

Insertion of Benzyne and Substituted Benzyne into the S-S Bond of Diphenyl and Di-*p*-tolyl Disulfides Yielding the Corresponding *o*-Bis(arylthio)benzenes

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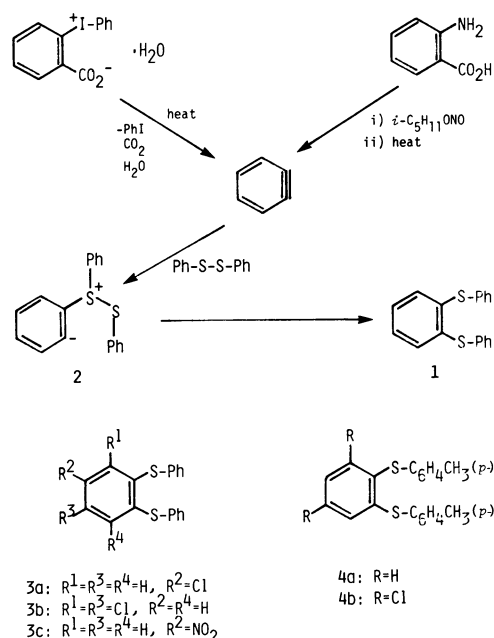
Synopsis. Benzyne and substituted benzyne undergo insertion into the S-S bond of diphenyl and di-*p*-tolyl disulfides to afford the corresponding *o*-bis(arylthio)benzenes in low but reproducible yields.

Petragnani and Toscano reported that benzyne, generated by thermolysis of diphenyliodonium-2-carboxylate monohydrate,¹⁾ inserts into the Se-Se and Te-Te bonds of diphenyl diselenide and bis(*p*-ethoxyphenyl) ditelluride to afford *o*-bis(phenylseleno)- and *o*-bis(*p*-ethoxyphenyltelluro)benzenes, respectively, but it fails to insert into the S-S bond of diphenyl disulfide, the latter being recovered quantitatively.²⁾ In connection with our continuing study on reactions of benzyne with sulfur compounds, we reexamined the reaction of benzyne with diphenyl disulfide and found that benzyne reacts with diphenyl disulfide to give *o*-bis(phenylthio)benzene in a low but reproducible yield. Herein we report the insertion of benzyne and substituted benzyne into the S-S bond of diphenyl and di-*p*-tolyl disulfides yielding the corresponding *o*-bis(arylthio)benzenes.

First the reaction of benzyne with diphenyl disulfide was reinvestigated under the conditions that were reported by Petragnani and Toscano.²⁾ Thus 2 equivalents of diphenyliodonium-2-carboxylate monohydrate was heated with diphenyl disulfide in boiling *o*-dichlorobenzene for 0.5 h. The resulting brown mixture was evaporated and the residue was chromatographed on a column of silica gel. Elution with hexane afforded *o*-bis(phenylthio)benzene (**1**) in 8% yield with quantitative recovery of the unreacted diphenyl disulfide. The structure of **1** was established by comparison with the authentic sample prepared by an alternative synthesis.³⁾

Next benzyne, generated by aprotic diazotization of anthranilic acid,⁴⁾ was allowed to react with diphenyl disulfide. Thus a solution of anthranilic acid in dioxane was added to a gently refluxing solution of isopentyl nitrite and diphenyl disulfide in 1,2-dichloroethane (anthranilic acid:isopentyl nitrite:diphenyl disulfide=2:2.1:1). Workup of the mixture with silica-gel column chromatography afforded the sulfide **1** in 14% yield with quantitative recovery of the unreacted disulfide.

Thus it is clear that, contrary to the previous report,²⁾ benzyne is able to insert into the S-S bond of diphenyl disulfide. The reaction probably proceeds via the initial formation of the betaine intermediate (**2**) as depicted below. The initial formation of betaine intermediates by reaction of benzyne with organic sulfides is well-documented.⁵⁾



In order to know more about the generality and characteristics of the present reaction, reactivities of substituted benzyne toward diphenyl and di-*p*-tolyl disulfides were examined. 4-Chloro-, 3,5-dichloro-, and 4-nitrobenzyne were generated by aprotic diazotization of 4-chloro-, 3,5-dichloro-, and 4-nitroanthranilic acids, respectively. These benzyne, produced from 2 equivalents of anthranilic acids, reacted with diphenyl disulfide to afford the sulfides **3a**, **3b**, and **3c** in 25, 19, and 30% yields, respectively. Benzyne and 3,5-dichlorobenzene reacted with di-*p*-tolyl disulfide to give the sulfides **4a** and **4b** in 17 and 14% yields, respectively.

The present reaction involves the initial electrophilic attack of benzyne on the sulfur atom of the disulfides, and therefore more electrophilic benzyne would be expected to give higher yields of the insertion products. However, the above results do not show such a tendency markedly. This is due to the fact that a competitive side reaction, addition of isopentyl alcohol (produced from isopentyl nitrite) to benzyne yielding isopentyl aryl ethers, occurs to consume benzyne, especially when benzyne are strongly electrophilic.

In conclusion insertion of benzyne and substituted benzyne into diaryl disulfides generally occurs to yield *o*-bis(arylthio)benzenes in low but reproducible yields.⁶⁾

Experimental

Diphenyliodonium-2-carboxylate monohydrate was purchased from Lancaster Synthesis Ltd. Anthranilic acid and 4-chloro- and 3,5-dichloroanthranilic acids were obtained from Tokyo Kasei Kogyo and 4-nitroanthranilic acid from Aldrich. Column chromatography was carried out on 70–230 mesh Merck silica gel. Isopentyl nitrite was prepared by the literature method.⁷

Reaction of Diphenyl Disulfide with Benzyne Generated from Diphenyliodonium-2-carboxylate Monohydrate. A mixture of 549 mg (2.5 mmol) of diphenyl disulfide and 1.717 g (5 mmol) of diphenyliodonium-2-carboxylate monohydrate in 10 ml of *o*-dichlorobenzene was refluxed for 0.5 h. The resulting brown mixture was evaporated under reduced pressure and the residue was chromatographed on a column of silica gel. Elution with hexane afforded 505 mg (92%) of diphenyl disulfide and then 56 mg (8%) of *o*-bis(phenylthio)benzene (**1**). ¹H NMR and IR spectra of **1** agreed with those of the authentic sample prepared by an alternative synthesis.³

Reaction of Diphenyl Disulfide with Benzyne Generated by Aprotic Diazotization of Anthranilic Acid. To a gently refluxing mixture of 2.18 g (10 mmol) of diphenyl disulfide and 2.46 g (21 mmol) of isopentyl nitrite in 100 ml of 1,2-dichloroethane was added dropwise a solution of 2.74 g (20 mmol) of anthranilic acid in 10 ml of dioxane over a period of 0.5 h. After the completion of the addition, the mixture was refluxed for 0.5 h and evaporated. The resulting residue was chromatographed on a column of silica gel. Elution with hexane gave 1.86 g (86%) of diphenyl disulfide and then 0.42 g (14%) of *o*-bis(phenylthio)benzene (**1**).

Reaction of Diphenyl Disulfide with 4-Chloro-, 3,5-Dichloro-, and 4-Nitrobenzynes. 4-Chloro-, 3,5-dichloro-, and 4-nitrobenzynes were generated by aprotic diazotization of two equivalents of 4-chloro-, 3,5-dichloro-, and 4-nitroanthranilic acids, respectively, and allowed to react with an equivalent of diphenyl disulfide in a similar manner described above. Chromatographic purification afforded the following new *o*-bis(phenylthio)benzenes.

1,2-Bis(phenylthio)-4-chlorobenzene (3a): Yield, 25%; viscous oil; ¹H NMR (CCl₄) δ=6.8–7.0 (3H, m), 7.23 (5H, s), and 7.30 (5H, s). Found: C, 65.73; H, 3.94; Cl, 10.80; S,

19.28%. Calcd for C₁₈H₁₃ClS₂: C, 65.74; H, 3.98; Cl, 10.78; S, 19.50%.

1,2-Bis(phenylthio)-3,5-dichlorobenzene (3b): Yield, 19%; mp 87–88 °C; ¹H NMR (CCl₄) δ=6.43 (1H, d, *J*=1.6 Hz), 6.9–7.3 (6H, m), and 7.36 (5H, s). Found: C, 59.37; H, 3.29; Cl, 19.72; S, 17.50%. Calcd for C₁₈H₁₂Cl₂S₂: C, 59.51; H, 3.33; Cl, 19.52; S, 17.65%.

1,2-Bis(phenylthio)-4-nitrobenzene (3c): Yield, 30%; yellow viscous oil; ¹H NMR (CCl₄) δ=6.70 (1H, d, *J*=9.0 Hz), 7.23 (5H, s), 7.30 (5H, s), and 7.6–7.9 (2H, m). Found: C, 63.56; H, 3.86; N, 4.22; S, 18.53%. Calcd for C₁₈H₁₃NO₂S₂: C, 63.69; H, 3.86; N, 4.13; S, 18.89%.

Reaction of Di-*p*-tolyl Disulfide with Benzyne and 3,5-Dichlorobenzene. Di-*p*-tolyl disulfide was allowed to react with benzyne and 3,5-dichlorobenzene generated from 2 equivalents of the corresponding anthranilic acids in a manner described above to give *o*-bis(*p*-tolylthio)benzene (**4a**) and 1,2-bis(*p*-tolylthio)-3,5-dichlorobenzene (**4b**).

4a: Yield, 17%; mp 75.5 °C; ¹H NMR (CCl₄) δ=2.32 (6H, s), 6.97 (4H, s), and 7.0–7.5 (8H, m). Found: C, 74.52; H, 5.63; S, 19.88%. Calcd for C₂₀H₁₈S₂: C, 74.49; H, 5.63; S, 19.88%.

4b: Yield, 14%; mp 70–72 °C; ¹H NMR (CCl₄) δ=2.23 (3H, s), 2.37 (3H, s), 6.43 (1H, d, *J*=2.0 Hz), and 6.8–7.5 (9H, m). Found: C, 61.42; H, 4.09; Cl, 18.25; S, 16.40%. Calcd for C₂₀H₁₆Cl₂S₂: C, 61.38; H, 4.12; Cl, 18.12; S, 16.38%.

References

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- 4) L. Friedman and F. M. Logullo, *J. Org. Chem.*, **34**, 3089 (1969).
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- 6) We are currently investigating the reaction of dialkyl disulfides with benzyne. The reaction does not afford the products resulting from the insertion of benzyne to the S–S bond. For example, the reaction of dimethyl disulfide with benzyne affords thioanisole and diphenyl sulfide as the major products.
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