

Chemistry Division, The Norwich Pharmacal Company

Synthesis of 5-Phenyl-2-furaldehyde

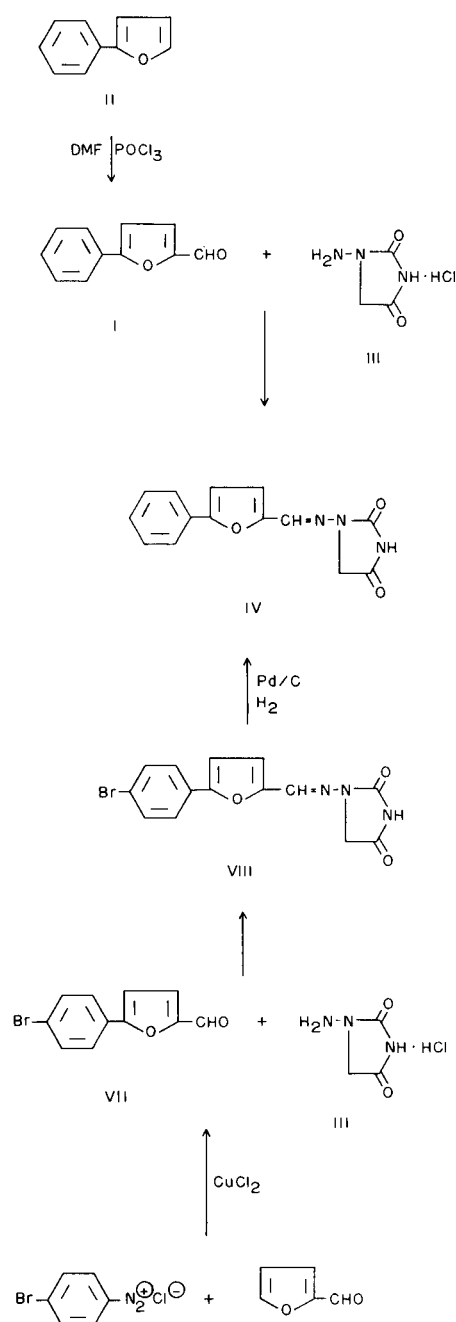
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Akashi and Oda (1) have reported the preparation of 5-phenyl-2-furaldehyde (I) by coupling benzenediazonium chloride with 2-furaldehyde in the presence of cupric chloride. Malinowski (2) has confirmed this method of preparation. Bailey, *et al.*, (3) synthesized 5-phenyl-2-furaldehyde by forming the furan ring, but reported physical constants significantly different from Akashi and Oda's. Repeated attempts by the authors to reproduce Akashi and Oda's method for the preparation of 5-phenyl-2-furaldehyde were unsuccessful. When electron withdrawing groups (*i.e.*, *p*-nitro and *p*-bromo) were attached to the benzenediazonium chloride, the condensation proceeded as reported (4a, b, c).

As a route to large quantities of 5-phenyl-2-furaldehyde (I), the formylation of 2-phenylfuran was investigated. The structure of 2-phenylfuran has been established (5). Because three isomers of phenylfuraldehyde are possible, location of the formyl group was accomplished by the following procedure: (a) The 5(2)-phenylfuraldehyde (I) was condensed with 1-aminohydantoin hydrochloride (III) to give a solid derivative (IV). (b) *p*-Bromobenzenediazonium chloride (V) and 2-furaldehyde (VI) were allowed to react to give 5-(*p*-bromophenyl)-2-furaldehyde (VII). Although the position of the 5-(*p*-bromophenyl) group may be questioned, the aldehyde group must be in the 2 position of the furan ring. (c) 5-(*p*-Bromophenyl)-2-furaldehyde (VII) was condensed with III to give 1-[5-(*p*-bromophenyl)furfurylidene]amino]hydantoin (VIII). (d) The bromo compound (VIII) was reduced with palladium on charcoal to give a material (IV) which was identical to the compound obtained from formylation of 2-phenylfuran.

This sequence of reactions illustrates the following points: (a) Formylation of 2-phenylfuran produced 5-phenyl-2-furaldehyde. (b) *p*-Bromobenzenediazonium chloride coupled with 2-furaldehyde in the 5 position.

Although Akashi and Oda (1) reported a lower boiling point for 5-phenyl-2-furaldehyde, the melting point of their semicarbazone agrees with our findings. The present work confirms the boiling point for 5-phenyl-2-furaldehyde reported by Bailey, *et al.* (3), but there is a slight discrepancy in the melting points of the oxime.



EXPERIMENTAL

The melting points were taken in a Mel-Temp apparatus and are corrected.

5-Phenyl-2-furaldehyde (I).

Into a flask equipped with a mechanical stirrer, thermometer, addition funnel, and a nitrogen inlet tube was placed dimethylformamide (21.9 g., 0.3 mole). To the dimethylformamide was added phosphorus oxychloride (45.9 g., 0.3 mole) with caution. The resulting solid was allowed to stand at room temperature for 0.5 hours before adding 2-phenylfuran (5) (37 g., 0.27 mole). The exothermic reaction was controlled with an ice bath (maximum temperature 40°). The mixture was stirred for 2 hours and then heated on a steam bath for 1 hour. The dark colored solution was poured into 500 ml. of ice water, neutralized with solid potassium carbonate, and then extracted with 2 x 1 l. portions of ether. The ethereal extracts were dried over sodium sulfate and concentrated under reduced pressure. The remaining residue was fractionally distilled to yield 31 g. (60%) of 5-phenyl-2-furaldehyde, b.p. 122-123°/0.25 mm. (lit. b.p. 90-92°/30 mm. (1) and 146°/5 mm. (3)).

5-Phenyl-2-furaldehyde (36 g., 0.21 mole) in 150 ml. of dimethylformamide was added to a solution of 1-aminohydantoin hydrochloride (6) (III) (45 g., 0.3 mole) in 250 ml. of water. The suspension was stirred for 2 hours and then poured into 2 l. of cold water to yield 51 g. (94%) of 1-[(5-phenylfurfurylidene)amino]hydantoin (IV). The analytical sample, m.p. 258-260°, was prepared by washing with acetone.

Anal. Calcd. for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61. Found: C, 62.52; H, 4.33; N, 15.78.

5-Phenyl-2-furaldehyde (5 g., 0.028 mole) and 4 ml. of pyridine in 15 ml. of ethanol were treated with hydroxylamine hydrochloride (5 g., 0.07 mole) and refluxed for 2 hours. The solution was cooled and diluted with 25 ml. of water to yield 5 g. (95%) of 5-phenyl-2-furaldehyde oxime. The oxime was recrystallized from methanol, m.p. 194-195° (lit. (3) m.p. 182-185°).

5-Phenyl-2-furaldehyde semicarbazone was prepared by the method of Akashi and Oda (1). The semicarbazone was recrystallized from ethanol to give a material melting at 199-202°.

Anal. Calcd. for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.87; N, 18.33. Found: C, 62.87; H, 5.03; N, 18.51.

1-[(5-(*p*-Bromophenyl)furfurylidene)amino]hydantoin (VIII).

A mixture of *p*-bromoaniline (86 g., 0.5 mole), 100 ml. of water and 75 ml. of concentrated hydrochloric acid was heated for 15-20 minutes before an additional 150 ml. of concentrated hydrochloric acid was added. The white suspension was cooled to 0° and then a solution of sodium nitrite (35 g., 0.5 mole in 150 ml. of water) was added. The solution was stirred for 20 minutes at 5° before the ad-

dition of cupric chloride (10 g. in 20 ml. of water) and 2-furaldehyde (48 g., 0.5 mole in 50 ml. of acetone). The green solution was stirred for 4 hours at 15-20°. After the evolution of nitrogen ceased, the aqueous solution was decanted and the solid was washed with 2 x 500 ml. portions of water.

The 5-(*p*-bromophenyl)-2-furaldehyde was dissolved in dimethylformamide (800 ml.) and then added to a solution of 1-aminohydantoin hydrochloride (III) (76 g., 0.5 mole) in 1 l. of water. The material was washed in hot acetone and then recrystallized from DMF to give 39 g. (22%) of VIII. The analytical sample was recrystallized from dimethylformamide, m.p. 284-285° dec.

Anal. Calcd. for $C_{14}H_{10}BrN_3O_3$: C, 48.30; H, 2.90; N, 12.07. Found: C, 48.28; H, 2.89; N, 12.15.

Reduction of 1-[(5-(*p*-Bromophenyl)furfurylidene)amino]hydantoin (VIII).

A solution of 1-[(5-(*p*-bromophenyl)furfurylidene)amino]hydantoin (VIII) (10 g., 0.03 mole) was hydrogenated at 50 psi using 2 g. of 5% palladium on charcoal. The theoretical amount of hydrogen was absorbed in 15 hours. Two hundred milliliters of water was added to the dimethylformamide solution to precipitate a solid. The solid was filtered and dried. The 1-[(5-phenylfurfurylidene)amino]hydantoin (6 g., 67%) was recrystallized from dimethylformamide and water to give a material melting at 257-259°. A mixture melting point with the product from the formylation of 2-phenylfuran (IV) gave no depression; the infrared spectra were identical.

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REFERENCES

- (1) H. Akashi and R. Oda, *J. Chem. Soc., Japan*, 53, 81 (1950). *Chem. Abstr.*, 47, 2164 (1953).
- (2) S. Malinowski, *Roczniki Chem.*, 27, 54 (1953). *Chem. Abstr.*, 48, 13678 (1954).
- (3) P. S. Bailey, W. W. Hakki, and H. W. Bost, *J. Org. Chem.*, 20, 1034 (1955).
- (4a) H. Akashi and R. Oda, *Repts. Inst. Chem. Research*, 19, 93 (1949). *Chem. Abstr.*, 45, 7519 (1951). (4b) H. Akashi and R. Oda, *J. Chem. Soc., Japan*, 53, 202 (1950). *Chem. Abstr.*, 46, 9312 (1952). (4c) R. Oda, *Mem. Fac. Eng. Kyoto Univ.*, 14, 195 (1952). *Chem. Abstr.*, 48, 1935 (1954).
- (5) A. W. Johnson, *J. Chem. Soc.*, 895 (1946).
- (6) W. Traube and E. Hoffa, *Ber.*, 31, 167 (1898).

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