



The First Isolation of Benzyne-Thiobenzophenone Adducts

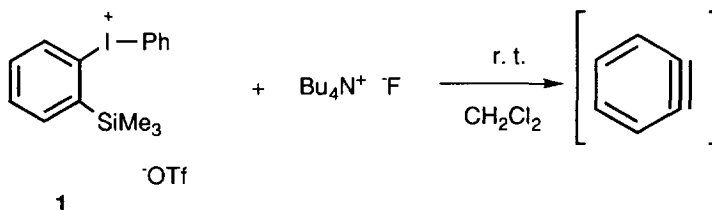
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Abstract: Reaction of thiobenzophenones with phenyl[2-(trimethylsilyl)phenyl]iodonium trifluoromethanesulfonate in the presence of tetrabutylammonium fluoride afforded the corresponding adducts, which are the first examples of benzyne-thiobenzophenone adducts.
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Benzyne is a reactive intermediate and reacts with many dienes to afford the corresponding cycloadducts.¹ However, no report on the reaction of thione with benzyne was available.² The reported examples of the reaction of the compounds relating thiones with benzyne are dithioacetals, products of thiophosgene and benzyne, and dibenzotrithiocin derivatives, products of 1,3-benzodithiole-2-thione and benzyne.³ Recently, one of the authors has introduced a new type of benzyne precursor, phenyl[2-(trimethylsilyl)phenyl]iodonium trifluoromethanesulfonate (**1**), which has been found to produce benzyne under very mild conditions (Scheme 1).⁴

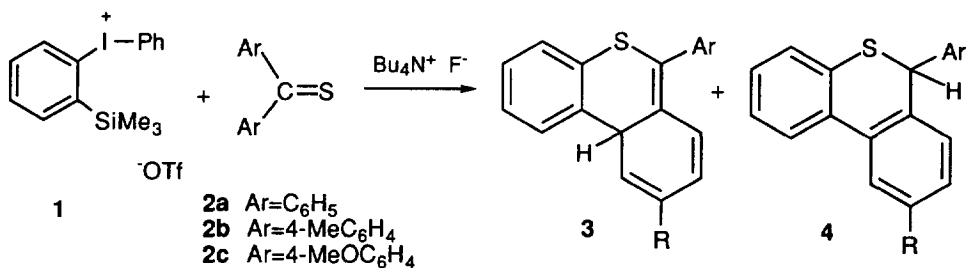


Scheme 1.

We report herein the reaction of thiobenzophenones (**2**) with this compound **1**, which forms completely different products from those previously reported.⁵

Treatment of **1** with 4,4'-dimethoxythiobenzophenone (**2a**) followed by the addition of tetrabutylammonium fluoride at room temperature resulted in the formation of cycloadduct (**3a**) and its

rearranged product (**4a**) in 15 and 29% yields, respectively (Scheme 2). Other reactions were carried out in a similar manner (Table 1).

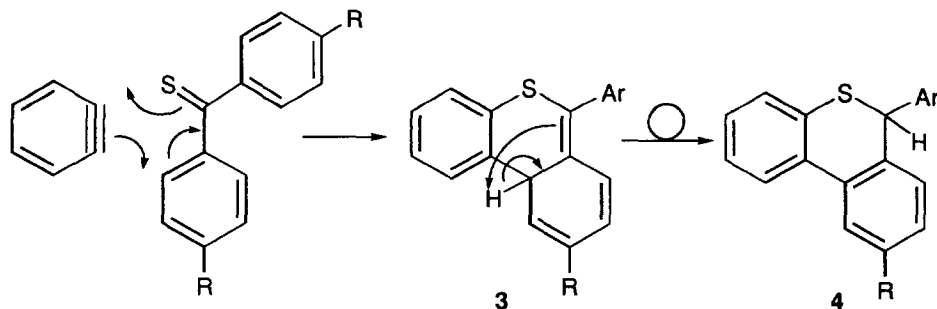


Scheme 2.

Table 1. Reaction of Thiobenzophenones with 1.

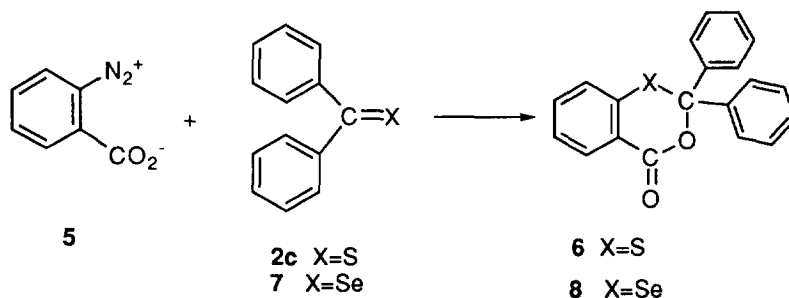
Entry	Ar	Solvent	Conditions		3	Products (Yield/%) ⁶	
			Temp./°C	Time/min.		4	4
1	4-MeOC ₆ H ₄	Dichloromethane	0	10	3a 10	4a 32	
2	4-MeOC ₆ H ₄	Dichloromethane	rt	5	3a 15	4a 29	
3	4-MeOC ₆ H ₄	Dichloromethane	reflux	3	3a 5	4a 44	
4	4-MeOC ₆ H ₄	Toluene	reflux	1	3a 0	4a 38	
5	4-Tol	Dichloromethane	0	5	3b 17	4b 28	
6	4-Tol	Dichloromethane	rt	2	3b 15	4b 45	
7	4-Tol	Toluene	reflux	1	3b 0	4b 37	

In all cases, the reaction completed within 10 min. When this reaction was carried out in refluxing toluene, the obtained products were only the rearranged ones (Entries 4 and 7). When the present reaction was carried out at 0 °C, the ratios of unrearranged **3** to **4** were higher (Entries 1 and 5). Interestingly, the reaction of thiobenzophenone **2c** with benzyne afforded adducts of the same type **3c** and **4c**, but **3c** was found to be unstable at room temperature. When the reaction mixture was subjected to column chromatography by elution with hexane-dichloromethane, the fraction containing **3c** and **4c** turned blue. The proton NMR spectrum of this mixture shows the adduct **4c** and thiobenzophenone, which suggested that a retro-Diels-Alder reaction was occurred under these conditions. Thus, the reaction might proceed as follows: when the benzyne was formed, thiobenzophenone is immediately attacked by benzyne to afford the corresponding Diels-Alder adduct **3**. This adduct is aromatized to give the rearranged product **4** (Scheme 3).



Scheme 3.

It has long been known that benzenediazonium 2-carboxylate (**5**), which is a well-known benzyne precursor, reacts with dienes to give the corresponding cycloadducts.^{1,7} However, thiobenzophenone **2c** reacted with **1** to afford benzo-1,3-oxathian-4-one (**6**), which is not a benzyne adduct.⁵ We also found that the reaction of selenobenzophenone (**7**) with **1** or diphenyliodonium-2-carboxylate afforded the corresponding benzo-1,3-oxaselenan-4-one (**8**) (Scheme 4).⁸ These results suggested that **5** and diphenyliodonium-2-carboxylate did not act as benzyne precursors under the conditions.



Scheme 4.

Recently, many benzyne precursors have been developed. However, the properties of thiobenzophenones are difficult to reconcile with the properties of the precursors of benzyne and also with the reaction conditions where benzyne is generated; acidic or basic conditions and the presence of oxidizing reagents or strong nucleophiles should be avoided. In the case of **5** and diphenyliodonium-2-carboxylate, much higher temperature was required. Similarly, generation of benzyne by using a strong base such as butyllithium is not acceptable for the reaction with thiobenzophenone, since butyllithium attacks thiobenzophenone to give tetraphenylethylene.⁹ Because of this limitation, no report describing the reaction of benzyne with thiones in the actual sense has appeared. The present reaction requires only a fluoride anion at room temperature and can be carried out under very mild conditions. Our work is the first true example of the reaction of thiones with benzyne.

The reaction of thiobenzophenone with dienes usually affords the Diels-Alder adducts, whereas the reaction with olefins results in the formation of bicyclic products.⁹ Schatz and Sauer have reported that thiobenzophenone shows high dienophilic reactivity by kinetic investigation.¹⁰ Huisgen *et al.* also reported that thiobenzophenone shows unusually high dipolarophilic activity.¹¹ However, some dienes such as

norbornadiene act as olefins but not as dienes.¹² We are interested in the reactivity whether the reaction proceeds through a [2+2] or [4+2] manner. The present result shows that [4+2] cycloaddition overcomes [2+2] cycloaddition. Thus, it has been clarified that benzyne acts as a dienophile in the present reaction.

This work was partly supported by Grants-in-Aid for Scientific Research (06640706 and 07804046) from the Ministry of Education, Science and Culture of Japan.

References and Notes

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- 6 Satisfactory mass spectra were obtained for all the new compounds. ¹H NMR spectra of **3** and **4**. **3a**: colorless oil; ¹H NMR (CDCl₃, 400 MHz) δ=3.72 (s, 3H, OMe), 3.80 (s, 3H, OMe), 5.21 (s, 1H, CH), 6.72 (d, 2H, Ar), 6.80 (d, 1H, Ar), 6.96 (d, 2H, Ar), 6.97 (d, 1H, Ar), 7.21 (dd, 2H, Ar), 7.28 (dd, 1H, Ar), 7.37 (d, 1H, Ar), 7.41 (d, 1H, Ar). **3b**: colorless oil; ¹H NMR (CDCl₃, 400 MHz) δ=2.24 (s, 3H, Me), 2.32 (s, 3H, Me), 5.24 (s, 1H, CH), 6.90 and 6.99 (d, 4H, MeC₆H₄), 7.05 (d, 1H, Ar), 7.28-7.28 (m, 4H, Ar), 7.37 (dd, 1H, Ar), 7.41 (dd, 1H, Ar). **4a**: pale yellow oil; ¹H NMR (CDCl₃, 400 MHz) δ=3.74 (s, 3H, OMe), 3.88 (s, 3H, OMe), 5.13 (s, 1H, CH), 6.75 (d, 2H, Ar), 6.84 (dd, 1H, Ar), 6.99 (d, 1H, Ar), 7.13 (d, 2H, Ar), 7.19 (dd, 1H, Ar), 7.23 (dd, 1H, Ar), 7.32 (dd, 2H, Ar), 7.78 (d, 1H, Ar). **4b**: Mp 93–95 °C; ¹H NMR (CDCl₃, 400 MHz) δ=2.26 (s, 3H, Me), 2.42 (s, 3H, Me), 5.12 (s, 1H, CH), 6.95 (d, 1H, Ar), 7.02 (d, 2H, Ar), 7.10 (d, 3H, Ar), 7.14-7.28 (m, 2H, Ar), 7.32 (d, 1H, Ar), 7.6 (br s, 1H, Ar), 7.81 (d, 1H, Ar). **4c**: Found: 274.0855. Calcd for C₁₉H₁₄S; 274.0816. ¹H NMR (CDCl₃) δ=5.17 (s, 1H, CH), 7.07 (d, 1H, Ar), 7.12-7.40 (m, Ar), 7.80 (d, 1H, Ar), 7.82 (d, 1H, Ar).
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(Received in Japan 13 September 1996; revised 18 October 1996; accepted 21 October 1996)