in these solvents (TABLE); e.g. the reaction in CH_3NO_2 at room temperature gave 2 (main product) and 11.

The formation of dihydrobaccharis oxide (1), together with the other reaction products, was observed in the reaction of 3 in ether and DME, while 1 was not produced in the reaction in nitromethane, benzene, toluene, hexane, acetonitrile, and in THF. The same treatment of 1 with BF_3-Et_2O in ether at a temperature range between -40 and 0 °C resulted in no initiation of the reaction.[5] No intermediacy of 1 was therefore suggested for the formation of the rearranged alcohols (7-9) in the reaction of 3 in ether at -30 and -5 °C (TABLE).

TABLE. Relative Amount Ratios of the Products in the Reaction of 3 with BF_3-Et_2O.[a)]

Solvents	Temp. (°C)	Time (min)	Products 10	1	7 (5-ene)	8 (5(10)-ene)	11 (8-ene)	9 (7-ene)	2 (12-ene)
CH_3NO_2	r.t.[b)]	5	0	0	0	0	30	0	70
CH_3NO_2	- 5	15	0	0	trace	0	35	30	35
Benzene	r.t.	5	0	0	15	20	20	15	30
Toluene	r.t.	5	0	0	10	15	25	15	35
Toluene	- 5	15	0	0	10	10	25	20	35
Hexane	r.t.	5	0	0	25	25	20	5	25
Hexane	- 5	5	0	0	25	25	15	25	10
CH_3CN	r.t.	5	0	0	15	35	25	15	10
CH_3CN	- 5	10	0	0	15	50	20	15	trace
Ether	r.t.	5	40	25	5	15	0	15	trace
Ether	- 5	50	30	25	10	20	0	15	trace
Ether	- 30	60	10	25	20	15	0	30	0
Ether[c)]	- 30	60	10	17	18	15	0	15	0
DME	r.t.	5	0	15	30	40	0	15	0
DME	- 5	20	0	15	30	30	0	25	0
THF	r.t.	5	0	0	45	50	0	5	0
THF[d)]	- 5	5	0	0	10	10	0	0	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 a RI detector; column: μ-PORASIL 1/8 (inch) X 1 (foot); solvent system: 1 or 10 % ether-n-hexane; flow rate: 1.0 or 1.2 ml/min; pressure: about 500 psi. b) Room temperature (r.t.) refers to a temperature range between 20 and 28 °C. c) Yields in this line are expressed as isolation yields (in %). d) The epoxide (3) was recovered in about 80 % yield.

Characterization of the products (7-11): D:B-friedo-bacchar-5-en-3β-ol (7), $C_{30}H_{52}O$,[6)] mp 124-125 °C, showed the following spectral data: IR (KBr) 3450, 1630 1100, 830, and 820 cm^{-1}; PMR ($CDCl_3$) δ 3.47 (1H, t-like, $W_{1/2}$= 6 Hz; $C_{(3\alpha)}$-H) and 5.62 (1H,m; $C_{(6)}$-H); MS m/e 428 (relative intensity: 8; M^+), 276 (39), 261 (100), and 152 (21). Acetylation of 7 yielded the corresponding acetate, which was oxidized with SeO_2 in acetic acid to give the known heteroannular diene (13).[4a)]

D:B-Friedo-bacchar-5(10)-en-3β-ol (8), mp 142-143 °C, proved to be identical (mp, mixed mp, IR, PMR, and MS) with an authentic sample (8).[7)]

D:C-Friedo-bacchar-7-en-3β-ol (9), mp 136.5-137.5 °C; IR (liquid) 3350, 1630, 1035, and 820 cm^{-1}; PMR ($CDCl_3$) 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); MS m/e 428 (25; M^+), 413 (100), and 247 (14).[8)] Found: 428.4000 (by high resolution MS). Calcd for $C_{30}H_{52}O$: 428.4015. Acetylation of 9 gave an acetate (14), which was oxidized with t-butyl chromate in benzene to afford an α,β-unsaturated ketone (15), an oil, IR (liquid) 1730, 1660, 1610, and 1245 cm^{-1}; UV λ_{max}^{EtOH} 248 nm (ε 12000); PMR ($CDCl_3$) δ 2.17 (s; $C_{(5\alpha)}$-H) and 5.81 (d, $J_{7,9\alpha}$= 2.4 Hz; $C_{(7)}$-H).[9)] Found: 484.3902 (by

high resolution MS). Calcd for $C_{32}H_{52}O_3$: 484.3913. Hydrogen chloride (gas) was passed through a solution of 14 in chloroform at 0 °C (5 min). The product was hydrolyzed with 5 % KOH-MeOH at 60 °C to give the 8-ene (11) (vide infra). Treatment of 14 with hydrochloric acid in acetic acid at 60 °C (19 hr), followed by alkaline hydrolysis gave the known 2[1b] together with 11.

4α-Fluoroshionan-3β-ol (10), $C_{30}H_{53}OF$[6], mp 174-175 °C, IR (KBr) 3450 cm^{-1}; PMR ($CDCl_3$) 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); MS m/e 448 (11; M^+), 428 (18;$(M-HF)^+$), and 95 (100). In the PMR measurements using $Eu(fod)_3$-d_{27} as a shift reagent, the $C_{(4\beta)}$-CH_3 signals suffered a considerable downfield shift and were observed as a doublet (J = 23 Hz; CH_3-C-F). When treated with KOH in MeOH under reflux, the 3β,4β-epoxide (4) was formed. The formation of a fluorohydrin in the reaction of an epoxide with boron trifluoride is often encountered.[10] A 4α-fluoro-configuration was suggested for 4 based on mechanistic considerations[10] and the spectral data described above.

D:B-Friedo-bacchar-8-en-3β-ol (11), an oil, IR (liquid) 3400 cm^{-1}; PMR ($CDCl_3$) δ 3.28 (1H, m; $C_{(3\alpha)}$-H) (the absence of olefinic proton was observed); MS m/e 428 (29; M^+), 413 (100), and 247 (13).[8] Found: 428.4018 (by high resolution MS). Calcd for $C_{30}H_{52}O$: 428.4015.

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