

Hypervalent iodine in synthesis 79: reductive homocoupling of diaryliodonium salts in the presence of palladium catalyst and indium[†]

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In the presence of palladium catalyst and indium diaryliodonium salts can undergo reductive homocoupling under mild reaction conditions to give biaryls in excellent yields.

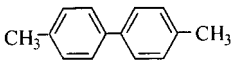
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Biaryls are structural features of a variety of biologically active natural products¹ and show specific properties as materials to form semiconducting charge transfer complexes² and optically active ligands.³ So the synthesis of biaryls is of considerable interest.⁴ The classical method for the synthesis of biaryls involves Ullmann reaction⁵ which produces biaryls by the copper-catalysed reductive coupling of aryl halides. One of the major disadvantages of the reaction is the requirement of a high reaction temperature. There are, however, several modifications of this reaction involving palladium^{4(d)} and other copper derived compounds.^{4(b)} Also, the direct synthesis of biaryls from aryl halides can be achieved by transition metal catalysis in the presence of a reductant, such as zinc,⁶ and hydroquinone.⁷ Recent developments in hypervalent iodine chemistry have shown that diaryliodonium salts are good substitutes for aryl halides in most cases due to their high reactivity which leads to improvements in many reactions.⁸ Tamura *et al.* reported that diaryliodonium salts react with methylmagnesium iodide in the presence of nickel chloride to give biaryls.⁹ Yamazaki *et al.*¹⁰ reported the reductive coupling of diaryliodonium halides catalysed by palladium and zinc.¹⁰ Kang *et al.*¹¹ reported the reductive coupling of hypervalent iodonium salts catalysed by palladium-diethylzinc.¹¹

In recent times, there has been increasing interest in indium-mediated transformations because of certain unique properties possessed by indium.¹² Because of the close resemblance of

indium with zinc, indium could be a potential reductive coupling agent. This prompted us to investigate indium-prompted reductive coupling of diaryliodonium salts in the presence of a palladium catalyst. Here we report a convenient and efficient synthesis of biaryls by the reductive coupling of diaryliodonium salts in the presence of palladium catalyst and indium (Scheme 1). We found that in the presence of palladium catalyst and indium the reductive coupling of diaryliodonium salts takes place smoothly in DMF at room temperature. In order to determine the optimum conditions for this reaction, we examined the effects of several factors on the reductive coupling of bis(4-methylphenyl)iodonium tetrafluoroborate (Table 1). We found that solvent and palladium catalyst have obvious effects on the reaction. Among the selected solvents including DMF, DME, THF and dioxane, DMF is the best choice. Among the three tested palladium catalyst, Pd(OAc)₂ is the most effective. Pd(PPh₃)₄ cannot catalyse this reaction effectively. The reaction catalysed by PdCl₂(PPh₃)₂ proceeds excellently at 40°C though it proceeds slowly at room temperature. In the absence of palladium catalyst, the reductive coupling of bis(4-methylphenyl)iodonium tetrafluoroborate takes place slowly at room temperature and gives 4, 4'-dimethylbiphenyl in 55% yield after 16h. We also briefly examined the effect of the amount of indium on the reaction and found that the reaction did not occur at all without the aid of indium and 0.5 mg-atom indium could make the reaction proceed completely.

Table 1 Effects of several factors on the reductive homocoupling of diaryliodonium salts^a

Entry	Solvent	Catalyst ^b	In (mg-atom)	Product	Yield (%) ^c
1	DMF	Pd(OAc) ₂	1		99
2	Dioxane	Pd(OAc) ₂	1	2a	55
3	THF	Pd(OAc) ₂	1	2a	82
4	DME	Pd(OAc) ₂	1	2a	66
5	DMF	Pd(PPh ₃) ₄	1	2a	33
6 ^d	DMF	PdCl ₂ (PPh ₃) ₂	1	2a	99
7 ^e	DMF	No catalyst	1	2a	55
8 ^e	DMF	Pd(OAc) ₂	0	2a	0
9	DMF	Pd(OAc) ₂	0.15	2a	28
10	DMF	Pd(OAc) ₂	0.5	2a	99

^aThe reaction was carried out at room temperature for 1h. ^b5mol% catalyst was added. ^cIsolated yield. ^dThis reaction was carried out at 40°C for 4h. ^eThis reaction was carried out at room temperature for 16h.

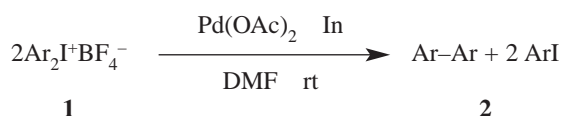
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[†] This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

Table 2 Reductive homocoupling of diaryliodonium salts^a

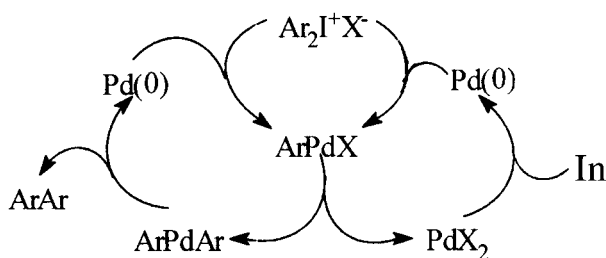
Entry	Diaryliodonium salt	Product	m.p.(°C) (lit.)	Yield (%) ^b
1	(p-Tol)2I+BF4 ⁻ 1a	2a	118–120 (119) ¹³	99
2	Ph2I+BF4 ⁻ 1b	2b	67–69 (70–71) ⁹	9
3	(p-ClC6H4)2I+BF4 ⁻ 1c	2c	148–150 (147–148) ¹⁴	94
4	(p-CH3OC6H4)2I+BF4 ⁻ 1d	2d	173–175 (176–177) ⁹	89
5	(m-NO2C6H4)2I+BF4 ⁻ 1e	2e	198–200 (202–202.5) ¹⁵	82
6	(p-BrC6H4)2I+BF4 ⁻ 1f	2f	163–165 (165–166) ⁹	90
7c	1g	2g	109–111 (112) ¹⁶	63

^aThe reaction was carried out in DMF at room temperature for 1h in the presence of 5mol% Pd(OAc)₂ and 0.5 mg-atom indium
^bIsolated yield. ^cThis reaction was carried out at 40°C for 3h

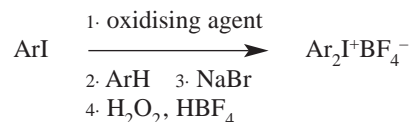
**Scheme 1**

Several diaryliodonium salts with various substituents including chloro, methoxy, nitro and bromo were tested. It was found that all of them can undergo the reductive coupling excellently in the presence of Pd(OAc)₂ and indium at room temperature. When diphenyliodonium-2-carboxylate **1g** (DPIC) was used in the reaction, we found interestingly that biphenyl-2-carboxylic acid was obtained as major product and biphenyl was obtained in 13% yield, but 2, 2'-biphenyldicarboxylic acid was not obtained. The results are summarised in Table 2. All the products gave satisfactory m.p. and ¹H NMR data consistent with literature data.

A plausible mechanism for the reductive coupling of diaryliodonium salts in the presence of palladium catalyst and indium is analogous to that of aryl iodide in the presence of palladium catalyst and zinc^{6(a)} and is shown in Scheme 2.

**Scheme 2**

As shown in Scheme 1, iodoarene was the another product in the reaction. However, it was easily converted to diaryliodonium salt in efficient yield as follows.¹⁷



In conclusion, the reductive coupling reaction of diaryliodonium salts can complete rapidly in the presence of Pd(OAc)₂ and indium at room temperature to give biaryls in excellent yields. With the advantage of simple operation, high yield and mild reaction conditions, it offers a convenient and efficient method for the preparation of biaryls. Furthermore, it has extended the range of useful application of indium-mediated transformations in organic synthesis.

Experimental

Melting points were uncorrected. ¹H NMR data were recorded on Avance 400 spectrometer using CDCl₃ as the solvent with TMS as an internal standard. IR spectra were determined on Vector 22 infrared spectrometer with KBr pallet.

Typical procedure for the preparation of biaryls: A mixture of bis(4-methylphenyl)iodonium tetrafluoroborate **1a** (395 mg, 1 mmol), indium (0.5 mg-atom, cut into small slices), Pd(OAc)₂ (5 mol%) and DMF (5 ml) was stirred under a nitrogen atmosphere at room temperature for 1h. The reaction mixture was diluted with 1M HCl (20 ml), and extracted with diethyl ether (3 × 15 ml). The combined organic layer was washed with brine, dried over anhydrous sodium sulfate. After removal of the solvent under vacuum, the residue was chromatographed on silica gel plate using *n*-hexane as a developer to give pure 4, 4'-dimethylbiphenyl **2a** 90 mg, yield 99%, m.p. 118–120°C, ¹H NMR δ_H 2.39 (s, 6H), 7.23 (d, 4H), 7.47 (d, 4H). IR ν_{max}/cm⁻¹ (KBr) 3040, 2942, 2881, 1610, 1488, 1451, 1398, 819, 799, 750, 691.

2b–2f were prepared by the same procedure, using *n*-hexane for **2b**, **2c** and **2e**, *n*-hexane/ethyl acetate (6:1) for **2d** and **2f** and *c*-hexane/ethyl acetate (1:1) for **2g** as a developer.

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