[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCIV. Persulfate Oxidation of *allo*-Pregnane Derivatives

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Although potassium persulfate has been used rather extensively to oxidize ketones of the terpene group[1,2,3] it has not been used to any appreciable extent in the oxidation of sterol ketones. In this Laboratory it was recently used in the oxidation of sarsasapogenin to pregnanetriol-3,16,20.[4]

The fact that persulfate oxidations bring about a cleavage of a carbon–carbon linkage adjacent to a carbonyl group suggested its possible use in the oxidation of C-20 keto *allo*-pregnane compounds to androstane derivatives. The oxidation of *allo*-preganone-20 with potassium persulfate yielded a neutral carbinol mixture which we were unable to separate. The acidic fraction from this oxidation gave an acid of the composition $C_{20}H_{32}O_2$, m. p. 228–230°. This formed a methyl ester, m. p. 141–143°. This acid is undoubtedly *etio-allo*-cholanic acid which was prepared by Tschesche.[5] His acid melted at 228–230° and the methyl ester at 140–142°.

The oxidation of *allo*-pregnanol-3(β)-one-20 yielded an acidic fraction which consisted of 3(β)-hydroxy-*etio-allo*-cholanic acid.[6,7] The neutral fraction which appeared to be a mixture was oxidized with chromic anhydride to yield androstanedione.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part[8]

Treatment of *allo*-Pregnanone-20 with Persulfuric Acid.—A mixture of 5 g. of *allo*-pregnanone-20, 500 cc. of 90% acetic acid, 5 cc. of concentrated sulfuric acid and 25 g. of potassium persulfate was refluxed for four hours, cooled, diluted with water and extracted with ether. The acids were removed from the ether by washing with water and sodium carbonate solution. The ether was evaporated and the residue was hydrolyzed with boiling ethanolic potassium hydroxide. Water was added and the neutral product extracted with ether. The carbinols were separated from the neutral fraction by means of their half-succinates. This apparently gave a mixture of epimeric carbinols which melted over a range of 110–142°, and could not be separated.

Anal. Calcd. for $C_{19}H_{32}O$: C, 82.8; H, 11.7. Found: C, 82.6; H, 11.5.

The water layer from the alkaline hydrolysis above was acidified and the precipitated acids taken up with ether. The solvent was removed and the product was recrystallized from ethyl acetate to give white crystals, m. p. 228–230°. This product is *etio-allo*-cholanic acid.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.9; H, 10.6. Found: C, 78.5; H, 10.6.

Upon treatment with diazomethane the acid gave a **methyl ester** which crystallized from dilute acetone as white crystals, m. p. 141–143°.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.2; H, 10.6.

Treatment of *allo*-Pregnanol-3(β)-one-20 with Persulfuric Acid.—A mixture of 2.3 g. of *allo*-pregnanol-3(β)-one-20 acetate, 250 cc. of 90% acetic acid, 2.5 cc. of concentrated sulfuric acid and 10 g. of potassium persulfate was refluxed for four hours. The products were separated and hydrolyzed as in the preceding experiment. The neutral fraction was freed from some unchanged ketones by means of Girard's reagent in ethanol. The non-ketonic fraction upon crystallization from dilute methanol and dilute acetone gave crystalline material melting at 170–185°, which apparently consisted of a mixture of epimeric carbinols. The solvent was removed and the total product was dissolved in 25 cc. of acetic acid and 1 g. of chromic anhydride in 5 cc. of 80% acetic acid added. After standing one hour at 25° water was added and the precipitated solid extracted with ether and the acids removed by washing with water and sodium carbonate solution. The residue remaining after evaporation of the ether was crystallized from ether–pentane and from dilute acetone to give a product m. p. 128–130°. This gave no depression in melting point when mixed with androstanedione, m. p. 130°.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.1; H, 9.8. Found: C, 78.9; H, 9.8.

The water layer from the above alkaline hydrolysis was acidified and the precipitated acids taken up with ether. After removal of the ether, the residue was crystallized from dilute methanol to give a product, m. p. 249–252°. It gave no depression in melting point when mixed with an authentic sample of 3(β)-hydroxy-*etio-allo*-cholanic acid, m. p. 250–252°.[7]

Anal. Calcd. for $C_{20}H_{32}O_3$: C, 74.9; H, 10.1. Found: C, 74.8; H, 10.1.

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[1] Baeyer and Villiger, *Ber.*, **32**, 3630 (1899).

[2] Ruzicka and Stoll, *Helv. Chim. Acta*, **11**, 1159 (1928).

[3] Rollett and Bratke, *Monatsh.*, **43**, 685 (1922).

[4] Marker, Rohrmann, Crooks, Wittle, Jones and Turner, THIS JOURNAL, **62**, 525 (1940).

[5] Tschesche, *Ber.*, **68**, 7 (1935).

[6] Steiger and Reichstein, *Helv. Chim. Acta*, **20**, 949 (1937).

[7] Marker and Wittle, THIS JOURNAL, **61**, 1329 (1939).

[8] Microanalyses by Dr. John R. Adams, Jr., of this Laboratory.

Summary

The persulfate oxidation of 20-keto-*allo*-pregnane compounds gave a mixture of androstanols-17 and *etio-allo*-cholanic acid.

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Osage Orange Pigments. III. Fractionation and Oxidation

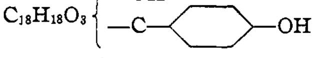
BY M. L. WOLFROM AND A. S. GREGORY

In continuation of our studies[1] on the pigments of the fruit of the osage orange tree (*Maclura pomifera* Raf.) we have made a rather exhaustive fractionation of the naturally occurring mixture of the two pigments, the results of which indicate that the two are probably present in about equal amounts.

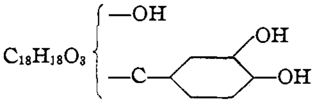
The melting point–composition diagram obtained from mixtures of the two pure substances is shown in Fig. 1. The melting point behavior obtained on mixing the pure compounds is probably slightly different from the behavior of mixtures of equal composition which have been formed by co-crystallization.

The trimethyl ether of pomiferin has been reported previously.[1b] We have now obtained the corresponding dimethyl ether of osajin. When the former is subjected to oxidation, in acetone solution, with alkaline hydrogen peroxide, veratric (3,4-dimethoxybenzoic) acid is produced. Under the same conditions, osajin dimethyl ether yields anisic (*p*-methoxybenzoic) acid. These two acids were identified by analysis, by preparation of the anilide and amide of each, and by comparison with authentic specimens in all cases. The two acids have practically identical melting points. This is also true for their amides and anilides. Mixed melting points, however, give definite depressions.

The formulas of osajin (I) and pomiferin (II), both of which are methoxyl-free, may now be developed as follows



(I)



(II)

Further work on the structure of these two substances is in progress in this Laboratory.

Experimental

Fractionation.—The whole fruit of the osage orange tree (*Maclura pomifera* Raf.) was cut, dried and crushed to a coarse meal. The meal (1500 g.) was extracted successively with petroleum ether and ether. From the latter extract was obtained a yellow solid; yield 47.8 g., m. p. 180–182°. This material was recrystallized from ten parts of hot xylene, the crop being removed by filtration when the temperature of the solution had reached approximately 40°. On repeated recrystallization in this manner pure pomiferin was obtained; yield 10.0 g., m. p. 200.5°. The combined mother liquors were concentrated to give a product melting at 173–175° and after repeated recrystallization from 95% ethanol pure osajin was obtained; yield 5.6 g., m. p. 189°.. By employing a method of crystallizing the xylene mother liquor material from 95% alcohol, and then the alcohol mother liquor material from xylene again, and continuing this cycle, a total of 14.1 g. of high purity osajin and 15.8 g. of high purity pomiferin was obtained.

Although not all the material was accounted for, the above results would seem to indicate that the two substances are present in the crude extract in very nearly equal amounts. The total yield of crude extract in this lot of material was not as high as in the crops of previous seasons. The melting point–composition diagram obtained from mixtures of the two pure substances is shown in Fig. 1. The melting point behavior obtained on mixing the two pure substances is probably slightly different from the behavior of mixtures of equal composition which have been formed by co-crystallization.

Osajin Dimethyl Ether.—To a boiling solution of osajin (2 g., m. p. 189°) in acetone (130 cc.) were added under reflux the following portions of reagents over a period of forty minutes: 24 cc. of dimethyl sulfate, 14 cc. of 50% aqueous potassium hydroxide, then six alternate portions of 6 cc. each of dimethyl sulfate and 8 cc. each of 50% aqueous potassium hydroxide. The refluxing was continued for two hours longer and then the reaction mixture was poured on 1.5 l. of crushed ice and allowed to stand until the ice had melted before filtration of the precipitated solid; yield 2.16 g., m. p. 109°. Pure material was obtained on several recrystallizations from ethanol (95%); m. p. 118.5° unchanged on recrystallization from methanol, propanol-1 and benzene–petroleum ether. The substance crystallized in long, colorless needles and gave a negative ferric chloride–alcohol phenol test.

Anal. Calcd. for $C_{25}H_{22}O_3(OCH_3)_2$: C, 74.98; H, 6.53; OCH_3, 14.35. Found: C, 74.91; H, 6.53; OCH_3, 14.3.

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(1) (a) E. D. Walter, M. L. Wolfrom and W. W. Hess, THIS JOURNAL, **60**, 574 (1938); (b) M. L. Wolfrom, F. L. Benton, A. S. Gregory, W. W. Hess, J. E. Mahan and P. W. Morgan, *ibid.*, **61**, 2832 (1939).