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### Rapid and Selective Reduction of Functionalized Fluoroaryl Azides to the Corresponding Anilines with Stannous Chloride Dihydrate

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RAPID AND SELECTIVE REDUCTION OF FUNCTIONALIZED  
FLUOROARYL AZIDES TO THE CORRESPONDING ANILINES  
WITH STANNOUS CHLORIDE DIHYDRATE

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**ABSTRACT:** Nitrofluorophenyl azide **1**, azidofluorobenzaldehyde **2**, azidofluorobenzoate ester **3**, and aminonitrofluorophenyl azide **4** were selectively reduced in high yield to the corresponding anilines **5-8** with excess stannous chloride dihydrate in 2:1 ethyl acetate/ethanol at ambient temperature.

A convenient method for the introduction of an amino group into fluorinated aromatics is by nucleophilic aromatic substitution of one of the fluorine atoms with azide ion<sup>1</sup> and then reduction of the azide group to the primary amine with lithium aluminum hydride or catalytic hydrogenation.<sup>2</sup> The substitution reaction is favored by the presence of electron withdrawing groups on the aromatic ring. Unfortunately, the most favorable groups such as nitro or carbonyl are also susceptible

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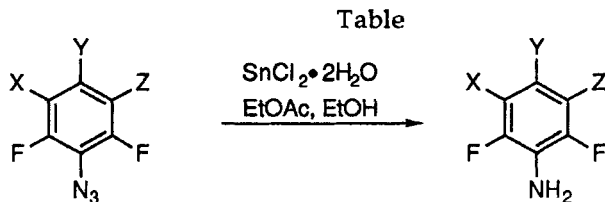
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toward reduction. Methods have been reported for the selective reduction of aryl azides to anilines in the presence of nitro groups, e.g.  $\text{Ph}_3\text{P}/\text{NH}_4\text{OH}$ ,<sup>3</sup>  $\text{Na}_2\text{S}/\text{MeOH}/\text{NEt}_3$ ,<sup>4</sup> and propane-1,3-dithiol.<sup>5</sup> However, these reagents require relatively long reaction times<sup>3,4</sup> or cumbersome work-up procedures.<sup>3,4,5</sup>

Recently Maiti et al.<sup>6</sup> reported the facile conversion of phenyl azide and several aliphatic azides to amines using stannous chloride in methanol. Since we had a series of functionalized perfluorophenyl azides available from our photolabeling program,<sup>7</sup> we investigated the selectivity of the stannous chloride method with these molecules. The Table shows that treatment of fluorinated aryl azides with stannous chloride dihydrate allows for the rapid and selective reduction of aryl azide groups to aryl amines in high yield in the presence of nitro, ester and aldehyde functionality.<sup>8</sup> It should be noted that refluxing solutions of stannous chloride dihydrate in ethyl acetate/ethanol have been previously reported to reduce aromatic nitro compounds to the corresponding anilines over periods of 30 minutes or longer.<sup>9</sup>

#### Selective Reduction of Aryl Azides: Representative Procedure

To a stirred solution of **37** (36 mg, 0.14 mmol) in ethyl acetate (2 mL) and ethanol (1 mL) at room temperature was added stannous chloride dihydrate (163 mg, 0.72 mmol). After all the solid dissolved (ca. 1 min), the reaction solution was poured into ice water (8 mL) and neutralized with saturated  $\text{NaHCO}_3$  (ca. 1 mL). The resulting mixture was extracted with ethyl acetate (2 x 6 mL). The extract was dried ( $\text{MgSO}_4$ ) and concentrated in vacuo to give **7** (30 mg, 94%) as a white microcrystalline powder: mp 113.5-115.0 °C (lit.<sup>7</sup> mp 113-114 °C); IR



$1^a$ Y = NO <sub>2</sub> , X, Z = F	$5^b$ Y = NO <sub>2</sub> , X, Z = F	96%
$2^a$ Y = CHO, X, Z = F	$6^c$ Y = CHO, <sup>d</sup> X, Z = F	99%
$3^a$ Y = CO <sub>2</sub> Me, X, Z = F	$7^a$ Y = CO <sub>2</sub> Me, X, Z = F	94%
$4^e$ Y = NO <sub>2</sub> , X = NH <sub>2</sub> , Z = H	$8^f$ Y = NO <sub>2</sub> , X = NH <sub>2</sub> , Z = H	94%

<sup>a</sup>Reference 7. <sup>b</sup>Reference 10. <sup>c</sup>Reference 11. <sup>d</sup>Isolated as a 1:1 mixture of 4-amino-2,3,5,6-tetrafluorobenzaldehyde and its diethyl acetal.

<sup>e</sup>Azide **4** was prepared by the reaction of sodium azide with 6-nitro-2,3,4-trifluoroaniline in refluxing acetone/water (1:1). Azide **4**: mp 92-93.5 °C; HRMS 215.0255 (215.0251 calcd for C<sub>6</sub>H<sub>3</sub>N<sub>5</sub>O<sub>2</sub>F<sub>2</sub>). <sup>f</sup>Diamine **8**: mp 175-177 °C; HRMS 189.0329 (189.0350 calcd for C<sub>6</sub>H<sub>5</sub>N<sub>3</sub>O<sub>2</sub>F<sub>2</sub>).

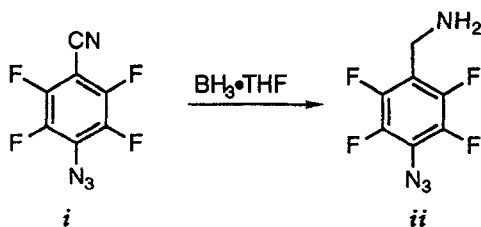
(CDCl<sub>3</sub>) 3414, 1727 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 3.92 (s, 3H), 4.36 (br s, 2H); m/e (rel. intensity) 223 (M<sup>+</sup>, 52), 192 (100).

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8. It is interesting to note that the *nitrile* group in perfluoroaryl azide *i* can be reduced selectively with  $\text{BH}_3 \cdot \text{THF}$  to the corresponding benzyl amine *ii* (48%) with preservation of the azide moiety.<sup>7</sup>



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