

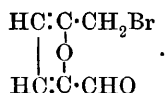
LXXXV.—*Derivatives of Methylfurfural.*

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IN previous communications (Trans., 1898, **73**, 554 ; 1899, **75**, 423), the authors have described the isolation, properties, and constitution of bromomethylfurfural,  $C_6H_5O_2Br$ . It was shown that this beautifully crystalline substance results from the action of hydrogen bromide on ketohexoses, such as lævulose and sorbose, or on carbohydrates, which are capable of giving rise to ketohexoses on hydrolysis, such as cane sugar or inulin, and that it may be obtained in a similar manner from various forms of cellulose (Trans., 1901, **79**, 361). The bromine in this compound is extremely reactive, so that it may be quantitatively estimated by direct precipitation with silver nitrate in the cold ; the substance itself is hydrolysed by boiling water, in presence of barium

carbonate, giving the corresponding hydroxy-compound ; and by oxidation with silver oxide yields the  $\omega$ -hydroxypyromucic acid previously obtained by Hill and Jennings from the corresponding bromo-acid.

From these considerations, it is evident that the bromine occupies the  $\omega$ -position, that is, it is present in the side chain and not in the main nucleus, the constitution of the compound being represented by the formula



Owing to the important relations of this compound to the carbohydrate family, and the bearing which its formation has upon questions in vegetable physiology, the authors have considered it advisable to make a further study of its derivatives, and it will be shown that owing to the extremely reactive nature of the substance it is capable of many interesting transformations.

The group or radicle  $\text{O}:\text{CH}\cdot\text{C}_4\text{H}_2\text{O}\cdot\text{CH}_2$  has evidently considerable permanence or stability, and it would be a matter of convenience if a simple name were given to it, as has been done in the case of benzyl and other analogous radicles.

*Chloromethylfurfural*,  $\text{O}:\text{CH}\cdot\text{C}_4\text{H}_2\text{O}\cdot\text{CH}_2\text{Cl}$ .—Recent experiments show that this compound may be produced by the action of hydrogen chloride on ketohexoses and on cellulose in a manner altogether similar to that employed in preparing the bromo-derivative, but that in the first case the action takes place more slowly, and the product is in the first instance more difficult to crystallise.

When lævulose, for example, is treated with hydrogen chloride under ether, there is at first no apparent change except that the solid tends to cake together. After standing for some hours, the mixture becomes pink or purple, but the colour is very much less intense than that given by the action of hydrogen bromide. In the latter case, the action begins almost immediately, and a very intense purple colour is developed within about 30 minutes.

In order to prepare the chloro-derivative, 'commercial' lævulose is covered with dry ether, and the mixture, surrounded by ice, is saturated, or nearly saturated, with dry hydrogen chloride. It is then allowed to stand for a day or two, and the resulting purple mixture is neutralised with sodium carbonate in the manner previously described for the preparation of the bromo derivative. This neutralisation process is somewhat tedious owing to the large quantity of hydrogen chloride which is necessarily present, but the operation may be economised without much loss by pouring off the ethereal part and shaking it with a small quantity of water, keeping the mixture cool,

and again extracting this aqueous solution two or three times with ether. Only the ethereal extracts and the remaining solid are then neutralised, the aqueous solution being neglected. The excess of acid may also be removed by drawing a current of air through the mixture slightly warmed on a water-bath.

The solid portion is then also extracted with ether, the joint ethereal solutions are dried over calcium chloride, and the ether is then distilled off. The yellow oil or syrup which remains generally refuses to crystallise, but when taken up with hot light petroleum and allowed to stand in a cold place it slowly deposits long, colourless, transparent prisms. In some cases, the substance separates again as an oil, but after this purification it soon sets to a crystalline mass on cooling and stirring, or, better, by sowing with a trace of either the chloro- or bromo-derivative.

The purified substance crystallises extremely well from solvents, whereas in the presence of impurities it exhibits, like the bromo-derivative, a great tendency to remain in a superfused condition. This fact, together with its low melting point, accounts for the difficulty first experienced in isolating it, the experiments having been made in hot weather.

In properties, the chloro-derivative very closely resembles the bromo-derivative, and the crystals appear to be isomorphous. It dissolves very easily in ether, alcohol, chloroform, or carbon tetrachloride, but is only sparingly soluble in hot light petroleum. It melts to a colourless liquid at 37—38°, that is, about 22° lower than the bromo-derivative; at a somewhat higher temperature, if cautiously heated, it vaporises unchanged, giving a colourless liquid which immediately crystallises when touched with a crystal of the substance.

For analysis, it was recrystallised from dry ether and dried in a vacuum desiccator.

0.1459 gave 0.2647 CO<sub>2</sub> and 0.0445 H<sub>2</sub>O. C = 49.47; H = 3.38.

0.3650 „ 0.3600 AgCl. Cl = 24.40.

C<sub>6</sub>H<sub>5</sub>O<sub>2</sub>Cl requires C = 49.82; H = 3.46; Cl = 24.56 per cent.

The halogen in this compound is, like that in the bromo-derivative, extremely reactive, so that it may be quantitatively estimated by direct precipitation by silver nitrate in aqueous alcoholic solution.

From cellulose, the compound may be prepared in the same way as the bromo-derivative (*loc. cit.*), and the product in this case usually crystallises directly from the first extraction without previous purification with light petroleum. Using carbon tetrachloride as solvent, saturated at about 0° with hydrogen chloride, and heating for two hours in a water-bath, 50 grams of Swedish filter paper gave 5.2 grams of pure crystals of the chloro-derivative. The product was in every way

identical with that prepared from lævulose ; it melted at the same temperature, and the following result was obtained on analysis :

0·3483 gave 0·3448 AgCl. Cl = 24·48 per cent.

It is evident that this is a highly economical way of obtaining the substance, and the yield may probably be considerably increased by longer heating and by further modification of the details.\*

Mixtures producing hydrogen chloride may be substituted for the gas itself ; thus, for example, a good yield is obtained from cellulose by using a mixture of phosphoryl chloride with about the calculated quantity of water and carbon tetrachloride as solvent. The substance is produced also by the direct action of dry hydrogen chloride on the carbohydrate without the use of a solvent, but the results are not so satisfactory.

When the chloro-derivative is dissolved in strong acetic acid and mixed with excess of phenylhydrazine acetate, a very voluminous, pale yellow or buff precipitate is immediately produced. This, after washing with acetic acid and then with water, contains no chlorine. It appears to consist of more than one substance, since only a part is soluble in benzene or ether, the residue being nearly insoluble even in boiling alcohol.

On adding light petroleum to the benzene or ether solution, an orange-yellow, flocculent precipitate separates which, after drying in a water-oven, melts at 118—120°. This product is being further investigated.

It seems not at all unlikely that a certain amount of the chloro-derivative may be formed in the process usually employed for the estimation of furfural in carbohydrates, &c., and in this case it is evident that its presence would considerably vitiate the results obtained by the phenylhydrazine method.

*Acetoxymethylfurfural*,  $O\cdot CH\cdot C_4H_2O\cdot CH_2\cdot O\cdot CO\cdot CH_3$ .—This substance is readily obtained by dissolving the bromo compound in glacial acetic acid and adding excess of silver acetate ; after warming and shaking for a short time, until the solution ceases to react with silver nitrate, the solution is filtered and allowed to evaporate in a vacuum desiccator over solid potash. The resulting syrup sets to a crystalline mass on stirring, and the product, after recrystallisation first from dry ether and then from boiling light petroleum, is obtained in the form of colourless, transparent prisms which melt at 55°.

\* Further experiments show that the yield is to some extent dependent on conditions such as quantity of solvent and duration of heating. This primary yield is in no sense to be regarded as the maximum obtainable ; if the residue be well washed, dried, and again subjected to the action of hydrogen chloride, a further yield is obtained which in amount appears to fall not far short of that originally produced.

The substance, after being dried in a vacuum, was analysed with the following results :

0·1473 gave 0·3082 CO<sub>2</sub> and 0·0603 H<sub>2</sub>O. C = 57·05 ; H = 4·54.

C<sub>8</sub>H<sub>8</sub>O<sub>4</sub> requires C = 57·14 ; H = 4·76 per cent.

*Benzoxymethylfurfural*, O·CH·C<sub>4</sub>H<sub>2</sub>O·CH<sub>2</sub>·O·CO·C<sub>6</sub>H<sub>5</sub>.—This compound was obtained in a manner similar to that employed in the preparation of the acetoxy-derivative, using silver benzoate, with acetone as solvent in place of acetic acid. After crystallisation from dry ether and from light petroleum, it was obtained in the form of stellate aggregates of long, colourless prisms melting at 56—57°.

0·1188 gave 0·2962 CO<sub>2</sub> and 0·0451 H<sub>2</sub>O. C = 67·99 ; H = 4·22.

C<sub>13</sub>H<sub>10</sub>O<sub>4</sub> requires C = 67·82 ; H = 4·34 per cent.

*Preparation of 5-Methylfurfural*.—Both the bromo- and the chloro-derivatives are easily reduced by stannous chloride in acid solution, giving methylfurfural identical in every respect with that obtained by fractionation of the product of dry distillation of wood, &c., and from rhamnose by the action of dilute acids.

Powdered crystals of the bromo-derivative were covered with excess of a strong solution of freshly prepared stannous chloride in hydrochloric acid and allowed to stand overnight. The mixture was then neutralised with solid sodium carbonate and distilled in steam, when a considerable quantity of nearly colourless oil separated in the distillate. The latter was shaken with ether, and the ethereal solution dried over calcium chloride. After distilling off the ether, the product boiled at 186—187°, and was analysed with the following results :

0·2135 gave 0·5135 CO<sub>2</sub> and 0·1015 H<sub>2</sub>O. C = 65·58 ; H = 5·28.

C<sub>6</sub>H<sub>6</sub>O<sub>2</sub> requires C = 65·45 ; H = 5·45 per cent.

Fourteen grams of the bromo-derivative gave about 1·9 grams of pure methylfurfural, or about 23 per cent. of that required by theory, and this yield could doubtless be increased by slight modification of the details of preparation.

The reactions of the product are in every way similar to those of the substance prepared in the other ways mentioned. With aniline acetate, it gives at first only a slight yellow colour and this, on standing for some time, changes to a bright orange-red. When a dilute solution of the substance in alcohol is carefully mixed with strong sulphuric acid, an intense and beautiful grass-green colour is developed in the upper layer of liquid (Maquenne's reaction).

The chloro-derivative also readily gives methylfurfural under similar treatment, and the yield appears to be as good or better. For this purpose, it is not necessary first to isolate the chloro-derivative ; the

mixture produced by action of hydrogen chloride on the carbohydrate may be mixed directly with excess of stannous chloride and the further operations conducted as before. It is advisable to remove most of the acid as above suggested in order to avoid excessive neutralisation. Bearing in mind the difficulty of obtaining pure methylfurfural by the older methods, it would appear that the process here described offers very considerable advantages.

*Difurfurylethanedialdehyde.*

When bromomethylfurfural, dissolved in an appropriate solvent, is heated with finely divided metallic silver, the bromine is entirely removed and a beautifully crystalline product results. Other metals in the ordinary state, such as zinc, sodium, or magnesium, appear to have little, if any, action, and in the case of silver the state of division is of great importance. The first experiments were made with silver precipitated by the sulphite method, toluene being used as solvent, and the mixture heated in sealed tubes for several hours to about 140°. Only a very small yield was obtained in this way, and it was afterwards found that by using silver reduced from the chloride by zinc, an energetic action takes place, the whole of the bromine being removed in about half an hour, and a large yield of the product obtained.

The method now adopted is as follows. Recrystallised bromomethylfurfural is mixed with a considerable excess ( $1\frac{1}{2}$  to 2 parts by weight) of finely divided silver (prepared by reducing the chloride with zinc, digesting for 24 hours with dilute sulphuric acid, washing successively with water, alcohol, ether, and benzene). The mixture is then covered with two or three times its volume of dry benzene, and heated to boiling in a reflux apparatus on a water-bath until a drop of the liquid gives no reaction with silver nitrate and nitric acid. Considerable heat is evolved in the action, the mixture becoming warm even before external heat is applied, and the operation is completed in about 30—45 minutes.

The solution is filtered off, the residue further extracted three or four times with boiling benzene, and the greater part of the benzene distilled off, when, on cooling, a bulky, yellow precipitate separates. This is drained on a porous plate and recrystallised from a mixture of boiling benzene and light petroleum. Thus obtained, the product is still bright yellow, but it may be further purified by recrystallisation from boiling water, from which it separates on cooling in long, slender prisms which are almost colourless. The substance dissolves easily in cold chloroform and fairly easily in cold glacial acetic acid, but is very sparingly soluble in most other cold solvents. It dissolves easily in hot benzene and sparingly in boiling water. It melts sharply without

decomposition at 119—120°, and at a higher temperature partly vaporises, giving a crystalline sublimate.

A dilute alcoholic solution of the substance when cautiously mixed with concentrated sulphuric acid gives a grass-green colour, resembling in this respect the behaviour of methylfurfural.

The substance, dried at 100°, was analysed with the following results :

0·1168 gave 0·2826 CO<sub>2</sub> and 0·0478 H<sub>2</sub>O. C = 65·98 ; H = 4·54.

0·1253 „ 0·3024 CO<sub>2</sub> „ 0·0483 H<sub>2</sub>O. C = 65·82 ; H = 4·28.

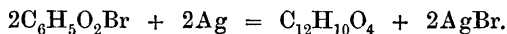
(C<sub>6</sub>H<sub>5</sub>O<sub>2</sub>)<sub>x</sub> requires C = 66·05 ; H = 4·54 per cent.

The molecular weight was determined by the freezing point method using acetic acid as solvent, and the results obtained were remarkably concordant.

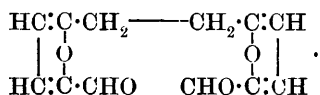
	Solvent.	Solute.	Depression.	Molecular weight.
I.	11·12	0·1974	0·307	224
II.	—	0·4093	0·635	225
III.	13·43	0·2053	0·264	224
IV.	—	0·3307	0·424	225

The calculated molecular weight for C<sub>12</sub>H<sub>10</sub>O<sub>4</sub> is 218.

The action therefore consists in the removal of two atoms of bromine from two molecules of bromomethylfurfural with linking of the residues.



From the constitution of bromomethylfurfural which was previously established (*Trans.*, 1899, 75, 429), it follows that the product at present under consideration must be represented by the following formula :



It is difficult to give this substance a simple name ; difurfurylethanedialdehyde seems to be the most appropriate.

*Action of Phenylhydrazine.*—Phenylhydrazine, benzylphenylhydrazine, and hydrazine all give white or buff precipitates with solutions of the above condensation product. A solution of the substance in strong acetic acid was mixed with rather more than twice the molecular proportion of phenylhydrazine as acetate, and the resulting bulky, nearly white precipitate was well washed with acetic acid and then with water. It was then dried in a vacuum desiccator and recrystallised from a cold mixture of absolute alcohol and ether, from which it separated in clusters of minute, transparent plates melting at 179—181°. These, dried in a vacuum desiccator, were analysed with the following result :

0.1501 gave 18.84 c.c. nitrogen at 17° and 747 mm. N = 14.53.

$C_{24}H_{22}O_2N_4$  requires N = 14.07 per cent.

The compound is therefore a *dihydrazone* having the formula  $C_{12}H_{10}O_2(N_2H \cdot C_6H_5)_2$ .

*Action of Hydroxylamine.*—A warm alcoholic solution of the dialdehyde was mixed with rather more than two molecular proportions of free hydroxylamine, also in alcoholic solution, prepared by Wohl's method. After standing for about 24 hours in a closed flask, the solution was allowed to evaporate in a vacuum desiccator over sulphuric acid, when a white, crystalline substance was deposited. This was washed with cold chloroform and recrystallised from a hot mixture of absolute alcohol and chloroform, from which it separated in colourless prisms melting at 182°. It dissolves fairly easily in warm alcohol, but is very slightly soluble in chloroform or ether. On analysis:

0.1825 gave 17.5 c.c. nitrogen at 16° and 746 mm. N = 11.15.

$C_{12}H_{12}O_4N_2$  requires N = 11.29 per cent.

The substance is therefore a *dioxime* having the formula  $C_{12}H_{10}O_2(NO_2H)_2$ .

#### *Difurfurylethanedicarboxylic Acid.*

The dialdehyde was oxidised with silver oxide in a manner similar to that employed by Hill and Jennings for the oxidation of methylfurfural (*Amer. Chem. Journ.*, 1893, 15, 167). The substance was mixed with water and an excess of freshly precipitated, well washed silver oxide, and heated in a water-bath to boiling for about half an hour. A slight excess of sodium carbonate was then added, the mixture again boiled for ten minutes, filtered, evaporated to smaller bulk, again filtered, and strongly acidified with hydrochloric acid. A voluminous white or yellowish precipitate was immediately produced, which, after cooling, was collected on a suction filter, well washed with cold water, and recrystallised, first from hot dilute alcohol and then from a mixture of absolute alcohol and toluene. The product is seen under the microscope to consist of minute, transparent prisms. It melts at 267—269°, turning black and decomposing at the same time. It is almost insoluble in cold water, acetic acid, benzene, &c., but dissolves fairly easily in hot alcohol, and easily in alkalis.

For analysis, the acid was dried at 100°:

0.1394 gave 0.2923  $CO_2$  and 0.0488  $H_2O$ . C = 57.25; H = 3.89.

$C_{12}H_{10}O_6$  requires C = 57.60; H = 4.00 per cent.

The *barium salt* was prepared by dissolving the acid in a considerable excess of hot barium hydroxide solution, removing the excess by carbon



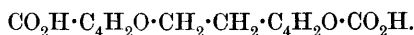
dioxide, boiling, and filtering. On allowing the solution to stand in a desiccator, the salt is slowly deposited in aggregates of transparent plates. For analysis, it was dried at 140°:

0.4813 gave 0.2872 BaSO<sub>4</sub>. Ba = 35.09.

C<sub>12</sub>H<sub>8</sub>O<sub>6</sub>Ba requires Ba = 35.58 per cent.

The barium salt is easily soluble in hot water; its solution is neutral to litmus and gives a white precipitate with silver nitrate or lead acetate.

From the mode of formation and composition of the acid and composition of the barium salt, it is evident that the acid is dibasic and has the constitution:



When the dry barium salt is mixed with quicklime and strongly heated, a yellowish oil distils over and partially crystallises on standing. It is probable that this is the parent substance, difurfurylethane, and the authors intend further to examine it.

*Condensation Product with Sulphurous Acid.*—It may be observed that the molecular formula for the dialdehyde described above, C<sub>12</sub>H<sub>10</sub>O<sub>4</sub>, differs by CH<sub>2</sub> from that of the product, which the authors previously obtained from the bromo-derivative by the action of sulphurous acid, and proved to have the molecular formula C<sub>11</sub>H<sub>8</sub>O<sub>4</sub> (Trans., 1899, 75, 431). Recent experiments with the latter compound indicate that it also reacts with two mols. of phenylhydrazine. The product does not crystallise well, so was analysed after washing carefully and then drying in a vacuum desiccator.

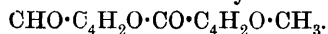
0.2169 gave 27.0 c.c. nitrogen at 19° and 731 mm. N = 14.04.

C<sub>23</sub>H<sub>20</sub>O<sub>2</sub>N<sub>4</sub> requires N = 14.58 per cent.

This phenylhydrazine derivative dissolves in concentrated sulphuric acid with a green colour, which is changed to an intense blue by the addition of manganese dioxide.

At first sight, therefore, it might be thought probable that this condensation product and the dialdehyde were homologous compounds of the same type, but this is probably not the case, since the former gives very remarkable colour reactions, which distinguish it in a marked way from the dialdehyde; with caustic alkalis, it gives an intense blue, and with aniline acetate a brilliant green colour. Further experiments are now being made with this product, and it is found that it may be produced in a similar way by the action of sulphurous acid on the chloro- and on the acetoxy-derivatives. The authors previously suggested that it might be methylfuryl, C<sub>4</sub>H<sub>3</sub>O·CO·CO·C<sub>4</sub>H<sub>2</sub>O·CH<sub>3</sub>, and the experiments

made up to the present time are in harmony, either with this assumption, or with the alternative ketone-aldehyde formula,



The isolation of the derivatives mentioned in this and preceding communications has suggested a large number of further investigations which the authors hope shortly to undertake. It would be of much interest, if, by a reversal of the change mentioned, a carbohydrate could be regenerated from one of these compounds, for example, from the hydroxy-derivative, and some experiments have already been made in this direction.

The study of the action of hydrogen cyanide on the dialdehyde and of hydrogen iodide on the dicarboxylic acid also promises to give results of considerable interest.

Most of the materials necessary for this research have been obtained by means of funds kindly supplied by the Government Grant Committee of the Royal Society.

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