Chemical Evidence for Transition-State Geometry in Reaction of Monoolefins with Singlet Oxygen[1]

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To examine the possibility of stereoelectronic control in formation of the C–O bond in oxygenation of monoolefins with singlet oxygen, steroidal substrates were studied having allylic methyl groups in which optimum C–H orientation for a cyclic process is readily attainable. Hematoporphyrin-sensitized oxygenation of 3-methyl-5α-cholest-2-ene (**13**) in pyridine followed by reduction of the initially formed hydroperoxides afforded 3β-methyl-5α-cholest-1-en-3α-ol (**21**) and 3-methylene-5α-cholestan-2α-ol (**15a**) in the ratio 7:3. Under similar conditions, 2-methyl-5α-cholest-2-ene (**23**) gave 2-methylene-5α-cholestan-3α-ol (**24**), 2-methylene-5α-cholestan-3β-ol (**2a**), and 2-methyl-5α-cholest-1-en-3α-ol (**11**) in the ratio 57:13:30. The products were identified by comparison with authentic samples obtained from straightforward synthetic procedures. The results indicate that the formation of a quasiaxial C–O bond may be slightly favored over a quasiequatorial one, but the preference is not as strong as that observed for cleavage of a quasiaxial C–H bond over a quasiequatorial C–H in endocyclic cyclohexene systems. A transition state for the cyclic, product-forming step that resembles starting olefin more than it does the allylic hydroperoxide product is advanced to account for these results.

Reactions of singlet oxygen are of considerable synthetic, biological, and environmental importance.[2] For synthetic work the activated oxygen is conveniently produced in solution by photosensitization and among its reactions with unsaturated compounds the one that converts a monoolefin to an allylic hydroperoxide with a rearranged double bond has received extensive mechanistic attention.[3]

In conformationally fixed cyclohexene rings the allylic hydroperoxidation shows a strong preference for quasiaxial C–H bond cleavage and can be retarded by 1,3-diaxial type hindrance to the developing C–O bond. These results are understood in terms of the one-step ene mechanism between singlet oxygen and olefin and on geometric factors that could affect such a path.[4,5]

In the cases studied that gave information on stereochemistry, a cyclic process involving a quasiaxial C–H bond on a six-membered steroidal ring necessarily created a quasiaxial C–O bond. The question arises whether there is any inherent stereoelectronic factor favoring formation of a quasiaxial C–O bond. To separate this factor from those involving C–H bond cleavage, it was necessary to study substrates in which the allylic C–H bond available for reaction was not conformationally fixed.[6] Because certain methylated steroid olefins appeared to satisfy this requirement, we examined the photosensitized oxygenation of 3-methyl-5α-cholest-2-ene (partial structure **13**) and 2-methyl-5α-cholest-2-ene (**23**).

Preparation of Potential Reaction Products.—The starting methylcholest-2-enes **13** and **23** were prepared as described elsewhere.[7] Allylic alcohols and other products related to 2-methyl-5α-cholestane were prepared as follows (Chart I). 2-Hydroxymethylene-5α-cholestan-3-one (**1**)[8-10] was reduced with lithium aluminum hydride and gave 2-methylene-5α-cholestan-3β-ol (**2a**) together with a sharp-melting 1:1 complex of **2a** and **3**,[11] which was separated into its components by precipitation of the digitonide of **2a**. The structure and stereochemistry of **2a** were revealed by its ir and nmr spectra, by its quantitative precipitation with digitonin, and by the nmr spectra of the corresponding acetate (**2b**), benzoate (**2c**), and 3,5-dinitrobenzoate (**2d**) derivatives. Hydrogenation of **2a** in alkaline ethanol over a platinum catalyst afforded the 3β-hydroxy-2β-methyl compound **4a**. Oxidation of this alcohol gave 2β-methyl-5α-cholestan-3-one (**5**), which was in turn epimerized to the more stable 2α-methyl isomer **6**.[7b,12a]

Attempted hydrogenation of **2a** in ethyl acetate over palladium/charcoal led to quantitative isomerization to the 2β-methyl ketone **5**. Hydrogenation of **5** with platinum in alkaline ethanol afforded a mixture of the epimeric 2α-methyl-5α-cholestan-3-ols **7** and **8**,[7b,12a] indicating that isomerization to **6** had taken place prior to hydrogenation.

The epimeric 3-hydroxy-2-methyl-5α-cholest-1-enes **10** and **11** were prepared by aluminum isopropoxide

(1) (a) This work was supported by the National Institutes of Health (Grant GM 09693) and by a postdoctoral fellowship to J. B. D. from the National Cancer Institute. (b) For a preliminary communication of some of these results, see A. Nickon, V. T. Chuang, P. J. L. Daniels, R. W. Denny, J. B. DiGiorgio, J. Tsunetsugu, H. G. Vilhuber, and E. Werstiuk, *J. Amer. Chem. Soc.*, **94**, 5517 (1972).

(2) (a) C. S. Foote, *Science*, **162**, 963 (1968); (b) T Wilson and J. W. Hastings, "Photophysiology," Vol. V, A. C. Giese, Ed., Academic Press, New York, N. Y., 1970, p 49; (c) I. R. Politzer, G. W. Griffen, and J. L. Laseter, *Chem.-Biol. Interactions*, **3**, 73 (1971); (d) R. A. Ackerman, J. N. Pitts, Jr., and I. Rosenthal, *Amer. Chem. Soc., Div. Petrol. Chem., Prepr.*, **16**, A25 (1971); (e) R. W. Denny and A. Nickon, *Org. React.*, in press.

(3) For reviews see (a) K. Gollnick, *Advan. Photochem.*, **6**, 1 (1968); (b) C. S. Foote, *Accounts Chem. Res.*, **1**, 104 (1968); (c) D. R. Kearns, *Chem. Rev.*, **71**, 395 (1971); (d) ref 2e.

(4) (a) A. Nickon and J. F. Bagli, *J. Amer. Chem. Soc.*, **81**, 6330 (1959); (b) *ibid.*, **83**, 1498 (1961); (c) A. Nickon, N. Schwartz, J. B. DiGiorgio, and D. A. Widdowson, *J. Org. Chem.*, **30**, 1711 (1965); (d) A. Nickon and W. L. Mendelson, *Can. J. Chem.*, **43**, 1419 (1965); (e) A. Nickon and W. L. Mendelson, *J. Amer. Chem. Soc.*, **87**, 3921 (1965).

(5) (a) F. A. Litt and A. Nickon, *Advan. Chem. Ser.*, **77**, 118 (1968). (b) K. Gollnick, *ibid.*, 672 (1968). (c) Alternative mechanisms involving dioxetane or perepoxide intermediates have been proposed but subsequently have been modified or withdrawn. Papers dealing with those aspects are cited in ref 1b.

(6) For the behavior of methyl olefins in ring-flexible octalin systems see (a) J. A. Marshall and A. R. Hochstetler, *J. Org. Chem.*, **31**, 1020 (1966); (b) J. A. Marshall, N. Cohen, and A. R. Hochstetler, *J. Amer. Chem. Soc.*, **88**, 3408 (1966); (c) Y. Kithara, T. Kato, T. Suzuki, S. Kanno, and M. Tanemura, *Chem. Commun.*, 342 (1969).

(7) (a) D. H. R. Barton, A. da S. Campos-Neves, and R. C. Cookson, *J. Chem. Soc.*, 3500 (1956); (b) C. Djerassi, N. Finch, R. C. Cookson, and C. W. Bird, *J. Amer. Chem. Soc.*, **82**, 5488 (1960).

(8) (a) L. Ruzicka, V. Prelog, and J. Batterjay, *Helv. Chim. Acta*, **31**, 1296 (1948); (b) M. W. Goldberg and H. Kirchensteiner, *ibid.*, **26**, 288 (1943); (c) E. T. Stiller and O. Rosenheim, *J. Chem. Soc.*, 353 (1938); (d) J. L. Beton, T. G. Halsall, E. R. H. Jones, and P. C. Phillips, *ibid.*, 753 (1957).

(9) We confirmed the position of the hydroxymethylene group in **1** by oxidation[10] to the known 2,3-seco diacid.

(10) A. Aebi, D. H. R. Barton, A. W. Burgstahler, and A. S. Lindsey, *J. Chem. Soc.*, 4659 (1954).

(11) B. Fuchs and H. J. E. Loewenthal, *Tetrahedron*, **11**, 199 (1960).

(12) (a) Y. Mazur and F. Sondheimer, *J. Amer. Chem. Soc.*, **80**, 5220 (1958); (b) J. A. Mills, *J. Chem. Soc.*, 4976 (1952).

CHART I

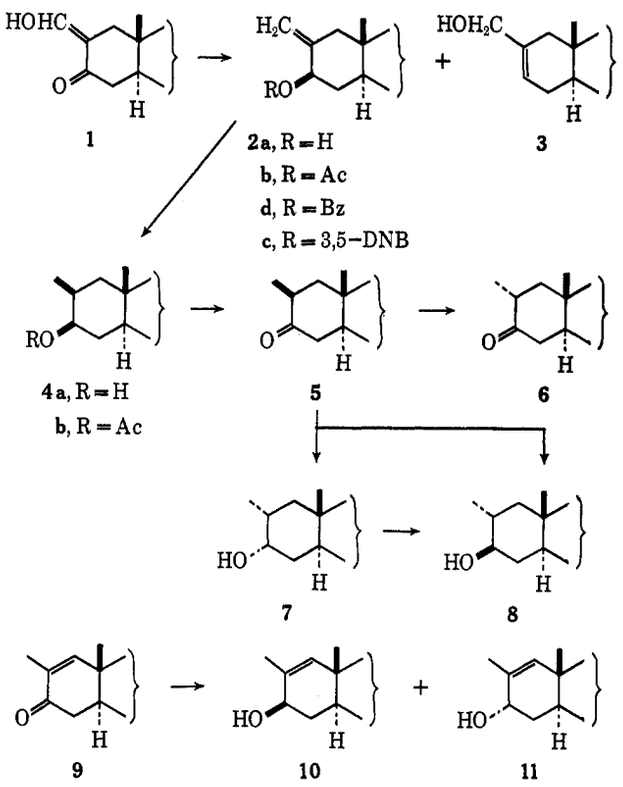
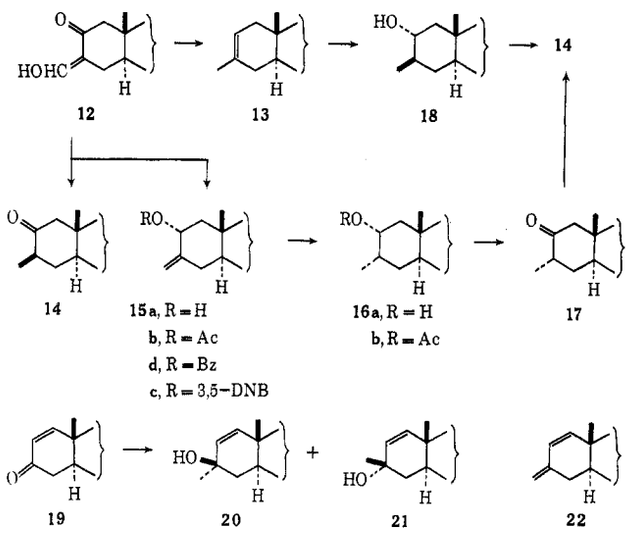


CHART II

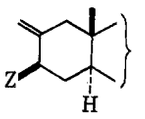


reduction of the known enone **9**.[7b,12a] The major product from our reduction was assigned the 3β-hydroxy structure **10** on the basis of nmr spectra and optical rotation considerations.[12b] Interestingly, when the isopropoxide reduction was run for longer periods, larger proportions of **10** were formed, indicating that equilibration favors **10**. This observation might be taken as further support for the quasiequatorial nature of the hydroxyl group; however, partial eclipsing by the vicinal methyl group could alter normal conformational preferences.

The preparation of allylic alcohols related to 3-methyl-5α-cholestane is shown in Chart II. Condensation of ethyl formate with 5α-cholestan-2-one afforded the hydroxymethylene derivative **12**, whose structure was proved by hydrogenation to a mixture of epimeric

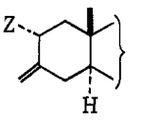
TABLE 1

MOLECULAR ROTATIONS IN CHLOROFORM



2

Compd	Z	$[\phi]^a$	$\Delta[\phi]$
	H	−19	
2a	OH	0	+19
2b	OAc	−80	−61
2c	OBz	−247	−228
2d	*O*-3,5-DNB[b]	−274	−255



15

	H	+96	
15a	OH	+112	+16
15b	OAc	−40	−136
15c	OBz[c]	−111	−207
15d	*O*-3,5-DNB	−155	−251

[a] $[\phi]$ = molecular rotation. [b] 3,5-DNB = 3,5-dinitrobenzoate. [c] Not obtained crystalline.

methyl ketones[13] followed by reduction with lithium aluminum hydride and dehydration to the known 3-methyl-5α-cholest-2-ene (**13**). Reduction of **12** with lithium aluminum hydride gave **15a** as well as a small amount of 3β-methyl-5α-cholestan-2-one (**14**).[14] Equatorial stereochemistry of the hydroxyl group in **15a** is supported as follows. Alcohol **15a** was readily converted into its esters **15b,c,d** and comparison of molecular rotation differences of these derivatives with the corresponding ones from the alcohol **2a** (Table I) shows striking similarities between the two series and indicates that the chirality of the two alcohols (**2a** and **15a**) is the same.[12b] Hydrogenation of the acetate **15b** in ethanol over platinum afforded a single compound **16b** in 80% yield. That **16b** possessed a 3α-methyl group was shown by lithium aluminum hydride reduction to the alcohol **16a** and oxidation to **17**,[14] which was separately isomerized to the more stable 3β-methyl ketone **14**. On the assumption that no epimerization of the acetate group occurs in the hydrogenation step steric considerations[15] are also consistent with the assigned stereochemistry of **15**. The C-3 methyl epimer **18** was prepared by hydroboration of **13**. Its structure follows from the known cis stereochemistry of such reactions[16] and by its oxidation to the ketone **14**.

The epimeric 3-hydroxy-3-methyl-5α-cholest-1-enes (**20** and **21**) were prepared by addition of methylmagnesium iodide to 5α-cholest-1-en-3-one (**19**). Assignment of stereochemistry to the hydroxyl groups in these compounds was based on their order of elution from alumina and on the considerable predominance of one isomer (**20**) in the reaction mixture, consistent

(13) H. J. Ringold, E. Batres, O. Halpern, and E. Necoechea, *J. Amer. Chem. Soc.*, **81**, 427 (1959).

(14) J. Hudec, Ph.D. Thesis, University of London, 1958.

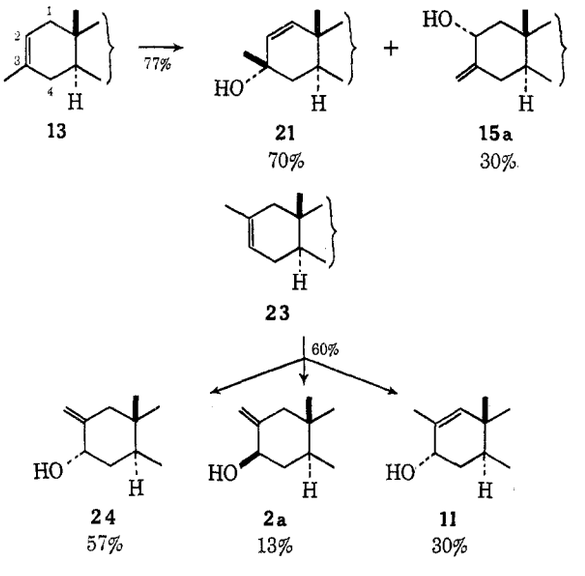
(15) As a model system the acetate **2b** was hydrogenated under the same conditions and afforded **4b** in 90% yield. Therefore, with **2b** and **15b** the hydrogen is delivered from the side opposite to that of the allylic substituent.

(16) H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, **83**, 2544 (1961).

with the expected preferential α attack of the Grignard reagent. When heated, both **20** and **21** were easily dehydrated to form a conjugated diene whose spectral data, hydrogenation behavior (see Experimental Section), and optical rotation indicated that it was largely **22**.[17]

Photooxygenations and Results.—Photooxygenations were conducted in pyridine solution with hematoporphyrin as sensitizer by methods described earlier.[4] The initially formed hydroperoxides were reduced directly to the corresponding alcohols with methanolic sodium iodide. The allylic alcohols were separated from small amounts of by-product by chromatography over alumina, and the mixtures were assayed by combinations of infrared and nmr spectroscopy and by optical rotations. The individual components of the mixtures were identified either spectroscopically or by isolation from the reaction mixtures. Chart III summarizes the results.

CHART III



Photooxygenation of 3-methyl-5α-cholest-2-ene (**13**) for 32 hr gave a mixture of allylic alcohols (77%) together with some ketonic material (6%). Assay of the alcohol mixture showed it to consist of **21** and **15a** in the ratio 7:3. Both alcohols were isolated and identified by comparison with our authentic samples. No evidence was found for the presence of 3-methylene-5α-cholestan-2β-ol (the epimer of **15a**) in the reaction product. Similar photooxygenation of 2-methyl-5α-cholest-2-ene (**23**) for 19 hr afforded a mixture of allylic alcohols in *ca.* 60% yield as well as some ketonic (*ca.* 7%) and unidentified material (*ca.* 6%). The allylic alcohol mixture was composed of 2-methylene-5α-cholestan-3α-ol (**24**), **2a**, and **11** in the ratio 57:13:30, and chromatography of the mixture afforded pure samples of **24** and **2a**. The axial allylic alcohol **24** was identified by analytical and spectral data (infrared and nmr) and by its nonidentity with authentic **2a**.

(17) For properties of **22** and possible isomeric dienes see (a) H. Ziffer and C. H. Robinson, *Tetrahedron*, **24**, 5803 (1968); (b) F. Sondheimer and R. Mechoulam, *ibid.*, **79**, 5029 (1957); (c) O. C. Musgrave, *J. Chem. Soc.*, 3121 (1951); (d) N. F. Kucherova and M. I. Ushakov, *Zh. Obshch. Khim.*, **23**, 315 (1953); *Chem. Abstr.*, **48**, 2744*b* (1954).

Discussion

Previous work has shown that steric hindrance to C–O bond formation in the photosensitized oxygenation reaction is more important than hindrance to C–H bond cleavage,[4d] and additional support for that view has since appeared.[6a] For six-membered rings, there is a strong preference for quasiaxial (a′) hydrogen abstraction, since such hydrogens are better oriented for participation in a cyclic process than are quasiequatorial (e′) ones.[4] However, if the allylic hydrogen is located on a conformationally mobile methyl group, optimum geometric alignment of the C–H should be readily achievable, and therefore the behavior of methyl olefins permits evaluation of other factors in the cyclic process. The presumed ease with which a methyl group can orient a C–H bond optimally was invoked by Marshall and coworkers to explain the preferred formation of exocyclic olefins in photooxygenation of some 1,10-dimethyl-1(9)-octalins,[6a,b] and other workers have also observed preferences for methyl hydrogen involvement.[18] A distinctive feature in olefins **13** and **23** is that ring A can adopt only one half-chair conformation, and ambiguities that might arise from ring inversions are largely avoided.

In the case of **13** attack by activated oxygen from the β face of the steroid could in principle occur at three sites, *viz.*, (a) at C-3 with abstraction of the quasiequatorial (e′) β hydrogen at C-1; (b) at C-2 with abstraction of the quasiaxial β hydrogen at C-4; (c) at C-2 with abstraction of a hydrogen from the methyl group. That a did not occur was expected, because e′ hydrogens in half-chair rings cannot easily participate in the cyclic process. That b did not take place supports earlier findings[4c] that syn-axial interactions exerted by an angular methyl simultaneously on the developing C–O bond and on the allylic C–H bond can strongly retard oxygenation and reveals that, if there is any stereoelectronic factor favoring creation of a quasiaxial C–O bond, it is overshadowed here by the combination of these two adverse steric factors. That c did not occur is particularly significant, because it suggests that any stereoelectronic preference for axial C–O formation is even overridden by a single 1,3-diaxial interaction with the angular methyl group.

There are also three possibilities for α attack on olefin **13**. Only two of these were realized experimentally (*viz.* **21** and **15a** obtained in the ratio 7:3), and the absence of the third product is understandable because it requires the geometrically difficult abstraction of a quasiequatorial hydrogen from C-4. The preference for a product with an endocyclic rather than an exocyclic double bond is noteworthy but not surprising, since geometric and stereoelectronic factors act synergistically, and oxygen preferentially attacks the more substituted olefinic site.[19] More signifi-

(18) (a) G. O. Schenck, S. Schroeter, and G. Ohloff, *Chem. Ind. (London)*, 459 (1962); (b) G. O. Schenck, H. Eggert, and W. Denk, *Justus Liebigs Ann. Chem.*, **584**, 177 (1953); (c) E. Klein and W. Rojahn, *Tetrahedron*, **21**, 2173 (1965).

(19) Other things equal, tertiary olefinic centers may be more susceptible to attack then secondary ones. For example, 2-methyl-2-butene gives approximately equal amounts of the two possible hydroperoxides despite a statistical factor that should favor oxygen attack at the less substituted carbon [(a) K. Gollnick and G. O. Schenck, *Pure Appl. Chem.*, **9**, 507 (1964); (b) ref 3, 6]. Statistical differences are virtually absent in **13** because all but the two types of attack observed are excluded on energetic grounds.

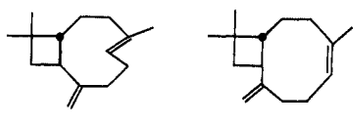
cantly, however, the exocyclic product has a quasi-equatorial OH (**15a**). Attack on the $CH_3C{=}C$ unit in the initial olefin from above and below the olefinic plane are *stereoelectronically* equivalent, and differences in allylic overlap (favoring axial C–O) develop only as the geometry approaches that of the final chair-like product.[20a] Therefore the degree of stereoelectronic control (*i.e.*, preference for axial C–O) reflects how far the transition-state geometry lies along the reaction coordinate. If orbital interaction between the new C–O bond and the π link were of paramount importance in a cyclic transition state that *resembles the allylic hydroperoxide*, the axial epimer of **15a** should have predominated over the equatorial epimer, in contrast to the experimental results. Evidently creation of an allylic axial C–O bond *per se* is not of paramount importance, and this finding implies a transition state that resembles starting olefin more than it does product.[20b] The oxygenation reaction contrasts with others where strong stereoelectronic preferences for axial have been observed in generation of allylic cyclohexenoid bonds, even in opposition to strong steric hindrance.[21]

Of the six possible oxygenation products from **23** (three from β attack and three from α attack) three were not expected on stereochemical and steric grounds. Thus β-oxygenation at C-2 was blocked by the angular methyl group (*cf.* behavior of **13**) and both α attack at C-2 and β attack at C-3 were precluded because these paths would involve quasiequatorial hydrogens. The remaining three possibilities fulfill the geometric requirements and lead to the observed products **24**, **2a**, and **11**. Product **2a** has an equatorial C–O bond and its formation supports the view that the cyclic transition state does not strongly prefer a geometry that stereoelectronically favors development of an axial C–O bond and further illustrates that an axial methyl group (at C-10) in a 1,4 relationship to an incipient C–O bond is not sterically prohibitive. The moderate predominance of the axial product **24** over **2a** could be due to an inherent steric preference for α attack along with a small stereoelectronic advantage.

The production of an appreciable proportion of **11** again shows that ring hydrogens can compete effectively with methyl hydrogens when geometric circumstances are favorable.

On the basis of our chemical evidence, we suggest that the geometry of the cyclic transition state in singlet oxygen reactions of monoolefins has more of the character of the starting olefin than of the final product, and that stereoelectronic preference for creation of an axial C–O bond is not an overriding factor. Although the chemical results say nothing about the extent of C–H bond breaking at the transition state, primary deuterium isotope effects have been found to be low ($k_H/k_D \sim 1.1$–2.4) and, along with the chemical evidence, point to a reactant-like transition state.[1b]

This picture of the transition state suggests that thermodynamic stability of the rearranged double bond should not provide a major driving force in the oxygenation. This expectation is borne out by the relative inertness of terminal open-chain olefins[21a,22] and of methylene cycloolefins such as methylenecyclopentane, methylenecyclohexane,[18c] 2-methylene-5α-cholestane, and 3-methylene-5α-cholestane (see Experimental Section). That double-bond stability plays but minor roles is also suggested by the only moderately faster rate of oxygenation (factor of *ca.* 5.8) of caryophyllene (**25**, strained trans endocyclic double bond) compared to its more stable isomer isocaryophyllene (**26**, cis double bond),[5a] although with these



25 **26**

isomers stereochemical and conformational differences preclude an unambiguous interpretation.[23]

A reactant-like transition state also clarifies why conformational ring inversion (which sometimes must accompany a double bond shift) does not block oxygenation,[4c,d] and why the susceptibility of the C–H to abstraction is not inherently related to whether it is primary, secondary, or tertiary.[3]

Experimental Section[24]

2-Hydroxymethylene-5α-cholestan-3-one (**1**) was prepared as described previously,[8a] mp 180.5–182°, $[\alpha]_D$ +54° (*c* 1.14). Oxidation with alkaline hydrogen peroxide according to the method of Barton and coworkers[10] gave 2,3-seco-5α-cholestan-2,3-dioic acid, mp 195.5–196.5°, $[\alpha]_D$ +30° (*c* 1.72) (reported[25] mp 196–197°, $[\alpha]_D$ + 33°).

2-Methylene-5α-cholestan-3β-ol (**2a**).—2-Hydroxymethylene-5α-cholestan-3-one (1, 9.3 g) was reduced with lithium aluminum hydride (9.6 g) in refluxing ether (500 ml) for 1 week. Water and 15% sodium hydroxide solution[26] were added and the ethereal filtrate was separated, dried, and evaporated. Chromatography of the residue (7.9 g) over alumina (250 g) and crystallization from methanol afforded needles of 2-methylene-5α-cholestan-3β-ol (**2a**), mp 132.5–133° (5.1 g). Further crystallization from methanol gave the analytical sample: mp 134°; $[\alpha]_D$ ±0° (*c* 2.37); ν 3610 (OH), 1653 (C=C), and 895 cm^{-1} (=CH_2).

(20) (a) We emphasize that these interpretations are based on normal half-chair → chair transformations. Presently there are no compelling reasons to invoke twist-boats. (b) The results of photosensitized oxygenations of monocyclic olefins such as carvomethene and limonene are understandable in these terms, although ring inversion involving more than one half-chair form limits the usefulness of those monocyclic systems for stereochemical conclusions. R. L. Kenney and G. S. Fisher, *J. Org. Chem.*, **28**, 3509 (1963); G. O. Schenck, K. Gollnick, G. Buchwald, S. Schroeter, and G. Ohloff, *Justus Liebigs Ann. Chem.*, **674**, 93 (1964); G. O. Schenck, O. A. Neumuller, G. Ohloff, and S. Schroeter, *ibid.*, **687**, 26 (1965).

(21) (a) G. Stork and S. D. Darling, *J. Amer. Chem. Soc.*, **82**, 1512 (1960); (b) G. Subrahmanyam, S. K. Malhotra, and H. J. Ringold, *ibid.*, **88**, 1332 (1966).

(22) K. R. Kopecky and H. J. Reich, *Can. J. Chem.*, **43**, 2265 (1965).

(23) (a) Photosensitized oxygenation of caryophyllene involves only the endocyclic olefinic link and gives mixtures of the expected products. Product identification was in progress in our laboratory but was discontinued when we learned that similar work had been carried out by K. H. Schulte Elte and G. Ohloff, *Helv. Chim. Acta*, **51**, 494 (1968). We are grateful to Dr. Ohloff for informing us of their work. (b) K. Gollnick and G. Schade, *Tetrahedron Lett.*, 689 (1968).

(24) Melting points are corrected and, unless stated otherwise, the following applies. Optical rotations were recorded at room temperature in chloroform solution with a sodium lamp light source. Ultraviolet spectra were taken in 95% ethanol and infrared spectra were recorded in chloroform. The light petroleum used (bp 40–60°) was distilled from potassium permanganate, the alumina for chromatography was obtained from Fisher Scientific Co. (Cat. No. A-540), and magnesium sulfate was the drying agent. Pyridine, acetic anhydride, and benzoyl chloride were distilled, and 3,5-dinitrobenzoyl chloride was crystallized from carbon tetrachloride. Sublimations were done at the high vacuum of an oil diffusion pump at temperatures 20–50° below the melting points of the compounds. Microanalyses were performed by Mr. Joseph Walter in this laboratory.

(25) B. Heath-Brown, I. M. Heilbron, and E. R. H. Jones, *J. Chem. Soc.*, 1482 (1940).

(26) V. M. Micovic and M. L. J. Mihailovic, *J. Org. Chem.*, **18**, 1190 (1953).

Anal. Calcd for $C_{28}H_{48}O$ (400.60): C, 83.93; H, 12.08. Found: C, 83.75; H, 12.18.

Concentration of the mother liquors afforded a 1:1 complex (1.4 g) of **2a** and **3** as plates, mp 155.5–156°, $[\alpha]D$ +28° (*c* 2.23). Separation of this complex by precipitation of **2a** with digitonin and regeneration afforded pure samples of **2a** and 2-hydroxymethyl-5α-cholest-2-ene (**3**): mp 141–141.5°; $[\alpha]D$ +61° (*c* 1.28); ν 3640 cm^{-1} (OH) (lit.[11] mp 140–142°; $[\alpha]D$ +63°). Acetylation of **3** afforded 2-acetoxymethyl-5α-cholest-2-ene, mp 80.5–81°, $[\alpha]D$ +54° (*c* 0.52) (lit.[11] mp 82–83°).

Derivatives of 2a.—Esterification of **2a** in the conventional manner in pyridine solution afforded 2-methylene-5α-cholestan-3β-yl acetate (**2b**), mp 106.5–107° (from methanol), $[\alpha]D$ −18° (*c* 2.41).

Anal. Calcd for $C_{30}H_{50}O_2$ (442.70): C, 81.39; H, 11.38. Found: C, 81.51; H, 11.42.

2-Methylene-5α-cholestan-3β-yl benzoate (**2c**) had mp 144.5–145° (from ether–methanol) and mp 143.5–144.5° after sublimation, $[\alpha]D$ −49° (*c* 2.06).

Anal. Calcd for $C_{35}H_{52}O_2$ (504.77): C, 83.28; H, 10.38. Found: C, 82.93; H, 10.48.

2-Methylene-5α-cholestan-3β-yl 3′,5′-dinitrobenzoate (**2d**) had mp 192.5–193° (from ether–methanol), $[\alpha]D$ −46° (*c* 1.88).

Anal. Calcd for $C_{35}H_{50}O_6N_2$ (594.78): C, 70.67; H, 8.47. Found: C, 70.81; H, 8.53.

Digitonide of 2a.—The alcohol **2a** formed an insoluble digitonide in 92% yield in ethanol.

3-Hydroxymethylene-5α-cholestan-2-one (**12**).—Hydroxymethylation of 5α-cholestan-2-one as described for 1[8a] afforded an 89% yield of **12**, mp 127–128°. Crystallization from acetone gave yellow granules: mp 128–128.5°; $[\alpha]D$ +52° (*c* 2.40); ν 1645 (C=O) and 1590 cm^{-1} (C=C).

Anal. Calcd for $C_{28}H_{46}O_2$ (414.65): C, 81.10; H, 11.18. Found: C, 81.45; H, 11.28.

Conversion of 12 to 3-Methyl-5α-cholest-3-ene (**13**).—The hydroxymethylene ketone **12** (0.32 g) in methanol (50 ml) was hydrogenated for 24 hr over a 10% palladium on charcoal catalyst to give a solid saturated ketone (0.30 g) as evidenced by its infrared spectrum. Part of this ketone (0.120 g) was reduced with an excess of lithium aluminum hydride in refluxing ether for 4 hr, the excess of hydride was decomposed with acid, and the ether layer was separated, dried, and evaporated to an oily residue (infrared shows hydroxyl, but no carbonyl absorption). The oily residue (0.105 g) in pyridine (5 ml) was heated with phosphorus oxychloride (0.2 ml) on the steam bath for 1.5 hr, evaporated to dryness *in vacuo*, and dissolved in a mixture of ether and water. The ethereal layer was separated, dried, and evaporated and the residue in light petroleum was filtered through alumina and crystallized from ethyl acetate–methanol to give 3-methyl-5α-cholest-2-ene (**13**) (0.02 g), mp 80–81°, identical by melting point, mixture melting point, and infrared spectrum with an authentic sample.[7a] The mother liquors were evaporated and treated with acetic acid–perchloric acid on the steam bath for 1 hr and on work-up gave an additional 0.04 g of **13**.

3-Methyl-5α-cholest-2-ene (**13**).—This olefin was prepared by the method of Barton, *et al.*,[7a] mp 82–82.5°, $[\alpha]D$ +71 (*c* 3.90) [reported[7a] mp 82–83°, $[\alpha]D$ +74° (*c* 1.39)].

2-Methyl-5α-cholest-2-ene (**23**) prepared by a method previously described for **13** had mp 97.5–98°, $[\alpha]D$ +67° (*c* 3.09) [reported[11] mp 100–101°, $[\alpha]D$ +68° (*c* 1)].[11]

3-Methylene-5α-cholestan-2α-ol (**15a**).—The hydroxymethylene ketone **12** (7.2 g) was refluxed in ether (400 ml) with lithium aluminum hydride (7.7 g) for 1 week. The reaction mixture was worked up as for **2a** to give 6.45 g of a solid which was chromatographed over alumina (200 g). Elution with light petroleum–benzene (1:1–1:4) afforded **15a** (3.33 g), mp 107–111°. Recrystallization from methanol gave mp 113–114°; $[\alpha]D$ +28° (*c* 1.06); ν 3610 (OH), 1655 (C=C), and 895 cm^{-1} (=CH_2). The compound formed no precipitate with digitonin.

Anal. Calcd for $C_{28}H_{48}O$ (400.66): C, 83.93; H, 12.08. Found: C, 83.89; H, 12.08.

Elution of the column with light petroleum–benzene (2:1) afforded 3β-methyl-5α-cholestan-2-one (**14**) (0.70 g), crystallized from ether–methanol: mp 149–149.5°; $[\alpha]D$ +48° (*c* 1.54); ν (KBr) 1710 cm^{-1} (C=O). The reported values are mp 148–150°, $[\alpha]D$ +50°.[14]

Derivatives of 3-Methylene-5α-cholestan-2α-ol.—By conventional methods **15a** gave the following ester derivatives.

3-Methylene-5α-cholestan-2α-yl acetate (**15b**), crystallized from methanol, had mp 99.5–100.5°; $[\alpha]D$ −9° (*c* 2.04).

Anal. Calcd for $C_{30}H_{50}O_2$ (442.70): C, 81.39; H, 11.38. Found: C, 81.60; H, 11.49.

3-Methylene-5α-cholestan-2α-yl benzoate (**15c**) was oily: ν 1710 (C=O), 1655 (C=C), and 1275 cm^{-1} (C—O); $[\alpha]D$ −22° (*c* 2.88). Since the material was an oil, it may not be entirely pure.

3-Methylene-5α-cholestan-2α-yl 3′,5′-dinitrobenzoate (**15d**) from ether–methanol had mp 188–188.5°, $[\alpha]D$ −26° (*c* 1.90).

Anal. Calcd for $C_{35}H_{50}O_6N_2$ (594.78): C, 70.67; H, 8.47. Found: C, 70.75; H, 8.46.

2β-Methyl-5α-cholestan-3β-ol (**4a**).—Alcohol **2a** was recovered unchanged from attempted hydrogenation in ethanol containing a drop of 10% aqueous sodium hydroxide and a 10% palladium on carbon catalyst.

The alcohol (0.189 g) in ethanol (100 ml) containing 5 drops of 10% sodium hydroxide solution was hydrogenated over platinum oxide (0.018 g) for 24 hr. Evaporation and crystallization of the residue from methanol gave **4a**: mp 134–135°; $[\alpha]D$ +42° (*c* 2.12); ν 3750 (OH) and 1030 cm^{-1} (C—O) (lit.[7b] mp 121–124°, $[\alpha]D$ +27°).

Anal. Calcd for $C_{28}H_{50}O$ (402.68): C, 83.51; H, 12.52. Found: C, 83.60; H, 12.33.

With ethanolic digitonin **4a** gave an essentially quantitative precipitate of a digitonide. The alcohol gave the following derivatives by conventional methods.

2β-Methyl-5α-cholestan-3β-yl acetate (**4b**) had mp 109–109.5° (from ethanol), $[\alpha]D$ +37° (*c* 2.04).

Anal. Calcd for $C_{30}H_{52}O_2$ (444.72): C, 81.02; H, 11.79. Found: C, 80.59; H, 11.72.

2β-Methyl-5α-cholestan-3β-yl benzoate had mp 135.5–136° (from ethanol), $[\alpha]D$ +33° (*c* 2.41). Interestingly, the infrared spectrum showed two C=O bands (1712 and 1708 cm^{-1}).

Anal. Calcd for $C_{35}H_{54}O_2$ (506.78): C, 82.95; H, 10.74. Found: C, 83.18; H, 10.84.

2β-Methyl-5α-cholestan-3β-yl 3′,5′-dinitrobenzoate had mp 164.5–165° (from ethanol), $[\alpha]D$ +30° (*c* 1.51).

Anal. Calcd for $C_{35}H_{52}O_6N_2$ (596.78): C, 70.44; H, 8.78. Found: C, 70.40; H, 8.56.

2β-Methyl-5α-cholestan-3-one (**5**). **A. From Isomerization of 2a.**—Alcohol **2a** (0.20 g) in ethyl acetate (100 ml) was shaken for 12 hr in an atmosphere of hydrogen over a 10% palladium on carbon catalyst (0.04 g). Evaporation of the solvent and recrystallization of the residue from ether–methanol gave **5**: mp 98–99°; $[\alpha]D$ +122° (*c* 1.36); ν (KBr) 1715 cm^{-1} (C=O) (lit.[12] mp 96–97°, $[\alpha]D$ +86°).

Anal. Calcd for $C_{28}H_{48}O$ (400.66): C, 83.93; H, 12.08. Found: C, 84.22; H, 12.08.

B. By Oxidation of 4a.—Alcohol **4a** (0.020 g) in 6 drops of acetic acid was stirred with chromium trioxide (0.005 g) for 5 min at room temperature and then for 10 min at 60°. Dilution with water and extraction with ether afforded the ketone **5**, mp 96–97°, $[\alpha]D$ +111° (*c* 1.04). The infrared spectrum was identical with that of the product from method A.

Equilibration of 2-Methyl-5α-cholestan-3-one. A.—2β-Methyl-5α-cholestan-3-one (**5**) (0.0187 g, mp 98–99°, $[\alpha]D$ +122°) was refluxed overnight in 2 ml of chloroform saturated with hydrogen chloride. After evaporation, the residual solid had $[\alpha]D$ +39.8 ± 0.6° (*c* 2.72).

B.—2α-Methyl-5α-cholestan-3-one (**6**, 0.0228 g, mp 119–120.5°, $[\alpha]D$ +36°) was similarly treated and afforded material with $[\alpha]D$ +39.5 ± 0.7° (*c* 2.66). The infrared spectra of the materials from A and B were identical and the rotation corresponded to an equilibrium mixture containing 96% of **6**.

Hydrogenation of 2β-Methyl-5α-cholestan-3-one (**5**).—The ketone (0.016 g) in ethanol (5 ml) containing a trace of 10% aqueous sodium hydroxide solution was hydrogenated for 12 hr over platinum oxide (0.006 g). The product after evaporation of the solvent was recrystallized from ether–methanol to give 2α-methyl-5α-cholestan-3β-ol (**8**), 0.005 g, mp 137–138°, ν 3590 cm^{-1} (OH) (lit.[12] mp 139–140°).

The crude reduction product from a larger run (0.046 g) was treated with ethanolic digitonin solution. The precipitated digitonide was filtered off and the filtrate was evaporated to dryness. Ether extraction of the residue afforded 2α-methyl-5α-cholestan-3α-ol (**7**, 0.032 g, 69%). The digitonide was dissolved in pyridine and an excess of ether was added to precipitate the digitonin. Filtration and evaporation afforded 0.012 g (26%) of 2α-methyl-5α-cholestan-3β-ol (**8**).

2-Methyl-5α-cholest-1-en-3-one (**9**), prepared by the method of Djerassi, *et al.*,[7b] had mp 74–76° (lit. mp 75–76°).

Reduction of Enone 9. A. With Aluminum Isopropoxide.—The enone (0.285 g) in dry isopropyl alcohol was heated at 88° for 8 hr with freshly distilled aluminum isopropoxide (4.5 g). After an additional 8 hr at room temperature, the mixture was poured into water and 25 ml of 6 *N* sodium hydroxide was added to dissolve the aluminum salts. Ether extraction afforded a gum (0.281 g, ν 994 cm^{-1}) which was chromatographed over alumina (15 g). Elution with hexane–ether (49:1), gave unchanged enone (0.037 g), mp 74–77° after one crystallization from methanol. Further elution with the same solvent afforded 2-methyl-5α-cholest-1-en-3α-ol (**11**) as an oil (0.067 g). Rechromatography over alumina and extensive drying (10 days under vacuum at 40–50°) afforded a crystalline sample: mp 90–92° (did not clear); $[\alpha]D$ −4° (*c* 2.85); ν 3580 (OH) and 994 cm^{-1}; δ 5.72 (H at C-1), 3.87 (broad H at C-3), and 0.77 ppm (methyl at C-2).

Anal. Calcd for $C_{28}H_{48}O$ (400.66): C, 83.93; H, 12.08. Found: C, 83.51; H, 11.90.

Further elution of the column with hexane–ether (19:1) afforded 2-methyl-5α-cholest-1-en-3β-ol (**10**, 0.121 g) as plates from methanol: mp 122–123°; $[\alpha]D$ +28° (*c* 2.5); ν 3600 (OH) and 1011 cm^{-1} (C—O); δ 5.63 (H at C-1) and 4.08 ppm (broad, H at C-3).

Anal. Calcd for $C_{28}H_{48}O$ (400.66): C, 83.93; H, 12.08. Found: C, 83.94; H, 12.11.

The alcohol formed a precipitate with ethanolic digitonin solution.

B. With Sodium Borohydride.—Enone **9** (0.062 g) in methanol (20 ml) was reduced with sodium borohydride. The crude product contained less than 10% of **11** by infrared inspection at 994 cm^{-1}. Crystallization from methanol afforded **10**, mp 118–120°.

C. With Lithium Aluminum Hydride.—The enone (0.021 g) in dry ether (2 ml) was treated with lithium aluminum hydride (0.015 g) at room temperature. After 1 min the excess of hydride was destroyed with ethyl acetate and the product was isolated as a gum. Infrared inspection indicated the presence of less than 10% of alcohol **11**. Recrystallization afforded **10**, mp 120.5–122°.

Hydrogenation of 3-Methylene-5α-cholestan-2α-yl Acetate (15b).—The acetate (0.050 g) in ethanol (20 ml) was hydrogenated over platinum oxide (0.006 g) for 22 hr. Filtration, evaporation, and crystallization from ether–methanol gave 3α-methyl-5α-cholestan-2α-yl acetate (**16b**) (0.028 g): mp 108–110°, raised to 112.5–113° after two recrystallizations; $[\alpha]D$ +18° (*c* 1.48); ν (KBr) 1740 (C=O), 1243 (sp^2 C—O), and 1026 cm^{-1} (sp^3 C—O).

Anal. Calcd for $C_{30}H_{52}O_2$ (444.72): C, 81.02; H, 11.79. Found: C, 81.13; H, 11.59.

3α-Methyl-5α-cholestan-2α-ol (16a).—Acetate **16b** (0.053 g) in ether (10 ml) was treated with lithium aluminum hydride for 5 hr. After work-up[26] the residue was crystallized from acetone: 0.032 g; mp 100–100.5°; ν 3600 (OH) and 1031 cm^{-1} (C—O). Further recrystallization from acetone gave pure **16a**, mp 101.5–102°, $[\alpha]D$ +42° (*c* 1.47). Esterification in pyridine afforded the 3,5-dinitrobenzoate **16c**, mp 188–189° from ether–methanol, $[\alpha]D$ +20° (*c* 1.38).

Anal. Calcd for $C_{35}H_{52}O_6N_2$ (596.78): C, 70.44; H, 8.78. Found: C, 70.76; H, 8.98.

3β-Methyl-5α-cholestan-2α-ol (18) To a slurry of lithium aluminum hydride (0.64 g) in ether (25 ml) was slowly added a solution of the olefin **13** (2.00 g) in ether (80 ml) containing boron trifluoride etherate (3.00 g). The mixture was stirred at room temperature in a nitrogen atmosphere for 2 hr. Saturated aqueous sodium sulfate (15 ml) was added to destroy the excess of hydride, followed by solid sulfate to dry the ether phase. The solids were removed by filtration and the solution was evaporated to an oily residue, which was dissolved in tetrahydrofuran (10 ml) and treated successively with 15% aqueous sodium hydroxide (0.5 ml) and 30% hydrogen peroxide (0.5 ml). After several minutes on the steam bath, the solution was treated with water (15 ml) and the product was obtained by ether extraction (1.82 g). Chromatography over alumina and elution with benzene–ether (9:1) afforded the crude alcohol (0.85 g). Recrystallizations from ether–methanol gave pure **18**: mp 114.5–115°; $[\alpha]D$ + 18° (*c* 1.84); ν 3580 (OH) and 1024 cm^{-1} (C—O).

Anal. Calcd for $C_{28}H_{50}O$ (402.68): C, 83.51; H, 12.52. Found: C, 83.85; H, 12.19.

Acetylation gave an acetate, mp 106.5–107° from ether–methanol, $[\alpha]D$ −38° (*c* 0.75).

Anal. Calcd for $C_{30}H_{52}O_2$ (444.72): C, 81.02; H, 11.79. Found: C, 80.92; H, 11.69.

Esterification with 3,5-dinitrobenzoyl chloride gave a 3,5-dinitrobenzoate, mp 200–201° (from ether–methanol), $[\alpha]D$ −24° (*c* 1.18).

Anal. Calcd for $C_{35}H_{52}O_6N_2$ (596.78): C, 70.44; H, 8.78. Found: C, 70.47; H, 8.72.

3α-Methyl-5α-cholestan-2-one (17).—Chromium trioxide–acetic acid oxidation of alcohol **16a** (0.025 g) gave the crude ketone, 0.019 g, mp 115–118°. Two recrystallizations from methanol gave pure **17**, mp 124.5–125.5°, $[\alpha]D$ +76° (*c* 0.37). The reported values are mp 116–118°, $[\alpha]D$ +70° (*c* 0.40).[14]

Acid equilibration (sulfuric acid–ethanol) of ketone **17** (0.005 g) gave the epimeric ketone **14** (0.003 g), mp 144.5–146.5°, which showed no melting point depression on admixture with an authentic sample of **14**.

Oxidation of Alcohol 18.—Chromium trioxide–acetic acid oxidation of alcohol **18** (0.020 g) afforded a crude ketone (0.015 g), mp 142–143°. Recrystallization from ether–methanol gave **14** (0.010 g), mp 148.5–149.5°, $[\alpha]D$ +45° (*c* 1.06).

Addition of Methylmagnesium Iodide to Enone 19.—To a stirred solution of methylmagnesium iodide (from 0.189 g of magnesium) in tetrahydrofuran (25 ml) at 0–5° was slowly added a solution of enone **19** (2.35 g) in tetrahydrofuran (30 ml). The mixture was warmed to 35° for 13 hr, then cooled to −10° and treated with 50 ml of cold 10% ammonium chloride solution. Extraction with ether afforded a crystalline solid, 2.19 g, mp 145–148°. One crystallization from methanol gave 3α-methyl-5α-cholest-1-en-3β-ol (**20**): 1.08 g; mp 155.5–157.5°, raised to 157–158.5° by further crystallization; $[\alpha]D$ +32° (*c* 0.83); ν 3620 (OH), 1642 (C=C), 1022 (C—O), and 758 cm^{-1} (CH=CH–). The compound gave no precipitate with digitonin.

Anal. Calcd for $C_{28}H_{48}O$ (400.86): C, 83.93; H, 12.08. Found: C, 84.20; H, 11.74.

The mother liquors from the reaction were evaporated and the residue was chromatographed over alumina. Elution with hexane–ether (100:1–50:1) gave a crystalline solid (0.22 g) which was rechromatographed and recrystallized from acetone to give 3β-methyl-5α-cholest-1-en-3α-ol (**21**) as plates, mp 102–103°, $[\alpha]D$ +4° (*c* 0.25). The compound gave no precipitate with digitonin and was identical (melting point, mixture melting point, and infrared spectrum) with the material obtained from the photosensitized oxygenation of olefin **13**. Further elution with hexane–ether (97:3) afforded more of the 3β-hydroxy compound (0.54 g).

3-Methylene-5α-cholest-1-ene (22).—Sublimation of alcohol **21** at 60° under vacuum afforded crude diene **22**, mp 82–82.5°. The same compound was formed during attempted chromatography of **21** over basic alumina (Woelm, activity I) or on activated silica gel (W. R. Grace, desiccant grade). Sublimation of the epimeric alcohol **20** at 130–140° also afforded crude **22**. Crystallization from ethyl acetate–methanol gave the diene **22**: mp 84–84.5°; $[\alpha]D$ +62° (*c* 1.45); λ 236 nm (ϵ 14,150); ν (KBr) 1738, 869 (C=CH_2), and 1625, 1588 cm^{-1} (conjugated C=C). In view of the low molar absorptivity and the value of $[\alpha]D$, the sample probably contains an isomeric impurity, which may be the unreported 3-methyl-5α-cholesta-1,3-diene.

Anal. Calcd for $C_{28}H_{46}$ (382.68): C, 87.88; H, 12.12. Found: C, 88.00, 87.98; H, 12.09, 12.18.

Hydrogenation of Diene 22.—The diene (0.011 g) in ethyl acetate–acetic acid (1:1, 6 ml) was hydrogenated over platinum oxide (0.020 g). A total of 2.0 mol of hydrogen was taken up in 40 min and the product was isolated by filtration and evaporation of the solvent. Crystallization from ethyl acetate–methanol afforded 3β-methyl-5α-cholestane, identified by melting point (105–106°) and mixture melting point with an authentic sample.

Photosensitized Oxygenation of 2-Methyl-5α-cholest-2-ene (23).—Oxygenations were conducted according to the general methods described previously.[4] A pyridine solution (50 ml) of olefin **23** (0.80 g) was irradiated and oxygenated in the presence of hematoporphyrin (0.013 g) for 19 hr. The solution was diluted with ether, decolorized with Norit-A charcoal, and evaporated. The residue was taken up in methanol (40 ml), sodium iodide (4 g) was added, and the solution was allowed to stand overnight. After evaporation of the solvent the residue was taken up in ether, washed with 5% sodium thiosulfate solu-

tion and with water, and dried and evaporated to a gum, which was chromatographed over alumina (30 g). Elution with hexane gave unidentified oily material (0.049 g). Elution with hexane–ether (199:1, 99:1) gave oily ketonic material (ν 1720, 1680 cm^{-1}) and further hexane–ether (97:3, 20:1) elution gave a mixture of hydroxy compounds (0.488 g), $[\alpha]D$ +27° (*c* 5.45). Most of this mixture (0.434 g) was rechromatographed over alumina (20 g). Elution with hexane–ether (97:3) gave 13 fractions (0.342 g) composed of mixtures of 2-methylene-5α-cholestan-3α-ol (**24**) and alcohol **11** identified by infrared and nmr measurements. Recrystallization of this material from acetone afforded 2-methylene-5α-cholestan-3α-ol (**24**) (0.076 g): mp 116–120°, raised by further recrystallization to 127–128° (0.033 g); $[\alpha]D$ +35° (*c* 0.7); ν 3560 (OH), 1647 (C=C), 902, and 705 cm^{-1}; δ 4.90 and 4.75 (=CH_2), 4.23 (C-3 H), and 2.08 ppm (OH).

Anal. Calcd for $C_{28}H_{48}O$ (400.66): C, 83.93; H, 12.08. Found: C, 84.10; H, 12.01.

Further elution with hexane–ether (24:1 and 20:1) gave mixtures of alcohols **24**, **11**, and **2a**. These combined fractions were recrystallized from methanol and gave a sharp-melting compound, mp 150.5–151.5°, $[\alpha]D$ +11° (*c* 1.30). Infrared analysis indicated that this compound was a complex (*ca.* 1:1) of **24** and **2a**.

Anal. Calcd for $C_{28}H_{48}O$ (400.66): C, 83.93; H, 12.08. Found: C, 83.90; H, 12.12.

Final elution with hexane–ether (47:3 and 9:1) gave alcohol **2a** (0.015 g) identified by melting point (132–133°), mixture melting point, and infrared spectrum.

Assay of the alcohol mixtures by quantitative infrared, nmr, and optical rotation indicated that the alcohols **24**, **2a**, and **11** were formed in the ratio of 57:13:30, respectively. The corrected total yield was 60%.

Photosensitized Oxygenation of 3-Methyl-5α-cholest-2-ene (13).—A pyridine solution (180 ml) of olefin **13** (3.00 g) was irradiated and oxygenated in the presence of hematoporphyrin (0.050 g). After 32 hr, the starting olefin was completely consumed and the reaction mixture was worked up as in the preceding experiment to give a light brown gum (3.1 g), which was chromatographed over alumina (90 g).[27] Elution with hexane and hexane–ether (99:1 to 97:1) afforded several oily fractions (0.170 g). Further elution with hexane–ether (9:1 to 7:3) gave a mixture of alcohols **15a** and **21**, 2.40 g, $[\alpha]D$ +18.6° (*c* 4.806). Rechromatography of most (2.18 g) of this material over alumina followed by several crystallizations from acetone afforded **21**: mp 107–108°; $[\alpha]D$ +9° (*c* 3.34); ν 3571 (OH), 1642 (C=C), 1034 (C—O), 898, and 762 cm^{-1}. This sample was identical with authentic **21** (infrared, mixture melting point). For analysis the sample was dried *in vacuo* for 2 days at room temperature.

Anal. Calcd for $C_{28}H_{48}O$ (400.66): C, 83.93; H, 12.08. Found: C, 84.02; H, 11.72.

Assay of the alcohol mixture by quantitative infrared and comparison with synthetic mixtures established that **21** and **15a** were formed in the ratio of *ca.* 70:30, respectively, and in a corrected total yield of 77%.

Attempted Photosensitized Oxygenations of 2-Methylene- and 3-Methylene-5α-cholestane.—Pyridine solutions (40 ml) of each olefin (0.1 g) were separately irradiated and oxygenated in the presence of hematoporphyrin (0.008 g) with additional dye (0.004 g) being added after 75 hr. Infrared examination of aliquots showed no evidence of hydroperoxide formation and work-up at the end of 100 hr gave only the starting olefins.

Registry No.—**2a**, 22599-96-8; **2b**, 37392-80-6; **2c**, 22599-97-9; **2d**, 37392-82-8; **4a**, 20997-60-8; **4b**, 37163-88-5; **4** (R = COPh), 37163-89-6; **4** (R = 3′,5′-dinitrobenzoate), 37406-79-4; **5**, 14528-10-0; **6**, 2097-78-1; **10**, 22599-98-0; **11**, 22599-94-6; **12**, 37392-87-3; **15a**, 37392-88-4; **15b**, 37392-89-5; **15c**, 37392-90-8; **15d**, 37413-07-3; **16a**, 37392-91-9; **16b**, 37392-92-0; **16c**, 37392-93-1; **18**, 37392-94-2; **18** acetate, 37392-95-3; **18** 3,5-dinitrobenzoate, 37392-96-4; **20**, 37392-97-5; **21**, 37392-98-6; **22**, 21152-07-8; **24**, 22599-92-4.

(27) Chromatography over activated silica gel gave diene **22** along with unidentified material.

Syntheses in the Noradamantane Series

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Preparations of several derivatives of noradamantane, including 1- and 2-noradamantanols, 1-bromonoradamantane, and noradamantane-1-carboxylic acid, are described. The reaction of deltacyclane (tetracyclo[4.3.0.$0^{2,4}$.$0^{8,7}$]nonane) with sulfuric acid is shown to lead to either 1- or 2-noradamantanol or noradamantane, depending on conditions. Other compounds, such as *exo*-2-brendanol and oxaadamantane, are also found in the reaction mixtures. Reaction pathways leading to the various products are discussed.

Investigations of the chemistry of adamantane (**1**) have been abetted considerably by the ease and simplicity of direct functionalization of the parent hydrocarbon.[1] Ionic substitutions, *e.g.*, bromination[2] and Koch–Haaf carboxylation,[3] give bridgehead products cleanly.[1] Adamantanone and several disubstituted adamantanes can be obtained by sulfuric acid oxidation of **1** under a variety of conditions.[4] Even nonselective substitution reactions, such as free-radical halogenations,[1] can be synthetically useful because of the high symmetry of adamantane, which limits the number of monosubstituted isomers to two.

Noradamantane (**2**),[5] only a single methylene removed from adamantane (**1**), behaves quite differently. Ring contraction decreases bridgehead reactivity at

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