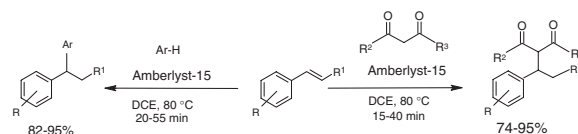


## Simple and Efficient Metal-free Hydroarylation and Hydroalkylation Using Strongly Acidic Ion-exchange Resin<sup>1</sup>

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Highly efficient hydroarylation and hydroalkylation of styrenes with various arenes and 1,3-dicarbonyl compounds respectively have been developed using Amberlyst-15 as a heterogeneous catalyst. The excellent yields, short reaction times, and high selectivity are the advantages of this method. The C–H functionalization has been achieved here under metal-free conditions.



Scheme 1.

Table 1. Hydroarylation of styrenes using Amberlyst-15<sup>a</sup>

Entry	Styrene 1	Arene 2	Product 3	Time /min	Yield /% <sup>b</sup>	Selectivity <sup>c</sup>
a				20	98	92:8
b				40	95	94:6
c				25	93	89:11
d				30	96	91:9
e				20	98	92:8
f				45	83	93:7
g				35	92	88:12
h				50	83	86:14
i				45	90	94:6
j				20	96	88:12
k				15	93	82:18
l				20	95	84:16
m				20	93	91:9
n				55	87	87:13
o				40	93	91:9

continued

The functionalization of aromatic compounds is highly useful for the synthesis of pharmaceuticals and agrochemicals. Classically this conversion is carried out by Friedel–Craft reactions with alkyl or acyl halides using Lewis acids as catalysts. However, the drastic reaction conditions, formation of by-products and low selectivity are drawbacks of these reactions. Recently several transition metals and organometallics have been applied as catalysts for C–H transformation of aromatic compounds.<sup>2</sup> The hydroarylation of styrenes using a metal catalyst or a Lewis acid has also emerged as an important method for this purpose.<sup>3</sup> The resulting diarylalkane motif has been found in various bioactive molecules.<sup>4</sup>

In continuation of our work<sup>5</sup> on the development of useful synthetic methodologies we have observed that hydroarylation of styrenes with aromatic compounds and hydroalkylation with 1,3-dicarbonyl compounds can easily and efficiently be carried out in the presence of Amberlyst-15 as a heterogeneous catalyst (Scheme 1).

Various styrenes were treated with different aromatic compounds following the above method to prepare a series of diarylalkanes (Table 1). The reaction was conducted in DCE at 80 °C. Initially different other solvents such as CH<sub>2</sub>Cl<sub>2</sub>, CHCl<sub>3</sub>, MeCN, and MeNO<sub>2</sub> were employed to carry out this reaction but considering the yields and reaction times DCE was preferred. The products were formed in excellent yields and the conversion was complete within 20–55 min.

The selectivity of the reaction is interesting. In the case of phenols the ortho-substituted products were major while in other cases the para-substituted products were major (Table 1). With 3-methoxyphenols the substitution took place mainly at C-2 position (Entries p and q) while with 3-methylphenol at the C-6 position (Entries k, l, and m).

The ethers were not formed in the present reaction of phenols and styrenes. The lone pairs of oxygen of the phenolic hydroxyl groups are engaged in resonance and so their availability is low to form the ethers (O-addition products).

The present method has successfully been extended to the hydroalkylation of styrenes with 1,3-dicarbonyl compounds. Typically the alkylation of 1,3-dicarbonyl compounds is carried out using stoichiometric amount of base and alkyl halides but the reaction has an overall low atom economy<sup>6</sup> and generates a large amount of salt by-products. Recently the addition of 1,3-dicar-

continued

p			50	85	85:15
q			35	90	89:11
r			30	91	83:17
s			35	87	88:12

<sup>a</sup>The structures of the products were established from the spectral (<sup>1</sup>H and <sup>13</sup>C NMR and MS) and analytical data. <sup>b</sup>Isolated yields after column chromatography. <sup>c</sup>Determined by <sup>1</sup>H NMR spectrum of the crude product and it is ortho-adduct:ortho-adduct for Entries a–d and k–m, and ortho-adduct:para-adduct for Entries e–j and n–s.

Table 2. Hydroalkylation of styrenes using Amberlyst-15<sup>a</sup>

Entry	Styrene 1	1,3-Di-ketone 4	Product 5	Time /min	Yield /% <sup>b</sup>
a				15	95
b				25	92
c				20	89
d				20	85
e				20	93
f				25	95
g				20	85
h				30	88
i				30	86
j				25	93
k				40	80 <sup>c</sup>
l				35	74 <sup>c</sup>

<sup>a</sup>The structures of the products were established from their spectral (<sup>1</sup>H and <sup>13</sup>C NMR and MS) and analytical data. <sup>b</sup>Isolated yield after column chromatography. <sup>c</sup>Two diastereomers were formed in almost equal amount.

bonyl compounds to alkenes catalyzed by transition metals or clay has appeared as an atom economical process.<sup>7</sup>

We have observed that facile hydroalkylation of styrenes with 1,3-dicarbonyl compounds can also easily be accomplished using Amberlyst-15 as a catalyst (Scheme 1).<sup>8</sup> The reaction was conducted in DCE at 80 °C. The alkylation of styrenes took place within 15–40 min to furnish the products in excellent yields (Table 2). Various styrenes and 1,3-dicarbonyl compounds were employed. Both 1,3-diketones and  $\beta$ -ketoesters underwent the conversion smoothly. However, in the case of  $\beta$ -ketoesters two diastereoisomers were formed in each case in almost equal amount (Table 2, Entries k and l). This was evident from the spectral (<sup>1</sup>H and MS) data.<sup>9</sup>

The catalyst Amberlyst-15 is commercially available and inexpensive. It works under heterogeneous conditions.<sup>8</sup> It was recycled for three times with a minimum variation of its activity. Transition metals and organometallics (which have usually been utilized<sup>3,7</sup> in the present conversions) can be avoided by using this catalyst.

In conclusion, we have described a highly convenient and facile practical procedure for hydroarylation and hydroalkylation of styrenes with arenes and 1,3-dicarbonyl compounds respectively in the presence of Amberlyst-15. Operational simplicity, metal-free transformations, excellent yields, high selectivity, rapid conversions, and heterogeneous conditions are the notable advantages of the present method. Thus we developed a highly efficient straightforward procedure for carbon–carbon bond formation. We feel the protocol will find important applications in organic synthesis.

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- General procedure for hydroarylation and hydroalkylation: To a stirred solution of an arene or 1,3-dicarbonyl compound (1 mmol) and styrene (1.1 mmol) Amberlyst-15 (100 mg) was added. The mixture was allowed to reflux at 80 °C and the reaction was monitored by TLC. After completion the mixture was cooled and filtered. The filtrate was concentrated and the residue was subjected to column chromatography (silica gel, hexane–EtOAc) to obtain pure hydroarylated or hydroalkylated styrene. The catalytic efficiency of Amberlyst-15 was tested on the reaction of styrene and 2-naphthol (Table 1, Entry a) following the above method. The yields of **3a** were found to be 98, 96, 95, and 92% in four consecutive uses of the catalyst.
- Supporting Information is available electronically on the CSJ-Journal Web site, <http://www.csj.jp/journals/chem-lett/index.html>.