Hidden Brønsted Acid Catalysis: Pathways of Accidental or Deliberate Generation of Triflic Acid from Metal Triflates

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Supporting Information

ABSTRACT: The generation of a hidden Brønsted acid as a true catalytic species in hydroalkoxylation reactions from metal precatalysts has been clarified in case studies. The mechanism of triflic acid (CF₃SO₃H or HOTf) generation starting either from AgOTf in 1,2-dichloroethane (DCE) or from a Cp*RuCl₂/AgOTf/phosphane combination in toluene has been elucidated. The deliberate and controlled generation of HOTf from AgOTf and cocatalytic amounts of *tert*-butyl chloride in the cold or from AgOTf in DCE at elevated



temperatures results in a hidden Brønsted acid catalyst useful for mechanistic control experiments or for synthetic applications.

INTRODUCTION

The development of metal-catalyzed additions of oxygen nucleophiles to nonactivated alkenes¹⁻⁴ had seen limited success prior to 2002,^{1,4-7} but the number of reports on such catalytic hydroalkoxylations (including hydroaryloxylations, if R = aryl; Scheme 1), or related hydroacyloxylations, dramatically

Scheme 1. Hydroalkoxylation Reactions



increased after 2004.^{1,8–33} Many of the new catalysts are electrophilic metal trifluoromethanesulfonate (triflate) salts that display a similar substrate range and product selectivity profile.³⁴

Bearing in mind Spencer's hypothesis that many hetero-Michael additions are catalyzed by Brønsted acidic metal aquo complexes rather than the precursor Lewis acids introduced,³⁵ some ambiguity remains for most of the reported examples with respect to the actual catalytic species. Indeed, the reactions shown in Scheme 1 have also been catalyzed by strong Brønsted acids,^{36,37} and Hartwig and co-workers have shown that traces of triflic acid (CF₃SO₃H/HOTf) are, in many cases, sufficient to reproduce experimental results previously obtained with metal triflate catalysts.^{38,39} However, the approach to show that the Brønsted acid will reproduce a certain set of results neither rules out competitive or exclusive metal catalysis nor does it explicitly prove that Brønsted acid catalysis is occurring.⁴⁰ This may be the reason why the implications of the suggestive results of the Spencer and Hartwig groups have not always been appreciated in work on Lewis-acid-catalyzed

hydroalkoxylations.¹ In a recent example, Cu(OTf)₂ was shown to be a precursor for HOTf via reduction to CuOTf under the conditions of a hydroalkoxylation reaction.⁴¹ In the current work, we have specifically investigated the role of silver triflate (AgOTf), which is used either as a catalyst itself or as a catalyst activator in combination with transition-metal chlorides. The key findings are that HOTf is released according to several specific mechanistic routes and acts as a Brønsted acid catalyst under conditions that have earlier been proposed to involve metal catalysis. We propose the term "hidden Brønsted acid catalysis" to denote cases in which Brønsted acid released from any kind of precursor is responsible for an observed catalytic activity, rather than the precursor itself. We have established conditions to deliberately and reliably generate HOTf in trace amounts from AgOTf under mild conditions. Paradoxically, such a hidden Brønsted acid catalyst may have specific advantages over the use of pure HOTf as catalyst.

RESULTS

Several literature reports suggest the use of AgOTf as a catalyst in halogenated organic solvents including 1,2-dichloroethane (hereafter abbreviated DCE), often at elevated temperatures.^{23,42–46} This is potentially problematic in view of the halide abstracting properties of the silver cation.⁴⁷ To investigate the stability of silver triflate in DCE, we heated a sample of the compound at reflux (84 °C) for 3 h. The resulting turbid suspension was filtered to leave an almost quantitative yield (99%) of AgCl on the filter (for a photograph; see Figure S1, Supporting Information).⁴⁸ The filtrate displayed two peaks in the ¹⁹F NMR spectrum, one for HOTf ($\delta = -77.6$ ppm in C_6D_6 ; $\delta = -78.0$ ppm in CDCl₃; see the discussion for a comment on the chemical shifts of HOTf samples recorded in air and moist solvents) and a second peak

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due to 2-chloroethyltriflate (1; $\delta = -74.9$ ppm in C₆D₆; $\delta = -74.5$ ppm in CDCl₃), which also gave rise to a characteristic triplet (δ {¹H}= 3.62 ppm, J = 5.4 Hz in C₆D₆; $\delta = 4.64$ ppm, J = 5.7 Hz in CDCl₃) in the ¹H NMR spectrum.^{48,49} This peak was more intense if the reaction of AgOTf with DCE was carried out at 80 °C for 2 h but disappeared with a concomitant increase of the HOTf peak after prolonged heating. The solvent therefore reacts with AgOTf via an initial substitution to 1, followed by release of HOTf, either by hydrolysis with trace water⁵⁰ or by an E1-type elimination, which would presumably lead to vinyl chloride oligomers (Scheme 2).

Scheme 2. Generation of HOTf from AgOTf in DCE

$$Cl \xrightarrow{Cl} AgOTf AgCl + \left[\begin{array}{c} Cl^{+} \\ \end{array} \right] OTF$$

The generation of organic triflates from haloalkanes and AgOTf has ample precedence.^{51–53} Our experiment implies that the generation of HOTf from solutions of AgOTf in DCE must be generally expected and is probably inevitable at higher temperatures or with prolonged reaction times. A reported condensation of phenol (2a) with isoprene (3) to 2,2-dimethylchromane (4a; Table 1, entry 1), mediated by catalytic

Table 1. Catalytic Phenol–Isoprene Cyclization to 2,2-Dimethylchromane^a

+	[cat.] (5 mol %)	\sim
ОН А	DCE, r.t.	~~~
2a 3		4a
catalyst	time (h)	yield (%) ^b
AgOTf	48	65
TfOH	2	21
TfOH (0.5 m	ol %) 2	63
p-TsOH	48	63
$Al(OTf)_3$	48	С
$Sn(OTf)_2$	2	89
$Zn(OTf)_2$	48	51
$Bi(OTf)_3$	48	15
$Cu(OTf)_2$	48	48
$Fe(OTf)_3$	2	50
$Ce(OTf)_3$	2	29
LaOTf	48	С
AgOTf + Et ₃ N	N ^d 48	С
AgOTf (1 mo	$(1\%)^e$ 0.3	79
	+ - 2a 3 2a 3 AgOTf TfOH TfOH TfOH TfOH (0.5 m p-TsOH Al(OTf)_3 Sn(OTf)_2 Zn(OTf)_2 Bi(OTf)_3 Cu(OTf)_2 Fe(OTf)_3 Ce(OTf)_3 LaOTf AgOTf (1 model)	$\begin{array}{c c} \begin{array}{c} (cat.] (5 \text{ mol } \%) \\ \hline \\ $

^{*a*}Reaction conditions: the catalyst (5 mol %) was added into a mixture of phenol (1 mmol) and isoprene (1.5 mmol) in DCE (5 mL), and the reaction was stirred at RT. ^{*b*}Yield of isolated product. ^{*c*}No product detected. ^{*d*}Added in large excess. ^{*e*}Catalyst prepared by refluxing AgOTf in DCE (5 mL).

AgOTf in DCE at room temperature or 40 °C over 1–3 days, might well represent an example of hidden acid catalysis rather than a specific silver ion catalysis.⁴³ It is known that fluorinated Brønsted acids are particularly efficient catalysts for this type of reaction, which involves a Friedel–Crafts alkylation followed by a hydroalkoxylation.⁵⁴ We find that Brønsted acids do indeed catalyze the reaction (entries 2–4). In agreement with the control experiment in an earlier report,⁴³ the catalytic activity of HOTf is inferior to that of AgOTf at catalyst loadings of 5 mol % (entries 1, 2).⁴² However, the low yield obtained in the experiment with HOTf (Table 1, entry 2) is misleading because the reaction is very fast,⁵⁵ and the product may undergo cationic polymerization.³⁸ When the reaction was performed with a lower quantity of HOTf (entry 3), the product yield was higher and similar to that earlier obtained with AgOTf (entry 1).⁴² Several other metal triflates among a range tested induced the isoprene–phenol condensation, which weakens the claim for a specific silver ion catalysis (entries 5–12).^{14,56–60}

A potent hidden acid catalyst was obtained by preheating AgOTf in refluxing DCE (84 °C) and cooling to RT prior to addition of the substrates; with only 1 mol % AgOTf, a fast reaction gave high yields of chromane 4a (Table 1, entry 14). Admitting that the role of the silver salt is to abstract chloride from the chlorinated solvent, followed by elimination of HOTf as the true catalyst, it follows that a hidden acid catalyst should be obtained under milder conditions by addition of an alkyl halide that is prone to E1 elimination to the reaction mixture. The addition of *tert*-butyl chloride (5) to a stirred solution of AgOTf at ambient temperature in DCE or chloroform- d_1 produced a white precipitate of AgCl immediately (for a photograph, see Figure S6, Supporting Information), and a major peak for HOTf in the ¹⁹F NMR indicated that E1 eliminiation had occurred (Scheme 3, route a).⁶¹⁻⁶⁴ When the

Scheme 3. HOTf Generation from AgOTf and t-BuCl



experiment was performed in the solvent benzene- d_6 , the generation of HOTf was also observed (¹⁹F NMR), but signals for *tert*-butyl benzene **6** (¹H, ¹³C NMR) show that acid had been generated via a Friedel–Crafts alkylation of the aromatic solvent as another distinct mechanistic route (Scheme 3, route b).

In situ hidden Brønsted acid catalysts prepared in the manner discussed above present distinct advantages over the direct use of HOTf, particularly in small-scale experiments, because HOTf does not readily dissolve homogeneously in apolar reaction mixtures. Either the "hot" (AgOTf + DCE at reflux) or "cold" (AgOTf + *t*-BuCl) protocol gave highly active catalysts for the condensation of isoprene and phenols to chromans (Table 2).

The examples discussed so far have been concerned with acid released from combinations of silver salt and a chlorinated solvent. On the other hand, many other examples of metal triflate catalyses in the literature involve nonchlorinated solvents but must still be considered suspicious with respect to the occurrence of hidden acid catalysis. Other mechanistic Table 2. Synthetic Applications of Deliberate Hidden Brønsted Acid Catalysts^a



^{*a*}All reactions were performed on an 1 mmol scale with AgOTf (1 mol %) as the catalyst precursor at RT with 1.5 equiv of isoprene. ^{*b*}Conditions: Procedure A: AgOTf was stirred for 10 min with *t*-BuCl (4 mol %) prior to addition of the reactants. Procedure B: AgOTf was refluxed in DCE (10 mL) for 3 h prior to addition of the reactants at RT. ^{*c*}The loading of AgOTf was 2 mol %.

pathways of HOTf generation might be operating. For example, it has been shown that a reduction of Cu(OTf), to Cu(OTf) and HOTf takes place in the presence of olefins and alcohols.⁴¹ Another intriguing organometallic catalyst is generated in situ from Cp*RuCl₂ (7),⁶⁵ phosphanes, and AgOTf (1:1:2 ratio) as the activator.⁸⁻¹² It was postulated that a $[Cp*Ru(PR_3)_n]^{2+}$ fragment (n = 1, 2) forms and activates olefins toward nucleophlic additions of oxygen nucleophiles to bring about a redox-neutral hydroalkoxylation (and hydroacyloxylation¹²) reaction.¹⁰ Any such catalytic reaction proceeding via organometallic intermediates is of major interest for synthesis because it has the potential to be carried out enantioselectively. It must be stressed that evidence for the realization of such a process in the literature is scarce and conflicting.^{1,2,35,38} A most remarkable aspect of the Cp*Ru(III) catalyst is a reported asymmetric cyclization of 2-allylphenol (8) to 2-methylcoumaran (9; coumaran is a trivial name for the 2,3-dihydrobenzofurane; Table 3) when the metal fragment is complexed to chelating chiral diphosphanes.¹⁰ The realization of an asymmetric catalytic reaction is probably the strongest argument for the involvement of a chiral phosphane complex rather than a hidden acid as the catalyst. Therefore, we decided to take a closer look at this particular in situ catalyst and to collect evidence for the nature of the catalytically active species formed under reaction conditions. Initially, it was established that the reaction $8\,\rightarrow\,9$ is catalyzed by pure Brønsted acids (Table 3, entry 1,2)³⁶ and also very efficiently by our hidden acid catalyst from AgOTf in DCE (entry 3). Next, the reported¹⁰ ruthenium-catalyzed cyclization was successfully repeated using PPh_3 as the phosphane ligand (entry 4).

Table 3. Catalytic Cyclization of 2-Allylphenol (8) to 2-Methylcoumaran (9)

	ОН	[cat.]		-Me	
	8		9		
entry	catalyst	mol	™ (°C)	time (h)	yield (%) ^c
1^a	p-TsOH	5	60	24	44
2^a	TfOH	5	60	2	63
3 ^{<i>a</i>}	AgOTf	5	50	48	54
4^b	Cp*RuCl ₂ /AgOTf/PPh	3 2	90	48	81
5 ^{<i>b</i>}	Cp*RuCl ₂ /AgOTf/(<i>R</i>)- BINAP	2	50	96	14
6 ^{<i>b</i>}	Cp*RuCl ₂ /AgOTf/(<i>R</i>)- BINAP	2	110	48	45
7 ^b	Cp*RuCl ₂ /AgOTf/ (R)- ^{Tol} BINAP	2	50	96	11
8 ^b	Cp*RuCl ₂ /AgOTf/ (R)- ^{Tol} BINAP	2	110	48	39
9 ^{<i>b</i>}	Cp*RuCl ₂ /AgOTf/(<i>R</i> , <i>S</i> JOSIPHOS	p)- 2	110	48	3

"General conditions: catalyst and 8 (1 mmol) were stirred in DCE (3 mL) at the indicated temperature. ^bGeneral conditions: catalyst prepared from Cp*RuCl₂ (0.02 mmol) and AgOTf (0.04 mmol) in PhMe (3 mL) at 90 °C for 3 h, followed by cooling and addition of a ligand (0.02 mmol) and substrate 8 (1 mmol). Coumaran 9 was isolated by chromatography and analyzed by NMR, GC/MS, and chiral HPLC.⁴⁸ Cyield of product after chromatography.

Notably, the conditions of this metal-catalyzed reaction (Table 3, entry 4) appear to be harsher than those of the acidcatalyzed reactions (entries 1–3), considering the temperature and reaction times. The in situ catalyst preparation asks for heating of Cp*RuCl₂ and AgOTf in toluene for 3 h, followed by cooling to ambient temperature and addition of the phosphane ligand. In order to study the chemical processes taking place, we first performed the procedure without addition of a phosphane. After evaporation of the solvent, NMR spectra of the in situ catalyst from Cp*RuCl₂ and AgOTf in toluene were recorded. The ¹H NMR spectrum showed the presence of a single major new organometallic Cp* species, which was isolated by chromatography and turned out to be the known complex [Cp*Ru(η^6 -toluene)]OTf (10) (Scheme 4).^{66,67}

Scheme 4. Reaction Chemistry of Cp*RuCl₂ (7) in Toluene



Related complexes have previously been prepared from either $HCp^*/RuCl_3$ or Cp^*RuCl_2 and arenes in refluxing alcoholic solution⁶⁸ or alternatively from Ru(II) precursors like [Cp*Ru-(MeCN)₃]OTf by ligand exchange with arenes.^{67,69}

We independently synthesized the complexes $[Cp*Ru(n^6)]$ toluene)]Cl (11)⁷⁰ and [Cp*Ru(η^{6} -toluene)]OTf (10) from Cp*RuCl₂ by heating in toluene/isopropanol, in the absence or presence of AgOTf, respectively (Scheme 4). The ruthenium-(II) cation Cp*Ru⁺ is a very strong arenophile in organometallic coordination chemistry⁶⁹ that might not readily exchange toluene for a phosphane ligand in toluene solution, particularly if the phosphane can complex to AgCl, which is present in the mixture in stoichiometric amounts. An in situ catalyst was prepared by heating Cp*RuCl₂ and AgOTf in toluene, followed by cooling and addition of PPh₃.¹⁰ The only detectable Cp* species by ¹H NMR in CDCl₃ was again due to [Cp*Ru(toluene)]OTf (10), with no other specific complex signals in the ³¹P NMR spectrum apart from broad resonances at $\delta(^{31}P) = 10-15$ ppm, which are ascribe to dynamic (PPh₃)_nAgX species.⁷¹ Because we had initially removed the toluene solvent from the in situ catalysts in vacuo before spectroscopic investigation, any HOTf that might have been formed was no longer present. A key experiment involved the generation of an in situ catalyst from Cp*RuCl₂ and AgOTf in hot toluene, followed by addition of (\pm) -BINAP (2,2'-bisdiphenylphosphino-1,1'-binaphthyl) as a potentially chelating diphosphane, which should increase chances of generating and observing a [Cp*Ru^{II}(BINAP)] complex. A filtered sample of this in situ catalyst was analyzed by NMR spectroscopy in CDCl₃ solution. The ¹H NMR spectrum revealed again the presence of [Cp*Ru(toluene)]OTf (10) as a single major Cp*containing substance. The ¹⁹F NMR spectrum displayed signals for both the OTf⁻ counterion ($\delta = -77.84$ ppm) and HOTf (δ = -78.55 ppm), though this may be due to the presence of a heterogeneous HOTf droplet phase; see the Discussion. The

Figure 1. ³¹P NMR spectrum of an in situ catalyst mixture prepared from Cp*RuCl₂, AgOTf, and (\pm) -BINAP.

³¹P NMR spectrum (Figure 1) displayed multiple signals, which could be interpreted as belonging to the complex species $[Ag((\pm)-BINAP)_2]Cl \ (\delta = 15.59 \text{ ppm}) \text{ and } [\{AgCl((\pm)-BINAP)\}_2] \ (\delta = 11.24, 10.25 \text{ ppm}), which appear each as$ characteristic combination doublets with couplings¹J(¹⁰⁹Ag,³¹P) and ¹J(¹⁰⁷Ag,³¹P) to silver isotopic nuclei (Figure1 and Figure S7, Supporting Information).⁷²

The conclusion is that an in situ catalyst prepared from $Cp*RuCl_2$, AgOTf, and PR_3 in hot toluene solution contains HOTf, $[Cp*Ru(\eta^{6}-toluene)]OTf$ (10), and several $[Ag_mCl_m(PR_3)_n]$ complexes. The HOTf must result from a redox reaction involving a $Cp*Ru^{III}$ species as the oxidant (eq 1). Our spectral observations give no hint as to the identity of the reductant (RH), but judging from color changes during the in situ catalyst preparation, the redox process occurs prior to addition of the phosphane and might thus involve the solvent toluene as a reducing agent.

$$Cp^{*}Ru^{III}(PhMe)(OTf)_{2} + RH$$

= [Cp^{*}Ru^{II}(PhMe)](OTf) + R + HOTf (1)

Triflic acid should induce cyclization of **8** to racemic **9** under conditions of the catalytic reaction, whereas neither the sandwich complex **10** nor the $[Ag_nCl_n(BINAP)_m]$ species would be expected to show catalytic activity for hydroalkoxylation.¹¹ In any case, a range of cyclizations performed with the Cp*RuCl₂/AgOTf/phosphane system using the enantiopure ligands (*R*)-BINAP, (*R*)-TolBINAP, and (1*R*,*S*_P)-Josiphos gave exclusively racemic product in our hands (Table 3, entries 5–9). Because the in situ Cp*RuCl₂-AgOTf-PR₃ catalyst is evidently of the hidden acid type, it remained to be shown whether some of its previously reported reactions might be performed with a simple deliberate hidden acid catalyst for preparative purposes. The results in Table 4 show that this is

Table 4. Application of Deliberate Hidden Acid Catalysts in Catalytic Hydroalkoxylation $\operatorname{Reactions}^a$

^{*a*}All reactions were performed for 1 h at 90 °C with 1 mol % AgOTf, with allylphenol (1 mmol) or a mixture of alcohol (1 mmol) and alkene (1.5 mmol) in 10 mL DCE (10 mL). ^{*b*}Catalyst prepared from AgOTf (1 mol %) and *t*-BuCl (4 mol %) in DCE at RT for 10 min. ^{*c*}Reaction performed in CH₂Cl₂ at 50 °C for 96 h.

indeed the case; catalytic hydroalkoxylations of allylphenols⁸ as well as intermolecular hydroalkoxylations of norbornene⁹ were performed with a hidden acid catalyst generated from AgOTf and either DCE or *t*-BuCl. As compared to the original procedures,^{8,9} which had used a loading of 2 mol % [Ru] and 4 mol % AgOTf at 70 or 85 °C over 48 or 18 h, respectively, the reactions with the deliberate hidden acid catalysts were all performed with a loading of 1 mol % AgOTf at 90 °C within 1 h.

DISCUSSION

Numerous reports on metal-catalyzed hydroalkoxylation reactions have appeared in recent years.^{1,5–32} The substrate scope and selectivity observed with those catalysts remain in a relatively narrow range and are hardly discernible from results obtained with Brønsted acid catalysts. This could, in principle,

be due to a common mechanistic scheme involving Lewis-acidassisted Brønsted acid catalysis.^{1,15,29,73} On the other hand, it has been implied that traces of acid from the hydrolysis of a metal salt precursor might be responsible for the observed acidlike catalytic activity of transition-metal salts.^{35,37,38,40,41} In support of this interpretation, some groups have shown that the results of apparent metal catalysts can be reproduced with respect to both activity and selectivity by use of small amounts of strong Brønsted acid. This approach does not necessarily prove that Brønsted acid catalysis is operating under the conditions of the catalytic reaction. In the present work, we have chosen the alternative approach of proving that HOTf is generated from metal triflate precursors under reaction conditions according to specific mechanistic pathways and acts as a hidden Brønsted acid catalyst for the catalytic reaction in question. The method used for detecting HOTf was ¹⁹F NMR spectroscopy. This technique was also successful for mixtures containing HOTf and soluble organometallic complex salts with OTf⁻ as the counterion, which remarkably gave rise to separate signals in apolar solvents, which may however be a consequence of the "wet" conditions of analysis.⁷⁴ In fact, the NMR analysis of HOTf solutions under regular laboratory conditions in air with moist solvent (a representative sample of CDCl₃ contained 274 ppm H₂O according to Karl Fischer titration) shows peculiarities; at concentrations of $\sim 1 \,\mu L$ HOTf per mL of CDCl₃, a sample will give rise to at least *two* peaks in the ¹⁹F NMR spectrum, one relatively sharp peak at $\delta = -76.3$ \pm 0.5 ppm corresponding to homogeneously dissolved HOTf in the organic phase and at least one second, broadened peak at $\delta = -79.5 \pm 0.5$ ppm, which is sometimes accompanied by smaller, similarly broadened peaks (Figure 2). Visual

Figure 2. ¹⁹F NMR spectra of HOTf in moist CDCl₃.

observation indicates that the additional signals are due to a separate droplet phase of HOTf, which also causes the turbid appearance of the NMR sample. The use of SiMe4 as an internal standard further complicates the analysis because reaction of HOTf with SiMe₄ forms TMSOTf (δ {¹H} = 0.52 ppm, δ {¹⁹F} = -76.9 ppm) and methane (δ {¹H} = 0.23 ppm). At higher concentrations of HOTf (>20 µL HOTf per mL of $CDCl_3$), the HOTf droplets collect to form an acid phase at the bottom of the NMR tube that escapes detection. The clear supernatant displays a signal for dissolved HOTf (-76.3 ppm). In more diluted samples (<0.5 μ L per mL of CDCl₃), the signal for dissolved HOTf becomes smaller and shifts to lower frequency, until a single peak for a water-rich HOTf droplet phase at δ ⁽¹⁹F) = -78.5 ± 0.5 ppm remains (0.2 μ L HOTf/mL $CDCl_3$). The use of a solvent like $CDCl_3$ or C_6D_6 in combination with sufficiently high concentrations appears to

be a secure way to prove the presence of HOTf by ¹⁹F NMR spectroscopy also in the presence of ionic triflates.⁷⁴ The observation of the droplet HOTf phase of dilute solutions of HOTf in moist solvents coincides with our difficulties in preparing dilute stock solutions of HOTf in DCE or similar nonprotic solvents for the sake of performing control experiments at low loadings of HOTf as the catalyst. Such stock solutions readily separate the acid in the form of small droplets at the bottom and walls of the vessel. Use of the supernatant then leads to erroneous experimental results and may be a cause for false negative control experiments in studies of metal versus acid catalysis.

The mechanistic pathways leading to HOTf release are not hydrolyses of metal aquo complexes³⁵ but irreversible reactions including eliminations (Schemes 2 and 3), Friedel-Crafts alkylations (Scheme 3), and redox processes including the solvent or substrates as reductants (eq 1). The oxidizing power and the halophilicity of the silver cation is responsible for the ease of all of those processes. Interestingly, similar arguments apply to cationic gold(I) complexes, which are readily reduced (thereby acting as a potential source of protic acid, similarly as illustrated for Ru(III) in eq 1) and whose halophilicity might even be superior to that of silver(I), if the solubility product of AgCl ($K_{\rm sp} = 1.77 \times 10^{-10}$) versus AuCl ($K_{\rm sp} = 2.0 \times 10^{-13}$)⁷⁵ is taken as an indication of the strength of the metal/halogen interaction. Cases of gold(I)-catalyzed hydroalkoxylations of nonactivated alkenes are certainly suspicious of accompanying hidden Brønsted acid catalysis. In several past studies, the interference of Brønsted acid catalysis has been excluded by performing control experiments, in which the Brønsted acid gave qualitatively or quantitatively different results from the metal catalyst in question. According to Hartwig and coworkers, the use of Brønsted acid at loadings equivalent to the metal catalyst in such control experiments induces polymerization of the reaction product and can create the false impression that Brønsted acid is a less efficient catalyst.³⁸ We would also argue that control experiments with Brønsted acids often show inferior catalytic performance because the control experiment hardly ever receives the amount of optimization that the key metal triflate experiment receives. We propose that such control experiments are more readily performed with deliberate hidden acid catalysts under the conditions of the original catalysis. Two simple protocols have been introduced to generate such a hidden acid catalyst from AgOTf; the first protocol (AgOTf + t-BuCl) produces HOTf in controlled amounts at ambient temperature or below, whereas the second protocol (AgOTf + DCE) slowly eliminates HOTf at elevated temperatures (>60 °C). Both procedures show advantages in synthetic applications because the hidden acid catalyst based on AgOTf is easier to handle in minute amounts than pure HOTf. Dilute solutions of HOTf in moist laboratory solvents may be inhomogeneous and difficult to dose, whereas in situ generation provides a finely dispersed form of HOTf.

CONCLUSION

Examples of assumed transition-metal-catalyzed hydroalkoxylation reactions have been investigated and shown to be catalyzed by hidden Brønsted acid. The mechanistic pathway of HOTf generation under reaction conditions was elucidated by spectroscopic analysis and by isolation of side products formed in reactions of the metal precursor. An earlier claim of an asymmetric catalytic hydroalkoxylation reaction of a nonactivated alkene has been refuted. ¹⁹F NMR spectroscopy is a suitable tool for studying the stability of metal triflate catalysts under the conditions of the catalytic reactions. This technique may prove or disprove the generation of HOTf, if peculiarities of the ¹⁹F NMR analysis of HOTf samples in moist air and solvents are taken into account. If the catalytic activity of Brønsted acids in hydroalkoxylation reactions is evaluated against the activity of metal catalysts, control experiments can be advantageously performed with a deliberate hidden acid catalyst rather than with pure Brønsted acids to circumvent problems arising from the handling of small amounts of strong acids.

EXPERIMENTAL SECTION

General. Reaction setup was carried out in air, but catalyses were performed in Schlenk vessels under nitrogen. Preparative chromatography (CC, column chromatography) was performed on silica gel 60 (0.040–0.063 mm) using pressurized air (0.1–0.3 bar) for flash elution. ¹H NMR and ¹³C NMR data are referenced to tetramethylsilane as the internal standard. Unless otherwise mentioned, chemicals were obtained from commercial suppliers and used as received. Solvents were stored over molecular sieves in air.

Isolation of AgCl from the Reaction of AgOTf with 1,2-Dichloroethane (DCE). A suspension of AgOTf (128.5 mg, 0.50 mmol) in DCE (5 mL) was heated in a pressure tube at 90 °C with stirring for 3 h. The precipitate was filtered to afford AgCl as a white powder (71 mg, 99%). See Figure S1 (Supporting Information) for a photograph. Identification of AgCl: the colorless solid was insoluble in water or dilute HNO₃ but soluble in aqueous ammonia. A sample was dissolved in diluted aqueous ammonia and warmed to 40 °C. Addition of a few drops of aqueous formaldehyde induced a black precipitate of metallic silver.

Generation of 2-Chloroethyl Triflate (1) and HOTf from the Reaction of AgOTf with DCE. In a dry Schlenk tube under an Ar atmosphere, AgOTf (100 mg, 389 μ mol) was suspended in 0.5 mL of DCE and heated to 80 °C for 2 h. After cooling to RT, a sample (~50 μ L) of the reaction was filtered and diluted with CDCl₃ or C₆D₆ for NMR analysis. ¹H NMR (500 MHz, CDCl₃): δ = 4.64 ppm, (t, *J* = 5.7 Hz; 1); ¹H NMR (250 MHz, C₆D₆): δ = 3.62 ppm (t, *J* = 5.4 Hz; 1). ¹⁹F NMR (471 MHz, CDCl₃): δ = -74.5 ppm (1), -78.0 ppm (HOTf); ¹⁹F NMR (235 MHz, C₆D₆): δ = -74.9 ppm (1), -77.5 ppm (HOTf). See Figures S2 and S3 (Supporting Information) for selected spectra.

Catalytic Phenol–Isoprene Condensation to 2,2-Dimethylchromane (Table 1): General Procedure. The catalyst (usually 5 mol %) was added to a stirred solution of phenol (2a; 1 mmol) and isoprene (3; 1.5 mmol) in DCE (5 mL). Reaction progress was monitored by TLC analysis. After completion of the reation, the solvent was evaporated and the residue separated by flash column chromatography (SiO₂, *n*-hexane) to give the product 4a as colorless oil. See Table 1 for results.

2,2-Dimethylchromane (4a). ¹H NMR (360 MHz, CDCl₃): δ = 1.33 (s, 6 H), 1.79 (t, *J* = 6.8 Hz, 2 H), 2.77 (t, *J* = 6.8 Hz, 2 H), 6.76–6.83 (m, 2 H), 7.03–7.10 (m, 2 H) ppm. ¹³C NMR (90 MHz, CDCl₃): δ = 22.6, 27.0, 32.9, 74.2, 117.4, 119.7, 121.0, 127.4, 129.6, 154.1 ppm. Known compound, CAS 1198-96-5.

Generation of Deliberate Hidden Acid Catalysts (NMR Experiments). (a). Generation of HOTf in $CDCl_3$ from t-BuCl + AgOTf. In a dry Schlenk tube under an Ar atmosphere, AgOTf (23.3 mg, 91 μ mol) was added to a solution of t-BuCl (10 μ L, 91 μ mol) in $CDCl_3$ (0.6 mL). The suspension was stirred vigorously for 10 min. The colorless suspension was directly filtered into an NMR tube for further analysis. See Figure S4 (Supporting Information) for the NMR spectrum.

(b). Generation of HOTf in C_6D_6 Using t-BuCl + AgOTf. In a dry Schlenk tube under an Ar atmosphere, t-BuCl (10 μ L, 91 μ mol) was dissolved in C_6D_6 (0.6 mL) and mixed with AgOTf (23.3 mg, 91 μ mol). The suspension was stirred vigorously for 180 min while a white precipitate appeared. The suspension was filtered and analyzed

by NMR without further purification. See Figure S5 (Supporting Information) for NMR spectra.

(c). Reaction of DCE with AgOTf. In a dry Schlenk tube under an Ar atmosphere, AgOTf (100 mg, 389 μ mol) was suspended in 0.5 mL of DCE and heated to 85 °C for 120 min. After cooling to RT, a sample (~50 μ L) of the reaction was filtered and diluted with CDCl₃ for NMR analysis. A second sample was treated the same way with the exception that it was mixed with a sample of freshly prepared TFA in CDCl₃. Compare Figures S2 and S3 (Supporting Information) for spectra.

Synthetic Applications of Deliberate Hidden Acid Catalysts. (a). Generation of a Hidden Acid Catalyst from AgOTf and t-BuCl (General Procedure A). By means of a microsyringe, t-BuCl (4 mol %) was added to a stirred solution/suspension of AgOTf (typically 1–2 mol %) in DCE (10 mL/mmol) or any other desired solvent (CH_2Cl_2 , benzene, toluene). The mixture was stirred for 10 min at RT before further use. See Figure S6 (Supporting Information) for a visual impression.

(b). Generation of a Hidden Acid Catalyst from AgOTf in DCE (General Procedure B). For a 1 mmol scale reaction, AgOTf (2.6 mg, 1 mol %) was added to DCE (10 mL/mmol) and heated with stirring to 90 °C (oil bath temperature) in a pressure tube (or alternatively, to reflux in an open system with refluxing condenser) for 3 h.

Phenol–Isoprene Condensations Catalyzed by Deliberate Hidden Acid Catalysts (Table 2). These reactions employ excess isoprene (1.5 equivs), which is added slowly to the reaction mixture. Batch addition may lead to isoprene polymerization, while overly slow addition can result in isoprenylation at C-6 of the chromane products. Individual optimization for each new phenol is necessary for optimal results.

2,2-Dimethylchromane (4a). The catalyst solution was prepared according to the procedure A from AgOTf (2.6 mg, 1 mol %) and *t*-BuCl (4.5 μ L, 4 mol %) in DCE (10 mL). Phenol (94 mg, 1 mmol) was added to the suspension, followed by slow addition of a solution of isoprene (150 μ L, 1.5 mmol) in DCE (2 mL) over 10 min. The mixture was stirred at RT for 20 min. The solvent was removed in vacuo and the residue purified by flash column chromatography (SiO₂, *n*-hexane) to give product 4a (139 mg, 86%) as a colorless oil.

2,2-Dimethyl-8-isopropylchromane (4b). A catalyst solution was prepared according to procedure A from AgOTf (5.2 mg, 2 mol %) and *t*-BuCl (4.5 μ L, 4 mol %) in DCE (10 mL). After addition of 2-isopropylphenol (136 mg, 1.0 mmol), a solution of isoprene (150 μ L, 1.5 mmol) in DCE (2 mL) was slowly added over 10 min to the reaction mixture. After stirring for 30 min at RT, the solvent was removed in vacuo and the residue purified by flash column chromatography (SiO₂, *n*-hexane) to give 4b (134 mg, 66%) as a colorless oil. ¹H NMR (360 MHz, CDCl₃): δ = 1.20 (d, *J* = 6.9 Hz, 6 H), 1.32 (s, 6 H), 1.78 (t, *J* = 6.8 Hz, 2 H), 2.77 (t, *J* = 6.8 Hz, 2 H), 3.26 (sept, *J* = 6.9 Hz, 1 H), 6.77 (t, *J* = 7.5 Hz, 1 H), 6.87–6.92 (m, 1 H), 6.99–7.04 (m, 1 H) ppm. ¹³C NMR (90 MHz, CDCl₃): δ = 22.5, 22.8, 26.9, 27.0, 32.7, 73.7, 119.1, 120.3, 123.6, 126.8, 136.5, 151.1 ppm. HRMS (EI) calcd for C₁₄H₂₀O⁺ 204.1509; found 204.1509.

8-tert-Butyl-2,2-dimethylchromane (4c). A catalyst solution was prepared according to procedure B from AgOTf (2.6 mg, 1 mol %) in DCE (10 mL). After cooling to RT, 2-*tert*-butylphenol (150 mg, 1.0 mmol) was added to the suspension. A solution of isoprene (150 μ L, 1.5 mmol) in DCE (2 mL) was slowly added over 10 min and the reaction mixture stirred at RT for 3 h. The solvent was removed in vacuo and the residue purified by flash column chromatography (SiO₂, *n*-hexane) to give **4c** (214 mg, 98%) as a colorless oil. ¹H NMR (250 MHz, CDCl₃): δ = 1.35 (s, 6 H), 1.38 (s, 9 H), 1.78 (t, *J* = 6.9 Hz, 2 H), 2.79 (t, *J* = 6.9 Hz, 2 H), 6.75 (t, *J* = 7.6 Hz, 1 H), 6.89–6.95 (m, 1 H), 7.10 (dd, *J* = 7.7, 1.6 Hz, 1 H) ppm. ¹³C NMR (62.5 MHz, CDCl₃): δ = 23.0, 27.0, 29.7, 32.7, 34.8, 73.8, 118.8, 120.9, 124.3, 127.5, 137.8, 152.5 ppm. HRMS (EI) calcd for C₁₅H₂₂O⁺ 218.1665; found 218.1668.

6-Methoxy-2,2-dimethylchromane (4d). A catalyst solution was prepared according to procedure B from AgOTf (5.2 mg, 2 mol %) in DCE (10 mL). In the resulting suspension, 4-methoxyphenol (124 mg, 1.0 mmol) was dissolved, and a solution of isoprene (150 μ L,

1.5 mmol) in DCE (2 mL) was slowly added over 10 min. After stirring the reaction mixture at RT for 1 h, the solvent was removed in vacuo and the residue purified by flash column chromatography (SiO₂, *n*-hexane) to give 4d (114 mg, 59%) as a colorless oil. ¹H NMR (360 MHz, CDCl₃): δ = 1.31 (s, 6H), 1.78 (t, *J* = 6.8 Hz, 2H), 2.75 (t, *J* = 6.8 Hz, 2H), 3.74 (s, 3H), 6.59–6.62 (m, 1H), 6.65–6.72 (m, 2H) ppm. ¹³C NMR (360 MHz, CDCl₃): δ = 22.8, 26.7, 32.8, 55.7, 73.7, 113.3, 113.9, 117.7, 121.4, 147.9, 152.8 ppm. Known compound, CAS 69888-41-1.

Catalytic Cyclization of 2-Allylphenol to 2-Methylcoumaran (Table 3). (*a*). Cyclization with Various Catalysts (Table 3, entries 1-3). A solution of the catalyst (5 mol %) and 8 (134 mg, 1.0 mmol) in DCE (3 mL) was stirred under the conditions indicated in Table 3. The solvent was evaporated and the product isolated by flash column chromatography (SiO₂, *n*-hexane).

2-Methylcoumaran (9). ¹H NMR (360 MHz, CDCl₃): δ = 1.46 (d, *J* = 6.3 Hz, 3H), 2.80 (dd, *J* = 15.4, 7.7 Hz, 1H), 3.29 (dd, *J* = 15.4, 8.8 Hz, 1H), 4.84–4.96 (m, 1H), 6.73–6.84 (m, 2H), 7.05–7.17 (m, 2H) ppm. ¹³C NMR (360 MHz, CDCl₃): δ = 21.7, 37.1, 79.4, 109.3, 120.1, 124.9, 127.0, 127.9, 159.5 ppm. Known compound, CAS 1746-11-8.

(b). Cyclization with In Situ Catalysts Derived from Cp*RuCl₂-AgOTf-phosphane (Table 3). In a dry Schlenk tube under an Ar atmosphere, Cp*RuCl₂ (6.1 mg, 0.02 mmol; 2 mol %) and AgOTf (10.3 mg, 0.040 mmol; 4 mol %) were added subsequently into freshly degassed toluene (3 mL). The resulting suspension was heated to 110 °C for 3 h. After cooling to RT, the ligand (PPh3, (R)-BINAP, (R)-Tol-BINAP, or $(1R_{s})$ -Josiphos; 2 mol %) and 2-allylphenol (134 mg, 1.0 mmol) were added. The mixture was heated at the temperature and time indicated in Table 3. The reaction mixture was directly chromatographed on SiO_2 (pentane/Et₂O = 50:1) to isolate pure coumaran 9, which was identified by NMR and GC/MS. The enantiomeric excess was analyzed by HPLC with UV detection (Chiralcel OJ, hexane/*i*-propanol = 98:2, flow = 0.8 mL/min, T = 15°C; UV detection at λ = 280 nm). No enantiomeric excess was observed within the accuracy of the analytical method (<1% ee). See Table 3, entries 5–9, and the Supporting Information for results.

NMR Analysis of the Cp*RuCl₂-AgOTf-BINAP In Situ Catalyst. In a dry Schlenk tube under an Ar atmosphere, Cp*RuCl₂ (13.3 mg, 43 μ mol) and AgOTf (20.5 mg, 80 μ mol) were added subsequently into freshly degassed toluene (3 mL), and the mixture was heated to 110 °C for 210 min. After cooling to RT, (±)-BINAP (25 mg, 40 μ mol) was added and the mixture stirred for 30 min at RT. A sample of the mixture was filtered, diluted with CDCl₃, and analyzed by ¹H, ¹⁹F, and ³¹P NMR. See Figure S7 (Supporting Information) for NMR spectra.

Synthesis of Ruthenium(II) Complexes from Cp*RuCl₂: η^5 -Pentamethylcyclopentadienyl(η^6 -toluene)ruthenium(II) Trifluoromethanesulfonate (10). (a). Direct Synthesis from 7. A mixture of Cp*RuCl₂ (7; 18 mg, 0.059 mmol) and AgOTf (30.9 mg, 0.12 mmol) in degassed toluene/*i*-PrOH (1:1, 4 mL) was heated at 90 °C for 4 h with stirring. The mixture was filtered to remove the precipitate (AgCl), and the filtrate was concentrated under reduced pressure. The residual solid was washed with Et₂O and hexanes to give 19 mg of tan solid 10 (68% yield).

(b). Synthesis of **10** by Chloride Abstraction from **11**. A mixture of **11** (30 mg, 0.082 mmol) and AgOTf (26 mg, 0.10 mmol) in degassed toluene/*i*-PrOH (1:1, 6 mL) was stirred at RT for 4 h. The mixture was filtered to remove the precipitate (AgCl), and the filtrate was concentrated under reduced pressure. The residual solid was washed with Et₂O and hexanes to give tan solid **10** (38 mg, 98% yield). ¹H NMR (360 MHz, CDCl₃): $\delta = 1.97$ (s, 15H), 2.19 (s, 3H), 5.73 (d, J = 6.0 Hz, 2H), 5.75–5.87 (m, 3H) ppm. ¹³C NMR (90.6 MHz, CDCl₃): $\delta = 10.6$, 18.5, 86.6, 87.3, 88.2, 96.1, 100.0, 120.9 (q, $J_{FC} = 320.6$ Hz) ppm. MS (FAB): m/z (%) = +329 (100) [Cp*Ru(C₇H₈)]⁺, -149 (100) OTf⁻. Analysis calcd for C₁₈H₂₃F₃O₃RuS: C 45.28, H 4.85, S 6.72; found: C 45.19, H 4.77, S 6.95. Spectral data in agreement with the literature values.^{66,67}

 η^{5} -Pentamethylcyclopentadienyl(η^{6} -toluene)ruthenium(II) Chloride (11). A suspension of Cp*RuCl₂ (7; 62 mg, 0.20 mmol) in degassed toluene/*i*-PrOH (1:1, 10 mL) was heated at 90 °C for 4 h with stirring. The mixture was filtered and the filtrate concentrated under reduced pressure. The residual solid was washed with Et₂O and hexanes to give a tan solid 11 (54 mg, 74%). ¹H NMR (360 MHz, CDCl₃): δ = 2.02 (s, 15H), 2.23 (s, 3H), 5.87 (d, *J* = 5.8 Hz, 2H), 5.95 (br t, *J* = 5.5 Hz, 1H), 6.03 (br t, *J* = 5.6 Hz, 2H) ppm. ¹³C NMR (90.6 MHz, CDCl₃): δ = 11.0, 18.7, 87.0, 87.7, 88.5, 96.0, 100.0 ppm. MS (FAB): *m/z* (%) = +329 (100) [Cp*Ru(C₇H₈)]⁺. Analysis calcd for C₁₇H₂₃ClRu: C 56.11, H 6.37; found: C 56.39, H 6.64. Data agree with literature values.⁷⁰

Deliberate Hidden Acid Catalysis of Hydroalkoxylation Reactions (Table 4): 2-Methylcoumaran (9). A catalyst solution was prepared according to general procedure B from AgOTf (2.6 mg, 1 mol %) in DCE (10 mL). After addition of 2-allylphenol (134 mg, 1.0 mmol), the mixture was heated at 90 °C for 1 h. After cooling, the solvent was removed in vacuo. The residue was purified by flash column chromatography (SiO₂, *n*-hexane) to give product 9 (119 mg, 89%) as a colorless oil.

5,7-Di-tert-butyl-2-methylcoumaran (12). (a) A catalyst solution was prepared according to general procedure B from AgOTf (2.6 mg, 1 mol %) in DCE (10 mL). After addition of 2-allyl-4,6-di-tertbutylphenol (1 mmol, 246 mg), the mixture was heated to 90 °C for 1 h. After cooling, the solvent was removed in vacuo, and the residue was purified by flash column chromatography (SiO₂, *n*-hexane) to give the product (161 mg, 65%) as a colorless oil. (b) The reaction was performed at a 1.03 mmol scale as under (a) but in CH₂Cl₂ as the solvent with heating to 50 °C (closed vessel) over 4 days to give a colorless oil (203 mg, 80%). ¹H NMR (250 MHz, CDCl₃): δ = 1.29 (s, 9H), 1.36 (s, 9H), 1.43 (d, J = 6.2 Hz, 3H), 2.75 (ddt, J = 15.2, 7.5, 0.9 Hz, 1H), 3.24 (ddt, J = 15.2, 8.8, 0.9, 1H), 4.87 (qdd, 8.8, 7.5, 6.2 Hz, 1H), 7.04 (dt, J = 2.1, 1.0 Hz, 1H), 7.11 (dt, J = 2.1, 0.8 Hz, 1H). ¹³C NMR (63 MHz, CDCl₃): δ = 21.9, 29.3, 31.9, 34.3, 34.4, 37.2, 78.6, 119.4, 121.5, 126.7, 131.7, 142.5, 155.2 ppm. HRMS (EI): calcd for C17H26O+ 246.1978; found 246.1972.

2-exo-Phenyloxybicyclo[**2.2.1**]**heptane** (13). A catalyst solution was prepared according to general procedure B from AgOTf (2.6 mg, 1 mol %) in DCE (10 mL). After addition of phenol (94 mg, 1.0 mmol) and norbornene (141 mg, 1.5 mmol), the reaction mixture was heated at 90 °C for 1 h. The solvent was removed in vacuo and the residue purified by flash column chromatography (SiO₂, *n*-hexane) to give the product (97%, 0.182 g) isolated as a colorless oil. ¹H NMR (360 MHz, CDCl₃): δ = 1.08–1.22 (m, 3 H), 1.41–1.79 (m, 5 H), 2.31 (t, *J* = 4.1 Hz, 1 H), 2.45 (d, *J* = 4.2, 1 H), 4.15 (d, *J* = 6.7, 1 H), 6.82–6.93 (m, 3 H), 7.21–7.27 (m, 2 H). ¹³C NMR (91 MHz, CDCl₃): δ = 24.3, 28.5, 35.2, 35.4, 40.0, 41.1, 79.9, 115.4, 120.1, 129.3, 157.7 ppm. Data are consistent with the *exo*-stereoisomer.⁷⁶ Known compound, CAS 50414-48-7.

2-exo-Benzyloxybicyclo[**2.2.1**]**heptane** (**14**). A catalyst solution was prepared according to procedure A from AgOTf (2.6 mg, 1 mol %) and *tert*-butylchloride in DCE (10 mL). Benzyl alcohol (108 mg, 1 mmol) and norbornene (141 mg, 1.50 mmol) were added with stirring, and the mixture was heated to 90 °C for 1 h. The solvent was removed in vacuo and the residue purified by flash column chromatography (SiO₂, *n*-hexane) to give product **2d** (117 mg, 58%) as a colorless oil. ¹H NMR (360 MHz, CDCl₃): δ = 0.91–1.16 (m, 3 H), 1.36–1.67 (m, 5 H), 2.24 (br. s, 1 H), 2.37 (d, *J* = 4.6 Hz, 1 H), 3.44 (dt, *J* = 6.7, 1.1 Hz, 1 H), 4.43 (d, *J* = 11.9 Hz, 1 H), 4.48 (d, *J* = 11.9 Hz, 1 H), 7.20–7.35 (m, 5 H) ppm. ¹³C NMR (90 MHz, CDCl₃): δ = 24.6, 28.6, 34.9, 35.2, 39.6, 40.4, 70.1, 82.1, 127.3, 127.5, 128.3, 139.1 ppm. Known compound.¹⁷

ASSOCIATED CONTENT

S Supporting Information

NMR spectra and photographs of key experiments, ¹H and ¹³C NMR spectra of pure reaction products, and additional data including HPLC chromatograms for attempted asymmetric experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) Hintermann, L. Top. Organomet. Chem. 2010, 31, 123 and cited literature.

(2) Beller, M.; Seayad, J.; Tillack, A.; Jiao, H. Angew. Chem., Int. Ed. 2004, 43, 3368.

(3) Alonso, F.; Beletskaya, I. P.; Yus, M. Chem. Rev. 2004, 104, 3079.

- (4) Tani, K.; Kataoka, Y. In *Catalytic Heterofunctionalization*; Togni, A., Grützmacher, H., Eds.; Wiley-VCH: Weinheim, Germany, 2001; p 171.
- (5) Hori, K.; Kitagawa, H.; Miyoshi, A.; Ohta, T.; Furukawa, I. *Chem. Lett.* **1998**, 1083.

(6) Marotta, E.; Foresti, E.; Marcelli, T.; Peri, F.; Righi, P.; Scardovi, N.; Rosini, G. Org. Lett. **2002**, *4*, 4451.

- (7) Loh, T.-P.; Hu, Q.-Y.; Ma, L.-T. J. Am. Chem. Soc. 2001, 123, 2450.
 - (8) Oe, Y.; Ohta, T.; Ito, Y. Chem. Commun. 2004, 1620.
 - (9) Oe, Y.; Ohta, T.; Ito, Y. Synlett 2005, 179.
- (10) Ohta, T.; Kataoka, Y.; Miyoshi, A.; Oe, Y.; Furukawa, I.; Ito, Y. J. Organomet. Chem. **2007**, 692, 671.

(11) Ito, Y.; Kato, R.; Hamashima, K.; Kataoka, Y.; Oe, Y.; Ohta, T.; Furukawa, I. J. Organomet. Chem. 2007, 692, 691.

- (12) Oe, Y.; Ohta, T.; Ito, Y. Tetrahedron Lett. 2010, 51, 2806.
- (13) Coulombel, L.; Favier, I.; Duñach, E. Chem. Commun. 2005, 2286.

(14) Lemechko, P.; Grau, F.; Antoniotti, S.; Duñach, E. *Tetrahedron Lett.* **2007**, 48, 5731.

- (15) Coulombel, L.; Rajzmann, M.; Pons, J. M.; Olivero, S.; Duñach, E. *Chem.—Eur. J.* **2006**, *12*, 6356.
- (16) Kelly, B. D.; Allen, J. M.; Tundel, R. E.; Lambert, T. H. Org. Lett. 2009, 11, 1381.
- (17) Taylor, J. G.; Whittall, N.; Hii, K. K. M. Chem. Commun. 2005, 5103.
- (18) Chaminade, X.; Coulombel, L.; Olivero, S.; Duñach, E. Eur. J. Org. Chem. 2006, 3554.
- (19) Yang, C. G.; He, C. J. Am. Chem. Soc. 2005, 127, 6966.
- (20) Reich, N. W.; Yang, C.; Shi, Z.; He, C. Synlett 2006, 1278.
- (21) Li, Z.; Zhang, J.; Brouwer, C.; Yang, C. G.; Reich, N. W.; He, C. Org. Lett. **2006**, *8*, 4175.
- (22) Grant, V. H.; Liu, B. Tetrahedron Lett. 2005, 46, 1237.
- (23) Yang, C. G.; Reich, N. W.; Shi, Z.; He, C. Org. Lett. 2005, 7, 4553.
- (24) Qian, H.; Han, X.; Widenhoefer, R. A. J. Am. Chem. Soc. 2004, 126, 9536.
- (25) Liu, C.; Bender, C. F.; Han, X.; Widenhoefer, R. A. Chem. Commun. 2007, 3607.

(26) Komeyama, K.; Morimoto, T.; Nakayama, Y.; Takaki, K. Tetrahedron Lett. 2007, 48, 3259.

- (27) Choi, J. C.; Kohno, K.; Masuda, D.; Yasuda, H.; Sakakura, T. *Chem. Commun.* **2008**, 777.
- (28) Dzudza, A.; Marks, T. J. Org. Lett. 2009, 11, 1523.
- (29) Dzudza, A.; Marks, T. J. Chem.-Eur. J. 2010, 16, 3403.
- (30) Zhang, X.; Corma, A. Chem. Commun. 2007, 3080.

(31) Vece, V.; Ricci, J.; Poulain-Martini, S.; Nava, P.; Carissan, Y.; Humbel, S.; Duñach, E. *Eur. J. Org. Chem.* **2010**, 6239.

- (32) Adrio, L. A.; Quek, L. S.; Taylor, J. G.; Hii, K. K. M. Tetrahedron 2009, 65, 10334.
- (33) Hirai, T.; Hamasaki, A.; Nakamura, A.; Tokunaga, M. Org. Lett. **2009**, *11*, 5510.

(34) Antoniotti, S.; Poulain-Martini, S.; Duñach, E. Synlett 2010, 2973.

- (35) Wabnitz, T. C.; Yu, J. Q.; Spencer, J. B. Chem.—Eur. J. 2004, 10, 484.
- (36) Coulombel, L.; Duñach, E. Green. Chem. 2004, 6, 499.
- (37) Li, Z.; Zhang, J.; Brouwer, C.; Yang, C. G.; Reich, N. W.; He, C. Org. Lett. **2006**, 8, 4175.
- (38) Rosenfeld, D. C.; Shekhar, S.; Takemiya, A.; Utsunomiya, M.; Hartwig, J. F. Org. Lett. **2006**, *8*, 4179.
- (39) Compare: Taylor, J. G.; Adrio, L. A.; Hii, K. M. Dalton Trans. 2010, 39, 1171.

(40) For additional studies addressing the question of metal versus acid catalysis, see: McKinney Brooner, R. E.; Widenhoefer, R. A. *Chem.—Eur. J.* **2011**, *17*, 6170.

(41) Tschan, M. J. L.; Thomas, C. M.; Strub, H.; Carpentier, J. F. Adv. Synth. Catal. 2009, 351, 2496.

(42) Bandini, M.; Eichholzer, A.; Kotrusz, P.; Tragni, M.; Troisi, S.; Umani-Ronchi, A. *Adv. Synth. Catal.* **2009**, 351, 319.

(43) Youn, S. W.; Eom, J. I. J. Org. Chem. 2006, 71, 6705.

- (44) Harrison, T. J.; Dake, G. R. Org. Lett. 2004, 6, 5023.
- (45) Deng, C.-L.; Zou, T.; Wang, Z.-Q.; Song, R.-J.; Li, J.-H. J. Org. Chem. 2009, 74, 412.
- (46) Arcadi, A.; Alfonsi, M.; Marinelli, F. J. Organomet. Chem. 2007, 692, 5322.
- (47) Silver in Organic Chemistry; Harmata, M., Ed.; Wiley: New York, 2010.
- (48) See the Supporting Information for additional data and NMR spectra.
- (49) Falzon, C. L.; Ackermann, U.; Spratt, N.; Tochon-Danguy, H. J.; White, J.; Howells, D.; Scott, A. M. J. Labelled Compds. Radiopharm. **2006**, *49*, 1089.

(50) 2-Chloroethyltriflate is described as sensitive to hydrolysis, fuming in air: Lown, J. W.; Joshua, A. V.; McLaughlin, L. W J. Med. Chem. **1980**, 23, 798.

- (51) Howells, R. D.; Mc Cown, J. D. Chem. Rev. 1977, 77, 69.
- (52) Chapman, R. D.; Andreshak, J. L.; Herrlinger, S. P.; Shackelford,
- S. A.; Hildreth, R. A.; Smith, J. P. J. Org. Chem. 1986, 51, 3792.
- (53) Chapman, R. D.; Andreshak, J. L.; Shackelford, S. A. J. Org. Chem. 1988, 53, 3771.

(54) Bonrath, W.; Haas, A.; Hoppmann, E.; Netscher, T.; Pauling, H.; Schager, F.; Wildermann, A. *Adv. Synth. Catal.* **2002**, 344, 37.

(55) The addition of a small quantity of HOTf to a mixture of 4methoxyphenol and isoprene (1:2 ratio) dissolved in CDCl_3 in an NMR tube produced an immediate exotherm. A ¹H NMR spectrum of the sample, measured within 1 h, showed peaks of the methoxychromane with no more remaining signals for isoprene.

(56) The reaction conditions with the metal triflates are not optimized. The results appear to depend as much on solubility of the precatalysts as on the nature of the cation. For other Lewis-acid-catalyzed isoprene/phenol condensations, see refs 57–60.

(57) Youn, S. W. Synlett 2007, 3050.

(58) Adrio, L. A.; Hii, K. K. Chem. Commun. 2008, 2325.

(59) Bigi, F.; Carloni, S.; Maggi, R.; Muchetti, C.; Rastelli, M.; Sartori, G. Synthesis **1998**, 301.

(60) De Felice, V.; De Renzi, A.; Funicello, M.; Panunzi, A.; Saporito, A. *Gazz. Chim. Ital.* **1985**, *115*, 13.

(61) The reaction of a silver salt AgY with t-BuX is an elegant method to generate strong protic acids HY in solution, particularly in cases where the pure substance HY is unstable; see refs 62 and 63.

(62) Jona, H.; Mandai, H.; Chavasiri, W.; Takeuchi, K.; Mukaiyama, T. Bull. Chem. Soc. Jpn. **2002**, 75, 291.

(63) Kato, T.; Tanaka, M.; Hoshikawa, M.; Yagi, M. *Tetrahedron Lett.* **1998**, *39*, 7553.

(64) Claims regarding the use of in situ prepared *t*-BuOTf can be found in the literature, but this compound has only been characterized by NMR spectroscopy at -60 °C and decomposes above -30 °C with generation of polyisobutene: Hommeltoft, S. I.; Ekelund, O.; Zavilla, J. *Ind. Eng. Chem. Res.* **1997**, *36*, 3491.

(65) The monomeric formula $Cp*RuCl_2$ is used to avoid confusion regarding stoichiometric ratios. Complex 7 is a dimer in the solid state:

Kölle, U.; Kossakowski, J.; Klaff, N.; Wesemann, L.; Englert, U.; Heberich, G. E. Angew. Chem., Int. Ed. Engl. 1991, 30, 690.

(66) Masuda, K.; Ohkita, H.; Kurumatani, S.; Itoh, K. Organometallics 1993, 12, 2221.

(67) Fagan, P. J.; Ward, M. D.; Calabrese, J. C. J. Am. Chem. Soc. 1989, 111, 1698.

(68) (a) Kaganovich, V. S.; Kudinov, A. R.; Rybinskaya, M. I. Russ. Chem. Bull. **1986**, 35, 456. (b) Kaganovich, V. S.; Kudinov, A. R.; Rybinskaya, M. I. Izv. Akad. Nauk SSSR, Ser. Khim. **1986**, 2, 492.

(69) Wheeler, D. E.; Hill, S. T.; Williams, J. D.; Wedyck, E. J. Inorg.

Chim. Acta 1995, 231, 133. (70) Suzuki, H.; Omori, H.; Lee, D. H.; Yoshida, Y.; Morooka, Y.

(70) Suduki, H.; Omori, H.; Lee, D. H.; Tosinda, T.; Morooka, T. Organometallics **1988**, 7, 2243.

(71) Bardají, M.; Crespo, O.; Laguna, A.; Fischer, A. K. Inorg. Chim. Acta 2000, 304, 7.

(72) The chemical shifts and $J(^{107/109}\text{Ag},^{31}\text{P})$ coupling constants are characteristic for complexes of the indicated stoichiometry; the [{AgCl(BINAP)}₂] complex is presumably occurring in meso- and rac-forms. For reference data in a AgPF₆/BINAP system, see: Ohkouchi, M.; Masui, D.; Yamaguchi, M.; Yamagishi, T. J. Mol. Catal. A: Chem. **2001**, 170, 1.

(73) Yamamoto, H.; Futatsugi, K. Angew. Chem., Int. Ed. 2005, 44, 1924.

(74) Performing a vacuum transfer of volatiles and recording of a $^{19}\mathrm{F}$ NMR spectrum of the distillate is another method to prove the presence of HOTf in a mixture with ionic triflate. 29

(75) Speight, J. G. *Lange's Handbook of Chemistry*, 16th ed.; McGraw-Hill: New York, 2005.

(76) Lajunen, M.; Himottu, M. Acta Chem. Scand. 1989, 43, 957.