

(Received July 12, 1977)

1

2

3

4 5(10)-ene

5 5-ene

6 18 β -H

7 R=H

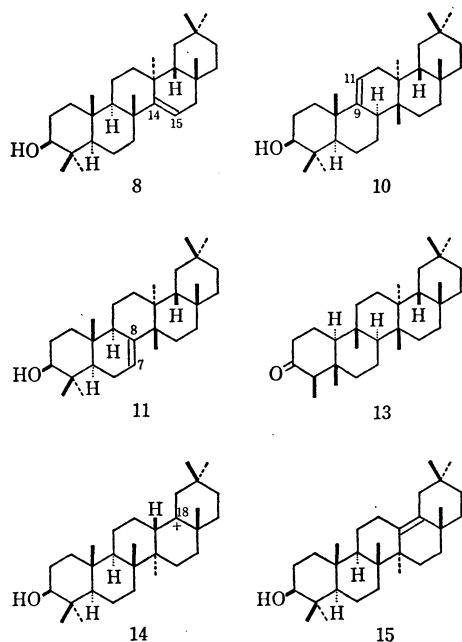
9 18 α -H

12 R=CH₃

TABLE 1. RELATIVE AMOUNT RATIOS OF THE PRODUCTS IN THE REACTION OF **2** WITH BORON TRIFLUORIDE ETHERATE^{a)}

Solvents	Temp (°C)	Time (min)	2	12	3	1	5 (5-ene)	4 5(10)-ene	6^{b)} (12-ene)	7^{b)} (18-ene)
Toluene	r.t. ^{c)}	10	0	5	0	0	10	15	25	45
Toluene	-5	10	0	5	0	0	10	10	30	45
Benzene	r.t.	10	0	5	0	0	15	15	25	40
CH ₂ Cl ₂	r.t.	20	0	0	0	0	20	10	30	40
CH ₂ Cl ₂	-5	20	0	0	0	0	30	5	25	40
Hexane	r.t.	20	0	5	0	0	15	10	30	40
Hexane	-5	20	0	5	0	25	20	15	15	20
Cyclohexane	r.t.	20	0	15	0	0	10	40	15	20
CH ₃ CN	r.t.	20	0	20	0	0	15	45	10	10
CH ₃ CN	-5	20	0	15	0	0	15	50	10	10
Ether	r.t.	20	0	5	60	15	5	15	trace	trace
Ether	-5	60	0	5	40	15	5	35	trace	trace
DME	r.t.	20	0	0	25	15	15	45	trace	trace
DME	-5	20	0	0	25	10	15	50	trace	trace
THF	r.t.	70	10	5	35	0	10	40	0	0
THF	-5	70	75	0	10	0	5	10	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 an RI detector; column: μ -PORASIL 1/8 (inch) $\times$ 1 (foot); solvent system: 10% ether-hexane; flow rate: 0.8 ml/min; pressure: *ca.* 450 psi. Even if HPLC analyses were carried out under these conditions, the retention times were variable. Mean values of their retention times were 5.1, 5.7, 6.9, 13.2, 14.5, 19.3, 21.2, and 21.8 min for **1**, **2**, **12**, **3**, **5**, **4**, **7**, and **6**, respectively. b) Errors are relatively large owing to the proximity of both retention times. c) Room temperature (r.t.) refers to a temperature range between 20 and 28 °C.



dichloromethane *etc.*) proceeded up to D/E rings to give germanicol (**7**; main product) and β -amyrin (**6**), besides **4** and **5**, as the cationic center survives longer in these solvents. Germanicol (**7**) could be derived from a cation (**14**; or its equivalent species);¹⁵⁾ olean-13(18)-en-3 β -ol (**15**) which might be also derived from **14** was not detectable in the reaction mixture. These results (Table 1) shown above are parallel to those observed for the solvent effects on the reaction of 3 β ,4 β -epoxyshionane.⁴⁾

Driving force to provoke backbone rearrangement in the rigid polycyclic ring is considered to be a release¹⁶⁾ of intercylic tension due to 1,3-diaxial interactions among the alkyl substituents (especially between the side chain and the 13 α -methyl group in shionane series) and due to *cis*-fused D/E rings (in friedelane series). Thus, the acid-catalyzed backbone rearrangement of friedelane derivatives proceeds from ring A towards ring E, and constitutes a reversal of the biogenesis¹⁷⁾ of friedelin (**13**) from β -amyrin-type intermediate.¹⁵⁾ In the rearrangement of 3 β ,4 β -epoxyshionane the formation of D: C-friedo-bacchar-7-en-3 β -ol and D: C-friedo-bacchar-8-en-3 β -ol was observed,⁴⁾ while the corresponding 7- and 8-enes were undetected in the product mixture from **2**. This is considered to be a structure difference between the two skeletons of friedelane and shionane. The acid-catalyzed backbone rearrangements hitherto reported for derivatives of friedelane,^{2,3,18)} alnusane (glutinane),¹⁹⁾ multiflorane,²⁰⁾ and of taraxane²¹⁾ are limited to proceed up to C/D rings. Germanicol is the first example of product in which the backbone rearrangement of friedelane-oleanane-type effected up to E-ring.

Experimental

General procedures and preparation of 3 β ,4 β -epoxyfriedelane (**2**) were the same as described in a previous paper.³⁾

Isolation and Characterization of Germanicol (7). A solution of 3 β ,4 β -epoxyfriedelane³⁾ (**2**; 175 mg) in anhydrous benzene (150 ml) was treated with boron trifluoride etherate (1 ml) at room temperature for 10 min and usual work-up gave a residue (*ca.* 170 mg). The residue was shown by HPLC examination to consist of germanicol¹⁵⁾ (**7**; 45%), D: B-friedo-

olean-5(10)-en-3 β -ol^{3,19}) (**4**; 15%), D: B-friedo-olean-5-en-3 β -ol^{3,19}) (**5**; 15%), and β -amyrin³) (**6**; 25%). This residue was dissolved in benzene, passed through a column of silica gel (30 g), and eluted with the same solvent (each fraction 50 ml). Fractions 6–14, containing β -amyrin (**6**) and germanicol (**7**), were combined (ca. 133 mg) and subjected to preparative HPLC separation to afford about 30 mg of germanicol (**7**). The isolation yield of germanicol (**7**) was very poor, because the separation of **6** and **7** by HPLC was carried out with much difficulty owing to the proximity of their retention times (21.2 and 21.8 min for **7** and **6**, respectively). Recrystallization from chloroform-methanol gave pure germanicol (**7**; 10 mg), mp 177–178.5 °C, (lit. 176–177 °C,^{5a}) 173–175 °C,^{5b}) 179 °C,^{5c}) 176.5–177 °C,^{5d}) 180 °C,^{5e}) and synthetic *dl*-germanicol, 220–223 °C,^{5f}); IR (KBr) 3450, 1630, and 840 cm⁻¹; NMR (CDCl₃) δ 0.74, 0.78, 0.89, 0.98, 1.02, 1.09 (each 3H, s, *t*-Me), 0.94 (6H, s, 2 $\times$ *t*-Me), 3.20 (1H, dd, $J_{2\beta,3\alpha}=10$ and $J_{2\alpha,3\alpha}=5$ Hz, C_(3 α)-H), and 4.85 (1H, d, $J=1.5$ Hz, C₍₁₉₎-H); MS *m/e* (%) 426 (M⁺; 50), 411 (31), 204 (100), 189 (83), and 177 (83).

Methylation of Germanicol (7). Potassium (100 mg) was added to a solution of germanicol (**7**; 5.7 mg) in anhydrous benzene (10 ml) and the mixture was refluxed for 2 h under a nitrogen atmosphere. A solution of methyl iodide (2 ml) in benzene (10 ml) was added and heating was continued for 4 h under reflux. After addition of methanol (2 ml) and benzene (10 ml), the organic solution was washed with water, 2M hydrochloric acid, and then with brine, dried over magnesium sulfate, and evaporated to afford a residue (7 mg). The residue was crystallized from acetone-benzene to give miliacin (**8**; 2.7 mg), mp 280–281.5 °C, (lit. 283 °C¹⁴); IR (KBr) 1635, 1180, 1110, 860, and 850 cm⁻¹; NMR (CDCl₃) δ 0.76 (6H, s, 2 $\times$ *t*-Me), 0.89, 1.02, 1.08 (each 3H, s, *t*-Me), 0.95 (9H, s, 3 $\times$ *t*-Me), 3.35 (3H, s, -OMe), and 4.85 (1H, d, $J=1.5$ Hz, C₍₁₉₎-H); MS *m/e* (%) 440 (M⁺; 44), 425 (23), 393 (5), 204 (100), 189 (75), and 177 (63). Identification of this compound with an authentic sample (mp 282.5–283 °C) of miliacin¹⁴) was effected on mixed mp (280–283 °C), TLC, IR, NMR, and on mass spectra.

Reaction of 3 β ,4 β -Epoxyfriedelane (2) with Boron Trifluoride Etherate in Various Solvents. Examination of the Products by HPLC. 3 β ,4 β -Epoxyfriedelane (**2**; 1–3 mg) dissolved in a solvent (2–10 ml) was treated with boron trifluoride etherate (2 drops) at -5 °C or at room temperature. After usual treatment, the reaction mixture was extracted with ether to give a residue on evaporation of the solvent. The residue was subjected to examination by HPLC. The results are listed in Table 1. Authentic samples (**1**, **3–6**, and **12**) used for an identification of the products are the compounds obtained in the previous work.³)

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