Catalytic defluorinative [3 + 2] cycloaddition of trifluoromethylalkenes with alkynes via reduction of nickel(II) fluoride species

Fujita Takeshi, Arita Tomohiro, Ichitsuka Tomohiro, Ichikawa Junji

journal or publication title: Dalton transactions
volume: 44
number: 45
page range: 19460-19463
year: 2015

(C) The Royal Society of Chemistry 2015
URL: http://hdl.handle.net/2241/00135046
doi: 10.1039/C5DT02160J
Catalytic Defluorinative [3+2] Cycloaddition of Trifluoromethylalkenes with Alkynes via Reduction of Nickel(II) Fluoride Species

Takeshi Fujita, Tomohiro Arita, Tomohiro Ichitsuka and Junji Ichikawa*

www.rsc.org/

Received 00th January 20xx, Accepted 00th January 20xx
DOI: 10.1039/x0xx00000x

Nickel-catalyzed [3+2] cycloaddition of 2-trifluoromethyl-1-alkenes with alkynes via domino C-F bond activation was achieved by sequential β-fluorine elimination. The nickel(II) fluoride species formed in this reaction was reduced by a diboron compound, regenerating the catalytically active nickel(0) species.

Transition metal-catalyzed carbon-fluorine bond activation has recently been established as one of the most significant areas of research in synthetic, organometallic, and fluorine chemistries. The activation not only is effective for cleaving strong chemical bonds but also provides synthetic methods toward partially fluorinated compounds from multi-fluorinated substrates. Although metal-mediated oxidative addition of C-F bonds has mostly been used for C-F bond activation, we have developed alternative approaches by employing β-fluorine elimination as the key elementary step.

Quite recently, we reported two types of nickel-mediated defluorinative coupling reactions between 2-trifluoromethyl-1-alkenes 1 and alkynes 2 via a combination of oxidative cyclization and β-fluorine elimination. When stoichiometric amounts of Ni(cod)$_2$ (cod = 1,5-cyclooctadiene) and PC$_6$I$_6$ are used, cleavage of two C-F bonds of the CF$_3$ group proceeds via β-fluorine elimination to afford the corresponding 2-fluoro-1,3-cyclopentadienes 3 (Scheme 1, path A). In contrast, the addition of Et$_3$SiH enables the catalytic synthesis of 1,1,3-trifluoro-1,4-dienes 4 via cleavage of a C-F bond of the CF$_3$ group (Scheme 1, path B). In this reaction, the Ni-F bond of the nickel(II) fluorides A would be formed from the intermediary nickelacylclopentenes via β-fluorine elimination and transformed into a Ni-H bond by Et$_3$SiH. The key to this successful catalysis is the regeneration of the active Ni(0) catalyst by employing a fluorophilic silicon reagent.

The more difficult challenge was the catalytic synthesis of 2-fluoro-1,3-cyclopentadienes 3 with the regeneration of catalytically active Ni(0) species from the NiF$_2$ species B formed with 3 (Scheme 1, path A’). Elemental metals were found to be ineffective for the electron-transfer reduction of the nickel(II) fluoride species. We thus attempted to individually remove the fluorine atoms on the nickel using a transmetalation/reductive elimination sequence employing bimetallic species (Scheme 2). As a result of screening for bimetallic reagents with good affinity for fluorine atoms, we consequently found that the use of bis(neopentylglycolato)diboron (B$_2$(nep)$_2$) in the presence of t-BuOK and MgF$_2$ successfully induced the nickel-catalyzed synthesis of 2-fluoro-1,3-cyclopentadienes 3 via [3+2] cycloaddition of 1 and 2.

---

Scheme 1 Nickel-mediated catalytic defluorinative coupling of 2-trifluoromethyl-1-alkenes 1 with alkynes 2.
Although the treatment of 1.1 equiv of disilane, silylboron, or diboron compounds afforded cyclopentadiene 3aa, its catalytic synthesis was not achieved (Entries 6–10). Among the diboron compounds examined (Fig. 1), the combination of B₂(nep)₂ and t-BuOK for borate formation improved the yield of 3aa up to 45% (Entry 13 vs. Entries 11 and 12). Finally, the ternary additive system of B₂(nep)₂ and t-BuOK with MgF₂ for fluorine abstraction was adopted, affording 3aa in 60% yield (Entry 14).

The substrate scope was then investigated using the optimized conditions (Table 2).† Unsymmetrical 4-methylpent-2-ynyl (2b) also participated in the catalytic [3+2] cycloaddition to afford 2-fluoro-1,3-cyclopentadienes 3ab–gb with complete regioselectivity, which is consistent with those obtained in other nickel-catalyzed coupling reactions via oxidative cyclization. 1α-Trifluoromethylstyrenes 1a–d bearing electron-withdrawing acetyl, fluoro, cyano, and further trifluoromethyl groups as well as unsubstituted and phenyl-substituted α-trifluoromethylstyrenes 1e–f provided the corresponding cyclopentadienes 3bb–fb. The cycloaddition of tert-butyl 2-(trifluoromethyl)acrylate (1g) with 2b also proceeded smoothly to afford cyclopentadiene 3gb in 42% yield.

Table 1 Screening of reagents for the catalytic synthesis of 2-fluoro-1,3-cyclopentadiene 3aa

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reagent (equiv)</th>
<th>Yield (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>Na (3.0)</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>K (3.0)</td>
<td>N.D.</td>
</tr>
<tr>
<td>4</td>
<td>Mn (2.0)</td>
<td>18</td>
</tr>
<tr>
<td>5</td>
<td>Zn (2.0)</td>
<td>18</td>
</tr>
<tr>
<td>6</td>
<td>Me₂SiMe₂SiMe₂ (1.1)</td>
<td>16</td>
</tr>
<tr>
<td>7</td>
<td>PhMe₂SiB(Bpin) (1.1)c</td>
<td>18</td>
</tr>
<tr>
<td>8</td>
<td>B₂(pin)₂ (1.1)</td>
<td>17</td>
</tr>
<tr>
<td>9</td>
<td>B₂(cat)₂ (1.1)d</td>
<td>4</td>
</tr>
<tr>
<td>10</td>
<td>B₂(nep)₂ (1.1)e</td>
<td>19</td>
</tr>
<tr>
<td>11</td>
<td>B₂(pin)₂ (1.1)f t-BuOK (1.1)</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>B₂(cat)₂ (1.1)g t-BuOK (1.1)</td>
<td>29</td>
</tr>
<tr>
<td>13</td>
<td>B₂(nep)₂ (1.1)h t-BuOK (1.1)</td>
<td>45</td>
</tr>
<tr>
<td>14</td>
<td>B₂(nep)₂ (1.1)h t-BuOK (1.1), MgF₂ (1.0)</td>
<td>60</td>
</tr>
</tbody>
</table>

a Yield was determined by 19F NMR measurement using PhCF₂ as an internal standard. b N.D. = Not detected. c pin = pinacolato. d cat = catecholato. e nep = neopentylglycolato.

Fig. 1 List of diboron compounds.

We sought appropriate reagents for the nickel-catalyzed [3+2] cycloaddition of 1 and 2. α-Trifluoromethylstyrene 1a bearing an acetyl group and 4-octyne (2a) were used as model substrates along with 20 mol% of Ni(cod)₂ and 40 mol% of PCy₃ (Table 1). First, to perform the electron-transfer reduction of the intermediary nickel(II) fluoride species, several elemental metals were examined as additives (Entries 2–5). Alkali metals, i.e., sodium and potassium, possessing strongly negative formal potentials afforded lower yields of cyclopentadiene 3aa, compared with the case when no additive was added (Entries 2 and 3 vs. Entry 1). Although manganese and zinc are often used as reductants for nickel(II) halides, no positive effect was observed for the present reaction (Entries 4 and 5). We expected fluorophilic bimetallic species to promote stepwise abstraction of fluoride from the nickel species, which might allow for the catalytic [3+2] cycloaddition (vide supra).
Scheme 3 Preparation and nickel-catalyzed intramolecular [3+2] cycloaddition of 1-trifluoromethyl-1-en-7-yne 5.

Notes and references
† Typical procedure for the synthesis of 2-fluoro-1,3-cyclopentadiene 3 via nickel-catalyzed [3+2] cycloaddition: In a 30-mL Schlenk tube were placed Ni(cod)₂ (14 mg, 0.051 mmol), PCy₃ (29 mg, 0.10 mmol), B₂(neop)₂ (62 mg, 0.27 mmol), BuOK (30 mg, 0.27 mmol), MgF₂ (16 mg, 0.26 mmol), and 1,4-dioxane (3 mL). After stirring for 10 min at room temperature, 2-trifluoromethyl-1-alkene 1a (53 mg, 0.25 mmol) and 4-octyne (2a, 30 mg, 0.28 mmol) were added to the mixture. After stirring for 3 h at 80 °C, the reaction was quenched with aqueous HCl (1 M). Organic materials were extracted with Et₂O two times. The combined extracts were washed with brine and dried over Na₂SO₄. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane:EtOAC = 50:1) to give 2-fluoro-1,3-cyclopentadiene 3aa (38 mg, 53%) as a yellow solid.
§ Crystal data for 9: CCDC 1402817, C₁₇H₁₇F₂; M = 228.30, monoclinic, space group P2₁/n; crystal size = 0.20 × 0.10 × 0.10 mm³, α = 10.246(4) Å, β = 10.133(4) Å, c = 11.645(4) Å, α = 90°, β = 91.857(4)°, γ = 90°, V = 1208.2(8) Å³, Z = 4, T = 120(2) K, D_calcd = 1.255 g/cm³, 2θ[scan] = 5.22°, 2θ[scan] = 55.02°, 6664 reflections measured, of which 2745 are unique (Rint = 0.034), R1 = 0.0449, wR2 = 0.1065, goodness of fit on F² = 1.049.
6 For transition metal-catalyzed reactions via β-fluorine elimination reported by other groups, see: (a) W. Heitz and A. Knebelkamp, Makromol. Chem., Rapid Commun., 1991, 12, 69–75; (b) A. A. Peterson and K. McNeil, Organometallics,


