constants such as viscosity, specific gravity, dielectric constant, refractive index, α, K_V, etc., are modified by the different substances present and corrections must be applied later to the data presented here. Only in this way can we obtain the final data freed from all normal and abnormal salt and solvent effects. It is believed from data obtained by adding some of these substances that these corrections will not be large enough to modify the general theory of the activity of both the ions and molecules of acids, bases, and salts.

JOHNS HOPKINS UNIVERSITY.
June, 1913.

[CHEMICAL SECTION, IOWA AGRICULTURAL EXPERIMENT STATION.]

A COMPARISON OF BARBITURIC ACID, THIOBARBITURIC ACID AND MALONYLGUANIDINE AS QUANTITATIVE PRECIPITANTS FOR FURFURAL.

BY ARTHUR W. DOX AND G. P. PLAISANCE.
Received July 27, 1916.

All of the methods for the quantitative determination of pentoses and pentosans in agricultural products are based upon the conversion of pentose into furfural by distillation with a mineral acid, preferably hydrochloric, and subsequent estimation of furfural in the distillate by means of a suitable reagent. Günther, Chalmot and Tollens[1] titrated the furfural with phenylhydrazine, using aniline acetate paper as an indicator. Stone[2] made use of the same reaction, but used Fehling's solution to determine the excess of phenylhydrazine. Later, Flint and Tollens[3] showed that this titration method was not accurate, on account of the levulinic acid resulting from the decomposition of hexoses, as well as the instability of the standard phenylhydrazine acetate reagent used. Jolles[4] titrated the furfural with potassium bisulfite and iodine. In the absence of other reducing substances, the furfural could be determined directly with Fehling's solution. Günther and Tollens[5] precipitated the furfural as hydrofurfuralimide by means of ammonia, while Chalmot and Tollens[6] used phenylhydrazine and weighed the resulting hydrazone. In both cases the condensation product was somewhat soluble.

Councilor[7] was the first to use phloroglucinol for the quantitative determination of furfural. This method was later studied and perfected by Tollens and his co-workers. The phloroglucinol method, although

[1] *Ber.*, **24**, 3577 (1891).
[2] *Ibid.*, **24**, 3019 (1891).
[3] *Ibid.*, **25**, 2912 (1892).
[4] *Ibid.*, **39**, 96 (1906).
[5] *Ibid.*, **23**, 1751 (1890).
[6] *Ibid.*, **24**, 694 (1891).
[7] *Chem. Ztg.*, **17**, 1743.

known to be faulty in several respects, is the one in general use to-day, having been adopted as provisional by the Association of Official Agricultural Chemists.[1] It is strictly empirical, since the nature of the reaction and the constitution of the condensation product have not been determined. Kröber[2] compiled a table in which the weight of furfural-phloroglucide obtained is interpreted in terms of furfural, xylose, arabinose or pentose. This table is purely empirical, being based on trial distillations and precipitations of the furfural, or the particular pentose employed, and not upon the molecular weight of the condensation product. Furthermore, this method calls for solubility corrections. Kröber assumes that two molecules of water are split out in the reaction between furfural and phloroglucinol. Goodwin and Tollens[3] claim that only one molecule of water is liberated at ordinary temperature, but if the reaction is carried out at a temperature of 80° three molecules are liberated. A slight variation in the conditions may, therefore, affect the result considerably. Kröber noted the fact also that when the phloroglucide is allowed to stand in the air for a time, it takes up moisture which cannot be expelled by subsequent drying. From this brief survey of the literature, it is obvious that the phloroglucinol method in common use is not altogether satisfactory.

Other reagents have also been tried with varying success. Kerp and Unger[4] used semioxamizine as a precipitant for furfural, but obtained results that were too low. Conrad and Reinbach[5] found that furfural and barbituric acid condensed in the presence of dilute hydrochloric acid. Subsequently, Unger and Jäger[6] applied this reaction to the quantitative determination of furfural. They found that six to eight times as much barbituric acid as the theory required was needed to give the calculated value for furfural. The condensation product had the advantage of being only very slightly soluble in hydrochloric acid (1.22 mg. per 100 cc.). They claim that barbituric acid does not precipitate the furfural derivatives of hexose origin and that these merely tend to color the solution yellow. The reaction is a very simple one, consisting in the condensation of one molecule of furfural and one molecule of barbituric acid, through the aldehyde group of the former and the methylene group of the latter, with the splitting out of one molecule of water. The product was found to contain 13.75% nitrogen, which is in close agreement with the calculated value of 13.63%. When prepared from the furfural distillate from natural sources, the product was found to contain 13.96% nitrogen.

[1] Bureau of Chem., *Bull.* **107**, 54 (1905).
[2] *J. Landw.*, **48**, 357.
[3] *Ber.*, **37**, 315 (1904).
[4] *Ibid.*, **30**, 590 (1897).
[5] *Ibid.*, **34**, 1339 (1901).
[6] *Ibid.*, **35**, 4440 (1902); **36**, 1222 (1903).

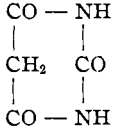
Fromherz[1] used barbituric acid as a precipitant for methyl furfural and found the condensation product to be not appreciably soluble. Fallada, Stein and Ravinka[2] found that barbituric acid and phloroglucinol gave very nearly the same results when pure xylose and arabinose were distilled and precipitated. On the other hand, when sucrose was added to the pentose, the results were very much higher when phloroglucinol was used as a precipitant than when barbituric acid was employed, the latter giving normal values. This substantiates the statements of other workers who found that hydroxymethylfurfural was not precipitated by barbituric acid.

The barbituric acid method possesses, therefore, certain advantages over the phloroglucinol method, in that the reaction is more specific and a definite condensation product is formed. The precipitate, however, is sufficiently soluble to render a solubility correction necessary. Then again, a large excess of the reagent appears to be necessary, indicating that possibly an occlusion of the precipitant leads to a compensation of errors.

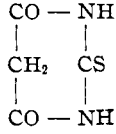
The possibility of obtaining better results by using some derivative of barbituric acid will be discussed in the experimental part of this paper.

Experimental.

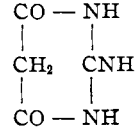
Barbituric acid is ordinarily prepared by the condensation of urea with the sodium salt of malonic ester. The corresponding thio derivative was prepared by Michael,[3] and by Gabriel and Colmann[4] by condensing thiourea with sodium malonic ester, and the imino derivative was prepared by Michael[5] and by Traube[6] from guanidine and malonic ester. These two derivatives are analogous in many respects to barbituric acid, as will readily be seen by a glance at the structural formulas given below.



Barbituric acid.



Thiobarbituric acid.



Malonylguanidine.

It remained to be determined whether they would react in a similar manner with furfural, and possibly give a more complete precipitation.

The barbituric acid used in this work was a Kahlbaum preparation, which we purified further by recrystallization from water. Analysis showed it to contain 21.80% nitrogen; theory, 21.87%.

Our first preparation of thiobarbituric acid was made according to

[1] *Z. physiol. Chem.*, **50**, 241 (1910).

[2] *Oesterr.-ung. Z. Zuckerind.*, **43**, 425.

[3] *J. prakt. Chem.*, **35**, 456 (1887); **49**, 37 (1894).

[4] *Ber.*, **37**, 3657 (1904).

[5] *Loc. cit.*

[6] *Ber.*, **26**, 2553 (1893).

the method of Gabriel and Colmann. 2.3 g. of sodium were dissolved in 50 cc. absolute alcohol, and 16 g. malonic ester added, then 7.6 g. dry thiourea, previously dissolved in absolute alcohol. The mixture was heated on a water bath for ten hours. The white pasty mass which resulted was then treated with 80 cc. water and 7.6 cc. hydrochloric acid and gently warmed until it had dissolved. Upon standing, thiobarbituric acid crystallized out. The yield was about 30% of the theory. In preparing a further quantity of thiobarbituric acid we found that a much better yield was obtained when less solvent was used and the mixture heated for 15 hours in a sealed tube at 105° with twice the theoretical amount of sodium, as recommended by Fischer and Dilthey[1] in their preparation of methylethyl- and dimethylthiobarbituric acid. The product, after acidifying with hydrochloric acid, was a slightly yellowish crystalline powder containing 19.61% nitrogen, whereas the theory calls for 19.45%. The yield in this case was 45% of the theory.

Malonylguanidine was made according to Traube from free guanidine and malonic ester. The condensation took place readily and gave an excellent yield. The product was used directly without further purification. It contained 32.71% nitrogen; theory, 33.06%.

Parallel determinations were now conducted, using barbituric acid (malonylurea), thiobarbituric acid (malonylthiourea) and malonylguanidine as precipitants for furfural. For this work a stock solution of pure, freshly distilled furfural of exactly 1% strength was prepared, and a 5 cc. aliquot taken for each determination. The furfural was diluted with 12% hydrochloric acid and solutions of the different precipitants in 12% hydrochloric acid added, the total volume of the reaction mixture being 400 cc. The conditions were, therefore, similar to those obtaining in pentosan determinations. Unless otherwise indicated, a slight excess of the precipitant was employed, the reaction carried out at room temperature, and the precipitate allowed to stand overnight before filtering on Gooch crucibles and drying to constant weight at 100°. The analytical results are set forth in the following tables.

From Table I it is at once apparent that the results with barbituric acid are uniformly low. The last three determinations show the effect of increasing amounts of the precipitant. With barbituric acid and furfural in molecular proportions of sixteen to one, the result is nearly quantitative. This observation is in accord with the statement of Unger and Jäger that eight times the theoretical amount of barbituric acid is necessary for complete recovery of the furfural.

With thiobarbituric acid, as shown in the table, the precipitation is quantitative without using a large excess of the reagent. The results

[1] *Ann.*, **335**, 350 (1904).

tend even to run just a trifle over the theory. The last two determinations show that the reaction should not be allowed to occur at a high temperature, since this leads to results that are too low.

TABLE I.

	Barbituric acid.			Thiobarbituric acid.			Malonylguanidine.		
Gram furfural taken.	Wt. of precipitate.	Gram furfural calculated.	Furfural recovered. %.	Wt. of precipitate.	Gram furfural calculated.	Furfural recovered. %.	Wt. of precipitate.	Gram furfural calculated.	Furfural recovered. %.
0.0583	0.1180	0.0550	94.3	0.1351	0.0584	100.2	0.0649	0.0305	52.3
0.0583	0.1180	0.0550[2]	94.3	0.1360	0.0588	100.8	0.0640	0.0300	51.5
0.0583	0.1171	0.0546[2]	93.6	0.1372	0.0593	101.7	0.0066[5]	0.0031	12.7
0.0583	0.1174	0.0547[2]	93.8	0.1367	0.0591	101.4	0.0035[5]	0.0016	6.6
0.0583	0.0976	0.0455[1]	78.0	0.1361	0.0588	100.8	0.0577	0.0270	46.3
0.0583	0.1194	0.0556[2]	95.4	0.1368	0.0591	101.4	0.0610	0.0286	50.9
0.0583	0.1238	0.0580[3]	99.5	0.1271[4]	0.0550	94.3			
				0.1294[4]	0.0559	95.9			

The condensation of furfural with malonylguanidine is not quantitative. The best yield in the determinations quoted above was only a little more than half the theory, hence under these conditions, malonylguanidine is not applicable for the qantitative determination of furfural.

Having shown that thiobarbituric acid in moderate excess gives quantitative results under the conditions of the above experiments, whereas barbituric acid under the same conditions gives less than 95% of the theoretical yield, it remains to compare these two reagents as regards their sensitiveness to smaller amounts of furfural. In the determinations recorded in Table II, four times the theoretical amount of barbituric acid was used.

TABLE II.—BARBITURIC ACID.

Gram furfural taken.	Wt. of precipitate.	Gram furfural calculated.	Error. Mg.	Furfural recovered. %.
0.0117	None	None	No ppt.	None
0.0117	0.0061	0.0028	— 8.9	26.5
0.0233	0.0225	0.0105	—12.8	45.6
0.0233	0.0334	0.0156	— 7.7	67.0
0.0350	0.0475	0.0221	—12.9	63.1
0.0350	0.0640	0.0298	— 5.2	85.1

It is obvious, therefore, that the barbituric acid method is inapplicable to the determination of small quantities of furfural.

In Table III, varying amounts of furfural are treated with varying amounts of thiobarbituric acid.

[1] Precipitated with a little more than the theoretical amount of barbituric acid.
[2] Precipitated with 4 times the theoretical amount of barbituric acid.
[3] Precipitated with 16 times the theoretical amount of barbituric acid.
[4] Precipitated at 60°.
[5] 0.0244 g. furfural taken.

TABLE III.—THIOBARBITURIC ACID.

Gram furfural taken.	Gram thiobarbituric acid taken.	Wt. of precipitate.	Gram furfural calculated.	Furfural recovered. %	Gram furfural taken.	Gram thiobarbituric acid taken.	Wt. of precipitate.	Gram furfural calculated.	Furfural recovered. %
0.0592	0.18	0.1369	0.0592	100.0	0.0244	0.08	0.0568	0.0247	101.2
0.0592	0.18	0.1398	0.0603	101.8	0.0244	0.08	0.0560	0.0243	99.6
0.0592	0.18	0.1370	0.0592	100.0	0.0244	0.06	0.0556	0.0240	98.3
0.0592	0.18	0.1400	0.0605	102.3	0.0244	0.16	0.0573	0.0248	101.6
0.0592	0.12	0.1390	0.0601	101.6	0.0119	0.04	0.0277	0.0120	100.8
0.0592	0.12	0.1400	0.0605	102.3	0.0119	0.04	0.0275	0.0119	100.0
0.0592	0.20	0.1372	0.0593	100.2	0.0119	0.03	0.0261	0.0113	95.0
0.0360	0.11	0.0835	0.0361	100.3	0.0119	0.08	0.0278	0.0120	100.8
0.0360	0.11	0.0852	0.0369	102.5					

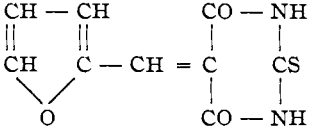
Here again, the results are just a trifle in excess of the theory. Even so small an amount of furfural as 12 mg. gave practically a quantitative yield, and variations in the amount of precipitant were of very little influence.

Analysis of the condensation products showed the percentage of nitrogen to be in close agreement with the values calculated from the formulas.

TABLE IV.—ANALYSIS OF CONDENSATION PRODUCTS.

	Nitrogen.		Sulfur.	
	Found. %	Calculated. %	Found. %	Calculated. %
Furfuralmalonylurea.....	13.60	13.65	.....	.....
Furfuralmalonylthiourea.....	12.61	12.61	14.47	14.41
Furfuralmalonylguanidine.....	15.61	16.01	.....	.....

Since the second of these products is the one with which we are chiefly concerned in this paper, the structural formula is given below.



The furfuralmalonylurea is a bright lemon-yellow, somewhat granular, precipitate which settles readily. Furfuralmalonylthiourea is also a brilliant lemon-yellow precipitate but very flocculent and voluminous. No difficulty was experienced in filtering and washing it, although the filtration was somewhat slow. It was practically insoluble in cold dilute mineral acids and only slightly soluble in hot acids. It was practically insoluble in alcohol, ether, petroleum ether, methyl alcohol, acetic acid, benzene, carbon disulfide and turpentine. In ammonia, pyridine and caustic alkalies it dissolves with ease, giving at first a greenish blue solution which gradually loses its color. From the alkaline solution it can be recovered by neutralizing with acid. The filtrates from both the furfuralmalonylurea and the furfuralmalonylthiourea had a very slight tinge of

yellow. Furfuralmalonylguanidine, on the other hand, is a very dark green, flocculent precipitate, appreciably soluble in hydrochloric acid. The filtrate is an intense greenish brown.

It was early noted that unless the thiobarbituric acid was carefully purified, the precipitation of furfural was not complete, only 90 to 95% of the latter being recovered, and the filtrate possessed a red color or sometimes a green color. In one set of determinations the difficulty was traced with reasonable certainty to the presence of cyanacetic ester in the malonic ester from which the thiobarbituric acid was made. In preparing malonic ester from chloroacetic acid in the usual way, some cyanacetic ester is apt to remain unless precautions are taken to carry the saponification to completion. This is difficult to separate from the malonic ester because the boiling points of the two substances lie only a few degrees apart. The cyanacetic ester in all probability reacts with the thiourea forming a dicyandiacetylthiourea. On fractional crystallization of one of our impure preparations of thiobarbituric acid, white needle shaped crystals were obtained, which on analysis yielded 26.66% nitrogen; calculated for dicyandiacetylthiourea, 26.65% nitrogen. These crystals when dissolved in 12% hydrochloric acid gave an intensely green precipitate with furfural, just as did the thiobarbituric acid before purification. For the preparation of thiobarbituric acid it is, therefore, recommended that the malonic ester be subjected to a repetition of the simultaneous saponification and esterification before condensation with thiourea, and that the thiobarbituric acid be purified by one or two crystallizations of its sodium salt.

Methylfurfural.—Methylpentosans often accompany the pentosans commonly found in plant structures. On hydrolysis they yield a methylpentose, usually rhamnose or fucose, and this on distillation with mineral acid is converted into methylfurfural which closely resembles furfural in most of its properties. Qualitatively, methylfurfural may be distinguished from furfural by the color reaction with aniline acetate which in this case is yellow instead of red.[1] When, however, furfural greatly predominates in the mixture, as is usually the case, the color test is not conclusive. Methylfurfural is precipitated by the same reagents which precipitate furfural, for example—phloroglucinol[2] and barbituric acid.[3] Ishida and Tollens[4] make use of the difference in solubility of the phloroglucides in alcohol for quantitative determinations, the loss in weight after extraction with alcohol being taken as representing the amount of methylfurfural phloroglucide. We have not been able to obtain satisfactory results by this method. For example, the phloroglucide prepared from pure furfural

[1] de Chalmot, *Am. Chem. J.*, **15**, 278 (1893).
[2] Votocek, *Ber.*, **30**, 1195 (1897).
[3] Fromherz, *loc. cit.*
[4] *J. Landw.*, **1911**, 60.

was appreciably soluble when subjected to continuous extraction with alcohol. At the same time the insoluble residue sometimes increased in weight during this operation. The loss in weight and the direct weight of the extracted material seldom agreed, the difference running as high as 25 mg.

Pure methylfurfural could not be obtained from the chemical supply houses or from other institutions, and the amount of rhamnose at our disposal was very limited, hence the reaction could not be carried out quantitatively with definite amounts as was done in our previous work with furfural. In the few experiments which we were able to carry out with methylfurfural, the distillate obtained by distilling rhamnose with 20% sulfuric acid was used. This was made 12% acid with hydrochloric acid and treated with thiobarbituric acid as already described. A flocculent yellow precipitate resulted, which closely resembled the corresponding furfural derivative, and showed practically the same solubilities as the latter. The filtrate was only slightly colored and gave no reaction with aniline acetate paper.

Calc. for $C_{10}H_8N_2O_3S$: N, 11.86%; N, 13.56%. Found: N, 11.91; S, 13.50.

It will be noted that methylfurfuralmalonylthiourea contains only 0.75% less nitrogen than furfuralmalonylthiourea. Owing to the relatively large size of the molecule, the introduction of a single methyl group makes only a slight difference in the percentage composition. The presence of methylfurfural in the proportion of one to three of furfural could undoubtedly be detected by analysis of the thiobarbituric acid condensation product. In mixtures where the ratio is less than one to four the lowering of the nitrogen content would be within the limit of analytical error, and hence inconclusive as evidence of the presence of methylfurfural.

Discussion.

Our experiments, quoted above, show that thiobarbituric acid condenses readily with furfural in the presence of 12% hydrochloric acid. The reaction is quantitative, giving a voluminous precipitate which can be filtered, dried and weighed. As a precipitant for furfural, thiobarbituric acid is superior to phloroglucinol, in that no correction for solubility of the product is necessary. It is also preferable to barbituric acid for the reason that the reaction is quantitative with as small amounts of furfural as 12 mg. and a large excess of the precipitant is not necessary, thus avoiding possible errors due to inclusion. Unlike the phloroglucinol product, the resulting furfurylmalonylthiourea is a definite substance resulting from the condensation of one molecule of furfural with one molecule of thiobarbituric acid by the elimination of one molecule of water, and a definite chemical formula can be assigned to it. It has a further advantage in that the percentages of nitrogen and sulfur, which agree with those

calculated from the formula, can be determined by analysis and used as a positive means of identification of the product to distinguish it from, or detect the presence of similar products which might result in case homologs of furfural were present. For example, if a mixture of furfural and sufficient methylfurfural were precipitated, the determinations of nitrogen and sulfur on the product should enable us to compute the relative amounts of these two aldehydes, and, therefore, the relative amounts of pentosans and methylpentosans in the original sample. At present the only means of estimating separately the furfural and methylfurfural present in a mixture such as is frequently met with in analysis, is the supposed differential solubility of their phloroglucides in alcohol, and this is admittedly unreliable.

It is suggested that thiobarbituric acid, which is not difficult to prepare in a pure state, may be found useful in the analysis of agricultural products, in place of phloroglucinol or barbituric acid, for the determination of pentoses and pentosans.

AMES, IOWA.

[CONTRIBUTION FROM THE CHEMICAL SECTION, IOWA STATE COLLEGE.]

CONDENSATION OF THIOBARBITURIC ACID WITH AROMATIC ALDEHYDES.

BY ARTHUR W. DOX AND G. P. PLAISANCE.

Received August 19, 1916.

The condensation occurring between aldehydes and the methylene group of malonic acid or its ester is well known. Less known, however, is the fact that the same reaction can be made to occur between aldehydes and the ureides of malonic acid. Conrad and Reinbach[1] condensed malonylurea (barbituric acid) with benzaldehyde, salicylaldehyde, *o*-nitrobenzaldehyde, *o*-aminobenzaldehyde, cinnamic aldehyde, and furfural. The reaction was carried out in aqueous solution at the temperature of the water bath. Salicylic aldehyde condensed with two molecules of barbituric acid, but in every other instance the condensation was in equimolecular proportions. Weinschenk[2] condensed barbituric acid with *p*-hydroxybenzaldehyde and with *p*-dimethylaminobenzaldehyde, heating the mixtures with alcohol on the water bath. Later, Whiteley[3] condensed 1,3-diphenylbarbituric acid with benzaldehyde and with cinnamic aldehyde, by heating with alcohol under a reflux. The same reaction was subsequently carried out by Whiteley and Mountain,[4] using 1,3-diphenylthiobarbituric acid. Jäger and Unger[5] found that in the pres-

[1] *Ber.*, **34**, 1339 (1900).
[2] *Ibid.*, **34**, 1685 (1900).
[3] *J. Chem. Soc.*, **91**, 1330 (1907).
[4] *Proc. Chem. Soc.*, **25**, 121 (1909).
[5] *Ber.*, **35**, 4440 (1902).