Molecular Rearrangement of 4,4-Dimethylcholestan-3β-ol and Derivatives[1]

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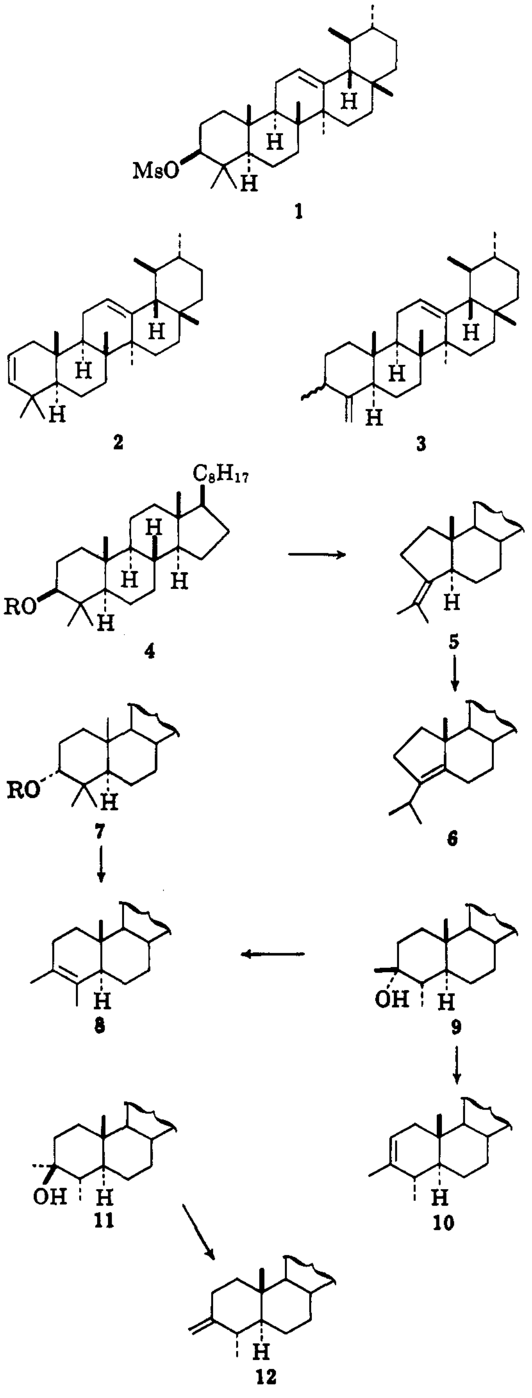
Dehydration of 4,4-dimethylcholestan-3β-ol (**4**, R = H) with phosphorus oxychloride in pyridine, or dehydrosulfonylation of the derived methane or toluenesulfonate esters by the action of basic alumina or hot pyridine gives a hydrocarbon mixture, the principal constituents of which are shown to be 4,4-dimethylcholest-2-ene (**13**) and the rearranged 3α-methyl-4-methylenecholestane (**14**). The structure of the latter is established by its oxidation to 3α-methylcholestan-4-one (**18**) followed by isomerization to 3β-methylcholestan-4-one (**19**), prepared independently from cholestan-4-one (**20**).

We have shown that sulfonate esters of the pentacyclic triterpenoid alcohols, α- and β-amyrin, on boiling with pyridine or simple filtration through alumina, undergo elimination of the sulfonic acid with formation of a hydrocarbon mixture, of which the two major constituents were separated and identified.[2] Thus, from α-amyrin methanesulfonate (**1**), for example, there was obtained ursa-2,12-diene (**2**) and a rearranged product formulated as 3ξ-methyl-24-norursa-4(23),12-diene (**3**) (Scheme I). We have now subjected the methanesulfonate and toluenesulfonate esters of 4,4-dimethylcholestanol to both of these conditions to examine the generality of the reaction and to gain information regarding the stereochemistry of the methyl group migration involved in the rearrangement (*e.g.*, **1** → **3**) and the configuration of the C-3 methyl group in the final product.

The 4,4-dimethylcholestan-3β-ol system was chosen for this purpose because of its ready availability, the simplicity of spectra interpretation of dehydration products in the absence of other ethylenic functions, and because a number of dimethylcholestenes and A-norcholestene isomers were known from previous studies.

The dehydration of 4,4-dimethylcholestan-3β-ol (**4**, R = H) by phosphorus pentachloride, a reaction frequently employed in triterpenoid chemistry to yield A-ring contracted products, has been reported to yield 3-isopropylidene-A-norcholestane (**5**) by three groups,[3-5] and the same hydrocarbon has been obtained as a product of acetolysis of the corresponding toluenesulfonate[5] (**4**, R = Ts). The endocyclic isomer, 3-isopropyl-A-norcholest-3-ene (**6**) has been obtained by the action of trichloroacetic acid on **5**, and also from the methanesulfonate (**4**, R = Ms) by solvolysis in aqueous dioxane in the presence of calcium carbonate.[4]

SCHEME I



3,4-Dimethylcholest-3-ene (**8**) has been obtained[5,6] by solvolysis of 4,4-dimethylcholestan-3α-yl toluenesulfonate (**7**, R = Ts) and by ionic dehydration of 3β,4α-dimethylcholestan-3α-ol (**9**). The latter reaction[7] also gave 3,4α-dimethylcholest-2-ene (**10**). In the same work, the dehydration of 3α,4α-dimethylcholestan-3β-ol (**11**) was reported to give 3-methylene-4α-methylcholestane (**12**). The preparation of 4,4-dimethylcholest-2-ene (**13**) in the conventional manner by heating the sulfonate ester (**4**, R = Ts) with collidine has also recently been indicated.[8] The reported

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[1] The award of a research grant (AM-3439) from the U. S. Public Health Service (to R. S.) and an Institutional Grant of the American Cancer Society (to F. K.) is gratefully acknowledged.

[2] F. Kohen, B. K. Patnaik, and R. Stevenson, *J. Org. Chem.*, **29**, 2710 (1964).

[3] N. W. Atwater, *J. Am. Chem. Soc.*, **82**, 2847 (1960).

[4] (a) J. F. Biellmann and G. Ourisson, *Bull. soc. chim. France*, 348 (1960); (b) *ibid.*, 331 (1962).

[5] C. W. Shoppee and G. A. R. Johnston, *J. Chem. Soc.*, 3261 (1961).

[6] G. Bancroft, Y. M. Y. Haddad, and G. H. R. Summers, *ibid.*, 3295 (1961).

[7] J. L. Beton, T. G. Halsall, E. R. H. Jones, and P. C. Phillips, *ibid.*, 753 (1957).

TABLE I

REPORTED MELTING POINTS AND SPECIFIC ROTATIONS OF HYDROCARBONS, $C_{29}H_{50}$

Compd.	M.p., °C.	[α]D, deg.	Ref.
3-Isopropylidene-A-norcholestane (5)	98–100	+121	a
	99–100	+5	b
	88–90	+19	c
	97–98	+10	d
3-Isopropyl-A-norcholest-3-ene	96–99	+20	b
(6)	98–99	+15	e
3,4-Dimethylcholest-3-ene (8)	107–108	+6	f
	106.5–108	+5	g
	105–106	+8	c
3,4α-Dimethylcholest-2-ene (10)	113–113.5	+20	g
3-Methylene-4α-methylcholestane (12)	66–67	+12.5	g
4,4-Dimethylcholest-2-ene (13)	89–90	+38	h
	89–90	+44	e
3α-Methyl-4-methylenecholestane (14)	125–127	+105	e

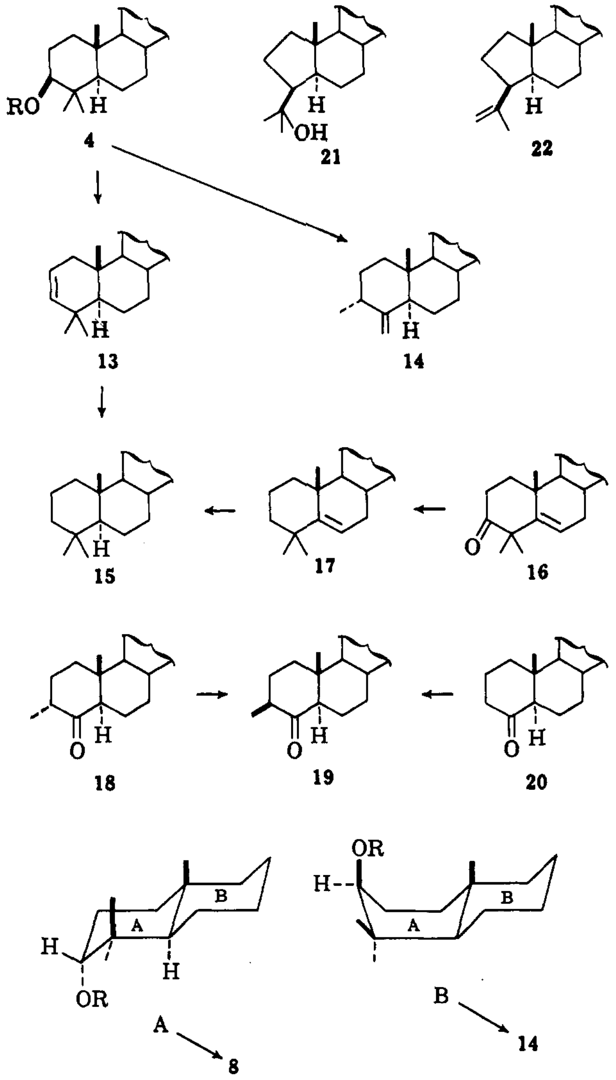
[a] Ref. 3. [b] Ref. 4b. [c] Ref. 5. [d] F. Kohen and R. Stevenson, unpublished. [e] This work, Experimental section. [f] Ref. 6. [g] Ref. 7. [h] Ref. 8.

constants of these hydrocarbons, together with those obtained in this work, are summarized in Table I.

The 4,4-dimethylcholestan-3β-ol (**4**, R = H) was prepared by catalytic hydrogenation of 4,4-dimethylcholest-5-en-3β-ol, either in ethanol solution under pressure or in acetic acid solution at atmospheric pressure, or by lithium aluminum hydride hydrolysis of the acetate (**4**, R = Ac), also obtained by catalytic hydrogenation of the Δ^5 precursor. Subjection of the derived toluenesulfonate or methanesulfonate of **4** to the action of pyridine under reflux for 6 days yielded a hydrocarbon mixture of which two major and two minor constituents could be detected by thin layer chromatographic techniques. A hydrocarbon mixture of the same constituents, although present in different ratio, could be obtained much more simply by filtration of a benzene solution of the sulfonate ester through basic chromatographic alumina. These observations corresponded to our previous experience with the sulfonate esters of the triterpenoids, α- and β-amyrin.[2]

The two major constituents, which represented about 90% of the total hydrocarbon mixture obtained by the pyridine method, were separated by thin layer chromatography and shown to be isomeric alkenes, $C_{29}H_{50}$. By the evidence outlined below, the product of higher R_f 0.39, m.p. 89–90°, [α]D +44°, is shown to be 4,4-dimethylcholest-2-ene (**13**) and that of lower R_f 0.20, m.p. 125–127°, [α]D +105°, to be 3α-methyl-4-methylenecholestane (**14**), a product of molecular rearrangement (Scheme II).

SCHEME II



The structure of **13** was rigorously established by the following: (a) the melting point is in good agreement with that reported for a product to which this structure had been assigned[8]; (b) the n.m.r. spectrum shows the presence of two vinyl protons; (c) it was identical with the hydrocarbon which we obtained by pyrolysis of the dimethylcholestanyl benzoate (**4**, R = Bz); and (d) on catalytic hydrogenation it yielded the saturated hydrocarbon, 4,4-dimethylcholestane (**15**), obtained unambiguously by Wolff–Kishner reduction of 4,4-dimethylcholest-5-en-3-one (**16**), followed by catalytic hydrogenation of the derived 4,4-dimethylcholest-5-ene (**17**).

The isomeric hydrocarbon of lower R_f 0.20 had an intense band at 11.20 μ in the infrared spectrum, which indicated the presence of a vinylidene group. This was confirmed by the n.m.r. spectrum which had signals characteristic of two vinyl protons; the fact that this spectrum lacked a methyl peak, characteristic of an allylic methyl function, excluded the possibility that the hydrocarbon was a product of retropinacolic dehydration with an isopropenyl group (*e.g.*, **22**). Evidence for the correctness of the postulated structure (**14**) was obtained by oxidation of the hydrocarbon with osmium tetroxide, followed by lead tetraacetate cleavage of the resultant diol. In addition to formaldehyde, isolated as its dimedone derivative, there was obtained a ketone $C_{28}H_{48}O$. The optical rotatory dispersion spectrum exhibited a strong rather symmetrical negative Cotton effect, characteristic of a 4-ketone. Of all positions in rings A, B, and C of cholestanones, only the 4- and 6-ketones exhibit this type of spectrum.[9] This indicates that the hydrocarbon has a methylene group at C-4 and consequently is a rearrangement product from **4**, in which one of the methyl groups originally

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(8) J. Levisalles, J. C. N. Ma, and J. P. Pete, *Bull. soc. chim. France*, 1126 (1963); A. L. Combier, J. Levisalles, J. P. Pete, and H. Rudler, *ibid.*, 1689 (1963).

(9) C. Djerassi, W. Closson, and A. E. Lippman, *J. Am. Chem. Soc.*, **78**, 3163 (1956).

located at C-4 has undergone a 1,2-shift to C-3. Since this ketone is readily converted by mild base treatment to an isomeric ketone which also exhibits a negative Cotton effect, we conclude that it is the less stable of the 3-methyl-4-keto epimers and has the 3α-axial configuration. In summary, this evidence is fully consistent with the postulate that the hydrocarbon is the 3α-methyl-4-methylenecholestane (**14**) which has yielded on oxidation 3α-methylcholestan-4-one (**18**) readily epimerized to 3β-methylcholestan-4-one (**19**).

We have sought to confirm these structural assignments by an unambiguous synthesis of the ketone **19**. Condensation of cholestan-4-one[10] (**20**) with ethyl formate, followed by alkylation with methyl iodide, gave both ketones **18** and **19**, from which the more stable 3β-methyl isomer was obtained in a pure state after chromatography. It was identical with the ketone obtained from the hydrocarbon **14**.

The demonstration that it is the 4α-methyl group which migrates to C-3 during the rearrangement deserves comment. There has been much recent discussion, particularly concerning steroids and triterpenoids, of molecular systems in which a ring exists in one of the flexible forms (where nonbonded interactions in the chair form are sufficiently reduced and compensate for the usual instability of the boat form relative to the chair form), or in which reactions occur in conformations other than their most stable.[11-13] We note that the interconversion of **4** to **13** and **14** is readily visualized if the ester (or derived cation) reacts in a boat conformation.

In the solvolysis of 3α-substituted derivatives of 4,4-dimethyl steroids, a migration of the 4β-methyl group occurs,[5,6] as expected from the *trans* diaxial disposition of the leaving and migrating groups in the chair form (A). Such a condition does not exist in the chair form of the 3β-equatorial-substituted derivatives; the adoption of the boat conformation (B) readily provides the desired geometry. It has already been pointed out[11] that the boat conformation of **4** is also suitably disposed for the bimolecular elimination yielding the hydrocarbon **13**, although recent evidence indicates that this elimination, performed by the action of boiling collidine on the toluenesulfonate ester, shows a high *cis* stereospecificity.[8] Consequently, although the conversion (**4** → **13**) is consistent with the intermediacy of a boat conformation species, definitive evidence is lacking.

The hydrocarbons **13** and **14**, the principal products obtained from elimination of the sulfonate esters under such disparate reactions as refluxing pyridine and basic alumina at room temperature, were also shown to be produced (a) by the action of acid alumina, along with 3-isopropyl-A-norcholest-3-ene (**6**); (b) by base hydrolysis in aqueous dioxane, along with **6** and 3β-(1-hydroxy-1-methylethyl)-A-norcholestane (**21**); and (c) by the action of phosphorus oxychloride in pyridine on the 4,4-dimethyl 3β-alcohol (**4**, R = H).

In achievement of one of the original aims of this work, the rearranged hydrocarbon obtained from the sulfonate esters of α-amyrin and β-amyrin, and originally called α- and β-amyradiene-IV, can now be definitely formulated, respectively, as 3α-methylnorursa-4(23),12-diene (**3**, 3α-methyl group) and 3α-methylnoroleana-4(23),12-diene.

Experimental

Specific rotations were determined in chloroform solution. Melting points were determined using a Gallenkamp melting point apparatus. Proton magnetic resonance spectra were determined in CCl_4 or $CDCl_3$ solution with tetramethylsilane as an internal standard using a Varian 4300B spectrophotometer. Petroleum ether, unless otherwise stated, refers to the fraction of b.p. 30–60°.

Thin Layer Chromatographic Technique.[14]—Aqueous silver nitrate solution (12.5%, 60 ml.) was added to silica gel G (30 g., Merck), and the mixture was shaken to a slurry for 1 min. For analytical purposes, the slurry was applied to glass plates in a 0.25-mm. layer, and for preparative purposes in a 1.00-mm. layer. The plates were dried at room temperature for 30 min., and activated, prior to use, at 125° for 2 hr. The R_f values reported are for carbon tetrachloride as developing solvent.

4,4-Dimethylcholestan-3β-yl Acetate (4, R = Ac).—A solution of 4,4-dimethylcholest-5-en-3β-yl acetate[15] (1.3 g.) in acetic acid (150 ml.) was added to a suspension of platinum (prereduced from 217 mg. of PtO_2) in acetic acid and shaken in hydrogen for 3 hr. Two recrystallizations of the product from acetone gave 4,4-dimethylcholestan-3β-yl acetate as needles (870 mg.), m.p. 132–133°, $[\alpha]_D$ +16° (*c* 2.1). It does not give a color with tetranitromethane in chloroform: lit.[16] m.p. 138–139°, $[\alpha]_D$ +19°.

Anal. Calcd. for $C_{31}H_{54}O_2$: C, 81.16; H, 11.87. Found: C, 81.4; H, 12.1.

4,4-Dimethylcholestan-3β-ol (4, R = H). A.—A solution of the acetate (550 mg.) in ether (50 ml.) was refluxed with lithium aluminum hydride for 1 hr. and worked up in the usual way. Crystallization from chloroform–methanol or acetone gave the product as a rather gelatinous solid, m.p. 151–153°, $[\alpha]_D$ +8° (*c* 1.6). Recrystallization from acetic acid gave 4,4-dimethylcholestan-3β-ol as flat needles: m.p. 152–153°, $[\alpha]_D$ +8°; lit.[16] m.p. 157–158°, $[\alpha]_D$ +11°.

Anal. Calcd. for $C_{29}H_{52}O$: C, 83.58; H, 12.58. Found: C, 83.5; H, 12.6.

B.—A solution of 4,4-dimethylcholest-5-en-3β-ol in acetic acid was shaken with prereduced platinum oxide in hydrogen for 4 hr. Crystallization from acetic acid gave the saturated alcohol as flat needles, m.p. 151–152°, $[\alpha]_D$ +7° (*c* 3.0). Acetylation by heating with pyridine and acetic anhydride gave the acetate as needles, m.p. 132–133°, $[\alpha]_D$ +16° (*c* 1.1), from acetone.

C.—A solution of 4,4-dimethylcholest-5-en-3β-ol (2.15 g.) in 95% ethanol (500 ml.) was hydrogenated at 1000 p.s.i. at 130° for 5 hr., using palladium–carbon (10%, 200 mg.) as catalyst. The residue obtained after removal of solvent and catalyst was crystallized from methylene chloride–methanol to give 4,4-dimethylcholestan-3β-ol as platelets (1.75 g.), m.p. 156–157°, $[\alpha]_D$ +7° (*c* 1.5).

4,4-Dimethylcholestan-3β-yl Toluene-*p*-sulfonate (4, R = Ts).—To a solution of the dimethylcholestanol (1.0 g.) in dry pyridine (20 ml.) was added toluene-*p*-sulfonyl chloride (1.8 g.), and the mixture was allowed to stand at room temperature for 3 days. Addition of ice–water produced a precipitate, which was collected and washed with methanol. Recrystallization from methylene chloride–methanol gave the toluene-*p*-sulfonate as prisms: m.p. 120–122° dec., $[\alpha]_D$ +10° (*c* 1.6), λ^{CHCl_3} 8.50 and 9.10 μ; lit.[5] m.p. 125–126°, $[\alpha]_D$ +7°; lit.[4b] m.p. 131°, $[\alpha]_D$ +106°.

4,4-Dimethylcholestan-3β-yl Methanesulfonate (4, R = Ms).—To a solution of the dimethylcholestanol (500 mg.) in pyridine (3 ml.) was added dropwise a solution of methanesulfonyl chloride (0.5 ml.) in pyridine (3 ml.). The mixture was allowed to stand at room temperature for 24 hr., poured into

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[10] C. W. Shoppee, M. E. Howden, R. W. Killick, and G. H. R. Summers, *J. Chem. Soc.*, 630 (1959).

[11] J. Levisalles, *Bull. soc. chim. France*, 551 (1960).

[12] D. H. R. Barton and G. A. Morrison, "Progress in the Chemistry of Organic Natural Products," Vol. 19, Springer-Verlag, Wien, 1961, pp. 212–217.

[13] M. Balasubramanian, *Chem. Rev.*, **62**, 591 (1962).

[14] C. B. Barrett, M. S. J. Dallas, and F. B. Padley, *Chem. Ind.* (London), 1050 (1962).

[15] R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelly, *J. Chem. Soc.*, 1131 (1957).

[16] Y. Mazur and F. Sondheimer, *J. Am. Chem. Soc.*, **80**, 5220 (1958).

water, extracted with ether, and worked up in the usual way. Crystallization of the product from methylene chloride–methanol gave the methanesulfonate as needles: m.p. 139–140° dec., $[\alpha]_D$ +10° (*c* 2.0), λ^{KBr} 8.55 μ; lit.[4b] m.p. 148°, $[\alpha]_D$ +13°.

Anal. Calcd. for $C_{30}H_{54}O_3S$: C, 72.83; H, 11.00; S, 6.50. Found: C, 73.04; H, 11.02; S, 6.38.

4,4-Dimethylcholestan-3β-yl Benzoate (4, R = Bz).—Benzoyl chloride (0.2 ml.) was added to the dimethylcholestanol (300 mg.) in pyridine (4 ml.) and the mixture was heated under reflux for 30 min. The solid, which separated on cooling, was collected and crystallized from methylene chloride–methanol as needles, m.p. 136–138°, $[\alpha]_D$ +39° (*c* 1.8).

Anal. Calcd. for $C_{36}H_{56}O_2$: C, 83.02; H, 10.84. Found: C, 82.76; H, 10.74.

Action of Pyridine on 4,4-Dimethylcholestan-3β-yl Sulfonate Esters. A.—A solution of the methanesulfonate (1.17 g.) in pyridine (54 ml.) was heated under reflux for 6 days, then evaporated to dryness under reduced pressure. The residue was extracted with ether, and the extract was washed successively with water, dilute hydrochloric acid, water, sodium bicarbonate solution, and water. The dried extract (820 mg.) was dissolved in petroleum ether and filtered through alumina (Savory and Moore, 25 g.). The eluate (60 ml.) was evaporated and the residue (710 mg.) crystallized from ethyl acetate to give a hydrocarbon mixture: m.p. 71–73°; $[\alpha]_D$ +53° (*c* 1.7); λ^{KBr} 6.00, 6.10, 11.20, and 13.65 μ. Thin layer chromatographic examination revealed four spots, two of strong intensity at R_f 0.20 and 0.39 and two of weak intensity at R_f 0.53 and 0.67. The hydrocarbon mixture (565 mg.) was separated by combining the appropriate fractions by elution with petroleum ether from seven preparative thin layer plates.

The fraction (275 mg.), R_f 0.39, was crystallized from methylene chloride–methanol to give **4,4-dimethylcholest-2-ene (13)** as long needles: m.p. 89–90°; $[\alpha]_D$ +44° (*c* 0.9); λ^{KBr} 6.00 and 13.67 μ; n.m.r. signals (in CCl_4) at δ 0.63, 0.79, 0.84, 0.89, 0.91, 1.19 (methyl groups), and 5.38 (two vinyl protons).

Anal. Calcd. for $C_{29}H_{50}$: C, 87.36; H, 12.64. Found: C, 87.46; H, 12.69.

The fraction (200 mg.), R_f 0.20, was crystallized from methylene chloride–methanol to give **3α-methyl-4-methylenecholestane (14)** as needles: m.p. 125–127°; $[\alpha]_D$ +105° (*c* 2.2); λ^{KBr} 6.10 and 11.20 μ; n.m.r. signals (in $CDCl_3$) at δ 0.65, 0.68, 0.82, 0.91, 1.14 (methyl groups), 4.40, and 4.70 (vinyl protons).

Anal. Calcd. for $C_{29}H_{50}$: C, 87.36; H, 12.64. Found: C, 87.36; H, 12.62.

B.—The same treatment of the toluenesulfonate ester (200 mg.) gave the same mixed hydrocarbon (200 mg.), m.p. 71–73°.

Action of Basic Alumina on 4,4-Dimethylcholestan-3β-yl Sulfonate Esters. A.—A solution of the toluenesulfonate (500 mg.) in petroleum ether (5 ml.) was added to a column of alumina (Woelm basic, 30 g.), allowed to stand for 1 hr., then eluted with the same solvent (100 ml.) to give a hydrocarbon mixture (325 mg.; m.p. 75–76°; R_f 0.20, 0.39, 0.53, and 0.67). From 200 mg. of this mixture there was obtained, by thin layer chromatographic separation, 3α-methyl-4-methylenecholestane (R_f 0.20, 14 mg.) and 4,4-dimethylcholest-2-ene (R_f 0.39, 63 mg.). The third fraction (R_f 0.53, 72 mg.) did not give a homogeneous identified product, and the fourth fraction (R_f 0.67, 10 mg.) failed to crystallize.

B.—Under the same conditions, the methanesulfonate (350 mg.) yielded a hydrocarbon mixture (210 mg.), which yielded 3α-methyl-4-methylenecholestane (30 mg.) and 4,4-dimethylcholest-2-ene (115 mg.).

Action of Acid Alumina on 4,4-Dimethylcholestan-3β-yl Methanesulfonate.—A solution of the methanesulfonate (242 mg.) in petroleum ether (4 ml.) was added to a column of alumina (Woelm acid), allowed to stand for 1 hr., then eluted with the same solvent (50 ml.) to yield a hydrocarbon mixture (179 mg.) shown to consist of three major products, R_f 0.21, 0.37, and 0.60, by thin layer chromatographic examination. The product, R_f 0.60, was crystallized from acetone to give **3-isopropyl-A-norcholest-3-ene** as platelets (72 mg.): m.p. 98–99°; $[\alpha]_D$ +16° (*c* 1.1); n.m.r. signals (in CCl_4) at δ 0.68, 0.81, 0.91, 1.00, 1.16 (methyl groups), and showed absence of vinyl protons.

Anal. Calcd. for $C_{29}H_{50}$: C, 87.36; H, 12.64. Found: C, 87.21; H, 12.48.

Base Hydrolysis of 4,4-Dimethylcholestan-3β-yl Methanesulfonate.—A solution of the methanesulfonate (400 mg.) and calcium carbonate (455 mg.) in aqueous dioxane (1:1, 136 ml.) was heated under reflux for 18 hr., concentrated under reduced pressure, and extracted with ether. Evaporation of the washed and dried extract gave a gummy solid (305 mg.) which was dissolved in petroleum ether (b.p. 66–67°) and chromatographed on alumina (Merck). Elution with the same solvent gave the hydrocarbon mixture (174 mg.; R_f 0.20, 0.37, and 0.60), m.p. 72–74° (from methylene chloride–methanol). From 150 mg. of this mixture there was obtained, by thin layer chromatographic separation, a product identified as **3-isopropyl-A-norcholest-3-ene (6)** [67 mg., R_f 0.60, m.p. 98–99°, $[\alpha]_D$ +15° (*c* 0.9)] by comparison of the R_f value with the authentic specimen. Elution with chloroform (50 ml.) yielded a product which, on crystallization from methylene chloride–methanol, gave **3β-(1-hydroxy-1-methylethyl)-A-norcholestane (21)** as needles (42 mg.): m.p. 97–98°, $[\alpha]_D$ +30° (*c* 1.0), λ^{KBr} 2.75 and 2.99 μ; lit.[4b] m.p. 101.5–102.5°, $[\alpha]_D$ +27°.

Dehydration of 4,4-Dimethylcholestan-3β-ol with Phosphorus Oxychloride.—Phosphorus oxychloride (1 ml.) was added to a solution of dimethylcholestanol (219 mg.) in pyridine (7 ml.), heated at 56° for 19 hr., poured into ice–water, and extracted with ether. The extract was washed successively with water, dilute hydrochloric acid, sodium bicarbonate solution, and water, dried ($MgSO_4$), and evaporated. The residue (165 mg.) was dissolved in petroleum ether, filtered through Merck acid alumina, and the hydrocarbon fraction was examined by thin layer chromatography. The two major spots (R_f 0.21 and 0.38) were identified as 3α-methyl-4-methylenecholestane (20 mg.) and 4,4-dimethylcholest-2-ene (65 mg.).

4,4-Dimethylcholest-5-ene (17).—A mixture of 4,4-dimethylcholest-5-en-3-one[15] (412 mg.), 99% hydrazine hydrate (3 ml.), and diethylene glycol (11 ml.) was heated at 150° for 10 min., potassium hydroxide (2 g.) then was added, and heating was continued at 150° for 45 min. Solvent was then distilled until a solution temperature of 210° was reached, and the mixture was refluxed for a further 6 hr., cooled, poured into water, and extracted with ether. The washed and dried extract was evaporated, and the residual gum (312 mg.) was chromatographed on Merck acid alumina (14 g.). Elution with petroleum ether (b.p. 66–68°, 50 ml.) gave **4,4-dimethylcholest-5-ene** (176 mg.), which crystallized from acetone as long needles: m.p. 72–73°, $[\alpha]_D$ −70° (*c* 1.2); lit.[17] m.p. 73–74°, $[\alpha]_D$ −73°; n.m.r. spectrum (in CCl_4) at δ 0.67, 0.82, 0.92, 1.07, 1.12 (methyl groups), and 5.35 (vinyl hydrogen).

Anal. Calcd. for $C_{29}H_{50}$: C, 87.36; H, 12.64. Found: C, 87.72; H, 12.40.

4,4-Dimethylcholest-2-ene (13).—4,4-Dimethylcholestan-3β-yl benzoate (200 mg.) was heated at 300° for 1 hr. in a nitrogen atmosphere. The residue was extracted with ether; the extract was washed with sodium bicarbonate solution and water, dried, and evaporated. A solution of the product in petroleum ether (b.p. 66–68°) was chromatographed on Merck acid alumina, elution with the same solvent giving 4,4-dimethylcholest-2-ene (80 mg.) as needles, m.p. 87–88°, $[\alpha]_D$ +48° (*c* 2.6), after two recrystallizations from acetone. A comparison of infrared and n.m.r. spectra with samples obtained from the sulfonate ester reactions confirmed their identity.

4,4-Dimethylcholestane (15). A.—A solution of 4,4-dimethylcholest-2-ene (165 mg.) in acetic acid (20 ml.) and cyclohexane (30 ml.) was stirred in a hydrogen atmosphere at room temperature and pressure for 2 hr. using prereduced platinum oxide (65 mg.) as catalyst. The residual solid, obtained after removal of solvent and catalyst, was purified by filtration through alumina and crystallized from acetone to give 4,4-dimethylcholestane as needles (130 mg.): m.p. 84–85°, $[\alpha]_D$ +9° (*c* 1.5); lit.[17] m.p. 86–87°, $[\alpha]_D$ −8°.

Anal. Calcd. for $C_{29}H_{52}$: C, 86.92; H, 13.08. Found: C, 87.06; H, 13.02.

B.—A solution of 4,4-dimethylcholest-5-ene (100 mg.) in cyclohexane (150 ml.) was hydrogenated at 1000 p.s.i. at 130° for 4 hr., using palladium–carbon (10%) catalyst. The product, purified as in A, gave 4,4-dimethylcholestane (74 mg.), m.p. 84–85°, $[\alpha]_D$ +8° (*c* 1.4), undepressed in mixture melting point with sample prepared in A.

3α-Methylcholestan-4-one (18).—A solution of osmium tetroxide (150 mg.) in dioxane (15 ml.) was added to a solution of 3α-methyl-4-methylenecholestane (145 mg.) in the same solvent (15 ml.), the mixture was allowed to stand at room temperature for 3 weeks, then saturated with hydrogen sulfide, and the precipitate was removed by filtration. The residue, obtained by evapo-

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[17] C. W. Shoppee and G. A. R. Johnston, *J. Chem. Soc.*, 1126 (1962).

ration of the filtrate under reduced pressure, was dissolved in *petroleum ether and chromatographed on Merck acid alumina.* Elution with the same solvent (50 ml.) gave unchanged hydrocarbon (5 mg.), and elution with chloroform (200 ml.) gave a solid (88 mg., λ^{CHCl_3} 2.70 and 2.90 μ), assumed to be the required diol and not further purified. To a solution of this diol (88 mg.) in acetic acid (20 ml.) was added freshly crystallized lead tetraacetate (180 mg.) in acetic acid (6 ml.). The mixture was allowed to stand at room temperature for 40 hr., diluted with water, and distilled. Sodium carbonate was added to the distillate, which was then redistilled and added to a solution of dimedone (60 mg.) in ethanol (2 ml.). A precipitate (17 mg.) formed and was collected and identified as formaldehyde dimedone by m.p. 192–193° and infrared comparison with authentic specimen. The residue from the initial distillation was extracted with ether; the extract was washed with sodium bicarbonate solution and water. Evaporation of the dried extract gave an oil (60 mg.) which was dissolved in petroleum ether and chromatographed on Savory and Moore alumina (7 g.). Elution with petroleum ether–benzene (1:1, 50 ml.) yielded a solid (26 mg.) which was crystallized from methylene chloride–methanol to give **3α-methylcholestan-4-one** as platelets, m.p. 90–92°, $[\alpha]_D$ +15° (*c* 1.3), λ^{KBr} 5.85 μ, R_f 0.45 (C_6H_6–$CHCl_3$, 1:1, as developing solvent on silica gel G).

Anal. Calcd. for $C_{28}H_{48}O$: C, 83.93; H, 12.08. Found: C, 84.11; H, 11.84.

Optical rotatory dispersion (O.R.D.)[18] in dioxane (*c* 0.045) gave: $[\alpha]_{345}$ −218°, $[\alpha]_{318.5}$ −980° (min.), and $[\alpha]_{278}$ +1420° (max.).

3β-Methylcholestan-4-one (19). **A. By Alkylation of Cholestan-4-one.**—Sodium methoxide (prepared from 385 mg. of sodium in 5 ml. of methanol) and ethyl formate (5 ml.) were added to a solution of cholestan-4-one[10] (455 mg.) in anhydrous ether (15 ml.), and the mixture was allowed to stand at room temperature for 5 days. Ether and buffered phosphate solution (pH 8, 40 ml.) were then added, and the aqueous layer was separated, acidified with 1 *N* hydrochloric acid, and extracted with ether. Evaporation of the washed and dried extract yielded the hydroxymethylene derivative, which was heated under reflux with a mixture of potassium carbonate (200 mg.) and methyl iodide (0.4 ml.) in dry acetone (10 ml.) for 16 hr. The mixture was then diluted with water and extracted with ether, and the extract was washed with 2 *N* sodium hydroxide solution and water and dried. The residue (290 mg.) obtained on evaporation was dissolved in petroleum ether and chromatographed on alumina (Savory and Moore, 20 g.). Elution with petroleum ether–benzene (1:1, 100 ml.) yielded a solid which, on crystallization from methylene chloride–methanol, gave **3β-methylcholestan-4-one** as needles (20 mg.), m.p. 118–119°, $[\alpha]_D$ +19° (*c* 0.8), λ^{KBr} 5.87 μ, R_f 0.53 (C_6H_6–$CHCl_3$, 1:1, as developing solvent and silica gel G as adsorbent).

Anal. Calcd. for $C_{28}H_{48}O$: C, 83.93; H, 12.08. Found: C, 84.20; H, 11.95.

O.R.D. in dioxane (*c* 0.031) gave: $[\alpha]_{345}$ −46°, $[\alpha]_{315.5}$ −680° (min.), and $[\alpha]_{275.5}$ +1380° (max.). Further elution with benzene gave a mixture of 3α- and 3β-cholestan-4-one (50 mg., R_f 0.45 and 0.53, respectively).

B. By Epimerization of 3α-Methylcholestan-4-one.—To 1% ethanolic potassium hydroxide solution (10 ml.) was added 3α-methylcholestan-4-one (14 mg.), and the mixture was heated under reflux for 1 hr. The solvent was then removed under reduced pressure, the residue was extracted with ether, and the extract was washed and dried. Evaporation gave a solid which was crystallized from methylene chloride–methanol to give 3β-methylcholestan-4-one as needles, m.p. 118–119°, with R_f and infrared spectrum identical with those of the specimen prepared as in A.

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[18] We are grateful to Mrs. Elke Mermelstein for O.R.D. data, determined on a Polaramatic 62 Bendix Ericsson polarimeter.

Bis(phenylsulfonyl)diazomethane[1]

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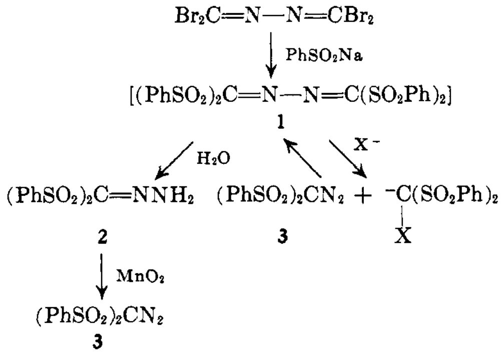
The preparation of the electrophilic bis(phenylsulfonyl)diazomethane (**3**) from carbonyl bromide azine is described. Photolysis of **3** is believed to give bis(phenylsulfonyl)carbene. A study of the reactions of this exceptionally electrophilic carbene and possible mechanisms are discussed.

A study of the reactions of divalent carbon has attracted the attention of many workers. In general, carbenes are highly reactive electrophilic reagents, although Wanzlick has rationalized reactions of bis[1,3-diphenylimidazolidinylidene-(2)] in terms of a nucleophilic diaminocarbene intermediate.[2] We were interested in studying the effect of strongly electron-withdrawing substituents on the reactivity of the divalent carbon atom in the hope of observing an exceptionally electrophilic carbene. The sulfonyl group is one of the strongest electron-withdrawing groups known and, therefore, we chose to prepare and study the reactions of bis(phenylsulfonyl)diazomethane (**3**), a possible source of bis(phenylsulfonyl)carbene.

Preparation.—A rapid reaction occurred upon treatment of carbonyl bromide azine with sodium benzenesulfinate in dimethylformamide. Addition of water precipitated bis(phenylsulfonyl)formaldehyde hydrazone (**2**) in 90% yield. Oxidation of **2** could be effected readily with active manganese dioxide or silver oxide to give bis(phenylsulfonyl)diazomethane in 55% yield. Bis(phenylsulfonyl)methane (**4**) was also isolated as a by-product; it was probably formed *via* a Wolff–Kishner-type reaction of **2** with the basic oxidizing agent.



In an attempt to prepare the intermediate tetrakis(phenylsulfonyl)formaldehyde azine (**1**), the reaction of carbonyl bromide azine with sodium benzenesulfinate was carried out in an anhydrous medium. Surprisingly, a good yield of **3** was isolated directly by this

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[1] A preliminary communication of this work appeared in *J. Org. Chem.*, **28**, 2933 (1963). The completed work was presented at the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964.

[2] H. W. Wanzlick, *Angew. Chem.*, **74**, 129 (1962).