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Enantioselective Nickel-Catalyzed Cross-Coupling Reactions of Trialkynylindium Reagents with Racemic Secondary Benzyl Bromides

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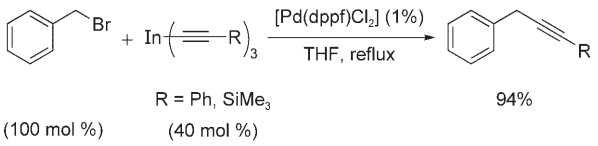
Abstract: The first enantioselective sp–sp^3 cross-coupling reaction between alkynyl organometals and racemic benzyl bromides is reported. The coupling is performed at room temperature by using $NiBr_2$·diglyme and (*S*)-(*i*Pr)-Pybox as the catalytic system and trialkynylindium reagents as nucleophiles. The reaction is stereoconvergent, both enantiomers of the racemic benzyl bromide are converted into one enantiomer of the product, and stereospecific. The reaction takes place efficiently in good yields and with high atom economy, as the triorganoindium reagents transfer the three organic groups attached to indium (only 40 mol% of R_3In is used).

Keywords: asymmetric catalysis · benzyl bromides · cross-coupling reactions · indium organometallics · nickel catalysis

Introduction

Indium organometallics are useful reagents in metal-catalyzed cross-coupling reactions.[1,2] The main features of indium reagents are their high versatility, their non-toxicity, and their ability to transfer all three metal-attached groups to the electrophile. A representative example of this usefulness is the particularly effective sp–sp^3 palladium-catalyzed cross-coupling reaction between alkynylindium reagents and benzyl halides (Scheme 1).[1b]



Scheme 1. Palladium-catalyzed cross-coupling reactions of trialkynylindium reagents with benzyl bromide.

Metal-catalyzed cross-coupling reactions using alkyl halides have traditionally faced significant limitations, associated with low reactivity in the oxidative addition step and undesired β-hydride elimination.[3] Benzyl halides are particularly interesting alkyl electrophiles, as they readily undergo oxidative addition, and do not suffer β-hydride elimination. Their utility in cross-coupling reactions has been proven with aryl and alkenyl metals,[4] but the alkynylation of benzyl halides is still a difficult task.[5] In 2001, our group reported the first efficient coupling reaction between primary benzyl halides and alkynyl organometallics by using organoindium reagents.[1b] Recently, Negishi has extended this reactivity to organozinc reagents.[5b] Nevertheless, the palladium-catalyzed cross-coupling of alkynylindium compounds with primary benzyl halides constitutes the method of choice to perform the sp-benzyl coupling in organic synthesis.[6] Despite of the interest, the reactivity with secondary benzyl halides still remains undeveloped. In this paper, we describe the first catalytic enantioselective sp–sp^3 cross-coupling reaction between alkynylindium reagents and racemic secondary benzyl electrophiles.

Results and Discussion

According to our previous experience, we explored the reaction of a secondary benzyl halide, such as α-methylbenzyl-bromide (**1**) with tri(phenylethynyl)indium (40 mol%) in refluxing THF by using [Pd(dppf)$_2$] (dppf = 1,1′-bis(diphenylphosphino)ferrocene; 2 mol%) as the catalyst. Under these reaction conditions, the cross-coupling product **2** was obtained in 65% yield (Table 1, entry 1), a slightly lower yield than that obtained by using the primary benzyl bromide. This result can be reasonably attributed to the lower reactiv-

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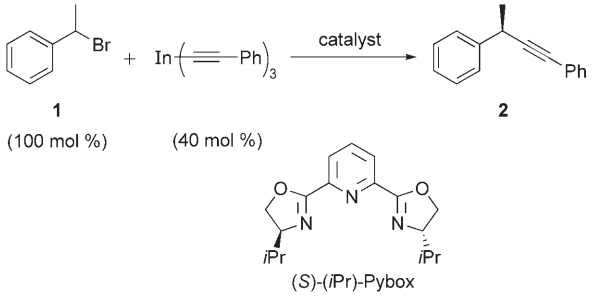
Table 1. Reaction of **1** with tri(phenylethynyl)indium under various catalytic systems.



Entry	Catalyst	Solvent	T [°C]	t [h]	Yield [%]	*ee* [%][a]
1	[Pd(dppf)Cl_2] (2%)	THF	reflux	21	65	–
2	[Pd_2(dba)$_3$] (2%), (R_p,*R*)-Josiphos I (4%)	THF	reflux	24	<5	–
3	[Pd_2(dba)$_3$] (2%), (R_p,*R*,*R*,R_p)-Mandyphos III (4%)	THF	reflux	24	<5	–
4	[Pd_2(dba)$_3$] (2%), (*R*)-BINAP (4%)	THF	reflux	24	22	10
5	$NiBr_2$·diglyme (4%), (*S*)-(*i*Pr)-Pybox (8%)	THF	reflux	24	11	–
6	$NiBr_2$·diglyme (4%), (*S*)-(*i*Pr)-Pybox (8%)	DMA/THF 1:1	RT	20	42	87
7	[Ni(cod)$_2$] (4%), (*S*)-(*i*Pr)-Pybox (8%)	DMA/THF 1:1	RT	20	30	82
8	$NiBr_2$·diglyme (10%), (*S*)-(*i*Pr)-Pybox (13%)	DMA/THF 1:1	RT	140	70	84
9	$NiBr_2$·diglyme (4%), (*S*)-(Ph)-Pybox (8%)	DMA/THF 1:1	RT	72	12	–
10	$NiBr_2$·diglyme (10%), (*S*)-(*i*Pr)-Pybox (13%)	DMA/THF 1:1	40	120	45	87

[a] The enantiomeric excess was determined by HPLC analysis.

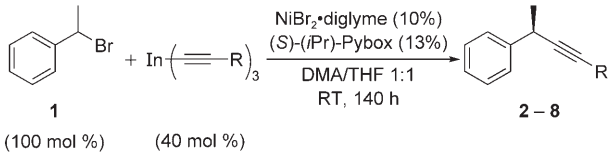
ity of the secondary center toward oxidative addition and the competitive β-hydride elimination process. Based on these results, we looked for a ferrocenyl-based chiral catalyst that could allow the reaction enantioselectively. To this end, we tried the reaction by using the commercially available chiral ligands (R_p,*R*)-Josiphos I and (R_p,*R*,*R*,R_p)-Mandyphos III (2–4 mol%) combined with [Pd_2(dba)$_3$] (dba = (*E*,*E*)-dibenzylideneacetone; 2 mol%) as a palladium source. Unfortunately, we observed lower reactivity and the coupling product **2** was only obtained in very low yields (Table 1, entries 2 and 3). The reaction with other chiral bidentate phosphine ligands, such as (*R*)-BINAP (BINAP = 2*R*,3*S*,2,2′-bis(diphenylphosphino)-1,1′-binaphthyl; 4 mol%), afforded the reaction product in low yield and enantioselectivity (22%, 10% *ee*; Table 1, entry 4).[7]

These results led us to assay the reaction under nickel catalysis. In this field, interesting sp^3–sp^3 cross-coupling reactions have been described by using nickel catalysts and Pybox-type ligands.[8] In our first attempt, the reaction of racemic α-methylbenzylbromide (**1**) with tri(phenylethynyl)-indium (40 mol%) by using $NiBr_2$·diglyme (4 mol%) and (*S*)-(*i*Pr)-Pybox (8 mol%), in THF at reflux, afforded the cross-coupling product **2** in 11% yield after a 20 h reaction, with low conversion of the starting benzyl bromide and with considerable amounts of the diyne resulting from reductive dimerization of the alkynylindium reagent (Table 1, entry 5). When the same reaction was performed at room temperature by using a 1:1 mixture of DMA/THF (DMA = dimethylacetamide) as the solvent, we reduced the amount of diyne and the yield of the coupling product **2** rose up to 42%, with high enantioselectivity (87% *ee*; Table 1, entry 6).[9] Encouraged by these results, we set out to optimize the reaction conditions. The use of other nickel catalysts, such as [Ni(cod)$_2$] (cod = 1,5-cyclooctadienyl) did not improve the yield, but using $NiBr_2$·diglyme at room temperature for 140 h, the reaction was complete and the coupling product **2** was obtained in 70% yield with high enantioselectivity (84% *ee*, Table 1, entry 8).[10] Other chiral ligands, such as (*S*)-(Ph)-Pybox, or different reaction conditions, led to lower yields, although maintaining the same level of enantioselectivity (≈85% *ee*; Table 1, entries 9 and 10).

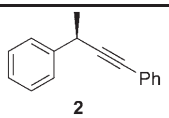
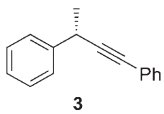
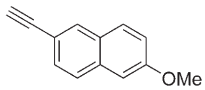
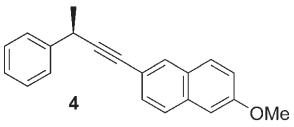
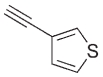
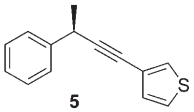
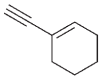
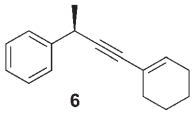
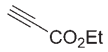
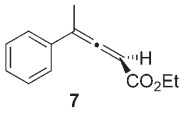
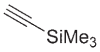
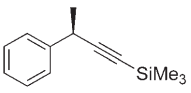
This novel reaction constitutes, to the best of our knowledge, the first enantioselective alkynyl–alkyl (sp–sp^3) cross-coupling. Other noteworthy features of this approach are: 1) that the reaction is stereoconvergent, that is, both enantiomers of the racemic starting material are preferentially transformed into one enantiomer of the product, 2) that the reaction shows high atom economy, that is, the organoindium reagent transfers more than one of its organic groups to the electrophile, 3) that all the catalyst components are commercially available and air-stable, and 4) that the reaction proceeds at room temperature without any special requirements. Additionally, we also found that the reaction is stereospecific; the reaction with the *R* enantiomer of (*i*Pr)-Pybox afforded **3** (enantiomer of **2**) in a similar yield and enantioselectivity (67% yield, 82% *ee*; Table 2, entry 2).

After having established optimal reaction conditions, we proceeded to extend the reaction to other alkynylindium reagents and various benzyl bromides. In this study, we found that reaction of α-methylbenzylbromide (**1**) with tri[(6-methoxy-2-naphthalenyl)ethynyl]indium or tri[(3-thienyl)ethynyl]indium gives the corresponding coupling products (**4** and **5**, respectively) in satisfactory yields and with high enantioselectivities (60–65% yield, 85–87% *ee*; Table 2, entries 3 and 4). The reaction of reagents that transfer a conjugate enyne moiety afforded the coupling product in lower yield, although maintaining a similar level of enantioselectivity (35% yield, 84% *ee*; Table 2, entry 5). Interestingly, the re-

Table 2. Results of the nickel-catalyzed cross-coupling reaction of trialkynylindium reagents with **1**.



1 (100 mol %) (40 mol %) **2 – 8**

Entry	Alkyne	Product	Yield [%]	*ee* [%]
1		 **2**	70	84
2[a]		 **3**	67	82
3		 **4**	60	85[b]
4		 **5**	65	87[b]
5		 **6**	35	84[b]
6		 **7**	30	77[b]
7		 **8**	57	–[c]

[a] Reaction performed with (*R*)-(*i*Pr)-Pybox (13 mol %) as the ligand. [b] The absolute configuration of the reaction product was not determined. [c] The percentage *ee* could not be determined by HPLC analysis.

action of **1** with the trialkynylindium derivative of ethyl propiolate afforded the allene **7** as the only product in 30% yield with good enantioselectivity (77% *ee*). The formation of related allenes was also observed by Buchwald in the Heck alkynylation of benzyl chlorides at high temperatures by using an excess of base.[5d] On the other hand, the reaction of the benzyl bromide **1** with alkynylsilanes, such as tris(trimethylsilylethynyl)indium, gave the corresponding cross-coupling product **8** in 57% yield (Table 2, entry 7).

During our work, we also explored the reaction of trialkynylindium reagents with other benzylic substrates (Table 3). The reaction of the previously prepared trialkynylindium reagents with 1-bromoindane (**9**), under the conditions described above, also afforded the corresponding cross-coupling products in satisfactory yields and with high enantioselectivities (40–65% yield, 80–84% *ee*; Table 3, entries 1–4). In these cases, the lower yields can be attributed to the lower stability of the reaction products. The reactivity of the benzyl bromide 1-bromobenzocyclobutene (**10**) was also studied. In these cases, the reactions with the various trialkynylindium reagents afforded stable coupling products, although with low enantioselectivity (57–82% yield, 6–7% *ee*; Table 3, entries 5–8).

Although the mechanism for this enantioselective cross-coupling reaction has not been established, according to previous mechanistic studies about the oxidative addition of Pd^0 to benzyl halides,[11] the stereoconvergence of the reaction could be explained by two possible pathways after the formation of the Ni–C_α bond: 1) a nucleophilic exchange process with Ni^0 to afford the most stable or reactive of the two diastereomeric intermediates of the nickel complex with the chiral ligand or 2) a rearrangement through a planar sp^2-benzyl species. In this last situation, the generation of a benzyl radical associated with a nickel(I) complex could be proposed, in a similar scenario to that proposed by Stille[12] and Vivic[13] for nickel-catalyzed cross-coupling reactions. This proposal could also explain the lack of enantioselectivity when 1-bromobenzocyclobutene (**10**) is used as the electrophile, because of the difficulty of isomerization through a planar sp^2-benzocyclobutene intermediate.

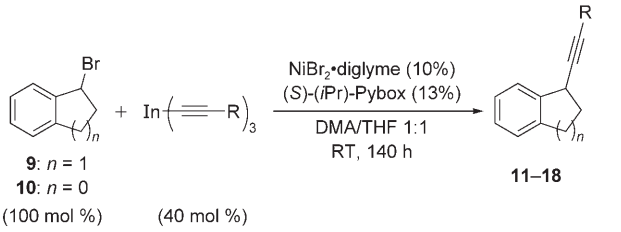
Conclusion

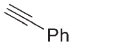
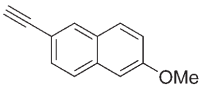
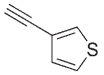
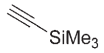
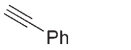
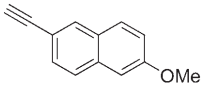
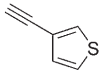
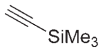
We have described the first enantioselective cross-coupling reaction between racemic secondary benzyl bromides and trialkynylindium reagents by using a commercially available catalytic system. The reaction occurs efficiently, as indium organometallics can transfer more than one organic group to the electrophile, and with high enantioselectivity. Current efforts are focused towards the application of this methodology to other organoindium reagents and different secondary electrophiles.

Experimental Section

General methods: All reactions were conducted in flame-dried glassware under a positive pressure of argon. Reaction temperatures refer to external bath temperatures. THF was dried by distillation from the sodium ketyl of benzophenone. All other commercially available reagents were used as received. Racemic 1-bromoindane (**9**) was prepared by following a previously published procedure.[8b] Liquid reagents or reagent solutions were added by syringe or cannula. Organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated by using a rotary evaporator at aspirator pressure (20–30 mmHg). TLC was effected on silica gel 60 F_{254} (layer thickness 0.2 mm) and components were located by observation under UV light and/or by treating the plates with a phosphomolybdic acid or *p*-anisaldehyde reagent followed by heating. Flash chromatography was performed on silica gel 60 (230–400 mesh) by Still's method.[14] NMR spectra were performed in Bruker Avance 300 or Bruker Avance 500 spectrometers in $CDCl_3$ by using the residual solvent signal at $\delta =$ 7.26 (^{1}H) or 77.0 ppm (^{13}C) as internal standard. DEPT was used to assign carbon types. LR-EIMS were measured on a Thermo Finnigan Trace MS spectrometer at 70 eV. The HRMS were measured on a Thermo Finnigan MAT 95XP spectrometer. IR spectra were taken with a Bruker Vector 22. Optical rotation values were determined at room tem-

Table 3. Results of the nickel-catalyzed cross-coupling reaction of trialkynylindium reagents with benzyl bromides **9** and **10**.



Entry	Benzyl bromide	Alkyne	Product[a]	Yield [%]	*ee* [%]
1	**9**		**11**	65	82
2			**12**	60	81
3			**13**	56	84
4			**14**	40	80
5	**10**		**15**	81	6
6			**16**	57	6
7			**17**	65	7
8			**18**	82	7

[a] The absolute configuration of the reaction products was not determined.

perature in a JASCO DIP-1000 Digital polarimeter. HPLC analyses were performed on a Hewlett Packard HP1100 Series system by using Daicel Chiralcel columns.

Trialkynylindium reagents: According to previously reported methods,[1b] trialkynylindium compounds were prepared by treatment of the corresponding alkynyllithium reagents (3 equiv) with $InCl_3$ (1.1 equiv) in dry THF at −78 °C and warming to room temperature. Alkynyllithium reagents were prepared from the corresponding alkynes (1.0 equiv) by treatment with *n*BuLi (1.0 equiv) in dry THF at −78 °C and warming to room temperature, except in the case of ethyl propiolate and 2-ethynyl-6-methoxynaphthalene which were metallated and used at −78 °C.

General procedure for the nickel-catalyzed enantioselective cross-coupling reaction: A solution of $NiBr_2$•diglyme (25 mg, 0.07 mmol) and (*S*)-(*i*Pr)-Pybox (25 mg, 0.09 mmol) in dry DMA (4 mL) was placed in an argon-filled Schlenk tube. After stirring for 15 min at room temperature, the benzyl bromide (0.7 mmol) and a solution of R_3In in dry THF (0.07 M, 0.28 mmol, 4 mL) were successively added, and the resulting mixture was stirred at room temperature for 140 h. The reaction was quenched by addition of a few drops of MeOH and diluted with Et_2O (25 mL). The organic phase was washed successively with aqueous HCl (5%, 30 mL), saturated aqueous $NaHCO_3$ (30 mL) and brine (30 mL), then dried and concentrated. The residue was purified by flash chromatography and enantiomer excess was determined by HPLC on Daicel Chiralpak columns.

(1-Methyl-3-phenyl-2-propynyl)benzenes 2 and 3:[15] According to the general procedure, the reaction of (±)-α-methylbenzylbromide (**1**, 125 mg, 0.678 mmol) with tri(phenylethynyl)indium (0.27 mmol) afforded, after purification by column chromatography (hexanes), (1-methyl-3-phenyl-2-propynyl)benzenes **2** and **3** as a colorless oil. With (*S*)-(*i*Pr)-Pybox as the catalyst, 97 mg of **2** (70%, 84% *ee*) was formed; however, with (*R*)-(*i*Pr)-Pybox as the catalyst, 93 mg of **3** (67%, 82% *ee*) was formed. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.53–7.30 (m, 10H), 4.04 (q, ^3J(H,H) = 7.1 Hz, 1H), 1.64 ppm (d, ^3J(H,H) = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 143.3 (C), 131.6 (2×CH), 128.5 (2×CH), 128.2 (2×CH), 127.7 (CH), 126.9 (2×CH), 126.6 (CH), 123.7 (C), 92.6 (C), 82.4 (C), 32.4 (CH), 24.5 ppm (CH_3); MS (70 eV, EI): *m*/*z* (%): 206 (53) [M^+], 191 [M^+-CH_3] (100), 189 (25), 165 (14), 128 (17); HRMS (EI): *m*/*z*: calcd for $C_{16}H_{14}$: 206.1090 [M^+]; found: 206.1090; HPLC: (Chiralcel OD-H): eluent: hexane, flow: 0.5 mL min^{-1}.

(*S*)-1,3-Diphenylbutane:[16] A mixture of (1-methyl-3-phenyl-2-propynyl)-benzene **2** (prepared from reaction of **1** with tri(phenylethynyl)indium and (*S*)-(*i*Pr)-Pybox as the catalyst, 39 mg, 0.368 mmol, 84% *ee*) and Pd/C (4 mg, 10% Pd) in hexane (2 mL) was hydrogenated for 5 h (balloon pressure). After this time, the mixture was filtered through a short pad of Celite. Concentration under reduced pressure afforded (*S*)-1,3-diphenylbutane (37 mg, 95%) as a colorless oil. $[\alpha]_D^{20} = +12.1$ cm^3 g^{-1} dm^{-1} (c = 1.85 g cm^{-3} in $CHCl_3$) (lit.[16] $[\alpha]_D^{20} = -11.6$ cm^3 g^{-1} dm^{-1} (c = 1.57 g cm^{-3} in $CHCl_3$)); data for the *R* enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.37–7.15 (m, 10H), 2.76 (m, 1H), 2.55 (m, 2H), 1.95 (m, 2H), 1.13 ppm (d, ^3J(H,H) = 6.7 Hz, 3H).

2-Methoxy-6-(3-phenyl-1-butynyl)naphthalene (4): According to the general procedure, the reaction of (±)-α-methylbenzylbromide (**1**, 128 mg, 0.692 mmol) with tri[(6-methoxy-2-naphthalenyl)ethynyl]indium (0.28 mmol) afforded, after purification by column chromatography (1% Et_2O/hexanes), compound **4** as a white solid (119 mg, 60%, 85% *ee*). M.p. 71–72 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.93–7.12 (m, 11H), 4.07 (q, ^3J(H,H) = 7.1 Hz, 1H), 3.94 (s, 3H), 1.66 ppm (d, ^3J-(H,H) = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 158.1 (C), 143.4 (C), 133.8 (C), 131.0 (CH), 129.3 (CH), 129.1 (CH), 128.6 (2×CH), 128.5 (C), 126.9 (2×CH), 126.6 (2×CH), 119.2 (CH), 118.6 (C), 105.7 (CH), 92.2 (C), 82.8 (C), 55.3 (CH_3), 32.5 (CH), 24.5 ppm (CH_3); MS (70 eV, EI): *m*/*z* (%): 286 [M^+] (75), 271 [M^+-CH_3] (100), 228 (40), 226 (22); HRMS (EI): *m*/*z*: calcd for $C_{21}H_{18}O$: 286.1352 [M^+]; found: 286.1365; HPLC (Chiralcel OJ): eluent: *i*PrOH/hexane (10:90), flow: 1.0 mL min^{-1}.

3-(3-Phenyl-1-butynyl)thiophene (5): According to the general procedure, the reaction of (±)-α-methylbenzylbromide (**1**, 130 mg, 0.700 mmol) with tri[(3-thienyl)ethynyl]indium (0.28 mmol) afforded, after purification by column chromatography (hexanes), compound **5** as a colorless oil (97 mg, 65%, 87% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.49–7.13 (m, 7H), 4.00 (q, ^3J(H,H) = 7.1 Hz, 1H), 1.61 ppm (d, ^3J-(H,H) = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 143.2 (C), 130.0 (CH), 128.5 (2×CH), 127.9 (CH), 126.9 (2×CH), 126.7 (CH), 125.0 (CH), 122.7 (C), 92.1 (C), 77.4 (C), 32.4 (CH), 24.4 ppm (CH_3); MS (70 eV, EI): *m*/*z* (%): 212 [M^+] (41), 197 [M^+-CH_3] (100), 178 (13); HRMS (EI): *m*/*z*: calcd for $C_{14}H_{12}S$: 212.0654 [M^+]; found: 212.066; HPLC (Chiralcel OD-H), eluent: hexane, flow: 0.5 mL min^{-1}.

(4-Cyclohexenyl-3-butyn-2-yl)benzene (6): According to the general procedure, the reaction of (±)-α-methylbenzylbromide (**1**, 130 mg, 0.700 mmol) with tri(1-cyclohexenylethynyl)indium (0.28 mmol) afforded, after purification by column chromatography (hexanes), compound **6** as a colorless oil (52 mg, 35%, 84% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.42–7.23 (m, 5H), 6.09 (m, 1H), 3.88 (q, ^3J(H,H) = 7.1 Hz, 1H), 2.18–2.07 (m, 4H), 1.69–1.57 (m, 4H), 1.51 ppm (d, ^3J(H,H) = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 143.7 (C), 133.7 (CH), 128.4 (2×CH), 126.9 (2×CH), 126.5 (CH), 120.9 (C), 89.7 (C), 84.2 (C), 32.3 (CH), 29.5 (CH_2), 25.6 (CH_2), 24.7 (CH_3), 22.4 (CH_2), 21.6 ppm (CH_2); MS (70 eV, EI): *m*/*z* (%): 210 [M^+] (56), 195 [M^+-CH_3] (72), 167 (100), 129 (62), 105 (76); HRMS (EI): *m*/*z*: calcd for $C_{16}H_{18}$: 210.1403 [M^+]; found: 210.1401; HPLC (Chiralcel OD-H): eluent: hexane, flow: 0.5 mL min^{-1}.

Ethyl 4-phenyl-2,3-pentadienoate (7):[17] According to the general procedure, the reaction of (±)-α-methylbenzylbromide (**1**, 130 mg, 0.700 mmol) with tri(3-methoxy-3-oxo-1-propynyl)indium (0.28 mmol) afforded, after purification by column chromatography (hexanes), compound **7** as a yellow oil (43 mg, 30%, 77% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.42–7.25 (m, 5H), 5.90 (q, J(H,H) = 2.9 Hz, 1H), 4.26

(q, ^3J(H,H) = 7.1 Hz, 2H), 2.22 (d, J(H,H) = 2.8 Hz, 3H), 1.30 ppm (t, ^3J(H,H) = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 213.9 (C), 165.7 (C), 134.4 (C), 128.6 (2×CH), 127.8 (CH), 126.2 (2×CH), 105.4 (C), 89.8 (CH), 60.9 (CH_2), 16.2 (CH_3), 14.3 ppm (CH_3); IR ($CHCl_3$): $\tilde{\nu}$ = 1948 (C=C=C), 1718 cm^{-1} (C=O); MS (70 eV, EI): m/z (%): 202 [M^+] (20), 174 (38), 158 (25), 129 (100); HRMS (EI): m/z: calcd for $C_{13}H_{14}O_2$: 202.0988 [M^+]; found: 202.0987; HPLC (Chiralcel OD-H): eluent: *i*PrOH/hexane 0.5:99.5, flow: 0.5 mL min^{-1}

(3-Phenyl-1-butynyl)trimethylsilane (8):[18] According to the general procedure, the reaction of (±)-α-methylbenzylbromide (**1**, 132 mg, 0.722 mmol) with tris(trimethylsilylethynyl)indium (0.29 mmol) afforded, after purification by column chromatography (hexanes), compound **8** as a colorless oil (82 mg, 57%). ^{1}H NMR (300 MHz, CD_2Cl_2, 25 °C): δ = 7.42–7.25 (m, 5H), 3.80 (q, ^3J(H,H) = 7.1 Hz, 1H), 1.49 (d, ^3J(H,H) = 7.1 Hz, 3H), 0.20 ppm (s, 9H); ^{13}C NMR (75 MHz, CD_2Cl_2, 25 °C): δ = 143.6 (C), 128.9 (2×CH), 127.3 (2×CH), 127.0 (CH), 109.9 (C), 86.4 (C), 32.2 (CH), 24.8 (CH_3), 0.2 ppm (3×CH_3); MS (70 eV, EI): m/z (%): 202 [M^+] (11), 187 [M^+-CH_3] (43), 159 (18), 105 (100); HRMS (EI): m/z: calcd for $C_{13}H_{18}Si$: 202.1172 [M^+]; found: 202.1168.

1-(Phenylethynyl)-2,3-dihydro-1*H*-indene (11):[19] According to the general procedure, the reaction of (±)-1-bromoindane (**9**, 140 mg, 95%, 0.675 mmol) with tri(phenylethynyl)indium (0.27 mmol) afforded, after purification by column chromatography (hexanes), compound **11** as a white solid (96 mg, 65%, 82% *ee*). M.p. 79–81 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.54–7.25 (m, 9H), 4.25 (t, ^3J(H,H) = 8.5 Hz, 1H), 3.12–2.90 (m, 2H), 2.63 (m, 1H), 2.25 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 143.6 (C), 142.9 (C), 131.7 (CH), 128.2 (CH), 127.7 (CH), 127.0 (CH), 126.6 (CH), 124.5 (CH), 124.3 (CH), 123.7 (C), 91.5 (C), 81.6 (C), 36.8 (CH), 34.4 (CH_2), 31.5 ppm (CH_2); MS (70 eV, EI): m/z (%): 218 [M^+] (100), 203 [M^+-CH_3] (51), 189 (14), 115 (34); HRMS (EI): m/z: calcd for $C_{17}H_{14}$: 218.1090 [M^+]; found: 218.1086; HPLC (Chiralcel OD-H): eluent: hexane, flow: 0.5 mL min^{-1}.

2-[(2,3-Dihydro-1*H*-inden-1-yl)ethynyl]-6-methoxynaphthalene (12): According to the general procedure, the reaction of (±)-1-bromoindane (**9**, 138 mg, 97%, 0.678 mmol) with tri[(6-methoxy-2-naphthalenyl)ethynyl]-indium (0.27 mmol) afforded, after purification by column chromatography (1% Et_2O/hexanes), compound **12** as a white solid (121 mg, 60%, 81% *ee*). M.p. 100–101 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.90–7.11 (m, 10H), 4.27 (t, ^3J(H,H) = 8.5 Hz, 1H), 3.93 (s, 3H), 3.12–2.90 (m, 2H), 2.64 (m, 1H), 2.26 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 158.1 (C), 143.7 (C), 143.0 (C), 133.8 (C), 131.0 (CH), 129.3 (CH), 129.2 (CH), 128.5 (C), 127.1 (CH), 126.6 (2×CH), 124.5 (CH), 124.3 (CH), 119.2 (CH), 118.7 (C), 105.8 (CH), 91.1 (C), 82.0 (C), 55.3 (CH_3), 36.9 (CH), 34.5 (CH_2), 31.5 ppm (CH_2); MS (70 eV, EI): m/z (%): 298 [M^+] (100), 283 [M^+-CH_3] (30), 252 (33), 239 (23); HRMS (EI): m/z: calcd for $C_{22}H_{18}O$: 298.1352 [M^+]; found: 298.1350; HPLC (Chiralcel OJ): eluent: *i*PrOH/hexane 30:70, flow: 1.0 mL min^{-1}.

3-[(2,3-Dihydro-1*H*-inden-1-yl)ethynyl]thiophene (13): According to the general procedure, the reaction of (±)-1-bromoindane (**9**, 140 mg, 97%, 0.689 mmol) with tri[(3-thienyl)ethynyl]indium (0.28 mmol) afforded, after purification by column chromatography (hexanes), compound **13** as a white solid (87 mg, 56%, 84% *ee*). M.p. 64–65 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.52–7.13 (m, 7H), 4.22 (t, ^3J(H,H) = 8.5 Hz, 1H), 3.10–2.89 (m, 2H), 2.61 (m, 1H), 2.24 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 143.5 (C), 142.9 (C), 130.0 (CH), 127.9 (CH), 127.1 (CH), 126.6 (CH), 125.0 (CH), 124.5 (CH), 124.3 (CH), 122.7 (C), 91.0 (C), 76.6 (C), 36.8 (CH), 34.3 (CH_2), 31.5 ppm (CH_2); MS (70 eV, EI): m/z (%): 224 [M^+] (100), 208 (21), 191 (29), 178 (21); HRMS (EI): m/z: calcd for $C_{15}H_{12}S$: 224.0654 [M^+]; found: 224.0654; HPLC (Chiralcel OD-H): eluent: hexane, flow: 0.5 mL min^{-1}.

[(2,3-Dihydro-1*H*-inden-1-yl)ethynyl]trimethylsilane (14): According to the general procedure, the reaction of (±)-1-bromoindane (**9**, 142 mg, 97%, 0.700 mmol) with tris(trimethylsilylethynyl)indium (0.28 mmol) afforded, after purification by column chromatography (hexanes), compound **14** as a colorless oil (60 mg, 40%, 80% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.36 (m, 1H), 7.24–7.15 (m, 3H), 4.00 (dd, J(H,H) = 9.0, 8.5 Hz, 1H), 2.95–2.85 (m, 2H), 2.49 (m, 1H), 2.05 (m, 1H), 0.17 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 143.8 (C), 143.5 (C), 127.3 (CH), 126.9 (CH), 124.8 (CH), 124.4 (CH), 108.8 (C), 85.5 (C), 37.5 (CH), 34.8 (CH_2), 31.7 (CH_2), 0.16 ppm (3×CH_3); MS (70 eV, EI): m/z (%): 214 [M^+] (32), 199 [M^+-CH_3] (34), 117 (69), 84 (92), 73 (100); HRMS (EI): m/z: calcd for $C_{14}H_{18}Si$: 214.1172 [M^+]; found: 214.1168; HPLC (Chiralcel OD-H): eluent: hexane, flow: 0.5 mL min^{-1}.

1-(Phenylethynyl)-1,2-dihydrocyclobutabenzene (15): According to the general procedure, the reaction of (±)-1-bromobenzocyclobutane (**10**, 126 mg, 0.690 mmol) with tri(phenylethynyl)indium (0.28 mmol) afforded, after purification by column chromatography (hexanes), compound **15** as a colorless oil (113 mg, 81%, 6% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.50–7.15 (m, 9H), 4.49 (dd, J(H,H) = 5.5, 2.8 Hz, 1H), 3.73 (dd, J(H,H) = 13.7, 5.5 Hz, 1H), 3.42 ppm (dd, J(H,H) = 13.9, 2.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 145.2 (C), 143.6 (C), 131.6 (2×CH), 128.2 (2×CH), 128.0 (CH), 127.7 (CH), 127.4 (CH), 123.6 (C), 123.2 (CH), 122.1 (CH), 89.7 (C), 82.3 (C), 38.9 (CH_2), 32.6 ppm (CH); MS (70 eV, EI): m/z (%): 204 [M^+] (88), 202 (100), 101 (20); HRMS (EI): m/z: calcd for $C_{16}H_{12}$: 204.0934 [M^+]; found: 204.0934; HPLC (Chiralcel OD-H): eluent: *i*PrOH/hexane 0.5:99.5, flow: 0.5 mL min^{-1}.

2-[(1,2-Dihydrocyclobutabenzen-1-yl)ethynyl]-6-methoxynaphthalene (16): According to the general procedure, the reaction of (±)-1-bromobenzocyclobutane (**10**, 128 mg, 0.700 mmol) with tri[(6-methoxy-2-naphthalenyl)ethynyl]indium (0.28 mmol) afforded, after purification by column chromatography (hexanes), compound **16** as a white solid (113 mg, 55%, 6% *ee*). M.p. 83–84 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.90–7.11 (m, 10H), 4.52 (dd, J(H,H) = 5.5, 2.8 Hz, 1H), 3.93 (s, 3H), 3.74 (dd, J(H,H) = 13.9, 5.6 Hz, 1H), 3.44 ppm (dd, J(H,H) = 13.9, 2.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 158.1 (C), 145.3 (C), 143.6 (C), 133.8 (C), 131.1 (CH), 129.2 (CH), 129.1 (CH), 128.4 (C), 128.0 (CH), 127.4 (CH), 126.6 (CH), 123.2 (CH), 122.1 (CH), 119.2 (CH), 118.4 (C), 105.7 (CH), 89.3 (C), 82.7 (C), 55.2 (CH_3), 39.0 (CH_2), 32.8 ppm (CH); MS (70 eV, EI): m/z (%): 284 [M^+] (72), 269 [M^+-CH_3] (22), 241 (100); HRMS (EI): m/z: calcd for $C_{21}H_{16}O$: 284.1196 [M^+]; found: 284.1200; HPLC (Chiralcel OD-H): eluent: *i*PrOH/hexane 0.5:99.5; flow: 0.5 mL min^{-1}.

3-[(1,2-Dihydrocyclobutabenzen-1-yl)ethynyl]thiophene (17): According to the general procedure, the reaction of (±)-1-bromobenzocyclobutane (**10**, 128 mg, 0.700 mmol) with tri[(3-thienyl)ethynyl]indium (0.28 mmol) afforded, after purification by column chromatography (hexanes), compound **17** as a colorless oil (96 mg, 65%, 7% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.42–7.11 (m, 7H), 4.45 (dd, J(H,H) = 5.5, 2.7 Hz, 1H), 3.70 (dd, J(H,H) = 14.0, 5.5 Hz, 1H), 3.36 ppm (dd, J(H,H) = 13.9, 2.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 145.1 (C), 143.5 (C), 129.9 (CH), 128.0 (2×CH), 127.4 (CH), 125.0 (CH), 123.2 (CH), 122.5 (C), 122.1 (CH), 89.2 (C), 77.4 (C), 38.2 (CH_2), 32.6 ppm (CH); MS (70 eV, EI): m/z (%): 210 [M^+] (100), 165 (73); HRMS (EI): m/z: calcd for $C_{14}H_{10}S$: 210.0498 [M^+]; found: 210.0493; HPLC (Chiralcel OD-H): eluent: hexane, flow: 0.5 mL min^{-1}.

[(1,2-Dihydrocyclobutabenzen-1-yl)ethynyl]trimethylsilane (18): According to the general procedure, the reaction of (±)-1-bromobenzocyclobutane (**10**, 126 mg, 0.690 mmol) with tris(trimethylsilylethynyl)indium (0.28 mmol) afforded, after purification by column chromatography (hexanes), compound **18** as a colorless oil (113 mg, 82%, 7% *ee*). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.29–7.03 (m, 4H), 4.28 (dd, J(H,H) = 5.5, 3.0 Hz, 1H), 3.62 (dd, J(H,H) = 13.9, 5.6 Hz, 1H), 3.30 (dd, J(H,H) = 14.1, 2.9 Hz, 1H), 0.20 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 145.0 (C), 143.6 (C), 127.9 (CH), 127.4 (CH), 123.1 (CH), 122.0 (CH), 106.4 (CH), 86.3 (C), 38.8 (CH_2), 32.9 (CH), 0.1 ppm (3×CH_3); MS (70 eV, EI): m/z (%): 200 [M^+] (4), 185 [M^+-CH_3] (100), 172 (17), 141 (23); HRMS (EI): m/z: calcd for $C_{13}H_{16}Si$: 200.1016 [M^+]; found: 200.1011; HPLC (Chiralcel OD-H): eluent: hexane, flow: 0.4 mL min^{-1}.

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