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Cobalt-Catalyzed Preparation of Arylindium Reagents from Aryl and Heteroaryl Bromides

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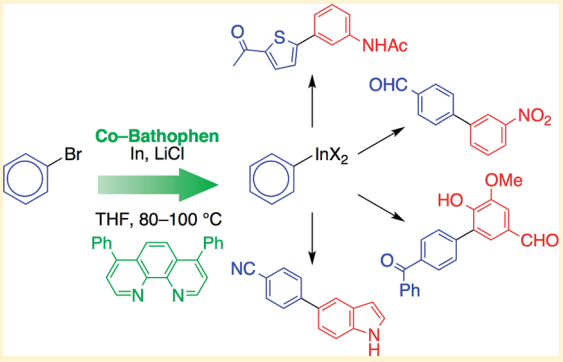
Supporting Information

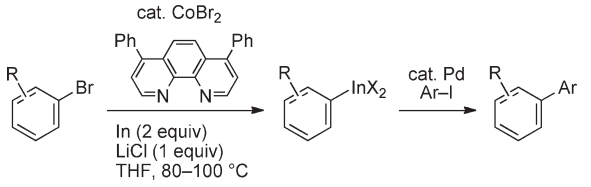
ABSTRACT: A cobalt−bathophenanthroline catalyst has been developed for the direct preparation of a variety of arylindium reagents from the corresponding aryl and heteroaryl bromides in the presence of indium metal and lithium chloride. The thus-formed arylindium reagents undergo efficient palladium-catalyzed cross-coupling reactions with aryl iodides, tolerating various functional groups including hydroxy and free amino groups.



Organoindium reagents occupy a unique position in the synthetic chemistry of nucleophilic organometallics; they exhibit sufficient reactivity toward a variety of C−C bond-forming reactions yet tolerate air, moisture, and sensitive functional groups, including hydroxy and amino groups.[1] While allyl- and propargylindium reagents are easily accessible from the corresponding halides and indium metal,[1] the preparation of other classes of organoindium reagents, aryl- and alkylindiums in particular, used to be less straightforward. Thus, their preparation has commonly resorted to transmetalation of the corresponding organolithium and magnesium reagents with indium trichloride,[2] which is less attractive in terms of operational simplicity, atom efficiency, and functional group compatibility. With this background, the recent developments of LiCl-assisted indium insertion into aryl halides by Knochel[3] and Minehan[4] and CuCl-assisted indium insertion into alkyl halides by Loh[5] represent breakthroughs in the preparative methods for organoindium reagents.[6]

The direct preparation of arylindiums by Knochel and Minehan is particularly attractive in the context of biaryl synthesis.[7] Nevertheless, their methods have been mostly limited to aryl iodides, in particular to those bearing activating functional groups (e.g., ester, ketone, aldehyde, cyano), while the use of aryl bromides is more desirable in terms of cost and availability. Encouraged by our recent development of a cobalt−Xantphos catalyst for the preparation of arylzinc reagents from aryl iodides, bromides, and chlorides via zinc insertion,[8−10] we became interested in the ability of cobalt complexes to catalyze indium insertion into aryl halides. We report here that a cobalt−bathophenanthroline catalyst promotes indium insertion into a wide range of aryl and heteroaryl bromides, thereby offering a convenient method for the preparation of arylindium reagents (Scheme 1). The thus-formed reagents participate in palladium-catalyzed cross-couplings with tolerance to various functional groups.

Scheme 1. Cobalt−Bathophenanthroline-Catalyzed Indium Insertion into Aryl Bromide



Screening of cobalt catalysts was performed on the reaction of 1-bromo-3,5-dichlorobenzene **1** with indium (2 equiv; preactivated with a catalytic amount of allyl chloride) and LiCl (1 equiv) in THF at 80 °C for 20 h. The degree of indium insertion was measured by iodolysis of the reaction mixture followed by GC analysis (Table 1). The cobalt−Xantphos catalyst,[8] which was the optimum catalyst for the zinc insertion, produced the iodination product **2** in moderate yield (49%, entry 1). The reaction was accompanied by a considerable amount (36%) of the reduction product **3**, which is considered to form via hydrogen abstraction of an arylcobalt species and not via protonation of an arylindium species (vide infra).[8] Other diphosphine ligands such

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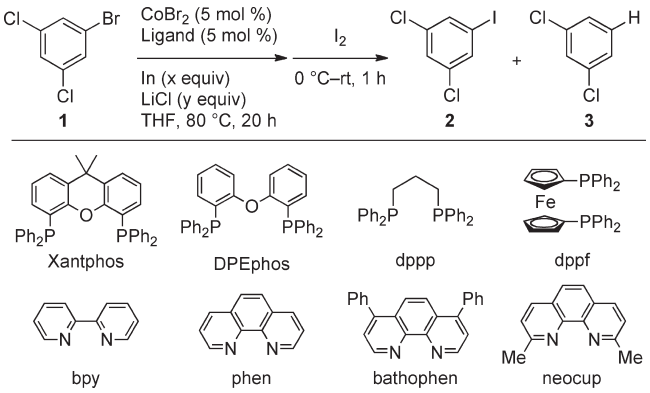
Table 1. Indium Insertion into 1-Bromo-3,5-dichlorobenzene[a]



				yield[b] (%)	
entry	ligand	*x*	*y*	**2**	**3**
1	Xantphos	2	1	49	36
2	DPEphos	2	1	30	20
3	dppp	2	1	48	33
4	dppf	2	1	31	13
5	bathophen	2	1	83	6
6	bpy	2	1	33	17
7	phen	2	1	12	7
8	neocup	2	1	16	9
9[c]	bathophen	2	1	0	0
10		2	1	0	7
11	bathophen	2	0	0	0
12	bathophen	2	2	42	37
13	bathophen	1.5	1	73	8

[a] Reaction was performed on a 1 mmol scale. [b] Determined by GC using *n*-tridecane as an internal standard. [c] $CoBr_2$ was omitted from the reaction.

as DPEphos, dppp, and dppf also gave unsatisfactory results in terms of conversion and selectivity (entries 2–4). Upon further ligand screening, bathophenanthroline emerged as an effective ligand, affording **2** in 83% yield together with a small amount (6%) of **3** (entry 5).

The performance of other bidentate nitrogen ligands, such as 2,2-bipyridine, 1,10-phenanthroline, and neocuproine, was much poorer (entries 6–8). Control experiments demonstrated that $CoBr_2$, bathophenanthroline, and LiCl are all essential components of the catalytic system (entries 9–11). The amount of LiCl was crucial because the use of 2 equiv of LiCl led to a significant increase in the reduction product **3** (entry 12). A decrease in the amount of indium to 1.5 equiv resulted in a slightly lower yield of **2** (entry 13). Note that, unlike the zinc insertion reaction,[8] no biaryl homocoupling product was observed.

The cobalt–bathophenanthroline system (Table 1, entry 5) was applicable to a variety of electron-neutral, -rich, and -poor aryl/heteroaryl bromides, affording the corresponding indium reagents **4a**–**u** in moderate to excellent yields as indicated by GC analysis after iodolysis (Figure 1). Some of the arylindium reagents (**4a**–**h**,**n**,**p**) were prepared at 100 °C, while most of these reactions could be performed at 80 °C with a slight decrease in the yield by 5–10%. The reaction became

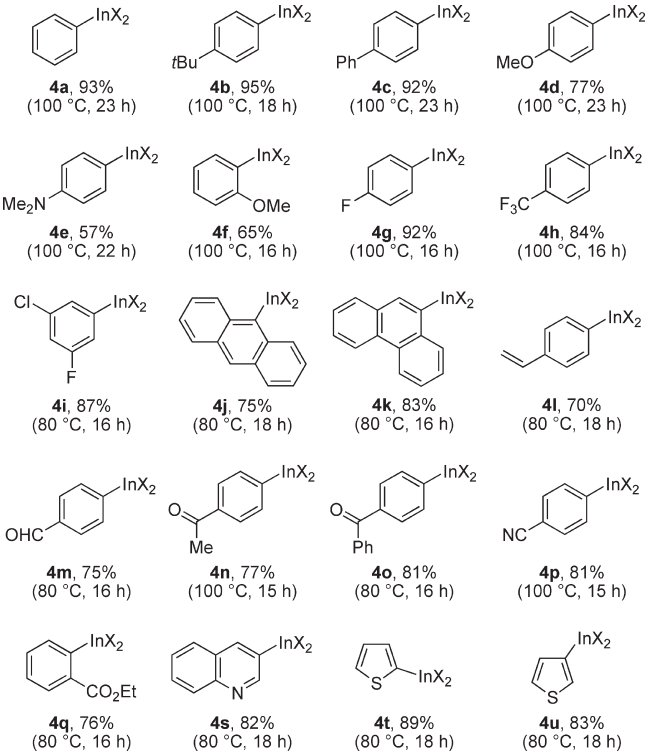


Figure 1. Arylindium reagents prepared from aryl bromides with the cobalt–bathophenanthroline catalyst (Table 1, entry 5). Yields were determined by GC after iodolysis.

particularly sluggish with 4-Me_2N and 2-MeO substituents (**4e** and **4f**). Polycyclic aromatic indium reagents **4j** and **4k** could be prepared in ca. 80% yield. The presence of an olefinic moiety, which could potentially coordinate to the cobalt catalyst, was tolerated (**4l**). Carbonyl and related functional groups (i.e., aldehyde, ketone, cyano, ester) were tolerated, as exemplified by the preparation of the indium reagents **4m**–**q** in 75–81% yield. Heteroaryl bromides such as 3-quinolyl bromide and 2- and 3-bromothiophene could be efficiently converted to the corresponding indium reagents **4s**–**u** in >80% yield.

Note that the formula "$ArInX_2$" used here is a formal representation of the arylindium reagent. ^1H and ^{13}C NMR analysis of the phenylindium reagent **4a** indicated that it mainly consists of two species in an approximate ratio of 2:1 (see Figure S1a in the Supporting Information). The chemical shifts of the major species were close to that of a phenylindium reagent prepared by transmetalation between $InCl_3$ and one equivalent of PhMgBr (Figure S1b, Supporting Information), while the minor one showed similar chemical shifts as a reagent prepared from $InCl_3$ and 2 equiv of PhMgBr (Figure S1c, Supporting Information). Thus, we presume that the reagent **4a** exists as a mixture of phenylindium(III) dihalide ($PhInX_2$) and diphenylindium(III) halide (Ph_2InX) and/or their aggregate species including phenylindium(III) sesquihalide ($Ph_3In_2X_3$).[1,11,12]

The indium insertion into aryl chlorides was also briefly studied (Scheme 2). In general, aryl chlorides were very reluctant to participate in the reaction. Even activated substrates such as 4-chlorobenzonitrile and 4-chlorobenzotrifluoride afforded only a small amount or none of the product (Scheme 2a). Nevertheless, 2-chlorothiophenes could be converted to the corresponding indium reagents in moderate yield (Scheme 2b).

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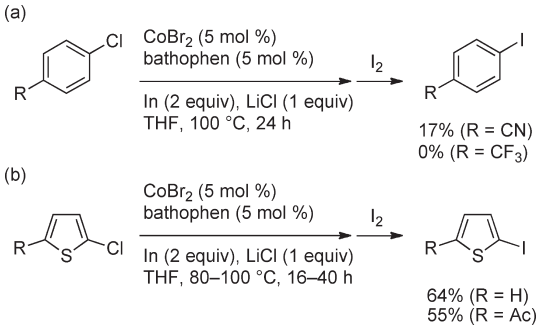
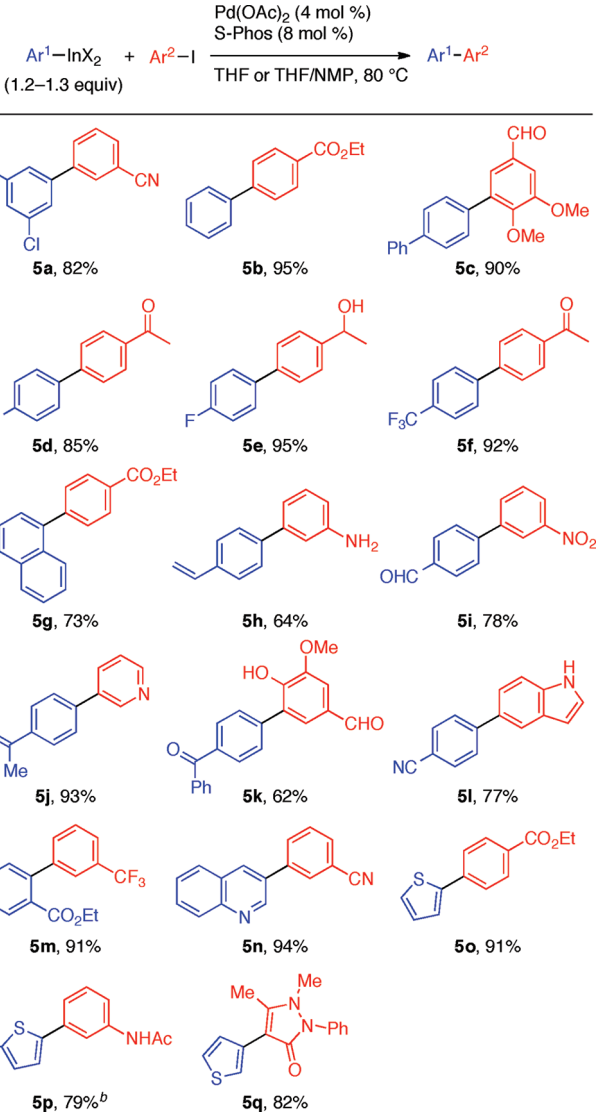
Scheme 2. Indium Insertion into Some Aryl Chlorides



Scheme 3. Palladium-Catalyzed Cross-Coupling of Arylindium Reagents[a]



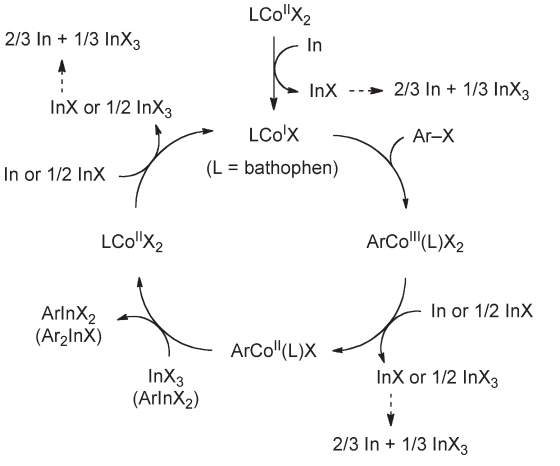
[a] Reaction was performed using 1 mmol of the starting aryl bromide and 0.75−0.46 mmol of the aryl iodide. Yields refer to isolated yields based on the aryl iodides. See the Experimental Section for details of the reaction conditions for each case. [b] 2-Chloro-5-acetylthiophene was used as the starting halide.

The arylindium reagents prepared by the present method readily participate in palladium-catalyzed cross-coupling reactions,[2c−m,3−5] without apparent interference from the cobalt catalyst (Scheme 3). Thus, cross-coupling with a variety of aryl/heteroaryl iodides took place smoothly with the Pd−SPhos catalyst[13] in THF or THF/NMP (NMP = *N*-methylpyrrolidinone),[3] affording a diverse array of biaryl products **5a**−**q** in moderate to excellent yield. Tolerable functional groups on the aryl iodides include electrophilic groups such as cyano (**5a**,**n**), ester (**5b**,**g**,**o**), aldehyde (**5c**,**k**), ketone (**5d**,**f**), and nitro (**5i**) groups and protic OH and NH groups of alcohol (**5e**), phenol (**5k**), aniline (**5h**), indole (**5l**), and acetanilide (**5p**). Heterocyclic iodides such as 3-iodopyridine and 4-iodoantipyrine are also excellent coupling partners (**5j**,**q**).

At this stage, we speculate that the present catalytic system for the indium insertion and the Co−Xantphos system for the zinc insertion share a similar catalytic cycle involving redox processes between Co(I), Co(II), and Co(III) species.[8,9] However, given that common oxidation states of indium are 0, I, and III and that In(I) can disproportionate to In(0) and In(III),[1] we consider that the redox processes in the present system may be more complicated than the case of the zinc insertion (Scheme 4). The reaction would be initiated by reduction of the cobalt(II) precatalyst to a cobalt(I) species by the indium metal. The catalytic cycle may involve (1) oxidative addition of an aryl halide to cobalt(I) to give an arylcobalt(III) species, (2) reduction of the arylcobalt(III) to an arylcobalt(II) species by In or InX, (3) transmetalation of the arylcobalt(II) species with InX_3 (or $ArInX_2$), which would be generated through the preceding reduction steps or disproportionation of InX, to afford $ArInX_2$ (or Ar_2InX) and cobalt(II) halide, and (4) reduction of cobalt(II) halide by In or InX to regenerate the cobalt(I) species. The reduction product may form via hydrogen abstraction of THF by the arylcobalt(II) species, as suggested for the zinc insertion reaction.[8]

In summary, we have developed a cobalt−bathophenanthroline catalyst for the efficient insertion of indium into a variety of aryl and heteroaryl bromides. The resulting arylindium reagents can be cross-coupled with aryl iodides under palladium catalysis with a high level of functional group compatibility. Because of the wider availability and lower cost of aryl bromides than of iodides, as well as the operational simplicity, the present preparative method has significantly expanded the accessibility to arylindiums as nucleophilic aryl donors. Further efforts will focus on

Scheme 4. Proposed Catalytic Cycle



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expansion of the substrate scope, applications of the arylindium reagents, and investigation into the reaction mechanism.

EXPERIMENTAL SECTION

General Methods. All reactions were performed by standard Schlenck techniques in oven-dried reaction vessels under nitrogen atmosphere. Unless otherwise noted, chemicals were purchased from commercial suppliers and were used as received. Indium powder of 99.99% purity (trace metals basis, excluding ~1% Mg as an anticaking agent) was used.[14] THF was distilled over Na/benzophenone before use. Flash chromatography was performed using 40−63 μm silica gel. ^{1}H and ^{13}C NMR spectra are reported in ppm downfield from an internal standard, tetramethylsilane (0 ppm) and $CHCl_3$ (77.0 ppm), respectively. Gas chromatographic (GC) analysis was performed on a GC system equipped with an FID detector and a (5% phenyl)-methylpolysiloxane capillary column (0.25 mm i.d. × 30 m, 0.25 μm film thickness). The melting points of solid materials were determined by a capillary melting point apparatus and are uncorrected. Mass spectrometry data were recorded on a high-resolution mass spectrometer with the ESI (positive) method.

General Procedure for Cobalt-Catalyzed Preparation of Arylindium Reagents. Anhydrous LiCl (42.4 mg, 1 mmol) was placed in a 10 mL Schlenk tube, dried under vacuum (1 mbar) at 150 °C for 1 h, and cooled to room temperature (20 °C) under N_2. To the Schlenk tube was added indium powder (230 mg, 2 mmol), and the tube was evacuated and backfilled with N_2 three times. The In/LiCl mixture was suspended with THF (1 mL), followed by the activation of In with allyl chloride (25 μL, 0.31 mmol) and stirring for 10 min. Then bathophenanthroline (16.8 mg, 0.05 mmol) and $CoBr_2$ (10.9 mg, 0.05 mmol) were added sequentially. After the solution was stirred for an additional 10 min, an aryl halide (1 mmol) was added in one portion. The reaction was stirred at 80 or 100 °C and monitored by GC analysis. After complete conversion of the starting material, the reaction was cooled to 0 °C, quenched by the addition of I_2 (0.38 g, 1.5 mmol), and then stirred at room temperature for 1 h. The resulting mixture was analyzed by GC using *n*-tridecane as an internal standard to determine the yield of the arylindium reagent. Note that, for some cases (**4m** and Scheme 2b, R = Ac), indium was activated by $BrCH_2CH_2Br$ (5 μL, 0.05 mmol) and Me_3SiCl (3 μL, 0.02 mmol) instead of allyl chloride.

Palladium-Catalyzed Cross-Coupling of Arylindium Reagents. *Procedure A.* An as-prepared arylindium reagent was diluted by the addition of THF (0.8 mL) at room temperature, followed by stirring for 15 min. The mixture was allowed to stand for 10 min, and the supernatant solution was carefully transferred via syringe to another Schlenk tube, which had been charged with an aryl iodide, $Pd(OAc)_2$ (4 mol %), S-Phos (8 mol %), and THF (0.5 mL). The resulting mixture was heated to 80 °C and stirred for 12−22 h. The reaction was allowed to cool to room temperature, diluted with EtOAc (5 mL), and quenched by the addition of saturated aqueous solution of NH_4Cl (1 mL). The aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel chromatography to afford a cross-coupling product.

Palladium-Catalyzed Cross-Coupling of Arylindium Reagents. *Procedure B.* An as-prepared arylindium reagent was diluted by the addition of THF (1.0 mL) at room temperature, followed by stirring for 15 min. The mixture was allowed to stand for 10 min, and the supernatant solution was carefully transferred via syringe to another Schlenk tube, which had been charged with an aryl iodide, $Pd(OAc)_2$ (4 mol %), S-Phos (8 mol %), and NMP (0.8 mL). The resulting mixture was heated to 80 °C and stirred for 12−20 h. Workup and purification were performed similarly as described for procedure A.

*3′,5′-Dichloro(1,1′-biphenyl)-3-carbonitrile (**5a**).* The reaction of 3,5-dichlorophenylindium reagent (Table 1, entry 5) was performed according to procedure A using 3-iodobenzonitrile (151.2 mg, 0.66 mmol) with a reaction time of 21 h. Silica gel chromatography (eluent: hexane/EtOAc = 9/1) of the crude product afforded the title compound as a white solid (134.5 mg, 82%): mp = 252−253 °C; R_f 0.51 (hexane/EtOAc = 9/1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65 (t, J = 1.8 Hz, 1H), 7.68 (t, J = 8.0 Hz, 1H), 7.86 (d, J = 1.8 Hz, 2H), 7.89−7.90 (m, 1H), 8.09−8.11 (m, 1H), 8.28−8.29 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 112.2, 118.5, 125.7 (2C), 127.7, 130.1, 130.8, 131.8, 132.1, 134.8 (2C), 138.2, 141.4; HRMS (ESI+) calcd for $C_{13}H_7Cl_2NNa$ $[M + Na]^+$ 269.9853, found 269.9852.

*Ethyl (1,1′-Biphenyl)-4-carboxylate (**5b**).* The reaction of phenylindium reagent (Figure 1, **4a**) was performed according to the procedure A using ethyl 4-iodobenzoate (126 μL, 0.75 mmol) with a reaction time of 21 h. Silica gel chromatography (eluent: hexane/EtOAc = 19/1) of the crude product afforded the title compound as a colorless solid (161.2 mg, 95%). The ^{1}H and ^{13}C NMR spectra showed good agreement with the literature data (see the Supporting Information).[15]

*5,6-Dimethoxy(1,1′:4′,1″-terphenyl)-3-carbaldehyde (**5c**).* The reaction of 4-biphenylindium reagent (Figure 1, **4c**) was performed according to procedure A using 3-iodo-4,5-dimethoxybenzaldehyde (219 mg, 0.75 mmol) with a reaction time of 19 h. Silica gel chromatography (eluent: hexane/EtOAc = 4/1) of the crude product afforded the title compound as a brown solid (215.0 mg, 90%): mp = 97−98 °C; R_f 0.30 (hexane/EtOAc = 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H), 3.99 (s, 3H), 7.36−7.40 (m, 1H), 7.45−7.49 (m, 3H), 7.54 (d, J = 1.8 Hz, 1H), 7.63−7.70 (m, 6H), 9.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2, 61.0, 109.7, 127.1 (2C), 127.2 (2C), 127.4, 127.6, 128.9 (2C), 129.7 (2C), 132.6, 135.8, 136.1, 140.6, 140.7, 152.2, 153.9, 191.3; HRMS (ESI+) calcd for $C_{21}H_{19}O_3$ $[M + H]^+$ 319.1334, found 319.1336.

*1-[4′-Methoxy(1,1′-biphenyl)-4-yl]ethanone (**5d**).* The reaction of 4-methoxyphenylindium reagent (Figure 1, **4d**) was performed according to procedure A using 4-iodoacetophenone (162.4 mg, 0.66 mmol) with a reaction time of 17 h. Silica gel chromatography (eluent: hexane/EtOAc = 4/1) of the crude product afforded the title compound as a white solid (127.1 mg, 85%). The ^{1}H and ^{13}C NMR spectra showed good agreement with the literature data (see the Supporting Information).[16]

*1-[4′-Fluoro(1,1′-biphenyl)-4-yl]ethanol (**5e**).* The reaction of 4-fluorophenylindium reagent (Figure 1, **4g**) was performed according to procedure B using 1-(4-iodophenyl)ethanol (188.5 mg, 0.76 mmol) with a reaction time of 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 3/2) of the crude product afforded the title compound as a light brown solid (156.2 mg, 95%): mp = 100−102 °C; R_f 0.58 (hexane/EtOAc = 3/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (d, J = 6.9 Hz, 3H), 2.04 (s, 1H), 4.95 (q, J = 5.9 Hz, 1H), 7.10−7.16 (m, 2H), 7.44 (d, J = 8.2 Hz, 2H), 7.52−7.56 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4, 70.3, 115.8 (d, $^2J_{C-F}$ = 21.9 Hz, 2C), 126.1 (2C), 127.3 (2C), 128.7 (d, $^3J_{C-F}$ = 8.6 Hz, 2C), 137.1 (d, $^4J_{C-F}$ = 2.9 Hz), 139.6, 145.0, 162.6 (d, $^1J_{C-F}$ = 245.2 Hz); HRMS (ESI+) calcd for $C_{14}H_{13}OFNa$ $[M + Na]^+$ 239.0848, found 239.0844.

*1-[4′-(Trifluoromethyl)(1,1′-biphenyl)-4-yl]ethanone (**5f**).* The reaction of 4-trifluoromethylphenylindium reagent (Figure 1, **4h**) was performed according to procedure A using 4-iodoacetophenone (172.2 mg, 0.70 mmol) with a reaction time of 18 h. Silica gel chromatography (eluent: hexane/EtOAc = 19/1) of the crude product afforded the title compound as a white solid (170.2 mg, 92%). The ^{1}H and ^{13}C NMR spectra showed good agreement with the literature data (see the Supporting Information).[17]

*Ethyl 4-(Phenanthren-9-yl)benzoate (**5g**).* The reaction of 9-phenanthrenylindium reagent (Figure 1, **4k**) was performed according to procedure A using ethyl-4-iodobenzoate (116 μL, 0.69 mmol) with a reaction time of 18 h. Silica gel chromatography (eluent: hexane/

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EtOAc = 19/1) of the crude product afforded the title compound as a white solid (164.4 mg, 73%): mp = 112−113 °C; R_f 0.35 (hexane/EtOAc = 19/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (t, J = 7.1 Hz, 3H), 4.46 (q, J = 7.1 Hz, 2H), 7.53−7.57 (m, 1H), 7.62−7.72 (m, 6H), 7.86 (d, J = 8.2 Hz, 1H), 7.91 (d, J = 7.8 Hz, 1H), 8.21 (d, J = 8.2 Hz, 2H), 8.73 (d, J = 7.8 Hz, 1H), 8.79 (d, J = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 61.3, 122.8, 123.2, 126.8, 126.9 (2C), 127.1, 127.2, 127.8, 129.0, 129.7, 129.8 (2C), 130.3 (3C), 130.8, 130.9, 131.5, 137.9, 145.7, 166.8; HRMS (ESI+) calcd for $C_{23}H_{19}O_2$ $[M + H]^+$ 327.1385, found 327.1389.

*4′-Vinyl(1,1′-biphenyl)-3-amine (**5h**).* The reaction of 4-styrylindium reagent (Figure 1, **4l**) was performed according to procedure B using 3-iodoaniline (70 μL, 0.58 mmol) with a reaction time of 20 h. Silica gel chromatography (eluent: hexane/EtOAc = 3/2) of the crude product afforded the title compound as a light brown solid (72.5 mg, 64%): mp = 69−70 °C; R_f 0.56 (hexane/EtOAc = 3/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (brs, 2H), 5.23 (d, J = 11.0 Hz, 1H), 5.77 (d, J = 17.4 Hz, 1H), 6.63 (d, J = 7.8 Hz, 1H), 6.72 (dd, J = 17.6, 11.0 Hz, 1H), 6.87 (s, 1H), 6.97 (d, J = 7.8 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 7.42−7.46 (m, 2H), 7.48−7.52 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.8, 113.9, 114.4, 117.6, 126.7 (2C), 127.3 (2C), 129.8, 136.6, 136.7, 140.8, 141.9, 146.8; HRMS (ESI+) calcd for $C_{14}H_{14}N$ $[M + H]^+$ 196.1129, found 196.1135.

*3′-Nitro(1,1′-biphenyl)-4-carbaldehyde (**5i**).* The reaction of 4-formylphenylindium reagent (Figure 1, **4m**) was performed according to procedure B using 3-iodonitrobenzene (154.4 mg, 0.62 mmol) with a reaction time of 16 h. Silica gel chromatography (eluent: hexane/EtOAc = 9/1) of the crude product afforded the title compound as a white solid (109.8 mg, 78%). The ^{1}H and ^{13}C NMR spectra showed good agreement with the literature data (see the Supporting Information).[18]

*1-[4-(Pyridin-3-yl)phenyl]ethanone (**5j**).* The reaction of 4-acetylphenylindium reagent (Figure 1, **4n**) was performed according to the procedure B using 3-iodopyridine (131.2 mg, 0.64 mmol) with a reaction time of 18 h. Silica gel chromatography (eluent: hexane/EtOAc = 3/2) of the crude product afforded the title compound as a faint yellow solid (117.4 mg, 93%). The ^{1}H and ^{13}C NMR spectra showed good agreement with the literature data (see the Supporting Information).[19]

*4′-Benzoyl-6-hydroxy-5-methoxy(,1′-biphenyl)-3-carbaldehyde (**5k**).* The reaction of 4-benzoylphenylindium reagent (Figure 1, **4o**) was performed according to procedure B using 5-iodovaniline (187.7 mg, 0.675 mmol) with a reaction time of 18 h. Silica gel chromatography (eluent: hexane/EtOAc = 3/2) of the crude product afforded the title compound as a colorless gummy oil (139.1 mg, 62%): R_f 0.33 (hexane/EtOAc = 3/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (s, 3H), 7.02 (s, 1H), 7.43−7.49 (m, 3H), 7.55−7.60 (m, 2H), 7.75 (d, J = 8.2 Hz, 2H), 7.82 (d, J = 8.2 Hz, 2H), 7.87 (d, J = 8.2 Hz, 2H), 9.87 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.5, 108.2, 126.5, 128.3, 128.4 (2C), 129.1 (2C), 129.4, 130.1 (2C), 130.2 (2C), 132.5, 136.5, 137.6, 140.7, 147.7, 149.1, 190.9, 196.4; HRMS (ESI+) clcd for $C_{21}H_{17}O_4$ $[M + H]^+$ 333.1127, found 333.1135.

*4-(1H-Indol-5-yl)benzonitrile (**5l**).* The reaction of 4-cyanophenylindium reagent (Figure 1, **4p**) was performed according to procedure B using 5-iodoindole(162.8 mg, 0.67 mmol) with a reaction time of 19 h. Silica gel chromatography (eluent: hexane/EtOAc = 3/2) of the crude product afforded the title compound as a white solid (112.6 mg, 77%). The ^{1}H and ^{13}C NMR spectra showed good agreement with the literature data (see the Supporting Information).[20]

*Ethyl 3′-(Trifluoromethyl)(1,1′-biphenyl)-2-carboxylate (**5m**).* The reaction of 4-ethoxycarbonylphenylindium reagent (Figure 1, **4q**) was performed according to the procedure A using 3-iodobenzotrifluoride (92 μL, 0.64 mmol) with a reaction time of 12 h. Silica gel chromatography (eluent: hexane/EtOAc = 19/1) of the crude product afforded the title compound as a colorless oil (171.4 mg, 91%): R_f 0.33 (hexane/EtOAc = 19/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, J = 7.1 Hz, 3H), 4.09 (q, J = 7.1 Hz, 2H), 7.35 (dd, J = 7.5, 1.2 Hz, 1H), 7.45−7.63 (m, 6H), 7.91 (dd, J = 7.8, 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 61.2, 124.1 (q, $^3J_{C-F}$ = 3.8 Hz), 124.3 (q, $^1J_{C-F}$ = 272 Hz), 125.5 (q, $^3J_{C-F}$ = 3.8 Hz), 128.1, 128.6, 130.4, 130.6 (q, $^2J_{C-F}$ = 32 Hz), 130.8, 131.2, 131.7, 132.0, 141.2, 142.6, 168.3; HRMS (ESI+) calcd for $C_{16}H_{14}F_3O_2$ $[M + H]^+$ 295.0946, found 295.0940.

*3-(Quinolin-3-yl)benzonitrile (**5n**).* The reaction of 3-quinolylindium reagent (Figure 1, **4s**) was performed according to procedure A using 3-iodobenzonitrile (155.7 mg, 0.68 mmol) with a reaction time of 17 h. Silica gel chromatography (eluent: hexane/EtOAc = 3/2) of the crude product afforded the title compound as a faint yellow solid (147.2 mg, 94%): mp = 141−142 °C; R_f 0.36 (hexane/EtOAc = 3/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−7.64 (m, 2H), 7.69−7.77 (m, 2H), 7.88 (d, J = 8.2 Hz, 1H), 7.92 (dt, J = 7.8, 1.6 Hz, 1H), 7.96 (t, J = 1.4 Hz, 1H), 8.14 (d, J = 8.2 Hz, 1H), 8.28 (d, J = 1.8 Hz, 1H), 9.10 (d, J = 2.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 113.6, 118.6, 127.6, 127.8, 128.3, 129.5, 130.2, 130.3, 131.0, 131.6, 131.7, 131.8, 133.9, 139.4, 147.9, 149.2; HRMS (ESI+) calcd for $C_{16}H_{11}N_2$ $[M + H]^+$ 231.0922, found 231.0927.

*Ethyl 4-(Thiophene-2-yl)benzoate (**5o**).* The reaction of 2-thienylindium reagent (Figure 1, **4t**) was performed according to procedure A using ethyl 4-iodobenzoate (124 μL, 0.74 mmol) with a reaction time of 16 h. Silica gel chromatography (eluent: hexane/EtOAc = 19/1) of the crude product afforded the title compound as a colorless solid (156.4 mg, 91%). The ^{1}H and ^{13}C NMR spectra showed good agreement with the literature data (see the Supporting Information).[21]

*N-[3-(5-Acetylthiophene-2-yl)phenyl]acetamide (**5p**).* The reaction of 2-(5-acetyl)thienylindium reagent (Scheme 2b, R = Ac) was performed according to the procedure A using *N*-(3-iodophenyl)acetamide (120.1 mg, 0.46 mmol) with a reaction time of 20 h. Silica gel chromatography (eluent: hexane/EtOAc = 1/4) of the crude product afforded the title compound as a yellow solid (94.3 mg, 79%): mp = 173−174 °C; R_f 0.34 (hexane/EtOAc = 1/4); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.09 (s, 3H), 2.55 (s, 3H), 7.39 (t, J = 7.8 Hz, 1H), 7.45 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 4.1 Hz, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.93 (d, J = 3.7 Hz, 1H), 8.05 (s, 1H), 10.12 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.0, 26.3, 116.2, 119.6, 120.5, 124.8, 129.7, 133.0, 135.0, 140.1, 142.7, 151.3, 168.6, 190.5; HRMS (ESI+) calcd for $C_{14}H_{14}NO_2S$ $[M + H]^+$ 260.0745, found 260.0742.

*1,5-Dimethyl-2-phenyl-4-(thiophene-3-yl)-1H-pyrazol-3(2H)-one (**5q**).* The reaction of 3-thienylindium reagent (Figure 1, **4u**) was performed according to procedure A using iodoantipyrine (216.7 mg, 0.69 mmol) with a reaction time of 22 h. Silica gel chromatography (eluent: hexane/EtOAc = 3/2) of the crude product afforded the title compound as a white solid (153.0 mg, 82%): mp = 157−158 °C; R_f 0.19 (hexane/EtOAc = 3/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.11 (s, 3H), 7.26−7.30 (m, 1H), 7.34−7.36 (m, 1H), 7.43−7.48 (m, 5H), 7.66−7.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.7, 36.2, 107.1, 122.0, 124.1 (2C), 125.1, 126.6, 127.1, 129.3 (2C), 131.6, 135.4, 151.5, 164.6; HRMS (ESI+) calcd for $C_{15}H_{15}N_2OS$ $[M + H]^+$ 271.0905, found 271.0914.

^{1}H and ^{13}C NMR Analysis of Phenylindium Reagents. *Phenylindium Reagent **4a**.* The reagent **4a** was prepared according to the general procedure, followed by removal of most of the THF solvent under vacuum. The NMR sample was prepared by dissolving the residue with THF-d_8 (conc = ca. 0.2 M): ^{1}H NMR (400 MHz, THF-d_8) δ 7.01−7.03 (m), 7.07−7.11 (m), 7.14−7.18 (m), 7.24−7.25 (m), 7.46−7.48 (m, 1H), 7.59−7.61 (m, 1H); ^{13}C NMR (100 MHz, THF-d_8) δ 127.1, 127.5, 128.1, 128.2, 137.5, 138.5. The signal of the *ipso* carbon was not detected.

Phenylindium Reagent Prepared from a 1:1 Mixture of $InCl_3$ and PhMgBr. To a solution of $InCl_3$ (466 mg, 2.1 mmol) in THF (4.6 mL) was added a THF solution of PhMgBr (1.49 M, 1.4 mL, 2 mmol) at −78 °C. The reaction was stirred for 2 h, and then most of the solvent was removed under vacuum. The NMR sample was prepared by dissolving the residue with THF-d_8 (conc = ca. 0.3 M): ^{1}H NMR

(400 MHz, THF-d_8) δ 7.12−7.15 (t, J = 7.9 Hz, 1H), 7.17−7.21 (t, J = 7.8 Hz, 2H), 7.45−7.48 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, THF-d_8) δ 128.2, 128.4, 137.4. The signal of the *ipso* carbon was not detected.

Phenylindium Reagent Prepared from a 1:2 Mixture of $InCl_3$ and PhMgBr. The reagent and the NMR sample were prepared by a similar procedure as described above: ^{1}H NMR (400 MHz, THF-d_8) δ 7.01−7.05 (t, J = 7.3 Hz, 1H), 7.08−7.13 (t, J = 7.3 Hz, 2H), 7.58−7.61 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, THF-d_8) δ 127.2, 127.6, 138.4. The signal of the *ipso* carbon was not detected.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra for the phenylindium reagents and the compounds **5a**−**q**. This material is available free of charge via the Internet at http://pubs.acs.org.

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$$12PhX + 8In + InX_3 \rightarrow 6PhInX_2 + 3Ph_2InX$$

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