

SYNTHESIS OF 4-HYDROXY-4'-BROMOTHIOBENZANILIDE

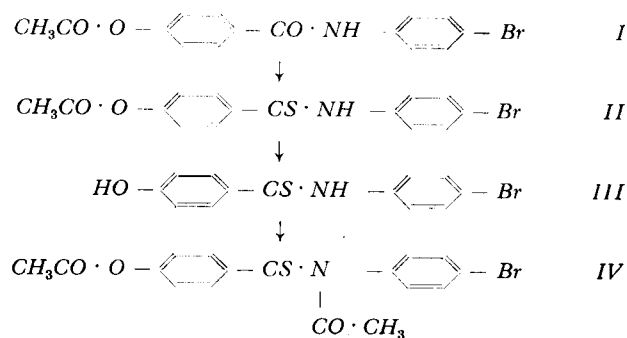
by

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As a continuation of our investigations in the field of hydroxythioamides and in connection with already reported conclusions (1,2) we have synthesized 4-hydroxy-4'-bromothiobenzanilide.

The starting substance was the corresponding hydroxybenzanilide in which the hydroxyl group was protected by an acetyl group, namely the 4-acetoxy-4'-bromobenzanilide (I) which was obtained from 4-acetoxybenzoyl chloride and 4-bromoaniline. By refluxing this compound with phosphorpentasulphide in anhydrous organic solvents (dioxane, pyridine, xylene) the corresponding acetoxythioamide (II) was obtained in a yield of about 80%. Alkaline hydrolysis of the product II yielded the desired 4-hydroxy-4'-bromothiobenzanilide (III).

The presence of the free hydroxyl group in compound III was proved by acetylation with acetic anhydride. However, upon treatment with acetic anhydride the thioamide group was acetylated as well, so that the corresponding O,N-diacetyl thioamide derivative (IV) was obtained. The same compound (IV) was also obtained by the acetylation of compound II.



EXPERIMENTAL

Melting points are not corrected.

4-Acetoxy-4'-bromobenzanilide (I)

Freshly prepared 4-acetoxybenzoyl chloride (3) (3.98 g; 0.02 mole) was added dropwise to the cooled, stirred solution of 4'-bromoaniline (4) (3.44 g; 0.02 mole) dissolved in pyridine (12 ml). After standing for half an hour the reaction mixture was poured into icy water (300 ml) and the separated crystalline product was filtered off, washed and dried. The yield of the crude product was 6.2 g (92.4%). Recrystallization from ethanol gave colorless needles melting at 214–215°.

Anal. $C_{15}H_{12}NO_3Br$ (334.17)

Calc.: C 53.94, H 3.62, N 4.19%

Found: C 53.86, H 3.78, N 3.90%

4-Acetoxy-4'-bromothiobenzanilide (II)

Phosphorus pentasulphide (2.22 g; 0.01 mole) was added to the hot solution of compound I (3.4 g; 0.01 mole) in dioxane (10 ml). The reaction mixture was heated under reflux in an oil-bath at 90–100° for 4½ minutes. In the course of heating the color of the reaction mixture changed from yellow to red and dark red, showing that the reaction was going in the desired direction. The warm reaction mixture was then poured into water (250 ml) and the separated darkyellow oil crystallized soon. After standing overnight at room temperature the yellow crystalline product was filtered off, washed with water and dried. The yield was 3.3 g (81.4%), m. p. 147–149°. Recrystallization from ethanol afforded crystals melting at 152–153°.

Anal. $C_{15}H_{12}NO_2SBr$ (350.24)

Calc.: C 51.18, H 3.44, N 3.98%

Found: C 50.93, H 3.22, N 3.70%

Some experiments were carried out in dry pyridine as solvent (5,6) but the yield of the crude product was practically unchanged (79.2%). The same yield was also obtained (81.7%) when dry xylene was used as solvent (2,7,8).

The attempts to brominate 4-acetoxy-thiobenzanilide (9) by the usual procedure with bromine in glacial acetic acid were unsuccessful. Under different reaction conditions non-sulphur compounds were obtained.

4-Hydroxy-4'-bromothiobenzanilide (III)

A mixture of compound II (3.5 g; 0.01 mole) and 1 N sodium hydroxide solution (15 ml) was heated on a water-bath for 10–15 minutes at 70–80°. The yellow alkaline solution was filtered, cooled and acidified with dilute hydrochloric acid (1 N HCl) to pH 7, whereby a yellow precipitate was obtained. The precipitate was filtered off, washed with water and dried yielding 2.9 g (94%) of the crude product of m. p. 200–202°. Recrystallization from water-ethanol (2 : 1) gave yellow prisms melting at 203–204°.

Anal. $C_{13}H_{10}NOSBr$ (308.20)

Calc.: C 50.61, H 3.30, N 4.55%

Found: C 50.62, H 3.45, N 4.56%

N-Acetyl-O-acetyl-4-hydroxy-4'-bromothiobenzanilide (IV)

Acetic anhydride (6 g; 0.006 mole) was added dropwise to a stirred solution of compound III (3 g; 0.01 mole) in anhydrous pyridine (10 ml). After standing

overnight at room temperature the red reaction mixture was poured into icy water (500 ml). The separated crystalline product was filtered off, washed with water and dried. The yield of the crude product of m. p. 114–115° was 3.4 g (97.3%). Recrystallization from water-ethanol (1 : 1) yielded red prisms melting at 117–118°.

Anal. $C_{17}H_{14}NO_3SBr$ (392,28)

Calc: C 52,08, H 3,70, N 3,59%

Found: C 51,98, H 3,89, N 3,62%

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ИЗВОД

СИНТЕЗА 4-ХИДРОКСИ-4'-БРОМТИОБЕНЗАНИЛИДА

од

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Дејством фосфорпентасулфида на 4-ацетокси-4-бромбензанилид (I) у сухом диоксану добивен је одговарајући тиоамид (II). у приносу од 80%. Након благе алкалне хидролизе из једињења (II) добивен је тражени хидрокситиоамид (III).

Присуство слободне хидроксилне групе у 4-хидрокси-4'-бромтиобензанилиду (III) доказано је ацетирањем анхидридом сирћетне киселине.

Овим поступком се ацетира и тиоамидна група и настаје O, N-диацетил-тиодериват (IV).

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