

A Convenient Approach to 2-Arylindenes via Suzuki Coupling Reaction of 2-Indenylboronate with Aryl Bromides

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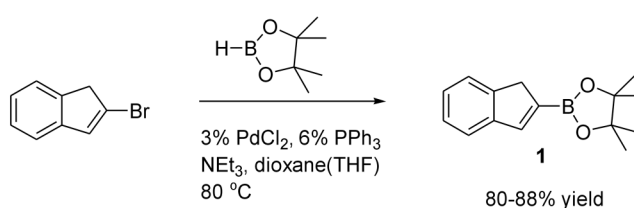
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Indenyl derivatives have been extensively employed in organometallic chemistry as ligands.¹ Group 4 metallocene catalysts containing such ligands have shown activities in olefin polymerization² as well as in various organic reactions of small molecules.³ Recently, unbridged bis(2-aryindenyl)-zirconium dichlorides were reported to produce elastomeric polypropylene with a stereoblock microstructure when activated by MAO (methylaluminoxane).⁴ Waymouth and coworkers investigated several zirconocene catalysts containing a different aryl substituent in the 2-position of the indenyl ligand for their polymerization behavior, and reported that the bis(2-aryindenyl) framework was important for the production of elastomeric polypropylene.⁵

Although the importance of 2-arylindenes as ligands for olefin polymerization catalysts is increasing, only a couple of synthetic methods to 2-arylindenes have been reported.^{4,5b} These reported procedures, however, have a serious limitation, as strongly basic reagents are required. The reaction of an organolithium reagent or arylmagnesium bromide with 2-indanone is troublesome due to the susceptibility of 2-indanone to enolization.⁶ This method is particularly ineffective for most organolithium nucleophiles as well as sterically demanding nucleophiles. The reaction utilizing 1,2-di(magnesiomethyl)benzene dichloride⁷ and the corresponding methyl ester of the substituent moiety was reported.^{5b} In this method, the starting methyl esters, if not commercially available, needed to be prepared separately and use of the di-Grignard reagent limited the functional group compatibility of this procedure. Therefore, a more convenient and general way to make a variety of 2-arylindenes is necessary.

We now report a synthetic route to a family of 2-arylindenes via Suzuki coupling reaction⁸ of 2-indenylboronate with various aryl bromides. To develop an efficient protocol, we initially focused on the preparation of an indenyl boron derivative as the coupling component. Since various aryl halides are commercially available, this approach seems more attractive than the coupling between bromoindene⁹ and arylboronic acids. We found that Masuda's borylation procedure¹⁰ could be employed to prepare the indenylboron derivative. The original reaction conditions^{10c} was modified by changing the catalyst from PdCl₂(dppf)/AsPh₃ to PdCl₂/PPh₃ and applied to bromoindene. The desired indenylboronate **1** was obtained in 80-88% yield in either THF or dioxane at 80 °C (Scheme 1).¹¹ In this reaction, using an



Scheme 1. Synthesis of 2-indenylboronate.

excess of toxic AsPh₃ ligand with regard to the precatalyst was not necessary, and carrying out the coupling with a mixture of PdCl₂ and PPh₃ was enough to give the desired product in high yield.

Next, reaction conditions for the Suzuki coupling reaction of indenylboronate **1** and bromobenzene were optimized¹² by using Pd(OAc)₂ as the precatalyst and K₃PO₄ as the base¹³ (Table 1). THF or dioxane was more effective than toluene as a solvent, and PPh₃ was a better ligand than the other bidentate ligands that were screened. The coupling product, 2-phenylindene was isolated in 92% yield under the optimized conditions.


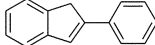
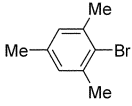
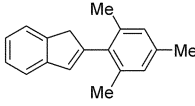
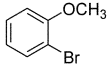
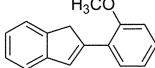

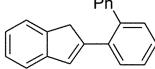
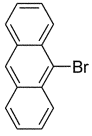
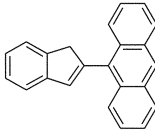

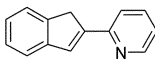
Other aryl halides were tested in the coupling reaction and the results are shown in Table 2.¹⁴ Sterically hindered aryl halides with ortho substituents were effectively coupled to afford the corresponding 2-aryl substituted indenes in good yields (Table 2, entries 2-4). Ortho substituents such as methyl, phenyl, and methoxy groups were accommodated. It

Table 1. Optimization of Suzuki coupling of 2-indenylboronate and bromobenzene

Entry	Ligand	Solvent	Yield (%) ^a
1	PPh ₃	THF	92
2	PPh ₃	dioxane	85
3	PPh ₃	THF	65 ^b
4	PPh ₃	toluene	48
5	DPPB ^c	THF	71
6	DPPB	toluene	50
7	BINAP ^d	toluene	55

^aIsolated yield, >95% pure by ¹H NMR. ^bK₃PO₄·H₂O was used instead of K₃PO₄. ^cDPPB=1,4-bis(diphenylphosphino)butane. ^dBINAP=2,2'-bis(di-*p*-tolylphosphino)-1,1'-binaphthyl.

Table 2. Suzuki coupling of aryl bromides^a

1 + Ar-Br		5% Pd(OAc) ₂ , 10% PPh ₃ 3 equiv K ₃ PO ₄ , THF, 80 °C		
Entry	Aryl bromide	Product	Time (h)	Yield (%) ^b
1			20	92
2			30	84
3			25	78
4			24	89
5			24	87
6			24	60

^aReaction conditions: 1.0 equiv aryl bromide, 1.1 equiv 2-indenylboronate, 3.0 equiv K₃PO₄, 5% Pd(OAc)₂, 10% PPh₃, THF (0.3 mmol aryl bromide/1 mL); reaction times have not been minimized. ^bIsolated Yields.

is notable that 9-bromoanthracene was reacted to form the corresponding product in good yield (Table 2, entry 5, 87%). The reaction conditions were also effective for the coupling of 2-bromopyridine (Table 2, entry 6).

In summary, this method provides a versatile way to prepare a variety of 2-arylidenes in good to high yield. The mild reaction conditions which do not require the use of strong bases both in the preparation of 2-indenylboronate and in the Suzuki coupling reaction potentially allow a broad range of functional group variation in the coupled products. Work to extend the scope of this reaction is in progress.

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- Synthesis of 2-Indenylboronate:** PdCl₂ (33.4 mg, 0.19 mmol), PPh₃ (98.6 mg, 0.38 mmol) and bromoindene (1.22 g, 6.27 mmol) were placed in an oven-dried Schlenk flask and dioxane (25 mL) was added. Triethylamine (2.62 mL, 18.8 mmol) and 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (1.36 mL, 9.40 mmol) were added successively by syringe at room temperature under nitrogen. The reaction flask was stirred at 80 °C for 5.5 h. The reaction mixture was cooled to room temperature and quenched with water, and saturated brine (5 mL) was added. The organic layer was separated and the aqueous layer was extracted with ethyl ether (2 × 20 mL). The combined organic layers were washed with brine, dried over MgSO₄ and concentrated. The residue was purified by Kugelrohr distillation to give 2-indenylboronate as a white solid (mp 73–74 °C) in 80% yield. The product can be stored and handled in air. ¹H NMR (300 MHz, CDCl₃) δ 7.58 (s, 1H), 7.50 (d, *J* = 7 Hz, 1H), 7.46 (d, *J* = 7 Hz, 1H), 7.30–7.21 (m, 2H), 3.54 (s, 2H), 1.33 (s, 12H); ¹³C NMR (75 MHz, CDCl₃) δ 147.0, 145.7, 145.0, 126.3, 126.0, 124.0, 122.0, 83.6, 41.7, 25.1.
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- General procedure for Suzuki coupling of 2-indenylboronate and aryl bromides:** An oven-dried resealable Schlenk tube was charged with Pd(OAc)₂ (3.4 mg, 0.015 mmol), PPh₃ (7.9 mg, 0.030 mmol), 2-indenylboronate (79.9 mg, 0.33 mmol) and K₃PO₄ (191 mg, 0.90 mmol). The Schlenk tube was evacuated and backfilled with nitrogen, and THF (1 mL) and the aryl bromide (0.30 mmol) were added through a rubber septum (aryl bromides which were solids at room temperature were added prior to the evacuation/backfill cycle). The reaction Schlenk tube was sealed and was heated to 80 °C for the indicated amount of time. The reaction mixture was cooled to room temperature and filtered through a plug of SiO₂. The filtrate was concentrated and the resulting residue was purified by flash chromatography to afford the desired product.