

An Improved Synthesis of Tetrabromo-2,1,3-benzothiadiazole

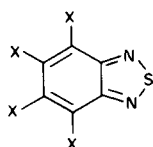
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An improved synthesis of tetrabromo-2,1,3-benzothiadiazole using bromine and reduced iron powered is presented.

The bromination of 2,1,3-benzothiadiazole (**1**) and certain of its derivatives under a variety of conditions has been the subject of a number of reports (1-5). The compounds prepared have ranged from mono to tribrominated substitution derivatives in addition to the tetrabromo-tetrahydro addition product. The absence of tetrabromo-2,1,3-benzothiadiazole is noteworthy (6) as the corresponding tetrachloro compound has been known for some time (4). A recent study of the bromination of 2,1,3-benzothiadiazole in refluxing 70% nitric acid reveals that a trace of tetrabromo-2,1,3-benzothiadiazole (**2**) has been obtained for the first time (7). An improved synthesis and some reactions of this uninvestigated compound are the subjects of this report.



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| 1. X = H | 3. X = CH ₃ S |
| 2. X = Br | 4. X = C ₆ H ₅ S |

Reaction of 2,1,3-benzothiadiazole with bromine has been shown to lead to the formation of 4,5,6,7-tetrabromo-4,5,6,7-tetrahydro-2,1,3-benzothiadiazole (**1**). The action of bromine on molten 5-bromo- or 4,5-dibromo-2,1,3-benzothiadiazole led to the formation of the 4,5,7-tribromo derivative (**3**). Bromination of the parent compound **1** in the presence of iron was found to give a quantitative yield of 4,7-dibromo-2,1,3-benzothiadiazole.

Chlorination of molten 2,1,3-benzothiadiazole in the presence of reduced iron has been shown to provide the 4,5,7-trichloro derivative. Upon further chlorination at elevated temperature, this material ultimately led to tetrachloro-2,1,3-benzothiadiazole (**4**). When the procedure in reference 3 was carried out in these laboratories using bromine, molten 2,1,3-benzothiadiazole and reduced iron powder, tetrabromo-2,1,3-benzothiadiazole was obtained.

The yield of purified product was 53%.

Treatment of tetrabromo-2,1,3-benzothiadiazole with five molar equivalents of sodium methylmercaptide in absolute methanol led to the formation of a red-orange compound identified as tetra(methylthio)-2,1,3-benzothiadiazole (**3**). When four molar equivalents of sodium benzenethiolate were employed, the reaction product was identified as tetra(phenylthio)-2,1,3-benzothiadiazole (**4**). The reaction of **2** with six molar equivalents of sodium methoxide in refluxing absolute methanol resulted in the formation of a mixture of mono-substituted derivatives.

EXPERIMENTAL

All melting points are uncorrected and were determined using a "mel temp" apparatus. An Atlas model CH4 mass spectrometer, a Varian model T-60 nuclear magnetic resonance spectrometer, and a Perkin Elmer model 257 infrared spectrophotometer were used to determine the respective spectra.

Preparation of Tetrabromo-2,1,3-benzothiadiazole (**2**).

A mixture of 50 g. (0.37 mole) of 2,1,3-benzothiadiazole and 2.0 g. (0.036 g.-atom) of reduced iron powder was heated slowly to 180° with concurrent dropwise addition of 10 ml. of bromine. The mixture was maintained at 180° for 1.5 hours while 15 ml. of bromine was added dropwise. The mixture was then heated to 225° and the remaining bromine (65 ml.) added dropwise over 4 hours. Analysis of the reaction mixture by glpc (250°, 5 ft.-5% SE-30, 60/80 Chromosorb W) indicated the presence of two materials. Samples of each of these materials were trapped and analyzed by mass spectrometry. The first material trapped was identified as a tribromo-2,1,3-benzothiadiazole (m/e 370). The second was identified as tetrabromo-2,1,3-benzothiadiazole (m/e 448).

An additional 1.0 g. of reduced iron powder and 10 ml. of bromine were added to the mixture and heating at 225° was continued for an additional 6 hours. The mixture was allowed to cool to room temperature. Analysis by glpc showed the presence of only one volatile constituent identified as tetrabromo-2,1,3-benzothiadiazole by its mass spectrum and comparison of its retention time with that of an authentic sample.

The reaction mixture was extracted in a Soxhlet apparatus with chloroform. The chloroform extract was passed through a short column of alumina to provide a clear solution. Evaporation of the solvent gave 87.0 g. (53%) of a buff colored solid having

m.p. 224-226° (lit. (7) m.p. 144-145°). The product was identified by means of elemental analysis and mass spectral data.

Anal. Calcd. for $C_6Br_4N_2S$: C, 15.95; N, 6.20; Br, 70.75. Found: C, 15.76; N, 6.39; Br, 70.68.

Reaction of Tetrabromo-2,1,3-benzothiadiazole with Sodium Methoxide.

To a solution of 2.7 g. (0.12 g.-atom) of sodium dissolved in 300 ml. of absolute methanol was added 9.0 g. (0.02 mole) of tetrabromo-2,1,3-benzothiadiazole. The mixture was maintained at reflux for 8 hours then filtered while still hot. The filter cake was found to contain 6.0 g. of starting material. As the filtrate cooled to room temperature, fine yellow crystals precipitated which were removed by filtration. After drying *in vacuo*, there was obtained 1.2 g. (14%) of product having m.p. 99-104°. The compound was identified as a mixture of monomethoxytribromo-2,1,3-benzothiadiazoles by means of elemental analysis in conjunction with infrared and nmr spectra. The nmr spectrum (deuteriochloroform) consisted of two sharp singlets at 4.07 and 4.45 ppm relative to an internal standard of tetramethylsilane. The relative intensities were 48 and 40, respectively.

Anal. Calcd. for $C_7H_3Br_3N_2OS$: C, 20.9; H, 0.8; N, 7.0. Found: C, 20.7; H, 0.7; N, 6.9.

When the above reaction was carried out using two molar equivalents of sodium methoxide in dry dimethyl sulfoxide at 95° for 2 hours, there was obtained 8.0 g. of starting material and 0.33 g. (4.6%) of a yellow solid having a melting point of 163-166°. Its elemental composition was determined by microanalysis and found to be that of a dibromodimethoxy-2,1,3-benzothiadiazole. The disposition of the methoxy groups was not established.

Anal. Calcd. for $C_8H_6Br_2N_2O_2S$: C, 27.1; H, 1.7; N, 7.9. Found: C, 27.2; H, 1.5; N, 8.5.

Reaction of Tetrabromo-2,1,3-benzothiadiazole with Sodium Methylmercaptide.

To a stirred solution of 2.3 g. (0.1 g.-atom) of sodium in 200 ml. of absolute methanol was added 10 ml. of methanethiol. The solution was stirred for 5 minutes and 9.0 g. (0.02 mole) of

tetrabromo-2,1,3-benzothiadiazole was added. The resulting suspension was heated at reflux for 3 hours during which time it turned deep red. During the heating period, an oil remained in the bottom of the flask. Upon cooling, the oil crystallized and fine needles deposited from the solution. Recrystallization of the product from methanol gave 5.0 g. (78%) of red-orange crystals having a melting point of 67°. The material was identified as tetra(methylthio)-2,1,3-benzothiadiazole.

Anal. Calcd. for $C_{10}H_{12}N_2S_5$: C, 37.5; H, 3.8; N, 8.7. Found: C, 37.1; H, 3.6; N, 8.7.

An attempt to prepare the mono-methylthio derivative of tribromo-2,1,3-benzothiadiazole resulted in the formation of an inseparable mixture of isomers.

A similar reaction using 0.08 mole of sodium thiophenolate and 0.02 mole tetrabromo-2,1,3-benzothiadiazole led to the formation of 9.0 g. (79%) of a red-orange solid identified as tetra(phenylthio)-2,1,3-benzothiadiazole (m.p. 173.5-176.0°).

Anal. Calcd. for $C_{30}H_{20}N_2S_5$: C, 63.3; H, 3.5; N, 4.9. Found: C, 63.9; H, 3.5; N, 5.4.

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