3.31 (m, 2), 4.40 (s, 1) 5.75 (td, 1, J = 11, 5 Hz), 6.14 (s, 3), 6.15 (s, 3), 6.46 (s, 3) 6.83 (dd, 1, J = 11, 4 Hz), 7.14 (s, 2), 7.71 (m, 4), 8.00 (td, 1, J = 12, 4 Hz); mass spectrum (rel intensity) 346 (52), 274 (4), 193 (24), 180 (27), 167 (51), 162 (30), 151 (100).

Anal. Calcd for $C_{19}H_{22}O_6$: C, 65.88, H, 6.40; *m/e* 346 (100), 347 (21.1), 348 (3.32). Found: C, 65.71; H, 6.36; *m/e* 346 (100), 347 (21.1), 348 (3.88).

Treatment of trimethylcatechinic acid with CH_2N_2 gave a product which was identical by tlc and ir.

Acetylation of permethylcatechinic acid with NaOAc and Ac_2O in benzene gave the acetate as a viscous oil: ir ($CHCl_3$) 1735 (s), 1660 (s), 1605 (s), 1522 (s) cm^{-1}; uv (95% EtOH) 237, 252 nm; nmr ($CDCl_3$) τ 3.25 (s, 1), 3.35 (m, 2), 4.35 (s, 1), 4.46 (m, 1), 6.15 (s, 3), 6.17 (s, 3), 6.49 (s, 3), 6.56 (m, 1), 7.14 (s, 2), 7.69 (m), 7.80–8.15 (m), 8.21 (s, 3); mass spectrum (rel intensity) 388 (26), 328 (100), 313 (7), 299 (12), 193 (46), 180 (25), 151 (60), 137 (22).

Anal. Calcd for $C_{21}H_{24}O_7$: *m/e* 388 (100), 389 (23.3), 390 (4.00). Found: *m/e* 388 (100), 385 (23.7), 390 (4.09).

Dihydropermethylcatechinic Acid (8). Permethylcatechinic acid (50 mg) was hydrogenated for 5 hr at 50 psi with 5% Pd/C (100 mg) in MeOH (30 ml). Preparative tlc (solvent B) gave 30 mg of amorphous product: ir ($CHCl_3$), 3620 (w), 3440 (w), 1647 (s), 1605 (s), 1522 cm^{-1}; uv (95% EtOH) 230, 258 nm; nmr ($CDCl_3$) τ 3.30 (m, 3), 4.55 (s, 1), 5.87 (m, 1), 6.16 (s, 3), 6.17 (s, 3), 6.55 (s, 3), 6.85 (br s), 7.45 (m), 7.9 (m), 8.65 (s, 3); mass spectrum (rel intensity) 348 (34), 193 (7), 181 (12), 179 (26), 164 (13), 151 (100), 138 (17).

Anal. Calcd for $C_{19}H_{24}O_6$: *m/e* 348 (100), 349 (21.1), 350 (3.32). Found: *m/e* 348 (100), 349 (21.1), 350 (3.35).

Acetylation with NaOAc and Ac_2O in benzene gave the diacetate as a white solid: ir ($CHCl_3$) 1732 (s), 1655 (s), 1608 (s), 1523 (s) cm^{-1}; uv (95% EtOH) 233, 255 nm; nmr ($CDCl_3$) τ 3.35 (m, 3), 4.48 (s, 1), 4.52 (m, 1), 6.14 (s, 3), 6,16 (s, 3), 6.52 (s, 3), 6.65 (m), 7.6–8.02 (m), 7.78 (s, 3), 8.17 (s, 3), 8.38 (s, 3).

Trimethyldihydrocatechinic Acid (9). Catechinic acid (400 mg) in MeOH was hydrogenated for 5 hr at 50 psi over 5% Pd/C (500 mg). The filtered reaction mixture was evaporated to dryness and then treated with excess CH_2N_2 at 4° for 3 days. Evaporation *in vacuo* gave a viscous oil which was purified by preparative tlc (solvent B) to give the major product (90 mg): ir ($CHCl_3$), 3620 (w), 3420 (w), 1649 (s), 1602 (s), 1520 (s) cm^{-1}; uv (95% EtOH) 232, 254 nm; nmr ($CDCl_3$) τ 3.42 (m, 3), 4.54 (s, 1), 5.94 (m), 6.17 (s, 3), 6.20 (s, 3), 6.34 (m), 6.54 (s, 3), 6.70 (dd, 1), 7.27 (m, 2), 7.93 (m); mass spectrum (rel intensity) 334 (55), 316 (4), 304 (8), 273 (4), 193 (10), 183 (11), 179 (15), 167 (27), 165 (28), 151 (100), 137 (81).

Anal. Calcd for $C_{18}H_{22}O_6$: *m/e* 334 (100), 335 (20.04), 336 (3.11). Found: *m/e* 334 (100), 335 (20.02), 336 (4.35).

Acetylation with Ac_2O, NaOAc, and benzene at reflux gave the diacetate as an amorphous white solid: ir ($CHCl_3$) 1738 (s), 1660 (s) 1605 (s), 1523 (s) cm^{-1}; uv (95% EtOH) 237, 252 nm; nmr ($CDCl_3$) τ 3.35 (m, 3), 4.43 (s, 1), 4.50 (m, 1), 4.80 (t, 1), 6.14 (s, 3), 6.16 (s, 3), 6.53 (s, 3), 6.65 (dd, 1), 7.06 (m, 2), 7.77 (s, 3), 8.02 (m), 8.20 (s, 3); mass spectrum (rel intensity) 418 (19), 358 (31), 298 (30), 283 (9), 266 (100), 255 (12), 251 (11), 239 (11), 214 (19), 193 (44), 180 (12), 165 (20), 151 (75), 137 (67).

Anal. Calcd for $C_{22}H_{26}O_8$: *m/e* 418 (100), 419 (24.4), 420 (4.5). Found: *m/e* 418 (100), 419 (24.7), 420 (4.6).

Acknowledgment. We thank Dr. F. W. Herrick, ITT Rayonier Inc., Shelton, Wash., for helpful discussions.

Registry No.—**2,** 154-23-4; **5,** 52484-79-4; **6,** 52358-31-3; **6** monoacetate, 52358-32-4; **7,** 52358-33-5; **7** monoacetate, 52358-34-6; **8,** 52358-35-7; **8** diacetate, 52358-36-8; **9,** 52358-37-9; **9** diacetate, 52358-38-0; trimethylisocatechinic acid, 52358-39-1; trimethylisocatechinic acid monoacetate, 52358-40-4; dihydrotrimethylisocatechinic acid, 52358-41-5; diazomethane, 334-88-3.

References and Notes

(1) H. L. Hergert, Abstracts of Papers, 161st National Meeting of the American Chemical Society, Los Angeles, Calif., March–April 1971, p 66 CELL; K. V. Sarkanen and H. L. Hergert in "Lignins," K. V. Sarkanen and C. H. Ludwig, Ed., Wiley-Interscience, New York, N.Y., 1971, pp 83–85.
(2) H. L. Hergert, L. E. Van Blaricom, J. C. Steinberg, and K. R. Gray, *Forest Prod. J.*, **15,** 485 (1965).
(3) These compounds are frequently referred to as "bark phenolic acids."
(4) H. J. Kiefer and E. F. Kurth, *Tappi,* **36,** 14 (1953); E. F. Kurth and J. E. Smith, *Pulp Paper Mag. Can.,* **55** (12), 125 (1954).
(5) W. F. Erman and W. I. Lyness, *Tappi,* **48,** 249 (1965).
(6) H. L. Hergert in "The Chemistry of Flavanoid Compounds," T. A. Geissman, Ed., Macmillan, New York, N. Y., 1962, pp 573–574.
(7) K. D. Sears and R. L. Casebier, *Phytochem.,* **4,** 1589 (1970); H. L. Hergert, Abstracts of Papers, 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, p 21D.
(8) Compare dimedone ethyl ether (1642, 1603 cm^{-1}): K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, San Francisco, Calif., 1962, p 69.
(9) A. J. Scott, "Ultraviolet Spectra of Natural Products," Macmillan, New York, N.Y., 1964, pp 69–71. Compare dimedone, 258 nm (ε 12,000), and its anion, 282.
(10) Dimedone methyl ether absorbs at τ 4.73.
(11) F. W. Lichtenthaler, *Chem. Ber.,* **96,** 2047 (1963).
(12) L. E. McCandlish and G. H. Stout, manuscript in preparation.

A Novel Synthesis of 4α- and 4β-Methylcholest-5-en-3β-ol from 6β-Bromo-4-methylcholest-4-en-3-one[1]

Furn F. Knapp, Jr., and George J. Schroepfer, Jr.*

Departments of Biochemistry and Chemistry, Rice University, Houston, Texas 77001

Received April 30, 1974

The reduction of 6β-bromo-4-methylcholest-4-en-3-one with a large excess of lithium aluminum hydride (19 equiv of H^-) in ether results in the formation of 4α-methylcholest-5-en-3β-ol in high yield (~84%). Reduction of the bromide with lithium aluminum deuteride under similar conditions gives [3α,4β-$^2H_2$]-4α-methylcholest-5-en-3β-ol. Unexpectedly, reduction of 6β-bromo-4-methylcholest-4-en-3-one with lithium aluminum hydride at a lower molar ratio (3 equiv of H^-) gave good (~31%) yields of 4β-methylcholest-5-en-3β-ol (in addition to 4α-methylcholest-5-en-3β-ol and a third compound which was not identified). The 4β-methylcholest-5-en-3β-ol formed under these conditions by reduction of the bromide with lithium aluminum deuteride was labeled in the 3α and 4α positions.

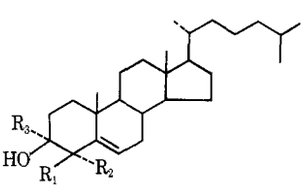
The C-4 demethylation of sterol precursors of cholesterol is an important process which has received considerable attention.[2] The initial demethylation of 4,4-dimethyl precursors has been reported to proceed with initial removal of the equatorial 4α-methyl group with subsequent inversion of the axial 4β-methyl group to the equatorial position.[3–5] We have been interested in the stereochemical fate of the C-4 hydrogen in the demethylation of 4α-monomethyl intermediates. Preliminary studies of the conversion of [2,2,4-$^3H_3$]-4α,14α-dimethylergosta-8,24(28)-dien-3β-ol into [2,2,4-$^3H_3$]-(24*R*)-24-ethylcholesta-5,22-dien-3β-ol by the Chrysophyte *Ochromonas malhamensis* have indicated that during the second demethylation the axial 4β hydrogen appears to be inverted to the equatorial 4α position.[6] We have now directed our efforts at developing a synthetic route to give a 4α-methyl-4β-tritio substrate which can be

used to study the second C-4 demethylation during cholesterol biogenesis. This paper describes our studies involving the hydride reduction of 6β-bromo-4-methylcholest-4-en-3-one.

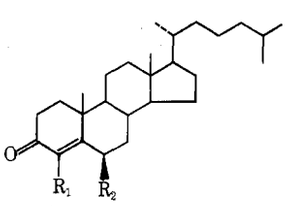
Several years ago Ireland, Wrigley, and Young[7] reported that lithium aluminum hydride reduction of 6β-chlorocholest-4-en-3β-yl benzoate yielded cholest-5-en-3β-ol. It was shown by chemical modification and infrared studies of the product formed by lithium aluminum deuteride reduction of the allylic chloride that the deuterium was stereospecifically introduced into the 4β position. These results were explained by a mechanism involving an intramolecular attack (SNi′) of hydride on the double bond at C-4 followed by double-bond rearrangement resulting in the loss of bromide ion to give [4β-^{2}H]-cholest-5-en-3β-ol. There have been no further studies, however, of the detailed mechanism of this reaction. More recently Knapp, Goad, and Goodwin[6] have found that reduction of 6β-chloro-(24*S*)-24-ethylcholesta-4,22-dien-3β-yl acetate by lithium aluminum deuteride gave [4β-^{2}H]-(24*S*)-24-ethylcholesta-5,22-dien-3β-ol. Degradation of this substance demonstrated that the isotopic hydrogen had been stereospecifically introduced into the 4β position. Collins and Hobbs[8] have reported that sodium borohydride reduction of 6β-bromocholest-4-en-3-one in diglyme gave cholesterol in high yield, although no experimental details were given. The combined results of these studies indicated that hydride reduction of 6β-bromo-4-methylcholest-4-en-3-one might provide an attractive route for the synthesis of 4α-methylcholest-5-en-3β-ol labeled with isotopic hydrogen at carbon atoms 3 and 4.

Results and Discussion

Methods that have been used successfully to deconjugate cholest-4-en-3-one (VII) proceed in only very low yields



Compd	R_1	R_2	R_3
I	H	H	H
II	H	^{2}H	H
III	H	CH_3	H
IV	CH_3	H	H
V	^{2}H	CH_3	^{2}H
VI	CH_3	^{2}H	^{2}H



Compd	R_1	R_2
VII	H	H
VIII	CH_3	H
IX	H	Br
X	CH_3	Br

when applied to the deconjugation of 4-methylcholest-4-en-3-one (VIII). For example, Birch reduction of 4-methylcholesta-3,5-dien-3-acetate, followed by hydride reduction gave the allylic alcohol, 4-methylcholest-4-en-3β-ol, demonstrating rapid reconjugation of the double bond prior to reduction of the C-3 ketone.[9] Similarly, sodium borohydride reduction of 4-methylcholesta-3,5-dien-3-acetate gave a complex mixture of which the major products are the two allylic alcohols, 4-methylcholest-4-en-3β-ol and 4-methylcholest-4-en-3α-ol. 4α-Methylcholest-5-en-3β-ol and 4β-methylcholest-5-en-3β-ol could be isolated in only low yield.[9-11] In addition, kinetically controlled protonation of the enolate anion of VIII gave only starting material.

The first step in our alternative approach to this problem involved bromination of 4-methylcholest-4-en-3-one (VIII) with *N*-bromosuccinimide to give 6β-bromo-4-methylcholest-4-en-3-one (X) in high yield.[12] Initially, we conducted the reductive rearrangement of 6β-bromo-4-methylcholest-4-en-3-one (X) with a large excess of lithium aluminum hydride (19 equiv of H^-). From the analogy of the similar hydride reduction of 6β-bromocholest-4-en-3-one (IX), we expected hydride reduction of X to proceed with the formation of 4α-methylcholest-5-en-3β-ol (III). Our results indicate that this is the case. Two minor components (<10%) of the crude reaction mixture, 4-methyl-cholest-4-en-3β-ol and 4-methylcholest-4-en-3α-ol, were inseparable from III on thin layer chromatography but could be removed by crystallization. After purification by crystallization, 4α-methylcholest-5-en-3β-ol (III), chromatographically homogeneous on thin layer and gas liquid chromatographic analysis, was obtained in high yield (~84%). Nuclear magnetic resonance (nmr) studies showed resonance compatible with an olefinic proton, the axial C-3 proton, and the secondary 4α-methyl group (d, J = 6 Hz). The latter was more easily seen in the 60-MHz spectrum by the use of the Eu(dpm)$_3$ shift reagent. Reduction of 6β-bromo-4-methylcholest-4-en-3-one (X) with lithium aluminum deuteride under the same conditions gave [3α,4β-^{2}H$_2$]-4α-methylcholest-5-en-3β-ol (V). The mass spectra of III and V were in accord with the assigned structures (see Experimental Section). The nmr spectrum of V contained a singlet for the C-4 methyl group which was more easily seen in the spectrum expanded with Eu(dpm)$_3$. No absorption due to the C-3 proton was present in the spectrum. The combined results of the nmr and mass spectral studies indicate the location of the isotopic hydrogen at C-3 and C-4. In analogy with examples cited earlier we interpret our results as compatible with an initial reduction of the C-3 ketone followed by intramolecular hydride attack with double-bond participation (SNi′) in the formation of III and V. A mechanism for this type of reaction has been suggested by Ireland, Wrigley, and Young.[7]

Unexpectedly, when the molar ratio of hydride to 6β-bromo-4-methylcholest-4-en-3-one (X) was decreased (3 equiv of H^-), it was found that 4β-methylcholest-5-en-3β-ol (IV) was formed in substantial amounts. Analysis of the crude reaction mixture by gas–liquid chromatography (glc) indicated the presence of two minor components with retention times corresponding to those of 4-methylcholest-4-en-3β-ol and 4-methylcholest-4-en-3α-ol and two major components with retention times corresponding to those of 4α-methylcholest-5-en-3β-ol (III) and 4β-methylcholest-5-en-3β-ol (IV). The former compound was partially purified by preparative thin layer chromatography (tlc) but was shown (by nmr and mass spectral (ms) studies; see Experimental Section) to be contaminated by one or more other compounds whose precise chemical nature has not been established. 4β-Methylcholest-5-en-3β-ol (IV) was isolated from the crude reaction mixture in pure form by preparative tlc and crystallization. The isolated compound showed mobilities identical with that of authentic 4β-methylcholest-5-en-3β-ol (IV) (prepared by an alternate route[13]) on tlc and glc analyses. The nmr spectrum showed the presence of an olefinic proton, the axial C-3 proton, the allylic C-4-proton, and the 4β-methyl group. The latter three-proton doublet was easily seen in the spectrum expanded with Eu(dpm)$_3$ (d, J = 8 Hz).

Assignment of the position of the C-4α proton in the spectrum of IV was confirmed by the reduction of X with a limiting amount of lithium aluminum deuteride. Purification of the material chromatographing with IV gave [3α,4α-^{2}H$_2$]-4β-methylcholest-5-en-3β-ol (VI). In the nmr spectrum of this substance the downfield methine proton

and the axial C-3 proton were not present, confirming that these two hydrogens originate from deuteride. In addition, in the spectrum of VI the C-4β methyl resonance was present as a singlet. The downfield position of the allylic C-4 proton and the C-3 proton in IV and the increased coupling of the axial C-4β methyl group must reflect considerable distortion of ring A. This distortion probably results from the large 1,3 interaction between the C-4β methyl group and the C-19 methyl group. In III this interaction is relieved and the C-4 allylic proton is evidently under the methylene envelope in the spectrum of this compound.

The formation of 4β-methylcholest-5-en-3β-ol (IV) by reduction of 6β-bromo-4-methylcholest-4-en-3-one with limiting amounts of hydride represents a unique and unexpected result. Additional detailed chemical and kinetic studies are indicated to define the precise mechanism of the reaction leading to the formation of IV under these conditions. The observed results do provide a new, simple synthetic route for the preparation of 4β-alkyl substituted Δ^5-sterols. Moreover, the results described herein provide an approach to the stereospecific introduction of isotopic hydrogen at carbon atoms 3 and 4 of 4-alkyl substituted Δ^5-3β-hydroxysterols.

Experimental Section

General. The 4-methyl-cholest-4-en-3-one was synthesized by the method of Atwater.[14] Tlc was performed on plates spread with silica gel H using chloroform as the developing solvent. For analytical purposes the plates were spread at a thickness of 0.25 mm and spot colors were detected by spraying the plate after development with molybdic acid spray followed by brief heating to 80°. For preparative experiments the plates were spread 0.50 or 1.0 mm thick and, after two developments in chloroform, the bands were visualized by spraying the plates with an acetone solution of Rhodamine 6G followed by uv irradiation. Glc was performed using a Hewlett-Packard Model 402 instrument equipped with dual flame ionization detectors. The columns were packed (6 ft × 0.25 in., o.d.) with the following phases: 1% SE-30, 1% QF-1, 3% OV-1, and 3% OV-17 on Gas-Chrom Q (100–120 mesh). The carrier gas was helium with a flow rate of 66 ml/min. Ms analyses were determined on a CEC Model 21-110 B double focusing instrument. Nmr spectra were recorded on a Perkin-Elmer HR-12 spectrometer in $CDCl_3$ solution with TMS as the internal standard. The nmr absorptions are reported as parts per million (δ) downfield from the TMS internal standard. The lanthanide shift reagent europium(III) dipivaloylmethanoate [Eu(dpm)$_3$] was purchased from Alpha Inorganics (Beverly, Mass.). Lithium aluminum hydride was purchased from Research Organic/Inorganic Chemicals (Sun Valley, Calif.). Lithium aluminum deuteride was purchased from E. Merck (Darmstadt). Authentic samples of 4-methylcholest-4-en-3α-ol and 4-methylcholest-4-en-3β-ol were prepared by hydride reduction of 4-methylcholest-4-en-3-one. An authentic sample of 4β-methylcholest-5-en-3β-ol was prepared by the method of Julia and Lavaux.[13] Melting points were recorded on a Thomas-Hoover melting point apparatus and are uncorrected. Infrared (ir) spectra were recorded on a Beckman IR-9 spectrometer using KBr pellets.

4α-Methylcholest-5-en-3β-ol (III). 4-Methylcholest-4-en-3-one (2.04 g) was refluxed with *N*-bromosuccinimide (960 mg) in CCl_4 (40 ml) for 30 min. The solution was cooled in an ice bath and the precipitated succinimide was removed by filtration. The filtrate was evaporated to dryness to give an orange gum which was dissolved in a small amount of ether. Addition of cold methanol resulted in the formation of fine needles. Recrystallization of the first and second crops gave pure 6β-bromo-4-methyl-cholest-4-en-3-one (X): 1.28 g; mp 132–133° dec (lit.[12] mp 135°); uv λ_{max} (ETOH) 262 nm (log ε 4.10) [lit.[12] λ_{max} (ETOH) 262 nm (log ε 4.11)]; ir ν_{max} (KBr) 1673 cm^{-1}; ms (rel intensity), 478 and 476 (M, 5% and 6%), 398 and 396 (100 and 75%), 397 (M − Br; 38%), 384 (12%), 283 (21%), 275 (16%), 261 (9%), 247 (24%), 243 (11%); nmr 1.48 (s, 3 H, deshielded C-19 CH_3), 1.86 (s, 3 H, C-4 CH_3), 5.45 (m, 1 H, C-6 H). The bromide (180 mg, 3 mmol) was dissolved in ether (10 ml) and added to a slurry of lithium aluminum hydride (500 mg, 53 mequiv of H$^-$) in ether (100 ml). After the mixture was stirred for 30 min, excess hydride was decomposed by the slow addition of ethyl acetate (50 ml). Hydrochloric acid (2 *N*, 50 ml) was added and the isolated organic layer was washed thoroughly with dilute sodium bicarbonate and water, dried over anhydrous sodium sulfate, and evaporated to dryness. Analysis of the crude product by glc indicated that the major component of the reaction mixture cochromatographed with authentic III. Two minor components (<10%) of the crude reaction mixture, 4-methylcholest-4-en-3β-ol and 4-methylcholest-4-en-3α-ol, were inseparable from III on tlc but could be removed by crystallization. Crystallization from ethanol–water yielded 4α-methylcholest-5-en-3β-ol in the form of fine needles (124 mg): mp 166–167° (lit.[13] mp 162–163°); uv, only end absorption; ir ν_{max} (KBr) 3440, 1064 cm^{-1}; ms (rel intensity) 400 (M, 100%), 385 (M − CH_3, 29%), 382 (M − H_2O, 38%), 367 (M − CH_3 − H_2O, 26%), 343 (8%), 331[15] (12%), 301 (7%), 287 (M − side chain, 8%), 275 (20%), 269 (M − H_2O − side chain, 9%), 261 (3%), 247 (7%), 227 (M − H_2O − side chain − 42, 8%); nmr 1.05 (s, 3 H, C-19 CH_3), 1.09 (d, 3 H, C-4 CH_3, J = 6 Hz), 3.11 (m, 3 H, C-3 H), 5.35 (m, 1 H, C-6 H). The isolated product showed a single component on tlc and on glc (on the four systems described above).

[3α,4β-$^2H_2$]-4α-Methylcholest-5-en-3β-ol (V). 6β-Bromo-4-methylcholest-4-en-3-one (X, 130 mg) was reduced with lithium aluminum deuteride (500 mg) as described above. Crystallization of the product from ethanol–water gave V as plates: mp 165–166°; ir ν_{max} (KBr) 3410, 1080 cm^{-1}; ms (rel intensity) 402 (100%), 387 (20%), 384 (43%), 369 (26%), 344 (12%), 331[15] (14%), 301 (9%), 289 (5%), 275 (29%), 271 (10%), 261 (5%), 247 (12%), 229 (10%); nmr 1.09 (s, 3 H, C-4 CH_3), 5.42 (m, 1 H, C-5 H), absence of the C-3 H resonance. The isolated product showed a single component on tlc and on glc (on the four systems described above).

4β-Methylcholest-5-en-3β-ol (IV). 6β-Bromo-4-methylcholest-4-en-3-one (130 mg) was reduced with lithium aluminum hydride (7 mg, 7.4 mequiv of H$^-$) as described above (except for the lower molar ratio of hydride). Analysis of the crude reaction mixture by glc indicated the presence of two minor components with retention times corresponding to those of 4-methylcholest-4-en-3β-ol and 4-methylcholest-4-en-3α-ol and two major components with retention times corresponding to 4α-methylcholest-5-en-3β-ol (III) and 4β-methylcholest-5-en-3β-ol (IV). Analysis of the crude reaction mixture by tlc indicated two major components with R_f values of 0.19 and 0.23. The mixture was subjected to preparative tlc.

The more polar major component was crystallized from ethanol–water to give 4β-methylcholest-5-en-3β-ol (IV, 30.4 mg) in the form of needles: mp 135–137° (lit.[13] mp 132–134°); ir ν_{max} (KBr) 3410, 1026, 1062 cm^{-1}; ms 400 (M, 100%), 385 (M − CH_3, 25%), 382 (M − H_2O, 32%), 367 (M − CH_3 − H_2O, 33%), 343 (9%), 331[15] (36%), 301 (7%), 387 (M − side chain, 9%), 275 (19%), 269 (M − H_2O − side chain, 10%), 261 (3%), 247 (9%), 227 (M − H_2O − side chain − 42, 8%); nmr 1.06 (s, 3 H, C-19 CH_3), 1.12 (d, 3 H, C-4 CH_3, J = 8 Hz), 2.60 (m, 1 H, C-4 H), 3.71 (m, 1 H, C-3 H), 5.40 (m, 1 H, C-6 H). The compound showed a single component on tlc and on glc (on the four systems described above) with the same mobility as authentic IV.

The less polar major component (52.8 mg) from the preparative tlc showed only one component on glc (on the four systems described above) and on tlc on silica gel H and silica gel H–silver nitrate plates as the free alcohol and in the form of the acetate derivative. The mobilities were the same as that observed with authentic III and its acetate derivative. However, both ms and nmr analyses indicated the presence of one or more other components. For example, the nmr spectrum showed the presence of absorptions, in addition to those of III, at 3.90 (m), 4.97 (m), 5.60 (m), and 8.44 (s). The latter signal is compatible with a methyl group attached to an olefinic carbon. The mass spectrum showed the same ions as seen in III and, in addition, showed ions at 398 (30%), 365 (4%), 332 (17%), 285 (3%), and 279 (6%). The precise nature of the component(s) present in addition to III is not known. However, these data suggest that one of the components has two double bonds. The ir spectrum showed no absorption due to a carbonyl function. Analysis of the uv spectrum of the product showed only end absorption in the 210-nm region, indicating the absence of a conjugated diene system.

[3α,4α-$^2H_2$]-4β-Methylcholest-5-en-3β-ol (VI). Reduction of 6β-bromo-4-methylcholest-4-en-3-one (X) with lithium aluminum deuteride (7 mg, 7.4 mequiv of D$^-$) in ether was effected and the crude reaction mixture was subjected to preparative tlc as described in the case of the synthesis of IV. The more polar major component on tlc was crystallized from ethanol–water to yield [3α,4α-$^2H_2$]-4β-methylcholest-5-en-3β-ol (VI, 19.1 mg) in the form of needles: mp 131°; ir ν_{max} (KBr) 3448, 1064 cm^{-1}; ms (rel intensity) 402 (100%), 387 (28%), 284 (41%), 369 (32%), 344 (10%), 331[15] (36%), 301 (7%), 289 (18%), 275 (11%), 271 (9%), 261 (3%), 247

(10%), 229 (7%); nmr 1.12 (s, 3 H, C-4 CH_3), no resonance for the C-3 proton. The compound showed a single component on analysis by tlc and glc (on four systems noted above).

The less polar major component (19.0 mg) on tlc showed a mass spectrum which was very similar to that of [3α,4β-$^2H_2$]-4α-methylcholest-5-en-3β-ol (V) with additional ions at 399 (90%) and 366 (3%). The nmr spectrum showed the presence of signals 4.95 (m), 5.62 (m), and 8.43 in addition to the resonances seen in the spectrum of III. The spectrum showed no absorbance at 3.71 (C-3 H) or at 3.90 seen in the spectrum of the less polar component obtained as a by-product in the synthesis of IV.

Registry No.—III, 15073-00-4; IV, 1251-98-5; V, 52259-51-5; VI, 52259-52-6; VIII, 2041-92-1; X, 2239-49-8.

References and Notes

(1) This investigation was supported by grants from the National Heart and Lung Institute (HL-15376) and the Robert A. Welch Foundation (C-583).

(2) J. L. Gaylor, *Advan. Lipid Res.*, **10**, 89 (1972), and references cited therein.
(3) K. B. Sharpless, T. E. Snyder, T. A. Spencer, K. K. Maheshwari, G. Guhn, and R. B. Clayton, *J. Amer. Chem. Soc.*, **90**, 6874 (1968).
(4) R. Rahman, K. B. Sharpless, T. A. Spencer, and R. B. Clayton, *J. Biol. Chem.*, **245**, 2667 (1970).
(5) E. L. Ghisalberti, N. J. De Souza, H. H. Rees, L. J. Goad, and T. W. Goodwin, *J. Chem. Soc. C*, 1403 (1969).
(6) F. F. Knapp, L. J. Goad, and T. W. Goodwin, *Chem. Commun.*, 149 (1973).
(7) R. E. Ireland, T. I. Wrigley, and W. G. Young, *J. Amer. Chem. Soc.*, **81**, 2818 (1959).
(8) D. J. Collins and J. J. Hobbs, *Aust. J. Chem.*, **17**, 677 (1964).
(9) T. Esmon, F. F. Knapp, and G. J. Schroepfer, unpublished experiments.
(10) A. D. Tait, *J. Chem. Soc.*, 1850 (1964).
(11) S. Julia and J. P. Lavaux, *Bull. Soc. Chim. Fr.*, 1231 (1963).
(12) C. W. Shoppee, F. P. Johnson, R. E. Lack, R. J. Rawson, and S. Sternhell, *J. Chem. Soc.*, 2476 (1965).
(13) S. Julia and J. P. Lavaux, *Bull. Soc. Chim. Fr.*, 81 (1963).
(14) N. W. Atwater, *J. Amer. Chem. Soc.*, **82**, 2847 (1960).
(15) This ion has been shown to result from an unusual intramolecular transfer of the 3β-hydroxyl group to the charge-retaining fragment with concomitant loss of carbon atoms 1 through 4 and their other substituents: F. F. Knapp and G. J. Schroepfer, Jr., *Chem. Commun.*, 537 (1974).

Studies in Mass Spectrometry. A Comparison of the Electron Impact and Chemical Ionization Fragmentations of 8,9-Dehydro-2-adamantanol and 2-*exo*-Protoadamantenol

Barbara L. Jelus, Burnaby Munson, Kevin A. Babiak, and Roger K. Murray, Jr.*

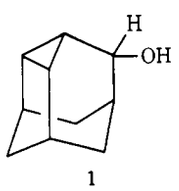
Department of Chemistry, University of Delaware, Newark, Delaware 19711

Received April 11, 1974

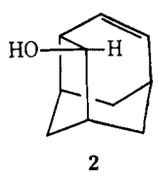
Electron impact (electron energies of 70, 20, and 14.2 eV) and chemical ionization (methane, isobutane, hydrogen, nitrogen, and nitric oxide–nitrogen mixtures as reagent gases) spectra were obtained for 8,9-dehydro-2-adamantanol (1) and 2-*exo*-protoadamantenol (2). Within the limits of experimental reproducibility, the mass spectrometric behavior of the two alcohols was identical when the site of ionization was the alcohol functional group. Only under conditions of electrophilic addition ionization were significant differences observed between 1 and 2.

Significant attention has been devoted to comparisons of the behavior of cyclopropylcarbinyl and homoallyl derivatives in solvolytic reactions.[1] Although it has been contended that "most of the [solvolytic] reactions of allylcarbinyl derivatives may be explained on the basis of the formation of a cyclopropylcarbinyl cation," [2] considerable controversy exists concerning the detailed structures of the intermediate species involved in these reactions.[1,3]

In light of these studies, it is striking that no detailed comparison of the mass spectrometric behavior of any cyclopropylcarbinyl and homoallyl derivatives has appeared. We now wish to report our results concerning the behavior of 8,9-dehydro-2-adamantanol (1) and 2-*exo*-protoadamantenol (2) in the mass spectrometer employing both electron impact and chemical ionization techniques.



1



2

Results and Discussion

Electron Impact Spectra. The partial electron impact mass spectra of 1 and 2 measured at 70, 20, and 14.2 eV are reported in Table I. The most striking conclusion resulting from a comparison of these data is that there is little difference in the electron impact fragmentations of 1 and 2 over this range of energies. Indeed, any differences in the ionic abundances of 1 and 2 reported in Table I are within the limits of experimental reproducibility. The absence of sig-

Table I
Partial Electron Impact Spectra of 1 and 2

	% ionization[a,b] ($100I_i/\sum_{sample} I_i$)						
	70 eV		20 eV		14.2 eV		
m/e	1	2	1	2	1	2	Comment
43	0.9	1.0	0.9	0.8	0.8	0.6	
54	2.6	2.4	3.5	3.1	3.0	1.8	
57	1.6	1.9	1.7	1.6	1.5	1.1	
72	3.2	4.4	6.8	6.3	9.4	8.9	
77	4.3	3.4	0.8	1.0			
78	4.9	4.9	5.3	5.4	4.9	4.9	
79	12.4	14.2	12.4	14.4	6.8	6.7	C_6H_7
80	6.9	9.7	11.4	11.2	11.9	10.8	
91	5.0	4.2	3.3	3.4	2.0	2.0	C_7H_7
92	1.1	1.1	1.0	1.1	0.7	0.7	
93	1.6	1.7	1.8	1.9	1.3	1.4	
104	1.8	2.5	3.1	2.9	3.9	3.3	M − (H_2O + C_2H_4)
108	1.2	1.5	2.3	2.1	2.8	2.5	
117	4.0	5.0	6.9	6.2	6.1	5.6	M − (OH + CH_4)
132	1.4	2.1	2.6	2.3	4.0	3.1	M − (H_2O)
133	0.3	0.7	0.9	0.7	1.3	0.8	M − (OH) and ^{13}C of M − (H_2O)
150	7.6	10.0	12.3	14.2	21.2	28.4	M

[a] The ion intensities reported are uncorrected for ^{13}C isotope. [b] The reproducibility of the per cent ionizations reported is ±15% of the reported value.