

*Anal.* Calcd. for  $C_{13}H_{16}O_4$ : C, 66.1; H, 6.8. Found: C, 65.8; H, 6.8. *Neutral equivalent.* Calcd.: 236. Found: 239.

**1,4-Dibromo-1,4-dianisoylbutane (XI).**—The bromination was carried out in hot carbon tetrachloride solution in the manner previously described for the dibenzoyl compound. The dibromide after one recrystallization from carbon tetrachloride melted at 158–169°, with decomposition. The yields from three runs varied from 67 to 90% of the theoretical. No attempt was made to separate the meso and racemic isomers.

*Anal.* Calcd. for  $C_{20}H_{20}O_4Br_2$ : Br, 33.0. Found: Br, 33.2.

**2-Anisyl-3-cyano-6-anisoyl-5,6-dihydro-1,4-pyran (XII).**—Sixteen grams of 1,4-dibromo-1,4-dianisoylbutane was treated with sodium cyanide in the manner outlined for the dibenzoyl compound. The product after four recrystallizations from ethyl acetate melted at 141–141.5° (corr.). The yields from two runs were 67 and 73% of the theoretical.

*Anal.* Calcd. for  $C_{21}H_{19}O_4N$ : C, 72.2; H, 5.5. Found: C, 72.1; H, 5.5.

### Summary

2-Phenyl-3-cyano-6-benzoyl-5,6-dihydro-1,4-pyran, 2-(*p*-tolyl)-3-cyano-6-(*p*-toluy)-5,6-dihydro-1,4-pyran and 2-anisyl-3-cyano-6-anisoyl-5,6-dihydro-1,4-pyran have been prepared from 1,4-dibromo-1,4-dibenzoylbutane, 1,4-dibromo-1,4-di-(*p*-toluy)-butane and 1,4-dibromo-1,4-dianisoylbutane, respectively. The closure of the ring was effected in each case by heating the dibromo compound for twenty-four to forty-eight hours with powdered sodium cyanide in a mixture of absolute alcohol and ethyl acetate. The yields varied from 50 to 73% of the theoretical.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

## 5-BROMOFURYLACETYLENE

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### Introduction

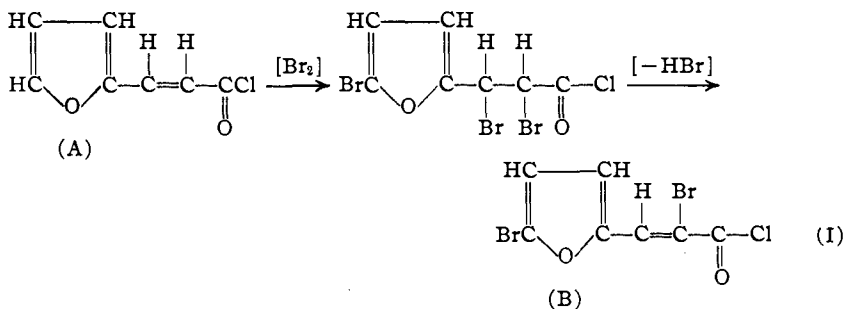
Furylacetylenes are rare and uncommonly difficult of preparation. The parent type, furylacetylene, was prepared by Moureu, Dufraisse and Johnson<sup>1</sup> after a long and difficult study by the action of alcoholic potassium hydroxide on furylbromoethylene. Their success was due in part to the use of the anti-oxidants or stabilizers elaborated by Moureu and co-workers in connection with polymerization studies on the related styrenes and other compounds. Long before those studies, Gibson and Kahnweiler<sup>2</sup> used the same reaction for the preparation of bromofurylacetylene, which they never succeeded in isolating in a pure condition.

Incidental to our studies on furan compounds, a need arose for 5-bromo-

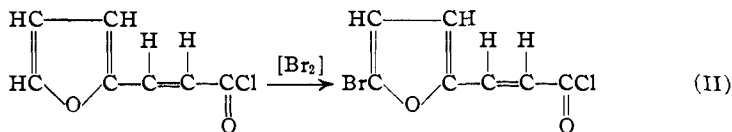
<sup>1</sup> Moureu, Dufraisse and Johnson, *Ann. chim.*, **7**, 1, 14 (1927).

<sup>2</sup> Gibson and Kahnweiler, *Am. Chem. J.*, **12**, 314 (1890).

furylacetylmagnesium bromide,  $\text{BrC}_4\text{H}_2\text{OC}\equiv\text{CCMgBr}$ . Investigations of bromine nuclear substituted furan types<sup>3</sup> suggested a different avenue of approach and there is now reported a series of reactions leading to the preparation of 5-bromofurylacetylene in satisfactory yields. The readily accessible furylacryloyl chloride (A) is smoothly brominated (when highly purified) to give  $\alpha$ -bromo- $\beta$ -(5-bromofuryl)-acryloyl chloride (B), in yields greater than 90%.<sup>4</sup>



The tendency for nuclear bromination is so great<sup>5</sup> that it is possible under selected conditions to prepare 5-bromofurylacryloyl chloride in satisfactory yields



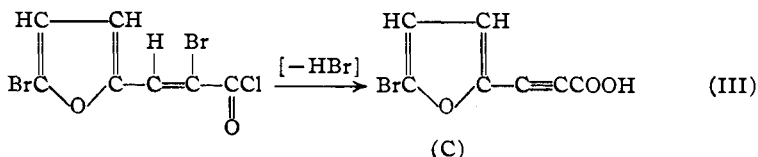
It is interesting to report in this connection that the allo- or *cis*-furylacrylic acid, when treated with one mole of bromine with a view to effecting lateral addition only, gave the tetrabromo addition compound of Moureu, Dufrasse and Johnson<sup>1</sup> in which two of the bromines are in the side chain and two on the ring.

$\alpha$ -Bromo- $\beta$ -(5-bromofuryl)-acryloyl chloride (B) with dilute aqueous sodium hydroxide gives 5-bromofurylpropionic acid (C).<sup>5</sup>

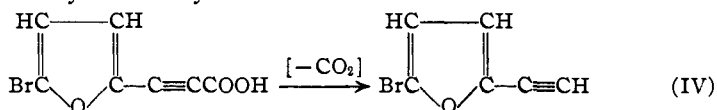
<sup>3</sup> Gilman and Wright, THIS JOURNAL, 52, 1170, 3349 (1930), etc.

<sup>4</sup> The nuclear bromine in furylacrylic acid derivatives has been shown to be in the 5-position [Gilman and Wright, *Rec. trav. chim.*, 49, 195 (1930)] and it is highly probable on the basis of some direct evidence as well as indirect evidence resting on analogies with related heterocycles (like thiophene, coumarone, etc.), that all 2-substituted furans orient to the 5-position. The reader is referred to current studies by Johnson and Rinkes. For absolute methods of orientation, see Gilman and Wright, *Iowa State Coll. J. of Sci.*, 5, 85 (1931). By analogy with related phenyl compounds, the lateral bromine in bromo-(5-bromofuryl)-acryloyl chloride is probably on the  $\alpha$ -carbon.

<sup>5</sup> Gibson and Kahnweiler<sup>2</sup> attempted unsuccessfully the preparation of bromofurylpropionic acid by removal of hydrogen bromide from the  $\alpha$ -bromo- $\beta$ -(5-bromofuryl)-acrylic acid.



Steam distillation of 5-bromofurylpropionic acid (C) gives 5-bromofurylacetylene by decarboxylation.



In addition, there are obtained varying quantities of 5-bromofuryl methyl ketone,  $\text{BrC}_4\text{H}_2\text{OCOCH}_3$ . This ketone is also obtainable by the action of aqueous sodium hydroxide on  $\alpha$ -bromo- $\beta$ -(5-bromofuryl)-acryloyl chloride. It is obtained in higher yields by the action of alkali on ethyl 5-bromofuryldibromopropionate,<sup>6</sup>  $\text{BrC}_4\text{H}_2\text{OCHBrCHBrCO}_2\text{C}_2\text{H}_5$ . The identity of 5-bromofuryl methyl ketone was confirmed by its synthesis from the recently available 5-bromofurfural<sup>7</sup> and diazomethane.

As was to be expected, the 5-bromofurylacetylene is readily converted by ethylmagnesium bromide to 5-bromofurylacetylenylmagnesium bromide, which underwent in turn some characteristic reactions of an acetylenic Grignard reagent.

The reduction of 5-bromofurylpropionic acid (C) by zinc to furylpropionic acid indicates that it may be possible to prepare at present the relatively inaccessible furylacetylene by a corresponding reaction from the now available and relatively more stable 5-bromofurylacetylene.

### Experimental Part

**$\beta$ -(5-Bromofuryl)-acryloyl Chloride,  $\text{BrC}_4\text{H}_2\text{OCH}=\text{CHCOCl}$ .**—Seventy-eight g. (0.5 mole) of carefully purified furylacryloyl chloride<sup>8</sup> was diluted with 150 cc. of carbon disulfide in a 500-cc. three-necked flask provided with a dropping funnel, stirrer and drying tube containing calcium chloride. The flask was immersed in a cold water-bath, 80 g. (0.5 mole) of bromine in 100 cc. of carbon disulfide was added slowly, and stirring was continued for one hour subsequent to addition. After keeping the reaction mixture under reduced pressure (25–50 mm.) for twenty-four hours, the residue was distilled under reduced pressure, and 66 g. or a 56% yield of bromo acid chloride distilling at 182–188° (6 mm.) was obtained. Redistillation gave the pure compound which melted at 54°.

*Anal.* Calcd. for  $\text{C}_7\text{H}_4\text{O}_2\text{BrCl}$ : Br, 34.04; Cl, 15.09. Found: Br, 34.44; Cl, 14.72.

Hydrolysis yielded 5-bromofurylacrylic acid, which was shown to be identical with an authentic specimen.<sup>9</sup>

<sup>6</sup> The halogenated esters will be reported subsequently.

<sup>7</sup> Gilman and Wright, *THIS JOURNAL*, **52**, 1170 (1930).

<sup>8</sup> The furylacryloyl chloride is obtainable in 90% yield from furylacrylic acid and thionyl chloride. See Gilman and Hewlett, *Iowa State Coll. J. of Sci.*, **4**, 27 (1929).

<sup>9</sup> Gilman and Wright, *Rec. trav. chim.*, **49**, 195 (1930).

$\alpha$ -Bromo- $\beta$ -(5-bromofuryl)-acryloyl Chloride,  $\text{BrC}_4\text{H}_2\text{OCH}=\text{CBrCOCl}$ .—In the preparation of this acid chloride, pure, freshly distilled furylacryloyl chloride must be used, the first and last fractions being rejected. A solution of 232 g. (1.5 moles) of furylacryloyl chloride in 920 cc. of dry carbon disulfide was placed in a 2-liter three-necked flask provided with a stirrer, dropping funnel and condenser holding a drying tube with calcium chloride. After the slow addition of 480 g. (3 moles) of bromine in 280 cc. of dry carbon disulfide, the solution was refluxed for three hours, and then the carbon disulfide was removed by distillation under reduced pressure. The thick oily residue was heated at  $100^\circ$  under 30 mm. pressure for four hours, at the end of which time evolution of hydrogen bromide had practically ceased. On distillation at  $190$ – $195^\circ$  (24 mm.) the residue gave 390–400 g. of the acid chloride, which solidified in the receiver and melted at  $70$ – $71^\circ$ . This yield is 83%, but yields as high as 92% were obtained in 0.5-mole runs. On redistillation at  $182$ – $183^\circ$  (21 mm.) the product melted at  $72^\circ$ . It can be crystallized from chloroform or carbon tetrachloride and is fairly stable when kept cold.

*Anal.* Calcd. for  $\text{C}_7\text{H}_3\text{O}_2\text{Br}_2\text{Cl}$ : Br, 50.95; Cl, 11.29. Found: Br, 50.67; Cl, 11.51.

Although the acid chloride was not directly hydrolyzed to the corresponding acid, the  $\alpha$ -bromo- $\beta$ -(5-bromofuryl)-acrylic acid was obtained by converting the acid chloride to its ethyl ester, which is readily hydrolyzed with cold alcoholic potassium hydroxide. The dibromo acid so obtained was shown to be identical with the previously described compound.<sup>2</sup>

5-Bromofurylpropionic Acid,  $\text{BrC}_4\text{H}_2\text{OC}\equiv\text{CCOOH}$ .—Seventy-eight and one-half g. (0.25 mole) of  $\alpha$ -bromo- $\beta$ -(5-bromofuryl)-acryloyl chloride was melted and poured into a solution of 30 g. (0.75 mole) of sodium hydroxide in 1.5 liters of water which had been heated to  $70$ – $80^\circ$ . After stirring for four hours, the mixture was filtered, and cracked ice was added to the filtrate after chilling. The cold filtrate was acidified with hydrochloric acid, and the precipitated acid, after filtration by suction and air-drying, weighed 37 g. or a 67% yield, and melted at  $127^\circ$ . This highly impure acid melted at  $143^\circ$  after several crystallizations from a water-alcohol mixture. The yield of crude acid in 0.5 mole and 1.44 mole runs was 69%.

*Anal.* Calcd. for  $\text{C}_7\text{H}_3\text{O}_3\text{Br}$ : Br, 37.21. Found: Br, 37.54.

The pure acid is more readily obtained by refluxing potassium  $\alpha$ -bromo- $\beta$ -(5-bromofuryl)-acrylate with an equimolecular quantity of alcoholic potassium hydroxide, filtering to remove unaltered potassium salt, evaporating the filtrate under reduced pressure and acidifying the iced solution with hydrochloric acid. The acid is obtained in this manner in a 30% yield and melts at  $143^\circ$ .

Furylpropionic Acid,  $\text{C}_4\text{H}_3\text{OC}\equiv\text{CCOOH}$ .—An excess of powdered zinc was added to a heated solution ( $80^\circ$ ) of 5-bromofurylpropionic acid in an excess of ammonium hydroxide. When the heat of reaction subsided, the suspension was filtered, and the cooled filtrate acidified to liberate unaltered 5-bromofurylpropionic acid. The filtrate from the bromo acid was extracted with ether to give furylpropionic acid, which may be purified by crystallization from petroleum ether (b. p.  $90$ – $120^\circ$ ). The furylpropionic acid melted at  $112$ – $113^\circ$  and had a neutralization equivalent of 138 (calcd. 136). These properties agree with those reported previously.<sup>1</sup>

5-Bromofurylacetylene,  $\text{BrC}_4\text{H}_2\text{OC}\equiv\text{CH}$ .—A suspension of 21.5 g. (0.1 mole) of crude 5-bromofurylpropionic acid in 125 cc. of water was steam distilled until about 700 cc. of distillate was collected. The oil which was collected in the bottom of a separatory funnel receiver was separated and then combined with two carbon disulfide extracts of the aqueous layer. After drying over sodium sulfate and removing the solvent, the

compound distilled at 63–64° (24 mm.) and weighed 5.4 g., which is equivalent to a 32% yield;  $n_D^{20}$  1.5510;  $d_{20}^4$  1.509.<sup>10</sup>

*Anal.* Calcd. for  $C_6H_5OBr$ : Br, 46.78. Found: Br, 46.84, 46.90.

In the distillation, care must be exercised that none of the higher boiling 5-bromofuryl methyl ketone distills. The yield of ketone melting at 96° after crystallization from alcohol was 4 g. The residual liquor from the steam distillation was found to contain appreciable quantities of 5-bromofurylacrylic acid and  $\alpha$ -bromo- $\beta$ -(5-bromofuryl)-acrylic acid.

The di-(5-bromofurylacetylene) melted at 126°, which agrees with that reported previously by Gibson and Kahnweiler.<sup>2</sup>

**5-Bromofuryl Methyl Ketone,  $BrC_4H_2OC(=O)CH_3$ .**—The ketone was obtained in a 14.4% yield by treating 3.76 g. (0.012 mole) of  $\alpha$ -bromo- $\beta$ -(5-bromofuryl)-acryloyl chloride with 4.7 g. (0.12 mole) of sodium hydroxide in 25 cc. of water. After several hours, the mixture was steam distilled and yielded 0.32 g. of the ketone melting at 94–95°. Larger yields are obtainable if ethyl  $\alpha$ , $\beta$ -dibromo- $\beta$ -(5-bromofuryl)-propionate,  $BrC_4H_2OCHBrCHBrCOOC_2H_5$ , is used. In an orienting experiment none of the ketone was obtained when 5-bromofurylacetylene was treated with concentrated alkali.

The ketone was also obtained in a 36% yield by the action of diazomethane on 5-bromofurfural,<sup>7</sup> and the method of mixed melting points showed the product to be identical with that obtained by the other reactions mentioned above.

*Anal.* Calcd. for  $C_6H_5O_2Br$ : Br, 42.33. Found: Br, 42.52.

The corresponding 5-bromofuryl methyl ketoxime was prepared in a customary manner, and when crystallized from an alcohol-water mixture melted at 79.5°. The oxime has a slightly astringent taste in aqueous solution.

*Anal.* Calcd. for  $C_6H_5O_2NBr$ : Br, 39.21. Found: Br, 39.43.

**5-Bromofurylacetylenylmagnesium Bromide,  $BrC_4H_2OC\equiv CMgBr$ .**—The Grignard reagent was prepared by the slow addition of 11 g. (0.065 mole) of 5-bromofurylacetylene in 50 cc. of ether to 0.1 mole of ethylmagnesium bromide. When carbonated in a customary manner,<sup>11</sup> there was obtained a 21.8% yield of 5-bromofurylpropionic acid.

The  $\alpha$ -naphthalide from 5-bromofurylacetylenylmagnesium bromide was prepared in a customary manner<sup>12</sup> from the  $RMgBr$  compound and  $\alpha$ -naphthyl isocyanate. Recrystallization from an alcohol-water mixture gave 5-bromofurylpropio- $\alpha$ -naphthalide,  $BrC_4H_2OC\equiv CCONHC_{10}H_7-\alpha$ , melting at 150°.

*Anal.* Calcd. for  $C_{17}H_{20}BrNO_2$ : Br, 23.53. Found: Br, 23.46.

The authors gratefully acknowledge assistance from W. M. Selby.

### Summary

A series of reactions is described for the preparation of 5-bromofurylacetylene and derivatives in satisfactory yields.

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<sup>10</sup> In 0.5 and 0.7 mole runs the yield of 5-bromofurylacetylene was 30%. It is probable that other variations for decarboxylation will give higher yields.

<sup>11</sup> Gilman and Parker, *THIS JOURNAL*, **46**, 2816 (1924).

<sup>12</sup> Gilman and Furry, *ibid.*, **50**, 1214 (1928).