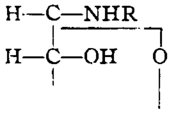
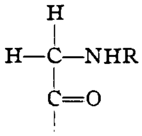
[Contribution from the Chemistry Department of Iowa State College]

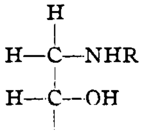
The Reaction of Glucose with Some Amines

By Eleanor Mitts and R. M. Hixon

The phenylhydrazine derivatives were recently prepared from several corn sirup dextrins as a check on other methods of determining molecular weights of these large molecules. The ease of hydrolysis of these compounds indicated that they were of a glycosidic structure analogous to similar derivatives prepared by the reaction of phenylhydrazine in organic solvents with simple sugars. The tendency of the phenylhydrazine derivatives to form highly solvated molecules as well as the ease of isomerization detracts from their value for characterization of the dextrins. In connection with the synthesis of Vitamin B_2, detailed studies have been made of the reaction of aromatic amines with glucose. These compounds are N-glucosides (I) and undergo the Amadori rearrangement (II) to form amino ketones. A comparative study of the relative stability of the N-glucosides was made as an indication of nitrogen derivatives better suited for characterizing the dextrins. The data on glucosylalkylamines and their hydrogenation products (III) has been extended.


(I) N-Glucoside


(II) Isoglucosamine formed from (I) by Amadori Rearrangement


(III) Glucamines formed from (I) or (II) by hydrogenation

The available literature indicates that glucose and other monosaccharides react in non-polar solvents to give N-glucosides (I) with ammonia,[1] alkylamines,[1a,2] arylamines,[3] acid amides,[4] hydroxylamine[5] and phenylhydrazine.[6] As a general class, these compounds are labile and undergo rearrangement as well as hydrolysis. In many cases they crystallize with one or more molecules of water, of alcohol, or of amine. The difficulties of isolation or recrystallization seem to depend upon these solvation characteristics as well as upon hydrolysis or isomerization.

With the exception of the first member of the series, 1-aminoglucose or glucose ammonia, hydrolysis of the N-glucosides appears to parallel the basic dissociation constant (K_B) of the nitrogen substituent. The extent of hydrolysis depends upon concentration and temperature. Experiments with representative members of the various series indicate that for dilute aqueous solutions (2% or less) the alkylamines come to equilibrium in about twenty hours with approximately 40% of hydrolysis; in contrast, the glucosyl-*n*-arylamines after approximately ninety hours are only 8% hydrolyzed, while the amide derivatives are not hydrolyzed in water or even by dilute acids at room temperature.

The isomerization of N-glucosides to isoglucosamines (II, the Amadori rearrangement) has been observed with arylamines only. Weygand[7] suggests this type of rearrangement to explain the formation of osazones. The presence of the methoxy group in 2-methylglucose is not sufficient to prevent the formation of the osazone[8]; it is, however, sufficient to prevent rearrangement of the *p*-toluidide. Repeated attempts to induce the Amadori rearrangement in N-acyl and N-alkylamine glucosides met with negative results. In fact, the conditions used for the production of aryl isoglucosamines were found to be ideal for the production of the N-alkylamine glucosides. These conditions were used to prepare *n*-butyl, *n*-amyl and *n*-heptyl glucosylamines and the melting points found were identical to those reported previously by Votoček.[2b]

Catalytic hydrogenation of the N-glucosides of alkylamines has been previously reported.[9] It was found that good yields of N-alkyl glucamines (III) could be obtained in several cases where it was not possible to isolate the intermediate N-glucoside in crystalline form. The glucamines are crystalline solids, soluble in water and quite stable to heat. They may be titrated potentiometrically with dilute acid and are stable to both strong acid or alkali. These compounds, especially those from amines of intermediate molecular weight, lower the surface tension of water noticeably and are good wetting agents. Properties for a number of such compounds are reported in Table I.

Experimental

Glucosyl-*n*-butylamine.—To 10 g. (0.056 mole) of glucose and 2 ml. of 0.5 *N* hydrochloric acid, 9 g. (0.12 mole) of *n*-butylamine was added. This mixture was heated

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[1] (a) Irvine, Thomsen and Garrett, *J. Chem. Soc.*, **103**, 238 (1913); (b) Levene, *J. Biol. Chem.*, **24**, 59 (1916); (c) Wayne and Adkins, This Journal, **62**, 3314 (1940).

[2] Votoček and Valentin, *Coll. Czechoslov. Chem. Commun.*, **6**, 77 (1934).

[3] (a) Sorokin, *J. prakt. Chem.*, (2) **37**, 291 (1888); (b) Marchlewski, *ibid.*, (2) **50**, 95 (1894); (c) Strauss, *Ber.*, **27**, 1284 (1894); (d) Irvine and Gilmour, *J. Chem. Soc.*, **93**, 1429 (1908); (e) Kuhn and Dansi, *Ber.*, **69**, 1745 (1936); (f) Kuhn and Birhofer, *ibid.*, **71**, 621 (1938).

[4] (a) Schoorl, *Rec. trav. chim.*, **22**, 31 (1903); (b) Helferich and Kasche, *Ber.*, **59**, 69 (1926).

[5] Wolfrom and Thompson, This Journal, **53**, 622 (1931).

[6] (a) Behrend and Lohr, *Ann.*, **362**, 78 (1908); (b) Behrend and Reinsberg, *ibid.*, **377**, 189 (1910).

[7] Weygand, *Ber.*, **73**, 1284 (1940).

[8] Brigl and Schinle, *ibid.*, **62**, 1716 (1929).

[9] (a) Karrer, Saloman, Kunz and Seebach, *Helv. chim. acta*, **18**, 1338 (1935). (b) Karrer and Harkenrath, *ibid.*, **20**, 83 (1937). (c) Flint and Saltzberg, U. S. Patent 2,016,962, Oct. 8, 1935; *C. A.*, **29**, 8007 (1935).

TABLE I

PROPERTIES OF SOME ALKYLGLUCAMINES

Alkyl-*d*-glucamine	Recrystd. from	M. p. uncor., °C.	% N Calcd.	% N Found		$[\alpha]^{25}\mathrm{D}$[a]	% Carbon (micro) Calcd.	% Carbon (micro) Found	% Hydrogen (micro) Calcd.	% Hydrogen (micro) Found
N-Butyl-	Methanol	127–128	5.91	6.02	5.87	−14	50.59	50.4	9.77	9.7
N-Amyl-	Methanol	129–130	5.57	5.42	5.52	−13.8	52.55	52.3	10.03	9.9
N-Heptyl-	Methanol	126–127	5.02	5.08	4.99	−14	55.86	55.5	10.47	10.4
N-Cyclohexyl-	Methanol	145–146	5.32	5.18		−11	...	...	...	..
N,N′-Ethylene-	Methanol–water	136–137	7.22	7.17		−15.5	43.26	43.0	8.3	8.3
N-Hexadecyl-	....	123–124[b]	3.45	3.42	3.25	..				
N-Octadecyl-	....	118–119[b]	3.23	3.19	3.14	..				
N-Isopropyl-	Methanol–ethyl acetate	126–127[b]	6.27	5.71	5.64	−13				
N-2-Octyl-	Ethyl acetate	107–108[b]	4.77	4.63		..				
N,N′-Propylene	Methanol–water	135–137	6.97	6.92		..				

[a] One per cent. solution in 50% ethanol. [b] Softened earlier.

under reflux on a water-bath at 70° until the glucose went into solution and for ten minutes thereafter. The solution was cooled and 20 ml. of ethanol, then 100 ml. of ether, was added. The needle-like crystals that formed were filtered by suction and washed repeatedly with ether; yield 11 g. The compound was recrystallized from dioxane and washed with petroleum ether. Recrystallization from alcohol and ether usually resulted in the formation of a gelatinous precipitate rather than the desired crystals. The product was dried over phosphorus pentoxide under reduced pressure. The melting point of the crystals was usually about 86–87° but, after repeated crystallization, the melting point was raised to 96–97°. The specific rotation after five minutes was $(\alpha)^{25}\mathrm{D}$ −22° (*c*, 2; C_2H_5OH); this changed to a constant value of −7.8° in less than one hour.

Anal. Calcd. for $C_{10}H_{23}O_6N$: N, 5.53. Found: N, 5.48, 5.49.

Glucosyl-*n*-amylamine.—The same procedure as given above was used; yield 11 g. The melting point of the compounds after thorough drying was 96–97°, which was not changed after recrystallization from alcohol-ether. The specific rotation after twelve minutes was $(\alpha)^{25}\mathrm{D}$ −22°; this changed to a constant value of −8° (*c*, 2; C_2H_5OH).

Anal. Calcd. for $C_{11}H_{25}O_6N$: N, 5.25. Found: N, 5.28, 5.28.

Glucosyl-*n*-heptylamine.—The same procedure was used for the preparation of this glucosylalkylamine as was employed for the preparation of the *n*-butyl compound. Thirteen grams of white needles, recrystallized from a butanol-Skelly D mixture, was obtained. The compound could also be recrystallized from methanol or methanol-water mixtures, or from water alone if the solution were cooled rapidly enough to preclude appreciable hydrolysis; m. p. 97–98°, $(\alpha)^{25}\mathrm{D}$ −13° after ten minutes, changing to a constant value of −7° (*c*, 2; C_2H_5OH).

Anal. Calcd. for $C_{13}H_{29}O_6N$: N, 4.74. Found: N, 4.70, 4.63.

Glucosyldicyclohexylamine.—To 9 g. (0.09 mole) cyclohexylamine was added 10 g. (0.056 mole) of glucose and 2 ml. of 0.5 *N* hydrochloric acid. This mixture was heated on the water-bath at 75° until the solution became homogeneous and for ten minutes thereafter. After the solution was cooled, 20 ml. of ethanol and 100 ml. of ether were added. After thirty-six hours in the refrigerator, 6 g. of crystals was obtained. The compound melted at 97–98°, with softening early. The specific rotation after four minutes was $(\alpha)^{25}\mathrm{D}$ −23.5°; this changed to −11.6° in six hours (*c*, 2; C_2H_5OH). On analysis, it was found that two molecules of the amine had combined with the hexose and one molecule of water had been eliminated.

Anal. Calcd. for $C_{18}H_{35}O_5N_2$: N, 7.77. Found: N, 7.60, 7.75.

Efforts to obtain a condensation product from one molecule of glucose and one molecule of the amine were not successful. The second molecule of cyclohexylamine could not be removed by heating the compound at the boiling point of acetone for three hours under reduced pressure. Heating at 100° resulted in the darkening of the compound and after several hours 20.44% of the total weight was lost. Upon analysis, the nitrogen content was found to be 8.26%, indicating that water was removed from the glucosylalkylamine more easily than a cyclohexylamine molecule.

Diglucosylethylenediamine.—To 3.5 g. (0.06 mole) of ethylenediamine in 50 ml. of methanol, 21 g. (0.12 mole) of glucose was added. This mixture was refluxed gently on a water-bath until the glucose went into solution. The refluxing was continued and soon a precipitate appeared on the side of the flask. After two hours, the refluxing was discontinued, the flask cooled and left in the refrigerator overnight. Eleven grams of the compound, m. p. 152–154° (with decomposition), was obtained after filtering, washing with cold methanol, and drying. The product was recrystallized from methanol-water. The specific rotation $(\alpha)^{25}\mathrm{D}$ −17° (*c*, 2; 50% C_2H_5OH) changed to a value of +14.5° in thirty-nine hours. This value represented partial hydrolysis as well as mutarotation.

Anal. Calcd. for $C_{14}H_{28}O_{10}N_2$: N, 7.29. Found: N, 7.35, 7.35.

Glucosyl-*n*-hexadecylamine.—Twenty-four grams (0.10 mole) of *n*-hexadecylamine was dissolved by warming in 50 ml. of ethanol and to this was added 18 g. (0.10 mole) of glucose and 50 ml. of ethanol. After the mixture was refluxed for several minutes, the glucose went into solution and the refluxing was continued for fifteen minutes. The precipitate that formed on cooling was filtered and washed with alcohol and ether; yield 31 g., m. p. 106–107° with softening somewhat earlier. The compound was purified by precipitation from hot ethanol. The specific rotation was not determined since the compound was not appreciably soluble in ordinary solvents at room temperature.

Anal. Calcd. for $C_{22}H_{47}O_6N$: N, 3.32. Found: N, 3.28, 3.26.

Glucosyl-*n*-octadecylamine.—Twenty-seven grams (0.10 mole) of *n*-octadecylamine was dissolved in 100 ml. of ethanol, and 18 g. (0.10 mole) of glucose added. This mixture was refluxed until the glucose went into solution and for fifteen minutes thereafter. The precipitate (37.5 g.) that formed on cooling the red-brown liquid was filtered and washed with alcohol and ether, then dried; m. p. 104–105° with softening earlier. The specific rotation was not determined.

Anal. Calcd. for $C_{24}H_{51}O_6N$: N, 3.12. Found: N, 3.01, 3.06, 3.01.

Attempted Condensations of Other Amines with Glucose.—Repeated attempts using the different methods of preparation for glucosylalkylamines were made to obtain pure crystalline condensation compounds from isopropylamine, 2-aminoöctane, and propylenediamine. Solid compounds were obtained by precipitation of the glucose-isopropylamine solution with ether, and by precipitation of the methanol or ethanol solution of propylenediamine and glucose, but the nitrogen analysis was high in all cases and the preparation melted over a range of several degrees. The compounds could not be recrystallized from any of the ordinary solvents. Evidence of reaction of all these amines with glucose was shown by the ease of solution of the sugar in the alcohol containing the anhydrous amine as well as by the analysis of the amorphous products obtained.

Reduction of the Glucosyl-*n*-alkylamines.—All of the glucosyl-*n*-alkylamines prepared were hydrogenated in a Parr type bomb using activated Raney nickel as a catalyst.[10] The physical constants and nitrogen analyses of the compounds are given in Table I. Ten grams of the glucosyl-*n*-alkylamines was dissolved in 200 ml. of solvent (methanol, ethanol or alcohol–water mixtures). The reduction was carried out below 100° (most often 70–83°) at pressures of 800 to 1300 lb. of hydrogen. The amount of catalyst was varied from 2.5 to 9 g. and the time of reaction from seven to fourteen hours. No effort was made to determine the minimum conditions necessary for complete reduction. Good yields were obtained except from glucosyl-*n*-hexadecylamine and glucosyl-*n*-octadecylamine which, after reduction and partial removal of the solvent, gelatinized and were difficult to obtain as solids.

N-Isopropyl-*d*-glucamine, N,N′-propylenediglucamine and N-2-octyl-*d*-glucamine were prepared, even though the corresponding glucosyl derivatives were not isolated in the pure state. A solution of the glucoside of 2-aminoöctane and of isopropylamine was obtained by the same method used for the preparation of the glucosyl-*n*-butylamine, except that after the solution was homogeneous, 75 ml. of ethanol was added and the solutions refluxed for one-half hour. In the reduction of diglucosylpropylenediamine, 12 g. (0.067 mole) of glucose was refluxed with 2.5 g. (0.034 mole) of propylenediamine in 60 ml. of methanol for one hour. Before reduction 150 ml. of 50% methanol was added. Although complete reduction of the diglucosylpropylenediamine occurred, only a very small amount of the reduced compound was isolated.

N-Isopropyl-*d*-glucamine was not pure as was shown by the nitrogen analysis. The compound gelatinized on attempted recrystallization from alcohol, but precipitated from a methanol-ethyl acetate mixture. Since the nitrogen value of the compound was still somewhat low, the impurity was believed to be sorbitol.

Hydrolysis of Glucosyl-*n*-alkylamines.—Glycosyl-*n*-butylamine was selected as a representative compound of this series, and the equilibrium of 0.5000 g. of the compound in 25 ml. of water was followed. From the change in optical rotation, it was evident that equilibrium was reached in twenty-two hours at room temperatures. On the assumption that only one form of the glucosylamine was present, and that it dissociated into glucose and the amine, the amount of the compound that had dissociated was calculated to be 56.9%. Potentiometric titration of the solution at equilibrium indicated that 39.5% of the compound had hydrolyzed. By extraction with ether an amount of the amine equivalent to 44% of the glucosyl-*n*-alkylamine was recovered. It was evident that mutarotation as well as hydrolysis occurred in aqueous solution. In methanol solution, mutarotation but no hydrolysis occurred. The other glucosyl-*n*-alkylamines behaved in much the same manner, the amount of hydrolysis depending upon the concentration and the temperature.

Hydrolysis of Other Amine Derivatives of Glucose.—Glucosyl-*n*-arylamine as well as the N-aryl-isoglucosamines were prepared by the method given by Weygand.[11] The change in rotation of *p*-toluidine-*d*-glucoside in aqueous solution was followed, and the amount of amine liberated after ninety hours was determined by extracting and weighing the extracted amine. Extraction of the 0.008 molar solution of the N-glucoside in water indicated only 8% hydrolysis. The isoglucosamine did not hydrolyze.

1-Aminoglucose was prepared by the method of Ling and Nanji.[12] The compound, after recrystallization from 95% methanol, appeared to be the hydrated compound, m. p. 120–121°, $(\alpha)^{24}\text{D}$ +19.1° (0.1001 g. in 1.694 ml. water. 1-dm. tube). Values found in the literature for the melting point of glucose ammonia and 1-aminoglucose vary from 120 to 131°, the rotation from +19.5 to +22.6°.

Anal. Calcd. for $C_6H_{15}O_6N$: N, 7.10. Found: N, 7.01.

1-Aminoglucose is remarkably stable in aqueous solution at ordinary temperatures as evidenced by the very slight change in rotation. This stability was confirmed by potentiometric titration of 1-aminoglucose with dilute acid, and titration of the amine in the presence of a known amount of ammonium hydroxide. After seventy-three hours, no measurable amount of ammonia had been liberated. However, slight acidity or higher temperatures cause immediate hydrolysis.

1-Aminoglucose pentaacetate was prepared from 1-aminoglucose and N-acetyl-1-aminoglucose was obtained from this compound according to the method of Brigl and Keppler.[13] This amide derivative was not hydrolyzed in aqueous solution or in dilute acid. It was hydrolyzed, however, by heating with 1 *N* acid.

Attempted Condensation of Acetamide with Glucose and Acetobromoglucose.—Two grams (0.034 mole) of acetamide was added to 6 g. (0.033 mole) of glucose in 100 ml. of methanol: after a few minutes refluxing on a water-bath, all of the glucose went into solution. The refluxing was discontinued after two hours and most of the solvent was removed under reduced pressure. Although no N-acetyl-1-aminoglucose was obtained even on seeding, the solution of the glucose in the alcohol and the inability to extract with hot chloroform more than one-third of the amide from the solvent-free residue indicated that a reaction had taken place. Such a reaction would be expected, in analogy to the glycosides of urea which have been reported.[4b]

When 10 g. (0.024 mole) of acetobromoglucose prepared by the method of Fischer[14] was refluxed with 4.0 g. (0.068 mole) of acetamide in 20 ml. of chloroform, crystals appeared in the solution after approximately thirty minutes. On analysis for bromine it was found that the crystals were diacetamide hydrobromide that sublimed 95–100° and melted 138–139°. No crystals of pentaacetyl-1-aminoglucose were obtained when the filtrate was seeded.

The Amadori Rearrangement.—Although this rearrangement was easily effected on N-glucosides of the arylamines, neither the alkylamine nor acylamine derivatives of glucose formed the rearranged product. In fact, the best method of preparation of the glucosylalkylamines from the low molecular-weight alkylamines was a procedure that was used for the preparation of the isoglucosamines in the aryl series. A further attempt to effect the rearrangement or partial rearrangement of the glucosylalkylamines was made by refluxing 1 g. of glucose in 10 g. of *n*-butylamine for three hours. Although the resulting gold-colored solution reduced methylene blue fairly rapidly (rapid reduction of methylene blue was used as evidence for the formation of isoglucosamine), only impure crystals of glucosyl-*n*-butylamine could be obtained after rapid removal of excess amine and precipitation with alcohol-ether. No evidence of any kind was obtained to indicate that the N-acyl derivative underwent even partial rearrangement.

Amine Derivatives of 2-Methylglucose.—The phenylhydrazine derivative of 2-methylglucose was prepared by allowing 1.65 g. of phenylhydrazine in 1 ml. of water to stand overnight in the presence of 0.55 g. of the monosaccharide (m. p. 150–155°) and one drop of glacial acetic acid. This derivative melted 176–177° and had a methoxyl content 11.1% as compared to the calculated value of 10.93%. Glucose phenylosazone was obtained by refluxing the phenylhydrazine derivative of 2-methylglucose with phenyl-

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[10] Mozingo in "Organic Syntheses," Editor, N. L. Drake, John Wiley and Sons, Inc., New York, N. Y., 1941, Vol. 21, p. 15.

[11] Weygand, *Ber.*, **72**, 1663 (1939); **73**, 1259 (1940).

[12] Ling and Nanji, *J. Chem. Soc.*, **121**, 1682 (1922).

[13] Brigl and Keppler, *Z. physiol. Chem.*, **180**, 38 (1929).

[14] Fischer, *Ber.*, **49**, 584 (1916).

hydrazine and glacial acetic acid in aqueous solution as had been reported by Brigl and Schinle.[8] The analysis for the glucose phenylosazone is as follows.

Anal. Calcd. for $C_{18}H_{22}O_4N_4$: N, 15.64; OCH_3, 0.00. Found: N, 15.93; OCH_3, 0.40.

The *p*-toluidide of 2-methylglucose was prepared by heating 1.04 g. of the monomethyl sugar (OCH_3, 15.27%) with 0.72 g. of *p*-toluidine and 0.30 ml. of water. The mixture was heated on a water-bath until the solution became homogeneous and for ten minutes thereafter to insure complete reaction. After cooling, 2 ml. of 95% ethanol and 4 ml. of ether was added. Cooling in the refrigerator yielded a precipitate (0.15 g.) that was identified as unchanged 2-methylglucose. The mother liquor was evaporated to 1.5 ml. and left overnight: needle-like crystals (0.55 g.), m. p. 150-151° after purification, were obtained.

Anal. Calcd. for $C_{14}H_{21}O_5N$: OCH_3, 10.95. Found: OCH_3, 10.7.

Prolonged refluxing in the water-ethanol solvent with dilute acetic acid and with dilute hydrochloric acid gave no evidence for the Amadori rearrangement: crystals of the glucoside were isolated in all cases.

Summary

Physical properties are reported for a number of glucosylalkylamines and the corresponding glucamines.

The glucamines formed from primary amines of intermediate molecular weight are good wetting agents.

An approximation of the degree of hydrolysis of the various N-substituted glucosides was made by comparison of changes in rotation, by potentiometric titration and by extraction of the hydrolyzed amine. With the exception of the first member of the series, 1-aminoglucose, ease of hydrolysis appears to parallel the K_B of the nitrogen substituent.

An attempt was made to effect the Amadori rearrangement of the glucosylalkylamines and the acyl derivatives of 1-aminoglucose. No rearranged product could be isolated in either case.

The *p*-toluidide and phenylhydrazine derivative of 2-methylglucose were prepared. The methoxyl group on the second carbon atom prevented rearrangement of the *p*-toluidide, but glucose phenylosazone was prepared from the phenylhydrazine derivative of 2-methylglucose.

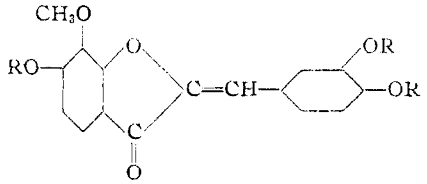
AMES, IOWA RECEIVED AUGUST 23, 1943

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES]

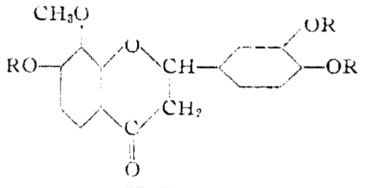
Anthochlor Pigments. V. The Pigments of *Coreopsis grandiflora*, Nutt. II

BY T. A. GEISSMAN AND CHARLES D. HEATON

In the preceding paper of this series,[1] structures were proposed for leptosin, leptosidin and a flavanone, constituents of the flower petals of *Coreopsis grandiflora*, Nutt. Leptosin and leptosidin are related as glycoside and aglycon, and to the latter was assigned the structure of 7-methoxy-3′,4′,6-trihydroxybenzalcoumaranone (I). The position of the sugar residue (presumably glucose) in leptosin was assumed to be 6, on the basis of certain distinctive color reactions of the glycoside. The structure of the flavanone was considered to be II, both because of the correspondence in the positions of the hydroxyl and methoxyl groups in this structure and in that chosen for leptosidin, and because of the similarity between certain color reactions of the flavanone and those of butin (3′,4′,7-trihydroxyflavanone).



I, R = H
III, R = CH_3



II, R = H
IV, R = CH_3

We have synthesized 3′,4′,6,7-tetramethoxybenzalcoumaranone (III) by the condensation of veratraldehyde with 6,7-dimethoxycoumaranone. The product, crystallizing in bright yellow needles, did not depress the melting point of fully methylated leptosidin. This establishes for the first time the occurrence in nature of a substance possessing the benzalcoumaranone nucleus.

3′,4′,7,8-Tetramethoxyflavanone (IV) has been described by Kostanecki and Rudse,[2] who reported its melting point as 144°. While the trimethyl ether of the naturally-occurring flavanone analyzed correctly for this structure and showed color reactions which left no doubt that it was a flavanone and pointed strongly to the probability that it had structure IV, it melted at 139-140°, a fact which left some doubt as to its identity with the flavanone described by Kostanecki and Rudse. The synthesis of IV has shown that the trimethyl ether of the naturally-occurring flavanone is indeed 3′,4′,7,8-tetramethoxyflavanone. The condensation of gallacetophenone 3,4-dimethyl ether with veratraldehyde yielded 2′-

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(1) Geissman and Heaton, THIS JOURNAL, **65**, 677 (1943).

(2) Kostanecki and Rudse, *Ber.*, **38**, 937 (1905).