

Highly efficient iodine-catalyzed hydroarylation of arenes with styrenes

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Received 25 June 2007; revised 24 July 2007; accepted 26 July 2007

Available online 31 July 2007

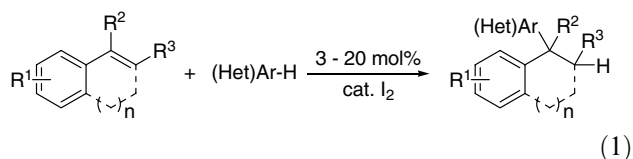
Abstract—Iodine mediates the hydroarylation of styrenes with arenes and heteroarenes to afford 1,1-diarylalkanes in good to high yields. Details regarding the substrate scope and selectivity of this hydroarylation reaction are discussed.

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Arenes and heteroarenes have important functionalization due to their essential role in chemical industry as well as in the pharmaceuticals, agrochemicals, and fine and bulk chemical industries. In general, Friedel–Crafts reaction of aromatic and heteroaromatic compound is one of the fundamental reactions for forming carbon–carbon bond. Recently, there has been considerable interest in developing C–H transformations of arenes and heteroarenes using various transition-metal and acid catalysts.¹ The addition of olefins to acetophenones (Murai reaction)² and aromatic imines,³ the addition of olefins to arenes^{4,5} and heterocyclic compounds,⁶ the addition of aromatics to alkynes⁷ or alcohols,⁸ and the cyclization of arene–alkyne substrates⁹ are elegant examples of this. Such reactions manifest significant drawbacks, for instance, the extreme reaction conditions of high temperature and strong acidic, poor regioselectivity, and a large amount of salt byproducts in essentially. Therefore, the development of new synthetic methods for hydroarylation of alkenes would be significant and the ongoing task is organic synthesis. Recently, several papers have been reported about the Friedel–Crafts hydroarylation of alkenes with electron-rich aromatic and heteroaromatic compounds, which were catalyzed by FeCl₃, Bi(OTf)₃, BiCl₃, and Sm(OTf)₃.¹⁰ In recent years, molecular iodine (I₂) has attracted more attention because of their diverse applicability as catalysts in organic synthesis.¹¹ As part of our continuous interest in employment of iodine as an

alternative, most simple, less expensive, and less toxic reagent,^{11o–u} herein we report a highly efficient Friedel–Crafts hydroarylation of alkenes with arenes or heteroarenes under solvent-free condition.

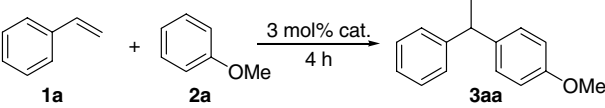
Interest in the direct addition of arenes to styrenes and by the fact that iodine is a highly efficient and mild catalyst for oxidation to aromatic,¹² we decided to inspect the iodine catalyzed hydroarylation of styrene (Eq. 1).



In general, styrene **1a** and anisole **2a** were used as a representative. Initially, endeavors were mainly focused on the efficiency of the iodide catalyzed reaction (entries 1–5 of Table 1). Several reactions were conducted at this stage by using 1 equiv of **1a** and 2 equiv of anisole **2a** under solvent-free conditions. Only a slight conversion of **1a** to **3aa** was observed in the presence of 3 mol% of hydriodic acid, suggesting that the different cation such as Li⁺, Na⁺, K⁺, or Cu⁺ or proton or the anion such as iodide I[−] catalyzed reaction is not favorable for hydroarylation. The parallel of the catalytic activity of the iodine was also observed in iodine monochloride (ICl)-catalyzed reactions. However, inferior results obtained (entries 6 and 7) are probably due to the high reactivity nature of ICl and this property makes ICl to decompose to the hydrogen chloride and hydrogen iodide rapidly in the presence of trace of moisture and also induces the rapid exothermic decomposition

Keywords: Friedel–Crafts reaction; Iodine; Heteroarenes; Hydroarylation; Styrene.

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Table 1. Reaction of anisole **2a** with styrene **1a** in the presence of various iodide catalyst


Entry	Catalyst ^a	Temperature (°C)	Conversion ^b (%)	3aa ^c (%)	Sel. ^d
1	LiI	80	3	—	—
2	NaI	80	2	—	—
3	CuI	80	1	—	—
4	KI	80	2	—	—
5	HI	80	10	4	5.3:1
6	ICl	80	39	20	4.0:1
7	ICl ^e	80	72	51	4.1:1
8	I ₂	80	100	98	5.7:1
9	Br ₂	80	3	—	—

^a Reaction condition: 3 mmol of styrene **1a**, 6 mmol of anisole **2a**, 3 mol % of catalyst, under solvent free condition at 80 °C.

^b GC conversion of styrene.

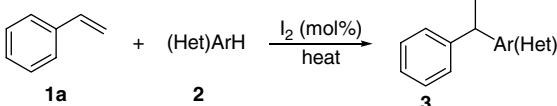
^c GC yields of product **3aa**.

^d 4-/2-substituted isomer were determined by ¹H NMR of the crude reaction.

^e 10 mol % of catalyst.

and the polymerization of styrene to occur in the reaction. The best result was observed when the reaction was carried out in the presence 3 mol % of iodine to quantitatively afford the corresponding product **3aa** after 4 h (entry 8).^{13,14} Finally, no catalytic effect was observed when the molecular bromine was used under the same conditions (entry 9).

The substrate scope of the reaction under the optimized conditions was investigated, and we first explored the extent of the iodine-catalyzed hydroarylation by changing the arene components and all the experimental results were summarized in Table 2. The reaction was amenable to a wide variety of arenes for the hydroarylation. When different arenes and heteroarenes were employed, regioisomeric products resulted from both *para*- and *ortho*-attack of the electrophile. Remarkably, to our great satisfaction, under iodine catalysis, even *ortho*-xylene and thiophene possessing less reactivity reacted smoothly and cleanly in good yield (entries 9 and 10), although slightly higher catalyst loads (20 mol %) or longer reaction times were required. However, electron-rich groups as strong as aniline were ineffective in this Friedel–Crafts hydroarylation.

Table 2. Reaction of styrene with various arenes in the presence of iodine^a


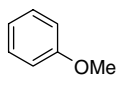
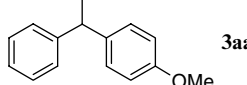
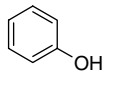
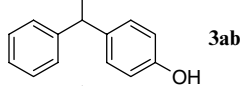
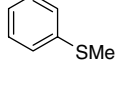
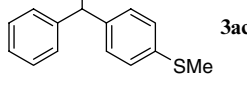
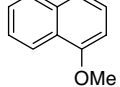
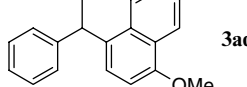
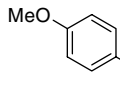
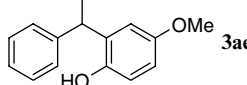
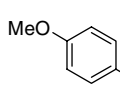
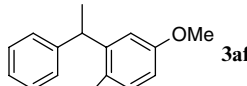
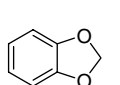
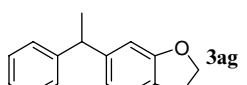
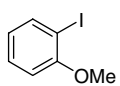
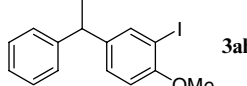

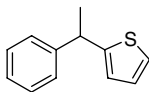

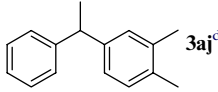
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1		1.5	3	80/3	 3aa	98/5.7:1
2		4	3	80/2	 3ab	94/2.2:1
3		2.5	10	100/12	 3ac^d	63/11.6:1
4		1.5	3	80/4	 3ad	98/99:1
5		2	3	80/4	 3ae	88/2.2:1
6		2	3	80/4	 3af	95/—
7		2	5	80/7	 3ag	75/24:1
8		5	5	80/5	 3ah	70/99:1

Table 2 (continued)

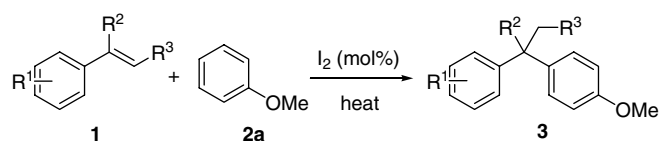
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9		5	5	100/16	 3ai	72/3.5:1
10		6	20	130/2	 3aj^d	58/9.2:1

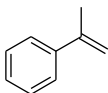
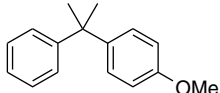
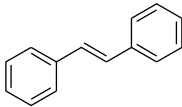
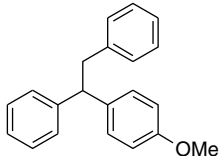
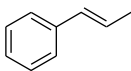
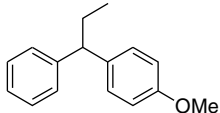
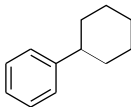
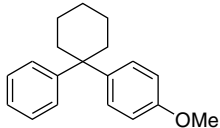
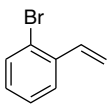
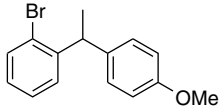
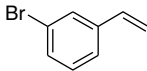
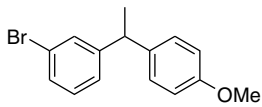
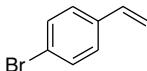
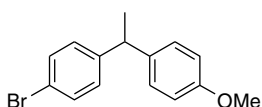
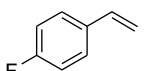
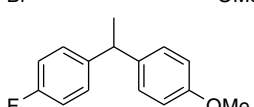
^a Reaction condition: 3 mmol of styrene under solvent free conditions.

^b GC yields.

^c Major and minor isomer were determined by ¹H NMR of the crude reaction.

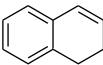
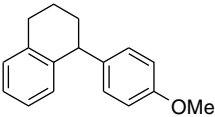
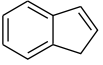
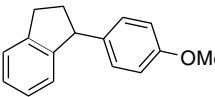
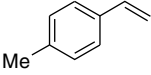
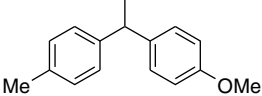
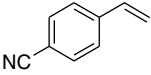
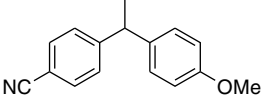
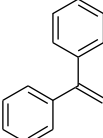
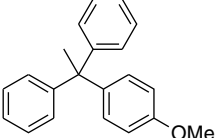
^d The side product is 1,3-diphenylbut-1-ene.

Table 3. Reaction of various styrene derivatives with anisole in the presence of iodine^a

Entry	Vinylarene	I ₂ (mol %)	T (°C)/time (h)	Product 3	Yield ^b (%)/sel. ^c
1 ^d		5	80/4	 3ba	98/99:1
2		5	135/24	 3ca	76/4.0:1
3		5	80/4	 3da	98/8.3:1
4		3	80/4	 3ea	99/99:1
5		5	80/8	 3fa	97/2.0:1
6		5	80/8	 3ga	98/2.5:1
7 ^d		5	80/4	 3ha	98/6.2:1
8		3	80/3	 3ia	98/2.6:1

(continued on next page)

Table 3 (continued)

Entry	Vinylarene	I ₂ (mol %)	T (°C)/time (h)	Product 3	Yield ^b (%) / sel. ^c
9		5	70/3	 3ja	75/4.3:1
10		3	70/2	 3ka	53/6.0:1
11		6	80/4	 3la	62/8.8:1
12		10	120/24	 3ma	94/1.5:1
13		10	120/36	 3na	95/99:1

^a Reaction condition: 2 mmol of styrene, 2 equiv of anisole in the presence of different amount of I₂ under solvent free condition.

^b GC yields.

^c Major and minor isomer were determined by ¹H NMR of the crude reaction.

^d 1.5 equiv of anisole.

We continued to elucidate the scope of the new methodology, this time in terms of differently substituted styrene derivatives in the reaction with anisole. This method demonstrated good compatibility with various functional substituted in phenyl group of styrene, including alkyl groups, cyano, and halides (Table 3). It was found that different halo-substituted styrenes reacted well in the hydroarylation, and the diarylalkane products were obtained in 97–98% yield (entries 5–8). The electron-releasing groups generally increased polymer reaction of these substrates and as such lower yields of the corresponding products were obtained. For example, styrene bearing one methyl group on the benzene nucleus was converted to diarylalkane **3la** in 62% isolated yield in the presence of 6 mol % of iodine (entry 11). However, 4-cyanostyrene containing an electron-withdrawing group was obtained in 94% yield in the presence of 10 mol % of iodine after 24 h (entry 12). Additionally, the α -substituted styrene derivatives could be converted to the corresponding products containing higher *para*-substituted selectivity in 95–99% yields as a greater than 99:1 mixture (entries 1, 4, and 13). The use of indene and dihydronaphthalene as substrates in the reaction can generate aryl-dihydroindene and tetrahydronaphthalene derivatives, which are the important intermediates in the preparation of different products such as agrochemicals and fungicides, and useful compounds such as nafenopin, a peroxisome proliferators.^{10b}

In summary, we have developed a mild and neutral method for hydroarylation of electron-rich arene and styrene substrates with promising efficiency and scope. Iodine demonstrated consistent performance with arene

and styrene substrates of diverse structural features providing good to excellent yields of the diarylalkane products. In contrast, iodine was shown to be cheap and easy to handle in opposition to transition-metal catalyst.

Acknowledgment

Financial support of this work by the National Science Council of the Republic of China and National Taiwan Normal University (96TOP001) is gratefully acknowledged.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.07.178.

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13. *General procedure for the FC-arylation of anisole 2a to styrene 1a in the presence of iodine to generate 1-methoxy-4-(1-phenylethyl)benzene (3aa)*¹⁴ (entry 8 of Table 1 or entry 1 of Table 2): In a typical experiment styrene **1a** (0.23 mL, 2.0 mmol) and anisole **2a** (0.65 mL, 6 mmol) were mixed together in a 7 mL glass bottle including PTFE seal and lid, and then iodine (0.016 g, 3 mol %) was added to the solution and stirred at room temperature under close system for 1 min. This setup was placed in an oil bath at 80 °C temperature. After heating for 3 h, the reaction mixture was cooled to room temperature and then washed with ice cold saturated sodium thiosulfate aqueous solution, the solution was extracted with dichloromethane (25 mL × 3) and then the dichloromethane solution was dried over magnesium sulfate, filtered, and the solvent was evaporated under reduced pressure. The crude products were purified by a flash column chromatography on silica gel with ethyl acetate–hexane (100:0.5, v/v) to afford 90% yield of **3aa** as a colorless oil whose spectral data are consistent with the literature report.¹⁴ ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.11 (m, 7H), 6.82 (d, J = 8.8 Hz, 2H), 4.11 (q, J = 7.2 Hz, 1H), 3.76 (s, 3H), 1.62 (d, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 157.84, 146.75, 138.54, 128.49, 128.31, 127.50, 125.90, 113.72, 55.20, 43.92, 22.03. *m/z* (relative intensity) 212 (M⁺, 90), 197 (100), 182 (30), 165 (45), 153 (42), 135 (10), 128 (7), 115 (6), 103 (8), 91 (10), 77 (13), 65 (5), 51 (6).
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