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Transition-Metal-Catalyzed Sequential Cross-Coupling of Bis(iodozincio)methane and -ethane with Two Different Organic Halides

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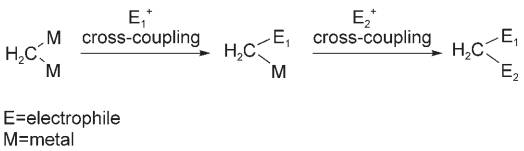
Abstract: Bis(iodozincio)methane, prepared from diiodomethane and zinc, reacts with an organic halide in the presence of a transition-metal catalyst to give an iodozinciomethylenated compound; this then reacts with another organic halide to form a C–C bond. The overall process connects two electrophiles with one carbon atom. Bis(iodozincio)ethane can also undergo this transformation, yielding a new stereogenic center. The asymmetric induction of this stereogenic center was investigated by using a chiral palladium catalyst.

Keywords: C–C bond formation · cross-coupling · *gem*-dizinc · nickel · palladium

Introduction

The cross-coupling reaction of an organometallic reagent with an organic electrophile in the presence of a transition-metal catalyst is one of the most important methods used to construct molecular skeletons.[1] The reaction has been studied with a variety of organometallic reagents and electrophiles, and has provided a general and efficient C–C bond-forming reaction. One can imagine that a sequential cross-coupling reaction at one carbon atom would make this transformation more useful, and thus provide a method for the connection of two electrophiles with one carbon atom. For this purpose, a *gem*-dimetallic reagent that contained two carbon–metal bonds was prepared by our group (Scheme 1).[2,3]



Scheme 1. General scheme for the sequential coupling reaction of a *gem*-dimetallic reagent.

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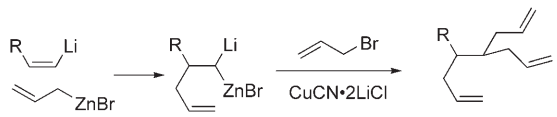
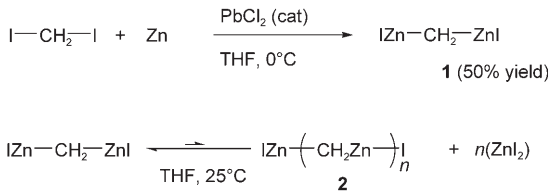
These *gem*-dimetallic reagents have previously been used for Wittig-type methylenation reactions of carbonyl compounds.[4] In these reactions, the nucleophilic addition of a *gem*-dimetallic reagent to a carbonyl group, followed by elimination of a metal oxide, produced a Wittig-type olefination product. In addition to the Wittig-type reaction, other synthetic applications of *gem*-dimetallic compounds were discovered by Knochel and Normant in the 1980's.[5] For their investigation, Knochel and Normant studied the reactivity of *gem*-dimetal species that were prepared by Gaudemar/Normant coupling (Scheme 2). These *gem*-dimetal species were treated with various electrophiles; however, cross-coupling reactions were not studied well.



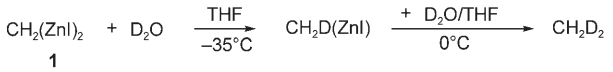
Scheme 2. Preparation of a *gem*-dimetal species by Gaudemar/Normant coupling and its copper salt-mediated allylation.[5]

Since we reported a preparation method for bis(iodozincio)methane (**1**) in 1998, we have investigated some specific molecular transformations.[2a–c,6] A solution of the *gem*-dizinc **1** in THF was obtained from the reaction of diiodomethane, zinc dust, and a catalytic amount of lead(II) chloride. Detailed structural studies of **1** concluded that it is monomeric in THF, although it is possible to form polymethylene zinc compounds, such as **2**, by the Schlenk equilibrium (Scheme 3).[7]



Scheme 3. Preparation of bis(iodozincio)methane (**1**) and its Schlenk equilibrium.[7]

The treatment of a solution of **1** in [D_8]THF with one molar equivalent of deuterium oxide in an NMR tube effected sequential deuteration (Scheme 4). From this result,



Scheme 4. Sequential deuteration of bis(iodozincio)methane (**1**).

we deduced that the reactivity of the C–Zn bond in **1** is significantly greater than that in methylzinc iodide when these species are reacting with water or iodine. Thus, we concluded that it was possible for two *gem*-C–Zn bonds to be used individually and sequentially for cross-coupling reactions. Our results for the cross-coupling reactions of the organometallic reagent **1** with organic halides are described herein.

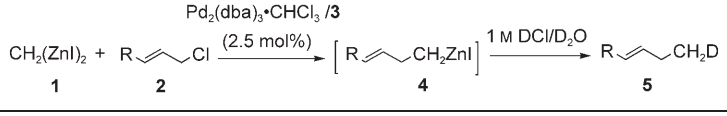
Results and Discussion

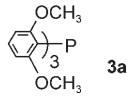
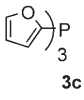
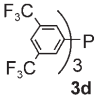
Treatment of diiodomethane with zinc powder in the presence of lead(II) chloride[10] in anhydrous THF produced bis(iodozincio)methane (**1**) in 50% yield (0.5 M solution in THF, as determined by ^{1}H NMR spectroscopic analysis, with 2,2,4,4-tetramethylbutane as an internal standard) by means of a slightly exothermic reaction.[11] Takai and Utimoto have shown that only a small amount of lead(II) chloride is required for it to work effectively as a catalyst.[10] Indeed, as little as 0.05 mol% lead(II) chloride/zinc is required for the reaction to be effective enough. Lead metal, lead(II) bromide, and lead(II) acetate are also effective catalysts for this reaction. When pyrometallurgy zinc, which contains approximately 0.04–0.07% lead, was used it was not necessary to add lead(II) chloride. In a previous investigation by our group, the structure of **1** was studied intensively by X-ray and neutron scattering,[12] and it was shown that the contribution of the Schlenk equilibrium was not significant, provided the concentration of **1** in THF was less than 0.5 M and the temperature less than that of room temperature. This means that when **1** is prepared as a solution in THF, it can keep its homogeneity as a monomeric form; this is crucial if the sequential coupling reaction is to work effectively.

Organomonozinc reagents have often been utilized for transition-metal-catalyzed cross-coupling reactions;[13] therefore, we decided to examine a palladium(0)-catalyzed cross-coupling reaction (Table 1). Four molar equivalents of various phosphines **3** and Pd_2dba_3·$CHCl_3$ were mixed in THF under an atmosphere of argon to prepare the palladium catalyst (Pd^0/PR_3 1:2).[14] The reactions were carried out by using 2.5 mol% of the palladium catalyst, and were quenched with 1 M DCl/D_2O (DCl = deuterium chloride) to give compounds **5**. By alternating the selection of the phosphine ligand, the yield of the coupling product was increased, with tris(2-furyl)phosphine (**3c**) and tris[3,5-bis(trifluoromethyl)]phosphine (**3d**) producing excellent results.[15]

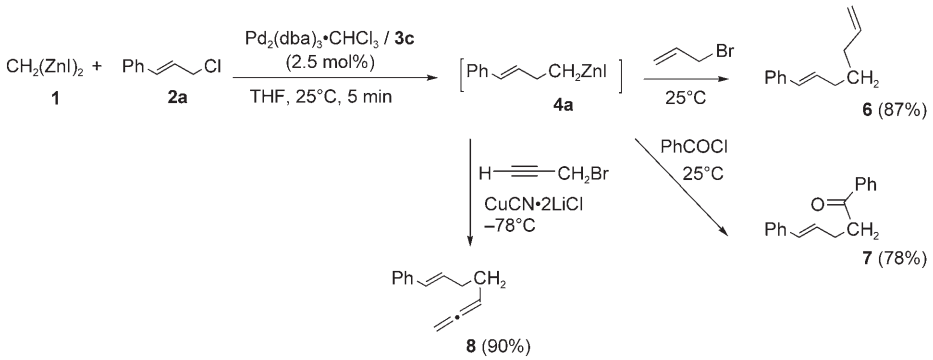
For the next step in our study, an organic halide was used as the second electrophile (versus DCl/D_2O) in these reactions (Scheme 5). Thus, organomonozinc species **4a**, obtained from the reaction of **1** with cinnamyl chloride in situ, was treated with allyl bromide and benzoyl chloride. The existing palladium catalyst was effective for the second cross-coupling reaction, and the sequential coupling products **6**

Table 1. Palladium-catalyzed cross-coupling of **1** with allylic chloride.[a]

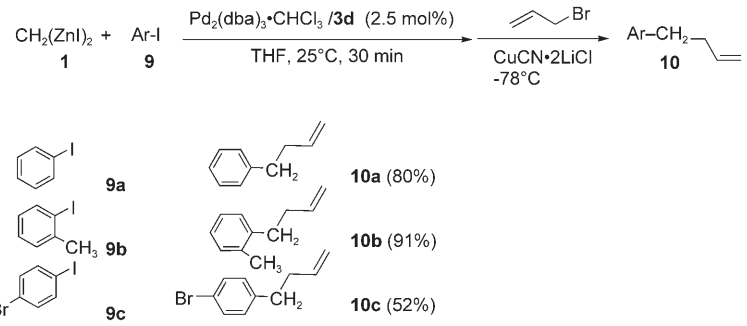


	 **3a**	Ph_3P **3b**	 **3c**	 **3d**	$(C_2H_5O)_3P$ **3e**
5a (R = Ph)	< 1%	16%	88%	97%	14%
5b (R = $nC_{11}H_{23}$)	< 1%	< 1%	82%	91%	< 1%

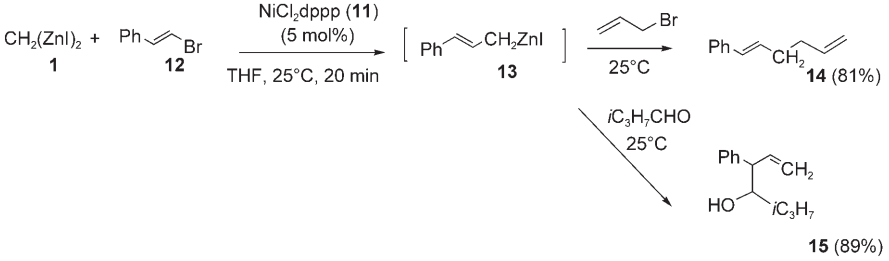
[a] **2a** = cinnamyl chloride and **2b** = 1-chloro-2-tetradodecene.



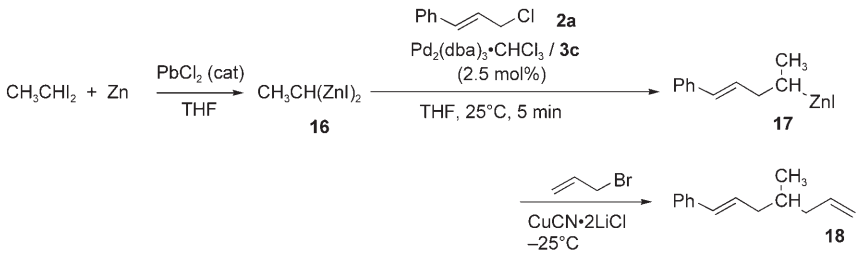
Scheme 5. Sequential cross-coupling of **1** with an allylic halide and another electrophile.



Scheme 6. Sequential cross-coupling of **1** with an aryl halide and allyl bromide.



Scheme 7. Sequential cross-coupling of **1** with β-bromostyrene and allyl bromide or aldehyde.



Scheme 8. Sequential cross-coupling of 1,1-bis(iodozincio)ethane (**16**) with cinnamyl chloride and allyl bromide.

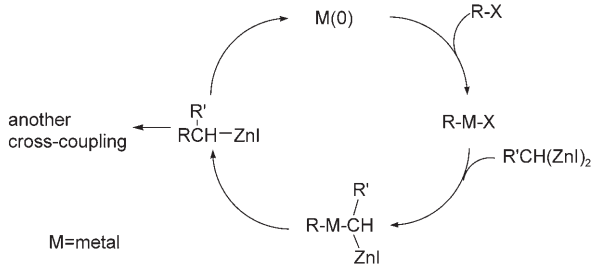
and **7** were obtained. However, when propargyl bromide was used as the second organic halide, the addition of a copper salt became necessary.

The coupling reactions of bis(iodozincio)methane (**1**) with different aryl iodides proceeded effectively in the presence of the palladium catalyst, prepared from $Pd(dba)_3{\cdot}CHCl_3$ and tris[bis(trifluoromethyl)phenyl]phosphine (**3d**), (Scheme 6) to produce benzylzinc intermediates, which were subsequently treated with allyl bromide. For these reactions, the second cross-coupling reaction would not proceed without the addition of additional copper salt.

For the sequential coupling reaction of **1** with a bromoalkene, such as β-bromostyrene (**12**), the first coupling reaction affords an allylic zinc intermediate. Following the procedure illustrated in Schemes 5 and 6, β-bromostyrene (**12**) was treated with bis(iodozincio)methane (**1**) in the presence of various palladium catalysts. Although all of the ligands listed in Table 1 were examined, none of the desired cross-coupling product was obtained. $NiCl_2$dppp (dppp = 1,3-diphenylphosphinopropane), however, was an effective catalyst for this reaction, and the resulting allyl zinc **13** formed in situ was treated with allyl bromide to give the diene **14**. Alternatively, treatment of **13** with isopropylaldehyde produced the homoallylic alcohol **15**, a product of C–C bond formation at the γ-position (Scheme 7).

Treatment of 1,1-diiodoethane with zinc dust in the presence of a catalytic amount of lead(II) chloride produced the *gem*-dizinc species **16**. Sequential coupling of **16** with cinnamyl chloride and allyl bromide produced **18** (Scheme 8).

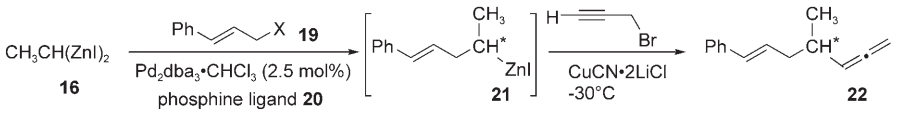
The sequential coupling reactions described above, should have proceeded by the normal cross-coupling mechanism; that is, oxidative insertion of a transition-metal catalyst into the first organic halide to give R–M–X, followed by a transmetallation reaction with the *gem*-dizinc reagent, and then reductive elimination to afford the iodozincioalkylated coupling product. The product from this sequence will become a reactant for other cross-coupling reactions (Scheme 9).



Scheme 9. Proposed mechanism for the sequential coupling.

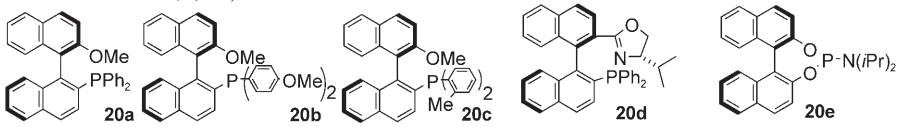
For compound **16**, sequential coupling with two different electrophiles resulted in the formation of an asymmetric carbon. If the enantiotopic iodozincio groups in *gem*-dizincioethane (**16**) are selectively transmetallated with a palladium species that contains chiral ligands, then the follow-

Table 2. Enantioselective preparation of configurationally stable organozinc compound **21**.[a]

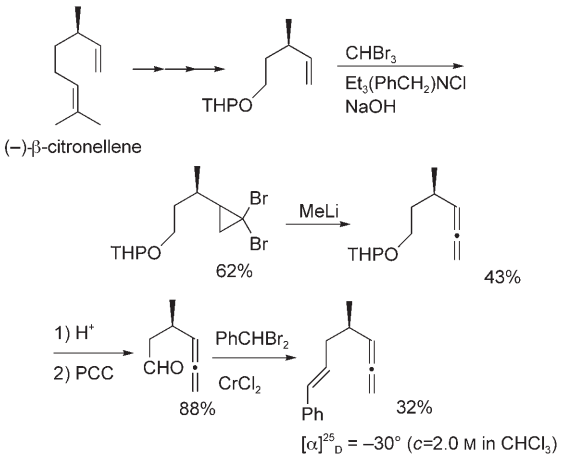


Entry	X in **19**	Ligand	Yield of **22** [%]	*ee* [%][b]	*R*/*S*
1	Cl	**20a**[9a]	81	10	*R*
2	OAc	**20a**	78	22	*R*
3	OBz	**20a**	68	31	*R*
4	OCO_2Me	**20a**	69	32	*R*
5	OCO_2iBu	**20a**	70	33	*R*
6	OCO_2iBu	**20b**[9b]	73	32	*R*
7	OCO_2iBu	**20c**[9c]	<1	–	–
8	OCO_2iBu	**20d**[9c]	<1	–	–
9	OCO_2iBu	**20e**[9d]	40	13	*S*

[a] Compound **16** (1.0 mmol), Pd_2dba_3·$CHCl_3$ (0.25 mmol), **20** (0.1 mmol), and **19** (1.0 mmol) were used for the preparation of **21**. This compound was treated with CuCN·2LiCl (1.2 mmol) at −30 °C and then reacted with propargyl bromide to give **22**. [b] Enantiomeric purity (*ee* = enantiomeric excess) was determined by GPLC (Chrompack CP-Chiralsil-Dex CB, 25 m × 0.25 mm, 40 °C, 60 min; 2 °C min^{-1} to 130 °C; 130 °C, 130 min for *(S)*-**22** and 140 min for *(R)*-**22**).



ing reductive elimination should afford secondary organozinc species **21** with enantiomeric excess (Table 2).[16] The copper-mediated reaction with organozinc reagent proceeds stereospecifically, thus the enantiomeric excess in **21** should be reflected in that of **22**.[17,18] Unfortunately, only very low values of asymmetric induction were realized, despite the investigation of many different types of phosphine ligand. However, a chiral monophosphine ligand carrying a biphenyl group (developed by Hayashi) and a chiral binol based phosphite ligand (developed by Feringa), did produce some enantiomeric excess.[19] The absolute configuration of **22** was determined by comparison with an authentic sample, prepared from (−)-β-citronellene (Scheme 10).



Scheme 10. Preparation of optically active *(R)*-**22**.

Conclusion

The cross-coupling reaction of bis(iodozincio)methane can be performed stepwise and sequentially. This method has provided a route for the combination two electrophiles with one carbon atom. Bis(iodozincio)methane is monomeric in THF with a high homogeneity, a crucial feature for these sequential coupling reactions. However, instead of bis(iodozincio)methane, one might also try Nysted reagent, prepared from dibromomethane and zinc in the presence of a lead catalyst, for these reactions (commercially available from Aldrich). Unfortunately, the use of Nysted reagent (polymethylene zinc) was not successful for our sequential coupling reactions.

Experimental Section

Dehydrated, stabilizer free THF was purchased from Kanto Chemical. [D_8]THF was distilled over benzophenone-ketyl. 1,3-dimethylimidazolidin-2-one (DMI) was distilled over calcium hydride. The zinc powder (Wako) was washed with 10% HCl before use, according to the reported procedure. 1,1-diiodoethane was prepared according to the literature procedure.[20] Chromatographic purification of products was accomplished by using forced-flow chromatography on silica gel (supplied by Kanto Chemical, 60 N, spherical, neutral). ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-2000 (300 and 75 MHz, respectively), and were internally referenced to residual proton solvent signals. For the ^1H NMR spectra, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet). HRMS were generated by a JEOL Mstation 700 spectrometer.

Preparation of bis(iodozincio)methane (1): A mixture of zinc powder (150 mmol) and diiodomethane (1.0 mmol) in THF (2 mL) was sonicated for 1 h. After this time, additional diiodomethane (49 mmol) in THF (48 mL) was slowly added at 0 °C, and the mixture was then stirred for a further 1 h at 25 °C. The integral of the α-proton peak relative to the internal standard in the ^1H NMR spectrum was used to measure the concentration factor. ^1H NMR (300 MHz, [D_8]THF): $\delta = -1.10$ ppm (br s, 2H); ^{13}C NMR (75 MHz, [D_8]THF): $\delta = -14.3$ ppm.

General procedure for the palladium-catalyzed cross-coupling of 1 with allylic chloride: Allylic chloride (1.0 mmol in THF, 1.0 mL) and **1** (0.5 M solution in THF, 2.0 mL, 1.0 mmol) were added to a solution of [$Pd_2(dba)_3$]·$CHCl_3$ (26 mg, 0.025 mmol) and phosphine (0.1 mmol) in THF (1.0 mL), and the mixture was stirred at room temperature for 30 min. After this time, DCl (2.0 mL, 1 M solution in D_2O) was added at 0 °C, and the resulting mixture was stirred for a further 5 min. Once the reaction was complete, the mixture was extracted with ether. The organic layers were then combined, washed with brine, and dried over Na_2SO_4. The product was isolated by silica-gel column chromatography.

4-Deuterio-1-phenyl-1-butene (5a): ^1H NMR (300 MHz, $CDCl_3$): $\delta =$ 7.41–7.23 (m, 5H), 6.38 (d, $J = 16.2$ Hz, 1H), 6.27 (dt, $J = 6.0$, 16.2 Hz,

2H), 2.27–2.02 (m, 2H), 1.09 ppm (tt, $J=2.1$, 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=138.21$, 132.91, 129.06, 128.74, 127.03, 126.19, 26.51, 13.92 ppm (t, $J=19.2$ Hz); HRMS: calcd for $C_{10}H_{11}D$: 133.1001 $[M]^+$; found: 133.0999.

1-Deuterio-3-pentadecene (5b): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=5.47$–5.36 (m, 2H), 2.00–1.94 (m, 4H), 1.38–1.26 (m, 18H), 0.94 (tt, $J=2.0$, 7.5 Hz, 2H), 0.88 ppm (t, $J=6.5$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=132.08$, 129.65, 34.08, 32.84, 32.18, 29.94, 29.92, 29.90, 29.80, 29.61, 29.45, 25.78, 22.95, 14.38, 13.97 ppm (t, $J=19.5$ Hz); HRMS: calcd for $C_{15}H_{29}D$: 214.2410 $[M]^+$; found: 211.2401.

1-Phenyl-1,6-heptadiene (6):[21] Cinnamyl chloride (1.0 mmol in THF, 1.0 mL) and **1** (0.5 M solution in THF, 2 mL, 1.0 mmol) were added to a solution of $[Pd_2(dba)_3]\cdot CHCl_3$ (26 mg, 0.025 mmol) and **3c** (0.1 mmol) in THF (1.0 mL), and the mixture was stirred at room temperature for 30 min. After this time, allyl bromide (1.5 mmol in THF 1.0 mL) was added to the mixture at room temperature. The resulting mixture was stirred for 2 h, and was then poured into saturated aqueous NH_4Cl solution and extracted with ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The product produced was isolated by silica-gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.38$–7.21 (m, 5H), 6.37 (d, $J=16.2$ Hz, 1H), 6.20 (dt, $J=7.5$, 16.2 Hz, 1H), 5.84 (ddt, $J=6.6$, 10.2, 17.1 Hz, 1H), 5.02 (d, $J=17.1$ Hz, 1H), 4.96 (d, $J=10.2$ Hz, 1H), 2.24 (dt, $J=7.2$, 7.5 Hz, 2H), 2.10 (dt, $J=6.6$, 7.2 Hz, 2H), 1.56 ppm (tt, $J=7.2$, 7.2 Hz, 2H).

1,5-Diphenyl-4-penten-1-one (7): Cinnamyl chloride (1.0 mmol in THF, 1.0 mL) and **1** (0.5 M solution in THF, 2 mL, 1.0 mmol) were added to a solution of $[Pd_2(dba)_3]\cdot CHCl_3$ (26 mg, 0.025 mmol) and **3c** (23 mg, 0.1 mmol) in THF (2.0 mL), and the resulting mixture was stirred at room temperature for 30 min. After this time, DMI (2.0 mL) and benzoyl chloride (140 mg, 1.0 mmol) were added at 0 °C, and the mixture was stirred for a further 2 h, before being poured into a solution of saturated aqueous NH_4Cl and extracted with ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The product was isolated by silica-gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$ 8.02 (d, $J=7.2$ Hz, 2H), 7.20–7.52 (m, 8H), 6.48 (d, $J=15.6$ Hz, 1H), 6.27 (dt, $J=6.8$, 15.6 Hz, 1H), 3.15 (t, $J=7.5$ Hz, 2H), 2.64–2.70 ppm (m, 2H).

7-Phenyl-1,2,6-heptatriene (8): Cinnamyl chloride (1.0 mmol in THF, 1.0 mL) and **1** (0.5 M solution in THF, 2 mL, 1.0 mmol) were added to a solution of $[Pd_2(dba)_3]\cdot CHCl_3$ (26 mg, 0.025 mmol) and **3c** (23 mg, 0.1 mmol) in THF (1.0 mL), and the resulting mixture was stirred at room temperature for 30 min. After this time, CuCN·2LiCl (1 M solution in THF, 1.2 mL) was added at −30 °C, and the mixture stirred for a further 5 min. Propargyl bromide (1.5 mmol) was then added at −78 °C. This mixture was warmed to room temperature and stirred for 1 h, before being poured into a solution of saturated aqueous NH_4Cl and extracted with ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The product was isolated by silica-gel column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.36$–7.18 (m, 5H), 6.43 (d, $J=15.9$ Hz, 1H), 6.24 (dt, $J=6.6$, 15.9 Hz, 1H), 5.17 (dt, $J=6.6$, 12.9 Hz, 1H), 4.70 (dt, $J=3.3$, 6.6 Hz, 2H), 2.35 (dt, $J=6.6$, 8.1 Hz, 2H), 2.24–2.14 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=208.70$, 138.00, 130.75, 130.19, 128.76, 127.19, 126.25, 98.73, 75.48, 33.01, 28.56 ppm; HRMS: calcd for $C_{13}H_{14}$: 170.1096 $[M]^+$; found: 170.1089.

General procedure for the sequential cross-coupling of 1 with aryl halide and allyl bromide: Aryl iodide (1.0 mmol in THF, 1.0 mL) and **1** (0.5 M solution in THF, 2 mL, 1.0 mmol) were added to a solution of $[Pd_2(dba)_3]\cdot CHCl_3$ (26 mg, 0.025 mmol) and **3d** (67 mg, 0.1 mmol) in THF (1.0 mL), and the mixture was stirred at room temperature for 30 min. After this time, CuCN·2LiCl (1 M solution in THF, 1.2 mL) was added to the mixture at −30 °C, and it was stirred for a further 5 min. Propargyl bromide (1.5 mmol) was then added at −78 °C. This mixture was warmed to room temperature and stirred for 1 h, before being poured into a solution of saturated aqueous NH_4Cl and extracted with ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The product was isolated by silica-gel column chromatography.

4-Phenyl-1-butene (10a):[22] ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.31$–7.16 (m, 5H), 5.87 (ddt, $J=6.6$, 10.2, 17.3 Hz, 1H), 5.05 (d, $J=17.3$ Hz, 1H), 4.98 (d, $J=10.2$ Hz, 1H), 2.72 (t, $J=7.8$ Hz, 2H), 2.38 ppm (td, $J=7.8$, 6.6 Hz, 2H).

4-(*o*-Tolyl)-1-butene (10b):[23] ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.17$–7.08 (m, 4H), 5.88 (tdd, $J=6.6$, 10.2, 17.3 Hz, 1H), 5.05 (d, $J=17.3$ Hz, 1H), 4.98 (d, $J=10.2$ Hz, 1H), 2.72 (t, $J=7.8$ Hz, 2H), 2.37 (td, $J=7.8$, 6.6 Hz, 2H), 2.31 ppm (s, 3H).

4-(4-Bromophenyl)-1-butene (10c): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.37$ (d, $J=8.2$ Hz, 2H), 7.06 (d, $J=8.2$ Hz, 2H), 5.80 (tdd, $J=6.6$, 10.2, 17.3 Hz, 1H), 5.05 (d, $J=17.3$ Hz, 1H), 4.98 (d, $J=10.2$ Hz, 1H), 2.67 (t, $J=8.2$ Hz, 2H), 2.35 ppm (m, 2H).

General procedure for the nickel-catalyzed cross-coupling of 1 with vinyl halides: β-Bromostylene (1.0 mmol in THF, 1.0 mL) and **1** (0.5 M solution in THF, 2 mL, 1.0 mmol) were added to a suspension of $NiCl_2$dppp (27 mg, 0.05 mmol) in THF (2.0 mL), and the mixture was stirred for 30 min at room temperature. After this time, a solution of the electrophile (1.5 mmol) in THF (1.0 mL) was added, and the reaction mixture was then stirred for a further 2 h, before being poured into a solution of saturated aqueous NH_4Cl and extracted with ether. The combined organic layers were washed with brine and dried over Na_2SO_4. The product was isolated by silica-gel column chromatography.

1-Phenyl-1,5-hexadiene (14):[24] ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.37$–7.16 (m, 5H), 6.40 (d, $J=16.2$ Hz, 1H), 6.24 (dt, $J=6.3$, 16.2 Hz, 1H), 5.84 (ddt, $J=6.6$, 10.2, 17.1 Hz, 1H), 5.00 (d, $J=17.1$ Hz, 1H), 4.98 (d, $J=10.2$ Hz, 1H), 2.38–2.20 ppm (m, 4H).

2-Methyl-4-phenyl-5-hexen-3-ol (15):[25] The product was obtained as a diastereomeric mixture in a ratio of *anti*/*syn* 93:7. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.33$–7.30 (m, 2H), 7.23–7.20 (m, 3H), 6.12 (ddd, $J=8.0$, 8.5, 16.5 Hz, 0.93H), 6.01 (ddd, $J=8.0$, 8.5, 16.5 Hz, 0.07H), 5.22–5.18 (m, 1.86H), 5.12–5.02 (m, 0.14H), 3.8–3.7 (m, 0.07H), 3.60 (ddd, $J=3.0$, 8.0, 8.5 Hz, 0.93H), 3.42 (dd, $J=8.0$, 8.0 Hz, 0.07H), 3.38 (dd, $J=8.0$, 8.0 Hz, 0.93H), 1.71 (d, $J=3.0$ Hz, 1H), 1.57–1.51 (m, 1H), 0.89 ppm (d, $J=$ 6.5 Hz, 6H).

Preparation of 1,1-bis(iodozinscio)ethane (16): A mixture of zinc powder (60 mmol) and 1,1-diiodoethane (1.0 mmol) in THF (2 mL) was sonicated for 1 h. After this time, additional 1,1-diiodoethane (19 mmol) in THF (18 mL) was added slowly at 0 °C, and the resulting mixture was stirred for 1 h at 25 °C. The integral of the α-proton peak relative to the internal standard in the ^{1}H NMR spectrum was used to measure the concentration factor. ^{1}H NMR (300 MHz, $[D_8]$THF): $\delta=1.45$ (d, $J=7.8$ Hz, 3H), −0.08 (q, $J=7.8$ Hz, 1H); ^{13}C NMR (75 MHz, $[D_8]$THF): $\delta=12.0$, 4.2 ppm.

General procedure for the sequential cross-coupling of 16 with cinnnamyl chloride and allyl bromide: Cinnamyl chloride (1.0 mmol in THF 1.0 mL) and **16** (0.5 M solution in THF, 2 mL, 1.0 mmol) were added to a solution of $[Pd_2(dba)_3]\cdot CHCl_3$ (26 mg, 0.025 mmol) and **3c** (23 mg, 0.1 mmol) in THF 1.0 mL, and the mixture was stirred at room temperature for 30 min. After this time, allyl bromide (1.5 mmol in THF, 1.0 mL) was added at room temperature and the resulting mixture was stirred for 2 h. The mixture was then poured into a solution of saturated aqueous NH_4Cl and extracted with ether. The combined organic layers were washed with brine and dried over Na_2SO_4. Finally, the product was isolated by silica-gel column chromatography.

4-Methyl-1-phenyl-1,6-heptadiene (18): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$ 7.37–7.19 (m, 5H), 6.39 (d, $J=16.0$ Hz, 1H), 6.22 (dt, $J=7.5$, 16.0 Hz, 1H), 5.82 (ddt, $J=7.0$, 8.0, 16.5 Hz, 1H), 5.04 (d, $J=16.5$ Hz, 1H), 5.02 (d, $J=8.0$ Hz, 1H), 2.30–2.22 (m, 1H), 2.18–2.12 (m, 1H), 2.10–2.04 (m, 1H), 1.98–1.93 (m, 1H), 1.74–1.65 (m, 1H), 0.95 ppm (d, $J=6.8$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=138.08$, 137.65, 131.39, 129.66, 128.74, 127.09, 126.19, 116.12, 41.22, 40.27, 33.53, 19.65 ppm. HRMS: calcd for $C_{14}H_{18}$: 186.1400 $[M]^+$; found: 186.1409.

4-Methyl-7-phenyl-1,2,6-heptatriene (22): ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.37$–7.19 (m, 5H), 6.39 (d, $J=16.0$ Hz, 1H), 6.22 (dt, $J=7.5$, 16.0 Hz, 1H), 5.17 (dt, $J=6.6$, 8.1 Hz, 1H), 4.74 (d, $J=6.6$ Hz, 1H), 4.73 (d, $J=$ 6.6 Hz, 1H), 2.37–2.29 (m, 2H), 2.25–2.19 (m, 1H), 1.07 ppm (d, $J=$ 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=207.74$, 138.00, 131.67, 129.11, 128.74, 127.18, 126.25, 95.81, 76.18, 40.76, 33.16, 20.09 ppm. HRMS: calcd for $C_{14}H_{16}$: 184.1248 $[M]^+$; found: 184.1252. Enantiomeric

purity was determined by GPLC (Chrompack CP-Chiralsil-Dex CB, 25 m × 0.25 mm, 40 °C, 60 min; 2 °C min^{-1} to 130 °C; 130 °C, 130 min for *(S)*-**7** and 140 min for *(R)*-**7**).

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[1] a) M. Kumada, *J. Organomet. Chem.* **2002**, *653*, 62; b) *Cross-coupling Reactions: A Practical Guide* (Ed.: N. Miyaura), Springer-Verlag, Berlin, **2002**.
[2] a) S. Matsubara, K. Oshima, K. Utimoto, *J. Organomet. Chem.* **2001**, *617*, 39; b) S. Matsubara, K. Oshima, *Proc. Jpn. Acad.* B **2003**, *79*, 71; c) S. Matsubara, K. Oshima in *Modern Carbonyl Olefination* (Ed.: T. Takeda), Wiley-VCH, Weinheim, **2004**, 200; d) I. Marek, J. -F, Normant in *Organozinc Reagents* (Eds.: P. Knochel, P. Jones), Oxford University Press, New York, **1999**, 119.
[3] a) I. Marek, J.-F. Normant, *Chem. Rev.* **1996**, *96*, 3241; b) I. Marek, *Chem. Rev.* **2000**, *100*, 2887; c) J.-F. Normant, *Acc. Chem. Res.* **2001**, *34*, 640; d) P. Knochel in *Handbook of Grignard Reagents* (Eds.: G. S. Silverman, P. E. Rakita), Marcel Dekker, New York, **1996**, 633; e) J. F. K. Müller, *Eur. J. Inorg. Chem.* **2000**, 789
[4] S. Matsubara, K. Oshima in *Modern Carbonyl Olefination* (Ed.: T. Takeda), Wiley-VCH, Weinheim, **2004**, 200.
[5] P. K. Knochel, J. F. Normant, *Tetrahedron Lett.* **1986**, *27*, 4427 and 4431.
[6] S. Matsubara, T. Mizuno, T. Otake, M. Kobata, K. Utimoto, K. Takai, *Synlett* **1998**, 1369.
[7] S. Matsubara, Y. Yamamoto, K. Utimoto, *Synlett* **1999**, 1471.
[8] P. Turnbell, K. Syoro, J. H. Fried, *J. Am. Chem. Soc.* **1966**, *88*, 4764.
[9] a) H. Hashimoto, M. Hida, S. Miyano, *Kogyo Kagaku Zasshi* **1966**, *69*, 174; b) H. Hashimoto, M. Hida, S. Miyano, *J. Organomet. Chem.* **1967**, *10*, 518.
[10] K. Takai, T. Kakiuchi, Y. Kataoka, K. Utimoto, *J. Org. Chem.* **1994**, *59*, 2668.
[11] S. Matsubara, T. Mizuno, T. Otake, M. Kobata, K. Utimoto, K. Takai, *Synlett* **1998**, 1369.
[12] S. Matsubara, K. Oshima, H. Matsuoka, K. Matsumoto, K. Ishikawa, E. Matsubara, *Chem. Lett.* **2005**, *34*, 952.
[13] a) E. Negishi in *Organozinc Reagents. A Practical Approach* (Eds.: P. Knochel, P. Jones), University Press, New York, 1999, pp. 213–243; b) P. Knochel, R. D. Singer, *Chem. Rev.* **1993**, *93*, 2117.
[14] C. Amatore, A. Jutand, G. Meyer, H. Atmani, F. Khalil, F. O. Chahdi, *Organometallics* **1998**, *17*, 2958.
[15] K. Utimoto, N. Toda, T. Mizuno, M. Kobata, S. Matsubara, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2804.
[16] S. Matsubara, N. Toda, M. Kobata, K. Utimoto, *Synlett* **2000**, 987.
[17] A. Boudier, F. Flachmann, P. Knochel, *Synlett* **1998**, 1438.
[18] R. W. Hoffmann, B. Holzer, *J. Am. Chem. Soc.* **2002**, *124*, 4204.
[19] a) Y. Uozumi, T. Hayashi, *J. Am. Chem. Soc.* **1991**, *113*, 9585; b) Y. Uozumi, A. Takahashi, S.-Y. Lee, T. Hayashi, *J. Org. Chem.* **1993**, *58*, 1945; c) T. Hayashi, H. Iwamura, M. Naito, Y. Uozumi, F. Matsumoto, *Synthesis* **1994**, 526; d) A. H. M. de Vries, A. Meetsma, B. L. Feringa, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2374.
[20] R. L. Letsinger, C. W. Kammeyer, *J. Am. Chem. Soc.* **1951**, *73*, 4476.
[21] E. Negishi, C. J. Rousset, D. Choueiry, J. P. Maye, N. Suzuki, T. Takahashi, *Inorg. Chim. Acta* **1998**, *280*, 8–20.
[22] D. H. R. Barton, J. Boivin, E. Crepon, J. Sarma, H. Togo, S. Z. Zard, *Tetrahedron* **1991**, *47*, 34, 7091.
[23] H. Kakiya, H. Shinokubo, K. Oshima, *Bull. Chem. Soc. Jpn.* **2000**, *73*, 9, 2139.
[24] Z. Li, K. M. Nicholas, *J. Organomet. Chem.* **1991**, *402*, 105.
[25] J. M. Coxon, S. J. Eyk, P. J. Sleel, *Tetrahedron* **1989**, *45*, 1029.

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