TABLE IV

METHALLYL ETHERS

Compounds	Boiling point °C.	Mm.	Formula	n^{20}_D	d^{20}_4	Molecular refraction Calcd.	Molecular refraction Found	Methallyl, % Calcd.	Methallyl, % Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Hexamethallyl-D-mannitol[a]	173–174	0.8	$C_{30}H_{50}O_6$	1.4713	0.9537	147.80	148.58	65.2	64.6	71.1	71.5	10.0	10.2
Hexamethallyl-D-sorbitol[b]	165–167	.3	$C_{30}H_{50}O_6$	1.4703	.9528	147.80	148.45	65.2	64.4	71.1	71.1	10.0	9.9
Trimethallyl glycerol	94– 96	.5	$C_{15}H_{26}O_3$	1.4532	.9142	75.00	75.23	65.0	64.5	70.8	70.9	10.3	10.0
Dimethallyl ethylene glycol	48– 50	.4	$C_{10}H_{18}O_2$	1.4383	.8779	50.73	50.93	64.7	64.1	70.6	70.6	10.7	10.6
Tetramethallyl pentaerythritol	128–129	.3	$C_{21}H_{36}O_4$	1.4621	.9285	103.88	104.15	62.5	62.1	71.6	71.4	10.3	10.1
Hexamethallyl dipentaerythritol	183–185	.3	$C_{34}H_{58}O_7$	1.4682	.9561	167.11	168.34	57.1	56.4	70.6	70.3	10.1	10.1

[a] $[\alpha]^{25}_D$ of an 8% solution in absolute alcohol, +15.7°. [b] $[\alpha]^{25}_D$ of an 8% solution in absolute alcohol, +5.9°.

0.4 mm. Step II gave a 70% yield of dimethallyl ethylene glycol.

Methallyl Starch.—Thirty-four grams of air-dried potato starch was treated with three times the stoichiometrically equivalent quantities of methallyl bromide and 50% alkali with 150 ml. of methyl ethyl ketone as solvent. The reaction mixture was stirred at 85° for ten hours. It was then steam distilled, and the resulting gummy material kneaded with water until free of alkali. The yield was 30 g. of methallyl starch containing 43.7% methallyl, or 2.25 methallyl groups, per glucose unit. This material was gummy while wet but soon became dry and crumbly. Thin films of the product polymerized to an insoluble infusible state in the same manner as allyl starch.[8]

Allyl Dipentaerythritol.—By Step I, 200 g. of dipentaerythritol gave a 59% yield of a partially allylated product containing 4.6 allyl groups and distilling at 174° at 0.3 mm.

Step II gave a 67% yield of hexaallyldipentaerythritol, boiling point 184–186° at 1 mm., n^{20}_D 1.4679, d^{20}_4 0.9777, molecular refraction, 140.03 (calcd. 140.20); allyl 49.9% (calcd. for $C_{28}H_{46}O_7$, 49.8%); carbon, 68.1% (calcd. 68.0%); hydrogen, 9.3% (calcd. 9.3%).

Isolation of Methacrolein as a By-product of Oxidation of Methallyl Ethers.—Methacrolein was isolated and identified essentially in the same manner as described for isolation of acrolein.[3] The pungent liquid which distilled off during oxidation of methallyl sorbitol at 97° was collected in the trap cooled with solid carbon dioxide in acetone. The 2,4-dinitrophenylhydrazone was prepared, and after two recrystallizations from xylene melted at 205.5–206° (reported in literature[9] 206.0–206.5). When this material was mixed with authentic methacrolein-2,4-dinitrophenylhydrazone, there was no depression in the melting point.

Preparation of Methallyl Bromide.—One mole of methallyl chloride and 1.5 moles of sodium bromide were heated with 360 ml. of absolute methanol for ten hours at reflux temperature. After filtration and removal of methanol by washing with water, the methallyl bromide was recovered by fractionation. The average yield of four preparations was 31%, as compared with 15 to 20% obtained by Tamele, Ott, Marple and Hearne.[10]

Unsaturation was determined as described in the second article of this series.[3] The method of Ogg, Porter and Willits[11] was used for determination of free hydroxyl.

Acknowledgment.—The assistance of Miss M. L. Fisher in making the Barcroft–Warburg measurements is acknowledged.

Summary

Eight new methallyl ethers of polyhydroxy compounds have been prepared. Their rates of oxygen absorption are higher than those for corresponding allyl ethers and they absorb more oxygen at the gelation point. Comparative gelation times for allyl and methallyl ethers have been determined. The mechanism of oxidation of methallyl ethers appears to be similar to that described for allyl ethers.

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[8] Nichols, Hamilton, Smith and Yanovsky, *Ind. Eng. Chem.*, **37**, 201 (1945).

[9] Shriner and Sharp, THIS JOURNAL, **62**, 2245 (1940).

[10] Tamele, Ott, Marple and Hearne, *Ind. Eng. Chem.*, **33**, 115 (1941).

[11] Ogg, Porter and Willits, *Ind. Eng. Chem.*, *Anal. Ed.*, **17**, 394 (1945).

RECEIVED JUNE 7, 1946

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

Chemical Interactions of Amino Compounds and Sugars. I[1]

BY LIEBE F. CAVALIERI[2] AND M. L. WOLFROM

In the processing of many foodstuffs the products often develop undesirable colors. Much of this coloring or "browning" has been ascribed to the reaction between the carbohydrates and proteins present, or, more specifically, to the reaction between reducing sugars and amino acids. This decomposition reaction, in its final stages, has been termed the Maillard[3] reaction. Attempts to determine the nature of the interaction between amino acids and sugars are numerous and many techniques have been employed. The principal investigative tools used have been polarimetry,[4] cryoscopy,[5] colorimetry,[3b] potentiometry[6] and chemical analysis, the latter including

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[1] The subject matter of this communication has been undertaken in coöperation with the Quartermaster Corps Committee on Food Research under a contract (W44-109QM-1027) with The Ohio State University Research Foundation. The opinions or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or indorsement of the War Department.

[2] Research Foundation Associate, The Ohio State University, Project 238.

[3] (a) L.-C. Maillard, *Compt. rend.*, **154**, 66 (1912); (b) *Ann. chim.*, [9] **5**, 258 (1916).

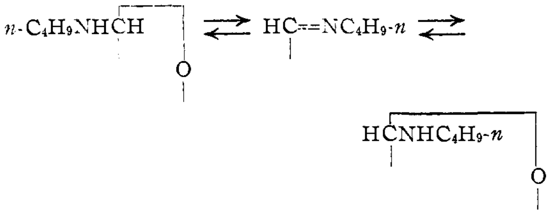
[4] C. Neuberg and Maria Kobel, *Biochem. Z.*, **162**, 496 (1925); *ibid.*, **174**, 464 (1926); H. v. Euler and K. Josephson, *Z. physiol. Chem.*, **153**, 1 (1926).

[5] H. v. Euler, E. Brunius and K. Josephson, *Z. physiol. Chem.*, **155**, 259 (1926); H. v. Euler and E. Brunius, *Ber.*, **59B**, 1581 (1926); *Ann.*, **467**, 201 (1928).

[6] M. Frankel and A. Katchalsky, *Biochem. J.*, **31**, 1595 (1937).

formol titrations, Van Slyke amino nitrogen assays and various methods for determining reducing sugars.

In the work herein reported, a relatively simple amino condensation product of a sugar was selected for study by ultraviolet absorption spectra methods. This substance was the crystalline D-glucosyl-N-butylamine, first synthesized by Mitts and Hixon.[7] Whatever the structure of the crystalline product may be, it is certain[8] that its solutions will contain the components shown in the equilibrium I. The aqueous solution slowly turns brown on standing at room temperature. Mitts and Hixon[7] have shown that hydrolysis to D-glucose and butylamine occurs to the extent of *ca.* 44% in *ca.* twenty hours. The resultant equilibrated solution is quite alkaline, the pH varying with concentration but being in the pH range 10.6–11.6.



$$n\text{-}C_4H_9NHCH \rightleftharpoons HC{=}NC_4H_9\text{-}n \rightleftharpoons HCNHC_4H_9\text{-}n$$

I

$$HC{=}NC_4H_9\text{-}n \overset{HOH}{\rightleftharpoons} HC{=}O + n\text{-}C_4H_9NH_2 \overset{HOH}{\rightleftharpoons} n\text{-}C_4H_9NH_3^+ + OH^-$$

While these high values of pH are outside of the normal range for foodstuffs, it was considered of interest to study D-glucosyl-N-butylamine as a model system. The nearest approach to such a system in a foodstuff is perhaps attained in dried egg white which exhibits a pH range of 8.5–9.5.[9]

The absorption spectra of D-glucose after standing for twenty hours at room temperature, in aqueous butylamine, dilute sodium hydroxide, and aqueous dimethylamine solutions, are shown in curves 1, 6 and 7, respectively, of Fig. 1. These solutions show absorption bands with maxima at 2620, 2650 and 2630 Å., respectively. Such agreement indicates that the alkaline decomposition products are essentially identical in all three cases.

If the concentration of sodium hydroxide is increased, the spectrum (after twenty-four hours at room temperature) changes considerably, as is shown by the data of Kwieciński and Marchlewski[10] reproduced in Fig. 2, curve 1. The band with a maximum at 2650 Å. is suppressed and a new band with a maximum at 3150 Å. is evident. An increase in the concentration of butylamine leads to a similar result. Thus, Fig. 2, curve 3 shows the spectrum of an aqueous D-glucose solution (after twenty hours at room temperature) in which the concentration of butylamine has been increased from a pH value of 11 (Fig. 1, curve 1) to 11.6. A new absorption maximum appears at 3180 Å. while the band occurring at 2620 Å. is nearly completely suppressed. Thus in either the sodium hydroxide system or in

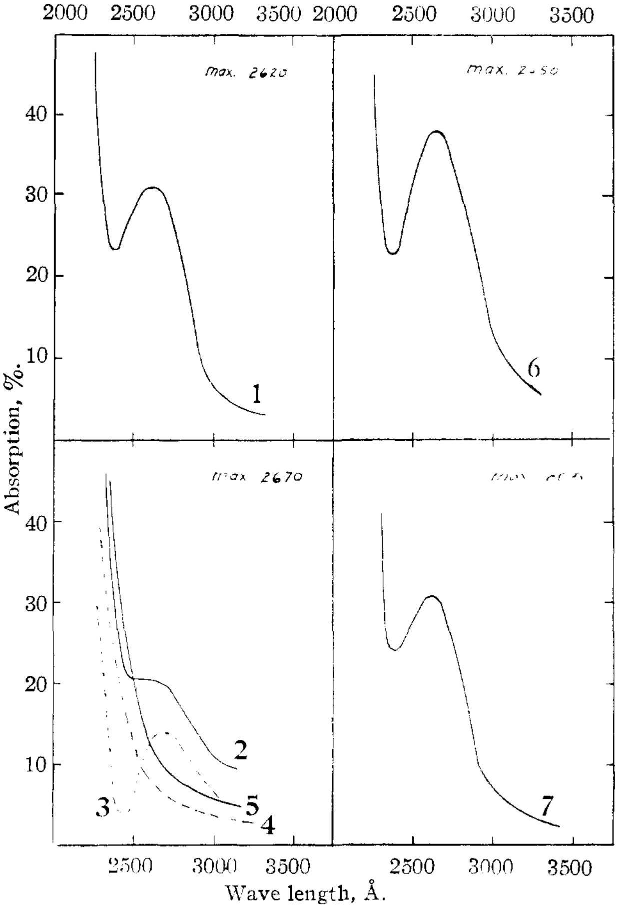


Fig. 1.[11]—Curve 1, 0.044 M D-glucose in aqueous butylamine at pH 11.0; curve 2, 0.034 M D-glucosyl-N-butylamine[12] at pH 11.0; curve 3, calcd. by subtracting curve 4 from curve 2; curve 4, calcd. spectrum of the residual 56% D-glucosyl-N-butylamine; curve 5, 0.034 M D-glucosyl-N-butylamine after five minutes; curve 6, 0.044 M D-glucose in sodium hydroxide at pH 10.6; curve 7, 0.044 M D-glucose in aqueous dimethylamine at pH 11.0. Beckman ultraviolet spectrophotometer (model DU); 1-cm. cell.

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[7] Eleanor Mitts and R. M. Hixon, THIS JOURNAL, **66**, 483 (1944).

[8] *Cf.* M. L. Wolfrom and A. Thompson, *ibid.*, **53**, 622 (1931); V. Deulofeu, M. L. Wolfrom, P. Cattaneo, C. C. Christman and L. W. Georges, *ibid.*, **55**, 3488 (1933).

[9] In pretzel manufacture dough containing added sugar is dipped in boiling caustic (0.75–1%) and baked.

[10] L. Kwieciński and L. Marchlewski, *Bull. intern. acad. polonaise*, **A**, 317 (1929); *C. A.*, **24**, 3711 (1930).

[11] Unless otherwise noted, all observations were made after a reaction period of twenty hours at room temperature. The pH values were those found at the end of this period.

[12] Prepared according to the procedure of Mitts and Hixon,[7] repeatedly recrystallized from dioxane and dried at room temperature over phosphorus pentoxide under reduced pressure.

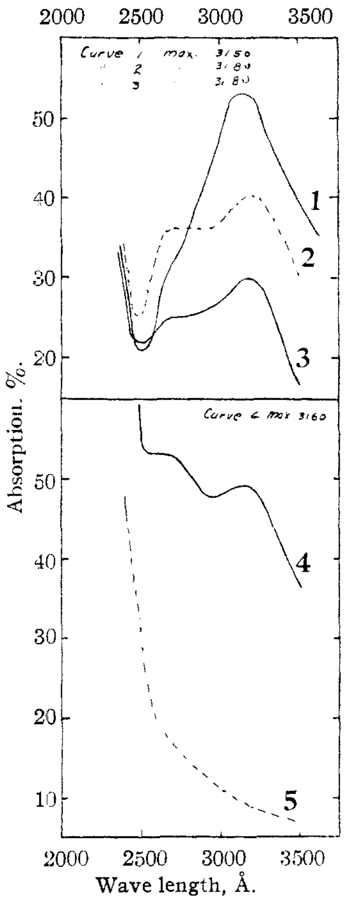

Fig. 2.[11]—Curve 1, 0.5 M D-glucose in 0.5 N sodium hydroxide after twenty-four hours (data of L. Kwieciński and L. Marchlewski[10]); curve 2, calcd. by subtracting curve 5 from curve 4; curve 3, 0.044 M D-glucose in aqueous butylamine at pH 11.6; curve 4, 0.1 M D-glucosyl-N-butylamine[12]; curve 5, calcd. spectrum of the residual 56% D-glucosyl-N-butylamine. Beckman ultraviolet spectrophotometer (model DU); 1-cm. cell.

the butylamine system, the absorption bands with maxima at 3150 and 2650 Å. may be made to vary in intensity, depending upon the hydroxyl ion concentration.

The absorption spectrum of a dilute solution (0.034 M) of D-glucosyl-N-butylamine determined immediately after the compound was dissolved in water, is shown in Fig. 1, curve 5. The spectrum taken after the solution was allowed to stand for twenty hours at room temperature is given in Fig. 1, curve 2. Since D-glucosyl-N-butylamine undergoes hydrolysis to the extent of 44%,[7] curve 2 is a summation of the spectrum of the remaining 56% D-glucosyl-N-butylamine and the spectrum of the alkaline degradation products formed by the action of the generated butylamine on D-glucose. Figure 1, curve 4, represents the spectrum of the 56% D-glucosyl-N-butylamine calculated from the equation $\epsilon = 1/c \log (100/T)$; wherein ϵ is the molar extinction coefficient, c is the molar concentration and T is the per cent. transmission. If curve 4 (Fig. 1) be subtracted from curve 2 (Fig. 1), there results curve 3 (Fig. 1), a more accurate spectrum of the alkaline decomposition products of D-glucose. Herein the absorption maximum occurs at 2670 Å. This value is in good agreement with the maxima shown in curves 1, 6 and 7 of Fig. 1. The maximum in curve 3 (Fig. 1) is displaced toward lower absorption values due to a lower concentration of free D-glucose in this case.

The absorption spectrum of a relatively concentrated solution (0.1 M) of D-glucosyl-N-butylamine is shown in Fig. 2, curve 4. If the correction for the remaining 56% D-glucosyl-N-butylamine (Fig. 2, curve 5) is taken into account, curve 2 (Fig. 2) results. It is seen that this spectrum is similar to that obtained by the action of butylamine on D-glucose at the same pH (Fig. 2, curve 3) and to that obtained by the action of relatively high concentrations of sodium hydroxide upon D-glucose (Fig. 2, curve 1). In curve 1. the band with a maximum at 3150 Å. is more pronounced because the hydroxyl ion concentration was considerably higher in this experiment.

Comparing the corrected spectrum of the dilute D-glucosyl-N-butylamine solution (Fig. 1, curve 3) with that of the concentrated D-glucosyl-N-butylamine solution (Fig. 2, curve 2), it is noted that a maximum appears at 3180 Å. in curve 2, whereas no such maximum is evident in Fig. 1, curve 3. This is due to the fact that the hydroxyl ion concentration was higher in the more concentrated solution. Thus, in the case of D-glucosyl-N-butylamine, as in the case of alkaline D-glucose, the bands with maxima at 2650 and 3180 Å. may be made to vary in intensity depending upon the hydroxyl ion concentration.

Since the spectra developed in alkaline D-glucose solutions are essentially identical with the spectra of equilibrated aqueous D-glucosyl-N-butylamine solutions (*cf.* curves 1, 6 and 7 of Fig. 1 with curve 3 of Fig. 1; and curves 1 and 3 of Fig. 2 with curve 2 of Fig. 2), we believe that at least the incipient "browning" of aqueous solutions of D-glucosyl-N-butylamine is due to hydrolysis of the amine-sugar compound followed by the action of the base so formed on the liberated D-glucose. We believe that this general type of process may well be the predominant one occurring in the "browning" of the amino condensation products of the sugars in this rather high range of pH (10.6–11.6). Such a conclusion is in harmony with that arrived at by Frankel and Katchalsky[6] from potentiometric measurements on aqueous solutions of sugars and amino acids. These workers noted the appearance of a second type of reaction at $p\text{H} > 10$ and they postulated that alkaline sugar decomposition was probably the main reaction in this range of pH.

Acknowledgment.—We are pleased to acknowledge the assistance of Doris K. Cavalieri.

Summary

1. Ultraviolet absorption spectra measurements are recorded for aqueous solutions of D-glucosyl-N-butylamine and are compared with those for similar solutions of D-glucose in alkali.
2. The above data are interpreted as demonstrating that the incipient coloration appearing when aqueous solutions of D-glucosyl-N-butylamine are allowed to stand at room temperature, is caused by hydrolysis of the compound followed by the action of the liberated hydroxyl ions upon D-glucose. It is probable that this is a general reaction of sugar-amino condensation products in these relatively high *p*H ranges.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

The Willgerodt Reaction. II. A Study of Reaction Conditions with Acetophenone and Other Ketones[1,2]

BY DELOS F. DETAR[3] AND MARVIN CARMACK

Although the Willgerodt reaction[4] has been applied to a large number of ketones for the preparation of carbonamides, no systematic study of the effect of variations of reaction conditions appears to have been published. The attempt of Willgerodt and Scholtz[5] to replace the ammonium polysulfide reagent with colorless ammonium sulfide gave poor results. One useful variant of the original procedure, introduced by Fieser and Kilmer,[6] involves the addition of dioxane to the reaction mixture; the presence of the organic solvent generally permits the use of lower reaction temperatures, and yields are often greatly improved.

In an effort to improve the usefulness of the Willgerodt synthesis of amides and to throw light on the reaction mechanism, we have made a study of the effect of the time, temperature, composition of the reagent, and presence of organic solvents on the reaction of acetophenone to form phenylacetamide. As a result of this study a

$$C_6H_5COCH_3 \xrightarrow{(NH_4)_2SS_x} C_6H_5CH_2CONH_2$$

modified procedure was developed which gave a total of 85.6% of phenylacetamide and phenylacetic acid as compared with the total of 63% by the original procedure of Willgerodt and Merk.[7] The improved methods were applied also to the reactions of a number of other ketones according to the general equation

$$\text{Aryl-CO}(CH_2)_nCH_3 \longrightarrow \text{Aryl-}CH_2(CH_2)_nCONH_2$$

The results are summarized in Tables II and III in the Experimental.

According to the classical procedure the ammonium polysulfide reagent is prepared by dissolving an excess of sulfur in concentrated ammonium hydroxide which has been previously "saturated" with hydrogen sulfide. Although the published procedures are rather indefinite the molecular proportions of reactants have probably been of the following order: ketone (1), ammonia (7), hydrogen sulfide (4) and sulfur (2).

Using a standardized procedure for small-scale runs with acetophenone, we determined that the temperature range of 160–190° gives the highest yields within a convenient reaction time of four to six hours. Using combinations of sulfur, ketone, and analyzed solutions of ammonium sulfide–ammonium hydroxide in varying proportions, we found that the highest yields of amide were obtained when a large excess of sulfur was used; the optimum ratio appeared to be approximately 10 gram-atomic weights of sulfur for each mole of ketone.

When the concentration of ammonium hydroxide and the proportions of sulfur and ketone were held approximately constant and the concentration of hydrogen sulfide added to the starting mixture was varied, the interesting result emerged that the best yields of amide were obtained when only low concentrations of hydrogen sulfide were added initially. Higher concentrations of hydrogen sulfide in the reagent markedly lowered the yields of amide. This finding suggested the desirability of omitting hydrogen sulfide entirely from the reagent, a modification which gave very satisfactory results with acetophenone. Runs in which only concentrated ammonium hydroxide, sulfur and acetophenone were present initially produced higher yields than runs using comparable proportions of the same reagents with added hydrogen sulfide.

It is apparent from a consideration of the stoichiometry of the Willgerodt reaction that the over-all process involves a net oxidation which is almost certainly at the expense of the added

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[1] For the previous paper of the series, see Cavalieri, Pattison and Carmack, THIS JOURNAL, **67**, 1783 (1945).

[2] From the Ph.D. Dissertation of DeLos F. DeTar, University of Pennsylvania, 1944.

[3] Present address: Chemistry Department, Cornell University, Ithaca, N. Y.

[4] Willgerodt, *Ber.*, **20**, 2467 (1887); **21**, 534 (1888).

[5] Willgerodt and Scholtz, *J. prakt. Chem.*, [2] **81**, 382 (1910).

[6] Fieser and Kilmer, THIS JOURNAL, **62**, 1354 (1940); a bibliography of earlier references to the Willgerodt reaction appears in this paper.

[7] Willgerodt and Merk, *J. prakt. Chem.*, [2] **80**, 192 (1909).