needles, m.p. 303–305° dec. (further recrystallization gave a much darker product, m.p. 306–307° dec.).

Anal. Calcd. for $C_{19}H_{12}Cl_2N_2O_2$: C, 61.47; H, 3.26. Found: C, 61.47; H, 3.36.

(B).—A solution of 9 g. (0.05 mole) of 5-chloro-8-quinolinol and 0.75 g. (0.025 mole) of paraformaldehyde in 100 ml. of acetic acid was heated under reflux for 90 minutes. Then, 0.5 g. more of paraformaldehyde was added and heating continued for about four hours. The solution was diluted with water and 6.5 g. (70% yield) of product was collected by filtration, m.p. 304–305° dec. with no depression upon admixture with the analytical sample from A.

(C).—A mixture of 5.4 g. (0.03 mole) of 5-chloro-8-quinolinol, 0.9 g. (0.03 mole) of paraformaldehyde, 3.1 g. (0.03 mole) of triethylamine and 100 ml. of alcohol was heated at reflux. After 20 minutes of heating a precipitate was noted and the quantity increased as the heating continued. At the end of two hours, less than a gram of XVII was obtained, m.p. 285–290° dec. After washing with alcohol, it melted at 297–302° and was not depressed by admixture with XVII (A).

(D).—About a gram of 5-chloro-7-diethylaminomethyl-8-quinolinol (I) dihydrochloride[4] was dissolved in 20 ml. of water. After the mixture had been covered with an equal volume of ether, it was shaken with an excess of ammonia. The ether solution was decanted and to it was added 10 ml. of alcohol. The resulting solution was evaporated until the volume was only about 5 ml. Ten milliliters of alcohol was added and the solution was heated at reflux for 90 minutes. A few milligrams of tan solid was collected on a funnel, m.p. 301–302° dec., undepressed by admixture with XVII (C).

5,5'-Methylene-bis-(7-chloro-8-quinolinol) (XVIII).—During an attempt to apply the procedure of III to the preparation of the diethylamino analog of IX, from the reaction mixture there separated 2.1 g. of light tan colored solid, m.p. 309–310° dec. Recrystallized from phenyl ether and then from xylene, it melted at 310–311° dec.

Anal. Calcd. for $C_{19}H_{12}Cl_2N_2O$: C, 61.47; H, 3.26. Found: C, 61.76; H, 3.62.

An appreciable amount of what was apparently the hygroscopic hydrochloride (dec. > 165°) of the desired analog of IX was isolated, but it could not be purified readily.

5,6,7-Trichloro-8-quinolinol (XIX).—Solution of 4.5 g. (0.025 mole) of 6-chloro-8-quinolinol[16] in 250 ml. of absolute alcohol was effected by warming. Then, at room temperature, a stream of chlorine was bubbled into the solution for 40 minutes. After 12 hours, 4.5 g. of yellow solid was collected on a filter, m.p. 215–218°. Concentration of the filtrate and neutralization with dilute ammonia gave 2.5 g. of white solid, m.p. 217–219°. The first crop was slightly acidic and it lost its yellow color when suspended in water. Recrystallization from alcohol–acetic acid gave 6 g. (96% yield) of crystalline product, m.p. 219–220°. Two recrystallizations from acetic acid elevated the melting point only to 220–220.5°.

Anal. Calcd. for $C_9H_4Cl_3NO$: C, 43.50; H, 1.62. Found: C, 43.72; H, 2.04.

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[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY]

The Constitution of Sapote Gum. III. A Structural Evaluation

BY E. V. WHITE[1]

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Previous communications have dealt with the monosaccharide components of sapote gum. The present study is concerned with that portion of the macromolecule which is extremely resistant to hydrolysis. This fraction is composed, for the most part, of aldobiouronic acid residues and can be separated from the methanolysis products of the methyl ether derivative as a mixture of alkylated aldobiosiduronates. Evidence is given to indicate the presence of two compounds of this type. The glycosidic linkage is evidently the same in each instance because complete methylation of the mixture, after reduction of the methoxycarbonyl group to the primary alcohol function, provides the anomeric forms of a single disaccharide. Hydrolysis of the latter furnishes equimolar parts of 2,3,4,6-tetra-O-methyl-D-glucose and 3,4-di-O-methyl-D-xylose thus demonstrating a 1–2-glycosidic linkage in the original aldobiosiduronates. This new information, together with previous data, permits some description of the molecular architecture of the sapote gum polysaccharide.

The previous communications[2a,b] in this series have dealt with some of the products formed upon methanolysis of sapote gum methyl ether. The glycosidic components of the methanolysate proved to be derived from 3-O-methyl-D-xylose, 2,3,4-tri-O-methyl-D-xylose, 2,3,4-tri-O-methyl-L-arabinose and other compounds of glycosiduronate character. The arabinose component evidently arises from a novel structure in the polysaccharides and reveals for the first time the natural occurrence of the arabopyranose unit in these macromolecules.[3] This finding, so far as it concerns the polysaccharides, removes one objection to the hypothesis that D-galactose and L-arabinose are biosynthetically interconvertible since the improbable shift in ring structure accompanying the conversion from D-galactopyranose to L-arabofuranose is not, of necessity, a requirement.[4]

The glycosiduronate fraction of the methanolysis sirup has been more difficult to investigate because of the extreme resistance of the glycosidic linkage in the uronic acids to hydrolysis. This fraction is, for the most part, of aldobiosiduronate character. Its further treatment with methanolic hydrogen chloride eventually provided a sirup from which, by the usual methods, methyl (methyl 3,4-di-O-methyl-D-glucopyranosid)-uronate was isolated in its anomeric forms as one of the components. The crystalline acid was obtained therefrom after removal of the ester and aglycone groups by hydrolysis. Certain of the uronic acid residues of sapote gum are therefore resident in the internal structure of the macromolecule and are joined therein at C-1 and C-2 to other carbohydrate units. The latter type of glycosidic union has not been reported previously for uronic acid units occurring in the polysaccharides, although Lythgoe and Trippett[5] have recorded its occurrence in the carbohydrate component of glycyrrhinic acid. Prolonged aqueous hydrolysis of the glycosiduronate fraction has furnished 3-O-methyl-D-xylose as the only sugar component.

(1) University of Toronto, Toronto 5, Canada.

(2) (a) E. V. White, THIS JOURNAL, **75**, 257 (1953); (b) **75**, 4692 (1953).

(3) The isolation of 3-O-(β-L-arabopyranosyl)-L-arabinose from larch ε-galactan and from peach and cherry gum has now been reported by J. K. N. Jones, *J. Chem. Soc.*, 1672 (1953), and by P. Andrews, D. H. Ball and J. K. N. Jones, *ibid.*, 4090 (1953), respectively.

(4) E. L. Hirst, *ibid.*, 70 (1942).

(5) B. Lythgoe and S. Trippett, *ibid.*, 1983 (1950).

A further study of this same fraction has assisted materially in clarifying certain structural features of the sapote gum system. In the present investigation, the aldobiosiduronate components were separated directly from the methanolysate of the methyl ether derivative by vacuum fractional distillation. The product, as the methyl ester, was reduced with lithium aluminum hydride[6] to produce the corresponding primary alcohol function and thus develop a glucosidic structure more susceptible to hydrolysis than was that of the original aldobiosiduronates. When a portion of the reduced product was hydrolyzed and examined on the paper chromatogram it became evident that three components were present. These, evidently, were derived from the hydrolysis of two disaccharides and were identified as 3-O-methyl-D-xylose, 3,4-di-O-methyl-D-glucose and 2,3,4-tri-O-methyl-D-glucose. Thus, relating back to the aldobiosiduronates prior to reduction and hydrolysis, in one instance, 3,4-di-O-methyl-D-glucuronic acid is united glycosidically with 3-O-methyl-D-xylose while in the second case 2,3,4-tri-O-methyl-D-glucuronic acid is similarly joined, again, with 3-O-methyl-D-xylose. The tri-O-alkylated glucuronic acid has not been identified previously as a component of sapote gum methyl ether although its presence as the corresponding glucose derivative was suspected in the chromatographic band containing 2,3,4-tri-O-methyl-L-arabinose. These two compounds move at about the same rate chromatographically in the ethyl acetate–acetic acid–water system and no convenient method of separation could be found. With the present information at hand, through the isolation of 2,3,4-tri-O-methyl-D-glucosaccharolactone methyl ester as a characterizing derivative of 2,3,4-tri-O-methyl-D-glucose, this chromatographic band can now be re-assessed.[7] The molar ratio of the components of sapote gum methyl ether is thus expressed as: 3-O-methyl-D-xylose, 2.80 parts; 3,4-di-O-methyl-D-glucuronic acid determined as 3,4-di-O-methyl-D-glucose, 1.11 parts; 2,3,4-tri-O-methyl-D-glucuronic acid determined as 2,3,4-tri-O-methyl-D-glucose, by difference, 1.07 parts; 2,3,4-tri-O-methyl-L-arabinose, 1.05 parts; and 2,3,4-tri-O-methyl-D-xylose, 0.97 part. Again, the complexity of the evaluation and the possibility for error is emphasized.

The above-described disaccharides evidently possess the same type of glycosidic linkage and differ only in regard to the position of their O-methyl substituents. Upon complete methylation a single product was obtained, namely, the anomeric forms of methyl 2-O-(2,3,4,6-tetra-O-methyl-D-glucopyranosyl)-3,4-di-O-methyl-D-xylopyranoside. The constitution of the disaccharide became evident, after hydrolysis, through the isolation of crystalline 2,3,4,6-tetra-O-methyl-D-glucose and 3,4-di-O-methyl-D-xylose in equimolar proportion. The latter compound, a sirup, was identified as the corresponding crystalline lactone of 3,4-di-O-methyl-D-xylonic acid. The α- or β-configuration of the disaccharide linkage was not determined. Curiously enough, the same completely methylated disaccharide, except for doubt as to the character of the glycosidic linkage, has been prepared[8a] from an aldobiouronic acid isolated from the hemicelluloses of aspen wood, *Populus tremuloides*, and also from Hemicellulose-B of corn cob.[8b]

The present evidence, together with prior experimental data, now permits a tentative consideration of the molecular architecture of the sapote gum system. For this purpose, it seems best to employ the concept of the repeating unit although it should be borne in mind that, as yet, there is no definite evidence to support the hypothesis of discrete, uniformly reproduced, repeating systems as constituting the structure of this or any other heteroglycan. In the present instance, the molar ratio of the component saccharides, produced upon hydrolysis of the methyl ether derivative, namely, 3-O-methyl-D-xylose, 2,3,4-tri-O-methyl-D-xylose, 2,3,4-tri-O-methyl-L-arabinose, 2,3,4-tri-O-methyl-D-glucuronic acid and 3,4-di-O-methyl-D-glucuronic acid approximates within experimental error the whole number ratio 3:1:1:1:1. The primary or main chain structure is therefore based largely, if not entirely, upon units of D-xylose. In the aggregate, two of the three branch centers must engage in main chain linkage by 1–4 glycosidic union since the side chain substituents are evidently attached at C-2. Presumably the third D-xylose residue is engaged in a similar manner to provide a uniform main chain system. The side chain substituent in one of the three primary chain units under consideration is a terminal residue of either D-xylopyranose or L-arabopyranose while the second and third units are joined with D-glucuronic acid residues. One of the latter units is of terminal character and one or other of these residues evidently bears an O-methyl substituent.[9] The non-terminal uronic acid residue bears at C-2 a glycosidic union with the final pentose residue and represents the only di-linked unit in the macromolecule. These deductions are set forward as a tentative description of the sapote gum system but are without the implication that the side-chain substituents are necessarily repetitive throughout the macromolecule on a repeating unit basis.

There is, of course, no information at hand concerning the molecular weight of the polysaccharide. Indeed, as is always the case with amorphous compounds of natural origin, the homogeneity of the material under consideration may be open to question despite rigorous purification. The present evidence appears to favor a basic constitution of the type described. In this, it is to be noted that the terminal unit of the primary chain should produce 3,4-di-O-methyl-D-xylose upon hydrolysis of the methyl ether derivative. No evidence has been found, as yet, in support of this concept although the relatively small amount of the compound derivable from a macromolecule of high

(6) M. A. Abdel-Akher and F. Smith, *Nature*, **166**, 1037 (1950).

(7) The ratio of 2,3,4-tri-O-methyl-L-arabinose to 2,3,4-tri-O-methyl-D-xylose, determined upon a representative sample using the method previously employed for the separation of these components,[2a] was found to be 1.05:0.97, respectively.

(8) (a) J. K. N. Jones and L. E. Wise, *J. Chem. Soc.*, 3389 (1952); (b) R. L. Whistler, H. E. Conrad and L. Hough, THIS JOURNAL, **76**, 1668 (1954).

(9) E. Anderson and H. D. Ledbetter, *J. Am. Pharm. Assoc.*, **40**, 623 (1951).

molecular weight could easily escape detection. The further characterization of the sapote gum system may well be achieved through the preferential action of periodic acid followed by mild hydrolysis. The resulting product, on the basis of present evidence, should be a substantially linear polysaccharide molecule based largely upon units of D-xylose.

Experimental Part

Preparation and Methanolysis of Sapote Gum Methyl Ether.—Sapote gum was dissolved in water and treated with dimethyl sulfate and alkali as previously described[2a] to prepare the ether derivative. The product was then dissolved in anhydrous methanol to furnish a 10% solution to which anhydrous hydrogen chloride was added to 7% concentration. The reaction mixture was heated under reflux for 8 hours, cooled, neutralized with silver carbonate, filtered and evaporated to a sirup which was extracted with ethyl ether. After removal of excess solvent the resulting sirup was distilled fractionally at 0.2 mm. to provide Fraction I, 10.6 g. (b.p. 60–180°); Fraction II, 7.3 g. (b.p. 180–200°); and a still residue of 1.3 g. The components of Fraction I have received previous consideration.[2a] The still residue, comprising undistilled fraction II and a reaction tar, was discarded.

Reduction of Fraction II with Lithium Aluminum Hydride.—Fraction II, 5.0 g., shown previously to consist for the most part of methyl aldobiosiduronate esters, was dissolved in 100 ml. of anhydrous tetrahydrofuran and added slowly to a well-stirred solution containing 1.0 g. of lithium aluminum hydride dissolved in 100 ml. of anhydrous tetrahydrofuran. The temperature of the reaction mixture was maintained at 40° during addition of the reagents and for the following 30 minutes. The excess hydride was then destroyed by the cautious addition of moist tetrahydrofuran followed by an excess of water to decompose the addition complex and to precipitate the hydroxides of lithium and aluminum. The latter were removed by filtration using Celite and the filtrate was evaporated to a sirup which was extracted with acetone, filtered, and excess solvent removed by distillation. The product, 4.8 g., gave a negative naphthoresorcinol test and its saponification number was zero.

Hydrolysis of the **Reduction Product** from **Fraction II.**—A portion, 1.0 g., of the reduction product from Fraction II was treated under reflux for 5 hours with *N* sulfuric acid. The hydrolyzate was isolated in the usual manner, yield 0.9 g. When the latter was examined on the paper chromatogram, developed with a mixture of ethyl acetate, acetic acid and water (9:2:2), against known reference standards there was evidence of three components. These, evidently, were 3-O-methyl-D-xylose and 3,4-di-O-methyl-D-glucose which have been isolated and identified previously[2a] in the course of these investigations together with a third, as yet unidentified, component. The two known compounds, eluted from the appropriate strips cut from several paper chromatograms and crystallized from suitable solvents, had melting points and mixed melting points identical with those of the corresponding authentic compounds.

Identification of 2,3,4-Tri-O-methyl-D-glucose.—The hydrolysate of the reduction product from fraction II, 3.6 g., was dissolved in 75 ml. of chloroform and placed on a no. 5 column of acid-washed Magnesol.[10] The chromatogram was developed with 750 ml. of 25:1 chloroform–ethanol (by vol.). The column was then extruded, streaked and sectioned. The individual sections were eluted with acetone and, after removal of excess solvent, furnished fraction I_t, 2.49 g., and fraction I_b, 1.01 g. Fraction I_t, comprising 3-O-methyl-D-xylose and 3,4-di-O-methyl-D-glucose, was not examined further. Fraction I_b was distilled at 0.2 mm. to provide a colorless sirup, b.p. 120°, with $[\alpha]^{20}D$ 65° (*c* 3.7, equilibrium in water).

Anal. Calcd. for $C_9H_{18}O_6$: OMe, 41.9. Found: OMe, 41.5.

An attempt to prepare the crystalline aniline derivative was not successful. However, when 0.2 g. of the sirup was oxidized with 5 ml. of nitric acid (d. 1.2) at 90° until the evolution of nitrogen oxides was complete (3 hours) 2,3,4-tri-O-methyl-D-glucosaccharic acid was formed. The reaction mixture was diluted with water and distilled under reduced pressure with periodic addition of fresh water and finally with addition of anhydrous methanol to remove most of the nitric acid. The sirupy residue, in ether solution, was then treated with diazomethane to destroy residual nitric acid and esterify the reaction product. After removal of excess reagent and solvent the sirup, 0.15 g., was distilled, b.p. 110° at 0.2 mm. It crystallized spontaneously and, recrystallized from ethyl ether, furnished the methyl ester of 2,3,4-tri-O-methyl-D-glucosaccharolactone with m.p. 107°[11] alone or admixed with an authentic specimen,[12] $[\alpha]^{20}D$ 55° (*c* 2.0 in methanol).

Anal. Calcd. for $C_{10}H_{16}O_7$: OMe, 50.0. Found: OMe, 50.0.

Methylation of the Reduction Product from Fraction II.—The reduction product from fraction II, 4.5 g., was dissolved in 20 ml. of methyl iodide and heated under reflux for 4 hours with 7 g. of freshly prepared silver oxide. The reaction products were separated in the usual manner and, after five separate treatments, the fully methylated derivative was eventually obtained in 4.0-g. yield. It distilled under 0.2 mm. at b.p. 150–155°.

Anal. Calcd. for $C_{18}H_{39}O_{10}$: OMe, 52.9. Found: OMe, 51.0.

When a sample of the sirup was hydrolyzed as previously described and the hydrolysate examined chromatographically under similar conditions as described above, evidence was obtained for the presence of two major components with minor traces of other substances.

Hydrolysis of the **Methylated Reduction Product** from **Fraction II.**—Three and one-half grams of the methylated reduction product from fraction II was dissolved in *N* sulfuric acid, 15 ml., and heated under reflux for 6 hours. The reaction mixture was then cooled, neutralized with barium carbonate, filtered and evaporated to a sirup, yield 3.2 g. The hydrolysate, 1.7 g., dissolved in 50 ml. of chloroform, was added in 25-ml. portions to two no. 3 columns packed with acid-washed Magnesol using 200 ml. of 25:1 chloroform–ethanol (by vol.) as the developer in each instance. The extruded columns were streaked, sectioned, and eluted with acetone in the usual manner to furnish, upon removal of solvent, fraction I_t, 0.09 g.; fraction I_m, 0.562 g.; and fraction I_b, 0.862 g. Fraction I_t moved at the same rate as the previously identified 3-O-methyl-D-xylose when developed on a paper chromatogram with a mixture of ethyl acetate, acetic acid and water, (9:2:2). This component is believed to be 3-O-methyl-D-xylose produced in the hydrolysis reaction from a small amount of incompletely methylated disaccharide or possibly by demethylation of the alkylated monose in the acidic medium. It was not investigated further.

Identification of 3,4-di-O-methyl-D-xylose.—Fraction I_m, a sirup which did not crystallize, was treated with 1 ml. of bromine in 10 ml. of water and 36 hours at room temperature in the absence of light. Upon removal of the bromine by aeration, the non-reducing solution was neutralized with silver carbonate and filtered. The filtrate was then treated with hydrogen sulfide to remove silver ion, filtered, evaporated to a sirup, and dried at 50°. The yield was 0.53 g. The sirup was extracted with ethyl ether and crystallized from the same solvent to furnish the lactone of 3,4-di-O-methyl-D-xylonic acid with m.p. 68°[13] alone or admixed with an authentic specimen, $[\alpha]^{20}D$ −26° (*c* 3.0 equilibrium in water).

Anal. Calcd. for $C_7H_{12}O_5$: OMe, 35.2. Found: OMe, 35.2.

Identification of 2,3,4,6-Tetra-O-methyl-D-glucose.—Fraction I_b was distilled under 0.2 mm. to furnish 0.7 g. of a colorless sirup. When the latter was dissolved in ethyl ether 2,3,4,6-tetra-O-methyl-D-glucose crystallized in good yield. The compound melted at 92°[14] and had $[\alpha]^{20}D$ 82° (*c* 2.9 equilibrium in water).

(10) I. A. Pearl and E. E. Dickey, This Journal, 73, 863 (1951).

(11) R. W. Humphries, J. Pryde and E. T. Waters, *J. Chem. Soc.*, 1298 (1931).

(12) The authentic specimen was prepared from 2,3,4-tri-O-methyllevoglucosan which was kindly supplied by Fred Smith.

(13) Sybil P. James and F. Smith, *J. Chem. Soc.*, 739 (1945).

(14) T. Purdie and J. C. Irvine, *ibid.*, 83, 1021 (1903).

Anal. Calcd. for $C_{10}H_{20}O_6$: OMe, 52.5. Found: OMe, 52.4.

When 0.1 g. of the crystalline compound was treated with 1.1 moles of aniline in the usual manner the aniline derivative of 2,3,4,6-tetra-O-methyl-D-glucose was obtained. It crystallized from ether solution and melted at 135°[15] alone or admixed with an authentic specimen.

(15) J. C. Irvine and Agnes M. Moodie, *J. Chem. Soc.*, **93**, 95 (1908).

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[CONTRIBUTION FROM THE COLLIP MEDICAL RESEARCH LABORATORY AND FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WESTERN ONTARIO, LONDON, CANADA]

Steroids and Related Products. I. The Synthesis of 17α-Methyldesoxycorticosterone

BY CH. R. ENGEL[1] AND G. JUST[2]

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A new hormone analog, 17α-methyldesoxycorticosterone, has been synthetized from desoxycorticosterone. In the course of this investigation it has been shown that the alkali-sensitive α,β-unsaturated 3-ketone, present in many natural steroid hormones, can be protected easily against strong alkaline treatment by the formation of the corresponding enol ethyl ether. 17α-Methyldesoxycorticosterone acetate was found to possess adrenal cortical activity.

Considering that 17α-methyltestosterone[3] is a highly potent, orally active androgen[4] and that 17α-methylprogesterone[5a,b,c] possesses two to three times the progestational activity of the natural corpus luteum hormone, progesterone,[5b,c,6] it seemed of interest to prepare the corresponding 17 homologs of the adrenal cortical hormones and to investigate their biological properties. The interest in such experiments seemed the greater because the important adrenal cortical hormones, cortisone (Kendall's compound E), dihydrocortisone (Kendall's compound F) and 17α-hydroxydesoxycorticosterone (Reichstein's compound S), also have a substituent in the 17α-position in the form of a hydroxyl group.

It was reported in 1950[5b] and again more recently[5c] that parts of such syntheses had been undertaken in the desoxycorticosterone series. The synthesis of 17α-methyldesoxycorticosterone has now been accomplished by different methods by Heusser and co-workers at the Swiss Federal Institute of Technology in Zurich in collaboration with one of us (C.R.E.) and by our laboratory in parallel experiments. It was agreed with the Swiss group to publish the results obtained in Zurich in the *Helvetica Chimica Acta* and to report the findings of our laboratory in THIS JOURNAL.

Whereas in the earlier attempts[5,7] Δ^5-3,β-hydroxysteroids were used as starting materials, the experiments of this series proceeded from 3α-hydroxysteroids with saturated nuclei belonging to the normal (bile acid) series, or from Δ^4-3-ketosteroids, today easily obtainable from the 3-keto derivatives of such compounds[8] or by Oppenauer oxidation of Δ^5-3-hydroxysteroids.[9] Desoxycorticosterone (I) was converted in good yield, according to Reichstein's method,[10] to a mixture of 21-tosyloxyprogesterone (IIa)[10,11] and 21-chloroprogesterone (IIb) in which the latter predominated considerably. We found that when the mixture was not eluted quickly from the chromatographic column (aluminum oxide) no tosylate could be isolated. The chloroketone IIb underwent a rearrangement of the Aston–Greenburg type[12] when treated with potassium methylate in methanol, according to the experimental conditions described by Plattner and co-workers,[13] and gave in 95% yield a mixture of the two epimeric methyl Δ^4-3-keto-17-methyletienates VI and VII. It was not necessary to employ chloroprogesterone of very high purity to obtain high yields. When a crude mixture of chloroprogesterone and tosyloxyprogesterone containing approximately 60% of chloroprogesterone (in this mixture the ratio of tosyloxyprogesterone was deliberately made greater than in the original reaction product obtained from desoxycorticosterone) was subjected to an identical treatment, the same mixture of VI and VII was isolated from the neutral fraction of the reaction product in approximately 53% yield; the relatively important acid fraction, not obtained when chloroprogesterone alone had been employed, gave upon methylation with diazomethane the same mixture of esters, bringing the total yield of these two esters to approximately 88%. The fact that the ester representing approximately 63% of the mixture was eluted with greater ease from the chromatogram and possessed a higher specific rotation than its

(1) Holder of a Medical Fellowship of the Canadian Life Insurance Officers Association.

(2) This paper is abbreviated from part of the doctoral thesis of G. Just to be presented to the Faculty of Graduate Studies of the University of Western Ontario.

(3) L. Ruzicka, M. W. Goldberg and H. R. Rosenberg, *Helv. Chim. Acta*, **18**, 1487 (1935).

(4) K. Miescher and E. Tschopp, *Schweiz. Med. Wochenschrift*, **68**, 1258 (1938).

(5) (a) Pl. A. Plattner, H. Heusser and P. Th. Herzig, *Helv. Chim. Acta*, **32**, 270 (1949); (b) H. Heusser, Ch. R. Engel, P. Th. Herzig and Pl. A. Plattner, *ibid.*, **33**, 2229 (1950); (c) Hs. H. Günthard, E. Beriger, Ch. R. Engel and H. Heusser, *ibid.*, **35**, 2437 (1952).

(6) See also A. Wettstein and F. Benz, *Ann. Rev. Biochem.*, **18**, 355 (1949).

(7) *Cf.* a forthcoming publication in the "Helvetica Chimica Acta."

(8) *Cf.*, for example, V. R. Mattox and E. C. Kendall, THIS JOURNAL, **70**, 882 (1948); **72**, 2290 (1950); *J. Biol. Chem.*, **188**, 287 (1951); W. F. McGuckin and E. C. Kendall, THIS JOURNAL, **74**, 5811 (1952); B. A. Koechlin, T. H. Kritchevsky and T. F. Gallagher, *J. Biol. Chem.*, **184**, 393 (1950).

(9) R. V. Oppenauer, *Rec. trav. chim.*, **56**, 137 (1937).

(10) T. Reichstein and H. G. Fuchs, *Helv. Chim. Acta*, **23**, 684 (1940).

(11) T. Reichstein and W. Schindler, *ibid.*, **23**, 669 (1940).

(12) J. G. Aston and R. B. Greenburg, THIS JOURNAL, **62**, 2590 (1940); see also Al. Faworsky, *J. prakt. Chem.*, [2] **88**, 658 (1913).

(13) Pl. A. Plattner, H. Heusser and S. F. Boyce, *Helv. Chim. Acta*, **31**, 603 (1948).