Improved Solubility of Hypervalent Iodine-Benzyne Precursors: Synthesis and Reaction of (Phenyl)[2-(trimethylsilyl)phenyl]iodonium Salts Bearing Long Alkyl Chains

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Abstract: Synthesis of new long-chained hypervalent iodine-benzyne precursors, (4-dodecylphenyl)[2-(trimethylsilyl)phenyl]iodonium triflate and the tetradecyl derivative, is described. The benzyne precursors dissolve even in organic solvents of low polarity such as diethyl ether, THF, cyclopentyl methyl ether, benzene, and toluene. The trapping reactions with furan and tetraphenylcyclopentadienone in the above solvent give the benzyne adducts in high yields without any loss of high reactivity of hypervalent iodine-benzyne precursors.

Key words: hypervalent iodine, benzyne, cycloaddition, high solubility, less polar solvent

Benzyne is one of the important reactive intermediates in organic chemistry and has been widely applied to mechanistic studies and syntheses of natural products and functional materials.1 Although many benzyne precursors have been reported to date,1 there are only a few examples of the precursors that are stable and efficiently yield benzynes under very mild conditions (room temperature and neutral conditions).

Recently, we have introduced ortho-(trimethylsilyl)phenyliodonium salts as new hypervalent iodine benzene precursors that meet the above criteria.2 The crystalline hypervalent iodine-benzyne precursors are very stable to air and moisture, and are very easy to handle. Moreover, quantitative generation of benzyne is achieved by treatment with potassium iodide gave the corresponding iodonobenzene 2a or 2b in good yield, respectively. Subsequent oxidation of 2a,b to (diacetoxyiodo)benzenes 3a,b was accomplished using peracetic acid (30% in acetic acid) in ethyl acetate at 40 °C. Treatment of 3a,b with trifluoromethanesulfonic acid (TfOH) in CH2Cl2 followed by reaction with 1,2-bis(trimethylsilyl)benzene (4) afforded (4-dodecylphenyl)[2-(trimethylsilyl)phenyl]iodonium triflate (5a) or the tetradecyl derivative 5b in good yield.

Scheme 1  Synthesis of long-chained hypervalent iodine-benzyne precursors 5a,b

Long-chained benzyne precursors 5 are colorless crystals (mp 83–84 °C for 5a and mp 81–82 °C for 5b) and stable to air and moisture. The solubility of 5 has been greatly improved over the ones without the side-chains. These long-chained benzyne precursors 5a,b are freely soluble in such common organic solvents as Et2O, THF, benzene, toluene, CH2Cl2, and acetonitrile.

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In order to test the generation of benzyne using the precursors 5, the trapping reactions with furan and tetraphenylcyclopentadienone were conducted in several solvents. Treatment of 5a,b with Bu4NF in the presence of furan in an appropriate solvent afforded the benzyne adduct, 1,4-dihydro-1,4-epoxynaphthalene (6), in high yield. In addition, 4-dodecyl-1-iodobenzene (2a) and 1-iodo-4-tetradecylbenzene (2b) could be recovered almost quantitatively. Cyclopentyl methyl ether (CPME), a new solvent, was also found to give the same result as the other solvents. These results are summarized in Table 1.

Next, the trapping reaction of benzyne with tetraphenylcyclopentadienone was examined using (4-tetradecylphenyl)[2-(trimethylsilyl)phenyl]iodonium triflate (5b). Since tetraphenylcyclopentadienone is insoluble in organic solvents such as THF and toluene, a mixed solvent system with CH2Cl2 was used for the trapping reaction. Treatment of 5b with Bu4NF in the presence of tetraphenylcyclopentadienone gave 1,2,3,4-tetraphenynaphthalene (7) in high yields, together with high yields of recovered 2b, as shown in Table 2.

In summary, we have developed novel long-chained hypervalent iodine-benzyne precursors 5 that dissolve in most organic solvents including nonpolar solvents such as diethyl ether, THF, CPME, benzene, and toluene. The generation and trapping reactions of benzyne using 5 gave high yields of benzyne adducts. Therefore, we believe that the present long-chained hypervalent iodine-benzyne precursors 5 would be used extensively as precursors for a benzyne in a wide range of solvents.

Melting points were measured with a Yanaco melting apparatus and are uncorrected. NMR spectra were taken with a Jeol JNM AL 300 spectrometer. Elemental analyses were conducted by the Service Center of the Elementary Analysis of Organic Compounds, Faculty of Science, Kyushu University.

### Table 1 Trapping Reaction of Benzyne with Furan in Several Solvents

<table>
<thead>
<tr>
<th>Entry</th>
<th>Benzyne Precursor</th>
<th>Solvent</th>
<th>Isolated Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a</td>
<td>Et2O</td>
<td>83</td>
</tr>
<tr>
<td>2</td>
<td>THF</td>
<td>89</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>toluene</td>
<td>86</td>
<td>92</td>
</tr>
<tr>
<td>4</td>
<td>hexane</td>
<td>87</td>
<td>93</td>
</tr>
<tr>
<td>5</td>
<td>CH2Cl2</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>5b</td>
<td>Et2O</td>
<td>83</td>
</tr>
<tr>
<td>7</td>
<td>THF</td>
<td>94</td>
<td>92</td>
</tr>
<tr>
<td>8</td>
<td>CPME</td>
<td>84</td>
<td>94</td>
</tr>
<tr>
<td>9</td>
<td>toluene</td>
<td>82</td>
<td>ca.100</td>
</tr>
<tr>
<td>10</td>
<td>hexane</td>
<td>89</td>
<td>90</td>
</tr>
<tr>
<td>11</td>
<td>CH2Cl2</td>
<td>94</td>
<td>91</td>
</tr>
</tbody>
</table>

* Compound 5 (0.5 mmol), furan (2.5 mmol), Bu4NF (0.6 mmol in THF) and a solvent (2 mL) at r.t. for 30 min.

### Table 2 Trapping Reaction of Benzyne with Tetraphenylcyclopentadienone in Some Solvents

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Isolated Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF–CH2Cl2</td>
<td>89</td>
</tr>
<tr>
<td>2</td>
<td>toluene–CH2Cl2</td>
<td>86</td>
</tr>
</tbody>
</table>

* Compound 5b (0.5 mmol), tetraphenylcyclopentadienone (1.0 mmol), Bu4NF (0.6 mmol in THF), CH2Cl2 (2 mL) and a solvent (2 mL) at r.t. for 30 min.

* Isolated by column chromatography on silica gel.

* Cyclopentyl methyl ether.

The unsubstituted (phenyl)[2-(trimethylsilyl)phenyl]iodonium triflate could not be used in nonpolar solvents such as diethyl ether, THF, CPME, and toluene because of its insolubility. However, the development of the long-chained benzyne precursors 5 has made it possible to use such solvents of low polarity. Although benzyne precursors 5 do not completely dissolve in hexane, but instead form an emulsion, the generation and trapping reactions of benzyne proceeded uneventfully even in such a nonpolar solvent.

Iodoarenes 2: General Procedure

To a suspension of 4-dodecyl or tetradecylaniline 1 (5.0 mmol) in H2O (15 mL) were added 10 M HCl (1.4 mL) and then a solution of NaNO2 (0.25 g, 5.0 mmol) in H2O (5 mL) dropwise at the same temperature. To the resulting amediazone chloride solution was added a solution of KI (0.83 g, 5.0 mmol) in H2O (5 mL) dropwise and the mixture was stirred at 40 °C for 20 min. After addition of an aqueous solution of Na2S2O3 the product was extracted with Et2O. The ethereal extract was washed with H2O and brine, dried (Na2SO4), and concentrated under reduced pressure. The residual oil was purified by column chromatography on silica gel. Elution with hexane gave iodoarene 2 as colorless crystals. An analytical sample was obtained by recrystallization from MeOH.

**4-Dodecyl-1-iodobenzene (2a)**

Yield: 49%; mp 21–23 °C.
1H NMR (300 MHz, CDCl3): δ = 0.88 (t, J = 7 Hz, CH3, 3 H), 1.25 (br s, CH2, 18 H), 1.54–1.59 (m, CH2, 2 H), 2.53 (t, J = 8 Hz, CH2, 2 H), 6.92 (d, J = 9 Hz, ArH, 2 H), 7.57 (d, J = 9 Hz, ArH, 2 H).

13C NMR (75 MHz, CDCl3): δ = 14.1, 22.7, 29.2, 29.3, 29.4, 29.6 (4 C), 31.3, 31.9, 35.4, 90.5, 130.6, 137.2, 142.5.

Anal. Calcd for C20H35IO4: C, 55.60; H, 7.58. Found: C, 55.97; H, 7.81.

2-Iodo-4-tetradecylbenzene (2b)

Yield: 66%; mp 81–82 °C.

1H NMR (300 MHz, CDCl3): δ = 0.45 (s, CH3, 9 H), 0.88 (t, J = 7 Hz, CH2, 2 H), 1.25 (br s, CH2, 22 H), 1.55–1.58 (m, CH2, 2 H), 2.62 (t, J = 8 Hz, CH2, 2 H), 7.26–8.00 (m, ArH, 8 H).

13C NMR (75 MHz, CDCl3): δ = 0.05, 14.1, 22.6, 29.1, 29.3, 29.5, 29.6 (5 C), 30.9, 31.9, 35.5, 110.1, 121.9, 132.1, 132.5, 133.3, 133.4, 138.3, 138.6, 148.1, 148.1.


Trapping Reaction of Benzyne with Furan Using Benzyne Precursor 5; General Procedure

To a solution of the benzyne precursor 5 (0.5 mmol) and furan (0.170 g, 2.5 mmol) in an appropriate solvent (2 mL) was added dropwise a THF solution of Bu4NF (1.0 M, 0.6 mL) at 0 °C and the reaction mixture was stirred at r.t. for 30 min. The solvent was evaporated and H2O was added to the residue. The product was extracted with CH2Cl2, the organic extract was dried (Na2SO4), and concentrated. The residue was submitted to column chromatography on silica gel. Elution with CH2Cl2 and hexane gave 1,4-dihydro-1,4-epoxynaphthalene (6) and iodoarene 2, respectively.

1,4-Dihydro-1,4-epoxynaphthalene (6)

M 85–95 °C (Lit. 1) mp 55–60 °C.

1H NMR (300 MHz, CDCl3): δ = 5.72 (s, CH, 2 H), 6.95–7.00 (m, ArH, 2 H), 7.03 (s, =CH, 2 H), 7.23–7.27 (m, ArH, 2 H).

13C NMR (75 MHz, CDCl3): δ = 125.3, 125.8, 126.4, 126.5, 127.0, 127.5, 129.0, 131.1, 131.3, 137.6, 176.4.

Anal. Calcd for C13H10IO3C: 55.50; H, 7.88. Found: C, 55.97; H, 7.61.

Benzyne Precursors 5; General Procedure

To a solution of 1-diactoxyiodoarene 3 (1.0 mmol) in CH2Cl2 (10 mL) was added dropwise TIOH (0.18 mL, 2.0 mmol) at −20 °C and the solution was stirred at −20 °C for 30 min. 1,2-Bis( trimethylsilyl)benzene (4; 0.222 g, 1.0 mmol) was added at the same temperature and the reaction mixture was stirred at −20 °C and at r.t. for 15 min. The mixture was washed with H2O, dried (Na2SO4), and the solvent was evaporated under reduced pressure to give light brown crystals. Recrystallization from CH2Cl2 and hexane afforded colorless crystals.

1-(Diacetoxyiodo)arenes 3; General Procedure

To a solution of 1-(diacetoxyiodo)arene 3; General Procedure

To a solution of peracetic acid in HOAc (30%, 16 mL) at 0 °C and the solution was stirred at −20 °C for 30 min. 1,2-Bis(trimethylsilyl)benzene (4; 0.222 g, 1.0 mmol) was added at the same temperature and the reaction mixture was stirred at −20 °C and at r.t. for 15 min. The mixture was washed with H2O, dried (Na2SO4), and the solvent was evaporated under reduced pressure to give light brown crystals. Recrystallization from CH2Cl2 and hexane afforded colorless crystals.

1,2,3,4-Tetraphenylnaphthalene (7)

Mp 203–205 °C (Lit. 3 mp 204 °C).

1H NMR (300 MHz, CDCl3): δ = 6.80–6.89 (m, ArH, 10 H), 7.16–7.28 (m, ArH, 10 H), 7.38–7.40 (m, ArH, 2 H), 7.62–7.66 (m, ArH, 2 H).

13C NMR (75 MHz, CDCl3): δ = 125.3, 125.8, 126.4, 126.5, 127.0, 127.5, 131.3 (2 C), 132.0, 138.4, 138.8, 139.5, 140.5.
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