in hexane and stored under N_2. The total weight of material recovered was 162 mg.
22. The elemental composition of the as-synthesized FePt particle materials was obtained by inductively coupled plasma–atomic emission spectrometry. The samples were precipitated from hexane dispersions by adding ethanol and then drying. The analysis was performed at Galbraith Laboratories (Knoxville, TN).
23. Although the particle dispersion can be handled without inert gas protection, it is advisable to store the hexane dispersion under N_2 for long-term protection.
24. An example is as follows: 0.02 ml of hexane-dispersed FePt nanoparticles (equivalent to $\sim$5 mg/ml) was deposited on a SiO_2/Si substrate ($\sim$0.5 cm by 1 cm). The solvent was allowed to evaporate slowly ($\sim$5 min) at room temperature. The as-deposited thin film was then transferred into a N_2 glove box (O_2 concentration <2 ppm) and annealed in a Thermolyne 1300 furnace. The temperature was raised to 550°C from room temperature over a period of 13 min and maintained for 30 min. The sample was taken out of the furnace and cooled to room temperature in the N_2 box. Composition and thickness of the FePt nanocrystal assembly were determined by Rutherford backscattering spectrometry. This procedure yielded a $\sim$120-nm-thick FePt nanocrystal assembly.
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Efficient Activation of Aromatic C–H Bonds for Addition to C–C Multiple Bonds

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Efficient electrophilic metalation of aromatic C–H bonds leading to new C–C bond formation through regio- and stereoselective addition to alkynes and alkenes has been realized by a catalytic amount (0.02 to 5 mole percent) of palladium(II) or platinum(II) compounds in a mixed solvent containing trifluoroacetic acid at room temperature. Various arenes undergo unexpected selective trans hydroarylation to terminal or internal $C\equiv C$ bonds inter- and intramolecularly with high efficiency (up to a turnover number of 4500 for palladium), especially for electron-rich arenes, giving thermodynamically unfavorable *cis*-alkenes, and the oxygen- and nitrogen-containing heterocycles. The simplicity, generality, and efficiency of this process should be very attractive to the possible industrial application for the functionalization of arenes.

Arenes such as benzenes, naphthalenes, phenols, and anilines are the large-quantity chemicals manufactured by chemical industries. Catalytically efficient activation of aromatic C–H bonds leading to useful organic reactions such as new C–C bond formation is of considerable interest for the chemical and pharmaceutical industries and remains a long-term challenge to chemists (*1–4*). It would provide simple, clean, and economic methods for making aryl-substituted compounds directly from simple arenes because no prefunctionalization, such as halogenation, is involved. The catalytic systems for such a purpose have been sought for many years, although there are many examples of stoichiometric reaction of aromatic C–H bonds with transition metal compounds (*1, 2*).

The few available catalytic systems based on transition metals (*4–12*) activate aromatic C–H bonds mainly through two routes. The first route is by chelation-assisted oxidative insertion of low-valent transition metal complexes, such as Ru(0) (*4, 5*) and Rh(I) (*6*) complexes, to aromatic C–H bonds in the hydroarylation of C–C multiple bonds. This insertion involves the coordination of a functional group in arenes to the metal complex, followed by the oxidative insertion of the metal to an ortho-aromatic C–H bond, resulting in the addition to unsaturated C–C bonds (*2*). These systems are apparently limited to functionalized arenes such as aromatic ketones at high temperature and give low stereoselectivity in the hydroarylation of alkynes. The second route involves electrophilic metalation of aromatic C–H bonds by Pd(II) complexes to give σ-aryl-Pd complexes in oxidative coupling of arenes with olefins in acetic acid (reaction 1 in Fig. 1). The σ-aryl-Pd complexes undergo cis arylpalladation to $C=C$ bonds followed by Pd-β-hydride elimination to give aryl alkenes (*9–12*). For this system, in situ regeneration of Pd(II) from Pd(0) is the crucial step for the catalytic cycle; the turnover number (TON) (the molar ratio of product formed to the catalyst) is still not high enough for possible industrial application. Therefore, it is still very desirable to find new, general, and efficient catalytic systems to activate the aromatic C–H bonds. Very few examples are available for the intramolecular version of this reaction type.

We report the efficient metalation of aromatic C–H bonds at room temperature by in situ generated highly electrophilic Pd(II) and Pt(II) cationic species in trifluoroacetic acid (TFA), leading to regio- and stereoselective addition of simple arenes to C–C multiple bonds inter- and intramolecularly (reactions 2 through 4 in Fig. 1). In most cases, the addition to alkynes exclusively affords the thermodynamically unfavorable *cis*-aryl alkenes, unlike most of the arylmetalations of $C\equiv C$ and $C=C$ bonds that occur mainly in a cis fashion and yield trans products, especially in Pd-catalyzed reactions (*13, 14*). The intramolecular hydroarylation of $C\equiv C$ bonds is very fast and regiospecific because the electrophilic metalation of aromatic C–H bonds by Pd(II) cationic species is assisted by ethynyl coordination, affording heterocycles in good to excellent yields. In fact, this intramolecular reaction combines the chelation assistance and electrophilic metalation.

The reaction of pentamethylbenzene with ethyl phenylpropiolate in a mixed solvent TFA/CH_2Cl_2 (4/1 by volume) at 25°C was used to screen catalysts among $Pd(OAc)_2$ (OAc, acetate), $Pd(PPh_3)_2(O_2CCF_3)_2$ (Ph, phenyl), $Pd(PPh_3)_4$, Pd/C, $PtCl_2$/2AgOAc, $RhCl_3$/3AgOAc, $IrCl_3$/3AgOAc, $RuCl_3$/3AgOAc, and $Ni(OAc)_2$. The highly electrophilic cationic species $[M(O_2CCF_3)_xL_y]^+$ (M, metal; L, ligand) are expected to be generated in situ through bonding weakly coordinating anions, $CF_3CO_2^-$, to transition metal ions by using TFA as a solvent (*15–18*). The cationic species should greatly enhance the metalation of aromatic C–H bonds and, at the same time, possibly activate $C\equiv C$ and $C=C$ bonds through the coordination to generate the acceptors of aryl nucleophiles. The reaction was carried out by simply mixing all of the reactants, a catalyst, and the solvent over an ice bath and then warming to room temperature (Table 1 and Fig. 2). The Pd(II) and Pt(II) catalysts were four times as active as other transition metals: Pd(II) > Pt(II) ≫ Rh(III) > Ru(III) > Ni(II), in accordance with the reactivity of these metal ions in electrophilic metalation of aromatic C–H bonds (*1*). The Pd(II) catalysts $Pd(OAc)_2$ and $Pd(PPh_3)_2(O_2CCF_3)_2$ are equally active; *cis*-ethyl 3-pentamethylphenyl cinnamate was obtained in 75% yield in 5 hours, and an almost

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quantitative yield of hydrolyzed acid, *cis*-3-pentamethylphenyl cinnamic acid, was obtained in 12 hours (entry 4 in Table 1). Pd(0) catalysts such as $Pd(PPh_3)_4$ and Pd(0)/C were much less active (<20% yield in 12 hours), indicating that the reaction may not involve Pd(0) species in the catalytic cycle. The Pt(II) catalyst exhibited lower activity than Pd(II), but it had a higher selectivity and gave higher yields of the 1/1 arene/alkyne adducts with fewer side products (such as the formation of a 1/2 arene/alkyne adduct) with the prolonged reaction time (compare entries 1 and 2 in Table 1). Replacement of TFA with either trifluoromethanesulfonic acid or toluenesulfonic acid (10% to alkyne in CH_2Cl_2) resulted in lower yields (<15% yield in 12 hours) with Pd(II) cationic systems such as $PdCl_2/2CF_3SO_3Ag/CF_3SO_3H$ and $PdCl_2/2CF_3SO_3Ag/CH_3C_6H_4SO_3H$.

The scope and generality of this reaction have been explored with various commercially available arenes, with alkynes from terminal and internal alkynes (see Table 1 and Web table 1, available at www.sciencemag.org/feature/data/1047418.shl), and also by intramolecular reactions (Table 2). The reaction exhibited very good chemoselectivity with unprotected OH, Br, CHO, and vinyl groups in arenes and with unprotected –CHO, –COMe, $-CO_2H$, and $-CO_2Et$ (Me, methyl; Et, ethyl) in alkynes, all proving to be compatible (Tables 1 and 2 and Fig. 2). The intermolecular reaction gave low to excellent yields, depending on the reactivity of arenes and alkynes. The yield increased with the increasing number of electron-donating groups of arenes, as expected for electrophilic substitution (*11, 12*). The electron-rich arenes can overcome the steric hindrance, and thus, the reactions of pentamethylbenzene with all acetylenes gave good yields of crowded molecules. The C≡C bonds conjugated to the electron-withdrawing groups such as CHO, CO_2H, COMe, and CO_2Et generally serve as good acceptors of aryl nucleophiles (Table 1). The reactions with internal alkynes were slower than those with terminal alkynes. For example, the reactivity of $RC{\equiv}CCO_2Et$ depends on R: H > Ph > Me (compare entries 1, 3, and 4 in Table 1). The increasing concentration of $Pd(OAc)_2$ greatly enhanced the reaction.

The regio- and stereochemistry of this reaction was unambiguously established on the basis of chemical shifts, coupling constants (J_{H-H}), and differential nuclear Overhauser effect experiments of ^1H nuclear magnetic resonance (NMR) of products. The cis configuration of adducts 1-(pentamethylphenyl)-1-phenyl propene and 1-(pentamethylphenyl)-1-phenyl-2-phenyl ethylene (entries 11 and 12 in Table 1) was further confirmed by x-ray crystal structure.

The structure of adducts shows that the addition of aryl and H groups across C≡C bonds is in a trans fashion exclusively (within the limit of ^1H NMR spectrum) in most cases and gives *cis*-alkenes (Table 1), which are difficult to prepare by known reactions (*14, 19*). In a few cases, the 1/2 or 2/1 arene/alkyne adducts (entries 1 and 21 in Table 1) were obtained. Control experiments revealed that the 2/1 arene/alkyne adduct resulted from further addition of another arene to the 1/1 arene/alkyne adduct. In some cases, the reaction can be stopped at the stage of 1/1 adducts by controlling reaction time or the concentration of $Pd(OAc)_2$. The reaction of arenes with an alkynone, 3-butyn-2-one, gave exclusively trans adducts, *trans*-4-aryl 3-buten-2-ones (entries 9, 20, and 21 in Table 1), whereas a cis adduct, *cis*-4-pentamethylphenyl-4-phenyl 3-buten-2-one, was iso-

Table 1. Intermolecular addition of arenes (Ar–H, 10 mmol) to alkynes (R^1–C≡C–R^2, 5 mmol) in TFA (4 ml) and CH_2Cl_2 (1 ml) by Pd [$Pd(OAc)_2$] and Pt ($PtCl_2$/2AgOAc) catalysts at 25°C, yielding products as shown in reaction 2 of Fig. 1. Stereo refers to the stereochemistry [exclusively cis or trans, otherwise cis/trans ratio (c/t) is given]; the bold numbers refer to the structures in Fig. 2. The isolated yields are given in general, and the yields given in parentheses were determined by gas chromatography. The yields and molar percentages of catalyst are based on alkyne. Products were isolated or purified by flash chromatography or recrystallization, and their structures were determined by ^1H and ^{13}C NMR, infrared spectroscopy, and elemental analysis. Other conditions are noted.

Entry	Ar–H	R^1	R^2	Catalyst	Molar percentage	Time (hours)	1/1 adduct	
							Stereo	Yield (%)
1	**1**	H	CO_2Et	Pd	1	3	cis	85*
2	**1**	H	CO_2ET	Pt	5	24	cis	92†
3	**1**	Me	CO_2Et	Pd	5	46	cis	78
4	**1**	Ph	CO_2Et	Pd	5	12	cis	96
5	**1**	Ph	CO_2H	Pt	5	24	cis	(71)
6	**1**	Ph	CHO	Pt	5	24	cis	62
7	**1**	EtO_2C	CO_2Et	Pd	5	48	cis	61
8	**1**	Ph	COMe	Pt	5	72	cis	(69)
9	**1**	H	COMe	Pd	0.02	96	trans	90
10	**1**	Ph	H	Pt	5	48	cis	60
11	**1**	Ph	Me	Pt	5	48	cis	73
12	**1**	Ph	Ph	Pt	5	48	cis	68
13	**1**	n-C_3H_7	C_3H_7-n	Pd	5	40	c/t = 1	61
14	**2**	H	CO_2Et	Pd	1	12	cis	49*
15	**3**	H	CO_2Et	Pd	1	24	cis	61
16	**4**	H	CO_2Et	Pd	1	46	cis	46
17	**5**	H	CO_2Et	Pd	1	12	cis	62‡
18	**6**	H	CO_2H	Pd	1	40	**14**	(71)§
19	**6**	Ph	CO_2H	Pd	1	5	**15**	(65)‖
20	**7**	H	COMe	Pd	1	5	trans	72
21	**8**	H	COMe	Pd	1	1	trans	(70)¶
22	**9**	H	CO_2Et	Pd	1	48	cis	46
23	**10**	H	CO_2Et	Pd	1	45	c/t = 12	(78)

*Six to 10% of 1/2 arene/alkyne adduct as **ArA_2** (see Fig. 2) was also isolated. †No **ArA_2** was found by ^1H NMR. ‡Ethyl propiolate (3 mmol) and **5** (1.5 mmol) were used, and the yield was based on **5**. §Thirty millimoles of **6** was used. ‖Trifluoroacetic anhydride (5 mmol) was added. ¶Five percent of 2/1 arene/alkyne adduct as **Ar_2A** (see Fig. 2) was formed.

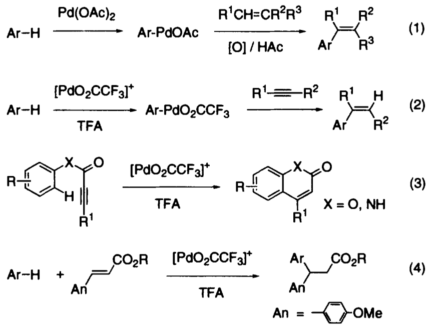


Fig. 1. Pd(II)-catalyzed C–C bond formation involving electrophilic aromatic C–H bond cleavage. $[PdO_2CCF_3]^+$ refers to the in situ generated Pd(II) cationic species in TFA.

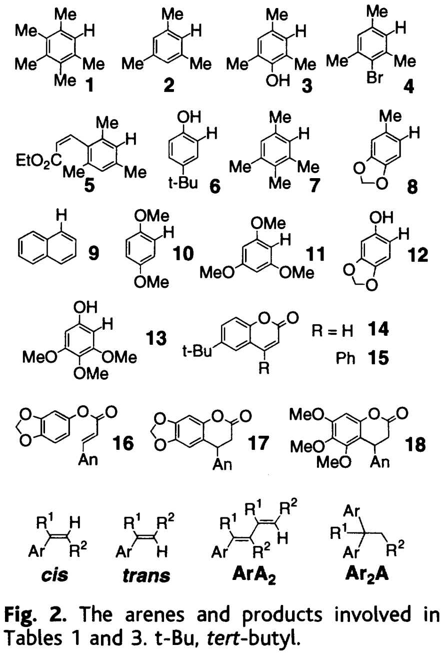
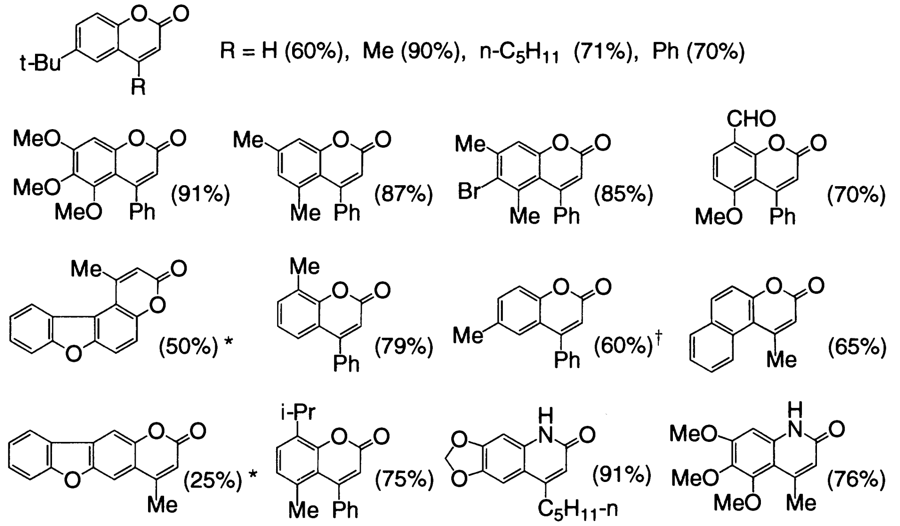


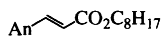
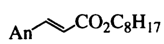
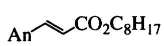
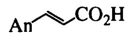
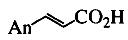
Fig. 2. The arenes and products involved in Tables 1 and 3. t-Bu, *tert*-butyl.

Table 2. The coumarins and 2(1*H*)-quinolinones from Pd-catalyzed intramolecular addition reactions (reaction 3 in Fig. 1) of the corresponding aryl alkynoates (1 mmol) and alkynalides (1 mmol), respectively, in the presence of 1 to 3% $Pd(OAc)_2$, TFA (1.5 ml), and CH_2Cl_2 (0.5 ml) at 25°C for 30 min to 5 hours. The isolated yields are given in the parentheses after the structure. i-Pr, isopropyl.



*Isolated as a mixture of two regioisomers from one reaction. †The yield was determined by ^1H NMR.

Table 3. The addition of arenes (Ar–H, 5 mmol) to activated alkenes (5 mmol) catalyzed by 1% $Pd(OAc)_2$ in TFA (4 ml) and CH_2Cl_2 (1 ml) at 25°C for 10 hours, yielding products as shown in reaction 4 of Fig. 1. The bold numbers refer to the structures in Fig. 2.

Entry	Ar–H	Olefin	Yield (%)
1	**8**		86
2	**10**		83
3	**11**		65
4	**12**		**17** 95
5	**13**		**18** 96
6	**16**		**17** 65*

*Benzoquinone (5 mmol) was added, and yield was determined by ^1H NMR.

lated as the sole product from the reaction of an internal alkynone, 4-phenyl-3-butyn-2-one, with pentamethylbenzene under the same conditions (entry 8 in Table 1). These findings suggest that the formation of cis adducts is kinetically controlled, and initially formed *cis*-4-aryl 3-buten-2-ones may isomerize to thermodynamically favorable *trans*-4-aryl 3-buten-2-ones through a vinyl-Pd intermediate as reported by Zargarrian and Alper (*20*). Two coumarins (**13** and **14**, see entries 18 and 19 in Table 1) were directly obtained from the reaction of *p*-tert-butylphenol with ethyl propiolate and phenyl propiolic acid in 71 and 65% yields, respectively, apparently through addition followed by cyclization.

The aryl alkynoates prepared from corresponding phenols and alkynoic acids underwent much faster and more regioselective addition than intermolecular reactions with this catalytic system (Table 2), and they afforded various coumarins in 60 to 91% yields. Almost all of the aryl alkynoates were converted to coumarins within 30 min (monitored by ^1H NMR and thin-layer chromatography), except for a few cases (for example, slow formation of 4-phenyl-6-methyl coumarin with 60% yield in 5 hours was observed). The reactivity of *m*-, *o*-, and *p*-methylphenyl 3-phenylpropiolates is in the order of $m \gg o > p$, as expected for typical electrophilic substitution. This intramolecular reaction is regiospecific, giving the coumarins (such as 4-phenyl-5-methyl-8-*iso*-propyl coumarin in high yield) that are not possible with intermolecular reaction. Pd(0) complex $Pd(PPh_3)_4$ is only active in intramolecular reactions, presumably through a mechanism of chelation-assisted oxidative insertion of Pd(O) to aromatic C–H bonds, similar to the case of Ru(0) (*4*). All of these facts indicate that electrophilic metalation of aromatic C–H by Pd(II) is accelerated and directed in orientation by C≡C coordination.

The reaction was further extended to inter- and intramolecular additions of alkoxyarenes to activated alkenes (Table 3). Two 3,4-dihydrocoumarins, **17** and **18**, were obtained almost quantitatively from the equimolar reaction of corresponding phenols with *p*-methoxycinnamic acid (entries 4 and 5 in Table 3), and **17** was also obtained from an intramolecular reaction (entry 6 in Table 3). Also, the intramolecular addition has been extended to the synthesis of nitrogen-containing heterocycles, 2(1*H*)-quinolinones, from corresponding alkynalides (Table 3). The alkynalides are readily prepared from the corresponding anilines and alkynoic acids.

The efficiency of this process can be seen from the following inter- and intramolecular reactions. The reaction of pentamethylbenzene with 3-butyn-2-one catalyzed by 0.02 mole percent $Pd(OAc)_2$ at 25°C for 96 hours (entry 9 in Table 1) gave *trans*-4-(pentamethylphenyl)-3-buten-2-one in 90% yield (TON of 4500), and the intramolecular reaction of 3′,4′,5′-trimethoxyphenyl 3-phenylpropiolate by 0.079% of $Pd(OAc)_2$ at 25°C for 6 hours resulted in 4-phenyl-5,6,7-trimethoxycoumarin in 95% yield (TON of 1200).

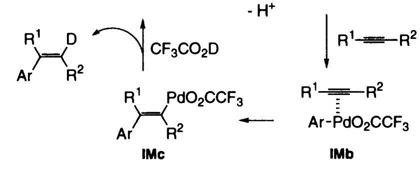


Fig. 3. A possible mechanism for addition of arenes to alkynes.

A possible mechanism for this reaction has been outlined in Fig. 3. The three isotope experiments shown in Fig. 4 revealed that one vinyl H or D in all adducts was mainly from the solvent acid, which presumably results from the protonation of vinyl-Pd complex **IMc** by TFA-d_1 or TFA (Fig. 3). The formation of **IMc** was also strongly supported by other evidence (*21*). The involvement of σ-aryl-Pd complexes **IMa** has been confirmed by the ^1H NMR spectrum from the disappearance of the aryl H of pentamethylbenzene in the reaction with 1 equivalent of $Pd(OAc)_2$ in TFA in a few minutes at room temperature. The facile formation of **IMa** through electrophilic metalation of the aromatic C–H bond either in TFA or with cationic metal ions has been documented (*1, 11, 15, 18*). The fact that the hydroarylation reaction failed in other solvents such as acetic acid indicates the necessity of TFA for the formation of cationic Pd(II) species (*22*) and for the protonation of a vinyl-Pd intermediate **IMc** to complete the catalytic cycle. A possible mechanism would be the electrophilic at-

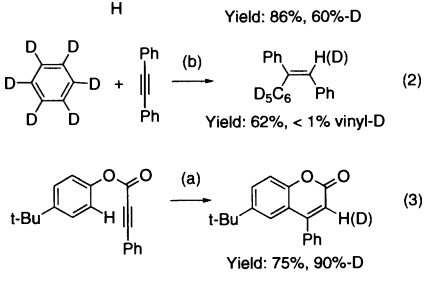


Fig. 4. Isotope experiments under the conditions of (a) 1% $Pd(OAc)_2$ in CF_3CO_2D at 25°C for 2 hours and (b) 5% $PtCl_2$/10% AgOAc in CF_3CO_2H at 25°C for 40 hours.

tack of the aromatic C–H bond by cationic Pd(II) species to form **IMa** followed by coordination of alkyne to give **IMb**. A trans insertion of C–C triple bonds to the σ-aryl-Pd bond (*23–25*) results in **IMc**, and 1/1 arene/alkyne adduct would be released from Pd(II) (*24*) upon protonation of **IMc**. The possible involvement of Pd(II)-vinylidine and Pd(II)-allenyl complexes could be excluded (*26, 27*). In the addition of alkoxyarenes to activated alkenes, the involvement of the carbocations from alkenes may be possible.

Many of the products offered by this reaction [such as coumarins, 2(1*H*)-quinolinones, and *cis*-aryl-α,β–unsaturated carbonyl compounds] are biologically relevant compounds and cannot otherwise be easily accessed by known reactions. This process offers a general, simple, and efficient method for converting simple arenes directly to potentially useful compounds in one step under mild conditions. This method should have many applications in organic and medical chemistry and possibly be applied by chemical and pharmaceutical industries.

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21. Two control reactions also support the formation of **IMc** in the reaction: (i) The D-containing adduct of reaction 1 in Fig. 4 cannot be formed from H/D exchange of the corresponding 1/1 arene/alkyne adduct in TFA-d_1, and (ii) the 1/2 arene/alkyne adduct as **ArA$_2$** (in Fig. 2) cannot result from the reaction in TFA-d_1 or from the reaction of 1/1 arene/alkyne adduct with another alkyne. **ArA$_2$** would be formed by cis addition of the vinyl-Pd complex **IMc** to the alkyne, followed by protonation.
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Thermal, Catalytic, Regiospecific Functionalization of Alkanes

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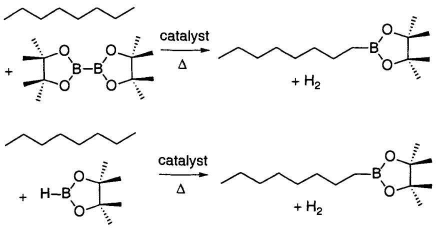
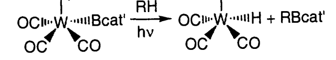
The formation of a single product from terminal functionalization of linear alkanes from a transition metal–catalyzed reaction is reported. The rhodium complex $Cp^*Rh(\eta^4\text{-}C_6Me_6)$ (Cp^*, C_5Me_5; Me, methyl) catalyzes the high-yield formation of linear alkylboranes from commercially available borane reagents under thermal conditions. These reactions now allow catalytic, regiospecific functionalization of alkanes under thermal conditions. The organoborane products are among the most versatile synthetic intermediates in chemistry and serve as convenient precursors to alcohols, amines, and other common classes of functionalized molecules.

Alkanes are among the most abundant but least reactive molecules. This low reactivity, particularly at the terminal position of the alkane, has prevented their direct conversion into industrially important chemicals such as linear alcohols, linear amines, and α-olefins. Instead of selectively producing these desired products, which contain a single functional group at the end of an alkyl chain, reactions of alkanes typically form mixtures. When good selectivity is observed, internal positions or both internal and terminal positions of the alkane react to produce, for example, *tert*-butylhydroperoxide from isobutane or maleic anhydride from *n*-butane (*1*). Certain transition metals do react cleanly at the end of the alkane to produce *n*-alkyl complexes (*2, 3*), but these transformations involve stoichiometric amounts of expensive metal reagents; catalytic reactions that selectively functionalize the terminal positions of alkanes are rare. Transition metal–catalyzed dehydrogenation gives alkene regioisomers (*4–6*), and photocatalytic carbonylation produces secondary photoproducts (*7*). Both processes also suffer from unfavorable thermodynamics. Enzymes that oxidize higher alkanes than methane and ethane give regioisomeric mixtures. Here, we report a regiospecific catalytic functionalization of linear alkanes under thermal conditions: the coupling of alkanes with borane reagents to form linear alkylboranes (Scheme 1). These borane products are common, well-developed synthetic intermediates in organic chemistry. They are easily converted to amines, alcohols, alkenes, and other classes of functionalized molecules in a single step (*8, 9*).



Scheme 1.

We previously reported the stoichiometric reaction of transition metal–boryl complexes ($L_nM\text{-}BR_2$, where L is a ligand, M is a metal, and R is an organic substituent) with alkanes to produce linear alkylboranes:



(1)

(*10, 11*). We then pursued a selective catalytic reaction of alkanes that incorporates a similar stoichiometric step into a catalytic cycle. We disclosed the reaction of diboron reagents (R_2BBR_2; R_2 = pinacolate) with alkanes catalyzed by $Cp^*Re(CO)_3$ (Cp^*, C_5Me_5; Me, methyl) to produce linear alkylboranes under photochemical conditions (*12*). This photochemistry led to the selective, catalytic reactions under the thermal conditions described below (*13*).

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