alkenyl and hydroxymethyl protons. After a simple column chromatographic purification (silica gel) **3**[5] was isolated in 71% yield (3.16 g): $n^{27}_D$ 1.4984; IR (neat) 3300 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, $Me_4Si$) $\delta$ 1.00 (s, 6 H), 1.2–2.4 (m with peaks at 1.61, 1.71, and 2.08, 17 H), 4.15 (d, $J$ = 7 Hz, 2 H), 5.41 (t, $J$ = 7 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$, $Me_4Si$) $\delta$ 13.90, 17.23, 17.42, 25.19, 26.27 (2C), 30.46, 32.64, 37.59, 37.78, 56.68, 120.81, 124.75, 134.56, 137.43. The stereoisomeric purity based on the $^{13}C$ NMR spectrum was ≥98%.

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**Registry No.** **3**, 18665-81-1; **4**, 79-77-6; **5**, 17283-81-7; **6**, 36772-04-0; **8**, 73395-75-2; **9**, 110-93-0; **10**, 22842-10-0; phenylethyne, 536-74-3; 3,3-dimethyl-1-butyne, 917-92-0; cyclohexylethyne, 931-48-6; 1-octyne, 629-05-0; 2-octanone, 111-13-7; acetophenone, 98-86-2; pinacolone, 75-97-8; cyclohexyl methyl ketone, 823-76-7.

## Stereochemical Course of the Catalytic Reduction and of the Acidic Isomerization of 14β Steroids. Synthesis of $\Delta^8$-14β and 8α,9α,14β Steroids

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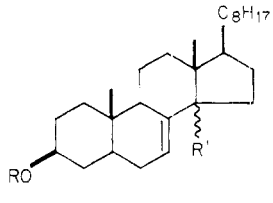
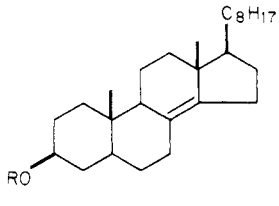
It is well-known[1b] that the $\Delta^7$ double bond in the normal steroid series is isomerized either under hydrogenation conditions or by acid to the 8(14) position. Indeed, treatment of 3β-(acetyloxy)-5α-cholest-7-ene (**1a**) with

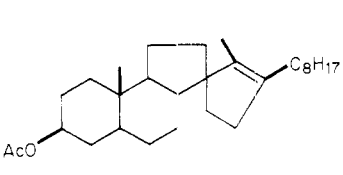



**1a**, R = Ac; R′ = α-H
**b**, R = H; R′ = α-H
**c**, R = H; R′ = β-H
**d**, R = Ac; R′ = β-H

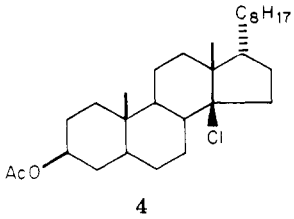



**2a**, R = Ac
**b**, R = H

$BF_3$·$OEt_2$ or toluene-4-sulfonic acid produces at first 3β-(acetyloxy)-5α-cholest-8(14)-ene (**2a**) and as the final product the backbone-rearranged steroid 3β-(acetyloxy)-12,14α-cyclo-12,13-seco-5α-cholest-13(17)-ene (**3**).[2]




**3**



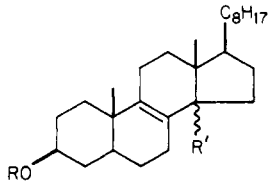

**4**

**Table I. $^{13}C$ NMR Chemical Shifts[a] for 3β-(Acetyloxy)-5α,14β-cholest-7- and -8-ene (1d and 5d) and 5α,8β,14β-Cholestan-3β-ol (6b)**

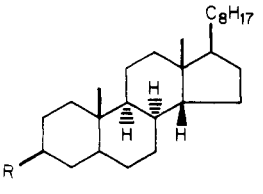
| carbon | 1d | 5d | 6b |
|---|---|---|---|
| 1 | 36.5 | 35.4[b] | 38.0 |
| 2 | 27.0[b] | 27.4 | 30.9 |
| 3 | 73.4 | 73.5 | 71.3 |
| 4 | 32.7 | 33.9 | 38.0 |
| 5 | 39.8 | 41.3 | 44.9 |
| 6 | 30.0 | 30.2 | 28.0 |
| 7 | 120.6 | 30.2 | 30.1 |
| 8 | 139.1 | 130.5 | 37.6 |
| 9 | 45.2 | 134.9 | 45.6 |
| 10 | 34.0 | 36.1 | 36.7 |
| 11 | 21.5 | 20.7 | 22.5 |
| 12 | 33.7 | 35.6[b] | 36.4 |
| 13 | 42.6 | 41.3 | 42.8 |
| 14 | 55.7 | 51.0 | 47.9[b] |
| 15 | 22.6 | 25.4 | 25.3 |
| 16 | 27.5[b] | 28.3 | 27.8 |
| 17 | 56.5 | 54.0 | 53.6[b] |
| 18 | 20.8 | 23.5 | 20.2 |
| 19 | 12.4 | 17.3 | 15.1 |
| 20 | 34.1 | 33.5 | 33.4 |
| 21 | 20.0 | 19.8 | 19.8 |
| 22 | 33.8 | 34.3 | 34.8 |
| 23 | 25.0 | 24.5 | 24.2 |
| 24 | 39.6 | 39.5 | 39.5 |
| 25 | 28.0 | 27.9 | 27.8 |
| 26 | 22.6 | 22.5 | 22.8 |
| 27 | 22.7 | 22.7 | 22.8 |
| $CH_3$ (Ac) | 21.5 | 21.4 | |
| C=O (Ac) | 170.4 | 170.3 | |

[a] In parts per million relative to $Me_4Si$. [b] These values can be reversed in any vertical column.

The action of hydrogen chloride at −60 °C on **1a** affords 3β-(acetyloxy)-14-chloro-5α,14β,17β*H*-cholestane (**4**) probably[3,4] via **3**. On the other hand 5α-cholest-7-en-3β-ol (**1b**) is reversibly isomerized to 5α-cholest-8-en-3β-ol (**5b**)




**5a**, R = Ac; R′ = α-H
**b**, R = H; R′ = α-H
**c**, R = H; R′ = β-H
**d**, R = Ac; R′ = β-H




**6a**, R = H
**b**, R = OH
**c**, R = OAc
**d**, R = OTos

by rat liver microsomal enzymes,[5] the equilibrium being almost completely shifted to the $\Delta^7$ isomer. Recently we synthesized[6] 5α,14β-cholest-7-en-3β-ol (**1c**) and demonstrated[7] that it was isomerized by rat liver enzymes into 5α-cholest-8(14)-en-3β-ol (**2b**). This result indicates that inversion of the configuration at C-14 alters the course of the enzyme-catalyzed isomerization of a $\Delta^7$ sterol. In

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continuation of our interest in steroids with unnatural stereochemistry, we report here on the action of hydrogenation catalysts and of acids on **1d** and on the hitherto unknown 3β-(acetyloxy)-5α,14β-cholest-8-ene (**5d**).

Treatment of **1d** with palladium on carbon in an atmosphere of hydrogen at room temperature and pressure gave in nearly quantitative yield the isomer **5d**. The structure of **5d** was assigned on the basis of its physicochemical properties and reactivity. The microanalysis and the mass spectrum were in accordance with the molecular formula $C_{29}H_{48}O_2$. The $^1H$ NMR spectrum did not exhibit signals in the olefinic region, and the positions of the 18- and 19-methyl signals were all within 0.02 ppm of the values calculated according to Zürcher's rules.[8] The $^{13}C$ NMR spectrum (Table I) revealed the presence of two quaternary $sp^2$ carbon atoms at δ 130.5 and 134.9 attributed to C-8 and C-9, respectively. The experimental values, the calculated values,[9] and the values reported[10] for **5a** are in agreement. The C-18 methyl resonance was at δ 23.5 in accordance with three hydrogen–carbon gauche interactions[9] due to the cis C/D ring junction. The resonances of C-6, C-7, and C-11 were within 2 ppm of the calculated values.[9] The assignments for all other nuclear carbon atoms and C-19 were supported by comparison with the corresponding carbon shifts of **5a**.[10] We also observed that the C-20 and the C-22 carbons are more shielded, whereas C-21 and the C-23 are less shielded than the same carbons in the 14α epimer **5a**.[10] Inspection of the spectrum of the 14β compound **1d** showed shifts of the same sign and of nearly identical magnitude for the C-20, C-21, C-22, and C-23 carbons with respect to the same carbons of the 14α isomer **1a**.[10]

The 8-position of the double bond in **5d** was confirmed by $RuO_4$ oxidation: a ten-membered seco diketone was obtained which was transformed by alkali treatment into an α,β-unsaturated ketone.[11] Both products showed the expected UV and IR absorptions. By use of deuterium in place of hydrogen in the isomerization of **1d** to **5d**, the incorporation of three deuterium atoms per molecule of **5d** was evidenced by the mass spectrum. Only one of them was in the allylic position 7 and possessed the α-axial configuration,[12] thus showing that only the α sides of both **1d** and **5d** face the catalyst.

In contrast to the known resistance of $\Delta^8$-unsaturated sterols in the 14α series toward catalytic hydrogenation, **5d** gave 3β-(acetyloxy)-5α,8α,14β-cholestane (**6c**) on hydrogenation in the presence of palladized charcoal for 48 h. The mass spectrum of **6c** and that of 3β-(acetyloxy)-5α,14β-cholestane[6] differed only in the relative intensities of peaks. The observed and calculated $^1H$ chemical shifts for the C-18 and C-19 methyls of **6c** agree within 0.02 ppm. The calculated values were obtained by adding the known effects of the 3β-acetoxy to the C-18 and C-19 chemical shifts of 5α,8α,14β-cholestane (**6a**).[8] Support for the assigned structure was derived from the inspection of the $^{13}C$ NMR spectrum of the corresponding alcohol **6b**. The C-18 methyl that resonates at δ 20.2 is indicative of three hydrogen–carbon gauche interactions which can originate only in a cis C/D ring juncture. In addition, the C-20, C-21, C-22, and C-23 resonances show the same anomalous values observed in compounds **1d** and **5d** having a C/D cis ring juncture. The signal at δ 15.1 for the C-19 methyl group could be reconciled[9] with either a trans–transoid–cis or a trans–cisoid–cis perhydrophenanthrene structure of ABC rings for **6b**. However, the resonances of C-7 and C-11 were in accordance only with a trans–transoid–cis perhydrophenanthrene structure of ABC rings of **6b**, ruling out the trans–cisoid–cis structure for which the calculated values differ (>5 ppm) from the observed ones. The assigned resonances of C-1 through C-5, C-10, C-15, C-16, and C-24 through C-27 are within 1.1 ppm of the corresponding carbon of 5α-cholestan-3β-ol.[10] The signals for C-6, C-8, C-9, and C-12 were within 2 ppm of the calculated values.[9] The low-field doublets at δ 47.9 and 53.6 were attributed to C-14 and C-17, respectively. The remaining singlet at δ 42.8 was assigned to C-13. Confirmation of the assigned structure of the alcohol **6b** was obtained by hydrogenolysis of the corresponding tosylate ester **6d** to the known hydrocarbon **6a**. Compound **6a** is of interest because the stereoisomers of steranes have become important factors in organic geochemistry. Preparation of **6a** from a 14β-$\Delta^7$ compound represents an alternative route to the known method of starting from a 14β-$\Delta^8$-11 ketone.[13,14]

The stereochemistry of **6c** is in accordance with that of the saturated compound obtained in the hydrogenation of 5α,14β-ergosta-7,9,22-trien-3β-ol.[15] No intermediate was isolated in that reaction. The authors did not conclude whether the 8α,9α configuration is the result of direct attack by hydrogen on the $\Delta^7$ and $\Delta^{9(11)}$ bonds from the α face or whether it is the result of attack on the $\Delta^8$ double bond formed by isomerization of $\Delta^7$. The course of our hydrogenation experiments with **1d** and **5d** shows that direct hydrogenation of a $\Delta^7$-14β compound cannot occur. In fact, although cis addition of hydrogen from the rear face of **1d** would give the observed **6c**, isomerization of the $\Delta^7$ double bond to the thermodynamically more stable $\Delta^8$ position occurs first, presumably via a π-allylic intermediate[16] formed by abstracting the α-hydrogen atom at C-9. The β configuration of the hydrogen atom at C-14 apparently precludes isomerization to the 8(14)-position. In the 14α series $\Delta^7 \rightarrow \Delta^8$ migration occurs under hydrogenation conditions when a methyl group is present at C-14 and prevents the isomerization to the 8(14)-position (cf. butyrospermol[17]). In the 14α series, however, saturation of the $\Delta^8$ double bond does not occur, probably because the intimate olefin–catalyst association required in the hydrogenation introduces large intramolecular repulsive interactions between the angular methyl groups at C-10 and C-13, as suggested for the $\Delta^{8(14)}$ isomer.[16] These interactions do not arise in the 14β series.

For the evaluation of the influence of the ring stereochemistry on the partial backbone rearrangement promoted by HCl,[3,4] the behavior of **1d** and **5d** in the presence of the acid at −60 °C was investigated. Treatment of **1d** and **5d** with HCl as described for the 14α isomer[3] affords **4** in quantitative yield. When the reaction was stopped after 20 min at −60 °C or the temperature was maintained at −30 °C for 30 min,[3] a mixture of **2a** and 3β-(acetyloxy)-5α-cholest-14-ene was obtained after base treatment. These results show that the first action of acid is isomerization of the double bond to the $\Delta^{8(14)}$ position. This

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was also supported by the isolation of **2a** and **3** in the treatment of **1d** and **5d** with either $BF_3$·$OEt_2$ or 4-toluenesulfonic acid under the reported conditions.[2] These results demonstrate that HCl-promoted partial backbone rearrangements of 14α and 14β olefins proceed in a similar manner. In both cases, the first stage is the isomerization of the double bond to the 8(14)-position. Isolation of 3β-(acetyloxy)-5α-cholest-14-ene on treatment of **1d** and **5d** with HCl at −30 °C is noteworthy because it affords the possibility of converting 14β into 14α steroids. In fact, it is well-known that hydrogenation of a $\Delta^{14}$ olefin yields a 14α saturated compound.

A literature survey showed that under acidic conditions 14α-$\Delta^8$ steroids are the most stable isomers when an A/B cis (5α,10α or 5β,10β) or an A/B trans (5β,10α) ring juncture is present in the molecule. In these cases a $\Delta^{8(14)}$ olefin is transformed into the 14β-$\Delta^8$ isomer by acids.[18,19] Now we report that a 14β-$\Delta^8$ system with a trans A/B ring junction (5α,10β) is isomerized to the 8(14)-position, thus paralleling the behavior of 14α-$\Delta^8$ olefins in the 5α,10β series.[1b]

These results show that the configuration of the A/B ring junction is a decisive factor in determining the relative stability of $\Delta^8$ and $\Delta^{8(14)}$ steroidal olefins under acidic conditions independently from C/D ring configuration.

## Experimental Section

All melting points are uncorrected. Infrared (IR) spectra were recorded for solutions in $CCl_4$. Optical rotations were measured for solutions in chloroform. The $^1H$ nuclear magnetic resonance spectra ($^1H$ NMR) were recorded on a Varian XL-100 spectrometer as chloroform-*d* solutions and are reported as δ units relative to $Me_4Si$. The $^{13}C$ nuclear magnetic resonance ($^{13}C$ NMR) spectra were recorded on a Varian XL-100 spectrometer operating at 25.2 MHz in the Fourier transform mode with 0.2–0.4 M solutions of the sterols in $CDCl_3$. Data were accumulated with a maximum of 0.68 Hz per data point. A 5-mm sample tube was utilized, and solvent-signal $CDCl_3$ was used as internal standard. The chemical shifts (δ) are expressed in parts per million relative to $Me_4Si$ and are estimated to be accurate to ±0.05 ppm [$\delta(Me_4Si) = \delta(CDCl_3) + 76.9$ ppm]. Mass spectra were recorded on a Varian 112-S by direct inlet. The progress of all reactions and column chromatographies (silica gel G–Celite, 50:50 v/v) was monitored by TLC on E. Merck silica gel $HF_{254}$ plates visualized by spraying with 70% sulfuric acid followed by heating. Gas–liquid chromatography (GLC) was performed on a Carlo Erba gas chromatograph using glass silanized columns 2 m long packed with 1% SE-30 on Gas-Chrom Q (100–120 mesh).

**3β-(Acetyloxy)-5α,14β-cholest-8-ene (5d).** A solution of 3β-(acetyloxy)-5α,14β-cholest-7-ene (**1d**, 200 mg) in diethyl ether (50 mL) was stirred with 10% palladium on carbon (100 mg) in an atmosphere of hydrogen at room temperature and pressure for 1 h to give, after column chromatography (hexane), 3β-(acetyloxy)-5α,14β-cholest-8-ene (**5d**): 170 mg; clear liquid; $[\alpha]^{22}_D$ +92°; IR 1725 $cm^{-1}$; $^1H$ NMR δ 0.93 (s, 3 H, 19-$CH_3$; calcd[8] 0.925), 0.86 (s, 3 H, 18-$CH_3$; calcd[8] 0.867); GLC (220 °C) relative retention time ($t_{rel}$) = 0.89 (relative retention time of **1d** = 1); mass spectrum, *m/e* (relative intensity) 428 ($M^+$, 40), 413 (25), 368 (13), 353 (100), 315 (16), 260 (23), 255 (24), 213 (30).

Anal. Calcd for $C_{29}H_{48}O_2$: C, 81.25; H, 11.30. Found: C, 81.3; H, 11.2.

Saponification of the acetate **5d** with methanolic potassium hydroxide gave the alcohol **5c** as an oil. The 4-bromobenzoate showed the following: mp 102–104 °C; $[\alpha]^{22}_D$ +97°.

Anal. Calcd for $C_{34}H_{49}O_2Br$: C, 71.6; H, 8.7. Found: C, 71.4; H, 8.5.

When the isomerization of **1d** to **5d** was conducted in an atmosphere of deuterium the obtained **5d** contained three deuterium atoms: mass spectrum, *m/e* (relative intensity) 431 (52), 416 (28), 371 (5), 356 (100), 318 (5), 262 (25); IR 2115 (axially attached 7α-$H^{12,16}$), 2170 $cm^{-1}$ (equatorial C–D, probably at C-6 and C-11).

When **5d** (50 mg) in carbon tetrachloride (8 mL) was treated with ruthenium tetraoxide (100 mg) at room temperature for 12 h,[11] followed by the usual workup and preparative TLC, a dicarbonyl compound was obtained: 30 mg; mass spectrum, *m/e* 460 ($M^+$); IR 1735 (OAc), 1700 $cm^{-1}$ (decane-1,6-dione). Saponification of the 3β-acetoxy group with methanolic potassium hydroxide causes also the known formation of an α,β-unsaturated ketone:[11] UV 251 nm (ε 9000); IR 3410, 1650, 1609 $cm^{-1}$.

**3β-(Acetyloxy)-5α,8α,14β-cholestane (6c).** 3β-(Acetyloxy)-5α,14β-cholest-8-ene (**5d**, 200 mg) was hydrogenated over 10% palladium on carbon (100 mg) in diethyl ether (100 mL) at room temperature and pressure for 48 h to give, after crystallization from methanol, 3β-(acetyloxy)-5α,8α,14β-cholestane (**6c**): mp 60–61 °C; $[\alpha]^{22}_D$ +34°; $^1H$ NMR δ 0.92 (s, 3 H, 18-$CH_3$ or 19-$CH_3$; calcd[8,13] 0.898), 0.88 (s, 3 H, 19-$CH_3$ or 18-$CH_3$; calcd[8,13] 0.900); GLC (220 °C) $t_{rel}$ = 1.00 ($t_{rel}$ of 3β-(acetyloxy)-5α-cholestane = 1.00); mass spectrum, *m/e* (relative intensity) 430 ($M^+$, 6), 415 (3), 370 (7), 355 (16), 315 (4), 276 (23), 262 (7), 230 (23), 216 (60), 215 (100).

Anal. Calcd for $C_{29}H_{50}O_2$: C, 81.0; H, 11.7. Found: C, 80.8; H, 11.4.

Saponification of the acetate **6c** gave the alcohol **6b**: mp 99–101 °C (from methanol); $[\alpha]^{22}_D$ +41°; $^1H$ NMR δ 0.92 (s, 3 H, 18-$CH_3$ or 19-$CH_3$; calcd[8,13] 0.898), 0.86 (s, 3 H, 19-$CH_3$ or 18-$CH_3$; calcd[8,13] 0.883).

Anal. Calcd for $C_{27}H_{48}O$: C, 83.43; H, 12.45. Found: C, 83.3; H, 12.3.

**5α,8α,14β-Cholestane (6a).** The alcohol **6b** (100 mg) in pyridine (1 mL) was treated with tosyl chloride (120 mg) in pyridine at room temperature for 24 h. The tosylate **6d** was isolated by addition of ether, extraction with dilute hydrochloric acid, evaporation, and crystallization from methanol: mp 66–67 °C; yield 100 mg. **6d** (50 mg) in THF (1 mL) was cooled at 0 °C. To this stirred solution was added lithium triethylborohydride[20] (0.1 mL of a 1 M solution in THF), and the ice bath was removed. The mixture was stirred for 4 h at 25 °C. Excess hydride was decomposed with water. The organoborane was oxidized with NaOH (3 N, 0.7 mL) and $H_2O_2$ (0.1 mL, 30%). After the usual workup 5α,8α,14β-cholestane (**6a**) (60 mg) was obtained as an oil (lit.[13] liquid): $[\alpha]^{22}_D$ +85° (lit.[13] +84°); $^1H$ NMR δ 0.89 (s, 3 H, 18-$CH_3$ or 19-$CH_3$; lit.[13] 0.89), 0.85 (s, 3 H, 19-$CH_3$ or 18-$CH_3$; lit.[13] 0.85); GLC (220 °C) $t_{rel}$ 1.00 ($t_{rel}$ of 14α-cholestane = 1.00); mass spectrum, *m/e* (relative intensity) 372 ($M^+$, 38), 357 (32), 262 (10), 259 (4), 232 (18), 219 (19), 218 (75), 217 (100), 203 (25), 175 (11), 163 (8), 151 (11), 149 (6). This mass spectrum is consistent with that reported[13] for **6a**.

**Reactions with Boron Trifluoride Diethyl Etherate.** A solution of the steroid (300 mg) in chloroform (30 mL) was treated with $BF_3$·$OEt_2$ (3 mL) for 30 min at room temperature. After the usual workup the crude residue was chromatographed. From acetates **1d** and **5d**, 3β-(acetyloxy)-12,14α-cyclo-12,13-seco-5α-cholest-13(17)-ene (**3**) was obtained as a glass (50% yield); in addition, 3β-(acetyloxy)-5α-cholest-8(14)-en-3β-ol (**2a**) (8% yield) was separated. The $^1H$ NMR and mass spectra of these compounds are consistent with those of authentic samples.[2] When the progress of the reaction was monitored by GLC/MS initial formation of **2a** was observed.

**Reactions with Toluene-4-sulfonic Acid.** The steroid (100 mg) was added to a mixture of anhydrous toluene-4-sulfonic acid (50 mg) and benzene (25 mL) and heated to reflux for 2 h. After the usual workup, the crude residue was chromatographed. The oil **3** was obtained (50% yield) accompanied by **2a** (6% yield) from both **1d** and **5d**. When the progress of the reaction was monitored by GLC/MS initial formation of **2a** was observed.

**Reaction with Hydrogen Chloride. (a) At −60 °C.** In typical experiments the acetates **1d** or **5d** (200 mg) in diethyl ether (20 mL) were treated with HCl at −60 °C for 3 h. The pressure in the reaction vessel was then lowered to about 20 mm without interrupting the cooling. The residue was poured into ice–water and extracted with diethyl ether. The organic layer was shaken with saturated $NaHCO_3$ solution, dried ($Na_2SO_4$), and evaporated

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in vacuo to give 14-chloro-5α,14β,17βH-cholestane (4; 200 mg, mp 104–106 °C) which exhibited physical and spectroscopic properties identical with those of authentic material.[3]

**(b) At −30 °C.** The acetates **1d** or **5d** (200 mg) in $CHCl_3$ (0.5 mL) were treated with HCl at −30 °C for 0.5 h. The usual workup afforded a solid which after chromatography on silica gel G–Celite–$AgNO_3$ (1:1:0.3) yielded 3β-(acetyloxy)-5α-cholest-8(14)-ene (**2a**, 35 mg) and 3β-(acetyloxy)-5α-cholest-14-ene (140 mg). Both compounds were identical with authentic samples. The same result was obtained when the reaction was conducted at −60 °C in diethyl ether for 20 min.

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**Registry No.** **1a**, 2465-00-1; **1d**, 59531-52-1; **2a**, 6562-21-6; **3**, 69224-70-0; **4**, 73465-15-3; **5c**, 73465-16-4; **5c** 4-bromobenzoate ester, 73396-47-1; **5d**, 73465-17-5; **6a**, 55123-81-4; **6b**, 73465-18-6; **6c**, 73465-19-7; **6d**, 73465-20-0; 3β-(acetyloxy)-5α-cholest-14-ene, 40446-06-8.

## Hexahydro-4,6-methanocyclopenta[*b*]pyran-2-(3*H*)-one and the Structural Proof for Brendan-4-one

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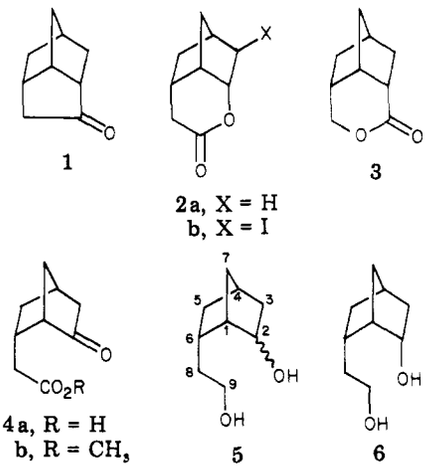
Recently Nickon and his colleagues have provided a synthesis and structural proof for brendan-4-one (**1**).[1] An important stage in the proof of structure is the Baeyer–Villiger oxidation of **1** to afford the two δ-lactones **2a** and **3** (Chart I) as a mixture, which could not be separated. Saponification of this mixture followed by acidification at 0 °C resulted in the regeneration of **3**, with **2a** being converted to the hydroxy acid. Without separation, this mixture of **3** and the hydroxy acid derived from **2a** was treated with diazomethane, oxidized with Brown's reagent and saponified. This resulted in the conversion of **2a** into the keto acid **4a**, which could now be separated from **3** and which on methylation with diazomethane afforded the keto ester **4b**, identical with authentic material. The reduction of **4b** with lithium aluminium hydride produced a crystalline diol given the structure **5**, for which the stereochemistry of the hydroxyl group at C-2 was not known but was thought to be endo as in **6**. Although other reported[1] evidence, such as the Wolff–Kishner reduction of **1** to brendane, supports the structure **1**, the above structural evidence is incomplete in view of (a) the failure to isolate **2a**, a compound which has never previously been prepared or isolated, and (b) an absence of knowledge of the C-2 stereochemistry in **5** which is needed to deduce with absolute certainty the stereochemistry of **1**. The structural proof is additionally unsatisfactory because the 60-MHz spectrum of **5** is reported[1] as δ 4.62–3.58 (m, 6), 2.57–1.66 (m, 6), and 1.45–0.78 (m, 4). Such a spectrum is inconsistent with a structure (**5**) for which only five protons in the region δ 4.62–3.58 corresponding to **CHOH** and **$CH_2$OH** would be anticipated.

We had available the iodo δ-lactone **2b**[2] and found that it could be smoothly deiodinated to the parent δ-lactone

Chart I




**2a** by using the tri-*n*-butyltin chloride plus sodium borohydride reagent of Corey and Suggs.[3] Reduction of **2a** with lithium aluminium hydride led to the diol **6** in which the stereochemistry of the hydroxyl group at C-2 is fixed as endo. The melting point of 71–72 °C for **6** compares with that of 73–74.5 °C reported[1] for **5**. The NMR spectral data at 60 MHz reported[1] for **5** are the same as those we now find for **6** with the exception that resonances in the range δ 4.65–3.58 correspond to five and not six protons. At 90 MHz the spectrum (the details of which are recorded in the Experimental Section) has less overlap and greater separation of resonances than that recorded at 60 MHz. Confirmation that the compound **5** prepared by Nickon does in fact have the structure **6** was obtained by converting **2a** into the keto ester **4b** by using the procedures employed by Nickon and then reducing **4b** with lithium aluminium hydride. The product was identical in all respects with **6** prepared by the direct reduction of **2a**, thus proving conclusively that **5** has the structure **6** in which the hydroxyl group at C-2 is endo.

The reduction of the ketonic carbonyl group in **4b** to afford **6** may be compared with the observation of Brown[4] that in the corresponding reduction of norbornan-2-one there is an 8.1:1 preference for exo hydride ion attack leading to the same preference for the production of an *endo*-hydroxyl group. The presence of the *endo*-$CH_2CO_2Me$ group at C-6 in **4b**, which is being simultaneously reduced to $CH_2CH_2OH$, results in a complete preference for exo hydride ion attack at C-2, leading to the exclusive formation of **6**.

### Experimental Section

**Hexahydro-4,6-methanocyclopenta[*b*]pyran-2(3*H*)-one (2a).** A solution of 7-*exo*-iodohexahydro-4,6-methanocyclopenta[*b*]pyran-2(3*H*)-one (**2b**; 2.78 g, 10 mmol) and tri-*n*-butyltin chloride (0.65 g, 20 mmol) in dry ethanol (200 mL) was prepared under a nitrogen atmosphere. A suspension of sodium borohydride (0.475 g, 12.5 mmol) in ethanol (50 mL) was added and the stirred mixture irradiated by a Philips 300-W ultraviolet lamp. Initially diborane gas was rapidly evolved, but this had largely ceased after 1 h when TLC analysis [30% ethyl acetate, 70% petroleum ether (bp 60–80 °C), Merck silica gel; $R_f$ 0.4 for **2b** and 0.5 for **2a**] of an aliquot of the reaction mixture showed that all the starting material (**2b**) had been consumed to afford a single product. A few drops of acetic acid were then added to the reaction mixture to destroy excess sodium borohydride, and the solvent was evaporated. The residue was dissolved in methylene chloride (100 mL) and the resultant solution washed with saturated aqueous

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