Celite[25] (5:1 by weight) using as developer four liters of a solution of *t*-butyl alcohol in benzene (1:75 v./v.). On extrusion the column was streaked with alkaline potassium permanganate.[7] The principal zone was eluted with acetone and evaporated to yield 0.538 g. of crude sirup. Decolorization with activated charcoal in absolute ethanol and evaporation produced crystalline octadeca-*O*-acetylmaltopentaitol. It was recrystallized from absolute ethanol; m.p. 197–197.5°, $[\alpha]^{25}\text{D}$ +132.7° (*c* 0.9, chloroform). An X-ray diffraction pattern confirmed the crystalline nature of the acetate.

Anal. Calcd. for $C_{66}H_{90}O_{44}$: C, 49.99; H, 5.67. Found: C, 49.63; H, 5.77.

R_{glucose} Values of Pure Corn Sirup Components.—Approximately equal amounts of the pure corn sirup oligosaccharides of degree of polymerization one through seven were placed on Whatman No. 4 grade paper at a distance of two centimeters from each other. The chromatograms eluted at 25° for 44 or 144 hours with butanol–ethanol–water (3:2:1) and developed with aniline hydrogen phthalate.[23] The paper eluted the shorter time was used to calculate the R_{glucose} values of maltose, maltotriose and maltotetraose. The R_{glucose} value of the higher oligosaccharides on the paper eluted longer were calculated from the R_{glucose} value of maltotriose. The R_{glucose} value of maltotetraose in both cases was used as a secondary reference point. The values are recorded in Table I.

Acknowledgments.—The authors wish to thank the Corn Industries Research Foundation for funds in support of this investigation, Dr. A. K. Balls for providing the crystalline sweet potato β-amylase, and Mr. Ben Moy for assisting in a portion of the work.

LAFAYETTE, INDIANA

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[25] No. 535, Johns-Manville, New York, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FACULTY OF SCIENCE, CAIRO UNIVERSITY, AND THE LABORATORIES OF THE MEMPHIS CHEMICAL COMPANY]

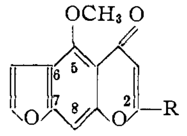
Furo-chromones and -Coumarins. IX. Reactions of Khellol Glucoside, Visnagin and Bergapten

BY ALEXANDER SCHÖNBERG, NASRY BADRAN AND NICOLAS A. STARKOWSKY

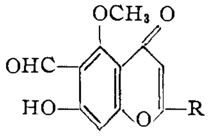
RECEIVED JUNE 28, 1954

A method is described for the hydrolysis of khellol glucoside and the subsequent transformation of khellol to visnagin. The oxidation of khellol with chromic acid yields 6-formyl-7-hydroxy-2-hydroxymethyl-5-methoxychromone (IIa) and that of bergapten 6-formyl-7-hydroxy-5-methoxycoumarin (apoxanthoxyletin) (IV). 5,6,7-Trimethoxy-2-methylchromone (VIId) can be obtained from visnagin through the intermediate 6-formyl-7-hydroxy-5-methoxy-2-methylchromone (IIc).

An improvement of the original method of Geissman[1] is described for the conversion of khellol glucoside (Id), a natural product extracted from the seeds of *Ammi visnaga* L., to another constituent of this plant, visnagin (Ic). The first step: acid hydrolysis of the glucoside, of a few minutes duration, yielded khellol (Ia) of high purity. Under more drastic conditions, khellol glucoside was not only hydrolyzed, but also demethylated to 5-norkhellol.[2] Khellol reacted with thionyl chloride to give (Ib) which was converted into visnagin by reduction with zinc and acetic acid. These reactions are analogous to the synthesis of allomaltol from kojic acid[3].



I

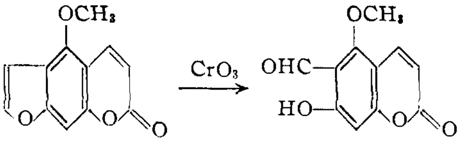


II

Ia, R = CH_2OH
Ib, R = CH_2Cl
Ic, R = CH_3
Id, R = $CH_2OC_6H_{11}O_5$

IIa, R = CH_2OH
IIb, R = CH_2Cl
IIc, R = CH_3

The oxidation of visnagin (Ic) with chromic acid to 6-formyl-7-hydroxy-5-methoxy-2-methylchromone[4] (IIc) has already been reported. Khellol (Ia) reacted with chromic acid in the same manner, with the destruction of the furan ring and the production of a formylchromone (IIa). The alcoholic group of khellol is probably protected from oxidation by the formation of an ester of chromic acid. The chloro derivative of khellol (Ib), when subjected to the same reaction, yielded 2-chloromethyl-6-formyl-7-hydroxy-5-methoxychromone (IIb). The structure of these derivatives of salicylaldehyde was proved by the fact that, when IIb was treated with alcoholic silver nitrate, the chlorine atom was replaced by a hydroxyl group; the product was identical with the IIa[5] produced by the oxidation of khellol with chromic acid. Furthermore, IIb on treatment with zinc and acetic acid yielded IIc which has already been obtained by the oxidation of visnagin with chromic acid.[4]



III IV

Like visnagin (Ic)[4] and khellol (Ia), bergapten (III) was oxidized with chromic acid with the destruction of the furan ring; it yielded the aldehydocoumarin, 6-formyl-7-hydroxy-5-methoxycoumarin (IV), which was shown to be identical with apoxanthoxyletin, the ozonolysis product of the natural coumarin xanthoxyletin.[6]

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[1] T. A. Geissman, THIS JOURNAL, **73**, 3355 (1951).

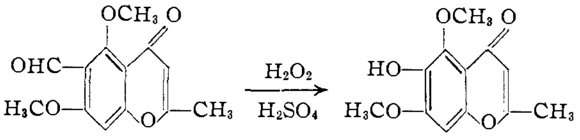
[2] A. Schönberg and G. Aziz, *ibid.*, **76**, 3265 (1953). *Cf.* also British Patent 687,755 and U. S. Patent 2,666,766 (The Memphis Chemical Company).

[3] T. Yabuta, *J. Chem. Soc.*, 575 (1924); F. H. Stodola, THIS JOURNAL, **73**, 5912 (1951).

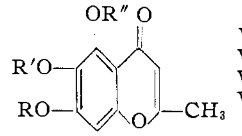
[4] A. Schönberg, N. Badran and N. A. Starkowsky, *ibid.*, **75**, 4992 (1953).

[5] IIa is probably identical with the ozonolysis product of khellol obtained by M. K. Hassan, M.Sc. Thesis, Faculty of Science, Egyptian University, Cairo, 1932; m.p. 213°, m.p. of IIa 217°. He tentatively identified his product as $C_9H_8O_5$, but his analytical data are closer to the values calculated for $C_{12}H_{10}O_6$ (IIa). *Anal.* Calcd. for $C_9H_8O_5$: C, 55.10; H, 4.08. Calcd. for $C_{12}H_{10}O_6$: C, 57.60; H, 4.00. Found: C, 56.76; H, 4.01.

[6] J. C. Bell, A. Robertson and T. S. Subramaniam, *J. Chem. Soc.*, 627 (1936).



V VI



VII

VIIa, $R = R' = H, R'' = CH_3$
VIIb, $R = R' = R'' = H$
VIIc, $R = CH_3, R' = R'' = H$
VIId, $R = R' = R'' = CH_3$

A number of 5,6,7-substituted 2-methylchromones were prepared from visnagin. 6-Formyl-5,7-dimethoxy-2-methylchromone (V), obtained from visnagin[4] was oxidized with hydrogen peroxide in sulfuric acid to a compound which is probably 5,-7-dimethoxy-6-hydroxy-2-methylchromone (VI). This structure for VI is supported by the fact that it can be prepared from 6,7-dihydroxy-5-methoxy-2-methylchromone (VIIa) by partial methylation with methyl iodide.

The oxidation product of visnagin with chromic acid (IIc) reacted with hydrogen peroxide in alkaline solution to give 6,7-dihydroxy-5-methoxy-2-methylchromone (VIIa). The structure of this compound is proved by the fact that it can be demethylated to the trihydroxy derivative (VIIb), and methylated to the trimethoxy derivative (VIId). The two latter substances recently have been synthesized by an independent method.[7]

Experimental[8]

Hydrolysis of Khellol Glucoside.—Ten grams of khellol glucoside (Id) dissolved in 15 ml. of 60% hydrobromic acid in a thin-walled glass vessel was immersed in a water-bath at 75° for exactly 2 minutes; the solution was then removed from the bath and shaken. A thick, yellow precipitate (presumably the oxonium salt of khellol with hydrobromic acid) was immediately formed. After the reaction mixture had stood at room temperature for a few minutes, it was diluted with 200 ml. of water and treated with a 10% sodium carbonate solution until it was alkaline. The mixture was then acidified with a little acetic acid, boiled and filtered while hot. On cooling, colorless crystals of khellol were deposited; yield 80%, m.p. 176–178°. The product sometimes gave a faint green ferric chloride reaction due to traces of 5-norkhellol, which was easily removed by recrystallization from hot water. The yield was not substantially affected by recrystallization and the melting point was raised to 179–180°.

When the glucoside was treated with hot hydrobromic acid for 10–15 min., the main product was 5-norkhellol which was isolated as yellow prisms melting, after repeated recrystallization from alcohol, at 200°.[9]

2-Chloromethyl-5-methoxyfuro-4′,5′,6,7-chromone (Ib).—One gram of khellol (Ia) was treated with 3 ml. of redistilled thionyl chloride in a porcelain crucible. The brownish green mixture was stirred with a glass rod and the excess thionyl chloride allowed to evaporate at room temperature. The solid residue was washed with petroleum ether, filtered and crystallized from 50% ethanol (charcoal) to give colorless needles of Ib; yield 75%, m.p. 140°. When Ib was pulverized with potassium hydroxide, it gave a deep green color which turned violet-red on addition of a drop of alcohol.[10]

Anal. Calcd. for $C_{13}H_9ClO_4$: C, 59.0; H, 3.4; Cl, 13.4. Found: C, 59.3; H, 3.3; Cl, 13.0.

One gram of Ib dissolved in 20 ml. of glacial acetic acid was refluxed with 2 g. of zinc dust and one drop of concentrated sulfuric acid for 3 hours. The mixture was then filtered and diluted with water. The colorless precipitate, which was recrystallized from hot water, melted at 140–142°; it was proved to be visnagin by a mixed melting point determination and by its oxidation with chromic acid to IIc.

6-Formyl-7-hydroxy-2-hydroxymethyl-5-methoxychromone (IIa).—One gram of finely powdered khellol was stirred with 20 ml. of 25% sulfuric acid for about 2 minutes and then with 20 ml. of 10% potassium dichromate solution. The mixture became warm and a colorless precipitate was formed after a few minutes. After standing for 30 minutes, the precipitate was filtered and crystallized from dilute ethanol as colorless needles of IIa; m.p. 217°, yield 0.5 g. IIa gave a red ferric chloride reaction and a yellow solution in dilute sodium hydroxide. An orange precipitate was formed when an alcoholic solution of *p*-phenylenediamine was mixed with a concentrated alcoholic solution of IIa.

Anal. Calcd. for $C_{12}H_{10}O_6$: C, 57.6; H, 4.0; two active H, 0.80. Found: C, 57.6; H, 4.1; active H, 0.77.

Anil of IIa.—A mixture of IIa (0.5 g.) in 10 ml. of glacial acetic acid and a solution of 0.4 g. of aniline in 2.5 ml. of the same solvent was allowed to stand for 10 min. and then diluted with 100 ml. of water. The orange condensation product which precipitated melted at 233° after recrystallization from ethanol; it gave a red ferric chloride reaction.

Anal. Calcd. for $C_{18}H_{15}O_5N$: N, 4.3. Found: N, 4.2.

Semicarbazone of IIa.—A mixture of IIa (0.24 g.) in 10 ml. of warm ethanol and a solution of 0.3 g. of semicarbazide hydrochloride and 0.4 g. of anhydrous sodium acetate in 4 ml. of water was heated to boiling and then cooled. The crystalline precipitate which formed had a melting point above 280°, depending on the rate of heating, and was very sparingly soluble in water and the usual organic solvents.

Anal. Calcd. for $C_{13}H_{13}O_6N_3$: N, 13.7. Found: N, 13.2.

2-Chloromethyl-6-formyl-7-hydroxy-5-methoxychromone (IIb).—Ib, treated with chromic acid under the conditions described for the oxidation of visnagin,[4] yielded colorless needles of IIb, m.p. 175–177°, which gave a red ferric chloride reaction. IIb gave a yellow solution with 4% sodium hydroxide; an orange deposit was formed immediately when a concentrated alcoholic solution of IIb reacted with *p*-phenylenediamine in alcohol.

Anal. Calcd. for $C_{12}H_9O_5Cl$: C, 53.6; H, 3.3; Cl, 13.2. Found: C, 53.5; H, 3.4; Cl, 13.6.

Zinc dust (0.5 g.) was added to a warm solution of 200 mg. of IIb in 6 ml. of glacial acetic acid. The mixture was stirred with a glass rod for 15 minutes and the residual zinc filtered. The filtrate, after dilution with water and neutralization with sodium bicarbonate solution, yielded colorless crystals, *m*.p. 189°. A mixture of this substance with 6-formyl-7-hydroxy-5-methoxy-2-methylchromone (IIc) gave no depression of melting point. The identity of the two substances was further confirmed by a mixed melting point determination of their respective oximes.[4]

IIb (200 mg.) was refluxed for 4 hours with 50 ml. of 1% alcoholic silver nitrate solution. The mixture was then filtered from the precipitated silver chloride and concentrated to a small volume on a water-bath. On cooling, colorless crystals were deposited, m.p. 215–217°. A mixed melting point determination showed them to be identical with 6-formyl-7-hydroxy-2-hydroxymethyl-5-methoxychromone (IIa), prepared directly from khellol as described previously.

6-Formyl-7-hydroxy-5-methoxycoumarin (IV) (Apoxanthoxyletin).—A mixture of 1 g. of bergapten (III) dissolved in 30 ml. of hot glacial acetic acid and 15 ml. of a 30% sodium dichromate solution was boiled gently on a hot-plate for 5 minutes; gas was evolved during the reaction. After standing at room temperature for 5 hours, the mixture was diluted with water to 200 ml. and kept in a refrigerator overnight. The yellowish needles of IV were filtered,

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(7) D. K. Chakravorty, S. K. Mukerjee, V. V. S. Murty and T. R. Sheshadry, *Proc. Indian Acad. Sci.*, **35A**, 34 (1952); *C. A.*, **47**, 6413 (1953).

(8) All melting points are uncorrected. For the ferric chloride reactions, a drop of an aqueous solution of ferric chloride was added to the substance dissolved in 95% ethanol. Elementary micro-analyses were made by Drs. Weiler and Strauss, Oxford.

(9) A. Schönberg and G. Aziz, THIS JOURNAL, **75**, 3265 (1953).

(10) A. Schönberg and A. Sina, *J. Chem. Soc.*, 3344 (1950).

washed with water (yield 0.6 g.) and recrystallized from alcohol; m.p. 222–223°, undepressed by an authentic sample of apoxanthoxyletin.[6] IV gave a yellow solution in dilute sodium hydroxide, a red ferric chloride reaction, a yellow color with concentrated sulfuric acid and an orange deposit with *p*-phenylenediamine in alcohol.

Anal. Calcd. for $C_{11}H_8O_5$: C, 60.0; H, 3.6. Found: C, 59.8; H, 3.5.

A solution containing IV (0.2 g.), phenylhydrazine hydrochloride (0.6 g.), acetic acid (20 ml.), sodium acetate (0.4 g.) and water (2 ml.) was refluxed for 20 minutes and then cooled to 0°. The phenylhydrazone of IV separated as yellow crystals, which were recrystallized from alcohol; m.p. 251°, reported m.p. for the phenylhydrazone of apoxanthoxyletin 251°.[6]

Anal. Calcd. for $C_{17}H_{14}O_4N_2$: C, 65.9; H, 4.5; N, 9.0. Found: C, 66.2; H, 4.7; N, 8.8.

5,7-Dimethoxy-6-hydroxy-2-methylchromone (VI).—Five ml. of a 30% solution of hydrogen peroxide were added to a suspension of 1 g. of V in 100 ml. of 20% sulfuric acid. The mixture was kept at room temperature for 6 hours with occasional shaking. When 100 ml. of water was added and the mixture cooled in ice, VI was precipitated. It was recrystallized from hot water as colorless needles; m.p. 222–223° (unchanged by sublimation). VI developed a brown color gradually with ferric chloride and dissolved in both 4% sodium hydroxide and concentrated sulfuric acid with a yellow color.

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.1; H, 5.1. Found: C, 61.3; H, 5.0.

5,6-Dihydroxy-7-methoxy-2-methylchromone (VIIc).—VI (0.5 g.) was refluxed with 50 ml. of 18% hydrochloric acid for 90 minutes. The solution was then diluted with water and cooled. The colorless crystals of VIIc separated, m.p. 234°; with ferric chloride in alcohol it gave a blue color changing to olive green. VIIc showed the typical reactions of a catecholic phenol, *e.g.*, when one drop of 1% sodium hydroxide solution was added to a solution of the substance in alcohol containing one drop of ferric chloride solution, a deep red color was produced.

Anal. Calcd. for $C_{11}H_{10}O_5$: C, 59.5; H, 4.5. Found: C, 59.2; H, 4.7.

6,7-Dihydroxy-5-methoxy-2-methylchromone (VIIa).—When IIc (4 g.), dissolved in 30 ml. of a 4% sodium hydroxide solution was treated with 10 ml. of a 30% hydrogen peroxide in an ice-bath, a copious white precipitate was formed after a few minutes. The mixture was left in the ice-bath with occasional shaking for 6 hours and was then neutralized with acetic acid. The precipitate was filtered and recrystallized from hot water, in which it was fairly soluble, to give colorless silky needles of VIIa, m.p. 229°. It gave a greenish black ferric chloride reaction and dissolved in 4% sodium hydroxide solution and concentrated sulfuric acid, giving a yellow color in both cases. VIIa displayed the reactions characteristic of a catechol derivative described for VIIc. Also, addition of a lead acetate solution to an alcoholic solution of the substance gave a yellow precipitate; addition of an aqueous titanium trichloride solution gave a red-brown deposit.

Anal. Calcd. for $C_{11}H_{10}O_5$: C, 59.5; H, 4.5. Found: C, 59.2; H, 4.5.

Demethylation of VIIa.—VIIa (1 g.) was demethylated under the conditions described for VI to yellowish plates of 5,6,7-trihydroxy-2-methylchromone (VIIb) which gave a green-brown ferric chloride reaction; m.p. 280–282°, reported m.p. 284–286°.[7]

Anal. Calcd. for $C_{10}H_8O_5$: C, 57.7; H, 3.8. Found: C, 57.5; H, 4.1.

Methylation of VIIa.—VIIa (1 g.) was refluxed for 8 hours with a mixture of 80 ml. of acetone, 5 ml. of methyl iodide and 5 g. of anhydrous potassium carbonate. The solvent was evaporated under reduced pressure, and the residue was acidified with dilute acetic acid and extracted with chloroform. The chloroform layer was washed with 4% sodium hydroxide solution and evaporated to dryness. The residue consisting of 5,6,7-trimethoxy-2-methylchromone (VIId) crystallized from water in colorless prisms; m.p. 100°, reported m.p. 99–100°.[7] VIId had a negative ferric chloride reaction; with potassium hydroxide pellets it gave the red color characteristic of 2-methylchromones having no free phenolic group.[10]

Anal. Calcd. for $C_{13}H_{14}O_5$: C, 62.4; H, 5.6. Found: C, 62.2; H, 5.5.

VIId is appreciably soluble in water (1 part in 150 at 24° and 1 part in 10 at 70°); 5,8-dimethoxy-2-methylchromone has been described as a water-soluble compound.[11]

Acidification of the alkaline washings from the above experiment yielded a small amount of a phenolic substance (m.p. 222°) which was identified as VI.

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.1; H, 5.1. Found: C, 60.9; H, 4.8.

The yield of VI was considerably increased at the expense of the completely methylated product (VIId) when the time of the reaction was cut down to 4 hours.

Acknowledgment.—We are indebted to Professor Alexander Robertson, F.R.S., for carrying out the m.p. determination of IV with an authentic sample of apoxanthoxyletin.

[11] L. Vargha and M. Rados, *Acta Chim. Acad. Sci. Hung.*, **3**, 223 (1953).

CAIRO, EGYPT

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

Transformation of D-Gulose to 1,6-Anhydro-β-D-gulopyranose in Acid Solution[1,2]

BY LAURA C. STEWART AND NELSON K. RICHTMYER

RECEIVED SEPTEMBER 30, 1954

D-Gulose is transformed by hot dilute acid to the extent of at least 43% to a crystalline anhydride whose structure has been established through periodate oxidation methods as 1,6-anhydro-β-D-gulopyranose.

In continuation of our studies on the formation of monomeric non-reducing anhydrides from reducing sugars under the influence of acids, and particularly from those with the *gulo* configuration, we now wish to describe the behavior of D-gulose (I) itself. When that sugar is heated with dilute acid it suffers a considerable loss of reducing power. After a suitable period of time has been allowed for establishing equilibrium and the unchanged D-gulose then destroyed by heating with alkali, an anhydro-D-gulose, melting at 154–155° and showing $[\alpha]^{20}D$ +50.4° in water, can be isolated without difficulty. At least 43% of the D-gulose is estimated to be converted to anhydride in this manner. The anhydride has been characterized further through its tri-*O*-acetyl, benzoyl, and tosyl derivatives; it has

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[1] Presented in part before the Division of Carbohydrate Chemistry at the Chicago Meeting of the American Chemical Society, September 10, 1953.

[2] For the preceding paper on anhydro sugars, see L. C. Stewart and N. K. Richtmyer, THIS JOURNAL, **76**, 424 (1954).