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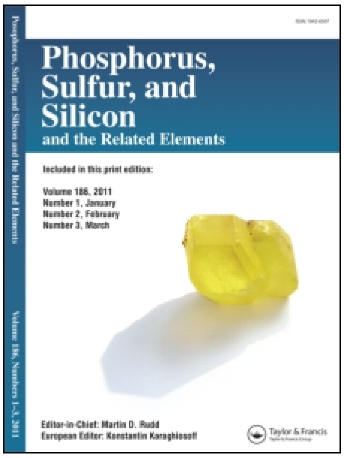

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REACTION OF BENZYNE WITH THIOPHOSGENE

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Benzyne, generated by thermal decomposition of benzenediazonium-2-carboxylate, reacts with thiophosgene to give 2,2,4,4-tetrachloro-2,4-dihydro-1,3-benzodithiin (**5**), 2,2,3,3-tetrachloro-2,3-dihydrobenzo[*b*]thiophene (**6**), and 2-(*o*-chlorophenylthio)-3-chlorobenzo[*b*]thiophene (**7**). Definite structure proof of compound **7** has been obtained by an X-ray analysis.

Reactions of benzyne with carbon–carbon double bonds have been investigated in detail both from a mechanistic and a synthetic point of view,[2] whereas those with carbon–heteroatom double bonds have been scarcely studied.[3,4,5] Reaction of benzyne with thioketones seemingly provides the most straightforward way to benzothietes. This reaction is, however, accompanied by some difficulty since thioketones are generally reactive toward oxidizing reagents and strong bases (nucleophiles), and hence generation of benzyne must be done without use of these reagents. Although benzenediazonium-2-carboxylate (**1**)[6] seemed to be the best precursor for the present purpose, thiobenzophenones unfortunately reacted with an intermediate in benzyne formation from **1** to give benzoxathianones (**2**).[7,8] Our choice of thiocarbonyl is thiophosgene in which the nucleophilicity of the sulfur is deactivated by electron-withdrawing chlorine atoms, which might prevent the reaction observed with thiobenzophenones.

RESULTS AND DISCUSSION

A suspension of benzenediazonium-2-carboxylate (**1**) in dichloromethane containing thiophosgene and propylene oxide[9] was heated at reflux until all the **1** disappeared (0.6–1.2 h). TLC of the mixture indicated that a complex reaction occurred. Chromatographic purification permitted isolation of three major products and elucidation of their structures.

The first oily product eluted (3–10%), which has a molecular formula $C_8H_4Cl_4S_2$ ($C_6H_4 + 2CSCl_2$), was identified as 2,2,4,4,-tetrachloro-2,4-dihydro-1,3-benzodithiin (**5**) on the basis of spectral and chemical data. ^{1}H NMR spectrum shows the unsymmetrical structure of **5**. The compound is thermally labile and also moisture-

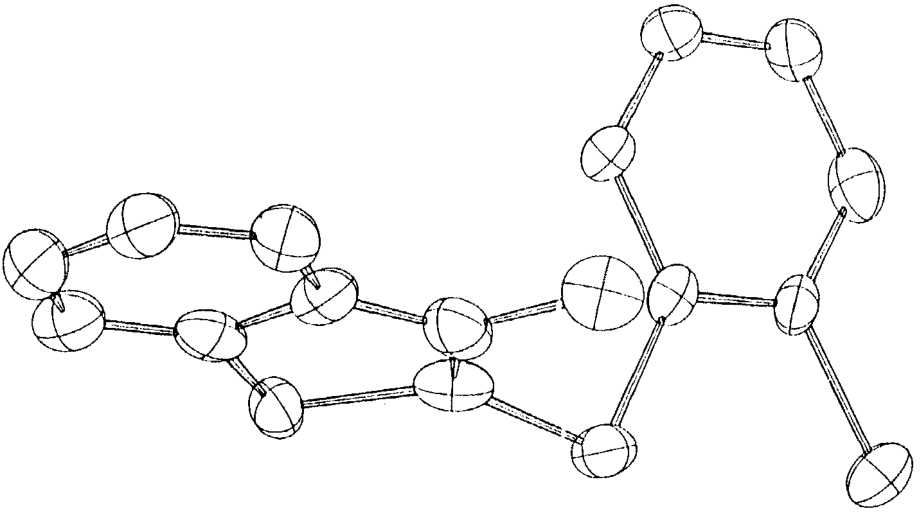


FIGURE 1. Perspective View of 2-(*o*-Chlorophenylthio)-3-chlorobenzo[*b*]thiophene (7).

sensitive, which is characteristic of α-halogenated sulfides.[10] Heating **5** in refluxing toluene gives 2,2,3,3,-tetrachloro-2,3-dihydrobenzo[*b*]thiophene (**6**) along with elemental sulfur in good yield. Reduction of **5** with lithium aluminum hydride gives *o*-toluenethiol, although in low yield, in accordance with the assigned structure.

The oily compound eluting second (4–12%), which has a molecular formula $C_8H_4Cl_4S$ ($C_6H_4 + 2CSCl_2 - S$), is identical to compound **6** obtained by thermolysis of **5**, and was consequently assigned to be dihydrobenzo[*b*]-thiophene **6**. ^1H NMR and ^{13}C NMR spectra indicated the unsymmetrical structure of **6** (symmetrical 1,1,3,3,-tetrachloro-1,3-dihydrobenzo[*c*]thiophene is a known crystalline compound[11]). On oxidation with *m*-chloroperbenzoic acid, the compound gave a mixture of crystalline sulfoxide (**8a**, 64%) and sulfone (**8b**, 20%).

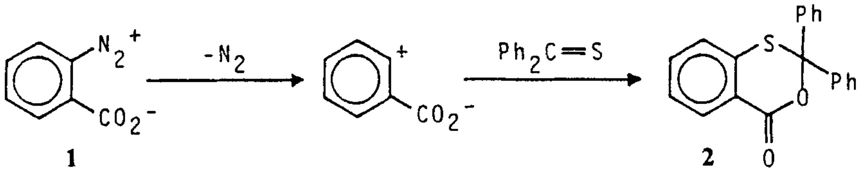
The slowest-eluting crystalline compound (1–6%) which has a molecular formula $C_{14}H_8Cl_2S_2$ ($2C_6H_4 + 2CSCl_2 - Cl_2$) was identified as 2-(*o*-chlorophenylthio)-3-chlorobenzo[*b*]thiophene (**7**). The structure of this compound could not be determined unambiguously on the basis of physical and chemical data, and definite structure proof was provided by an X-ray crystallographic analysis. A perspective view of the compound is shown in Figure 1.

The present reaction was repeated over ten times. The results are reproducible and the above three products were repeatedly obtained although their yields varied within the limits identified above.

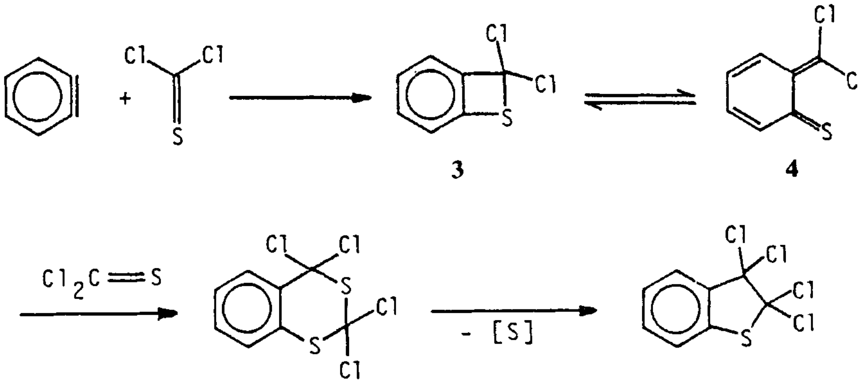
In one case, the crude reaction mixture was subjected to GC/MS analysis which revealed the presence of a small amount of a compound of molecular formula $C_7H_4Cl_2S$ ($C_6H_4 + CSCl_2$) to which we have tentatively assigned the structure 2,2-dichloro-2H-benzothiete (**3**).[12]

The formation of these products can best be rationalized as follows. The initial 1,2-cycloaddition of benzyne with thiophosgene gives benzothiete **3** which tautomerizes to a ring-opened isomer (**4**); then **4** reacts with thiophosgene to yield **5**. A precedent for this type of reaction is found in reactions of benzyne with *N*-benzilideneaniline[3a] and aromatic aldehydes.[4b] As ascertained by a separate experiment, compound **5** loses sulfur to give **6**. The mechanism of the formation of compound **7** is uncertain. We initially thought that it was formed from **5** or **6** by reaction with benzyne. However, separate experiments have shown that neither **5** nor **6** gives **7** on reaction with benzyne.

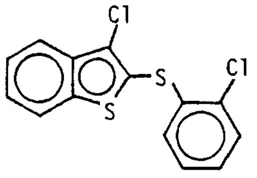
In summary, we have demonstrated the first example of reaction of benzyne with a thiocarbonyl, in which the thiocarbonyl group most probably reacts with benzyne in a 1,2-cycloaddition manner.



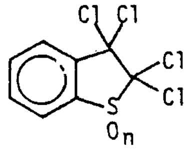
1 **2**



3 **4** **5** **6**



7



8a : n = 1

8b : n = 2

EXPERIMENTAL

Reaction of Benzyne with Thiophosgene. Caution! Benzenediazonium-2-carboxylate (**1**) *is explosive, and thiophosgene is toxic.* Anthranilic acid (20 mmol) was diazotized with isoamyl nitrite in tetrahydrofuran according to the procedure described in *Organic Syntheses*.[6] The resulting **1** was collected by filtration, washed successively with tetrahydrofuran and dichloromethane, and then transferred to a three-necked round-bottomed flask (in which a solution of 4 ml of thiophosgene and 4 ml of propylene oxide in 30 ml of dichloromethane was placed) carried by *ca.* 150 ml of dichloromethane. Throughout this operation **1** was never allowed to become dry, because solvent-free **1** is highly explosive. The mixture was heated at reflux until all the **1** disappeared (0.6–1.2 h). TLC of the mixture indicated that a complex reaction occurred (more than seven products were detected). The orange mixture was concentrated under normal pressure. The resulting oily residue was chromatographed on a silica gel column (Merck, 70-230 mesh, 85 g). Elution with hexane first gave a small amount of an oil of unpleasant odor whose structure was not examined further. Further elution with the same solvent afforded 2,2,4,4-tetrachloro-2,4-dihydro-1,3,-benzodithiin (**5**) (0.15–0.56 g or 3–10%), 2,2,3,3-tetrachloro-2,3-dihydrobenzo[*b*]thiophene (**6**) (0.27–0.76 g or 4–12%), and 2-(*o*-chlorophenylthio)-3-chlorobenzo[*b*]thiophene (**7**) (0.03–0.18 g or 1–6%). Although the column was further eluted with hexane and then with carbon tetrachloride, no other products could be obtained in a pure form; only a small amount of polymeric material was isolated.

The reaction was repeated over ten times. The results are reproducible and the above three products were repeatedly isolated in yields within the ranges described above.

The use of 1,2-dichloroethane as solvent (a solvent of higher boiling point than dichloromethane) gave a decreased yield of **5**, partially compensated by a somewhat increased yield of **6**.

In one case the crude oily residue was subjected to GC/MS analysis which revealed the presence of a compound of molecular formula $C_7H_4Cl_2S$; *m/e* 190 : 192 : 194 (100 : 71 : 15) (M^+), 155 : 157 (100 : 37) (M^+—Cl, base peak), 120 (M^+—2Cl), and 111 (M^+—SCCl), to which we have tentatively assigned structure **3**.

Characterization of Compound **5**. This thermally labile and moisture-sensitive oil turns orange to brown on standing. ^{1}H NMR ($CDCl_3$) δ 7.0–7.8 (complex multiplet). ^{13}C NMR: in addition to four strong absorptions (δ 127.71, 129.91, 130.34, and 133.01) due to benzene ring carbons carrying a hydrogen, five weak absorptions (δ 120.43, 121.48, 126.03, 131.80, and 135.34; one of these originates from an impurity) were observed. IR (film) 1575, 1455, 1435, 1116, 1037, 810, and 742 cm^{-1}. MS *m/e* 272 : 274 : 276 : 278 : 280 (100 : 133 : 67 : 16 : 2) (M^+), 237 : 239 : 241 : 243 (M^+—Cl), and 202 : 204 : 206 (100 : 67 : 14) (M^+—2Cl, base peak). A satisfactory elemental analysis could not be obtained because of the instability of the compound. The following is the most satisfactory among several attempts: Calcd for $C_8H_4Cl_4S_2$: C, 31.39; H, 1.33; Cl, 46.34; S, 21.16. Found: C, 32.08; H, 1.44; Cl, 45.44; S, 21.16.

Conversion of **5** *to* **6** *by Thermolysis.* A solution of 183 mg of **4** in 20 ml of toluene was refluxed for 4.5 h. The mixture was evaporated, and the residue was chromatographed on a silica gel column (45 g). Elution with hexane gave elemental sulfur, 83 mg (67%) of **6**, and 27 mg of an unidentified product.

Reduction of **5** *with Lithium Aluminum Hydride.* A mixture of 357 mg (1.17 mmol) of **5** and 300 mg (7.9 mmol) of lithium aluminum hydride in 15 ml of tetrahydrofuran was refluxed for 7 h. The mixture was quenched with 2 N HCl and extracted with ether (2 × 50 ml). The ether extracts were reextracted with 10% NaOH (2 × 5 ml). Usual workup of the ether layer gave 86 mg of a complex oily mixture. The alkaline layer was acidified and extracted with ether. The extracts were washed with water, dried, and evaporated to give 100 mg of the oily residue. ^{1}H NMR analysis indicated that this is a mixture of two compounds. The minor component having absorptions at δ 2.30 (3 H, s, aromatic methyl) and 3.26 (1 H, s, SH) was identified as *o*-toluenethiol by comparison with the spectrum of the commercial product. The major component shows a singlet at δ 3.87 probably due to SH and a complex multiplet in the aromatic region. Methylation of this compound with methyl iodide afforded an oil having absorptions at δ 2.44 (3 H, s, SMe) and 6.9–7.5 (*ca.* 5 H, m, aromatic H).

Alkaline Hydrolysis of **5** was carried out in aqueous ethanol with KOH as base. The reaction gave a complex mixture containing a carboxylic acid as one of products.

Reaction of **5** *with Benzyne.* 586 mg (1.85 mmol) of **5** was allowed to react with benzyne (generated from **1** prepared from 5 mmol of anthranilic acid) in boiling dichloromethane. Workup of the mixture by column chromatography gave **6** (4%) and some unidentified products with 21% recovery of **5**. However, no **7** was observed in this product mixture.

Characterization of Compound **6**. Colorless oil; bp 114°C/0.5 mm Hg (Kugelrohr). ^{1}H NMR ($CDCl_3$) δ 7.1–7.6 (complex multiplet). ^{13}C NMR ($CDCl_3$) δ 125.27, 127.56, 129.70, 130.29, 130.64, 132.49, 135.71, and 156.88. IR (film) 3050, 1540, 1456, 1435, 1038, 1033, 880, and 750 cm^{-1}. Anal. Calcd for $C_8H_4Cl_4S$: C, 35.07; H, 1.47; Cl, 51.76; S, 11.70. Found: C, 35.08; H, 1.53; Cl, 51.70; S, 11.87.

Oxidation of **6** *with m-Chloroperbenzoic Acid.* A mixture of 113 mg (0.41 mmol) of **6** and 382 mg (2.21 mmol) of *m*-CPBA in 20 ml of dichloromethane was refluxed for 4 h. The mixture was evaporated, and the residue was chromatographed on a silica gel column (45 g). Elution with dichloromethane gave 76 mg (64%) of 2,2,3,3-tetrachloro-2,3-dihydrobenzo[*b*]thiophene 1-oxide (**8a**) and 20 mg (18%) of 2,2,3,3-tetrachloro-2,3-dihydrobenzo[*b*]thiophene 2,2-dioxide (**8b**).

Heating **8a** with *m*-CPBA in refluxing dichloromethane for 3.5 h gave **8b** in 5% yield with 70% recovery of **8a**.

Compound **8a**. Mp 103–104°C (from hexane). Anal. Calcd for $C_8H_4Cl_4OS$: C, 33.13; H, 1.39; Cl, 48.90; S, 11.06. Found: C, 33.34; H, 1.41; Cl, 48.63; S, 11.13.

Compound **8b**. Mp 114–114.5°C (from hexane). Anal. Calcd for $C_8H_4Cl_4O_2S$: C, 31.40; H, 1.32; S, 10.48. Found: C, 31.54; H, 1.27; S, 10.37.

Reaction of **6** *with Benzyne.* Compound **6** (217 mg; 0.79 mmol) was allowed to react with benzyne (produced from 3 mmol of anthranilic acid) in refluxing dichloromethane. Workup of the mixture by column chromatography gave 52% recovery of **6**. No **7** was observed in the product mixture.

Both attempted hydrolysis of **6** by potassium hydroxide and attempted dechlorination with zinc-copper couple gave complex mixtures.

Characterization of Compound **7**. Mp 104–104.5°C (from hexane). UV (hexane) (log ε) 313 (3.9), 302 (4.0), 292 (4.0), 278 (4.0), 260 (4.0), 249 (4.4), 234 (4.4), and 210 nm (4.6). ^1H NMR ($CDCl_3$) δ 6.9–8.1 (complex multiplet). Anal. Calcd for: $C_{14}H_8Cl_2S_2$: C, 54.02; H, 2.59; Cl, 22.78; S, 20.60. Found: C, 53.94; H, 2.51; Cl, 22.79; S, 20.60.

X-ray Analysis of Compound **7**. A single crystal of **7** was prepared by slow crystallization from cyclohexane. The crystal data are orthorhombic, space group $Pna2_1$, a = 7.737 (2), b = 22.996 (6), c = 7.574 (3) Å, d_{calcd} = 1.53 g cm^{-1} for Z = 4 (asymmetric unit, $C_{14}H_8Cl_2S_2$). The intensity data were measured on a Rigaku automated Mo K_α radiation unit. A single crystal of approximate dimensions 0.35 × 0.20 × 0.20 mm was used. The number of the significant reflections ($|F_0| > 3\sigma(|F_0|)$) is 1282 ($2\theta \leqq 60°$). The structure was solved by the direct method and refined by block-diagonal least-squares methods. The final refinement, with anisotropic temperature factors for C, S, and Cl and anisotropic temperature factors for H, gave an R factor of 0.082.

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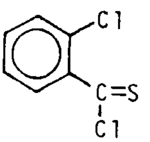

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