dimethoxypyrimidine and the completely rearranged 1,3-dimethyl-4-methoxyuracil.

3. The preparation of 2-amino-4,6-dimethoxypyrimidine is described.

NEW HAVEN, CONNECTICUT

2-IODOFURAN AND 2-FURYLMAGNESIUM IODIDE

BY HENRY GILMAN, HARVEY E. MALLORY AND GEORGE F. WRIGHT

Introduction

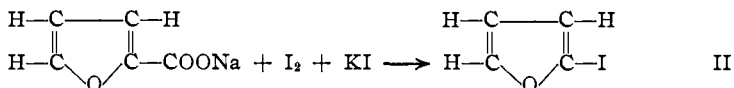The chemistry of furan compounds is markedly circumscribed by present limitations on methods for the introduction of nuclear substituents, and by want of definite information on the positions assumed by substituents together with an inadequate understanding and formulation of rules of orientation. Within recent years, the number of direct nuclear substitution products of furfural and derivatives has been extended significantly. However, such substituents have not as yet lent themselves to widely diversified transformations.

One of several highly reactive key-groupings of this type, through which a miscellany of functions can be introduced indirectly, is the —MgX group attached to carbon. The ready reaction of 2,5-diiodofuran with activated

$$\text{I—C} \underset{\text{O}}{\overset{\text{H—C——C—H}}{\diagdown\diagup}} \text{C—I} + \text{Mg} \longrightarrow \text{I—C} \underset{\text{O}}{\overset{\text{H—C——C—H}}{\diagdown\diagup}} \text{C—MgI} \qquad \text{I}$$
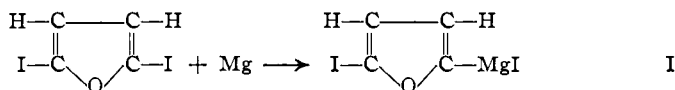
magnesium–copper alloy leading to the formation of 5-iodo-2-furylmagnesium iodide[1] suggested that the simple mono-iodofurans might react smoothly with magnesium to form the corresponding Grignard reagents. Unfortunately, however, no mono-iodofuran was known although attempts[2] have been made to prepare them. After a series of studies, we have devised a method for the preparation of pure 2-iodofuran from the accessible furoic acid and iodine.

$$\text{H—C} \underset{\text{O}}{\overset{\text{H—C——C—H}}{\diagdown\diagup}} \text{C—COONa} + \text{I}_2 + \text{KI} \longrightarrow \text{H—C} \underset{\text{O}}{\overset{\text{H—C——C—H}}{\diagdown\diagup}} \text{C—I} \qquad \text{II}$$

Despite the fact that the present yield of 2-iodofuran is only 20% it is the most accessible simple halogen-furan which can be prepared conveniently in large quantities. 2-Iodofuran is not of a high order of stability, as might have been predicted from the known relative instabilities of chloro

---

[1] Gilman and Wright, *Iowa State Coll. J. Sci.*, **5**, 85 (1931).

[2] (a) Shepard, Winslow and Johnson, THIS JOURNAL, **52**, 2083 (1930); (b) Ciusa and Grillo, *Gazz. chim. ital.*, **57**, 323 (1927).

and bromofurans.[2a]   However, it has so far offered no particular obstacles in manipulation, and it is, of course, more stable in dry ether solutions.

The reaction of 2-iodofuran leading to the formation of 2-furylmagnesium iodide proceeded with an ease that exceeded expectations, no activated magnesium–copper alloy being necessary. Of even greater importance is the excellent yield (95%) of Grignard reagent. Actually, this yield is in excess of that obtained with iodobenzene and is about equal to the yield of phenylmagnesium bromide.[3]   This is not the first furylmagnesium halide, because 2-furylmagnesium bromide was prepared earlier[2a] from the less readily available 2-bromofuran by means of the activated magnesium–copper alloy.   It is, however, the most accessible and unquestionably the most useful furan Grignard reagent despite the increasing number of such compounds prepared very recently, and in very high yields in some cases.[4] By means of 2-furylmagnesium iodide it should prove possible to prepare the widest variety of furan compounds with substituents in the 2-position. The immediately important applications are those turning on the proof of structure of some debatable mono-substituted furans and the synthesis of hitherto inaccessible types.

The general procedure for replacing carboxyl by iodine is one that can be extended from dehydromucic[1] and furoic acids to others like the alkyl and halogen substituted mono- and dibasic furancarboxy ic acids.[5]   Another procedure which it is hoped will yield iodofurans is that involving the following sequence of reactions: nitro compound to amine to diazonium compound to iodo compound.[1]

Experimental Part

2-Iodofuran, C_4H_3OI.—To a solution of 120 g. (3 moles) of sodium hydroxide in 2500 cc. of water is added 336 g. (3 moles) of furoic acid[6] and 332 g. (2 moles) of potassium iodide.   This solution, contained in a 5-liter, round-bottomed flask provided with a reflux condenser, is heated in an oil-bath until the temperature of the mixture reaches 95–97°.   Then 254 g. (1 mole) of iodine is added quickly[7] and the mixture refluxed for three hours by maintaining the oil-bath temperature between 130 and 140°.

At the end of the refluxing period, the flask and contents are cooled with tap water, and to the cooled mixture is added 200 to 500 cc. of a 10% solution of sodium thiosulfate to reduce any unaltered iodine.   The solution is then steam distilled from a 12-liter flask until oil ceases to come over (about fifteen minutes).   This oil is then subjected to another steam distillation, subsequent to a treatment with sodium thiosulfate to remove any iodine.   The steam distillate is collected in two fractions.   The first fraction

[3] Gilman, Zoellner and Dickey, THIS JOURNAL, 51, 1576 (1929).

[4] Gilman and Hewlett, *Rec. trav. chim.*, in press.   This article refers to other furan Grignard reagents.

[5] Among the studies for the preparation of 3-iodofuran is one starting with the known tetraiodofuran.

[6] The technical furoic acid used was purified by crystallizing once from water.

[7] It is necessary that the iodine be added rapidly.   This can be effected by adding it at one time and promptly affixing the condenser to the reaction flask.

is collected in a short stemmed separatory funnel. The second fraction is collected as soon as the oil which steam distils becomes semi-solid in the condenser. The solid in the second fraction yields iodoform, to the extent of about 3.4 g. in a one mole run.

The first fraction is then distilled under reduced pressure, observing the following precautions. First, all parts of the distillation apparatus must be thoroughly steamed out or washed with dilute sodium hydroxide to remove traces of acid which induce re-sinification. Second, the capillary bubbling tube in the Claisen distilling flask is provided with a drying tube containing calcium chloride in order to dry incoming air. Third, the receiver is immersed in an iced-water bath. After carefully transferring the oil from the separatory funnel with a minimum of water, about 5 to 10 g. of anhydrous calcium chloride is added to the flask,[8] and the pressure is reduced immediately to about 15 mm. The 2-iodofuran distils at 43–45° (15 mm.) from a warm water-bath. At the first indication of decomposition in the water condenser, the pressure must be released[9] and the receiver removed immediately. The distillate weighs 39.5 g. (20% of the theoretical amount based on the iodine used); d_{20}^4 2.024; n_D^{20} 1.5661. The 2-iodofuran should be immediately diluted with anhydrous ether because it is relatively more stable in solution and because this ether solution can also be used for the preparation of the corresponding Grignard reagent.

Anal. Calcd. for C_4H_3OI: I, 65.46. Found: I, 65.26, 65.58.

2-Furylmagnesium Iodide, C_4H_3OMgI.—A solution of 35.4 g. (0.18 mole) of 2-iodofuran in 100 cc. of ether is added dropwise to a suspension of 6 g. (0.25 atom) of magnesium (either turnings or 30–80 mesh) in 50 cc. of ether contained in a 200 cc. three-necked flask provided with a mercury-sealed stirrer, condenser and dropping funnel. The reaction flask is previously swept out with dry, pure nitrogen. When the 2-iodofuran and the flask are dry, reaction sets in immediately without addition of iodine or other catalyst. The heat of reaction is large, and care must be exercised that not too much of the halide is added initially. When addition is complete, the mixture is refluxed for one-half hour and then preferably filtered in an inert atmosphere prior to use. Great care should be taken in opening the flask containing magnesium residues, after the Grignard solution is removed by filtration or decantation. The residues are unusually active and *ignite spontaneously* on contact with the air. They may be destroyed by the rapid addition of a large volume of water in an atmosphere of dry nitrogen. There is a possibility that the residues might contain some inflammable di-2-furylmagnesium. Analysis by the acid-titration method[3,10] showed that the Grignard reagent was formed in a 95% yield. Methyl red is recommended as an indicator for the titration of this RMgI compound because of the colored solution.

Two characteristic derivatives of the Grignard reagent were prepared. First, carbonation in a customary manner[11] gave furoic acid, C_4H_3OCOOH, in a 42.5% yield. Second, treatment with phenyl isocyanate gave furoyl anilide, $C_4H_3OCONHC_6H_5$, in an 85% yield. Each of these products was identified by mixed melting point determinations with authentic specimens. It was subsequently found by R. A. Franz that the

---

[8] The calcium chloride is present during the distillation, and the temperature of the water-bath is kept low enough to effect smooth distillation at the pressure indicated. A long stemmed funnel is recommended for the transferal in order to avoid having the iodide touch the side of the neck of the distilling flask.

[9] The pressure can be released by breaking the capillary bubbling tube against the side of the distilling flask. An inert atmosphere of dry nitrogen reduces decomposition during distillation.

[10] Gilman, Wilkinson, Fishel and Meyers, THIS JOURNAL, **45**, 150 (1923).

[11] Gilman and Parker, *ibid.*, **46**, 2816 (1924).

Grignard reagent can be prepared without distillation under reduced pressure, by separating carefully the steam-distilled iodide from water and subsequently drying its ether solution with barium oxide.

The authors are grateful to W. H. Zugschwerdt and E. A. Zoellner for experimental assistance, and to the Cyrus M. Warren Fund of the American Academy of Arts and Sciences for a grant which partially defrayed expenses.

Summary

Pure 2-iodofuran has been prepared from furoic acid and iodine. It forms the corresponding Grignard reagent with uncommon ease and in excellent yields. Both compounds should prove suitable in determining the constitution of nuclear substituted furan compounds and in making accessible hitherto unavailable furan types.

AMES, IOWA

ADDITION REACTIONS OF VINYL PHENYL KETONE. II. DESOXYBENZOIN

BY C. F. H. ALLEN AND W. E. BARKER[1]

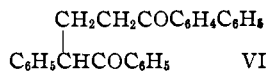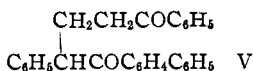In the first paper in this series[2] it was shown that β-chloropropiophenone could be used in place of vinyl phenyl ketone in addition reactions. In continuation of this work we have selected desoxybenzoin as addend, and compared the reactions of the 1,5-diketone (I) thus formed with those of the isomeric benzaldiacetophenone (II).[3]

$$CH_2CH_2COC_6H_5 \qquad\qquad C_6H_5CHCH_2COC_6H_5$$
$$C_6H_5CHCOC_6H_5 \quad I \qquad\qquad CH_2COC_6H_5 \quad II$$
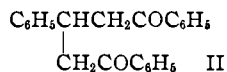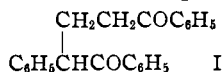
We have transformed it into cyclopropane derivatives (III) isomeric with those (IV) investigated by Kohler and Jones.[4]

$$CH_2\text{—}CHCOC_6H_5 \qquad\qquad C_6H_5CH\text{———}CHCOC_6H_5$$
$$C\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad$$
$$C_6H_5 \quad COC_6H_5 \quad III \qquad\qquad CHCOC_6H_5 \quad IV$$
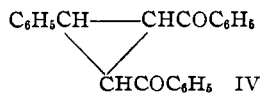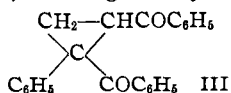
We have also prepared two of the p-phenyl derivatives, one (V) by starting with p-phenyldesoxybenzoin and the other (VI) with p-phenyl-β-chloropropiophenone.

$$CH_2CH_2COC_6H_5 \qquad\qquad CH_2CH_2COC_6H_4C_6H_5$$
$$C_6H_5CHCOC_6H_4C_6H_5 \quad V \qquad\qquad C_6H_5CHCOC_6H_5 \qquad VI$$

---

[1] Acknowledgment is hereby made of a bursary granted to one of us by the National Research Council of Canada.

[2] Allen and Bridgess, THIS JOURNAL, 51, 2151 (1929).

[3] Kostanecki, Ber., 29, 1493 (1891).

[4] Kohler and Jones, THIS JOURNAL, 41, 1249 (1919),