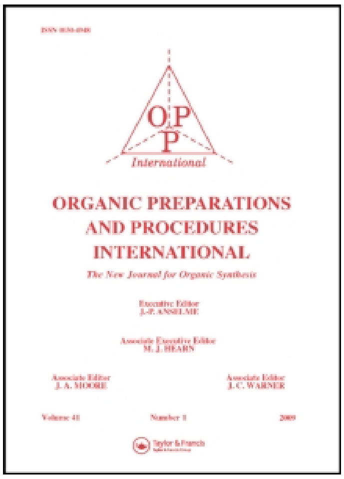

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AN IMPROVED SYNTHESIS OF THE ISOMERIC AMINODIBENZOFURANS

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AN IMPROVED SYNTHESIS OF THE ISOMERIC AMINODIBENZOFURANS

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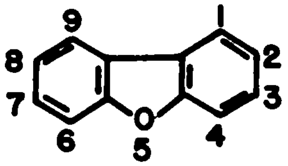
Our continuing interest in the carcinogenic properties of heterocylic analogs of p-N,N-dimethylphenylazobenzene (DAB) required synthesis of the isomeric aminodibenzofurans in substantial amounts. Although routes have been reported[1,2] the conciseness of the experimental procedures made them at times difficult to reproduce. The methods described here represent a significant improvement in yields and procedures. Those procedures which were not improved or altered are referred to without discussion.



1-Aminodibenzofuran was synthesized from the 1-bromo rather than the 1-nitrodibenzofuran since in our hands a low yield (25%) of product was obtained upon nitration of 4-acetamidodibenzofuran and three recrystallizations from ethanol were required to obtain the reported melting point. The utility of our procedures is shown by the high yield, melting point, and crystalline state of the compound as isolated. In particular, the excellent conversion of the halogenated dibenzofurans to the aminodibenzofurans may be of general interest, e.g. 1-bromodibenzofuran gave 1-aminodibenzofuran in 90% yield as compared to the 24% previously reported.[3]

EXPERIMENTAL

2-Aminodibenzofuran. - Into a 1700 ml glass liner from a Parr stirrer autoclave was placed 2-iododibenzofuran (55 g, 0.17 mol) and cuprous bromide (55 g). To this was added conc. ammonium hydroxide (500 ml) and the autoclave heated at 200-210° with stirring for 24 hr. The autoclave was cooled and the basic mixture filtered. After water washing to remove copper salts, the autoclave and filter cake were treated with acetone to dissolve all organic materials. The acetone mixture was filtered and diluted with twice its volume of water. The precipitated 2-aminodibenzofuran was collected by filtration as white flakes (30 g, 95%) mp. 127° (lit.[4], mp. 125-126°).

4-Aminodibenzofuran. - This amine was synthesized as described by Gilman with the exception that to n-butyllithium (22% in hexane, 230 ml) was added an equimolar amount of dibenzofuran (84 g, 0.5 mol) in absolute ether (500 ml) and refluxed until a copious canary yellow precipitate formed (3-4 hrs). At this point, the reaction mixture was cooled to (-10) in a dry ice-acetone bath. Stirring was begun and methoxyamine (30 ml, 0.5 mole) in anhydrous ether (100 ml) was then admitted slowly. After allowing the mixture to come to room temperature, it was refluxed for 1 hr. The mixture was cooled and water was slowly admitted. The ether solution was separated from the water, dried with anhydrous sodium sulfate, diluted to a volume of 1 - 1.5 liters with more ether and hydrogen chloride gas passed in. A thick copious precipitate of the 4-aminodibenzofuran hydrochloride formed. The product was removed by filtration and the 4-aminodibenzofuran hydrochloride was obtained as a white solid in 50 per cent yield, (55 g), mp. of the free amine 85° (lit[5] mp. 83-4°).

4-Acetamidodibenzofuran. - 4-Aminodibenzofuran (1 g) was treated with 5 ml. of acetic anhydride to dissolve it. As soon as the material dissolved a solid mass of yellow needles formed. This material was treated with carbon tetrachloride, filtered; the crystals were washed with carbon tetrachloride and dried to give 4-acetamidodibenzofuran as short yellow needles, 80%, mp. 180-181°, (lit.[6], 172.5°).

1-Bromo-4-acetamidodibenzofuran. - 4-Acetamidodibenzofuran (19.4 g, 0.096 mol) was treated with sufficient glacial acetic acid to dissolve it. Bromine (13.8 g, 4.1 ml, 0.09 mol) was added at such a rate that no color developed until the end of the addition. After an additional 10 min., a solution of sodium thiosulfate (10% by wt) was added to discharge the brown coloration and the mixture poured onto ice. By filtering this mixture, 1-bromo-4-acetamidodibenzofuran was obtained as silvery flakes, 26.2 g, 100%, mp. 228°, (lit.[3], mp. 228°).

1-Bromo-4-aminodibenzofuran. - 1-Bromo-4-acetamidodibenzofuran (30.5 g, 0.1 mol) was hydrolyzed by refluxing 2.5 hr with ethanol (500 ml) and potassium hydroxide (56 g, 1.0 mol). The lightly pink solution was poured onto ice and the solid, collected by filtration, was a white powder, 25 g, 95%, mp. 118-120° (lit.[3], mp. 119-120°).

1-Bromo-4-aminodibenzofuran was converted to 1-bromodibenzofuran as previously described.[3]

1-Aminodibenzofuran. - 1-Bromodibenzofuran was converted to 1-aminodibenzofuran as described for the 2-aminodibenzofuran. The amine was isolated by washing the bomb and the filter cake with ether, drying the ethereal solution with sodium sulfate, and bubbling in hydrogen chloride. From 7 g of 1-bromodibenzofuran, there was obtained, lit, 6.5 g of 1-aminodibenzofuran hydrochloride (90%), mp. free amine 74°, (lit.[3], mp. 74°).

<u>3-Aminodibenzofuran</u>. - 3-Nitrodibenzofuran, prepared by nitration of dibenzofuran in glacial acetic acid with fuming nitric acid, was reduced by hydrogenation in absolute ethanol with 10% Pd/C at 40 psi. The catalyst was removed by filtration through a Celite bed. The ethanol was removed in vacuo, the residue dissolved in ether and hydrogen chloride gas bubbled into the ether. The solid was removed by filtration to give 3-aminodibenzofuran hydrochloride, 90% mp. free amine 94°, (lit.[7], mp. 94°).

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