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I The relative aromaticity of furan II Heavy hydrogen in some naturally occurring organic compounds and mixtures

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14

I. THE RELATIVE AROMATICITY OF FURAN.
II. HEAVY HYDROGEN IN SOME NATURALLY
OCCURRING ORGANIC COMPOUNDS AND MIXTURES.

By

James M. Straley

A Thesis Submitted to the Graduate Faculty
for the Degree of

DOCTOR OF PHILOSOPHY

Major Subject - Organic Chemistry

Approved

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1936

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I. THE RELATIVE AROMATICITY OF FURAN

INTRODUCTION

A study of the relative aromaticity or electronegativity of any nucleus is desirable for several reasons. First, from an academic standpoint, effects of position and kind of nuclear atoms may lead to a more thorough understanding of their individual properties, and serve to classify organic compounds accurately. Secondly, a practical knowledge of nuclear behavior is invaluable in predicting orientation, conditions of synthesis, methods of isolation, and the general behavior of substances containing the nucleus or nuclei in question.

Since there is some confusion concerning the methods by which aromaticity is to be measured, and since there is the existence of diverse definitions of the term, a presentation of the status quo must preface any discussion embracing the generality "aromaticity". Usually, the term is made to imply a benzoid structure or one exhibiting properties similar to those of benzene, although in reality there is no sharp line of demarcation between aliphatic and aromatic properties.

Primarily, aromatic properties are due to a peculiar type of unsaturation existent in cyclic molecules, but are influenced to a great extent by the number and kind of groupings attached to the ring.

The confusion mentioned has arisen only in recent years due to investigations which have shown that some aliphatic compounds have properties which were formerly ascribed only to benzenoid types, and vice versa. For instance, nuclear substitution in benzene and related types is probably preceded by addition to a double or conjugated bond. The addition does not occur as readily as to some aliphatic double bonds, but after addition groups are eliminated with great ease, a circumstance which may best be laid at the door of a labilized hydrogen atom. Thus the differences between aliphatic and aromatic compounds are merely of degree, and not of kind.

However, in order to classify organic types, it becomes necessary to impose some more or less rigid boundaries limiting aliphaticity and aromaticity. These boundaries, which are a matter of general acceptance, hinge upon rather general properties some of which follow. (1) Nuclear substitution in reactions such as halogenation, nitration, mercuration, sulfonation, and the Friedel-Crafts class of reactions. None of these can be considered unequivocally critical, since all are encountered to some extent in aliphatic chemistry. Yet from the standpoint of ease of accomplishment, yields and the lack of side reactions, they are quite typical of benzenoid chemistry. This definition is the one usually first presented to the student, and constitutes the mental picture normally evoked

when aromaticity is mentioned. (2) Idiosyncracies of the group attached to the nucleus; e.g., the acidity of phenols and the inertness of nuclear halogens. (3) Resistance of the ring to addition reactions. (4) Stability of the nucleus, especially in preserving its identity throughout a series of reactions. (5) The effect of the nucleus on reactions such as decarboxylation, the pinacol-pinacolone rearrangement, and the reactions involving labile alpha-hydrogen atoms.

That all of these criteria do not always serve the same end may be illustrated by an appropriate example. Aniline, viewed with an eye to ease of nuclear substitution, is certainly more aromatic than benzene. On the other hand, it is certainly less stable than benzene in reactions such as oxidation, and by some would doubtless be considered less aromatic than benzene on these grounds. One thus reaches a point where it becomes imperative to select arbitrarily a definition of aromaticity. For instance, it may be considered that nuclei possessing a lesser degree of ring stability and exhibiting smoother and more easily controlled susceptibility to substitution reactions are more aromatic. One might designate benzene as the zero mark in a series of aromaticity and molecules such as nitrobenzene and carbomethoxybenzene would be definitely sub-aromatic.

The preceding definition seems to be well established by the fact that results reported here and elsewhere coincide

rather well with those found by interpretation of Kharasch's series (1), part of which follows in the decreasing order of electronegativity.

p-anisyl > o-anisyl > alpha-naphthyl > o-tolyl > p-tolyl > phenyl > p-chlorophenyl, etc.

This series was derived from the reaction



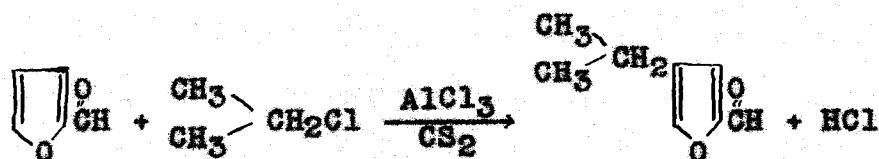
the more electronegative radical combining with the positive hydrogen to give the hydrocarbon.

The leading opponents of the above definition hold the view that the stability of a molecule to chemical treatment is a measure of the aromaticity (2). Their chief criticism of the application of substitution methods to heterocycles is that the ease of substitution is influenced by and is a function of the hetero atom, rather than significant of the reactivity of the molecule as a whole (2b). This may well be; in fact, it must be granted. However, if the hydrogen atoms attached to the molecule's carbon atoms are more easily replaced the aro-

1. (a) Kharasch, J. Chem. Ed., 13, 9 (1936); (b) Kharasch, et al, J. Am. Chem. Soc., 47, 1948 (1925); ibid., 48, 3130 (1926); ibid., 54, 674 (1932).
2. (a) Fieser, et al, J. Am. Chem. Soc., 46, 858 (1924); ibid., 48, 1097 (1926); ibid., 49, 2604 (1927); ibid., 56, 1565 (1934); ibid., 57, 1611, 1835, 1844 (1935). (b) Ibid., 57, 1840 (1935).

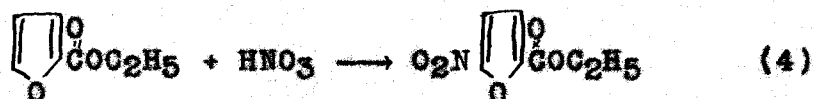
maticity of the molecule has been increased, whether such increase be due to the introduction or presence of a hetero atom or to other reasons. These critics have confused cause with effect and their arguments appear to be of little relation to the main issue.

Fieser has based his aromaticity series upon the lowering of potential in oxidation-reduction of certain binuclear quinones containing a heterocyclic nucleus fused to contiguous carbon atoms of a 1-4 quinone nucleus (2). From some of his results, namely those measuring the aromaticity of the pyridine ring attached with the nitrogen atom in two different positions, the point arises that in regard to heterocycles it may not be altogether accurate to speak of the aromaticity of the molecule as a whole, but rather of the various carbon atoms differing in their relation to the hetero atom. This point is further established by a glance at the history of furan chemistry. Only in one instance, and that proceeding from a reaction notorious for unreliability, has a substituent entered a beta-position while an alpha-position was available (3).



3. Gilman, Calloway and Burtner, J. Am. Chem. Soc., 57, 906, (1935).

All other alkyl halides used reacted with the free alpha-carbon atom. Even when the group already present in an alpha-substituted furan is one of strict meta-orienting proclivities in benzene chemistry, the reaction product is a di-alpha-substituted furan. One reaction is written to illustrate this point.



In the following pages the term "relative aromaticity of furan" is used with respect to the alpha-carbon atom, unless specified otherwise.

The first competitive reactions between furan and another aromatic nucleus were performed by Phelps and Hale (5), who attempted to brominate and nitrate 2-5-dibenzoylfuran. During the process of bromination the furan ring was ruptured and the products isolated were all three of the possible bromobenzoic acids and bromomaleic acid. Upon attempts to oxidize dibenzoylfuran with nitric acid the three nitrobenzoic acids were isolated, as well as a compound which gave the correct analysis for a mononitrodibenzoylfuran and a higher melting compound. These products were not studied further.

4. Marquis, Compt. rend., 137, 520 (1903); Ann. chim. phys., 8 4, 196 (1905).
5. Phelps and Hale, Am. Chem. J., 25, 458 (1903).

From that work to the studies of Gilman and co-workers in this laboratory no mention is made of similar reactions. These investigators have established a case for the superaromaticity of furan by means of the following methods. (1) The acid cleavage of furyl aryl lead compounds (6). (2) The Friedel-Crafts reaction (7). (3) The nitration of symmetrical furyl aryl compounds (8). (4) Metalation of furyl compounds (9).

In the studies concerning unsymmetrical lead compounds use was made of the following reaction.



and, as in Kharasch's work, the more electronegative grouping combines with the positive hydrogen from the acid.

The Friedel-Crafts reaction is one whose reliability is in some doubt (the reaction is greatly maligned in this respect), but it has presented the most overwhelming evidence thus far obtained supporting the greater aromaticity of furan in a reaction where the question of unreliability does not enter. This evidence involves the acetylation of methyl 2-furoate by means of acetic anhydride and stannic chloride in benzene solution. Here indeed is adequate proof of the extraordinary re-

6. Gilman and Towne, Rec. trav. chim., 51, 1054 (1932).
7. Gilman and Calloway, J. Am. Chem. Soc., 55, 4197 (1933).
8. Gilman and Young, ibid., 56, 464 (1934).
9. Gilman and Breuer, ibid., 56, 1123 (1934).

activity of the furan alpha-carbon atom, as there is a group which normally prohibits further substitution in Friedel-Crafts reactions present in the molecule. Further, benzene alone was not converted readily into acetophenone by the same reagents, even under drastic conditions, and the alkylation of 2-benzoylfuran with iso-propyl chloride and aluminum chloride in carbon disulphide gave only 5-iso-propyl-2-benzoylfuran.

The studies were continued on 2-benzoylfuran using this symmetrical compound in competitive nitrations. The nitro group entered the furan ring only. Analogous results were obtained when 2-thenoylfuran was nitrated, the product being 5-nitro-2-thenoylfuran.

Metalation of furan and derivatives was based in principle on the fact that it is possible to arrange hydrocarbons in a series correlating acid strengths, deriving the data from reactions with organo-metallic compounds (10).

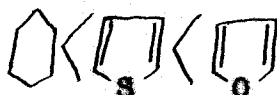


the metal combining with the hydrocarbon radical of stronger acidity or greater electronegativity. For example, it is

10. Wooster and Mitchell, J. Am. Chem. Soc., 52, 688 (1930);
Zeigler, et al, Ann., 473, 1 (1929), Ber., 61, 253 (1928);
Conant and Wheland, J. Am. Chem. Soc., 54, 1212 (1932).

possible to prepare phenylsodium from benzene and ethylsodium. It is also known that benzene undergoes no reaction with metallic sodium and potassium (11), and while the same was thought to be true of furan (12), Gilman and Breuer (9) found that furan reacts with potassium to form 2-furylpotassium.

The results reviewed briefly in the preceding discussion may be collected to provide the following series arranged in the order of increasing aromaticity.



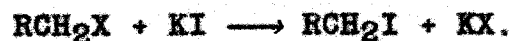
Another series arranged in order of increasing strength of acidity has been derived.



The work already mentioned does not constitute all of the material accumulated. Catlin (13) has adduced evidence substantiating the superior aromaticity of furan, his conclusions deriving from two sources. One is the activating influence of an aromatic nucleus upon a lateral halogen atom, the reaction

11. Schlenck and Mayer, *Ber.*, 46, 4060 (1913).
12. Limpricht, *Ann.*, 165, 282 (1873).
13. Ph.D. dissertation of W. E. Catlin, *Iowa State Coll. J. Sci.*, 10, 65 (1935). C.A., 30, 935 (1936)/.

employed being



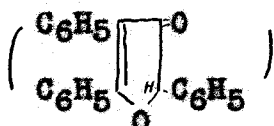
For example, 2-furfuryl chloride is about sixteen times more reactive than is benzyl chloride. His second method comprises a study of the ionization constants of some aromatic carboxylic acids. Here the furan nucleus is found to be more aromatic than the benzene ring, and the 2-furyl radical is more reactive than the 3-furyl radical. It is extremely probable, however, that ionization constants and decarboxylation temperatures are of little value in respect to aromaticity (14).

In a study of the rates of reaction of organic nitriles with phenylmagnesium bromide (15) the speed of the reaction was found in general to vary inversely with the electronegativity (in the light of Kharasch's series) of the radical attached to the cyano group. Astonishingly enough, 2-furonitrile reacted with such uncommon speed that the authors were inclined to place the 2-furyl radical with those of very high aliphaticity. Such an anomaly led to the interesting, at least, theory of a closed or cyclic arrangement of organic radicals, and on such an hypothesis the aromatic and aliphatic radicals would merge

14. Marshall, Rec. trav. chim., 51, 233 (1932); Gilman, Janney and Bradley, Iowa State Coll. J. Sci., 7, 429 (1933).
15. Gilman and Lichtenwalter, Rec. trav. chim., 55, 000 (1936).

with each other in two regions. While this is not an unpleasant speculation we are not assured that the reaction employed is actually a measure of the electronegativity. Only one reaction with furan nuclei was performed, so that the validity of any conclusion based on that evidence is problematical. It is entirely possible that furonitrile possesses some unorthodox properties of which we are as yet unaware; a contingency that will be discussed at greater length under another heading.

Kohler and co-workers appear to frown upon the idea of furan having super-aromatic properties (16). In justification of this view they have pointed out the surprisingly unaromatic properties of beta-hydroxytriphenylfuran. This substance (which was not isolated) gave a peroxide which upon catalytic reduction formed 2-hydroxy-2,4,5-triphenylfuranone-3. The tautomer

() of the beta-hydroxyfuran was obtained by treat-

ment of beta-acetoxytriphenylfuran with methylmagnesium iodide and gave a crystalline peroxide. It must be admitted that the above properties do not correspond to those expected of an aromatic compound. This work is one of passing interest only as regards its effect upon the problem of aromaticity, since the paucity of hydroxy furans must be relieved before a general

16. Kohler, Westheimer and Tishler, J. Am. Chem. Soc., 58, 264 (1936).

study of this nature can be pursued (17).

While the evidence already presented supporting the superaromaticity of furan is excellent, the scope and nature of the methods employed may leave doubt in the minds of some. For example, the Friedel-Crafts reaction is still considered unreliable, however undeservedly, and nitration is but one of several reliable substitution reactions. It is the purpose of this thesis to attempt a definite removal of the doubts with which one is now confronted.

17. It is interesting to note that Mr. W. M. Hoehn, in unpublished studies upon beta-hydroxyfurans, has observed no evidence of peroxide formation and his evidence for enolization is not prepossessing.

EXPERIMENTAL

A. Studies on Aryl Furoic Esters

Nitration of Phenyl 2-Furoate.

Ten grams (0.057 mole) of phenyl 2-furoate (18) dissolved in 30 g. of acetic anhydride were added dropwise, at a temperature below -10° , to a nitrating mixture prepared by dropping 34 g. of fuming nitric acid into 60 g. of acetic anhydride at -5° . The mixture was stirred for one hour after complete addition, poured cautiously onto ice, and extracted six times with ether. The ether extract was neutralized with a sodium bicarbonate solution, and the ether layer allowed to stand twelve hours with 15 cc. of pyridine. The ether solution was then washed well with 2% hydrochloric acid followed by water, dried over anhydrous sodium sulfate, and the ether removed by distillation. The residue was crystallized twice from 60% alcohol, using Norite once. The yield was 5.2 g. (44% of the theoretical) of phenyl 5-nitro-2-furoate, melting at $121-1.5^{\circ}$.

Anal. Calcd. for $C_{11}H_7O_5N$: N, 6.38. Found: N, 6.48, 6.33.

Hydrolysis, effected by refluxing with 20% hydrochloric acid, gave 5-nitro-2-furoic acid, melting at $183-4^{\circ}$. A mixed

18. Baum, Ber., 37, 2951 (1904).

melting point determination with an authentic specimen (4) showed no depression. Upon working up the mother liquors, phenol, identified by preparation of the tribromo derivative, was obtained.

Preparation of 3-Methoxyphenyl 2-Furoate.

Ten grams (0.075 mole) of furoyl chloride were heated at 150° with 9.4 g. (0.075 mole) of m-methoxyphenol (19) until hydrogen chloride ceased to be evolved. The heavy black oil was washed with dilute sodium hydroxide and water, dried in ether over anhydrous sodium sulfate and distilled under reduced pressure. The yield was 12.3 g. (76%) of 3-methoxyphenyl 2-furoate, boiling at 179-80° under 10 mm. pressure.

Anal. Calcd. for C₁₂H₁₀O₄: -OCH₃, 14.18. Found: -OCH₃, 13.99 and 13.95.

Nitration of 3-Methoxyphenyl 2-Furoate.

This was performed exactly as in the nitration cited above, using 4 g. (0.018 mole) of the ester and proportional amounts of acetic anhydride and nitrating mixture. The isolation of the product also followed the above procedure, resulting in a mixture melting from 81-86°. Steam distillation of the product resulted in 1.3 g. (43%) of yellow needles melting at 94-4.5°

19. Perkin, Ray, and Robinson, J. Chem. Soc., 1926, 945

after one recrystallization from water.

Anal. Calcd. for $C_7H_7O_4N$: N, 8.28. Found: N, 8.44 and 8.47.

This compound was definitely established as 3-methoxy-6-nitrophenol by the preparation of 3-methoxy-6-nitrophenyl benzoate (20) by means of the Schotten-Baumann reaction. The ester, after crystallization from 50% alcohol, melted at 96° . A mixed melting point determination with the original 3-methoxy-6-nitrophenol showed a melting range of $71-83^\circ$.

That portion of the mixture not volatile with steam was crystallized eight times from alcohol and water, using Norite twice, obtaining 0.47 g. (11%) of 3-methoxy-6-nitrophenyl 2-furoate, melting at $106-6.5^\circ$.

Anal. Calcd. for $C_{12}H_9O_6N$: N, 5.30. Found: N, 5.56 and 5.48.

Acid hydrolysis of the ester gave 2-furoic acid and 3-methoxy-6-nitrophenol, both identified by mixed melting points with authentic specimen.

Preparation of Diphenyl Dehydromucate.

Nine and seven-tenths grams (0.05 mole) of dehydromucyl chloride (21) were heated at 150° with 10 g. (excess) phenol

20. Meldola and Eyre, Proc. Chem. Soc., No. 238, 132 (1901).

21. Klinkhardt, J. prakt. Chem., 2 25, 46 (1882).

until hydrogen chloride ceased to be evolved. After cooling, the product was washed with dilute sodium hydroxide and water, and crystallized from a 50% mixture of alcohol and ethyl acetate. After four recrystallizations a light yellow, amorphous compound, melting at 138.5-139°, was obtained. The yield was 14.3 g., or 89% of the theoretical.

Anal. Calcd. for $C_{18}H_{12}O_5$: C, 67.91; H, 3.81. Found: C, 67.70 and 67.74; H, 3.98 and 3.89.

Nitration of Diphenyl Dehydromucate.

Several ineffectual attempts to nitrate this ester were performed before success was attained. These included nitration with acetic anhydride-fuming nitric acid mixture at a low temperature, fuming nitric acid alone at both low and room temperatures, and nitric-sulfuric acid mixtures at low temperatures.

Four grams (0.0125 mole) of diphenyl dehydromucate were stirred for two hours at room temperature with a mixture composed of 27 g. of concentrated nitric acid and 27 g. of concentrated sulfuric acid. The mixture was poured onto ice, filtered and extracted twice with hot water. The extract, after chilling, yielded 0.9 g. (15.7% based on the starting amount of ester; 28.6% based on the amount of ester actually used) of picric acid, melting at 121°. A mixed melting point determination with a specimen of authentic picric acid showed no de-

pression. The recovery of diphenyl dehydromucate was 1.8 g. (45%). Upon investigation of the mother liquors, 0.11 g. of oxalic acid were obtained. No other organic compounds were isolated, nor was any other method of nitration successful.

Preparation of 2-Naphthyl 2-Furoate.

Fourteen and four-tenths grams (0.1 mole) of beta-naphthol and 13.3 g. (0.1 mole) of furoyl chloride were heated at 150° until no more hydrogen chloride was evolved. The resulting mass was washed with hot 20% alcohol, and the residue recrystallized four times from alcohol, using Norite twice. The product was 19 g. (79%) of the desired ester, melting at 121-2°. This was not beta-naphthol, which melts in about the same range, as was shown by the depression in a mixed melting point determination. The saponification equivalents of the compound were 234 and 233, while that calculated for $C_{14}H_{10}O_3$ is 238.

Nitration of 2-Naphthyl 2-Furoate.

This was effected in the same manner as with phenyl furoate, using 7 g. (0.029 mole) of the ester and corresponding amounts of nitrating mixture and acetic anhydride. Upon working up the product in the described manner, a red tar which would yield to no methods of purification was isolated. This product is probably a mixture of isomers produced by substitution occurring in several of the available naphthyl alpha-posi-

tions.

That nitration occurred in the naphthyl radical only was demonstrated by the fact that upon acid hydrolysis no nitro-furoic acid could be isolated in the reaction mixture. However, furoic acid, identified by mixed melting point, was found.

Friedel-Crafts Reaction with Phenyl 2-Furoate.

There are several difficulties encountered in Friedel-Crafts reactions with aryl furoic esters. For some as yet unperceived reason aluminum chloride has not been used successfully in acylations of furoic esters, and in the case of aryl furoates induces Fries rearrangements rather easily. On the other hand, catalysts such as stannic chloride, titanium tetrachloride, etc., are ineffective in alkylation. These obstacles do not leave a very wide field in the choice of Friedel-Crafts substitutions with phenyl furoate.

To a mixture of 18.8 g. (0.1 mole) of phenyl furoate, 10.2 g. (0.1 mole) of acetic anhydride and 75 cc. of dry thiophene-free benzene, 52 g. (0.2 mole) of anhydrous stannic chloride were added dropwise with efficient stirring and cooling by means of an ice-bath. After thirty minutes the ice-bath was removed and the mixture refluxed for four hours, cooled and poured cautiously onto ice. The aqueous layer was extracted with benzene and the combined benzene layers dried over anhy-

drous sodium sulfate and distilled. In this manner there was recovered 9.4 g. (50%) of phenyl furoate, boiling at 165-7° at 12 mm. The identity of the product was established by acid hydrolysis to furoic acid and phenol. The only other reaction product was a large amount of a black, resinous tar which would yield to no purification methods.

B. Studies on 1-(2)Furyl-2-phenylethylene

Preparation of 1-(2)Furyl-2-phenylethylene.

While the action of sulfuric acid on α,β -diphenylacrylic nitrile results in satisfactory yields of stilbene (22), application of this method to β -(2)furyl- α -phenylacrylic nitrile (23) resulted in the formation of red tars only. Attempts to decarboxylate β -(2)furyl- α -phenylacrylic acid (24) by boiling with 50% sulfuric acid in the absence of air gave similar results.

Six grams (0.028 mole) of β -(2)furyl- α -phenylacrylic acid were heated with 10 g. of quinoline and 3 g. of copper-bronze in a 10-inch Pyrex test tube immersed to the level of its contents in a metal-bath. Nitrogen was passed through the mix-

22. Meisenheimer and Heim, Ann., 355, 275 (1907).

23. Frost, Ann., 250, 159 (1888).

24. Röhmer, Ber., 31, 282 (1898).

ture continuously and heating was maintained at such a temperature that the quinoline vapor condensed two inches above the liquid. At the end of about two hours carbon dioxide had ceased to be evolved, so the mixture was cooled, 100 cc. of ether added and the mixture filtered. The ether solution was washed with 10% hydrochloric acid and water, dried over anhydrous sodium sulfate and distilled under reduced pressure. In this manner there was obtained 2.9 g. (59%) of 1-(2)furyl-2-phenylethylene, boiling at $145-6^{\circ}$ at 14 mm. This product, a yellow oil, after standing for two weeks boiled at $132-4^{\circ}$ at 10 mm., and the product solidified to a compound melting at $53-4^{\circ}$ (25). Upon recrystallization from alcohol and water a compound melting at $54-4.5^{\circ}$ was obtained. This substance readily decolorized dilute permanganate and bromine solutions, and a qualitative analysis disclosed the presence of C, H and O only.

Anal. Calcd. for $C_{12}H_{10}O$: C, 84.44; H, 5.92. Found: C, 84.09 and 83.96; H, 5.86 and 5.82.

Oxidation of the olefine with alkaline 3% potassium permanganate solution gave benzoic and furoic acids, which were separated by fractional crystallization from water. The identities of the two products were established by mixed melting point methods. Oxidation with potassium ferricyanide solution

25. Similar results are experienced in the preparation of stilbene from α,β -diphenylacrylic acid or its nitrile.

gave benzoic acid, but no furcic acid could be isolated. Hydrogen peroxide oxidations were quite ineffective.

Bromination of 1-(2)Furyl-2-phenylethylene.

Three grams (0.018 mole) of furylphenylethylene were dissolved in 15 cc. of carbon tetrachloride and 2.8 g. (0.0175 mole) of bromine in 5 cc. of carbon tetrachloride were added dropwise at room temperature. No hydrogen bromide was evolved and, upon cooling in a freezing mixture, a precipitate of white platelets was formed. However, during filtration hydrogen bromide was suddenly evolved and the precipitate decomposed into a black tarry mass which was resistant to purification methods. All precautions to preserve the product, which was apparently quite stable in carbon tetrachloride, resulted in complete failure upon removal of the reaction solvent.

Nitration of 1-(2)Furyl-2-phenylethylene.

A solution of three grams (0.018 mole) of the olefine in 6 g. of acetic anhydride was added at -10° to a nitrating mixture prepared at -5° from 5 g. of acetic anhydride and 1.2 g. (0.018 mole) of fuming nitric acid. During the addition the mixture turned a greenish-black, an occurrence which, in the light of previous experience, indicates decomposition. The mixture was immediately poured onto ice and worked up in the manner described under A, but to no avail, as the addition of

pyridine precipitated a black tar, a further indication of departure from the normal course of nitration. Investigation of the supernatant ether resulted in the isolation of absolutely no organic compound. Larger runs were performed in an identical manner, with similar failures.

When runs were made omitting the use of pyridine, the removal of the ether resulted in a tar, from which benzoic acid only could be isolated. Apparently oxidation with ring scission had occurred in these experiments. It is not unlikely that these were preceded by lateral nitration.

Mercuration of 1-(2)Furyl-2-phenylethylene.

Seventeen grams (0.1 mole) of furylphenylethylene were shaken for twelve hours with 500 cc. (0.1 mole of mercuric chloride) of Wright's mercurating solution (26)(mercuric chloride buffered with sodium acetate) and the mixture filtered. Thus 22 g. of a compound or mixture of compounds which neither melted nor charred in the range of the mercury thermometer were obtained. Boiling with alcohol appeared to have no effect upon the product. Treatment with 10% hydrochloric acid resulted in a tarry mass, as did attempted replacements of the chloromercuri groups with bromine or iodine. Analyses for mercury gave values ranging from 68 to 81 per cent of mercury. Some calcu-

26. Gilman and Wright, J. Am. Chem. Soc., 55, 3302 (1933).

lated values are: $C_{12}H_9OClHg$; Hg, 49.24; $C_{12}H_9OCl_2Hg_2$; Hg, 62.58; $C_{12}H_7OCl_3Hg_3$; Hg, 68.51.

Attempted purifications by means of extractions with chloroform, alcohol, acetone, carbon tetrachloride, benzene, xylene and carbon disulphide proved ineffective.

C. Studies on 2-Furylphenylmethane

Preparation of 2-Furylphenylmethane.

Attempts to effect a satisfactory preparation of furylphenylmethane by treatment of 2-benzoylfuran with hydrazine hydrate in the manner of the Kirschner reaction on furfural were found to be of little value, traces only of the desired product being isolated. The procedure of Kariyone (27), in which an alcoholic solution of 2-benzoylfuran is treated with sodium in small portions, the mixture steam distilled and the process repeated six times on the product, was found to be quite tedious and devoid of any desirable features. The method about to be mentioned was very satisfactory and quite facile.

To 34.2 g. (0.2 mole) of 2-benzoylfuran dissolved in 300 cc. of boiling absolute ethanol 40 g. (1.75 moles) of sodium wire were added over a period of four hours. The mixture was

27. Kariyone, J. Pharm. Soc. Japan, 428, 8913 (1917).

then saturated with carbon dioxide and distilled with steam, pouring the distillate into a saturated solution of calcium chloride. This mixture was then extracted six times with ether, the extract dried over anhydrous sodium sulfate and fractionated. The yield was 18.8 g. (59%) of 2-furylphenylmethane, boiling at $102-3^{\circ}$ at 14 mm., no other fraction being isolated. The boiling point at atmospheric pressure was $217-8^{\circ}$, while that reported (27) is 219° . This compound should be handled with care, since it possesses sternutatory properties, as well as a mild vesicant action.

Anal. Calcd. for $C_{11}H_{10}O$: C, 84.51; H, 6.40. Found: C, 84.31 and 84.28; H, 6.21 and 6.30.

Oxidation with neutral 3% potassium permanganate solution gave benzoic acid only, no furoic acid being isolated. A mixed melting point determination with authentic benzoic acid melted at $121-2^{\circ}$.

That the furan ring remained intact in the above reduction is established by the following description of a successful diene synthesis.

A solution of 2.5 g. (0.025 mole) of maleic anhydride and 3.8 g. (0.025 mole) of furylphenylmethane in 20 cc. of dry thiophene-free benzene was warmed gently to start the reaction and allowed to stand in the ice-box. Three days later 4.2 g. (67%) of Δ^4 -3-benzyl-3, 6-endoxytetrahydrophthalic anhydride,

which, after crystallization from ethyl acetate, melted without decomposition at $102-2.5^{\circ}$, were obtained. The adduct was not dehydrated since the product which would be obtained is apparently unavailable at present.

Anal. Calcd. for $C_{15}H_{12}O_4$: C, 70.34; H, 4.68. Found: C, 69.92 and 70.01; H, 4.41 and 4.32.

Nitration of 2-Furylphenylmethane.

To a nitrating mixture prepared at a -5° from 17 g. of fuming nitric acid and 30 g. of acetic anhydride, 7.9 g. (0.05 mole) of furylphenylmethane in 7 g. of acetic anhydride were added, maintaining the temperature below -10° . Stirring was continued at this temperature for thirty minutes after addition was complete. All attempts to isolate a stable nitro compound according to previously mentioned methods, with or without pyridine encountered failure only. To be sure, some benzoic acid was found in some cases, but all other products were refractory tars. As in the case of furylphenylethylene the nitration had apparently occurred laterally, rather than nuclearly. These nitration products were quite stable in ether solution but upon removal of the solvent, even at room temperature in vacuo, voluminous clouds of nitrogen oxides were evolved, leaving the black or red tars only.

Mercuration of 2-Furylphenylmethane.

A suspension of 7.9 g. (0.05 mole) of furylphenylmethane suspended in 250 cc. (0.05 mole of mercuric chloride) of Wright's mercurating solution was shaken for six days. No reaction had occurred at this time, so the mixture was refluxed in an oil bath for four hours. A substance precipitated which, after filtration, was refluxed two hours with n-propyl alcohol cooled and filtered. Twelve grams of a mercury-containing compound, charring at 198° were thus obtained. Analyses for mercury showed values of 72.3 and 71.9 per cent of mercury, quite out of agreement with calculated values for mono- or polymer-mercurated molecules. Some of these latter values are: $C_{11}H_9OClHg$; Hg, 52.25; $C_{11}H_8OCl_2Hg_2$; Hg, 64.76; $C_{11}H_7OCl_3Hg_3$; Hg, 70.51. Treatment with hydrochloric acid resulted in tars only.

Mercuration of furylphenylmethane with mercuric acetate in the cold gave similar results. Refluxing furylphenylmethane with equivalent amounts of mercuric acetate dissolved in water resulted in mercuric oxide and black tars which contained no mercury.

D. Studies on Furyl Aryl Ketones

Bromination of 2-Benzoylfuran.

To a solution of 17.1 g. (0.1 mole) of 2-benzoylfuran (28) dissolved in 200 cc. of carbon tetrachloride 16 g. (0.1 mole) of bromine in 50 cc. of carbon tetrachloride were added slowly, refluxing gently and stirring constantly. The addition consumed perhaps 90 minutes. The bromine was consumed readily without evolution of hydrogen bromide, although it was found necessary to subject the contents of the flask to the light from a 50-watt bulb, held about four inches from the flask, in order to start the reaction. Four or five minutes after addition was complete the evolution of hydrogen bromide began and continued throughout a period of about four hours refluxing. The solvent was then removed by distillation, and the residue heated for twelve hours at a temperature of 100° and a pressure of 25 mm., and then distilled under diminished pressure. The yield was 14.9 g. (62%) of 5-bromo-2-benzoylfuran, boiling at 172-4° under 4 mm. pressure. The bromo ketone melts at 37-7.5°. In this reaction it is absolutely necessary to employ adequate lighting and heating of the mixture. If the former is neglected, the reaction will not commence, and if the latter be omitted insurmountable difficulties in distillation will be encountered.

28. Marquis, Compt. rend., 129, 111 (1899).

ered.

Anal. Calcd. for $C_{11}H_7O_2Br$: Br, 31.82. Found: Br, 32.08 and 31.99.

The oxime of the bromo ketone was prepared in the usual manner, two days refluxing being necessary for completion of the reaction. The melting point of the oxime was $139-40^\circ$.

5-Bromo-2-benzoylfuran was also prepared from 5-bromo-2-furoyl chloride, benzene and aluminum chloride (29). The oxime, prepared as above, showed no depression in melting point when mixed with the oxime of the bromo ketone prepared by direct bromination.

Anal. Calcd. for $C_{11}H_8O_2BrN$: N, 5.29. Found: N, 5.60 and 5.39.

The position of the bromine in the above ketone was established in the following manner (30).

Two grams (0.0083 mole) of 5-bromo-2-benzoylfuran were placed in a 50 cc. Erlenmeyer flask and heated to 60° in an oil bath. Nitrogen trioxide, generated by dropping concentrated nitric acid onto sodium nitrite, was passed over the compound for 20 hours, maintaining the original temperature. The residual nitrogen trioxide was then removed by suction, and the

29. This reaction was performed by Mr. D. F. Eaton.

30. The replacement of furan alpha-halogens by nitrogen trioxide (N_2O_3) has been developed (as yet unpublished) by Mr. J. A. V. Turck, Jr.

yellow solid recrystallized from ethyl alcohol, melting finally at 109.5-10°. A mixed melting point determination with a specimen of authentic 5-nitro-2-benzoylfuran (8) showed no depression. The yield was 1.6 g., or 93% of the theoretical.

Sulfonation of 2-Benzoylfuran.

This particular substitution was attempted under a variety of conditions before a satisfactory result was obtained. Some of the less satisfactory methods employed were sulfonation with 15% or 30% fuming sulfuric acid at 0° or at room temperature, 15% fuming sulfuric acid at 40°, and 30% fuming sulfuric acid at 50°. The optimum conditions are reported in the following detailed directions.

Seventeen and one-tenth grams (0.1 mole) of 2-benzoylfuran were mixed thoroughly with 40 cc. of 15% fuming sulfuric acid. The mixture was then stirred and heated at 55° until a drop of the mixture when placed in water no longer exhibited any turbidity. The solution was then poured onto ice, diluted to twelve times the original volume, neutralized with solid barium carbonate, boiled vigorously and filtered hot. The precipitate was washed with a liter of boiling water and the combined filtrates evaporated almost to dryness on a steam bath. The residue was cooled under the water tap, and recrystallized twice from a small amount of water. In this manner there was

obtained 26.2 g. (69%) of the barium salt of 5-benzoylfuran 2-sulfonic acid.

Anal. Calcd. for $C_{22}H_{14}O_{10}S_2Ba$: Ba, 21.49. Found: 21.89 and 21.76.

Three grams (0.008 mole) of the barium salt thus obtained were allowed to stand overnight with 5 g. of fuming nitric acid, and then poured onto ice. The mixture was extracted with ether, dried over anhydrous sodium sulfate and the ether removed by distillation. The residue was fractionally crystallized from dilute alcohol, obtaining 0.59 g. (46%) of 5-nitro-2-benzoylfuran (8), identified by a mixed melting point determination. There was also obtained 0.48 g. of a compound melting at $136-7^{\circ}$, which has not yet yielded to analytical or identification methods. Oxidation with acid 3% potassium permanganate solution, however, resulted in benzoic acid only, demonstrating that sulfonation (or replacement followed by nitration, perhaps) had not occurred in the benzene fragment of the molecule.

Attempts to replace the sulfonic group in the above ketonic sulfonic acid were made, using the barium salt and bromine in water solution, bromine in carbon tetrachloride, bromine in glacial acetic acid and without a solvent. In these experiments no reaction occurred when heating was omitted, and when heated the only compound obtained was a light yellow oil which

would yield to no purification methods. Oxidation of this oil with acid 3% permanganate solution gave benzoic acid only, which was identified by mixed melting point methods. Attempts to prepare an oxime of the yellow oil met with failure. The oil contained bromine, but when treated with nitrogen trioxide as in the case of 5-bromo-2-benzoylfuran, the compound was apparently unaltered.

Mercuration of 2-Benzoylfuran.

1st Run. A mixture of 500 cc. (0.1 mole of mercuric chloride) of Wright's mercurating solution and 17.1 g. (0.1 mole) of 2-benzoylfuran in 50 cc. of alcohol were shaken for one week at room temperature. No apparent reaction had occurred at the end of this time, and upon working up the mixture through an ether extraction and subsequent distillation, a quantitative recovery of unchanged ketone resulted. The product was identified by means of a mixed melting point determination of its oxime (melting at 132-3°) with an authentic sample (28).

2nd Run. A mixture of 31.9 g. (0.1 mole) of mercuric acetate and 17.1 g. (0.1 mole) of 2-benzoylfuran in 250 cc. of 25% ethanol were allowed to shake for 60 hours at room temperature. The filtered precipitate was refluxed four hours with 95% ethanol, cooled and filtered. After drying under reduced

pressure, the yellow amorphous precipitate weighed 29.5 g., and began charring at 208°, but had not melted at 360°. Analyses for mercury showed 72.9 and 72.6 per cent. Some calculated values for mercury are listed here in order to show the complexity of the product. Calcd. for $C_{13}H_{10}O_4Hg$: Hg, 46.7; $C_{15}H_{12}O_6Hg_2$: Hg, 58.2; $C_{17}H_{14}O_8Hg_3$: Hg, 63.5.

Upon refluxing a sample of the mercurial with 20% hydrochloric acid for 12 hours, an oil was obtained which gave the oxime of 2-benzoylfuran, identity being established by mixed melting point methods.

Five grams of the mercurated 2-benzoylfuran was suspended in 25 cc. of glacial acetic acid heated to 50° and solid sodium chloride added until all of the mercurial had dissolved. Upon chilling the solution 4.2 g. of a substance containing both mercury and chlorine were obtained. After boiling with 95% ethanol, filtering and drying, the compound remained apparently unaltered when heated to 360°. One gram of the product was refluxed with 2 g. of bromine in 10 cc. of carbon tetrachloride for seven days, and the solvent removed by distillation. Thus were obtained 0.9 g. of a substance which was probably mercuric bromide since it failed to burn upon ignition and melted at 235-40°, and a few drops of a brown oil which gave the oxime of 2-benzoylfuran. The product failed to react with iodine in a potassium iodide solution. Analyses for mer-

cury performed on this suspected chloromercuri compound gave values of 79.6 and 78.2. Some calculated values for expected mercurials follow. Calcd. for $C_{11}H_7O_2ClHg$: Hg, 49.3; $C_{11}H_6O_2Cl_2Hg_2$; Hg, 62.5; $C_{11}H_5O_2Cl_3Hg_3$; Hg, 68.5.

3rd Run. A mixture of 17.1 g. (0.1 mole) of 2-benzoylfuran was refluxed 36 hours with 500 cc. (0.1 mole of mercuric chloride) of Wright's mercurating solution. There was obtained 12.3 g. of a compound or mixture of compounds which was probably identical with the product obtained by the sodium chloride replacement described above, inasmuch as its behavior was entirely similar. In view of this fact, analyses were not performed.

4th Run. Thirty-two grams (slightly more than 0.1 mole) of mercuric acetate were boiled with 250 cc. of water until no more red mercuric oxide was formed. After filtering, the solution was refluxed with 17.1 g. (0.1 mole) of 2-benzoylfuran for 30 minutes, cooled and filtered. The precipitate was boiled one hour with 95% ethanol, filtered and dried. The product was apparently identical with that obtained in the 2nd Run, since analysis for mercury resulted in values of 72.3 and 72.1. Its chemical behavior was exactly that of the former substance, as was its resistance to heat.

Preparation of 2-(p)Toluylfuran.

To a solution of 100 cc. of dry toluene and 13.1 g. (0.1 mole) of 2-furoyl chloride, cooled in ice-bath, 20 g. (0.15 mole) of Eastman resublimed aluminum chloride were added slowly during the course of 30 minutes. The ice-bath was then removed and the mixture allowed to stir six hours at room temperature. At the end of this period the mixture was poured cautiously onto ice, the layers separated, and the water extracted once with toluene. The combined toluene layers were dried over anhydrous sodium sulfate and distilled under reduced pressure. The yield was 12 g. (70%) of 2-(p)toluylfuran boiling at 185-7° at 18 mm. pressure.

Anal. Calcd. for $C_{12}H_{10}O_2$: C, 77.49; H, 5.39. Found: C, 77.28 and 77.36; H, 5.35 and 5.31.

Oxidation of the ketone with acid 3% permanganate solution resulted in p-toluic acid (31), melting at 176-7° after vacuum sublimation. A mixed melting point determination with a sample of authentic p-toluic acid showed no depression. A small amount of a substance which did not melt but ignited to leave no residue was also obtained. This substance sublimed at 300° at 10 mm. pressure, but there was not enough for identification purposes. It was probably terephthalic acid.

An oxime of the ketone was prepared and melted at 142-3°

31. Herb, Ann., 258, 10 (1890).

after two recrystallizations from alcohol and water. It was not analyzed.

Nitration of 2-(p)Toluylfuran.

A nitrating mixture was prepared at -5° from 11 g. of fuming nitric acid and 20 g. of acetic anhydride. The solution was cooled to -10° , and maintained below that temperature during the addition of 5 g. (0.027 mole) of 2-(p)toluylfuran dissolved in 10 g. of acetic anhydride. After addition was complete, the solution was stirred for one hour, poured cautiously onto ice and treated in a manner already described, using pyridine. The yield was 2.1 g. (34%) of 5-nitro-2-(p)toluylfuran, melting at $122-3^{\circ}$.

Anal. Calcd. for $C_{12}H_9O_4N$: N, 6.04. Found: N, 6.18 and 6.22.

The nitro ketone was oxidized with acid 3% permanganate solution, giving as the only product p-toluic acid, which was identified by mixed melting point methods.

Preparation of 2-(p)Anisoylfuran.

This compound has already been prepared by the methylation of 2-(p)hydroxybenzoylfuran (32), and a reaction between ani-

32. Gilman and Dickey, Rec. trav. chim., 52, 389 (1933).

sole, furoyl chloride and aluminum chloride in carbon disulphide (33). However, the first method has the disadvantage of indirect procedure, and in the second the yields are not as satisfactory as could be desired.

To a solution of 26.6 g. (0.2 mole) of 2-furoyl chloride in 200 g. of anisole cooled in an ice-bath, 50 g. (0.375 mole) of Eastman resublimed aluminum chloride were added during the course of forty minutes, stirring vigorously. The ice-bath was then removed and the solution, which had assumed a deep red color, was stirred an additional eight hours at room temperature. At this point the solution was poured cautiously upon ice and extracted twice with ether. The ether extract was dried over anhydrous sodium sulfate and distilled under reduced pressure, collecting that fraction which boiled at 210-11° at 17 mm. The product weighed 36 g., a yield of 94% of the theoretical, and upon standing solidified. The melting point was 63-4° and without recrystallization showed no depression in a mixed melting point determination with a sample prepared according to Dickey (32). A small amount of phenol was isolated during distillation and the recovery of anisole was almost quantitative.

33. Gilman and Hewlett, Iowa State Coll. J. Sci., 4, 27 (1929).

Bromination of 2-(p)Anisoylfuran.

1st Run. To a boiling solution of 8 g. (0.04 mole) of 2-(p)anisoylfuran in 200 cc. of anhydrous petroleum ether (boiling at 60-68°) 7 g. (0.044 mole) of bromine in 30 cc. of petroleum ether were added dropwise. A precipitate of red needles formed, and after 15 minutes further reflux, the flask was cooled under the water tap and its contents filtered. Since no hydrogen was evolved during the addition, the product was probably 2-(p)anisoyl-4,5-dibromo-4,5-dihydrofuran. The compound is rather unstable in the solid form, hydrogen bromide evolving, a circumstance which caused poor values for bromine upon analysis. The yield was 13.1 g. (91%), melting with decomposition at 131-2° after one recrystallization from glacial acetic acid. The solution must not be warmed to the boiling point of acetic acid, since the product decomposes rather rapidly above 100°, even in solution. Moisture likewise accelerates decomposition, even at room temperature.

Bromination was also run in carbon tetrachloride and in chloroform, but the products obtained were sticky red masses, formed probably by partial decomposition during removal of the solvent.

Anal. Calcd. for $C_{12}H_{10}O_3Br_2$: Br, 44.09. Found: Br, 43.06 and 42.74.

The product was oxidized with acid 3% permanganate solu-

tion, obtaining only *p*-anisic acid (34), melting at 180-1°. A mixed melting point determination with authentic *p*-anisic acid showed no depression.

Two grams (0.006 mole) of the red compound were boiled briskly for 10 minutes in 25 cc. of glacial acetic acid and poured into 100 cc. of water. The resultant yellow oil was recrystallized twice from alcohol and water, obtaining 1.4 g. (89%) of 5-bromo-2-(*p*)anisoylfuran, melting at 73-4°. A mixed melting point determination with the product to be described under "2nd Run" showed no depression.

2nd Run. To a boiling solution of 8 g. (0.04 mole) of 2-(*p*)anisoylfuran dissolved in 150 cc. of chloroform 7 g. (0.044 mole) of bromine in 20 cc. of chloroform were added dropwise. When addition was complete, the flask was exposed to the light of a 100-watt bulb, held four inches from the reaction mixture. After about three minutes, hydrogen bromide was copiously evolved and had practically ceased to be evolved after about 40 minutes refluxing. The solvent was removed under reduced pressure at room temperature, obtaining a light yellow oil which, after crystallization from ethanol and water (using Norite), melted at 73-4°. The yield was 9.4 g. (84%) of 5-bromo-2-(*p*)anisoylfuran.

34. Graebe, Ann., 340, 211 (1906).

Anal. Calcd. for $C_{12}H_9O_3Br$: Br, 28.54. Found: Br, 28.24 and 28.36.

The bromo ketone was treated with nitrogen trioxide at 120° for 12 hours, at the end of which the contents of the flask solidified. After cooling and removing the nitrogen trioxide by suction, the product was recrystallized from alcohol, melting at $126-7^\circ$. From one gram of 5-bromo-2-(p)anisoylfuran there was obtained in this manner 0.76 g. (83%) of 5-nitro-2-(p)anisoylfuran in the form of light yellow needles. Oxidation with acid 3% permanganate solution gave p-anisic acid only, which was identified by mixed melting point methods.

Anal. Calcd. for $C_{12}H_9O_5N$: N, 5.67. Found: N, 5.55 and 5.49.

Since the experimental procedure may be a bit difficult to follow, the proof of orientation in the above substitutions is presented here. In the compound obtained by addition of bromine to anisoylfuran the bromine must have entered the furan ring, since oxidation gave p-anisic acid only. Elimination of hydrogen bromide from this product by two methods resulted in a monobrominated ketone (as shown by analysis) in which the bromine was still in the furan ring. That the remaining bromine was in the 5-position is established by replacement with nitrogen trioxide, since numerous attempts to replace furan

beta-halogens by this method have been entirely unsuccessful (35). Rearrangement of either the bromine or the nitro group from the furan ring to the anisyl nucleus did not occur, since analysis of the final product in the series of transformations resulted in p-anisic acid only.

In order to establish the identity of the dinitrated ketone described under the next heading, the following experiment was performed.

To 0.5 g. of fuming nitric acid contained in a watch-glass, cooled in tap-water, there was added 0.2 g. of 5-nitro-2-(p)anisoylfuran during the course of three minutes, stirring vigorously. The solution was at once diluted with five volumes of water and filtered. Upon two recrystallizations from ethanol 0.11 g. of 5-nitro-2-(4)methoxy(3)nitrobenzoylfuran, melting at 123-4°, were obtained. A mixed melting point determination with 5-nitro-2-(p)anisoylfuran showed a range of 102-110°. Weights in this experiment were only approximate, and accordingly the percentage yield was not calculated.

Anal. Calcd. for $C_{12}H_8O_7N_2$: N, 9.59. Found: N, 9.47 and 9.43.

Oxidation of the product with acid 3% permanganate solution gave 3-nitro-4-methoxybenzoic acid (36) only, melting at

35. Unpublished work of Mr. J. A. V. Turck, Jr.

36. Steermer and Behn, Ber., 34, 2459 (1901).

186-7°. The identity of this acid was established by mixed melting point methods.

Nitration of 2-(p)Anisoylfuran.

1st Run. To a nitrating mixture prepared from 11 g. of fuming nitric acid and 20 g. of acetic anhydride at -5°, there was added dropwise a solution of 5 g. (0.025 mole) of 2-(p)anisoylfuran in 10 g. of acetic anhydride, maintaining the temperature below -10°. After an hour's additional stirring at this temperature the mixture was poured cautiously onto ice and worked up in the previously described manner, using pyridine. The product was a red tar which finally was purified by repeated crystallization from alcohol to yield 3.2 g. (44%) of 5-nitro-2-(4)methoxy(3)nitrobenzoylfuran melting at 123-4°. A mixed melting point determination with the compound obtained by nitration of 5-nitro-2-(p)anisoylfuran showed no depression. A mixed melting point taken with 5-nitro-2-(p)anisoylfuran melted over a range of 100-110°.

2nd Run. The nitration was repeated exactly as in the above run, except that the amount of fuming nitric acid used was only 4.5 g. The results were similar to those recorded above, the yield of 5-nitro-2-(4)methoxy(3)nitrobenzoylfuran being 41% of the theoretical.

3rd Run. A procedure exactly the same as the first case

was employed here, except that the nitrating mixture was prepared from 4.5 g. of fuming nitric acid and 40 g. of acetic anhydride, and the mixture was hydrolyzed immediately after addition was complete. The product obtained was a mixture of the dinitro ketone and unnitrated starting material. Separation, effected by a rather tedious fractional crystallization from alcohol and water, resulted in a 29% yield of 5-nitro-2-(4)methoxy(3)nitrobenzoylfuran and a 12% recovery of the original ketone. Both were identified by mixed melting points.

4th Run. To a nitrating mixture prepared in the usual manner from 3.15 g. (0.05 mole) of fuming nitric acid and 30 g. of acetic anhydride, a solution of 10.1 g. (0.05 mole) of 2-(p)anisoylfuran in 15 g. of acetic anhydride was added dropwise with efficient stirring, maintaining the temperature below -56 by means of dry ice and acetone. Immediately after complete addition the mixture was poured onto ice and worked up as in the 3rd Run. There were thus obtained 3.5 g. (24%) of 5-nitro-2-(4)methoxy(3)nitrobenzoylfuran and 5.2 g. (52%) of 2-(p)anisoylfuran. Both products were identified by mixed melting point methods.

All of the above runs were repeated at least once and the results varied only slightly from those given above.

Attempts to Nitrate 5-Nitro-2-benzoylfuran.

1st Run. To a nitrating solution of 5 g. of fuming nitric acid in 9 g. of acetic anhydride prepared at -5° , there was added 3 g. (0.0145 mole) of 5-nitro-2-benzoylfuran, prepared according to Young (8), stirring incessantly and maintaining the temperature below -10° . One hour after addition was complete the mixture was poured onto ice, filtered, and the yellow solid recrystallized from alcohol. The yield was 3 g. of unchanged 5-nitro-2-benzoylfuran identified by a mixed melting point determination with the starting material. The compound melts at $109-110^{\circ}$ (8).

2nd Run. Three grams (0.0145 mole) of 5-nitro-2-benzoylfuran were allowed to stand twelve hours at room temperature with 6 g. of fuming nitric acid and the solution poured onto ice. Subsequent treatment (see 1st Run) resulted in a quantitative recovery of the starting material.

3rd Run. Precisely the same amounts of ketone and fuming nitric acid as in 2nd Run were warmed at 50° for thirty minutes, cooled and worked up in the manner described. An almost quantitative recovery (91%) of the original nitro ketone resulted. Longer heating (one hour) at this temperature produced almost identical results, and higher temperatures ($70-80^{\circ}$) gave some oxidation as evidenced by isolation of benzoic acid as well as recovered 5-nitro-2-benzoylfuran (mixed melting point).

4th Run. Three grams (0.0145 mole) of 5-nitro-2-benzoyl furan were warmed at 50° for thirty minutes with a mixture of 6 g. of concentrated sulfuric acid and 6 g. of concentrated nitric acid with stirring. The heat source was removed and stirring continued for twelve hours. After treatment with ice the product was worked up as before, obtaining 2.6 g. (87%) of the original nitro ketone (mixed melting point).

In none of these runs was any dinitro ketone isolated, nor was there any indication of nitration.

Nitration of 2,5-Dibenzoylfuran.

The method described by Phelps and Hale (5) (refluxing the diketone with concentrated nitric acid) proved rather ineffective, only a mixture of nitrobenzoic acids and the high-melting compound being isolated. After several ineffective experiments in which either no nitration occurred or else only the highly nitrated compound resulted, a fair method was found. This method did not, however, always give identical results, and did not always produce some of the mononitro compound; a difficulty which seemed to predominate when larger runs than that about to be described were performed.

Ten grams (0.16 mole) of fuming nitric acid were cooled in a freezing mixture and 10 g. (0.036 mole) of 2,5-dibenzoylfuran were added at such a rate that no fumes evolved and the

temperature remained below 15°. The ice-bath was removed and the solution allowed to stand at room temperature for twelve hours, then poured onto ice. The gummy solid was extracted twice with boiling alcohol and the residue recrystallized from acetic anhydride, melting then at 193-4°. The yield was 6.7 g. (51%) of a product which was probably 2,5-di(m)nitrobenzoyl 3-nitrofuran.

Anal. Calcd. for $C_{16}H_9O_9N_3$: N, 10.47. Found: N, 10.66 and 10.59.

Oxidation of the product gave m-nitrobenzoic acid only, melting at 138-9°. A mixed melting point determination with a specimen of the authentic acid showed no depression.

The alcohol-soluble portion was fractionally crystallized from alcohol and water, yielding, after a tedious manipulation, 0.85 g. (7.4%) of what may have been 2,5-dibenzoyl-3-nitrofuran melting at 130-1°, and 2.2 g. (22%) of unchanged dibenzoylfuran, identified by mixed melting point methods. 2,5-Dibenzoylfuran melts at 106-7° (5).

Anal. Calcd. for $C_{16}H_{11}O_5N$: N, 4.36. Found: N, 4.58 and 4.51.

Oxidation of one gram of the suspected nitro diketone, using two methods; namely, acid 3% permanganate solution and 20% chromic acid in acetic acid solution, gave respectively 0.21 g. and 0.11 g. of an acid containing carbon, hydrogen, and oxygen

only, and melting at 133-4° after recrystallization from water. Although a qualitative test for nitrogen was negative a mixed melting point determination with m-nitrobenzoic acid was performed, and as expected the melting range was very low; 110-115°. A series of mixed melting point determinations failed to establish the identity of the unknown as furoic acid, mandelic acid, cinnamic acid, maleic acid or benzoic acid. Saponification equivalents of 155 and 154 were obtained. The substance did not respond to tests for alpha-hydroxy or keto groups. It did not decolorize permanganate or bromine solutions. It is probable that the original nitro compound contained no furan ring, since similar oxidations of the unsubstituted 2,5-dibenzoylfuran resulted in benzoic acid only.

Attempts to Mercurate 2,5-Dibenzoylfuran.

1st Run. Five grams (0.018 mole) of 2,5-dibenzoylfuran were shaken with 6 g. (0.018 mole) of mercuric acetate in 50 cc. of 25% ethanol for seven days at room temperature. The mixture was filtered, obtaining 5 g. (100%) of the original diketone melting at 106-7° without purification. A mixed melting point determination with authentic 2,5-dibenzoylfuran confirmed the product's identity.

2nd Run. Precisely the same quantities of material as above were refluxed in an oil-bath for six hours, cooled and

filtered. One recrystallization from ethanol resulted in 4.8 g. (96%) of pure 2,5-dibenzoylfuran, identified by mixed melting point methods.

3rd Run. Five grams (0.018 mole) of 2,5-dibenzoylfuran were refluxed with 6 g. (0.019 mole) of mercuric acetate in 70 cc. of glacial acetic acid for 24 hours. The solution was cooled, poured into water and the slightly gummy solid was recrystallized twice from ethanol. Thus were recovered 4.6 g. (92%) of the original dibenzoylfuran, identified by mixed melting point.

Preparation of 2-Cyanopyridine.

This preparation is mentioned because of the long period of time consumed in futile efforts to repeat previous methods, and because an excellent method of synthesizing ethyl picolinate has been devised.

The first synthesis attempted was that illustrated by the following series of transformations.



The first two steps were carried out in one series of operations, the method employed being a combination and slight modification of Wibaut's preparation of picolinic acid (37) and

37. Wibaut, Rec. trav. chim., 45, 657 (1928).

Engler's esterification of the acid (38).

One hundred grams (1.08 moles) of 2-picoline (Eastman) were dissolved in one liter of water and heated to 70°. The solution was stirred constantly while adding a solution of 340 g. (2.14 moles) of potassium permanganate in two liters of water during the course of three hours, maintaining the temperature at 70-80°. The mixture was allowed to cool overnight, filtered and the brown precipitate extracted thrice with 500 cc. of boiling water. The combined filtrates were neutralized (using methyl orange) with sulfuric acid and evaporated to dryness under reduced pressure, not allowing the temperature to rise above 75° because of the volatility of picolinic acid. The residue was extracted for 20 hours with 500 cc. of absolute ethanol in a Soxhlet apparatus, taking precautions to exclude moisture.

The extract was placed in a liter 3-neck flask and a rapid stream of hydrogen chloride introduced, stirring constantly and refluxing vigorously. A solid hydrochloride was first formed, but dissolved slowly upon long heating (three to four hours after formation). The condenser was then set for distillation and the alcohol removed by distilling in a continuous stream of hydrogen chloride. The cooled mixture was neutralized with a saturated solution of sodium carbonate, not allowing the tem-

38. Engler, Ber., 27, 1784 (1894).

perature to rise above 10° . The resulting emulsion was then saturated with solid sodium carbonate and extracted six times with ether. The combined extracts were dried over anhydrous potassium carbonate and fractionated. The product was 83 g. (55%) of ethyl picolinate boiling at $241-2^{\circ}$. This figure checks Engler's boiling point (38) and identity was firmly established by an alkaline hydrolysis to ethanol and picolinic acid, melting at $136-7^{\circ}$. A mixed melting point determination with a sample of the acid prepared according to Wibaut (37) showed no depression.

The amide was prepared by allowing the above ester to stand 12 days at room temperature with 10 times its weight of concentrated ammonium hydroxide (38). The yields ranged from 55-60%. The melting point of the product agreed with that of Engler, which was $105-6^{\circ}$. Recrystallization from ether did not raise the melting point.

Attempts to prepare 2-cyanopyridine by dehydration of picolinamide with thionyl chloride according to H. Meyer (39) gave none of the desired compound. The reaction was run three times, resulting in a hard polymerization product and tar each time.

1st Run. Fifteen grams (0.11 mole) of picolinamide, dried

39. Meyer, Monatsh., 23, 438, 900 (1902).

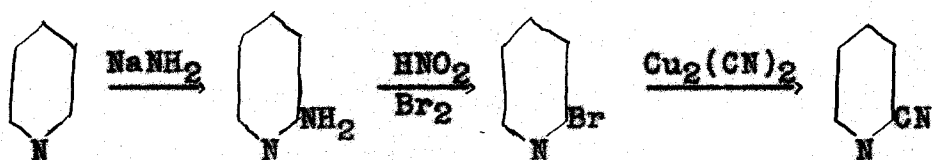
in vacuo over potassium hydroxide, dissolved in 150 cc. (excess) thionyl chloride (Rubber Service Laboratories Co.) were refluxed eight hours, using a spiral condenser which was fitted with a trap filled with chloroform. After cooling, the mixture was poured cautiously onto ice and the hard granular substance removed by filtration. The filtrate was extracted with the chloroform from the trap, the extract washed with 10% sodium carbonate solution and distilled. The extraction was repeated four times using the same chloroform throughout. The small amount of tarry material remaining in the distillation flask was extracted with hot ether and the extract allowed to stand in the ice-box for several weeks. No product had separated from solution at the end of this time, and no residue was left upon distillation. An attempt to distill the tarry material resulted in failure only. Attempted extraction and distillation of the hard material previously removed were also futile.

2nd Run. The same operations as above were performed using Eastman thionyl chloride. The results did not vary from those of the first run.

3rd Run. The thionyl chloride (Eastman) was distilled thrice from 50 g. of beeswax in 100 cc. of cottonseed oil (a fresh solution was used for each distillation) since it has been observed that some chlorination and polymerization occurs when attempts to prepare the acid chloride of picolinic acid

were made using impure thionyl chloride (40). Other conditions were as before, and the result also followed the previous course.

The above method of preparation of 2-cyanopyridine was then abandoned and attention was directed to the following series of reactions (41).



Because of the uneventful manner in which the above syntheses allowed themselves to be performed, detailed directions will not be given here. The over-all yield of 2-cyanopyridine was 41%, and the physical constants observed compared very favorably with those reported. The boiling point was 221-2°, and the melting point was 26° after one recrystallization from ether. The reported values are 222-3° (41) and 26° (39) respectively.

Attempt to Prepare 2-(2)Furoylpyridine.

2-Furylmagnesium iodide was prepared from 9.3 g. (0.048 mole) of 2-iodofuran (42) and 1.15 g. (0.048 mole) of magnes-

40. Spaeth and Spitzer, *Ber.*, 59, 1477 (1926).

41. Craig, *J. Am. Chem. Soc.*, 56, 231 (1934).

42. 2-Iodofuran was prepared from 2-Chloromercurifuran and iodine solution according to Gilman and Wright (26).

ium turnings in 50 cc. of anhydrous ether under an atmosphere of nitrogen. To the filtered Grignard reagent was added a solution of 5 g. (0.047 mole) of 2-cyanopyridine in 20 cc. of anhydrous ether, stirring vigorously and cooling in an ice-bath. A color test was negative at the end of twenty minutes, and after an hour's additional stirring at room temperature the solution was hydrolyzed with iced 10% hydrochloric acid. When the initial reaction had subsided the mixture was refluxed for three hours and made strongly alkaline with 10% sodium hydroxide. The aqueous layer was extracted twelve times with 50 cc. portions of ether, the combined extracts dried over anhydrous potassium carbonate and the solvent removed by distillation. The residue was a few drops of a tarry solid which would respond to neither distillation nor crystallization from a variety of solvents; alcohol, acetone, acetic acid, benzene, carbon tetrachloride, xylene and pyridine.

Three more attempts were made in the same general manner as above, but the final results were invariably the same. In one run the reaction mixture was refluxed for three hours before hydrolysis, and the acidified product was exactly neutralized with sodium carbonate. In another run the hydrolyzed mixture was not heated after addition of the hydrochloric acid, and worked up according to the detailed procedure. In the final run the mixture was heated for six hours after hydrolysis,

and after neutralization with sodium carbonate, the mixture was extracted with 24 portions of ether.

E. Miscellaneous Studies

Preparation of 2-Furonitrile.

Although furonitrile is by no means a new compound and the following procedure does not differ radically from previous methods (43), from a standpoint of yields and ease of manipulation a more satisfactory synthesis has been developed.

Sixty grams (0.54 mole) of 2-furamide, prepared from 2-furoyl chloride and ammonium hydroxide (44), were heated with 160 g. (excess) of phosphorous pentachloride for one hour. Caution must be observed in the initial application of the heat source (a free flame) since once started, the reaction proceeds with some violence. The resulting phosphorous oxychloride was then removed by distillation, stopping when a vapor temperature of 110° was attained. After cooling, the residue was poured cautiously onto ice and distilled rapidly (an imperative condition) with steam. The distillate was extracted thoroughly with ether, and after drying over anhydrous calcium chloride, the extract was fractionated at atmospheric pressure. The yields

43. Wallach, Ann., 214, 228 (1882); Douglas, Ber., 25, 1313 (1892); Pinner, ibid., 25, 1415 (1892).

44. Lies and Bodart, Ann., 100, 327 (1856).

were 48-49.5 g. (96-98% of the theoretical) of 2-furonitrile boiling at 146-7°. Acid hydrolysis gave 2-furoic acid which was identified by mixed melting point methods.

Nitration of 2-Furonitrile.

1st Run. Sixteen grams (0.17 mole) of furonitrile dissolved in 28 g. of acetic anhydride were added dropwise with efficient stirring to a nitrating mixture prepared from 68 g. of fuming nitric acid and 120 g. of acetic anhydride, maintaining the temperature below -10°. The temperature did not rise appreciably during addition, about fifteen minutes sufficing. Two hours later the reaction mixture was poured onto ice and worked up in a manner previously described, omitting the use of pyridine. The product weighed 14.1 g. (88%), and was apparently unchanged 2-furonitrile, boiling at 146-7°. Identity was firmly established by acid hydrolysis to 2-furoic acid.

2nd Run. Sixteen grams (0.17 mole) of furonitrile were added dropwise to 20 cc. of fuming nitric acid stirring vigorously and maintaining the temperature below 10°. The mixture was stirred for two hours after complete addition, poured onto ice and extracted with ether. The ether extract was washed with a saturated bicarbonate solution, dried over anhydrous sodium sulfate and distilled. The product was 12.4 g. (78%) of unchanged 2-furonitrile identified as before.

3rd Run. Twelve grams (0.13 mole) of furonitrile were dropped into 25 cc. of fuming nitric acid with vigorous stirring, maintaining the temperature below 50°. The mixture was then worked up as in the 2nd Run, recovering 8.1 g. (67%) of furonitrile. Investigation of the mother liquors resulted in the isolation of 1.8 g. of oxalic acid, melting at 99-100°. A mixed melting point determination with authentic oxalic acid showed no depression.

4th Run. Ten grams (0.11 mole) of 2-furonitrile were added dropwise with efficient stirring to a mixture of 27.5 g. of concentrated nitric acid and 27.5 g. of concentrated sulfuric acid, maintaining the temperature below 0°. After addition was complete the mixture was stirred for one hour at room temperature and poured onto ice. The resulting mixture was worked up as before, resulting in 2.4 g. (16%) of 5-nitro-2-furonitrile, melting at 67-8° after two recrystallizations from petroleum ether (b.p., 60-68°).

Anal. Calcd. for $C_5H_2O_3N_2$: N, 20.29. Found: N, 20.40 and 20.47.

Acid hydrolysis of the product resulted in an 80% yield of 5-nitro-2-furic acid (4), melting at 183-4°. A mixed melting point determination with an authentic specimen showed no depression.

No furonitrile could be recovered from this run, but 0.75 g.

of oxalic acid were isolated (identity was established by mixed melting point).

Nitration of Methyl Benzoate.

This experiment was performed in order to compare the conditions of nitration to those successful for methyl 2-fur-oate.

To a mixture of 40 g. of acetic anhydride and 22 g. of fuming nitric acid prepared at -5° , 10 g. (0.074 mole) of methyl benzoate were added dropwise, maintaining the temperature below -5° , and stirring vigorously. There was no appreciable rise in temperature during addition, and after this was complete the mixture was stirred for two hours and poured onto ice. The resulting mixture was treated in a manner already described, omitting the use of pyridine. Finally there was obtained 9.2 g. (92%) of methyl benzoate boiling at $106-7^{\circ}$ at 22 mm. pressure. The product was identified by an alkaline hydrolysis to benzoic acid and methanol.

Two runs identical to that just described, except that ethyl benzoate was used in one, were carried out. The results were, as before, practically quantitative recovery of the un-nitrated ester.

Attempts to Acetylate Methyl 5-Bromo-2-furoate.

1st Run. To a solution of 20.5 g. (0.1 mole) of methyl 5-bromo-2-furoate (45) and 10.4 g. (0.1 mole) of acetic anhydride in 100 cc. of dry benzene there was added 54 g. (0.2 mole) of anhydrous stannic chloride with vigorous stirring, cooling meanwhile in an ice-bath. After stirring for one hour at room temperature the mixture was refluxed briskly for four hours, cooled and poured onto ice. The aqueous layer was extracted thoroughly with benzene and the combined benzene layers dried over anhydrous sodium sulfate and distilled under reduced pressure. The product was 19.6 g. (95%) of methyl 5-bromo-2-furoate boiling at 120-22° under 16 mm. pressure, and melting at 66-7° (45). A mixed melting point determination with a sample of the starting material was not depressed. A slight odor of acetophenone was perceptible, but none could be isolated.

2nd Run. When the above reaction was run in precisely the same manner using toluene in place of benzene and, instead of refluxing, maintaining the temperature of the mixture at 80°, 24.1 g. of a mixture boiling at 110-20° under 13 mm. pressure were obtained. This oil was treated with warm 10% sodium hydroxide solution and filtered. After washing the precipitate (which was probably the sodium salt of the enol form of p-methyl-

45. This ester was prepared according to an unpublished method of Dr. R. J. VanderWal. The procedure is the ordinary absolute methanol-hydrogen chloride method. The pure ester melts at 66-7°.

acetophenone) with a small quantity of ether, it was shaken a few minutes with 10% hydrochloric acid and extracted with ether. After drying over anhydrous sodium sulfate the extract was distilled in vacuo, obtaining 4.9 g. (36%) of p-methylacetophenone, boiling at 116-7° at 14 mm. The product was identified by preparation of the oxime (melting at 87-8°), and a mixed melting point determination with an authentic specimen of p-methylacetophenone oxime. This oxime melts at 88° (46).

The mixture which was filtered from the sodium enolate was crystallized from water and proved to be unchanged methyl 5-bromo-2-furoate (mixed melting point methods). The recovery was 18 g. or 87%.

3rd Run. The reaction was next investigated using as a solvent 100 cc. of dry nitrobenzene and maintaining the temperature at 120°. Other quantities and conditions were not altered. Upon distillation (steam distillation of the nitrobenzene can not be used because of the volatility of the ester) 3.4 g. (17%) of methyl 5-bromo-2-furoate were recovered, while a large amount of an intractable tar remained in the distillation flask. The recovered ester was identified as before.

Acetylation of Ethyl 2-Furoate.

This acetylation was performed exactly as in the 2nd Run

46. Widman and Bladin, Ber., 19, 587 (1886).

on methyl 5-bromo-2-furoate, except that the toluene solution was refluxed for four hours after addition was complete. Fourteen and one-tenth grams (0.1 mole) of ethyl 2-furoate were used. Upon distillation there was obtained 6.8 g. (37%) of ethyl 2-furoate boiling at $195-7^{\circ}$, and 5.2 g. of ethyl 5-acetyl-2-furoate, boiling at $128-31^{\circ}$ at 12 mm., and melting at $85-6^{\circ}$. A mixed melting point determination with an authentic sample confirmed the identity of the latter product. According to Calloway (7), pure ethyl 5-acetyl-2-furoate melts at $85-6^{\circ}$. The ethyl furoate was identified by an alkaline hydrolysis to ethanol and furoic acid. No *p*-methylacetophenone could be isolated after a thorough investigation, although a faint odor of this substance could be detected.

This reaction was checked, obtaining similar results.

Acetylation of 2,5-Dimethylfuran.

To a solution of 20.4 g. (0.2 mole) of acetic anhydride and 19.2 g. (0.2 mole) of 2,5-dimethylfuran in 125 cc. of dry toluene, 104 g. (0.4 mole) of anhydrous stannic chloride were added dropwise during the course of one hour, stirring vigorously and cooling in an ice-bath. After addition was complete the cooling bath was removed, the contents of the flask allowed to come to room temperature and then refluxed for six hours. After cooling, the mixture was poured cautiously onto ice, the layers separated, and the aqueous layer extracted well with

toluene. The combined toluene solutions were dried over anhydrous sodium sulfate and fractionated. The yield was 16.3 g. (59%) of 3-acetyl-2,5-dimethylfuran boiling at 89-90° at 14 mm. pressure. The compound was identified by preparation of the oxime which melted at 77-8°. A mixed melting point determination with a sample of authentic 3-acetyl-2,5-dimethylfuran oxime (melting at 78°) (7) showed no depression.

No *p*-methylacetophenone was isolated from the reaction mixture, the only other product than the acetylated dimethylfuran being a large amount of a non-volatile resin, which is always present when positively substituted furans are treated with acidic reagents. There was no noticeable odor of *p*-methylacetophenone; any such odor, however, would have been masked by the pungent odor of the main reaction product.

E. General Observations on Experimental Technique.

This topic is introduced here since the fine points of experimental detail, which are in many instances the most important, are too often neglected. The following observations have been gathered not only from the work embraced in the previous pages, but also from other investigations outside the scope of this thesis.

Nitration.

When nitrating compounds containing furan nuclei with the nitric acid-acetic anhydride mixture several interesting points arise. In the process of neutralization of the hydrolysis mixture it has been found that the use of sodium bicarbonate is very desirable, although a tedious process. Some prefer to partially neutralize with sodium hydroxide until a brown color is observed and then finish the neutralization with bicarbonate. In the experience of the writer the use of sodium hydroxide or carbonate has always been followed by a lowering of the yield.

In the nitration process some attention must also be paid to the pyridine employed. Pyridine which has been allowed to remain in contact with strong alkali should not be used, since it is apparently contaminated with traces of alkali, toward which nitrofurans are decidedly unstable. Pyridine is not absolutely necessary in all cases, since long standing in ether solution (six weeks in the case of methyl 5-nitro-2-furoate) accomplishes the same end.

Many times it will be observed that a brown, resinous substance separates from solution after the pyridine has been added. This occurrence is always accompanied by poor yields, or none at all, and the problem of its circumvention has not yet been solved nor adequately attacked.

The final removal of the solvent from the nitro compound

is best performed in vacuo at room temperature, since some nitrogen oxides are evolved at higher temperatures; yet the purified products are stable towards heat, although it is inadvisable to attempt distillation of them.

Oxidation.

In most cases, a 3% potassium permanganate solution, acidified with twice the calculated amount of sulfuric acid, was used. Apart from the fact that the use of acid oxidation is imperative for derivatives of nitrofuran, it is also the quickest and requires fewer manipulations after completion. To cite one example, an acid permanganate oxidation of p-(4)nitrophenyl-stearophenone was complete in twenty minutes, whereas an alkaline oxidation of the same strength required three days of constant refluxing.

Friedel-Crafts Reactions.

The path of this reaction in furan chemistry is beset with difficulties, most of which have been thoroughly discussed elsewhere (47). Nevertheless, there remain one or two points not yet covered.

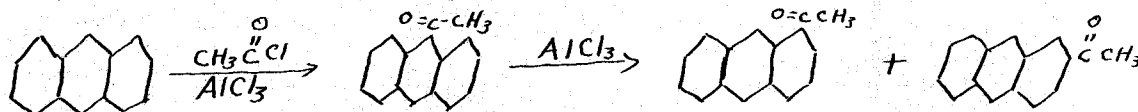
When using furcyl chloride in this type of reaction, es-

47. Ph.D. dissertation of N. O. Calloway (1934).

pecially when the other reactant does not serve as the solvent, the aluminum chloride should be added last. Departure from this order increases the amount of resinous product and decreases the yield of furyl aryl ketone.

Eastman's resublimed aluminum chloride, free from iron, has been found to be very satisfactory in furanic Friedel-Crafts reactions. Other brands, which for the most part, have a yellow color denoting iron, greatly enhance the probabilities of resinification.

It may be well to add here that the unreliability of the Friedel-Crafts reaction is of consequence for the most part in alkylation only, or in reactions involving a halogenated nucleus. Only one instance is to be found in the literature where acylation is irregular. This evidence is the migration of an acetyl group in an anthracene molecule (where rearrangement is relatively common) (48). By careful use of exactly the theo-



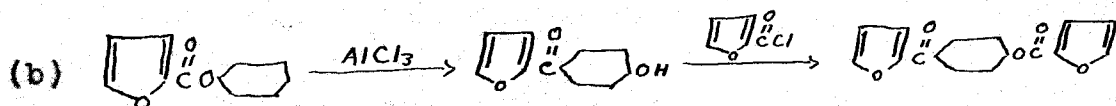
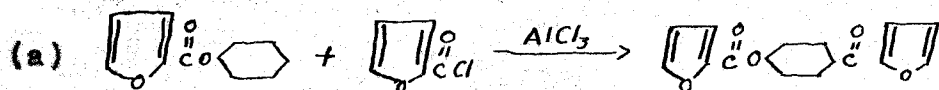
retical amount of aluminum chloride it is possible to stop at the 9-acetylanthracene.

48. German Patent 492,247 (1926) Chem. Zentr., 1930, I, 2631.]

DISCUSSION OF RESULTS

Perhaps one of the most striking items of evidence supporting the hypothesis that furan is more aromatic than benzene is to be found in a substitution reaction upon phenyl 2-furoate. Upon nitration of phenyl benzoate, 4-nitrophenyl benzoate is obtained (49), demonstrating that the carboxylic group markedly inhibits substitution in the acidic fragment of the molecule. In view of this evidence it will be readily conceded that in the phenyl furoate molecule the phenolic fragment has a decided advantage over the acidic fragment—if all else were equal. Nitration of phenyl 2-furoate, however, resulted in a satisfactory yield of phenyl 5-nitro-2-furoate, no other organic compound being isolated, establishing beyond doubt the greater aromaticity of the furan nucleus.

To be sure, in a reaction between phenol, furoyl chloride and aluminum chloride (32) some *p*-furoylphenyl 2-furoate is formed, which might be attributed to a Friedel-Crafts reaction between phenyl furoate and furoyl chloride (a), or more likely, to the furoylation of *p*-hydroxybenzoylfuran (b).



49. Schiaparelli, Gazz. chim. ital., 11, 78 (1880).

That the first mechanism may not be correct is indicated by the results of an attempted acetylation of phenyl 2-furoate by means of the Friedel-Crafts reaction, reported in this thesis, where neither aromatic nucleus was attacked. This may be a rather broad statement since only a portion of the original ester was recovered. It may be that the molecule was partially acetylated, and the resulting substituted ester combined with part of the stannic chloride to give the resin which was observed during isolation of the product. It is not unusual for furoic esters to form refractory resins in this particular type of the Friedel-Crafts reaction (50), especially when run in carbon disulphide solution.

However, even if the first mechanism were assumed to be correct the discrepancy between this reaction and the nitration of phenyl furoate might be explained by the fact that the furan nucleus is not known to undergo substitution in Friedel-Crafts reactions employing aromatic acid chlorides or anhydrides and aluminum chloride (51). On the basis of that fact it would be expected that substitution would occur in the phenolic fragment of the molecule.

The nitration of aryl furoates in which the phenolic res-

50. Unpublished work of the author.

51. A few instances are known where this reaction is successful when stannic chloride is used instead of aluminum chloride (7).

idue was much more aromatic than benzene itself unfortunately did not take the course of that with phenyl furoate. 3-Methoxyphenyl furoate and 2-naphthyl 2-furoate gave products in which the nitro group had entered the phenolic and naphthyl fragments of the molecules. It must not be assumed on that account, however, that these nuclei are more aromatic than furan, since the carboxylated furan residue is at a distinct disadvantage, and the results obtained are therefore of little value to the issue. They do show that the benzene nucleus is susceptible to nitration under the conditions of the nitric acid-acetic anhydride technique; a point which had not previously been established.

It would be difficult to indicate the point in the nitration of 3-methoxyphenyl 2-furoate where hydrolysis occurred, nor is it necessary to do so since the small amount of nitro ester which was obtained was not substituted in the furan ring.

The unsuccessful attempts to nitrate diphenyl dehydromucate emphasize the difficulty of introducing a group in the beta-position; a difficulty which is greatly increased in this case because of the presence of two carboxylic groups in the molecule. The only nitrated product obtained in this reaction was picric acid, the formation of which may have followed hydrolysis of the ester, or the nitro ester may have been formed first and hydrolysis occurred later.

In the case of furylphenylethylene it was thought that

bromination might occur in the furan ring rather than at the ethylenic bond, since symmetrical diaryl ethylenes do not add bromine too readily (52). For instance, it is necessary to reflux a solution of stilbene and bromine in carbon tetrachloride in order to effect addition in good yields (53). It is difficult to say where bromination did occur because the reaction product decomposed upon attempted isolation. The attempt to nitrate furylphenylethylene was rather optimistic when one considers the ease with which arylated olefines undergo lateral nitration (54).

It is not surprizing that furylphenylmethane did not undergo nuclear substitution in view of the highly activated lateral hydrogens. Although Paul (55) prepared a mercurial of furylphenylmethane, duplication of his results could not be effected in this laboratory. Not even traces of his reported compound were to be found (56). While asserting that the chloromercuri group entered the furan residue in the 5-position, he offers no proof of his statement.

The bromination, sulfonation and nitration of furyl aryl

52. Bauer and Moser, *Ber.*, 48, 919 (1915).
53. Unpublished work of the author.
54. Lorenz, *Ber.*, 7, 1097 (1874); *ibid.*, 8, 1050 (1875).
Blythe and Hofmann, *Ann.*, 53, 297 (1845).
55. Paul, *Compt. rend.*, 200, 1481 (1935).
56. Page 30, this thesis.

ketones quite adequately attest the super-aromaticity of furan. From these experiments it will be perceived that the furyl radical is more aromatic than even the *p*-anisyl radical, which is one of the most electronegative radicals in Kharasch's series. It is quite likely that the *p*-anisyl and 2-furyl radicals occupy very nearly the same position in an aromaticity series if one may judge from the results of competitive nitration of 2-(*p*)anisoylfuran. Here two nitro groups were introduced into the molecule in spite of reasonable precautions, a result which has not previously been reported in experiments employing this particular technique. Incidentally, since the *p*-anisyl radical nitrates readily under these conditions while the *p*-toluyl and phenyl radicals do not, anisole is shown to be more aromatic than toluene or benzene; a fact which did not need confirmation.

Competitive bromination of 2-(*p*)anisoylfuran resulted in substitution in the furan ring only. That the bromine was in the 5-position was established by replacement with nitrogen trioxide to give a nitrofuryl anisyl ketone. This reaction has not yet been successful with beta-halogenated furans (57). Oxidation of the bromo ketone gave *p*-anisic acid only, so the bromine must have been in the furan ring.

57. Unpublished work of Mr. J. A. V. Turck, Jr.

Sulfonation of 2-benzoylfuran resulted in a compound in which the sulfonic group had entered the furan ring. Thus, to repeat, we have three orthodox reactions, sulfonation, bromination and nitration, which confirm the theory that furan is super-aromatic.

The mercuration of furan derivatives is at best a reaction difficult to control, and is unsatisfactory from several standpoints. Complexes of the mercurating agent with the functional group may be formed, and polymercurated compounds are quite common. Throughout the series of mercurations reported in these pages none of the desired results was realized. At what door these failures are to be laid is an open question. They may have been due to the presence of lateral unsaturation, lateral labile hydrogens, keto groups, or to possible impurities in the reagents used, etc., but one may not speak of these reasons with any degree of confidence. The amount of mercury present in the molecule of the reaction product was in each case inordinately high, and corresponded to no calculated values for mono- or polymercuration.

Another group of experiments which furnished unexpected results was the failure to effect successful nitration of 5-nitro-2-benzoylfuran. The phenyl radical was granted in this case a certain advantage which it failed to utilize. To state on the basis of these data that the furan beta-carbon atom is

possessed of about the same order of aromaticity as the benzene ring would, of course, be an unwarranted conclusion.

2,5-Dibenzoylfuran was nitrated in an only partially successful attempt to extend the work of Phelps and Hale. The higher melting compound obtained was most probably 2,5-di(m)nitrobenzoyl-3-nitrofurane, but the identity of the lower melting product is still undetermined. Analysis was satisfactory for a mononitrodibenzoyl furan, but its peculiar behavior toward oxidation methods points to the possibility of a ring scission structure. Upon oxidation of the nitro compound an unidentified acid containing no nitrogen was obtained, while if the furan ring had remained intact one would have expected either benzoic or nitrobenzoic acid to be formed. In contrast to this result is the oxidation of the unnitrated dibenzoylfuran, where benzoic acid only was isolated. Oxidation of the trinitro compound gave, as was to be expected, m-nitrobenzoic acid. All three oxidations were performed under precisely the same conditions. In regard to the monitro compound, it is the opinion of the author that had nitration occurred in a benzene ring both benzene residues would have been substituted because of the symmetry of the molecule, and such a compound would have upon oxidation undoubtedly yielded a nitrogen-containing product, if not nitrobenzoic acid.

The stubborn resistance of the furan beta-carbon towards

substitution is excellently portrayed by the reluctance of 2,5-dibenzoylfuran to undergo mercuration, even under strenuous conditions. The diketone was recovered unchanged in good yields from every attempted mercuration.

The contingency of 2-furonitrile possessing some hitherto unsuspected anomalous properties has been cited on a previous page of this dissertation. The probability is by no means lessened when one considers the nitration of furonitrile, carbomethoxyfuran and their benzene analogs. Methyl and ethyl benzoates do not exhibit the slightest indications of nitration under conditions where eminently satisfactory nitration of the corresponding furcic esters is attained (4). On the other hand, benzonitrile is nitrated readily at -10° in fuming nitric acid (58), while 2-furonitrile requires much more drastic treatment to effect nitration. Both the cyano and carboalkoxy groupings are strong negative groupings and both are strong meta-orientors, in benzene chemistry at least. From the results of others and those described here, there can remain no doubt of the greater aromaticity of the furyl radical when compared to that of the phenyl radical, so there is no obvious reason why the two types, RCN and RCOOR', should exhibit different properties in substitution reactions. To repeat, since neither of the two groupings of the molecule can be at fault when taken singly,

58. Flürscheim and Holmes, J. Chem. Soc., 1928, 2239.

the non-conformity to rule must be due to some property of the molecule formed (C_4H_3OCN) when the two are united. Accordingly, studies performed upon 2-furonitrile cannot assume significance until the cause for irregularity is discovered, and its effect duly taken into account.

Since Calloway (7) has established the super-aromaticity of some derivatives of furan by acetylation of them in benzene solution among other methods, the thought arose that perhaps this technique might be extended to other solvents and other furan derivatives, especially in regards to the beta-carbon. About the only data relative to the aromaticity of the furan beta-carbon atom is the fact that acetylation of 2,5-dimethylfuran using stannic chloride and acetic anhydride in benzene solution, results in satisfactory yields of 3-acetyl-2,5-dimethylfuran only (7). Therefore, in this positively substituted furan, at least, the beta-carbon is more aromatic than the benzene carbon atoms. To be sure, as mentioned in the Introduction of this thesis, it is well known that the furan alpha-carbon atom is probably more aromatic than the beta-carbon atom, since, except in one instance, the substituent always enters an alpha-position if one be available.

Acetylation of 2,5-dimethylfuran with acetic anhydride and stannic chloride in toluene solution gave a good yield of 3-acetyl-2,5-dimethylfuran. No p-methylacetophenone was found,

indicating that the beta-carbon atom in 2,5-dimethylfuran is more aromatic than the toluene nuclear carbon atoms.

Acetylations of methyl 5-bromo-2-furoate were attempted, using acetic anhydride and stannic chloride in benzene and toluene solutions. Since acetylation of the ester just mentioned was not successful in either solvent, yet the toluene, but not the benzene, was acetylated perceptibly, it may be safe to say that the beta-carbon atom in the furan molecule under discussion is of a lesser degree of aromaticity than are the toluene nuclear atoms, and is likely of about the same order, roughly speaking, of the aromaticity of benzene. It will be borne in mind that the furan nucleus in this case is negatively substituted.

Quite the opposite of the data just discussed, acetylation of ethyl 2-furoate with acetic anhydride and stannic chloride in toluene solution, resulted in a fair yield of ethyl 5-acetyl-2-furoate and no p-methylacetophenone. The latter was probably present in traces inasmuch as its distinctive odor was noticeable in the reaction product before purification.

SUMMARY

In a competitive reaction where the phenyl radical was granted an extraordinary advantage the furyl radical has been shown to be super-aromatic.

Nitration, sulfonation and bromination of symmetrical furyl aryl compounds have been employed to demonstrate the super-aromaticity of furan.

Mercuration proved to be devoid of any interpretable results.

The Friedel-Crafts reaction has been used to investigate the relative aromaticity of the furan beta-carbon atom. Negative results only were obtained in an attempt to acetylate an aryl furoic ester in a Friedel-Crafts synthesis.

Some evidence has been obtained to show that 2-furonitrile possesses some unorthodox property or properties, the exact nature of which is unknown.

On the basis of nuclear substitution furan is more aromatic than benzene, toluene or anisole (59), and its aromaticity is of about the same order as that of the last-mentioned structure.

59. Cleavage of organic lead compounds also indicates that furan is more aromatic than anisole [Gilman, et al, J. Am. Chem. Soc., 57, 886 (1935)].

II. HEAVY HYDROGEN IN SOME NATURALLY OCCURRING ORGANIC COMPOUNDS AND MIXTURES

INTRODUCTION

Since the discovery of the heavy isotope of hydrogen in 1932 by Urey (1) and co-workers the investigation of this substance has progressed by leaps and bounds. Due to the differences in association and ionization (2) between heavy water and normal water, it is natural to expect that the selective power of living organisms might effect a partial separation of isotopes in some of the organs or substances necessary to sustain life, although it now appears improbable that important deuterium sources are to be found in such processes.

Among the estimations of the natural abundance of deuterium are to be found those concerned with the amount of heavy water obtained in the combustion of hydrogen-containing organic substances. This work embraces material ranging from mineral products such as coal and kerosene to living bodies such as animal tissues and fruit. The investigation of mineral products is especially interesting, since they may throw some light on the deuterium distribution of the geological age in which the deposits were formed or upon the chemistry of the

1. Urey, Brickwedde and Murphy, Phys. Rev., 39, 164 (1932).
2. Stevens, J. Chem. Physics, 2, 107 (1934); Abel, Bratu and Redlich, Z. Physik. Chem., A170, 153 (1934).

growth and decay of the organic matter responsible.

The substances under investigation were usually burned in the solid state in an air-stream. Where possible, the compound or mixture was vaporized and burned in a torch.

The measurements were made by comparing the specific gravities of the water samples in question with that of a standard. Ordinary water was used for this purpose in most cases. While the exact deuterium content of the standard is not known, it will probably not differ greatly from the value for rain water obtained by Bleakney and Gould (3). This value is generally accepted as the average deuterium content of normal water and is numerically one part in five thousand.

For convenience Table I summarizes the values thus far obtained. Although the table is for the most part self-explanatory, it may be well to state that Δd indicates the density difference between the water under investigation and normal water, expressed in parts per million.

3. Bleakney and Gould, Phys. Rev., 44, 265 (1933).

Table I.

Abundance of Heavy Hydrogen in
Some Naturally Occurring Organic Substances

Origin	Oxygen Source	Δd	Reference
Benzene	Air	7.9	(4) Dole, <u>J. Chem. Phys.</u> , <u>2</u> , 337 (1934)
Benzene	Electr.	0.0	(5) Dole, <u>ibid.</u> , <u>2</u> , 548 (1934)
Oklahoma Kerosene	Air	6.2	(4)
Oklahoma Butane	Linde	6.1	(6) Snow and Johnston, <u>Science</u> , <u>80</u> , 210 (1934)
Petroleum	---	11.0	(7) Fillipova, <u>J. Chem. Physics.</u> , <u>3</u> , 316 (1935)
Natural Gas	Air	5.7	(8) Greene and Voskyl, <u>J. Am. Chem. Soc.</u> , <u>56</u> , 1694 (1934)
Illuminating Gas	---	0.0	(9) Moser, <u>Physik. Z.</u> , <u>35</u> , 682 (1934)
Anthracite Coal	---	0.0	(9) (10) Washburn and Smith, <u>Bur. Standards J. Research</u> , <u>12</u> , 305 (1934)
Natural Propane	---	0.0	(10)
Bamboo	Air	4.4	(11) Okabi and Titani, <u>Bull. Chem. Soc. Japan</u> , <u>10</u> , 465 (1935)
Cedar Wood	Air	4.5	(11)
Willow Wood	Linde	3.2	(12) Washburn and Smith, <u>Science</u> , <u>79</u> , 188 (1934)
Cotton	Air	5.7	(11)

Table I (Continued)

Origin	Oxygen Source	Δd	Reference
Filter Paper	Air	6.3	(11)
Alcohol	Air	3.0	(13) <u>Briscoe, et al, J. Chem. Soc., 1934, 1207, 1948.</u>
Beet Molasses	Air	5.3	(13)
Fusel Oil	—	4.0	(13)
Cane Sugar	Air	7.4	(13)
		7.8	(14) <u>Titani and Harada, Bull. Chem. Soc. Japan, 10, 41 (1935)</u>
Beet Sugar	Air	6.5	(14)
Dextrose	Air	6.4	(14)
Lactose	Air	5.9	(14)
Soluble Starch	Air	3.9	(14)
Rice Flour	Air	6.0	(14)
Wheat Flour	Air	6.0	(14)
Dextrin	Air	5.4	(14)
Potato Starch	Air	5.9	(14)
Galactan	Air	4.8	(14)
Mannan	Air	5.8	(14)
Corn Oil	Air	4.9	(8)
Honey	Air	4.1	(4)
Fruits	—	0-5	(13)
Human Blood	—	1.5	(13)

Table I (Continued)

Origin	Oxygen Source	Δd	Reference
Human Milk	—	3.0	(13)
Human Urine	—	0.0	(13)
Cows Milk	—	-1.0	(13)
Ox Blood	—	3.0	(13)
Cholesterol	Air	0.0	(5)
Beef Hide	Air	1.8	(15) Unpublished work of Gilman, <u>et al.</u>
Beef Kidney	Air	2.1	(15)
Beef Prostate	Air	2.3	(15)
Beef Spinal Cord	Air	2.5	(15)
Beef Pancreas	Air	3.2	(15)
Beef Thyroid	Air	3.3	(15)
Beef Muscle	Air	4.4	(15)
Beef Ovary	Air	4.6	(15)
Beef Thymus	Air	4.7	(15)
Beef Heart	Air	4.9	(15)
Beef Aorta	Air	5.0	(15)
Beef Testis	Air	5.0	(15)
Beef Marrow	Air	5.8	(15)
Beef Spleen	Air	5.8	(15)
Beef Lung	Air	6.6	(15)

Table I (Continued)

Origin	Oxygen Source	Δd	Reference
Beef Brain	Air	8.1	(15)
Beef Liver	Air	9.5	(15)
Beef Liver Water	Air	0.7	(15)
Beef Blood (Defibrinated)	Air	4.5	(15)
Beef Blood Water	Air	0.7	(15)
Beef Blood Fibrin	Air	5.0	(15)
Beef Haemoglobin	Air	1.6	(15)
Beef Blood Serum	Air	3.8	(15)
Beef Tallow	Air	1.5	(15)

Unfortunately, all of these experiments were not performed under identical conditions. For instance, some samples were burned with air, some with oxygen obtained by fractional distillation of liquid air, others with electrolytic oxygen, and some with oxygen of unknown or unreported origin. Also, in samples difficult to burn, such as wood, some material may have

been lost in uncondensable gases. Perhaps the latter objection might be removed had some oxidizing agent been mixed with the sample to be burned.

Aside from the possible sources of error due to dissolved impurities or to error in density measurement, Dole (16) has presented a timely criticism of the reliability of calculations of deuterium concentrations from the data of the preceding table. His observations are worthy of note and are reviewed briefly in the following paragraphs.

First, the atomic weight of the oxygen used in the combustion may not be the same as that of normal atmospheric oxygen. It has been found that oxygen from fractional distillation of liquid air has a slightly higher atomic weight than has atmospheric oxygen (17), while on the other hand, electrolytic oxygen should have an atomic weight less than that of oxygen in normal water since the isotopes of oxygen may be definitely fractionated by electrolysis (8)(18).

Secondly, the oxygen in the water from combustion may not have a normal atomic weight if the original substance contained oxygen. The oxygen in the water may be abnormal for another

16. Dole, J. Am. Chem. Soc., 58, 580 (1936).
17. Smith, J. Chem. Physics, 2, 298 (1934); Science, 79, 454 (1934). Klar and Kraus, Naturwiss., 22, 119 (1934).
18. Washburn, et al, Bur. Standards J. Research, 11, 453 (1933); ibid., 13, 599 (1934). Johnston, J. Am. Chem. Soc., 57, 484 (1935). Bleakney, et al, ibid., 57, 642 (1935).

reason; that of isotopic exchange between water and carbon dioxide (19)(a). Further, there is a possibility that the isotopes



of oxygen may be fractionated in the combustion reaction, although there are no definite theoretical or experimental indications of such an occurrence.

If the substance is not completely oxidized, a separation of the hydrogen isotopes might occur. During combustion with air a large volume of uncondensable gases passes through the system, carrying off water vapor, and perhaps causing fractionation of the water isotopes.

The isotopes of water might also be fractionated in the purification process.

Finally, unless it is true that normal atmospheric oxygen has the same atomic weight as the oxygen in normal water, the calculation of deuterium abundance from the data presented in Table I is meaningless. That there is a discernible difference between the atomic weight of oxygen from normal water and that of atmospheric oxygen is indubitable. Upon comparing the densities of water made from oxygen in the air and water made

19. Urey, et al, J. Am. Chem. Soc., 57, 321 (1935); J. Chem. Physics, 3, 129 (1935).

from oxygen originally in water, the air-oxygen water was found to be denser by six parts per million!

Dole (16) has shown that of the preceding possible sources of error, only two are important enough to be significant. The atomic weight of the oxygen used in the combustion must be determined, and correction must be made for the difference between the atomic weight of oxygen in the air and in water. In order to correct the values in the table for the latter error it is necessary to subtract six parts per million from Δd for each sample reported, and to correct for the differences in atomic weight of the oxygen used and atmospheric oxygen one must subtract 0.5 parts per million (Airco oxygen), 1.6 parts per million (Linde oxygen), or add 8.1 parts per million (Burdette electrolytic oxygen). These correction values were secured by Dole (16) in experimental investigations concerning the oxygen samples mentioned. It must be evident that even with these data the values in Table I cannot be reduced to a basis satisfactory for comparison, since the oxygen used was not given in all cases, and Dole has shown that while the deuterium content of the standard does not vary greatly, there is in some instances a significant difference.

The work comprising the investigation of beef organs has not been described elsewhere and will be reviewed here. The work was performed under the direction of Dr. Henry Gilman and

was made possible only by the kind coöperation and intimate collaboration of Mr. V. Conquest, Dr. A. W. Ralston, and Dr. H. L. Keil in the ignition of the samples, and Dr. W. H. Jennings, Dr. W. E. Catlin and Mr. M. T. Kelley in performing the density measurements.

The fresh beef tissues were dried at 60° and ground in a meat chopper. One hundred grams of the finely divided tissues were intimately mixed with approximately twice its volume of carefully washed and screened sand. The mixture was distilled to dryness in a two-liter balloon flask and the distillate passed twice through an electrically heated combustion tube filled with coarse copper oxide. The tube was kept at a bright red heat throughout the combustion. The resulting water was then refluxed with potassium permanganate for six hours and distilled to dryness from the same flask. After three more distillations from alkaline permanganate the sample was distilled from oxalic acid to remove alkaline impurities, and then from barium hydroxide to remove acidic impurities. Prior to determination of the density, the sample was freshly distilled through a seasoned Pyrex system, the dissolved air first being removed by boiling under reduced pressure.

The standard of reference was prepared by redistilling ordinary distilled water from potassium permanganate and rejecting the first and last portions. Repeated distillation or passage over red-hot copper oxide resulted in no change in density

of the water thus obtained.

The relative densities of the water samples were determined by a modification of the method reported by Lamb and Lee (20). The apparatus consisted of a submerged magnetic float, the movements of which could be controlled by a measured electric current in a solenoid surrounding the float. The container of the float was mounted in a constant temperature bath. The temperature was maintained at about 25° , and kept constant within a range of 0.0002° . The movements of the float were observed through a window in the water bath by means of a cathetometer.

The limit of accuracy of the measuring apparatus was about one part per million. An interchange of samples with Dr. Malcolm Dole, who used the temperature equilibrium method, demonstrated the accuracy of the technique employed.

The results of these investigators are included in Table I, and while they are open to the objections already mentioned, it is at least interesting to observe the apparent differences in density of the water obtained from the various beef organs. The water obtained by combustion of the dried beef liver proved to be the most abundant in heavy hydrogen. At present there exist no obvious reasons or data with which one may correlate these differences in the amount of isotope present.

Since ordinary ignition is rather slow and is seldom ade-

quate because of the possible escape of unburned gases and the presence of unoxidized organic compounds in the water obtained, this thesis was undertaken in an attempt to devise a simple yet adequate method for the combustion of organic substances, such as yeast, fungi, etc., which are not readily combustible.

EXPERIMENTAL

Apparatus

The apparatus employed was rather simple and the individual units are to be found in any laboratory. For the ignition of the sample a one-liter Pyrex balloon flask was fitted with a two-hole stopper in which was mounted a small-bore glass tube for introduction of oxygen and an ordinary glass still-head. To the still-head was connected a water-cooled copper condenser 2.5 feet in length, which in turn was connected by means of a glass adapter and cork to a water-cooled glass spiral condenser, mounted vertically. The spiral condenser was connected by means of a two-hole stopper to a 500 cc. Erlenmeyer flask. Leading from the latter was a Hopkins water-cooled condenser with a gas outlet leading to the hood.

The stopper for the ignition flask was prepared by winding two-inch strips of asbestos paper about the two pieces of apparatus which it bore. The asbestos was then thoroughly saturated with sodium silicate solution and oven-dried for three days. When put into use it was well covered with tin-foil and firmly wired into place.

The purification unit was constructed from a 36-inch electric furnace and a Pyrex combustion tube. The tube was filled with coarse C.P. copper oxide held in place by two rolls of

oxidized copper gauze. A 500-cc. distilling flask with a straightened side-arm was connected to one end of the tube, the other end of which led to an inclined glass condenser. The receiving flask was fitted with a Hopkins condenser to prevent as far as possible the loss of water by evaporation.

All glass used in this apparatus was of Pyrex and all stoppers, with the exception of the asbestos stopper previously described, were of cork and all were covered with tin-foil when in use.

Procedure

Five hundred grams of the substance to be ignited were powdered finely and mixed intimately with an equal weight of finely powdered C.P. copper oxide. The mixture was then placed in the ignition flask, which was usually about half full then, and the asbestos stopper wired tightly into place. The oxygen was not admitted at once, but the flask was heated with a free flame until admission of oxygen promoted spontaneous combustion, the rate of combustion being controlled by the speed of the oxygen stream. Ignition was controlled thus at such a pace that water was collected at the rate of three to five drops per minute. Speedier ignition results in the loss of much unburned gases. Throughout ignition the receiving flask was cooled in an ice-salt mixture. This process is rather hard on both

ignition flask and stopper so both were renewed for each run.

The water collected above was then distilled through the purification train, the combustion tube being heated to a bright red heat. A stream of air which had been passed through two calcium chloride towers and one soda-lime tower was introduced into the distillation flask at a moderate rate throughout the distillation by means of a glass tube extending to within two or three centimeters of the liquid. This process was repeated on the distillate.

To the water thus obtained a few pellets of potassium hydroxide and enough potassium permanganate to impart a permanent color were added and the mixture refluxed for six hours and then distilled to dryness. This procedure was repeated twice. The final distillate was then distilled from one gram of oxalic acid and then from a few crystals of barium hydroxide, rejecting the first and last small portions. In this manner 125 to 175 cc. of water ready for density determination could be obtained from 500 g. of dried yeast.

The author is indebted to Mr. W. M. Hoehn for assistance in the purification of the water samples.

Materials

The oxygen used was a commercial product supplied by the Air Reduction Sales Co., Bettendorf, Iowa, and was prepared by

fractionation of liquid air.

The substances burned and purified in the above apparatus include six different samples of yeast and one of the dried mycelium (fat-free) of Penicillium javanicum van Beijma. With the exception of one sample of yeast the substances were obtained already dry and ready for investigation. The wet yeast was kindly dried at 40° by Dr. H. E. Stavely.

Determination of densities of the water samples obtained from these ignitions is not yet complete.

The author is indebted for liberal samples of yeast to Dr. Charles N. Frey of the Fleischmann Laboratories, Dr. G. S. Bratton of the Anheuser-Busch Co., Dr. M. H. Givens of the Northwestern Yeast Co., and Dr. Charles H. Keipper of the National Distilling Co., and to Dr. O. E. May of the Bureau of Chemistry and Soils, U. S. Department of Agriculture for several pounds of the dried mycelium of Penicillium javanicum van Beijma.

SUMMARY

A satisfactory procedure for the combustion of organic compounds and mixtures and for the purification of the water thus obtained has been described.