

m. p. 63–64° (unchanged on admixture with an authentic sample), spec. rot. +156° (22°, *c* 1.5, abs. EtOH, D line). For this ethyl α -thio-D-glucoside tetraacetate, Schneider and Sepp⁸ recorded the constants: m. p. 63°, spec. rot. +155° (20°, EtOH, D line).

Anal. Calcd. for C₁₈H₂₄O₉S: C, 48.98; H, 6.17. Found: C, 49.17; H, 6.00.

Oxidation of the Ethyl α -Thio-D-glucoside of Schneider and Sepp⁸ by Sodium Metaperiodate.—The parent substance of the above-described tetraacetate was oxidized in dilute solution and at room temperature with an excess of sodium metaperiodate. The reaction was followed with time and the results are tabulated in Table I. The formaldehyde was assayed by the dimedon procedure¹⁵ and the acidity was that titratable with methyl red indicator. The results tabulated represent the initial phases of the reaction. On long standing, further oxidation occurs with this substance under these conditions.

(2,3,4,5)-O-Dibenzylidene-D-glucose Dimethyl Acetal (V).—(2,3,4,5)-O-Dibenzylidene-D-glucose diethyl mercaptal¹¹ (20 g.) was added to a suspension of 24 g. of cadmium carbonate in 300 cc. of absolute methanol and to this was added a solution of 100 cc. of methanol containing 56 g. of mercuric chloride. The mixture was then refluxed for twelve hours with constant stirring, whereupon the mixture was filtered and the solids washed with warm methanol. The filtrate was then poured into a mixture of 500 cc. each of chloroform and water and the chloroform layer was washed free of halides with water, treated with decolorizing charcoal and dried with Drierite and cadmium carbonate. The residue obtained on solvent removal was crystallized from 50% methanol; yield 15 g., m. p. 177–178°. Pure material was obtained on further crystallization from the same solvent; m. p. 183–184°, spec. rot. +14° (25°, *c* 4, CHCl₃, D line).

Anal. Calcd. for C₈H₈O₅(C₆H₅CH)₂(OCH₃)₂: OCH₃,

(15) D. Vorländer, C. Ihle and H. Volkholz, *Z. anal. Chem.*, **77**, 321 (1929).

15.42; C₆H₅CH, 44.79. Found: OCH₃, 15.25; C₆H₅CH,¹⁶ 44.53.

(2,3,4,5)-O-Dibenzylidene-D-glucose dimethyl acetal was treated at room temperature with essentially anhydrous methanol containing 0.05% dry hydrogen chloride. A gradual change in rotation occurred, with the liberation of benzaldehyde. No crystalline product was isolated from the reaction.

The assistance of Mr. Irving Auerbach in a portion of this work is acknowledged. One of us (A. T.) acknowledges a stipend from the funds of The Ohio State University Research Foundation administered by the Graduate School.

Summary

1. The synthesis in crystalline form of 6-O-triphenylmethyl-D-glucose diethyl mercaptal tetraacetate (I), D-glucose diethyl mercaptal tetraacetate (IIa) and (2,3,4,5)-O-dibenzylidene-D-glucose dimethyl acetal (V) is reported.

2. IIa was formed by the detritylation of I and by the mercaptalation of D-glucose 2,3,4,6-tetraacetate.

3. Demercaptalation of IIa yielded the ethyl α -thio-D-glucoside tetraacetate of Schneider and Sepp.⁸

4. It is conclusively demonstrated by periodate oxidation that the ethyl α -thio-D-glucoside of Schneider and Sepp⁸ has a furanoside structure.

5. V lost benzaldehyde on treatment with methanol containing 0.05% hydrogen chloride.

(16) Method of W. Alberda van Ekenstein and J. J. Blankensma, *Rec. trav. chim.*, **26**, 153 (1906).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Reactivity of the Monothioacetals of Glucose and Galactose in Relation to Furanoside Synthesis¹

BY M. L. WOLFROM, D. I. WEISBLAT AND A. R. HANZE

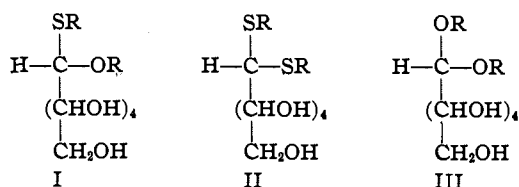
The synthesis of the crystalline monothioacetals (I) of D-galactose² and of D-glucose³ has been reported from this Laboratory. Since these compounds have been postulated by Green and Pacsu⁴ as intermediates in the reaction of sugar mercaptals or thioacetals (II) with mercuric chloride in alcohol containing yellow mercuric oxide, their behavior under such conditions and under other ring closure conditions is of interest. The behavior of the acetals (III) and mercaptals under similar conditions was also studied in order to compare their reactivity with that of the monothioacetals.

(1) Presented before the Division of Sugar Chemistry and Technology at the 101st meeting of the American Chemical Society, St. Louis, Missouri, April 10, 1941.

(2) M. L. Wolfrom and D. I. Weisblat, *THIS JOURNAL*, **62**, 878 (1940).

(3) M. L. Wolfrom, D. I. Weisblat and A. R. Hanze, *ibid.*, **62**, 3246 (1940).

(4) J. W. Green and E. Pacsu, *ibid.*, **60**, 2288 (1938); E. Pacsu, *ibid.*, **61**, 1671 (1939).



When the monothioacetals were placed in dilute hydrochloric acid (0.05%) or in alcohols containing dry hydrogen chloride (0.05%), a reaction took place which proceeded at 25° with a speed suitable for polarimetric observation. The polarimetric data which we have obtained for D-glucose S-ethyl O-methyl monothioacetal and for D-galactose diethyl monothioacetal under such conditions are diagrammed in Figs. 1 and 2. The plots (Fig. 2) of the polarimetric data for the two compounds in alcohols containing dry hydrogen chloride yield continuous exponential curves. In dilute hydrochloric acid (Fig. 1)

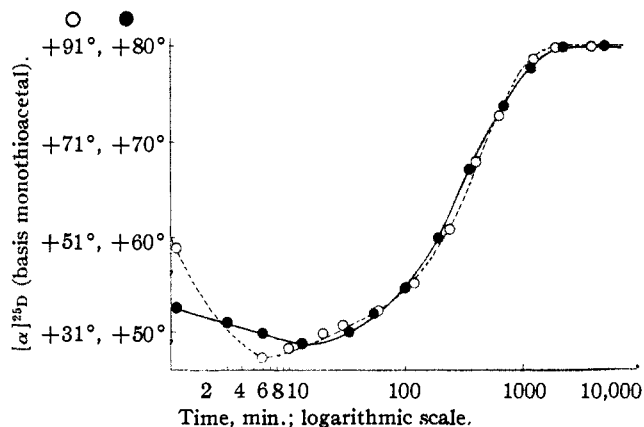


Fig. 1.—Rotation changes at 25° of D-glucose S-ethyl O-methyl monothioacetal (c 1.7), O, and of D-galactose diethyl monothioacetal (c 1.5), ●, in hydrochloric acid (0.05%).

both substances yield curves showing initial minima followed by a gradual increase in dextro-rotation until equilibrium is attained.

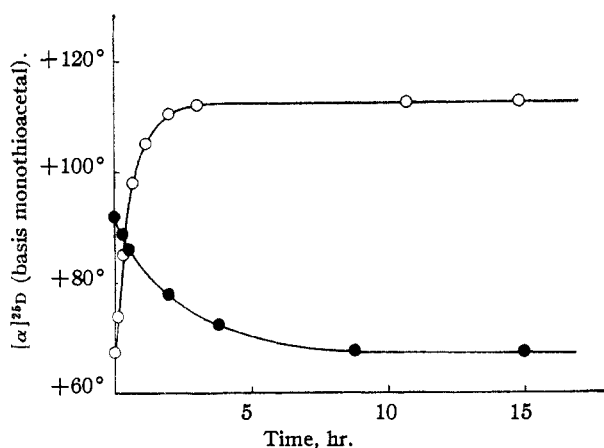


Fig. 2.—Rotation changes at 25° of D-glucose S-ethyl O-methyl monothioacetal, O, in methanol (c 0.7) containing hydrogen chloride (0.05%); and of D-galactose diethyl monothioacetal, ●, in ethanol (c , 0.6) containing hydrogen chloride (0.05%).

The glucose monothioacetal gave ethyl α -thio-D-glucufuranoside as an end-product both in methanol containing hydrogen chloride and in dilute hydrochloric acid, the final equilibrium mixture in both cases being non-reducing toward Fehling solution. In ethanol containing hydrogen chloride, the galactose monothioacetal yielded an isolated mixture of sulfur-free ethyl galactosides as the end-product, the exact nature of which was not determined. D-Galactose was the only final product isolated in the dilute hydrochloric acid reaction, although the high final specific rotation (calculated on the basis of the original weight of monothioacetal, *cf.* Fig. 1) would indicate the presence of a more dextrorotatory product than D-galactose. The further interesting observation

was made that ethyl β -D-galactofuranoside was stable in 0.05% hydrochloric acid at 25°. Any free D-galactose formed in the ethanol reaction would probably undergo glycoside formation in the presence of the dry hydrogen chloride, as indicated by the work of E. Fischer.⁵

E. Fischer⁶ showed qualitatively that D-glucose diethyl mercaptal was decomposed by mercuric chloride with the formation of thioethoxy mercuric chloride (C_2H_5SHgCl). Schneider and Sepp⁷ demonstrated that when this reaction was kept neutral by the stepwise addition of dilute sodium hydroxide, there was obtained from D-glucose diethyl mercaptal a compound which was later shown⁸ to be ethyl α -thio-D-glucufuranoside. Green and Pacsu⁸ extended and improved the reaction by replacing the dilute sodium hydroxide with yellow mercuric oxide. These authors postulated⁴ that, except in the case of the glucose compound, the mixed acetal was the probable intermediate in the reaction of sugar mercaptals with mercuric chloride in alcohol containing mercuric oxide.

On treating D-glucose diethyl mercaptal with mercuric chloride in *methanol* in the presence of mercuric oxide at room temperature, we have obtained ethyl α -thio-D-glucufuranoside in low yield. D-Glucose S-ethyl O-methyl monothioacetal under identical conditions gave a 95% yield of a sirup whose rotation agreed with the value given for methyl β -D-glucufuranoside by Haworth, Porter and Waine.⁹ This compound was characterized by a crystalline tetracarbanilate on application of the general technique previously reported¹⁰ from this Laboratory. *These data indicate that, in the formation of ethyl α -thio-D-glucufuranoside from D-glucose diethyl mercaptal, the mixed acetal, at least in this anomeric form, is not the probable intermediate.* It would be of interest to study the relative behavior of the anomer under the same conditions.

D-Galactose diethyl monothioacetal, on treatment with mercuric chloride in ethanol containing yellow mercuric oxide, yielded 85–90% of ethyl β -D-galactofuranoside, an increase of 15–20% over that recorded by Green and Pacsu⁸ from the diethyl mercaptal. Under similar conditions, D-galactose diethyl acetal¹¹ was apparently unaffected. D-Galactose diethyl mer-

(5) E. Fischer, *Ber.*, **26**, 2400 (1893); **28**, 1145 (1895).

(6) E. Fischer, *ibid.*, **27**, 673 (1894).

(7) W. Schneider and Johanna Sepp, *ibid.*, **49**, 2054 (1916).

(8) J. W. Green and E. Pacsu, *THIS JOURNAL*, **59**, 1205 (1937);

E. Pacsu and E. J. Wilson, *ibid.*, **61**, 1450, 1930 (1939); P. Brigl,

K. Gronemeier and A. Schulz, *Ber.*, **72B**, 1052 (1939); M. L. Wolfrom,

S. W. Waisbrot, D. I. Weisblat and A. Thompson, *THIS JOURNAL*, **66**, 2063 (1944).

(9) W. N. Haworth, C. R. Porter and A. C. Waine, *J. Chem. Soc.*, 2254 (1932).

(10) M. L. Wolfrom and D. R. Pletcher, *THIS JOURNAL*, **62**, 1151 (1940).

(11) M. L. Wolfrom, L. J. Tanghe, R. W. George and S. W. Waisbrot, *ibid.*, **60**, 132 (1938).

capital on treatment with mercuric chloride (2 moles) and cadmium carbonate¹² (excess) in absolute ethanol for six hours at room temperature gave a 50% yield of ethyl β -D-galactofuranoside. The pentaacetate of D-galactose diethyl monothioacetal on treatment with mercuric chloride and cadmium carbonate in absolute ethanol gave an excellent (77%) yield of D-galactose diethyl acetal pentaacetate. *These data indicate that, in the formation of ethyl β -D-galactofuranoside from D-galactose diethyl mercaptal, the mixed acetal is the probable intermediate.*

Experimental

Behavior of Monothioacetals in 0.05% Hydrochloric Acid Solution at 25° (Fig. 1)

(a) **Conversion of D-Glucose S-Ethyl O-Methyl Monothioacetal into Ethyl α -Thio-D-glucufuranoside.**—D-Glucose S-ethyl O-methyl monothioacetal³ (0.467 g.) was dissolved in 27.23 cc. of water containing hydrogen chloride (0.05%). The solution was quickly transferred to a polarimeter tube and the mutarotation observed until equilibrium was attained. The reaction mixture was neutralized with silver carbonate, filtered through a bed of filter cell (Johns-Manville Super-Cel), and the solvent removed at 30° under diminished pressure. The sirupy residue was taken up in a minimum of dry methanol, the solution treated with active charcoal and filtered through a bed of filter cell. The ethyl α -thio-D-glucufuranoside crystallized on cooling; yield 0.12 g. (30%), m. p. 151–153°, spec. rot. +121° (23°, c 2.1, H₂O, D line); mixed melting point with an authentic sample unchanged. For this substance, Schneider and Sepp⁷ recorded the constants: m. p. 153°, spec. rot. +121° (H₂O, D line).

(b) **Conversion of D-Galactose Diethyl Monothioacetal into D-Galactose.**—Under identical conditions, D-galactose diethyl monothioacetal³ (1.500 g.) in 100.0 cc. of hydrochloric acid (0.05%) gave a crystalline mass of D-galactose. On recrystallization from ethanol pure D-galactose was obtained; yield 0.54 g. (54%), m. p. 161–163°, spec. rot. (equilibrium) +80° (25°, c 2.8, H₂O). At the minimum point of the curve (Fig. 1), D-galactose and starting material were isolated.

(c) **Behavior of Ethyl β -D-Galactofuranoside in Hydrochloric Acid Solution.**—The rotation of ethyl β -D-galactofuranoside in water containing hydrogen chloride (0.05%) was taken at various time intervals ranging from two minutes to forty hours. The specific rotation, –98° (22°, c 1.1), remained constant throughout this period. Upon processing this solution in the previously-described manner, unchanged starting material was obtained.

Behavior of Monothioacetals in Alcohol Containing 0.05% Dry Hydrogen Chloride at 25° (Fig. 2)

(a) D-Glucose S-ethyl O-methyl monothioacetal (0.70 g.) was dissolved in 99.92 cc. of methanol containing dry hydrogen chloride (0.05%). At equilibrium the reaction mixture was neutralized with silver carbonate and the product, ethyl α -thio-D-glucufuranoside, was isolated as described above; yield 60%, m. p. 149–151°, identification by mixed melting point and specific rotation.

(b) Similar treatment of D-galactose diethyl monothioacetal (0.591 g.) in 100.0 cc. of ethanol containing dry hydrogen chloride (0.05%) yielded at equilibrium a mixture of galactosides whose exact nature was not determined. The product was sulfur-free and reduced Fehling solution only after acid hydrolysis.

Conversion of D-Galactose Diethyl Monothioacetal into Ethyl β -D-Galactofuranoside.—An amount of 4.75 g. of D-galactose monothioacetal was converted into the ethyl β -D-galactofuranoside with mercuric chloride and yellow

mercuric oxide in absolute ethanol, according to the procedure of Green and Pacsu,⁴ yield 3.2 g. (87%) of recrystallized product, m. p. 86–87°, spec. rot. –97.5° (25°, c 1.7, H₂O, D line); mixed melting point with an authentic sample unchanged. For this substance Schlubach and Meisenheimer¹⁴ recorded the constants: m. p. 86°, spec. rot. –97° (H₂O, D line).

The Action of Mercuric Chloride–Mercuric Oxide on D-Galactose Diethyl Acetal.—D-Galactose diethyl acetal¹¹ was recovered unchanged in good yield under the conditions described above for the conversion of D-galactose diethyl monothioacetal into ethyl β -D-galactofuranoside.

Conversion of D-Glucose S-Ethyl O-Methyl Monothioacetal into Methyl β -D-Glucufuranoside.—A mixture of D-glucose S-ethyl O-methyl monothioacetal (1.15 g., 1 mole), yellow mercuric oxide (1.5 g., excess) and mercuric chloride (1.92 g., 2 moles) in 25 cc. of absolute methanol was stirred vigorously for two hours at room temperature and the sirupy product isolated by the procedure described by Green and Pacsu⁴; yield 0.83 g. (95% of calcd.), spec. rot. –74° (26° c 5.5, H₂O, D line). Haworth, Porter and Waive⁹ reported a specific rotation of –77° (H₂O, D line) for sirupy methyl β -D-glucufuranoside.

Methyl β -D-Glucufuranoside Tetracarbanilate.—Methyl β -D-glucufuranoside (0.65 g., 1 mole) was dissolved in 5 cc. of hot, dry pyridine and the solution cooled to room temperature. The addition of phenyl isocyanate (2 cc., 5.5 moles) produced an exothermic reaction. The mixture was heated for three hours under a reflux condenser equipped with drying tube. The solution was then cooled, 15 cc. of ligroin added and the whole placed in an ice-chest overnight. A semi-crystalline mass separated which was removed by filtration and extracted with dry ether in a Soxhlet apparatus. The residue was crystallized from warm ethanol by the addition of water. Pure material was obtained, in the form of sheaves of long, delicate needles, after two recrystallizations from the same solvent mixture; yield 0.56 g. (28%), m. p. 215–217° (uncor.), spec. rot. +7.6° (26°, c 1.2, dry acetone, D line).

Anal. Calcd. for C₁₄H₁₄O₁₀N₄: C, 62.67; H, 5.07; N, 8.35. Found: C, 62.66; H, 5.05; N, 8.28.

Ethyl α -Thio-D-glucufuranoside from D-Glucose Diethyl Mercaptal.—When D-glucose diethyl mercaptal (5.0 g.) was substituted for the D-glucose S-ethyl O-methyl monothioacetal and treated as described above for the conversion of the latter compound into methyl β -D-glucufuranoside, a low yield of ethyl α -thio-D-glucufuranoside (0.25–0.50 g., identified by m. p. and mixed m. p.) was obtained.

Conversion of D-Galactose Diethyl Monothioacetal Pentaacetate into D-Galactose Diethyl Acetal Pentaacetate.—D-Galactose diethyl monothioacetal pentaacetate (4.0 g., 1 mole) and finely powdered cadmium carbonate (4.4 g., excess) were added to 80 cc. of absolute ethanol and the mixture heated to 70–80° while stirring with a mercury-sealed mechanical stirrer. Mercuric chloride (7.0 g., 3 moles), dissolved in 20 cc. of absolute ethanol, was added rapidly in one portion. The mixture was stirred under reflux for two and one-half hours. The hot reaction mixture was filtered through a bed of Super-Cel (Johns-Manville) and the residue washed with a small volume of hot ethanol. The clear, colorless filtrate was transferred to a separatory funnel containing equal volumes (300 cc. of each) of chloroform and cold water. The chloroform layer was washed once with 10% potassium iodide solution and then repeatedly (three times) with 100 cc. of water until free of halide. The solution, dried over anhydrous calcium sulfate (Drierite), was then concentrated at 30° under diminished pressure to a crystalline mass. Recrystallization from hot 50% ethanol yielded D-galactose diethyl acetal pentaacetate; yield 3.0 g. (77.5%), m. p. 78–79°, spec. rot. +17.2° (25°, c 2.0, abs. CHCl₃, D line); mixed melting point with an authentic sample showed no depression. Wolfrom and co-workers¹¹ record the following constants for this compound: m. p. 79°, spec. rot. +17.5° (abs. CHCl₃, D line).

(12) M. I. Wolfrom, *THIS JOURNAL*, **51**, 2188 (1929).

(13) c throughout denotes g. per 100 cc. of soln.

(14) H. Schlubach and K. Meisenheimer, *Ber.*, **67B**, 429 (1934).

Conversion of D-Galactose Diethyl Mercaptal into Ethyl β -D-Galactofuranoside with Mercuric Chloride and Cadmium Carbonate.—A mixture of D-galactose diethyl mercaptal (5.0 g., 1 mole) cadmium carbonate (6.0 g., excess) and mercuric chloride (9.2 g., 2 moles) in 100 cc. of absolute ethanol was stirred vigorously for two hours at room temperature and the product isolated as described above for the isolation of ethyl β -D-galactofuranoside. The crystalline material was found to be a mixture of D-galactose diethyl mercaptal and ethyl β -D-galactofuranoside. When the reaction time was extended to six hours at room temperature, only ethyl β -D-galactofuranoside was isolated, in approximately 50% yield.

Summary

1. D-Glucose S-ethyl O-methyl monothioacetal exhibited a simple mutarotation at 25° in methanol containing 0.05% hydrogen chloride and exhibited a complex mutarotation in 0.05% aqueous hydrochloric acid. Ethyl α -thio-D-glucoside was isolated as a final product in both cases.

2. Similar mutarotation phenomena were exhibited by D-galactose diethyl monothioacetal. D-Galactose was isolated as a final product in the aqueous medium.

3. Ethyl β -D-galactofuranoside was not detectably hydrolyzed by 0.05% hydrochloric acid at 25°.

4. Mercuric chloride and cadmium carbonate in absolute ethanol reacted with D-galactose

diethyl monothioacetal to yield ethyl β -D-galactofuranoside and with D-galactose diethyl monothioacetal pentaacetate to yield D-galactose diethyl acetal pentaacetate.

5. Mercuric chloride and yellow mercuric oxide in methanol reacted with D-glucose S-ethyl O-methyl monothioacetal to give a practically quantitative yield of the sirupy methyl β -D-glucoside of Haworth and co-workers, herein characterized by a crystalline tetracarbanilate.

6. Mercuric chloride and yellow mercuric oxide in ethanol reacted with D-galactose diethyl monothioacetal to give a practically quantitative yield of the crystalline ethyl β -D-galactofuranoside. D-Galactose diethyl acetal was stable toward these reaction conditions.

7. The above data indicate that D-glucose S-ethyl O-methyl monothioacetal, at least in this anomeric form, is not the probable intermediate in the formation of ethyl α -thio-D-glucoside from D-glucose diethyl mercaptal but that the mixed acetal is the probable intermediate in the formation of ethyl β -D-galactofuranoside from D-galactose diethyl mercaptal. These deductions are in accord with the postulations of Pacsu and Green.

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[CONTRIBUTION FROM THE WILLIAM G. KERCKHOFF LABORATORIES OF THE BIOLOGICAL SCIENCES OF THE CALIFORNIA INSTITUTE OF TECHNOLOGY AND THE EMERGENCY RUBBER PROJECT, BUREAU OF PLANT INDUSTRY, U. S. DEPARTMENT OF AGRICULTURE]

Chemical Investigations in Guayule. I. Essential Oil of Guayule, *Parthenium argentatum*, Gray

By A. J. HAAGEN-SMIT AND R. SIU¹

Aside from the identification of α -pinene by Alexander,² very little is known about the essential oil of the guayule rubber plant. This meager chemical knowledge could not furnish a sound basis for the understanding of the injurious effects of the oil on rubber, of its role in the plant, and of its possibilities as a by-product in the guayule rubber industry. The following investigation was carried out to fill this gap in the chemical knowledge of the oil.

The oil was obtained from the steam distillation of fresh guayule plants. Two-thirds of the total oil was obtained after one and one-half hours of steam distillation. About 25% more was obtained with an additional one and one-half hours. After four and one-half hours further steam distillation gave only a negligible amount of oil. The oil obtained after three hours of steam dis-

tillation emitted an odor suggestive of decomposition. For this reason later steam distillations were carried out for only two and one-half hours, yielding about 80% of the total oil.

According to Table I, the leaves possess the highest essential oil content on a fresh weight basis (1.04%), followed next by the flowers, then the bark. Only a small amount of oil can be obtained from the wood.

TABLE I
ESSENTIAL OIL CONTENT OF DIFFERENT PARTS OF THE
GUAYULE PLANT

Part of plant	Fresh wt. of tissue in g.	Wt. of oil in g.	% of oil on fresh wt. basis
Leaves	6,870	71.2	1.04
Flowers	890	6.7	0.75
Bark	10,265	24.7	.24
Wood	5,910	6.3	.11
Total	23,935	108.9	.45

When the entire guayule plant was steam distilled, the oil separating from the steam distillate

(1) The authors greatly appreciate the hearty cooperation and keen interest of Dr. A. C. Hildreth and Dr. H. Traub during the course of this work. The help of Dr. J. Kirchner is also gratefully acknowledged.

(2) Alexander, *Ber.*, 44, 2320 (1911).