

XLI.—*Bromomethylfurfuraldehyde.*

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IN a previous communication (Trans., 1898, '73, 554), it was shown by the present authors that certain carbohydrates, when treated with hydrogen bromide in ethereal solution, give an intense and beautiful purple colour. It was suggested that the reaction would probably be of service in distinguishing certain typical classes of carbohydrates, and that it might be employed for the detection of these in natural products.

The examination of a considerable number of carbohydrates of various classes led to the following generalisations.

1.—With *ketoheposes* (lævulose, sorbose), the purple colour appears after a few minutes, and becomes very intense in about one hour; and substances which, by hydrolysis, are capable of giving rise to these compounds (cane sugar, inulin) give a similar effect, only rather more slowly, the maximum colour being attained in about two hours.

2.—*Hexaldoses* (dextrose, galactose), and substances capable of giving rise to them (milk sugar, maltose, dextrin), show, in the first instance, various shades of yellow, brown, or red, and it is only after long standing that a purple colour is apparent. This colour, however, never approaches in brilliancy or intensity that obtained with substances mentioned in 1.

424 FENTON AND GOSTLING : BROMOMETHYLFURFURALDEHYDE.

3.—Carbohydrates whose molecules contain less than 6 atoms of carbon (arabinose, glycollic aldehyde) give brown or red colours without any appearance of purple, and the polyhydric alcohols show only a yellow colour.

A curious exception to this general behaviour is found in the case of *xylose*, with which a deep purple colour is obtained after a few hours; this circumstance is being further investigated.

The function of the ether in the above reaction appears to be merely that of a convenient solvent, since similar colour changes can be brought about by conducting gaseous hydrogen bromide over the dry carbohydrate. In making the experiments, it is advisable, for the sake of comparison, to employ a definite proportion of the ethereal solution and carbohydrate to be examined; in the experiments mentioned, 0.5 gram of the substance was mixed with 7.5 c.c. of a solution of hydrogen bromide in dry ether which had been saturated at about 15°, and allowed to remain in a closed vessel.

An investigation has now been undertaken with the object of throwing light upon the nature and mode of formation of this colour-giving substance, and, after some considerable difficulties, it has been isolated in a crystalline state.

If the purple ethereal solution is evaporated in a vacuum desiccator over solid potash and sulphuric acid, a purplish-black, gummy mass is obtained, and a similar result is brought about by precipitating the ethereal solution by light petroleum. On the addition of water or alkalis to the solution, the purple colour is at once discharged with separation of a dark precipitate. If, after shaking the purple mixture with excess of sodium carbonate, the ether solution is evaporated, a dark, yellowish-brown oil remains, which gives again the purple colour on the addition of hydrogen bromide. Strong hydrochloric or nitric acids give a beautiful rose colour, and strong sulphuric acid a fine but transient purple.

This oil is practically non-volatile, even under reduced pressure or in steam, and the product first obtained, which was prepared from *cane sugar*, obstinately refused to crystallise; later experiments however, have shown that even this product may be made to crystallise, in part, at any rate, by 'sowing' with a crystal of the substance subsequently obtained.

With *levulose*, however, if certain precautions be taken, the product obtained in a similar way invariably crystallises when the strong ethereal solution is allowed to evaporate. In order to obtain this result, the following method is now employed.

Five hundred c.c. of a solution prepared by saturating dry ether with dry hydrogen bromide at 15° is poured on to about 100 grams

of crystallised lævulose,* and the mixture is occasionally shaken and cooled if necessary, since a somewhat violent action often sets in after a few minutes. After standing for some time, generally 12 to 24 hours, the dark purple mixture is shaken with a saturated solution of sodium carbonate, in small portions at a time, and then with dry sodium carbonate until the reaction is decidedly alkaline to litmus; the ethereal solution is then decanted, and the dark brown residue repeatedly extracted with ether. The joint ether-extracts, which are deep yellow or orange, are left over calcium chloride for 12 hours or more, and the greater part of the ether is then distilled off, preferably under somewhat diminished pressure; the deep orange or brown oil thus obtained is again taken up with a small quantity of dry ether and filtered, if necessary, from a small quantity of a black insoluble substance. This solution, on being allowed to evaporate in an open dish, soon begins to deposit beautiful, orange-yellow, transparent prisms; crystallisation may be promoted, if necessary, by stirring, or by the addition of a little light petroleum. The yield of crude crystals is about 20—25 grams. The substance, which dissolves very easily in ether, chloroform, alcohol, or benzene, but with difficulty in boiling light petroleum, crystallises well from any of these solvents; light petroleum, however, affords the best means of purifying it. The impure crystals soon darken and decompose on keeping, so that it is advisable to purify them at once in this way. When pure, they are quite permanent.

The original orange, or deep golden-yellow, crystals behave with acids exactly in the same way as the oil above mentioned, giving intense and beautiful colours with strong hydrochloric, nitric, sulphuric, and hydrobromic acids; after one or two recrystallisations, however, they become pale yellow, and now give little, if any, colour with hydrochloric or nitric acids, and only a brown with sulphuric acid. With *hydrogen bromide*, however, best in ethereal solution, they give an intense purple exactly resembling the colour originally obtained; this colour appears even more quickly than in the case of ketohexoses, and becomes intense after a few minutes. The colours which the other acids give with the impure crystals are evidently due to the presence of traces of hydrogen bromide.

From these observations, it is evident that the substance here isolated is the cause of the purple colour obtained in the original

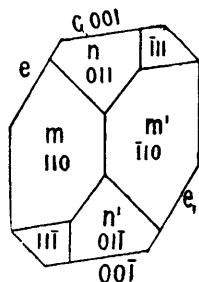
* The first experiments were made with the pure substance, but it is now found that the 'commercial' crystallised lævulose answers perfectly well for this preparation. Ordinary methylated ether is used after it has been carefully washed and dried in the usual manner. It occasionally happened that a specimen of methylated ether was supplied, which, after careful washing, and drying over calcium chloride and even over sodium, gave an indifferent or abnormal colour. But by making use of the distillate from the subsequent operation, the results are uniformly good, even after the ether has been dried for only 24 hours over calcium chloride.

experiments. The pure crystals, which contain bromine, melt sharply at 59.5° – 60.5° ; heated to a higher temperature, they decompose suddenly and somewhat explosively, giving a dense, black smoke mixed with a pink or light purple sublimate, the latter being apparently due to the action of liberated hydrogen bromide on traces of the original substance which escape decomposition.

Professor Lewis has very kindly undertaken the examination of these crystals, and the authors wish to express to him their best thanks. His report is as follows.

“The crystals of bromomethylfurfuraldehyde are oblique, and belong to the holohedral (plinthoid) class. The habit of the best crystals is well given by the plan, Fig. 1, in which the plane of symmetry is in

FIG. 1.



the paper. The forms are: $c\{001\}$, $e\{201\}$, $m\{110\}$, $n\{011\}$, $o\{111\}$; and the crystal elements are: $\beta = 80^{\circ} 42'$; $a : b : c = 1.2427 : 1 : 1.0071$.

“The following are some of the principal angles calculated and observed.

	Calculated.	Observed (mean).
ce	$52^{\circ}15.6'$	$52^{\circ}2'$
nm'	$78\ 31$	$78\ 22$
nn'	$89\ 2$	$89\ 5$
co	$56\ 21.2$	$56\ 35$
cm'	$95\ 52$	$95\ 56$
oo'	$99\ 2$	$98\ 50$
no	$31\ 44$	$31\ 48$
nm'	$61\ 18$	$61\ 26$
nm	$51\ 24$	$51\ 24$

“The crystals are very brittle, and the optic characters have not been determined. The plane of the optic axes seems to lie in the plane of symmetry, and the extinction is inclined to the vertical at an angle of 44° , and the line lies in the obtuse angle between the axes of x and z .”

In cold water, the substance is practically insoluble, but it is soluble to some extent in boiling water, and dissolves in caustic alkalis with

FENTON AND GOSTLING: BROMOMETHYLFURFURALDEHYDE. 427

a deep orange-red colour; its solutions permanently stain the skin a deep brown. Its solution in dilute alcohol quickly reduces ammoniacal silver nitrate and Fehling's solution, and with a solution of rosaniline salt decolorised by sulphurous acid it gives, after some time, a deep purplish-red colour.

Phenylhydrazine acetate gives a buff or salmon-coloured precipitate, which, however, is very unstable; it soon turns dark-coloured, and cannot be recrystallised from any of the ordinary solvents without decomposition.

For analysis, the substance was recrystallised first from light petroleum, and afterwards from ether or chloroform, and dried in a vacuum.

- I. 0.1478 gave 0.2060 CO₂ and 0.0361 H₂O.
 II. 0.1712 „ 0.2379 CO₂ „, 0.0416 H₂O.
 III. 0.2380 „ 0.3340 CO₂ „, 0.0550 H₂O.
 IV. 0.2478 „ 0.2460 AgBr. V. 0.2915 gave 0.2935 AgBr.

If an alcoholic solution of silver nitrate is added in excess to a solution of the substance, also in alcohol, the whole of the bromine is immediately precipitated as silver bromide.

VI. Treated in this way, 0.2145 gave 0.2126 AgBr.

	Found.					
	I.	II.	III.	IV.	V.	VI.
C.....	38.01	37.89	38.26			
H	2.71	2.69	2.56			
Br				42.16	42.84	42.08

The simplest formula which corresponds to these numbers is C₆H₅BrO₂; this requires C = 38.09; H = 2.64; Br = 42.32 per cent.

The molecular weight was determined by Raoult's method, using acetic acid (m. p. 16.9°) as solvent.

Weight of solvent.	Weight of substance.	Depression of freezing point.	Molecular weight.
18.94	0.2762	0.312	182.1
—	0.8302	0.902	189.5

Molecular weight for C₆H₅BrO₂ = 189.

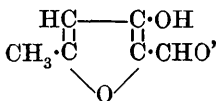
From this formula, and from certain properties of the substance, such as the yellow colour and the power of staining the skin, it was at first thought possible that it might be a quinone derivative, C₆H₄O₂.HBr, or, from the formula, it might be a substituted dihydroxybenzene, C₆H₃Br(OH)₂; but by no process of reduction or oxidation, &c., could any recognisable benzenoid compound be obtained from it.

An alternative, however, is that the substance may be a bromo-derivative of methylfurfuraldehyde, C₆H₆O₂. This supposition ap-

428 FENTON AND GOSTLING : BROMOMETHYLFURFURALDEHYDE.

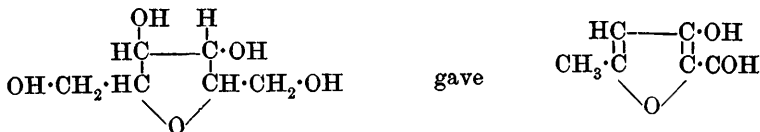
peared probable from some of the reactions of the substance; with aniline acetate paper, for example, its solutions give at first only a pale yellow colour, but this, after some time, becomes changed to a bright orange, the behaviour in this respect entirely resembling that of methylfurfuraldehyde itself (Hill and Jennings, *Amer. Chem. Journ.*, 1893, 15, 162).

Moreover, it has been shown by Düll (*Chem. Zeit.*, 1895, 19, 216) that, by heating inulin with oxalic acid solution under pressure, a derivative of methylfurfuraldehyde is produced; this substance was afterwards further examined by Kiermayer (*loc. cit.*, 1903), who prepared it in a similar way from cane sugar, the dextrose being apparently unacted on. It is described as a colourless syrup which rapidly turns yellow on exposure to the air; it is soluble in water, alcohol, and ethylic acetate, and gives a colour reaction with aniline acetate similar to that produced by furfuraldehyde. It also gives colour reactions with thymol and with phloroglucinol. It cannot be distilled unchanged. On oxidation with ammoniacal silver nitrate, it yields a hydroxymethylpyromucic acid melting at 148°. The hydr-azone and the two oximes (*anti* and *syn*) are crystalline. The substance is considered to be β -hydroxy- δ -methylfurfuraldehyde,



produced from lævulose by loss of $3\text{H}_2\text{O}$, $\text{C}_6\text{H}_{12}\text{O}_6 - 3\text{H}_2\text{O} = \text{C}_6\text{H}_6\text{O}_3$. Its formation is explained by supposing that the two terminal $\text{CH}_2 \cdot \text{OH}$ groups of lævulose lose a molecule of water, one becoming oxidised and the other reduced, so that a methyl and an aldehyde group result.

The position of the hydroxyl group is uncertain, but on various grounds it is considered to occupy the β -position. In explanation of the formation of a furfuran nucleus, reference is made to Tollens' 'lacton' formula for lævulose, so that, upon this view, the relation might perhaps be indicated in some such way as the following.



On the supposition just mentioned, it would therefore follow that there should be a close relation between the new bromo-derivative and the compound discovered by Düll. It was mentioned that the bromine in the former compound is entirely precipitated by silver nitrate, and the solution might then contain a substance identical or isomeric with

Düll's compound. Oxidation with silver oxide should yield one of the hydroxymethylpyromucic acids, and perhaps, by careful oxidation with other agents, it should be possible to obtain one of the bromomethylpyromucic acids.

Oxidation with Silver Oxide.—Following the method employed by Hill and Jennings in the oxidation of methylfurfuraldehyde (*loc. cit.*, 167), the substance was mixed with a considerable excess of freshly precipitated silver oxide suspended in water and heated to boiling for 20 minutes; sodium carbonate was then added to precipitate the silver in solution, the mixture was again boiled, filtered, evaporated to small bulk, again filtered, acidified with hydrochloric acid, and, as no acid separated on cooling, extracted with ether. The ethereal solution, on evaporation, left a brownish residue which, when re-crystallised from ethylic acetate with the addition of a little animal charcoal, gave a white, crystalline mass; better crystals were obtained, however, by using a mixture of absolute alcohol and toluene. Under the microscope, the lustrous, crystalline mass was seen to consist of long, transparent prisms or plates. The acid was fairly easily soluble in water, alcohol, and hot ethylic acetate, but only very sparingly in boiling chloroform. It melted and decomposed at 162–163°. It was dried in a vacuum and analysed, with the following result.

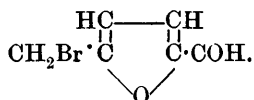
0.1264 gave 0.2334 CO₂ and 0.0495 H₂O. C = 50.35; H = 4.35.

C₆H₆O₄ requires C = 50.70; H = 4.23 per cent.

The melting point and properties of this acid entirely agree with the *ω*-hydroxymethylpyromucic acid obtained by Hill and Jennings by the action of water on the corresponding bromo-acid (*loc. cit.*, 181), and the acid is different, therefore, from that obtained by Kiermayer from Düll's compound.

The constitution of the former acid may be taken as well established. That the methyl group occupies the *δ*-position follows from Maquenne's formation of methylfurfuraldehyde from rhamnose, and the constitution of the latter as determined by Fischer and Tafel; moreover, the position of the hydroxyl group in the side chain is concluded from the 'reactive' properties of the bromo-acid from which it is derived, properties which are in striking contrast with those of the isomeric *β*-acid.

For these reasons, there can be but little doubt that the substance at present under discussion is *ω*-bromo-*δ*-methylfurfuraldehyde,



Its formation may be expressed by the relation C₆H₁₂O₆ + HBr - 4H₂O = C₆H₅BrO₂, and it is evident that, in representing the formation

430 FENTON AND GOSTLING : BROMOMETHYLFURFURALDEHYDE.

of the terminal groups an explanation must be offered which is somewhat different from that which accounts for the production of Düll's compound.

Action of Silver Nitrate.—It has been already stated that the bromine in the original substance is quantitatively separated by precipitation with silver nitrate in alcoholic solution; in order to examine the nature of this solution, a weighed quantity of the substance was dissolved in dilute (50 per cent.) alcohol, and mixed with slightly more than the calculated amount of silver nitrate dissolved in the same solvent. After filtration, the liquid was treated with a few drops of barium chloride solution to remove excess of silver, and, being strongly acid, it was then shaken with excess of barium carbonate and again filtered. After being kept in a vacuum desiccator for a day or two, yellow drops began to separate, and collected as a heavy oil at the bottom of the vessel. When most of the supernatant liquid had evaporated, the residue was taken up with absolute alcohol, filtered from barium salts, and the alcohol again evaporated. The oil or syrup thus obtained was moderately soluble in cold water, and dissolved easily in alcohol or ether; the solutions readily reduce Fehling's solution and ammoniacal silver nitrate, and with aniline acetate paper give a bright orange to brick-red coloration. With *thymol* and a few drops of moderately strong sulphuric acid, a fine pink colour is obtained, and *phloroglucinol*, with acids, gives an intense brownish-red. An ethereal solution of *hydrogen bromide* gives, immediately, an intense purple colour.

On heating, the oil begins to show signs of boiling at about 80°, but the temperature continues to rise, and no fixed boiling point is indicated. A small quantity of liquid distils over at about 200°, and behaves generally like the unaltered substance.

If the aqueous solution is treated with the calculated quantity (1 mol.) of phenylhydrazine as acetate, the liquid at once turns milky, and a red oil slowly separates, but this shows no signs of solidification, even after being kept for some days in a vacuum desiccator, or after purification by dissolving in hot dilute alcohol, from which it separates on cooling.

On oxidising this substance with silver oxide in the manner already described, an acid is obtained which melts at 162—163°, and is evidently identical with that obtained from the original substance.

From these observations, it is evident that this product bears a close resemblance to Düll's hydroxymethylfurfuraldehyde, but differs from it in some important particulars—for example, in the formation of a liquid hydrazone, and the character of the hydroxymethylpyromucic acid obtained from it on oxidation.

Action of Water.—A solution of the substance in dilute alcohol is

neutral to litmus, but on boiling it with water it slowly dissolves and the solution becomes strongly acid. If it is boiled with water, and excess of barium carbonate added to the hot solution, the filtered liquid, on extraction with ether, gives a product which appears to be identical in every way with that obtained by the action of alcoholic silver nitrate.

It appears, therefore, that the substance very readily undergoes hydrolysis, giving hydrogen bromide and hydroxymethylfurfuraldehyde. This fact, and the ease with which the original substance reacts with silver nitrate, further support the view, expressed above, that the bromine occupies a position in the side chain rather than in the nucleus.

Action of Sulphurous Acid.—When powdered crystals of the purified substance are covered with water, and sulphur dioxide is passed into the mixture, the gas is rapidly absorbed for a considerable time, and on allowing the mixture to remain for some hours, with further saturation by the gas if necessary, the whole of the solid dissolves; this solution, when treated with excess of caustic alkali, gives a magnificent blue or plum colour. Ether, chloroform, or benzene extract this colour-giving substance from the solution, and leave it as a crystalline solid on evaporation.

For the isolation of this substance, the mixture, after saturation with sulphur dioxide, was allowed to stand for 24 hours or more, and then neutralised with barium carbonate. (For convenience, it is advisable, before neutralising, to remove the excess of sulphur dioxide and part of the liquid by distillation under reduced pressure). It is then extracted 5 or 6 times, or more, with one of the above-mentioned solvents, the solution dried over calcium chloride, and the solvent distilled off, when a yellow or orange oil is left which generally sets to a crystalline mass on cooling, but sometimes remains in a superfused condition, and requires shaking, or the addition of a few drops of water, to promote crystallisation. It is then recrystallised from the smallest possible quantity of boiling water, from which it separates on cooling as a bulky yellow or orange, crystalline precipitate; under the microscope, this is seen to consist of long, transparent needles. After again crystallising from hot water or hot dilute alcohol, with the addition, if necessary, of animal charcoal, the colour is very pale golden-yellow. It is easily soluble in cold acetone, chloroform, glacial acetic acid, or hot alcohol or benzene, and dissolves sparingly in cold alcohol or ether, or hot water. It melts sharply at 116·5—117·5°, and when heated to a higher temperature, a considerable portion vaporises unchanged and condenses as a crystalline sublimate. It is also slightly volatile with steam. Its alcoholic or aqueous solutions give, with caustic potash or soda, a

432 FENTON AND GOSTLING : BROMOMETHYLFURFURALDEHYDE.

magnificent *blue* colour, which in deep layers appears red or plum-coloured ; this colour soon fades on standing. With hydrogen bromide in ether, it gives an intense but transient purple colour.

With *aniline acetate*, solutions of this product give immediately a beautiful, bright *green* colour ; a mixture of aniline with the substance in alcoholic solution gives no colour, but on the addition of acetic, tartaric, or other organic acid, the green colour appears at once. Mineral acids appear only to produce a similar effect in certain states of dilution.

The substance, crystallised from hot water and dried at 100°, was analysed.

I. 0.1268 gave 0.2991 CO₂ and 0.0455 H₂O. C = 64.33 ; H = 3.98.

This result appeared to be anomalous, since it could not be reconciled to any C₆-formula, or multiple thereof, consequently several more analyses were made with specimens which were variously treated. The melting point, however, continued to be quite constant, and the results of analysis practically the same.

II. Recrystallised from hot water and then from hot alcohol and dried in a vacuum. M. p. 116.5—117°.

III. Recrystallised from hot water containing sulphur dioxide. Dried in a vacuum. M. p. 117°.

IV. Recrystallised from hot water and then from hot alcohol, both containing sulphur dioxide. Dried at 100°. M. p. 117.5°.

II. Found, C = 64.50 ; H = 4.00 per cent.

III. „ C = 64.48 ; H = 3.98 „

IV. „ C = 64.47 ; H = 3.83 „

The simplest formula which can satisfactorily explain these numbers appears to be C₁₁H₈O₄, which requires C = 64.70 ; H = 3.92 per cent.

The molecular weight was determined by Raoult's method, with acetic acid as solvent.

	Weight of solvent.	Weight of substance.	Depression of freezing point.	Molecular weight.
I.	9.92	0.2760	0.504	215.2
II.	—	0.4203	0.774	213.4
III.	15.57	0.1461	0.169	216.5
IV.	—	0.3756	0.436	215.7

It must, therefore, be concluded that the formula is C₁₁H₈O₄, the molecular weight of which is 204.

The substance is a powerful reducing agent and acts decidedly, though feebly, as a photographic developer ; it also reacts with phenylhydrazine, but does not give the aldehydic reaction with Schiff's reagent. It would be easy, of course, to make assumptions

A REACTION OF SOME PHENOLIC COLOURING MATTERS. 433

as to its constitution; it might, for example, be methylfural, $C_4H_3O \cdot CO \cdot CO \cdot C_4H_2O \cdot CH_3$, but this is a mere conjecture, and the authors prefer to reserve the discussion of its nature and mode of formation, for a future communication, when further experiments are completed.

Oxidation with Chromic Acid.—If the original bromo-derivative is finely powdered, covered with dilute sulphuric acid, and a solution of chromic acid is slowly added to the mixture, a violent action takes place with considerable rise of temperature. By using only 1 atomic proportion of oxygen and keeping the mixture cool, a crystalline acid was obtained which closely resembled the ω -bromomethylpyromucic acid of Hill and Jennings. Its solutions gave no precipitate with silver nitrate in the cold, but after boiling the aqueous solution there was copious precipitation of silver bromide. The quantity of the acid obtained, however, was very small, the greater part of the substance remaining unchanged, so that it has not yet been fully examined. But if excess (5 atoms) of oxygen is added, and the temperature allowed to rise, another crystalline acid is obtained which is very sparingly soluble in water, and sublimes on heating.

These acids, together with several other interesting derivatives of the aldehyde, are being investigated.

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