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A Conversion of 4α-Bromoshionan-3-one into D: B-Friedo-bacchara-1,5(10)-dien-3-one and A Preparation of D: B-Friedo-bacchar-5(10)-en-3-one

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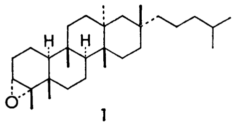
Synopsis. A mixture of D: B-friedo-bacchar-5(10)-en-3-one (**2**) and D: B-friedo-bacchar-5-en-3-one (**4**), prepared from 4α-bromoshionan-3-one (**3**) by the known procedures, was converted into a mixture of 2ξ-bromo-D: B-friedobacchar-5(10)-en-3-one (**6**) and 2ξ-bromo-D: B-friedo-bacchar-5-en-3-one (**7**) by bromination with pyridinium tribromide. The mixture (**6** and **7**) was subjected to dehydrobromination to give D: B-friedo-bacchara-1,5(10)-dien-3-one (**5**). Hydrogenation of the dienone (**5**) gave D: B-friedo-bacchar-5(10)-en-3-one (**2**).

In connection with studies on a backbone rearrangement of 3α,4α-epoxyshionane (**1**),[1] a pure sample of D: B-friedo-bacchar-5(10)-en-3-one (**2**) was required for identification of rearrangement products. It has been reported that 4α-bromoshionan-3-one (**3**) was treated with silver acetate to give a mixture[2] of D: B-friedo-bacchar-5(10)-en-3-one (**2**) and D: B-friedo-bacchar-5-en-3-one (**4**) and that a treatment of the mixture (**2** and **4**) in acetic acid with hydrochloric acid at 100 °C resulted in an isomerization of a double bond in **4** to give mainly **2** (mp 78—80 °C).[2] However, the 5(10)-en-3-one (**2**) thus prepared was found to be always contaminated with some amounts of **4**. An attempt to separate the the mixture (**2** and **4**) by chromatography under various conditions was hardly successful.

We now wish to report a synthesis of D: B-friedo-bacchara-1,5(10)-dien-3-one (**5**) and a preparation of pure D: B-friedo-bacchar-5(10)-en-3-one (**2**) from **5**.

Treatment of 4α-bromoshionan-3-one (**3**)[2] with silver acetate gave a mixture (mp 81—82 °C) of **2** and **4** in a ratio of about 1 : 1. Signals due to an olefinic proton of **4** appeared at δ 5.70 as a broad multiplet with an integrated intensity due to about a half proton. Then the mixture (**2** and **4**) was brominated with pyridinium tribromide in acetic acid[3,4] to yield a mixture of 2ξ-bromo-D: B-friedo-bacchar-5(10)-en-3-one (**6**) and 2ξ-bromo-D: B-friedo-bacchar-5-en-3-one (**7**) as white crystals, mp 136—137 °C, which showed PMR signals at δ 4.57—5.00 (1H, m; $C_{(2)}$-H) and 5.75 (*ca.* 0.5H, br; $C_{(6)}$-H of **7**). In the mass spectrum the molecular ion peaks appeared at *m/e* 506 and *m/e* 504. The mixture (**6** and **7**) was dehydrobrominated with hexamethylphosphoric triamide[5] to give D: B-friedo-bacchara-1,5-(10)-dien-3-one (**5**). The conjugated dienone (**5**) was a yellow oil and showed a characteristic ultra violet absorption maximum at 324 nm (ε 5300) and PMR signals due to olefinic protons at δ 5.98 (1H, d, J=10 Hz) and 7.12 (1H, d, J=10 Hz).

Finally, the dienone (**5**) was hydrogenated in the presence of palladium-charcoal to afford pure D: B-friedo-bacchar-5(10)-en-3-one (**2**), mp 84—84.5 °C. No other enone such as the 5-en-3-one (**4**) was formed. D: B-Friedo-bacchar-5(10)-en-3β-ol (**8**)[2] free from its 5-en-3β-ol isomer was also prepared by reduction of pure **2** with lithium aluminium hydride.



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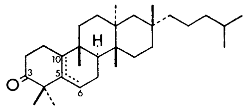
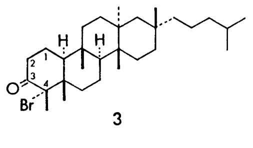


2; 5(10)-ene
4; 5-ene



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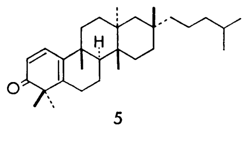

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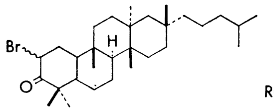
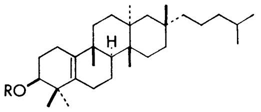


6; 5(10)-ene
7; 5-ene



8; R=H
9; R=Ac

Experimental

IR spectra were measured on a Hitachi EPI-G2 spectrometer. UV spectra were measured using a Hitachi EPS-2 spectrometer. 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. 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.

Treatment of 4α-Bromoshionan-3-one (3) with Silver Acetate. 4α-Bromoshionan-3-one[2] (**3**; mp 122—123 °C; 2.62 g) in ether (600 ml) was added to a solution of silver acetate (2.63 g) in acetic acid (1 l) and water (60 ml). The mixture was heated, concentrated until the vapor temperature reached to 110 °C and then refluxed for 2 h. The reaction mixture, after removal of precipitates, was evaporated under reduced pressure and the residue was extracted with ether. The ethereal layer was washed with water, 10% aqueous sodium carbonate solution and then with brine, and dried over sodium sulfate. On evaporation, an oily residue (2.31 g) was obtained, which was subjected to separation by silica gel (150 g) column chromatography using benzene as an eluent to give an oil (1.23 g). This was crystallized from dichloromethane–methanol to afford a mixture (672 mg) of D: B-friedo-bacchar-5(10)-en-3-one (**2**) and D: B-friedo-bacchar-5-en-3-one (**4**), mp 81—82 °C (lit,[2] 81—81.5 °C); IR (KBr) 1710 and 825 cm^{-1}; PMR (60 MHz, $CDCl_3$) δ 5.70 (*ca.* 0.5H, br).

Bromination of the Mixture of D: B-Friedo-bacchar-5(10)-en-3-one (2) and D: B-Friedo-bacchar-5-en-3-one (4). A mixture (3.62 g) of the enones (**2** and **4**) in acetic acid (100 ml) was treated at 60 °C with pyridinium tribromide (4.53 g) for 15 min. The brownish solution, after removal of the solvent under reduced pressure, was extracted with ether. The ethereal extract was washed with water, 10% aqueous sodium carbonate solution, and with brine, and then dried over sodium sulfate. The solvent was removed and the residue was dissolved in petroleum ether. The solution was passed through a column of silica gel (450 g). Elution with a mixture of petroleum ether–benzene (2: 1 and then 1: 1) gave a mixture (1.75 g) of 2ξ-bromo-D: B-friedo-bacchar-5(10)-en-3-one (**6**) and 2ξ-bromo-D: B-friedo-bacchar-5-en-3-one (**7**) as an oil, which was crystallized from dichloromethane–methanol to give white crystals (1.22 g), mp 136—137 °C; IR (KBr) 1720, 760, 655, and 630 cm^{-1}; PMR (60 MHz, $CDCl_3$) δ 4.57—5.00 (1H, m) and 5.75 (*ca.* 0.5H, br); mass spectrum *m/e* 506, 504 (M$^+$; $C_{30}H_{49}OBr$), and 261 (base peak).

Dehydrobromination of the Mixture of 2ξ-Bromo-D: B-friedo-bacchar-5(10)-en-3-one (6) and 2ξ-Bromo-D: B-friedo-bacchar-5-en-3-one (7). A mixture (64 mg) of the bromo-derivatives (**6** and **7**) was dissolved in freshly distilled hexamethylphosphoric triamide (5 ml) and the solution was heated at 130—140 °C for 10 h under a nitrogen atmosphere. The reaction mixture, after cooling, was poured into ice water, extracted with petroleum ether. The organic layer was washed with water, 2M hydrochloric acid, 20% aqueous sodium carbonate solution, and with brine and then dried over sodium sulfate. The residue, after removal of the solvent, was dissolved in a mixture of chloroform and benzene (1: 1), passed through a column of silica gel (100 g) and eluted with the same solvent mixture to give D: B-friedo-bacchara-1,5(10)-dien-3-one (**5**; 11 mg), a yellow oil, IR (liquid) 1655 and 1620 cm^{-1}; UV $\lambda_{\max}^{\mathrm{EtOH}}$ 324 nm (ε 5300); PMR (100 MHz, $CDCl_3$) δ 5.98 (1H, d, J=10 Hz) and 7.12 (1H, d, J=10 Hz); molecular weight (by high resolution mass spectrometry) Found: 424.3642. Calcd for $C_{30}H_{48}O$: 424.3705; mass spectrum *m/e* 424 (M$^+$) and 203 (base peak).

Hydrogenation of D: B-Friedo-bacchara-1,5(10)-dien-3-one (5). The dienone (**5**; 11 mg) in ethanol (5 ml) was hydrogenated in the presence of palladium–charcoal (10%, 2 mg) for 3 h. A yellow color of the solution faded and finally a colorless solution was obtained, which on filtration followed by evaporation, gave a colorless oil. The oil was subjected to separation by preparative tlc (SiO_2, 0.25 mm in thickness, developed with benzene) to give a colorless oil (5 mg), which was crystallized from methanol to give D: B-friedo-bacchar-5(10)-en-3-one (**2**) as fine needles, mp 84—84.5 °C (lit,[2] mp 78—80 °C); IR (KBr) 1715 cm^{-1}; PMR (60 MHz, $CDCl_3$) δ 2.40 (2H, m), no signal due to olefinic proton; mass spectrum *m/e* 426 (M$^+$; $C_{30}H_{50}O$) and 109 (base peak).

Reduction of D: B-Friedo-bacchar-5(10)-en-3-one (2) with Lithium Aluminium Hydride. To a solution of D: B-friedo-bacchar-5(10)-en-3-one (**2**; 37 mg), obtained by the above procedure, in ether (5 ml) was added lithium aluminium hydride (in excess), and the reaction mixture was allowed to stand overnight. After dilution with additional ether, the solution was washed with 1M hydrochloric acid, 5% aqueous sodium hydrogen carbonate solution and with brine, and then dried over sodium sulfate. On removal of the solvent, an oily residue was obtained, which gave a major spot with a smaller R_f value accompanied by a minor spot due to 3α-isomer on tlc developed with chloroform.

The major product was separated by preparative tlc developed with chloroform to afford D: B-friedo-bacchar-5(10)-en-3β-ol (**8**), mp 141.5—142 °C (lit,[2] mp 140.5—141 °C); IR (Nujol) 3350, 1065, 1040, 1025, and 975 cm^{-1}; PMR (60 MHz, $CDCl_3$) δ 3.42 (1H, dd, J=5 and 10 Hz), no signal due to olefinic proton; mass spectrum *m/e* 428 (M$^+$; $C_{30}H_{52}O$) and 135 (base peak).

Acetylation of D: B-Friedo-bacchar-5(10)-en-3β-ol (8). D: B-Friedo-bacchar-5(10)-en-3β-ol (**8**; 23 mg) in pyridine (0.2 ml) was treated with acetic anhydride (0.1 ml), and was kept at room temperature overnight. Usual work-up and crystallization from chloroform–methanol gave D: B-friedo-bacchar-5(10)-en-3β-yl acetate (**9**; 18 mg), mp 146.5—149 °C (lit,[2] mp 148.5—149.5 °C); IR (KBr) 1730, 1250, 1110, and 975 cm^{-1}; PMR (60 MHz, $CDCl_3$) δ 2.03 (3H, $-COCH_3$), 4.64 (1H, dd, J=5 and 10 Hz), no signal due to olefinic proton.

References

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