of the ethanol, was distilled (b.p. 139° at 6 mm., n^{25}_{D} 1.5431) and the distillate was treated with alcoholic hydrogen chloride to form the hydrochloride salt of N-(4-methoxybenzyl)-ethanolamine. The latter was converted back to base which was then obtained as a solid. After recrystallization from Skellysolve B it melted at 38–39°.

The bases, described in Table I, were recrystallized from ether or a Skellysolve fraction or a mixture of the two. The hydrochlorides were recrystallized from acetone or isopropyl alcohol.

Preparation of N-Benzylpropanolamines.—The following compounds were prepared from the appropriate dichlorobenzyl chloride and propanolamine.

N-(2,4-Dichlorobenzyl)-2-hydroxypropylamine, m.p. 73.8–75.0° (Skellysolve B). *Anal.* Calcd. for $C_{10}H_{14}Cl_2NO$: N, 5.99. Found: N, 5.95.

N-(3,4-Dichlorobenzyl)-2-hydroxypropylamine, m.p. 54.4–56.4° (Skellysolve B). *Anal.* Found: N, 6.17.

N-(2,4-Dichlorobenzyl)-3-hydroxypropylamine, b.p. 150–155° (0.5 mm.), n^{25}_{D}, 1.5600. *Anal.* Found: N, 6.00.

N-(3,4-Dichlorobenzyl)-3-hydroxypropylamine, b.p. 155–160° (0.8 mm.), n^{25}_{D}, 1.5539. *Anal.* Found: N, 6.11.

Preparation of N-Benzyl-N-(hydroxyalkyl)-dichloroacetamides.—The following example illustrates the general procedure employing dichloroacetyl chloride as the acetylating agent.

Method A. A solution of 4.63 g. of dichloroacetyl chloride in 20 ml. of ethylene dichloride was added dropwise with stirring and cooling (0–5°) to a solution of 14 g. of N-(4-butoxybenzyl)-ethanolamine in 100 ml. of ethylene dichloride. After the addition was completed the reaction mixture was allowed to stand overnight at room temperature and ether was added to precipitate N-(4-butoxybenzyl)-ethanolamine hydrochloride (8 g.). The solid was filtered off and the filtrate was washed with 1 *N* hydrochloric acid and then water. After drying over Drierite, the solvents were removed by distillation. The residue was dissolved in ether, filtered with charcoal and Skellysolve A added to incipient turbidity; yield 5 g., m.p. 81–85° (uncor.). Recrystallization from ether–Skellysolve A gave a product melting at 88–88.9°.

With N-(4-nitrobenzyl)-ethanolamine the reaction was carried out at 25°.

A variation of the above method was used in the preparation of N-(2-chlorobenzyl)-N-(2-hydroxyethyl)-dichloroacetamide. Twelve grams of dichloroacetyl chloride in 30 ml. of ethylene dichloride was added with stirring over a period of one hour to a mixture of 15 g. of N-(2-chlorobenzyl)-ethanolamine in 100 ml. of ethylene dichloride and 80 ml. of 1 *N* sodium hydroxide. The temperature was kept below 0° with external cooling. The reaction mixture was then allowed to come to room temperature with stirring and the organic layer was separated. This was washed successively with 1 *N* sodium hydroxide, water, 1 *N* hydrochloric acid, water, and dried. The residue, after removing the solvent by distillation, was recrystallized from benzene-Skellysolve A.

Method B. This method is illustrated by the preparation of **N-(2,4-dichlorobenzyl)-N-(2-hydroxyethyl)-dibromoacetamide**. A mixture of 5.5 g. of N-(2,4-dichlorobenzyl)-ethanolamine and 7 g. of ethyl dibromoacetate was heated at 60° for 3–4 hours. The mixture, which became quite viscous, was stirred in dilute hydrochloric acid and the product was extracted with chloroform. The chloroform solution was then washed with water and the solvent removed by distillation. The resulting solid residue was recrystallized from ethylene dichloride and a small amount of Skellysolve B to give 3.5 g. (33%) of product melting at 115.0–117.2°.

Anal. Calcd. for $C_{11}H_{11}Br_2Cl_2NO_2$: Br, 38.07; C, 31.46; H, 2.64. Found: Br, 37.75; C, 31.43; H, 2.85.

N-(3,4-Dichlorobenzyl)-N-(2-hydroxyethyl)-dibromoacetamide was prepared in a similar manner; yield 38%, m.p. 115.5–128.8°.

Anal. Calcd. for $C_{11}H_{11}Br_2Cl_2NO_2$: Br, 38.07; C, 31.46; H, 2.64. Found: Br, 38.39; C, 31.54; H, 2.41.

The following dichloroacetamides were also prepared according to method B starting with methyl dichloroacetate and the appropriate secondary amine:

N-(2,4-Dichlorobenzyl)-N-(2-hydroxypropyl)-dichloroacetamide, 69% yield, m.p. 135.1–138.0° (ethylene dichloride). *Anal.* Calcd. for $C_{12}H_{13}Cl_4NO_2$: C, 41.77; H, 3.80; Cl, 41.10. Found: C, 41.56; H, 3.97; Cl, 40.66.

N-(3,4-Dichlorobenzyl)-N-(2-hydroxypropyl)-dichloroacetamide, 31% yield, m.p. 120.0–121.8° (ethylene dichloride). *Anal.* Calcd. for $C_{12}H_{13}Cl_4NO_2$: C, 41.77; H, 3.80; Cl (KOH), 20.55. Found: C, 42.00; H, 3.86; Cl(KOH), 20.52.

N-(2,4-Dichlorobenzyl)-N-(3-hydroxypropyl)-dichloroacetamide, 58% yield, m.p. 83.7–86.7° (benzene–Skellysolve A). *Anal.* Calcd. for $C_{12}H_{13}Cl_4NO_2$: C, 41.77; H, 3.80; Cl, 41.10. Found: C, 4.60; H, 3.88; Cl, 41.23.

N-(3,4-Dichlorobenzyl)-N-(3-hydroxypropyl)-dichloroacetamide, 70% yield, m.p. 91.9–97.5° (benzene–Skellysolve A). *Anal.* Calcd. for $C_{12}H_{13}Cl_4NO_2$: C, 41.77; H, 3.80; Cl, 41.10. Found: C, 41.70; H, 3.89; Cl, 41.44.

RENSSELAER, NEW YORK

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE OHIO STATE UNIVERSITY]

Benzylation and Xanthation of Cellulose Monoalkoxide[1]

BY M. L. WOLFROM AND M. A. EL-TARABOULSI[2]

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A monobenzylcellulose was prepared by the reaction of sodium 2-cellulosate with benzyl chloride. Water, if present, causes a progressive lowering in the degree of benzylation. A topochemical, macroheterogeneous type of reaction is indicated. No glycol group was detectable in the product. Xanthation of dry sodium 2-cellulosate was not possible and required water as a catalyst; a maximum of 0.4 xanthate group per C_6-unit could be introduced. Replacement by zinc of the sodium in the cellulose alkoxide is described.

Alkali cellulose very probably consists of an addition compound in equilibrium with a true alkoxide. In the procedures established by Gaver,[3] working mainly with starch, the water in the alkali–carbohydrate reaction is removed by azeotropic distillation with a higher alcohol. A large excess of sodium

$$\mathrm{ROH + NaOH \rightleftarrows ROH\cdot NaOH \rightleftarrows RONa + HOH}$$

hydroxide is employed and when the reaction is heterogeneous, the alkoxide of the carbohydrate remains on removal of other sodium compounds with ethanol.

One hydroxyl group in glycosidically bound carbohydrates forms an alkoxide much more readily than the others. Thus, in the presence of an excess of alkali, the reactions of these polyhydric units

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[1] Reported in part in *Abstracts Papers Am. Chem. Soc.*, **121**, 8P (1952); presented before the XIIIth International Congress of Pure and Applied Chemistry, Stockholm, Sweden, Aug. 1, 1953.

[2] Fellow of the Egyptian Government.

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show a sharp leveling off at a monoalkoxide composition. Further reaction with the other hydroxyl groups then occurs very slowly. Considerable evidence has been advanced that this acidic hydroxyl is the one adjacent to the acetal or glycosidic function. Michaelis[4] and Kuhn and Sobotka[5] determined the acidic dissociation constants of a number of glycosides and alcohols. They considered that the aglycon influenced primarily the electrochemical character of the hydroxyl group adjacent to the glycosidic or acetal carbon. The glycosides exhibited acid dissociation constants that were of a much higher order than those shown by the monohydric or polyhydric alcohols. Fox, Cavalieri and Chang[6] demonstrated that variations in the ultraviolet absorption spectra of pyrimidine nucleosides dissolved in strong alkali are due to the ionization of the 2-hydroxyl group of the sugar, with a very limited contribution from the other hydroxyl groups. Lieser and Leckzyck[7] obtained 2-*O*-methyl-D-glucose diethyl thioacetal by shaking D-glucose diethyl thioacetal at 0–10° with methyl iodide and silver oxide. Papadakis[8] had encountered the same monomethyl ether on partial methylation of D-glucose diethyl thioacetal with alkali and dimethyl sulfate. Schmidt and Wernicke[9] selectively alkylated 4,5-di-*O*-isopropylidene-D-fucose dimethyl acetal in the second position with sodium and benzyl chloride in ether.

Evidence that the Gaver procedure for obtaining a monoalkoxide forms such at position two in starch[3] and in methyl α-D-glucopyranoside[10] has been presented. Starting with an alkoxide so formed and considered to be essentially sodium 2-cellulosate, Sugihara and Wolfrom[11] have described its employment to yield a methylcellulose largely substituted in position two of the component anhydro-β-D-glucopyranose units. In the work herein described, this sodium derivative of cuprammonia-regenerated cellulose has been utilized in a study of the benzylation and xanthation of cellulose.

The benzylation of sodium 2-cellulosate with benzyl chloride, under essentially anhydrous conditions, is a difficult reaction to effect since the halide employed does not swell the cellulose alkoxide. Benzylation proceeds by what is probably a topochemical, macroheterogeneous type of reaction related to that delineated by Lorand and Georgi[12] for the benzylation of cellulose in an aqueous system. On shaking the monosodium cellulosate with an excess of benzyl chloride at 90 ±5°, an apparent end-point was attained in about 24 hours (Table I) when essentially one-third of the material had reacted. Further reaction then proceeded very slowly. The benzylated portion was isolated through its insolubility in cuprammonia. Small amounts of water decreased the degree of benzylation (Table I), probably by hydrolyzing the alkoxide. Unreacted sodium alkoxide was removed on treatment of the product with water. The benzylation reaction with the sodium cellulosate can be considered as a typical nucleophilic replacement.

$$RO^- + C_6H_5CH_2Cl \longrightarrow RO—CH_2C_6H_5 + Cl^-$$

The monobenzyl cellulose was an amorphous solid of verified analysis in which no significant amount of glycol grouping was detectable by the procedure of Cramer, Hockett and Purves.[13]

TABLE I

BENZYLATION[a] OF SODIUM 2-CELLULOSATE IN THE PRESENCE OF VARYING AMOUNTS OF WATER

Expt.	H_2O, ml.	Yield,[b] g.	Carbon, %[c]	Hydrogen, %[c]	Benzyl groups per C_6-unit
1	0.0	0.63	61.01	6.40	0.92
2	.0	.63	61.90	6.37	1.00
3	.3	.65	59.26	6.51	0.78
4	.5	.50	58.62	6.61	.74
5	1.00	.55	57.47	6.45	.65

[a] Sodium 2-cellulosate, 1.5 g.; benzyl chloride, 15 ml. in expt. 1–2 and 30 ml. in 3–5; time, 24 hr. except expt. 2 (48 hr.); see Experimental portion for details. [b] After cuprammonia treatment. [c] Corrected for a combustion residue varying from 0.4–2.7%.

Following Gaver,[3] the cation of sodium 2-cellulosate was replaced by a divalent metal. On reaction of the sodium alkoxide with zinc chloride in ethanol, a salt was obtained the analysis of which closely approximated that for $(C_6H_9O_5)_2Zn$.

In contrast to the successful benzylation of dry sodium 2-cellulosate with benzyl chloride, no xanthation could be effected with carbon disulfide under anhydrous conditions. Here, water is apparently required as a catalyst for this reaction (Fig. 1). On the other hand, water hydrolyzes the alkoxide so that the reaction necessarily passes through a maximum, in the presence of increasing amounts of water, with a maximum replacement efficiency of

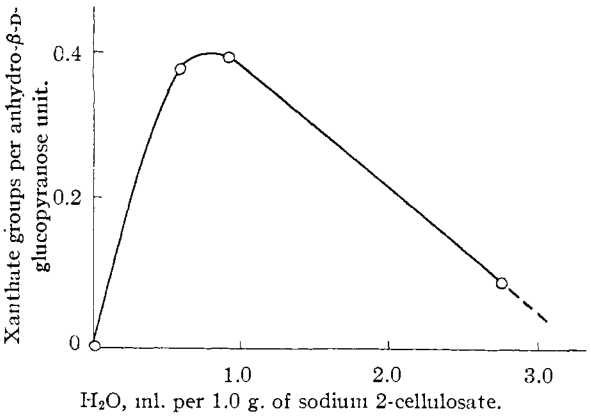

Fig. 1.—Xanthation of sodium 2-cellulosate (0.94 equiv. Na per anhydro-β-D-glucose unit); 25 ± 2°; time, 24 hr.; 100 ml. of carbon disulfide; see Experimental portion for details. No xanthation at the initial anhydrous point was found in a reaction period of two weeks.

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about 40%. This makes the allocation of the xanthate group to the 2-position somewhat uncertain. This result is in harmony with the established fact that xanthation of alcohols does not proceed under anhydrous conditions.[10,14,15] At relatively high concentrations of water (Fig. 1), the competing hydrolytic reaction predominates and the degree of xanthation becomes very low.

Experimental

Sodium 2-Cellulosate.—This was prepared as described previously.[11] The yield was 14 g. from 20 g. of cotton linters and contained 1 (0.9–1.2) equiv. of sodium per anhydro-β-D-glucopyranose unit.

Reaction of Sodium 2-Cellulosate with Zinc Chloride.—An amount of 1 g. of sodium cellulosate (1.2 Na per anhydro-D-glucose unit) was stirred vigorously, in a moisture-guarded apparatus, at 70° for 6 hr. with a solution of zinc chloride (1.2 equiv.) in 70 ml. of 100% ethanol. The mixture was then allowed to stand overnight at room temperature. The product was removed by centrifugation and washed successively with 100% alcohol and ether. The amorphous solid was dried in a desiccator under reduced pressure. The product so isolated contained some sodium chloride.

Anal. Calcd. for $C_6H_7O_2(OH)_{1.8}(OZn/2)_{1.2}$: Zn, 19.60. Found (after correction for a sodium chloride content of 3.9%): Zn, 20.6.

Monobenzylcellulose.—An amount of 6.9 g. of dry, finely ground sodium 2-cellulosate was shaken mechanically at atmospheric pressure and under anhydrous conditions, with 72 ml. of benzyl chloride at 90 ± 5° for 48 hr. The excess benzyl chloride was removed by steam distillation and the product was filtered on sintered glass, digested at room temperature with 5% sulfuric acid for a few minutes, washed thoroughly with boiling water, then with 95% ethanol and dried in a vacuum desiccator; yield 5.2 g. The product was digested under occasional stirring with cuprammonia solution[16] at room temperature for 4 days and was then removed by centrifugation and washed successively on a sintered glass funnel with a few ml. of 5% sulfuric acid, boiling water and ethanol; yield 3.0 g. of a white, amorphous powder. It was swollen by and was partially soluble in chloroform. It was insoluble in acetone, benzene, toluene and ethyl acetate. It was insoluble in water and appeared to be water-repellent.

Anal. Calcd. for $C_6H_7O_2(OH)_2(OCH_2C_6H_5)$: C, 61.90; H, 6.35; OH, 13.5. Found[17]: C, 61.52; H, 6.35; OH,[18] 12.9.

The **2-*O*-benzylcellulose diacetate** isolated in the hydroxyl analysis was an amorphous solid that was soluble in chloroform, acetone, ethyl acetate and warm benzyl chloride; it was insoluble in water.

An amount of 55 mg. of dry monobenzylcellulose (0.96 benzyl group per anhydro-D-glucose unit) was swollen in a mixture of 10 ml. each of anhydrous acetic acid and abs. chloroform (freshly distilled from phosphorus pentoxide), 5 ml. of 0.1 *N* lead tetraacetate in anhydrous acetic acid was added and the whole was maintained in the dark at room temperature. The amount of apparent reagent consumption over a blank was determined according to Cramer, Hockett and Purves.[13] The amount of oxidant consumed (moles per C_6-unit) as a function of time was found to be: 0.03 at 19 hr., 0.08 at 72 hr. and 0.15 at 132 hr.

In all of the benzylation experiments recorded in Table I, the finely ground sodium 2-cellulosate was added first, followed by the benzyl chloride. The temperature was adjusted to 90 ± 5° and the amounts of water noted were added at this point.

Xanthation of Sodium 2-Cellulosate.—In the xanthation experiments, 1 g. of finely ground sodium 2-cellulosate was treated with 100 g. of carbon disulfide, and water, if any, was added. The mixture was shaken mechanically in a closed system for 24 hr. at room temperature. The sticky xanthate was separated by decantation and residual solvent was removed by evaporation under reduced pressure. The reddish-brown xanthate was immediately dissolved in 3% sodium hydroxide and a 25-ml. aliquot was assayed for its xanthate content by the de Wyss method.[19] Another 25-ml. aliquot was treated with 1 ml. of 12 *N* hydrochloric acid and mixed with preignited (at 800°) asbestos fiber. The mixture was filtered through a weighed Gooch crucible and washed with water. The crucible and contents were dried at 105° to constant weight and were then ignited at 800° for 3 hr. The loss in weight on ignition was considered to represent the weight of the cellulose. The data are plotted in Fig. 1. In an additional experiment, sodium cellulosate of 1.2 Na per $C_6H_{10}O_5$ unit yielded with 1.1 g. of water per gram of sodium cellulosate, a product containing 0.57 xanthate group per $C_6H_{10}O_5$ unit.

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