4. Within the limits of experimental error all the molecules of a dilute solution of hemocyanin from *Helix pomatia* at *P*H 4.7 are found to be of equal weight and size and this protein is therefore probably to be regarded as a chemical individual.

5. As to shape, the calculations based on our experimental data indicate that at *P*H 4.7 the molecules are practically spherical with a radius of 12.1 × 10^{-7} cm.

UPSALA, SWEDEN

[COMMUNICATION FROM THE DEPARTMENT OF INDUSTRIAL AND CELLULOSE CHEMISTRY, McGILL UNIVERSITY]

STUDIES ON REACTIONS RELATING TO CARBOHYDRATES AND POLYSACCHARIDES. XIII. PROPERTIES OF GAMMA-DELTA-DIHYDROXY-CARBONYL DERIVATIVES AND THEIR BEARING ON THE POLYMERIZATION OF POLYSACCHARIDES

BY HAROLD HIBBERT AND C. PAULINE BURT[1]

RECEIVED NOVEMBER 30, 1927 PUBLISHED MAY 5, 1928

In previous communications[2] the important role played by adjacent hydroxyl groups in the γ,δ-positions to the carbonyl group has been emphasized and evidence submitted of the tendency of such compounds to readily lose a molecule of water with subsequent formation of a highly polymerized product. The bearing of such phenomena on the problem of the constitution of cellulose and related compounds has been repeatedly indicated.[2]

Further evidence is now available in that a second dihydroxy carbonyl derivative, namely, methyl γ,δ-dihydroxy amyl ketone has been synthesized and found to show a similar behavior to that of the methyl γ,δ-dihydroxy butyl ketone previously investigated.[2c]

Thus in presence of a trace of concentrated sulfuric acid at about 90°, it readily loses a mole of water per mole of the ketone, yielding a viscous, resinous substance which is found to be a polymerized product having a molecular weight in benzene solution of 553–590.

The molecular weight of the corresponding product from methyl γ,δ-dihydroxy butyl ketone is shown to vary between 395 and 445 in phenol solution and to increase to 3706 when camphor is used as the solvent.

Assuming the methyl γ,δ-dihydroxy amyl ketone to possess the butylene oxide structure, the change may be represented as follows.

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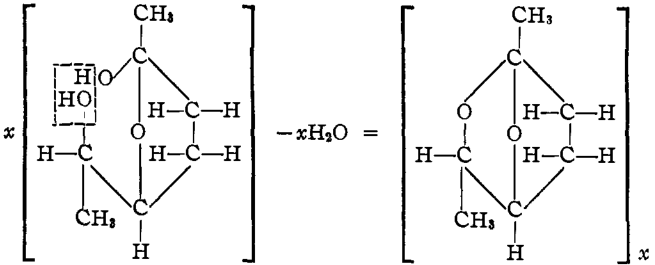
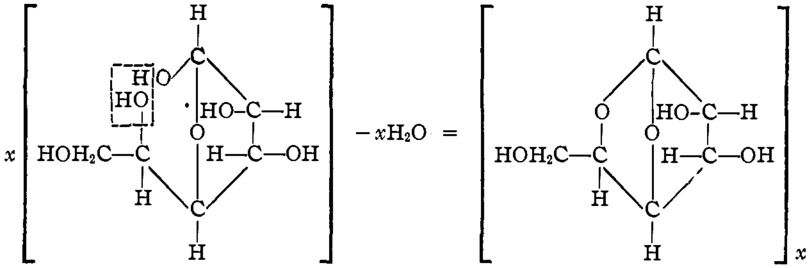
[1] Constructed from the dissertation presented by C. Pauline Burt to the Faculty of the Graduate School of Yale University, June, 1925, in candidacy for the degree of Doctor of Philosophy.

[2] (a) Hibbert, *Chem. Met. Eng.*, **22**, 838 (1920); (b) *J. Ind. Eng. Chem.*, **13**, 256, 334 (1920); (c) Hibbert and Timm, THIS JOURNAL, **45**, 2433 (1923).



I

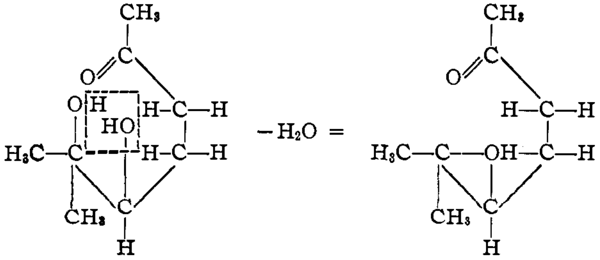
Its formation is thus probably analogous to the change taking place in the transformation of glucose into cellulose.[2a,b]



II Polymerized glucose anhydride

Whether the nucleus (cellulose) consists of one[3] or several[4] glucose anhydride units is at present unknown, as is also the nature of the forces (secondary valence, crystallographic, etc.)[5] which serve to hold the larger aggregate together.

On the other hand, the next higher homolog, methyl γ,δ-dihydroxy *iso*valeryl ketone, under the same conditions, readily loses a molecule



III

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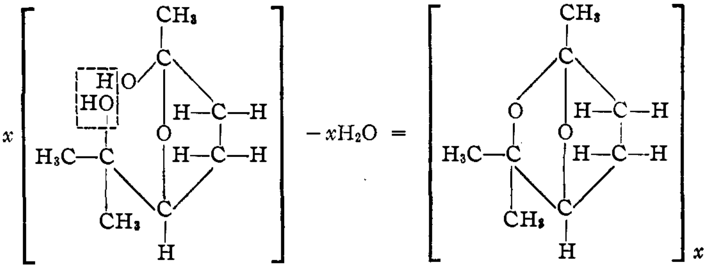
[3] Hess and Messmer, *Ann.*, **435,** 7, 111 (1923); Hess, Messmer and Ljubitsch, *Ann.*, **444,** 287 (1925); Hess, *Ann.*, **450,** 65 (1926); Pringsheim and co-workers, *Ann.*, **448,** 163 (1926).

[4] Hibbert, *loc. cit.;* Irvine, *Brit. Assocn. Adv. Sci.*, **1922,** p. 14; Karrer, "Die Polysaccharide," Akademische Verlagsgesellschaft, Leipzig, **1925,** pp. 217–240; Schorger, *Ind. Eng. Chem.*, **16,** 1274 (1924); Gray, *Ind. Eng. Chem.*, **18,** 811 (1926).

[5] For synopsis see "Handbuch der normalen und pathologischen Physiologie," Verdauung und Verdauungsapparat-Verlag, Julius Springer, Berlin, Vol. III, **1927,** pp. 922–924.



IV

of water from the γ,δ-hydroxyl groups with formation of a 1:2 oxide, and exhibits practically no tendency toward a dehydration involving the carbonyl group; that is, Reaction III is favored rather than IV. The reason for this difference in behavior is, in all probability, to be found in the alteration in the valence angle of the carbon atom to which the two methyl groups are attached,[6] the latter producing a deviation favorable to the formation of a three-membered ring, but operating against a reaction between the ketohydrol and the γ-hydroxyl group.[7]

Experimental

Synthesis of Methyl γ,δ-Dihydroxy Amyl Ketone ($CH_3CHOH\text{-}CHOH(CH_2)_2\text{-}COCH_3$).—This was prepared by the following synthetic reactions: crotonaldehyde ⟶ crotyl alcohol ⟶ crotyl bromide ⟶ crotyl ethyl aceto-acetate ⟶ Δ^{5-6} heptene-2-one ⟶ methyl γ,δ-dihydroxy amyl ketone.

Reduction of Crotonaldehyde to Crotyl Alcohol.—This was carried out by Charon's method[8] in acetic acid solution by means of the zinc-copper couple. The yield after purification (b. p. 116–118°) is small, the principal product being dipropenyl glycol.

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[6] Ingold, *J. Chem. Soc.*, **119**, 305 (1921); the phenomenon would appear to be closely related to the general inability, or very small tendency, of ketones to form six-membered cyclic ketals; Fischer and Pfähler, *Ber.*, **53**, 1606 (1920); Boeseken, Schaefer and Hermans, *Rec. trav. chim.*, **41**, 722 (1922). That such can be formed is further evident from the recent work of Fischer and Taube, *Ber.*, **60**, 487 (1927), on the condensation of acetone with dioxyacetone.

[7] The structure of the three γ,δ-hydroxy ketones referred to in this communication is under investigation. Judging from analogy with the cyclic ketals, it seems probable that they will be found to be tautomeric mixtures of the free ketone with the butylene oxide ring isomer; in other words, the amylene oxide isomer is absent.

It is regretted that due to unavoidable delay the properties of the γ,δ-dihydroxy aldehydes have not as yet been investigated. In the light of recent investigations by Hibbert and co-workers on the isomeric forms of the aryl and alkyl glycerols and the close analogy found to exist between these derivatives and carbohydrates, glucosides and polysaccharides, it seems to be more than likely that the aldehydes corresponding to the ketones discussed in this communication will be found to consist of a mixture of the free aldehyde together with the corresponding butylene and amylene forms of the aldehydrol, the last named being present in by far the largest amount.

It is proposed to push this work intensively, and to give a resumé of the bearing of cyclic acetal and ketal formation on the constitution and properties of carbohydrates and polysaccharides in a forthcoming publication. H. H.

[8] Charon, *Ann. chim. phys.*, [7] **17**, 217 (1899).

Conversion into Crotyl Bromide.—The method used was that employed for the manufacture of allyl bromide.[9]

Seventy-five grams of crotyl alcohol (containing, by bromine titration, 90% of the alcohol) was dropped slowly into a flask containing 258 g. of 48% hydrobromic acid and 78 g. of concentrated sulfuric acid, and the mixture, after digestion and stirring for a period of one hour, then distilled. The crude bromide (b. p. 95–110°) was washed with potassium carbonate, dried with fused calcium chloride and fractionated. The product boiled at 101–105° and was practically free from butyl bromide; yield, 69%.

Preparation of Crotyl Ethyl Aceto-acetate.—Seven and six-tenths grams of sodium was dissolved in 100 cc. of absolute alcohol, 44 g. of ethyl aceto-acetate added and the mixture well shaken. Forty-seven grams of crotyl bromide was then dropped slowly into the cooled mixture. After digesting for twelve hours on the steam-bath, the sodium bromide was filtered off and the alcohol removed by distillation. The product was taken up with ether, washed, then dried with fused calcium chloride. Removal of the ether and fractionation under reduced pressure yielded a colorless liquid, b. p. 135–139° (46 mm.); yield, 66%.

Synthesis of **Δ^{5-6}-Heptene-2-one.**—The saponification of the crotyl aceto-acetate was carried out by the method used by Wislicenus[10] in saponifying various substituted ethyl aceto-acetates with alcoholic potash.

Method.—Thirty-eight grams (one mole) of crotyl ethyl aceto-acetate was heated for four hours with 313 g. (2.75 moles) of a 10% solution of potassium hydroxide in absolute alcohol. The precipitated potassium carbonate was separated by filtration and the alcohol removed by slow, careful fractionation, using a column of beads. The product left (50–60 cc.) was cooled by adding a small amount of ice, and the solution acidified by the addition of 10% hydrochloric acid. The precipitated potassium chloride was removed by suction filtration, the salt washed with ether and the combined solution and ether washings diluted with about half of its volume of ether. After washing with sodium carbonate, then with water, it was dried with calcium chloride. The ether was removed, and several refractionations using a column of beads, gave a product, b. p. 150–152°; yield, 54%.

Preparation of Methyl γ,δ-Dihydroxyl Amyl Ketone.—This was prepared by oxidizing the Δ^{5-6}-heptene-2-one with a 2% aqueous solution of barium permanganate. The procedure gave only a 54% yield indicating that other oxidation products were formed.

Method.—Ten grams of the Δ^{5-6}-heptene-2-one was mixed with 100 cc. of water, cooled to 0° and a cooled solution of 14.6 g. of barium permanganate in 730 cc. of water slowly added during the course of three hours, the mixture being stirred vigorously throughout the addition. The solution was then filtered and the water removed by distillation at 40° under 20 mm. pressure. The residual oil in the flask was dissolved in chloroform, the solution filtered and the chloroform removed by evaporation. The product left was a pale yellow liquid boiling at 139–143° (10 mm.); yield, 54%.

Anal. Calcd. for $C_7H_{14}O_3$: C, 57.54; H, 9.59. Found: C, 57.99, 58.05; H, 9.01, 9.30.

Conversion of Methyl γ,δ-Dihydroxy Amyl Ketone into its Anhydro Derivative.—On warming the ketone with a trace of concentrated sulfuric acid, the viscosity of the liquid increased rapidly, resulting within a few minutes in the formation of a thick, resinous product. Water was given off during the process. A quantitative estima-

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[9] Adams, "Organic Syntheses," John Wiley and Sons, Inc., New York, **1920,** Vol. I, p. 3.

[10] Wislicenus, *Ann.*, **190,** 280 (1878).

tion showed that the polymerized product was formed by the loss of one molecule of water from each molecule of the dihydroxy ketone.

Method.—Into a specially constructed tube there was introduced about 0.5 g. of the ketone and about 0.002 g. of concentrated sulfuric acid and the contents heated in a glycerine bath at about 90° in a slow stream of dry air until constant weight was obtained. The water eliminated was absorbed by connecting with a weighed drying tube containing fused calcium chloride.

Subs. 0.4481; H_2O, 0.0536; loss in weight of ketone product 0.0672 or 14.99%. Calcd. for loss of 1 molecule of water; 12.33. Found: 11.96.

Analysis of Resulting Resin.—This was washed with water to remove sulfuric acid and then carefully dried.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.62; H, 9.37. Found C, 65.32, 65.26; H, 9.18, 9.14.

The resin is insoluble in dilute alkali and acid but readily soluble in concentrated acids (H_2SO_4; HCl). It dissolves readily in the common organic solvents.

Molecular Weight. Sample I. 0.2414; benzene, 43.65; ΔT, 0.050°. Mol. wt., 553. Sample II. (slightly less pure), 0.2833, 0.1588, 0.1131, 0.0794; benzene, 21.80; ΔT, 0.110°, 0.062°, 0.044°, 0.031°. Mol. wt., 591, 588, 590, 588.

The carefully washed and dried resin from methyl γ,δ-dihydroxy butyl ketone gave the following results.

Anal. Substance, 0.0974, 0.0994, 0.1530, phenol, 25.07, 28.11, 28.11; ΔT, 0.070°, 0.068°, 0.093°. Mol. wt., 422, 395, 445.

A determination, using camphor as solvent [Rast, *Ber.*, **54,** 1979 (1921); **55B,** 1051 (1922)] gave the surprisingly high value of 3706.

Ratio of camphor to resin, approximately 15:1. Subs., 0.0208; camphor, 0.3351; ΔT, 0.67° (mean of 14 readings); $k = 40$. Mol. wt., 3706.

Preparation of Methyl γ,δ-Dihydroxy *Iso*Valeryl Ketone.—This ketone was prepared by two different methods starting with methyl heptenone as the raw material.

1. Methyl heptenone was oxidized with a dilute aqueous solution of potassium permanganate, exactly according to the directions of Harries.[11]

2. Methyl heptenone was first converted into methyl heptenone oxide by the action of benzoyl hydroperoxide,[12] and then allowed to combine with the theoretical amount of water by allowing it to stand in contact with water at ordinary temperature for two hours. The oxide is a colorless liquid, b. p. 148–150°, and reacts with water with great readiness at ordinary temperature; in fact, unless it is kept in a very tightly stoppered bottle, it will only remain pure for a short time. On seeding with a little of the solid ketone it crystallized immediately into a thick, white mass. The crude product melted at 64° but, on crystallization from ligroin, at 67–68°, in agreement with the value found by Harries.[11]

Action of Heat on Methyl γ,δ-Dihydroxy *Iso*-Valeryl Ketone.—The ketone is readily converted into the oxide under the influence of heat at 150° with the formation of only a very small amount of resin. The same change takes place in the presence of a trace of concentrated sulfuric acid, but with the difference that the speed of reaction is much increased and there is slightly more resinification.

Method.—Five grams of the ketone was heated in a distilling flask at 150° (inside temperature). A mixture of water and methyl heptenone oxide distilled over. Ether was added to the distillate, the product dried with anhydrous sodium sulfate, the ether

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[11] Harries, *Ber.*, **35,** 118 (1902).

[12] Prileschaeff, *J. Russ. Phys.-Chem. Soc.*, **43,** 609 (1911).

removed and the residue fractionated. There was obtained 3 g. of methyl heptenone oxide, b. p. 145–155°; yield, 60%.

0.9651 g. of the ketone was heated under the same conditions and the residue weighed. The brown resinous product amounted to 0.0704 g., equivalent to 7.29%.

Additional experiments in which quantities of 1 to 2 g. of the ketone were heated with small amounts of concentrated sulfuric acid (0.02 to 0.08 g.) under the same conditions, gave results similar to those under the influence of heat alone. There is, therefore, no pronounced tendency for dehydration and polymerization to a resinous product as in the case of methyl γ,δ-dihydroxy amyl ketone.

Summary

1. Attention is drawn to the important role, in the case of dihydroxycarbonyl derivatives, played by the hydroxyl groups in the γ,δ-positions to the carbonyl group.

2. It is found that methyl γ,δ-dihydroxy amyl ketone behaves similarly to methyl γ,δ-dihydroxy butyl ketone in that it readily undergoes dehydration and polymerization in the presence of a trace of concentrated sulfuric acid. The change corresponds to a loss of one molecule of water from each molecule of the dihydroxy ketone.

3. Under the same conditions methyl γ,δ-dihydroxy *iso*valeryl ketone readily undergoes dehydration with formation of methyl heptenone oxide and shows little tendency towards polymerization. The introduction of the second methyl group in the δ-position thus facilitates to a pronounced degree the splitting off of water from the two adjacent hydroxyl groups.

4. The bearing of such changes on the formation of polysaccharides such as cellulose is indicated.

MONTREAL, CANADA

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY, CORNELL UNIVERSITY]

2,7-DIMETHYLSULFONEFLUORAN, 2'-HYDROXY-5'-METHYLBENZOYL-2-BENZENESULFONIC ACID AND SOME OF THEIR DERIVATIVES

BY W. R. ORNDORFF AND I. T. BEACH[1]

RECEIVED DECEMBER 19, 1927 PUBLISHED MAY 5, 1928

Fluoran was discovered by Baeyer[2] and its constitution established by Meyer.[3] 2,7-Dimethylfluoran was first made by Drewson.[4] Sulfonephthaleins have been prepared by Remsen and his students[5] and also

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[1] From a dissertation presented by I. T. Beach to the Faculty of the Graduate School, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[2] Baeyer, *Ann.*, **212**, 347 (1882).

[3] Meyer, *Ber.*, **24**, 1412, 3586 (1891).

[4] Drewson, *Ann.*, **212**, 340 (1882).

[5] Remsen and co-workers, *Am. Chem. J.*, **6**, 180 (1884); **9**, 372 (1887); **11**, 73 (1889); **16**, 513, 328 (1894); **17**, 352, 656 (1895); **20**, 257 (1898).