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Furfural and some of its derivatives

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FURFURAL AND SOME OF ITS DERIVATIVES

BY

Amiot P. Hewlett

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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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Head of Major Department

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Iowa State College

1930

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The author wishes to take this occasion to express his indebtedness to Dr. O. R. Sweeney under whose direction a portion of this work was done.

GG

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INTRODUCTION

Furfural was first prepared exactly one hundred years ago. In 1830 Dobereiner (1), while preparing formic acid by the action of sulfuric acid and manganese dioxide on sugar, noticed that a yellow oil separated from his distillate. This oil, on account of its odor and method of preparation, was given the name of "artificial oil of ants". Later Stenhouse (2), by treating oatmeal and sawdust with sulfuric acid, was the first to prepare an appreciable quantity of this oil. He determined the physical properties and composition of the oil and gave to it the formula $C_5H_4O_2$. Fownes (3), five years later, secured an oil by the distillation of bran with sulfuric acid. He found this to be identical with the oil of Stenhouse and, on account of its method of preparation, suggested the name furfurol (furfur-bran, oleum-oil). Ultimately when the aldehyde character of the substance had been demonstrated, it received the name of furfural.

Cahours (4) also obtained furfural by the distillation of wheat with sulfuric acid while Stenhouse (5) prepared oils from various vegetable sources and found them all to be similar. However, Stenhouse (5) secured from seaweeds an oil

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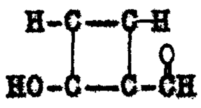
(1) Dobereiner, Ann., 3:141 (1832).
(2) Stenhouse, Ann., 35:301 (1840).
(3) Fownes, Ann., 54:52 (1845).
(4) Cahours, Ann., 69:82 (1849).
(5) Stenhouse, Ann., 74:279 (1850).

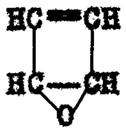
which he assumed to be an isomer of furfural and to which he gave the name fucusol. Later Maquenne (6) and Tollens (7) found fucusol to be a mixture of furfural and methyl furfural. After the preparation of furfural from various substances such as cane sugar (8), wood (9), glucose (10) and numerous other substances, it was found that, in general, pentoses and pentosans were the substances ordinarily producing furfural.

Structure.

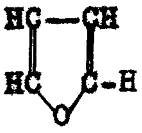
Limpricht (11) after a study of the action of the halogens on furfural, proposed the formula



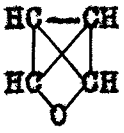
However, Pawlinoff (12) established the absence of an hydroxyl group in furfural by the use of zinc ethyl reactions. Baeyer (13) proposed the following three structures for furan, giving preference to I.



I.



II.



III.

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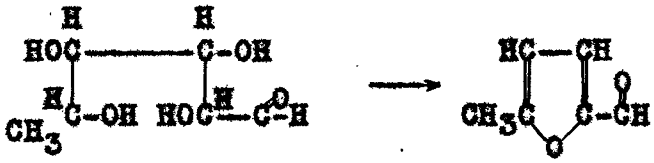
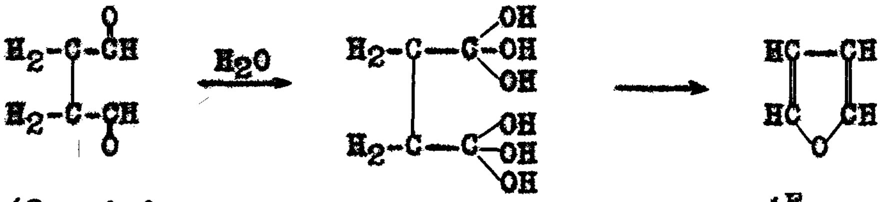
(6) Maquenne, Ber., 22:751 (1889).
✓(7) Tollens, Ber., 22:3062 (1889).
(8) Volckel, Ann., 85:59 (1853).
(9) Heill, Ber., 10:936 (1870).
(10) Fischer, Ann., 270:64 (1895).
(11) Limpricht, Ber., 2:211 (1869).
(12) Pawlinoff, Ber., 17:967 (1884).
(13) Baeyer, Ber., 10:(1)358 (1877).

Much evidence has accumulated in favor of formula II. Markwald (14) prepared furylacrylic acid from furfural, by means of the Perkin condensation and from this prepared a keto acid having the structure $HOOCCH_2CH_2\underset{O}{C}CH_2CH_2COOH$ (15). Assuming formula II is correct, the action may be expressed as follows:

Tollens (16) and Maquenne (17) determined the structure of methyl furfural by its synthesis from isodulcide by dehydration, thus


(Isodulcide) (Methyl furfural)

The final proof of structure is due to Harries (18) who synthesized furan directly from succinic dialdehyde and water.



(Succinic dialdehyde) (Furan)

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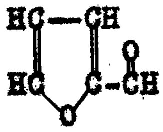
(14) Markwald, Ber., 20:2811 (1887).
(15) Markwald, Ber., 21:398 (1888).
(16) Tollens, Ber., 33:143 (1900).
(17) Maquenne, Ann. Chim. Phys., (6), 22:76 (1891).
(18) Harries, Ber., 34:1488 (1901).

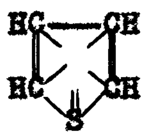
The formula for furfural, which is now accepted universally is,

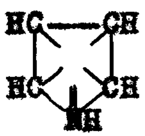


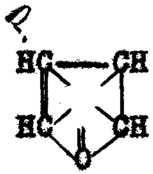
However, it will probably be found that this structure does not explain the exact reactions of furfural and its derivatives any more accurately than the Kekulé formula does for benzene.

A very popular method of showing the structural relationship of furan to other cyclic compounds is as follows:


(Benzene)


(Thiophen)


(Pyrrol)


(Furan)

This, however, should not be taken too literally as a marked difference in activity and stability of these compounds and their derivatives is evident.

Leading literature references to work in furan chemistry may be found in the various texts on organic chemistry; Meyer Jacobson, "Lehrbuch der Organischen Chemie"; and Beilstein, "Handbuch der Organischen Chemie". A complete bibliography of furan chemistry up to 1889 is given by Adolf Bender, "Das Furfuran und sein Derivate", while a bulletin, "Furfural and its Derivatives", published by the Miner Laboratories, Chicago, Illinois gives a bibliography up to 1925. For later work, one should consult the abstracts of the American and British Chemical Societies.

Sources.

Agricultural waste products are the sources of furfural in this country. Any pentose or pentosan containing material may be used for the commercial manufacture of furfural. Among these waste materials are corn stalks, corncobs, oat hulls, peanut hulls, cottonseed hulls, beet pulp, sugar cane pulp, rice bran, rice chaff, and wheat, oat, rye and flax straw. At the present time the commercial manufacture of furfural has been confined to the use of corncobs and oat hulls, which give a relatively high yield of furfural. Practically all of the furfural manufactured in this country, at present, is produced from oat hulls. This does not mean that other materials are not suitable for furfural production but can be explained by the fact that the Quaker Oats Company has control of the patents and the supply of oat hulls is more than sufficient to meet the present demand for furfural. Oat hulls are also supplied at all times of the year and storage is unnecessary.

It is interesting to follow the development of furfural manufacture. In 1920 furfural was quoted at thirty dollars a pound and it is doubtful if 50 pounds of it were used in this country during that year (19). In 1924 furfural was quoted at twenty-five cents a pound and Mains and LaForge (19) pub-

(19) Mains and LaForge, J. Ind. Eng. Chem., 16:356 (1924).

lished specifications for plant which could manufacture furfural from corn cobs at a total cost of 6.15 cents per pound. At the present time, furfural is quoted at ten cents per pound, which makes it the cheapest of aldehydes and therefore desirable for many purposes.

The possible supply of furfural in this country is practically unlimited, the amount being manufactured at the present time depending only on the demand for that material. In the year 1929, 1,500,000 (20) pounds of furfural were produced in this country. To manufacture this quantity of furfural required only a part of the supply of oat hulls. The annual oat hull supply in this country is about 220,000 tons (21) and the yield of furfural from oat hulls is 20%. This would mean a possible production of 88,000,000 pounds of furfural each year from the oat hull supply alone. The yearly yield of corn in this country is about 2,622,189,000 bushels (22) and figuring 14 pounds of cobs to the bushel, the yearly yield of corn cobs is about 5,645,556 tons. Figuring a yield of 10% furfural (23) from corn cobs, the annual production from that source alone would be 1,016,200,080 pounds of furfural. The total annual production from corn cobs and oat hulls alone would be 1,104,200,080 pounds while the demand in 1929 was only 1,500,000 pounds. At ten cents per pound the

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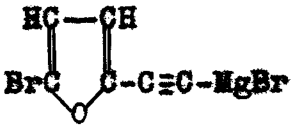
(20) Unofficial.
(21) Miner, Trickey and Brownlee, Chem. and Met. Eng., 27:299 (1922).
(22) U.S. Department of Agriculture, Year book, 1930, p.626.
(23) LaForge, J. Ind. Eng. Chem., 15:499 (1923).

value of the possible annual yield from corn cobbs and oat hulls alone would amount to $11,042,000 from farm waste products. We also have an annual acreage of 61,141,000 in corn which, at an average of 1.5 tons per acre, will produce 147,027,000 tons of corn stalks (22). In addition to these, we have large quantities of other farm waste products.

Since the production of furfural from agricultural waste products is dependent upon the demand for that compound, the problem is to find uses for furfural. At the present time, furfural is being used as a substitute for the more expensive formaldehyde in resins of the bakelite type, in insecticides, fungicides and as an embalming fluid. It is used in the production of varnish resins and as a solvent for varnish resins and cellulose esters (19). Other uses for furfural are being continually developed.

This is a part of the work being done on utilization of agricultural wastes at Iowa State College. In this work the problem of utilization of furfural is being attacked from the chemical point of view. Numerous new compounds have been prepared from furfural. These compounds are to be used as insecticides, fungicides, antiseptics, antipyretics, dyes, sweetening agents, and for the synthesis of more valuable and more useful compounds.

5-BROMOFURYLACETENYLMAGNESIUM BROMIDE



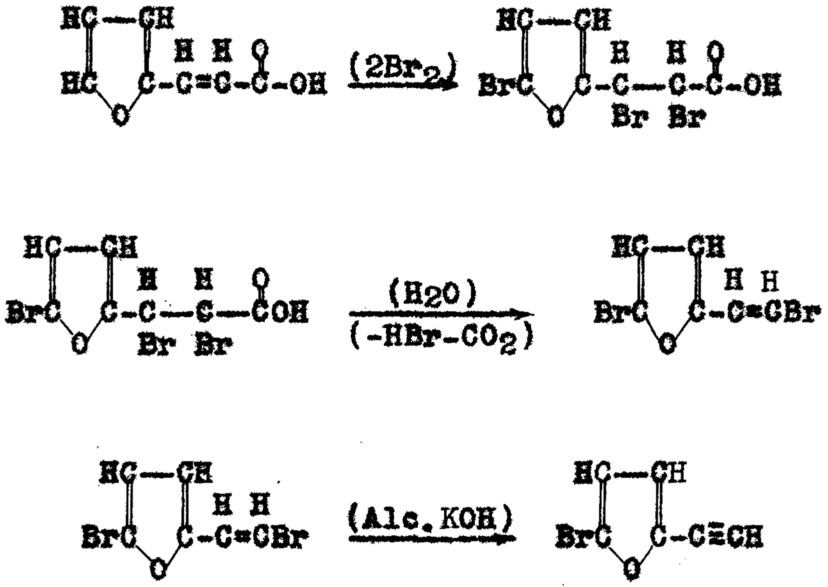
Introduction.

There is a wide demand for Grignard reagents containing the furyl grouping in the synthesis of numerous compounds. Moureu, Dufraisse and Johnson (1) were successful in the preparation of furylacetenylmagnesium bromide by the action of furylacetylene on ethylmagnesium bromide. This Grignard reagent was treated with carbon dioxide to produce furylpropiolic acid. The furylacetylene was secured in very poor yields by bromination of furylethylene and treatment of the resulting furylbromoethylene with potassium hydroxide. The furylethylene was secured simultaneously with the preparation of furylacrylic acid.

There is a possibility that better results may be obtained by use of 5-bromofurylacetylene, which was first prepared by Gibson and Kahnweiler (2). The method used by Gibson and Kahnweiler (2) consisted of brominating furylacrylic acid and treating the resulting 5-bromofuryldibromopropionic acid with water to produce 5-bromofurylbromoethylene. The 5-bromofurylbromoethylene was then treated with alcoholic potassium hydroxide to produce impure 5-bromofurylacetylene. No yields are given, but they may safely be assumed as being poor, and

(1) Moureu, Dufraisse and Johnson, Ann. Chim., (10)7:1 (1927).
(2) Gibson and Kahnweiler, Am. Chem. J., 12:314 (1890).

the compound was never secured in a pure condition. However, the copper salt was prepared and analyzed. The following reactions serve to illustrate this method of Gibson and Kahnweiler (2).

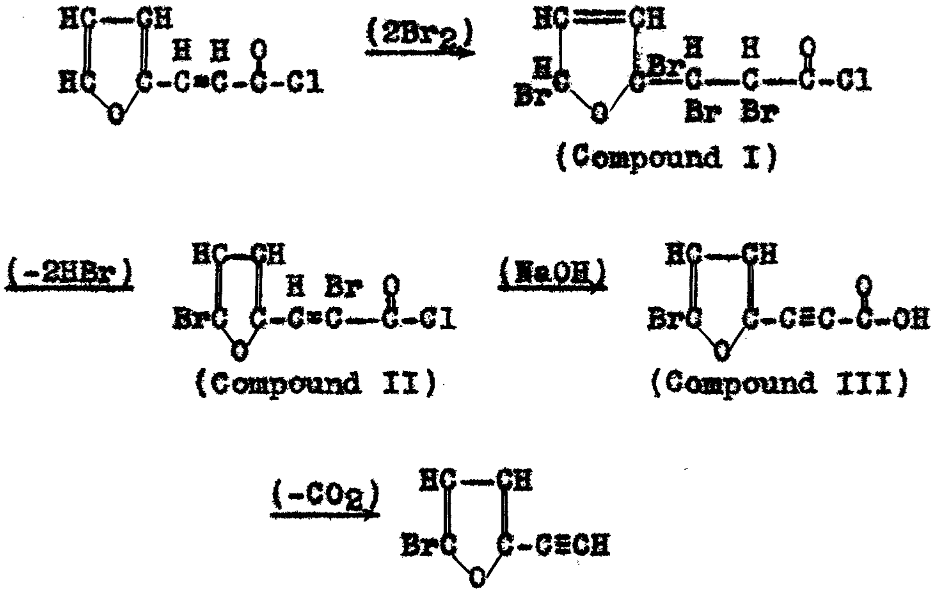


In the preparation of 5-bromofurylacetylene we have used the method of Gilman and Wright (3), which consists of brominating furylacryloyl chloride to produce a substance, compound (I), which evolves hydrogen bromide to produce 5-bromofurylbromoacryloyl chloride. This intermediate product, compound (I), is formed by addition of one molecule of bromine to the ethylenic linkage and the addition of one molecule of bromine to the ring. There is evidence (3) that 1-4 addition takes place in the ring, although other forms of addition are possible. The 5-bromofurylbromoacryloyl chloride, compound

(3) Gilman and Wright, *J. Am. Chem. Soc.*, *53*:3349 (1930).

(II), is treated with dilute aqueous sodium hydroxide to produce 5-bromofurylpropiolic acid, compound (III), which in turn is converted by steam distillation to 5-bromofurylacetylene, compound (IV).

The following reactions serve to illustrate this method for the preparation of 5-bromofurylacetylene.



(Compound I)

(Compound II)

(Compound III)

(Compound IV)

During the decarboxylation of 5-bromofurylpropiolic acid (compound III), small amounts of 5-bromofurylbromoacrylic acid, 5-bromofurylacrylic acid, and 5-bromofurylmethyl ketone are also formed.

<u>Experimental</u>.

<u>Furylacryloyl Chloride</u>, $(C_4H_3OCH{=}CHCOCl$. This compound was prepared by the method described by Gilman and Hewlett (4).

(4) Gilman and Hewlett, <u>Iowa State College Journal of Science</u>, 4:31 (1930).

A solution of 178.5 g. (1.5 moles) of thionyl chloride in 500 cc. of dry benzene was added to 138 g. (1 mole) of furylacrylic acid, contained in a round-bottom flask. The mixture was refluxed for three hours, the benzene distilled from a water-bath and the residue distilled under reduced pressure (water-pump). The yield of furylacryloyl chloride boiling at 145° at 30 mm. pressure was 141 g. or 90%.

5-Bromofurylbromoacryloyl Chloride (3), $BrC_4H_2OCH=CBrCOCl$. In the preparation of this compound, there is an absolute necessity for using pure furylacryloyl chloride. The furylacryloyl chloride was redistilled, the first and last 10-15% being rejected. Two hundred thirty-two grams (1.5 moles) of pure furylacryloyl chloride was dissolved in 920 cc. of dry carbon disulphide and a solution of 480 g. (6 atoms) of bromine in 280 cc. of carbon disulphide added slowly. About one-half hour was required for the addition of the bromine. The solution was then refluxed for three hours and the carbon disulphide removed with aid of a water-pump. The thick oily residue was then heated under about 30mm. pressure at 100° for four hours, at the end of which time evolution of hydrogen bromide had practically ceased. The residue was then distilled under reduced pressure to yield 450 g. or 96% of crude 5-bromofurylbromoacryloyl chloride boiling at 190°-195° at 24 mm. pressure and melting at 69°-70°. The pure material boils at 182°-183° at 21 mm. pressure and melts at 72°. In a subsequent run using 78.25 g. (0.5 mole) of furylacryloyl chloride in 307 cc. of carbon disulphide and 160 g. (2 atoms) of bromine in 93 cc. of carbon disulphide, the yield of 5-bromofurylbromoacryloyl chloride boiling at 181°- 185° at 21 mm. pressure and melting at 69°- 70° was 145 g. or 92%.

5-Bromofurylpropiolic Acid (3), $BrC_4H_2OC{\equiv}C{-}COOH$. Four hundred fifty grams (1.44 moles) of crude 5-bromofurylbromoacryloyl chloride was melted and poured into a solution of 9000 cc. of water containing 180 g. (4.5 moles) of sodium hydroxide. This solution was then heated to 70°-80° and the mixture stirred at that temperature for four hours. Norite was then added and the mixture filtered with suction and allowed to cool. The solution was chilled with ice and carefully acidified with hydrochloric acid. The 5-bromofurylpropiolic acid was filtered and dried to yield 215 g. or 69.5% melting at 127°. This acid may be purified by crystallization from a mixture of alcohol and water, but the loss is great. Thirty grams of the crude acid was placed in 50 cc. of alcohol and warmed to 70°. Water at 70° was added until the mixture just became turbid and was then filtered and allowed to cool. As the solution cooled, an oil with the odor of 5-bromofurylacetylene separated out. Just as the first crystals were formed, the solution was decanted from the oil and then cooled to yield 10 g. or 50% of pure 5-bromofurylpropiolic acid melting at 143° (3). In a second run using 157.25 g. (0.5 mole) of 5-bromofurylbromoacryloyl chloride and 3000 cc. of water containing 60 g. (1.5 mole) of sodium hydroxide, the yield of 5-bromofurylpropiolic acid melting at 127° was 60.5 g. or 69%.

5-Bromofurylacetylene (3), $BrC_4H_2OC{\equiv}CH$. One hundred fifty grams (0.7 mole) of crude 5-bromofurylpropiolic acid was suspended in 1000 cc. of water and subjected to steam distillation. The steam distillation was continued until a clear distillate was secured. This distillate was then cooled and extracted with ether. The ether solution was dried over sodium carbonate and the ether removed by distillation from a water-bath. The residue was then distilled under reduced pressure to yield 35 g. or 29.4% of 5-bromofurylacetylene boiling at 63°- 64° at 24 mm. pressure. Care should be taken not to distill over any higher boiling material. The residue in the distillation flask solidified upon cooling. This solid was crystallized from alcohol to yield 4 g. of material which was identified as 5-bromofurylmethyl ketone. This material melted at 94° and a mixed melting point with the 5-bromofurylmethyl ketone of Gilman and Wright (3) showed no depression. On account of the high vapor pressure of the 5-bromofurylmethyl ketone, it was found necessary to redistill this constant boiling 5-bromofurylacetylene two or three times to completely separate the two.

A solid residue remained in the flask after the steam distillation was complete. This was removed by filtration while still hot. This residue was dissolved in ammonium hydroxide and acidified with hydrochloric acid to yield 15 g. of acid which was identified, by mixed melting point, as 5-bromofurylbromoacrylic acid. This material melted at 174° while a mixed melting point with 5-bromofurylbromoacrylic acid, prepared by the method of Gibson and Kahnweiler (2), was 176°. The pure acid melts at 178°- 179°.

The hot aqueous filtrate from above was chilled to yield 10 g. of acid melting at 140°-145°. Repeated recrystallization from water indicated that this acid was a mixture of 5-bromofurylbromoacrylic and 5-bromofurylacrylic acids. Finally, 2 g. of 5-bromofurylbromoacrylic acid melting at 176°, mixed melting point remaining unchanged, and 5 g. of 5-bromofurylacrylic acid melting at 174°, mixed melting point remaining unchanged, were secured from the mixture. It is evident that these two acids and the 5-bromofurylmethyl ketone are produced from 5-bromofurylpropiolic acid during the steam distillation, as Gilman and Wright (3) have secured the same substances under similar conditions by use of pure 5-bromofurylpropiolic acid.

In two subsequent runs using 107.5 g. (0.5 mole) of 5-bromofurylpropiolic acid, the yields of 5-bromofurylacetylene were, respectively, 56.8 g. or 28% and 60.9 g. or 30%.

Di(5-bromofuryl)diacetylene, $BrC_4H_2O-C\equiv C-C\equiv C-OH_2C_4Br$. This compound was previously prepared by Gibson and Kahnweiler (2) who followed the method used by Baeyer and Landsberg

(5) for diphenyldiacetylene. Two grams (0.0117 mole) of 5-bromofurylacetylene was added dropwise with shaking to a solution containing an excess of ammoniacal cuprous chloride. The copper salt was immediately formed as a yellow solid, which was separated from the liquid by filtration. The copper salt was suspended in 50 cc. of water and a solution of 0.5 g. (0.0117 mole) of sodium hydroxide in 5 cc. of water added. To this mixture was then added a saturated solution of 3.8 g. (0.0117 mole) of potassium ferricyanide in water. This mixture was then allowed to stand for twenty-four hours. At the end of this time the mixture was filtered and the precipitate extracted with 50 cc. of hot alcohol. Upon cooling the alcohol solution the dibromodifuryldiacetylene crystallized in the form of small plates which melted at 126°. This exactly checks the melting point given by Gibson and Kahnweiler (2). The yield of di(5-bromofuryl)diacetylene was 1 g. (0.003 mole) or 50%.

5-Bromofurylacetenylmagnesium Bromide, $BrC_4H_2O{-}C{\equiv}CMgBr$. This Grignard reagent was prepared by treatment of an ether solution of ethylmagnesium bromide with 5-bromofurylacetylene. A solution of 10.8 g. (0.1 mole) of ethyl bromide in 100 cc. of anhydrous ether was added to 2.43 g. (0.1 atom) of magnesium. After the reaction was complete a solution of 11 g. (0.0645 mole) of 5-bromofurylacetylene in 50 cc. of anhydrous

(5) Baeyer and Landsberg, *Ber.*, **15**:57 (1882).

ether was slowly added. The mixture became warm enough to cause free refluxing of the ehter and gas was evolved. This solution gave a violet color when tested for the Grignard reagent by the method of Gilman and Schulze (6).

The above solution was cooled with an ice-salt mixture and treated with carbon dioxide in the usual manner. The mixture was hydrolyzed by pouring onto cracked ice and adding the calculated quantity of dilute sulphuric acid. The ether layer was separated and washed with 50 cc. of 5% sodium hydroxide. The water layer was separated and acidified with hydrochloric acid to yield 5 g. (0.014 mole) or 21.8% of 5-bromofurylpropiolic acid melting at 140°. A mixed melting point with pure 5-bromofurylpropiolic acid was found to be 142°, the pure acid melting at 143°.

α-Naphthalide of 5-Bromofurylpropiolic Acid, $C_{10}H_7NHCO-C\equiv C-C_4H_2OBr$. A solution of ethylmagnesium bromide was prepared by addition of a solution of 5.45 g. (0.05 mole) of ethyl bromide in 50 cc. of anhydrous ether to 1.5 g. (0.062 atom) of magnesium. After the reaction was complete, the solution was separated from the unchanged magnesium and a solution of 6.84 g. (0.04 mole) of 5-bromofurylacetylene in 50 cc. of ether then slowly added. The mixture became warm and evolution of gas was evident. After the evolution of gas was complete, a solution of 8.45 g. (0.05 mole) of α-naphthyliso-

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(6) Gilman and Schulze, J. Am. Chem. Soc., 47:2002 (1925).

cyanate in 50 cc. of ether was added dropwise. A gummy material settled out of the solution. This mixture was stirred for one hour and hydrolyzed by pouring onto ice and ammonium chloride. The residue in the flask was washed out with benzene and added to the hydrolyzed mixture. The ether-benzene layer was then separated, dried and the solvent removed by distillation from a water-bath. The residue was then crystallized from a water-alcohol mixture to yield 7 g. of material melting at 135°. This material was then recrystallized from alcohol-water mixture and finally crystallized twice from benzene to yield 5 g. (0.014 mole) or 35% of material melting constantly at 150°.

Analysis. Calculated for $C_{17}H_{20}BrNO_2$: Br, 23.53. Found: Br, 23.46.

Reaction of 5-Bromofurylethinylmagnesium Bromide with Triphenyl Lead Chloride. An unsuccessful attempt at preparation of triphenyl-5-bromofurylacetenyl lead was made. A solution of ethylmagnesium bromide was prepared by the addition of 10.9 g. (0.1 mole) of ethyl bromide in 100 cc. of anhydrous ether to 3 g. (0.123 atom) of magnesium. After the reaction was complete, the ether solution was decanted from the undissolved magnesium and a solution of 15.39 g. (0.09 mole) of 5-bromofurylacetylene in 100 cc. of ether added slowly. After the evolution of gas was complete, this solution was added dropwise to a suspension of 25 g. (0.045 mole) of triphenyl lead chloride in 100 cc. of benzene. (The triphenyl lead chloride was prepared and purified by the method described by Gilman and Robinson (7)). A slight heat of reaction was observed when the Grignard reagent was added to the triphenyl lead chloride. This mixture was gently refluxed for two hours and hydrolyzed with ice and ammonium chloride. After hydrolysis the mixture was filtered to remove 3 g. of triphenyl lead chloride, which after recrystallization from alcohol melted at 204°, mixed melting point with triphenyl lead chloride remaining unchanged. The ether-benzene layer was separated, dried and the solvent removed by distillation from a water-bath. The residue was then crystallized from alcohol to yield 15 g. of triphenyl lead chloride melting at 200°, mixed melting point with pure triphenyl lead chloride being 204°. Thus, 18 g. or 72% of the triphenyl lead chloride was secured unchanged. Upon concentration of the alcoholic solution, after removal of the triphenyl lead chloride, 5 g. of a tarry material separated out upon cooling. This tarry material resisted all attempts at crystallization.

Apparently triphenyl lead chloride does not react with 5-bromofurylethinylmagnesium bromide in the expected manner under the conditions of this experiment.

Summary.

A description of the methods for the preparation of furylacryloyl chloride, 5-bromofurylbromoacryloyl chloride, 5-bro-

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(7) Gilman and Robinson, J. Am. Chem. Soc., 51:3112 (1929).

mofurylpropiolic acid and 5-bromofurylacetylene have been given. Upon steam distillation of 5-bromofurylpropiolic acid, moderate yields of 5-bromofurylacetylene are secured along with small quantities of 5-bromofurylmethyl ketone. The residue from the steam distillation consists of a mixture of 5-bromofurylacrylic and 5-bromofurylbromoacrylic acids. 5-Bromofurylacetenylmagnesium bromide has been prepared and characterized by conversion to 5-bromofurylpropiolic acid and also to the α-naphthalide of 5-bromofurylpropiolic acid. Apparently triphenyl lead chloride does not react in the expected manner with 5-bromofurylacetenylmagnesium bromide under the conditions of this experiment.

1-FURYL-3-CHLOROPROPANE AND 1-TETRAHYDROFURYL-3-CHLOROPROPANE.

Introduction.

The preparation of furyl-alkyl halides is of interest because of their possible synthetic value. Kirner (1) prepared α-furfuryl chloride and has used this compound in many interesting syntheses. The chlorine is said to be very active, but no mention is made as to its action on magnesium, In this instance, it is interesting to recall that α-furfuryl chloride has given us the first definite example of molecular rearrangement in the furan series. Runde, Scott and Johnson (2) have definitely shown that α-furfuryl chloride, by treatment with sodium cyanide followed by alkaline hydrolysis of the resulting nitrile, is converted to 5-methyl furoic acid and not to the expected 2-furylacetic acid.

Dox and Jones (3) prepared tetrahydrofurfuryl bromide while Gilman and Brown (4) have prepared tetrahydrofuryl chloride and iodide. Also, Gilman and Dickey (5) have recently prepared methyl-1-tetrahydrofuryl-3-bromopropane. In this study, 1-furyl-3-chloropropane and 1-tetrahydrofuryl-3-chloropropane have been prepared and the action of these substances on magnesium determined. The former is inactive toward mag-

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(1) Kirner, *J. Am. Chem. Soc.*, *50*:1955 (1928).
(2) Runde, Scott and Johnson, *J. Am. Chem. Soc.*, *52*:1284 (1930).
(3) Dox and Jones, *J. Am. Chem. Soc.*, *50*:2033 (1928).
(4) Unpublished results.
(5) Gilman and Dickey, *J. Am. Chem. Soc.*, *52*:2144 (1930).

nesium while the latter reacts vigorously with formation of RMgX in 90% yields.

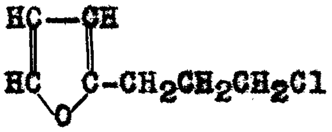
1-Furyl-3-chloropropane was prepared from the corresponding alcohol by the method used by Kirner (1) in the preparation of α-furfuryl chloride. 1-Tetrahydrofuryl-3-chloropropane is best prepared by the action of thionyl chloride on tetrahydrofurylpropyl alcohol, the latter being prepared by the reduction of furylacrolein by the method of Adams and Bray (6). While there is a possibility of the alcohol or the chloride or both being splitting products, this does not seem probable. Furylacrolein is split upon reduction (6) and in every case the normal splitting products, the heptanediols, are isolated. These bodies, however, boil much higher than the compound which we assume to be tetrahydrofurylpropyl alcohol. We have observed, however, that the reaction does not stop, as stated by Adams and Bray (6), when 4.2 to 4.4 molecular equivalents of hydrogen have been absorbed. We have not, however, made any attempt to determine the maximum amount of hydrogen that can be absorbed. It is naturally assumed that further absorption of hydrogen would increase the amount of splitting products. It is also possible that the action of thionyl chloride or the resulting hydrochloric acid, upon the alcohol, might lead to splitting. On the basis of the high yield of product obtained and upon the analysis of

(6) Adams and Bray, J. Am. Chem. Soc., **49**;2101 (1927).

this product, such splitting would seem improbable as the resulting molecule would contain either two or more atoms of chlorine or oxygen (from water splitting).

Experimental.

1-Furyl-3-Chloropropane,



1-Furyl-3-chloropropane was prepared from furylpropyl alcohol by the method used by Kirner (1) in the preparation of α-furfuryl chloride. A mixture of 63 g. (0.5 mole) of furylpropyl alcohol, 300 cc. of anhydrous ether and 67 g. (0.85 mole) of pyridine was treated with 89 g. (0.75 mole) of thionyl chloride. The thionyl chloride was added dropwise with vigorous stirring. After about an hours time the mixture began to darken and was then removed from the flask and the ether solution washed repeatedly with water. The ether layer was separated, dried over sodium sulfate and distilled. The yield of 1-furyl-3-chloropropane boiling at 60° at 5 mm. pressure was 14 g. or 20%. This compound is a colorless liquid with pleasant odor. It distills without decomposition but darkens rapidly upon standing. d_{25}^{25} 1.0813; n_D^{25} 1.4730.

Analysis. Calculated for C_7H_9OCl: Cl, 24.57. Found: Cl, 24.73 and 24.49.

This compound is inactive toward magnesium, 1 g. of the substance dissolved in 15 cc. of anhydrous ether giving a negative test for RMgX after having been heated with 0.5 g. of activated 12.5% copper-magnesium alloy in a sealed tube at 100° for 12 hours. The halide was recovered unchanged. Eight grams of the halide dissolved in 100 cc. of anhydrous ether gave a negative RMgX test after having been refluxed with one gram of copper-magnesium alloy for 7 days.

Furylpropyl Alcohol, $C_4H_3OCH_2CH_2CH_2OH$. This compound was prepared by reduction of furylacrolein (7), according to the method of Adams and Bray (6), with hydrogen and platinum-oxide platinum black (8). To a solution of 61 g. (0.5 mole) of furylacrolein in 200 cc. of absolute alcohol was added 0.5 g. of platinum oxide and 0.1 g. of ferrous sulfate. This mixture was reduced at 2 - 3 atmospheres pressure and the reaction was stopped when 3 molecular equivalents of hydrogen had been absorbed. The time required for the reduction was 8 hours and the catalyst was reactivated twice during the reaction. The ease of reduction depends upon the degree of purity of the furylacrolein and upon the activity of the catalyst. After the reduction, the alcohol solution was filtered from the catalyst and distilled to yield 69 g. or 55% of furylpropyl alcohol boiling at 90°-91° at 4 mm. pressure. The α-naphthyl urethan melted at 49° which is in agreement with that reported elsewhere (6).

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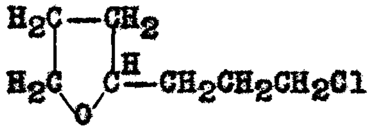
(7) König and Hey, Frdl., 13:110 (1927).
(8) Adams and Shriner, J. Am. Chem. Soc., 45:2171 (1923).

1-Tetrahydrofuryl-3-Chloropropane,



Method 1. Various method of preparation of 1-tetrahydrofuryl-3-chloropropane were used. The first method consisted of treating the corresponding alcohol with thionyl chloride in ether solution in the presence of pyridine (1). To a solution of 65 g. (0.5 mole) of tetrahydrofurylpropyl alcohol in 300 cc. of anhydrous ether and 67 g. (0.85 mole) of pyridine, was added 69 g. (0.75 mole) of thionyl chloride. After addition of the thionyl chloride was complete, the mixture was stirred for one hour and then washed repeatedly with water. The ether layer was separated, dried over sodium sulfate and distilled to yield 35 g. or 48% of 1-tetrahydrofuryl-3-chloropropane boiling at 75° at 4 mm. pressure, when distilled from a steam-bath.

This compound is a colorless liquid of characteristic odor. It distills without decomposition and remains colorless after long standing. d^{25}_{25} 1.0425; n^{25}_{D} 1.4540.

Analysis. Calculated for $C_7H_{13}OCl$: Cl, 23.90. Found: Cl, 23.74 and 23.76.

Method 2. A solution lf 13 g. (0.1 mole) of tetrahydrofurylpropyl alcohol in 100 cc. of anhydrous ether was saturated with dry hydrogen chloride under reflux over a period of three hours. The mixture, which had become black, was then distilled under reduced pressure to yield 5 g. or 34% of 1-tetrahydrofuryl-3-chloropropane boiling at 75° at 4 mm.

pressure.

Method 3. Same as method 2 except that a few drops of concentrated sulphuric acid was added as catalyst. A greater amount of decomposition appeared to take place, however, the yield of chloride boiling at 75° at 4 mm. was 7 g. or 47%.

Method 4. Same as method 3 except that a small amount of anhydrous zinc chloride was added as catalyst. The yield of chloride boiling at 75° at 4 mm. was 7.5 g. or 50%.

Method 5. Same as method 4 except that the benzene solution was washed with water and dried before distillation. The water layer became darkly colored while the benzene layer became less darkly colored. The yield of chloride boiling at 75° at 4 mm. was 7.7 g. or 52%.

Method 6. The best conditions for preparation of 1-tetrahydrofuryl-3-chloropropane was found to be by treatment of a boiling benzene solution of the alcohol with the calculated quantity of thionyl chloride.

1st Run. A solution of 13 g. (0.1 mole) of tetrahydrofurylpropyl alcohol in 100 cc. of dry benzene was placed in a 250 cc. three-neck flask equipped with reflux condenser, mercury-sealed mechanical stirrer, dropping funnel and provision for sucking a rapid stream of dry air through the reaction flask, the top of the reflux condenser being the exit point. The purpose of the air is to remove the reaction products (HCl and SO_2) as rapidly as possible. After heating the contents of the flask to vigorous boiling, the passage of air through the apparatus was started and 11.9 g. (0.1 mole) of thionyl chloride was added dropwise over a period of 15 minutes. The mixture was then refluxed for one-half hour and distilled under reduced pressure from a steam-bath. The yield of chloride boiling at 75° at 4 mm. pressure was 12.2 g or 82%.

<u>2nd Run.</u> This run was the same as the first except that 130 g. (1 mole) of the alcohol in 500 cc. of dry benzene was used and 119 g. (1 mole) of thionyl chloride was added. The yield of chloride boiling at 75° at 4 mm. was 122.5 g. or 82.5%. A small amount of higher boiling material (5 g.) was secured. This material boiled over a range of temperature, 100-120° at 4 mm. and probably consisted of some unchanged alcohol, some chloride and some decomposition products.

<u>3rd Run.</u> The conditions for this run were the same as above except that 1.2 times the calculated amount of thionyl chloride was used. From a 0.2 mole run using 26 g. (0.2 mole) of tetrahydrofurylpropyl alcohol in 150 cc. of benzene and 28.56 g. (0.24 mole) of thionyl chloride, the yield of chloride boiling at 75° at 4 mm. was 19 g. or 64%.

<u>4th Run.</u> The conditions of this run were the same as

above except that 0.8 of the calculated amount of thionyl chloride was used. From a 0.2 mole run using 26 g. (0.2 mole) of alcohol in 150 cc. of benzene and 19 g. (0.16 mole) of thionyl chloride, the yield of chloride boiling at 75° at 5 mm. was 12 g. or 40.5%.

Thus it appears that the better method for the preparation of 1-tetrahydrofuryl-3-chloropropane consists of treating a boiling benzene solution with the calculated amount of thionyl chloride, provision being made for removal of as much of the gaseous reaction products as rapidly as possible. Thionyl chloride seems to cause some decomposition of the alcohol as is shown by the darkening of the solution and by the decreased yield when excess thionyl chloride is added. Thus it is possible that one molecule of thionyl chloride causes decomposition of two or more molecules of the alcohol, in which event an excess of thionyl chloride over the unchanged alcohol may exist. It is to be remembered that the yield based on thionyl chloride would also be 82%.

Tetrahydrofurylpropyl Alcohol, $C_4H_7O(CH_2)_3OH$. The tetrahydrofurylpropyl alcohol (6) was prepared by reduction of furylacrolein in the manner described for furylpropyl alcohol, except that the reaction was continued until 4.4 molecular equivalents of hydrogen had been absorbed. From 122 g. (1 mole) of furylacrolein, 1 g. of platinum oxide and 0.2 g. of ferrous sulfate in 200 cc. of absolute alcohol, the yield of tetrahydrofurylpropyl alcohol boiling at 103°-105° at 4 mm. pressure was 77 g. or 60%. The higher boiling fraction consisted of 25 g. of heptane-diol-1-4, boiling at 127°-129° at 4 mm. pressure. The 3-5-dinitrobenzoic ester of tetrahydrofurylpropyl alcohol melted at 66° which is in agreement with that recorded elsewhere (6).

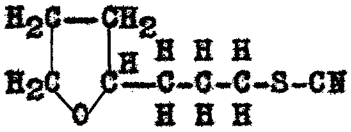
Tetrahydrofuryl-n-propylmagnesium Chloride. A solution of 29.7 g. (0.2 mole) of 1-tetrahydrofuryl-3-chloropropane in 200 cc. of anhydrous ether was added dropwise to 5 g. (0.2 mole) of powdered magnesium (80-200 mesh) and 0.5 g. of activated 12.5% copper-magnesium alloy in a 500 cc. three-neck flask, equipped with mercury-sealed mechanical stirrer, dropping funnel and reflux condenser. A few drops of the solution were added at first and the contents of the flask warmed gently until the reaction started. Stirring was then started and the remainder of the solution added dropwise over a period of one hour. At the end of the reaction a 5 cc. portion of the solution was withdrawn and titrated, the yield of RMgX by titration being 91.61%.

Tetrahydrofuryl-n-butyric Acid. The above solution of tetrahydrofuryl-n-propylmagnesium chloride was cooled in an ice and salt mixture and treated with dry carbon dioxide in the usual manner for preparation of acids from RMgX. The product was hydrolyzed with dilute sulphuric acid and the ether layer removed. This ether solution of the acid was then extracted with a solution of sodium hydroxide and the water layer removed, acidified and extracted with ether. The ether solution was dried and distilled. The yield of tetrahydrofuryl-n-butyric acid boiling at 145° at 5 mm. was 15 g. or 47.5% of the original halide.

This acid is a colorless liquid with faint unpleasant odor. Solubility in water at 25° is 5%. d_{25}^{25} 1.2286; n_D^{25} 1.4572. The neutralization equivalent was 165.

Analysis. Calculated for $C_8H_{14}O_3$: C, 60.76; H, 8.86. Found: C, 60.89 and 60.72; H, 8.66 and 8.69.

Tetrahydrofurylpropyl Thiocyanate,



There is a possibility that tetrahydrofurylpropyl thiocyanate may prove useful as an insecticide.

This compound was prepared by the action of tetrahydrofurylpropyl chloride on potassium thiocyanate in absolute alcohol. 14.85 g. (0.1 mole) of tetrahydrofurylpropyl chloride, 14.5 g. (0.15 mole) of potassium thiocyanate and 50 cc. of absolute ethyl alcohol were sealed in a tube and heated at 120° for twelve hours. At the end of this time the tube was opened and the potassium chloride removed by filtration. The alcohol was then removed by distillation from a water-bath and the residue treated with 100 cc. of anhydrous ether. This caused precipitation of the remainder of the salts. This solution was filtered and distilled to yield 17 g. or 99.4% of tetrahydrofurylpropyl thiocyanate boiling at 138° at 8 mm. pressure.

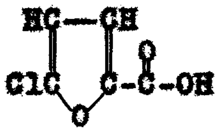
This is a colorless liquid with characteristic odor. n_D^{30} 1.4890; d_4^{30} 1.0660.

<u>Analysis</u>. Calculated for $C_8H_{13}ONS$: S, 18.71. Found: S, 18.93 and 19.16.

<u>Summary</u>.

1-Furyl-3-chloropropane and 1-tetrahydrofuryl-3-chloropropane have been prepared and described. The former is inactive toward magnesium, while the latter is quite reactive. Tetrahydrofuryl-<u>n</u>-propylmagnesium chloride has been prepared and characterized by its conversion to tetrahydrofuryl-<u>n</u>-butyric acid. Tetrahydrofurylpropyl thiocyanate has been prepared and described.

5-CHLOROFUROIC ACID



Introduction.

There is a wide demand for 5-chlorofuroic acid in the snythesis of many valuable compounds. Hill and Jackson (1) first prepared this compound by the action of dry chlorine on ethyl furoate. Upon this basis, it seems possible that 5-chlorofuroic acid may be successfully prepared by the action of chlorine on furoyl chloride. Also, in view of the preparation of 5-chlorofurfural, by Gilman and Wright (2), by the action of sulfuryl chloride on furfural diacetate, it seemed reasonable to expect that 5-chlorofuroic acid might be prepared by the action of this reagent on furoic acid, furoyl chloride or ethyl furoate. It also seemed possible that in this manner 5-chlorofuroic acid might be secured without the formation of other chloro-acids.

Experimental.

For identification purposes, we first prepared 5-chlorofuroic acid by the method of Hill and Jackson (1). Twenty-eight grams (0.2 mole) of pure ethyl furoate was placed in a flask and warmed gently with a low flame until a temperature of 145° was registered by a thermometer, which was placed in the liquid. A slow stream of dry chlorine gas was then pas-

(1) Hill and Jackson, Am. Chem. J., 12:22 (1890).
(2) See p.86, THIS THESIS.

sed through the liquid until the gain in weight of the flask corresponded to substitution of one hydrogen atom by chlorine. The contents of the flask was then allowed to cool and was added slowly to an excess of a saturated solution of sodium hydroxide in alcohol. When the action was complete, the sodium salt was filtered and dried. This was then dissolved in a small amount of water and acidified with hydrochloric acid. The acid thus precipitated was filtered and dried. In order to purify this material it was dissolved in twenty times its weight of water by addition of a slight excess of ammonium hydroxide. A solution of barium chloride was then added as long as precipitation took place. This mixture was filtered and the solution chilled, by placing the flask in ice, and acidified with hydrochloric acid to yield 8.8 g. (0.6 mole) or 30% of 5-chlorofuroic acid melting at 177°. Hill and Jackson (1) report a yield of 38% melting at 177°.

Ethyl Furoate, $C_4H_3OCOOC_2H_5$. Ethyl furoate may be prepared by condensation of furoic acid with ethyl alcohol by use of sulphuric or hydrochloric acids. Hill and Jackson (1) report a yield of 68% by heating a mixture of three parts of furoic acid and three parts of sulphuric acid (sp. gr. 1.84) in five parts of absolute alcohol. After heating on a water bath for four hours the mixture was cooled and the ester precipitated by addition of water. The ester was then washed with a dilute solution of sodium carbonate, dried by exposure to air and distilled. Hill and Jackson (1) considered this method to be more convenient than the hydrochloric acid method.

Marquis (3) secured a yield of 82% of ethyl furoate, boiling at 196.75° (corr.) at 759 mm., by treating a solution of furoic acid in four parts by weight of absolute alcohol with hydrogen chloride gas. The gas was passed through the solution at room temperatue for 2-3 hours and the alcohol then removed by distillation from a water bath. The residue was poured onto cracked ice and neutralized with dilute sodium carbonate solution. The precipitated ester was then dissolved in ether, dried and distilled.

Perhaps the most convenient method for the preparation of ethyl furoate is by the reaction of furoyl chloride on ethyl alcohol. When furoyl chloride is heated with an excess of absolute ethyl alcohol, it is converted quantitatively to the ester. A solution of 65.25 g. (0.5 mole) of furoyl chloride in 150 cc. of absolute ethyl alcohol was refluxed for two hours and distilled. The larger portion of the alcohol was removed at atmospheric pressure and the residue distilled under reduced pressure. The yield of ethyl furoate boiling at 85° at 15 mm. and 105° at 40 mm. and melting at 34° was 68 g. or 98%. From a second run, made under exactly the same conditions, 130.5 g. (1 mole) of furoyl chloride in 300 cc. of absolute alcohol gave a yield of 137 g. or 98% of ethyl furoate boiling at 85° at 15 mm. pressure and melting at 34°.

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(3) Marquis, Ann. chim. phys., (8) 4:256 (1905).

In a third run made, under exactly the same conditions except after removal of most of the alcohol at atmospheric pressure, the solution was diluted with water to give quantitative yield. Thirteen grams of furoyl chloride was dissolved in 30 cc. of absolute alcohol and the mixture refluxed for two hours. At the end of this time most of the alcohol was distilled off at atmospheric pressure. The residue was diluted with 100 cc. of cold water, which caused precipitation of the ester in the form of a white solid. This material was filtered with suction, washed thoroughly with 100 cc. of water and dried in a vacuum desiccator to constant weight, to give 14 g. or 100% of ethyl furoate melting at 34°.

Furoyl Chloride, C_4H_3OCOCl. Furoyl chloride was prepared by Lies-Bodart (4) by heating a mixture of 2 moles of phosphorous pentachloride and one mole of furoic acid at 100° and then distilling the mixture at atmospheric pressure. Frankland and Aston (5) found this method to give very poor yields, but claim practically a quantitative yield by use of an especially designed piece of apparatus in which chloroform was used as a solvent. In this manner two moles of phosphorous pentachloride was treated with one mole of furoic acid, the furoic acid being added by the principle of constant extraction. The resulting solution was then distilled under

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(4) Lies-Bodart, Ann., 100:325 (1856).
(5) Frankland and Aston, J. Chem. Soc., 79:515 (1901).

reduced pressure, the furoyl chloride boiling at 66° at 10 mm. pressure.

Winslow (6) following the method of Frankland and Aston (5) secured a yield of 70% of furoyl chloride, boiling at 70°-76° at 20 mm. pressure, and secured a yield of 52.5% by the action of thionyl chloride on furoic acid. Two hundred fifty grams (2.1 mole) of thionyl chloride was dissolved in 250 g. of carbon tetrachloride and 250 g. (2.22 moles) of furoic acid added in 20 g. portions to the boiling solution. The mixture was refluxed for two hours after addition of the furoic acid was complete and then filtered and distilled. The yield was 137 g. (1.05 moles) or 50% of furoyl chloride, based on thionyl chloride, boiling at 71°-74° at 19 mm. pressure.

The method used in this laboratory, for preparation of furoyl chloride, is that described by Gilman and Hewlett (7). To 112 g. (1 mole) of furoic acid, contained in a round-bottom flask was added a solution of 178.5 g. (1.5 mole) of thionyl chloride in 500 cc. of dry benzene. After ten hours refluxing, this mixture was cooled, filtered and distilled at atmospheric pressure to yield 98 g. (0.75 mole) or 75% of furoyl chloride boiling at 176°. A long period of heating is evidently necessary as similar runs, made exactly as described above, gave yields of 50% and 65% after heating for three and five hours respectively.

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(6) N. R. Winslow, Thesis, Cornell University.

(7) Gilman and Hewlett, Iowa State College Journal of Science, 4:29 (1930).

<u>5-Chlorofuroyl Chloride</u>, ClC_4H_2OCOCl. A 65.25 g. (0.5 mole) portion of furoyl chloride was placed in a flask and one gram of iron powder added. The mixture was heated at 100° and a stream of dry chlorine passed through. The mixture gradually became yellow in color and finally began to darken, becoming deep red in color. At this point, without determination of increase in weight, the reaction was stopped and the mixture fractionated at 10 mm. pressure. The fraction boiling at 92°-110° at 10 mm. was collected and refractionated to yield 55 g. or 66% of material boiling at 92°-95° at 10 mm. No constant boiling fraction could be separated from the higher boiling material, which formed no amide. A small amount of the fraction boiling at 92°-95° was dissolved in ether and ammonia gas passed through. The amide thus secured, when crystallized from alcohol, melted at 154° which corresponds to the melting point given by Hill and Jackson (1) for 5-chlorofuryl amide. A small amount of the 5-chlorofuroyl chloride was dissolved by refluxing with a slight excess of 10% sodium hydroxide. The resulting solution was just neutralized with hydrochloric acid and concentrated by evaporation. The resulting solution was then cooled and made acid with hydrochloric acid to yield an acid melting at 177°. A mixture of this acid and that prepared by the method of Hill and Jackson (1) melted at 177°. A 16.5 g. (0.1 mole) portion of the above 5-chlorofuroyl chloride was dissolved by refluxing with 50 cc. of 10% sodium hydroxide. This solution

was chilled in ice and acidified with hydrochloric acid to yield 8 g. or 54% of 5-chlorofuroic acid melting at 177°. There does not seem to be much preference between the preparation of 5-chlorofuroic acid from the acid chloride and from the ester. In each case the over-all yield, based on furoic acid as the starting point, is about the same. The yield from the acid chloride would be 35.64% while Hill and Jackson (1) secured 38% from the ester. The yields of acid chloride and ester, from the acid, are about the same. There is no apparent advantage of either method over the other.

Action of Sulfuryl Chloride on Furoic Acid. A solution of 11.2 g. (0.1 mole) of furoic acid in 50 cc. of chloroform was treated with 27 g. (0.2 mole) of sulfuryl chloride. The mixture was refluxed gently for three hours and the solvent and sulfuryl chloride removed under reduced pressure. The white residue, which became gummy, when exposed to air, was crystallized from hot water to yield 9 g. of unchanged furoic acid. No other products of reaction could be isolated. A 11.2 g. (0.1 mole) portion of furoic acid was then added to 27 g. (0.2 mole) of sulfuryl chloride without solvent, and the mixture gently warmed until all the furoic acid had dissolved. This solution was then gently heated for one hour and finally dissolved in 50 cc. of chloroform. The solution was cooled and the crystallized material again crystallized from chloroform to yield 3 g. or 20% of 5-chlorofuroic acid melting at 176°-177° and mixed melting point with 5-chlorofuroic acid by the method of Hill and Jackson (1) remaining unchanged. The chloroform solutions were concentrated by evaporation and finally the chloroform removed under reduced pressure to leave a large amount of a gummy mass which could not be crystallized and from which no constant boiling fraction could be separated by distillation. This material dissolved in alkali to give a dark colored solution. Upon acidification of this solution, no precipitation occurred. This solution was made slightly alkaline with ammonium hydroxide and barium chloride added without precipitation taking place. The nature of this material is as yet unknown.

By treating furoic acid with sulfuryl chloride, we had hoped to find a method for securing 5-chlorofuroic acid to the exclusion of other chlorofuroic acids. This indeed seems to be the case, as no other chloro-acids have been isolated from the reaction product. However, the very low yield of 5-chlorofuroic acid makes the method undesirable.

Action of Sulfuryl Chloride on Ethyl Furoate. There seemed to be a possibility that ethyl furoate might be successfully chlorinated by treatment with sulfuryl chloride. With this idea in view, two runs were made in which ethyl furoate was treated with two molecular equivalents of sulfuryl chloride.

First, 70 g. (0.5 mole) of ethyl furoate was dissolved in 200 cc. of carbon disulphide and 135 g. (1 mole) of sulfuryl chloride added. This mixture was refluxed for five hours and, after removal of the solvent from a water-bath, the residue was distilled under reduced pressure to yield 65 g. of unchanged ethyl furoate boiling at 85° at 15 mm. pressure. A small amount of decomposition material remained in the distillation flask.

Second, 70 g. (0.5 mole) of ethyl furoate was added to 135 g. (1 mole) of sulfuryl chloride, without solvent, and the mixture refluxed gently for five hours and distilled. After the sulfuryl chloride had been removed, the receiver was changed and 35 g. or 50% of the ethyl furoate, boiling at 85° at 15 mm. pressure, was recovered. The residue in the flask was a dark tarry material which decomposed upon attempted distillation.

Evidently sulfuryl chloride does not react upon ethyl furoate in the expected manner, under the conditions described.

Action of Sulfuryl Chloride on Furoyl Chloride. An unsuccessful attempt at chlorination of furoyl chloride with sulfuryl chloride was made. Thirteen grams (0.1 mole) of furoyl chloride was added to 27 g. (0.2 mole) of sulfuryl chloride and the mixture refluxed gently for five hours and then distilled. Ten grams of unchanged furoyl chloride, boiling at 176° was recovered and a small amount of tarry material remained. This residue decomposed upon attempted distillation.

Summary.

5-Chlorofuroic acid was prepared by the method of Hill and Jackson (1) and also by hydrolysis of 5-chlorofuroyl chloride. There seems to be no great advantage of either of these methods over the other. 5-Chlorofuroyl chloride may be prepared by the action of chlorine on furoyl chloride. Sulfuryl chloride reacts with furoic acid, in the absence of a solvent, to produce 5-chlorofuroic acid, but the yield is not satisfactory. Furoyl chloride and ethyl furoate do not appear to react with sulfuryl chloride, under the conditions of our experiments.

LACHRYMATORS OF THE FURAN SERIES

Introduction.

Furoyl chloride is a marked lachrymator and is very unpleasant to handle on account of this property. This suggested the possibility of other furan derivatives having similar properties. With this in view we have prepared, in addition to furoyl chloride (1), tetrahydrofurfuryl chloroacetate, tetrahydrofurfuryl iodo-acetate and 5-chloro-furoyl chloride (2). The physiological properties of these substances are listed below.

Furoyl Chloride. Pure compound on the skin of man gives no reaction. As lachrymator, 0.0035 mg. per liter, gave slight irritation. Lethal point for mice is greater than 2.5 mg. per liter, on 10 minute exposure.

Tetrahydrofurfuryl Iodo-Acetate. Pure compound on the skin of man gave redness. As lachrymator, 0.0035 mg. per liter gave slight irritation. Lethal point for mice, 10 minute exposure, is greater than 2.5 mg. per liter.

Tetrahydrofurfuryl Chloro-Acetate. Pure compound on the skin of man gave no reaction. As lachrymator, 0.0065 mg. per liter gave irritation but no lachrymation. Lethal Point for mice, 10 minute exposure, is greater than 2.5 mg. per liter.

5-Chloro-Furoyl Chloride. Pure compound on skin of man gave no reaction. As lachrymator, 0.0065 mg. per liter gave

(1) See p.38, THIS THESIS.
(2) See p.40, THIS THESIS.

slight lachrymation. Lethal Point for mice, 10 minute exposure, was greater than 2.5 mg.

It is known that chloroacetophenone lachrymates in 194 seconds at a concentration of 0.0004 mg. per liter.

Experimental.

Tetrahydrofurfuryl Chloro-Acetate, $C_4H_7OCH_2OCOCH_2Cl$. This compound was previously prepared by Gilman and Dickey (3). A 33.9 g. (0.3 mole) portion of chloro-acetyl chloride was added dropwise to a boiling solution of 30.3 g. (0.3 mole) of tetrahydrofurfuryl alcohol in 250 cc. of benzene. The reaction was carried out in a three-neck flask equipped with mechanical stirrer, reflux condenser and dropping funnel. After refluxing until evolution of hydrogen chloride ceased, the benzene was removed under reduced pressure and the ester distilled. The yield of ester boiling at 110° at 5 mm. pressure was 52.5 g. or 99%.

Tetrahydrofurfuryl Iodo-Acetate, $C_4H_7OCH_2OCOCH_2I$. This compound was prepared by treating an alcoholic solution of tetrahydrofurfuryl chloro-acetate with sodium iodide. A 35.7 g. (0.2 mole) portion of the chloro-ester was dissolved in 200 cc. of alcohol and 30 g. (0.2 mole) of sodium iodide added. The mixture was warmed, with vigorous stirring, for two hours and the alcohol removed under reduced pressure.

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(3) Unpublished results.

After the removal of the alcohol 50 cc. of dry ether was added. This caused the separation of sodium salts. The solution was then filtered and distilled. The yield of tetrahydrofurfuryl iodo-acetate boiling at 130° at 5 mm. was 35 g. or 65%. This is a colorless liquid which darkens upon standing.

Analysis. Calculated for $C_7H_{11}O_3I$: I, 47.21. Found: I, 46.99, 47.14.

Summary.

While furoyl chloride, 5-chloro-furoyl chloride, tetrahydrofurfuryl chloro-acetate and tetrahydrofurfuryl iodoacetate are unquestionably lachrymators, they are very much less powerful than substances like chloroacetophenone. Tetrahydrofurfuryl chloro-acetate and tetrahydrofurfuryl iodoacetate have been prepared and described.

ATTEMPTED FRIEDEL-CRAFT REACTION WITH SOME ACYL FURYL COMPOUNDS

Introduction.

The Friedel-Craft reaction is a very important one for the synthesis of many interesting and valuable compounds. At the present time no work has been reported upon the Friedel-Craft reaction as applied to acyl furyl compounds. However, Reichstein (1) has successfully applied the Friedel-Craft reaction with furan and methyl furan in the synthesis of 2-acetylfuran, 5-methylacetylfuran and other interesting compounds.

Experimental.

Furoic Acid. To a solution of 11.2 g. (0.1 mole) of furoic acid in 200 cc. of carbon disulphide was added 13.35 g. (0.1 mole) of anhydrous aluminium chloride. A solution of 11.3 g. (0.1 mole) of chloroacetyl chloride in 50 cc. of carbon disulphide was then added dropwise and the mixture refluxed for two hours. A small amount of hydrochloric acid was evolved. The mixture was then poured onto cracked ice and the carbon disulphide solution separated from the water layer and washed with 50 cc. of 10% sodium hydroxide solution. The sodium hydroxide solution was then acidified to yield 5 g. (0.044 mole) of unchanged furoic acid. The carbon disulphide solution was distilled from a water-bath to remove the solvent. A small amount of tarry material, which re-

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(1) Reichstein, Helvetica Chim. Act., 13:356 (1930).

sisted attempted crystallization and distillation, remained. Unsuccessful attempts at preparation of an oxime from this tar were made. It was, therefore, assumed that this reaction either did not go or did not go in the expected manner with furoic acid. No variation in the order of addition of reactants was made.

Furoyl Chloride. Thirteen grams (0.1 mole) of furoyl chloride was dissolved in 200 cc. of carbon disulphide and 13.35 g. (0.1 mole) of anhydrous aluminium chloride added. To this mixture was then added 11.3 g. (0.1 mole) of chloroacetyl chloride in 50 cc. of carbon disulphide. The mixture was refluxed gently for three hours, a small amount of hydrochloric acid being evolved. The mixture was poured onto ice and the carbon disulphide solution separated and dried. This solution was then distilled from a water-bath to remove the solvent. Only a tarry material, which decomposed upon attempted distillation, remained. Attempts to convert this material to an oxime were not successful.

Ethyl Furoate. Twenty-eight grams (0.2 mole) of ethyl furoate was dissolved in 300 cc. of carbon disulphide and 26.7 g. (0.2 mole) of anhydrous aluminium chloride added. To this mixture was then added 22.6 g. (0.2 mole) of chloroacetyl chloride and the solution refluxed gently for three hours. The mixture was then poured onto ice and the carbon disulphide solution separated and dried. The carbon disulphide was removed by distillation from a water-bath and the residue distilled under reduced pressure to yield 22 g. (0.16 mole) of unchanged ethyl furoate boiling at 105° at 40 mm. and melting at 34°. In addition to this a small amount of tar remained. Attempts to convert this tar to an oxime were not successful.

Summary.

Unsuccessful attempts at condensation of chloroacetyl chloride with furoic acid, furoyl chloride and ethyl furoate were made. No evidence of a Friedel-Graft reaction were observed.

ANTISEPTICS OF THE FURAN SERIES

Introduction.

Many well known antiseptics and germicides are esters, and many of the more important ones are phenolic esters. Thus it seems that esters of the furan series may prove valuable as antiseptics or germicides. With this idea in view, two groups of esters have been prepared. The first is a group of phenolic esters of furoic and furylacrylic acids. This group includes the furoic and furylacrylic esters of phenol, guaiacol, p-cresol, m-cresol, resorcinol, catechol and hydroquinone. Of these, only phenol furoate (1) and resorcinol difuroate (1) have been previously described. Also, for methods of comparison, the previously described resorcinol, catechol and hydroquinone esters of cinnamic (2) acid have been included.

The second group of esters includes the salicylic and oxalic esters of the furfuryl alcohols. Of these, tetrahydrofurfuryl oxalate, tetrahydrofurylpropyl oxalate and tetrahydrofurfuryl salicylate were successfully prepared. Unsuccessful attempts at preparation of furfuryl oxalate, furylpropyl oxalate, furylallyl oxalate and furfuryl salicylate were made.

All attempts at preparation of the formic esters of the

(1) Baum, Ber., 37:2951 (1904).
(2) Einhorn, Buletinul de Chimie, 17:110 (1925); C. 1916 (1), p.209.

above alcohols, resulted in complete decomposition.

Preliminary tests of the antiseptic property of these compounds is now in progress. The results of these tests will be reported at a later date.

Experimental.

I. Phenolic Esters of Furoic and Furylacrylic Acids.

Phenyl Furoate, $C_6H_5OCOC_4H_3O$. This compound was prepared by the action of furoyl chloride on the sodium salt of phenol. A 9.4 g. (0.1 mole) of phenol was added to 50 cc. of water and 4 g. (0.1 mole) of sodium hydroxide added. To this solution was added, with stirring, 13 g. (0.1 mole) of furoyl chloride. An oil immediately settled out. The mixture was then extracted with alcohol free ether, dried over calcium chloride and distilled. The yield of phenyl furoate melting at 42° and boiling at 145° at 44 mm. pressure was 17.7 g. or 94%. The melting point given by Baum (1) is 41.5°.

This ester is a colorless solid which darkens slightly upon standing. It was subjected to hydrolysis and the acid identified by mixed melting point.

Analysis. Calculated for $C_{11}H_8O_3$: H, 4.25; C, 70.21. Found: H, 4.46 and 4.42; C, 69.80 and 70.16.

Phenyl Furylacrylate, $C_6H_5OCOCH{=}CHC_4H_3O$. This substance was prepared by the method described for phenyl furoate, by the use of 9.4 g. (0.1 mole) of phenol, 4 g. (0.1 mole) of sodium hydroxide and 15.65 g. (0.1 mole) of furylacryloyl chloride. The yield of phenyl furylacrylate boiling at 185° at 4 mm. pressure was 10 g. or 47%.

A better method for preparation of this ester consists of refluxing furylacryloyl chloride with phenol in benzene solution. A 9.4 g. (0.1 mole) portion of phenol and 15.65 g. (0.1 mole) of furylacryloyl chloride were added to 250 cc. of dry benzene and the mixture refluxed for two hours and distilled. The yield of phenyl furylacrylate boiling at 185° at 4 mm. was 18 g. or 84%. This ester was subjected to hydrolysis and the acid identified by mixed melting point.

Analysis. Calculated for $C_{13}H_{10}O_3$: H, 4.67; C, 72.88. Found: H, 5.02 and 4.87; C, 72.36 and 72.78.

Guaiacol Furoate, o-$CH_3OC_6H_4OCOC_4H_3O$. This compound was prepared by the method described for phenyl furoate, using 12.4 g. (0.1 mole) of guaiacol, 4 g. (0.1 mole) of sodium hydroxide and 13 g. (0.1 mole) of furoyl chloride. The yield of guaiacol furoate melting at 76° and boiling at 175° at 5 mm. pressure was 18 g. or 82.5%.

This ester was saponified, the saponification equivalent being 225, and the acid identified by mixed melting point.

Analysis. Calculated for $C_{12}H_{10}O_4$: H, 4.59; C, 66.05. Found: H, 4.74 and 4.78; C, 65.92 and 66.19.

Guaiacol Furylacrylate, o-$CH_3OC_6H_4OCOCH{=}CHC_4H_3O$. This ester was prepared by the methods described for phenyl furylacrylate. The action of the acid chloride upon the sodium salt gave a yield of only 33% while refluxing with the acid chloride in benzene solution gave much better results. A 15.65 g. (0.1 mole) portion of furylacryloyl chloride in 200 cc. of dry benzene was refluxed with 12.4 g. (0.1 mole) of guaiacol for two hours and distilled. The yield of guaiacol furylacrylate boiling at 210° at 6 mm. pressure and melting at 105° was 17 g. or 70%. The ester was hydrolyzed and the acid identified by mixed melting point.

Analysis. Calculated for $C_{14}H_{12}O_4$: H, 4.92; C, 68.85. Found: H, 4.70 and 5.12; C, 69.23 and 68.29.

p-Cresol Furoate, p-$CH_3C_6H_4OCOC_4H_3O$. This ester was prepared by the method described for phenyl furoate, using 10.8 g. (0.1 mole) of p-cresol, 4 g. (0.1 mole) of sodium hydroxide and 13 g. (0.1 mole) of furoyl chloride. The yield of p-cresol furoate melting at 55° and boiling at 152° at 5 mm. pressure was 18 g. or 64%.

Analysis. Calculated for $C_{12}H_{10}O_3$: H, 4.95; C, 71.28. Found: H, 4.95 and 4.82; C, 70.83 and 71.66.

p-Cresol Furylacrylate, p-$CH_3C_6H_4OCOCH{=}CHC_4H_3O$. This ester was prepared by refluxing a mixture of 15.65 g. (0.1 mole) of furylacryloyl chloride with 10.8 g. (0.1 mole) of p-cresol in 200 cc. of dry benzene. The mixture was refluxed for two hours and distilled under reduced pressure. The yield of p-cresol furylacrylate melting at 75° and boiling at 195° at 6 mm. pressure was 15 g. or 71%. The saponification equivalent was determined as 213 and the acid was identified by mixed melting point.

Analysis. Calculated for $C_{14}H_{12}O_2$: H, 5.26; C, 73.68. Found: H, 5.31 and 5.51; C, 72.88 and 73.56.

m-Cresol Furoate, *m*-$CH_3C_6H_4OCOC_4H_3O$. This ester was prepared by the method described for phenyl furoate, using 13 g. (0.1 mole) of furoyl chloride, 4 g. (0.1 mole) of sodium hydroxide and 10.8 g. (0.1 mole) of *m*-cresol. The yield of *m*-cresol furoate melting at 39.5° and boiling at 155° at 5 mm. was 19 g. or 90%. The ester was hydrolyzed and the acid identified by mixed melting point.

Analysis. Calculated for $C_{12}H_{10}O_3$: H, 4.95; C, 71.28. Found: H, 4.96 and 4.90; C, 70.95 and 70.62.

m-Cresol Furylacrylate, *m*-$CH_3C_6H_4OCOCH{=}CHC_4H_3\ O$. This ester was prepared by refluxing a mixture of 15.65 g. (0.1 mole) of furylacryloyl chloride with 10.8 g. (0.1 mole) of *m*-cresol in 200 cc. of dry benzene for two hours. The yield of *m*-cresol furylacrylate boiling at 185° at 5 mm. pressure was 15 g. or 61%. This compound is a colorless liquid, d_4^{34} 1.0728, n_D^{34} 1.5980. The ester was hydrolyzed and the acid identified by mixed melting point.

Analysis. Calculated for $C_{14}H_{12}O_3$: H, 5.26; C, 73.68. Found: H, 5.45 and 5.39; C, 73.96 and 74.00.

Resorcinol Furoate, *m*-$(C_4H_3OCOO)_2C_6H_4$. Attempts were made to secure the half ester by treatment of resorcinol with equimolecular quantities of furoyl chloride in the presence of potassium hydroxide, in aqueous sodium carbonate and by refluxing in benzene solution. In all cases the same compound was secured. The properties of this compound indicate the formation of the full ester.

The better method of preparation consists of addition of 26 g. (0.2 mole) of furoyl chloride to a well stirred solution of 11 g. (0.1 mole) of resorcinol in 50 cc. of water containing 11.2 g. (0.2 mole) of potassium hydroxide. The ester separates as a solid which may be filtered off and crystallized from alcohol. The yield of resorcinol furoate melting at 130° was 5 g. where 0.1 mole of furoyl chloride was used and 11 g. or 37% where 0.2 mole of furoyl chloride was used. The melting point of this compound as given by Baum (1) is 128°-129°.

The saponification equivalent was determined as 147 which would indicate the full ester.

Analysis. Calculated for $C_{16}H_{10}O_6$: H, 3.35; C, 64.43. Found: H, 3.19; C, 64.10.

Catechol Furoate, o-$(C_4H_3OCOO)_2C_6H_4$. Attempts at preparation of this compound by the methods described for resorcinol furoate were not successful. However, by heating at 100° a mixture of 26 g. (0.2 mole) of furoyl chloride and 11 g. (0.1 mole) of catechol and crystallizing first from benzene and then from alcohol the ester, melting at 116°, may be secured in 10 g. or 34% yield. The saponification equivalent was determined as 145, which corresponds with that of the full ester.

Analysis. Calculated for $C_{16}H_{10}O_6$: H, 3.35; C, 64.43. Found: H, 3.81; C, 64.73.

Hydroquinone Furoate, p-$(C_4H_3OCOO)_2C_6H_4$. Attempts at preparation of this compound by the action of furoyl chloride on hydroquinone in the presence of potassium hydroxide resulted in a very low yield of substance melting at 199°. Refluxing hydroquinone with furoyl chloride in benzene solution resulted in no reaction. However, by heating directly a mixture of 26 g. (0.2 mole) of furoyl chloride and 11 g. (0.1 mole) of hydroquinone just below the boiling point of the furoyl chloride (176°) until the mass became solid, better results were obtained. The solid mass was extracted with benzene, then with alcohol and finally crystallized from acetone. The yield of hydroquinone furoate melting at 200° was 8 g. or 26.9%. The saponification equivalent was determined as 150 which would indicate the full ester. Mixed melting point with hydroquinone was 60°. The ester was hydrolyzed and the acid identified by mixed melting point.

Analysis. Calculated for $C_{16}H_{10}O_6$: H, 3.35; C, 64.43. Found: H, 3.81; C, 64.59.

Resorcinol Furylacrylate, m-$(OH)(C_4H_3OCH{=}CHCOO)C_6H_4$. This ester was secured by action of furylacryloyl chloride on resorcinol in benzene solution and the product secured seems to be the half ester, when one equivalent of the acid chloride was used and the full ester when two equivalents were used (see p. 59). In a typical run, 15.65 g. (0.1 mole) of furylacryloyl chloride and 11 g. (0.1 mole) of resorcinol were dissolved in 200 cc. of dry benzene and the mixture refluxed until evolution of hydrogen chloride ceased. About one-half of the benzene was then distilled off and the residue chilled, the ester crystallizing on cooling. This material melted at 126° and further crystallization from benzene raised the melting point to 128°. The yield of this material was 8 g. or 35% based on formation of the half ester.

The saponification equivalent was determined as 208 and 211, the molecular weight of the half ester being 230. The low values for saponification equivalent are probably due to error in titration. The solutions after saponification were highly colored and in order to see the end point it was necessary to dilute the solutions considerably and to place a strong light behind them.

Analysis. Calculated for $C_{20}H_{14}O_6$ (full ester): H, 4.00; C, 68.57. Calculated for $C_{13}H_{10}O_4$(half ester): H, 4.35; C, 67.83. Found: H, 4.50 and 4.78; C, 67.83 and 67.94.

Hydroquinone Furylacrylate, p-$(OH)(C_4H_3OCH{=}CHCOO)C_6H_4$. This ester was prepared by the method described for resorcinol furylacrylate, the same product being obtained with one or two equivalents of the acid chloride; 15.65 g. (0.1 mole) furylacryloyl chloride with 11 g. (0.1 mole) of hydroquinone in 200 cc. of dry benzene to yield 7 g. or 30.4% of material melting at 173°. A mixed melting point with hydroquinone was 145°. Saponification equivalent was determined as 208, the molecular weight of the half ester being 230. The saponification equivalent could not be determined with great accuracy on account of the dark color of the solution.

Analysis. Calculated for $C_{13}H_{10}O_4$: H, 4.35; C, 67.83. Found: H, 4.34 and 4.19; C, 67.50 and 68.32.

Catechol Furylacrylate, o-$(C_4H_3OCH{=}CHCOO)C_6H_4(OH)$. This compound was prepared by the method described for hydroquinone furylacrylate, the half ester being secured in all cases. A solution of 15.65 g. (0.1 mole) of furylacryloyl chloride and 11 g. (0.1 mole) of catechol in 200 cc. of dry benzene gave 8 g. or 35% yield of material melting at 132°. A mixed melting point with catechol was 118°. The saponification equivalent was determined as 208 with the same difficulties described in the case of hydroquinone furylacrylate.

Analysis. Calculated for $C_{13}H_{10}O_4$: H, 4.35; C, 67.83. Found: H, 4.72 and 4.74; C, 67.64 and 67.76.

Resorcinol Di-Furylacrylate, m-$(C_4H_3OCH{=}CHCOO)_2C_6H_4$. Eleven g. (0.1 mole) of resorcinol was refluxed with 31.3 g. (0.2 mole) of furylacryloyl chloride in 250 cc. of dry benzene until evolution of hydrogen chloride ceased. Most of the benzene was then distilled off and the residue allowed to crystallize. This material when recrystallized from alcohol to constant melting, melted at 112° and gave a mixed melting point of 95° with the previously described half ester. Yield, 12 g. or 34.3%. Mixed melting point with resorcinol was 94°. The saponification equivalent was determined as 165, the theoretical saponification equivalent for the full ester being 175. The dark color of the solution made titration difficult.

Analysis. Calculated for $C_{20}H_{14}O_6$: H, 4.00; C, 68.57. Found:H, 4.25 and 4.23; C, 69.23 and 69.02.

Hydroquinone Cinnamate. This previously described (2) compound was prepared by warming 11 g. (0.1 mole) of resorcinol with 33.3 g. (0.2 mole) of cinnamoyl chloride until a solid mass was formed. One hundred cubic centimeters of acetone was then added and the mixture refluxed for three hours. The mixture was then allowed to cool and the ester filtered off to yield 20 g. or 54% of material melting at 189°. This melting point is in agreement with that previously reported (2).

Resorcinol Cinnamate. This compound (2) was prepared by the method described for hydroquinone cinnamate. The yield from 11 g. (0.1 mole) of resorcinol and 33.3 g. (0.2 mole) of cinnamoyl chloride was 18 g. or 49%. This substance when crystallized from alcohol melted at 120° and the melting point remained unchanged when recrystallized from acetone. This melting point is in agreement with that previously reported (2).

II. Oxalic and Salicylic Esters of Furfuryl Alcohols.

Furfuryl Oxalate. Several unsuccessful attempts were made at preparation of furfuryl oxalate. To 9.8 g. (0.1 mole) of furfuryl alcohol was added 4.5 g. (0.05 mole) of anhydrous oxalic acid at room temperature. The mixture gradually darkened and rapid decomposition took place, leaving only a carbonous residue. A second attempt was made under the same conditions except that 50 cc. of anhydrous ether was used as a solvent. The mixture darkened in color but after two hours standing at room temperature, distillation under reduced pressure was attempted. After the solvent had been removed, with aid of a water-pump, and the temperature raised slightly, violent decomposition took place. Attempts at preparation of the ester by treatment of 9.8 g. (0.1 mole) of the alcohol in 50 cc. of anhydrous ether with 6.35 g. (0.05 mole) of oxalyl chloride resulted in the formation of a dark colored solution which decomposed upon attempted distillation at 10 mm. pressure. The same result was secured upon attempted preparation of the ester by the action of oxalyl chloride on the sodium salt of the alcohol, both with and without a solvent. The same results were also obtained upon treatment of furfuryl alcohol with a pyridine-oxalyl chloride complex. To 12.7 g. (0.1 mole) of oxalyl chloride was added dropwise a solution of 17.4 g. (0.22 mole) of pyridine in 200 cc. of dry chloroform. To this mixture was added dropwise, with stirring, a solution of 19.6 g. (0.2 mole) of furfuryl alcohol in 50 cc.

of chloroform. The mixture gradually darkened and finally became black. After two hours stirring at room temperature, the mixture was thoroughly washed with water and dilute acetic acid and finally again with water. The chloroform solution was separated, dried over sodium sulfate and the solvent removed with aid of a water-pump. A dark viscous residue remained in the distillation flask. Upon attempted distillation of this residue at 4 mm. pressure violent decomposition took place, resulting in a sudden explosion which shattered the containing flask. The product of decomposition was scattered over the room, taking fire as it touched the air. No further attempts at preparation of this compound have been made.

Tetrahydrofurfuryl Oxalate, $(C_4H_7OCH_2OCO)_2$. Tetrahydrofurfuryl oxalate was prepared by the method used by Wahl (3) in the preparation of various esters of oxalic acid. A 8.4 g. (0.0824 mole) portion of tetrahydrofurfuryl alcohol was dissolved in 6 g. of benzene and 3 g. (0.0333 mole) of anhydrous oxalic acid added to the resulting solution. To this mixture was then added 1.79 g. (0.0183 mole) of concentrated sulfuric acid and the mixture stirred at room temperature for 10 hours. The solution was then washed with a small amount of dilute sodium bicarbonate solution, dried over sodium sulfate and distilled. The yield of tetrahydrofurfuryl oxalate boiling

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(3) Wahl, Bull. soc. chim., 35:304 (1924); Bull. soc. chim., 37:713 (1925).

at 203° at 4 mm. pressure was 5 g. or 58.4%, based upon oxalic acid.

In a second preparation, 30.6 g. (0.3 mole) of tetrahydrofurfuryl alcohol was added to 9 g. (0.1 mole) of anhydrous oxalic acid and the mixture heated at 120° for 12 hours. The mixture was then distilled to yield 16 g. or 62%, based on oxalic acid, of tetrahydrofurfuryl oxalate boiling at 203° at 4 mm. pressure.

This ester is a colorless liquid with little odor. d_4^{25} 1.1835; n_D^{25} 1.4650. The saponification equivalent was determined as 127.5, the theoretical value being 129.

Analysis. Calculated for $C_{12}H_{18}O_6$: C, 55.81; H, 6.98. Found: C, 55.79 and 56.05; H, 7.21 and 6.77.

Tetrahydrofurylpropyl Oxalate, $(C_4H_7OCH_2CH_2CH_2OCO)_2$. Attempts at preparation of the oxalic ester of tetrahydrofurylpropyl alcohol (4) by the action of anhydrous oxalic acid were not successful. Signs of decomposition were evident and complete decomposition resulted upon attempted distillation at 4 mm. pressure. We were, however, successful in securing this compound by the action of oxalyl chloride upon the sodium salt of the alcohol. Thirteen grams (0.1 mole) tetrahydrofurylpropyl alcohol was dissolved in 50 cc. of dry benzene and 2.3 g. (0.1 atom) of sodium added. This mixture was refluxed until no further reaction was evident. The small particle of un-

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(4) See p.31, THIS THESIS.

used sodium was then removed and 6.35 g. (0.05 mole) of oxalyl chloride was added dropwise with vigorous stirring. The mixture was refluxed for two hours, filtered and distilled to yield 8 g. or 51% of tetrahydrofurylpropyl oxalate boiling at 210° at 3 mm. pressure.

This ester is a colorless liquid with little odor. d_4^{25}1.1045; n_D^{25} 1.4675. The saponification equivalent was determined as 157.9, the theoretical value being 157.

Analysis. Calculated for $C_{16}H_{26}O_6$: C, 61.15; H, 8.25. Found: C, 60.63 and 61.00; H, 8.61 and 8.14.

Furylpropyl Oxalate. Attempts at preparation of the oxalic ester of furylpropyl alcohol (5) were unsuccessful, all of the methods above described being attempted. In every case, violent decomposition took place upon attempted distillation under reduced pressure.

Furylallyl Oxalate. Furylallyl alcohol was prepared by the method of Adams and Bray (6). To a solution of 61 g. (0.5 mole) of furylacrolein in 200 cc. of absolute ethyl alcohol was added 0.5 g. of platinum oxide catalyst (7) and 0.05 g. of ferrous sulfate. The mixture was reduced at 2 - 3 atmospheres pressure and the reaction was stopped when one molecular equivalent of hydrogen had been absorbed. After re-

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(5) See p.27, THIS THESIS.
(6) Adams and Bray, J. Am. Chem. Soc., 49:2101 (1927).
(7) Adams and Schriner, J. Am. Chem. Soc., 45:2171 (1923).

duction, the alcohol solution was separated from the catalyst by filtration and the solution distilled under reduced pressure. The yield of furylallyl alcohol boiling at 108°-110° at 4 mm. pressure was 50 g. or 64.5%.

Note: Freshly distilled furylacrolein is slightly yellow in color and darkens rapidly unless kept in an ice chest. If this material is crystallized from petroleum ether (b.p. 40°-60°) a material is secured which remains practically colorless after long standing at room temperature. This crystallized material, however, gave no better yield of alcohols upon reduction.

All attempts at preparation of furylallyl oxalate by the above described methods resulted upon complete decomposition, either during the reaction or upon attempted distillation of the reaction products under reduced pressure.

Tetrahydrofurfuryl Salicylate, o-$(OH)(C_4H_7OCH_2OCO)C_6H_4$. Tetrahydrofurfuryl salicylate was prepared by the action of the acid chloride on tetrahydrofurfuryl alcohol. The salicyloyl chloride was prepared by the method of Adams and Ulich (8) by the action of oxalyl chloride on salicylic acid. A 13.8 g. (0.1 mole) portion of salicylic acid was dissolved in 50 cc. of dry benzene and 31.8 g. (0.25 mole) of oxalyl chloride added dropwise with stirring. The mixture was refluxed gently for two hours and the excess oxalyl chloride and benzene re-

(8) Adams and Ulich, J. Am. Chem. Soc., 42:604 (1920).

moved by distillation under reduced pressure. No attempt was made to distill the salicyloyl chloride.

The crude salicyloyl chloride was added to a solution of 10.2 g. (0.1 mole) of tetrahydrofurfuryl alcohol in 100 cc. of benzene and the solution refluxed until evolution of hydrogen chloride ceased. The mixture was then distilled to yield 15 g. or 78% of tetrahydrofurfuryl salicylate boiling at 166° at 5 mm. pressure.

This ester is a colorless liquid with a very pleasant odor. d_4^{34} 1.1831; n_D^{34} 1.5217.

Analysis. Calculated for $C_{12}H_{14}O_4$: C, 63.26; H, 5.77. Found: C, 63.25 and 63.57; H, 5.92 and 5.94.

Furfuryl Salicylate. Attempts to secure this ester by the method described for tetrahydrofurfuryl salicylate were unsuccessful, complete decomposition taking place upon attempted distillation at 4 mm. pressure. The same results were secured when a solution of the alcohol in chloroform was treated with a chloroform solution of the pyridine-acid chloride complex, a 10% excess of pyridine being used.

Summary.

The furyl and furylacrylic esters of phenol, guaiacol, p-cresol, m-cresol, resorcinol, catechol and hydroquinone have been prepared and described. Also for methods of comparison, the previously prepared cinnamic esters of hydroquinone and resorcinol have been prepared. In general, the furoic esters may be prepared in very good yields by the Schotten-Baumann reaction. This method, however, is not so desirable in the case of the furylacrylic esters, it being preferable to reflux the acid chloride with the phenolic body in benzene solution. In some cases it is necessary to heat directly a mixture of the acid chloride and the phenol. In the case of the dihydroxy benzene compounds, the full ester only is secured with furoyl chloride while the half ester may be formed with furylacryloyl chloride. In the case of resorcinol only was it possible to secure both the full and half ester.

Tetrahydrofurfuryl salicylate, tetrahydrofurfuryl oxalate and tetrahydrofurylpropyl oxalate have been prepared and described.

Unsuccessful attempts were made to secure furfuryl salicylate, furfuryl oxalate, furylpropyl oxalate and furylallyl oxalate.

INSECTICIDES OF THE FURAN GROUP

Introduction.

At the present time no correlation exists between the chemical constitution of compounds and their power to act as insecticides. Substances which are good germicides may be also good insecticides, but this is not necessarily the case. The method followed by the manufacturers of insecticides, in their search for new and better insecticides, is simply to test everything. With this idea in mind, the action of a series of furan compounds on flies has been determined. The preparation and properties of these compounds have been previously described in this series.

Method of Testing.

One hundred flies that have been raised under optimum conditions, and whose resistance to the solvent has been determined, are placed in a test chamber. No flies are used in which a check, with the solvent alone, shows over 5% down.

The chamber is a cubical room six feet on a side, with windows on two sides, well lighted and previously well aerated. Twelve cubic centimeters of the solution to be tested is sprayed in at the top of the ceiling, from a standard atomizer, at a pressure of 12 pounds. Exactly 10 minutes after spraying, the inactive flies on the floor are counted, at the end of 30 minutes the chamber is opened and the inactive flies picked up, placed in cages with food and water and observed at the end of 24 hours. In case nearly all of the flies are down at the end of 10 minutes, the chamber is then opened. Under these conditions a good pyrethrum spray will down all of the flies in less than 10 minutes and at the end of 24 hours from 20% to 30% will have recovered.

The results of tests with furan compounds is given in the following table.

Compound	Conc.	Sol-vent.	Downs 10 min.	30 min.	24 hours
Hydroquinone monofuroate	S	$K^{60}N^{40}$	4	23	—
Hydroquinone difurylacrylate	S	K	12	41	20
m-Cresol furylacrylate	S	$K^{60}N^{40}$	1	5	—
m-Cresol furoate	2%	K	12	31	—
Phenyl furylacrylate	2%	K	62	82	37
Phenyl furoate	2%	$K^{90}N^{10}$	42	57	28
p-Cresol furylacrylate	2%	K	48	59	48
Guaiacol furoate	2%	$K^{80}N^{20}$	15	52	17
Resorcinol difuroate	S	$K^{60}N^{40}$	10	31	—
Guaiacol furylacrylate	2%	$K^{60}N^{40}$	6	39	—
Hydroquinone difuroate	S	$K^{60}N^{40}$	2	19	—
p-Cresol furoate	2%	$K^{80}N^{20}$	67	81	61
Hydroquinone cinnamate	S	$K^{60}N^{40}$	7	24	7
Resorcinol furylacrylate	2%	$K^{60}N^{40}$	3	17	—
Benzoylfuran (1)	4%	$K^{80}N^{20}$	60	85	58
Tetrahydrofurylpropyl thiocyanate	1%	K	100	—	32

(1) Gilman and Hewlett, Iowa State College Journal of Science, 4:29 (1930).

In the above table, S represents a saturated solution the concentration of which is less than 2%. K represents kerosene; H, cyclohexanone; N, high flash naphtha. Thus, $K^{60}N^{40}$ represents 60% kerosene and 40% naphtha.

Summary.

A description is given for the method of testing the action of compounds on flies. A table is given in which the action of 16 furan compounds is listed. None of these compounds is remarkably good and some have little if any effect at all. The more active compounds are shown to be tetrahydrofurylpropyl thiocyanate, benzoylfuran, the p-cresol and the phenyl esters.

THE PREPARATION OF FURFURAL DIACETATE

Introduction.

Furfural diacetate is in demand for the preparation of various substituted furfurals, such as 5-chlorofurfural and 5-bromofurfural. The purpose of this study was to determine the optimum conditions for preparation of furfural diacetate, using the method of Gilman and Wright (1).

The method consists of treatment of furfural with acetic anhydride in the presence of stannous chloride dihydrate, $SnCl_2 \cdot 2H_2O$. Following the method of Gilman and Wright (1) it was found that improved yields of furfural diacetate were secured by use of a larger quantity of catalyst and by keeping the temperature of the reaction mixture as low as possible during the reaction. Thus by the use of four grams of catalyst to four moles of furfural, and a slight excess of acetic anhydride, yields as high as 78% of furfural diacetate from technical furfural were secured by allowing the reaction mixture to stand in the open during the severe cold spells of winter. Under these conditions, practically all of the furfural diacetate crystallized, thus making the product easier to work up.

Naturally, the preparation of furfural diacetate in warm weather and also in warmer climates is desirable. We have

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(1) Gilman and Wright, <u>Iowa State College Journal of Science</u>, **4**:35-36 (1929).

found that good yields of furfural diacetate may be secured by allowing the reaction mixture to stand in an electric refrigerator and that moderate yields may be secured by use of a large amount of catalyst at a higher temperature and over a shorter interval of time.

The mixture after reaction consists of a mass of coarse crystals of furfural diacetate and some liquid, the whole mixture being very dark in color. The crystals are separated from the liquor by filtration with suction. The separated liquor is then shaken with sufficient water to cause it to solidify and then is filtered through the crystal mat already present in the filter. This affords rapid filtration. The material is then dried and distilled. The stannous chloride, however, during the water treatment is hydrolyzed to the basic chloride which is insoluble and which seems to cause some decomposition upon distillation. In cases where very large quantities of catalyst were used, complete decomposition has resulted upon attempted distillation. Therefore, it seems desirable to remove the catalyst by crystallization of the material before distillation. In cases where more than one gram of catalyst per mole of furfural is used, the crystallization is necessary, in other cases it is optional. In all cases where crystallization is used a better yield and a purer product is obtained. Carbon disulphide has been used as the solvent in crystallization of this material, as it is almost completely miscible with furfural diacetate at the boiling point of carbon disulphide and the solubility is very low at 0°. From the same run, 323 g. of crude material gave 295 g. of very pure furfural diacetate by crystallization from carbon disulphide and subsequent distillation, while the same weight of crude material gave 272 g. of less pure product by direct distillation. In this run three grams of catalyst had been used to four moles of furfural.

Experimental.

In all cases the acetic anhydride used was 95% pure and the weights given will represent the actual weights of this material used while the number of moles will be based upon the acetic anhydride content. In cases where crude furfural is used, this material will be assumed to contain 95% furfural. Typical runs will be described while the data accumulated in this work will be given in tables I and II.

Method I. Three grams of stannous chloride dihydrate dissolved in 384 g. (4 moles) of freshly distilled furfural. This solution was placed in an ice and salt mixture and cooled to -8° to -10°. A solution of 459 g. of 95% acetic anhydride (4.27 moles) was also cooled to -8° to -10° and was then poured into the furfural. This was thoroughly mixed and allowed to remain in the freezing mixture for one hour and was then placed in an electric refrigerator and allowed to stand for 48 hours. At the end of this time, practically all of the material was crystallized. The mass was broken up and the crystals separated from the liquid by filtration through a Büchner funnel. The separated liquid was then shaken with two liters of water and the solid thus formed was filtered on top of the crystals in the funnel. This mass was thoroughly washed with water and sucked as dry as possible, and was then removed from the filter and dried on porous plates. The weight of the crude dry material was 647 g. (This material may be distilled directly or may be subjected to crystallization from carbon disulphide and subsequently distilled or recrystallized from carbon disulphide). In this run the crude material was divided into two equal portions of 323.5 g. each. The first was distilled directly under reduced pressure to yield 272 g. or 68.65% of furfural diacetate boiling at 140°-144° at 20 mm. The other portion was dissolved in 500 cc. of boiling carbon disulphide, filtered and cooled in cracked ice. This material was then filtered and sucked free of carbon disulphide. The slightly colored product was distilled to yield 295 g. or 74.5% of entirely colorless material boiling at 143°-144° at 20 mm. pressure.

Method II. The object of this method is the preparation of furfural diacetate without use of a refrigerator and also to avoid the loss in time by allowing the material to stand for 48 hours. Also, since acetic anhydride is more expensive than furfural, it is desirable to use an excess of furfural rather than an excess of acetic anhydride.

A series of runs was made using a large amount of catalyst, and adding the acetic anhydride to the furfural at room temperature. The product of reaction was worked up as described above. It was found, however, that much decomposition took place upon distillation and crystallization from carbon disulphide before distillation was found necessary. If the amount of catalyst is cut down to a minimum, 2 g. per mole, the material may be distilled directly, but the yields are much poorer when the crystallization is not used.

A typical run is given. Eight grams of stannous chloride dihydrate was dissolved in 384 g. (4 moles) of distilled furfural contained in a flask equipped with mechanical stirrer, dropping funnel and thermometer. The flask was placed in a vessel of water and 408 g. of 95% acetic anhydride (3.8 moles) added dropwise with stirring. The addition of the acetic anhydride was regulated so that the temperature of the mixture remained at 20°-30°. After the addition of the acetic anhydride was complete, the mixture was stirred for two hours. It was then poured into a large flask and was shaken with water until the mass solidified, about three liters of water being used. This mixture was then filtered with suction, washed and dried. The dry material was dissolved in 800 cc. of carbon disulphide by adding carbon disulphide and heating it to its boiling point under reflux condenser. This solution was then filtered and cooled in cracked ice. The furfural diacetate was separated by filtration, dried and distilled. The yield of furfural diacetate boiling at 143°-144° at 20 mm. was 380 g. or 50.51%, based on the acetic anhydride.

Table I.

Method I.

No.	Wt. F.	Moles F.	Grade F.	Wt. A.	Moles A.	Wt. Cat.	Time hours	Wt. P.	Yield on F., %	Yield on A., %
1	384	3.8	Crude	459	4.28	2	48	530	70.40	62.50
2	384	3.8	Crude	428	4.00	2	48	460	61.13	58.08
3	384	3.8	Crude	438	4.08	2	48	460	61.13	56.93
4	384	4.0	Pure	428	4.00	3	48	580	73.22	73.22
5	384	4.0	Pure	459	4.28	3	48	544	70.70	66.07
6	384	3.8	Crude	428	4.00	3	48	472	62.87	59.72
7	384	3.8	Crude	459	4.28	3	48	550	73.08	64.88
8	384	3.8	Crude	510	4.75	3	48	483	64.21	51.45
9	384	3.8	Crude	428	4.00	3	100	490	65.10	61.85
10	384	3.3	Crude	459	4.28	3	100	500	66.45	59.00
11	384	3.8	Crude	459	4.28	4	48	480	64.00	56.82
12	384	3.8	Crude	428	4.00	4	60	360	47.85	45.45

F represents furfural; A, acetic anhydride; P, furfural diacetate.

Table II.

Method II.

No.	Wt. F.	Moles F.	Grade F.	Wt. A.	Moles A.	Wt. Cat.	Treatment of P.	Wt. P.	Yield on F., %	Yield on A., %
1	96	0.095	Crude	102	0.095	10	Dist.	——	——	——
2	96	0.095	Crude	102	0.095	5	Dist.	39.6	21.05	21.05
3	96	0.095	Crude	102	0.095	3	Dist.	50.0	26.58	26.58
4	96	0.095	Crude	102	0.095	2	Dist.	62.5	33.23	33.23
5	96	0.095	Crude	102	0.095	2	Cryst. Dist.	97.0	51.58	51.58
6	96	0.095	Pure	107	1.000	2	Cryst. Dist.	110.0	55.55	55.55
7	384	4.000	Pure	428	4.000	8	Cryst. Dist.	405.0	51.12	51.12

F represents furfural; A, acetic anhydride; P, furfural diacetate.

Summary.

Two methods are described for the preparation of furfural diacetate in good yields. During very cold weather or where an ice box is available, the first method is more desirable. It is found preferable to crystallize the crude product before distillation.

NITROFURFURAL DIACETATE AND NITROFURFURAL

Introduction.

Nitrofurfural may prove to be a very useful compound in the manufacture of dyes and many other valuable compounds. This compound was first prepared by Gilman and Wright (1) by nitrating furfural diacetate in acetic anhydride. The direct product of this nitration is assumed, by Gilman and Wright (1), to be an intermediate ring fission compound which, when treated with pyridine, is converted to nitrofurfural diacetate. The nitrofurfural is secured from the diacetate by hydrolysis with sulfuric acid.

It is of interest to note that nitrofurfural diacetate may also be prepared directly from furfural by the method described by Gilman and Wright (1) for nitration of furfural diacetate. The yield of nitrofurfural diacetate from the direct nitration of furfural in acetic anhydride is practically the same as that secured by nitration of furfural diacetate. However, if the yield in both cases is referred back to furfural, the yield by direct nitration of furfural will be found superior to that secured by nitration of furfural diacetate. In addition to this, the necessity for the preparation of furfural diacetate is avoided.

X(1) Gilman and Wright, J. Am. Chem. Soc., 52:2550 (1930).

Experimental.

Nitrofurfural Diacetate, $NO_2C_4H_2OCH(OCOCH_3)_2$. A nitrating mixture was prepared by slow addition of 175 g. (2.76 moles) of fuming nitric acid (sp. gr. 1.5) to 560 g. (5.5 moles) of well chilled acetic anhydride, the temperature of the mixture being kept at -5° during the addition of the nitric acid. A solution of 96 g. (1 mole) of freshly distilled furfural in 210 g. (2 moles) of acetic anhydride was then added dropwise to the nitrating mixture, the temperature being kept below -5° during the addition and during three hours subsequent stirring. The mixture was then poured onto 1 kg. of cracked ice and a saturated solution of sodium hydroxide added with vigorous stirring until the solution was faintly but distinctly alkaline to litmus. During the addition of sodium hydroxide, ice was added from time to time to keep the temperature down, an excess of ice being kept in the mixture. The water layer was then decanted from the heavy oil which separated out. The oil was as nearly as possible freed from the water layer and dissolved by addition of pyridine. Just enough pyridine is added to completely dissolve this oil. Usually, no vigorous reaction occurs when the pyridine is added, however, in some cases the action has been known to become quite vigorous. If this occurs, it may be checked by addition of cracked ice. If ice is added, a larger amount of pyridine will be required to dissolve the oil. After standing for about one hour the solution was diluted with about three volumes of water and then allowed to stand over night. The solid nitrofurfural diacetate was then separated from the solution by filtration and dried to yield 100 g. or 41% of material melting at 85°. This material was crystallized from alcohol to yield 80 g. or 33% of pure nitrofurfural diacetate melting at 92°. The yield secured by Gilman and Wright (1) by nitration of furfural diacetate was given as 40% of material melting at 87°.

Nitrofurfural. Nitrofurfural was prepared by hydrolysis of nitrofurfural diacetate by the method of Gilman and Wright (1). Eighty grams (0.33 mole) of pure nitrofurfural diacetate was suspended in a solution of 100 cc. of concentrated sulfuric acid in 356 cc. of water and the mixture refluxed for 15 minutes in an atmosphere of carbon dioxide. The mixture was then chilled in ice, nitrofurfural crystallizing from the solution. This was separated from the solution by filtration and dried. The nitrofurfural may be recrystallized from petroleum ether (b.p. 40°-60°) or may be distilled. After filtration, the above solution was extracted with ether, the ether extract dried over sodium sulfate and the solid nitrofurfural added to this ether solution. The whole was then distilled to yield 38 g. or 80% of nitrofurfural boiling at 132°-134° at 11 mm. pressure and melting at 33°-34°.

Summary.

Nitrofurfural diacetate may be secured either by the nitration of furfural diacetate or by the direct nitration of furfural in acetic anhydride. The yields are about the same by either method, but the use of furfural itself is an advantage in that the preparation of furfural diacetate is avoided. Nitrofurfural may be prepared from nitrofurfural diacetate by hydrolysis in sulfuric acid.

PREPARATION OF SECONDARY AND TERTIARY FURYL CARBINOLS BY USE OF THE GRIGNARD REAGENT

Introduction.

Hale, McNally and Pater (1) found that the Grignard reagent reacted smoothly with ethyl furoate to produce the expected tertiary carbinol in good yields. In this manner they prepared, among others, diphenyl furyl carbinol. In the reaction of phenylmagnesium bromide on ethyl furoate, very little diphenyl was formed. Their attempts, however, at preparation of secondary furyl carbinols by reaction of furfural on the Grignard reagent were not successful. When phenylmagnesium bromide and benzylmagnesium chloride were treated with furfural only coupling products, diphenyl and dibenzyl, respectively, were formed.

Peters and Fischer (2), however, found that the Grignard reagent reacted normally with furfural and were successful in preparation of phenyl furyl carbinol and a number of other secondary furyl carbinols. No mention is made, however, as to the amount of coupling products formed.

We have followed the work of Hale, McNally and Pater (1) in preparation of diphenyl furyl carbinol and that of Peters and Fischer (2) in preparation of phenyl furyl carbinol and agree with their results except that our compounds seem to be more stable than has been previously indicated. We have also

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(1) Hale, McNally and Pater, Am. Chem. J., 35:68 (1906).
(2) Peters and Fischer, J. Am. Chem. Soc., 52:2079 (1930).

prepared the phenyl 5-chlorofuryl and phenyl 5-bromofuryl carbinols and have attempted the preparation of di-tert.butyl furyl carbinol. In all cases where phenylmagnesium bromide was used, the usual amount of diphenyl was formed.

Experimental.

Diphenyl Furyl Carbinol, $(C_6H_5)_2C(OH)C_4H_3O$. Diphenyl furyl carbinol was prepared by the method of Hale, McNally and Pater (1) by the action of phenylmagnesium bromide on ethyl furoate. The Grignard reagent was prepared by addition of a solution of 34.54 g. (0.22 mole) of bromobenzene in 200 cc. of anhydrous ether to 6 g. (0.25 atom) of magnesium. After the reaction was complete, a solution of 14 g. (0.1 mole) of ethyl furoate in 50 cc. of anhydrous ether was added dropwise with vigorous stirring. After two hours refluxing, a positive test for Grignard reagent was secured. This mixture was then hydrolyzed by pouring onto ice and the calculated quantity of 10% acetic acid. The ether layer was then separated, washed with sodium carbonate solution and dried over anhydrous sodium sulphate. The ether was removed by distillation from a water-bath and the residue subjected to steam distillation to yield 1.15 g. or 3.41% of diphenyl melting at 70°. The residue in the flask was then extracted with ether and dried over anhydrous sodium sulphate. The ether was sucked off with the aid of a water pump and the solid residue crystallized from petroleum ether, (b.p. 30°-60°) to yield

18 g. or 75% of diphenyl furyl carbinol melting at 92°. Hale, McNally and Pater (1) report a yield of 70% of material melting at 92.5° (corrected).

Contrary to former work (1) reported on this compound, decomposition appears to take place very slowly. The appearance and melting point remained unchanged at the end of one week and noticeable decomposition began at the end of fifteen days. At the end of thirty days about one-half of the original material was recovered unchanged by crystallization from petroleum ether, (b.p. 30°-60°). At the end of six months the whole mass had become plastic and could be moulded in the fingers, while at the end of two years only a hard resinous insoluble material remained.

Phenyl Furyl Carbinol, $C_6H_5CH(OH)C_4H_3O$. Hale, McNally and Pater (1) attempted the preparation of this compound without success. Upon this basis, the statement is made that furfural does not react normally with the Grignard reagent. Peters and Fischer (2) have prepared phenyl furyl carbinol by the reaction of furfural on phenylmagnesium bromide.

We have duplicated this preparation of Peters and Fischer (2). The phenylmagnesium bromide was prepared by addition of a solution of 18.84 g. (0.12 mole) of bromobenzene in 150 cc. of anhydrous ether to 3.6 g. (0.15 atom) of magnesium. After the reaction was complete a solution of 9.6 g. (0.1 mole) of freshly distilled furfural in 50 cc. of anhydrous ether was added dropwise with stirring. This mixture was refluxed for two hours and then allowed to stand over night. It was hydrolyzed by pouring onto ice and adding the calculated amount of 10% acetic acid. The ether layer was removed, washed with sodium bisulphite solution to remove any unchanged furfural and dried over sodium carbonate. The ether was then removed by distillation from a water-bath and the residue in the flask subjected to steam distillation to yield 0.5 g. (0.00325 mole) or 2.71% diphenyl melting at 70°. The residue in the flask was then extracted with ether, dried over sodium carbonate and distilled under reduced pressure to yield 4.5 g. or 25.9% of material boiling at 128°-130° at 5 mm. pressure. Peters and Fischer (2) report a yield of 26% of material boiling at 122°-125° at 2 mm. and 138°-142° at 10 mm. pressure. This material remained unchanged for 2 - 3 days but at the end of a week it had completely changed to a dark gummy mass.

Di-tert. Butyl Furyl Carbinol, (Tert. $C_4H_9)_2C(OH)C_4H_3O$. Attempted preparation of this compound was made by treatment of ethyl furoate with tert. butylmagnesium chloride. A solution of 46.25 g. (0.5 mole) of tert. butyl chloride in 5 moles of anhydrous ether was added slowly to 12 g. (0.5 atom) of magnesium. After the reaction was complete, a solution of 28 g. (0.2 mole) of ethyl furoate in 50 cc. of ether was added slowly After reluxing this mixture for two hours, a positive test for the Grignard reagent was secured. It was then hydrolyzed by pouring onto ice and adding the calculated quantity of 10% acetic acid. The ether solution was separated and dried over anhydrous sodium sulphate. The ether was then removed by distillation from a water-bath and the residue subjected to steam distillation. A yellow oil which collected in the distillate was assumed to be di-tert. butyl furyl carbinol. The steam distillate was extracted with ether and the ether solution dried over sodium sulphate and distilled under reduced pressure. The yield was 10 g. of material boiling at 80°-85° at 1 mm. pressure. This is a yellow substance with a pinene odor, d_4^{34} 0.9486; n_D^{34} 1.4749. Analysis would indicate this material to be a mixture of secondary and tertiary carbinols. A light red tar which remained as a residue in the flask after steam distillation was dissolved in ether and the solution dried over sodium sulphate. Upon evaporation of the ether, 11 g. of a red resinous material with a very pleasant odor remained. This material has shown no tendency to crystallize after two years standing. Both products of the reaction are stable and no apparent change has taken place in either compound over a period of two years. The above liquid was analyzed for carbon and hydrogen.

Analysis. Calculated for $C_{13}H_{22}O_2$ (tert. carbinol): C, 74.29; H, 10.48. Calculated for $C_9H_{14}O_2$ (sec. carbinol): C, 70.13; H, 9.09. Calculated for $C_{16}H_{24}O_3$ (ether): C, 72.72; H, 9.09. Calculated for $C_9H_{12}O_2$ (ketone): C, 71.05; H, 7.89. Found: C, 73.56 and 73.45; H, 9.87 and 9.73.

Attempts at preparation of the tertiary carbinol by action of furoyl chloride on tert. butylmagnesium chloride gave approximately the same results. A solution of tert. butylmagnesium chloride was prepared by addition of a solution of 46.25 g. (0.5 mole) of tert. butyl chloride in 5 moles of ether to 12 g. (0.5 atom) of magnesium. After the reaction was complete, a solution of 26.1 g. (0.2 mole) of furoyl chloride in 100 cc. of anhydrous ether was slowly added. The mixture was then refluxed for two hours and hydrolyzed by pouring onto ice and adding the calculated quantity of 10% acetic acid. The ether solution was removed, dried over anhydrous sodium sulphate and the ether removed from a water-bath. The residue was then subjected to steam distillation to yield 9 g. of material boiling at 80°-85° at 1 mm. pressure. The residue in the flask was dissolved in ether and dried. On evaporation of the ether solution, 15 g. of a light red viscous material remained. This viscous substance had the appearance of the resinous material secured by action of ethyl furoate upon tert. butylmagnesium chloride.

Phenyl 5-Bromofuryl Carbinol, $C_6H_5CH(OH)C_4H_2OBr$. This compound was prepared by the action of phenylmagnesium bromide on 5-bromofurfural. 5-Bromofurfural was previously prepared by Gilman and Wright (3) who describe three methods of securing this material.

X(3) Gilman and Wright, J. Am. Chem. Soc., 52:1170 (1930).

Two of the methods of Gilman and Wright (3) were used in preparation of the bromofurfural. The first of these consists of treating a solution of furfural diacetate (4) in carbon disulphide with bromine at low temperature. A solution of 396 g. (2 moles) of furfural diacetate was added to a flask containing 700 cc. of dry carbon disulphide and this mixture cooled with ice. A solution of 640 g. (8 atoms) of bromine in 200 cc. of dry carbon disulphide was then slowly added. The rate of addition of the bromine solution was so regulated that the temperature of the mixture remained at about 10°. The time required for the addition of the bromine solution was usually about 30 minutes. The mixture was then stirred for three hours, at the end of which time the mixture was filtered to remove 80 g. of a white solid which is insoluble in carbon disulphide. At the present time the composition of this material is unknown, however, further work is being done on this compound. The carbon disulphide solution may then be worked up in either of two ways. Typical runs will be described.

First, the filtered carbon disulphide solution was cautiously added to 400 g. (4 moles) of powdered calcium carbonate which had been previously moistened and covered with water. This mixture was allowed to stand until the vigorous reaction was complete and then subjected directly to steam

(4) See p.71, THIS THESIS.

distillation. The distillation flask should not be filled more than one-fourth full as a vigorous foaming begins as the last of the carbon disulphide passes over. After all of the carbon disulphide is removed, the temperature rises rapidly to 100° and pure 5-bromofurfural is collected in the steam distillate. The distillate is best condensed by running water over the receiver, the use of water in the condenser is to be avoided because of clogging the condenser. Care must be exercised that the distillate is completely condensed as 5-bromofurfural has a very high vapor pressure and is easily lost in this manner. The yield of 5-bromofurfural melting at 82° was 110 g. or 31.43%. This method gives a very pure product, but the steam distillation is tedious.

Second, the carbon disulphide was removed by distillation under reduced pressure and the residue subjected to steam distillation. After the removal of the carbon disulphide, the volume of the residue is estimated and three or four volumes of water added prior to the introduction of steam. The steam is passed through very slowly so as to raise the temperature gradually until the distillation begins. Unless these precautions are taken, violent decomposition takes place at about 70°. In case a violent reaction should occur, this may be checked by addition of cracked ice. After standing for a time the steam distillation may proceed as before. The decomposition is probably caused by the high concentration of hydrogen bromide in the aqueous layer. The larger volume of water reduces this concentration.

Probably the more convenient method for preparation of 5-bromofurfural is by the action of a pyridine-bromine complex on furfural diacetate (4) dissolved in a mixture of chloroform and carbon disulphide (3). The pyridine-bromine complex was prepared in a two-gallon bottle by slow addition of 640 g. (8 atoms) of bromine to a mixture of 800 cc. of chloroform, 800 cc. of dry carbon disulphide and 316 g. (4 moles) of pyridine. After addition of the bromine was complete, the pyridine-bromine complex was broken up by means of a rod and a solution of 396 g. (2 moles) of furfural diacetate in 800 cc. of chloroform added. This mixture was agitated by shaking, on a machine, for three days and then subjected directly to steam distillation. The passage of steam was regulated so that the carbon disulphide and chloroform passed over smoothly. As the last of the solvent passed over the temperature rose quickly and pure 5-bromofurfural was collected in the distillate. No precautions are necessary in this steam distillation except to provide for complete condensation of the vapors. The yield of 5-bromofurfural melting at 82° was 150 g. or 40%. Carbon disulphide appears to be necessary in this bromination as similar runs in which the carbon disulphide was replaced entirely by chloroform gave no bromofurfural.

The phenylmagnesium bromide was prepared by addition of a solution of 18.84 g. (0.12 mole) of bromobenzene in 150 cc.

of anhydrous ether to 3.6 g. (0.15 atom) of magnesium. After the reaction was complete, a saturated solution of 17.5 g. (0.1 mole) of 5-bromofurfural in ether was slowly added. This mixture was then refluxed for two hours and allowed to stand over night. After standing, a color test for the Grignard reagent indicated excess of phenylmagnesium bromide. This mixture was hydrolyzed by pouring onto ice and adding the calculated quantity of 10% acetic acid. The ether layer was separated, washed with sodium bisulphite solution to remove any excess aldehyde and dried over anhydrous sodium carbonate. The ether was then removed by distillation from a water-bath and the residue subjected to steam distillation to yield 0.45 g. or 2.4% of diphenyl melting at 70°. The residue from the steam distillation was dissolved in ether, dried over sodium carbonate and the ether removed by distillation from a water-bath. This residue was then crystallized from petroleum ether, (b.p. 30°-60°), to yield 6 g. or 23.6% of a white crystalline material melting at 128°. Upon further crystallization from petroleum ether the melting point remained unchanged.

Analysis. Calculated for $C_{11}H_9O_2Br$: Br, 24.69. Found: Br, 24.38 and 24.11.

A second run under the same conditions gave 6.2 g. or 24.5% of material melting at 128°. This material gradually darkens on standing and evolves hydrogen bromide. At the end of three days the material was quite dark. At the end of one week, the decomposition appeared to be complete. The dark mass was then crystallized from petroleum ether, (b.p. 30°-60°), to yield 0.2 g. of a white crystalline solid which melted sharply at 86° and gave a negative Beilstein test for halogen. Further work will be reported on this compound at a later date.

Phenyl 5-Chlorofuryl Carbinol, $C_6H_5CH(OH)(ClC_4H_2O)$. This compound was prepared by the action of phenylmagnesium bromide on 5-chlorofurfural. The 5-chlorofurfural was prepared by the method of Gilman and Wright (5) by the action of sulfuryl chloride on a solution of furfural diacetate (4) in carbon disulphide. A 198 g. (1 mole) portion of furfural diacetate was dissolved in 1000 cc. of dry carbon disulphide and to this mixture was added 270 g. (2 moles) of sulfuryl chloride. The sulfuryl chloride used was not freshly distilled. The flask was equipped with a long reflux condenser and the mixture allowed to stand for three or four hours without heating. The mixture was then gently refluxed from a water-bath for an additional seven hours and the carbon disulphide then removed by distillation from a water-bath at atmospheric pressure. The residue in the flask was then heated under a pressure of about 30 mm., using a water pump, until the temperature of the vapor passing over was 60°. At this point most of the hydrogen chloride and sulphur dioxide had been driven out and the residue was then distilled at 10 mm. pressure.

(5) Unpublished results.

The fraction boiling at 60°-85° at 10 mm. pressure contained the 5-chlorofurfural in addition to some furfural and some high boiling material. This fraction may then be refractionated under reduced pressure or subjected to fractional steam distillation. The steam distillation gives a more stable product and is therefore more desirable. The steam distillate was collected in four fractions, the receiver being changed when about one-fourth of the volume of the original liquid had collected in the distillate. These fractions were then cooled by placing in ice, the last two fractions solidifying completely and crystals appearing in the first two. These were then filtered through Buchner funnels and the contents of the funnels allowed to come to room temperature. As the contents of the funnels reached room temperature, some of the material melted and dripped through into the filtrate. This oil was collected and again subjected to steam distillation in the manner above described. The yield of 5-chlorofurfural boiling at 70° at 10 mm. and at 92° at 30 mm. pressure and melting at 35° was 39.2 g. or 30%.

The phenyl 5-chlorofuryl carbinol was prepared by exactly the same method as that described for 5-bromofuryl phenyl carbinol. A solution of 18.84 g. (0.12 mole) of bromobenzene, 3.5 g. (0.15 atom) of magnesium and 13 g. (0.1 mole) of 5-chlorofurfural gave a product which was crystallized from petroleum ether, (b.p. 40°-60°), to yield 5 g. or 24% of a white crystalline compound melting at 113°. The melting point of this compound remained unchanged upon recrystallization from petroleum ether.

Analysis. Calculated for $C_{11}H_9O_2Cl$: Cl, 17.07. Found: Cl, 17.28 and 17.19.

This compound seems to be much more stable than phenyl 5-bromofuryl carbinol, as no signs of decomposition were evident until after 10 days standing. This compound, however, gradually darkened, with evolution of hydrogen chloride, and finally after standing for 30 days was crystallized from petroleum ether to yield 0.2 g. of a white crystalline solid melting at 86°. This compound gave a negative Beilstein test for halogen and mixed melting point with the compound secured by decomposition of phenyl 5-bromofuryl carbinol showed no depression.

Summary.

The previous preparations of diphenyl furyl carbinol and furyl carbinol have been duplicated. Impure furyl di-*tert.* butyl carbinol has been prepared and described. Analysis would indicate that this material was a mixture of the secondary and tertiary alcohols. A light red viscous material of very pleasant odor was also isolated as a product of the reaction of both ethyl furoate and furoyl chloride with *tert.* butylmagnesium chloride.

Phenyl 5-bromofuryl and phenyl 5-chlorofuryl carbinols have been prepared and described. It is of interest to note that these two compounds undergo decomposition with the formation of identical, halogen free, compounds.

DYES OF THE FURAN SERIES

Introduction.

Various types of dyes, prepared from furfural, have been reported in the literature. Fischer (1) in his study of the reaction of aldehydes on tertiary amines, condensed furfural with dimethylaniline, in the presence of zinc chloride, to produce the furan analog of malachite green. Later, Renshaw and Naylor (2) repeated this work of Fischer and reported the furan analog of malachite green, tetramethyldiaminodiphenylfurylmethane, as giving upon oxidation a stable dye. This dye gave gray-blue shades on silk, wool and mordanted cotton.

Numerous investigators have studied the reaction of furfural on amines. Persoz (3) in the year 1860 noticed the formation of a red color when a solution of aniline in acetic acid was added to a water solution of furfural. Stenhouse (4) observed the formation of a red colored solution upon addition of furfural to a concentrated solution of aniline hydrochloride in alcohol. Upon standing, this solution was found to deposit a mass of purple crystals, the analysis of which indicated the addition of one molecule of aniline and one molecule of aniline hydrochloride to one molecule of furfural, without the elimination of water. No constants are

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(1) Fischer, Ber., 10:1626 (1877); Ann., 206:141 (1883).
(2) Renshaw and Naylor, J. Am. Chem. Soc., 44:862 (1922).
(3) Persoz, Rep. chim. appl., p.220 (1860).
(4) Stenhouse, Ann., 156:199 (1870).

given for this compound.

Later, a number of investigators (5) assumed that the compound of Stenhouse was formed by the addition of one molecule of aniline hydrochloride and one molecule of aniline to one molecule of furfural, one molecule of water being eliminated. Dieckman and Beck (6) found that this colored compound of Stenhouse and others (4,5) could also be produced by the action of cyanogen bromide and aniline on β-hydroxypyridine, thus showing this colored compound to be β-hydroxyglutaconaldehydedianilide hydrobromide. Mixed melting point of the compounds prepared by the two methods, aniline and aniline hydrobromide on furfural and cyanogen bromide and aniline on β-hydroxypyridine, indicated that these two compounds were identical. Also these compounds when heated with alcohol, acetic acid or nitrobenzene were converted to the same compound, 3-hydroxy-1-phenylpyridinium bromide. The β-hydroxyglutaconaldehydedianilide hydrobromide and hydrochloride being colored compounds, dyeing red on cotton, wool, silk and artificial silk, while the pyridinium salts are colorless. The following reactions indicate the formation of these compounds.

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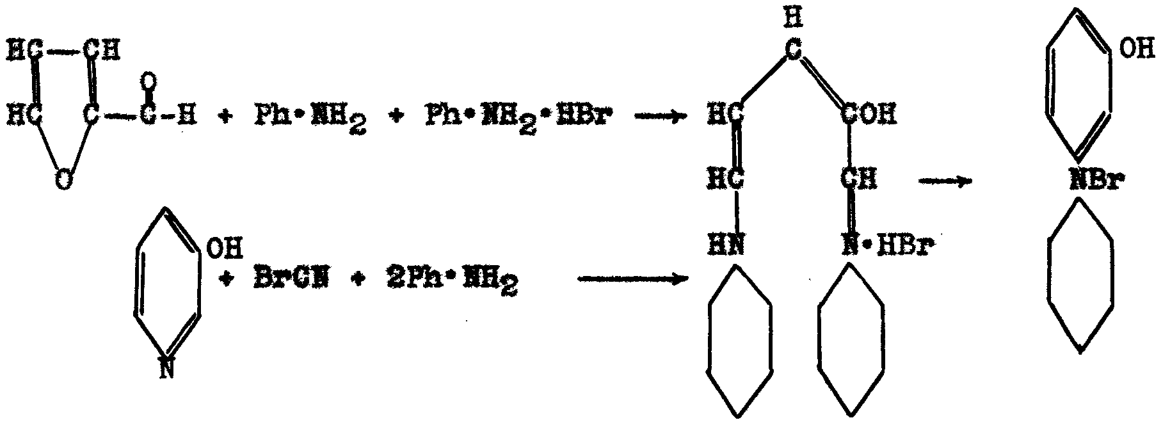
(5) Zincke and Mulhausen, Ber., 38:3824 (1905); Konig, J. prakt. Chim. 69:105 (1904); ibid, 72:555 (1905).

(6) Dieckmann and Beck, Ber., 38:4122 (1905).



(β-hydroxy-glutaconaldehyde-dianilide.)

(3-hydroxy-1-phenyl-pyridinium bromide.)

Mahood and Harris (7) prepared the furan analog of benzoflavine or dimethyldiaminofurylacridine hydrochloride, which was found to dye cotton, silk, artificial silk and wool a rich brown color the fastness of which could not be distinguished from benzoflavine. Lederer and Lederer (8) report the formation of brown dyes by heating furfural with alkali sulfides while Konig (9) prepared a series of azomethin dyes by treatment of furylacrolein with amines. Konig (9) explains the formation of these dyes by the following reaction.

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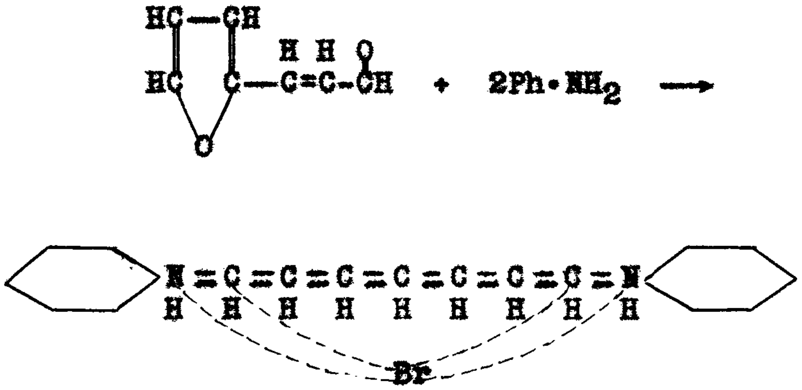
(7) Mahood and Harris, J. Am. Chem. Soc., 46:2810 (1924).
(8) Lederer and Lederer, Aust., 72:235 (Aug.10, 1916).
(9) Konig, J. prakt. Chim., 88:193 (1913).



In our work on dyes of the furan series, we have prepared the 5-bromofuryl and the 5-chlorofuryl analogs of malachite green and, for methods of comparison, have duplicated the preparation of the furyl analog by the method of Renshaw and Naylor (2). In order to establish with certainty the presence of a furan ring in the compound of Renshaw and Naylor (2), we have prepared what appears to be the same compound by the action of p-dimethylaminophenylmagnesium bromide on ethyl furoate. While the compound thus produced and the dye base obtained by oxidation of the tetramethyldiaminodiphenylfurylmethane of Renshaw and Naylor appear to be identical, no stable derivatives of either could be secured. The dye base and its various salts all decompose without melting. Analyses of the platinum salts and the colors produced on fibers, by the zinc chloride double salts, would indicate that these compounds are identical. The 5-chlorofuryl and 5-bromofuryl analogs of malachite green are much more stable than the furyl analog and give much better colors. These compounds dye blue on silk, artificial silk, wool and mordanted cotton and a variety of shades ranging from a light blue to a purple may be secured by varying the concentration of the dye bath.

The nitrofuryl analog of malachite green was prepared by condensation of nitrofurfural with dimethylaniline in the presence of zinc chloride. Under these conditions, we were unable to isolate the leuco base but oxidized the reaction product in the usual manner to the dye base. The dye base was separated as the zinc chloride double salt which dyes blue on silk, artificial silk, wool and mordanted cotton. The dye base was isolated from the zinc chloride double salt and this compound and its salts were found to decompose without melting. The platinum salt was prepared and analysis for platinum agreed with the theoretical value for the nitrofuryl analog of malachite green. It is interesting to note, however, that a crystalline compound, which appears to be the leuco base of the nitrofuryl analog of malachite green was secured by merely mixing dimethylaniline with nitrofurfural, in the absence of a condensing agent, and allowing the mixture to stand for several days. Water is eliminated during the reaction and it was found possible to secure the same compound, in poorer yields, by heating the mixture with or without phosphorous pentoxide as a dehydrating agent.

At first, it was thought possible that this compound might be β-hydroxy-nitroglutaconaldehydedianilide which would be analogous to the compounds previously (4,5,6) formed from furfural. This compound, however, does not exhibit the properties of the glutaconaldehydedianilides. The compound is an orange crystalline material which is insoluble in water but dissolves in strong acids to give a colorless solution which may be neutralized to precipitate the original compound. Analysis of the base for carbon and hydrogen and analysis of its platinum salt for platinum agree with the theoretic value for the leuco base of the nitrofuryl analog of malachite green. Oxidation of the compound with lead dioxide or treatment with strong alcoholic alkali lead to the formation of a dye. The hydrochloride and the zinc chloride double salt of this base, dye blue on silk, artificial silk, wool and mordanted cotton and analysis of its platinum salt for platinum agree with the theoretic value for the dye base of the nitrofuryl analog of malachite green. The base and its salts decompose without melting.

It is to be remembered that Hill and White (10) secured a highly colored compound by the action of aniline or aniline salts on nitrofuroic acid and demonstrated the fact that the nitro-group was involved in the condensation. However, in the case of the compound secured by the action of nitrofurfural on dimethylaniline, analyses would indicate that the nitro group was not involved in the condensation. In order to demonstrate this fact more clearly, dimethylaniline was treated, under the same conditions, with nitrofurfural di-

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(10) Hill and White, Am. Chem. J., 27:201 (1902).

acetate, ethyl nitrofuroate and the intermediate ring scission compound secured by nitration of furfural or furfural diacetate in acetic anhydride (11). In all three cases the original compounds were recovered unchanged, except in the case of the ring scission compound which was recovered as nitrofurfural diacetate, dimethylaniline having produced the same conversion as has been previously demonstrated with pyridine. These results would indicate that dimethylaniline did not undergo condensation with the nitro group nor did it cause ring scission. In order to demonstrate more clearly the probability of para condensation with the aldehyde group, nitrofurfural was treated with p-bromodimethylaniline. No signs of reaction were evident and the original materials were recovered unchanged.

An unsuccessful attempt was made at preparation of the tetrahydrofurylpropyl analog of malachite green by the reaction of tetrahydrofurylpropylmagnesium chloride (12) on Michler's ketone, tetramethyldiaminobenzophenone. Only a gummy mass, which resisted all attempts at crystallization, was secured. This material did not form colored salts with hydrochloric acid, acetic acid, zinc chloride or oxalic acid and no further work on this compound was attempted.

In view of the conversion of furfural to β-hydroxyglutaconaldehydedianilide and the corresponding pyridinium

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(11) See p.79, THIS THESIS.
(12) See p.32, THIS THESIS.

salt, it seemed possible that these reactions might be used with substituted furfurals to determine accurately the position of the substituted groups. Thus 5-chlorofurfural, 5-bromofurfural and 5-nitrofurfural should be converted to 3-hydroxy-6-chloro, 3-hydroxy-6-bromo- and 3-hydroxy-6-nitro-1-phenylpyridinium bromide, respectively. This, however, does not seem to be the case as during the condensation of substituted furfurals with aniline and aniline salts, the substituted group is lost. Thus, in the case of nitrofurfural with aniline and aniline hydrobromide, the mixture became quite warm with vigorous evolution of gas and the only product isolated was a green tar which resisted all attempts at crystallization. When 5-chlorofurfural was treated with aniline and aniline hydrobromide an orange colored crystalline mass was secured. Analysis of this compound demonstrated the absence of chlorine and it was found possible to prepare the same identical compound, as shown by mixed melting point, by treating 5-bromofurfural with aniline and aniline hydrobromide under the same conditions. Analysis of this compound for bromine would indicate the condensation of one molecule of the substituted furfural with one molecule of aniline and one molecule of aniline hydrobromide with the loss of a molecule of halogen acid. It is also assumed that one molecule of water is lost during the condensation, but analysis would indicate that the compound formed contained one molecule of water of crystallization. No mention is made in the literature of hydroxyglutaconaldehydedianilides crystallizing with water, but the fact that pyridinium salts contain water of crystallization has been thoroughly demonstrated (5,6). It is also to be remembered that the analyses of Stenhouse (4) did not show loss of water during the condensation. It is very probable that the compound of Stenhouse contained one molecule of water of crystallization.

That the halogen of the ring is the one which is lost is clearly shown since the compound formed by the action of 5-chlorofurfural on aniline and aniline hydrobromide was shown to contain no chlorine and also since under the same conditions, 5-chlorofurfural and 5-bromofurfural lead to the formation of one and the same compound. This loss of the halogen of the furan ring might have been expected for two reasons. First, the halogen in the 5-position is attached at the point of attack, the ring scission taking place between the 5-carbon atom and the oxygen of the ring. Second, while the halogen substituent in the furan ring is remarkably inactive, it may become labile under the influence of ring scission. The loss of halogen acid in the case of the 5-bromofuryl- and 5-chlorofuryl-phenyl carbinols (13) has been shown and is assumed to be the result of increased activity of the halogen atom due to the influence of the phenyl or hydroxyl group. 5-Chlorofurfural, when treated with aniline and aniline hydrochloride gives rise to an analogous compound which is

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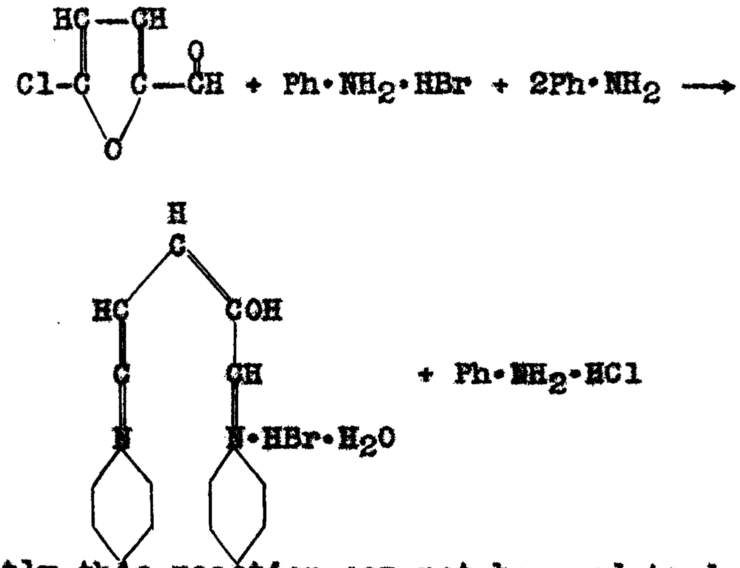
(13) See p.93, THIS THESIS.

shown by analysis to contain only one atom of chlorine. Neutralization of a water solution of these compounds causes precipitation of a material which contains no halogen. Thus the halogen content of these compounds is shown to be ionizable halogen.

While these compounds are evidently not analogous to the hydroxyglutaconaldehydedianilides secured from furfural, they seem to be very good dyes. They are slightly soluble in water, giving rise to a yellow solution, and readily dye silk, artificial silk, wool and cotton in beautiful golden-yellow shades. These dyes are stable and are apparently quite fast.

In addition to the facts already stated, the fact that these compounds are not converted to pyridinium salts when heated with alcohol, acetic acid or nitrobenzene leads to the suggestion of the following structure for these compounds.



Evidently this reaction can not be used to determine the position of substituted halogen and nitro groups in furfural, unless we assume that only those groups in the 5-position can give rise to compounds of this type. At the present time there is no basis for such an assumption. It would, however, be of interest to apply this reaction to 5-methylfurfural and to furfurals containing substituted halogen atoms in positions other than the 5-positions. At the present time, substituted furfurals in which the halogen atom is in a position other than the 5-position are unknown.

Since, in our preparation of the furyl analog of malachite green or tetramethyldiaminodiphenylfurylmethane, we have used *p*-dimethylaminophenylmagnesium bromide, it is of interest at this time to review the previous work on this Grignard reagent.

The preparation of *p*-dimethylaminophenylmagnesium bromide seems to be difficult and the yields are uncertain. Ehrlich and Sachs (14) claim to have secured a quantitative yield of this Grignard reagent by the use of magnesium which had previously been activated by treatment with ethyl bromide. Powdered magnesium was placed in the reaction flask, covered with anhydrous ether and ethyl bromide added. This was allowed to react for a few minutes and then the flask chilled by placing in ice water. The liquid was then decanted from the magnesium and a solution of *p*-bromodimethylaniline in anhydrous ether added. Although a quantitative yield of the Grignard reagent is claimed and although methylviolet and

(14) Erhlich and Sachs, *Ber.*, 36:4296 (1903).

malachite green were prepared from this reagent by treatment with Michler's ketone and ethyl benzoate, respectively, no yields of these dyes were given and their formation seems to have been assumed merely by the color of the products. No derivatives, no constants and no analyses are given.

Baeyer (15) prepared the *o*-, *m*-, and *p*-dimethylaminophenylmagnesium iodides by the use of magnesium which had been previously activated by heating with iodine. He found the *o*-iododimethylaniline reacted easily while the reaction of the *p*-iododimethylaniline was slight and the formation of tarry materials resulted. The Grignard reagent from the *ortho* compound was treated with the methyl ester of anthranilic acid to give tetramethyl-*o*-diaminobenzophenone the melting point and analysis of which are given. Nothing was accomplished with the *para* compound except to carry out the color reactions of Erhlich and Sachs (14).

Hurd and Webb (16) claim to have secured *p*-dimethylaminophenylmethyl carbinol in 85% yield (crude) from magnesium *p*-bromodimethylaniline and an excess of acetaldehyde. The details of preparation, constants, derivatives and analysis are not given in the paper. However, we have a private communication from the authors in which the details are given. "Three grams of magnesium (0.12 mole) and a little (few drops) of ethyl bromide with 25 cc. of absolute ether gave

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(15) Baeyer, *Ber.*, *38*:2763 (1905).
(16) Hurd and Webb, *J. Am. Chem. Soc.*, *49*:546 (1927).

rise to a vigorous reaction. Then 20 g. (0.1 mole) of p-bromodimethylaniline in 100 cc. of absolute ether was added and the mixture heated for 2.5 hours. In this operation a large share of the magnesium disappeared".

This Grignard solution was then treated with an excess of acetaldehyde which was generated by heating paraldehyde with sulphuric acid. The acetaldehyde was passed over calcium chloride and condensed in a tube, from which it was allowed to distill slowly into the flask containing the Grignard reagent, the latter being cooled in an ice and calcium chloride mixture. The aldehyde was passed into the Grignard solution during the course of three hours. The mixture was allowed to stand over night. It was then hydrolyzed with dilute sulphuric acid and the ether layer removed and evaporated, yielding about four grams of a semi-solid. The water layer was made ammoniacal, extracted with ether, the ether layer removed, dried and evaporated. Fourteen grams (0.085 mole) of solid remained. The melting point of this substance was 43° - 48° while the pure product melts at 60°. The method of purification and yield of pure product is not given.

Chamberlain and Dull (17) prepared p-bromodimethylaniline and from it secured the Grignard reagent by the method of Erhlich and Sachs (14). A quantitative yield of the Grignard reagent is claimed but the method of determining the yield is

(17) Chamberlain and Dull, J. Am. Chem. Soc., 50:3088 (1928).

not given. From 12.5 g. (0.0625 mole) of p-bromodimethylaniline and 15 g. of Michler's ketone was secured 9 g. of crude product. Nine grams would represent 0.0226 mole or 36% yield provided this product was the pure methyl violet carbinol base. The carbinol was purified by crystallization from alcohol, the yield and constants for this pure substance not being given. It is of interest to note that in the preparation of the above Grignard, the magnesium entirely dissolved. This, however, is not strange as 1.3 g. of magnesium (0.0625 atom) was used with 12.5 g. p-bromodimethylaniline (0.0625 mole) and the magnesium was activated by addition of an ether solution containing 8 g. (0.0735 mole) of ethyl bromide. The volume of ether used was not given, but after the ethyl bromide had reacted for three or four minutes, the bulk of the liquid was decanted. It seems to us that this would necessarily mean that quite a bit of ethyl bromide probably remained in the flask and that a quite a bit of the magnesium would be reacted upon by the ethyl bromide during three or four minutes contact.

Thus it would seem that although it is possible to prepare p-dimethylaminophenylmagnesium bromide, by activating the magnesium with ethyl bromide, and to prepare p-dimethylaminophenylmagnesium iodide by the use of magnesium which has been previously activated by heating with iodine, there is no definite data as to the rate or extent of these reactions. It is significant that Baeyer (15) detected a marked difference in reactivity toward magnesium of ortho, para and iodo-amino compounds and that the reaction products of the p-dimethylaminophenylmagnesium iodide were not successfully crystallized.

We have attempted to secure definite data upon the approximate rate of reaction and yields of the Grignard reagent from p-bromodimethylaniline and magnesium.

Our first step was to attempt to duplicate the results of Hurd and Webb (16). Following their method as outlined above we were able to secure 13 g. of material melting at 40°-45°. Attempts to purify this material were not successful but by steam distillation of the product, we were able to recover 5 g. of p-bromodimethylaniline which would mean that our maximum possible yield of the tertiary alcohol was 48.5%. Moreover in these runs a large part of the magnesium did not dissolve in 2.5 hours nor after an interval of 100 hours. Attempts were next made to prepare this Grignard reagent without the use of ethyl bromide. Activated 12.5% copper-magnesium alloy was found to be entirely inactive. It was found, however, that p-bromodimethylaniline will react with magnesium in the presence of one equivalent of magnesious iodide and that in such cases the addition of ethyl bromide is not necessary.

Experimental.

p-Dimethylaminophenylmagnesium Bromide. The p-bromodimethylaniline used was that furnished by the Eastman Kodak

Company, only the technical grade being obtainable. This material usually has a light blue color. Two methods of purification were used, first, crystallization from dilute alcohol to constant melting point. This gives a colorless product melting at 55°. Second, by distillation under reduced pressure. The crystallization is tedious and distillation under reduced pressure is found to produce a compound of the same degree of purity. No difference was noted in the activity of material which had been crystallized, distilled or crystallized and distilled. *p*-Bromodimethylaniline was found to boil at 105° at 2 mm. and 130° at 10 mm. and distills to give a colorless product melting at 55°.

In all of the following runs the equipment used consisted of 500 cc. three-neck flasks equipped with Hopkins reflux condenser, mercury-sealed mechanical stirrer and dropping funnel. The runs made over long periods of time were protected with an oil trap (18). The magnesium used was 80 - 200 mesh and the alloy used was 12.5% copper and was 200 mesh. Where activated alloy is mentioned, we refer to 12.5% copper-magnesium alloy of 200 mesh which had been previously activated by heating with iodine. All runs were 0.1 mole runs. Where the amount of Grignard was determined by titration, the acid titration was used. An excess of acid was added to the hydrolyzed sample and the excess acid titrated with standard alkali.

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(18) Gilman and Hewlett, *Rec. trav. chim.*, *48*:1124 (1929).

It was found that the presence of p-bromodimethylaniline did not interfere with the end-point. In standardization of acid and base, the same values were secured in the presence of p-bromodimethylaniline as were secured when this substance was absent.

Run 1. Three grams (0.123 mole) of magnesium and 0.5 g. of activated alloy were placed in the reaction flask and covered with anhydrous ether. Ten drops of ethyl bromide were then added and after a few minutes a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 100 cc. of absolute ether was added to the mixture. The mixture was then stirred and refluxed. From time to time small portions were withdrawn and the Schulze test (19) for Grignard reagent applied. A weak test was secured after 28 hours and a strong test after 50 hours. The presence of p-dimethylaminophenylmagnesium bromide may be detected in the presence of small amounts of ethylmagnesium bromide due to the difference in color, the former giving an intense violet coloration due to the formation of methyl violet by the interaction of the Grignard reagent with Michler's ketone. At the end of 145 hours the mixture was hydrolyzed with dilute sulphuric acid, then made alkaline with ammonium hydroxide, after addition of ammonium chloride, and the ether layer distilled. Seventeen grams or 85% of the p-bromodimethylaniline boiling at 105° at 2 mm. and melting at 55° was

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(19) Gilman and Schulze, J. Am. Chem. Soc., 47:2002 (1925).

recovered unchanged.

Run 2. Three grams (0.123 mole) of magnesium and 0.5 g. of activated alloy were placed in the reaction flask and a solution of 5 cc. of ethyl bromide in 25 cc. of anhydrous ether was added. After the reaction was well started the flask was chilled and the ether solution siphoned off and a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 200 cc. of anhydrous ether added. After 50 hours of refluxing a negative Schulze test was secured. A few drops of ethyl bromide were then added and a strong test secured after 50 hours. This solution was then cooled in an ice and salt mixture and treated with carbon dioxide by the usual method. We were not successful in isolating the corresponding acid but did recover 15 g. or 75% of p-bromodimethylaniline melting at 55°.

Run 3. Three grams of activated alloy was placed in the reaction flask and a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 200 cc. of anhydrous ether added. A negative test was secured after 24 hours refluxing. A few drops of ethyl bromide were then added and a positive test secured after 48 hours. After 100 hours the solution was hydrolyzed by the usual method and 16 g. or 80% of p-bromodimethylaniline melting at 55° was recovered.

Run 4. One gram of activated alloy and two grams of magnesium were added to the reaction flask and covered with 25 cc. of ether containing a few drops of ethyl bromide. After the reaction started a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 100 cc. of ether was added. A strong Schulze test was secured after 24 hours and after 90 hours the mixture was treated with an excess of acetaldehyde according to the method of Hurd and Webb as described in a private communication from those authors. The flask containing the Grignard reagent was fitted with a tube to admit the gas; an apparatus for generating acetaldehyde was attached to this tube. This apparatus consisted of a flask containing 20 g. (0.34 mole) of paraldehyde and 1 cc. of 6N sulphuric acid; also a condenser; a drying train filled with calcium chloride; an air inlet protected with a calcium chloride tube and a tube in which to liquefy the acetaldehyde. The aldehyde was slowly passed into the Grignard during the course of three hours. This gave rise to a grey-blue precipitate. The mixture was allowed to stand over night and was then hydrolyzed with 8 cc. of sulphuric acid in 100 cc. of water and 100 g. of fine ice. The water layer was made ammoniacal, extracted with ether and the ether solution dried and evaporated. The resulting material was dried in a vacuum desiccator. The yield was 13 g. melting at 40°-45° as compared to that secured by Hurd and Webb who obtained 14 g. melting at 43°-48°. We were not successful in purifying this material but upon subjecting it to steam distillation recovered from it 5 g. of p-bromodimethylaniline melting at 55°. This reduces the possible amount of tertiary carbinol to 8 g. as a maximum which would represent a yield of 48.5%.

Run 5. Two grams (0.085 atom) of magnesium was placed in the reaction flask and covered with 25 cc. of ether. Eight grams (0.063 atom) of iodine was then added in small portions with stirring. After the color of iodine disappeared 3 g. (0.123 atom) of magnesium and a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 100 cc. of ether were added. A negative test was secured after five hours. A few drops of ethyl bromide was added and a negative test secured after five hours. After 10 hours a feeble test was secured. After 55 hours refluxing the mixture was treated with acetaldehyde and worked up as described above. Thirteen grams of material melting at 40°-43° was secured. This material was subjected to steam distillation to yield 6 g. of unchanged p-bromodimethylaniline melting at 55°. This reduces the maximum possible yield of tertiary carbinol to 42.5%.

Run 6. Three and one-half grams (0.15 atom) of magnesium was placed in the reaction flask, covered with 25 cc. of anhydrous ether and one gram of iodine added in small portions with stirring. After the iodine color had disappeared, a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 125 cc. of anhydrous ether was added. After five hours refluxing a negative test for the Grignard reagent was secured. Five drops of ethyl bromide were then added and after 10 hours refluxing a positive test was secured. After 50 hours refluxing the mixture was hydrolyzed in the usual manner and

15 g. or 75% of unchanged p-bromodimethylaniline melting at 55° was recovered.

Run 7. One gram of activated alloy was placed in the reaction flask and covered with 25 cc. of ether. One gram of iodine was then added in small portions with stirring and, after the disappearance of the iodine color, three grams of activated alloy and a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 100 cc. of ether were added. After 24 hours refluxing, a negative test for the Grignard reagent was secured and the p-bromodimethylaniline was recovered unchanged.

Run 8. Four grams of 12.5% copper-magnesium alloy was placed in the reaction flask and covered with 25 cc. of ether. Twelve grams (0.095 atom) of iodine was then added in small portions with stirring. After the iodine color had disappeared, 4 g. of alloy and a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 100 cc. of ether was added. A positive test for the Grignard reagent was secured after six hours refluxing and after 50 hours refluxing a 5 cc. portion was withdrawn and titrated. The yield of Grignard reagent based on the titration value was 40%. This solution was treated with ethyl furoate as will be described later in this paper.

Run 9. Four grams of activated alloy was refluxed with a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 100 cc. of ether for 50 hours without evidences of reaction.

The solution gave a negative test for the Grignard reagent and the p-bromodimethylaniline was recovered unchanged.

Run 10. Two grams of alloy were placed in the reaction flask and covered with 25 cc. of ether. Four grams (0.031 atom) of iodine were then added and after the reaction was complete a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 100 cc. of ether and 3 g. (0.123 atom) of magnesium were added to the mixture. After 60 hours refluxing, a negative test for the Grignard reagent was secured and the p-bromodimethylaniline was recovered unchanged.

Run 11. The same conditions were used as in Run 10 except that 8 g. (0.063 atom) of iodine were used. At the end of 60 hours refluxing a negative test was secured and the p-bromodimethylaniline was recovered unchanged.

Run 12. Four grams of alloy were added to the reaction flask and covered with 25 cc. of ether. Twelve grams (0.095 atom) of iodine were then added in small portions with stirring. After the iodine color had disappeared, 4 g. of alloy and a solution of 20 g. (0.1 mole) of p-bromodimethylaniline in 200 cc. of ether were added. Ten cubic centimeter portions were withdrawn and titrated at different intervals of time with the following results.

Time of refluxing in days	Yield of Grignard
1	1.35%
2	20.45%
3	29.86%
7	37.77%
9	37.75%
13	37.75%

We were unable to find a suitable derivative for this Grignard reagent and finally decided to check the titration yields by hydrolysis and separation of the dimethylaniline from the p-bromodimethylaniline. The solution was hydrolyzed with ammonium chloride and a sufficient quantity of ammonium hydroxide added to dissolve the magnesium. The ether layer was separated, dried and the ether removed by distillation from a water-bath. The residue was then subjected to steam distillation which gave a rough separation of the dimethylaniline from the p-bromodimethylaniline, the dimethylaniline steam distilling with greater ease than the p-bromodimethylaniline. The steam distillate was extracted with ether and the ether solution distilled at atmospheris pressure. Thus 3.9 g. or 32% of dimethylaniline boiling at 195° was secured. The picrate, melting at 161°, was prepared and a mixed melting point with the picrate prepared from dimethylaniline of known purity showed no depression. The picrate of p-bromodimethylaniline was found to melt at 140° while a mixture of the two picrates melted at 110°.

Run 13. The conditions of Run 12 were duplicated. The following titration values were secured at the stated intervals of time.

Time of refluxing in days	Yield of Grignard
2	23.62%
3	26.59%
7	34.25%
24	39.50%

This run gave 4.1 g. or 34% of dimethylaniline boiling at 195°. The picrate melted at 161°.

Furyl Analog of Malachite Green (Tetramethyldiaminodiphenylfurylmethane), C_4H_3OCH-p-$(C_6H_4N(CH_3)_2)_2$. For purposes of comparison, this compound was prepared by the method of Renshaw and Naylor (2) by condensation of furfural with dimethylaniline in the presence of zinc chloride. Forty-eight grams (0.5 mole) of furfural, 61 g. (0.5 mole) of dimethylaniline and 34 g. (0.25 mole) of powdered anhydrous zinc chloride were mixed and heated in a porcelain dish, with frequent stirring, on a water-bath for four hours. The mass was then melted by the addition of hot water and transferred to a flask, where it was subjected to steam distillation until no more dimethylaniline passed over. A dark gummy mass remained as a residue in the distillation flask. This was dissolved in dilute hydrochloric acid and filtered. A tarry material remained on the filter paper. The filtrate was cautiously neutralized with 10% sodium hydroxide to precipitate a gummy mass. This mass was redissolved and reprecipitated several times, finally giving a solid precipitate which was dried and crystallized from petroleum ether (b.p. 40°-60°) to yield 11 g. or 6.9% of a slightly yellow crystalline compound melting sharply at 87°. Renshaw and Naylor (2) give no yields or melting point while Fischer (1) gave the melting point of the leuco base of the furyl analog of malachite green as 83°.

This leuco base was then oxidized to the carbinol base by the usual method employed with malachite green. Ten grams of the leuco base was dissolved in a quantity of dilute hydrochloric acid, corresponding to 2.7 g. of hydrogen chloride. The slightly red solution of the leuco base was then diluted with 800 cc. of water and 10 cc. of 40% acetic acid added. The solution was cooled to 0° by placing in ice and a thin paste of 7.5 g. of lead dioxide in water was slowly added with stirring. The stirring was continued for two hours and the lead dioxide removed by filtration. The lead in solution was precipitated by the addition of 10 g. of sodium sulfate in 50 cc. of water and the resulting lead sulfate removed by filtration. The solution was then heated to boiling and 15 g. of sodium chloride added for each 100 cc. of dye solution. While this solution was still hot, a saturated solution of 8 g. of zinc chloride was added. Upon cooling, this solution deposited 6 g. or 30% of dark blue solid. This solid is soluble in water, giving a highly colored solution which dyes grey on silk and blue on artificial silk and wool.

A solution of the zinc chloride double salt was made distinctly alkaline with sodium hydroxide and extracted with ether. On evaporation of the ether, a small amount of dark solid remained. Attempts at crystallization of this solid carbinol base resulted in decomposition. This base and its salts were found to decompose without melting.

Preparation of a compound which seems to be identical with the one just described was accomplished by the action of ethyl furoate on p-dimethylaminophenylmagnesium bromide. The solution of the Grignard reagent was prepared from 20 g. (0.1 mole) of p-bromodimethylaniline by the method previously described in this paper. This solution gave a titration value of 40% Grignard reagent. The contents of the flask were chilled by placing in ice and a solution of 7 g. (0.05 mole) of ethyl furoate in 50 cc. of ether added slowly with stirring. The mixture was then allowed to stand at room temperature over night and was hydrolyzed with ice and ammonium chloride, sufficient quantity of ammonium hydroxide being added to dissolve the magnesium. The ether solution was then separated, dried and the ether removed by distillation from a water-bath. All attempts at purification of the resulting gummy mass by crystallization were unsuccessful. Purification by dissolving in acid and neutralizing by alkali was also unsuccessful due to the interference of the excess p-bromodimethylaniline. Finally, the residue was subjected to steam distillation to remove the excess ethyl furoate and p-bromodimethylaniline. This distillation resulted in partial decomposition of the substance. The residue in the distillation flask was dissolved in dilute hydrochloric acid and precipitated by addition of sodium hydroxide. The solid thus obtained decomposed upon attempted crystallization and the base and its salts decomposed without melting. The base was then redissolved in dilute hydrochloric acid and warmed. The solution turned red in color. Fifteen grams of sodium chloride for each 100 cc. of solution was then added and while the solution was still warm a saturated solution of 5 g. of zinc chloride was added. Upon cooling, this solution deposited 1 g. of a dark blue solid which had the appearance of the compound secured by condensation of furfural with dimethylaniline. This solid dissolved in water and dyed silk, artificial silk and wool in the same shades as the furyl analog of malachite green as prepared by condensation of furfural with dimethylaniline. Analysis of the platinum salt of the carbinol base would indicate that this compound was the furyl analog of malachite green.

Analysis. Calculated for $C_{21}H_{26}O_2N_2PtCl_6$: Pt, 26.1. Found: Pt, 26.42 and 25.77.

Tetramethyldiaminodiphenyl-5-bromofurylmethane (5-Bromofuryl Analog of Malachite Green), $BrC_4H_2OCH\text{-}p\text{-}(C_6H_4N(CH_3)_2)_2$. This compound was prepared by the condensation of 5-bromofurfural (20) with dimethylaniline in the presence of anhy-

(20) See p.88, THIS THESIS.

drous zinc chloride by exactly the same method as that described for the furan analog of malachite green. A mixture of 87.5 g. (0.5 mole) of 5-bromofurfural, 181.5 g. (1.5 moles) of dimethylaniline and 54.5 g. (0.4 mole) of zinc chloride gave a product which was crystallized from petroleum ether (b.p. 40°-60°) to yield 21 g. or 12.9% of the leuco base melting at 132°. This compound is a slightly yellow crystalline substance and is quite stable. Twenty grams or 23% of unchanged 5-bromofurfural was recovered during the steam distillation.

Analysis. Calculated for $C_{21}H_{23}BrN_2O$: Br, 20.05. Found: Br, 19.88 and 19.75.

The leuco base was oxidized to the dye in the usual manner. Five grams of the leuco base was dissolved in 20 cc. of water containing 1.4 g. of hydrogen chloride. This solution was diluted to 400 cc. and 5 cc. of 40% acetic acid added. The solution was then cooled with ice and a paste of 3.7 g. of lead dioxide in water gradually added with stirring. The mixture was stirred for two hours and the excess lead dioxide filtered off. The lead in solution was then precipitated by addition of sodium sulphate solution containing 5 g. of sodium sulphate in 25 cc. of water. The solution was then filtered and heated to boiling. Fifteen grams of sodium chloride was then added to each 100 cc. of dye solution, and to this solution, while still hot, was added a saturated solution of 4 g. of zinc chloride. Upon cooling, this solution deposited 4 g. or 60% of a brown solid. This dye salt is quite soluble in water, giving a deep blue solution, and dying in blue shades on silk, artificial silk, wool and mordanted cotton. This dye is more stable than the furyl analog of malachite green and appears to be fast.

The carbinol base was secured from a solution of the dye salt by addition of sodium hydroxide and extraction with ether. The ether solution was then extracted with dilute hydrochloric acid and the acid solution neutralized to precipitate the base. This compound and its salts were found to decompose without melting. The platinum salt was prepared and analyzed for platinum.

Analysis. Calculated for $C_{21}H_{25}BrN_2O_2PtCl_6$: Pt, 23.65. Found: Pt, 23.61 and 23.60.

Tetramethyldiaminodiphenyl-5-chlorofurylmethane (5-Chlorofuryl Analog of Malachite Green), $ClC_4H_2OCH\text{-}p\text{-}(C_6H_4N(CH_3)_2)_2$. This leuco base was prepared by the method just described for leuco base of the 5-bromofuryl analog, by the condensation of 5-chlorofurfural (21) with dimethylaniline in the presence of anhydrous zinc chloride. Thirteen grams (0.1 mole) of chlorofurfural was mixed with 24.4 g. (0.2 mole) of dimethylaniline and 5 g. of anhydrous zinc chloride. The mixture was heated over a water bath for four hours and subjected to steam distillation to remove excess dimethylaniline and the unchanged

(21) See p.93, THIS THESIS.

5-chlorofurfural. The residue was then dissolved in dilute hydrochloric acid and the base precipitated with sodium hydroxide. This was dried and crystallized from petroleum ether (b.p. 40°-60°) to yield 5 g. or 14.1% of leuco base melting at 117°.

Analysis. Calculated for $C_{21}H_{23}ClN_2O$: Cl, 10.01. Found: Cl, 10.11 and 10.09.

The leuco base was oxidized to the dye by the method described for oxidation of the leuco base of the 5-bromofuryl analog. One gram of the leuco base dissolved in 4 cc. of water, containing 0.3 g. of hydrogen chloride, and diluted with 100 cc. of water was cooled with ice and treated with 0.5 cc. of acetic acid and 1 g. of lead dioxide to yield 1 g. or 73% of the dye salt. This salt is quite soluble in water to give a dark blue solution which dyes silk, artificial silk, wool and mordanted cotton in blue shades. The dye seems to be stable and fast. The carbinol base was prepared by the method used to secure the carbinol base of the 5-bromo analog. This compound and its salts decompose without melting. The platinum salt was prepared and analyzed.

Analysis. Calculated for $C_{21}H_{25}ClN_2O_2PtCl_6$: Pt, 25.00. Found: Pt, 24.96 and 24.93.

Tetramethyldiaminodiphenylnitrofurylmethane (Nitrofuryl Analog of Malachite Green), $NO_2C_4H_2OCH\text{-}p\text{-}(C_6H_4N(CH_3)_2)_2$. This compound was prepared by the method described for the

5-bromofuryl analog of malachite green. A mixture of 14.1 g. (0.1 mole) of nitrofurfural (11), 24.4 g. (0.2 mole) of dimethylaniline and 5 g. of anhydrous zinc chloride was heated over a water-bath for four hours. The excess dimethylaniline was removed by steam distillation to leave a tarry mass as a residue in the distillation flask. This tar was extracted with dilute hydrochloric acid and the acid solution carefully neutralized with sodium hydroxide causing precipitation of a tarry material. However, by repeated precipitations a dark colored solid was finally secured. Attempts at crystallization of this solid from alcohol and from petroleum ether (b.p. 40°-60°) resulted in decomposition. No further attempts at purification of this material were made. This crude material was oxidized by the method described for the oxidation of the 5-bromofuryl analog, the same proportions being used. The yield of dye salt secured was 5 g. or 10%. This compound, when treated with water, partially dissolved but some insoluble material was formed. The dye solution was found to produce blue colors on silk, wool, artificial silk and mordanted cotton. This dye is less stable and less fast than the bromofuryl and chlorofuryl analogs and appears to be of about the same stability as the furyl analog. The platinum salt was prepared by the usual method and analyzed.

<u>Analysis.</u> Calculated for $C_{21}H_{25}N_3O_4PtCl_6$: Pt, 24.65. Found: Pt, 24.22.

What appears to be the leuco base of the nitrofuryl analog of malachite green was secured by merely mixing nitrofurfural with dimethylaniline. It was noticed that a red color formed when nitrofurfural was added to dimethylaniline. In order to investigate the nature of the red colored material, a mixture of nitrofurfural and dimethylaniline was allowed to stand for an indefinite length of time. The mixture finally set to a crystalline mass which was crystallized from alcohol to produce an orange-red crystalline material.

In order to determine the length of time required for the formation of this compound, 28.1 g. of nitrofurfural was dissolved in 24.4 g. (0.2 mole) of dimethyl aniline and the mixture tightly corked and set aside. At the end of seven days the mass was crystallized from alcohol to yield 17 g. or 23.5%, based on dimethylaniline and assuming condensation of two molecules of dimethylaniline with one molecule of nitrofurfural with elimination of one molecule of water. This compound melted at 135° and recrystallization from alcohol failed to raise the melting point.

This compound was found to be distinctly basic in nature, dissolving in dilute acids and being precipitated unchanged upon addition of alkali. The substance is quite stable toward alkali, remaining unchanged when warmed with 50% sodium hydroxide, while upon being heated with alcoholic alkali and then precipitated by addition of water to the alcoholic solution, a blue solid was formed. This blue solid dissolved in acids to give a blue solution which dyed silk, artificial silk and wool in blue shades.

The stability of this compound toward alkali would indicate that the nitro group had been evolved in the reaction. A nitro group attached to the furan ring is known to be very unstable toward alkali (10) and it was at first suspected that this compound was analogous to that secured by Hill and White (10) by the action of nitrofuroic acid on aniline. These workers were able to demonstrate the fact that their compound was formed by condensation of the nitro group with the amino group of aniline. In our case, however, we have a tertiary amino group involved and the result of analyses indicate that only one molecule of water was lost in the condensation. The fact that water is lost during the condensation is easily demonstrated as droplets of water may be observed on the walls of the containing flask during the reaction. Also, we were able to secure this same compound by heating a mixture of nitrofurfural and dimethylaniline for one-half hour at 110° and also by treating a mixture of nitrofurfural and dimethylaniline with phosphorous pentoxide. The yields by these methods were very poor as much decomposition took place.

In order to determine whether or not the nitro group alone was involved in the reaction, we treated dimethylaniline with nitrofurfural diacetate, ethyl nitrofuroate and the intermediate ring scission compound produced in nitration of furfural or furfural diacetate in acetic anhydride (11). In the above cases no reaction occurred, either on long standing at room temperature or upon heating the mixtures, except that the ring scission compound was converted into nitrofurfural diacetate. The nitrofurfural diacetate, melting at 92° and mixed melting point remaining unchanged, and the ethyl nitrofuroate, melting point 100° and mixed melting point remaining unchanged, were recovered. The ring scission product was recovered as nitrofurfural diacetate, melting at 92° and mixed melting point remaining unchanged. It is evident that the nitro group in these compounds is not affected by dimethylaniline, although this compound does have the same reaction as that previously described (11) with pyridine upon the ring scission compound. In view of these facts, it seems probable that the aldehyde group is involved in the reaction.

As evidence in favor of <u>para</u> condensation with the aldehyde group as against any possible reaction between the amino and nitro groups, it was found that <u>p</u>-bromodimethylaniline does not react with nitrofurfural, either upon standing or upon heating the mixture at 120°. The <u>p</u>-bromodimethylaniline was recovered unchanged.

Thus it seems that the reaction must have been one of <u>para</u> condensation with the aldehyde group and analyses of the base for carbon and hydrogen and analysis of its platinum salt for platinum would indicate this to be the case. It is, however, of interest to note that dimethylaniline does not react with furfural or with 5-bromofurfural under these conditions. We can only explain the reaction of nitrofurfural in this manner by the fact that in this compound the aldehyde group is extremely reactive. A possible explanation of the stability of the nitro group, in the base produced by the action of dimethylaniline on nitrofurfural, is that of steric hindrance, produced by the two p-dimethylaminophenyl groups, thus preventing the enolization of the nitro group.

It was at first thought possible that this compound might be analogous to the hydroxyglutaconaldehydedianilides (4,5,6) but these compounds are dyes while our compound dissolves in acid to give a colorless solution. In addition to this, attempts at preparation of β-hydroxynitroglutaconaldehydedianilide by the action of nitrofurfural on aniline and aniline hydrobromide indicate that these compounds are unstable. Our base was analyzed for carbon and hydrogen and its platinum salt for platinum with the following results. The formulas on which the calculations are based are that of the leuco base of the nitrofuryl analog of malachite green and its platinum salt.

Analysis. Calculated for $C_{21}H_{23}N_3O_3$: C, 69.04; H, 6.30. Found: C, 68.66 and 68.93; H, 6.27 and 6.42.

Calculated for $C_{21}H_{23}N_3O_3 \cdot H_2PtCl_6$: Pt, 25.19. Found: Pt, 25.60.

This base was oxidized in the usual manner with lead dioxide, producing a substance which had the appearance of the compound secured from the condensation of nitrofurfural with dimethylaniline in the presence of zinc chloride. Five grams of the base was dissolved in 20 cc. of water containing 1.4 g. of hydrogen chloride and the resulting solution diluted to 400 cc. with water. This solution was cooled with ice and a paste of 3.7 g. of lead dioxide in water slowly added with stirring. After two hours additional stirring, the excess lead dioxide was filtered off and the lead removed from the solution by addition of sodium sulphate. The lead sulphate was filtered off and the filtrate heated to the boiling point and 15 g. of sodium chloride added for each 100 cc. of solution. A saturated solution of 4 g. of zinc chloride was then added and the solution allowed to cool. A black solid settled out on cooling. This substance was only partly soluble in water, giving a green solution with a dark solid suspended. The solution was filtered and was found to dye silk, artificial silk, wool and mordanted cotton in blue shades. The platinum salt was prepared in the usual manner and analyzed for platinum, the result of this analysis agreeing with the theoretic value for the nitrofuryl analog of malachite green.

Analysis. Calculated for $C_{21}H_{25}N_3O_4PtCl_6$: Pt, 24.67. Found: Pt, 24.85.

Reaction of Aniline and Aniline Salts with Substituted Furfurals. In view of the preparation of β-hydroxyglutaconaldehydedianilides, by the reaction of furfural on a mixture of aniline and aniline salts, and the subsequent conversion of these dianilides to 3-hydroxy-1-phenylpyridinium salts

(4,5,6), it seemed possible that these reactions might be of value in determination of the position of substituent groups in substituted furfurals.

With this idea in view, a solution of 13 g. (0.1 mole) of 5-chlorofurfural in 80 cc. of alcohol was added to a solution of 9.3 g. (0.1 mole) of aniline and 17.4 g. (0.1 mole) of aniline hydrobromide in 80 cc. of alcohol. The mixture was allowed to stand at room temperature for six hours, at the end of which time a mass of orange colored crystals had formed. This crystal mass was separated from the solution by filtration and recrystallized from alcohol to yield 27 g. of a crystalline compound melting at 145°. The compound melts with decomposition and for that reason is not introduced into the melting point bath until the latter has reached a temperature of about 130°. Mixed halogen analysis of this compound indicated the absence of chlorine. If the halogen substituent of the furan ring was really lost during the reaction, it seemed possible that the same compound might be secured, in the same manner, by the use of 5-bromofurfural.

This indeed proved to be the case. A solution of 17.5 g. (0.1 mole) of 5-bromofurfural in 200 cc. of alcohol was added to a solution of 9.3 g. (0.1 mole) of aniline and 17.4 g. (0.1 mole) of aniline hydrobromide in 80 cc. of alcohol to yield 27 g. of an orange colored compound which melted at 145°. The melting point of a mixture of this compound and the compound secured from 5-chlorofurfural was also 145°, thus showing these two substances to be identical. Halogen analyses of the compound from both sources also agree. Halogen analyses would indicate the combination of one molecule of the substituted furfural with one molecule of aniline and one molecule of aniline hydrobromide with loss of one molecule of halogen acid. It is also assumed that one molecule of water was lost in the condensation, but that the resulting compound contained one molecule of water of crystallization. It is to be remembered that the analysis of Stenhouse (4) did not show loss of water and compounds of this type do frequently contain water of crystallization.

Analysis. Calculated for $C_{17}H_{15}BrN_2O \cdot H_2O$: Br, 22.16. Found: Br, 22.16 and 21.94. Found: Cl, none.

Assuming the formula for this compound to be as given above, the yields of this substance from the two sources would be 77%.

As a check on these results, a solution of 13 g. (0.1 mole) of chlorofurfural in 80 cc. of alcohol was added to a solution of 9.3 g. (0.1 mole) of aniline and 12.9 g. (0.1 mole) of aniline hydrochloride in 80 cc. of alcohol to yield 20 g. or 63% of an orange colored compound melting at 158° with decomposition.

Analysis. Calculated for $C_{17}H_{15}ClN_2O \cdot H_2O$: Cl, 10.87. Found: 11.04 and 10.97.

Attempts at determination of the water content of these compounds by heating at 100° over a period of two hours resulted in partial decomposition.

Although these compounds are evidently not analogous to the hydroxyglutaconaldehydedianilides, they seem to be very good dyes. They are only moderately soluble in water but produce a yellow color, which seems to be quite fast, on silk, artificial silk, wool and cotton. For the proposed structure of these compounds, see the introduction to this chapter.

An unsuccessful attempt was made at preparation of the nitro analog of these compounds by the action of a solution of 14.1 g. (0.1 mole) of nitrofurfural in 150 cc. of alcohol to a solution of 9.3 g. (0.1 mole) of aniline and 17.4 g. (0.1 mole) of aniline hydrobromide in 80 cc. of alcohol. The mixture became warm with rapid evolution of gas and deposited a green tar which resisted all attempts at crystallization from alcohol. Thus it is evident that this reaction can not be used to determine the position of the substituted groups in the nitro and halogenated furfurals which compounds are known.

Attempts at conversion of these compounds to pyridinium salts were unsuccessful. Heating with alcohol, acetic acid and nitrobenzene caused some decomposition leading to the formation of a green tar, but in every case the only crystalline compound recovered was the unchanged original compound.

<u>Tetrahydrofurylpropyl Analog of Malachite Green.</u> An unsuccessful attempt at preparation of the tetrahydrofurylpropyl analog of malachite green was made by treating tetra-

hydrofurylpropylmagnesium chloride with Michler's ketone, tetramethyldiaminobenzophenone. A solution of 37.2 g. (0.25 mole) of tetrahydrofurylpropyl chloride (12) in 200 cc. of anhydrous ether was added to 7.3 g. (0.3 atom) of magnesium. After the reaction was complete, the ether solution was decanted from the unchanged magnesium and treated with a saturated solution of 53.66 g. (0.2 mole) of Michler's ketone in anhydrous benzene. This mixture was then stirred at room temperature for four days and hydrolyzed by pouring onto ice and the calculated quantity of dilute sulphuric acid. The ether-benzene layer was separated, dried over sodium sulfate and the solvent removed under reduced pressure. A gummy semisolid residue remained. This residue was light green in color. All attempts at crystallization of this material were unsuccessful. This material dissolved in acids to give colorless solutions which had no properties of a dye. No further work was attempted on this compound.

Summary.

p-Dimethylaminophenylmagnesium bromide may be prepared in yields as high as 40% by the action of p-bromodimethylaniline on magnesium, using one equivalent of "magnesious iodide." Usually about 5 - 7 days refluxing is required for a maximum yield. This Grignard reagent was used in preparation of the furyl analog of malachite green, the extremely poor yields of the dye being possibly due to its instability

and the difficulty of purification.

The 5-chlorofuryl, 5-bromofuryl and the nitrofuryl analogs of malachite green have been prepared and described. A compound which appears to be the leuco base of the nitrofuryl analog of malachite green may be prepared in good yields by merely mixing nitrofurfural with dimethylaniline in the absence of a condensing agent.

When substituted furfurals are treated with a mixture of aniline and aniline salt, the substituted group is lost and the resulting compounds were not converted into pyridinium salts after the manner of the known hydroxyglutaconaldehyde-dianilides. The compounds thus secured from 5-chloro and 5-bromo furfural are yellow dyes.

An unsuccessful attempt was made at preparation of the tetrahydrofurylpropyl analog of malachite green by the action of tetrahydrofurylpropylmagnesium chloride on Michler's ketone.

ANTIPYRETICS OF THE FURAN SERIES

Introduction.

The purpose of this study was the preparation of furan compounds of the phenacetin, aceto-p-phenetidine, type in which the aceto- group is replaced by the furoyl group. Phenacetin and some of its analogs are known as very efficient antipyretics. For purposes of comparison, in order to determine the effect of replacement of the aceto by the furoyl group, we have prepared furoylanilide and furoyl-p-phenetidine. A study of the antipyretic property of these compounds is now in progress and the results will be reported at a later date.

Experimental.

Furoylanilide, $C_4H_3CO \cdot NHC_6H_5$. This compound was previously prepared by Baum (1) by the action of furoyl chloride on aniline. Exact yields were not given. Furoylanilide is most conveniently prepared by addition of one molecular equivalent of furoyl chloride to two molecular equivalents of aniline, 65 g. (0.5 mole) of furoyl chloride being added dropwise into a well cooled flask containing 93.1 g. (1.0 mole) of aniline. The flask was then fitted with a reflux condenser and warmed over a water-bath for one-half hour. At the end of this time, cold water was added and the mixture filtered. This solid

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(1) Baum, Ber., 37:2951 (1904).

material was then crystallized from alcohol to yield 60 g. or 64% of material melting at 123.5°. This melting point exactly checks that previously given for this compound (1).

Furoyl-p-phenetidine, $C_4H_3OCO \cdot NHC_6H_4$-p-OC_2H_5. To a well cooled flask containing 54.8 g. (0.4 mole) of p-phenetidine was added 26 g. (0.2 mole) of furoyl chloride. The flask was then equipped with reflux condenser, heated over a water-bath for one-half hour, treated with cold water and filtered. The solid product was crystallized from alcohol to yield 30 g. or 65% of material melting at 135.5°.

Analysis. Calculated for $C_{13}H_{13}NO_3$: C, 67.53; H, 5.63. Found: C, 67.95; H, 5.85.

Summary.

Furoylanilide and furoyl-p-phenetidine have been prepared and described.

SULFUR COMPOUNDS OF THE FURAN SERIES

Introduction.

In recent years use has been made of furfuryl mercaptan and a number of its analogs in the production of synthetic coffee flavor. For this reason numerous patents, covering the preparation of these compounds, have been granted (1). In this connection it is also interesting to note that furfural and furfuryl alcohol have been isolated from coffee and chicory (2).

In connection with other work, Gilman and Hewlett (1) have prepared furfuryl mercaptan as an intermediate product in the preparation of chloro-alkyl furfuryl sulfides.

The preparation of tetrahydrofurylpropyl thiocyanate has been previously described in this thesis (3).

Experimental.

Tetrahydrofurylpropyl Mercaptan, $C_4H_7OCH_2CH_2CH_2SH$. Tetrahydrofurylpropyl mercaptan was prepared by the action of tetrahydrofurylpropyl chloride (4) on thiourea, the resulting compound being treated with ammonium hydroxide. A mixture of 14.85 g. (0.1 mole) of tetrahydrofurylpropyl chloride, 7.6 g. (0.1 mole) of thiourea and a few drops of water was placed in a flask and warmed gently on a hot plate until

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(1) Gilman and Hewlett, J. Am. Chem. Soc., 52:2141 (1930).
(2) Reichstein and Beitter, Ber., 63:816 (1930).
(3) See p.33, THIS THESIS.
(4) See p.28, THIS THESIS.

the water had been removed by evaporation. The heavy viscous residue was then treated with an excess of ammonium hydroxide at room temperature. After standing for a time the mercaptan settled out as a heavy liquid. The mixture was then extracted with ether and the ether solution dried over sodium sulfate and distilled to yield 5 g. or 34% of tetrahydrofurylpropyl mercaptan boiling at 85° at 10 mm. pressure. This compound is a colorless liquid with an extremely unpleasant penetrating odor. d_4^{25} 1.0006; n_D^{34} 1.4807.

Analysis. Calculated for $C_7H_{14}SO$: S, 21.92. Found: S, 21.60.

Tetrahydrofurylpropyl Phenacyl Sulfide, $C_4H_7OCH_2CH_2CH_2$-S-$CH_2CO \cdot C_6H_5$. Tetrahydrofurylpropylthiomagnesium bromide was prepared by the action of tetrahydrofurylpropyl mercaptan on ethylmagnesium bromide. The ethylmagnesium bromide was prepared by addition of a solution of 3.8 g. (0.035 mole) of ethyl bromide in 25 cc. of ether to 1 g. (0.04 atom) of magnesium. After the reaction was complete, the solution was decanted from the unused magnesium and a solution of 5 g. (0.034 mole) of tetrahydrofurylpropyl mercaptan in 50 cc. of ether added. A vigorous reaction took place and a solid precipitate was formed. To this mixture was then added a solution of 5.78 g. (0.034 mole) of phenacylchloride in 25 cc. of ether. During the addition of the phenacylchloride, the mixture became warm and free refluxing of the ether resulted.

This mixture was then refluxed for two hours and hydrolyzed by pouring onto cracked ice and the calculated quantity of dilute sulfuric acid. The ether solution was separated, dried and distilled to yield 3 g. or 33.4% of material which distilled with decomposition at 210°-215° at 10 mm. pressure. Redistillation of this compound resulted in partial decomposition and, for that reason, it was found impossible to purify the substance.

This compound is a liquid with a slight odor of tetrahydrofurylpropyl mercaptan, d_4^{34} 1.0741; n_D^{34} 1.5410.

Analysis. Calculated for $C_{15}H_{20}SO_2$: S, 11.89. Found: S, 13.56 and 13.45.

Furfuryl Phenacyl Sulfide, $C_4H_3OCH_2\text{-}S\text{-}CH_2CO\cdot C_6H_5$. This compound was prepared by the action of furfurylthiomagnesium bromide (1) on phenacylchloride. A solution of 5.45 g. (0.5 mole) of ethyl bromide in 25 cc. of ether was added to 1.2 g. (0.5 atom) of magnesium. After the reaction was complete, the solution was decanted from the unused magnesium and 5 g. (0.044 mole) of furfuryl mercaptan added. A vigorous reaction resulted with separation of a solid precipitate. This mixture was then diluted by addition of 100 cc. of ether and a solution of 6.8 g. (0.044 mole) of phenacylchloride in 25 cc. of ether added. This mixture was then refluxed for two hours and hydrolyzed by pouring onto ice and the calculated amount of dilute sulfuric acid. The ether layer was separated, dried and distilled to yield 2 g. or 19.7% of a compound which distilled with decomposition at 185°-190° at 10 mm. pressure. It was found impossible to purify this compound by redistillation. This compound is a liquid with a slight odor of furfuryl mercaptan, d_4^{34} 1.0725; n_D^{34} 1.5775.

Analysis. Calculated for $C_{13}H_{12}SO_2$: S, 13.78. Found: S, 15.07 and 15.12.

Summary.

Tetrahydrofurylpropyl mercaptan has been prepared and described. Attempts were made at preparation of tetrahydrofurylpropyl and furfuryl phenacyl sulfides. These compounds distill with decomposition and were not secured in a pure condition. For this reason, analyses for sulfur run quite high.

SOME CORRELATIONS OF CONSTITUTION WITH TASTE IN THE FURAN SERIES

Introduction.

For the correlation of constitution with sweet taste in the furan series, see Gilman and Hewlett (1) and Gilman and Dickey (2).

Although much work has been reported in the literature on the correlation of pungent taste with chemical constitution, no such correlation has been attempted with furan compounds. The proof of the structure of capsicin, 8-methylnonenovanillylmethylamide, the pungent principle of cayenne pepper, by Kobayashi (3) and the study of piperine derivatives by Staudinger and Schneider (4) have led to a very definite correlation of pungency with constitution of acid amides.

These studies have shown that the piperine molecule may be varied considerably without destroying the pepper taste. An essential factor is the amide-like union of piperidine with an aliphatic-aromatic acid, the grouping $Ph\cdot CH_2CH_2CH_2CH_2CO\cdot N(CH_2CH_2)_2CH$ seeming to be of importance in the production of pepper taste. It is found that in the case of piperidides of acids which do not contain the phenyl group, and also those

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(1) Gilman and Hewlett, *Iowa State College Journal of Science*, 4:27 (1929).
(2) Gilman and Dickey, *J. Am. Chem. Soc.*, 52:2010 (1930).
(3) Kobayashi, *Sci. Paper Ins. Phys. Chem. Research*, 6:166; Nelson, *J. Am. Chem. Soc.*, 41:1118 (1919).
(4) Staudinger and Schneider, *Ber.*, 56:699 (1923).

which contain a partially saturated ring, the acute pepper taste disappears (5).

In the case of vanillylamides, it was found that a free phenolic OH group in the fatty-aromatic acid interfered with the pungency while it was necessary in the fatty-aromatic amine. It was also shown that only a single methylene group may be present in the fatty-aromatic amine portion of the compounds.

For the purpose of determination of the effect of the furan ring upon the pungency of acid amides we have prepared furoylpiperonylmethylamide, furoylvanillylmethylamide and furylacryloylvanillylmethylamide. All three of these compounds are entirely without pungent taste.

Experimental.

Furoylpiperonylmethylamide, $CH_2O_2:C_6H_3CH_2NHCOC_4H_3O$. Piperonylmethylamine was prepared by the method of Mannich and Kuphal (6). A solution of 25 g. (0.15 mole) of piperonal oxime in 100 cc. of alcohol was warmed to 50° and 500 g. of 5% sodium amalgum slowly added. A solution of 50% acetic acid was added from time to time to keep the mixture acid, the temperature of the mixture being kept at 50°-70°. The alcohol was removed by distillation from a water-bath and the residue

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(5) Riccomanni, Atti. Acad. Lincei. (V) 33:145 (1924); C.A., 18:2900 (1924).

(6) Mannich and Kuphal, Ber., 45:318 (1914).

dissolved in a minimum amount of water. The solution was then made alkaline by addition of solid sodium hydroxide, an oil precipitating. This was extracted with ether and the ether solution dried and distilled to yield 20 g. or 88% of amine boiling at 135°-137° at 12 mm. pressure.

The amide was prepared by addition of 13 g. (0.1 mole) of furoyl chloride to a mixture of 15.1 g. (0.1 mole) of piperonylmethylamine and 50 cc. of water containing 10.6 g. (0.1 mole) of sodium carbonate. Upon shaking this mixture, a solid separated out. This solid was crystallized from alcohol to yield 15 g. or 61% of furoylpiperonylmethylamide melting at 108°. This compound is tasteless in the solid form and has a slight bitter taste in alcoholic solution.

Analysis. Calculated for $C_{13}H_{11}NO_4$: C, 61.80; H, 4.72. Found: C, 61.54; H, 4.87.

Furoylvanillylmethylamide, $1\text{-}C_4H_3OCO\cdot NHCH_2\text{-}3\text{-}CH_3O\text{-}4\text{-}OH\text{-}C_6H_3$. This compound was prepared by the action of furoyl chloride on vanillylmethylamine hydrochloride in the presence of aqueous sodium carbonate. The vanillylmethylamine hydrochloride was prepared by the method of Nelson (3). To a solution of 3.1 g. (0.02 mole) of vanillylmethylamine hydrochloride in 25 cc. of water was added 2.6 g. (0.02 mole) furoyl chloride and 0.2 g. (0.02 mole) of anhydrous sodium carbonate. After shaking until the material solidified, the solid was filtered off and crystallized from alcohol to yield 3 g. or

61% of the amide melting at 165°. This compound is practically tasteless and has no pungent taste.

Analysis. Calculated for $C_{13}H_{13}NO_4$: C, 62.71; H, 5.26. Found: C, 63.16 and 62.90; H, 5.55 and 5.13.

Furylacryloylvanillylmethylamide, $1\text{-}C_4H_3OCH{=}CHCO\cdot NHCH_2\text{-}3\text{-}CH_3O\text{-}4\text{-}OH\text{-}C_6H_3$. Furylacryloylvanillylmethylamide was prepared by the action of vanillylmethylamine on a furylacryloyl chloride-pyridine complex. To a solution of 3.95 g. (0.05 mole) of pyridine in 50 cc. of ether was added 7.3 g. (0.05 mole) of furylacryloyl chloride. A vigorous reaction resulted and a solid separated out. To this mixture was then added an ether solution of 7 g. (0.05 mole) of vanillylmethylamine. The mixture was then refluxed for two hours, washed with water and the ether solution dried. The ether was removed by evaporation and the residue crystallized from alcohol to yield 7 g. or 50% of the amide melting at 140°. This compound has practically no taste and has no pungent taste.

Analysis. Calculated for $C_{15}H_{15}NO_4$: C, 65.94; H, 5.49. Found: C, 65.52; H, 5.26.

Summary.

Furoylpiperonylmethylamide, furoylvanillylmethylamide and furylacryloylvanillylmethylamide have been prepared and described. These compounds have no pungent taste.