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# Efficient generation and trapping of acylbenzynes from hypervalent iodine compounds

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**Abstract**—[5-Acyl-2-(trimethylsilyl)phenyl]iodonium triflates were prepared for the generation of benzynes bearing ketone function. Treatment of the iodonium triflates with $Bu_4NF$ in $CH_2Cl_2$ in the presence of furan at room temperature gave 6-acyl-1,4-epoxy-1,4-dihydronaphthalenes in high yields. The mild conditions and the tolerance of the ketone function on benzyne generation are attributable to the advantage of hypervalent iodine compounds.

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Benzyne is an important reactive intermediate and has been used in organic synthesis, mechanistic studies, and synthesis of functional materials.[1] Recently, there has been considerable progress in the application of benzyne chemistry to natural product synthesis.[2] If benzynes having various functional groups can be generated readily, the synthetic applications using benzynes become more important.

The carbonyl group is one of the most important functional groups. Introduction of a carbonyl group into a benzyne skeleton greatly increases the potential for synthetic utility. Although generation of various types of benzynes has been studied to date, surprisingly, there are only a few examples concerning benzynes bearing carbonyl groups. Benzynes with ester and amide groups were generated from different precursors, aryliodonium salts,[3] and triflates,[4] respectively. Very recently, it has been reported that benzynes bearing electrophilic substituents such as ester, amide, and cyano groups can be generated by the reaction of functionalized bromobenzenes with lithium dialkyltetramethylpiperidinozincates.[5] However, the generation of a benzyne bearing a more reactive functional group such as an acyl group is still limited. For the generation of 4-acetylbenzyne, for example, it is necessary that the carbonyl group is protected as an acetal because the acetyl group cannot be tolerable under the reaction conditions.[6] To the best of our knowledge, there are no examples of benzynes bearing an acyl group. Here, we wish to report a more efficient and milder method for generation of benzynes bearing acyl groups.

Taking efficient generation and mild reaction conditions into consideration, the combination of a hypervalent iodine and a silyl group is the best way to generate a functionalized benzyne under mild conditions.[7] In order to avoid the basic conditions which ketones cannot tolerate, we adopted the Diels–Alder reaction of 5-acylpyran-2-ones with 1,2-bis(trimethylsilyl)acetylene, directly giving 1,2-bis(trimethylsilyl)benzenes bearing acyl groups at the 5 position. Cycloaddition of 5-acylpyran-2-ones **1**[8,9] with 1,2-bis(trimethylsilyl)acetylene was conducted in a sealed tube in the absence or presence of xylene as a solvent. For example, heating a mixture of 5-benzoylpyran-2-one (**1a**), bis(trimethylsilyl)acetylene, and xylene at 200 °C for 24 h gave 4-benzoyl-1,2-bis(trimethylsilyl)benzene (**2a**) in 72% yield. The results are given in Table 1.

The benzyne precursors, [2-(trimethylsilyl)phenyl]iodonium triflates **3** bearing an acyl group, were prepared

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*Keywords*: Benzyne; Cycloaddition; Hypervalent iodine compounds; Ketones.

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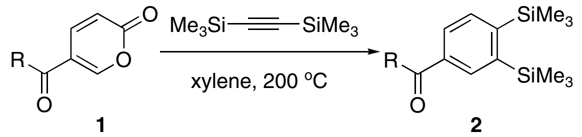
**Table 1.** Synthesis of 4-acyl-1,2-bis(trimethylsilyl)benzenes **2**

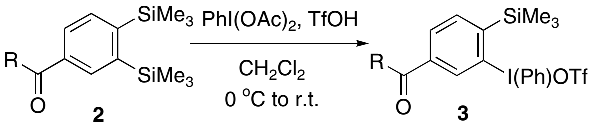


| Entry | Product | Yield[a] (%) |
|---|---|---|
| 1 | **2a** R = Ph | 72 |
| 2 | **2b** R = 4-MeC$_6$H$_4$ | 59 |
| 3 | **2a** R = $^t$Bu | 91 |
| 4 | **2a** R = Me | 60 |

[a] Isolated yields.

by the reaction of 1,2-bis(trimethylsilyl)benzenes **2** with (diacetoxyiodo)benzene [PhI(OAc)$_2$] activated with trifluoromethanesulfonic acid (TfOH) in CH$_2$Cl$_2$ at room temperature. The results are shown in Table 2. The phenyliodination of the silyl groups occurred only at the *meta* position to the acyl group to give the *meta*-acyl substituted benzyne precursors **3**. No benzyne precursors bearing the acyl group at the *para*-position were obtained at all. The high regioselectivity of the phenyliodination is attributable to the *para*-deactivating effect of the carbonyl group. In the cases of aroyl and pivaloyl-substituted 1,2-bis(trimethylsilyl)benzenes **2a–c**, [2-(trimethylsilyl)phenyl]iodonium triflates **3a–c** were obtained in good yields, while the yield of [5-acetyl-2-(trimethylsilyl)phenyl]iodonium triflate (**3d**) was low (Table 2, entries 1–4). This result means that ketones are reactive toward hypervalent iodine reagents. It is well-known that ketones react with hypervalent iodine reagents to give α-functionalized ketones.[10] However, even in this case, we considered that the keto groups were still tolerable under the reaction conditions because more reactive silyl groups existed on the benzene ring. Thus, we used iodosylbenzene (PhIO) instead of PhI(OAc)$_2$, where a Lewis acid, BF$_3$·Et$_2$O, was used for activating PhIO. When 4-acetyl-1,2-bis(trimethylsilyl)benzene (**2d**) was reacted with iodosylbenzene activated with BF$_3$·Et$_2$O and then treated with aqueous NaOTf solution, the yield of **3d** was much improved to be 43% (Table 2, entry 5).[11]

**Table 2.** Synthesis of benzyne precursors **3**



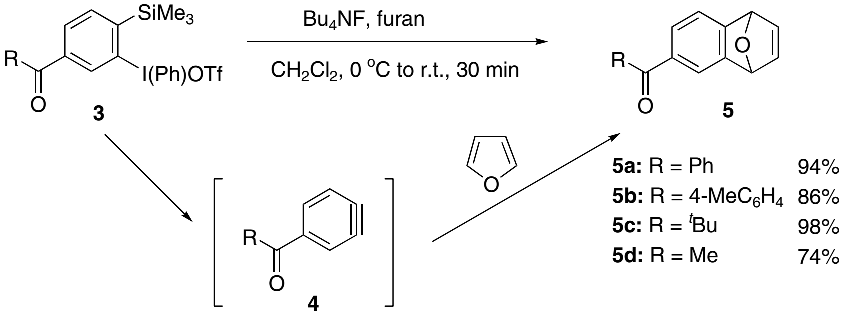
| Entry | Reagent | Product | Yield[a] (%) |
|---|---|---|---|
| 1 | PhI(OAc)$_2$/TfOH | **3a** R = Ph | 63 |
| 2 | PhI(OAc)$_2$/TfOH | **3b** R = 4-MeC$_6$H$_4$ | 54 |
| 3 | PhI(OAc)$_2$/TfOH | **3c** R = $^t$Bu | 49 |
| 4 | PhI(OAc)$_2$/TfOH | **3d** R = Me | 10 |
| 5 | PhIO/BF$_3$·Et$_2$O[b] | **3d** R = Me | 43 |

[a] Isolated yields.

[b] Reaction with PhIO/BF$_3$·Et$_2$O followed by treatment with aqueous NaOTf.

The generation of benzynes **4** bearing keto groups was induced by desilylation of [2-(trimethylsilyl)phenyl]iodonium triflates **3** with a fluoride anion and confirmed by the trapping reaction of **4** with furan to give 1,4-epoxy-1,4-dihydronaphthalene derivatives **5**, which method is conventionally used for the confirmation of benzyne formation because of their reactive and short-lived nature.[1] In the present case, a solution of acyl group-substituted [2-(trimethylsilyl)phenyl]iodonium triflate **3** in CH$_2$Cl$_2$ was treated with a THF solution of Bu$_4$NF in the presence of furan at 0 °C and the reaction mixture was stirred at room temperature for 30 min. Usual workup of the reaction mixture (extraction with CH$_2$Cl$_2$ and separation by column chromatography on silica gel) gave benzyne adduct **5** in a high yield.[12] This simple procedure was enough to generate acylbenzynes **4** and to trap them with an appropriate agent. As shown in Scheme 1, the cycloadducts **5** were isolated in high yields in all cases employed in the present study.

Apparently, it is synthetically useful that benzynes **4** bearing an acyl group were generated and trapped with furan without any damage to the acyl group to give the corresponding 1,4-epoxy-1,4-dihydronaphthalenes **5** in high yields. The benzyne **4c** with a sterically hindered pivaloyl group was generated quantitatively to give the cycloadduct **5c** in 98% yield. Similarly, it was found that the acetyl group on the benzyne **4d** did not suffer serious damage under the reaction conditions and acetyl-substituted benzyne **4d** was efficiently trapped with furan to give the cycloadduct **5d** in 74% yield. These results indicate that [2-(trimethylsilyl)phenyl]iodonium triflates **3** bearing acyl groups generate the corresponding



**Scheme 1.** Generation of acylbenzynes **4** and the trapping reaction with furan.

benzynes **4** almost quantitatively and provide the cycloadducts **5** with furan in high yields. The successful generation of benzynes **4** bearing a reactive ketone function is attributable to the selective desilylation by the fluoride anion due to the high affinity and to the extremely high leaving ability of the hypervalent iodine. Therefore, it is considered that the hypervalent iodine benzyne precursors have excellent advantages over the previously reported benzyne precursors.

In conclusion, we have found a mild and general method for generation of functionalized benzynes, especially benzynes with a ketone function. The high efficiency for generation of benzynes and the high yields of the cycloadducts are important factors in mechanistic studies as well as synthetic applications. In addition to the ketone function, the resultant 1,4-epoxy-1,4-dihydronaphthalene moiety also has high synthetic utility for transformation into new functionalized naphthalene derivatives.[13]

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11. *General procedure for synthesis of [2-(trimethylsilyl)-phenyl]iodonium triflates* **3**: A glass tube was charged with **1** (4 mmol), 1,2-bis(trimethylsilyl)acetylene (6 mmol), and mesitylene (2 mL). The tube was placed in a 20-mL stainless steel autoclave. The autoclave was closed and heated at 200 °C for 24 h. The product **2** was purified by column chromatography on silica gel (eluent: EtOAc/hexane). To a suspension of $PhI(OAc)_2$ (1 mmol) in $CH_2Cl_2$ (5 mL) was added TfOH (1.6 mmol) at 0 °C and the mixture was stirred at that temperature for 30 min. A solution of **2** (1 mmol) in $CH_2Cl_2$ (2 mL) was added at 0 °C and then the reaction mixture was stirred at room temperature for 30 min. After evaporation of the solvent, the residue was treated with ether and crystallized. The crystals were collected, washed with ether, and dried to give **3**. The spectral data are as follows. Compound **3a**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 0.50 (s, 9H), 7.45–7.53 (m, 4H), 7.58–7.68 (m, 2H), 7.75–7.80 (m, 4H), 7.84 (d, $J = 7.8$ Hz, 1H), 8.04 (dd, $J = 7.8$, 1.5 Hz, 1H), 8.36 (d, $J = 1.5$ Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 0.02, 114.00, 121.94, 128.77, 130.23, 132.05, 132.30, 132.48, 133.30, 133.57, 135.70, 138.23, 139.37, 141.68, 151.64, 193.61. Anal. Calcd for $C_{23}H_{22}F_3IO_4SSi$: C, 45.55; H, 3.66. Found: C, 45.55; H, 3.70. Compound **3b**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 0.49 (s, 9H), 2.45 (s, 3H), 7.30 (d, $J = 7.8$ Hz, 2H), 7.47 (t, $J = 7.8$ Hz, 2H), 7.60 (t, $J = 7.8$ Hz, 1H), 7.68 (d, $J = 7.8$ Hz, 2H), 7.78 (d, $J = 7.8$ Hz, 2H), 7.83 (d, $J = 7.5$ Hz, 1H), 8.02 (dd, $J = 7.5$, 1.2 Hz, 1H), 8.35 (d, $J = 1.2$ Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 0.06, 21.77, 114.01, 129.55, 130.42, 132.36, 132.59, 132.63, 133.03, 133.38, 138.36, 139.02, 142.36, 144.89, 148.45, 151.36, 193.05. Anal. Calcd for $C_{24}H_{24}F_3IO_4SSi$: C, 46.46; H, 3.90. Found: C, 46.68; H, 4.00. Compound **3c**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 0.45 (s, 9H), 1.30 (s, 9H), 7.46 (t, $J = 7.8$ Hz, 2H), 7.59 (t, $J = 7.8$ Hz, 1H), 7.74 (d, $J = 7.7$ Hz, 1H), 7.83 (d, $J = 7.8$ Hz, 2H), 7.90 (dd, $J = 7.7$, 1.5 Hz, 1H), 8.29 (d, $J = 1.5$ Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ −0.02, 27.48, 44.50, 114.05, 121.93, 130.60, 132.24, 132.46, 133.49, 137.43, 137.91, 142.55, 149.97, 206.30. Anal. Calcd for $C_{21}H_{26}F_3IO_4SSi$: C, 43.01; H, 4.47. Found: C, 42.83; H, 4.38. Compound **3d**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 0.45 (s, 9H), 2.62 (s, 3H), 7.46 (t, $J = 7.8$ Hz, 2H), 7.59 (t, $J = 7.8$ Hz, 1H), 7.80–7.84 (m, 3H), 8.15 (d, $J = 7.2$ Hz, 1H), 8.65 (s, 1H). Anal. Calcd for $C_{18}H_{20}F_3IO_4SSi$: C, 39.71; H, 3.70. Found: C, 39.48; H, 3.67.
12. *General procedure for trapping reaction of benzynes* **4**: To a solution of **3** (0.2 mmol) and furan (1.0 mmol) in $CH_2Cl_2$ (3 mL) was added a THF solution of $Bu_4NF$ (1.0 M in THF, 0.24 mL) at 0 °C, and the mixture was stirred at room temperature for 30 min. Then, water was added and the product was extracted with $CH_2Cl_2$. The organic extracts were dried over anhydrous $Na_2SO_4$ and concentrated. The residue was purified by column chromatography on silica gel (eluent: hexane/$CH_2Cl_2$) to give benzyne adducts **5**. The spectral data are as follows. Compound **5a**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 5.78–5.79 (m, 2H), 7.04 (dd, $J = 1.8$, 5.4 Hz, 1H), 7.08 (dd, $J = 1.8$, 5.4 Hz, 1H), 7.33 (d, $J = 7.5$ Hz, 1H), 7.45–7.50 (m, 3H), 7.58 (t, $J = 7.8$ Hz, 1H), 7.72 (d, $J = 1.8$ Hz, 1H), 7.77 (d, $J = 7.8$ Hz, 2H); $^{13}$C NMR (75 Hz, $CDCl_3$): $\delta$ 82.16, 119.67, 121.07, 128.25, 129.10, 129.89, 132.28, 134.87, 137.86, 142.32, 143.35, 149.51, 153.89, 196.41. Anal. Calcd for $C_{17}H_{12}O_2$: C, 82.24; H, 4.87. Found: C, 82.02; H, 4.94. Compound **5b**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.36 (s, 3H), 5.69 (s, 2H), 6.95 (dd, $J = 1.8$, 5.6 Hz, 1H), 6.99

(dd, $J = 1.8$, 5.6 Hz, 1H), 7.18–7.25 (m, 3H), 7.36 (dd, $J = 1.2$, 7.2 Hz, 1H), 7.59–7.62 (m, 3H); $^{13}$C NMR (75 Hz, $CDCl_3$): $\delta$ 21.59, 82.14, 119.58, 121.02, 128.78, 128.91, 130.10, 135.11, 135.19, 142.32, 143.04, 143.30, 149.41, 153.58, 196.13. Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.21; H, 5.40. Compound **5c**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 1.34 (d, 9H), 5.75 (s, 2H), 7.01 (dd, $J = 1.5$, 5.4 Hz, 1H), 7.05 (dd, $J = 1.5$, 5.4 Hz, 1H), 7.26 (d, $J = 7.4$ Hz, 1H), 7.42 (dd, $J = 1.2$, 7.4 Hz, 1H), 7.59 (d, $J = 1.2$ Hz, 1H); $^{13}$C NMR (75 Hz, $CDCl_3$): $\delta$ 28.15, 44.12, 82.11, 82.23, 119.49, 119.81, 125.88, 135.44, 142.37, 143.20, 149.09, 151.99, 208.57. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.55; H, 7.04. Compound **5d**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 2.48 (s, 3H), 5.67 (s, 2H), 6.91 (dd, $J = 1.5$, 5.4 Hz, 1H), 6.97 (dd, $J = 1.5$, 5.4 Hz, 1H), 7.23 (d, $J = 7.5$ Hz, 1H), 7.56 (dd, $J = 1.2$, 7.5 Hz, 1H), 7.74 (d, $J = 1.2$ Hz, 1H); $^{13}$C NMR (75 Hz, $CDCl_3$): $\delta$ 26.63, 81.99, 82.03, 119.02, 119.82, 127.20, 134.52, 142.19, 143.27, 149.71, 154.39, 197.47. Anal. Calcd for $C_{12}H_{10}O_2$: C, 77.40; H, 5.41. Found: C, 77.12; H, 5.43.

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