

3, 65. Neckers, D. C. *J. Chem. Educ.* **1975**, *52*, 695. Ellinger, L. P. *Annu. Rep. Prog. Chem., Sect. B.* **1973**, *70*, 322. Heitz, W. *Adv. Polym. Sci.* **1977**, *23*, 1. Ledwith, A.; Sherrington, D. C. In "Molecular Behavior and the Development of Polymeric Materials". Ledwith, A., and North, A. M., Ed.; Chapman and Hall: London, 1975; Chapter 9. Patchornik, A.; Kraus, M. A. In "Encyclopedia of Polymer Science and Technology." Mark, H. F., Gaylord, N. G., Bikales, N. M., Ed.; Interscience: New York, 1976; Vol. 1 Supplement, p 468. Blosssey, E. C., Neckers, D. C., Ed. "Solid Phase Synthesis". Halsted Press: New York, 1975. Marnett, L.; Neckers, D. C.; Schaap, P. In "Applications of Biochemical Systems in Organic Chemistry, Part II". Jones, J. B., Sih, C., Perlman, D., Ed.; Wiley-Interscience: New York, 1976; p 995 ff.

- (2) Allum, K. G.; Hancock, R. D.; Howell, I. V.; McKenzie, S.; Pitkethly, R. C.; Robinson, P. *J. Organomet. Chem.* **1975**, *87*, 203.
- (3) Analysis indicated: C, 12.60; H, 1.54; Cl, 1.38; P, 1.73.
- (4) (a) For a review see Fréchet, J. M. J.; Farrall, M. J. In "Chemistry and Properties of Crosslinked Polymers", Academic Press: New York, 1977; pp 59–83. (b) The polystyrene was purified by the method recommended by Hartley, F. R.; Vezey, P. N. *Adv. Organomet. Chem.* **1977**, *15*, 189.
- (5) (a) Pepper, K. W.; Paisely, H. M.; Young, M. A. *J. Chem. Soc.* **1953**, 4097. For 30 g of resin, 150 g of chloromethyl methyl ether and 7.5 g of stannic chloride for 1.5 h at reflux were employed. (b) Phosphide displacement was adapted from Regen, S. L.; Lee, D. P. *J. Org. Chem.* **1975**, *40*, 1669. (c) Capka, M.; Svoboda, P.; Hettflejš, J. *Collect. Czech. Chem. Commun.* **1973**, *38*, 1242. Capka, M.; Hettflejš, J. *ibid.* **1974**, *39*, 154. After submission of our paper, the following two reports of reactions catalyzed by Pd(0) on polymer supports appeared. Card, R. J.; Neckers, D. C. *J. Org. Chem.* **1978**, *43*, 2958. Pittman, C. U.; Ng, Q. *J. Organomet. Chem.* **1978**, *153*, 85.
- (6) (a) Anal. Cl, 21.98, 22.04. (b) Anal. Cl, 0.70, 0.80; P, 8.95, 9.02. (c) Anal. P, 7.75, 7.90; Pd, 1.57, 1.62.
- (7) In the continuous extractions of the palladated catalyst with benzene as a purification, use of paper thimbles in a Soxhlet extractor led to substantial decomposition. All glass systems must be used for maximum results.
- (8) For a recent review see Trost, B. M. *Tetrahedron.* **1977**, *33*, 2615.
- (9) (a) Trost, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1976**, *98*, 630. (b) *J. Org. Chem.* **1976**, *41*, 3215. (c) *J. Am. Chem. Soc.* **1977**, *99*, 3867. (d) *ibid.* **1978**, *100*, 3435. (e) Trost, B. M.; Matsumura, Y. *J. Org. Chem.* **1977**, *42*, 2036.
- (10) All new compounds have been characterized.
- (11) Ⓢ -Pd denotes the polystyrene catalyst; Ⓢ -Pd denotes the silica gel catalyst.
- (12) Trost, B. M.; Genet, J. P. *J. Am. Chem. Soc.* **1976**, *98*, 8516. Trost, B. M.; Godleski, S.; Genet, J. P. *ibid.* **1978**, *100*, 3930.
- (13) As in the related series,^{9b} couplings of H_a and H_b in **3** and **4** allow assignment. In **3** H_a appears at δ 1.5 (q, $J = 12$ Hz) indicative of an axial proton with only geminal and axial-axial couplings. In **4**, both H_a and H_b appear as a pseudotriplet ($J = 6$ Hz) at δ 1.9 indicative of conformationally averaged couplings.
- (14) Determined by VPC analysis on a 10 ft \times 0.25 in 20% SE-30 on Chromosorb P column at 150 °C.
- (15) Apparently in THF the primary amine is preferentially absorbed onto the polymer and the dissociation is very slow. In benzene, this equilibrium appears to be fast and reversible thereby allowing the allylic acetate to compete.
- (16) In this case, THF was required to dissolve tryptamine. Use of either solvent alone led to poor results.

Barry M. Trost,* Ehud Keinan

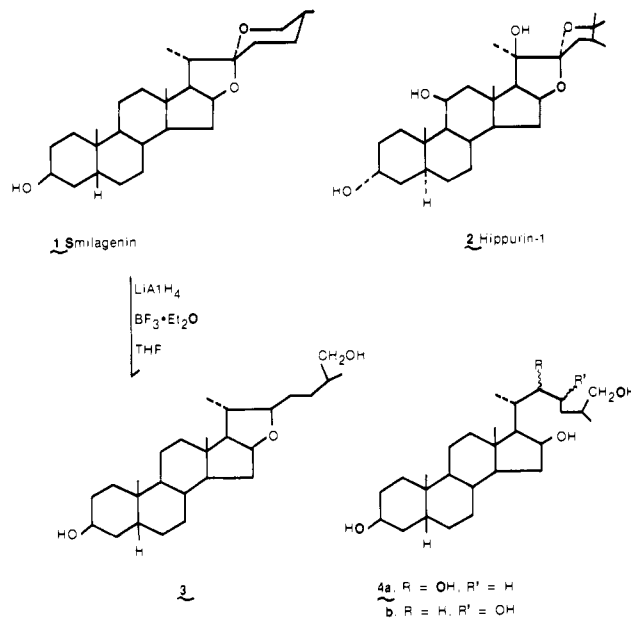
Department of Chemistry
University of Wisconsin—Madison
Madison, Wisconsin 53706

Received July 6, 1978

Synthesis of 3 β ,16 β ,23(R),26-Tetrahydroxy-5 β -cholestane¹

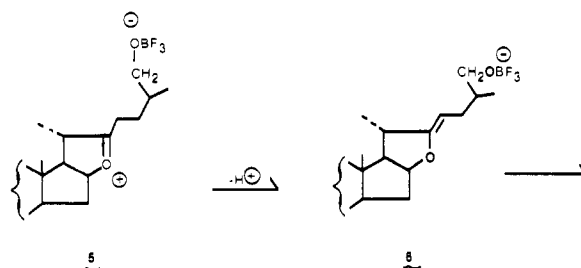
Sir:

Steroidal sapogenins² bearing spiro ketal systems such as smilagenin (**1**) are well-known plant constituents and even occur (cf. **2**) in certain marine animals.³ Some 20 years ago we⁴ found that a reagent prepared from lithium aluminum hydride and boron trifluoride in ethyl ether would readily cleave the spiro ketal unit to yield the corresponding dihydrosapogenin and a series of new products. For example, application of the reduction reaction to smilagenin (**1**) afforded dihydrosmilagenin (**3**) and a mixture of polyhydroxy steroids.⁵ We now report that the latter substances correspond to the hitherto unknown and potentially important C-22 and C-23 epimeric tetraols **4a** and **4b**. The novel introduction of oxygen (presumably a new hydroboration sequence) was found to be general for such spiro ketal systems and is illustrated in the sequel utilizing smilagenin.



Boron trifluoride etherate (11 mL) in tetrahydrofuran (40 mL) was slowly (10–15 min) added to a cold (ice bath) mixture of smilagenin (**1**, 1.0 g) and lithium aluminum hydride (1.0 g) in tetrahydrofuran (50 mL). After 2 h the mixture was heated at reflux for 3 h, cooled, and allowed to stand at room temperature for 18 h. The reaction was terminated by addition of water (100 mL) and the boron-containing steroids and dihydrosmilagenin were isolated by extraction with ether. After solution in ethanol (10 mL) and addition of potassium hydroxide (1.0 g), water (0.5 mL), and hydrogen peroxide (1 mL, 30%), the mixture was warmed. The products were isolated by dilution with water, extraction with ether, and careful chromatographic separation (through silica gel columns in series at 50 psi, elution with 4:1 chloroform–acetone, and flame ionization detection). Recrystallization using acetone–methanol led to dihydrosmilagenin (0.5 g), and two sets of tetrahydroxy sterols epimeric at C-22 (**4a**, 0.147 g of 22*R*, mp 137–138.5 °C, and 0.071 g of 22*S*, mp 115.5–119.5 °C, absolute configurational assignments provisional) and C-23 (**4b**, 0.241 g of 23*R*, mp 196–202.5 °C with sintering from 193 °C, and 0.050 g of 23*S*, mp 229.5–231 °C). Structural elucidation by X-ray crystallographic methods of the tetraol melting at 196–202.5 °C allowed the unequivocal assignment 3 β ,16 β ,23(R),26-tetrahydroxy-5 β -cholestane (**4b**, 23*R*). Comparison and interpretation of other physical measurements (principally NMR and mass spectral), elemental composition, and chemical degradation (e.g., to 5 β -cholestane) results for this substance with that obtained for the other isomers allowed the structural assignments noted above.

Based on our earlier mechanistic studies^{6,7} concerned with metal hydride reduction of the steroidal sapogenin spiro ketal, the lithium aluminum hydride-boron trifluoride etherate catalyzed formation of dihydrosmilagenin (**3**) most probably proceeds by an intermolecular hydride insertion (**5** \rightarrow **3**) from the least hindered side of intermediate **5** to yield the 22*R* derivative. The competitive production of tetraols **4a** and **4b** may



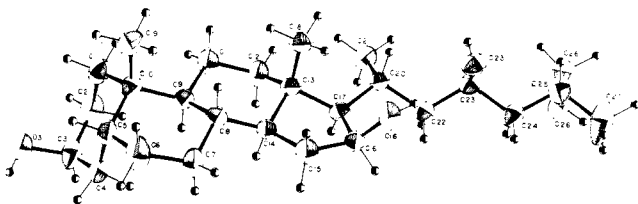
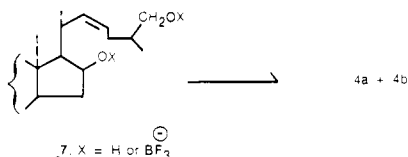


Figure 1. Perspective of 3 β ,16 β ,23(R),26-tetrahydroxy-5 β -cholestane.

involve concomitant formation of a transitory vinyl ether such as **6** that easily cleaves to olefin **7**. Addition of in situ generated diborane (hydroboration sequence) to the olefin intermediate (**7**) would proceed mainly from the least hindered carbon po-

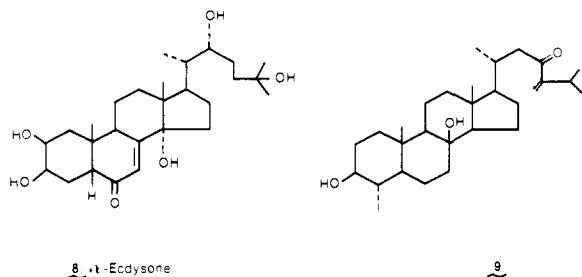


sition (and side) to yield as major product the 23R alcohol. The experimental observations, including the fact that dihydrosmilagenin (**3**) is not an intermediate in this unusual reaction, seem consistent with such a mechanistic pathway.

Single crystals of the C-23R isomer of tetraol **4b** were obtained from a saturated acetone and methanol solution. Precession photographs revealed Laué symmetry and systematically extinct reflections corresponding uniquely to monoclinic space group $P2_1$ with cell constants $a = 17.826$ (5) Å, $b = 7.682$ (2) Å, $c = 10.996$ (4) Å, and $\beta = 122.38$ (2)°. Crystal density, measured by flotation in carbon tetrachloride-toluene, was found to be 1.12 g cm^{-3} ($\rho_{\text{calcd}} = 1.14 \text{ g cm}^{-3}$, for $Z = 2$). Diffraction intensity measurements were made on a Syntex PT four-circle diffractometer using graphite monochromated $\text{CuK}\alpha$ ($\lambda = 1.54178$ Å) radiation. Reflections were scanned in a variable speed (between 1 and 12 deg min^{-1}) 2θ - θ mode. Of 2849 reflections measured with $(\sin \theta)/\lambda < 0.50$ in one quadrant of reciprocal space, 2645 unique reflections were accepted with $|F_o| > 0$. Corrections were made for Lorentz and polarization effects but not for absorption ($\mu = 5.4 \text{ cm}^{-1}$) or extinction.

Direct methods were used to solve the structure using MULTAN-74.⁸ Large-block least-squares refinement⁹ with anisotropic thermal parameters, fixed C-H hydrogen positions (placed at idealized locations 1.0 Å from respective C atom), and variable O-H hydrogen positions (located by a difference Fourier synthesis) converged at residual $R = 0.058$ and $R_w = 0.048$, where weighted residual $R_w = (\sum w(|F_o| - |F_c|)^2 / \sum w|F_o|^2)^{1/2}$ and $w = 1/\sigma_{F_o}^2$. Since 3 β ,16 β ,23(R),26-tetrahydroxy-5 β -cholestane was obtained by reduction of the 5 β -cholestane, smilagenin, the absolute configuration and conformation displayed in the perspective view in Figure 1 are those of the correct enantiomer.

Naturally occurring sterols bearing oxygen at C-22 or C-23 such as the insect molting hormone α -ecdysone¹⁰ (**8**) and the



new soft coral component **9**¹¹ require extensive structural maneuvers to elaborate the necessary side-chain oxygen sub-

stituents. The unique one-step conversion of steroidal saponins to C-22 and C-23 alcohols greatly improves the accessibility of such intermediates for synthetic purposes.

Acknowledgments. We are grateful for support of this investigation by the National Cancer Institute, Public Health Research Grants CA-16049-05 from the National Cancer Institute, the Fannie E. Rippel Foundation, Mrs. Mary Dell Pritzlaff, The Olin (Spencer T. and Ann W.) Foundation, and the Phoenix Coca Cola Bottling Co.

References and Notes

- (1) Steroids and Related Natural Products. 96. For part 95, refer to Y. Kamano, G. R. Pettit, M. Inoue, M. Tozawa, and Y. Komeichi, *J. Chem. Res. (M)*, 837 (1977).
- (2) W. H. Faul, A. Failli, and C. Djerassi, *J. Org. Chem.*, **35**, 2571 (1970); G. R. Pettit, *Experientia*, **19**, 124 (1963).
- (3) R. Kazlauskas, P. T. Murphy, R. J. Quinn, and R. J. Wells, *Tetrahedron Lett.*, 4439 (1977).
- (4) Unpublished experiments (autumn, 1957) by G.R.P., employing diosgenin acetate.
- (5) G. R. Pettit and T. R. Kasturi, *J. Org. Chem.*, **26**, 4553 (1961).
- (6) A. H. Albert, G. R. Pettit, and P. Brown, *J. Org. Chem.*, **38**, 2197 (1973).
- (7) G. R. Pettit, A. H. Albert, and P. Brown, *J. Am. Chem. Soc.*, **94**, 8095 (1972).
- (8) (a) P. Main, M. M. Woolfson, L. Lessinger, G. Germain, and J. P. Declercq, MULTAN 74, "A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data", Universities of York, England, and Louvain, Belgium, 1974; (b) J. P. Declercq, G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Part A*, **29**, 231 (1973); (c) G. Germain, P. Main, and M. M. Woolfson, *Ibid.*, **27**, 368 (1971).
- (9) All calculations other than data reduction and direct methods were performed using a modification (J.J.E. and R. B. von Dreele) of the CRYSTALS computing package: R. S. Rollett and J. R. Carruthers, personal communication.
- (10) For leading references, see M. Koreeda, D. A. Schooley, K. Nakanishi, and H. Hagiwara, *J. Am. Chem. Soc.*, **93**, 4084 (1971), and D. H. R. Barton, P. G. Feakins, J. P. Poyser, and P. G. Sammes, *J. Chem. Soc.*, 1584 (1970).
- (11) M. Bortolotto, J. C. Braekman, D. Daloz, and B. Tursch, *Steroids*, **30**, 159 (1977).

George R. Pettit,* James J. Einck, John C. Knight

Cancer Research Institute and Department of Chemistry
Arizona State University, Tempe, Arizona 85281

Received June 19, 1978

Quantitative Assessment of pp- σ Overlap in a Topologically Convex Triene. Electronic and Crystal Structure Analysis of C₁₆-Hexaquinacene

Sir:

C₁₆-Hexaquinacene (**1**) is the third and newest member¹ of a select group of trienes, which includes triquinacene (**2**) and *cis*³-1,4,7-cyclononatriene (**3**), whose constituent double bonds adopt an arrangement potentially suitable for effective pp- σ overlap.² Thus, the question arises as to whether one or more members of this series might partake of neutral homoaromatic character.³ Photoelectron (PE) spectroscopic investigations of **3**⁴ have revealed a sizable interaction between its π bonds. The energy difference between the bands corresponding to ionization from the $\epsilon(\pi)$ and $a_1(\pi)$ orbitals was found to be 0.9 eV. This split corresponds to a resonance integral (β) of -0.3 eV, a value consistent with the distance (2.46 Å)⁵ between the ethylene units. Although the distance in **2** (2.533 Å)⁶ is close to that found for **3**, a split of only 0.35-0.4 eV has been found.⁷ This difference between **2** and **3** has been explained by hyperconjugative effects.^{7,8} Thus, in **3** the interactions of $\epsilon(\pi)$ and $a_1(\pi)$ with the σ frame are of similar magnitude, while in

