

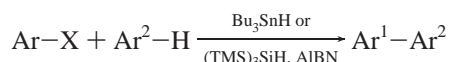
## Radical Additions of Aryl Iodides to Arenes Are Facilitated by Oxidative Rearomatization with Dioxigen

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A diverse assortment of useful synthetic transformations are based on inter- and intramolecular additions of radicals to aromatic rings.<sup>1</sup> Such reactions are often conducted under reducing conditions with reagents such as tributyltin hydride and tris(trimethylsilyl)silicon hydride,<sup>2</sup> even though the reactions are not reductions and often finish with oxidative rearomatization.<sup>3,4</sup> Typically, nonchain mechanisms are proposed for these formal homolytic aromatic substitution reactions, and suggestions for rearomatization pathways include reaction of an intermediate cyclohexadienyl or related radical with solvent, with initiator, with other radicals, or with itself, among other possibilities.<sup>5</sup>

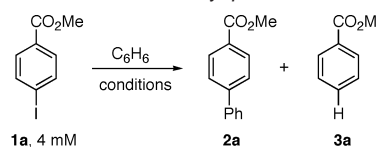


Homolytic aromatic substitutions often require high temperatures and long reactions times and typically occur in moderate yields, perhaps because of the relative stability of cyclohexadienyl radical intermediates. We hypothesized that cyclohexadienyl radicals could be intercepted by using even more stable radicals, taking advantage of the "persistent radical effect".<sup>6,7</sup> We report herein the discovery that radical additions of aryl iodides to arenes can be effected under exceptionally mild conditions and in high yields in the presence of air. We suggest that the selective interception of cyclohexadienyl radicals by dioxigen, a stable triplet diradical, is a key step in this process.

We initially selected stable nitroxide radicals such as TEMPO to intercept the intermediate cyclohexadienyl radicals.<sup>7</sup> The identification of the air-mediated reaction conditions stemmed from control experiments for the TEMPO-mediated process. Results from several key exploratory reactions are summarized in Table 1. Under conditions typical of those used currently,<sup>1,2</sup> the addition of methyl *p*-iodobenzoate **1** to benzene at reflux was promoted ineffectively by tributyltin hydride and a stoichiometric quantity of AIBN (entry 1). Biphenyl-4-carboxylic acid methyl ester **2** was formed in 27% yield along with methyl benzoate **3** in 9% yield. Consistent with the results of Alvarez-Builla,<sup>2a</sup> a better but still moderate yield of **2** (67%) was obtained with tris(trimethylsilyl)silane (1 equiv) and AIBN (1 equiv) (entry 3). The addition of TEMPO improved both reactions, providing **2** in 68% yield in the tin hydride reaction (entry 2) and in 90% yield in the tris(trimethylsilyl)silane reaction (entry 4).

To our surprise, a routine control reaction under argon but in nondegassed benzene in the absence of both AIBN and TEMPO worked beautifully, providing **2** in 87% yield (entry 5). Further, TLC analysis showed the reaction was complete in only 3 h at room temperature. We initially had difficulty reproducing this control experiment, but soon discovered that reliable results were obtained on small scale only when nondegassed benzene was used. On larger scale, it was helpful to actually expose the reaction mixture to air. Attempted reactions under degassed conditions resulted in little or no conversion of **1**. Tributyltin hydride was not

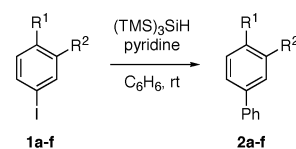
**Table 1.** Yields of Addition of Methyl *p*-iodobenzoate to Benzene



entry	hydride 1.2 equiv	AIBN	TEMPO	temp, time	% <b>1</b> <sup>a</sup>	% <b>2</b> <sup>a</sup>	% <b>3</b> <sup>a</sup>
1	Bu <sub>3</sub> SnH	1 equiv	–	80 °C, 3 h	0	27	9
2	Bu <sub>3</sub> SnH	1 equiv	1 equiv	80 °C, 18 h	8	67	10
3	(TMS) <sub>3</sub> SiH	1 equiv	–	80 °C, 14 h	0	68	6
4	(TMS) <sub>3</sub> SiH	1 equiv	1 equiv	80 °C, 18 h	0	90	0 <sup>b</sup>
5	(TMS) <sub>3</sub> SiH	–	–	rt, 3 h	0	87 <sup>c</sup>	0 <sup>d</sup>

<sup>a</sup>yield determined by GC with octadecane as an internal standard; <sup>b</sup>not detected; <sup>c</sup>isolated yield; <sup>d</sup>not isolated

**Table 2.** Intermolecular Additions of Aryl Iodides to Arenes<sup>a,b</sup>



entry	aryl iodide	R <sup>1</sup>	R <sup>2</sup>	product	% yield <sup>b</sup>
1	<b>1a</b>	CO <sub>2</sub> Me	H	<b>2a</b>	87
2	<b>1b</b>	H	H	<b>2b</b>	75
3	<b>1c</b>	OMe	H	<b>2c</b>	90
4	<b>1d</b>	H	CO <sub>2</sub> Et	<b>2d</b>	82
5	<b>1e</b>	<i>t</i> -Bu	H	<b>2e</b>	90
6	<b>1f</b>	H	OMe	<b>2f</b>	89

<sup>a</sup>rxn conds: **1**, (TMS)<sub>3</sub>SiH (1.2 equiv), and pyridine (5 equiv) were dissolved in benzene (50 mL, 4 mM); <sup>b</sup>isolated yields

an effective substitute for tris(trimethylsilyl)silane in this ambient temperature, air-mediated process. These results showed that neither AIBN, nor TEMPO, nor high temperatures were essential for a high-yielding reaction.

For preparative reactions (Table 2), tris(trimethylsilyl)silane (1.2 equiv) and pyridine (5 equiv, to neutralize HI) were added to a nondegassed benzene solution of the aryl iodide **1a–f** (1 equiv, 0.004 M). The reaction mixture was stirred in an open flask and, if rapid precipitation of pyridine hydroiodide was not observed, then a small amount of iodine (0.02 equiv) was added.

As soon as the aryl iodide was consumed (TLC analysis), the mixture was filtered, the solvent was removed, and the crude product was directly subjected to flash chromatography to provide the target biaryls **2a–f**. Reactions were rapid (15–30 min) and clean and isolated yields of biaryl adducts **2a–f** were uniformly high (75–90%).

Although these conditions are much milder and the yields are higher than typical bimolecular additions of aryl radicals to arenes, standard limitations presumably apply: the arene acceptor must

