

SYNTHESIS OF 4-HYDROXY-4'-IODOTHIOBENZANILIDE

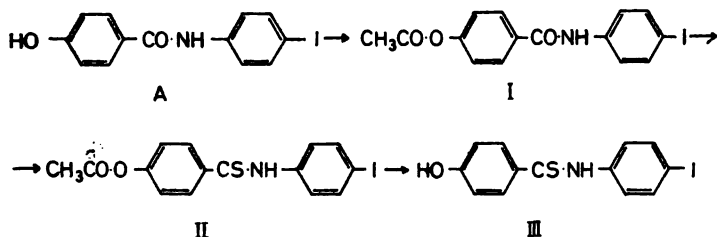
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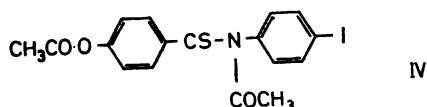
The amides of carbonic acids can easily be transformed into the corresponding thioamides by means of phosphorus pentasulphide in dry organic solvents (pyridine, dioxane, benzol, xylene, and others)^(1, 2, 3, 4). This simple and general method cannot be applied to amides which have a free phenol-hydroxyl group, unless the hydroxyl group is previously protected^(5, 6). Protection is only possible achieved with acyl protective groups which can be introduced in a simple way into the hydroxy-amide molecule and which, after interacting with phosphorus pentasulphide, can again be easily liberated, leaving the thioamide group unchanged.

Attempts at obtaining halogen-substituted hydroxythioamide by halogenation of the corresponding acetoxythio derivative under different reaction conditions have been unsuccessful. Substances without sulphur were always obtained.

It was therefore necessary to approach the synthesis of 4-hydroxy-4'-iodothiobenzanilide in another way. It is similar to the previously described synthesis of 4-hydroxy-4'-bromothiobenzanilide⁽⁷⁾ and can be represented by the following schema:



Compound III reacting with the anhydride of acetic acid involves simultaneous acetylation of the hydroxyl group and of the thioamide group, and the corresponding *O, N*-diacetylthio derivative with the following structure is formed:



EXPERIMENTAL

The melting points are not corrected.

4-acetoxy-4'-iodobenzanilide (I)

Into a solution of 2.19 g (0.01 mol) 4-iodoaniline⁽⁶⁾ in 20 ml of pyridine, cooled to 0°, 1.98 g (0.01 mol) of 4-acetoxybenzoylchloride⁽⁹⁾ (freshly prepared and dissolved in 10 ml of dry ether) was gradually added with continuous mixing through 15 minutes. The reaction mixture was mixed for another 30 minutes at room temperature and then poured into 250 ml of ice-cold water. 3.65 g (96%) of the raw product, m.p. 209—210°C, was obtained. By recrystallization from ethanol colorless flakes were obtained, m.p. 218—219°C.

Analysis: $C_1 H_{12} NO_3 I$ (381.18)

Calculated: C 47.28, H 3.17, N 3.68%

Found: C 47.26, H 3.40, N 3.55%

4-acetoxy-4'-iodothiobenzanilide (II)

3.81 g (0.01 mol) of dried compound I was dissolved in 10 ml of dry pyridine with mild heating on an oil bath. 2.22 g (0.01 mol) of powdered phosphorus pentasulphide was added to the warm solution and the heating continued so that the solution boiled gently for 45 minutes. The dark red reaction mixture was poured into 300 ml of water, whereupon a dark crystalline substance separated out, which was filtered, washed with water and dried. 3.46 g (87%) of raw product was obtained, m.p. 169—172°C. By recrystallization from ethanol yellow needles were obtained, m.p. 178—179°C.

This synthesis was also done with dry xylene as the solvent, with a yield of 80% of dry product.

Analysis: $C_{15} H_{12} NO_2 S I$ (397.25)

Calculated: C 45.38, H 3.05, N 3.53%

Found: C 45.22, H 2.38, N 3.64%

4-hydroxy-4'-iodothiobenzanilide (III)

3.97 g (0.01 mol) of compound II was dissolved in 20 ml NaOH with heating on a water bath at 60—70°C for 10—15 min. The yellow alkaline solution (pH 8—9) was filtered and after cooling was acidified with 1 N HCl to pH 5—6. The yellow crystalline substance formed was filtered, washed with water and dried. 3.3 g (93%) of raw product was obtained, m.p. 190—193°C. By recrystallization from ethanol yellow prisms were obtained, m.p. 197—198°C.

Analysis: $C_{13}H_{10}NO_3SI$ (355.20)
 Calculated: C 43.98, H 2.84, N 3.95%
 Found: C 44.01, H 3.07, N 3.77%

O,N-diacetyl-4-hydroxy-4'-iodothiobenzanilide (IV)

3.55 g (0.01 mol) of substance III was dissolved in 15 ml of pyridine, and 5.12 g (0.05 mol) of acetic acid anhydride added into the solution. After 2—3 hours at room temperature the red reaction mixture was poured into 300 ml of ice-cold water. The red crystalline product was filtered, washed and dried. The yield of raw product was 3.5 g (82%), m.p. 126—128°C. By recrystallization from ethanol red needles were obtained, m.p. 135—136°C.

Analysis: $C_{17}H_{14}NO_3SI$ (439.28)
 Calculated: C 46.51, H 3.23, N 3.19%
 Found: C 46.68, H 3.47, N 3.30%

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