TABLE I

FRACTIONATION OF METHYLATED GUARAN

Fraction	Bath temp., °C.	Weight obtained, g.	n^{19}D	% OCH_3
I	107–110	3.596	1.4515	60.0
II	110–118	0.643	1.4585	..
III	118–120	1.999	1.4605	52.8
IV	120–155	0.547	1.4635	..
V	155–170	3.043	1.4735	43.5
Residue	.....	0.350	....	..
Total		10.178		

Assuming that the refractive indices of the methyl tetra-, methyl tri- and methyl dimethylglycosides are n^{19}D 1.4515, 1.4616 and 1.4730, respectively, the above fractions I, II, III, IV and V contained methyl 2,3,4,6-tetramethyl-D-galactoside (3.793 g.), methyl 2,3,6-trimethyl-D-mannoside (2.899 g.) and methyl 2,3-dimethyl-D-mannoside (3.142 g.). The mole ratios of the methyl tetra-, methyl tri- and methyl dimethylglycosides were 1.23:1:1.15. The amount of the 2,3,4,6-tetramethyl-D-galactoside corresponded to 38.4% of the methylated gum from which it followed that the unmethylated gum contained 34% galactose (approx.).

These figures approximate those previously reported.[3,4] In another experiment the mole ratios of the tetra-, tri- and dimethylglycosides were found to be 1.3:0.82:0.86 and the amount of galactose corresponded to 35% of the unmethylated gum.

Identification of the 2,3,4,6-Tetramethyl-D-galactose.—Hydrolysis of fraction I (2 g.) with *N* sulfuric acid at 90° for twenty hours yielded 2,3,4,6-tetramethyl-D-galactose (1.85 g.) b. p. (bath temp.) 115–120° (0.01 mm.); n^{19}D 1.4675. By treatment with ethanolic aniline, it was converted to the anilide[10,11]; after recrystallization from ethanol–ether, m. p. 193°; $[\alpha]^{20}$D −140° in pyridine (*c*, 0.5), (*Anal.* Calcd. for $C_{16}H_{25}O_5N$: OCH_3, 39.8; N, 4.5. Found: OCH_3, 40.1; N, 4.5).

Identification of the 2,3,6-Trimethyl-D-mannose.—Hydrolysis of fraction III (2 g.) with 2 *N* sulfuric acid at 90° for twenty-four hours yielded 2,3,6-trimethyl-D-mannose (1.75 g.) which was dissolved in water (5 ml.) and oxidized with bromine (2.5 ml.) at room temperature for three days. The corresponding lactone was produced and, when isolated in the usual manner, gave 2,3,6-trimethyl-D-mannono-γ-lactone[10] (1.15 g.), b. p. (bath temperature) 135–140° (0.01 mm.); m. p. 84° (from ethyl acetate–ether), $[\alpha]^{20}$D +64.8° (initial in water, *c*, 0.5). The lactone yielded the phenylhydrazide[10,12]; after recrystallization from ether, m. p. 130.5°; $[\alpha]^{20}$D −20.1° in water (*c*, 0.5); (*Anal.* Calcd. for $C_{15}H_{25}O_6N_2$: N, 8.5. Found: N, 8.5), and an amide[10,13]; after recrystallization from methanol–ether, m. p. 125°; $[\alpha]^{20}$D −15.4° in water (*c*, 0.55); (*Anal.* Calcd. for $C_9H_{19}O_6N$: N, 5.9. Found: N, 5.9).

Identification of 2,3-Dimethyl-D-mannose.—Hydrolysis of fraction V (2 g.) for thirty hours at 90° with *N* sulfuric acid yielded 2,3-dimethyl-D-mannose which was converted to the corresponding lactone by bromine oxidation in the usual manner (0.8 g.), b. p. (bath temp.) 130–140° (0.01 mm.). The lactone yielded a crystalline phenylhydrazide[10,12]; after recrystallization from methanol–ether, m. p. 158°, remelting at 168°; $[\alpha]^{20}$D −25° in water (*c*, 0.5) (*Anal.* Calcd. for $C_{14}H_{22}O_6N_2$: N, 8.9; OCH_3, 19.7. Found: N, 8.8; OCH_3, 19.9).

Acknowledgment.—The authors wish to thank the General Mills, Inc., for supplying the guar flour used in this work.

Summary

Methylated guaran, obtained directly by the agency of dimethyl sulfate and sodium hydroxide, gives upon methanolysis the glycosides of 2,3,4,6-tetramethyl-D-galactose, of 2,3,6-trimethyl-D-mannose and of 2,3-dimethyl-D-mannose in approximately equal parts. These constituents have been characterized by the formation of identifiable crystalline derivatives. A proposed structure for the galactomannan is given.

---

(11) J. C. Irvine and D. MacNicoll, *J. Chem. Soc.*, **97**, 1449 (1910).

(12) F. Klages, *Ann.*, **509**, 159 (1934); **512**, 185 (1935).

(13) J. I. Cunneen and F. Smith, *J. Chem. Soc.*, 1154 (1948).

LAFAYETTE, INDIANA RECEIVED OCTOBER 14, 1949

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

Phenyl Ketones and Derivatives of Desoxyequilenin and Desoxyisoequilenin Intermediates[1]

BY W. E. BACHMANN AND FAUSTO RAMIREZ[2]

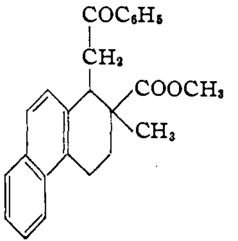
In a study of the intermediates involved in the synthesis of desoxyequilenin and desoxyisoequilenin, the acid chlorides of *cis* and *trans* 2-carbomethoxy - 2 - methyl - 1,2,3,4- tetrahydrophenanthrene-1-acetic acid were converted into the phenyl ketones (I) by reaction with diphenylcadmium. Bromination of the *cis* phenyl ketone in acetic acid took place on the methylene group next to the carbonyl group to give the monobromoketone in 82–85% yields. The bromoketone was converted into the ketol (II) in 90% yield by reaction with sodium formate in methanol. The ketol was not affected by periodic acid at room temperature. An attempt to oxidize the ketol to the diketone IV by a boiling mixture of copper sulfate in pyridine yielded the lactone III. The pyridine was responsible for the cyclization, for the lactone resulted when the ketol was heated with pyridine alone. The presence of a ketone group in the lactone was shown by the formation of a 2,4-dinitrophenylhydrazone. The ketol reacted with lead tetraacetate in acetic acid but, instead of cleavage to an aldehyde, oxidation occurred, presumably to the diketone IV, in spite of the presence of some methanol in the mixture to promote the cleavage reaction.[3] Fusion of the oxidation product with potassium hydroxide gave 2-methyl-1,2,3,4-tetrahydrophen-

---

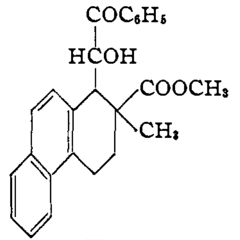
[1] From the Ph.D. dissertation of Fausto Ramirez.

[2] Cobb Chemical Laboratory, University of Virginia, University, Va.

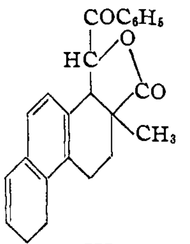
[3] Baer, THIS JOURNAL, **62**, 1597 (1940); **64**, 1416 (1942).



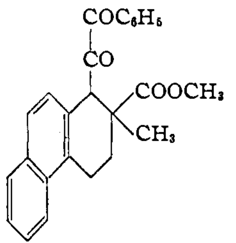
I



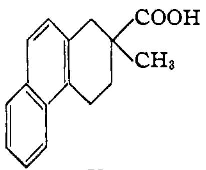
II



III



IV



V

anthrene-2-carboxylic acid (V), and oxidation with alkaline hydrogen peroxide yielded benzoic acid and acidic material which has not been characterized. Further studies are being carried out in attempts to degrade the compounds to 2-methyltetrahydrophenanthrene-1,2-dicarboxylic acid.

Experimental

***cis*-2-Carbomethoxy-2-methyl-1-phenacyl-1,2,3,4-tetrahydrophenanthrene (I)**.[4]—Anhydrous cadmium chloride (7.6 g.) was added to the Grignard reagent prepared from 6.8 ml. of bromobenzene in 100 ml. of ether. To the chilled solution of diphenylcadmium was added a benzene solution (80 ml.) of the ester acid chloride prepared from 10 g. of *cis*-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene-1-acetic acid (m. p. 133–134°)[5] by the procedure employed on the 7-methoxy derivative in the Arndt–Eistert reaction.[6] The mixture was refluxed for four hours, kept at room temperature for twelve hours and hydrolyzed with ice-cold 10% sulfuric acid. After the organic layer had been washed with water and dilute sodium hydroxide, the solvents were evaporated under reduced pressure and the residual ketone (I) was recrystallized from acetic acid; yield, 8.15 g. (68%); m. p. 131–133°. After three recrystallizations from methanol a sample formed colorless needles; m. p. 133–134°. The ketone gives a red color with concentrated sulfuric acid.

Anal. Calcd. for $C_{25}H_{24}O_3$: C, 80.6; H, 6.5. Found: C, 80.2; H, 6.6.

The **2,4-dinitrophenylhydrazone**, formed in aqueous methanol, crystallized from methanol in orange-red rhombic plates; m. p. 193–194°.

Anal. Calcd. for $C_{31}H_{28}N_4O_6$: C, 67.4; H, 5.1; N, 10.1. Found: C, 67.7; H, 5.3; N, 10.3.

When a mixture of 220 mg. of the ketone and 400 mg. of powdered 85% potassium hydroxide was heated cautiously with stirring over a free flame,[7] a sudden reaction took place. After ten minutes the cooled melt was dissolved in hot water and the filtered solution was acidified. The precipitated acid (140 mg.) was evaporatively distilled at 180° and 0.01 mm. and the distillate was recrystallized from methanol; m. p. 227–229° alone and when mixed with *cis*-2-carboxy-2-methyl-1,2,3,4-tetrahydrophenanthrene-1-acetic acid.[8]

Bromination of the Phenyl Ketone.—A solution of 2.98 g. of bromine in 65 ml. of acetic acid was added in two equal portions, with a fifteen-minute interval, with stirring to a suspension of 6.77 g. of the ketone (I) in 100 ml. of acetic acid containing 2 ml. of 35% hydrogen bromide in acetic acid. The bromine was absorbed rapidly and the solid went into solution. The bromoketone which began to crystallize after an hour was collected on a filter after three hours and washed with acetic acid; yield, 4.39 g.; m. p. 146–148°. The crude product obtained by addition of water to the filtrate was dried, dissolved in a mixture of 60–75° petroleum ether and benzene (3:1), the solution was passed through a column of Brockmann alumina, and the column was washed with a large volume of the same solvent. From the solution was isolated 2.31 g. of the bromoketone with m. p. 146–147° (total yield, 82%); ***cis*-1-benzoylbromomethyl-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene** crystallized from methanol in glistening, colorless needles.

Anal. Calcd. for $C_{25}H_{23}BrO_3$: C, 66.5; H, 5.1; Br, 17.7. Found: C, 66.2; H, 5.2; Br, 17.2.

The first time this bromination was carried out the bromoketone was obtained from benzene–petroleum ether as long prismatic needles with m. p. 132–133°. This lower melting product was not obtained again and, unfortunately, none was at hand for comparison when the higher melting form was obtained.

Hydrolysis of the Bromoketone to the Hydroxyketone.—Following the procedure for a similar case,[9] a mixture of 460 mg. of the bromoketone (m. p. 146–148°), 50 ml. of anhydrous methanol and 560 mg. of anhydrous sodium formate was refluxed for twenty-four hours with protection from moisture. After the removal of the solvent, the residue was stirrred with water and the insoluble hydroxyketone (360 mg.; m. p. 150–155°; no Beilstein test for halogen) was collected. After four recrystallizations from methanol the ***cis*-1-benzoylhydroxymethyl-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene** (II) formed stout colorless needles; m. p. 167–168°. The melting point remained the same after the melt had been heated to 270° and then cooled to solidification. The compound gave a pale-yellow color with concentrated sulfuric acid and in alcoholic solution reduced Fehling solution.

Anal. Calcd. for $C_{25}H_{24}O_4$: C, 77.3; H, 6.2. Found: C, 77.2; H, 6.6.

The **2,4-dinitrophenylhydrazone**, which formed readily, was practically insoluble in methanol. After two recrystallizations from acetic acid it formed stout yellow hexagons; m. p. 236–237°.

Anal. Calcd. for $C_{31}H_{28}N_4O_7$: C, 65.6; H, 5.0; N, 9.9. Found: C, 66.1; H, 4.6; N, 10.1.

When a solution of 70 mg. of crude hydroxyketone (m. p. 152–155°) in 10 ml. of pyridine and 2 ml. of water was refluxed for seventeen hours, the lactone of *cis*-1-benzoylhydroxymethyl-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene (III) was obtained as a colorless liquid. The same product was formed in an attempted oxidation of the hydroxy ketone to the diketone by a hot mixture of copper sulfate and pyridine. The **2,4-dinitrophenylhydrazone of the lactone** crystallized from ethyl acetate–methanol in fine yellow needles, m. p. 222–223°,

---

[4] Our work had been completed before the appearance of the paper by Billeter and Miescher, *Helv. Chim. Acta*, **31**, 1302 (1948), describing the preparation of the phenyl ketone of the 7-methoxy derivative by the same method.

[5] Bachmann and Wilds, THIS JOURNAL, **62**, 2084 (1940).

[6] Bachmann, Cole and Wilds, *ibid.*, **62**, 834 (1940).

[7] Bachmann, *ibid.*, **57**, 737 (1935).

[8] Billeter and Miescher, *Helv. Chim. Acta*, **31**, 1302 (1948), obtained a similar result from the 7-methoxy derivative.

[9] Levene and Walti, "Org. Syntheses," Coll. Vol. II, 5 (1943).

which was depressed by the same derivative of the hydroxyketone.

Anal. Calcd. for $C_{30}H_{24}N_4O_6$: C, 67.1; H, 4.5; N, 10.4. Found: C, 66.7; H, 4.8; N, 10.2.

Oxidation of the Hydroxyketone.—Lead tetraacetate (220 mg.) was added portionwise over a six-hour period to a solution of 194·mg. of crude hydroxyketone (m. p. 152–157°) in 10 ml. of acetic acid and 2 ml. of water kept at 90–95°; frequent tests with starch-potassium iodide paper showed that the oxidizing agent was being consumed. The lemon-yellow solution, after removal of the lead as lead sulfate, was warmed with methanolic 2,4-dinitrophenylhydrazine reagent for a few minutes. After three recrystallizations of the product (230 mg.) from ethyl acetate–methanol the **mono-2,4-dinitrophenylhydrazone** presumably of 1-phenylglyoxylyl-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene (IV) was obtained as microscopic crimson plates; m. p. 214–215°.

Anal. Calcd. for $C_{31}H_{26}N_4O_7$: C, 65.7; H, 4.6; N, 9.9. Found: C, 65.7; H, 4.3; N, 10.2.

Fusion of a sample of the crude oxidation product with potassium hydroxide yielded an acid which after evaporative distillation crystallized from acetone–petroleum ether in platelets; m. p. 183–185° alone, and 188–191° when mixed with a sample of 2-methyl-1,2,3,4-tetrahydrophenanthrene-2-carboxylic acid (m. p. 190–191°). The latter acid was prepared by refluxing a solution of 1.3 g. of 1-keto-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene with amalgamated zinc and hydrochloric acid for twenty-three hours, analogous to the preparation of the 7-methoxy derivative.[10] The isolated product was treated with diazomethane and evaporatively distilled at 100–120° at 0.05 mm. and the distillate was hydrolyzed with hot 14% aqueous-methanolic potassium hydroxide to the acid (330 mg.), which gave no test for carbonyl group. After evaporative distillation at 0.05 mm. and three recrystallizations from methanol the **2-methyl-1,2,3,-4-tetrahydrophenanthrene-2-carboxylic acid** formed colorless platelets; m. p. 192–193°.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 80.0; H, 6.7. Found: C, 80.0; H, 6.7.

A solution of 260 mg. of the crude oxidation product in 40 ml. of methanol, 2 ml. of Superoxol (30% hydrogen peroxide) and 4 ml. of *N* sodium hydroxide was stirred for twelve hours at room temperature. After the removal of the solvents at 60° in a current of air, the residue was boiled with water and the aqueous solution, after removal of a small amount of insoluble liquid with benzene, chloroform, and ethyl acetate, was filtered and acidified. The precipitated acidic material (120 mg.), isolated with ether, was evaporatively distilled at 130–160° and 0.05 mm. The crystalline product (33 mg. or 40%, m. p. 121–122°) which collected at the upper end of the tube, proved to be benzoic acid. The higher-boiling distillate (50 mg.) was a viscous liquid which is being investigated further.

***trans*-2-Carbomethoxy-2-methyl-1-phenacyl-1,2,3,4-tetrahydrophenanthrene.**—The phenyl ketone obtained by reaction of diphenylcadmium with the acid chloride of 0.05 g. of *trans*-2-carbomethoxy-2-methyl-1,2,3,4-tetrahydrophenanthrene-1-acetic acid (m. p. 155–157°)[5] crystallized from methanol in colorless needle-like prisms; yield, 0.33–0.36 g. (56–62%); m. p. 119–120°. After three recrystallizations a sample melted at 120–121°; it gave an orange color with concentrated sulfuric acid.

Anal. Calcd. for $C_{25}H_{24}O_3$: C, 80.6; H, 6.5. Found: C, 80.0; H, 6.6.

The **2,4-dinitrophenylhydrazone** after two recrystallizations from ethyl acetate–methanol formed red rectangular plates; m. p. 215–216°.

Anal. Calcd. for $C_{31}H_{28}O_6$: C, 67.4; H, 5.1; N, 10.1. Found: C, 67.6; H, 5.2; N, 9.9.

Bromination of 330 mg. of the phenyl ketone (m. p. 119–121°) in 8 ml. of acetic acid by the procedure described for the *cis* isomer gave 370 mg. of solid which was purified by passage of a 1:2 benzene–petroleum ether solution through alumina. After one recrystallization from petroleum ether the **monobromo derivative** melted at 126–130°; yield, 200 mg. (50%). After another recrystallization the bromo derivative formed colorless rosettes; m. p. 129–130°.

Anal. Calcd. for $C_{25}H_{23}BrO_3$: C, 66.5; H, 5.1; Br, 17.7. Found: C, 65.7; H, 5.1; Br, 17.7.

Summary

The *cis* and *trans* forms of 2-carbomethoxy-2-methyl-1-phenacyl-1,2,3,4-tetrahydrophenanthrene have been prepared by the reaction of diphenylcadmium with the corresponding acid chlorides. The formation of the *cis* 1,2-ketol and a study of its behavior toward oxidizing agents are described.

ANN ARBOR, MICHIGAN RECEIVED DECEMBER 5, 1949

---

[10] Heer and Miescher, *Helv. Chim. Acta*, **28**, 1506 (1945).

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

Studies on the Configuration of the C/D Ring Juncture of Steroids. The Lactams Corresponding to Desoxyequilenin and Desoxyisoequilenin[1]

BY W. E. BACHMANN AND FAUSTO RAMIREZ[2]

Although a *trans* configuration has been assigned to the C/D ring juncture of the female sex hormones, more experimental evidence is desirable in order to establish unequivocally this configuration.[3] We have investigated the nature of the C/D ring configuration in desoxyequilenin and desoxyisoequilenin by degrading the two diastereoisomeric 2-carbomethoxy-2-methyl-1,2,3-4-tetrahydrophenanthrene-1-acetic acids (Ia and IIa) in the form of racemic mixtures to the aminoesters (Ib and IIb) by the Curtius reaction and studying the tendency of the aminoesters to form lactams (Ic and IIc).

The acid chlorides of Ia and IIa were converted into azides by reaction with sodium azide in aqueous acetone. Rearrangement of the azides and hydrolysis of the resulting isocyanates with concentrated hydrochloric acid gave the hydrochlorides of the *cis* and *trans* forms of the aminoesters Ib and IIb in 71–80% over-all yields. A

---

[1] From the Ph.D. dissertation of Fausto Ramirez, 1949.

[2] Cobb Chemical Laboratory, University of Virginia.

[3] (a) Shoppee, *Nature*, **161**, 207 (1948); (b) Heer and Miescher, *Helv. Chim. Acta*, **29**, 1895 (1946); (c) Heer and Miescher, *ibid.*, **30**, 550 (1947); (d) Fieser and Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1949, 3rd ed., p. 626.