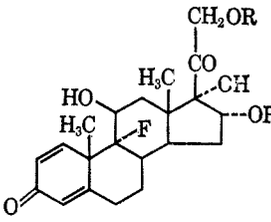
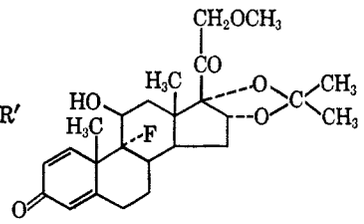
For the added purpose of structure elucidation, the 16α-acetate-21-methoxy compound (**1e**) was saponified to give the 21-methoxy-11β,16α,17α-triol (**1f**), in turn converted in the conventional manner into the 21-methoxy-16α,17α-acetonide (**2**).



1a, R = Ac; R′ = CH_3
b, R = Ac; R′ = H
c, R = H; R′ = Ac
d, R = R′ = H
e, R = CH_3; R′ = Ac
f, R = CH_3; R′ = H
g, R = R′ = CH_3



2

Thus, the previous implication[1] that carbonate hydrolysis of **1e** gave a new compound (**1g**), the indicated reaction being replacement of an acetate by a methyl ether group, must be withdrawn. In conclusion, it should be noted that the acid-catalyzed diazomethane reaction discussed herein proceeded in a normal manner without acetate hydrolysis or acetyl migration.

In Table I are listed the significant diagnostic signals of the nmr spectra of these methoxycorticoids which support the assigned structures.

TABLE I

NMR SPECTRA OF METHOXYCORTICOIDS (PARTS PER MILLION)

Compd	21-H[a]	Methyl ether	Acetate	19-H	18-H
Triamcinolone (**1d**)	4.29	3.27	...	1.49	0.87
21-Acetate 16-methyl ether (**1a**)	4.91	3.09	2.09	1.49	0.89
16-Acetate 21-methyl ether (**1e**)	4.25	3.25	1.98	1.49	0.88
16,21-Dimethyl ether (**1g**)	4.34	3.36 3.12	...	1.49	0.88
21-Methyl ether 16,17-acetonide (**2**)	4.37	3.42	...	1.57[b]	0.91

[a] Center of a pair of doublets. [b] This slight deshielding of a C-19-methyl grouping is common in many 16α,17α-acetonides.

Experimental Section[4]

21-Acetoxy-9α-fluoro-11β,17α-dihydroxy-16α-methoxypregna-1,4-diene-3,20-dione (**1a**).—A solution of highly purified 21-acetoxytriamcinolone (**1b**, 0.98 g) in methylene chloride (1 l.) was treated with fluoroboric acid and diazomethane as previously described.[1] After discharge of the excess diazomethane with a few drops of acetic acid and removal of polymethylene by filtration, the solution was evaporated *in vacuo* to give an oil. Crystallization of this oil gave starting material **1b** (0.53 g). Concentration of the mother liquors afforded a glass (0.32 g) which was partition chromatographed on Celite using the system cyclohexane–dioxane–water (82:20:8). Evaporation of holdback volumes 1.5 to 3 gave **1a** (0.17 g), mp 247–247.5°, upon crystallization from acetone–hexane. Its infrared spectrum was identical with that of the compound previously reported.[1] No other steroidal material was found in the remainder of the chromatographic fractions. Final methanol washings of the column on evaporation yielded a very small amount (0.02 g) of starting material **1b**.

9α-Fluoro-11β,16α,17α-trihydroxy-21-methoxypregna-1,4-diene-3,20-dione (**1f**).—To a solution of 16α-acetoxy-9α-fluoro-11β,17α-dihydroxy-21-methoxypregna-1,4-diene-3,20-dione (**1e**, 0.4 g)[5] in methanol (95 ml) under nitrogen was added a 10% potassium carbonate solution (1.35 ml). The solution was allowed to stand for 20 min and neutralized with acetic acid, and the solvent was removed *in vacuo*. Acetone was added to the residue, the mixture was filtered, and water was added to the solution to give a solid (0.215 g). The material was partition chromatographed on Celite using a heptane–ethyl acetate–methanol–water (55:45:17:4) system. The recovered material (0.099 g), crystallized from methanol, had mp 280–281.5°; λ_{max}^{MeOH} 239 mμ (ε 15,300); ν_{max}^{KBr} 3420 (OH), 1722 (20-C=O), 1670 (3-C=O), 1627 and 1611 ($\Delta^{1,4}$), and 1132–1017 (COC) cm^{-1}; $[\alpha]^{25}D$ +42° (chloroform).

Anal. Calcd for $C_{22}H_{29}FO_6$ (408.45): C, 64.69; H, 7.16; F, 4.65. Found: C, 65.09; H, 7.44; F, 4.71.

9α-Fluoro-11β-hydroxy-16α,17α-isopropylidenedeioxy-21-methoxypregna-1,4-diene-3,20-dione (**2**).—A solution of the 21-methyl ether 11,16,17α-triol (**1f**, 67 mg) in acetone (10 ml) and 10% perchloric acid (0.2 ml) was stirred for 1.5 hr and then was neutralized with sodium bicarbonate; water was added, and the resultant precipitate was filtered. Crystallization from acetone–hexane gave **2**: mp 265.5–267°; λ_{max}^{MeOH} 239 mμ (ε 15,400); ν_{max}^{KBr} 3400 (OH), 1732 (20-C=O), 1665 (3-C=O), 1618 and 1610 ($\Delta^{1,4}$), and 1076–1055 (COC) cm^{-1}; $[\alpha]^{25}D$ +110° (chloroform).

Anal. Calcd for $C_{25}H_{33}FO_6$ (448.51): C, 66.94; H, 7.42; F, 4.24. Found: C, 67.18; H, 7.44; F, 4.34.

Registry No.—**1a**, 1597-93-9; **1d**, 124-94-7; **1e**, 7704-75-8; **1f**, 7721-43-9; **1g**, 7704-76-9; **2**, 7704-77-0.

(4) All melting points are uncorrected. The analyses were carried out by Louis M. Brancone and associates. The infrared, ultraviolet absorption, nmr, and optical rotational data were supplied by William Fulmor and associates. The nmr spectra were taken in deuterated dimethyl sulfoxide (referred to tetramethylsilane). We are also indebted to George O. Morton for discussions concerning the nmr spectra, and to Charles Pidacks for carrying out the partition chromatography.

(5) The melting points of **1e** has been redetermined to be 291–295°.

The Action of Triphenylphosphine Dibromide on α-Amyrin and Derivatives[1,2]

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The use of triphenylphosphine dibromide as a reagent for conversion of alcohols to alkyl bromides has been described[3] and, in certain simple systems, advantages have been realized in minimizing the formation of undesirable products of elimination and molecular rearrangement.[4] In the steroid field, we have shown that, whereas the equatorial alcohol groups at C-3, in both the normal and *allo* series, are displaced by bromine with this reagent, axial alcohols at C-7 and C-12 in the normal series undergo elimination.[5] We wished to examine the action of triphenylphosphine dibromide on the widely occurring *gem*-dimethylcyclohexanol (4,4-dimethyl-3β-ol) grouping, which is particularly prone to molecular rearrangement on ionic dehydration or solvolysis of ester derivatives. For this purpose, we chose α-amyrin (I) as the representative sub-

(1) The award of a research grant (AM-03439) from the U. S. Public Health Service (to R. S.) and an Institutional grant of the American Cancer Society (to D. L.) is gratefully acknowledged.

(2) For a preliminary communication of part of this work, see D. Levy and R. Stevenson, *Tetrahedron Letters*, 341 (1965).

(3) L. Horner, H. Oediger, and H. Hoffman, *Ann.*, **626**, 26 (1959).

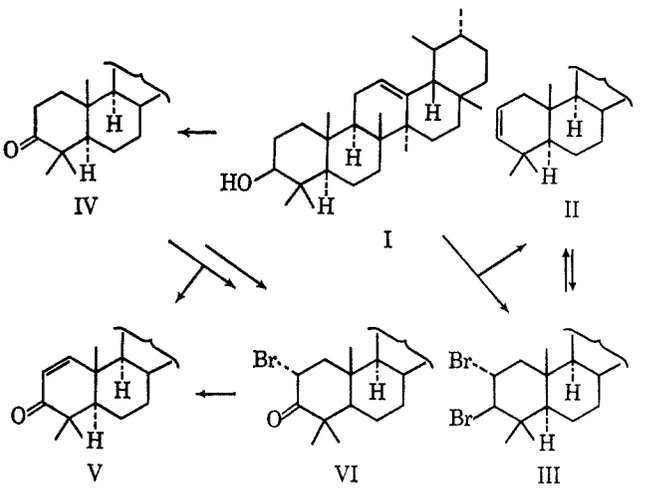
(4) G. A. Wiley, R. L. Hershkowitz, B. M. Rein, and B. C. Chung, *J. Am. Chem. Soc.*, **86**, 964 (1964).

(5) D. Levy and R. Stevenson, *J. Org. Chem.*, **30**, 3469 (1965).

strate, since a wide variety of its dehydration products of known structure is available for comparison purposes.[6]

On treatment with an excess of triphenylphosphine dibromide, α-amyrin (I) yielded two products readily separated by chromatography. The first, a hydrocarbon, isolated in about 60% yield, was identified as ursa-2,12-diene (II), *i.e.*, the product of elimination *without* molecular rearrangement. This contrasts with the action of phosphorus pentachloride[7] and phosphorus pentoxide[8] on I, in which retropinacolic dehydration products are obtained. The second product, a high-melting dibromide isolated in 15% yield, gave II on debromination with zinc dust, and could also be obtained by addition of 1 molar equiv of bromine to II. We conclude that the addition of bromine to ursa-2,12-diene (II) has occurred at the considerably less hindered Δ^2-unsaturated center, rather than to the Δ^{12} site, which is known to yield the 12-monobromours-12-ene derivative on treatment with the halogen.[9] Since the dibromide is stable toward Woelm neutral alumina, a condition known to isomerize the 2,3-diaxial dibromocholestane to the 2,3-diequatorial isomer,[5] it is consequently formulated as 2α,3β-dibromours-12-ene (III). The formation of III from I by the action of triphenylphosphine dibromide has undoubtedly occurred through the intermediacy of the hydrocarbon II; treatment of II with the phosphine dihalide under the same conditions yielded III in comparable yield. From the viewpoint of experimental convenience, yield, and absence of isomers, the general preparation of Δ^2-unsaturated hydrocarbons by the action of triphenylphosphine dibromide probably represents the method of choice. Although with cyclohexanone, triphenylphosphine dibromide yields the *gem*-dibromide,[3] we have shown with the 3-keto steroid, cholestanone, that α,β-unsaturated and α-bromo α,β-unsaturated ketone products can be obtained.[5] We have now examined the action of the reagent on the ketone, α-amyrenone (IV), readily obtained from α-amyrin by oxidation with Jones reagent.[10] The principal product, obtained in 45% yield, was shown by infrared and ultraviolet spectra to be a conjugated unsaturated ketone, and is accordingly formulated as ursa-1,12-dien-3-one (V). A second major product was a bromo ketone, $C_{30}H_{47}BrO$, which could also be obtained by the action of bromine on IV in acetic acid solution. Since the infrared spectrum indicates that the α-bromo atom has an equatorial conformation,[11] this product is assigned the structure, 2α-bromours-12-en-3-one (VI). In agreement with this formulation dehydrobromination of VI with collidine yielded V (see Scheme I).

SCHEME I



Experimental Section

Specific rotations were determined in chloroform solution unless otherwise stated. Melting points were determined using a Gallenkamp melting point apparatus. Petroleum ether refers to the fraction, bp 38–54°.

Action of Triphenylphosphine Dibromide on α-Amyrin (Urs-12-en-3β-ol).—To a solution of triphenylphosphine dibromide (3.0 g) in dry dimethylformamide (25 ml) was added a solution of α-amyrin (200 mg) in the minimum volume of the same solvent. The mixture was stirred for 20 hr at 90° under a nitrogen atmosphere, cooled, diluted with water, and extracted with ether. The extract was washed successively with water, sodium hydrogen carbonate solution, and water, dried ($MgSO_4$), and evaporated. The residue was triturated with petroleum ether and filtered, and the filtrate was chromatographed on alumina (Spence Type H). The first eluate (20 ml) on evaporation gave a solid (120 mg) which on one recrystallization from ether–methanol gave **ursa-2,12-diene** as needles (108 mg): mp 120–121°, $[\alpha]_D$ +130° (*c* 1.1) (lit.[12] mp 119–120°, $[\alpha]_D$ +137°). Further elution with petroleum ether (40 ml) gave a solid (40 mg, positive Beilstein test) which on recrystallization from ether–methanol yielded **2α,3β-dibromours-12-ene**: mp 295–297°, $[\alpha]_D$ +37° (*c* 1.2).

Anal. Calcd for $C_{30}H_{48}Br_2$: C, 63.38; H, 8.45; Br, 28.17. Found: C, 63.65; H, 8.49; Br, 28.07.

Ursa-2,12-diene from 2α,3β-Dibromours-12-ene.—To a solution of the dibromide (20 mg) in ether (5 ml), methanol (5 ml), and acetic acid (1 ml) was added zinc dust (600 mg) and the mixture was heated under reflux with stirring for 20 hr. The mixture was then filtered, the filtrate was evaporated, and the residue was dissolved in petroleum ether and chromatographed on Woelm neutral alumina. Elution with the same solvent (10 ml) gave a solid, which on crystallization from ether–methanol yielded ursa-2,12-diene as needles (11 mg, mp 120–121°, $[\alpha]_D$ +126°) with an infrared spectrum identical with an authentic specimen.

2α,3β-Dibromours-12-ene from Ursa-2,12-diene. A.—Ursa-2,12-diene (100 mg) was added to a solution of triphenylphosphine dibromide (1.51 g) in dimethylformamide (10 ml) and subjected to the conditions applied to α-amyrin described above. A solution of the product in petroleum ether was chromatographed on Spence Type H alumina. Elution with the same solvent (30 ml) gave, after one crystallization from ether–methanol, unchanged ursa-2,12-diene (56 mg, mp 119–120°). Further elution (40 ml) yielded 2α,3β-dibromours-12-ene (27 mg): mp and mmp 294–296°, $[\alpha]_D$ +37° (*c* 1.4).

B.—A solution of bromine (39.2 mg) in acetic acid (1.60 ml) was added to a solution of ursa-2,12-diene (100 mg) in dry ether (25 ml) and the mixture was allowed to stand for 5 hr. It was then diluted with water, and the ether layer and extracts were washed with sodium bicarbonate solution and water and dried ($MgSO_4$). The residue obtained after solvent evaporation was dissolved in petroleum ether and chromatographed as in A. The first eluate (20 ml) gave unchanged ursa-2,12-diene (70 mg). Further elution with petroleum ether gave 2α,3β-dibromours-12-ene [50 mg, mp 293–295°, $[\alpha]_D$ +39° (*c* 1.2)] after one crystallization from ether–methanol.

α-Amyrenone (Urs-12-en-3-one).—A solution of Jones chromium trioxide solution[10] (0.5 ml) was added to a solution of α-amyrin (426 mg) in acetone (125 ml) at 10° and the mixture was stirred for 5 min and then diluted with water (300 ml). Removal

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(8) M. B. E. Fayez, J. Grigor, F. S. Spring, and R. Stevenson, *ibid.*, 3378 (1955).

(9) O. P. Arya and R. C. Cookson, *ibid.*, 972 (1957).

(10) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *ibid.*, 39 (1946).

(11) R. C. Cookson, *ibid.*, 282 (1954).

(12) A. Winterstein and G. Stein, *Ann.*, **502**, 223 (1933).

of some solvent (*ca.* 50 ml) by distillation caused precipitation of a solid. After cooling, there was obtained by filtration α-amyrenone (390 mg): mp 125–126°, $[\alpha]_D$ +124° (*c* 1.2, pyridine) [lit.[13] mp 125–126°, $[\alpha]_D$ +119° (pyridine)].

Action of Triphenylphosphine Dibromide on α-Amyrenone.—To a solution of triphenylphosphine dibromide (3.0 g) in dry dimethylformamide (25 ml) was added a solution of α-amyrenone (250 mg), and the mixture was stirred for 20 hr at 90° under a nitrogen atmosphere. The product was worked up in the usual way and chromatographed on Spence Type H alumina. Elution with petroleum ether–benzene (4:1, 100 ml) yielded an oil (positive Beilstein test) that crystallized from methanol to give **2α-bromours-12-en-3-one** as needles (90 mg): mp 184–187°, $[\alpha]_D$ +26° (*c* 1.0), λ^{CHCl_3} 5.80 μ.

Anal. Calcd for $C_{30}H_{47}BrO$: C, 71.53; H, 9.41. Found: C, 71.43; H, 9.32.

Further elution with petroleum ether–benzene (4:1, 75 ml) gave a product (negative Beilstein test) that crystallized from ether–methanol to give **ursa-1,12-dien-3-one** as small needles (110 mg): mp 177–178°, $[\alpha]_D$ +36° (*c* 1.4), λ^{EtOH} 232 mμ (ε 10,200), λ^{CHCl_3} 6.01 μ.

Anal. Calcd for $C_{30}H_{46}O$: C, 85.23; H, 10.98. Found: C, 85.35; H, 11.07.

Action of Bromine on α-Amyrenone.—A solution of bromine (18.9 mg) in acetic acid (5 ml) was added dropwise over 10 min to α-amyrenone (50 mg) in the same solvent (5 ml). The mixture was then stirred for a further 10 min, diluted with water, and extracted with ether. Evaporation of the washed and dried ether extract yielded the product which on crystallization from methanol gave 2α-bromours-12-en-3-one as needles: mp and mmp 184–187°, $[\alpha]_D$ +30° (*c* 1.3).

Dehydrobromination of 2α-Bromours-12-en-3-one.—The bromo ketone (25 mg) was added to collidine (5 ml), and the mixture was heated at 100° for 5 hr, cooled, diluted with water, and extracted with ether. The extract was washed successively with dilute hydrochloric acid, dilute sodium bicarbonate solution, and water. Evaporation of the dried extract gave a solid which crystallized from methanol to give ursa-1,12-dien-3-one as small needles (14 mg): mp and mmp 175–177°, $[\alpha]_D$ +32° (*c* 0.9), λ^{EtOH} 232 mμ (ε 10,100), λ^{CHCl_3} 6.00 μ.

Registry No.—I, 638-95-9; III, 2309-00-4; II, 2309-01-5; IV, 638-96-0; VI, 2308-99-8; V, 2672-44-8; triphenylphosphine dibromide, 1034-39-5.

(13) W. A. Jacobs and E. E. Fleck, *J. Biol. Chem.*, **88**, 137 (1930).

A Synthesis of 2-Deoxy-D-*erythro*-pentose[1]

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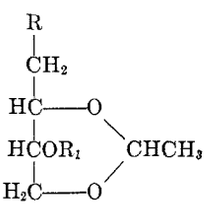
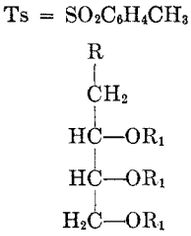
Nucleophilic displacement reactions of a 1-deoxy-1-halogeno-D-erythritol derivative or of a 1-*O*-(*p*-tolylsulfonyl)-D-erythritol derivative with a cyanide anion to form 2-deoxy-D-*erythro*-pentononitrile, followed by partial reduction of the nitrile, could offer a simple route to 2-deoxy-D-*erythro*-pentose. By this way no epimeric pair has to be separated, while it may also be used for labeling the anomeric carbon of the 2-deoxy sugar with radioactive carbon. Using 1-deoxy-2,4-*O*-ethylidene-1-iodo-D-erythritol (**5**), 2-deoxy-D-*erythro*-pentose was synthetized by the suggested procedure. When this work had been completed, a synthesis of 2-deoxy-D-*erythro*-pentose-(1-^{14}C), similar in its essential steps to the one described here, was reported by Bayly and Turner.[2]

1-Amino-1-deoxy-2,4-*O*-ethylidene-D-erythritol (**1**)[3] was hydrolyzed to 1-amino-1-deoxy-D-erythritol (**8**), and isolated as 1-[(benzyloxycarbonyl)amino]-1-deoxy-D-erythritol (**9**). Benzoylation of **9** formed 2,3,4-tri-*O*-benzoyl-1-[(benzyloxycarbonyl)amino]-1-deoxy-D-erythritol (**10**), which was converted by hydrogen bromide in acetic acid to 1-amino-2,3,4-tri-*O*-benzoyl-1-deoxy-D-erythritol hydrobromide (**11**). 2,3,4-Tri-*O*-benzoyl-1-chloro-1-deoxy-D-erythritol (**12**) was prepared from the amine (**11**), and 2,3,4-tri-*O*-benzoyl-1-bromo-1-deoxy-D-erythritol (**13**), was prepared from the mother compound (**10**) (without isolation of the amine) *via* the respective nitrosyl halides. 2,3,4-Tri-*O*-benzoyl-1-deoxy-1-iodo-D-erythritol (**14**) was prepared from the bromine analog (**13**) with sodium iodide.



1, R = NH_2; R_1 = H
2, R = OH; R_1 = H
3, R = Ts; R_1 = Ts
4, R = Ts; R_1 = H
5, R = I; R_1 = H
6, R = CN; R_1 = H
7, R = CHO; R_1 = H
Ts = $SO_2C_6H_4CH_3$ (*p*)



8, R = NH_2; R_1 = H
9, R = $NHCOOCH_2C_6H_5$; R_1 = H
10, R = $NHCOOCH_2C_6H_5$; R_1 = Bz
11, R = $NH_2 \cdot HBr$; R_1 = Bz
12, R = Cl; R_1 = Bz
13, R = Br; R_1 = Bz
14, R = I; R_1 = Bz
Bz = COC_6H_5

In attempted displacement reactions of **13** with sodium, silver, mercuric, or cuprous cyanide in refluxing *N*,*N*-dimethylformamide (DMF) no evidence for nitrile formation was found. On the other hand **13** reacted with sodium benzoate in DMF under reflux for 4 hr to form tetra-*O*-benzoylerythritol, as described by Kent, *et al.*,[4] for **12**. Nucleophilic displacements by cyanide anion of the *p*-toluenesulfonyloxy anion from a primary alcohol *p*-toluenesulfonate or of the iodide anion from 6-deoxy-6-iodo hexose and hexitol derivatives to form nitriles have recently been reported.[5]

In an alternative procedure, which is similar to that of Bayly and Turner,[2] 2,4-*O*-ethylidene-1-*O*-(*p*-totylsulfonyl)-D-erythritol (**4**)[6,7] was converted to 1-deoxy-

(1) (a) Taken from a thesis to be submitted by I. Z. to the Senate, The Hebrew University, Jerusalem, in partial fulfilment of the requirements for the degree of Ph.D. (b) A short communication of this paper has been presented at the 36th Meeting of the Israel Chemical Society, Oct 1966; *Israel J. Chem.*, **4**, 92p (1966).

(2) R. J. Bayly and J. C. Turner, *J. Chem. Soc., Org. Sect.*, 704 (1966).
(3) I. Ziderman and E. Dimant, *J. Org. Chem.*, **31**, 223 (1966).
(4) P. W. Kent, K. R. Wood, and V. A. Welch, *J. Chem. Soc.*, 2493 (1964).
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