other combinations containing the chaulmoogryl group. A light yellow product was obtained that crystallized from ligroin in hard crystalline masses melting at 73–74°.

Anal. Subs., 0.0647: CO_2, 0.1886; H_2O, 0.0649. Calcd. for $C_{24}H_{40}O_3$: C, 79.93; H, 11.19. Found: C, 79.50, H, 11.23.

Bacteriological Study

Preliminary experiments with chaulmoogrylresorcinol indicate a very low toxicity when given by mouth to rabbits or intramuscularly to rats. Tested against *B. thyphosum* the compound exerts little bactericidal or antiseptic action. It seems not improbable that this compound and lower homologs may be bactericidal for the acid-fast organisms such as leprosy and tuberculosis bacillus, through the ability of the compound to dissolve in the fat complexes of these organisms, even though the substance appears to be inert against the typhoid bacillus. Its bactericidal study is now in progress and a clinical investigation will follow.

Summary

1. The preparation of chaulmoogrylresorcinol and some of its derivatives are described.
2. The ketones prepared have been shown to be easily reduced to the corresponding alkyl resorcinols by the action of zinc amalgam.
3. The cyclopentenyl group in chaulmoogric acid is not reduced by the action of zinc amalgam.
4. The investigation of lower members of this homologous series will be continued in the Sterling Laboratory.

NEW HAVEN, CONNECTICUT

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

THE ACTION OF METALLIC SODIUM ON BROMINATED CYCLIC ACETALS[1]

BY HAROLD S. HILL[2] AND G. J. C. POTTER

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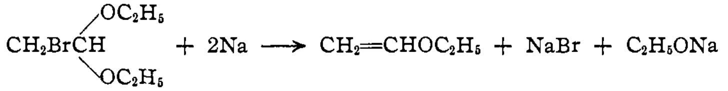
Wislicenus[3] showed that the reaction of bromo-ethylal with metallic sodium proceeded according to the following equation



$$\mathrm{CH_2BrCH}\begin{array}{l}\diagup \mathrm{OC_2H_5}\\ \diagdown \mathrm{OC_2H_5}\end{array} + 2\mathrm{Na} \longrightarrow \mathrm{CH_2{=}CHOC_2H_5} + \mathrm{NaBr} + \mathrm{C_2H_5ONa} \qquad (1)$$

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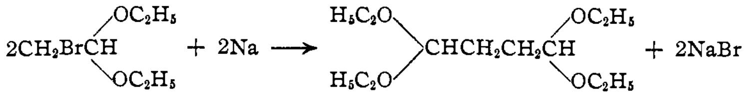
[1] This paper represents one of a series of publications carried out under the joint auspices of the Canadian Pulp and Paper Association, the Pulp and Paper Division of the Forest Products Laboratories of Canada and the Department of Industrial and Cellulose Chemistry, McGill University. The authors wish to express their appreciation of the facilities placed at their disposal by the three coöperating agencies.

[2] Research Fellow, Canadian Pulp and Paper Association.

[3] Wislicenus, *Ann.*, **192**, 106 (1878).

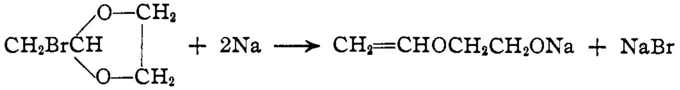
and that this unusual change took place to the exclusion of a Wurtz synthesis which might be expected to link up two molecules of the acetal



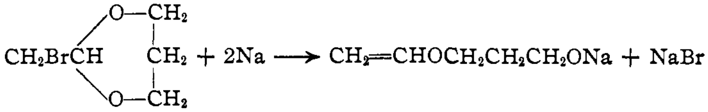
(2)

Quite recently the action of sodium on bromo-ethylidene ethylene glycol and bromo-ethylidene trimethylene glycol has been investigated.[4]

It has been found that these cyclic acetals in dry ether solution react smoothly at low temperatures with the metal and that a change similar to (1) takes place, yielding a vinyl derivative as the only product.



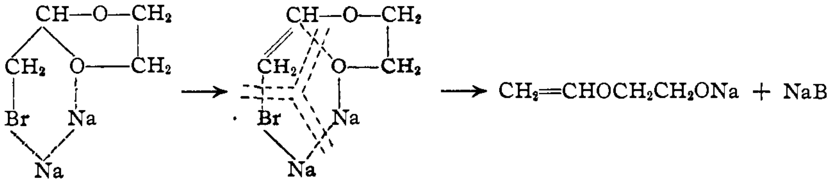
(3)



(4)

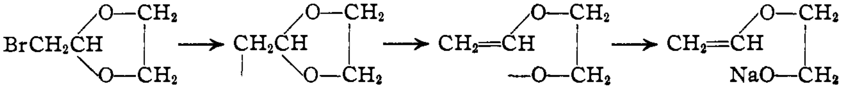
There are two obvious though nevertheless significant points regarding these reactions: (1) the absence of the usual Wurtz synthesis, as in (2); (2) the fact that the metal attacks the bromine and only one of the oxygen atoms. There may also be added the observations that: (3) without the oxygen in the molecule (substitution of O by CH_2, for example,) no unsaturation would have resulted; (4) without the bromine in the molecule no reaction at all would have resulted. (Ethylidene glycol may be refluxed over sodium without change.)

A conclusion may be drawn, therefore, that the above reactions are due to some combined influence of the bromine and oxygen atoms and that the role played by the one is dependent on that of the other. With these requirements in mind a mechanism scheme was proposed earlier[5] which embodied Erlenmeyer's theory of intermediate cyclization in chemical reaction as follows



(A)

An alternative series of changes may be



(B)

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[4] Hill and Pidgeon, This Journal, **50**, 2718, 2725 (1928).

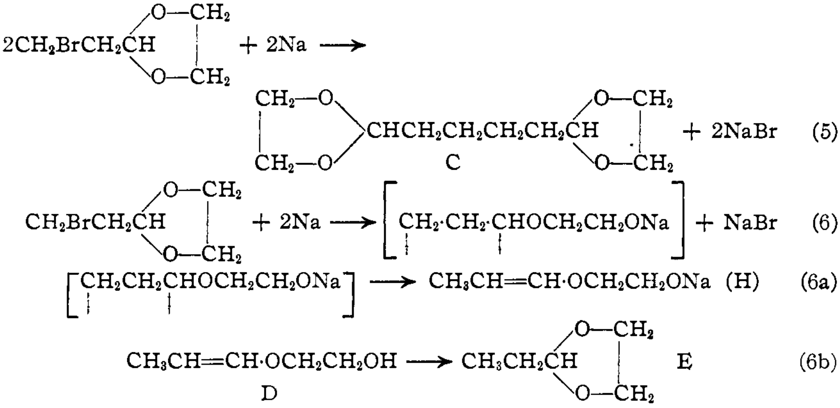
[5] Hibbert and Hill, *ibid.*, **45**, 740 (1923).

but in this scheme it is more difficult to account for the absence of a Wurtz synthesis.

In all of the above cases the bromine is on the α-carbon of the aldehyde residue. It seemed that similar reactions carried out with cyclic acetals having the halogen on the β-carbon might throw further light on the nature of the changes taking place. Such information might also have a bearing on the question regarding the function of sodium as a polymerization catalyst.

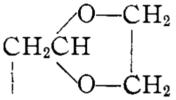
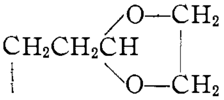
For this investigation β-bromopropylidene glycol and β-bromobutylidene glycol were synthesized by the reaction of acrolein and crotonaldehyde, respectively, with ethylene glycol in the presence of an excess of dry hydrogen bromide.

The Action of Sodium on β-Bromopropylidene Glycol.—β-Bromopropylidene glycol was found to react smoothly with metallic sodium in dry ether solution. The product instead of being exclusively a vinyl derivative as in the case of the α-bromo homolog proved to be a mixture of di-1,6-hexylidene glycol, C, hydroxy-ethyl-β-methylvinyl ether, D, and propylidene glycol, E, as well as smaller amounts of indefinite products. Propylidene glycol is presumably a secondary product resulting from a partial rearrangement (6b) of the vinyl derivative during distillation. The two primary reactions are, therefore, as indicated in (5) and (6)



The latter transformation (6b) takes place very rapidly in the presence of a trace of 50% sulfuric acid although it does not have the explosive or quantitative nature of the similar rearrangement of hydroxyethylvinyl ether.[4] Other products besides E are noticeable and it is possible that the rearrangement is complicated by a partial reversal of the reaction indicated in (6a).

Reaction (6a) is of interest since it is an example of unsaturation shifting from one atom to another, a process which undoubtedly takes place in the intermediate stages of many organic reactions.

In (5) a Wurtz synthesis has taken place and from this it may be concluded that the interdependence of the halogen and oxygen atoms is much less marked in the reaction of sodium with a β-bromo- than with an α-bromoalkylidene glycol. If Mechanism A is accepted, this may be explained as due to a less tendency to form the necessary seven-membered cyclic intermediate. On the other hand, if Mechanism B should prove correct, it means that the radical  is less stable than  in the presence of sodium.

The structure of the diacetal, C, was established by its hydrolysis to hexyl dialdehyde which underwent intramolecular "crotonization" to give Δ-cyclopentene aldehyde as described by Read and Hibbert.[6] The cyclic aldehyde was not isolated in a pure state but was identified by its semicarbazone.

The Action of Sodium on β-Bromobutylidene Glycol.—β-Bromobutylidene glycol reacted with sodium in an analogous manner to its lower homolog, β-bromopropylidene glycol. The reaction took a mixed course, effecting a union of two acetal residues on the one hand and attacking both the bromine and one oxygen atom to give a vinyl derivative and its rearrangement product, butylidene glycol on the other. Here also much of the unsaturated product underwent cyclization during isolation.

Conclusions

The results of the above and earlier experiments indicate that the position of the halogen in brominated cyclic acetals has a marked influence on the course of their reactions with metallic sodium. If the bromine is on the α-carbon a vinyl derivative is formed almost exclusively. A bromine attached to a β-carbon, however, causes more complicated changes, for in addition to the latter reaction, a Wurtz synthesis takes place. A bromine on a γ-carbon would presumably still further increase the tendency toward the linking up of two molecules.

Experimental Part

Preparation of β-Bromopropylidene Glycol.—One hundred and sixty g. (2.5 moles) of ethylene glycol was put in a 1-liter three-necked flask equipped with a mechanical stirrer operating through a mercury seal, a calcium chloride drying tube, a dropping funnel cooled by an ice-bath and containing 112 g. (2 moles) of pure acrolein, and a delivery tube. The latter was connected with a source of dry hydrogen bromide (prepared catalytically by passing a mixture of bromine and hydrogen over an electrically heated platinum spiral). The flask was cooled in an ice-bath and about 100 g. of dry hydrogen bromide was bubbled into the glycol with stirring. At this point acrolein was allowed to drop in slowly, continuing the passage of hydrogen bromide until about 100 g. more had been passed in (2.5 moles in all). After this and all of the acrolein had been

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[6] Read and Hibbert, This Journal, **46**, 1281 (1924).

added, the mixture was stirred for two hours, allowed to stand overnight without further cooling, and then stirred for two hours more at room temperature. The mixture was extracted three times with ether and the latter solution neutralized with solid sodium bicarbonate, filtered, washed several times with small amounts of cold water and dried over potassium carbonate. Fractionation under reduced pressure gave a small fore-run of sharp smelling products and 236 g. of β-bromopropylidene glycol, b. p. 72–73° (10 mm.); yield, 65% reckoned on the amount of acrolein used. There appeared to be a slight amount of decomposition during distillation and the final product possessed a somewhat sharp odor. There is less decomposition if no air is admitted through the capillary tube used to aid boiling.

Anal. Subs., 0.1539: AgBr, 0.1577. Calcd. for $C_5H_9O_2Br$: Br, 44.17. Found: Br, 43.61.

Preparation of β-Bromobutylidene Glycol.—This was prepared in an identical manner to β-bromopropylidene glycol, substituting crotonaldehyde for acrolein. From 124 g. (2 moles) of ethylene glycol, 200 g. (2.5 moles) of hydrogen bromide and 140 g. (2 moles) of crotonaldehyde, there was obtained from the first distillation 278 g. of β-bromobutylidene glycol, b. p. 70–78° (10 mm.). Refractionation gave 220 g., b. p. 76–78° (10 mm.), or 56% of the theoretical yield reckoned on the amount of crotonaldehyde used.

Anal. Subs., 0.1683: AgBr, 0.1667. Calcd. for $C_6H_{11}O_2$: Br, 41.02. Found: Br, 42.15.

This product on long standing decomposed, giving off hydrogen bromide. A sample in a well stoppered, brown glass bottle had changed to a black, solid mass on standing for one year.

Action of Sodium on β-Bromopropylidene Glycol.—Fifty-four g. of β-bromopropylidene glycol was dissolved in 100 cc. of absolute ether in a three-necked flask equipped with a reflux condenser and an efficient mechanical stirrer protected from the atmosphere. Fourteen g. of freshly cut sodium was added and the mixture warmed to gentle boiling for sixteen hours with vigorous stirring. The reaction was slower than in the case of α-bromo acetals. The sludge of accumulated salts was flushed with ether through a wire gauze to filter out unchanged sodium amounting to 6 g. The difference in the reaction of α- and β-brominated acetals is noticeable at this point from the relative amount of sodium used up by each. The β-bromo derivative used up considerably less sodium, indicating that more of the reaction linking up two molecules had taken place. Enough water to dissolve the salts was added cautiously, the mixture extracted three times with ether and the ether extract dried over potassium carbonate. Preliminary fractionation separated the product roughly into four parts: (1) b. p. 104–109° (760 mm.), yield, 7 g. (it is better to take this fraction off at about 100 mm. pressure in order to avoid overheating subsequent fractions); (2) b. p. 60–63° (16 mm.), yield, 2 g.; (3) b. p. 144–150° (11 mm.), yield, 5 g.; (4) residue, yield, 5 g.

Fraction (1). Propylidene Glycol.—This when refractionated gave pure propylidene glycol, b. p. 106–107° (760 mm.).

Anal. Subs., 0.2090: CO_2, 0.4470; H_2O, 0.1792. Calcd. for $C_5H_{10}O_2$: C, 58.82; H, 9.80. Found: C, 58.44; H, 9.52.

This product was identical in every way with propylidene glycol prepared from propionaldehyde and ethylene glycol.

Fraction (2). Hydroxyethyl-β-methylvinyl Ether.—The combined yield of this product from several runs was refractionated, giving a product of b. p. 60–61° (16 mm.).

Anal. Subs., 0.2021: CO_2, 0.4365; H_2O, 0.1742. Calcd. for $C_5H_{10}O_2$: C, 58.82; H, 9.80. Found: C, 58.90; H, 9.61.

The product was unsaturated against bromine in carbon tetrachloride and gave test reactions for the hydroxyl group. With a trace of 50% sulfuric acid it underwent a rapid reaction, from the product of which propylidene glycol was isolated, b. p. 106° (760 mm.).

The relative yields of Fractions (1) and (2) varied in different preparations, thus further indicating that the former is a secondary rearrangement product of the latter.

Fraction (3). Di-1,6-hexylidene Glycol.—This product on refractionation gave a colorless, viscous oil, b. p. 139–140° (10 mm.), which crystallized on cooling in an ice-bath.

Anal. Subs., 0.2074: CO_2, 0.4480; H_2O, 0.1662. Calcd. for $C_{10}H_{18}O_4$: C, 59.40; H, 8.91. Found: C, 59.02; H, 8.90.

Identification of Fraction (3).—Two g., b. p. 139–140° (10 mm.), was heated for two hours under reflux with 5 cc. of 5% phosphoric acid. The reaction mixture was extracted several times with ether and the latter solution neutralized with potassium carbonate and dried over the same salt. Distillation of the solvent left a small amount of an oil having the pungent aromatic odor described by Read and Hibbert for Δ-cyclopentene. The semicarbazone prepared in the usual manner gave m. p. 209° (corr.) (R. and H. give 208–209°).

Anal. Subs., 0.1529; CO_2, 0.3062; H_2O, 0.0972. Calcd. for $C_7H_{11}ON_3$: C, 54.90; H, 7.19. Found: C, 54.61; H, 7.06.

Action of Sodium on β-Bromobutylidene Glycol.—The reaction was carried out in the same manner as with β-bromopropylidene glycol, and here also fractionation of the product yielded three main fractions and a residue.

Fraction (1), butylidene glycol, b. p. 128–135° (760 mm.), yielded for the most part butylidene glycol, b. p. 132–133° (760 mm.).

Anal. Subs., 0.2024: CO_2, 0.4589; H_2O, 0.1827. Calcd. for $C_6H_{12}O_2$: C, 62.07; H, 10.30. Found: C, 61.88; H, 10.03.

Fraction (2), hydroxyethyl-β-ethyl vinyl ether, b. p. 60–65° (10 mm.). This product was unsaturated against bromine in carbon tetrachloride, gave positive tests for the hydroxyl group and underwent cyclization in the presence of a trace of 50% sulfuric acid, yielding butylidene glycol, b. p. 135°.

Anal. (Fraction (2)). Subs., 0.1990: CO_2, 0.4521; H_2O, 0.1790. Calcd. for $C_6H_{12}O_2$: C, 62.07; H, 10.30. Found: C, 61.96; H, 10.00.

Fraction (3), dimethyl-di-1,6-hexylidene glycol (?), b. p. 150–170° (15 mm.). It was impossible to obtain a sharp boiling product from this fraction but it is presumably an impure diacetal derivative corresponding to the di-1,6-hexylidene glycol isolated in the similar reaction with β-bromopropylidene glycol.

For the purpose of preparing these diacetal derivatives it would probably be more advantageous to extract them with dry ether from the original reaction mixture before the addition of water. This would effect their separation from hydroxyvinyl products, which would be left in the residue in the form of their sodium salts.

Summary

1. The synthesis of β-bromopropylidene glycol and β-bromobutylidene glycol has been carried out.

2. The reaction of these compounds with metallic sodium is described and compared with corresponding reactions of α-bromo acetals.

3. The mechanism of these reactions is discussed.

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