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J. Am. Chem. Soc., **Just Accepted Manuscript** • DOI: 10.1021/ja4052153 • Publication Date (Web): 04 Jun 2013

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Iridium-Catalyzed, Intermolecular Hydroetherification of Unactivated Aliphatic Alkenes with Phenols

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Supporting Information Placeholder

ABSTRACT: Metal-catalyzed addition of an O–H bond to an alkene is a desirable process because it allows for rapid access to ethers from abundant starting materials without formation of waste, without rearrangements, and with the possibility to control stereoselectivity. We report the intermolecular, metal-catalyzed addition of phenols to unactivated α-olefins. Mechanistic studies on this rare catalytic reaction reveal a dynamic mixture of resting states that undergo O–H bond oxidative addition and subsequent olefin insertion to form ether products.

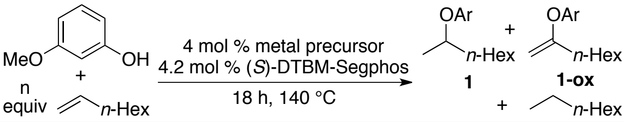
Metal-catalyzed hydrofunctionalization of alkenes offers the potential to control regioselectivity, diastereoselectivity and enantioselectivity of the addition process and to form products from readily accessible starting materials without formation of waste. Metal-catalyzed hydrofunctionalizations also could be more tolerant of auxiliary functionality than acid-catalyzed additions and could occur without the rearrangements that are characteristic of acid-catalyzed additions to alkenes. Hydroamination, the addition of an N–H bond across an unsaturated C–C bond, remains one of the most studied transformations in hydrofunctionalization chemistry,[1] but hydroetherification, the addition of an O–H bond across an unsaturated C–C bond, is much less developed.

The ether products of hydroetherification are more often formed by substitution reactions than addition reactions.[2] The electrophiles in substitution reactions are typically prepared by a multistep sequence that often includes oxidation or reduction and functional group interconversion or activation of an alcohol. Moreover, these substitution reactions generate salt by-products. Alternatively, ethers are formed by acid-catalyzed additions of alcohols to alkenes.[3] However, these additions often require strong acids and high temperatures, form side products from isomerization of carbocationic intermediates, and occur without control of the stereochemistry of the product. Moreover, acid-catalyzed additions of phenols to alkenes occur with competitive reaction of the alkene at the O–H bond and at an *ortho* or *para* C–H bond.[4] Thus, metal-catalyzed hydroetherification would exploit the abundance and stability of alkene starting materials, and could overcome many of the limitations of the classical syntheses of ethers.

However, current hydroetherification reactions are limited in scope. Most reported metal-catalyzed hydroetherifications of unsaturated C–C bonds are intramolecular and occur with carbon-carbon multiple bonds that are more reactive than those of unactivated alkenes.[5] Cationic gold complexes catalyze the cyclization of allenyl-alcohols in high yield and excellent ee, but the reactions do not occur intermolecularly or with mono-enes.[6] Likewise, Ir, Pd, Pt, and lanthanide complexes catalyze intramolecular additions of alcohols to alkenes and alkynes, but the intermolecular additions to alkenes catalyzed by such complexes are unknown.[7] Intermolecular hydroetherification of allenes with both carboxylic acids and phenols to form allylic ethers has been reported to occur in high yield and ee in the presence of a Rh catalyst, but the reactions do not occur with mono-enes.[8] Finally, the intermolecular additions of alcohols to unstrained, isolated alkenes have been reported to occur in the presence of triflates of coinage metals.[9] In these cases, the reactions form side products that are characteristic of carbocation intermediates.[10]

Here, we report intermolecular, metal-catalyzed additions of phenols to unactivated α-olefins in good yields. The measurable enantioselectivity and lack of reaction in the presence of acid, but absence of the metal, show that the iridium complex, not a proton, catalyzes the addition reaction. Mechanistic studies imply that the reaction proceeds by reversible oxidative addition of the O–H bond of the phenol, followed by turnover-limiting insertion of the alkene.

Table 1. Reaction Development for the Ir-Catalyzed Addition of 3-OMe-Phenol to 1-Octene[a]



entry	metal precursor	additive (4 mol %)	n equiv 1-octene	% 1-octene[b] remaining	% **1**[b]	% **1-ox**[b]
1	$[Ir(coe)_2Cl]_2$	--	10	11	30	4
2	$[Ir(cod)Cl]_2$	--	10	26	46[c]	10
3	--	4% HOTf	10	88	0	0
4	$[Ir(cod)Cl]_2$	17 % Et_3N	10	48	35	6
5	$[Ir(cod)Cl]_2$	$AgBF_4$	10	2	68[d]	0
6	$[Ir(cod)_2][BF_4]$	--	10	2	0	0
7	$[Ir(cod)_2][BF_4]$	KHMDS	10	5	18	2
8	$[Ir(cod)Cl]_2$	--	5	3	24	5
9	$[Ir(cod)Cl]_2$	--	20	48	60[e]	16
10	$[Ir(cod)Cl]_2$	--	40	64	51[f]	17
11	$[Ir(cod)Cl]_2$	--	80	70	38	20

[a]Reactions were performed with 0.2 mmol phenol. [b]Determined by GC analysis. [c]19% ee. [d]1:1:1 racemic mixture of 2-, 3-, 4-aryloxy octane. [e]25% ee. [f]36% ee.

We previously showed that the combination of iridium and DTBM-Segphos catalyzes the additions of amides to alkenes.[11] On the basis of these studies we tested the combination of $[Ir(coe)_2Cl]_2$ and a series of phosphine, bisphosphine, and chelating nitrogen ligands as catalyst for the addition of 3-OMe-phenol to 1-octene (see Supporting Information for studies with various ligands). Only Ir complexes of (*S*)-DTBM-

Segphos (DTBM = 3,5-di-*tert*-butyl-4-methoxy) led to substantial amounts of ether and enol-ether products. Further experiments conducted with (*S*)-DTBM-Segphos as ligand are summarized in Table 1. Isomerization of the terminal alkene to unreactive internal olefin isomers was observed over the course of the reaction; because internal alkenes are less reactive than terminal alkenes, this isomerization limited conversion of the alkene to the ether. Reactions conducted with $[Ir(cod)Cl]_2$ as a precursor with a slight excess of bisphosphine, relative to Ir, occurred with less alkene isomerization and concomitantly greater yield of products, compared to reactions conducted with $[Ir(coe)_2Cl]_2$ as the iridium precursor (entry 2 vs. 1).

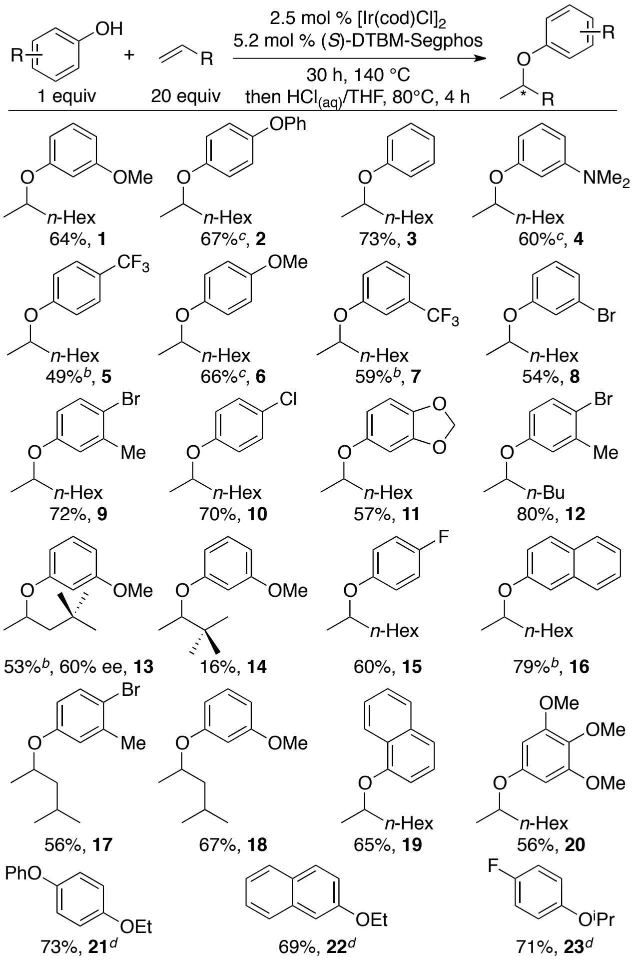
Several experiments provide strong evidence that the reaction is catalyzed by iridium, not a proton. Measurable, albeit modest, ee values for this reaction (19-40%) rule out alkene hydroetherification catalyzed by a proton alone. Products were not detected from reactions conducted in the presence of ligand and HOTf (entry 3), excluding an addition catalyzed by a phosphonium salt. Reactions conducted with excess tributylamine relative to iridium, which would quench trace acid, occurred with comparable yields (entry 4) to the reaction in the absence of this additive. Reactions conducted by initial halide abstraction from iridium with $AgBF_4$ led to the formation of a mixture of racemic ether products, consistent with an acid-catalyzed process. Reactions conducted with a cationic Ir precursor and ligand did not yield product (entry 6), but those conducted with a cationic Ir precursor, ligand, and base formed product (entry 7), presumably after generating a neutral Ir complex. A greater fraction of 1-octene vs. other isomers was observed for reactions conducted with 20 equivalents of olefin than reactions conducted with 5 or 10 equivalents of alkene and resulted in a 60% yield of **1** (entry 9).

The scope of the Ir-catalyzed addition of phenols to α-olefins by the procedure we developed is summarized in Chart 1. Products containing the phenoxy group at the 2-position of the alkyl chain were formed exclusively with ee's ranging from 8% to 60%, the highest value being observed for reaction of an alkene containing steric bulk proximal to the alkene (**13**). Upon completion of the reaction, the enol-ether products that result from oxidative etherification of the alkene were hydrolyzed with acid to facilitate isolation of the alkyl aryl ether products. A broad range of functional groups located *meta* and *para* to the OH-group were compatible with the addition process; the reaction between olefins and phenols containing halides, ethers, and tertiary amines occurred in good yields. Although reactions of 1-naphthol formed product **19** in good yield, other phenols containing substituents *ortho* to the OH-group did not add to the α-olefins under similar conditions.

The electronic properties of the substituents on the phenol influenced the reaction conversion and yield. Reactions of electron-poor phenols typically occurred in lower yields than reactions of electron-rich phenols because there was a greater amount of alkene isomerization during the reaction of the electron-poor phenol. Complete isomerization of the terminal alkene was observed after 24 h for reactions of 4-CF_3-phenol while only half of the terminal alkene isomerized during reactions of 4-OMe-phenol. Consequently, reactions of electron-rich phenols conducted with 10 equivalents of olefin, rather than the 20 equivalents used for a majority of the reactions, formed the addition products in good yield.

The scope of the reaction in alkene also was examined. Addition products were not detected from reactions of phenols with olefins containing activated allylic C–H bonds, such as allylbenzene, under the conditions we developed. Rapid isomerization of these terminal alkenes occurred. Alkenes with steric bulk in close proximity to the reactive alkene reacted more slowly than alkenes lacking this property. For example, the reaction of *tert*-butyl ethylene formed addition product **14** in low yield. However, reaction of 4,4-dimethyl-1-pentene and 4-methyl-1-pentene did form products **13**, **17**, and **18** in substantial yields. Reactions of phenols with ethylene and propene occurred with only 2.5 atm of alkene to form ether and enol ether products. Catalyst decomposition was observed upon accumulation of the enol ether during the reactions with ethylene. Nonetheless, the yields of reactions with these alkenes were higher than those with longer chain olefins because alkene isomers cannot form during reactions of these two alkenes.

Chart 1. Ir-Catalyzed Additions of Phenols to α-Olefins[a]



[a]Isolated yields. Reaction was performed with: [b]40 equivalents or [c]10 equivalents of alkene relative to ArOH. [d]Reactions were conducted in mesitylene solvent.

Mechanistic studies were conducted to gain insight into the elementary steps of this unusual process. Kinetic analysis of the additions of 4-F-phenol to propene was conducted. Initial rates (to 15% conversion) were measured by ^{19}F NMR spectroscopy (see Supporting Information). The reaction was found to be first-order in catalyst, zero-order in the concentration of alkene and partial positive order (0.6) in the concentration of 4-F-phenol.

Monitoring the reactions by ^{31}P NMR spectroscopy indicated that an unsymmetrical bisphosphine complex persisted throughout the course of the reaction (Figure 1a, spectrum *V*). This observed species was characterized to allow interpretation of the kinetic data. The oxidative addition of O–H bonds to Ir(I) is well established.[12] However, addition of 4-F-phenol to a solution of $[Ir(cod)Cl]_2$ and DTBM-Segphos in benzene did not form any new species. In contrast, the combination of Ir, ligand, and olefin in the absence of alcohol did react; the original orange solution turned light yellow in 1 h at 294 K. A similar color change was observed at the start of the catalytic reaction. The product of this reaction was shown by NMR spectroscopy to be the Ir(allyl)hydride complex **24** shown in Figure 1.

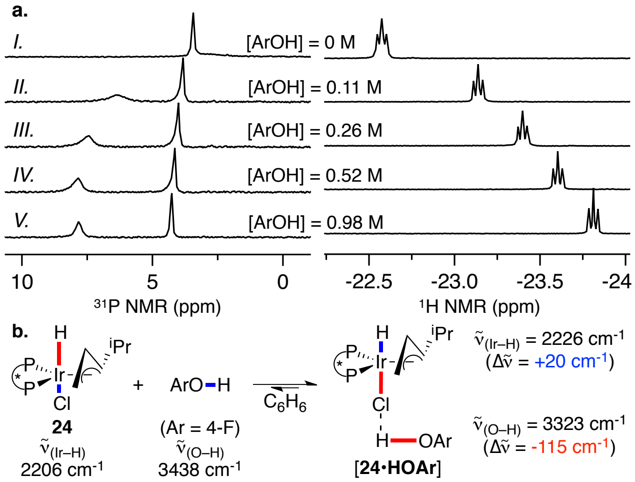


Figure 1. a. ^{31}P (left) and ^{1}H (right, Ir–H region only) NMR spectra *i.-v.* of **24** in the presence of varying concentrations of 4-F-phenol at 294 K. b. IR stretching frequencies of the Ir–H and O–H bonds of **24**, free 4-F-phenol, and [**24•HOAr**].

$$\delta_{obs} = \delta_{24}\mu_{24} + \delta_{[24\cdot HOAr]}\mu_{[24\cdot HOAr]} \qquad (1)$$

$$\delta_{obs} = \frac{\delta_{24} + \delta_{[24\cdot HOAr]}K_{eq}[ArOH_o]}{1 + K_{eq}[ArOH_o]} \qquad (2)$$

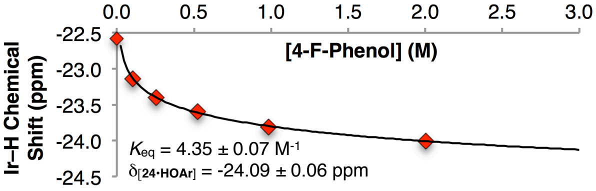


Figure 2. Plot of the Ir–H chemical shift as a function of 4-F-phenol concentration in C_6D_6 at 294 K, fit to Eq 2.

The hydride resonance and phosphorus resonances observed by NMR spectroscopy of isolated **24** in C_6D_6 (spectrum *I*) did not match those of the species in the catalytic reaction (spectrum *V*). However, the hydride chemical shift in the ^{1}H NMR spectrum of solutions of **24** containing varying concentrations of 4-F-phenol depended on the concentration of the phenol, and the ^{1}H and ^{31}P NMR spectra of the solution containing a 1 M concentration of alcohol matched those of the complex observed in the catalytic reactions (Figure 1a, spectra *I-V*).

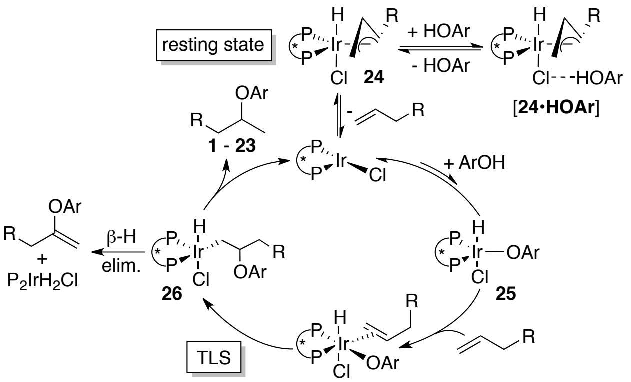
The interaction of the phenol with **24** was investigated by NOESY and IR spectroscopy (Figure 1b). Metal-hydride complexes are known to be hydrogen-bond acceptors. NOE correlations between metal-hydrides and alcoholic protons, as well as a reduced metal-hydride IR stretching frequency in the presence of an alcohol, are commonly observed for systems containing these hydrogen-bonding interactions.[13] In contrast to these characteristics of a M-H•HX interaction, no NOE was observed between the Ir–H resonance of **24** and the OH resonance of 4-F-phenol. In addition, the IR stretching frequency of the Ir–H bond of **24** *increased* by 20 cm^{-1} to 2226 cm^{-1} in the presence of 1 M 4-F-phenol (vs. **24** in the absence of alcohol), while the O-H stretching frequency of the phenol decreased by 115 cm^{-1} to 3323 cm^{-1} (vs. 1 M 4-F-phenol in the absence of **24**). These data suggest that the hydrogen-bond acceptor in complex [**24•HOAr**] is a ligand other than the hydride. The remaining likely hydrogen-bond acceptor in the coordination sphere of **1** is the chloride ligand (Figure 1b). We suggest that the reduced electron donation by a hydrogen-bound Ir–Cl ligand strengthens the Ir–H bond *trans* to the chloride and accounts for the increased Ir–H stretching frequency observed by IR spectroscopy.

The fraction of **24** and **24•HOAr** was determined by ^{1}H NMR spectroscopy, and this ratio was consistent with the order of the reaction in phenol. The resonance in the Ir–H region of the ^{1}H NMR spectrum results from the average of the fractional contributions of the absolute Ir–H chemical shifts of **24** and [**24•HOAr**] (Eq 1). The equilibrium concentrations of the two complexes were determined by measuring the observed chemical shift of the Ir–H resonance as a function of the concentration of 4-F-phenol (Figure 2). The value of K_{eq} from fitting the data to eq 2 is 4.4 M^{-1}, and the chemical shift of the Ir–H of [**24•HOAr**] is -24.1 ppm at 294 K. Van't Hoff analysis of the equilibrium constants determined by conducting this experiment at temperatures from 294 to 335 K (see supporting information) revealed the following thermodynamic parameters for the equilibrium: ΔH_{eq} = -1.9 kcal/mol and ΔS_{eq} = -3.5 eu.[14] From these thermodynamic parameters, an equilibrium constant of 1.6 M^{-1} at the 140 °C temperature of the reaction was calculated; this equilibrium constant corresponds to a 40:60 ratio of **24**:[**24•HOAr**]. A significant concentration of both complexes is consistent with the measured partial-order (0.6) of the catalytic addition reaction in [4-F-phenol].

A comparison of the initial rates for the addition of *O*-deuterated 4-F-phenol and proteo 4-F-phenol to propene in separate vessels revealed a kinetic isotope effect (KIE) of 1.6. Although greater than unity, this KIE is likely too small to be consistent with a turnover-limiting protonolysis or oxidative addition of the O–H bond,[6d] but it would be consistent with reversible oxidative addition of the alcohol O–H bond to the Ir center prior to a turnover-limiting step. In this case, the product of oxidative addition would be less stable than the catalyst resting state. This conclusion is consistent with the lack of O-H addition product from the reaction of DTBM-Segphos, $[Ir(coe)_2Cl]_2$ and 4-F-phenol.

These mechanistic data are consistent with the proposed catalytic cycle in Scheme 1. In this mechanism, the (allyl)iridium hydride resting state **24**, which equilibrates with hydrogen bonded **24•HAr**, undergoes C–H bond-forming reductive elimination to release olefin and form an Ir(I) complex that can undergo reversible, endergonic oxidative addition of the O–H bond of the phenol to form **25**. Subsequent olefin coordination and turnover-limiting insertion into the Ir–O bond forms an alkyl-Ir complex **26**. C–H bond-forming reductive elimination would then release the ether product, whereas β-H elimination from the same intermediate would form the enol-ether side product. This mechanism is consistent with the observed zero-order dependence of the rate on the concentration of alkene because the alkene is released and added prior to the turnover-limiting transition state. This mechanism is also consistent with the partial positive order dependence of the rate on the concentration of alcohol because a significant fraction of the resting state exists as the alcohol adduct [**24•HOAr**]. The alcohol dissociates and adds prior to the turnover-limiting step of a reaction initiated from [**24•HOAr**].

Scheme 1. Proposed Catalytic Cycle for the Ir-Catalyzed Hydroetherification of α-Olefins



Several aspects of this mechanism are distinct from those for addition of the N-H bonds of amides to alkenes catalyzed by the combination of $[Ir(coe)_2Cl]_2$ and Segphos.[11] The product from oxidative addition of the amide was the resting state of the catalyst in the hydroamidations of alkenes; the open coordination site of the $L_2IrCl(H)(amide)$ complex formed by oxidative addition was occupied by a second amide. The system for the catalytic additions of phenols lacks a basic component, making the stable 18-electrin Ir(III) complex in the system the allyl hydride complex **24** and its phenol adduct **24•HOAr**. Consequently, isomerization of the alkene occurs faster during the Ir-catalyzed additions of phenols to alkenes than during the additions of amides to alkenes.

In summary, we report a rare example of a metal-catalyzed intermolecular addition of an alcohol to an unactivated alkene. The lack of products from rearrangements and addition of the *ortho* C–H bond, the measurable enantiomeric excess, the absence of product from phosphonium salts, the lack of an effect of added tertiary alkylamine, and kinetic data that are consistent with the observed species show that the reaction is not purely acid-catalyzed. Instead, it likely occurs by generation of an Ir(I) intermediate by reductive elimination of the observed allyliridium hydride species, followed by reversible O–H bond oxidative addition, turnover-limiting olefin insertion, and product-releasing reductive elimination. Efforts to mitigate olefin isomerization and increase the enantioselectivity of the reaction are in progress.

ASSOCIATED CONTENT

Experimental procedures and characterization of all new compounds including NMR spectroscopy data, conditions for HPLC separations on a chiral stationary phase, kinetic studies, and optimization data are supplied. This material is available free of charge via the Internet at http://pubs.acs.org.

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ACKNOWLEDGMENT

This work was supported by the Director, Office of Science, of the U.S. Department of Energy under Contract No. DE-AC02-05CH11231. We thank Johnson-Matthey for a gift of $[Ir(cod)Cl]_2$, and Takasago for a gift of (*S*)-DTBM-Segphos. C.S.S. thanks the NSF for a graduate research fellowship.

REFERENCES

(1) (a) Müller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev*. **2008**, *108*, 3795. (b) Hannedouche, J.; Schulz, E. *Chem. Eur. J*. **2013**, *19*, 4972.

(2) (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc*. **1999**, *121*, 4545. (b) Muci, A. R.; Buchwald, S. L. *Cross-Coupling Reactions* **2002**, *219*, 131. (c) López, F.; Ohmura, T.; Hartwig, J. F. *J. Am. Chem. Soc*. **2003**, *125*, 3426. (d) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev*. **2004**, *248*, 2337. (e) Onitsuka, K.; Okuda, H.; Sasai, H. *Angew. Chem. Int. Ed*. **2008**, *47*, 1454.

(3) Smith, M. B.; March, J. In *March's Advanced Organic Chemistry*; 5 ed.; John Wiley and Sons: New York, NY, 2001, p 996.

(4) (a) Ronchin, L.; Quartarone, G.; Vavasori, A. *J. Mol. Catal. A-Chem*. **2012**, *353*, 192. (b) Ronchin, L.; Vavasori, A.; Toniolo, L. *J. Mol. Catal. A-Chem*. **2012**, *355*, 134.

(5) Hintermann, L.; Vigalok, A., Ed.; Springer Berlin / Heidelberg: 2010; Vol. 31, p 123.

(6) (a) Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496. (b) Zhang, Z. B.; Widenhoefer, R. A. *Angew. Chem. Int. Ed*. **2007**, *46*, 283. (c) Wang, Z. J.; Brown, C. J.; Bergman, R. G.; Raymond, K. N.; Toste, F. D. *J. Am. Chem. Soc*. **2011**, *133*, 7358. (d) Brown, T. J.; Weber, D.; Gagné, M. R.; Widenhoefer, R. A. *J. Am. Chem. Soc*. **2012**, *134*, 9134. (e) Butler, K. L.; Tragni, M.; Widenhoefer, R. A. *Angew. Chem. Int. Ed*. **2012**, *51*, 5175.

(7) (a) Qian, H.; Han, X.; Widenhoefer, R. A. *J. Am. Chem. Soc*. **2004**, *126*, 9536. (b) Li, X.; Chianese, A. R.; Vogel, T.; Crabtree, R. H. *Org. Lett*. **2005**, *7*, 5437. (c) Patil, N. T.; Lutete, L. M.; Wu, H.; Pahadi, N. K.; Gridnev, I. D.; Yamamoto, Y. *J. Org. Chem*. **2006**, *71*, 4270. (d) Messerle, B. A.; Vuong, K. Q. *Organometallics* **2007**, *26*, 3031. (e) Yu, X.; Seo, S.; Marks, T. J. *J. Am. Chem. Soc*. **2007**, *129*, 7244. (f) Seo, S. Y.; Yu, X. H.; Marks, T. J. *J. Am. Chem. Soc*. **2009**, *131*, 263. (g) Weiss, C. J.; Marks, T. J. *Dalton Trans*. **2010**, *39*, 6576. (h) Atesin, A. C.; Ray, N. A.; Stair, P. C.; Marks, T. J. *J. Am. Chem. Soc*. **2012**, *134*, 14682.

(8) (a) Kim, I. S.; Krische, M. J. *Org. Lett*. **2008**, *10*, 513. (b) Kawamoto, T.; Hirabayashi, S.; Guo, X.-X.; Nishimura, T.; Hayashi, T. *Chem. Commun*. **2009**, 3528. (c) Koschker, P.; Lumbroso, A.; Breit, B. *J. Am. Chem. Soc*. **2011**, *133*, 20746.

(9) (a) Yang, C.-G.; He, C. *J. Am. Chem. Soc*. **2005**, *127*, 6966. (b) Yang, C.-G.; Reich, N. W.; Shi, Z.; He, C. *Org. Lett*. **2005**, *7*, 4553. (c) Hirai, T.; Hamasaki, A.; Nakamura, A.; Tokunaga, M. *Org. Lett*. **2009**, *11*, 5510.

(10) For a discussion of the parallels between intermolecular O–H bond additions to unactivated alkenes catalyzed by metal triflates and Brønsted acids see: (a) Li, Z.; Zhang, J.; Brouwer, C.; Yang, C.-G.; Reich, N. W.; He, C. *Org. Lett*. **2006**, *8*, 4175. (b) Rosenfeld, D. C.; Shekhar, S.; Takemiya, A.; Utsunomiya, M.; Hartwig, J. F. *Org. Lett*. **2006**, *8*, 4179.

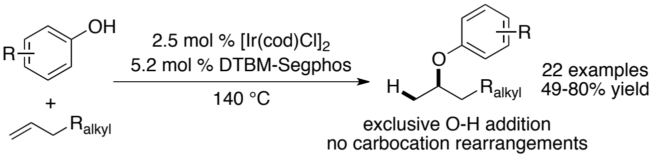
(11) Sevov, C. S.; Zhou, J.; Hartwig, J. F. *J. Am. Chem. Soc*. **2012**, *134*, 11960.

(12) (a) Ladipo, F. T.; Kooti, M.; Merola, J. S. *Inorg. Chem*. **1993**, *32*, 1681. (b) Blum, O.; Milstein, D. *J. Organomet. Chem*. **2000**, *593–594*, 479. (c) Dorta, R.; Rozenberg, H.; Shimon, L. J. W.; Milstein, D. *J. Am. Chem. Soc*. **2001**, *124*, 188. (d) Blum, O.; Milstein, D. *J. Am. Chem. Soc*. **2002**, *124*, 11456. (e) Schaub, T.; Diskin-Posner, Y.; Radius, U.; Milstein, D. *Inorg. Chem*. **2008**, *47*, 6502.

(13) (a) Stevens, R. C.; Bau, R.; Milstein, D.; Blum, O.; Koetzle, T. F. *J. Chem. Soc., Dalton Trans*. **1990**, *0*, 1429. (b) Lee, J. C.; Peris, E.; Rheingold, A. L.; Crabtree, R. H. *J. Am. Chem. Soc*. **1994**, *116*, 11014. (c) Siegbahn, P. E. M.; Eisenstein, O.; Rheingold, A. L.; Koetzle, T. F. *Acc. Chem. Res*. **1996**, *29*, 348.

(14) The small negative value of ΔSeq is consistent with an equilibrium between a self associated phenol and [24•HOAr], as would be expected in the nonpolar organic solvent benzene.

TOC Graphic


OH
R
+
R$_{alkyl}$
2.5 mol % [Ir(cod)Cl]$_2$
5.2 mol % DTBM-Segphos
140 °C
O
R
H
R$_{alkyl}$
22 examples
49-80% yield
exclusive O-H addition
no carbocation rearrangements