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# Reaction of 1,2-dihalogen substituted arenes with lanthanum metal: a new generation method of benzyne

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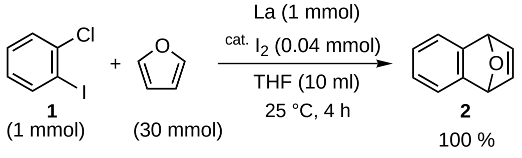
**Abstract**—A new generation method of benzyne has been developed. When 1,2-dihalogen substituted arenes were allowed to react with lanthanum metal in the presence of dienes, Diels–Alder products between benzyne and dienes were formed in moderate to good yields. © 2002 Elsevier Science Ltd. All rights reserved.

The use of lanthanoid salts and organolanthanoid compounds in organic synthesis has been steadily increasing in recent years.[1] In particular; low-valent, trivalent, and tetravalent lanthanoid compounds have been widely used as versatile reagents in organic reaction. Up to now the direct use of cerium,[2] samarium,[3] and ytterbium[4] metals has been developed; however, to the best of our knowledge, there are no reports on the direct use of lanthanum metal in organic synthesis. Recently, we have succeeded in the first direct use of lanthanum metal as a reducing agent,[5] which is a relatively stable metal under aerobic conditions and has the largest redox potential among the lanthanoid metals, in organic synthesis. In connection with a study on the direct use of lanthanum metal in organic synthesis, we found that generation of benzyne from 1,2-dihalogen substituted arenes was accomplished by the efficient transfer of available electrons from the lanthanum metal.[6]

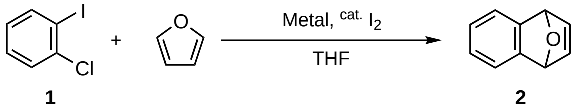
When 1-chloro-2-iodobenzene (**1**) was treated with an equivalent amount of lanthanum metal[9] in the presence of an excess amount of furan (30 equiv.) under a nitrogen atmosphere, 1,4-dihydro-1,4-epoxynaphthalene (**2**), which is a Diels–Alder product of benzyne and furan, was obtained in almost quantitative yield (Scheme 1). Although the reaction efficiently proceeded at lower reaction temperature (at 0°C: 100%), in the absence of iodine, the reaction did not occur.[10,11]



**Scheme 1.**

In order to know the reactivity of other lanthanoid metals, 1-chloro-2-iodobenzene was allowed to react with various lanthanoid metals in the presence of excess amount of furan (30 equiv.) at 25°C for 4 h, and these results are shown in Table 1. Although the use of Ce, Pr, Nd, and Yb led to the formation of **2**, the yield was decreased. In the case of samarium metal, which is widely used in organic synthesis, the yield of **2** was very low owing to the formation of various complex prod-

**Table 1.** Effect of lanthanoid metal[a]



| Metal | Yield (%)[b] | Metal | Yield (%)[b] |
|---|---|---|---|
| La | 100 | Tb | 0 |
| Ce | 89 | Dy | 0 |
| Pr | 77 | Ho | 0 |
| Nd | 59 | Er | 0 |
| Sm | Trace | Tm | 0 |
| Eu | 0 | Yb | 54 |
| Gd | 0 | Lu | 0 |

[a] *Reaction conditions*: 1-chloro-2-iodobenzene (1 mmol), furan (30 mmol), metal (1 mmol), $I_2$ (0.04 mmol) and THF (10 ml) at 25°C for 4 h.

[b] GC yield.

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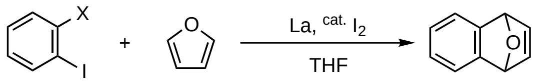
ucts. In the reaction of other lanthanoid metals, the reaction did not proceed, and **1** was recovered. To understand the scope and limitation of the reaction, 1-fluoro-, 1-bromo-2-iodobenzene, and 1,2-diiodobenzene instead of 1-chloro-2-iodobenzene were treated with lanthanum metal in the presence of furan, and the results are shown in Table 2. For every *o*-halogen substituted iodobenzene, the Diels–Alder adducts **2** were obtained in moderate yields; however, the yields were slightly decreased compared with that of 1-chloro-2-iodobenzene, owing to the formation of fluoro-, bromo- and iodobenzene, reductive deiodination products, as by-products. In the case of 2-trifluoromethanesulfonyl-1-iodobenzene, the reaction did not proceed at all. The treatment of *o*-halogen substituted iodobenzene with lanthanum metal in the presence of 2-methylfuran or cyclopentadiene was examined. In contrast to the case of furan, the Diels–Alder addition efficiently proceeded to form the Diels–Alder products in moderate to good yields, by the use of 1-bromo-2-iodobenzene instead of 1-chloro-2-iodobenzene (Scheme 2). In the case of isoprene, the yield of product was low owing to the formation of various complex products. Similarly, various benzyne derivatives was successfully generated by the reaction of 1,2-, 1,3-, 1,4-dichloro-6-iodobenzene, 4-chloro-3-iodotoluene, and 4-chloro-3-iodoanisole with lanthanum metal, and the corresponding 1,4-dihydro-1,4-epoxynaphthalenes were obtained in relatively high yields (Table 3).

By this method, reductive deiodinated products were formed as by-products. From these results, we speculated that benzyne was formed via elimination of the halogen anion from the 2-halogen substituted phenyl anion (**6**). In order to gain information on the reaction pathway for the generation of benzyne, we carried out some experiments. 1-Chloro-2-iodobenzene was treated with lanthanum metal in the presence of trimethylchlorosilane giving 1-chloro-2-trimethylsilylbenzene **3** in 58% yield (Scheme 3). In addition, the treatment of 1,4,5-trichloro-2-iodobenzene (**4**) with lanthanum metal in the presence of an excess amount of furan followed by quenching with $DCl/D_2O$ instead of $HCl/H_2O$ provided a *C*-deuterated product (**5**) (Scheme 4).[13] At the present time, while the reaction pathway for the generation of benzyne is not shown in detail, a reaction pathway including a phenyl anion species is strongly suggested (Scheme 5). Transfer of two electrons from lanthanum metal or low-valent lanthanum species, which were generated in situ by the reaction of lanthanum metal with iodine, to 1,2-dihalogen substituted benzenes, followed by elimination of the iodine anion forms the corresponding phenyl anion species (**6**). The halogen anion was easily eliminated from **6** to form

**Table 2.** Reaction of various 1-halogeno-2-iodobenzene[a]

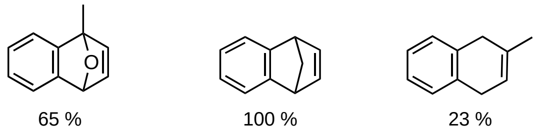


**2**

| Entry | X | Yield (%)[b] |
|---|---|---|
| 1 | F | 80 |
| 2 | Cl | 100 |
| 3 | Br | 87 |
| 4 | I | 82 |
| 5 | OTf | 0 |

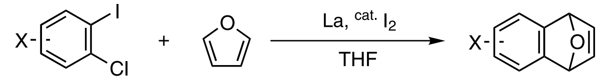
[a] *Reaction conditions*: 1-halogeno-2-iodobenzene (1 mmol), furan (30 mmol), La (1 mmol), $I_2$ (0.04 mmol) and THF (10 ml) at 25°C for 4 h.

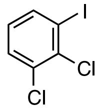
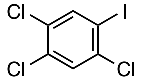
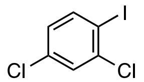
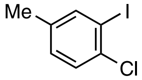
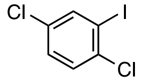
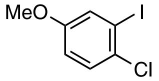
[b] GC yield.



**Scheme 2.** Reaction of 1-bromo-2-iodobenzene with various dienes.

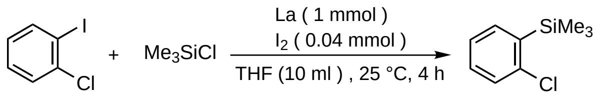
**Table 3.** Reaction of various 1-chloro-2-iodobenzene derivatives[a]



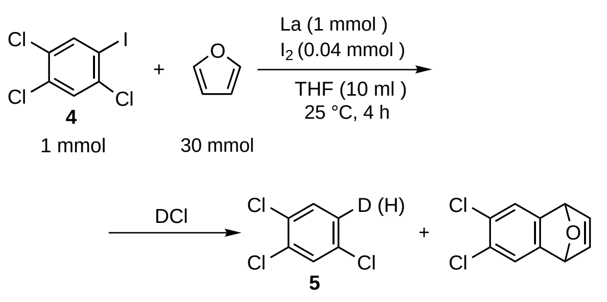
| entry | substrate | yield (%)[b] | entry | substrate | yield (%)[b] |
|---|---|---|---|---|---|
| 1 |  | 55 | 4 |  | 29 |
| 2 |  | 44 | 5 |  | 47 |
| 3 |  | 60 | 6 |  | 48 |

[a] *Reaction conditions*: substrate (1 mmol), furan (30 mmol), La (1 mmol), $I_2$ (0.04 mmol) and THF (10 ml) at 25°C for 4 h.

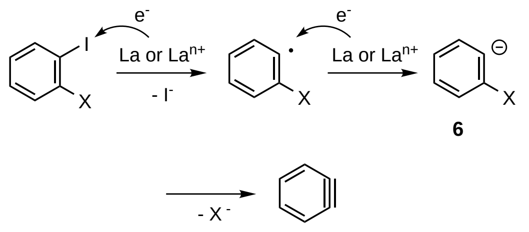
[b] GC yield.



**Scheme 3.**



**Scheme 4.**



Scheme 5. Plausible reaction path.

the corresponding benzyne intermediate. In the case of 1,2-dihalogeno benzenes substituted electron-withdrawing group, it seems likely that elimination of the halogen anion from **6** was suppressed owing to the stability of the phenyl anion, giving the corresponding deiodination product.

In summary, we have found that an efficient transfer of available electrons from lanthanum metal successfully achieved the generation of benzyne from *o*-dihalogen substituted benzene. Further work on application and elucidation of the reaction pathway are now in progress.

## Acknowledgements

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6. Since Wittig showed a generation method of benzyne by the reaction of *o*-dihalogen substituted benzene with lithium metal,[7] many methods of generating benzyne have been developed.[8]
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9. Lanthanum metal was commercially available high-grade product and was used after powderization (ca. 40 mesh).
10. We have already shown that the addition of a catalytic amount of iodine dramatically enhanced the reductive dimerization of carbonyl compounds or imine with lanthanum metal. See Ref. 5.
11. In the reaction used ytterbium or samarium metal, it was disclosed that various reactions were promoted by the addition of a catalytic amount of methyl iodide or iodine; however, the mechanism of the effect of methyl iodide or iodine was not explained.[12]
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13. At present, the formation pathway of 1,3,4-trichlorobenzene has not been explained; however, it was suggested that 1,3,4-trichlorobenzene was formed by the hydrogen abstraction of the phenyl radical, which was generated in situ by the one-electron transfer from lanthanum metal to 1,4,5-trichloro-2-iodobenzene (**4**), followed by the elimination of $I^-$ from THF as a solvent.