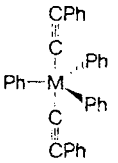
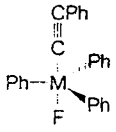


**A**



**B**

At the equimolar ratio of 2 and CuCl, compound A is probably formed. On heating, it is decomposed following the pattern of reductive elimination of a—a-substituents to give diphenyldiacetylene **3**, as was suggested earlier.[5] When CuCl is deficient, the formation of compound **B** predominates. Owing to coupling of substituents from a—e positions (probably, because of the strength of the M—F bond), it gives mainly tolan **4**.

## Experimental

The reaction mixtures were analyzed on a Chrom-5 chromatograph fitted with a flame-ionization detector and a column (3.5 m) with OV-1. Diphenyldiacetylene **3**, used as the standard and for calibration, was synthesized by the literature procedure,[8] difluorides **1a** and **1b** were obtained using the procedures reported earlier.[9,10] Commercial samples of tolan **4** and biphenyl (5) were used. Bi- and Sb-containing products were not isolated nor analyzed.

**Reaction of phenylacetylene with $Ph_3MF_2$. General procedure.** Triethylamine ($9.3 \cdot 10^{-4}$ mol) was added to a suspension of CuCl ($6.2 \cdot 10^{-4}$ mol) in 5 mL of a solvent (benzene, toluene) under argon; the resulting mixture was stirred for 10 min, and phenylacetylene ($6.2 \cdot 10^{-4}$ mol) and either difluoride **1a** or difluoride **1b** ($3.1 \cdot 10^{-4}$) were added in succession. The mixture was refluxed for 5 to 6 h under argon and analyzed by GLC. The reactions with other **2** : CuCl ratios were carried out similarly.

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# Synthesis of bromine- and iodine-containing perhaloisothiazoles

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A method was developed for the synthesis of bromine- and iodine-containing perhaloisothiazoles by bromination and iodination of 3-bromoisothiazole prepared from the available 3-hydroxyisothiazole.

**Key words:** isothiazole; 3-bromoisothiazole, bromination, iodination; polyhaloisothiazoles.

It is known that perchloroisothiazole can be used as a chemical means for plant protection[1] and as an intermediate for the synthesis of bactericides, fungicides, and dyes.[1–3] Preparation of bactericides based on perbromoisothiazole[2] is mentioned in the patent literature; however, we were not able to find an experimental proce-

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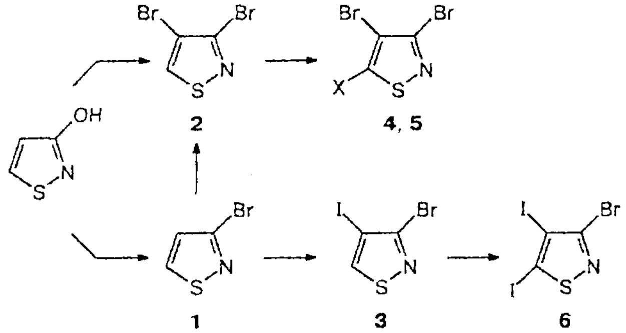
dure for the synthesis of this compound. To the best of our knowledge, potentially biologically active perhaloisothiazoles containing iodine atoms are not described.

We have developed a method for the synthesis of bromine- and iodine-containing perhaloisothiazoles on the basis of readily available 3-hydroxyisothiazole.[4,5] The latter was transformed into 3-bromoisothiazole (**1**) in 81% yield by the reaction with $POBr_3$. The reaction of compound **1** with *N*-bromosuccinimide (NBS) in concentrated $H_2SO_4$ or with an $I_2$—$HIO_4$ system afforded 3,4-dibromo- (**2**) or 3-bromo-4-iodothiazoles (**3**) in 79 and 70% yield, respectively. Compound **2** was also obtained in one step by treatment of 3-hydroxyisothiazole with $PBr_5$. In addition to dibromide **2** (yield 66%), the latter reaction afforded a small amount (~4%) of 3-bromoisothiazole **1**.



X = Br (**4**), I (**5**)

It is known that isothiazole derivatives do not usually enter into reactions with electrophilic agents at the C(5) atom of the isothiazole cycle.[7,8] For example, 3,4-dibromoisothiazole **2** is not transformed into perbromoisothiazole (**4**) under the action of different brominating agents ($Br_2$, dibromoamines) in $H_2SO_4$ at temperatures up to 100 °C. If the process is carried out in concentrated oleum, this allows one to intensify in some cases the bromination of heterocycles.[9] In fact, the reaction of compound **2** with bromine in 40% oleum at 40 °C yielded 85% of 3,4,5-tribromoisothiazole **4**.

We synthesized iodine-containing perhaloisothiazoles **5** and **6** in 23 and 61% yields, respectively, by the reaction of compounds **2** or **3** with an $I_2$—$HIO_4$ iodinating mixture in concentrated $H_2SO_4$. As might be expected, the above-mentioned iodination reactions require higher temperatures (70—90 °C) than the transformation of 3-bromoisothiazole **1** into 3-bromo-4-iodoisothiazole **3** (30 °C). The bromine- and iodine-containing perhaloisothiazoles **4—6** synthesized are crystalline compounds. Diiodide **6** is, probably, rather unstable since its melting point gradually decreases on storage at room temperature for several days. The structures of products **1—6** are proved by the $^{13}C$ NMR spectra; the purity of perhaloisothiazoles **4—6** is confirmed by elemental analysis.

## Experimental

$^{13}C$ NMR spectra were obtained on a Bruker AM-300 spectrometer at 75.5 MHz ($^{13}C$) in DMSO-$d_6$ and $CDCl_3$. Chemical shifts of the $^{13}C$ signals were measured relative to DMSO-$d_6$ (δ 39.5) and $CDCl_3$ (δ 76.9). TLC was carried out on a Silpearl UV-250 silica gel with $CCl_4$ as the eluent.

**3-Bromoisothiazole (1).** $POBr_3$ was obtained *in situ* by modification of a known procedure.[10] Bromine (0.36 mL, 1.12 g, 6.98 mmol) was added dropwise at −70 °C to $PBr_3$ (1.88 g, 6.95 mmol). The hardened mixture was heated to 20 °C and kept at 50 °C for 30 min. To the $PBr_5$ that formed, 100% HCOOH (0.26 mL, 0.32 g, 6.88 mmol) was added dropwise at −70 °C (frothing was observed), and the reaction mixture was gradually heated to 50 °C and kept at this temperature until the evolution of gas ceased (~1 h). 3-Hydroxyisothiazole (0.70 g, 6.93 mmol)[5] was added to the $POBr_3$ that formed (liquid that solidifies at ~20 °C to form yellow crystals), and the reaction mixture was heated at 100 °C for 1 h, cooled to 20 °C, and diluted with an ice-water mixture. The dark mixture formed was neutralized with $NaHCO_3$ and extracted with $CH_2Cl_2$ (5×10 mL) and the extract was dried with $MgSO_4$. Distillation afforded 0.92 g (81%) of bromide **1** as yellow liquid, b.p. 70—73 °C (20 Torr), $R_f$ 0.24, $n_D^{15}$ 1.5938. $^{13}C$ NMR ($CDCl_3$), δ: 128.2 (C(3)); 126.6 (C(4)); 150.4 (C(5)).

**3,4-Dibromoisothiazole (2).** *A.* NBS (5.44 g, 30.56 mmol) was added to a solution of 3-bromoisothiazole **1** (2.95 g, 18 mmol) in concentrated $H_2SO_4$ (200 mL). The reaction mixture was stirred at 20 °C for 1 h, and the solution that formed was kept at 50 °C for 30 h, poured onto ice (~300 g), and extracted with $CHCl_3$ (3×50 mL). The combined extracts were washed with water (2×30 mL) and dried with $MgSO_4$. The solvent was removed, and the residue was distilled at reduced pressure to give 3.48 g (79%) of dibromide **2** as a yellow liquid, b.p. 80—82 °C (20 Torr), $R_f$ 0.38, $n_D^{15}$ 1.6502. $^{13}C$ NMR ($CDCl_3$), δ: 140.9 (C(3)); 112.0 (C(4)); 147.7 (C(5)).

*B.* 3-Hydroxyisothiazole (0.10 g, 0.99 mmol) was added to $PBr_5$ prepared as described above from $PBr_3$ (0.20 mL, 0.57 g, 2.11 mmol) and bromine (0.12 mL, 0.37 g, 2.33 mmol) and the mixture was heated at 100 °C for 1 h. The dark reaction mixture was diluted with an ice-water mixture (~20 g), neutralized with $NaHCO_3$, extracted with $CHCl_3$ (3×5 mL), and dried with $MgSO_4$. The solvent was removed, and the residue was chromatographed to give 0.16 g (66%) of dibromide **2** and 0.01 g (4%) of bromide **1**, which were identical with the products obtained by other methods.

**3-Bromo-4-iodothiazole (3).** Iodine (0.20 g, 0.79 mmol) was added to a solution of 3-bromoisothiazole **1** (0.20 g, 1.22 mmol) in concentrated $H_2SO_4$ (10 mL) at 20 °C with stirring and after 30 min $NaIO_4$ (0.12, 0.56 mmol) was added in small portions to the reaction mixture. The dark-violet solution that formed was stirred at 20 °C for 2 h and at 30 °C for 10 h. The reaction mixture was poured onto ice (~100 g), decolorized with $Na_2SO_3$, and extracted with $CHCl_3$ (3×10 mL). The combined organic extracts were washed with water (2×10 mL) and dried with $MgSO_4$. The solvent was removed and the residue was crystallized from hexane to give 0.25 g (70%) of compound **3**, m.p. 64.0—65.5 °C, $R_f$ 0.38. $^{13}C$ NMR ($CDCl_3$), δ: 145.5 (C(3)); 82.6 (C(4)); 153.8 (C(5)).

**3,4,5-Tribromoisothiazole (4).** A mixture of 3,4-dibromoisothiazole **2** (0.16 g, 0.66 mmol), 40% oleum (20 mL), and bromine (0.04 mL, 0.12 g, 0.77 mmol) was heated at 80 °C for 6 h. The reaction mixture was cooled to 20 °C and poured onto ice (~100 g). The precipitate that formed was filtered off, washed with a small amount of water, dried in air, and crystallized from hexane to give 0.18 g (85%) of tribromide **4**, m.p. 81—83 °C, $R_f$ 0.64. $^{13}$C NMR ($CDCl_3$), δ: 140.7 (C(3)); 116.6 (C(4)); 136.4 (C(5)). Found (%): C, 11.96; Br, 74.60; N, 4.32; S, 9.83. $C_3Br_3NS$. Calculated (%): C, 11.19; Br, 74.51; N, 4.35; S, 9.95.

**3,4-Dibromo-5-iodoisothiazole (5).** Iodine (0.20 g, 0.79 mmol) was added to a solution of 3,4-dibromoisothiazole **2** (0.28 g, 1.15 mmol) in concentrated $H_2SO_4$ (10 mL) at 20 °C with stirring and after 30 min $NaIO_4$ (0.12, 0.56 mmol) was added in small portions to the reaction mixture. The reaction mixture was stirred at 30 °C for 4 h and at 80—90 °C for 4 h, cooled to 20 °C, and poured onto ice (~100 g). The mixture was decolorized with $Na_2SO_3$ and extracted with $CHCl_3$ (3×10 mL). The combined organic extracts were washed with water (2×10 mL) and dried with $MgSO_4$. The solvent was removed and the residue was crystallized three times from hexane to obtain 0.10 g (23%) of compound **5**, m.p. 154—157 °C, $R_f$ 0.56. $^{13}$C NMR ($CDCl_3$), δ: 139.7 (C(3)); 122.3 (C(4)); 104.0 (C(5)). Found (%): C, 10.31; Br, 43.29; I, 34.36; N, 3.71; S, 8.67. $C_3Br_2INS$. Calculated (%): C, 9.76; Br, 43.34; I, 34.42; N, 3.80; S, 8.68.

**3-Bromo-4,5-diiodoisothiazole (6).** Iodine (0.63 g, 2.36 mmol) was added to a solution of 3-bromo-4-iodoisothiazole **3** (1.67 g, 6.76 mmol) in concentrated $H_2SO_4$ (50 mL) at 20 °C with stirring and after 30 min $NaIO_4$ (0.39, 1.64 mmol) was added in small portions to the reaction mixture. The dark solution that formed was stirred at 20 °C for 2 h and kept at 70 °C for 24 h. The reaction mixture was poured onto ice (~100 g) and decolorized with $Na_2SO_3$. The residue was filtered, washed with water (~100 mL), dried in air, and crystallized three times from $CHCl_3$ to obtain 1.47 g (61%) of compound **6**, m.p. 168—169 °C, $R_f$ 0.56. $^{13}$C NMR (DMSO-$d_6$), δ: 144.7 (C(3)); 117.2 (C(4)); 101.0 (C(5)). Found (%): C, 8.82; Br, 19.48; I, 61.74; S, 7.80. $C_3BrI_2NS$. Calculated (%): C, 8.66; Br, 19.22; I, 61.05; S, 7.70.

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# Improved synthesis of bis[*p*-(phenylethynyl)phenyl]hetarylenes

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Bis[*p*-(phenylethynyl)phenyl]hetarylenes were synthesized in high yields by an improved method using cross-coupling between phenylacetylene and 4,4′-dibromobenzil followed by condensation of the 4,4′-di(phenylethynyl)benzil obtained with either *o*-phenylenediamine and 3,4-diaminobenzoic acid or with benzaldehyde and *p*-nitrobenzaldehyde in the presence of ammonium acetate.

**Key words:** phenylacetylene, cross-coupling reaction, dibromobenzil; bis[*p*-(phenylethynyl)phenyl]hetarylenes.

Earlier, we developed a method for the synthesis of bis[*p*-phenylethynyl)phenyl]hetarylenes[1] using Pd-catalyzed cross-coupling[2] of heterocyclic dibromides prepared from 4,4′-dibromobenzil (**1**)[3] with a twofold molar excess of phenylacetylene (Scheme 1, pathway *A*).

The major disadvantage of this method is the low activity of heteroaromatic dibromides **2a—d** in the cross-coupling reactions; this results in small yields of bis[*p*-(phenylethynyl)phenyl]hetarylenes **4a—d** (Table 1). The low activity of heteroaromatic dibromides is associated

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