

A Suzuki Coupling Based Route to 2,2'-Bis(2-indenyl)biphenyl Derivatives

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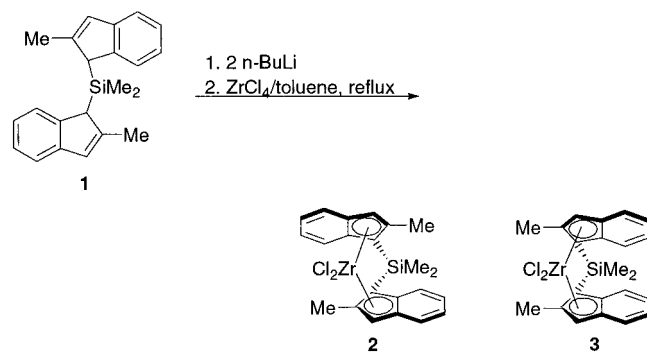
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Because of the promising performance in olefin polymerization of 2,2'-bis(2-indenyldiyl)biphenyl zirconium dichloride, we developed a new and broadly applicable route to 2,2'-bis(2-indenyl)biphenyl derivatives. Reaction of the known 2,2'-diiodobiphenyl (**26**) with the new 2-indenyl boronic acid (**23**) did not result in the desired 2,2'-bis(2-indenyl)biphenyl (**10**); instead an isomer thereof, (spiro-1,1-(2,2'-biphenyl)-2-(2-indenyl)indane) (**27**), was obtained. It was found that compound **10** could be made via a palladium-catalyzed reaction of 2,2-biphenyldiboronic acid (**31**) with 2-bromoindene (**21**) under standard Suzuki reaction conditions. However, the yield of this reaction was low at low palladium catalyst loadings, due to a competitive hydrolysis reaction of 2,2-biphenyldiboronic acid (**31**). HTE techniques were used to find an economically viable protocol. Thus, use of the commercially available 1.0 molar solution of (*n*-Bu)₄NOH in methanol with cosolvent toluene led to precipitation of the pure product in a fast and clean reaction, using only 0.7 mol % (0.35 mol % per C–C) of the expensive palladium catalyst.

Introduction

For the isotactic polymerization of propylene, an isospecific catalyst is required. Many examples have been reported in the literature, e.g., the *ansa* bis(1-indenyl)-dimethylsilane (**1**) derivatives of Hoechst and BASF¹ and the *ansa* bis-cyclopentadienyl compounds of Chisso.² The main disadvantage of most of these systems is that two isomers (*rac* (**2**) and *meso* (**3**)) are formed in the synthesis



of these organometallic complexes, often in a ratio of near 1:1 depending on the solvent used in the synthesis (eq 1).

Only the *rac*-isomer (**2**) is isospecific and catalyzes formation of isotactic polypropylene. The *meso*-isomer (**3**) is nonspecific and produces atactic polypropylene (a-PP). To avoid the presence of undesired, sticky a-PP, a separation of the *rac*/*meso* mixture is often necessary. These separations are usually not straightforward and

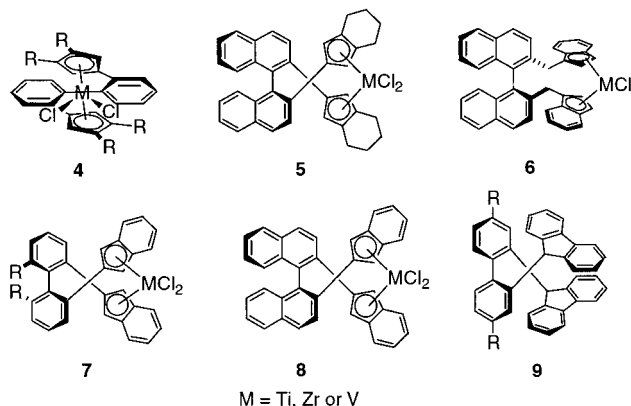


Figure 1. Published examples of biaryl-bridged metallocenes: **4**,⁴ **5**,⁵ **6**,⁶ **7**,⁷ **8**,⁷ **9** (R = H, *tert*-Bu).⁸

often rely on difficult crystallizations to obtain pure *rac*-isomer. The unwanted *meso*-isomer is often discarded at the end of a long route.

The synthesis of an isospecific metallocene is more efficient if the *rac*/*meso* separation can be avoided by smart design of the ligand-system. An example is the family of *ansa*-fluorenyl-cyclopentadienyl complexes described by Ewen et al.³ Another example is the use of biaryl bridged ligands and/or complexes (Figure 1). The spatial arrangement of the biaryl-bridge prohibits formation of the *meso*-form.

To avoid the introduction of additional isomers, the Cp or indenyl moiety needs to have C_{2v} symmetry. This C_{2v}

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(1) Spaleck, W.; Kueber, F.; Winter, A.; Rohrmann, J.; Bachmann, B.; Antberg, M.; Dolle, V.; Paulus, E. F. *Organometallics* **1994**, 13, 954.

(2) (a) Yoshimura, T.; Mise, T.; Miya, S.; Yamazaki, H.; EP 0316155 A2, Chisso Corp. (b) Mise, T.; Miya, S.; Yamazaki, H. *Chem. Lett.* **1989**, 1853.

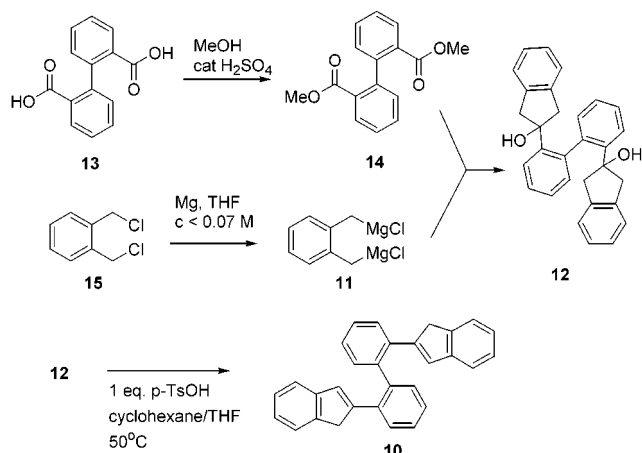
(3) Ewen J. A. *J. Mol. Catal. A: Chem.* **1998**, 128, 103 and references therein.

symmetry is present in the 2-indenyl moieties that were developed by us,⁹ and later by Waymouth,¹⁰ Halterman,¹¹ and Montell,¹² as ligands for homogeneous Ziegler–Natta (Z–N) polymerization. To the best of our knowledge, biaryl-bridged 2-indenyl-based compounds were reported in only one publication by Bosnich et al. (**7** and **8**).⁷ However, the application of these biaryl-bridged 2-indenyl catalysts in olefin polymerization has not been described. Bosnich et al. studied these complexes as catalysts for enantioselective Diels–Alder reactions.

Results and Discussion

The synthesis of 2,2'-bis(2-indenyl)biphenyl (**10**) according to Bosnich et al. was repeated by us (Scheme 1).

Scheme 1. Synthesis of 2,2'-Bis(2-indenyl)-biphenyl According to Bosnich et al.



Conversion of **10** into the zirconium dichloride complex **7** proceeded in 95% yield.

Initial results in olefin polymerization using zirconium complex **7** were very promising.⁹ Therefore, we decided to further develop this type of catalyst system. Unfortunately, the route by Bosnich et al. was not amenable to scale-up, as the yield of bis-Grignard **11** is only high at low concentration (max 0.075 M).¹³ We also found that increase of the scale to 0.60 mol (8 L) gave a significant

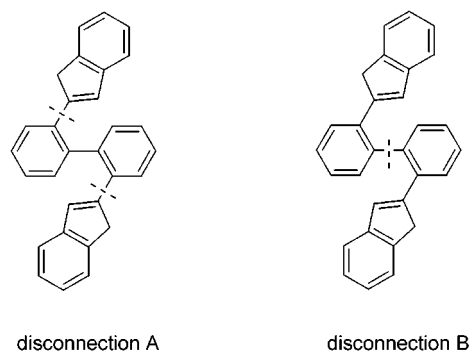
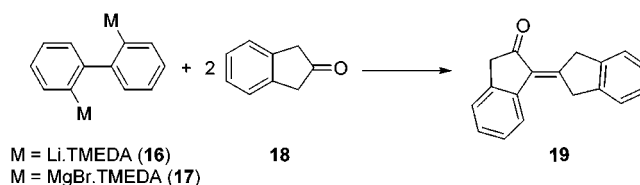


Figure 2. Two of the possible disconnections.

lower yield (10%) at this concentration of bis-Grignard **11**, although we could reach similar yields of diol **12** at small scale (37 mmol). It thus became necessary to develop a new route to **10**.

Route Exploration. Logical disconnections (Figure 2) can be made in the biphenyl–indene bond (disconnection A) or between the two phenyl rings of the biphenyl moiety (disconnection B). Since biphenyl is an attractively cheap starting material and 2-indene derivatives are easily accessible, we chose disconnection A.

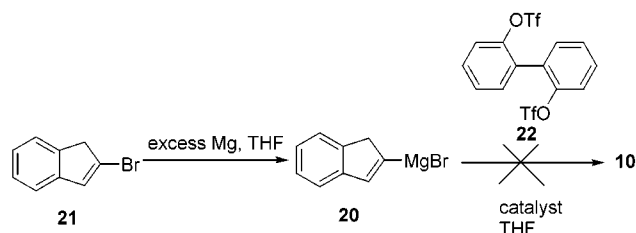
Synthesis of **10 Using Noncatalyzed Reactions.** Reaction of 2,2'-dilithiobiphenyl bis TMEDA adduct¹⁴ (**16**) or its corresponding bis-Grignard **17**, obtained via transmetalation of **16** with magnesium bromide, with 2-indanone (**18**) in diethyl ether did not result in formation of diol **12**. Instead, the condensation product of 2-indanone, 1-(2'-indanylidene)-2-indanone (**19**) (eq 2) was isolated after workup in 46% yield (see Supporting Information). This compound has also been reported by Treibs et al.¹⁵



Synthesis of **10 Using Metal-Catalyzed Cross-Coupling Reactions.** Cross-coupling reactions are effective methods to prepare biaryls.¹⁶ However, the double Kumada coupling of 2-(bromomagnesio)indene (**20**) (prepared by reaction of 2-bromoindene (**21**)¹⁷ with magnesium in THF) with 2,2'-bis(trifluoromethylsulfonyl)-biphenyl (**22**)¹⁸ was unsuccessful with various catalysts¹⁹

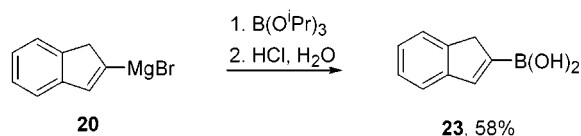
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(eq 3). All starting materials were still present in the reaction mixture, according to the GC-MS spectra.

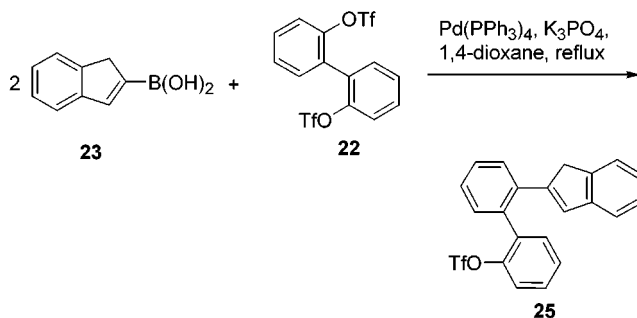
To explore the use of a Suzuki approach,²⁰ 2-indenyl boronic acid (**23**) was prepared. This was done by the reaction of **20** with an excess (5 equiv) of triisopropoxyborane (at $-30\text{ }^{\circ}\text{C}$) or trimethoxyborane (at $-100\text{ }^{\circ}\text{C}$) and subsequent warming to room temperature, followed by acidic hydrolysis (eq 4).



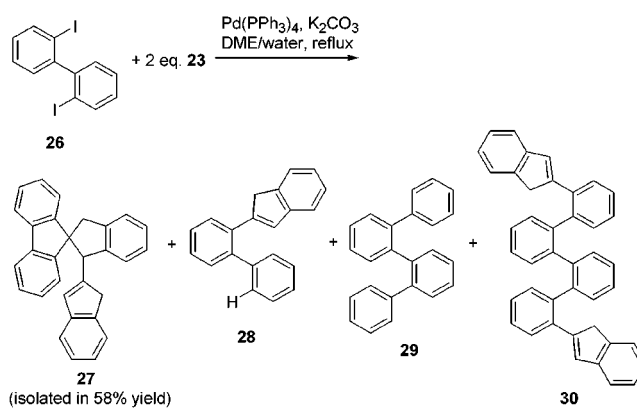
The yields of the 2-indenyl boronic acid **23** obtained via this reaction varied between 50 and 60%. Higher reaction temperatures ($-30\text{ }^{\circ}\text{C}$) can be applied when triisopropoxyborane is used instead of the more common trimethoxyborane ($-100\text{ }^{\circ}\text{C}$) to reach comparable yields.²¹

Attempted Suzuki couplings of boronic acid **23** with bistriflate **22** or the bismesylate of 2,2'-biphenol (**24**) in refluxing toluene, however, did not give the desired product under catalysis of $[\text{Pd}(\text{PPh}_3)_4]$ with K_2CO_3 and

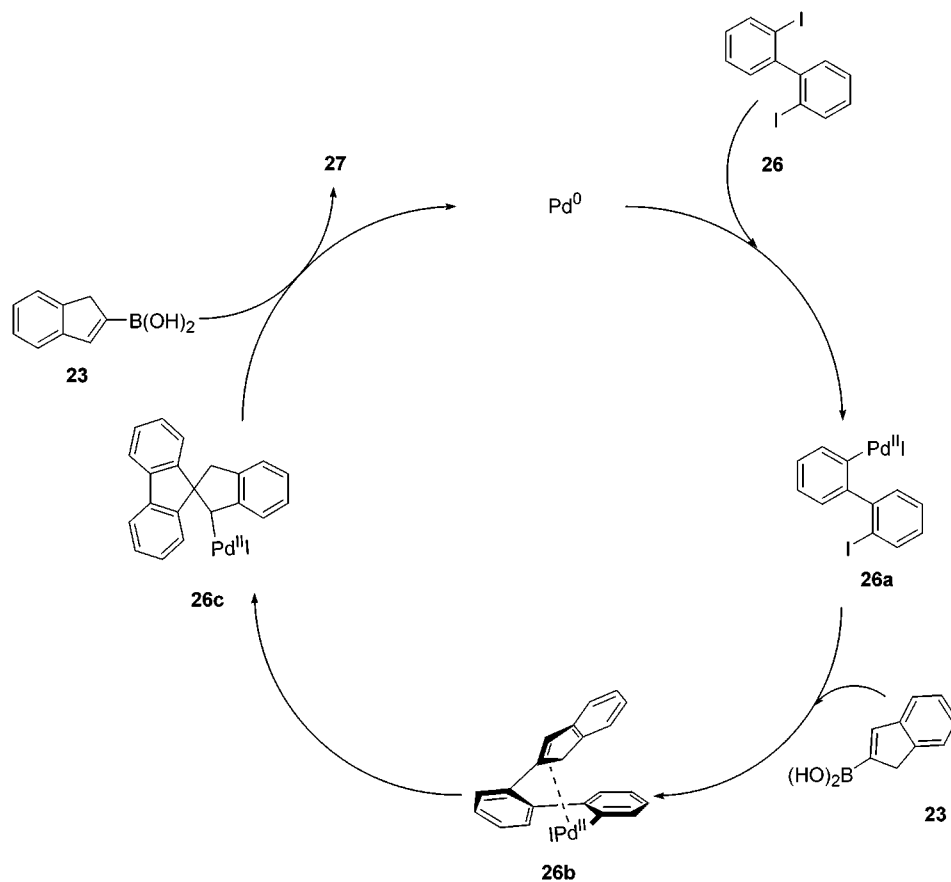
LiBr. As indicated by GC-MS, the monosubstituted product (**25**) was formed when **22** was used in 1,4-dioxane with K_3PO_4 (eq 5).



Reaction of 2,2'-diiodobiphenyl¹⁴ (**26**) with 2 equiv of boronic acid **23** and K_2CO_3 in DME/water gave a mixture of 4 products (eq 6) as indicated by GC-MS analysis.



Scheme 2. Proposed Mechanism (strongly simplified) for the Formation of 27



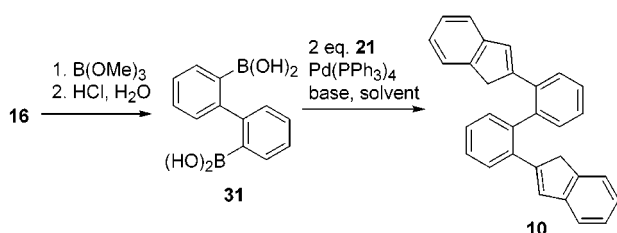
base solvent	K ₂ CO ₃	LiOH·H ₂ O	CsCO ₃	CsF	<i>n</i> -Bu ₄ NF	KO ^t Bu	K ₃ PO ₄	NaOH
DME								
toluene								
1,4-dioxane								
DMF								
ethanol								
THF								

Figure 3. First generation (6 by 8) array for the optimization of the synthesis of **10**. The red balls indicate the hot spots (where **10** was formed). Reactions performed on 50 mg (0.256 mmol) of 2-bromoindene and 31 mg (0.128 mmol) of 2,2'-biphenyl diboronic acid in 1 mL of solvent. All bases except Bu₄NF (1.0 M) added as 2.0 M aqueous stock solutions in 1.5 equiv per coupling under catalysis of [Pd(PPh₃)₄] (1 mol % per coupling). The reaction vessels were heated at 70 °C during 6 h and analyzed by LC-MS.

The major product was isolated and characterized as spiro-1,1-(2,2'-biphenyl)-2-(2-indenyl)indane (**27**) by ¹H, ¹³C, ¹H–¹H-COSY, and ¹³C–¹H correlation NMR spectroscopy (see Supporting Information).

For the mechanism for the formation of **27**, we propose a cascade as depicted in Scheme 2.

Identical Disconnection, Reversed Approach. Since the approach above suffered from the occurrence of an intramolecular Heck-type insertion (**26b** to **26c**), the opposite approach was performed. This translates to a Suzuki-coupling of 2 equiv of **21** with 2,2'-biphenyl diboronic acid (**31**). Diboronic acid **31** was prepared by the reaction of **16** with trimethoxyborane in diethyl ether at –30 °C (eq 7).



Yields dropped significantly if the temperature exceeded –20 °C. The use of triisopropoxyborane instead of trimethoxyborane in diethyl ether gave only low yields (~10%). These lower yields may be explained by the formation of the monoboronic acid (**32**) and side products, similar to those in the formation of the described binaphthylidiboronic acid.²²

Reaction of **31** with 2 equiv of **21** in DME/water with K₂CO₃ as base under catalysis of 7 mol % [Pd(PPh₃)₄] indeed resulted in the formation of **10** (equation 7), which was isolated after crystallization from ethanol–acetone in 79% yield. We wanted to reduce the amount of [Pd(PPh₃)₄] significantly, since this catalyst is expensive. However, reduction of the Pd-catalyst concentration to 3 mol % resulted in significant lower yields (50% of the desired product). Mono-substituted product **28** was formed as the single side product.

HTE Approach in the Optimization of the Suzuki Coupling. Many aspects, such as base, solvent, cosolvent, and catalyst, may have an influence on this standard Suzuki reaction. For this reason, a HTE approach was used for the optimization of the amount of the catalyst. In the first experiment an array of six solvents and eight bases was explored in a custom build 96-well heating block located on the bed of a TECAN Genesis 150 automated pipetting robot. The results are depicted in Figure 3.

It is clear that for most bases, toluene is the best solvent. Additionally, use of K₂CO₃ as base has hot spots in DME and dioxane. Remarkably, common Lewis bases for Suzuki reactions, such as CsF and Bu₄NF,^{16a} gave low yields, even in toluene.

Base, solvent, and catalyst were varied in the second generation 4 by 3 by 4 array: four bases (K₂CO₃, LiOH·H₂O, KOAc, and BaOH·H₂O all as aqueous solutions), three solvents (DMF, DME, and toluene), four catalysts ([Pd(PPh₃)₄], Pd(OAc)₂, [PdCl₂(dppf)], and 5% Pd/C. [Pd(PPh₃)₄] appeared to be the best catalyst, toluene the best solvent, and LiOH·H₂O and Ba(OH)₂·H₂O the best bases. Furthermore, an inert atmosphere (nitrogen) appeared to be very important to avoid degradation.

An important observation made during a control experiment (no catalyst present) was that **31** decomposed to the mono-boronic acid (**32**) under the reaction conditions, presumably due to hydrolysis (proto-deboronation). Usually, boronic acids are stable toward hydrolysis,

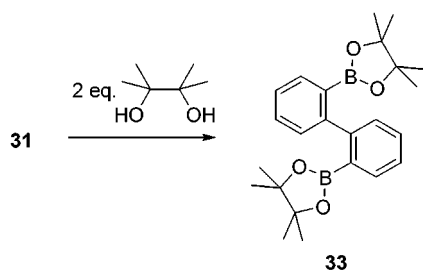
(20) (a) Suzuki, A. *J. Organomet. Chem.* **1999**, 576, 147. (b) Suzuki A. In *Metal-catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Ed.; Wiley-VCH Verlag GmbH: New York, 1998; Chapter 2. (c) Gröger, H. *J. Prakt. Chem.* **2000**, 342, 334.

(21) To avoid multiple alkylation, see: (a) Brown, H. C.; Cole, T. E. *Organometallics* **1983**, 2, 1316. (b) Brown, H. C.; Bhat, N. G.; Srebnik, M. *Tetrahedron Lett.* **1988**, 29, 2631. (c) Brown, H. C.; Rangaishenvi, M. V. *Tetrahedron Lett.* **1990**, 49, 7113 and 7115.

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although some boronic acids are reported to hydrolyze under Suzuki reaction conditions.^{23–27} We believe that the decomposition of **31** (and reported compounds in refs 20–24) is related to the high acidity of the boronic acid groups: (i) the protons of the OH groups of diboronic acid **31** have a very low-field chemical shift at 9.15 ppm in DMSO-*d*₆, indicating exceptionally high acidity; (ii) the *pK*_a was determined by base titration and appeared to be 5.4 (!) (in comparison: the *pK*_a of phenylboronic acid is 8.8¹⁶). Diboronic acid **31** and the reported boronic acids in refs 20–24 have in common that they have a neighboring acceptor atom, which can induce hydrogen bond formation that causes increased acidity. Modeling studies of diboronic acid **31** (and the boronic acids from refs 20–24) with Spartan Pro both semiempirical (PM3) and DFT (pBP/DN**) showed qualitatively significant intramolecular hydrogen bond formation with the neighboring acceptor atoms.

Apparently, reduction of the catalyst amount leads to a slow Suzuki reaction. Consequently, the decomposition of **31** becomes more important, resulting in decreasing yields of the desired product. Obviously, to obtain high yields of **10** at low catalyst loadings, the side reaction (presumably proto-deboronation) that leads to the decomposition of **31** has to be prevented by using anhydrous conditions. Remarkably, anhydrous conditions, like DMF/Et₃N, also led to decomposition of **31** to **32**. As another option to prevent proto-deboronation, diboronic acid **31** was esterified with 2 equiv of pinacol to give **33**, in analogy to the method of Gronowitz et al. (eq 8).²³

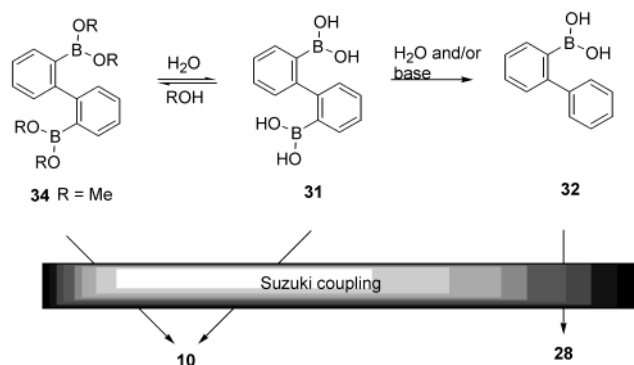


Remarkably, we found that pinacol ester **33** was hydrolyzed very rapidly to **31** in DME/water with K₂CO₃, in contrast to what was observed by Gronowitz.

A much better solution found in the screening was in situ esterification of **31** to **34** in methanol (Scheme 3).²⁷ This is in contrast to the method described by Suzuki et al.,²⁵ where the boronic esters are prepared in an extra reaction step.

Use of the commercially available 1.0 molar solution of (n-Bu)₄NOH in methanol with toluene as cosolvent appeared to be a good choice. Accordingly, catalyst concentrations could be decreased to 0.7 mol % Pd (0.35 mol % per C–C), and yields up to 82% were obtained (also on 0.35 molar scale). A second advantage is that the product precipitates out of the reaction mixture. Thus, filtration of the reaction mixture at room temperature

Scheme 3. Equilibria between **31, **34** and the Irreversible Decomposition of **31** to **32** and Their Subsequent Suzuki Reactions**



yielded **10** in high purity after washing the precipitate with toluene and methanol. Also, the reaction appeared to be very fast, being finished after approximately 10–15 min. On the basis of these observations, even lower Pd-concentrations might be possible.

Scope of the Method. To vary the indenyl moiety of the ligand, the 2-bromoindene derivatives **35**, **36**, and **37** were prepared via the route as depicted in Scheme 4.

Bromoindenes and **35**, **36**, and **37**²⁸ were successfully converted to the corresponding biphenyl-bridged bisindenes **46**, **47**, and **48**, using the new Suzuki conditions (Figure 4).

Conclusions

A new route to **10** has been developed, which is broadly applicable and economically feasible. This route involves a Suzuki coupling of 2 equiv of 2-bromoindene (**21**) with 2,2'-biphenyl diboronic acid (**31**) with [Pd(PPh₃)₄]. Standard Suzuki reaction conditions (in DME/water with K₂CO₃ as base) proved unsatisfactory for our needs due to a competitive proto-deboronation of the 2,2'-biphenyl diboronic acid (**31**), necessitating the use of high loadings of the expensive Pd-catalyst.

HTE techniques proved a very useful tool to rapidly optimize the scale-up of this Suzuki reaction. By use of the commercially available 1.0 molar solution of (n-Bu)₄NOH in methanol optionally with cosolvent toluene, pure product could be easily obtained in a fast and clean reaction, using only 0.7 mol % (0.35 mol % per C–C) of the expensive palladium catalyst.

Experimental Section

Experiments were performed under a dry and oxygen-free nitrogen atmosphere using Schlenk-line techniques. ¹H NMR (200, 300 or 400 MHz) and ¹³C NMR spectra (50, 75 or 100 MHz) were measured on a Bruker AC200, Bruker Avance 300, Varian Unity 300 or Bruker DPX 400. GC-MS spectra were measured on a Fisons MD-800 GC-MS equipped with a CPSil8 low bleed column (dimensions: 30 m × 0.25 mm, film thickness: 1.0 μm) or on a HP5890–HP5971-MSD equipped with a CPSil8 low bleed column (dimensions: 25m × 0.25 mm; film thickness: 0.4 μm). Diethyl ether and ligroin were distilled from sodium/potassium alloy; THF and toluene from potassium and sodium, respectively, all having benzophenone as indica-

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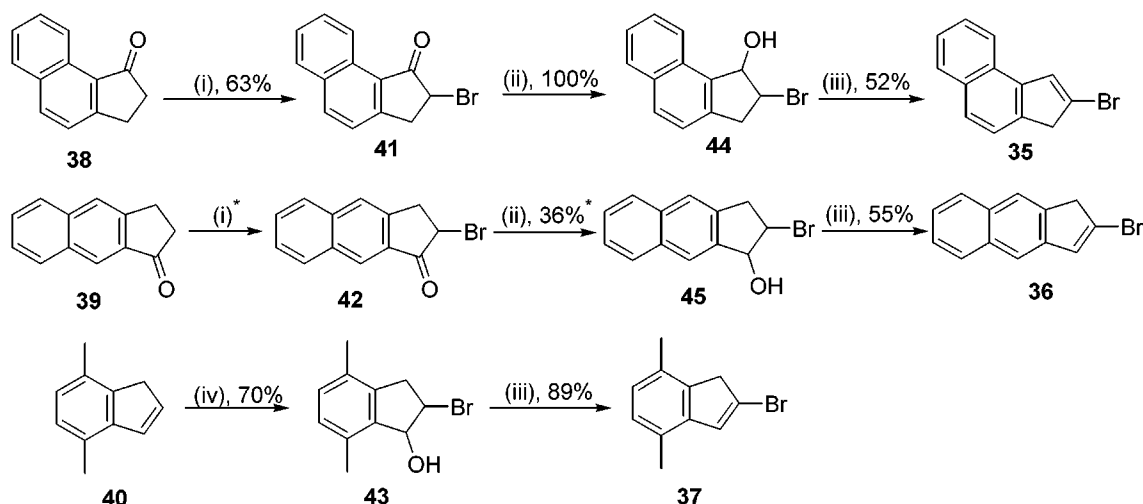
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Scheme 4. Synthesis of Substituted 2-Bromoindenes^a

^a Asterisk (*) denotes overall yield over two steps. (i) $\text{PhNMe}_3\text{Br}_3$, THF, 0 °C; (ii) NaBH_4 , THF, MeOH, 0 °C; (iii) $\text{p-TsOH}\cdot\text{H}_2\text{O}$, toluene, reflux; (iv) NBS, H_2O , DMSO.

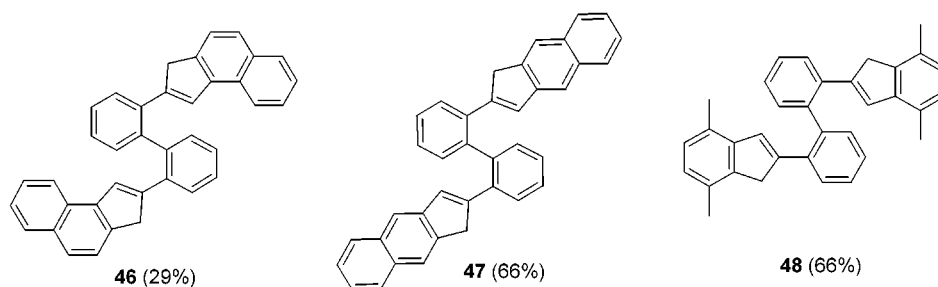


Figure 4. Suzuki coupling products of the substituted 2-bromoindenes (isolated yields between parentheses).

tor. *n*-Butyllithium (1.6 M in hexane), dimethoxyethane (anhydrous), trimethoxyborane, triisopropoxyborane, palladium acetate, triphenylphosphine, palladium tetrakis(triphenylphosphine), 2-indanone, sodium borohydride, and biphenyl were used as received from Aldrich. Phenyltrimethylammonium bromide was obtained from Fluka. 2-Bromoindene (**21**) was prepared according to a literature procedure by the dehydration of 2-bromo-1-indanol (Aldrich) followed by a vacuum distillation.¹⁷ 2,2'-Dilithiobiphenyl (**16**), 2,2'-diiodobiphenyl (**26**),¹⁴ benz(6,7)indanone (**38**),²⁹ benz(5,6)indanone (**39**),³⁰ 4,7-dimethylindene (**40**),³¹ 2-bromo-4,7-dimethylindene (**37**),²⁸ and 2,2'-bis(2-indenyl)diyl)biphenyl zirconium dichloride (**7**)⁷ were prepared according to literature procedures.

2-Indenyl Boronic Acid (23). Magnesium turnings (9.72 g, 0.40 mol) covered with dry THF (50 mL) were activated with 10 drops of 1,2-dibromoethane. A solution of 2-bromoindene (39.01 g, 0.20 mol) in dry THF (200 mL) was added slowly during 45 min under cooling with an ice-bath to maintain the temperature below 20 °C. The mixture was stirred at room temperature for 2 h after complete addition. Via a syringe, the Grignard solution was decanted from the excess magnesium turnings and added slowly to a solution of triisopropoxyborane (92 mL, 0.40 mol) in dry THF (250 mL) keeping the temperature between -30 to -50 °C. After addition, the temperature was allowed to rise to room temperature, and stirring was continued overnight. The mixture was quenched with water (100 mL), and then dilute hydrochloric acid (25 mL, 37 weight % in 250 mL water) was added. The mixture

was stirred for 30 min and then transferred into a separatory funnel. The organic phase was separated, and the aqueous phase extracted with ether (3 × 100 mL). The combined organic phases were extracted 3× with 50 mL of saturated brine. The organic phase was dried over sodium sulfate, filtered, and evaporated to dryness. The residue was dissolved in boiling ether (200 mL), and then hexanes were added (400 mL). Quick filtration of the hazy solution through paper gave a clear filtrate. The clear filtrate was evaporated slowly and partly on the rotary evaporator to afford a white powder. After filtration, washing, and drying, **23** was obtained as a white powder (18.54 g, 58%), mp 222 °C (dec). ¹H NMR (CDCl_3): δ 8.0–7.6 (3 peaks, ratio and exact shift concentration dependent; sum 1H), 7.45 (m, 2H), 7.20 (m, 2H), 3.7–3.5 (multiple peaks, ratio and exact shift concentration dependent; sum 2H) ppm. ¹³C NMR (CDCl_3): δ 148.5, 147.8, 147.5, 146.8, 146.0, 145.1, 144.9, 126.5 (m), 124.2, 124.1, 122.5, 122.2, 42.1, 41.5, 41.0 ppm. Anal. Calcd for $\text{C}_{27}\text{H}_{21}\text{B}_3\text{O}_3\cdot 2\text{H}_2\text{O}$: C, 70.20; H, 5.46. Found: C, 69.99; H, 5.39.

Spiro-1,1-(2,2'-Biphenyl)-2-(2-indenyl)indane (27). To a solution of 2-indenyl boronic acid (1.72 g, 10.73 mmol) and 2,2'-diiodobiphenyl (1.98 g, 4.88 mmol) in dimethoxyethane (10 mL), a solution of K_2CO_3 (1.54 g; 11.1 mmol) in degassed water was added. Then, $[\text{Pd}(\text{PPh}_3)_4]$ (0.11 g, 0.1 mmol, 2.0 mol %) was added, and the yellow mixture was heated to reflux. During this process, the color quickly changed (within one minute) to cognac brown. Reflux was continued for a period of 16 h. After cooling, the mixture was poured into 5% aqueous HCl (50 mL). The mixture was extracted with ether (3 × 50 mL). The combined organic phases were subsequently extracted with an aqueous solution of HCl (5 wt %, 3 × 25 mL), saturated sodium bicarbonate, and saturated brine. The organic phase was dried over sodium sulfate, filtered, and evaporated to dryness. The residue was dissolved in warm

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ethanol/water 9:1 v/v, and treated with active carbon. Cooling followed by slow partial evaporation gave a yellow-brown solid powder (1.08 g, 58%). An analytical pure sample was obtained by crystallization from acetone/ethanol 1:1 v/v by slow evaporation in air, mp 158–159 °C. ^1H NMR (CDCl_3): δ 7.7 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 6.8–7.5 (m, 13H), 6.47 (s, 1H), 5.03 (s, 1H), 3.72 (d, J = 16 Hz, 1H), 3.46 (d, J = 16 Hz, 1H), 2.70 (s, 2H) ppm. ^{13}C NMR (CDCl_3): δ 150.0, 148.8, 147.0, 144.5, 144.2, 143.0, 142.5, 140.1, 139.6, 129.5, 128.4, 127.1, 127.0, 126.7, 126.0, 125.6, 124.9, 124.5, 124.1, 123.6, 123.5, 122.9, 122.1, 120.0, 119.5, 63.2, 57.3, 43.8, 40.7 ppm. Anal. Calcd for $\text{C}_{30}\text{H}_{22}$: C, 94.20; H, 5.80. Found: C, 94.05; H, 5.84.

2,2'-Biphenyl Diboronic Acid (31). To a suspension of 2,2'-dilithiobiphenyl bis TMEDA adduct (**16**) (62.1 g; 156 mmol) in diethyl ether (1000 mL), kept at -40 °C (with a dry ice/acetone bath), trimethoxyborane (80 mL; 73.2 g; 705 mmol) was slowly added. The reaction mixture was allowed to warm to room temperature and then stirred overnight. A sticky lump had formed which was dissolved by the addition of dry THF (400 mL). The reaction mixture was stirred for an additional 1 h. To the resulting reaction mixture, water (200 mL) was added, followed by hydrochloric acid (5%, 500 mL). The reaction mixture was vigorously stirred for 4 h. The organic solvents were removed under reduced pressure. The remaining aqueous phase was extracted with dichloromethane (3×300 mL). The combined organic phases were dried over sodium sulfate. The drying agent was filtered off, and the solvents were removed under reduced pressure. Pure white microcrystalline **31** was obtained after crystallization from toluene/ligroin (23.9 g, 63%), mp 140 °C (dec). ^1H NMR ($\text{DMSO}-d_6$): δ 9.15 (bs, 4H), 7.72 (d, J = 8.0 Hz, 2H), 7.57 (m, 4H), 7.37 (dt, J = 8.0 Hz and J = 1.6 Hz) ppm. ^{13}C NMR ($\text{DMSO}-d_6$): δ 145.2, 134.1, 133.7, 130.7, 129.4, 126.5 ppm. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{B}_2\text{O}_4 \cdot \text{H}_2\text{O}$: C, 64.39; H, 4.50. Found: C, 64.00; H, 4.56.

Bis-pinacol Ester of 2,2'-Biphenyl Diboronic Acid (33). A suspension of 2,2'-biphenyl diboronic acid (**31**) (1.00 g; 4.12 mmol) and pinacol (0.98 g; 8.24 mmol) in toluene (25 mL) was heated under reflux with Dean–Stark trap for 16 h. During the first hour, water separated. The solution was cooled, and the resultant hazy solution was filtered and evaporated to dryness to afford crude product. Analytical sample was prepared by dissolving in ligroin (50 mL), filtering, and slowly evaporating in air (to approximately 10 mL) to afford large colorless platelike crystals (1.05 g, 63%), mp 109–110 °C. ^1H NMR (CDCl_3): δ 7.6 (d, J = 7.2 Hz, 2H), 7.2–7.4 (m, 6H), 1.0 (s, 24H) ppm. ^{13}C NMR (CDCl_3): δ 149.9, 134.0, 129.5, 129.4, 126.1, 83.5, 25.0 ppm. Anal. Calcd for $\text{C}_{24}\text{H}_{32}\text{B}_2\text{O}_4$: C, 70.98; H, 7.94. Found: C, 71.18; H, 8.00.

2-Bromobenz(6,7)indene (35). Bromine (4.70 g; 29.6 mmol) was added to a suspension of phenyltrimethylammonium bromide (6.39 g; 29.6 mmol) in THF (50 mL) at 0 °C. The resulting red solution was brought to room temperature, and this solution was added to a cold (0 °C) solution of benz(6,7)indanone (**38**) (5.39 g; 29.6 mmol) in THF (50 mL). The ice bath was removed, and the resulting reaction mixture was stirred overnight. The color had changed from yellow to colorless, and a white precipitate had formed. Water (100 mL) was added, and the mixture was extracted with diethyl ether (2×200 mL). The organic phase was separated from the aqueous phase. The organic phase was extracted with water (3×75 mL), dried over sodium sulfate, and filtered. The solvents were removed under reduced pressure, resulting in a yellow oil containing some solid material. The 2-bromobenz(6,7)indanone (**41**) was precipitated from ethanol at -20 °C, filtered, and washed with cold (-20 °C) ethanol twice, resulting in 3.50 g (45%) of a yellow powder. A second fraction of a yellow powder (1.36 g; 18%) was obtained after precipitation from the concentrated mother liquor at -20 °C. ^1H NMR (CDCl_3): δ 9.0 (d, J = 8.2 Hz, 1H), 8.0 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.57 (m, 2H), 7.38 (d, J = 8.4 Hz, 1H), 4.67 (dd, J = 7.2 and 2.8 Hz, 1H), 3.83 (dd, J = 18.6 and 7.2 Hz, 1H), 3.42 (dd, J = 18.6 and 2.8 Hz, 1H) ppm. ^{13}C NMR (CDCl_3): δ 198.8, 153.4, 136.3, 131.9, 128.5, 127.3, 126.9, 126.2, 123.0, 122.3, 51.5, 43.6, 37.2 ppm.

To a solution of **41** (6.50 g; 24.9 mmol) in THF (65 mL) and methanol (35 mL) was added sodium borohydride (1.03 g; 27.1 mmol) at 0 °C. A gas evolved, and the yellow color disappeared during this event. The ice bath was removed and stirred for 1 h at room temperature. A solution of hydrochloric acid in water (5%, 100 mL) was added to the reaction mixture. The reaction mixture was extracted with dichloromethane (2×150 mL). The combined organic phases were dried over sodium sulfate and filtered. The organic solvents were removed under reduced pressure to give 6.54 g (100%) of white powder of **44**. ^1H NMR (CDCl_3): δ 8.14 (d, J = 8.1 Hz, 1H), 7.76 (m, 2H), 7.43 (m, 2H), 7.26 (d, J = 8.3 Hz, 1H), 5.38 (d, J = 4.9 Hz, 1H), 4.77 (m, 1H), 3.43 (d, J = 6.4 Hz, 2H) ppm.

The crude indanol (**44**) was dissolved in toluene (150 mL), and *p*-toluenesulfonic acid (0.82 g; 4.3 mmol) was added. The mixture was heated to reflux for 2 h, and a Dean–Stark trap removed the evolved water. The mixture was cooled to room temperature and extracted subsequently with a saturated sodium carbonate solution and water. The solvents were removed under reduced pressure. Filtration of the residue over silica (eluent: ligroin) gave **35** as a light yellow solid (3.23 g, 53%), mp 92.0–93.8 °C. ^1H NMR (CDCl_3): δ 8.0–7.1 (m, 7H), 3.83 and 3.68 (2 s, sum: 2H), mixture of two double bond isomers. ^{13}C NMR (CDCl_3): δ 142.3, 141.1, 141.0, 139.9, 134.3, 133.3, 132.1, 131.5, 130.1, 129.6, 129.2, 128.3, 127.5, 127.3, 126.7, 126.0, 125.7, 125.6, 125.1, 124.3, 122.4, 120.2, 47.4, 45.3 ppm, mixture of two double bond isomers. Anal. Calcd for $\text{C}_{13}\text{H}_9\text{Br}$: C, 63.70; H, 3.70. Found: C, 63.55; H, 3.69.

2-Bromobenz(5,6)indene (36). 2-Bromobenz(4,5)indanone (**42**) was prepared in the same way as **41** from **39** with the difference that the reaction mixture was extracted with dichloromethane instead of diethyl ether. The solvents were removed under reduced pressure, and the crude mixture of the bromoindanone synthesis (9.78 g) was treated as described in the synthesis for **44**. After trituration with diethyl ether, pure bromoindanol **45** was obtained (3.41 g, 36%). ^1H NMR (CDCl_3): δ 7.75 (m, 3H), 7.61 (s, 1H), 7.30 (m, 2H), 5.05 (dd, J = 9.5 and 4.4 Hz, 1H), 4.91 (m, 1H), 3.48 (bs, 2H), 2.50 (d, 10.0 Hz) ppm. After dehydration and crystallization from ligroin, pure **36** (decomposes slowly at room temperature) was obtained (1.72 g, 55%). ^1H NMR (CDCl_3): δ 7.73 (m, 3H), 7.60 (s, 1H), 7.37 (m, 2H), 6.96 (bs, 1H), 3.67 (tr, J = 1.4 Hz, 2H) ppm. ^{13}C NMR (CDCl_3): δ 142.6, 140.2, 133.1, 132.9, 131.6, 128.0, 127.9, 126.8, 125.6, 125.3, 121.7, 117.9, 44.8 ppm.

2,2'-Bis(2-indenyl)biphenyl (10) via the Standard Suzuki Procedure. To a solution of **21** (15.60 g; 80.0 mmol) in degassed DME (800 mL) were added **31** (9.40 g; 38.8 mmol), $[\text{Pd}(\text{PPh}_3)_4]$ (3.23 g; 2.80 mmol), and a degassed solution of K_2CO_3 (16.72 g; 121 mmol) in water (400 mL). After stirring at reflux overnight, the reaction mixture was poured in a solution of hydrochloric acid in water (5%; 250 mL). The organic phase was dried over sodium sulfate and filtered, and the solvents were removed under reduced pressure. Crystallization of the residue from ethanol gave analytically pure **10** (11.6 g, 79%), mp 210–212 °C (lit. 211–213 °C).⁷

First Generation Array HTE Run for the Synthesis of 10. The 48 reaction vessels were charged with 2-bromoindene (50 mg; 0.256 mmol) and 2,2'-biphenyl diboronic acid (31 mg; 0.128 mmol), and $[\text{Pd}(\text{PPh}_3)_4]$ (3.0 mg; 2.60 μmol). To each vessel was added the desired solvent (1 mL). Then, all bases were added as aqueous stock solutions (2.0 M, except Bu_4NF (1.0 M), 1.5 equiv per coupling). The reaction vessels were heated at 70 °C during 6 h. After cooling to room temperature, the reaction mixtures were filtered, and the residues were extracted with acetone. Combined filtrate and acetone extract were analyzed by LC-MS.

Second Generation Array HTE Run for the Synthesis of 10. The 48 reaction vessels were charged with 2-bromoindene (50 mg; 0.256 mmol) and 2,2'-biphenyl diboronic acid (31 mg; 0.128 mmol). Then, the 48 minireactors were divided in 4 blocks of 12 vessels, and those were charged with catalyst $[\text{Pd}(\text{PPh}_3)_4]$ (8.9 mg; 7.71 μmol); $[\text{PdCl}_2(\text{dppf})]$ (5.6 mg; 7.71 μmol); $\text{Pd}(\text{OAc})_2$ (1.7 mg; 7.71 μmol) and Pd/C (5%, 10 mg). These 4 blocks of 12 mini reactors were each divided in blocks of 4 mini reactors and each block of 4 reactors was charged with the

solvent (1 mL; toluene; DMF and DME). Then, each reactor was charged with an aqueous solution of the base (1.5 M; K₂CO₃; LiOH; KOAc or Ba(OH)₂). The reactor block was heated to 70 °C for 6 h. After being cooled to room temperature, the reaction mixtures were filtered, and the residues were extracted with acetone. Combined filtrate and acetone extract were analyzed by LC-MS.

Bisindenyl Compound 10 via the Optimized Suzuki Procedure (0.70 mol % [Pd(PPh₃)₄]). To a solution of tetra(*n*-butyl)ammonium hydroxide (25.0 mL; 1.0 M; 25 mol) in methanol (used as obtained from Aldrich) were added toluene (30 mL), 2-bromoindene (3.20 g, 16.5 mmol), 2,2'-biphenyl diboronic acid (**31**) (2.00 g, 8.30 mmol), and [Pd(PPh₃)₄] (44 mg, 30 μmol, 0.7 mol %). The mixture was heated to reflux. At the boiling point, the color changed from yellow to cognac brown, and the product immediately started to precipitate. After stirring overnight at reflux, the reaction mixture was cooled to room temperature. Diluted hydrochloric acid (5%, 75 mL) was added, and the precipitate was filtered off. The residue was subsequently washed with water, ligroin, and ethanol and dried, resulting in pure **10** (2.49 g, 79%).

Bis(2-benz(4,5)indenyl)biphenyl (46) via the Optimized Suzuki Procedure. The same procedure as described for **10**, using **31** (1.18 g; 4.88 mmol), **35** (2.39 g; 9.76 mmol), tetra(*n*-butyl)ammonium hydroxide (14.0 mL; 1.0 M in MeOH; 14.0 mmol). Yield: 0.69 g (29%), mp 214–215 °C. ¹H NMR (CDCl₃): δ 7.9–7.1 (m, 12H), 6.28 and 6.25 (2 s, sum: 2H), 3.6–3.0 (m, sum: 4H) ppm, remark: mixture of double bond isomers. ¹³C NMR (CDCl₃): δ 146.9, 141.3, 141.0, 140.8, 139.8, 136.3, 132.5, 131.4, 131.0, 128.8, 128.3, 128.0, 127.8, 127.6, 127.4, 127.0, 126.0, 125.4, 124.9, 124.6, 124.4, 123.6, 123.4, 122.1, 120.4, 42.0, 39.8 ppm, remark: mixture of double bond isomers. HRMS calcd for C₃₈H₂₆: 482.20345. Found: 482.20172.

Bis(2-benz(5,6)indenyl)biphenyl (47) via the Optimized Suzuki Procedure. The same procedure as described for **10**, using **31** (0.86 g; 3.55 mmol), **36** (1.76 g; 7.19 mmol), and tetra(*n*-butyl)ammonium hydroxide (11.0 mL; 1.0 M in MeOH; 11.0 mmol). Yield: 1.13 g (66%), mp. 300–302 °C (dec).

¹H NMR (CDCl₃): δ 7.69 (dd, 4H), 7.55 (s, 2H), 7.43–7.29 (m, 14H), 6.24 (s, 2H), 3.39 (d, *J* = 22.5 Hz, 2H), 3.09 (d, *J* = 22.5 Hz, 2H) ppm. ¹³C NMR (CDCl₃): 148.6, 144.9, 142.0, 141.5, 136.7, 133.7, 132.5, 131.7, 131.2, 129.4, 128.3 (three peaks), 125.7, 125.3, 122.3, 119.1, 40.6 ppm. HRMS calcd for C₃₈H₂₆: 482.20345. Found: 482.20486.

Bis(4,7-dimethyl-2-indenyl)biphenyl (48) via the Optimized Suzuki Procedure. The same procedure as described for **10**, using **31** (3.80 g; 15.7 mmol), **37** (6.20 g; 27.8 mmol), and tetra(*n*-butyl)ammonium hydroxide (50.0 mL; 1.0 M in MeOH; 50.0 mmol). Yield: 4.0 g (66%), mp. 229–230 °C. ¹H NMR (CDCl₃): δ 7.35–7.28 (m, 8H), 6.82 (d, *J* = 7.6 Hz, 2H), 6.72 (d, *J* = 7.6 Hz, 2H), 6.13 (s, 2H), 3.10 (d, *J* = 22.7 Hz, 2H), 2.71 (d, *J* = 22.7 Hz, 2H), 2.02 (s, 6H), 2.00 (s, 6H) ppm. ¹³C NMR (CDCl₃): 146.2, 144.3, 142.6, 141.7, 137.2, 131.7, 130.5, 129.8, 129.3, 128.4, 128.2, 128.0, 126.4, 40.7, 18.9, 18.6 ppm. Anal. Calcd for C₃₄H₃₀: C, 93.11; H, 6.89. Found: C, 93.00; H, 6.92.

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Supporting Information Available: An experimental procedure for **19** and spectral data for **27**, **41**, **44**, **35**, **46**, **45**, **36**, **47**, and **48** are available free of charge via the Internet at <http://pubs.acs.org>.

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