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FURFURAL AND SOME OF ITS DERIVATIVES

By

Joseph B. Dickey

A Thesis submitted to the Graduate Faculty for
the Degree of

DOCTOR OF PHILOSOPHY

Major subject Organic Chemistry

Approved

Signature was redacted for privacy.

In Charge of Major Work.

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1930

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The writer wishes to express his appreciation to Dr. Henry Gilman for the suggestion of these problems and for his kindly aid in the work.

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INTRODUCTION

Furfural was first prepared in 1830 by Döbereiner[1] while treating sugar with sulfuric acid and manganese dioxide in order to prepare formic acid. He noted a yellow oil in his distillate which because of its odor and method of preparation was called the "artificial oil of ants." From this date until the year 1922, furfural was a laboratory curiosity found only in the more fortunate laboratories where cost was not an item to be considered. Much of the early work on this compound was done on furfural obtained by fractionation of the high boiling residues from the destructive distillation of wood[2] of various kinds.

Killeffer[3] states that in 1922 the price of furfural was $6.50 to $30.00 per pound. Soon after, the investigations of LaForge and others[4] with corn cobs and Brownlee and others[5] with oat hulls caused the price of furfural to fall to 15 cents per pound in May 1926[3]. Mains and LaForge[6] have published specifications for a plant which could manufacture furfural from

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[1] Döbereiner, _Ann._, _3_, 141 (1832).
[2] Hill, _Am._ _Chem._ _J._, _3_, 33 (1881-2).
[3] Killeffer, _Ind._ _Eng._ _Chem._, _18_, 1217 (1926).
[4] LaForge, _Chem._ _Age_ _(N.Y.)_, _28_, 332 (1920); _C.A._, _14_, 3761 (1920); LaForge, _Ind.Eng._ _Chem._, _13_, 1024 (1921); _15_, 499 (1923); _15_, 105 (1923); Mains and LaForge, _ibid._, _16_, 356 (1924).
[5] Brownlee, _Ind._ _Eng._ _Chem._, _19_, 422 (1927); Miner, Trickey and Brownlee, _Chem._ _Met._ _Eng._, _27_, 299, 362 (1922).

corn cobs at a total cost of 6.15 cents per pound. It is quite possible that if the demand were large enough the price of production could be appreciably reduced.

The amount of furfural used at present is "about 2,000,000 pounds"[7]. Because of its low cost, the ease with which it baffles one and its great variety of as yet unexploited reactions, furfural is attracting research workers and industrialists in ever increasing numbers.

Any organic compound in order to be of commercial significance must be obtainable in large quantities and at a price which will enable it to compete with other compounds of similar chemical and physical properties. There are in the United States large quantities of untouched raw materials for the production of furfural in an inexpensive manner. At present as far as is known, all the furfural of commerce is produced from oat hulls[5] or from corn cobs[4]. Oat hulls and corn cobs are apparently the only raw materials that have been studied for the production of furfural from the commercial point of view. It is well at this time to call attention to the following facts. There is much difference between the

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6 Mains and LaForge, Ind. Eng. Chem., 16, 356 (1924).

7 We are indebted to Mr. H. T. Herrick, Principal Chemist in Charge, Color and Farm Waste Division of the United States Department of Agriculture, Bureau of Chemistry and Soils at Washington, D. C., for the above information and for the quantities of farm waste materials.

amount of furfural that can be shown to be formed from a pentosan containing raw material by one of the many methods for its production, and that economically obtainable in a commercial process. Much of the literature on the production of furfural is old. The determinations recorded were made with analytical methods not equal to those used at present.

Table I contains a list of waste[9] agricultural materials available in large quantities. This Table also shows literature references when possible to the theoretical and commercial yields of furfural. The materials listed are for the United States.

An inspection of the Table will show that furfural can theoretically be produced in large quantities. It is safe to say that the present price of furfural can be materially reduced if the demand for it were large enough. A compound potentially available in the amounts noted is surely worthy of study from an economical point of view.

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[8] Pervier, Ind. Eng. Chem., 15, 1167, 1255 (1923). These articles contain a very excellent review of the literature of the analysis of pentosan materials for furfural with pertinent references. Association of Official Agriculture Chemists Methods (1920) p. 96.

[9] The term "waste agricultural materials" is used advisedly, because there are some who maintain that these materials are worth more to the agriculturist as a soil and plant food than as a commercial commodity.

TABLE I

Source	Av. Annual Yield in Tons.	% Furfural on Comm.Basis	% Furfural on Lab.Basis	Yield in Tons on Comm.Basis	Yield in Tons on Lab.Basis
Corn stalks[7]	100,000,000		16.21[10]		16,210,000
Cereal straws[7]	115,000,000		14.5 [11]		16,670,000
Corn cobs[7]	20,000,000	9.8[12]	16.5 [10]	1,900,000	3,300,000
Oat hulls[7]	3,000,000	12.6[20]	20. [13]	378,000	600,000
Cotton stalks[7]	18,000,000		[21]		
Cottonseed hulls[7]	1,800,000		3.4 [14]		61,200
Flax straw[7]	2,200,000		14.5 [12]		319,000
Peanut hulls[7]	70,000		4.38[15]		3,066
Sugar cane bagasse	500,000		28. [16]		140,000
Beet pulp[14]	415,000		15.5 [17]		64,325
Wheat husks[19]	160,000		7.16[18]		11,456
					37379047

10 Thesis, Iowa State College Chemical Engineering Department, Ericson, Experiments with Furfural Yields from Corn Cobs and Oat Hulls, p. 13 and 23.
11 Smith, J. Chem. Soc., 65, 479 (1894).
12 LaForge and Mains, Ind. Eng. Chem., 15, 1057 (1923).
13 Miner, Trickey and Brownlee, Chem. Met. Eng., 27, 299 (1922).
14 The yield of furfural given is an unofficial statement by Mr. Arnold of the Chemical Engineering Department of Iowa State College.
15 DeBelsunce, Bull. mat. grasses, (1926) 1; C.A., 20, 2230 (1926).
16 Browne, J. Am. Chem. Soc., 26, 1221 (1904).
17 Sweeney and Creighton, (Unpublished). This work was done by the Chemical Engineering Department of Iowa State College.
18 Stone, Ber., 24, 3019 (1891).
19 U. S. Department of Agriculture, Year Book, 1930, p. 626. The yearly yield of wheat in this country is about 806,508,000 bushels and the yield of husks is about 0.4 pound per bushel.
20 Brownlee, Ind. Eng. Chem., 19, 422 (1927).
21 Reference giving the yield of furfural from cotton stalks has not yet been found.

OTHER SOURCES

The materials listed in the Table are thought to be those most easily obtained in large quantities. There are however many other sources a few of which are worth noting here.

Rice husks, when treated with 30% sulfuric acid gave a yield of furfural equal to 4%[22]. Furfural is a by-product of the sulfite process in the paper industry. In the condensate from each ton of pulp there was shown to be present 2.2 to 3.3 pounds of furfural[23]. Furfural can be produced from esparto straw in a yield of 12.8%, and from jute fiber in a yield of 5.2%[24]. Any pentosan containing material is a potential source of furfural.

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[22] Scurti and Zay, Staz. Sper. Agar. Ital., 52, 278 (1919); C.A., 14, 3673 (1920).
[23] Bergstrom, Papienfabr., 12, 1040 (1914); C.A., 9,149(1915).
[24] Cross, Bevan and Smith, Ber., 28, 1940 (1895).

PREPARATION OF SOME UNSATURATED KETONES AND FURYLACROLEIN

INTRODUCTION

The compounds whose preparation will be described were synthesized in connection with a series of studies on the 1,4-addition of various groups to conjugated furan ketones, and in a series of toxicity studies with insects[1].

Leuck and Cejka[2] have published an excellent set of directions for the preparation of furfuralacetone using furfural, acetone and dilute sodium hydroxide in water. The yields are between 60% and 66%. Schmidt[3], and Claisen[4], and Claisen and Ponder[5] have prepared furfuralacetone in a similar manner, but have not reported their yield of the compound.

Furylacrolein is the most difficult of the compounds studied to prepare in good yields. Ivanov[6], using a method which will be described in detail in the Experimental Part, reported a yield of 70%. In no case has a yield higher than 51% been obtained. Frequently yields as low as 20% were obtained. In runs in which freshly distilled furfural was used

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[1] A great variety of furan compounds have been prepared in this laboratory by Gilman, Hewlett, Wright and Dickey and their properties as insecticides have been studied.
[2] Leuck and Cejka, Org. Syn., 7, 42.
[3] Schmidt, Ber., 14, 574, 1459 (1881).
[4] Claisen, Ber., 14, 2468 (1881).
[5] Claisen and Ponder, Ann., 223, 137 (1884).
[6] Ivanov, Bull. Soc. chem., (4) 35, 1658 (1924).

in place of the commercial product there was not a noticeable increase in the yield of furylacrolein. A number of modifications of Ivanov's original directions were tried but the yields were not improved. Konig[7] has prepared furylacrolein in 61% yields by adding a 40% water solution of acetaldehyde to furfural in water with dilute sodium hydroxide at 0°. Two equivalents of acetaldehyde to one of furfural were used. Schmidt[8], and Röhmer[9] have prepared furylacrolein by warming a mixture of furfural and acetaldehyde with dilute sodium hydroxide to 50°-60°. No yields were reported by these authors. König and Hey[10] prepared furylacrolein by running acetaldehyde into furfural in the presence of small quantities of alkaline condensing agents. Their yields were not reported.

Furfuralacetophenone was prepared after the directions of Kostanecki and Podrajansky[11] with yields of 90%. The original authors did not report their yields. Semmler[12] has prepared furfuralacetophenone in practically quantitative yields by condensing furfural with acetophenone, using sodium ethylate as the condensing agent. Semmler[12] repeated the work

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[7] König, Ber., 58, 2559 (1925).
[8] Schmidt, Ber., 13, 2342 (1880).
[9] Röhmer, Ber., 31, 283 (1898).
[10] König and Hey, Ger. pat., 330, 358 (1919); C.A., 15,2102(1921).
[11] Kostanecki and Podrajansky, Ber., 29, 2248 (1896).
[12] Semmler, Ber., 39, 726 (1906); ibid., 42, 2356 (1909).

of Kostanecki and Podrajansky[10], but failed to give the yield that he obtained.

Kasiwagi[13] has prepared furyl-1-methyl-4-pentene-1-one-3, furyl-1-pentene-1-one-3, and furyl-1-methyl-2-pentene-1-one-3, in good yields by adding dilute sodium hydroxide to a mixture of furfural and the desired ketone in water.

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[13] Kasiwagi, <u>Bull</u>. <u>Chem</u>. <u>Soc</u>. <u>Japan</u>, <u>1</u>, 90 (1926); <u>C.A.</u>, <u>20</u>, 3004 (1926).

EXPERIMENTAL PART

Furfuralacetone, ($C_4H_3OCH{=}CHCOCH_3$).- Furfuralacetone was prepared after the directions of Leuck and Cejka[1]. The reaction was carried out in a 5-l. flask equipped with a mechanical stirrer, thermometer and cooling-bath. To 385 g. (3.8 moles) (335 cc.) of 95% commercial furfural in 3-l. of water was added 500 g. (8.6 moles) (630 cc.) of acetone. The reaction mixture was cooled to 10° and 75 cc. of 33% sodium hydroxide was added. After the sodium hydroxide was added the mixture was stirred for four hours and was then made slightly acid to litmus by adding 350 cc. of 10% sulfuric acid. The mixture then separated into two layers which were separated by the aid of a separatory funnel. After separation the furfuralacetone was washed with water and distilled. There were obtained 314 g. of furfuralacetone boiling at 114°-118°/10 mm. or a yield of 64%. A small amount of furfuralacetone can be obtained by extracting the water residue with ether. A large number of runs gave equally good yields.

An undetermined amount of difurfuralacetone can be obtained by distilling the high boiling residue after the furfuralacetone has been distilled off.

Furylacrolein, $C_4H_3OCH{=}CHCHO$).- 1st. Run. This compound was prepared after the directions of Ivanov[2]. To 96 g. (1.0 mole) of commercial furfural and 1000 g. of cracked ice was added 30 g. of 20% sodium hydroxide and the reaction mixture was stirred for five hours and was then neutralized with dilute acetic acid. The liquid furylacrolein was separated from the water in a separatory funnel and was well washed with water. The water residue was extracted with ether and the ether extract washed with water and added to the furylacrolein fraction. There were obtained 62 g. of furylacrolein boiling at 97°/10 mm. or a yield of 51%. A series of runs gave yields varying between 20% and 51%. Furylacrolein when pure is a white crystalline compound melting at 51° and if protected from the atmosphere will hold its color for several months.

<u>2nd. Run</u>. Run No. 1 was repeated as described except that the reaction flask was immersed in an ice-bath. The yields from 3 runs were 41%, 45% and 50%.

<u>3rd. Run</u>. Run No. 1 was repeated as described substituting pure, freshly distilled furfural for the commercial product. The yields from two runs were 40% and 45% respectively.

<u>4th. Run</u>. To 96 g. (1.0 mole) of commercial furfural in one liter of water in a 3-l. flask cooled to -10° in a bath of ice and salt was added 88 g. (2.0 moles) of acetaldehyde which had been previously cooled to 0°. To this mixture was added drop by drop over a period of one hour, 30 g. of a 20% sodium hydroxide solution. The mixture was stirred for six hours

from the beginning of the addition of the sodium hydroxide and was worked up as previously described. By this method the yields from two runs were 35% and 46% respectively.

<u>5th. Run</u>. Run No. 4 was repeated using 288 g. (3.0 moles) of commercial furfural and 264 g. (6.0 moles) of acetaldehyde in three liters of water. To this mixture cooled to 0° was added, drop by drop, over a period of two hours, 90 g. of 20% sodium hydroxide. The reaction mixture was stirred for six hours from the beginning of the addition of the sodium hydroxide. It was then worked up in the usual manner and the yield was 36.5%.

There is no obvious reason why the yield of 70% reported by Ivanov[6] was not checked. A number of other investigators in this laboratory[14] have been unable to obtain a yield of furylacrolein greater than 51%.

In every run there was left in the distillation flask a large amount of a high boiling compound or compounds. The weight of this material was such as to eliminate the possibility that an appreciable amount of furfural had not condensed with the acetaldehyde. It is quite possible that an appreciable amount of the furylacrolein formed reacted with one or more molecules of acetaldehyde to give the high boiling sub-

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[14] Gilman, Hewlett and Brown have repeated Ivanov's work and have obtained results comparable to those reported by us.

stance and thus decreased the yield of furylacrolein. In some work in connection with the attempted 1, 4-addition of ammonia and aniline with furfuralacetophenone, using dilute sodium hydroxide as the condensing agent, it was found that furfuralacetophenone polymerized to give a high melting solid. The time necessary for this polymerization was fourteen days. It is believed that a similar polymerization may have taken place in this preparation.

Furfuralacetophenone, ($C_4H_3OCH=CHCOC_6H_5$).- *1st. Run*. Furfuralacetophenone was prepared after the directions of Kostanecki and Podrajansky[11]. The reaction was carried out in a 2-l., 3-neck flask equipped with a mechanical stirrer and dropping funnel. To 96 g. (1.0 mole) of commercial furfural dissolved in one liter of 95% ethyl alcohol was added 120 g. (1.0 mole) of acetophenone. This solution was then cooled in a bath of cracked ice, and 60 g. of 10% sodium hydroxide was run in over a period of two hours. The reaction mixture was kept in a bath of ice and stirred for twelve hours after the addition of the sodium hydroxide. The reaction product was poured into two liters of water and made acid to litmus paper with acetic acid. A heavy red oil soon precipitated which was separated from the water fraction in a separatory funnel, and was well washed with water. The yield of furfuralacetophenone boiling at 187°-190°/11 mm. was 179 g. or 90%. Furfuralacetophenone when pure has a light yellow color and is quite stable.

2nd. Run. A second run using the quantities and procedure described above was carried out in methyl alcohol over a period of ten hours instead of twelve hours. The yield was 158 g. or 80%.

3rd. Run. A third run using 3 times the quantities, but the same procedure was carried out as previously described. In this run ethyl alcohol was used as the solvent and the time was the same as in the first run. The yield was 538 g. or 90%. It is quite possible that the yield of furfuralacetophenone can be increased by using pure furfural. The distillation of furfuralacetophenone is facilitated by using an oil-bath, but care must be taken to prevent superheating.

Furyl-1-methyl-4-pentene-1-one-3, ($C_4H_3OCH{=}CHCOCH CH_3CH_3$).- This compound was prepared after the directions of Kasiwagi[13]. A mixture of 9.6 g. (0.1 mole) of furfural and 25.8 g. (0.3 mole) of methylisopropyl ketone in 250 cc. of water was treated with 10 g. of 10% sodium hydroxide. The sodium hydroxide was added dropwise with stirring to the mixture cooled on an ice-bath, and the stirring was continued for seven hours. At the end of this time the reaction mixture was made acid to litmus paper with acetic acid and was worked up in the usual manner. The yield of furyl-1-methyl-4-pentene-1-one-3, boiling at 133°-136°/18 mm. was 9.6 g. or 60%. The ketone is a clear yellow, stable compound.

Furyl-1-pentene-1-one-3, ($C_4H_3OCH{=}CHCOC_2H_5$).- This compound was prepared after the directions of Kasiwagi[13]. Thirty grams of 10% sodium hydroxide was added with stirring to 28.8 g. (0.3 mole) of furfural and 64.8 g. (0.9 mole) of ethylmethyl ketone in 750 cc. of water. The reaction mixture was cooled to 0° before the addition of the sodium hydroxide and was stirred at 0°-5° for seven hours. At the end of this time the reaction mixture was made acid to litmus with acetic acid and the ketone was separated and worked up in the usual manner. The yield of furyl-1-pentene-1-one-3 boiling at 90°-95°/2 mm. was 42 g. or 93%. The ketone is a clear yellow stable compound.

Furyl-1-methyl-2-pentene-1-one-3, ($C_4H_3OCH{=}CCH_3COC_2H_5$).- This compound was prepared after the directions of Kasiwagi[13]. To 28.9 g. (0.3 mole) of furfural and 77.4 g. (0.9 mole) of diethyl ketone in 750 cc. of water cooled to 0°-5° was added with stirring 30 g. of 10% sodium hydroxide. The reaction mixture was stirred in the ice-bath for seven hours and was then made acid to litmus paper with acetic acid. The resulting ketone was separated and worked up in the usual manner. The yield of furyl-1-methyl-2-pentene-1-one-3 boiling at 135°-136°/12 mm. was 49.2 g. or 60%. Kasiwagi[13] failed to report the yield of this compound. We were able to check the yields reported by him for the other two compounds described above.

SUMMARY

A description of the methods of preparation of furfuralacetone, furylacrolein, furfuralacetophenone, furyl-1-methyl-4-pentene-1-one-3, furyl-1-pentene-1-one-3, and furyl-1-methyl-2-pentene-1-one-3 have been given.

The results of some studies on the synthesis of furylacrolein and furfuralacetophenone are reported.

THE PREPARATION OF SOME ESTERS OF TETRAHYDROFURFURYL ALCOHOL, FUROIC ACID, β-FURYLACRYLIC ACID AND SOME STUDIES ON FURFURYL ALCOHOL

INTRODUCTION

The halogenated esters of many aliphatic acids are known to be of value as insecticides and as fumigants[1]. A search of the literature has failed to uncover the report of a study in this field of chemistry with esters of the furan series. As this field is practically untouched, any halogenated ester of the furan series would be worth studying.

Many organic esters are of value as perfume bases, and for this reason the preparation of any new ester containing the saturated or unsaturated furan ring is of interest. Gilman and Wright[2] have prepared a series of esters of β-furylacrylic acid which are potential commercial perfumes and flavoring extracts.

Furfuryl alcohol has proven to be unstable in the presence of mineral acids and the halogen substituted acetic acids. This property of furfuryl alcohol has eliminated as methods of preparation many of the common methods of esterification. Tetrahydrofurfuryl alcohol is quite stable with the reagents mentioned above which is in sharp contrast with furfuryl alcohol.

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[1] Roark and Cotton, Ind. Eng. Chem., 20, 512 (1928).

[2] Gilman and Wright, Iowa State College J. Sci., 3, 109 (1929); C.A., 23, 3993 (1929).

Wissell and Tollens[3] have prepared furfuryl acetate by the action of acetic anhydride on furfuryl alcohol. In the same study they prepared furfuryl benzoate by treating furfuryl alcohol with benzoyl chloride and dilute sodium hydroxide. Zanetti[4], and Miner[5] have prepared esters of furfuryl alcohol in good yields by the action of the acid anhydride on the alcohol in benzene. Zanetti[6] has prepared furfuryl furoate using the Schotten and Baumann reaction which involves the addition of an acid chloride to a dilute sodium hydroxide solution of the alcohol.

The esters of furoic acid are easily prepared by the action of the acid chloride on various aromatic and aliphatic alcohols as described by Zanetti[6]. Hill and Jackson[7], and Zanetti and Beckmann[8] have prepared various aliphatic esters of furoic acid using sulfuric and hydrochloric acids as catalysts. In general the yields are good.

Marckwald[9] has shown the peculiar effect of hydrogen chloride on α-furylacrylic acid which eliminates this acid as a catalyst for esterification purposes. Marckwald[10]

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[3] Wissell and Tollens, Ann., 272, 301 (1890).
[4] Zanetti, J. Am. Chem. Soc., 47, 535 (1925).
[5] Miner, Org. Syn., 7, 44.
[6] Zanetti, J. Am. Chem. Soc., 47, 1452 (1925).
[7] Hill and Jackson, Am. Chem. J., 12, 24 (1890).
[8] Zanetti and Beckmann, J. Am. Chem. Soc., 48, 1067 (1926).
[9] Marckwald, Ber., 20, 2813 (1887).
[10] Marckwald, Ber., 21, 1404 (1888).

has shown that ethyl β-furylacrylate can be prepared in unsatisfactory yields by the action of concentrated sulfuric acid on β-furylacrylic acid and ethyl alcohol.

Gilman and Pickens[11] prepared the hydrochloride of β-diethylamino-ethyl β-furylacrylate by the action of the acid chloride on the alcohol in benzene solution in a yield of 78%. In a paper published since this work was completed Gilman and Wright[2] have prepared the *n*-propyl and furfuryl esters of βfurylacrylic acid in good yields by adding a benzene solution of the alcohol to a solution of the acid chloride in benzene.

Furfuryl alcohol when treated with monochloroacetic acid and dichloroacetic acid or their acid chlorides, literally exploded. This was true when dilute solutions of the alcohol in dry benzene were used. The method of Ferns and Lapworth, and Einhorn[12] in which an alcohol was added to an acid chloride-pyridine complex in a suitable solvent was investigated. This method was tried with monochloroacetyl chloride and with dichloroacetyl chloride but in each case tar was the only product.

Gilman and Brown[13] have prepared tetrahydrofurfuryl

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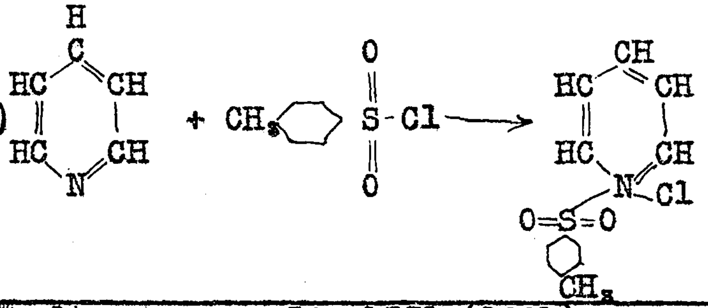
[11] Gilman and Pickens, *J. Am. Chem. Soc.*, *47*, 245 (1925).
[12] Ferns and Lapworth, *J. Chem. Soc.*, *101*, 273 (1912); Einhorn, *Ann.*, *301*, 95 (1898).
[13] Gilman and Brown in unpublished work in this laboratory.

p-toluenesulfonate using the method of Hahn and Walter[14], and Gilman and Beaber[15]. The yield of the stable ester was 93%. Ferns and Lapworth[16] and Gilman and Beaber[14] have developed an excellent method for the introduction of alkyl and alkyl-aryl groups into the benzene ring by treating the esters of *p*-toluenesulfonic acid with various substituted arylmagnesium halides. The application of the method developed by these authors would be of great assistance in synthesizing furan compounds not now known.

A number of attempts were made to prepare furfuryl *p*-toluenesulfonate after the directions of Gilman and Beaber[15] but in no case was a trace of the desired ester obtained. The method of Ferns and Lapworth, and Einhorn[12] proved to be equally unsuccessful even though a reaction took place as indicated by a rise in temperature of the reaction mixture. Ferns and Lapworth[12] reported a similar result from the attempted preparation of benzyl *p*-toluenesulfonate. They explained the non-formation of the desired ester by the following equations.

(1)



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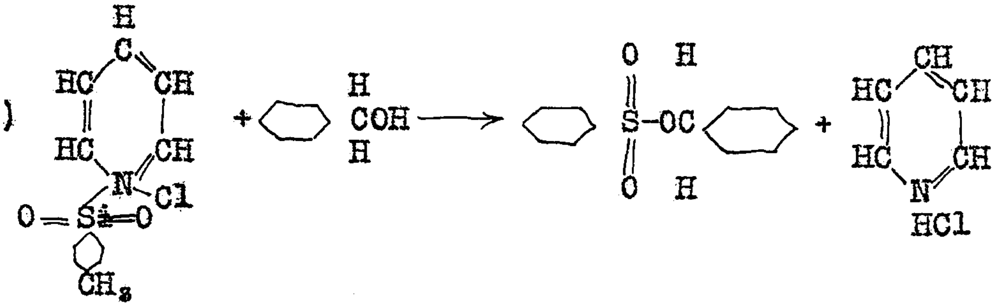
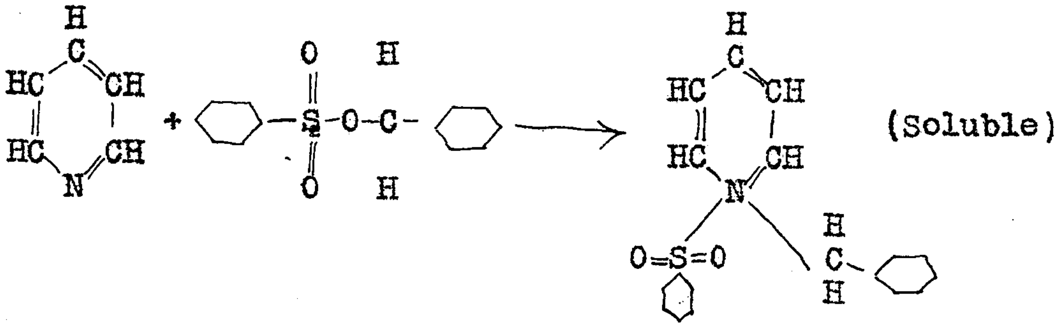
14 Hahn and Walter, *Ber.*, *54*, 1531 (1921).
15 Gilman and Beaber, *J. Am. Chem. Soc.*, *45*, 839 (1923); *ibid.*, *47*, 518 (1925).
16 Ferns and Lapworth, *Proc. Chem. Soc.*, *28*, 18 (1912).

(2)



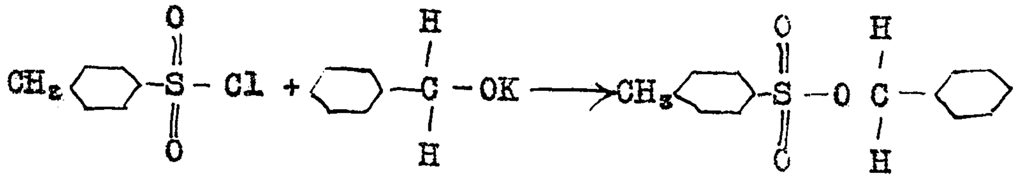
(3)

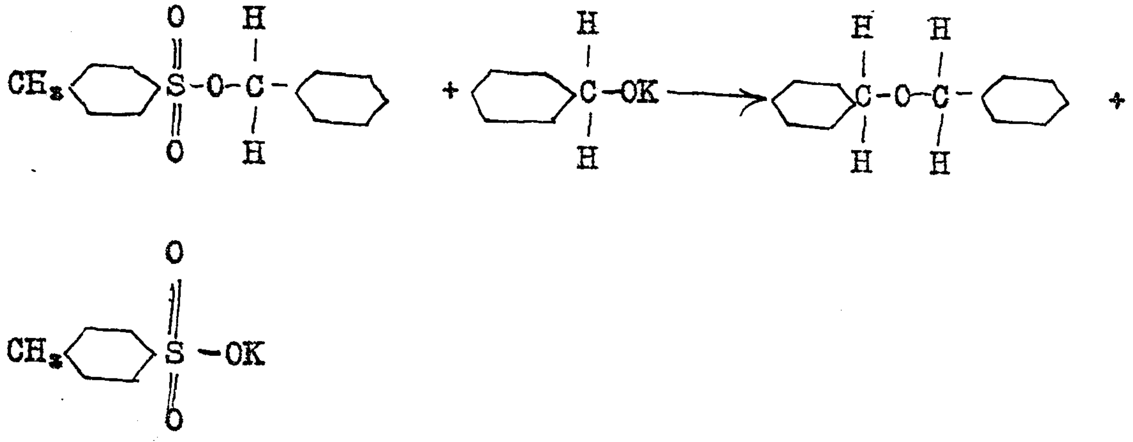


The above equations postulate the formation of the ester which then reacts with pyridine to form a water soluble complex which would be lost under the conditions the reaction was worked up. It is possible that a similar thing happened with furfuryl alcohol.

Sodium furfurylate was prepared by heating furfuryl alcohol with sodium or by heating furfuryl alcohol and sodium in toluene. The sodium furfurylate was characterized by treating it with acetyl chloride to prepare furfuryl acetate[3] in a yield of 75%. When sodium furfurylate was treated in ether with p-toluenesulfochloride a vigorous reaction took place and a white water soluble precipitate was formed. The ether solution was then distilled and yielded a colorless stable liquid which had the boiling point reported by Zanetti[17] for di-α-furfuryl ether.

This compound did not contain sulfur and could not be hydrolyzed with boiling alcoholic potassium hydroxide. Ferns and Lapworth[12] prepared dibenzyl ether by treating potassium benzylate with *p*-toluenesulfochloride in benzene. They have proposed the following mechanism to account for the formation of dibenzyl ether.

(1)


(2)


It is quite possible that the di-α-furfuryl ether isolated was formed in a similar manner.

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[17] Zanetti, *J. Am. Chem. Soc.*, *49*, 1061, 1065 (1927).

Gangloff and Henderson[18] have reported the formation of a black crystalline solid when furfural was treated with anhydrous aluminum chloride in the cold. This complex was unstable. Several attempts were made to condense furfuryl alcohol with benzene using anhydrous aluminum and zinc chlorides as the condensing agents. In each case a vigorous reaction took place which became violent as the temperature rose. Tar was the only product.

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[18] Gangloff and Henderson, J. Am. Chem. Soc., 39, 1424 (1917).

EXPERIMENTAL PART

Reagents.

The acid chlorides and acids used in the preparation of the esters were C. P. materials. All of the solvents used were dried over sodium.

The furoyl chloride and β-furylacryloyl chlorides were prepared after the directions of Gilman and Hewlett[19] in the yields reported by them. It was found that furoyl chloride if distilled under reduced pressure is water white and will remain so indefinitely. This method will prevent the slow decomposition of the acid chloride.

All reactions unless otherwise stated were carried out in a 3-neck flask equipped with a mercury seal stirrer, dropping funnel and Hopkins condenser. The Hopkins condenser and dropping funnel were protected from the atmosphere by means of calcium chloride tubes.

The trimethylacetyl chloride used was prepared from trimethylacetic acid[20]. The reaction was carried out in a 3-neck flask equipped with a mercury seal stirrer, dropping funnel and Hopkins condenser. To 30.6 g. (0.3 mole) of trimethylacetic acid in 60 cc. of anhydrous ether was added with stirring 46.1 g. (0.36 mole) of thionyl chloride over a

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[19] Gilman and Hewlett, *Iowa State College J. Sci.*, *4*, 27(1929).

[20] We are indebted to Mr. A. E. Zoellner of this laboratory for the trimethylacetic acid.

period of one hour. The heat of reaction caused the ether to reflux and when the reaction had subsided to the point at which no refluxing of the ether took place the reaction mixture was warmed on a water-bath for one hour. The product was distilled after removal of the ether and low boiling decomposition products. There were obtained 14.8 g. of trimethylacetyl chloride boiling at 105.5°-107°/740 mm. or a yield of 41%. The acid chloride is a stable compound of pungent odor.

Tetrahydrofurfuryl Acetate, ($C_4H_7OCH_2OCOCH_3$).- Seventeen and three-tenths grams (0.22 mole) of acetyl chloride were dissolved in 75 cc. of boiling benzene. To this boiling solution was added with stirring over a period of two hours 20.4 g. (0.2 mole) of tetrahydrofurfuryl alcohol in 50 cc. of benzene. Hydrogen chloride was evolved from the start of the reaction and the solution turned a greenish blue color. The reaction was heated for four hours from the first addition of the alcohol. After the benzene was distilled off the resulting product was taken up in ether and washed with 5% sodium bicarbonate, and then dried over anhydrous sodium sulfate. The ether solution was then distilled. The yield of tetrahydrofurfuryl acetate[21] boiling at 61°-62°/4 mm. was 23.2 g. or 80.5%. This compound is water white and stable and has a slight fruity odor, and flat taste.

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[21] Zanetti, J. Am. Chem. Soc., 50, 1821 (1928). This work was published shortly after our work was completed.

The following esters were prepared as described for tetrahydrofurfuryl acetate; tetrahydrofurfuryl benzoate[21], ($C_4H_7OCH_2OCOC_6H_5$), tetrahydrofurfuryl β-furylacrylate ($C_4H_7OCH_2OCOCH{=}CHC_4H_3O$), tetrahydrofurfuryl cinnamate, ($C_4H_7OCH_2OCOC(CH_3)_3$) and 2-chloroethyl β-furylacrylate ($C_4H_3OCOOCH_2CH_2Cl$). The analyses and physical constants of these compounds will be given in Table II. The esters named are stable with the exception of 2-chloroethyl β-furylacrylate which decomposed to a tar at room temperature in two weeks. Tetrahydrofurfuryl acetate and 2-chloroethyl furoate were the only esters prepared with a pleasant odor.

<u>Tetrahydrofurfuryl Monochloroacetate</u>, ($C_4H_7OCH_2OCOCH_2Cl$).- This compound was prepared after the general directions of Hill and Jackson[7], and Zanetti and Beckmann[8]. Forty and eight-tenths grams (0.4 mole) of tetrahydrofurfuryl alcohol and 37.8 g. (0.4 mole) of monochloroacetic acid were added to 100 cc. of benzene saturated with dry hydrogen chloride. The solution was treated with hydrogen chloride from time to time over a period of fifty hours. After the benzene had been distilled off the residue was taken up in ether and washed with 5% sodium bicarbonate and dried over anhydrous sodium sulfate. The yield of tetrahydrofurfuryl monochloroacetate boiling at 101°-104°/4 mm. was 35 g. or 49.3%. The

compound is a stable water white liquid of pungent taste and practically no odor. It is soluble in ether, alcohol, and benzene and insoluble in water. The analysis and physical constants for this ester are given in Table II.

Tetrahydrofurfuryl Dichloroacetate, $C_4H_7OCH_2OCO$ $CHCl_2$).- This compound was prepared exactly as described for tetrahydrofurfuryl monochloroacetate. The yield of tetrahydrofurfuryl dichloroacetate boiling at 106°-108°/4 mm. was 49.5 g. or 58.1%. The compound is a stable colorless liquid of practically no odor but a sharp taste. It is soluble in alcohol, benzene and ether and insoluble in water. The analysis and physical constants of this ester will be given in Table II.

2-Chloroethyl Furoate, ($C_4H_3OCOOCH_2CH_2Cl$).- Twenty-six and two-tenths grams (0.22 mole) of furoic acid were dissolved in 100 cc. of benzene with 16.2 g. (0.2 mole) of ethylene chlorohydrin. The reaction mixture was saturated with dry hydrogen chloride gas and this was continued intermittently for five days. After the benzene was distilled off the product was taken up in ether and washed with 5% sodium bicarbonate. The ether solution was dried over anhydrous sodium sulfate and distilled. The yield of 2-chloroethyl furoate boiling at 116°-117°/4 mm. was 2.8 g. or 8%. 2-Chloroethyl furoate is a stable water white liquid. It is soluble in alcohol, ether and benzene and insoluble in water. The compound has an odor similar to ethyl furoate but not so strong. It has a sharp pungent taste. The analysis and physical constants for this ester are given in Table II.

Action of the Chloroacetic Acids and Acid Chlorides on Furfuryl Alcohol.- Mono and dichloroacetic acids reacted violently with furfuryl alcohol when added to the alcohol, or to the alcohol in dry benzene. The alcohol was completely decomposed. The acid chlorides reacted with explosive violence with the alcohol or with the alcohol in a dilute benzene solution[22].

Reaction Between Mono- and Dichloroacetyl Chloride and Furfuryl Alcohol in a Pyridine-Chloroform Solution.- The reactions noted above indicated that it would be necessary to carry out any esterification of furfuryl alcohol with the acid chlorides in an anhydrous basic medium such as pyridine.

Twenty-two and six-tenths grams (0.2 mole) of monochloroacetyl chloride were added in small portions to a well cooled solution of 18.2 g. (0.23 mole) of pyridine in 50 cc. of anhydrous chloroform. To this solution was added 19.6 g. (0.2 mole) of furfuryl alcohol in 25 cc. of chloroform over a period of one hour at 25°. It was noted that the solution became a deep brown color. After the addition of the acid chloride the solution was heated for five hours at 70°-75° on a water-bath. The reaction mixture was then allowed to

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[22] Gilman and Hewlett in this laboratory, after the above observation treated sodium furfurylate with monochloroacetyl chloride in toluene. The alcohol was completely decomposed.

stand at 25° overnight and diluted with 100 cc. of chloroform. The black solution was then washed 5 times with water. There was much decomposition material and it was necessary to filter the solution. It was then well dried over anhydrous sodium sulfate and the chloroform removed on a water-bath. After the removal of the chloroform there was a small amount of a black liquid. An attempt was made to distil the liquid at 4 mm. but it exploded. The experiment was repeated using a 300% excess of pyridine in place of a 15%excess. The same results were obtained.

Twenty-nine and four-tenths grams (0.2 mole) of dichloroacetyl chloride were added in small portions to a well cooled solution of 63.2 g. (0.8 mole) of pyridine in 50 cc. of chloroform. To this solution was added over a period of one hour 19.6 g. (0.2 mole) of furfuryl alcohol in 50 cc. of chloroform. The reaction was started at 25° and turned black with the addition of the alcohol. There was evidence of a reaction as shown by the evolution of heat. The reaction mixture was heated for five hours on a water-bath at 70°-75° after the alcohol had been added. It was worked up as previously described. As soon as all the chloroform was removed the residue exploded. These experiments indicate that if the mono- and dichloroacetyl esters of furfuryl alcohol were formed they are unstable, and that the alcohol is very unstable in contact with the acids and acid chlorides.

Sodium Furfurylate, ($C_4H_3OCH_2ONa$).- Zanetti[6] has described an attempted condensation between sodium ethylate and a solution of sodium in furfuryl alcohol. Zanetti expressed the opinion that sodium furfurylate had been formed and mentioned his intention to prepare and prove the presence of this compound. A search of the literature has failed to show further mention of the reaction between furfuryl alcohol and sodium.

The sodium was prepared for use by cutting it up into small pieces in a tared beaker containing anhydrous ether or benzene. Two and three-tenths grams of sodium (0.1 atom) were added portionwise to 9.8 g. (0.1 mole) of furfuryl alcohol in a 50 cc. Erlenmeyer flask. The flask was equipped with a Hopkins condenser and protected from the atmosphere by a calcium chloride tube. A vigorous reaction took place with the evolution of hydrogen and heat. Towards the end of the reaction the mixture set to a solid and it was necessary to apply heat to cause the reaction to continue. It was estimated that approximately 70% of the theoretical amount of sodium was used. The solid that was formed was of a deep red color which deepened with heating.

This method was modified by the use of toluene. Toluene was chosen because its boiling point is above the melting point of sodium. It was hoped that this would facilitate the reaction. The reaction was carried out in a 250 cc.

3-neck flask equipped with a mercury sealed stirrer and Hopkins condenser. Nine and eight-tenths grams (0.1 mole) of furfuryl alcohol and 50 cc. of anhydrous toluene were placed in the reaction flask. The sodium cut in small pieces was added to this solution and a vigorous reaction took place. After the reaction had abated the mixture was heated to boiling until hydrogen ceased to be evolved. All of the sodium was not added. The amount of sodium used was approximately 80% of the theoretical. It was desired to test the stability of sodium furfurylate and its possible value in the synthesis of esters of furfuryl alcohol. With these points in mind the reaction mixture described above was exposed to the atmosphere and 7.8 g. (0.1 mole) of acetyl chloride was poured in. A vigorous reaction took place and the mixture darkened. The mixture was warmed for one-half hour after the reaction had subsided. It was then washed with water and distilled. The yield of furfurylacetate boiling at 84°-85°/25 mm. was 10.5 g. or 75%. By the use of a more refined technique the yield of esters from sodium furfurylate should be improved.

<u>Some Studies on the Attempted Preparation of Furfuryl p-Toluenesulfonate</u>, ($C_4H_3OCH_2O{-}SO_2C_6H_4CH_3$-p).- The following reaction was carried out after the directions of Hahn and Walter[15]. Twenty-two and four-tenths grams (0.4 mole) of finely powdered potassium hydroxide was added in 0.5 g. portions to 38.1 g. (0.2 mole) of dry p-toluenesulfo chloride and 19.6 g.

(0.2 mole) of furfuryl alcohol dissolved in 500 cc. of anhydrous ether. The ether solution was cooled to 0° before the addition of potassium hydroxide, which was added over a period of three hours. The temperature of the reaction mixture was kept between 0°-4° and for ten hours from the time of the first addition of potassium hydroxide. It was noted that the reaction mixture turned a grey color towards the end of the reaction. After the reaction mixture had been poured into iced water, it was extracted with ether. The ether layer after separation was washed with water and then dried with potassium carbonate. It was found very difficult to separate the ether-water layer due to a considerable amount of decomposed material and a very troublesome colloid. This was overcome by filtering on a Büchner funnel. The ether was removed on a water-bath and a considerable amount of a yellow liquid remained. The liquid soon decomposed to a resin.

A second experiment was carried out as described for the previous one. The dry ether solution was treated with phenylmagnesium bromide as described by Gilman and Beaber[15]. There was a reaction between the supposed ester and the Grignard reagent and a white precipitate was formed. After the reaction was completed it was hydrolyzed by pouring into cold water containing a small amount of acetic acid. The hydrolyzed mixture was extracted with ether and distilled. Apparently no products were formed other than diphenyl.

A third experiment was carried out as described. The resulting oil was analyzed for sulfur by the Carius method. The results showed that the oil was a mixture, probably of p-toluenesulfonic acid, p-toluenesulfo chloride, furfuryl alcohol, and traces of furfuryl p-toluenesulfonate if formed. The amount of sulfur found to be present was 4.39% against the theoretical of 12.72%.

A fourth experiment was carried out as described except that the reaction mixture was filtered and not washed with water as it was thought that water might have caused the decomposition of the ester if formed. A sulfur analysis showed 2.20% sulfur. This experiment indicates that the ester was not formed as a sulfur analysis of the product should show more approximately the theoretical amount of 12.72%. A number of runs were made in which the reaction time was varied from ten to thirty hours. There was no evidence of the formation of furfuryl p-toluenesulfonate.

One attempt was made to prepare furfuryl p-toluenesulfonate by heating the alcohol and p-toluenesulfo chloride in dry benzene. Nineteen and six-tenths grams (0.2 mole) of furfuryl alcohol and 38.1 g. (0.2 mole) of p-toluenesulfo chloride were dissolved in 100 cc. of benzene. The solution was refluxed and the furfuryl alcohol decomposed to a tar. Hydrogen chloride was not evolved.

A number of attempts were made to prepare furfuryl p-toluenesulfonate after the directions of Ferns and Lapworth, and Einhorn[12]. To 38.1 g. (0.2 mole) of p-toluenesulfo chloride in 50 cc. of anhydrous chloroform was added with stirring 23.7 g. (0.3 mole) of pyridine. The chloroform solution was cooled in an ice-bath before the addition of the pyridine. After the addition of the pyridine the ice-bath was removed and the mixture was allowed to warm to 25°. A solution containing 19.6 g. (0.2 mole) of furfuryl alcohol and 7.9 g. (0.1 mole) of pyridine in 25 cc. of chloroform was run in slowly. The temperature of the reaction mixture rose from 25° to 60° and the mixture turned brown. At the end of two hours the reaction mixture was heated to boiling for four hours and poured into water, and extracted with chloroform. It was dried over potassium carbonate and distilled. The only product was a small amount of tar. A second run was carried out on an ice-bath and not refluxed. The result was the same. A series of runs using both methods failed to produce a trace of the desired ester.

p-Toluenesulfo chloride reacted vigorously with sodium furfurylate. The sodium furfurylate was prepared as described in the first method and suspended in anhydrous ether. When the sodium furfurylate from 9.6 g. (0.1 mole) of furfuryl alcohol suspended in 50 cc. ether was treated with 19.0 g. (0.1 mole) of p-toluenesulfo chloride in 50 cc. ether a vigorous reaction took place and a white precipitate formed. After the reaction had subsided the mixture was washed with water, dried and distilled. The ether solution yielded a small amount of furfuryl alcohol and p-toluenesulfo chloride.

A second run containing the sodium furfurylate from 49 g. (0.5 mole) of furfuryl alcohol suspended in 250 cc. ether was treated with 95 g. (0.5 mole) of p-toluenesulfo chloride in 250 cc. ether. After the first vigorous reaction had subsided the mixture was refluxed for two hours. The ether solution was washed with water and 5% sodium bicarbonate and dried. After the ether was removed on a water-bath the resulting product was distilled. A yield of 8 g. of a light yellow liquid was obtained boiling at 110°-112°/6.5 mm. This compound did not contain sulfur and could not be hydrolyzed by boiling it with alcoholic potassium hydroxide.

Ferns and Lapworth[12] prepared dibenzyl ether by treating potassium benzylate with p-toluenesulfo chloride in benzene and explained the formation of the ether as discussed in the Introduction to this study.

It is believed that the compound is di-α-furfuryl ether and formed by a similar series of reactions as that advanced to explain the formation of dibenzyl ether. Zanetti[17] has prepared di-α-furfuryl ether by the action of α-furfuryl bromide and iodide on the alcohol in presence of potassium hydroxide, and reported its boiling point as 101°-102°/2 mm. No further information was obtained to prove the identity of the compound.

Reaction Between Furfuryl Alcohol, Benzene and Anhydrous Aluminum and Zinc Chlorides.- Nineteen and six-tenths grams (0.2 mole) of furfuryl alcohol were dissolved in 50 g. (0.64 mole) of anhydrous benzene, and to this solution was added 26.6 g. (0.1 mole) of anhydrous aluminum chloride at room temperature. The reaction mixture was stirred and after a short time the temperature of the reaction mixture rose and a violent reaction took place with decomposition of the alcohol. Tar was the only product.

Zinc chloride was substituted for aluminum chloride in the reaction just described with similar results. Tar was the only product.

TABLE II

CONSTANTS AND ANALYSES OF ESTERS OF FUROIC ACID, β -FURYLACRYLIC ACID AND TETRAHYDROFURFURYL ALCOHOL

Ester	Yield	B. P.	d_{20}^{20}	Analysis Carbon		Hydrogen	
				Calc.	Found	Calc.	Found
Tetrahydrofurfuryl acetate	80.5%	61-62/45mm.	1.0587				
" benzoate	72.8%	164-166/5mm.	1.1239				
" β-furylacrylate	84.7%	163-167/4mm.	1.1450	64.83	64.95 64.90	6.36	6.20 6.24
" cinnamate	77.5%	180-181/4mm.	1.1199	72.37	72.05 72.14	6.94	6.75 6.81
" trimethyl acetate	79.0%	137-138/40.5 mm.	0.9764	64.46	64.36 64.12	9.75	9.80 9.53
				Chlorine			
" monochloro acetate	48.8%	101-104/4mm.	1.2282	19.86	20.01 20.00		
" dichloro acetate	58.1%	106-108/4mm.	1.3095	31.66	31.84 31.62		
2 - Chloroethyl furoate	8.0%	116-117/9mm.	1.2952	20.31	19.95 20.05		
2 - Chloroethyl β-furyl-acrylate	80.0%	130-132/4mm.	1.2343	17.68	17.56 17.50		

SUMMARY

A number of esters of tetrahydrofurfuryl alcohol, _-furylacrylic acid and furoic acid have been prepared with a view to their utilization as insecticides, fumigants or perfumes. The attempted preparation of mono-and dichloroacetyl esters of furfuryl alcohol and of furfuryl *p*-toluenesulfonate has been discussed.

Sodium furfurylate has been prepared and characterized.

Several experiments with furfuryl alcohol and anhydrous zinc and aluminum chlorides have been described.

SOME STUDIES ON THE PREPARATION OF KETONES CONTAINING THE FURAN RING AND THE MONO- AND DIHYDROXYBENZENES

INTRODUCTION

This study was carried out in order to prepare some furan ketones containing one or more hydroxyl groups for physiological studies and as insecticides.

Phelps and Hale[1] were the first to prepare a ketone containing the furan ring by means of the Friedel-Crafts reaction. They prepared 2,5-dibenzoyl furan in a yield of 96% by the action of dehydromucyl chloride on benzene in the presence of anhydrous aluminum chloride.

Marquis[2] prepared 2-benzoyl furan in a similar manner using furoyl chloride, benzene and anhydrous aluminum chloride in a yield of 85%.

Gilman and Hewlett[3] by the method of Phelps and Hale[1] prepared a number of 2-benzoyl furans in which the benzene ring contained various substituents.

Renshaw and Naylor[4] treated pyrogallol with furoic acid and anhydrous zinc chloride and obtained a red-brown substance. The structure of the substance was not given.

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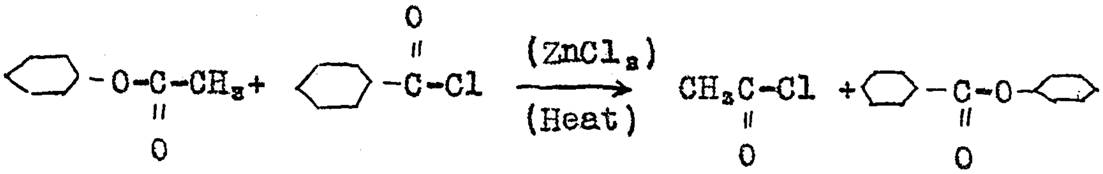
[1] Phelps and Hale, Am. Chem. J., 25, 445 (1901).
[2] Marquis, Ann. chim. phys., (8) 4, 196 (see 276) (1905).
[3] Gilman and Hewlett, Iowa State College J.Sci., 4, 27 (1930).
[4] Renshaw and Naylor, J. Am. Chem. Soc., 44, 862 (1922).

Kostanecki and Podrajansky[5] prepared furfuralacetophenone by the action of a 10% sodium hydroxide solution on an alcoholic solution of furfural and acetophenone. We were unable to prepare this compound by the action of furylacryloyl chloride on benzene in the presence of anhydrous aluminum chloride.

Döbner[6] prepared p-hydroxybenzophenone by heating benzoyl chloride and phenyl benzoate with zinc chloride at 180°. He also prepared the mono-substituted benzoyl ketones of catechol, resorcinol and hydroquinone using the same method, and the dibenzoate of each phenol. A reaction was carried out between phenyl acetate, benzoyl chloride and zinc chloride. The reaction that took place is illustrated by the following equation. A ketone was not formed.



In this study the diacetate and dibenzoate of catechol and hydroquinone were used. The reaction products were worked up in such manner as to hydrolyze any esters formed. The desired ketones were not obtained.

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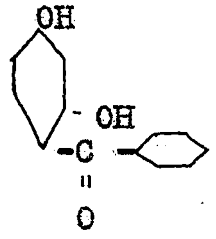
[5] Kostanecki and Podrajansky, Ber., 29, 2248 (1896).
[6] Döbner, Ann., 210, 246 (1881).

Komarowsky and Kostanecki[7] assigned the following structure to the ketone prepared by Döbner[6] by the action of benzoyl chloride on resorcinol dibenzoate in the presence of zinc chloride with the aid of heat:



They prepared the compound using the method of Nencki and Siebier[8] by heating equal parts of benzoic acid, resorcinol and zinc chloride to 160°. The structure assigned to the compound given above was the basis for the structure given to 2,4-dihydroxybenzoyl furan.

A reaction was carried out using phenol, furylacrylic acid and zinc chloride[8], with results described in the Experimental Part of this paper.

Behn[9] and others have used nitrobenzene as a solvent in the preparation of ketones by means of the Friedel-Crafts reaction. Hinegardner and Johnson[10] used nitrobenzene as a solvent in the preparation of chaulmoogrylresorcinol by means of the Friedel-Crafts reaction. They did not use carbon di-

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[7] Komarowsky and Kostanecki, *Ber.*, *27*, 1997 (1894).

[8] Nencki and Siebier, *J. prakt. Chem.*, (2) *23*, 147 (1881).

[9] Behn, *Chem. Zentr.*, (1898), I, 1223.; *Ger. pat.*, *95*, 901 (1897) (*Frdl.*, *5*, 143 (1897-1900)); Klarmann, *J. Am. Chem. Soc.*, *48* 791 (1926); Bartlett and Garland, *ibid.*, *49*, 2098 (1927).

[10] Hinegardner and Johnson, *ibid.*, *51*, 1503 (1929).

sulfide as a solvent when free resorcinol was used but employed the 1,3-dimethoxybenzene instead. They obtained a mixture of the dimethyl ethers of chaulmoogrylresorcinol.

In this study similar reactions were carried out between furoyl chloride, 1,3-dimethoxybenzene and aluminum chloride using carbon disulfide and nitrobenzene as solvents. In both cases one ether group was removed and the resulting product was completely soluble in sodium hydroxide. The position of the ether group is now known. It was found possible to prepare 2,4-dihydroxybenzoyl furan in carbon disulfide from furoyl chloride and resorcinol in the presence of aluminum chloride. One or more of the hydroxyl groups were esterfied in a small fraction of the product.

EXPERIMENTAL PART

Chemicals.

The various phenols used (phenol, resorcinol, catechol, hydroquinone) were C. P. chemicals. All solvents were dry and pure. The furoyl chloride and furylacryloyl chloride were prepared as described by Gilman and Hewlett[3]. The aluminum chloride employed was the C. P. sublimed chemical. All the esters used in this study were freshly crystallized from alcohol and then dried.

Apparatus.

All the reactions leading to the formation of ketones or esters were carried out in a 3-neck balloon flask of suitable size. In every case the flask was equipped with a mercury seal stirrer, dropping funnel and Hopkins condenser when needed. The dropping funnel and condenser were protected from moisture with drying tubes filled with anhydrous calcium chloride.

Reactions Between Phenol and Furoyl Chloride.

1st. Run. A solution of 32.6 g. (0.25 mole) furoyl chloride dissolved in 75 cc. of carbon disulfide was added dropwise over a period of three hours to a mixture of 18.8 g. (0.2 mole) of phenol and 57 g. (0.214 mole) of aluminum chloride in 100 cc. of carbon disulfide. The addition was carried out at room temperature and a slow reaction started at once as was evidenced by the evolution of hydrogen chloride. The mixture was stirred at room temperature for six hours and was then heated on a water-bath to refluxing for thirty hours. Hydrogen chloride gas was evolved slowly to the end of the reaction. After removal of the carbon disulfide on a water-bath the resulting yellow mass was hydrolyzed with cracked ice and then steam distilled. The water residue was extracted with ether and the ether solution was dried and distilled. The yield of phenyl furoate boiling at 138°-139°/3mm. was 12 g. or 31.9%. This compound is a yellow oil which when crystallized from petroleum ether melts at 42°. This compound was identified by an analysis and a mixed melting point determination with the compound previously prepared by Hewlett[11]. They prepared the ester by the action of furoyl chloride on a water solution of sodium phenolate.

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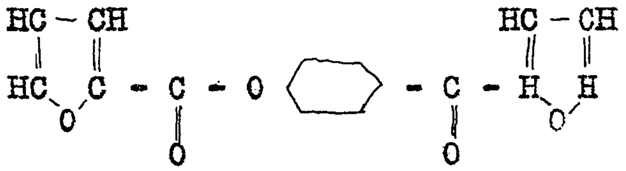
[11] From the Ph.D. dissertation of A. P. Hewlett (1930).

Anal. Calcd. for $C_{11}H_8O_3$: C, 70.19; H, 4.29. Found: C, $\begin{matrix}69.98\\70.10\end{matrix}$; H, $\begin{matrix}4.48\\4.39\end{matrix}$.

There was some unchanged furoyl chloride, phenol and considerable tar in the waste material.

A high boiling fraction remained in the flask after the phenyl furoate had been distilled off. After the identification of the first fraction as phenyl furoate it was thought that the high boiling fraction might have the following structure:



This compound after one crystallization from a mixture of benzene and petroleum ether (b.p.40°-68°) melts at 84°. It is a white crystalline compound and stable. With this structure in mind the substance was hydrolyzed with alcoholic potassium hydroxide. The alkaline solution was saturated with carbon dioxide and extracted with ether. After drying, the ether solution was evaporated and yielded a white solid which was recrystallized from hot benzene. The yield of 4-hydroxybenzoyl furan, ($HOC_6H_4COC_4H_3O$), melting at 163°-164° was 5.9 g. or 15.8%. 4-Hydroxybenzoyl furan is a white crystalline stable compound and soluble in alcohol, ether and in hot benzene and carbon tetrachloride.

Anal. Calcd. for $C_{11}H_8O_3$: C, 70.19; H, 4.29. Found: C, $\begin{matrix}69.95\\69.99\end{matrix}$; H, $\begin{matrix}4.40\\4.35\end{matrix}$.

The water solution from which the 4-hydroxybenzoyl furan was removed was acidified and shown to contain furoic acid. No other compound was isolated.

Identification of 4-Hydroxybenzoyl Furan.-

The methyl and ethyl ethers were prepared after the directions of Hiers[12]. In this method the phenolic body is treated in a cold sodium hydroxide solution with a calculated amount of the desired alkyl sulfate. The methyl ether melts at 60° after two crystallizations from hot benzene. It is a white crystalline stable compound. The ethyl ether melting at 70° was identified as 4-ethoxybenzoyl furan. It had previously been prepared by Gilman and Hewlett[3] and was identified by a mixed melting point determination with the compound prepared by them.

4-Methoxybenzoyl furan was oxidized to 4-methoxybenzoic acid by means of a neutral potassium permanganate solution. One gram (0.00495 mole) of the ether was added to 20 cc. of water in a 50 cc. Erlenmeyer flask equipped with a reflux condenser. Small crystals of potassium permanganate were added from time to time over a period of twenty-four hours

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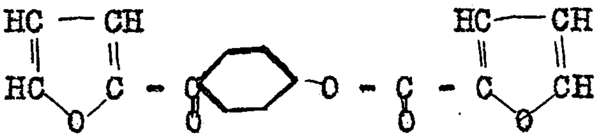
[12] Hiers, Org. Syn., 9, 12.

until the solution remained colored. This solution yielded a white crystalline compound melting at 184°. It was further identified as 4-methoxybenzoic acid by a mixed melting point determination with an authentic sample of the acid. By this means the furan ring was proved to be in the 4-position with respect to the hydroxyl group.

4-Hydroxybenzoyl furan was further identified by the preparation of the oxime of the ethyl ether as described by Gilman and Hewlett[3]. The oxime melting at 145° is a white crystalline compound. A mixed melting point determination was made with this compound and the compound prepared by Gilman and Hewlett[3] and there was no depression in the melting point.

<u>2nd. Run</u>. Run No. 1 was repeated using a slight excess of phenol as follows. Twenty and seven-tenths grams (0.22 mole) of phenol and 27 g. (0.101 mole) aluminum chloride were added to 75 cc. of carbon disulfide. To this mixture was added dropwise over a period of three hours 26.1 g. (0.2 mole) of furoyl chloride dissolved in 50 cc. of carbon disulfide. The reaction was carried out and worked up as before. A yield of 58.5% of phenyl furoate was obtained. No trace of



could be found. Considerable unchanged phenol and tar were the other products of the reaction. It is possible that the yield of phenyl furoate was reduced by hydrolysis during steam distillation. Furoic acid in traces could be isolated from the water solution.

The two runs previously described have shown that 4-hydroxybenzoyl furan was not prepared in satisfactory yields by the method used. The next step was to block the hydroxyl group with an easily removed radical.

Reaction Between Furoyl Chloride and Phenyl Benzoate.-

Twenty-nine and seven-tenths grams (0.15 mole) of phenyl benzoate were dissolved in 75 cc. of carbon disulfide containing 20 g. (0.075 mole) of aluminum chloride. To this mixture was added dropwise with stirring over a period of three hours 19.5 g. (0.15 mole) of furoyl chloride dissolved in 50 cc. of carbon disulfide. The reaction started slowly at room temperature and darkened. The reaction mixture was stirred for four days and was then poured on cracked ice and steam distilled. There was much furoyl chloride and tar present. The water residue was extracted with ether and the ether solution was dried and evaporated. The residue was hydrolyzed with alcoholic potassium hydroxide and saturated with carbon dioxide and extracted with ether. After drying, the solution was evaporated and crystallized from benzene. There was obtained 2.0 g. of 4-hydroxybenzoyl furan melting at 163°-164°. The yield was 7.1%.

The previous experiment was repeated after the directions of Hinegardner and Johnson[10]. Twenty-nine and seven-tenths grams of phenyl benzoate were dissolved in 75 cc. of nitrobenzene containing 20 g. (0.075 mole) of aluminum chloride. To this mixture was added dropwise with stirring over a period of three hours 19.5 g. (0.15 mole) of furoyl chloride dissolved in 50 cc. of carbon disulfide. There was but little reaction at room temperature. The mixture was then heated on a water-bath at 45° for nine hours and at 85-90° for thirty hours. The black reaction mixture was then poured onto cracked ice and steam distilled to remove the nitrobenzene and other volatile impurities. After the water residue had cooled it was extracted with ether and worked up as previously described. The yield of 4-hydroxybenzoyl furan was 8.8 g. or 31.8%. The other products of the reaction were furoic acid, furoyl chloride, phenol, benzoic acid, phenyl benzoate and tar.

Reaction Between Furoyl Chloride and Phenol in Nitrobenzene.-

The previous experiment was repeated substituting phenol for phenyl benzoate. Eighteen and eight-tenths grams (0.2 mole) of phenol and 27 g. (0.101 mole) of aluminum chloride were added to 100 cc. nitrobenzene. To this mixture was added dropwise with stirring over a period of three hours a solution of 26.1 g. (0.2 mole) of furoyl chloride dissolved in 50 cc. of nitrobenzene. The reaction flask was immersed in an ice-bath for six hours. The ice-bath was then removed and the reaction mixture was stirred at room temperature for thirty hours and at 60°-65° for three hours. Hydrogen chloride was evolved slowly throughout the reaction. After hydrolysis the reaction product was steam distilled and extracted with ether. The ether solution was dried and evaporated, and the product was crystallized from benzene. The yield of 4-hydroxybenzoyl furan was 9.2 g. or 24.5%. After removal of the 4-hydroxybenzoyl furan the residue was distilled and there was obtained 21.6 g. of phenyl furoate or a yield of 57.5%. The other products of reaction were phenol, tar, furoyl chloride and furoic acid.

Attempted Preparation of the Oxime of 4-Hydroxybenzoyl Furan.-

Three attempts were made to prepare the oxime after the method of Goldschmidt and Zanoli[13]. The ketone was dissolved in water containing enough sodium hydroxide to react with the hydroxyl group. To this solution was added two equivalents of hydroxylamine prepared by neutralizing the hydrochloride with the calculated amount of sodium hydroxide. The reaction product was neutralized with dilute acetic acid and the product was identified. A fourth attempt was made as described above except that the reaction was carried out on a water-bath at 50° for ten hours. In every case no trace of the desired oxime was found.

Two attempts were made to prepare the oxime after the directions of Hinegardner and Johnson[10]. In this method the ketone was treated with the desired quantity of hydroxylamine hydrochloride in anhydrous pyridine and warmed on a water-bath at 70° for ten hours. The reaction product was then poured into water, filtered and crystallized from benzene. It was shown to be the unchanged ketone.

The preparation of the oxime of 4-ethoxybenzoyl furan has been previously described.

Preparation of 2,4-Dihydroxybenzoyl Furan.-

1st. Method. A solution containing 65.5 g. (0.50 mole) of furoyl chloride dissolved in 100 cc. of carbon disulfide was added slowly to a mixture of 55 g. (0.50 mole) of resorcinol and 67 g. (0.25 mole) of aluminum chloride in 500 cc. of carbon disulfide. The acid chloride was added over a period of four hours with stirring. After the addition of the acid chloride the reaction mixture was stirred at room temperature for twenty-four hours and at its boiling point on a water-bath for twelve hours. Most of the carbon disulfide was removed on a water-bath and the resulting heavy mass was hydrolyzed by adding cracked ice and steam distilled. The product was treated with alcoholic potassium hydroxide to hydrolyze any ester groups present and recovered by treatment with carbon dioxide. The yield of 2,4-dihydroxybenzoyl furan melting at 123°-124° after 4 crystallizations from hot benzene was 81.6

g. or 80%. It is soluble in dilute sodium hydroxide and in hot benzene, carbon tetrachloride, chloroform and alcohol. 2,4-Dihydroxybenzoyl furan is a yellow crystalline compound and stable.

<u>Anal</u>. Calcd. for $C_{11}H_8O_4$: C, 64.68; H, 3.95. Found: C, 64.72, 64.78; H, 4.01, 4.08.

<u>2nd. Method</u>. A solution containing 26.1 g. (0.2 mole) of furoyl chloride in 75 cc. of nitrobenzene was added dropwise with stirring over a period of one and five-tenths hours to a solution containing 22 g. (0.2 mole) of resorcinol and 26 g. (0.098 mole) of aluminum chloride in 100 cc. of nitrobenzene. The reaction started at room temperature and was allowed to continue at this temperature for two hours. It was then heated on a water-bath for one hour. A vigorous reaction then took place as was evidenced by a vigorous evolution of hydrogen chloride gas. The reaction mixture was hydrolyzed by pouring onto cracked ice. It was then steam distilled and worked up as described for the previous preparation. The yield of 2,4-dihydroxybenzoyl furan was 16.1 g. or 79%. It is believed that the yield can be improved by heating the reaction mixture at a temperature lower than 70° as considerable tar was formed in the reaction described above.

Attempted Preparation of the Oxime and Proof of Structure of 2,4-Dihydroxybenzoyl Furan.-

The compound was proved to contain two active hydrogens using the Zerewitenoff[14] method. This determination[15] was carried out by treating 2,4-dihydroxybenzoyl furan in n-butyl ether with methylmagnesium iodide in n-butyl ether. The reaction mixture was warmed to complete the reaction. The active hydrogen equivalents from two samples of 0.2015 g. and 0.2106 g. weight were 1.95 and 2.00, respectively.

Six attempts were made to prepare the oxime after the directions of Goldschmidt and Zanoli[13]. The ketone was recovered unchanged. In each case 2 equivalents of hydroxylamine hydrochloride and 4 of sodium hydroxide were used. The time of reaction varied from one day to one week.

One run was made as described above keeping the reaction mixture at 50° for ten hours on a water-bath.

Two runs were made using the method of Hinegardner and Johnson[10]. The ketone was heated with 2 equivalents of hydroxylamine hydrochloride on a water-bath at 60°-70° for ten hours. No oxime could be detected. A third method using sodium carbonate to neutralize the hydroxylamine hydrochloride was tried. The ketone was dissolved in 95% ethyl alcohol and

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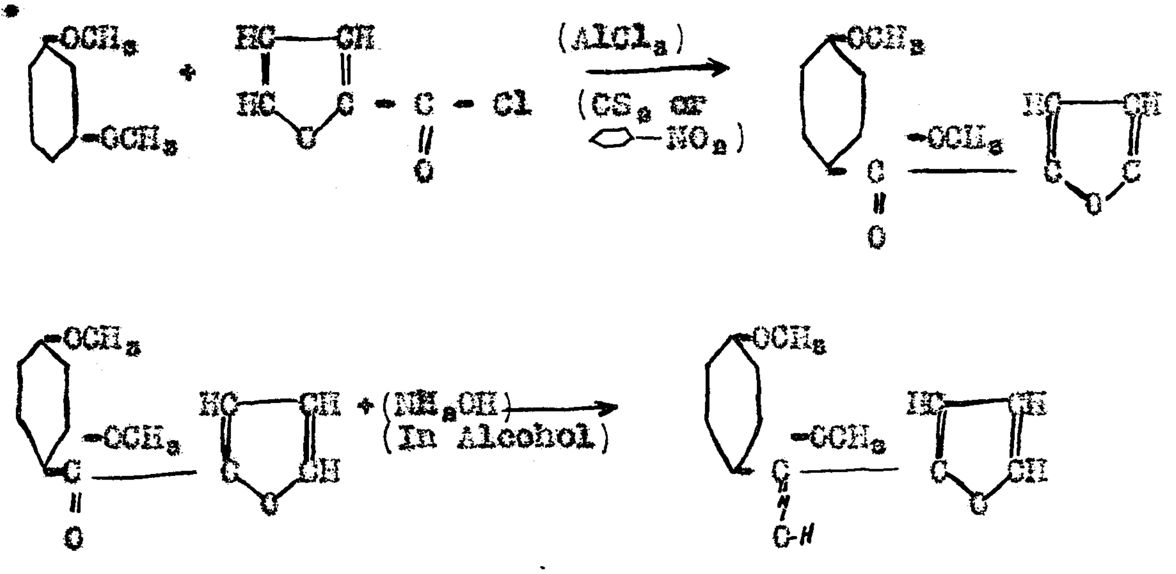
[14] Zerewitenoff, Ber., 40, 2023 (1907).

[15] This opportunity is taken to express our appreciation to Mr. R. J. Vander Wal and Mr. R. E. Fothergill for their kindness in determining the active hydrogens reported in this study.

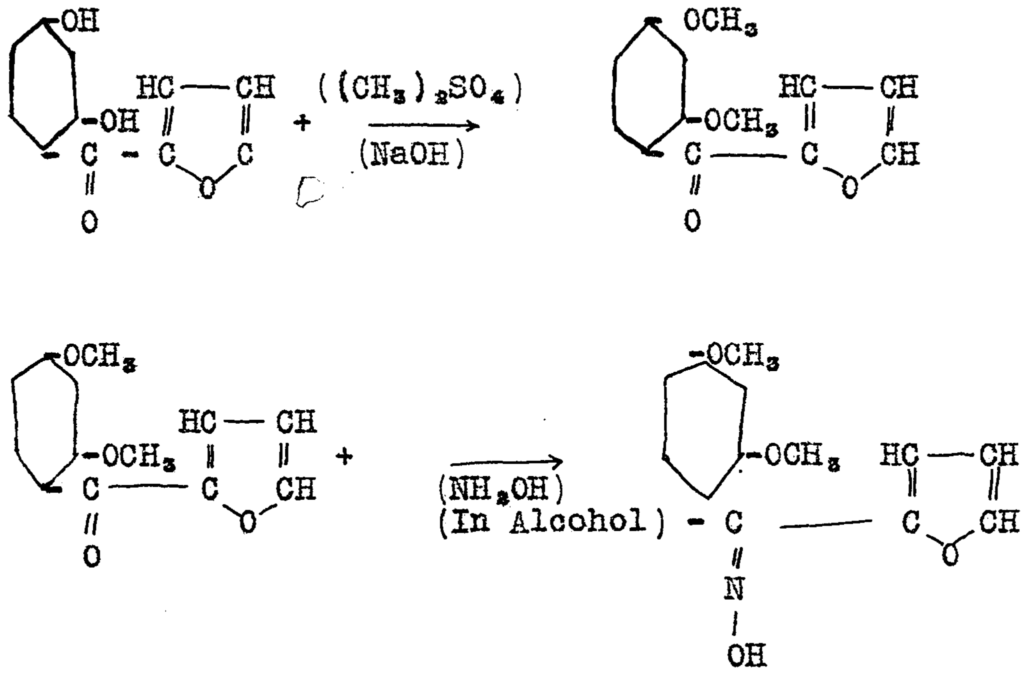
two equivalents of the free hydroxylamine were added in sufficient alcohol to just keep the ketone in solution. This solution was worked up after four days with the usual negative result. Three attempts were made to prepare each of the semicarbazone and phenyl hydrazone derivatives. The reaction mixtures were allowed to stand a week and then worked up. The results were negative in every case.

In attempting to prepare the oxime of 4-hydroxybenzoyl furan it was found necessary to ethylate the phenol group. When this was done the oxime was prepared with ease[3]. With this point in mind it was proposed to carry out the following reactions:

I.



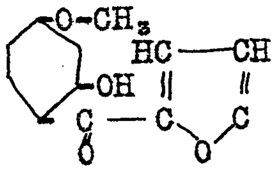
II.



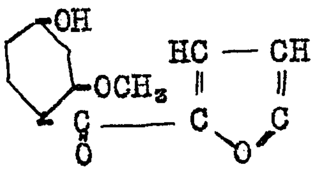
Two attempts were made to carry out the reactions proposed by Scheme I as follows: A solution of 26.1 g. (0.2 mole) of furoyl chloride in 75 cc. nitrobenzene was added dropwise with stirring over a period of one hour to a solution of 27.6 g. (0.2 mole) of 1,3-dimethoxybenzene and 26 g. (0.098 mole) of aluminum chloride in 100 cc. of nitrobenzene. The reaction mixture was cooled on an ice-bath during the addition of the acid chloride solution, and for two hours afterward. After the time noted had elapsed the ice-bath was removed and the reaction allowed to proceed at room temperature for four hours. A vigorous reaction took place with the addition of the acid chloride and continued to the end of the reaction. The mixture was poured onto cracked ice and steam distilled. After the water residue had cooled it was extracted with ether. The ether solution was extracted with 20% sodium hydroxide and distilled.

One and four-tenths grams or 5% of the 1,3-dimethoxybenzene used was recovered. A small amount of tar was left in the distillation flask. The alkaline solution was treated with carbon dioxide and a yellow crystalline compound was precipitated. A portion of this compound or mixture of compounds was crystallized 4 times from petroleum ether (b.p., 40°-60°). It melts between 75°-82°.

The presence of one or more hydroxyl groups was proved by the solubility of the substance in sodium hydroxide. If one methyl group has been removed there is no way of showing which one with the evidence at hand. It is believed that if two methyl groups were removed some of the compound prepared by the action of furoyl chloride on resorcinol in carbon disulfide would have been obtained. There was no trace of a compound melting at 123°-124° though it would be difficult to separate it from the other compounds present if formed. The yield calculated on the basis of one of the following formulas



or



was 39.2 g. or 90%.

The above experiment was repeated using carbon disulfide as a solvent with the same result. However, as this synthesis was carried out for the purpose of identifying 2,4-dihydroxybenzoyl furan the product of the above reactions was not analyzed. One attempt was made to oxidize the compound with neutral potassium permanganate. The compound was destroyed.

An attempt was made to carry out the reactions proposed by Scheme II after the method of Hiers[13]. Twenty and four tenths grams (0.1 mole) of 2,4-dihydroxybenzoyl furan was dissolved in 400 cc. water with 8g. (0.2 mole) sodium hydroxide. The solution was cooled to 5° and 12.6 g. (0.1 mole) of dimethyl sulfate was run in. After the addition of the dimethyl sulfate the reaction was stirred at 5° for one hour and then heated to boiling for fifteen hours. A compound was obtained which was soluble in sodium hydroxide. This compound was crystallized from petroleum ether (b.p., 40°-60°). It melts between 75°-82° and caused no noticeable lowering in a mixed melting point determination with the compound obtained from the reaction between furoyl chloride and 1,3-dimethoxybenzene in the presence of aluminum chloride. The yield was 90% of the theoretical if calculated on the basis that one hydroxyl group was methylated. An attempt was made to methylate the partly methylated compound as described above without success.

The compounds prepared after Schemes I and II were slightly soluble in boiling petroleum ether (b.p., 40°-60°) and soluble in boiling benzene, carbon tetrachloride and alcohol and soluble in cold ether and sodium hydroxide.

Reaction Between Catechol, Furoyl Chloride and Aluminum Chloride in Carbon Disulfide and Nitrobenzene.-

A solution of 32.5 g. (0.25 mole) of furoyl chloride in 100 cc. of carbon disulfide was added dropwise with stirring over a period of three hours to a mixture of 27.5 g. (0.25 mole) catechol and 37 g. (0.139 mole) of aluminum chloride in 200 cc. of carbon disulfide. The reaction started slowly at room temperature and was heated on a water-bath to the boiling point of carbon disulfide for forty-eight hours. After the carbon disulfide was removed on a water-bath the resulting white mass was hydrolyzed with cracked ice, steam distilled and allowed to evaporate. The product was apparently in solution, but separated as the water evaporated. This substance once precipitated was very slightly soluble in boiling water. The substance is of a greenish blue color. It is soluble in acetone, sodium hydroxide, alcohol and ether and slightly soluble in benzene and carbon tetrachloride. This compound could not be crystallized from any of the solvents mentioned or combination of them, and separated from solution in an amorphus condition.

The compound will dye cotton cloth a color much like that of the furan analogue of malachite green.

Four runs were made using 11 g. (0.11 mole) of catechol, 13 g. (0.1 mole) of furoyl chloride and 13 g. (0.048 mole) of aluminum chloride as described above. The product from each run was similar to that obtained and described in the first run. The yield of material was 90% of the theoretical for ketone formation. A number of fusions on platinum foil failed to show more than a trace of aluminum. The product could not be hydrolyzed with alcoholic potassium hydroxide or 10% hydrochloric acid.

Two reactions were carried out as described, substituting nitrobenzene for carbon disulfide as a solvent. The reaction proceeded rapidly and was completed in two hours. The products were similar to those previously described.

Reaction Between Furoyl Chloride and the Diacetate and Dibenzoate of Catechol.-

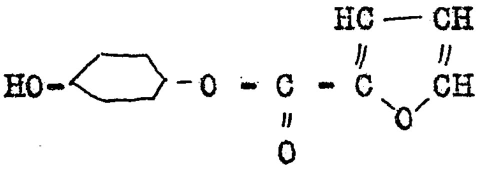
Four experiments were carried out using the diacetate and dibenzoate of catechol in carbon disulfide and nitrobenzene, respectively. All of the reactions were carried out and their products worked up as described in the following experiment. Nineteen and five-tenths g. (0.15 mole) of furoyl chloride in 25 cc. of carbon disulfide were added to 21 g. (0.15 mole) of catechol diacetate and 20 g. (0.075 mole) aluminum chloride in 50 cc. of carbon disulfide. This mixture was heated to boiling for four days on a water-bath. After most of the carbon disulfide had been removed the product was hydrolyzed by adding cracked ice and steam distilled. The resulting black mass was removed from the water residue with ether and the ether evaporated. The products of reaction after hydrolysis with alcoholic potassium hydroxide were found to be acetic acid, catechol, furoic acid and tar. All materials were identified by mixed melting point determinations with authentic samples. When nitrobenzene was used as a solvent the temperature of the reaction mixture was 70°. The amount of hydrogen chloride gas evolved in these experiments was small. Not a trace of the green substance was found.

Reaction Between Hydroquinone, Furoyl Chloride and Aluminum Chloride.-

1st. Method. A solution containing 26.1 g. (0.2 mole) furoyl chloride dissolved in 75 cc. of carbon disulfide was added slowly to a mixture of 22 g. (0.2 mole) hydroquinone and 26 g. (0.0975 mole) of aluminum chloride in 100 cc. of carbon disulfide. The acid chloride was added at room temperature and the reaction started at once and proceeded slowly for four days. After removal of the carbon disulfide on a water-bath the product was hydrolyzed with cracked ice, filtered and dried. The resulting white solid was crystallized from boiling benzene and melted at 193°-195°. It is a white semi-crystalline solid and soluble in sodium hydroxide.

The substance was hydrolyzed with sodium hydroxide, and the products of hydrolysis were hydroquinone and furoic acid.

No trace of the expected ketone could be found. If the compound be represented by the following formula

 [16]

it should give one active hydrogen as determined by the Zerewitenoff[14] method. This determination[15] was carried out as previously described. The active hydrogen equivalents from two samples of 0.2099 g. and 0.2165 g. weight were 0.95 and 0.97 respectively.

Anal. Calcd. for $C_{11}H_8O_4$: C, 64.68; H, 3.95. Found: C, 65.17, 65.01; H. 3.67, 3.75.

The yield of the ester was 34.3 g. or 84%.

Hewlett[11] has prepared hydroquinone difuroate by the action of furoyl chloride on a water solution of hydroquinone in dilute sodium hydroxide. The compound melts at 200°. A mixed melting point determination with his compound and the supposed hydroquinone monofuroate showed a melting point lowering of from 7°-10°. Hewlett[11] was unable to prepare hydroquinone monofuroate by his method.

2nd. Method. The reaction described in 1st. method was repeated using nitrobenzene as the solvent. The reaction was completed in three hours at room temperature. After the

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[16] The saponification equivalent was determined and found to be 184.8 and 188.1 against the theoretical value of 204.06. The solutions were so highly colored as to obscure the end-point of the titration.

reaction mixture had been poured on cracked ice it was steam distilled and treated as previously described. The product was identified with that previously described. Hydroquinone monofuroate was obtained in a yield of 80%. There was considerable tar formed which can probably be prevented with cooling.

Attempted Preparation of a Ketone Containing the Benzene or Substituted Benzene Ring and the Furylacryloyl Group.-

A solution containing 31.3 g. (0.2 mole) of furylacryloyl chloride in 150 cc. of carbon disulfide was added dropwise with stirring over a period of five hours to a mixture containing 18.8 g. (0.2 mole) of phenol and 27 g. (0.101 mole) of aluminum chloride in 200 cc. of carbon disulfide. The reaction mixture was cooled with a freezing mixture of ice and salt, and was stirred for five hours in the bath. It was noticed that the reaction mixture turned a deep red color when the first few drops of furylacryloyl chloride solution were added. After the carbon disulfide had been removed on a water-bath the reaction mixture was poured onto cracked ice. A black carbonaceous mass was the result. The product was extracted with ether and worked up in the usual manner. One gram of a red oil was obtained which did not give an oxime[13]. This oil decomposed to a resin on standing.

A second attempt was made using the same amount of materials at a temperature of -5° to -10°. Enough calcium carbonate was added to react with the hydrogen chloride theoretically formed in the reaction. The results were as described in the first experiment.

A third run using ferric chloride was carried out as described in the first experiment. Carbon and tar were the products of the reaction.

An attempt was made to prepare furfuralacetophenone from benzene, furylacryloyl chloride and aluminum chloride. A solution containing 21 g. (0.134 mole) of furylacryloyl chloride in 50 cc. of benzene was added dropwise with stirring over a period of seven hours to a mixture of 21 g. (0.078 mole) aluminum chloride in 150 cc. of benzene. The reaction flask was immersed in an ice-bath and a stream of well dried nitrogen was passed through the reaction mixture to remove as much as possible of the hydrogen chloride that was formed. The reaction mixture was worked up as previously described and the results were as before.

One attempt was made to condense furylacrylic acid with phenol after the directions of Nencki and Siebier[8]. Twenty-seven and six-tenths grams (0.2 mole) of furylacrylic acid and 18.8 g. (0.2 mole) of phenol were heated to 160° in an Erlenmeyer flask with 30 g. (0.22 mole) of anhydrous zinc chloride. A vigorous reaction took place and a heavy red tar was the only product. This tar resisted all attempts at crystallization.

One attempt was made to condense furylacrylic acid with phenol in a sealed tube at 180°-190°. Eighteen and eight-tenths grams (0.2 mole) of phenol and 27.6 g. (0.2 mole) of furylacrylic acid were mixed and heated in a sealed tube at 180°-190° for forty-eight hours. The products isolated were phenol, furylacrylic acid and a small amount of tar.

SUMMARY

Phenyl furoate was prepared in good yields from phenol and furoyl chloride by Friedel-Crafts reaction in carbon disulfide and nitrobenzene.

4-Hydroxybenzoyl furan was prepared in a yield of 15.8% when phenol was treated with an excess of furoyl chloride in carbon disulfide. 4-Hydroxybenzoyl furan was obtained in a yield of 7.1% when phenyl benzoate was treated with furoyl chloride and aluminum chloride in carbon disulfide. When the reaction was carried out in nitrobenzene the yield of 4-hydroxybenzoyl furan was 31.8%. 4-Hydroxybenzoyl furan was prepared in a yield of 24.5% when phenol was treated with furoyl chloride and aluminum chloride in nitrobenzene. In the same reaction the yield of phenyl furoate was 57.5%.

2,4-Dihydroxybenzoyl furan was prepared in a yield of 80% when resorcinol was treated with furoyl chloride and aluminum chloride in carbon disulfide. When nitrobenzene was used as a solvent the yield was 79%. The position of the ketone group has not been established.

Hydroquinone monofuroate was prepared in a yield of 84% when hydroquinone was treated with furoyl chloride and aluminum chloride in carbon disulfide. When the reaction was carried out in nitrobenzene the yield of the ester was 80%. All attempts to prepare a ketone from the diacetate and dibenzoate of hydroquinone failed.

Catechol failed to yield either ester or ketone.

SOME STUDIES ON THE ATTEMPTED PREPARATION OF p-AMINOBENZOYL FURAN

INTRODUCTION

It was desired to prepare p-aminobenzoyl furan for some physiological studies and as a possible insecticide. This compound would be valuable as a basis for a series of dyes containing the furan ring and for synthetic purposes.

The introduction of ketonic groups into a benzene ring which contains an amino group can be effected by a variety of methods.

Kunckell[1] has prepared a number of p-substituted acetanilides by treating acetanilide with the desired acid chloride in carbon disulfide in the presence of a large excess of aluminum chloride. The free amine can be easily obtained by treating the acetanilide with dilute hydrochloric acid, followed by sodium carbonate. Good yields are reported for this method.

Döbner[2] has made use of a similar method in an ingenious manner. p-Aminobenzophenone was prepared by hydrolyzing the compound formed by treating phthal-anil with benzoyl chloride and finely powdered zinc chloride at 180°. The phthal-anil

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[1] Kunckell, Ber., 33, 2641 (1900).
[2] Döbner, Ann., 210, 246 (see 260) (1881).

used was prepared in practically quantitative yields by treating aniline with phthalic anhydride. Torrey and Rafsky[3] have repeated the work of Döbner[2] and have described an improved method for working up the product of the reaction.

Clarke and Esselen[4] have prepared *p*-aminobenzophenone by hydrolyzing the product obtained by treating benzanilide at 200°-210° with benzoyl chloride and zinc chloride. The maximum yield reported was 42%. Chattaway[5] has reviewed the literature of the preparation of ketones by the action of acid chlorides on aniline at high temperatures with or without zinc chloride as a catalyst. The preparation of *p*-aminobenzophenone in good yields is described.

Several attempts were made to prepare *p*-dimenthylaminobenzoyl furan after the directions of Hurd and Webb[6] for *p*-dimethylaminobenzophenone without success.

Nitrobenzene has been used as a solvent in Friedel-Crafts reaction by Behn[7] and others. This method was tried without success.

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[3] Torrey and Rafsky, *J. Am. Chem. Soc.*, *32*, 1489 (1910).
[4] Clarke and Esselen, *J. Am. Chem. Soc.*, *33*, 1135 (1911).
[5] Chattaway, *J. Chem. Soc.*, *85*, 386 (1904).
[6] Hurd and Webb, *Org. Syn.*, *7*, 24.
[7] Behn, *Chem. Zentr.*, (1898), I, 1223. *Ger. pat.*, 95901 (1897). (*Frdl.*, *5*, 143 (1897-1900)):,Klarmann, *J. Am. Chem. Soc.*, *48*, 791 (1926); Bartlett and Garland, *ibid.*, *49*, 2098 (1922); Hinegardner and Johnson, *ibid.*, *51*, 1503 (1929).

EXPERIMENTAL PART

Apparatus.-

All Friedel-Crafts reactions were carried out in a 3-neck balloon flask of suitable size equipped with a dropping funnel, mercury seal stirrer and Hopkins condenser. The condenser and dropping funnel were protected from the atmosphere with drying tubes filled with anhydrous calcium chloride.

Furoylanilide, ($C_4H_3OCONHC_6H_5$).- This compound was prepared after the directions of Baum[8]. The reaction was carried out in a 250 cc. Erlenmeyer flask equipped with a dropping funnel, reflux condenser and drying tube. To 61.4 g. (0.66 mole) of freshly distilled aniline was added 39 g. (0.3 mole) of furoyl chloride[9] over a period of three hours. After the first vigorous reaction had subsided the reaction mixture was heated to 130° until no more hydrogen chloride was evolved. The product was dissolved in hot 95% alcohol, treated with Norite and allowed to crystallize. The yield of furoylanilide melting at 123° was 50 g. or 90%.

Phthal-anil, ($C_6H_4C_2O_2NC_6H_5$).- This compound was prepared after the directions of Döbner[2]. To 18.6 g. (0.2 mole) aniline in a 150 cc. Erlenmeyer flask was added with vigorous shaking 29.6 g. (0.2 mole) of phthalic anhydride.

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[8] Baum, Ber., 37, 2949 (1904).
[9] Gilman and Hewlett, Iowa State College J. Sci., 4, 27 (1929).

A very vigorous reaction took place and water was evolved. The solid product formed was heated on a hot-plate at 210° for one hour to complete the reaction. A practically quantitative yield of phthal-anil melting at 204° was obtained. This compound was used without further purification.

Reaction Between Acetanilide and Furoyl Chloride in Carbon Disulfide.-

The following experiment was carried out after the directions of Kunckell[1]. To 26 g. (0.2 mole) of furoyl chloride and 38 g. (0.142 mole) of finely powdered anhydrous aluminum chloride in 50 cc. of carbon disulfide[10] was added with stirring 13.5 g. (0.1 mole) of acetanilide in 20 cc. of carbon disulfide. The acetanilide was added over a period of three hours at 34°. Hydrogen chloride was slowly evolved throughout this period. After the acetanilide had been added the reaction mixture was heated to the boiling point of carbon disulfide on a water-bath for three hours. Hydrogen chloride was evolved rapidly during this time and a heavy red aluminum chloride complex separated. The reaction mixture was poured onto cracked ice and steam distilled. After the residue had cooled it was extracted with ether to remove both solids and liquids from the water. A part of the ether extract was evapor-

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[10] The carbon disulfide used was well dried over anhydrous calcium chloride and filtered.

ated and refluxed with 15% hydrochloric acid for five hours. The hydrochloric acid solution was worked up and yielded aniline and tar. An investigation of the steam distillate revealed analine. The ether fraction not hydrolyzed was evaporated and hydrolyzed with 10% alcoholic sodium hydroxide and yielded aniline and tar. Acetic acid, furoic acid and traces of furoyl chloride were isolated from all water residues.

A second run was made as described except that the reaction mixture was refluxed for eight hours. After hydrolysis the product was filtered and the filtrate was extracted with ether and added to the solid that had been removed by filtration. The ether was removed and the residue was hydrolyzed with 15% hydrochloric acid at 90°-95° for five hours. After the solution had cooled it was neutralized with dilute sodium hydroxide and extracted with ether. The ether was removed on a water-bath and the residue was distilled under reduced pressure. After the aniline present had distilled over there remained in the distillation flask a small amount of a solid compound. This material crystallized from boiling water in the form of thin yellow plates. It melts at 140° without decomposition and is stable. This compound contains nitrogen and is soluble in dilute hydrochloric acid.

A third run was carried out as follows: To 13 g. (0.1 mole) of furoyl chloride and 19 g. (0.071 mole) of aluminum chloride in 25 cc. of carbon disulfide was added 13.5 g.

(0.1 mole) acetanilide in 20 cc. carbon disulfide at 34°. This mixture was stirred at 34° for eight hours and worked up as previously described using the hydrochloric acid method of hydrolysis. A few crystals of the 140° compound were obtained.

A fourth run was carried out in which the furoyl chloride was added to a mixture of acetanilide and aluminum chloride. To 6.8 g. (0.05 mole) of acetanilide and 24 g. (0.089 mole) of aluminum chloride in 50 cc. of carbon disulfide was added 13 g. (0.1 mole) of furoyl chloride in 20 cc. of carbon disulfide. The reaction mixture was refluxed on a water-bath for forty hours and hydrogen chloride was evolved slowly throughout. After hydrolysis of the aluminum chloride complex the product was hydrolyzed with hydrochloric acid as previously described. The products were aniline, tar and a trace of the 140° compound. The reaction just described was repeated and refluxed for eight hours instead of forty with similar results.

It was thought to be of interest to investigate the product from the reaction between acetanilide, furoyl chloride and aluminum chloride after the reaction product had been poured onto cracked ice. With this in mind a run was made like that described in the previous paragraph. The reaction mixture after hydrolysis with cracked ice was filtered and the solid material thus obtained was dried and crystallized from benzene. There was obtained two fairly well defined grey amorphous solids. The first fraction melts between 150°-160°

and the second between 186°-197° without noticeable decomposition. Repeated recrystallizations from benzene failed to improve the melting points reported. The two solids were combined and hydrolyzed with 15% hydrochloric acid and yielded tar, aniline and a trace of the 140° compound.

Two general methods have been described in which acetanilide in carbon disulfide was added to a mixture of aluminum chloride and furoyl chloride, and in which furoyl chloride in carbon disulfide was added to a mixture of acetanilide and aluminum chloride in carbon disulfide. It was thought to be of value to add aluminum chloride portionwise to a solution of acetanilide and furoyl chloride in carbon disulfide. To 13.4 g. (0.1 mole) of acetanilide and 19.5 g. (0.15 mole) furoyl chloride dissolved in 50 cc. of carbon disulfide was added 30 g. (0.112 mole) of aluminum chloride portionwise with stirring over a period of six hours. After the aluminum chloride was added the reaction mixture was refluxed for thirty hours. Hydrogen chloride was evolved throughout the reaction. The reaction mixture was poured onto cracked ice and hydrolyzed with 15% hydrochloric acid as previously described. The products of reaction were aniline, tar and a trace of the 140° compound.

Reaction Between Acetanilide, Furoyl Chloride and Aluminum Chloride in Nitrobenzene.-

The following reactions were carried out after the general directions of Behn, and others[7].

To 24 g. (0.089 mole) of aluminum chloride and 13 g. (0.1 mole) furoyl chloride dissolved in 50 cc. of nitrobenzene was added with stirring 6.8 g. (0.05 mole) of acetanilide dissolved in 20 cc. of nitrobenzene. As practically no hydrogen chloride was evolved at 30° the temperature of the reaction mixture was raised to 80° for thirty hours. At 80° the evolution of hydrogen chloride was rapid during the first part of the reaction but decreased as time progressed. The black reaction mixture was cooled and poured onto cracked ice and steam distilled until all the nitrobenzene was removed. It was then worked up as previously described and hydrolyzed with 15% hydrochloric acid. The products of the reaction were tar and a small amount of aniline.

The reaction just described was repeated and the temperature of reaction was kept between 70°-71° for eight hours. After hydrolysis the reaction products were worked up in the usual manner. There was obtained tar, aniline and a trace of the 140° compound.

Reaction Between Furoyl Chloride, Phthal-anil and Zinc Chloride.-

This reaction was carried out as described by Dobner[2]. Thirteen grams (0.1 mole) of furoyl chloride were added to a mixture of 22.3 g. (0.1 mole) of phthal-anil and 0.4 g. of anhydrous zinc chloride. The reaction was carried out in a 150 cc. Erlenmeyer flask immersed in an oil-bath equipped with a reflux condenser, thermometer and drying tube. When the temperature of the reaction mixture reached 120° small quantities of hydrogen chloride were evolved. The reaction mixture was heated at 180° for eight hours and a sample was removed and crystallized from alcohol and proven to be unchanged phthal-anil by a mixed melting point determination with the known compound. Apparently much of the furoyl chloride was decomposed by the zinc chloride present judging from the decomposition material formed.

The experiment just described was repeated with similar results.

Reaction Between Furoyl Chloride, Phthal-anil and Aluminum Chloride in Nitrobenzene.-

To 6.5 g. (0.05 mole) of furoyl chloride and 11.2 g. (0.05 mole) of phthal-anil dissolved in 30 cc. of nitrobenzene was added 16 g. (0.06 mole) of aluminum chloride. The temperature of the reaction mixture was slowly raised to 80° and kept at that temperature for eight hours. Hydrogen chloride was evolved slowly and the mixture turned dark. The reaction product was poured onto cracked ice, steam distilled to remove the nitrobenzene and other steam volatile solids.

After the solids present were removed by filtration the mother liquor was extracted with ether and the ether extract added to the solids. The ether was removed on a waterbath and the residue was hydrolyzed by boiling with alcoholic potassium hydroxide, and when worked up yielded aniline, phthalic acid and much tar.

Reaction Between Aniline, Furoyl Chloride and Zinc Chloride.-

This reaction was carried out after the directions of Chattaway[5]. Twenty-six grams (0.2 mole) of furoyl chloride were added dropwise to 9.3 g. (0.1 mole) of aniline. The reaction was vigorous and seemed to go in two steps, the second taking place at 130°. After the reaction product had been heated at 160° on an oil-bath for one hour to complete the reaction 1 g. of finely powdered zinc chloride was added slowly at 160°. A vigorous reaction took place with evolution of hydrogen chloride and production of a black tar. The resulting mass was boiled with alcoholic potassium hydroxide for ten hours, cooled and extracted with ether and dried over sodium sulfate. It was distilled and yielded a small amount of aniline. There was much carbonaceous material not soluble in ether. The reaction just described was repeated with similar results.

Reaction Between Aniline and Furoyl Chloride at High Temperatures.-

The reaction described above was repeated without the use of zinc chloride and was heated on an oil-bath at 180° for twenty-four hours. There was obtained tar and aniline. A second attempt gave similar results.

Condensation Reaction Between Furoylanilide, Dimethyl Aniline and Phosphorous Oxychloride.-

This reaction was carried out after the directions of Hurd and Webb[6] in a 150 cc. Erlenmeyer flask equipped with a dropping funnel, thermometer and drying tube for the dropping funnel. Ten and four-tenths grams (0.06 mole) of pure phosphorous oxychloride were added to 9.4 g. (0.05 mole) of furoylanilide and 20.3 g. (0.168 mole) of dimethyl aniline cooled to 30° in a water-bath. When the phosphorous oxychloride was added the temperature of the reaction mixture rose to 39°. Heat was then applied by means of the water-bath until the temperature of the reaction mixture rose to 94°. The water-bath was then removed and the reaction mixture was heated with a smoky flame to 105° at which point a vigorous exothermic reaction took place and the temperature rose to 180°. While the exothermic reaction was taking place the flask was thrust as quickly as possible into an ice-salt mixture. After the reaction had subsided it was heated on a water-bath at 90° for five hours and worked up as described by Hurd and Webb[6]. Tar was the product.

A second run was warmed to 103° at which point the temperature rose quickly to 113° where it remained for three minutes and then started to fall. The reaction mixture was then warmed by means of a free flame to 119° where a second exothermic reaction took place and the temperature quickly rose to 132°. It was then cooled in an ice-salt bath to 105° and was heated on a boiling water-bath for three hours. The reaction mixture was worked up as described by Hurd and Webb[6] and yielded a small amount of furoylanilide, aniline and much tar.

SUMMARY

Acetanilide has been treated with furoyl chloride in the presence of aluminum chloride as a catalyst in carbon disulfide and nitrobenzene as solvents, under a variety of conditions. A trace of a compound melting at 140° has been obtained. Enough of the 140° compound was not obtained for an analysis.

Phthal-anil has been treated with furoyl chloride in the presence of zinc chloride at 180°. Tar was obtained. Phthal-anil was treated with furoyl chloride in nitrobenzene at

80° in the presence of aluminum chloride. Tar was the only product of the reaction.

Aniline was treated with two equivalents of furoyl chloride at high temperatures with, and without zinc chloride as a catalyst. Some decomposition took place as shown by the formation of tar.

Dimethyl aniline was condensed with furoylanilide using phosphorous oxychloride as the condensing agent. A vigorous decomposition reaction took place.

THE ATTEMPTED PREPARATION OF 2-FURYL-α-AMINOACETIC ACID AND SOME STUDIES ON FURYLACROLEIN.

INTRODUCTION

It was desired to prepare 2-furyl-α-aminoacetic acid for some studies on the physiological properties of the compound and to extend the synthetic possibilities of furfural.

Furfural is the least costly of all organic aldehydes and obtainable in large quantities. It is therefore quite natural that any attempt to prepare an amino acid which contains the furan ring should use furfural and correspondingly inexpensive inorganic salts.

A review of the literature has disclosed the following references to furan α-amino acids. Sasaki[1] has prepared d 1, (furyl-2)-α-alanin in good yields. Furfural was condensed with glycine anhydride in acetic anhydride in the presence of anhydrous sodium acetate. The condensation product was reduced with sodium amalgam and hydrolyzed with barium hydroxide to give the acid named above.

Posner[2] treated ethyl β-furylacrylate with hydroxylamine as described by him and obtained a 20% yield of the α-amino acid. Flatow[3] prepared the acid by the action of

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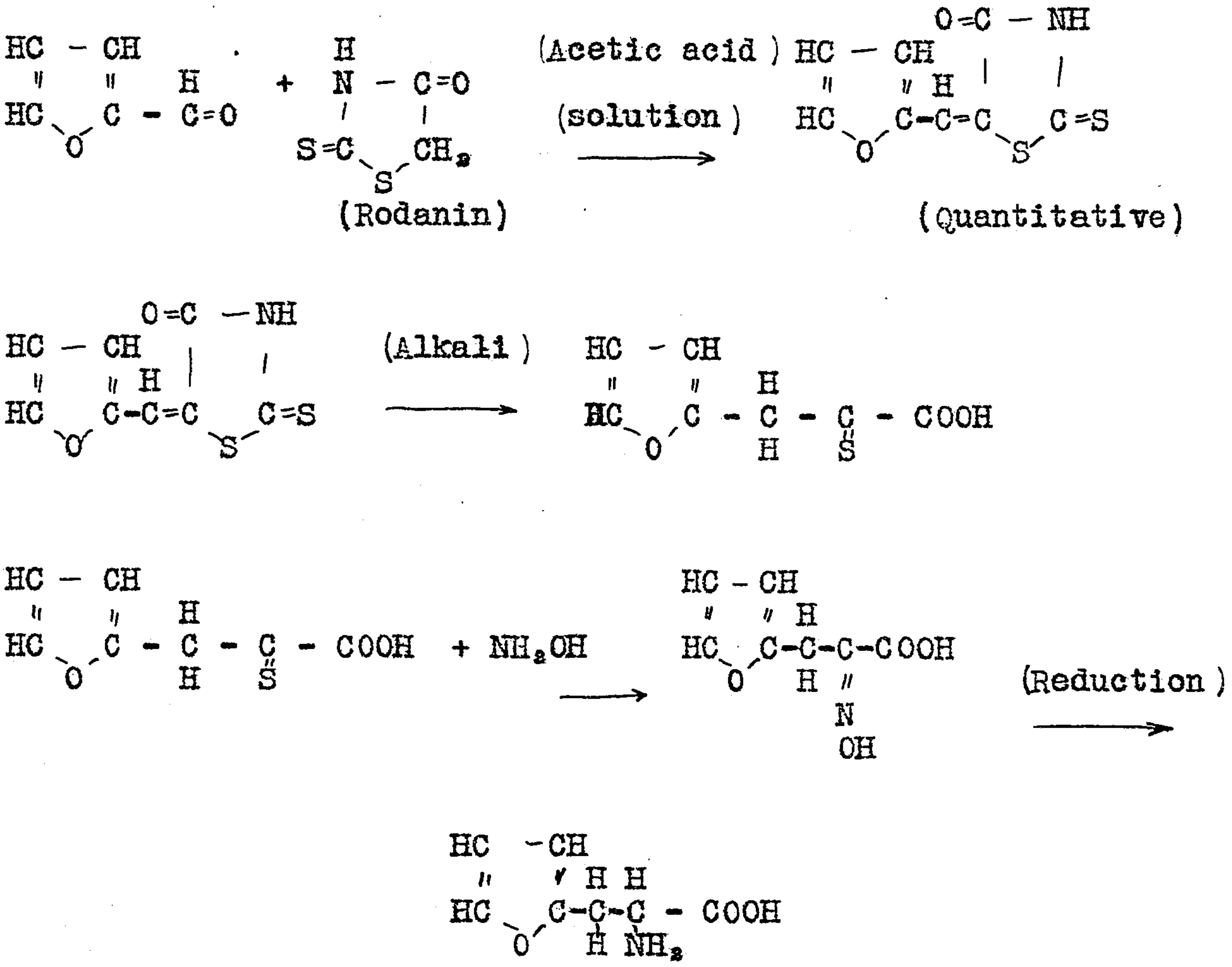
[1] Sasaki, *Ber.*, *54*, 2056 (1921).
[2] Posner, *Ann.*, *389*, 1 (see 107) (1912).
[3] Flatow, *Zeit. fur physiol. Chem.*, *64*, 367 (1910).

hippuric acid in acetic anhydride in the presence of anhydrous sodium acetate. The product of the condensation was then reduced and hydrolyzed.

Gränacher[4] obtained the α-amino acid as shown by the following equations:



In every case the compound was reported to be stable and resistant to an alkaline medium. With these points in mind there is no reason to predict that 2-furyl-α-aminoacetic acid once formed would be unstable. A series of attempts were made

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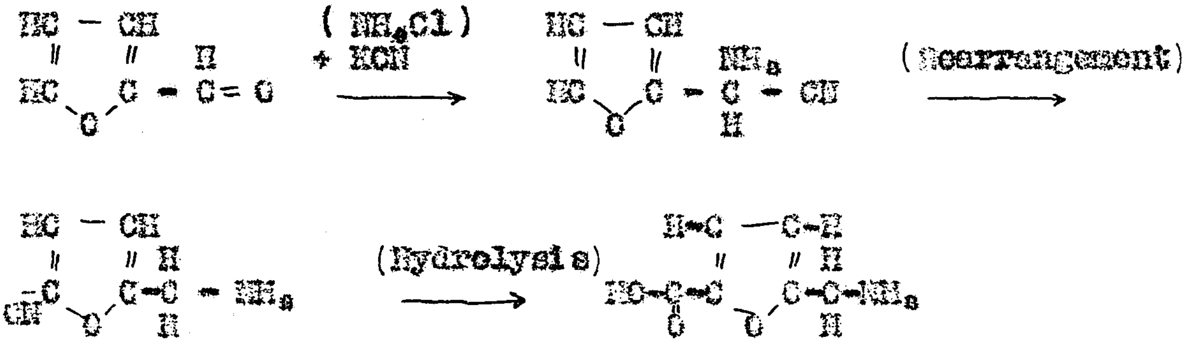
[4] Gränacher, Helv. Chem. Acta., 5, 610 (1922).

to prepare the acid by the action of potassium cyanide and ammonium chloride on furfural after the directions of Zelinsky and Stadnikoff[5]. In no case was a trace of the desired compound obtained and apparently the product of reaction was unstable.

Reichstein[6] has shown that dry hydrogen cyanide in ether split 2,5-dimethylfuran to give acetonyl acetone. This being true the results obtained by us are not startling. Runde, Scott and Johnson[7], and Reichstein[6] have shown that 2-furylacetonitrile undergoes rearrangement to form 2-methyl-5-cyanofuran which on hydrolysis gave 5-methylfuroic acid. It is not impossible that the intermediate compound formed would rearrange as illustrated by the following equations:



However we were not able to isolate either of the compounds proposed, but did obtain a small amount of furoin melting at 135°.

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[5] Zelinsky and Stadnikoff, *Ber.*, *39*, 1722 (1906).
[6] Reichstein, *Helv. Chem. Acta.*, *13*, 345 (1930).

EXPERIMENTAL PART

Action of Sodium Cyanide and Ammonium Chloride on Furfural and Furylacrolein.-

1st. Run. This run was carried out after the directions of Zelinsky and Stadnikoff[2]. All reactions were carried out in 3-neck flask of suitable size equipped with a mercury seal stirrer and dropping funnel. To a saturated solution of 5.4 g. (0.092 mole) of sodium cyanide and 5.0 g. (0.094 mole) of ammonium chloride in water was added with stirring 8.9 g. (0.094 mole) of furfural in 23 cc. of methyl alcohol. A vigorous reaction took place as was shown by the evolution of heat and the precipitation of a heavy viscous oil. The reaction mixture was allowed to stand over night and then decanted after which the oil was treated with 50 cc. of 10 % hydrochloric acid. The product was hydrolyzed and worked up as described by Zelinsky and Stadnikoff[2] and yielded amorphous carbon and tar.

2nd. Run. The reaction just described was repeated using furylacrolein in place of furfural and 50 cc. of methyl alcohol. A red oil began to separate as soon as the furylacrolein was added and continued for three hours. The water was decanted as before and the resulting red oil was refluxed with a slight excess of dilute (5%) alcoholic potassium hydroxide for five hours. After the reaction product was cool it was treated with cold dilute hydrochloric acid until neutral and extracted with ether. The ether solution yielded a small amount of an amorphous substance which could not be crystallized. There was much tar formed in the hydrolysis reaction.

3rd. Run. Run No. 1 was repeated exactly as described except that the reaction was run in ice and hydrolyzed by boiling with 5% alcoholic potassium hydroxide for six hours. The resulting solution was cooled and treated with cold 5% hydrochloric acid and extracted with ether and the ether extract yielded a small amount of a yellow amorphous substance which could not be crystallized. A second attempt gave a similar result.

4th. Run. The run just described was repeated. The resulting red oil was hydrolyzed by boiling for five hours with the calculated amount of 5% hydrated barium hydroxide in 50% alcohol. After the reaction mixture had cooled it was treated with the calculated amount of 0.2 N. sulfuric acid. The precipitated barium sulfate and tar was filtered out and extracted with ether. The ether solution yielded a small amount of a yellow crystalline compound from alcohol. This compound was shown to contain no nitrogen and melts at 135°, which is the melting point of furoin. A mixed melting point was not taken as an authentic sample was not available. No other substance was found to be present. A fractional evaporation of the water residue from the ether extraction failed to yield any other compound. This experiment was repeated as described with similar results.

<u>5th. Run.</u> The red oil from a run carried out as in No. 3 was treated with the calculated amount of hydrated barium hydroxide in 50% alcohol at room temperature for six days. It was then treated with 0.2 N. sulfuric acid as in No. 4. The products were tar, carbon and a small amount of a red oil which soon decomposed.

<u>6th. Run.</u> The red oil from a run carried out as in No. 3 was refluxed with a two equivalents of 10% acetic acid for five hours. After the resulting black solution had cooled it was filtered to remove the tar and neutralized with cold dilute sodium hydroxide and extracted with ether. Tar was the only product.

<u>7th. Run.</u> The red oil from a run carried out as in No. 3 was allowed to stand with two equivalents of 10% alcoholic potassium hydroxide for ten days and worked up as previously described. Tar was the only product. Furylacrolein was treated as described in runs 3, 4, 5, 6 and 7 with similar results.

SUMMARY

Furfural and furylacrolein have been treated with sodium cyanide and ammonium chloride to yield a red unstable oil. These oils have been treated with a variety of hydrolyzing agents under a variety of conditions. The desired $\underline{\alpha}$-amino acids were not isolated.

SOME STUDIES ON THE ATTEMPTED PREPARATION OF FURAN AMINES. THE PREPARATION OF TRIFURFURYL AMINE

INTRODUCTION

Aromatic and aliphatic amines are finding many uses as insecticides, in physiological studies and in the production of lacquers and varnishes. Amines are being extensively studied in connection with the preparation of oil and water emulsions for the destruction of plant and tree pests.

An amine to be of value in the last two fields must be available in large quantities and for a reasonable price. Furfural is the least expensive and can be produced in the largest quantities of all organic aldehydes. The preparation of furan amines from furfural is a field as yet unexploited. It was the purpose of this study to prepare furan amines from furfural and readily available inexpensive inorganic compounds.

Furfuryl amine has been prepared by reducing furonitrile with zinc and sulfuric acid[1], and with sodium amalgam[2] in alcohol. Goldschmidt[3] prepared furfuryl amine by reducing furfuraldoxime[4] in alcohol and acetic acid with sodium amal-

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[1] Wallach, Ber., 14, 751 (1881); Ciamician and Dennstedt, Ibid. 1475 (1881); Ciamician and Dennstedt, Ibid., 14, 1055 (1881) Wallach, Ann., 214, 193 (see 226) (1882).

[2] Taefel, Ber., 20, 398 (1887).

×[3] Goldschmidt, Ibid., 20, 728 (1887).

[4] Goldschmidt, Ibid., 25, 2583 (1892).

gam. Gilman and Hewlett[5] obtained furfuryl amine in a yield of 40% by reducing furfuraldoxime in absolute alcohol with sodium which is the best yield yet reported. Zanotti and Beckmann[6] obtained a mixture of mono-, di -, and trifurfuryl amines by the action of α-furfuryl bromide on ammonia in alcohol.

Furyl ethyl amine has been prepared by the action of hydrazine on ethyl β-furylacrylate as described by Windaus and Dalmer[7]. Asahina and Fujita[8] prepared the amine by condensing furfural with α-chloroethyl acetate and sodium in ether. The resulting furyl glycide ester was treated with hydroxylamine hydrochloride and reduced with sodium amalgam in 50% acetic acid to give furyl ethyl amine. Takamoto[9] has prepared furyl ethyl amine by the electrolytic reduction of furylnitroethylene in yields of 91%. Yabuta and Kambe[10] prepared the amine by reducing furylnitroethylene with aluminum amalgam to 2-furylacetaldoxime, which was then reduced with sodium amalgam.

Williams[11] obtained di-α-furfuryl amine by reducing furfuraldoxime in absolute ether with palladiumized animal charcoal.

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[5] Gilman and Hewlett, Iowa State College J. Sci., 4, 27 (1930).
[6] Zanetti and Beckmann, J. Am. Chem. Soc., 50, 2031 (1928).
[7] Windaus and Dalmer, Ber., 53, 2304 (1920).
[8] Asahina and Fujita, J. Pharm. Soc. Japan, No. 490, 1084, (1922); C.A., 17, 2578 (1923).
[9] Takemoto, Ibid., 48, 136 (1928); C.A., 22, 2004 (1928).
[10] Yabuta and Kambe, Proc. Imp. Acad. (Japan) 4, 120 (1928); C.A., 22, 4503 (1928).
[11] Williams, Ber., 60, 2069 (1927).

Some Proposed Reactions.- Ammonium formate is a comparatively inexpensive reagent. Leuckart[12] and others have prepared a variety of primary secondary and tertiary amines by heating aldehydes and ketones with ammonium formate. Wallach[13] has given an excellent discussion of this method and the preparation of a number of amines from various aldehydes and ketones. However, this method when applied to furfural leads to decomposition.

Mignonac[14] has prepared a variety of primary and secondary amines in good yields by treating the aldehyde or ketone in absolute alcohol with the calculated amount of dry ammonia for the formation of the imine. Finely divided nickel was then added and the reaction product was shaken with hydrogen under one atmosphere pressure. When furfural is treated with dry ammonia in absolute alcohol hydrofuramide is formed. The reduction of this compound will be described in the Experimental Part of this study.

Mignonac[15] prepared benzylamine by reducing hydrobenzamide in absolute alcohol with nickel. The yield of the amine was 27.5%.

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[12] Leuckart, Ber., 18, 2341 (1885); Leuckart and Bach, ibid. 19, 2128 (1886).
[13] Wallach, Ann., 343, 54 (1905).
[14] Mignonac, Compt. rend. 172, 223 (1921).
[15] Mignonac, Compt. rend., 171, 1148 (1920).

EXPERIMENTAL PART

Hydrofuramide, $((C_4H_3OCH)_3N_2)$.- This compound was prepared after the directions of Hartley and Dobbie[16]. To 96 g. (1.0 mole) of commercial furfural in 1000 cc. of water was added an excess of ammonia water. Heat was evolved during the first part of the reaction. After standing for fifteen hours the whole mass had crystallized. The crystals were filtered out on a Büchner funnel and well washed with cold water and dried. There was obtained a yield of 80 g. or 90% of hydrofuramide melting at 117°-118°. The product was slightly yellow in color but sufficiently pure for the work at hand.

Furylnitroethylene, $(C_4H_3OCH{=}CHNO_2)$.- This compound was prepared after the directions of Bouveault and Wahl[17]. The reaction was carried out in a 1000 cc. 3-neck flask equipped with a mercury seal stirrer, dropping funnel and protected from moisture with a drying tube. Five-tenths mole of sodium methylate was prepared by adding 11.5 g. (0.5 atom) of sodium to 120 cc. of absolute methyl alcohol. Forty-eight grams (0.5 mole) of furfural and 30.5 g. (0.5 mole) of nitromethane dissolved in 200 cc. of absolute methyl alcohol were added dropwise over a period of four hours to the sodium ethylate cooled to -3°. Some difficulty was encountered in hydrolyzing the sodium salt to furylnitroethylene. A part of the material was

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[16] Hartley and Dobbie, J. Chem. Soc., 73, 598 (1898).
[17] Bouveault and Wahl, Compt. rend., 135, 42 (1902).

removed and treated with 10% hydrochloric acid at 0° and decomposition took place. However when 19% HCl was used under the same conditions no decomposition took place and furylnitroethylene was obtained as a bright yellow solid. The compound was crystallized from petroleum ether (b. p. 40°-60°) and melts at 74°- 75°. After crystallization the yield was 41 g. or 60%. The yield was low because considerable was lost in orientation experiments with hydrochloric acid as described above. Bouveault and Wahl[17] did not report their yield or the strength of the hydrochloric acid used in hydrolysis of the sodium salt.

Reduction of Furfuraldoxime.- To 11.1 g. (0.1 mole) of furfuraldoxime dissolved in 50 cc. of 95% ethyl alcohol was added 0.05 g. of platinum oxide catalyst of Adams, Voorhees and Shriner[18]. The theoretical amount of hydrogen for the formation of furfuryl amine was added in ten hours. After the solution had been filtered to remove the catalyst it was distilled. There was recovered 50% of the furfuraldoxime and oils that did not have a definite boiling point. No trace of furfuryl amine was found. A second run gave similar results.

Reduction of Furylnitroethylene.- Thirteen and nine-tenths grams (0.1 mole) of furylnitroethylene were dissolved in 75 cc. of 95% ethyl alcohol and to this solution was added 0.15 g. of platinum oxide catalyst and a trace of ferric chloride. The solution was shaken with hydrogen for two hours and

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[18] Adams, Voorhees and Shriner, *Org. Syn.*, *8*, 92.

at the end of this time the theoretical amount of hydrogen had been added for the formation of furylethylamine. When the reaction bottle was opened in order to filter out the catalyst a strong odor of ammonia was noted, and the solution was black. The alcohol was distilled off and an attempt was made to distill the black residue under 4 mm. pressure. A violent explosion took place.

A second attempt was made using the quantities reported above in a solution containing 50 cc. of 95% alcohol and 50 cc. of glacial acetic acid. In this run 65% of the theoretical amount of hydrogen was absorbed in ten minutes and then no further reduction could be caused to take place after the catalyst had been reactivated. The solution was neutralized with sodium carbonate and extracted with ether. After the ether solution had been dried over anhydrous sodium sulfate it was distilled. There was obtained a small amount of furylnitroethylene and tar.

Attempted Reduction of Hydrofuramide with Nickel.- The nickel catalyst was prepared by precipitating nickel as the hydroxide from the nitrate with sodium hydroxide. The resulting nickel hydroxide was washed with water and heated to give the oxide which was reduced in a pyrex tube at 300° with a stream of hydrogen.

To 26.8 g. (0.1 mole) of hydrofuramide[19] suspend-

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[19] The hydrofuramide used was prepared by adding freshly distilled furfural to an absolute alcohol solution of dry ammonia in excess. Hydrofuramide prepared in this

ed in 75 cc. of absolute alcohol was added 5 g. of nickel catalyst. The mixture was shaken with hydrogen under one atmosphere pressure for forty-eight hours. No reduction took place. A second run using 26.8 g. (0.1 mole) of hydrofuramide was treated with hydrogen in 150 cc. of absolute alcohol as before. No reduction took place. The third run was carried out in 150 cc. of 95% alcohol under forty-five pounds pressure with the quantities used in the second run and no hydrogen was absorbed.

Reduction of Hydrofuramide with Platinum Oxide Catalyst.- To a solution of 55 g. (0.205 mole) of hydrofuramide in 150 cc. of glacial acetic acid and 25 cc. of 95% ethyl alcohol was added 0.3 g. of platinum oxide catalyst. The mixture was shaken with hydrogen and (0.615 mole) of hydrogen was added in four hours, after two reactivations. After the black solution had been filtered to remove the catalyst it was neutralized with dilute sodium carbonate and extracted with ether. The ether solution was washed with water, dried over sodium sulfate and distilled. There was obtained 21 g. or 38.2% of trifurfuryl amine boiling at 133°-138°/1 mm. Trifurfuryl amine is a yellow oil of slight odor and quite stable.

The hydrochloride was prepared as described by Zanetti and Beckmann[6] and checked the melting point reported by them. This is also true for the boiling point of the amine. Two

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manner melts at 121° and is a beautiful white crystalline compound with a yellow tinge.

grams of the amine were dissolved in 25 cc. of anhydrous ether and precipitated with dry hydrogen chloride. The ether was decanted from the white solid and it was then crystallized from a mixture of absolute ether and absolute ethyl alcohol. It is a white crystalline compound melting at 156°-157° and quite stable even in the atmosphere.

The picrate of trifurfuryl amine was prepared by treating a dilute solution of the amine in ether with a concentrated solution of picric acid in ether in excess. A heavy yellow crystalline solid was precipitated which was recrystallized from 95% ethyl alcohol. The picrate[20] is stable and melts at 132°.

Two additional runs were made as described and the yields of trifurfurylamine obtained were 38.3% and 37% respectively.

<u>2nd. Run</u>. The reaction described in Run No. 1 was repeated in 200 cc. of 95% ethyl alcohol. No hydrogen was added after ten hours. A second attempt gave the same result.

<u>3rd. Run</u>. Thirty grams (0.112 mole) of hydrofuramide was dissolved in 200 cc. of 95% ethyl alcohol with the theoretical amount of hydrochloric acid to form the hydrochloride and shaken with hydrogen as before. No reduction took place.

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[20] A description of this compound has not been reported in the literature.

4th. Run. Run No. 2 was repeated in ether with a negative result.

5th. Run. Twenty-six and eight-tenths grams (0.1 mole) of hydrofuramide were dissolved in 100 cc. of acetic anhydride and shaken with 0.3 g. of platinum oxide catalyst and hydrogen. The theoretical amount of hydrogen for the formation of trifurfuryl amine was absorbed in three hours. Most of the excess acetic anhydride was removed on a water-bath under 15 mm. pressure. The resulting heavy tar was treated with sodium carbonate and worked up as described in previous experiments. No trace of any amine could be detected. A second run gave the same result.

Reduction of Hydrofuramide With Sodium.- Fifty grams (0.186 mole) of hydrofuramide was added to 800 cc. of 95% ethyl alcohol in a 2000 cc. 3-neck flask equipped with a mercury seal stirrer and Hopkins condenser. Thirty-seven grams (1.58 atoms) of sodium were added as rapidly as possible with stirring. After the reaction was complete the reaction solution was made slightly acid with dilute sulfuric acid and the alcohol removed under reduced pressure. The product was made slightly alkaline with sodium hydroxide and extracted with ether. After the ether solution had been dried over anhydrous sodium sulfate it was distilled. An intractable tar was the result.

Reaction Between Furfural and Ammonium Formate.- The following reactions were carried out after the directions of Wallach[13]. Eighteen and eight-tenths grams (0.2 mole) of freshly distilled furfural were placed in a 250 cc. balloon flask with 40 g. (1.56 moles) of ammonium formate. The flask was equipped with an air condenser and drying tube. The reaction mixture was heated on an oil-bath at 110°, for five hours, cooled and extracted with ether to remove any free amine but none was present. After this operation the tar-like residue was boiled with 10% alcoholic potassium hydroxide and worked up. No amines were present. All of the furfural was decomposed.

The first experiment was repeated as described, using 40 cc. of glacial acetic acid as a solvent. Tar and carbon were the products of the reaction. A third run was carried out at 180° with negative results. All the runs described were checked with similar results.

SUMMARY

All attempts to prepare furfuryl amine and furyl ethyl amine from furfuraldoxime and furylnitroethylene failed.

A number of unsuccessful attempts were made to prepare amines from furfural and ammonium formate.

Hydrofuramide was reduced with hydrogen and platinum oxide as a catalyst to trifurfuryl amine in yields of 38% in a mixture of alcohol and acetic acid. The reduction could not be effected in ether or 95% alcohol.

PREPARATION OF ETHYL 5-NITROFUROATE AND SOME OF ITS DERIVATIVES

INTRODUCTION

Marquis[1] has prepared methyl 5-nitrofuroate and ethyl 5-nitrofuroate by nitrating the esters in acetic anhydride. The free 5-nitrofuroic acid is easily obtained by treating the ester with hot 50% sulfuric acid.

Klinkhardt[2] prepared 5-nitrofuroic acid by warming dehydromucic acid with a mixture of ten parts of sulfuric acid and one of nitric.

Priebs[3] nitrated furylnitroethylene with fuming nitric acid to obtain 5-nitrofurylnitroethylene which was oxidized with chromic acid mixture to 5-nitrofuroic acid.

Hill and Palmer[4], and Hill and White[5] have prepared 5-nitrofuroic acid by treating 5-sulfofuroic acid with fuming nitric acid at 60°.

Gilman and Wright[6] have prepared 5-nitrofuroic acid by oxidizing 5-nitrofurfural.

The nitrofuroic acids prepared by the six methods mentioned are identical and the position of the nitro group is

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[1] Marquis, Compt. rend., 137, 520 (1903); Ann. chim. phys. (8) 4, 196 (1905).

[2] Klinkhardt, J. prakt. Chem., (2) 25, 41 (1882).

[3] Priebs, Ber., 18, 1362 (1885).

[4] Hill and Palmer, Am. Chem. J., 10, 380 (1888).

[5] Hill and White, ibid., 27, 193 (1902).

[6] Gilman and Wright, J. Am. Chem. Soc., 52, 2550 (1930).

generally accepted as 5[4], though not definitely proven as yet.

5-Nitrofuroyl chloride was prepared in this study by treating 5-nitrofuroic acid with phosphorous pentachloride after the directions of Marquis[7]. A series of attempts was made to prepare the acid chloride by treating 5-nitrofuroic acid with thionyl chloride, without success.

Several attempts were made to prepare 5-nitrofuroic acid by nitrating furoic acid with fuming nitric acid in acetic anhydride[1]. In every case violent decomposition reactions took place when the reaction mixture was poured onto ice.

Ethyl 5-nitrofuroate was reduced with aluminum amalgam after the directions of Marquis[7]. The yields obtained were below those reported by Marquis. However, Gilman and Wright[6] in this laboratory have remedied the difficulty. Several attempts were made to prepare ethyl 5-aminofuroate by reducing the ester in 95% alcohol with hydrogen and platinum oxide as a catalyst without success. Gilman and Wright have repeated this work and report similar results, but when absolute alcohol is used a good yield of ethyl 5-aminofuroate is obtained.

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[7] Marquis, Ann. chim. phys., (8) 4, 196 (1905).

EXPERIMENTAL PART

Apparatus. All nitration reactions were carried out in a three-neck balloon flask of suitable size equipped with a mercury seal stirrer, dropping funnel and thermometer. The dropping funnel and thermometer were protected from moisture with a drying tube filled with anhydrous calcium chloride.

Ethyl Furoate, ($C_4H_3OCOOC_2H_5$).- The ethyl furoate used was prepared after the directions of Leimbach[8]. Three hundred thirty-six grams (3.0 moles) of commercial furoic acid were dissolved in 1350 cc. of 95% ethyl alcohol in a three liter flask fitted with a two hole rubber stopper, glass tube and calcium chloride tube. The alcohol solution was saturated with dry hydrogen chloride and treated intermittently at room temperature over a period of two days and distilled to remove most of the alcohol. After the residue had been dissolved in ether it was washed with dilute sodium bicarbonate followed by water and dried over anhydrous sodium sulfate. The solution was then heated on a water-bath to remove the ether and distilled with a free flame and the fraction boiling between 193°-196° /740 mm. was collected. The yield was 252 g. or 60%.

A second run using furoic acid crystallized from carbon tetrachloride, and absolute alcohol was run as described for the previous experiment. The yield of ethyl furoate was

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8 Leimbach, J. prakt. Chem., (2) 65, 20 (1902).

340 g. or 81%. There is some decomposition in the two reactions described as proven by the formation of carbon. Marquis[7] reported an 82% yield of ethyl furoate from a run similar to the second reported above.

Ethyl 5-Nitrofuroate, ($NO_2C_4H_3OCOOC_2H_5$).- This compound was prepared after the directions of Marquis[2]. The nitrating solution was prepared by adding 350 g. (sp.g.1.51) (5.45 moles) of fuming nitric acid to 560 g. (5.49 moles) of acetic anhydride dropwise with stirring over a period of three hours. The acetic anhydride was cooled to -10° with a bath of ice and salt. To the nitrating solution was added dropwise with stirring 140 g. (1.0 mole) of ethyl furoate in 210 g. (2.0 moles) of acetic anhydride over a period of two and one-half hours. During the time of addition and for three hours afterward the temperature of the reaction mixture was not allowed to rise above -5°. The reaction mixture was poured onto cracked ice[9] in a 4-l Erlenmeyer flask immersed in a mixture of ice and salt. A milky white emulsion was formed which settled out as a yellow oil over a period of six hours. After the ice and water had been decanted the oil was treated with pyridine until the mixture was no longer acid to litmus paper. The dark colored crystalline solid that was formed was dissolved in boiling alcohol, treated with Norite and filtered through

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[9] About 2.5 kilos of ice were used.

a hot-water funnel. A beautiful yellow crystalline compound separated on cooling the solution. Ethyl 5-nitrofuroate melts at 101° without decomposition. The yield was 110 g. or 60% of the theoretical. Marquis[7] reported a yield of 65% from 50 g. (0.357 mole) of ethyl furoate. A number of runs were made with similar results.

<u>5-Nitrofuroic Acid</u>, ($NO_2C_4H_2OCOOH$).- This compound was prepared as described by Marquis[7]. Thirty-five grams (0.162 mole) of ethyl 5-nitrofuroate were added in small portions to 200 cc. of 50% sulfuric acid heated to 150°. The ester dissolved rapidly in the sulfuric acid and as soon as the solution was complete 400 cc. of cold water was added and the whole cooled in an ice-bath. After the mixture was cold it was extracted with ether, and the ether was removed on a water-bath. The resulting yellowish white solid was crystallized from boiling water, and the yield was practically quantitative. It is a stable compound melting at 185°.

<u>5-Nitrofuroyl Chloride</u>, ($NO_2C_4H_2COCl$).- This compound was prepared after the directions of Marquis[7]. To 15.7 g. (0.10 mole) of 5-nitrofuroic acid in a small balloon flask was added 20.8 g. (0.10 mole) of phosphorous pentachloride. The reaction mixture was protected from the atmosphere with a calcium chloride tube. After the phosphorous pentachloride was added the reaction started at once and hydrogen chloride was evolved. The reaction mixture was heated on a water-bath until

the hydrogen chloride ceased to escape and the phosphorous oxychloride was distilled off under reduced pressure. After the phosphorous oxychloride had been removed the oily product was crystallized from a mixture of petroleum ether (b.p. 40°-60°) and chloroform. The yield of the pure compound melting at 38° was 5.7 g. or 50%[10].

Reaction Between 5-Nitrofuroic Acid and Thionyl Chloride.- Thirteen and one-tenth grams (0.11 mole) of thionyl chloride were added dropwise to 15.7 g. (0.10 mole) of 5-nitrofuroic acid suspended in 200 cc. of dry benzene. The reaction mixture was heated to boiling for four hours but no hydrogen chloride was evolved.

A second run using the quantities given above was carried out in ether in which 5-nitrofuroic acid is soluble. The reaction mixture was refluxed for six hours without more than a trace of hydrogen chloride being formed.

Reaction Between Furoic Acid and Nitric Acid in Acetic Anhydride.- This reaction was carried out after the directions of Marquis[7] for ethyl 5-nitrofuroate. The nitrating solution was prepared by adding 70 g. (sp. gr. 1.51) (1.09 moles) of fuming nitric acid to 112 g. (1.08 moles) of acetic anhydride cooled to -5° over a period of two hours. Twenty-four grams (0.2 mole) of furoic acid dissolved in 42 g.

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[10] The yield reported can be raised as the reaction was carried out but once. Marquis[7] failed to report his yield.

(0.40 mole) of acetic anhydride were added over a period of two hours to the nitration mixture. The reaction mixture was kept below -5° and stirred for four hours after the addition of the furoic acid. No color change took place during the reaction. A small portion of the reaction mixture was removed with a pipette and run onto ice and a violent reaction took place with complete decomposition of the product. A second run gave a similar result.

Ethyl 5-Aminofuroate, ($NH_2C_4H_2OCOOC_2H_5$).- The reduction of ethyl 5-nitrofuroate was carried out after the directions of Marquis[7] who reported a yield of 52%. The aluminum amalgam used was prepared after the directions of Wislicenus[11]. Aluminum foil of the thickness of a thin sheet of paper was cut into strips 0.5 cm. wide and 3.5 cm. long. These strips were placed in an Erlenmeyer flask and treated with a dilute solution of sodium hydroxide until a vigorous evolution of hydrogen took place after which the hydroxide was quickly decanted and the aluminum washed well with water, 95% ethyl alcohol and absolute ether[12]. A 5% solution of mercuric chloride was added after the ether was decanted. If the operations are carried out rapidly and thoroughly with a good grade of aluminum foil a very active aluminum amalgam can be prepared.

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[11] Wislicenus and Kaufmann, Ber., 28, 1323 (1895).

[12] The ether employed was that commonly used in preparing the Grignard reagent. It had not been dried with sodium.

Fifteen grams (0.081 mole) of ethyl 5-nitrofuroate were dissolved in a mixture of 250 cc. ether and 75 cc. 95% ethyl alcohol. The solution was treated with 5 g. (0.18 atom) of aluminum amalgam prepared as previously described. A very vigorous reaction took place upon adding the amalgam which was controlled by using an ice-bath. The evolution of hydrogen diminished after a short time and the mixture was allowed to stand for eleven hours. The formation of a large amount of a red precipitate was noted. After the mixture was filtered the ether and alcohol were removed on a water-bath and the resulting gummy residue was crystallized from a mixture of three volumes of benzene and one of 95% ethyl alcohol. There was obtained 3.3 g. of ethyl 5-aminofuroate melting at 95°, or a yield of 21%. There was considerable material left which did not crystallize. There was recovered 12.5% of ethyl-5-nitrofuroate. Ten runs were made with similar results. The red precipitate was shown to contain aluminum and resisted all attempts at hydrolysis.

Catalytic Reduction of Ethyl 5-Nitrofuroate.- The catalytic reduction of ethyl 5-nitrofuroate was carried out as described by Adams and Cohen[13] using the platinum oxide catalyst of Adams, Voorhees and Shriner[14].

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[13] Adams and Cohen, Org. Syn., 8, 66.
[14] Adams, Voorhees and Shriner, Org. Syn., 8, 92.

Nine and two-tenths grams (0.05 mole) of ethyl 5-nitrofuroate were added to 150 cc. of 95% ethyl alcohol with 0.157 g. of platinum oxide catalyst. The mixture was shaken with hydrogen at room temperature and the theoretical amount of hydrogen was absorbed for the formation of ethyl 5-aminofuroate in five minutes. After the theoretical amount of hydrogen had been added the reduction was stopped and the alcohol was removed on a water-bath. The resulting black viscous tar was treated as previously described. No ethyl 5-aminofuroate could be obtained. Several additional runs gave similar results. Gilman and Wright in this laboratory have obtained similar results in 95% alcohol but have obtained good yields of the desired compound in absolute alcohol.

SUMMARY

Ethyl 5-nitrofuroate, 5-nitrofuroic acid, 5-nitrofuroyl chloride have been prepared as previously described. 5-Nitrofuroic acid was shown to be inactive towards thionyl chloride.

Ethyl 5-aminofuroate was obtained in yields of 21% by reducing ethyl 5-nitrofuroate with aluminum amalgam. Several attempts to prepare ethyl 5-aminofuroate by the catalytic reduction of ethyl 5-nitrofuroate failed.

Two unsuccessful attempts were made to prepare 5-nitrofuroic acid by nitrating furoic acid in acetic anhydride.

THE ATTEMPTED PREPARATION OF A DI-NITROFURFURAL

INTRODUCTION

HISTORICAL. Gilman and Wright[1] have prepared 5-nitrofurfural diacetate by nitrating furfural diacetate[2] and furfural[3] in acetic anhydride. Marquis[4] has prepared ethyl and methyl 5-nitrofuroate by nitrating the esters in acetic anhydride.

Marquis[5] has nitrated furan in acetic anhydride and obtained 2-nitrofuran. In the preparations mentioned the technique is the same in that the nitration reactions are carried out in acetic anhydride, poured onto cracked ice and the ring closed with pyridine.

Klinkhardt[6] has prepared 5-nitrofuroic acid by warming dehydromucic acid with a mixture of ten parts of concentrated sulfuric acid and one of concentrated nitric acid. The formation of some 2,5-dinitrofuran was reported.

Hill and Palmer[7], and Hill and White[8] have prepared 5-nitrofuroic acid, 2-nitro-5-sulfofuran and 2,5-dinitrofuran by the action of fuming nitric acid on 5-sulfofuroic acid. Attention is called to the fact that the reactions reported

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[1] Gilman and Wright, *J. Am. Chem. Soc.*, *52*, 2550 (1930).

[2] Gilman and Wright, *Iowa State College J. Sci.*, *4*, 35 (1929).

[3] Gilman and Wright, *J. Am. Chem. Soc.*, *52*, 4165 (1930).

[4] Marquis, *Ann. Chim. phys.*, (8) *4*, 196 (1905); *Compt. rend.*, *137*, 520 (1903).

[5] Marquis, *Compt. rend.*, *132*, 140 (1901), *ibid.*, *134*, 776 (1902); *ibid.*, *135*, 505 (1902); *ibid.*, *137*, 520 (1903).

[6] Klinkhardt, *J. prakt. Chem.* (2) *25*, 41 (1882).

[7] Hill and Palmer, *Am. Chem. J.*, *10*, 380 (1888).

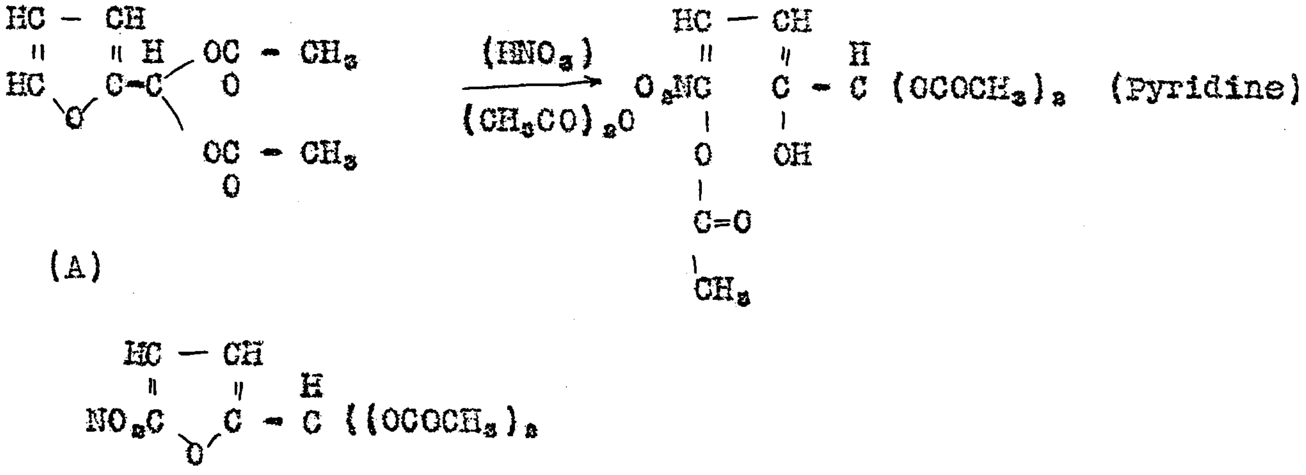
[8] Hill and White, *ibid.*, *27*, 193 (1902).

by Hill and coworkers did not give substitution reactions with the furan ring other than on the 2,5-positions.

Priebs[9] has prepared 5-nitrofuroic acid by oxidizing the nitration product of furylnitroethylene with chromic acid mixture.

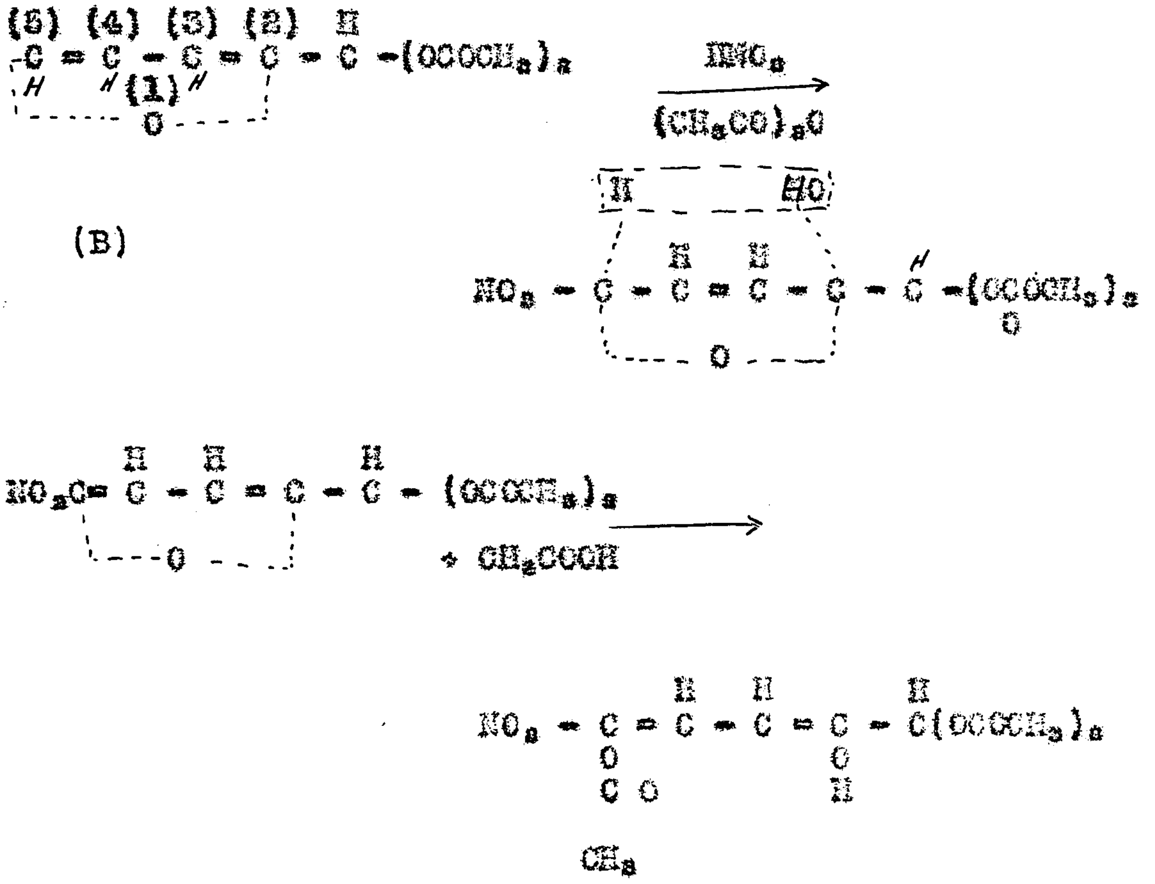
<u>THEORETICAL.</u> Gilman and Wright[10] have reviewed the literature of the addition of bromine to conjugated systems, especially, benzene, anthracene, phenanthrene, pyridine, furan, thiophene and pyrrole, and have proved the preliminary addition of a molecule of bromine to one of the conjugated systems of ethyl furylacrylate. One molecule of hydrogen bromide is then removed and ethyl 5-bromofurylacrylate is formed.

Gilman and Wright[1] have isolated the intermediate compound which is formed when furfural or furfural diacetate is nitrated in acetic anhydride. This compound conforms with that ascribed by Marquis[4] to the 2-nitrofuran ring fission products and can be illustrated by the following formulas:



(A)

If this explanation be true the nitration of the furan ring is not 1,4-addition but substitution. The following equation illustrates the nitration of furfural diacetate by 1,4-addition and elimination of water:



(B)

This explanation is open to attack for several reasons, namely: What is the catalyst that causes the acetic acid to add to the ether oxygen in the furan ring, and why is it that when 5-nitrofurfural diacetate is treated with fuming

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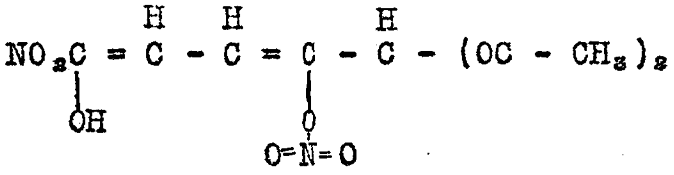
9 Friess, *Ber.*, 18, 1382 (1885).

10 Gilman and Wright, *J. Am. Chem. Soc.*, 52, 3349 (1930).

nitric acid in acetic anhydride the intermediate compound noted above is not formed. The explanation of the nitration of furfural diacetate and ethyl furoate would be much simpler if the intermediate nitration product had been proven to have the following formula for obvious reasons:



$$\mathrm{NO_2}\underset{\mathrm{OH}}{\mathrm{C}} = \overset{\mathrm{H}}{\mathrm{C}} - \overset{\mathrm{H}}{\mathrm{C}} = \underset{\underset{\mathrm{O{=}N{=}O}}{\mathrm{O}}}{\mathrm{C}} - \overset{\mathrm{H}}{\mathrm{C}} - (\mathrm{OC} - \mathrm{CH_3})_2$$

If the 1,4-addition explanation is correct the failure to obtain a dinitrofurfural diacetate is not surprising but if the explanation proposed by Gilman and Wright[1] and Marquis[4] is correct the formation of a dinitro body is a matter of reaction conditions or ring stability. The matter of steric hinderance is one of which little is known in connection with furan chemistry. The reaction is complicated by the reaction between acetic anhydride and nitric acid to form tetranitromethane, acetic acid and water. It is not impossible that the addition of acetic acid takes place to the 1,4-addition product between furfural diacetate and nitric acid represented by (B).

EXPERIMENTAL PART

Apparatus. All reactions where necessary were carried out in a 3-neck flask equipped with a dropping funnel, mercury seal stirrer and thermometer.

Furfural Diacetate, ($C_4H_3OCH(OCOCH_3)_2$).– This compound was prepared after the directions of Gilman and Wright[2]. The yields obtained from a large number of runs varied between 40% and 76%. There was no obvious reason why this was so. Attention is called to the fact that the flask from which the crude furfural diacetate is to be distilled should be free of mineral acids. The yield can be improved by careful drying of the crude product which can be done in the atmosphere on paper or waste cloth. In filtering and washing the crude product a piece of old laboratory towel cut to fit a Büchner funnel is far superior to paper or glass wool as a filter base.

The use of sodium carbonate is not necessary. It was found convenient to pour 100 g. to 200 g. portions of the liquid into cold water and stir vigorously. The water was decanted through the filter and the process repeated until the furfural diacetate had solidified. After shaking the material vigorously with several quantities of water pour the solid furfural diacetate onto the cloth filter. The crude furfural diacetate itself should not be poured onto the filter until it has solidified.

Tetranitromethane, ($C(NO_2)_4$).- This compound was prepared after the directions of Chattaway[11]. Thirty-one grams (0.5 mole) of absolute nitric acid[12] were placed in a 250 cc. Erlenmeyer flask fitted with a one hole rubber stopper, burette, and the burette was protected from moisture with a calcium chloride tube. Fifty-one grams (0.5 mole) of acetic anhydride were added in 2 cc. portions to the nitric acid. The temperature of the reaction mixture was not allowed to rise above 20°-25°. When all the acetic anhydride had been added the burette was removed and the flask was covered with an inverted beaker for seven days, poured into 200 cc. of cold water and steam distilled to remove the tetranitromethane. The tetranitromethane was washed with water and dried over anhydrous calcium chloride. There was obtained 19 grams of pure tetranitromethane or a yield of approximately 80%.

5-Nitrofurfural Diacetate, ($NO_2C_4H_2O-CH(OCOCH_3)_2$).- This compound was prepared after the directions of Gilman and Wright[1]. The nitrating mixture was prepared by adding dropwise 87.4 g. (1.38 mole) of fuming nitric acid (sp.gr.1.51) to 286 g. (2.8 moles) of acetic anhydride chilled to 0°. A solution of 99.0 g. (0.50 mole) of furfural diacetate in 102. g. (1.0 mole) of acetic anhydride was added slowly to the

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[11] Chattaway, J. Chem. Soc., 97, 2099 (1910).

[12] The nitric acid was prepared by treating nitric acid (sp. gr.1.51) with concentrated sulfuric acid (sp.gr.1.84) and distilling.

nitrating mixture which was not allowed to rise above -5°. The time required for the addition was about thirty minutes, after which the mixture was stirred for three hours and poured onto one kilo of cracked ice. A 40% sodium hydroxide solution was added with vigorous stirring until the precipitation of the oil was complete. The water layer was decanted and a volume of pyridine equal to that of the oil was added with crushed ice. The yield of 5-nitrofurfural diacetate melting at 92° from hot alcohol, was 49 g. or 40%.

The ring fission compound was obtained as described by Gilman and Wright[1]. It melts at 106°- 107°.

Attempted Nitration of the Furan Ring With Tetranitromethane.- The following reactions were carried out after the directions of Schmidt and Fischer[13].

Four and eight-tenths grams (0.05 mole) of furfural and 3.95 g. (0.05 mole) of dry pyridine were dissolved in 10 cc. of absolute alcohol. To this solution chilled to 0° was added 9.9 g (0.055 mole) of tetranitromethane with stirring in 10 cc. of absolute alcohol over a period of thirty minutes. The reaction mixture was stirred for eight hours at 0° and for twelve at 25°. At the end of the time mentioned the reaction mixture was poured into cold water and extracted with ether. After the ether solution had been dried it was distilled and yielded a small quantity of water soluble oils. A second run

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[13] Schmidt and Fishher, Ber., 53, 1537 (1920).

gave similar results.

Six and nine-tenths grams (0.05 mole) of furylacrylic acid and 3.95 g. (0.05 mole) of pyridine were dissolved in 20 cc. of dry acetone. To this solution chilled to 0° was added 9.9 g. (0.055 mole) of tetranitromethane in 10 cc. of acetone with stirring over a period of three hours. After the tetranitromethane had been added the reaction mixture was stirred at 0° for eight hours and at 25° for ten. It was then poured into water and extracted with ether. The ether solution was treated as above and yielded a small amount of unchanged furylacrylic acid and water soluble oils. A second run gave similar results.

Furfural diacetate was treated as described for furylacrylic acid. Most of the diacetate was recovered unchanged.

<u>Nitration of Furfural Diacetate</u>.- This reaction was carried out after the directions of Gilman and Wright[1], except that the amount of nitric acid was doubled and the temperature of the reaction mixture was allowed to rise to 17°.

The nitration mixture was prepared by adding dropwise with stirring 35 g. (0.545 mole) of fuming nitric acid (sp.gr.1.51) to 28 g. (0.274 mole) of acetic anhydride cooled to -5°. To the nitrating mixture was added 9.9 g. (0.05 mole) of furfural diacetate dissolved in 11 g. (0.108 mole) of acetic anhydride, over a period of fifteen minutes. The temperature of the reaction mixture was allowed to rise to 5° at the end of two hours and kept at 17° for two hours. After the resulting red solution had been poured onto crushed ice it was worked up as described for the preparation of 5-nitrofurfural diacetate. The product was crystallized from alcohol and proved to be 5-nitrofurfural diacetate by means of a mixed melting point determination. The yield was 26%.

Furfural diacetate was nitrated in acetic acid after the general directions of Orton[14]. To 9.9 g.(0.05 mole) of furfural diacetate in 34 g. of glacial acetic acid was added 10 g. (0.155 mole) of fuming nitric acid (sp. gr. 1.51) in 10 g. of glacial acetic acid. The temperature at the start of the reaction was 25° and rose to 35° when half of the nitric acid had been added and was then cooled to 26°. After the rest of the nitric acid had been added the temperature rose to 45° and the solution was stirred at that temperature for three hours and poured onto crushed ice. The product was worked up as previously described. There was obtained a small amount of a sweet smelling water soluble yellow oil.

Several attempts were made to nitrate furfural diacetate after the directions of Menke[15]. A solution of 9.9 g. (0.05 mole) of furfural diacetate in 10 g. of acetic anhydride was added to a mixture of finely powdered ($Cu(NO_3)_2 \cdot 3H_2O$) in

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[14] Orton, J. Chem. Soc., 81, 806 (1902).
[15] Menke, Rec. trav. chim., 44, 141 (1925).

25 g. of acetic anhydride at 0°. After a short time a reaction started that soon became so vigorous as to remove most of the reactants from the flask.

The reaction was repeated as described with use of a more efficient cooling-bath. After standing at -2° for several hours the reaction mixture was removed and warmed to 25° and finally to 80° on a steam-bath. The residue was poured into cold water and extracted with ether which after evaporation yielded furfural diacetate and a small quantity of a yellow oil soluble in water.

One attempt was made to nitrate furfural diacetate in anhydrous nitrobenzene. To 9.9 g. (0.05 mole) of furfural diacetate in 20 cc. of nitrobenzene was added dropwise with stirring 6.5 g. (0.10 mole) of fuming nitric acid (sp. gr. 1.51) in 5 cc. of nitrobenzene. The reaction was started at 25° and then cooled to 0° for eight hours. After the reaction mixture had been poured onto cracked ice it was neutralized with pyridine and steam distilled to remove the nitrobenzene. The water residue was extracted with ether and the ether was removed on a water-bath. As the residue was a liquid it was distilled to give some low boiling oils and furfural.

One run using the quantities given above was carried out in carbon tetrachloride at room temperature. The reaction product was poured onto cracked ice and treated with pyridine until neutral, after which the residue was extracted with ether, dried and distilled. The products were low boiling oils, furfural and furfural diacetate. A second run was carried out at -5° and worked up as described with similar results.

An attempt was made to nitrate furfural diacetate in carbon tetrachloride in the presence of phosphorous pentoxide. Nine and nine-tenths grams (0.05 mole) of furfural diacetate were added to 25 cc. of anhydrous carbon tetrachloride which contained 7.1 g. (0.05 mole) of phosphorous pentoxide. To this mixture chilled to -5° was added with stirring 6.5 g. (0.10 mole) of fuming nitric acid (sp. gr. 1.51). After five hours the oily black reaction mixture was poured onto cracked ice, and neutralized with dilute sodium hydroxide (10%). A small quantity of pyridine was then added and the black mixture was extracted with ether. The ether extract yielded tar.

Attempted Nitration of 5-Nitrofurfural Diacetate.- The following experiment was carried out after the directions of Gilman and Wright[1] for the preparation of 5-nitrofurfural diacetate, and is a rather significant experiment.

The nitration mixture was prepared by adding 17.5 g. (0.27 mole) of fuming nitric acid (sp.gr.1.51) to 28 g. (0.27 mole) of acetic anhydride cooled to -5°. To the nitrating mixture was added dropwise with stirring a solution of 11 g. (0.045 mole) of 5-nitrofurfural diacetate in 28 g. (0.27 mole) of acetic anhydride over a period of thirty minutes. Approximately half of the reaction mixture was poured onto crushed ice three hours after the addition of the last of the 5-nitrofurfural diacetate. A white crystalline solid separated at once which was proven to be 5-nitrofurfural diacetate by means of a mixed melting point determination. The rest of the reaction mixture was allowed to stand for an additional fifteen hours in an ice-box and worked up as described for the first half. The recovery of 5-nitrofurfural diacetate was practically quantitative.

5-Nitrofurfural diacetate was nitrated in carbon tetrachloride with negative results. To 1.0 g. (0.004 mole) of 5-nitrofurfural diacetate in 5 cc. of anhydrous carbon tetrachloride was added 0.3 g. (0.0046 mole) of fuming nitric acid (sp. gr. 1.51) in 5 cc. of carbon tetrachloride in a 20 cc. pyrex tube. The tube was sealed and the mixture was shaken for twelve hours. Considerable gas was formed which escaped with force when the tube was opened. The contents were poured onto crushed ice and the acid was neutralized with 10% sodium hydroxide after which a few drops of pyridine were added. After the solution had been extracted with ether the ether extract was dried and worked up. There was obtained a small amount of decomposition products and 5-nitrofurfural diacetate, which was identified by a mixed melting point determination.

The experiment just described was repeated with similar results.

Nitration of 5-Nitrofurfural Diacetate With a Mixture of Concentrated Nitric and Sulfuric Acids in Various Solvents.- To 1 g. (0.0041 mole) of 5-nitrofurfural diacetate in 5 cc. of anhydrous carbon tetrachloride was added a mixture of 0.3 g. (0.0046 mole) of fuming nitric acid (sp.gr.1.51) and 0.6 g. (0.0058 mole) of concentrated sulfuric acid (sp.gr.1.84). The resulting mixture was sealed in a 20 cc. pyrex text tube and shaken for twenty-one hours at 25° and at the end of this time some white crystalline substance had separated out. The tube was opened and the substance was placed on a porous plate. It decomposed slowly in the air. A melting point was taken and the substance started to soften at 155° and melted with decomposition at 170°-174°. The substance was soluble in water. When treated with pyridine it changed to an oil which could not be crystallized. A part was put onto crushed ice, treated with pyridine and an uncrystallizable oil was the result. A second run gave similar results.

One attempt was made to nitrate 5-nitrofurfural diacetate in acetic anhydride with a mixture of concentrated nitric and sulfuric acids. To 5.4 g. (0.0223 mole) of 5-nitrofurfural diacetate in 40 g. (0.392 mole) of acetic anhydride at 25° was added with stirring 4.9 g. (0.048 mole) of concentrated sulfuric acid (sp.gr.1.84). The temperature of the reaction mixture rose to 34° and was then cooled to 0° with a mixture of ice and salt. Three and four-tenths grams (0.054 mole) of fuming nitric acid (sp. gr. 1.51) was then added to the reaction mixture. The evolution of fumes of nitrogen dioxide took place followed by a violent reaction which removed most of the reaction mixture from the flask. After the residue had been treated with crushed ice it was neutralized with dilute sodium hydroxide and treated with pyridine. The products of the reaction were tar and a small amount of 5-nitrofurfural diacetate which was identified by a mixed melting point determination.

The reaction just described was repeated with the same quantities of materials as follows. After the sulfuric acid had been added to the 5-nitrofurfural diacetate cooled to -10° the nitric acid was run in at the same temperature. No decolorization of the reaction mixture took place, but an exothermic reaction took place as was shown by a rise in the temperature of the reaction mixture to 0°. After the reaction mixture was stirred for eight hours at -5°-0° it was poured onto crushed ice and the white solid which separated was filtered out on a Büchner funnel. This solid was proven to be 5-nitrofurfural diacetate by means of a mixed melting point determination. After the 5-nitrofurfural diacetate had been removed the ice-cold residue was neutralized with 10% sodium hydroxide and treated with pyridine and extracted with ether. No further material could be isolated.

An attempt was made to nitrate 5-nitrofurfural diacetate after the directions of Menke[15]. One gram (0.004

mole) of 5-nitrofurfural diacetate was treated with 1.5 g. (0.006 mole) of ($Cu(NO_3)_2 \cdot 3H_2O$) in 5 g. of acetic anhydride at 50° for seventy-two hours. Practically quantitative recovery of the 5-nitrofurfural diacetate was effected.

When 5-nitrofurfural diacetate was heated with fuming nitric acid in nitrobenzene in a sealed tube at 80° the tube exploded with violence. Twelve and two-tenths grams (0.05 mole) of 5-nitrofurfural diacetate was treated in a sealed tube with 20 cc. of nitrobenzene and 6.4 g. (0.10 mole) of fuming nitric acid (sp. gr. 1.51). The tube was heated in a furnace to 80° at which temperature a violent explosion took place.

<u>Reaction Between 5-Nitrofurfural Diacetate and Fuming Nitric Acid, and a Mixture of Nitric and Sulfuric Acids</u>.- Four grams (0.009 mole) of 5-nitrofuraldiacetate was treated with 6.4 g. (0.1 mole) of fuming nitric acid (sp. gr. 1.51) at room temperature for two hours. The reaction mixture was poured onto crushed ice, neutralized with 10% sodium hydroxide and pyridine. No 5-nitrofurfural diacetate could be recovered. Small quantities of water soluble oils were extracted from the water residue.

Four grams (0.009 mole) of 5-nitrofurfural diacetate was treated with a mixture of 3.5 g. (0.054 mole) of fuming nitric acid (sp. gr. 1.51) and 5.5 g. (0.054 mole) of concentrated sulfuric acid (sp. gr. 1.84). The mixed acids were added to the diacetate in an Erlenmeyer flask immersed in a bath of ice and salt. It was noted that the 5-nitrofurfural diacetate dissolved without apparent decomposition in the mixed acids. The reaction mixture was then placed in a water-bath and its temperature raised to 70° over a period of one hour. At the end of this time the reaction mixture was poured onto crushed ice and worked up as previously described. There was obtained a small quantity of 5-nitrofurfural.

A third reaction using the quantities given above was quickly heated to 160° and poured onto crushed ice to quiet the violent reaction that was taking place. The compound was completely destroyed.

A fourth run was carried out and heated to 105°. There was obtained a small quantity of a white crystalline solid melting at 120°. This compound was water soluble and did not contain nitrogen.

One attempt was made to nitrate the ring fission product with nitric acid (sp. gr. 1.2) but the compound decomposed.

SUMMARY

A series of attempts have been reported in an endeavor to prepare a dinitro derivative of furfural. No evidence was found of the formation of the desired compound.