The direct arylation of benzoquinones with arylboronic acid promoted by iron(II) oxalate

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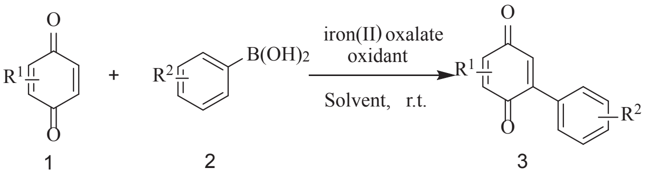
Arylations of various quinones with several arylboronic acids have been developed. The reactions proceed readily at ambient temperature using iron(II) oxalate as a catalyst and potassium persulfate as a co-oxidant. The mechanism is presumed to proceed through a nucleophilic radical addition to the quinone with *in situ* reoxidation of the resulting dihydroquinone.

Keywords: arylation, benzoquinones, arylboronic acid, iron(II) oxalate

The quinone moiety is an important structural feature of compounds involved in chemistry, material science, and medicine.[1] The structures of quinones are embedded in a series of natural products and drugs.[2–4] The visual and electronic properties of the arylated quinones make them useful in photosynthesis and in the dye industry. However, methods of the direct arylation of quinones are sparse.

Among them, some carbon–carbon bond formation reactions between organohalides and organometallic species can be applied to afford the direct arylation of quinones.[5,6] A popular protocol is the transition metal-catalysed coupling reaction *via* C–H activation. Several groups such as those of Molina,[7] Demchuk[8] and Renaud[9] have made notable advances in this research field. The Baran group has made an important contribution using an $AgNO_3/K_2S_2O_8$ system involving a radical pathway.[10–11] However, most protocols of them require rare metals under high temperature conditions. Therefore, the development of a more practical method for the direct arylation of benzoquinones is desirable.

Iron-based catalysts have drawn much attention as cheap, non-toxic and environmentally friendly materials in recent years.[12–14] Many transformations, however, are concerned with complex ligands. Recently, some ligand-free iron salts have[15,16] also been reported to promote the direct arylation of quinones as green catalysts. Here we report the direct arylation of benzoquinones promoted by iron(II) oxalate (Scheme 1), and suggest a radical reaction mechanism.



Scheme 1 The direct arylation of benzoquinones.

Results and discussion

First of all, we selected the reaction of 1,4-benzoquinone and phenylboronic acid as the model reaction to optimise the conditions, as shown in Table 1. The reaction cannot take place without the iron catalyst (Table 1, entry 1). With the catalysts, $Fe_2(SO_4)_3$ and $FeCl_3{\cdot}6H_2O$ containing Fe(III) only trace amounts of products could be obtained (entries 2 and 3). $FeSO_4{\cdot}7H_2O$, $FeCl_2{\cdot}4H_2O$ and $FeC_2O_4{\cdot}2H_2O$, however, afforded the products with moderate or good yields (entries 5–7). If the oxidant loading amounts varied from 3.0 equiv. to 1.0 equiv., the yield decreased gradually (entries 7–9). The solvent system of chlorobenzene/H_2O and α,α,α-trifluorotoluene/H_2O were as effective as DCM/H_2O (entries 7, 10 and 11). If the loading amounts of $FeC_2O_4{\cdot}2H_2O$ varied from 0.5, 1.0 to 2.0 equiv., the corresponding yields were 64%, 77%, 78% (entries 12, 7, 13). When potassium persulfate was replaced by other oxidants such as sodium persulfate and TBHP, the reaction did not proceed at all (entries 14 and 15).

Table 1 The optimisation of reaction conditions for the direct arylation of 1,4-benzoquinones[a]

Entry	Iron salt/equiv.	Oxidant/equiv.	Solvent	Yield/%[b]
1	None	$K_2S_2O_8$ 3.0	DCM / H_2O	ND[d]
2[c]	$Fe_2(SO_4)_3$ (1.0)	$K_2S_2O_8$ (3.0)	DCM / H_2O	5
3[c]	$FeCl_3{\cdot}6H_2O$ 1.0	$K_2S_2O_8$ 3.0	DCM / H_2O	5
4	$Fe(OAc)_2$ 1.0	$K_2S_2O_8$ 3.0	DCM / H_2O	35
5	$FeSO_4{\cdot}7H_2O$ 1.0	$K_2S_2O_8$ 3.0	DCM / H_2O	63
6	$FeCl_2{\cdot}4H_2O$ 1.0	$K_2S_2O_8$ 3.0	DCM / H_2O	53
7	$FeC_2O_4{\cdot}2H_2O$ 1.0	$K_2S_2O_8$ 3.0	DCM / H_2O	77
8	$FeC_2O_4{\cdot}2H_2O$ 1.0	$K_2S_2O_8$ 2.0	DCM / H_2O	65
9	$FeC_2O_4{\cdot}2H_2O$ 1.0	$K_2S_2O_8$ 1.0	DCM / H_2O	57
10	$FeC_2O_4{\cdot}2H_2O$ 1.0	$K_2S_2O_8$ 3.0	PhCl / H_2O	70
11	$FeC_2O_4{\cdot}2H_2O$ 1.0	$K_2S_2O_8$ 3.0	4-CF_3Ph / H_2O	73
12	$FeC_2O_4{\cdot}2H_2O$ 0.5	$K_2S_2O_8$ 3.0	DCM / H_2O	64
13	$FeC_2O_4{\cdot}2H_2O$ 2.0	$K_2S_2O_8$ 3.0	DCM / H_2O	78
14	$FeC_2O_4{\cdot}2H_2O$ 1.0	$Na_2S_2O_8$ 3.0	DCM / H_2O	ND[d]
15	$FeC_2O_4{\cdot}2H_2O$ 1.0	TBHP 3.0	DCM / H_2O	ND[d]

[a] Reaction condition: 1,4-benzoquinone 0.5 mmol; phenylboronic acid 1.5 mmol; 4 mL solvent (1:1, V/V); 25 °C, 24 h.

[b] Isolated yield.

[c] GC yield.

[d] ND, Not detected.

Next, we investigated the scope of the reaction of 1, 4-benzoquionone with various arylboronic acids under the optimised conditions. The results are summarised in Table 2. Most reactions proceeded smoothly to afford the expected products in moderate or good yields except for entry 10. The effects of changing the substituents in the benzenoid ring of the arylboronic acid was quite small (yields 68–82%, entries 1–9). In addition, the arylboronic acid containing a heterocyclic ring also formed the product with a moderate yield (entry 11).

Subsequently, we studied the scope of the reaction of phenylboronic acid with different benzoquinones. The corresponding results were listed in Table 3. As seen the desired products could be obtained in moderate yields using symmetrically substituted benzoquinones containing fluorochloro, trifluoromethyl or methoxyl groups.

Finally, we examined the mechanistic pathway using 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as a radical scavenger. When 2.0 equiv. of TEMPO was added to the model reaction, only a 20.5% yield of product **3a** was obtained. A

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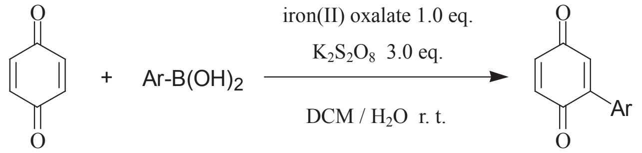
Table 2 The arylation of 1,4-benzoquinone with various arylboronic acids[a]

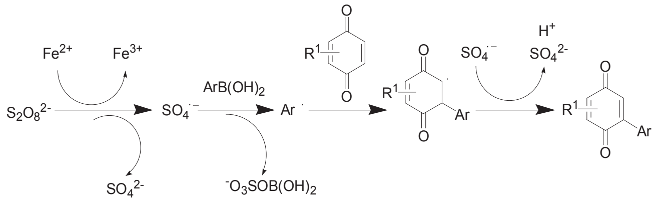


Entry	Ar	Product	M.p./°C		Yield/%[b]
			Observed	Reported	
1	C_6H_5-	**3a**	113–115	113–114[17]	77
2	4-$CH_3C_6H_4$-	**3b**	138–140	138–139[18]	82
3	3-$CH_3C_6H_4$-	**3c**	78–80	76–80[10]	78
4	2--$CH_3C_6H_4$-	**3d**	–	–[10]	72
5	4--$CH_3OC_6H_4$-	**3e**	120–122	120–12[10]	68
6	4-FC_6H_4-	**3f**	157–160	158–160[10]	70
7	4-ClC_6H_4-	**3g**	128–130	129–130[19]	73
8	3-ClC_6H_4-	**3h**	142–144	142–143[19]	74
9	4-$CF_3C_6H_4$-	**3i**	106–108	105–108[10]	68
10	Naphthyl	**3j**	173–175	173–174[20]	40
11	Thienyl	**3k**	–	–[15]	70

[a] 1,4-benzoquinone 0.5 mmol, arylboronic acid 1.5 mmol; iron(II) oxalate 0.5 mmol; potassium persulfate (1.5 mmol); 4 mL solvent of DCM:H_2O (1:1, V/V); 25 °C, 24 h.

[b] Isolated yield.

plausible mechanistic pathway is demonstrated in Scheme 2, which is analogous to the initial reports.[10,16] The single electron transfer of Fe^{2+} to $S_2O_8^{2-}$ could produce sulfate radical, which initiates the transformation with the liberation of SO_4^{2-} and Fe^{3+}. The sulfate radical could react with aryl boronic acids to give an aryl radical species, which could attack benzoquinones to afford the intermediate. Then, the target products could be obtained by overall oxidation and deprotonation of the intermediate.



Scheme 2 Proposed catalytic cycle.

Conclusions

We have described a practical method for the direct mono-arylation of benzoquinones using the cheap and environmentally friendly catalytic system of $FeC_2O_4{\cdot}2H_2O$ and $K_2S_2O_8$. A broad range of substrates have been explored to afford the coupling products. A plausible radical mechanism was also proposed. Studies of other applications of the catalytic system are in progress.

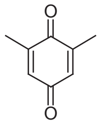
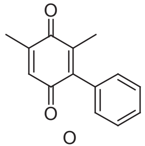
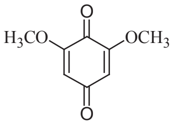
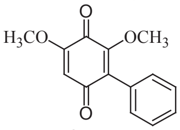
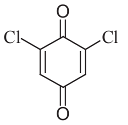
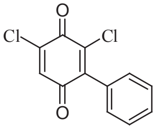
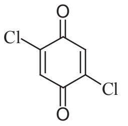
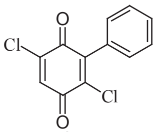
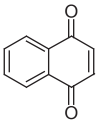
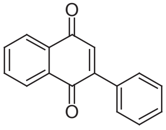
Experimental

All chemicals and solvents were obtained from commercial sources. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Varian NMR spectrometer using TMS as an internal standard; chemical shift values were given in ppm. Mass spectra were obtained on a Sectorfield-MS instrument. All products were known compounds and were identified by comparing their physical and spectroscopic data with those reported in the literature. Flash chromatography separations were performed on a YAMAZEN AI-580 system with silica gel (12 g, 230–400 μm mesh) cartridges.

Arylation of benzoquinones; general procedure

The mixture of 1,4-benzoquionone (0.5 mmol), phenylboronic acid (1.5 mmol), iron salt as a catalyst (0.5 mmol) and persulfate as a oxidant (1.5 mmol) was added to DCM/H_2O (1:1, 4 mL V/V) at room temperature. The resulting mixture was stirred vigorously for

Table 3 The arylation of various 1,4-benzoquinones with phenylboronic acid[a]

Entry	Benzoquinone	Product		M.p./°C		Yield/%[b]
				Observed	Reported	
1			**3l**	94–96	–[c] [15]	66
2			**3m**	108–110	109–110[5]	62
3			**3n**	120–122	–[c] [15]	72
4			**3o**	126–128	127–128[21]	66
5			**3p**	108–110	108–110[22]	50

[a] 1,4-benzoquinone derivatives 0.5 mmol, phenylboronic acid 1.5 mmol; iron(II) oxalate 0.5 mmol; potassium persulfate (1.5 mmol); 4 mL solvent of DCM:H_2O (1:1, V/V); 25 °C, 24 h.

[b] Isolated yield.

[c] M.p.s not reported

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24 h. After the finish of the reaction, the crude product was directly filtered through a pad of celite and washed with DCM (2 mL). The filtrate was washed with a saturated solution of $NaHCO_3$ (3 × 2 mL) and the aqueous layer was extracted again with DCM (3 × 2 mL). The combined organic layer was concentrated under reduced pressure. The corresponding crude product was purified on a flash column using ethyl acetate and hexane as eluate to afford the pure compounds. All the products were characterised by MS, ^{1}H NMR and ^{13}C NMR, and were compared with authentic samples.[5,10,15,17–22] The spectroscopic data of typical compounds are as follows.

2-Phenyl-1,4-benzoquionone (**3a**): Yellow solid, m.p. 113–115 °C (lit.[17] 113–114 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (br 5 H), 6.89–6.83 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.5, 186.6, 145.9, 137.1, 136.3, 132.7, 130.1, 129.2, 128.6; MS (ESI) *m/z*: 184.

2-(4-Chlorophenyl)-1,4-benzoquinone (**3g**): Yellow solid, m.p. 128–130 °C (lit.[19] 129–130 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (brs, 4 H), 6.90–6.83 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.4, 186.4, 144.8, 137.0, 136.6, 136.4, 132.7, 131.0, 130.6, 128.9; MS (EI) *m/z* 218 (for ^{35}Cl).

2,6-Dimethyl-3-phenyl-1,4-benzoquinone (**3l**):[15] Yellow solid, m.p. 94–96 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.39 (m, 3 H), 7.16 (d, J = 2.0 Hz, 1 H), 7.14 (d, J = 1.2 Hz, 1H), 6.66 (d, J = 1.0 Hz, 1 H), 2.11 (d, J = 1.4 Hz, 3 H), 1.97 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.6, 186.8, 145.6, 143.7, 141.6, 133.2, 132.9, 129.5, 128.5, 128.1, 16.0, 14.1; MS (EI) *m/z* 212.

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