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Microwave accelerated, Ni/C-catalyzed cross-couplings of in situ-derived zirconocenes

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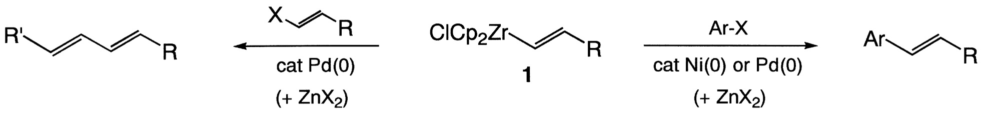
Abstract—Both vinyl and alkyl zirconocenes undergo rapid couplings with aryl halides under heterogeneous conditions in a microwave reactor using Ni/C as catalyst. Ligand variations both in type and stoichiometry play major roles in the extent of conversion.

1. Introduction

As amply documented by the very recent monograph on ‘Titanium and Zirconium in Organic Synthesis’, edited by Ilan Marek,[1] use of zirconocene intermediates in a wide range of synthetic situations continues to blossom. One of the more fundamental processes associated with organozirconium chemistry is generally regarded as cross-coupling reactions, or the zirconium version of ‘Negishi couplings’.[2] As originally disclosed in the mid-to-late 1970’s,[3] diene or styrene formation could be achieved via treatment of an in situ generated vinyl zirconocene with a vinyl or aryl halide, respectively (Scheme 1). Nickel(0) was the catalyst employed at first,[3a] although palladium is now regarded in most circles as more broadly applicable.[4] While these seminal studies offered new inroads to valued C–C bond constructions, the relatively low electronegativity (1.2–1.4) of Zr and unreactive nature of the C–Zr bond toward carbon-based electrophiles oftentimes necessitates transmetalations, thereby significantly expanding the scope of zirconocene-based couplings. In the specific case of Negishi couplings, addition of a zinc salt (e.g. $ZnCl_2$) results in a marked rate acceleration leading to extremely valuable technology,[5] especially in light of the many alternatives for preparing (functionalized) organozinc reagents.[6] Notwithstanding these developments, which greatly enhance the utility of zirconocene derivatives (especially those resulting from hydrozirconations,[7] e.g. **1**), we have returned to the basic concept of utilizing sp^2- and sp^3-C–Zr bonds directly. That is, how can vinyl and alkyl zirconocenes be employed more effectively without recourse to zinc salt additives and which rely on a base metal like nickel, rather than palladium? Our focus has also included a shift to a more environmentally benign, inexpensive, and recyclable heterogeneous approach to catalysis, in particular using nickel-on-charcoal (Ni/C).[8] Since the combination of less reactive ziconocenes (e.g. vs the corresponding zinc species) together with catalyst heterogeneity would be expected to depress reaction rates of the desired Negishi couplings, microwave irradiation[9–11] was postulated as a potential means of reaction acceleration. Although such reactions of Ni/C under the influence of microwaves had not been studied previously, there was evidence in the literature that Pd/C could function in a related capacity.[12] Thus, in this report we describe the remarkable effect that microwave irradiation exerts on various types of cross-couplings of organozirconium species catalyzed by heterogeneous Ni/C (Scheme 2).

2. Results and discussion

Reactions of vinyl zirconocenes, prepared in the usual fashion from terminal alkynes with $Cp_2Zr(H)Cl$,[7] were



Scheme 1.

Keywords: Microwave; Negishi couplings; Nickel-on-charcoal; Alkyl/vinyl zirconocenes.

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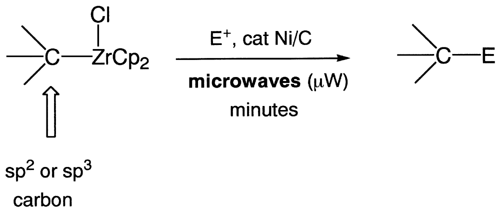
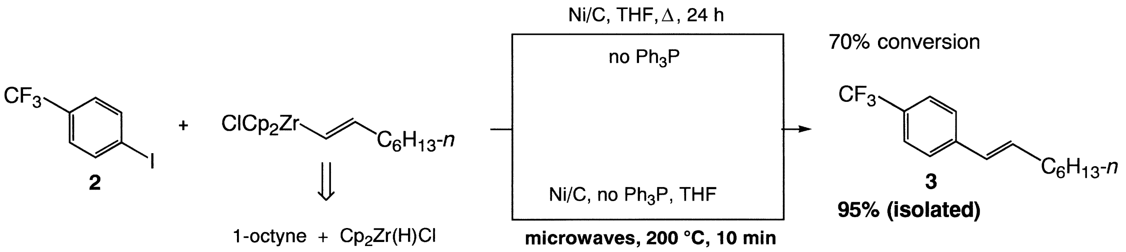


Scheme 2.

initially surveyed in combination with aryl halides in the presence of Ni/C. Unlike the related Suzuki-like couplings mediated by this catalyst,[13] complete consumption of starting material (initially on activated iodide **2**, Scheme 3) could not be accomplished even under reflux conditions (THF) after 24 h. Conversions below 70% were observed when room temperature conditions were applied. Interestingly, while these early trials were mainly unsuccessful, the importance of phosphine concentrations became apparent, as the greatest extent of conversion was noted in the absence of Ph_3P (rt: 4 Ph_3P, <5%; 2 Ph_3P, 20%; no PPh_3, 40% product **3**). Thus, under microwave irradiation and in the absence of phosphines, **2** was converted to **3** within 10 minutes in high yield.

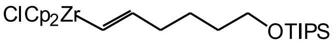
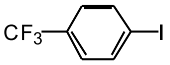
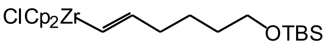
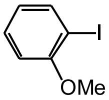
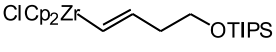
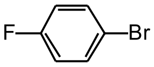
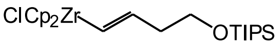
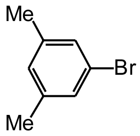
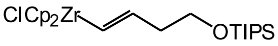
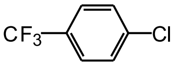
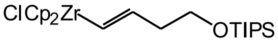
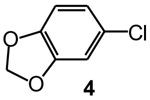
As illustrated in Table 1 (entries 1 and 2), couplings of representative vinyl zirconocenes under these phosphine-free conditions on both an electron-rich and electron-poor substrate proceed with equal facility. In the case of aryl bromides, 2 equiv. of PPh_3 were required (relative to the % Ni/C present) for total conversion (entries 3 and 4). Noteworthy are the cases of aryl chlorides (entries 5 and 6), which are notoriously unreactive toward vinyl zirconocenes even with Ni(0) in solution.[3] Reaction of highly electron-rich chloride **4** was unexceptional under the standard conditions employed, reaching completion within 40 min. However, in going from bromides to chlorides, 4 equiv. of Ph_3P (as opposed to 2 equiv. of PPh_3 with bromides and 0 equiv. of PPh_3 with iodides) were needed to fully consume the aryl halide.

In all of the above cases, Ph_3P was the ligand used. To quickly ascertain the importance of this reaction parameter, four other phosphines were screened: another monodentate



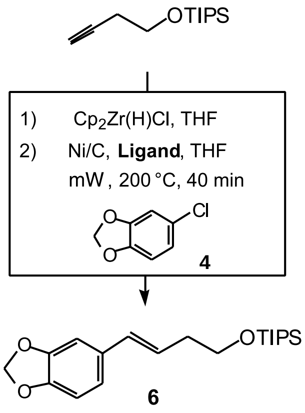
Scheme 3.

Table 1. 'Negishl couplings' of vinyl zirconocenes with aryl halides catalyzed by Ni/C under microwave irradiation at 200 °C in THF

Entry	Vinyl zirconocene	Aryl halide	Time (min)	Yield (%)[a]
1			10	**83**[b]
2			15	**83**[b]
3	 **5**		15	**86**[c]
4			20	**77**[c]
5			30	**76**[d]
6		 **4**	40	**75**[d]

[a] Isolated, chromatographically purified material.
[b] Reaction performed using 5% Ni/C and 0% PPh_3 relative to aryl iodide.
[c] Reaction performed using 5% Ni/C and 10% PPh_3 relative to aryl bromide.
[d] Reaction performed using 5% Ni/C and 20% PPh_3 relative to aryl chloride.

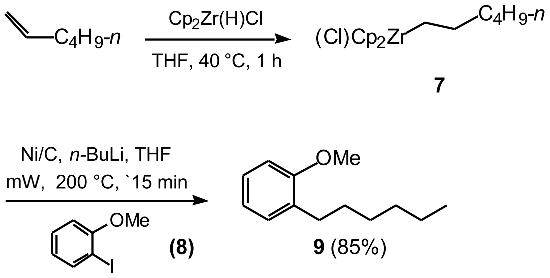
Table 2. Effect of ligands on cross-couplings of vinyl zirconcenes



Phosphine ligand	Ligand (equiv) vs Ni/C	Conversion (%)
Cy_3P	4	5
dppe	2	9
rac BINAP	2	11
dppf	2	18
Ph_3P	**4**	**95**

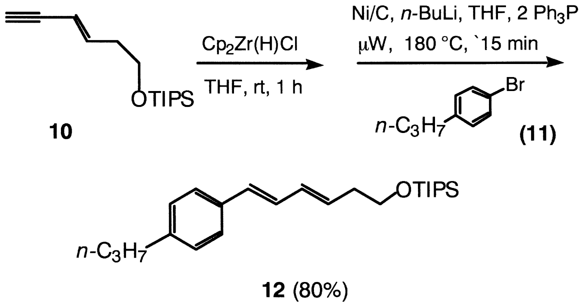
species (Cy_3P), and three of the bidentate variety: dppe, racemic BINAP, and dppf (Table 2). Our findings, based on the coupling of chloride **4** with vinyl zirconocene **5** to afford **6**, clearly indicate that Ph_3P is the only ligand in this group capable of assisting in the oxidative addition step; the recovered mass was the starting chloride.

The corresponding coupling using an sp^3-based C–Zr bond, from hydrozirconation of an alkene, was also tested under microwaves conditions. The combination of alkyl zirconocene **7** and aryl halide **8** led to a smooth conversion to adduct **9** (Eq. (1)).



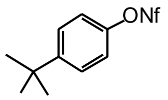
(1)

A more highly conjugated skeleton could be fashioned by hydrozirconation of enyne **10**, followed by Ni/C-catalyzed coupling with aryl bromide **11**. As previously observed for such educts, 2 equiv. of triphenylphosphine (i.e. 8 mol%) led to the desired dienic product **12** in good yield (Eq. (2)).

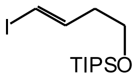


(2)

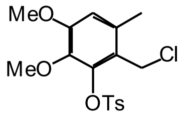
Several additional types of substrates were examined under these microwave enhanced, Ni/C-catalyzed conditions without success. Thus, nonaflate **13** and vinyl iodide **14** each led to many unidentified side products in reactions with a vinyl zirconocene. Each was also found to be sluggish, with considerable amounts of starting material remaining. Likewise, benzylic chloride **15**,[14] which couples at room temperature with vinyl alanes under Ni/C catalysis,[15] led to no reaction even at 180 °C for 10 min. It was also disappointing to observe even a simple vinyl zirconocene derived from octyne could not be induced to add in a conjugate fashion[16] to cyclohexenone under microwave irradiation at 200 °C in THF (10 min).



13



14



15

Finally, we have questioned the extent of leaching of nickel from the Ni/C used in these studies, as done in all previous uses of this heterogeneous support.[17] A quantitative ICP AES determination[18] was made based on the reaction mixture associated with entry 1 in Table 1. The data indicated that 2.86% of the 5% Ni/C present (or 2.86% of the 2.18 mg nickel for the amount of catalyst used) in the reaction mixture could be detected. This figure corresponds to 62.36 μg of nickel in solution, or the presence of 1.25 ppm.

3. Summary and conclusions

This study suggests that Ni/C is a viable catalyst for mediating cross-coupling reactions between organozirconium intermediates and aryl halides under microwave irradiation. Aromatic iodides, bromides, and in some cases even chlorides are amenable to these conditions. Microwave accelerated couplings related to these zirconium-based Negishi couplings, for example, involving aryl halides and boronic acids or amines, are also underway and will be reported in due course, as will our study on the use of CuCl as a trivial means of sequestering mono- and bidentate phosphines as used in some of the workups herein.[19]

4. Experimental

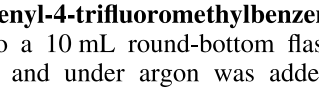
4.1. General

Reactions were performed in oven-dried glassware under an argon atmosphere containing a Teflon coated stir bar and dry septum. THF was freshly distilled from Na/benzophenone ketyl prior to use. Ni/C was stored and weighed out as a black powder in a glove box. All commercially available reagents were distilled either from CaH_2 or molecular sieves under an inert atmosphere before use. Schwartz's reagent, $Cp_2Zr(H)Cl$, was prepared using the standard procedure[20] and titrated using octyne and then analyzed by GC in triplicate and found to be >99% pure. 1-Octyne, 5-hexyn-1-ol, 3-butyn-1-ol, 2-iodoanisole, 5-chloro-1,3-benzodioxole, CuCl, and NaOMe were purchased from Aldrich. 1-Bromo-3,5-dimethylbenzene and 4-chlorobenzotrifluoride were purchased from Lancaster. 1-Hexene, 4-iodobenzotrifluoride, and 4-bromofluorobenzene were purchased from Acros. 3,4-Dimethoxy-6-methyl-2-toluene-sulfonyloxybenzyl chloride was obtained from Optima. All microwave experiments were performed using an Emrys Optimizer in 2–5 mL pyrex reaction vessels which were flame dried under an argon atmosphere. Each contained a Teflon stir bar and Teflon coated reaction vessel cap. ICP-AES analyses was performed on a Thermo Jarrell Ash IRIS plasma spectrometer. GC analyses were carried out using an HP-5 capillary column (0.25 μm×30 m; cross-linked 5% PH ME siloxane) and a time program beginning with 5 min at 50 °C followed by 20 °C/min ramp to 280 °C, then 20 min at this temp. Column chromatography was performed using Davisil Grade 633 Type 60A silica gel. TLC analyses were performed on commercial Kieselgel 60 F_{254} silica gel plates. NMR spectra were obtained on Varian Inova systems using $CDCl_3$ as solvent, with proton and carbon resonances at 400 and 100 MHz, respectively. FTIR spectra were obtained on an ATI Mattson Infinity series spectrometer neat on NaCl plates and are reported in cm^{-1}. Mass spectral data were acquired on a VF Autospec or an analytical VG-70-250 HF instrument.

4.2. Preparation of Ni(II)/C

Darco® KB (5.00 g, 100 mesh) activated carbon (25% H_2O content) was added to a 100 mL round bottom flask containing a stir bar. A solution of 727 mg (Aldrich, 24,407-4, Ni content by ICP determination: 92%; 2.30 mmol) $Ni(NO_3)_2{\cdot}6H_2O$ in 35 mL deionized H_2O was added to the activated carbon and 40 mL of deionized H_2O was added to wash down the sides of the flask. The flask was purged under argon and stirred vigorously for 1 min. The flask was submerged in an ultrasonic bath under a positive argon flow for 30 min. The flask was attached to an argon purged distillation setup and placed in a pre-heated 175–180 °C sand bath with stir plate. As the distillation ended, the flask temperature rises automatically but should be held below 210 °C for an additional 15 min. Upon cooling to rt, the black solid was washed with H_2O (2×50 mL) under argon into a pre-dried in vacuo 150 mL course fritted funnel. The 100 mL of H_2O used to wash the Ni/C was rotavaped and analyzed for any remaining nickel. The fritted funnel was turned upside down under vacuum for 3 h until the Ni/C falls from the frit into the collection flask. The collection flask is then dried in vacuo at 100 °C for 18 h. Using these specific amounts, all of the nickel is mounted on the support, which corresponds to 0.552 mmol Ni(II)/g catalyst, or 3.2% Ni/catalyst by weight.

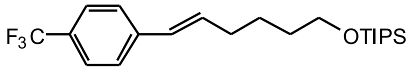
4.3. General procedure for Ni/C-catalyzed cross-couplings of vinyl zirconocenes with aryl halides



4.3.1. E-1-Octenyl-4-trifluoromethylbenzene (3). *Hydrozirconation.* To a 10 mL round-bottom flask wrapped in aluminum foil and under argon was added $Cp_2Zr(H)Cl$ (259 mg, 99% pure, 1.00 mmol). THF (2.0 mL) was added followed by 1-octyne (149 μL, 1.00 mmol) via syringe. After 30 min, the hydrozirconation was complete by GC.

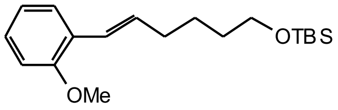
Nickel-on-charcoal catalyzed coupling. To an Emrys Optimizer 2–5 mL pyrex reaction vessel was added Ni/C (67.3 mg, 0.04 mmol) under argon at rt. THF (1 mL) was added followed by BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol). The solution was allowed to stir at rt for 5 min after which 4-iodobenzotrifluoride (117 μL, 0.80 mmol) was added dropwise at rt and the mixture allowed to stir for 5 min. The vinyl zirconocene was then transferred via cannula to the Ni/C mixture at rt. The reaction vessel was placed in the Emrys Optimizer and exposed to microwave irradiation according to the following specifications: temperature: 200 °C, time: 600 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. After cooling to room temperature, the crude reaction mixture was filtered through a glass frit containing Fullers Earth to remove the Ni/C and the zirconium salts, and the filter cake was further washed with ether and hexanes. The filtrate was collected, solvents were removed on a rotary evaporator, and the crude mixture was purified by flash chromatography on silica gel with pet ether. The title compound was obtained (244 mg; 95%) as a clear, viscous oil; R_f 0.80 (pet ether).

IR (neat): 2929, 2858, 2254, 1916, 1616, 1466, 1413, 1324, 1127, 1068, 1017, 909, 731 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58–7.53 (m, 2H), 7.47–7.42 (m, 2H), 6.43 (d, J=16.1 Hz, 1H), 6.36 (dt, J=6.1, 16.1 Hz, 1H), 2.26 (apparent quartet, J=7.4 Hz, 2H), 1.56–1.46 (m, 2H), 1.44–1.27 (m, 8H), (0.93, t, J=7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.66, 138.25, 134.34, 128.77, 126.22, 125.69, 125.65, 125.61, 125.57, 33.33, 31.96, 29.36, 29.15, 22.86, 14.31. MS (EI): m/z (relative %) 256 (16), 185 (29), 172 (100), 165 (12), 115 (19), 55 (10), 43 (13). HREIMS: m/z calcd for $C_{15}H_{19}F_3$ 256.1433; found 256.1438.



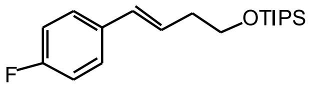
4.3.2. Table 1, entry 1. E-Triisopropyl-[6-(4-trifluoromethylphenyl)-hex-5-enyloxy]-silane. TIPS protected 5-hexynol (254 mg, 1 mmol), $Cp_2Zr(H)Cl$ (259 mg, 99% pure, 1.00 mmol) and THF (2.0 mL) were added to a 10 mL flasked protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. A mixture containing Ni/C (67.3 mg, 0.04 mmol), THF (1 mL), *n*-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 4-iodobenzotrifluoride (117 μL, 0.80 mmol) was prepared using the typical procedure above, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 900 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. After a standard workup, chromatography of the residue on silica gel with pet ether afforded 333 mg (83%) of the title compound as a clear oil; R_f 0.38 (pet ether).

IR (neat): 2941, 2865, 1616, 1462, 1325, 1165, 1126, 1068, 1015, 967, 882, 680 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58–7.52 (m, 2H), 7.46–7.41 (m, 2H), 6.44 (d, J=16.0 Hz, 1H), 6.28 (dt, *J*=7.1, 16.0 Hz, 1H), 3.75 (t, *J*=6.8 Hz, 2H), 2.29 (apparent q, 2H), 1.69–1.54 (m, 4H), 1.16–1.08 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.59, 134.09, 128.96, 128.68, 126.24, 125.90, 125.67, 125.63, 125.60, 125.56, 123.20, 63.39, 33.10, 32.74, 25.69, 18.25, 18.17, 12.23. MS (EI): *m/z* (relative %) 357 (100), 207 (18), 185 (10), 179 (24), 159 (11), 153 (10), 127 (13), 83 (17), 75 (20), 61 (14), 43 (10). HREIMS: *m/z* calcd for $C_{22}H_{35}F_3OSi$ ($M^+-C_3H_7$) 357.1853; found 357.1861.



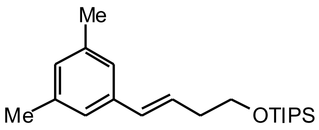
4.3.3. Table 1, entry 2. E*t*-Butyl-[6-(2-methoxyphenyl)-hex-5-enyloxy]-dimethylsilane. TBDMS protected 5-hexyn-1-ol (212 mg, 1 mmol), $Cp_2Zr(H)Cl$ (259 mg, 99% pure, 1.00 mmol) and 2.0 mL of THF were added to a 10 mL flask and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. A mixture containing Ni/C (67.3 mg, 0.04 mmol), THF (1 mL), BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 2-iodoanisole (104 μL, 0.80 mmol) was prepared using the typical procedure above followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 900 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. After a standard workup, chromatography of the residue on silica gel with pet ether–methylene chloride (95:5) afforded 212 mg (83%) of the title compound as a clear oil; R_f 0.08 (pet ether–methylene chloride).

IR (neat): 2959, 2252, 1701, 1459, 1367, 1148, 1013, 911, 733, 647 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.42 (m, 1H), 7.23–7.17 (m, 1H), 6.96–6.85 (m, 2H), 6.73 (d, *J*=16.0 Hz, 1H), 6.23 (dt, *J*=7.0, 16.0 Hz, 1H), 3.86 (s, 3H), 3.66 (t, *J*=6.5 Hz, 2H), 2.27 (ddt, *J*=1.2, 7.0, 7.0 Hz, 2H), 1.65–1.50 (m, 4H), 0.92 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.43, 131.82, 128.00, 127.13, 126.56, 124.62, 120.82, 110.94, 63.35, 55.62, 33.46, 32.64, 26.20, 25.96, 18.59, −5.05. MS (EI): *m/z* (relative %) 263 (100), 147 (10), 121 (38), 91 (12), 75 (31), 73 (14). HREIMS: *m/z* calcd for $C_{19}H_{32}O_2Si$ ($M^+-C_4H_9$) 263.1460; found 263.1467.



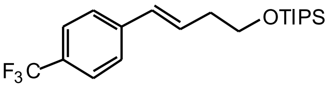
4.3.4. Table 1, entry 3. E-[4-(4-Fluorophenyl)-but-3-enyloxy]-triisopropylsilane. TIPS protected 3-butyn-1-ol (226 mg, 1 mmol), $Cp_2Zr(H)Cl$ (259 mg, 99% pure, 1.00 mmol) and 2.0 mL of THF were added to a 10 mL flask and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. A mixture containing Ni/C (67.3 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), THF (1 mL), *n*-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 4-bromofluorobenzene (88 μL, 0.8 mmol) was prepared using the typical procedure above, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 900 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. After standard workup, chromatography of the residue on silica gel with pentane afforded 277 mg (86%) of the title compound as a clear oil; R_f 0.36 (pentane).

IR (neat): 2942, 2865, 1602, 1508, 1463, 1382, 1230, 1157, 1104, 1013, 964, 882, 850, 774, 733, 680 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.29 (m, 2H), 7.03–6.97 (m, 2H), 6.43 (d, *J*=16.0 Hz, 1H), 6.19 (dt, *J*=7.1, 16.0 Hz, 1H), 3.82 (t, *J*=6.8 Hz, 2H), 2.47 (ddt, *J*=1.2, 6.8, 6.8 Hz, 2H), 1.13–1.08 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.38, 160.93, 134.14, 134.10, 130.54, 127.61, 127.53, 127.33, 127.31, 115.63, 115.41, 63.42, 36.98, 18.23, 12.21. MS (EI): *m/z* (relative %) 332 (1), 303 (2), 289 (100), 159 (54), 145 (34), 129 (30), 115 (23), 103 (20), 75 (35), 59 (33), 43 (31). HREIMS: *m/z* calcd for $C_{19}H_{31}FOSi$ ($M^+-C_3H_7$) 279.1575; found 279.1580.



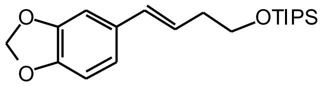
4.3.5. Table 1, entry 4. E-[4-(3,5-Dimethylphenyl)-but-3-enyloxy]-triisopropylsilane. TIPS protected 3-butyn-1-ol (226 mg, 1 mmol), $Cp_2Zr(H)Cl$ (259 mg, 99% pure, 1.00 mmol) and 2.0 mL of THF were added to a 10 mL flask and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. Ni/C (67.3 mg, 0.04 mmol), PPh_3 (21 mg, 0.08 mmol), THF (1 mL), *n*-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 5-bromo-2,3-dimethylbenzene (109 μL, 0.8 mmol) were used according to the typical procedure, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 1200 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. After standard workup, chromatography of the residue on silica gel with petroleum ether afforded 204 mg (77%) of the title compound as a clear oil; R_f 0.22 (pet. ether).

IR (neat): 2865, 2728, 2248, 1602, 1464, 1382, 1248, 1202, 1109, 1013, 996, 965, 909, 883, 851, 793, 734, 681 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.02 (apparent s, 2H), 6.89 (apparent s, 1H), 6.43 (d, *J*=16.0 Hz, 1H), 6.28 (dt, *J*=7.1, 16.0 Hz, 1H), 3.84 (t, *J*=6.8 Hz, 2H), 2.51 (ddt, *J*=1.2, 6.8, 6.8 Hz, 2H), 2.34 (s, 6H), 1.16–1.10 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.05, 137.86, 131.84, 128.87, 127.00, 124.12, 63.57, 37.11, 21.48, 18.24, 12.23. MS (EI): *m/z* (%) 332 (1), 303 (2), 289 (100), 159 (54), 145 (34), 129 (30), 115 (23), 103 (20), 75 (35), 59 (33), 43 (31). HREIMS: *m/z* calcd for $C_{21}H_{36}OSi$ 332.2547; found 332.2535.



4.3.6. Table 1, entry 5. E-Triisopropyl-[4-(4-trifluoromethylphenyl)-but-3-enyloxy]-silane. The TIPS protected 3-butyn-1-ol (226 mg, 1 mmol), $Cp_2Zr(H)Cl$ (259 mg, 99% pure, 1.00 mmol) and 2.0 mL of THF was added and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. Ni/C (67.3 mg, 0.04 mmol), PPh_3 (42 mg, 0.16 mmol), THF (1 mL), BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 4-chlorobenzotrifluoride (107 μL, 0.8 mmol) were prepared using the typical procedure followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 1800 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. After standard workup, followed by evaporation of most of the solvent, CuCl (5.3 mg, 0.053 mmol) was added and swirled for 10 min to sequester the triphenylphosphine. Chromatography of the residue on silica gel with petroleum ether afforded 227 mg (76%) of the title compound as a clear oil; R_f 0.35 (pet. ether).

IR (neat): 2943, 2866, 1503, 1465, 1325, 1165, 1125, 1067, 908, 736 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ 6.91–6.90 (m, 1H), 6.79–6.73 (m, 2H), 6.37 (d, J=15.7 Hz, 1H), 6.28 (dt J=7.1, 15.7 Hz, 1H), 3.80 (t, J=6.8 Hz, 2H), 2.51 (ddt, J=1.2, 6.8, 6.8 Hz, 2H), 1.12–1.07 (m, 21H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 141.45, 130.68, 130.52, 129.10, 126.29, 125.70, 125.66, 125.63, 125.59, 63.15, 37.01, 18.22, 12.21. MS (EI): m/z (%) 329 (100), 198 (11), 128 (14), 120 (45), 92 (15), 74 (11), 58 (10), 42 (28). HREIMS: m/z calcd for $C_{20}H_{31}F_3OSi$ $M^+-(C_3H_7)$ 329.1550; found 329.1549.



4.3.7. Table 1, entry 6. E-(4-Benzo[1,3]dioxol-5-yl-but-3-enyloxy)-triisopropylsilane. TIPS protected 3-butyn-1-ol (226 mg, 1 mmol), Cp$_2$Zr(H)Cl (259 mg, 99% pure, 1.00 mmol) and 2.0 mL of THF were added to a 10 mL flask and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. Ni/C (67.3 mg, 0.04 mmol), PPh$_3$ (42 mg, 0.16 mmol), THF (1 mL), n-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 4-chloro-1,3-benzodioxole (93 μL, 0.8 mmol) were used according to the typical procedure, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 2400 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. After standard workup followed by evaporation of most of the solvent, CuCl (5.3 mg, 0.053 mmol) was added and the mixture swirled for 10 min to sequester the triphenylphosphine. Chromatography of the residue on silica gel with petroleum ether afforded 208 mg (75%) of the title compound as a clear oil; R_f 0.10 (pet. ether).

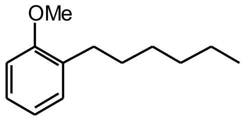
IR (neat): 2943, 2866, 1503, 1490, 1250, 1104, 908, 734, 680, 650, 450 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ 6.91–6.90 (m, 1H), 6.79–6.73 (m, 2H), 6.37 (d, J=15.7 Hz, 1H), 6.28 (dt, J=7.1, 15.7 Hz, 1H), 3.80 (t, J=6.8 Hz, 2H), 2.51 (ddt, J=1.3, 6.8, 6.8 Hz, 2H), 1.12–1.07 (m, 21H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 148.10, 146.85, 132.51, 131.25, 125.73, 120.55, 108.39, 105.58, 101.11, 63.51, 36.93, 18.22, 12.20. MS (EI): m/z (%) 348 (24), 305 (100), 174 (53), 156 (53), 144 (86), 134 (34), 130 (32), 116 (68), 114 (50), 102 (30), 86 (22), 74 (37), 58 (49), 44 (25). HREIMS: m/z calcd for $C_{20}H_{32}O_3Si$ 348.2129; found 348.2121.

4.3.8. Table 2; Cy$_3$P. TIPS protected 3-butyn-1-ol (226 mg, 1 mmol), Cp$_2$Zr(H)Cl (259 mg, 99% pure, 1.00 mmol) and 2.0 mL of THF were added to a 10 mL flask and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. Ni/C (67.3 mg, 0.04 mmol), Cy$_3$P (44.9 mg, 0.16 mmol) THF (1 mL), n-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 4-chloro-1,3-benzodioxole (93 μL, 0.8 mmol) were used according to the typical procedure, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 2400 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. After standard workup, GC of the title compound indicated 5% conversion.

4.3.9. Table 2; dppe. TIPS protected 3-butyn-1-ol (226 mg, 1 mmol), Cp$_2$Zr(H)Cl (259 mg, 99% pure, 1.00 mmol) and 2.0 mL of THF were added to a 10 mL flask and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. Ni/C (67.3 mg, 0.04 mmol), dppe (31.8 mg, 0.08 mmol), THF (1 mL), n-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 4-chloro-1,3-benzodioxole (93 μL, 0.8 mmol) were used according to the typical procedure, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 2400 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. Upon standard workup, GC of the title compound indicated 9% conversion.

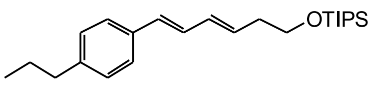
4.3.10. Table 2; BINAP. TIPS protected 3-butyn-1-ol (226 mg, 1 mmol), Cp$_2$Zr(H)Cl (259 mg, 99% pure, 1.00 mmol) and 2.0 mL of THF were added to a 10 mL flask and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. Ni/C (67.3 mg, 0.04 mmol), (R)-BINAP (49.8 mg, 0.08 mmol), THF (1 mL), n-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 4-chloro-1,3-benzodioxole (93 μL, 0.8 mmol) were used according to the typical procedure, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 2400 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. Upon standard workup, GC of the title compound indicated 11% conversion.

4.3.11. Table 2; dppf. TIPS protected 3-butyn-1-ol (226 mg, 1 mmol), Cp$_2$Zr(H)Cl (259 mg, 99% pure, 1.00 mmol) and 2.0 mL of THF were added to a 10 mL flask and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. Ni/C (67.3 mg, 0.04 mmol), dppf (44.4 mg, 0.08 mmol), THF (1 mL), n-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 4-chloro-1,3-benzodioxole (93 μL, 0.8 mmol) were used according to the typical procedure, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 2400 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. Upon standard workup, GC of the title compound indicated 18% conversion.



4.3.12. Eq. 1. 1-n-Hexyl-2-methoxybenzene (9). 1-Hexene (124 μL, 1 mmol), Cp$_2$Zr(H)Cl (259 mg, 99% pure, 1.00 mmol) and THF (2.0 mL) were added to a 10 mL flask and protected from light using aluminum foil. After 60 min, the hydrozirconation was complete by GC. Ni/C (67.3 mg, 0.04 mmol), THF (1 mL), n-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 2-iodoanisole (104 μL, 0.80 mmol) were used according to the typical procedure, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 900 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. Upon standard workup, chromatography of the residue on silica gel with hexanes afforded 131 mg (85%) of the title compound as a clear oil; R_f 0.41 (hexanes).

IR (neat): 2926, 2856, 1729, 1601, 1493, 1464, 1377, 1289, 1241, 1177, 1128, 1051, 1033, 751 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.20–7.12 (m, 2H), 6.91–6.83 (m, 2H), 3.83 (s, 3H), 2.61 (apparent t, J=7.7 Hz, 2H), 1.44–1.18 (m, 8H), 0.90 (t, J=7.1 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 157.63, 131.57, 129.93, 126.93, 120.49, 110.40, 55.46, 31.99, 30.36, 30.04, 29.53, 22.88, 14.35. MS (EI): *m/z* (%) 192 (21), 122 (12), 121 (100), 91 (44), 43 (19). HREIMS: *m/z* calcd for $C_{13}H_{20}O$ 192.1510; found 192.1514.



4.3.13. Eq. 2. E,E-Triisopropyl-[6-(4-propylphenyl)-hexa-3,5-dienyloxy]-silane (12). Hex-3-en-5-ynyl-oxytriisopropylsilane[21] (252 mg, 1 mmol), Cp$_2$Zr(H)Cl (259 mg, 99% pure, 1.00 mmol) and THF (2.0 mL) were added and protected from light using aluminum foil. After 90 min, the hydrozirconation was complete by TLC. Ni/C (67.3 mg, 0.04 mmol), PPh$_3$ (21 mg, 0.08 mmol), THF (1 mL), *n*-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 1-bromo-4-*n*-propylbenzene (124 μL, 0.8 mmol) were prepared using the typical procedure followed by the cross-coupling reaction using the following conditions: temperature: 180 °C, time: 900 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. The filtrate was collected, most of the solvents were removed on a rotary evaporator, and CuCl (2.7 mg, 0.026 mmol) was added and the mixture swirled for 10 min to sequester the triphenylphosphine. Chromatography of the residue on silica gel with hexanes afforded 237 mg (80%) of the title compound as a clear oil; R_f 0.15 (hexanes).

IR (neat): 3019, 2941, 2865, 1509, 1462, 1380, 1246, 1105, 1070, 1013, 985, 931, 882, 779, 739, 681, 658 cm^{-1}. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.34 (apparent d, 2H), 7.16 (apparent d, 1H), 6.76 (dd, J=15.7, 15.7 Hz, 1H) 6.48 (d, J=15.7 Hz, 1H), 6.30 (dd, J=15.7, 15.7 Hz, 1H), 5.87 (dt, J=7.4, 15.7 Hz, 1H), 3.80 (t, J=6.8 Hz, 2H), 2.61 (t, J=7.4 Hz, 2H), 2.44 (apparent q, 2H), 1.67 (qt, J=7.4, 7.4 Hz, 2H), 1.16–1.10 (m, 21H), 0.99 (t, J=7.4 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 142.05, 135.26, 132.60, 131.38, 130.67, 128.87, 128.60, 126.29, 63.41, 37.99, 36.92, 24.72, 18.23, 14.04, 12.20. MS (EI): *m/z* (%) 372 (31), 329 (100), 199 (26), 197 (38), 157 (63), 145 (71), 136 (33), 133 (36), 131 (27), 129 (28), 122 (33), 115 (47), 103 (30), 75 (22), 59 (31), 43 (32). HREIMS: *m/z* calcd for $C_{24}H_{40}OSi$ 372.2847; found 372.2848.

4.4. Sample preparation for ICP-AES

Octyne (149 μL, 1 mmol), Cp$_2$Zr(H)Cl (259 mg, 99% pure, 1.00 mmol) and THF (2.0 mL) were added to a 10 mL flask and protected from light using aluminum foil. After 30 min, the hydrozirconation was complete by GC. Ni/C (67.3 mg, 0.04 mmol), THF (1 mL), *n*-BuLi (31 μL, 2.55 M in hexanes, 0.08 mmol), and 4-iodobenzotrifluoride (117 μL, 0.80 mmol) were used according to the typical procedure, followed by the cross-coupling reaction using the following conditions: temperature: 200 °C, time: 600 s, fixed hold time: on, sample absorption: normal, pre-stirring: 30 s. The reaction mixture was filtered using a 60 mL course filter funnel after cooling to room temperature. The reaction mixture was then washed through the funnel with ether (3×20 mL). The filtrate was refilltered with ether washings (3×10 mL). The solvent was evaporated and the crude material digested with 10 mL of 20% HNO$_3$ and 5 mL concentrated HCl at reflux for 8 h. Upon cooling and dilution with H$_2$O (20 mL), the mixture was extracted with hexanes (10 mL) and CH$_2$Cl$_2$ (2×10 mL) and the combined organic layers washed with H$_2$O. The solvents were removed from the combined aqueous phases and the ICP-AES sample was prepared by adding 2% HCl in a way that the final (estimated) nickel concentration was between 1 and 35 ppm. The analytical sample prepared was determined to have 1.25 ppm Ni in solution (2.86% Ni in solution).

Acknowledgements

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