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# ZrCl$_4$-promoted halogen migration during an electrophilic amination of halogenated phenols†‡

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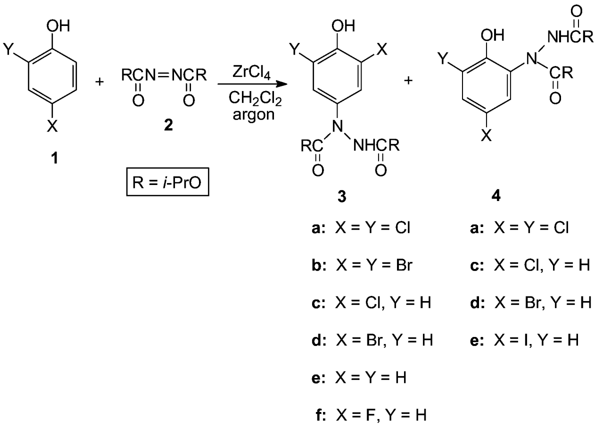
**An electrophilic amination of halogenated phenols with diisopropyl diazenedicarboxylate in the presence of ZrCl$_4$ as a Lewis acid, accompanied by a halogen migration, was demonstrated for the first time; the fluorine, chlorine, bromine, or iodine atom migrated during the amination process under mild reaction conditions.**

Halogen migration on aromatic substrates in the presence of a strong base, also known as the 'halogen dance', was discovered in the 1950s;[1] since then it has been thoroughly investigated[2] and remains a subject of interest for the groups of Quéguiner,[3] Schlosser,[4,5] and others.[6] In contrast, acid-promoted halogen migration occurs rarely on aromatic molecules,[7] and is limited to iodine[8,9] and bromine[10–14] atoms.

As a result of our interest in hydrazides and other N–N-containing compounds,[15] we recently described an electrophilic amination of aromatic substrates with various alkyl arylaminocarbonyldiazenecarboxylates in the presence of ZrCl$_4$.[16] Here we report that the ZrCl$_4$-promoted electrophilic amination of halogenated phenols was accompanied by the migration of a halogen atom. Thus, diisopropyl diazenedicarboxylate **2** and 2,4-dichlorophenol (**1**, X = Y = Cl) were reacted in the presence of ZrCl$_4$ to produce a mixture of regioisomers **3a** and **4a** (Scheme 1, Table 1).[17] We also noticed that 2,4-dichlorophenol did not react with **2** if ZrF$_4$ or ZrBr$_4$ was used instead of ZrCl$_4$. The amination performed on the 2,4-dibromophenol with the diazene **2** led exclusively to **3b**. The compound **4a** can be considered as a 'normal' product of amination. On the other hand, the products **3a** and **3b** can be formed in the process that involves the migration of one halogen atom from the starting 2,4-dihalophenol. As far as we know the formation of the products **3a** and **3b** represents the first evidence of Lewis-acid-promoted halogen migration taking place during an electrophilic amination of a haloarene.[18]



**Scheme 1**

Encouraged by these results we used the diazene **2** and ZrCl$_4$ for the amination of 4-halophenols. Under similar reaction conditions, 4-chlorophenol, 4-bromophenol and 4-iodophenol were transformed to the mixtures of **3c** and **4c**, **3d** and **4d**, or **3e** and **4e**, respectively. The isolation of **3c** and **3d**, though as minor products, again indicated a migration of the chlorine or the bromine atom from the *para* position to the *ortho* position regarding the phenolic OH. The product **3e** can be formed by following the same reaction pathway, the only difference being that the iodine atom was eliminated during the amination process, giving the isolated compound instead of its 2-iodo derivative.

Although fluorine migrations on organic substrates are rare and involve high-energy intermediates or excited molecules,[19] it was reasonable to examine the possibility of Lewis-acid-promoted fluorine migration on the appropriate fluorophenol. Thus, 4-fluorophenol reacted with the diazene **2** in the presence of ZrCl$_4$. Surprisingly, the isolated product was not the fluorophenol **3f**, which might have appeared on amination accompanied by a fluorine migration, but its chloro analogue **3c**. The formation of the latter can be explained by electrophilic amination, fluorine migration and substitution of the fluorine with the chlorine atom. In spite of the fact that the exchange of the fluorine by the chlorine is a thermodynamically unfavourable reaction it has already been observed on treatment of perfluorocycloalkenes with aluminium trichloride.[20]

To exclude the possibility of a halogen migration prior to or after electrophilic amination we performed several additional experiments: (a) starting materials (2,4-dichlorophenol, 2,4-dibromophenol, 4-chlorophenol, 4-bromophenol, 4-iodophenol, and 4-fluorophenol) remained unchanged when treated with ZrCl$_4$ in the absence of the diazene **2**. (b) Products aminated at the 2 position relative to the phenolic OH (**4a**, **4c**, **4d**, and **4e**) did not react with ZrCl$_4$ under the reaction conditions (time, temperature, solvent), required for their formation. Furthermore, the phenol **3f** (obtained from 2-fluorophenol and **2** in the

**Table 1** Amination of halogenated phenols with the diazene **2**

| Substrate | Time/h | Temp./°C | Product **3** (%)[a] | Product **4** (%)[a] |
|---|---|---|---|---|
| 2,4-Dichlorophenol | 5 | −10 | **3a** (57) | **4a** (10) |
| 2,4-Dibromophenol | 6 | −42 | **3b** (76) | — |
| 4-Chlorophenol | 4 | −42 | **3c** (5) | **4c** (86) |
| 4-Bromophenol | 4 | −62 | **3d** (5) | **4d** (79) |
| 4-Iodophenol | 3 | −62 | **3e** (8) | **4e** (69) |
| 4-Fluorophenol | 4 | −62 | **3c** (66) | — |
| 2-Fluorophenol | 4 | −62 | **3f** (83) | — |

[a] Yield of the product after radial chromatography.

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† Electronic supplementary information (ESI) available: spectroscopic data ($^1$H NMR,$^{13}$C NMR, IR, MS), mp and elemental analysis (or HRMS) for the products **3** and **4**. See http://www.rsc.org/suppdata/cc/b2/b203622c/

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presence of $ZrCl_4$ in the reaction that did not involve a fluorine migration) survived the treatment with $ZrCl_4$ under conditions applied for the synthesis of **3c** from 4-fluorophenol. These results suggest that the migration of a halogen atom always took place during an electrophilic amination.

In conclusion, an electrophilic amination of halogenated phenols with diisopropyl diazenedicarboxylate **2** was carried out using $ZrCl_4$ as a Lewis acid. The formation of products bearing the corresponding hydrazino functionality at the 4 position indicated that the amination was accompanied by a halogen migration. This is, to the best of our knowledge, the first example of a halogen migration promoted by $ZrCl_4$ during the electrophilic amination process. It is worth mentioning that the fluorine, the chlorine, the bromine, or the iodine atom can migrate under mild reactions conditions.

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