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A Novel and Efficient Coupling Reaction of Sodium Tetraphenylborate with Hypervalent Iodonium Salts

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Abstract: The novel coupling reaction of sodium tetraphenylborate with hypervalent iodonium salts was achieved in acidic water, providing an efficient and rapid method for the formation of carbon–carbon bonds in excellent yield.

Key words: coupling reaction, sodium tetraphenylborate, iodonium salt

The Suzuki reaction is one of the most versatile and utilized reactions for the selective construction of carboncarbon bonds, in particular for the formation of biaryls.¹ These coupling reactions are utilized extensively in the synthesis of pharmaceuticals, herbicides, and natural products as well as conducting polymers and liquid crystalline materials because they use nontoxic readily available organoboranes, yield easily removable nontoxic byproducts, and tolerate many functional groups. However, the use of heavy metals as catalysts leads to the generation of waste, which can have a number of problems associated with it, thus the eradication of the catalyst from the Suzuki reaction offers significant advantages. Recently, Leadbeater and Marco reported the first catalyst-free Suzuki coupling reaction under microwave irradiation.² They investigated the coupling of aryl halides with arylboronic acids, which afforded biaryls in excellent yields when aryl bromides were reacted with arylboronic acids in water under microwave heating at 150 °C for five minutes. However, due to the development of pressure and the need for specialized sealed vessels this method is not suitable for organic reactions carried out at atmospheric pressure and it is also difficult to apply on an industrial scale. In order to extend the scope of the catalyst-free Suzuki reaction the development of mild, efficient, and environmentally more benign metal-catalyst-free conditions are required.

During the past few years the chemistry of hypervalent iodine compounds has experienced an unprecedented growth.³ As powerful electrophilic reagents, hypervalent iodine compounds, in particular, hypervalent iodonium salts have found synthetic application due to their high reactivity toward various nucleophiles, their ready availability, and their nontoxic properties. They have been widely used in the Suzuki reaction to replace aryl halides or triflates affording products in excellent yield under mild reaction conditions.⁴ As part of a program to investigate the catalyst-free Suzuki reaction, we explored the coupling reaction of sodium tetraphenylborate with iodonium salts in acidic water. In this paper, we would like to report a novel and efficient coupling reaction of sodium tetraphenylborate with iodonium salts in acidic water. This method was successfully applied to the synthesis of biaryls, and to the best of our knowledge, the metal-catalyst-free Suzuki-type coupling reaction of sodium tetraphenylborate with iodonium salts in acidic water has not been reported.

Initially, we investigated the catalyst-free coupling reaction of phenylboronic acid with diphenyliodonium chloride in water by traditional heating methods. We found that the coupling was difficult to effect and the desired biphenyl was not obtained either in the presence or absence of a base (Na₂CO₃), even prolonged heating of the reaction mixture was unsuccessful. We then used a stronger nucleophilic reagent - sodium tetraphenylborate - in place of phenylboronic acid, however, the same result was obtained. Next, we explored the coupling reaction in acidic conditions. It was found that diphenyliodonium chloride decomposed quickly when p-TsOH was added to a mixture of phenylboronic acid and diphenyliodonium chloride. Fortunately, when sodium tetraphenylborate was used in place of phenylboronic acid, the product biphenyl was obtained, in good yield, when the mixture was stirred for 30 minutes at 50 °C. Prompted by this exciting result a series of experiments were performed on the coupling of sodium tetraphenylborate with diphenyliodonium chloride in the presence of *p*-TsOH in order to determine suitable reaction conditions. The reaction of four equivalents of sodium tetraphenylborate, two equivalents of p-TsOH, and one equivalent of diphenyliodonium chloride in water at 50 °C for 30 minutes afforded biphenyl in 95% yield. Then we extended this protocol to other iodonium salts, both symmetrical and unsymmetrical biaryls were readily synthesized in high yields under the optimum conditions (Scheme 1, Table 1).

With the exception of iodonium salt **2c** (Table 1, entry 3), all iodonium salts afforded the desired products in excellent yields. Electron-poor iodonium salt **2f** gave a slightly

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SHORT PAPER

Table 1 Coupling Reaction of Sodium Tetraphenylborate with Iodonium Salts^a

Entry	Iodonium salt	Product	Time (h)	Yield (%) ^b
1	$Ph_2I^+CI^-$ 2a	PhPh 3a	0.5	95
2	(<i>p</i> -MeC ₆ H ₄) ₂ I ⁺ Br ⁻ 2b	p-MeC ₆ H ₄ Ph 3b	0.5	92
3	$(p-\mathrm{BrC}_{6}\mathrm{H}_{4})_{2}\mathrm{I}^{+}\mathrm{Br}^{-}$ 2c	p-BrC ₆ H ₄ Ph 3 c	1	61
4	$p\text{-MeC}_6\text{H}_4\text{I}^+\text{PhBr}^-$ 2d	3b	1	94
5	<i>p</i> -MeOC ₆ H ₄ I⁺PhBr [_] 2e	p-MeOC ₆ H ₄ Ph 3d	1	92
6	$(m-\mathrm{NO}_2\mathrm{C}_6\mathrm{H}_4)_2\mathrm{I}^+\mathrm{Br}^-$ 2f	m-NO ₂ C ₆ H ₄ Ph 3e	1	80
7	Short I+—PhOTs−	S Ph	2	81
	2g	3f		
8	$(p-\mathrm{MeC}_{6}\mathrm{H}_{4})_{2}\mathrm{I}^{+}\mathrm{BF}_{4}^{-}$ 2h	3b	1	78°
9	$(p-MeOC_6H_4)_2 I^+BF_4^-$ 2i	3d	2	72°

^a Reaction conditions: Ph₄BNa (4 equiv), iodonium salt (1 equiv), *p*-TsOH (2 equiv), and H₂O (5 mL).

^b Isolated yields.

^c The amount of *p*-TsOH used was increased to 6 equivalents.

$$\begin{array}{rrrr} \mathsf{Ph_4BNa} & + & \mathsf{Ar_1l^+Ar_2X^-} & \xrightarrow{\rho\mathsf{-}\mathsf{TsOH}} & \mathsf{Ph}\mathsf{-}\mathsf{Ar} \\ \mathbf{1} & \mathbf{2} & & \mathbf{3} \end{array}$$

Scheme 1

lower yield than electron-rich phenyl iodonium salts 2b, 2d, and 2e. We also observed that the anions of iodonium salts affected the yield greatly: with 2b the reaction was complete after only 30 minutes affording **3b** in 92% yield; when 2h was used in place of 2b under the same reaction conditions, even after a prolonged reaction time of 28 hours, 3b was obtained in a poor 29% yield. To try to improve the yield, we increased the amount of acid to six equivalents and found that the coupling reaction was complete after one hour, giving the desired product in a muchimproved 78% yield. Similarly, 2i was reacted under these modified reaction conditions giving the desired product in 72% yield, compared to a yield of 20% after a reaction time of 35 hours under the standard conditions. The prolonged reaction time for tosylate iodonium salt 2g and the somewhat reduced yield, compared to 2a, can be attributed to the influence of the anion (Table 1, entry 7).

We also used HCl in place of *p*-TsOH to examine the effect on the reaction. The reactions occurred easily in a shorter time, however, lower isolated yields were obtained in dilute aqueous HCl (0.1 N; Table 2).

To date, iodonium salts had been reacted with a series of nucleophiles to form carbon–carbon bonds, generally in basic conditions,⁵ while our new coupling reaction em-

 Table 2
 Coupling Reaction in Aqueous HCl^a

Iodonium salt	Product	Time (min)	Yield (%)
2a	3 a	15	92
2e	3d	15	92
2h	3b	50	65
	Iodonium salt 2a 2e 2h	Iodonium saltProduct2a3a2e3d2h3b	Iodonium saltProductTime (min)2a3a152e3d152h3b50

^a Concentration of HCl was 0.1 N.

ploys acidic conditions. The mechanism is thought to involve an anion exchange of the iodonium salt with Ph_4B^- , promoted by the formation of HX, while an intramolecular coupling reaction follows to furnish the product.

In summary, a novel and efficient method for the formation of carbon–carbon bonds in acidic water has been reported. This method has advantages over other procedures in that it is simple, mild, high-yielding, and more environmentally benign. Furthermore, the scope of the metal-catalyst-free Suzuki-type coupling reaction could be extended to other substrates.

Mps were determined on a digital mp apparatus and were not corrected. IR spectra were recorded on a FT-170 SX instrument, ¹H NMR spectra were measured on a Bruker AM-400 FT-NMR spectrometer, and mass spectra were determined on HP5989A mass spectrometer. Iodonium salts were prepared according to literature procedures.⁶⁻⁸ Sodium tetraphenylborate is commercially available.

Reaction of Sodium Tetraphenylborate with Iodonium Salts; General Procedure

 Ph_4BNa (1; 137 mg, 0.4 mmol, 4 equiv), iodonium salt (2; 0.1 mmol, 1 equiv), and *p*-TsOH (38 mg, 0.2 mmol, 2 equiv) in H_2O (5 mL) were stirred at 50 °C until the reaction was complete (Table 1). After cooling to r.t., the mixture was extracted with Et_2O (3 × 20 mL), the organic layer was dried over anhyd MgSO₄, and the solvent was evaporated in vacuo. The crude product was purified by preparative thin-layer chromatography (silica gel, hexane) to afford pure products **3** in good yields.

Biphenyl (3a)

Mp 68–69 °C (Lit.⁹ 69–72 °C).

IR (KBr): 3035, 1569, 1481, 730 cm⁻¹.

¹H NMR (CDCl₃): δ = 7.32–7.36 (m, 2 H), 7.42–7.46 (m, 4 H), 7.58–7.61 (m, 4 H).

MS (70 eV, EI): m/z (%) = 154 (M⁺, 100).

p-Methylbiphenyl (3b)

Mp 43-46 °C (Lit.¹⁰ 44-47°C).

IR (KBr): 3067, 3033, 1488, 1007, 823, 766, 690 cm⁻¹.

 ^1H NMR (CDCl_3): δ = 2.39 (s, 3 H), 7.23–7.26 (m, 2 H), 7.30–7.34 (m, 1 H), 7.40–7.44 (m, 2 H), 7.48–7.51 (m, 2 H), 7.56–7.59 (m, 2 H).

MS (70 eV, EI): m/z (%) = 168 (M⁺, 100).

p-Bromobiphenyl (3c)

Mp 83–85 °C (Lit.¹¹ 85–87 °C).

IR (KBr): 3064, 3031, 1477, 1393, 1080, 830, 767, 691 cm⁻¹.

¹H NMR (CDCl₃): δ = 7.33–7.37 (m, 1 H), 7.42–7.46 (m, 4 H), 7.52–7.57 (m, 4 H).

MS (75 eV, EI): m/z (%) = 234 (M + 1), 233 (M⁺, 13.3), 232 (100).

p-Methoxybiphenyl (3d)

Mp 86–87 °C (Lit.¹² 88 °C).

IR (KBr): 3068, 3033, 1262, 1035, 835, 761 cm⁻¹.

¹H NMR (CDCl₃): δ = 3.83 (s, 3 H), 6.96–6.98 (m, 2 H), 7.27–7.31 (m, 1 H), 7.38–7.42 (m, 2 H), 7.51–7.55 (m, 4 H).

MS (70 eV, EI): m/z (%) = 184 (M⁺, 100).

m-Nitrobiphenyl (3e)

Mp 56-58 °C (Lit.13 58-60 °C).

IR (KBr): 3064, 3036, 1536, 1362, 877, 772, 733 cm⁻¹.

¹H NMR (CDCl₃): δ = 7.40–7.67 (m, 6 H), 7.83–7.95 (m, 1 H), 8.11–8.23 (m, 1 H), 8.40–8.45 (m, 1 H).

MS (75 eV, EI): m/z (%) = 199 (M⁺, 100).

2-Phenylthiophene (3f)

Oil.4a

IR (KBr): 3103, 3062, 3036, 1496, 1451, 747 cm⁻¹.

¹H NMR (CDCl₃): δ = 7.10–7.13 (m, 1 H), 7.30–7.34 (m, 2 H), 7.37–7.40 (m, 1 H), 7.46–7.49 (m, 2 H), 7.62–7.66 (m, 2 H). MS (70 eV, EI): *m*/*z* (%) = 160 (M⁺, 100).

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