A Study of the Normal and Abnormal Reactions of Certain Compounds in the Beta Furan Series.

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A STUDY OF THE NORMAL AND ABNORMAL REACTIONS OF CERTAIN COMPOUNDS IN THE BETA FURAN SERIES

by

Edward Sherman

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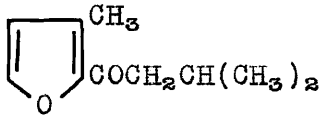
Reactions in the β-Furan Series

Introduction

Mono-β-substituted furan compounds have not been studied as extensively as their α-analogs. The paucity of such compounds in the literature is attributable to the fact that they are uncommonly difficult of synthesis. Usually the methods of preparation entail formation of the ring from suitable linear starting materials followed by the preferential removal of certain substituents from the α-position(s). In one instance only, a furan monosubstituted in the β-position has been isolated from a reaction which involves nuclear substitution.

Of the β-monosubstituted furans, one of the oldest is 3-furoic acid. It was first isolated by Rogerson (1) in 1912 from the root-bark of the "wahoo" or "burning bush" (Euonymus atropurpureus Jacquin) and then from the root of the scarlet runner (Phaseolus multiflorus Lamark) by Power and Salway (2) the following year. Confirmation of the structure assigned to this acid was not obtained until 1932 when it was prepared first by Reichstein and Zschokke (3) by the preferential α-decarboxylation of the 2,3- and 2,4-furandicarboxylic acids and subsequently by Gilman and coworkers (4,5) from the 2,4-dicarboxylic acid.

Asahina and coworkers (6) prepared 3-methylfuran by decarboxylation of elsholtzic acid (3-methylfuroic acid), a compound which they had obtained from elsholtzione* by



Elsholtzione

treatment with amyl nitrite and sodium in absolute ether. 3-Methylfuran has also been prepared by Rinkes (8) through decarboxylation of the isomeric 4-methylfuroic acid which he had synthesized. The furan has been obtained by other methods which are discussed below.

In a series of investigations (9,10) on β-methylfuroic acids, Reichstein and coworkers (9) prepared the 3-methylfuran by decarboxylation of 4-methyl-2,3-furandicarboxylic acid. Formylation of the furan (10) by the method of Gattermann and Koch yielded 3-methylfuraldehyde. Proof of orientation followed on oxidation of the aldehyde with silver oxide to the known elsholtzic acid.

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*Elsholtzione, a naturally occurring ketone, was isolated from Elsholtzia cristata Wildenow (Labiatae) by Asahina and Murayama (7) in 1914.

The clear-cut orientation depicted above was the first established case of the directing influence of a mono-β-substituted furan. A study of orientation in the β-furan series was then undertaken by Gilman and Burtner. During the course of this investigation (5) 3-furaldehyde was synthesized by the catalytic (Rosenmund) reduction of 3-furoyl chloride obtained from 3-furoic acid in the usual manner. The authors also prepared 3-methylfuran from the hydrazone of 3-furaldehyde by a Wolff-Kishner reduction.

From the results of their studies, Gilman and Burtner (5) proposed the following rules of orientation for β-monosubstituted furans: (1) the entering group assumes an α-position; (2) if the β-group is an ortho, para-director in the benzene series, the entering group goes to the contiguous α-carbon atom and if the β-group is a meta-director in the benzene series, the entering group goes to the more remote or opposite α-carbon atom.

Mono-β-substituted furans have also been prepared from such readily available starting materials as furan and furoic acid. In this group are to be found the β-halofurans, 3-chloromercurifuran, 3-furylsodium, 3-benzoylaminofuran, 3-hydroxyfuran, 3-furansulfonic acid, 3-p-chlorophenylfuran and tri-3-furylarsine.

Both the 3-bromo- and 3-chlorofuran were prepared by J. R. Johnson and coworkers (11). The method entailed

dihalogenation of furoic acid, removal of the α-halogen atom with zinc and ammonium hydroxide and subsequent decarboxylation of the 4-halofuroic acid.*

Gilman and Wright (14) prepared 3-chloromercurifuran from furoic acid by treatment with mercuric acetate followed by heating to 200°C., dissolution in acetic acid and treatment with aqueous sodium chloride. They obtained 3-iodofuran from the chloromercuri compound by reaction with a solution of iodine in aqueous potassium iodide. The authors also prepared the β-iodofuran by stripping three of the iodine atoms from tetraiodofuran by means of aluminum amalgam.

From 3-iodofuran, Gilman and Wright (15) were able to prepare 3-furylsodium (potassium)** by treatment with sodium-potassium alloy in a sealed tube under reduced pressure (30 mm.). Subsequent carbonation of the product resulted in 3-furoic acid in very low yield.

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*Due to Hill's earlier work (12), Johnson referred to these compounds as 3-halofuroic acids. It was later shown (13) that the major dihalofuroic acid was the 4,5-compound and that none of the 3,5-acid was formed. The removal of the α-halogen atom therefore resulted in the 4-halofuroic acid and not the 3-haloacid as reported.

**This was the first time an organosodium compound had been prepared by the direct action of the halide and the metal. The authors offered this as supporting evidence for that mechanism of the Wurtz-Fittig reaction which postulated the intermediate formation of organometallic compounds.

In 1934, Burtner (16) synthesized 3-benzoylaminofuran with the intention of preparing the diazonium salt for the purpose of orientation studies. The β-acylaminofuran compound was obtained from 3-furoic acid as shown in the following sequence of reactions

$$3\text{-}C_4H_3OCO_2H \longrightarrow 3\text{-}C_4H_3OCO_2C_2H_5 \xrightarrow{NH_2NH_2}$$
$$3\text{-}C_4H_3OCONHNH_2 \xrightarrow{HONO} 3\text{-}C_4H_3OCON_3 \xrightarrow{\Delta}$$
$$3\text{-}C_4H_3ONCO \xrightarrow{C_6H_5MgBr} 3\text{-}C_4H_3ONHCOC_6H_5 \ .$$

Furans containing arsenic linked to the nucleus in the β-position were prepared by Beck and Hamilton (17). They obtained tri-3-furylarsine when three equivalents of 3-chloromercurifuran were treated with one equivalent of arsenic trichloride in benzene solution. Unlike the α-isomer which undergoes cleavage of the carbon-arsenic bond, this compound yielded a complex mercurichloride on treatment with alcoholic mercuric chloride.

In a series of controversial papers,* Hodgson and Davies reported the preparation of the hydroxyfurans (18)

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*The methods used by these investigators were of such nature as to lead Wright and Gilman to make the following comment in closing their article on the synthesis of substituted furans (20), "The experiments by Hodgson and Davies are so unusual compared to the experiences of other furan chemists that it would seem worth while to repeat this work in other laboratories in order to develop techniques not known to furan chemists."

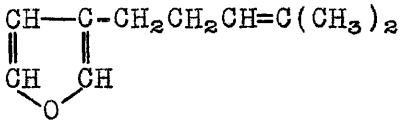
and offered further proof of the structures of the isomeric compounds (19). The 3-hydroxyfuran was prepared by sodium amalgam debromination of 2-bromo-3-hydroxyfuran which was obtained from furoic acid by the action of bromine and water.

In the preparation of 2-arylfurans by interaction of furan with aryldiazonium chlorides in the presence of alkali, A. W. Johnson (21) obtained minor quantities of the isomeric 3-arylfurans. The reaction between furan and p-chlorobenzenediazonium acetate was investigated in detail and 3-p-chlorophenylfuran was isolated in 0.7% yield as compared with a 29% yield of 2-p-chlorophenylfuran. The author differentiated between the isomers by relating their ultra-violet absorption spectra to those of styrene and 1-phenylbutadiene respectively.

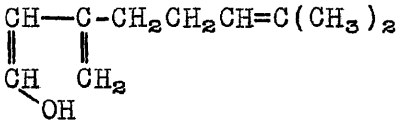
Furansulfonamides have been reported by Cinńeide in a recent preliminary communication (22). 3-Furansulfonic acid and its derivatives were prepared in the following manner: Furoic acid was brominated to the 5-bromoacid which was sulfonated and then the carboxyl group replaced by bromine. The barium 2,5-dibromosulfonate thus obtained was treated with zinc and ammonium hydroxide, giving barium 3-furansulfonate. The barium salt was converted to the sodium salt from which the sulfonyl chloride and the sulfonamides were prepared.

Rinkes (23) obtained 3-nitrofuran when 3-nitrofuroic acid was decarboxylated in quinoline with the aid of a copper chromite catalyst. The 3-nitrofuroic acid was prepared by the decarboxylation of 2-methyl-3-nitro-5-furoic acid and subsequent oxidation of the resulting 2-methyl-3-nitrofuran with potassium ferricyanide in an aqueous solution of potassium acetate.

In addition to 3-furoic acid, two other β-monosubstituted furans occur in nature, perillene and perilla ketone. Perillene was isolated from the essential oil of Perilla citriodora Makina by Kondo and Yamaguchi (24). From a study of its degradation products, Kondo and Suzuki (25) determined the structure of perillene. They also suggested a possible mode of formation of the compound in nature from an "iso-enolate" form of citral.



Perillene



Citral ("iso-enolate")

Goto (26) obtained perilla ketone from the ethereal oil of Perilla frutescens Brit. He proved its structure by degradation studies and through a Clemmensen reduction to dihydroperillene. Perilla ketone is 3-furyl isoamyl ketone.

The preceding summary of the studies on the mono-β-substituted furans discloses the fact that there is one major omission in the literature. In no instance has there been reported a linear derivative of 3-methylfuran. Such furylmethyl compounds, if prepared, would serve for the purpose of comparing the relative reactivities of the α- and β-isomers. Furthermore, since the β-substituted furans are generally less reactive than their α-isomers, it is to be expected that 3-furylmethyl compounds would exhibit more of the aromatic nature inherent to this class of heterocycles.

Another interesting factor has drawn our attention to this undertaking. If the presently accepted graphical formula for furan is truly representative, then there should be present in β-furylmethyl compounds an allylic system capable of exhibiting the abnormal reactions which commonly occur in that class of substances. Such being the case, 3-furylmethyl compounds could then be related to analogous aromatic compounds of the benzyl series.

With the introduction (27) of lithium aluminum hydride as an agent for reducing carboxylic acids directly to the corresponding carbinols without effect on carbon-carbon unsaturations and circumventing treatment of the resulting complexes with mineral acids, so deleterious to sensitive furan compounds, an approach to the

synthesis of 3-furylmethyl compounds presented itself. Thus from 3-furoic acid there may be prepared successively 3-furylcarbinol and 3-furylmethyl chloride. The latter compound could then be compared with its α-isomer, furfuryl chloride, which was first prepared by Kirner (28) in 1928.

When Kirner and Richter (29) added α-furfuryl chloride to a warm aqueous solution of potassium cyanide, they obtained a nitrile which they described as 2-furylacetonitrile (furfuryl nitrile) and the acid obtained on subsequent hydrolysis as furylacetic acid. It was later shown (30) that Kirner and Richter were in error and that the compounds they reported really were 5-methylfuronitrile and 5-methylfuroic acid. Actually a mixture of isomers was obtained, for Reichstein (30) succeeded in isolating each of the compounds by fractionation of the nitrile and by fractional crystallization of the acids obtained on hydrolysis of the nitriles. From the physical properties of 5-methylfuronitrile and furylacetonitrile, prepared by independent methods, and of the nitrile prepared by Kirner and Richter, Scott and J. R. Johnson (31) performed a rough calculation which indicated that the nitrile obtained from furfuryl chloride consisted of approximately 85% of 5-methylfuronitrile and 15% of α-furfuryl cyanide.

One other reaction of α-furfuryl chloride is of importance to this study, namely Grignard formation. It has been reported (32) that the conditions for obtaining a useful Grignard reagent from furfuryl chloride have not been ascertained but that such a reagent does form. This is indicated by the formation of sym-di-2-furylethane as one of the products when furfuryl chloride is treated with magnesium in ether. This is understandable in view of the fact that the halogen in furfuryl chloride is very reactive and would be expected to react with any Grignard reagent that may be formed.

The investigations described in this dissertation were concerned with the synthesis of 3-furylcarbinol and 3-furylmethyl chloride, and a study of their properties. Our interest in these compounds, as depicted earlier, was well founded for it has been shown that 3-furylmethyl chloride not only reacts abnormally to a certain extent but also lends itself to Grignard formation thereby making available to organic chemistry a new synthetically useful tool.

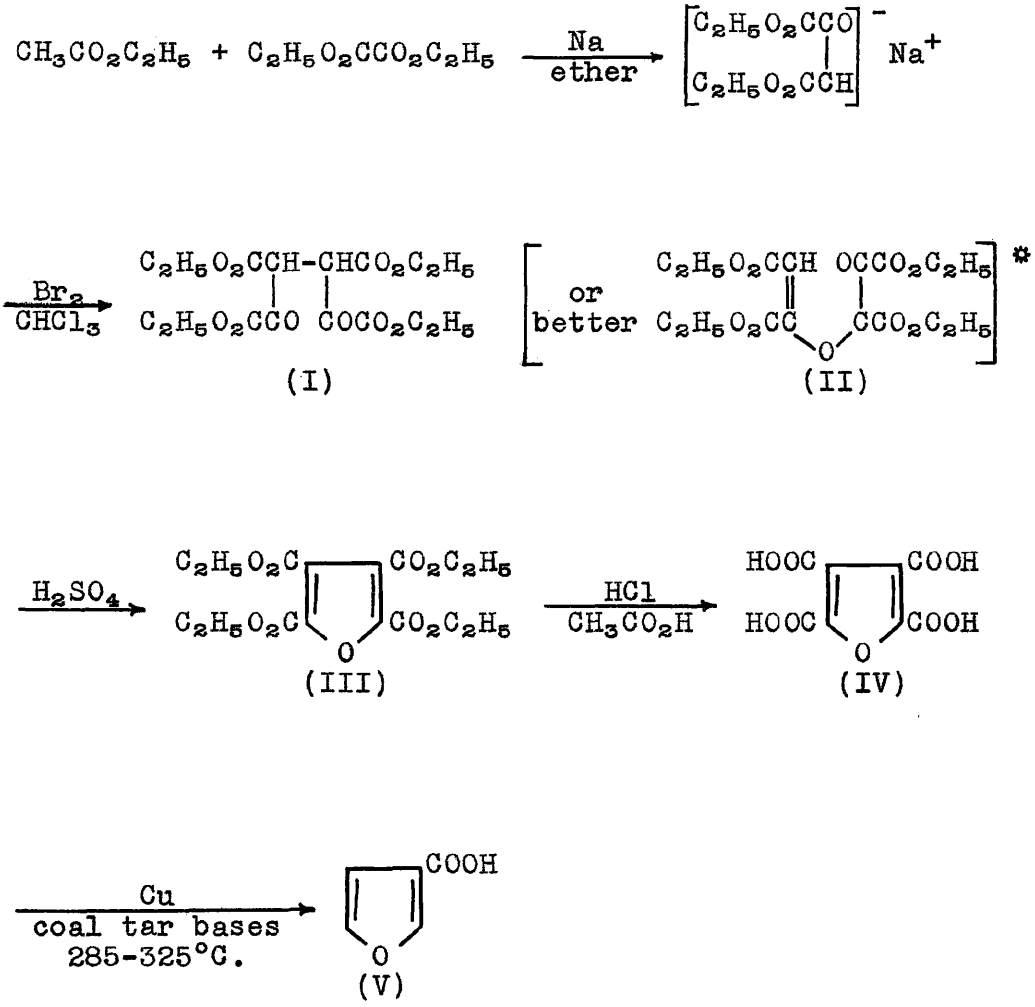
Discussion of Results

The preparation of large quantities of 3-furoic acid for starting material necessitated a procedure which was not fraught with difficulties and which would give relatively good yields. Of the several available methods (3,5,33) only the last met these requirements. Thus, after slight modifications necessary for large-scale work, it was possible to prepare 3-furoic acid in average overall yields of approximately 47% (based on the bromine used) according to the scheme shown on the next page.

The conversion of 3-furoic acid to 3-furylcarbinol by reduction with lithium aluminum hydride according to the general procedure of Nystrom and Brown (27) was accomplished initially in yields of 52-57% of the theoretical amount. By a chance error, a considerable excess of ether was used in one experiment and the yield was raised to 91.5%. Thereafter, yields averaging 90% of the theoretical were obtained. Schematic representation of the preparation of 3-furylcarbinol and of the compounds subsequently derived from it is to be found on page 14.

3-Furylcarbinol, a water-white liquid, is soluble in water and the common organic solvents. It is oxidized slowly in the presence of air, but can be preserved for about a week without noticeable decomposition if stored

The Synthesis of β-Furoic Acid



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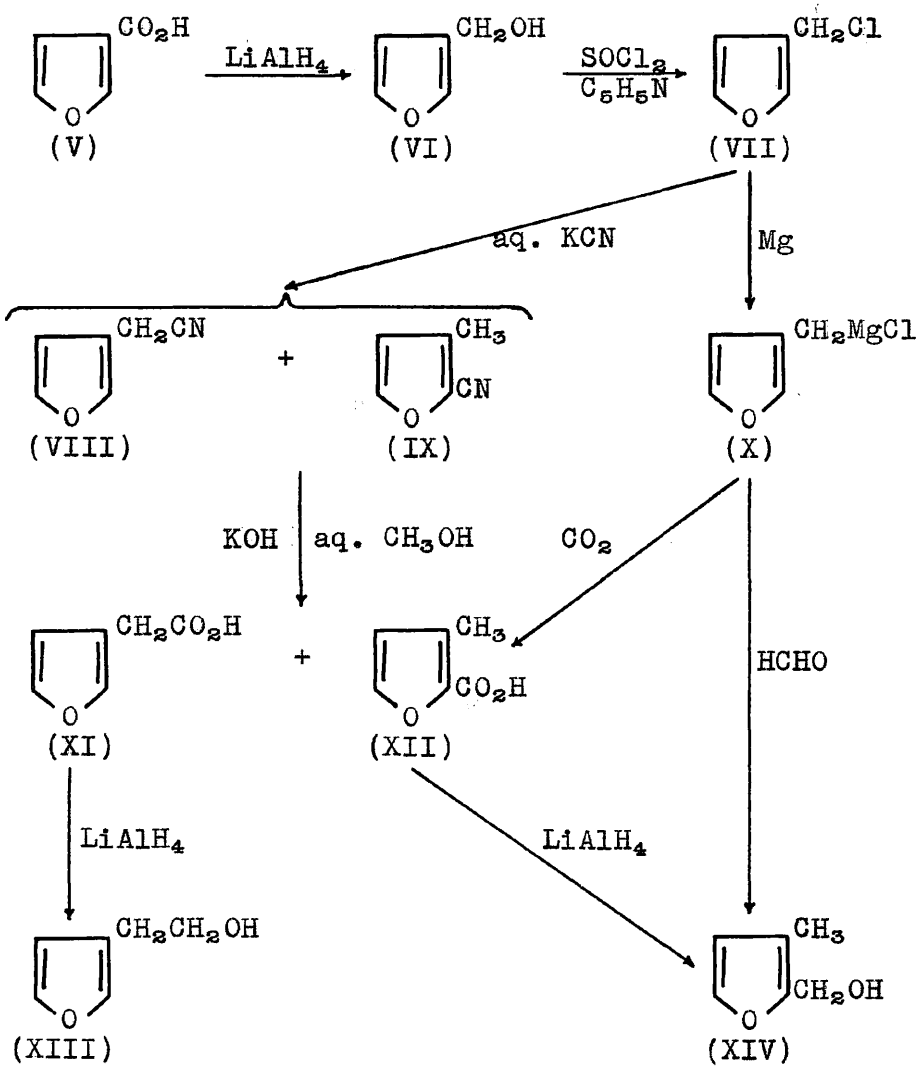
*Structure II was proposed by Reichstein et al. (33) to account for the fact that ring closure with concentrated hydrochloric acid yielded 2,3,4-furantricarboxylic acid presumably through initial ketone cleavage of the β-keto-ester.

Reactions in the β-Furan Series



under refrigeration in a well-stoppered flask from which the atmospheric oxygen has been displaced by nitrogen.

That 3-furylcarbinol is less susceptible to the action of mineral acids than its α-isomer was shown in the following manner: To each of two test tubes was added 1 ml. of a 5% hydrochloric acid solution and 0.9 ml. of distilled water. Furfuryl alcohol (0.1 ml.) was added to one, and the same amount of 3-furylcarbinol to the other. The tubes were then stoppered and placed in a rack. The test tube which contained the α-alcohol clouded up immediately and started to deposit a yellow oil within five minutes. The other tube remained clear for about five hours before developing a slight cloudiness. Further evidence of this greater stability toward mineral acids is given on page 16.

Adaptations of each of two modifications of the Darzens procedure served for the preparation of 3-furylmethyl chloride from 3-furylcarbinol. By the method of Kirner (28), 3-furylmethyl chloride was obtained in average yields of approximately 33% of the theoretical. The reaction time was consuming, two and one-half to three hours being required, and necessitated constant watching. When the modification due to Reichstein (30) was applied, yields were consistently better and reaction time was reduced to less than half an hour.

In one instance 3-furylmethyl chloride was prepared in the absence of a base to take up the free acid. The procedure employed was essentially that of Kirner (28) but excluding the pyridine. Although a fair yield (25%) was obtained, the method is not recommended as a means of preparing the chloride. Its description here serves only as further evidence of the lesser sensitivity of 3-furylcarbinol towards free hydrochloric acid.

The formation of 3-furylmethyl chloride in lower yield than its α-isomer requires some explanation, especially in view of the observation that its precursor is less susceptible to the presence of free mineral acid. The fact that both α-positions are unoccupied in 3-furylmethyl compounds undoubtedly has some bearing on the matter. Furthermore, it has been observed that relatively large amounts of a compound having an ester-like odor are formed during the preparation of the chloride. Attempted distillation of the substance(s) under reduced pressure invariably resulted in decomposition to sulfur dioxide and intractable tars. In view of these observations, it was assumed that this by-product is a sulfite ester.

3-Furylmethyl chloride distills as a clear, water-white liquid. It is insoluble in water but soluble in the common organic solvents. It is more stable than its α-isomer, furfuryl chloride, for unlike the latter, it does not

decompose on distillation in equipment in which special precautions were not taken to remove adsorbed mineral acid. Neither is it lachrymatory.

On treatment with strong aqueous potassium cyanide, 3-furylmethyl chloride is converted to a mixture of 3-furylacetonitrile and elsholtzonitrile (3-methylfuronitrile) contaminated with isocyanides and some polymeric material. The nitriles could not be separated by fractional distillation and so the mixture was hydrolyzed directly to the corresponding acids. These were separated by fractional crystallization alternately from low-boiling petroleum ether and water. The acids were found present in the approximate ratio of 90% of 3-furylacetic acid to 10% of elsholtzic acid.

Aside from the difficulties usually encountered in fractional crystallizations, one other factor complicated the separation of 3-furylacetic acid from elsholtzic acid. It was found that 3-furylacetic acid, like its α-isomer, is sensitive to decomposition especially when in the impure state. Once purified, it is relatively stable and can be converted to the acid chloride by treatment with thionyl chloride and thence to the amide and anilide by which derivatives it was characterized. That the abnormal product was elsholtzic acid was shown in several ways. First, like all α-furoic acids it is acidic to congo red indicator and

gives an orange precipitate when treated with an aqueous solution of ferric chloride. Secondly, it was converted to the known acid chloride and subsequently to the known methyl and ethyl esters, amide and anilide. Unequivocal confirmation was obtained in a private communication from Dr. T. Reichstein, University of Basel, Switzerland, who reported that there was no depression in the melting point, as determined on a Kofler block, when a sample of this compound was mixed with a sample of the acid he had synthesized as described earlier on page 3.

For the purpose of studies on the Grignard reagent prepared from 3-furylmethyl chloride (see page 19), 3-furylacetic acid and elsholtzic acid were converted to the corresponding alcohols by reduction with lithium aluminum hydride. The yield in each instance was better than 90%. β-3-Furylethanol, a colorless liquid, soluble in water and the common organic solvents, appears to be as stable as its α-isomer. It was characterized as the phenyl- and α-naphthylurethan.

3-Methylfurfuryl alcohol, also a colorless liquid, exhibits the same solubility behavior. It is sensitive to atmospheric oxygen and colors green on exposure to air for several hours. It can be stored without apparent decomposition if precautions are taken to displace the oxygen from the container in which it is placed. Although it was not

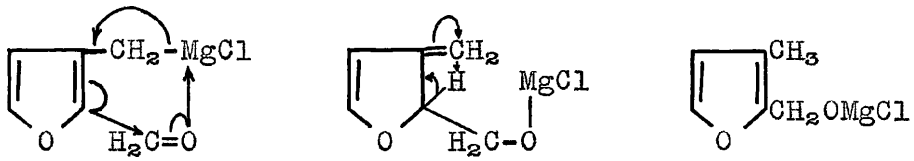
possible to prepare a phenylurethan, the alcohol was characterized as the α-naphthylurethan.

When an ethereal solution of 3-furylmethyl chloride is treated with magnesium, a Grignard reagent is formed to the extent of approximately 70%. It is unfortunate that the properties of this reagent cannot be compared with those of an α-isomer for furfuryl chloride does not form a Grignard reagent in measurable amounts.

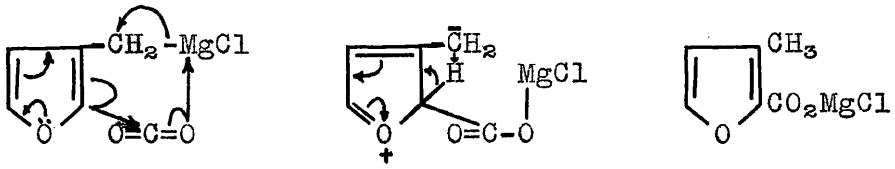
Carbonation of the Grignard reagent results in the formation of large amounts of an abnormal product. Thus when 3-furylmethylmagnesium chloride is treated with Dry Ice there is obtained 33.5% of a mixture of crude acids consisting of approximately 10% of 3-furylacetic acid, the normal product, and 90% of elsholtzic acid.

The reaction between formaldehyde and the Grignard reagent results in the formation of the abnormal product, 3-methylfurfuryl alcohol. This was confirmed by the fact that a phenylurethan could not be prepared and also that there was no depression in the melting point of a sample of the α-naphthylurethan prepared from the product of this reaction when mixed with a sample of the α-naphthylurethan prepared from 3-methylfurfuryl alcohol synthesized in an independent manner (see page 18). The similarity in the boiling points and refractive indices serves as further confirmatory evidence.

The similarity in behavior of 3-furylmethyl chloride and its benzene analog, benzyl chloride, is exhibited in the action of formaldehyde on the respective Grignard reagents. Each adds the aldehyde to an allylic carbon atom; 3-furylmethylmagnesium chloride gives 3-methylfurfuryl alcohol and benzylmagnesium chloride yields o-tolylcarbinol (34). This abnormal reaction may be explained on the basis of the following mechanism shown for the furan compound.



Unlike benzylmagnesium chloride which yields phenylacetic acid on carbonation, 3-furylmethylmagnesium chloride is converted largely to the abnormal product, elsholtzic acid, on treatment with carbon dioxide. This abnormality is attributable to the activating influence of the ring oxygen on the α-positions. It is interesting to note that the closely related thiophene analog, 3-thenylmagnesium bromide, has been reported (35) to yield the abnormal product, 3-methylthenoic acid, in 12.5% yield (plus only the expected coupling product, sym-di-3-thienylethane in 48% yield) when poured onto crushed Dry Ice. A similar mechanism, together with the additive effect of the ring oxygen, which may also be operative in the above, serves to explain this abnormality in behavior.



Another reaction which serves for comparative purposes is that between the halides and alkali cyanides. When treated with strong aqueous potassium cyanide, α-furfuryl chloride (29) gives a mixture of nitriles consisting 15% of 2-furylacetonitrile (normal product) and 85% of 5-methylfuronitrile (abnormal product). Under comparable conditions 3-furylmethyl chloride yields a mixture of nitriles consisting of 90% of 3-furylacetonitrile (normal product) and 10% of elsholtzonitrile (abnormal product). Both 3-thenyl chloride (35) and benzyl chloride (36) yield only the normal product.

Experimental

Diethyl Oxalacetate (Sodium Salt). - This compound was initially prepared according to the literature by means of Fischer's (37) modification of the method due to Wislicenus (38). Fischer reported yields of 75% while Wislicenus was less definite, having ascribed the limits of 70-80%. Two runs using the amounts specified by Fischer and one run using four times the quantity of reagents resulted in yields of 80-85%. Difficulty was encountered in working up the product as it absorbed the ether quite freely forming a pasty mass which was not readily filterable and consequently was washed free of impurities only after many hours of filtration.

Tetraethyl "Dioxalosuccinate" (I or II). - The method used for the preparation of this compound is essentially that of Sutter (39) modified for use in large-scale runs. It eliminates the formation of the jelly-like mass which results when the sodium salt of diethyl oxalacetate is suspended in the quantity of chloroform recommended by Sutter. Furthermore, it circumvents the slow and tedious filtration of the sodium bromide which, in this reaction, is generally formed as a near-colloidal suspension that rarely settles out in a period of 24 hours.

In a two-liter, three-necked, round-bottomed flask equipped with a stirrer, dropping funnel and salt funnel, 105.1 g. (0.5 mole) of the sodium salt of diethyl oxalacetate* was suspended in 700 ml. of dry chloroform. The flask was cooled in an ice-salt bath and a solution of 37.0 g. (0.232 mole) of bromine in 40 ml. of dry chloroform was added gradually with constant stirring. The bromine was taken up almost instantaneously. When about three-fourths of the bromine solution had been added, another 105.1 g. (0.5 mole) of the sodium salt was added portionwise to the flask, followed by 100 ml. of dry chloroform, and 37.0 g. (0.232 mole) of bromine in 40 ml. of dry chloroform to the dropping funnel. This method of addition was repeated two more times.

The reaction mixture was stirred for 15 minutes after the addition of the bromine solution was complete and then transferred to a five-liter separatory funnel. Most of the excess organic sodium salt and the sodium bromide was removed by washing the suspension with water until no more color was imparted to the aqueous extract. The chloroform solution was then dried over anhydrous

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*Both the sodium salt as prepared above and in the practical grade as produced by U.S. Industrial Chemicals, Inc., have been used. There was no great difference in the respective yields.

calcium chloride and the chloroform removed by distillation. The oily residue was then taken up in enough ether (ca. one liter) so that the solution separated easily when shaken with water. The ethereal solution was washed thoroughly with water, dried over anhydrous magnesium sulfate and then most of the solvent distilled off. The residue was transferred to a 400-ml. beaker and heated on the steam bath for about an hour. The resulting golden-yellow oil solidified on cooling to a white crystalline mass. The product was filtered off and washed with a small amount of ice-cold ether. The mother liquor yielded a second and, in several instances, a third crop of white crystals.

Sutter reported a yield of 63% (crude). By the procedure described above yields of 218.0-260.0 g. (63.0-75.2%) of the ester have been obtained. The compound was not purified further.

Tetraethyl Furantetracarboxylate (III). - Ring closure of the above described tetraester was effected with concentrated sulfuric acid according to the method due to Reichstein and coworkers (33). Inasmuch as a pure product was not essential, the crude having been subjected directly to hydrolysis, the following modification of the procedure was expedient.

To 800 ml. of ice-cold concentrated sulfuric acid in a four-liter beaker equipped with an efficient stirrer was added, portionwise, 211.0 g. (0.563 mole) of "dioxalosuccinic" ester which had been ground to a fine powder. After all the ester had gone into solution, the mixture was heated slowly to 50°C. and kept there for 5 minutes. The solution was then chilled in an ice bath and poured slowly, with stirring, onto approximately 2.5 kg. of ice in a four-liter beaker. The product precipitated out under those conditions and was filtered off with suction into a large Büchner funnel. The precipitate was washed thoroughly with cold water, then with cold dilute sodium hydroxide solution and again several times with ice-cold water. It was then pressed as dry as possible on the filter. After drying in air* there was obtained 198.7 g. (99.0%) of crude furantetracarboxylic ester which melted slightly below 30°C.

Other runs using the above procedure invariably resulted in yields that were almost quantitative. Reichstein reported a 92.6% yield of crude melting at 32-33°C.

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*In similar runs performed during the summer months when the laboratory temperature exceeded 25°C., drying in air was not feasible and the slightly damp crude ester, while still cold, was transferred to the flask in which the hydrolysis was to be effected.

Furantetracarboxylic Acid (IV). - The hydrolysis of furantetracarboxylic ester was performed in essentially the same manner as that reported by Reichstein and co-workers (33). The procedure was modified slightly for large-scale preparations and gave a somewhat less pure product containing a slight amount of water. The crude tetraacid so obtained was used without further purification or drying for the preparation of 3-furoic acid (V).

The method employed was as follows: To 179.5 g. (0.503 mole) of crude tetraethyl furantetracarboxylate in a two-liter, round-bottomed, standard taper flask equipped with a reflux condenser was added 750 ml. of water and 750 ml. of concentrated hydrochloric acid. The mixture was refluxed for six hours at which time all of the ester had gone into solution. The liquid was concentrated to one-half its volume and then filtered. It was returned to the flask and a mixture of 350 ml. of glacial acetic acid and 350 ml. of concentrated hydrochloric acid was added. The solution was refluxed for an additional six hours, concentrated as before, filtered and returned to the flask. The addition of the same amount of mixed acids was repeated and the solution once again refluxed for six hours. Most of the solvents was then distilled off at atmospheric pressure and the residue evaporated to dryness under vacuum (water pump) over the steam bath. There was

obtained in this manner 118.0 g. (96.8%) of crude furan-tetracarboxylic acid as a white, crystalline powder.

By using the method described above for larger runs, the yields were generally higher than that required by theory because of the water retained by the tetraacid. Reichstein did not list a yield for his preparation but showed that for analysis the product had to be dried at 0.2 mm. and 150°C. after purification by crystallization from an acetone-benzene mixture.

3-Furoic Acid (V). - This naturally occurring compound (1,2) has been prepared by the decarboxylation of 2,3-furandicarboxylic acid (3), 2,4-furandicarboxylic acid (3,5) and 3,4-furandicarboxylic acid (33), and by the carbonation of 3-furylsodium (15). Of these, the best procedure considering the relative ease of synthesis of starting material was the one due to Reichstein and coworkers (33) utilizing the 3,4-dicarboxylic acid, a stepwise decarboxylation product of furantetracarboxylic acid. Taking advantage of the fact that it was not necessary to isolate the intermediate decarboxylation products, the following method was devised whereby the 3-furoic acid was prepared directly as the desired product.

A 250-ml. distilling flask provided with an alembic prepared from a 125-ml. flask was charged with an intimate mixture of 40 g. (0.164 mole) of finely ground furantetracarboxylic acid, 4 g. of copper powder and 50 ml. of crude coal tar bases (boiling range: 145-220°C. at 12 mm.). A gas inlet tube was inserted and a 250-ml. distilling flask provided as a receiver (see figure 1 on the next page). Nitrogen was admitted into the system and a steady stream maintained throughout the reaction to sweep out the 3-furoic acid as fast as it was formed. The reaction flask was then heated cautiously by alternately raising and lowering a metal bath maintained at about 285°C. The mixture foamed considerably at the outset of the decarboxylation and was kept under control by playing the flame of a micro bunsen burner at the surface of the mixture. As the mixture came up to temperature, the viscosity decreased and the color changed from a bright coppery red to a deep reddish brown. When this point was reached, it was found safe to leave the metal bath fixed in position. The decarboxylation proceeded smoothly as the temperature of the bath was raised gradually to 325°C. When no more liquid was apparent in the reaction flask, the metal bath was removed and the system allowed to cool.

The distillate was transferred to a 250-ml. separatory funnel, the receiver washed twice with 50-ml. portions

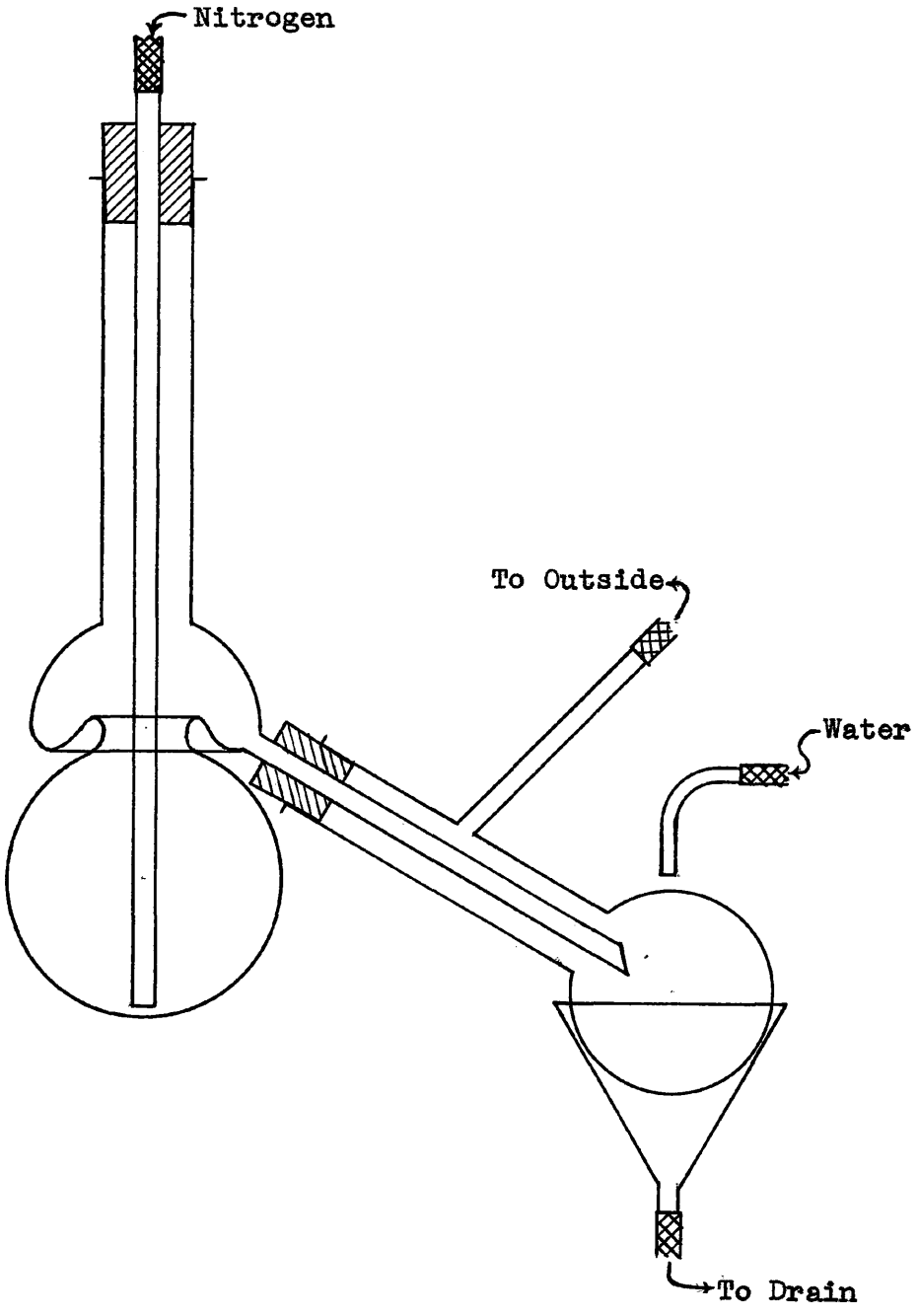

Figure 1. - Apparatus for the decarboxylation of furantetracarboxylic acid.

of ether, and the washings added to the distillate. The ethereal solution was then cautiously extracted five to six times with 25-ml. portions of saturated sodium bicarbonate solution, the extracts combined, washed with ether and finally heated on the steam bath to remove the dissolved ether. The solution was treated with charcoal while still hot, chilled in an ice bath and filtered. Cautious addition of a large excess of concentrated hydrochloric acid liberated the acid from its sodium salt as fine white crystals. After filtering and drying in air, there was obtained 10.4-12.0 g. (56.6-65.3%) of practically pure 3-furoic acid melting at 120-121°C. Extraction of the mother liquor with ether and evaporation of the solvent gave an additional 2.1-1.8 g. of slightly colored less pure acid (m.p. 117-120°C.) making the total yield 12.5-13.8 g. (67.9-75.1%).

The acid was purified further by recrystallization from water (charcoal) using 10 ml. of fresh solvent (or mother liquor from previous recrystallizations) per gram of compound. The recovery of pure 3-furoic acid melting at 121-122°C. is 88-98%.

3-Furylcarbinol (VI). - This new alcohol was prepared by an adaptation of the general method of reduction of carboxylic acids with lithium aluminum hydride due to

Nystrom and Brown (27). This elegant procedure eliminates the use of mineral acids which generally have drastic effects on sensitive furan compounds.

In a dry two-liter, three-necked, round-bottomed flask equipped with a stirrer, 500-ml. dropping funnel and a long reflux condenser, and protected from moisture with calcium chloride guard-tubes, was placed one liter of absolute ether and 15 g. (0.395 mole) of lump lithium aluminum hydride (Metal Hydrides, Inc.). The mixture was refluxed, with stirring, for six to eight hours, or until all of the lumps had disintegrated.*

Heating was discontinued and a solution of 33.6 g. (0.3 mole) of 3-furoic acid in 450 ml. of absolute ether was added dropwise at such a rate that the ether refluxed gently.** The mixture was stirred for about 30 minutes after the addition was complete. With continued stirring and cooling of the flask (ice bath), the excess hydride was decomposed by the cautious addition of water (a few drops at a time). The alcohol was then liberated from the complex by cautious addition of 200 ml. of 20% sodium

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*Finely divided hydroxides remained suspended in the solution and were disregarded.

**If the reaction started too vigorously, the flask was cooled in an ice bath that was kept in readiness throughout the reaction.

hydroxide solution.* The ethereal solution was decanted into a two-liter Erlenmeyer flask and the solid residue of mixed hydroxides was washed twice by stirring with 50-ml. portions of ether. The washings were added to the original ethereal solution and the whole was dried over anhydrous magnesium sulfate.

After removal of the solvent by distillation, the product was distilled under reduced pressure in an atmosphere of dry nitrogen. In the runs performed using this procedure there was obtained 25.3-26.9 g. (86.2-91.5%) of 3-furylcarbinol, a colorless liquid boiling at 54-55°C. at 2 mm., 79-80°C. at 17 mm.; n^{20}_D 1.4842; d^{20}_4 1.1391; MR_D (calcd.) 25.32, MR_D (obsd.) 24.65.

Anal. Calcd. for $C_5H_6O_2$: C, 61.21; H, 6.17. Found: C, 61.06; H, 6.35.

The phenylurethan, fine white needles, melted at 105.2-105.6°C. after recrystallization from aqueous ethanol.

Anal. Calcd. for $C_{12}H_{11}O_3N$: N, 6.45. Found: N, 6.42.

The α-naphthylurethan, fine white needles, melted at 118.4-118.7°C. after recrystallization from aqueous ethanol.

Anal. Calcd. for $C_{16}H_{13}O_3N$: N, 5.24. Found: N, 5.23.

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*In a private communication, Nystrom and Brown recommended this strength alkali in the reduction of 2-furoic acid.

3-Furylmethyl Chloride (VII). - Adaptations of each of two modifications of the Darzens procedure were used in the preparation of this compound from 3-furylcarbinol.

A. Method of Kirner (28): In a 100-ml., three-necked, round-bottomed flask equipped with a dropping funnel, stirrer and loosely-stoppered thermometer was placed a mixture of 9.8 g. (0.1 mole) of 3-furylcarbinol, 9.5 g. (0.12 mole) of anhydrous pyridine and 20 ml. of absolute ether. The flask was cooled in an ice-bath, the stirrer started, and when the temperature fell to 1°C., a solution of 13.1 g. (0.11 mole) of purified thionyl chloride (40) in 20 ml. of absolute ether was added at such a rate that the temperature of the reaction did not exceed 10°C. The addition required about two and one-half hours.

The reaction mixture, in which pasty brown lumps had formed, was stirred for an additional 30 minutes and then the ether solution was decanted into a 250-ml. separatory funnel. The lumps were broken up by means of a curved glass rod and were washed by stirring for five minutes at ice-bath temperature with 25 ml. of absolute ether. The extraction was repeated twice at ice-bath temperature and once after permitting the mixture to come to room temperature. The ether extracts were added to the original ethereal solution and then washed with 20 ml. of an ice-cold 50% potassium

hydroxide solution which was added in small portions in order to prevent undue heating. The ether layer was separated and dried over anyhdrous potassium carbonate or anhydrous magnesium sulfate.

The solvent was removed under reduced pressure in a system protected from moisture as recommended by Kirner (28). Vacuum distillation of the residual orange-colored oil in an atmosphere of nitrogen resulted in 3.8-4.2 g.* (32.5-35.9%) of a water-white liquid boiling at 42-43°C. at 17 mm., 51-52°C. at 27 mm.; n^{20}_D 1.4863; d^{20}_4 1.1855; MR_D (calcd.) 28.67, MR_D (obsd.) 28.24.

B. Method of Reichstein (30): A 200-ml., three-necked, round-bottomed flask equipped as described above and containing 19.6 g. (0.2 mole) of the alcohol, 19.1 g. (0.24 mole) of anhydrous pyridine and 25 ml. of absolute ether was cooled in an ice-salt bath. The stirrer was started and when the temperature fell to -10°C. a solution of 26.2 g. (0.22 mole) of purified thionyl chloride in 15 ml. of pentane was added as rapidly as possible yet keeping the reaction temperature below 30°C. The addition required no more than 15 minutes.

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*About 4 g. of an oily residue did not distill. On elevation of the bath temperature it decomposed to sulfur dioxide and a dark-colored tar.

The mixture was stirred for an additional 15 minutes and then allowed to settle for a short while. The supernatant liquid was decanted into a 250-ml. separatory funnel, stoppered and set in an ice-water bath. To the residue in the flask was added 25 ml. of pentane and then 25 ml. of ice-cold dilute hydrochloric acid was dropped in gradually with stirring (ice-salt bath). The mixture was transferred to another separatory funnel and the layers separated, the pentane layer being added to the first separatory funnel. The aqueous layer was extracted once with 25 ml. of fresh pentane and then discarded. The pentane layer was added to the others and the combined ether-pentane solution was washed once (cautiously) with ice-cold dilute hydrochloric acid and twice with ice-cold dilute sodium hydroxide solution.

After drying over potassium hydroxide pellets for about an hour, the solvent was distilled off at atmospheric pressure. The red-colored oily residue was transferred to a 25-ml. Claisen flask and distilled under reduced pressure (nitrogen atmosphere) in a protected system. The distillate (11.1-12.7 g.; 47.7-54.5%) exhibited the same physical properties as listed in method A. Approximately 8 g. of non-distillable material remained in the distilling flask.

Anal. Calcd. for C_5H_5OCl: Cl, 30.42. Found: Cl, 30.47.

3-Furylmethylisothiouronium picrate, fine mustard-colored needles, melted at 142-143°C. after two recrystallizations from aqueous ethanol.

Anal. Calcd. for $C_{12}H_{11}O_8N_5S$: N, 18.18. Found: N, 18.11.

3-Furylacetonitrile (VIII) and 3-Methylfuronitrile (Elsholtzonitrile) (IX). - 3-Furylmethyl chloride (9.0 g., 0.077 mole) was added to a solution of 8 g. (0.12 mole) of 98% potassium cyanide in 10 ml. of water contained in a 100-ml., three-necked, round-bottomed flask equipped with a stirrer, thermometer and reflux condenser with a tube leading to the outside. The mixture was heated with stirring for two hours at 70°C.; potassium chloride separated and some polymeric material formed during this period. The reaction mixture was cooled, diluted with water to bring the potassium chloride into solution and transferred to a 125-ml. separatory funnel. The brown-colored, oily, upper layer was separated and the aqueous layer extracted several times with ether. The extracts were added to the oil and the mixture was dried with anhydrous magnesium sulfate. After removal of the solvent, the reddish-orange residue was distilled under reduced pressure in an atmosphere of nitrogen. The product (5.5 g.; 67.2%) consisted of a mixture of 3-furylacetonitrile and 3-methylfuronitrile and was

contaminated with isocyanides. It boiled at 50-60°C. at 3 mm., the main portion coming over at 58-59°C.*

3-Furylacetic Acid (XI) and 3-Methylfuroic Acid (Elsholtzic Acid) (XII). - The mixed nitriles (5.5 g.; 0.051 mole) were hydrolyzed by refluxing with 30 ml. of a 20% solution of potassium hydroxide in aqueous methanol (1:1) in a 100-ml., round-bottomed, standard taper flask equipped with a reflux condenser. When the evolution of ammonia ceased, the solution was cooled, washed with ether and then heated to remove dissolved ether. While still hot it was treated with charcoal, then chilled and filtered. The filtrate was acidified strongly with concentrated hydrochloric acid, chilled and extracted thoroughly with ether. Evaporation of the combined extracts which had been dried over anhydrous magnesium sulfate resulted in 5.5 g. (84.7%) of slightly colored material melting at 50-55°C. and having an odor somewhat like phenylacetic acid.

The mixture of crude acids was taken up in low boiling petroleum ether, filtered and allowed to cool slowly. A crop of fairly pure 3-furylacetic acid, translucent white plates, m.p. 60-62°C., was separated in this manner. The mother liquor was evaporated to dryness and taken up in hot

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*Pure elsholtzonitrile boils at 54.5-55°C./12 mm. (10).

water, treated with charcoal, filtered and allowed to cool slowly. Under these conditions crude elsholtzic acid, m.p. 128-132°C., separated.

The aqueous mother liquor was extracted with ether and the ether evaporated after drying with anhydrous magnesium sulfate. The process of crystallizing first from petroleum ether and then from water was repeated twice, yielding in each instance a crop of the respective acid.

The crops of crude elsholtzic acid were combined and recrystallized from water (charcoal). There was obtained 0.55 g. (10% of the crude acid mixture) of pure elsholtzic acid, long white needles, m.p. 134-135°C. A mixed melting point with the acid prepared by carbonation of 3-furylmethyl magnesium chloride showed no depression.

The impure 3-furylacetic acid was recrystallized from petroleum ether (b.p. 60-68°C.). Pure acid (3.8 g.; 68% of the crude acid mixture) was obtained after a second recrystallization from the same solvent, lustrous plates, m.p. 61.9-62.2°C.

Anal. Calcd. for $C_6H_6O_3$: C, 57.14; H, 4.80; neut. equiv., 126.1. Found: C, 57.16; H, 4.90; neut. equiv., 127.1.

Treatment of 1 g. (0.008 mole) of 3-furylacetic acid with 2 ml. of purified thionyl chloride converted it to the acid chloride, $b.p._3$ ca. 53°C., in 54% yield.

The amide was prepared by adding a portion of the acid chloride to excess anhydrous ammonia in absolute ether. The ethereal solution was filtered free of ammonium chloride, washed with saturated sodium bicarbonate solution, dried with anhydrous magnesium sulfate and evaporated to dryness. The residue was recrystallized from benzene-petroleum ether (b.p. 60-68°C.). The amide, white feathery needles, melted at 114-115°C.

Anal. Calcd. for $C_6H_7O_2N$: N, 11.20. Found: N, 11.31.

The anilide was prepared by adding a portion of the acid chloride to an excess of freshly distilled aniline in absolute ether. After removal of the aniline hydrochloride by filtration, the ethereal solution was washed first with dilute hydrochloric acid and then with 5% potassium carbonate solution. After drying with anhydrous magnesium sulfate, the ether was removed by evaporation and the residue was recrystallized from benzene-petroleum ether (b.p. 60-68°C.). The anilide, slender white blades, melted at 122.6-123.2°C.

Anal. Calcd. for $C_{12}H_{11}O_2N$: N, 6.96. Found: N, 6.97.

β-3-Furylethanol (XIII). - This new compound was prepared from 3-furylacetic acid by reduction with lithium aluminum hydride as in the procedure described on page 31.

Thus when 3.15 g. (0.025 mole) of 3-furylacetic acid in 50 ml. of absolute ether was added to a solution of 1.5 g. (0.04 mole) of lithium aluminum hydride in 100 ml. of absolute ether contained in a 300-ml., three-necked, round-bottomed flask and the reaction mixture worked up in the prescribed manner, there was obtained 2.7 g. (96.5%) of β-3-furylethanol as a clear, colorless liquid, b.p.$_3$ 64-65°C., b.p.$_{18}$ 89-90°C.; n^{20}_D 1.4828; d^{20}_4 1.0941; MR_D (calcd.) 29.94, MR_D (obsd.) 29.24.

Anal. Calcd. for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 63.98; H, 7.40.

The phenylurethan, stout white needles from petroleum ether (b.p. 60-68°C.), melted at 58.3-58.8°C.

Anal. Calcd. for $C_{13}H_{13}O_3N$: N, 6.06. Found: N, 6.04.

The α-naphthylurethan, clusters of fine white needles from petroleum ether (b.p. 60-68°C.), melted at 85.2-85.9°C.

Anal. Calcd. for $C_{17}H_{15}O_3N$: N, 4.98. Found: N, 5.01.

3-Methylfurfuryl Alcohol (XIV). - This new alcohol was prepared in the same manner as β-3-furylethanol (page 39). When 2.96 g. (0.023 mole) of elsholtzic acid was reduced with 1.5 g. (0.04 mole) of lithium aluminum hydride and the product separated in the usual way, there

was obtained 2.35 g. (90.3%) of 3-methylfurfuryl alcohol, a water-white liquid, b.p.$_3$ 79-80°C.; n^{20}_D 1.4871; d^{20}_4 1.0917; MR_D (calcd.) 29.94, MR_D (obsd.) 29.54.

Anal. Calcd. for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.03; H, 7.44.

The α-naphthylurethan, clusters of white needles from benzene-petroleum ether (b.p. 60-68°C.), feathery white needles from petroleum ether (b.p. 90-100°C:), colored at 143°C., softened at 148°C., and melted at 151-153°C. with decomposition.

Anal. Calcd. for $C_{17}H_{15}O_3N$: N, 4.98. Found: N, 4.91.

3-Furylmethylmagnesium Chloride (X). - A Grignard reagent was prepared from 3-furylmethyl chloride in the following manner: To 2.82 g. (0.116 gram atom) of magnesium submerged in 25 ml. of absolute ether in a 500-ml. Grignard flask equipped with a stirrer, dropping funnel and reflux condenser, and protected from moisture in the usual manner, was added 10 ml. of a solution of 13.5 g. (0.116 mole) of 3-furylmethyl chloride in 125 ml. of absolute ether. The stirrer was started and the flask heated* for a short period of time when a vigorous reaction set in.

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*It was discovered later that the application of heat is not required to initiate the reaction.

The balance of the chloride solution was added at a rate that maintained moderate reflux (about 30 minutes). The mixture was kept at reflux for an additional 15 minutes by means of a water bath. Titration (41) of an aliquot indicated the presence of 71% of Grignard reagent.

A. Reaction with Carbon Dioxide: The Grignard reagent described above was poured onto about 300 g. of crushed solid carbon dioxide. The reaction product was hydrolyzed with cold 25% sulfuric acid and then transferred to a 250-ml. separatory funnel. The aqueous layer was separated, extracted several times with ether and then discarded. The ether layers were combined, extracted twice with dilute sodium hydroxide solution and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue (orange-colored oil) was subjected to vacuum fractionation in an atmosphere of nitrogen. There was obtained 1.3 g. of a straw-colored liquid boiling at 74-77°C./3 mm., 1.1 g. of a colorless liquid boiling at 92-95°C./3 mm., and ca. 0.2 g. of a substance which boiled at 147-152°C./3 mm. and solidified to a white crystalline compound, m.p. 83-89°C. Recrystallization of the solid from pentane resulted in long white needles, m.p. 90.7-91.4°C. The liquids discolor on exposure to air. Further investigation of these substances has not been undertaken.

The alkaline extracts were combined, washed with ether, heated to remove the dissolved ether, treated with charcoal, chilled and filtered. The filtrate was acidified strongly with concentrated hydrochloric acid and the precipitate which formed was filtered off and dried. There was obtained 3.5 g. of crude, tan-colored, elsholtzic acid, m.p. 125-131°C. The mother liquor was extracted thoroughly with ether, the extracts combined and dried with anhydrous magnesium sulfate. On evaporation of the ether 1.4 g. of a slightly oily solid was obtained. Total yield of crude acid was 4.9 g. (33.5%).

After several recrystallizations from water there was obtained 3.9 g. (80% of the crude acid) of pure elsholtzic acid, m.p. 134-135°C.* When mixed with an authentic specimen (10) the melting point showed no depression.**

Anal. Calcd. for $C_6H_6O_3$: C, 57.14; H, 4.80; neut. equiv., 126.1. Found: C, 57.06; H, 4.96; neut. equiv., 126.9.

The acid was converted to the acid chloride in the usual manner and the latter was used to prepare the methyl and ethyl esters, amide and anilide according to the method

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*Reichstein and coworkers (10) report a melting point of 136-137°C. (corr.).

**The author is indebted to Dr. T. Reichstein of the University of Basel, Switzerland, for this determination.

given by Reichstein and coworkers (10). The results are listed in the following table of melting points.

Table of Melting Points

Derivative	Found	Reported (10)
Chloride	18.5-19.5°C. ($b.p._4$ 61°C.)	18.5-19.5°C. ($b.p._{12}$ 80°C.)
Methyl ester	35-36°C.*	37.5-38°C.
Ethyl ester	46.5-47.5°C.	47-48°C.
Amide	89-90°C.	90-90.5°C.
Anilide	89.5-90.5°C.	90.5-91°C.

The aqueous mother liquors from the recrystallizations of the elsholtzic acid were combined and extracted with ether. The combined extracts were dried with anhydrous magnesium sulfate and then evaporated. The residue was taken up in low-boiling petroleum ether and allowed to cool slowly. The mother liquor was decanted from the needles of elsholtzic acid that had formed. On chilling, 0.25 g. (5% of the crude acid) of impure 3-furylacetic acid, m.p. 48-59°C., was deposited. Slow recrystallization from low-boiling petroleum ether raised the melting point to 59-61°C. When mixed with a specimen of pure 3-furylacetic acid, the melting point was 60-62°C.

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*This derivative was lost due to evaporation before final purification was effected.

B. Reaction with Formaldehyde: The Grignard reagent was prepared from 14.3 g. (0.123 mole) of 3-furylmethyl chloride and 3 g. (0.123 gram atom) of magnesium as described on page 41. In this instance the reaction started without the use of heat. The reagent was treated with gaseous formaldehyde prepared by the depolymerization of 7.5 g. of paraformaldehyde in essentially the same manner as described in Org. Syn., Coll. Vol. I, 188 (1941). A brown oil separated initially followed by a flocculent white precipitate. The reaction was complete at the end of two hours as was indicated by a negative test for the presence of Grignard reagent (42).

The reaction product was hydrolyzed by the gradual addition of an ice-cold solution of 13 g. of ammonium chloride in 38 ml. of water. The ether layer was separated, washed with saturated sodium bicarbonate solution and dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was distilled under reduced pressure in a nitrogen atmosphere. There was obtained 4.6 g. (33.4%) of 3-methylfurfuryl alcohol, b.p.$_3$ 79-81°C., n^{20}_D 1.4880.

The α-naphthylurethan melted at 151-153°C. (dec.) after recrystallization from petroleum ether (b.p. 90-100°C.), and showed no depression when mixed with an authentic specimen of the compound.

Summary

Several new mono-β-substituted furans have been synthesized and characterized. Among these are 3-furylcarbinol, 3-furylmethyl chloride, 3-furylacetic acid and β-3-furylethanol.

The reaction between 3-furylmethyl chloride and strong aqueous potassium cyanide resulted in the formation of a mixture of nitriles consisting of approximately 90% of 3-furylacetonitrile and 10% of elsholtzonitrile (3-methylfuronitrile).

A Grignard reagent has been prepared from 3-furylmethyl chloride in 71% yield. Carbonation of the reagent resulted in the formation of a mixture of acids in the ratio of 90% of elsholtzic acid (abnormal product) to 10% of 3-furylacetic acid (normal product).

Treatment of the Grignard reagent with formaldehyde produced the abnormal product, 3-methylfurfuryl alcohol. The structure of the latter was proved by comparison of the alcohol and its derivative with authentic specimens synthesized in an unambiguous manner.

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Vita

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Edward Sherman, the son of Israel and Sarah Baron Sherman, was born on February 8, 1919, in New York, New York. He attended the public schools for six and one-half years in Brooklyn, New York, and for one year in Jacksonville, Florida, where he graduated from the Edmund Kirby-Smith Junior High School. During the next three years he completed the science course at the Thomas Jefferson High School in Brooklyn, New York, graduating in June, 1935, with an average high enough to enable him to enter the City College of the College of the City of New York the following September on a tuition-free basis. He completed one year there while enrolled in the chemical engineering curriculum before leaving college to move to the Middle West to work for a short period of time.

In February, 1937, Mr. Sherman returned to school and attended the evening sessions of the spring and summer semesters at the Central Y.M.C.A. College in Chicago, Illinois. The following September he matriculated at the University of Illinois where he spent the next three years in the chemistry curriculum and, in addition to working his way through, he was quite active in extracurricular activities, serving on the Independent Council and as president of his house group. The degree of Bachelor of

Science in Chemistry was conferred on him on June 10, 1940, on completion of the requirements and submission of an unpublished thesis, "The Catalytic Hydrogenation of Protohemin Chloride," which embodies the results of attempts to reduce cattle hemin and lists a series of hemochromogens several of which were new at the time.

Mr. Sherman began his graduate studies in September, 1940, at the University of Alabama where he held a teaching assistantship. Due to his draft status, he left school at the end of the academic year and, a short while later, accepted an appointment as Junior Inspector (P-1) with the United States Food and Drug Administration. He worked out of the New Orleans office of that administration until he was ordered to active duty in the United States Marine Corps on January 31, 1942. He had enlisted in the Reserve on July 12, 1941, for assignment to the Platoon Leaders' Class.

While in the Marine Corps, Mr. Sherman spent nine weeks at the Marine Corps Schools in Quantico, Virginia, and was commissioned a second lieutenant in the Reserve on April 4, 1942, and in the Regular service on June 13, 1942, in recognition of his high attainment. He then served with the Guard Detachment at the President's Summer Camp and with the 23rd Marine Regiment, Fleet Marine Force, Camp Lejeune, North Carolina, where he performed

such duties as platoon commander, company executive officer and company commander. On May 1, 1943, as a first lieutenant, he was part of a cadre that formed the 25th Marine Regiment in which unit he served as a battalion adjutant and as commanding officer of a headquarters company.

During November, 1943, he was appointed an Acting Assistant Quartermaster, promoted to captain and assigned to duty as the Quartermaster and S-4 of the 25th Marines. It was in this capacity that he served overseas with the Fourth Marine Division in the assault invasions of Roi-Namur, Saipan, Tinian and Iwo Jima. Captain Sherman was awarded the Bronze Star Medal with Combat "V", the Purple Heart Medal, the Presidential Unit Citation with two bronze stars, the Asiatic-Pacific Campaign Medal with four stars, the American Campaign Medal, the World War II Victory Medal and a letter of commendation from the Commanding General of the Fourth Marine Division. During February, 1946, while stationed at the Depot of Supplies, Camp Lejeune, North Carolina, he resigned his commission in order to return to college.

Mr. Sherman entered Lehigh University on March 1, 1946, and continued his graduate studies under the Raybestos-Manhattan Company Research Fellowship, working on air-blown oils and related materials. He completed the

requirements for the Master of Science in Chemistry, the degree being conferred on June 29, 1947.

Continuing his graduate work at Lehigh University, Mr. Sherman resigned his full-time fellowship in August, 1947. The following month he accepted a position on a half-time basis preparing certain heterocyclic compounds for the William S. Merrell Company for antitubercular testing. In October, 1948, he resigned this appointment in order to devote more time to his studies and to the investigations which are embodied in the foregoing dissertation.

Mr. Sherman is a member of Sigma Xi, the American Chemical Society, the American Association for the Advancement of Science and the Illinois State Academy of Science. He was married to the former Laurel June Kaplan of Chicago, Illinois, on December 15, 1945.