THE NITRATION OF sym-TRIAZOLO[3,4-b]BENZOTHIAZOLE

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The nitration of sym-triazolo[3,4-b]benzothiazole (I) with a mixture of nitric and sulfuric acids has given 6-nitro-sym-triazolo[3,4-b]benzothiazole (II). The structure of II was established by comparing its properties (mp, PMR spectrum) with those of the 7-nitro-sym-triazolo[3,4-b]-benzothiazole (III) obtained by the ring closure of 2-hydrazino-6-nitrobenzothiazole (VI) with orthoformic ester. Compounds II and III have been converted into the corresponding acetylamino derivatives. Saponification of the acetyl groups has given amino derivatives of I.

In a preceding communication [1] it was shown that sym-triazolo[3,4-b]benzothiazole (I) readily takes part in the Mannich and Vilsmeier reactions with the formation of the corresponding 3-substituted derivatives. The present paper is devoted to a study of the nitration of I.

Attempts to perform the nitration of I with nitric acid in acetic acid even at an elevated temperature did not lead to a satisfactory result: the starting material was recovered. On nitration with a mixture of nitric and sulfuric acids, a mononitro derivative (II) was obtained in which, according to the PMR spectrum, the nitro group was present in the benzene nucleus.

The PMR spectrum of II obtained on a JNM-4H-100 instrument (working frequency 100 MHz) in CF_3COOH with TMS as internal standard, contains four signals. An isolated unresolved signal at 10.17 ppm corresponds to a proton in position 3. Three signals correspond to the protons of the benzene ring: a doublet at 8.28 ppm with a spin-spin coupling constant of 8 Hz; a quartet at 8.68 ppm with splittings of 8 and 2 Hz; and a doublet with a splitting of 2 Hz at 9.29 ppm. It is clear from this that the nitro group must be in position 6 or 7.

The actual position of the nitro group in compound II was established by comparing its properties (mp, PMR spectrum) with those of 7-nitro-sym-triazolo[3,4-b]benzothiazole (III), obtained from 2-mercapto-6-nitrobenzothiazole (IV).

2-Mercapto-6-nitrobenzothiazole [2] was subjected to oxidation with potassium permanganate, giving the potassium salt of 6-nitrobenzothiazole-2-sulfonic acid (V) which was converted by the action of hydrazine hydrate into 2-hydrazino-6-nitrobenzothiazole (VI) the synthesis of which by other methods has been described previously [3, 4].

In the reaction of VI with orthoformic ester, we isolated an intermediate ethoxymethylene derivative (VII) which cyclized at a higher temperature into 7-nitro-sym-triazolo[3,4-b]benzothiazole (III). The melting point of the latter was different from that of the nitro compound II.

The PMR spectrum of III shows the same splitting of the signals of the protons of the benzene ring as the PMR spectrum of compound II, but their chemical shifts differ. A quartet with constants of 8 and 2 Hz at 8.76 ppm corresponds to a proton in position 6, a doublet at 8.60 ppm with a constant of 8 Hz to proton 5, and a doublet at 9.07 ppm with a constant of 2 Hz to proton 8. An isolated peak corresponding to H_3 is at 10.11 ppm. On this basis, the chemical shift of 8.28 ppm for compound II can be assigned to the proton in position 8, that at 8.68 ppm to proton 7, and that at 8.29 ppm to proton 5; the nitro group is present in position 6. Consequently, the nitration of I with a mixture of nitric and sulfuric acids forms 6-nitro-sym-triazolo[3,4-b]benzothiazole (II).

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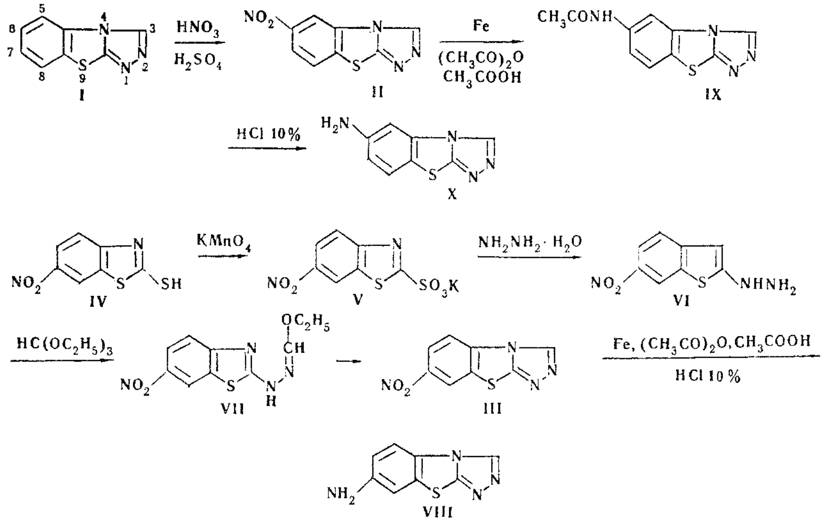

Compounds II and III were reduced with iron in a mixture of acetic acid and acetic anhydride. The resulting 6- and 7-acetylamino-sym-triazolo[3,4-b]benzothiazoles were saponified with 10% hydrochloric acid and converted into the corresponding amines (X) and (VIII). The structures of the reduced compounds were confirmed by their PMR spectra.

In attempts to perform the reaction of X with phenyl isothiocyanate in butanol in order to obtain the corresponding thiourea derivatives, the starting material was recovered unchanged.

EXPERIMENTAL

6-Nitro-sym-triazol[3,4-b]benzothiazole (II). In portions, 2 g (11.4 mmoles) of I was added to 9.7 g of concentrated sulfuric acid cooled to –5°C in such a way that the temperature did not exceed 25°C. The resulting suspension was treated at –5°C in drops with a mixture of 1.52 ml of nitric acid (d 1.5) and 1.62 ml of concentrated sulfuric acid. Then the reaction mixture was stirred at room temperature for 30 min. The solid matter gradually dissolved. The light brown solution was poured onto ice. The yellow precipitate formed was filtered off and washed with water. Yield 2.3 g (91.5%), mp 298-300°C (dimethylformamide). Found %: C 43.37; H 1.79; S 14.22. $C_8H_4N_4SO_2$. Calculated %: C 43.63; H 1.83; S 14.56.

Potassium 6-Nitrobenzothiazole-2-sulfonate (V). With ice cooling, a solution of 13.5 g of potassium permanganate and 5 ml of acetic acid in 200 ml of water was gradually added to a suspension of 8.49 g (40 mmoles) of 2-mercapto-6-nitrobenzothiazole [4] in 65 ml of acetone. After the end of the addition, oxidation was carried out at room temperature until the solution had become decolorized. The precipitate of manganese dioxide was filtered off and washed with hot water, the filtrate was evaporated to one-fourth of its initial volume, and the precipitate was filtered off and washed with saturated potassium chloride solution. Yield 7.06 g (65%).

2-Hydrazino-6-nitrobenzothiazole (VI). A suspension of 2 g (6.7 mmoles) of V in 45 ml of water was treated with 4.42 ml of hydrazine hydrate and stirred at 20°C for 6 h. The yellow precipitate was filtered off and washed with cold water. Yield 1.02 g, mp 253-255°C (butanol) (compare mp 244°C [3], 264-266°C [4]). Found %: C 39.88; H 2.60; S 15.33; N 26.93. $C_7H_6N_4O_2S$. Calculated %: C 39.99; H 2.87; S 15.25; N 26.65.

2-(Ethoxymethylenehydrazino)-6-nitrobenzothiazole (VII). A suspension of 2 g (9.55 mmoles) of VI in 16 ml of orthoformic ester was slowly heated. The substance gradually dissolved, and at 80°C a new precipitate formed. Heating with stirring was continued for 1 h 30 min at about 100°C with the simultaneous elimination of the ethanol formed by distillation. Then the reaction mixture was cooled and the precipitate was washed with orthoformic ester and then with ether. Yield 1.78 g (65.5%). Bright yellow crystals, mp on slow heating 180°C (aqueous dimethylformamide). Found %: C 44.74; H 3.66; S 12.49. $C_{10}H_{10}N_4SO_3$. Calculated %: C 45.11; H 3.78; S 12.04.

7-Nitro-sym-triazolo[3,4-b]benzothiazole (III). A suspension of 1.3 g (4.89 mmoles) of VII in orthoformic ester (the filtrate from the preceding experiment) was heated at 150°C with the elimination of ethanol by distillation. The solid matter gradually dissolved and a new precipitate formed. The bath temperature was raised to 190°C, whereupon a small amount of orthoformic ester distilled over. Stirring with heating was continued for another 3 h. Then the reaction mixture was cooled and the precipitate was filtered off and washed with ether. Yield 0.95 g (98%), decomp. temperature 306°C (dimethylformamide). Found %: C 43.62; H 1.75; N 25.27; S 14.20. $C_8H_4N_4SO_2$. Calculated %: C 43.63; H 1.83; N 25.44; S 14.56. A mixture with compound II had decomp. temperature 272°C (depression).

6-Acetylamino-sym-triazolo[3,4-b]benzothiazole (IX). A suspension of 1 g (4.55 mmoles) of II in 14 ml of glacial acetic acid was treated with 0.8 g of iron powder and 1 ml of acetic anhydride. The mixture was boiled with stirring for 1 h and cooled to 20°C, the unchanged iron was filtered off, and the filtrate was poured into cold water. The light-colored precipitate was filtered off and washed with water. Yield 1 g (94.6%). Colorless substance with decomp. temperature 315-316°C (glacial acetic acid). Found %: C 51.38; H 3.61; N 23.66; S 13.42. $C_{10}H_8N_4OS$. Calculated %: C 51.71; H 3.47; N 24.12; S 13.80.

6-Amino-sym-triazolo[3,4-b]benzothiazole (X). A suspension of 0.2 g (0.862 mmole) of IX in 15 ml of 10% hydrochloric acid was heated to the boil for 30 min. The solution was cooled and neutralized with 40% caustic soda solution, and the precipitate was filtered off and washed with water. Yield 0.14 g (85.4%). Colorless substance with mp 234-235°C (ethanol). Found %: C 50.56; H 3.15; S 16.36. $C_8H_6N_4S$. Calculated %: C 50.51; H 3.18; S 16.85.

7-Amino-sym-triazolo[3,4-b]benzothiazole (VIII). A mixture of 2 g (9.1 mmoles) of III, 28 ml of glacial acetic acid, 1.59 g of iron powder, and 2 ml of acetic anhydride was boiled with stirring for 4 h. On heating, the substance dissolved, and then a new precipitate formed. It was filtered off in the hot state together with the iron residues and was dissolved with heating in a new portion of glacial acetic acid, and the solution was filtered from the iron and diluted with water. The first mother liquor was also poured into water. The precipitates were filtered off, combined (1.68 g), heated with 10% hydrochloric acid until they dissolved, and the solution was treated with carbon and, after cooling, made alkaline with 40% caustic soda solution. This gave 1.1 g of light yellow crystals with decomp. temperature 254-256°C (ethanol). Found %: C 50.42; H 3.29; S 17.25. $C_8H_6N_4S$. Calculated %: C 50.51; H 3.18; S 16.85.

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