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How to cite

LI, Houhua, FIORITO, Daniele, MAZET, Clement. Exploring site selectivity of Iridium hydride insertion into allylic alcohols: serendipitous discovery and comparative study of organic and organometallic catalysts for the vinylogous peterson elimination. In: ACS catalysis, 2017, vol. 7, n° 3, p. 1554–1562. doi: 10.1021/acscatal.6b03376

This publication URL: https://archive-ouverte.unige.ch//unige:95401
Publication DOI: 10.1021/acscatal.6b03376

ACS Catalysis

Research Article

pubs.acs.org/acscatalysis

Exploring Site Selectivity of Iridium Hydride Insertion into Allylic Alcohols: Serendipitous Discovery and Comparative Study of Organic and Organometallic Catalysts for the Vinylogous Peterson Elimination

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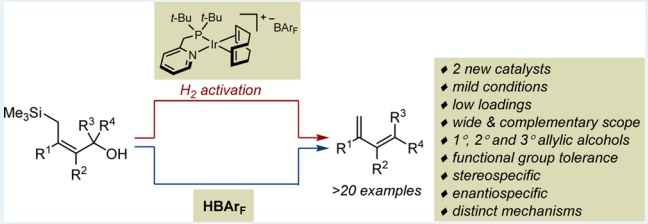
Supporting Information

ABSTRACT: The vinylogous Peterson elimination of a broad range of primary, secondary, and tertiary silylated allylic alcohols by two distinct and complementary catalytic systems—a cationic iridium complex and a Brønsted acid—is reported. These results are unexpected. Nonsilylated substrates are typically isomerized into aldehydes and silylated allylic alcohols into homoallylic alcohols with structurally related iridium complexes. Although several organic acids and bases are known to promote the vinylogous Peterson elimination, the practicality, mildness, functional group tolerance, and generality of both catalysts are simply unprecedented. Highly substituted C=C bonds, stereochemically complex scaffolds, and vicinal tertiary and quaternary (stereo)centers are also compatible with the two methods. Both systems are stereospecific and enantiospecific. After optimization, a vast number of dienes with substitution patterns that would be difficult to generate by established strategies are readily accessible. Importantly, control experiments secured that traces of acid that may be generated upon decomposition of the in situ generated iridium hydride are not responsible for the activity observed with the organometallic species. Upon inspection of the reaction scope and on the basis of preliminary investigations, a mechanism involving iridium−hydride and iridium−allyl intermediates is proposed to account for the elimination reaction. Overall, this study confirms that site selectivity for [Ir−H] insertion across the C=C bond of allylic alcohols is a key parameter for the reaction outcome.



KEYWORDS: *iridium catalysis, Brønsted acid catalysis, vinylogous Peterson elimination, dienes, selective catalysis*

INTRODUCTION

The 1,2-insertion of an olefin into a transition-metal hydride (i.e., migratory insertion) is a fundamental elementary step in organometallic chemistry that constitutes the basis of a plethora of catalytic processes.[1] The site selectivity of insertion is primarily dictated by the nature and the size of the substituents of the C=C bond. Modification of the catalyst structure allows either altering or even overriding the inherent electronic and steric biases imposed by the olefin substituents and, consequently, changing the outcome of the transformation. Therefore, gaining an understanding of the parameters that control site selectivity of [M−H] insertion across a C=C bond provides a means to elaborate improved catalyst structures (more reactive, more selective) or to access unconventional reactivity patterns by deviating transient intermediates toward novel catalytic manifolds.

In recent years, we and others have pursued the development of late-transition-metal catalysts for the selective isomerization of allylic and alkenyl alcohols into the corresponding carbonyl derivatives.[2−4] Specifically, we have shown that iridium complexes of the general formula [(P,N)Ir(cod)]BAr$_F$ were competent candidates for the isomerization of primary allylic alcohols. Once activated by molecular hydrogen and after degassing of the solution, these typical hydrogenation catalysts can be diverted from their initial task and favor exclusive isomerization into aldehydes instead.[5] The Pfaltz-modified version of Crabtree's catalyst **1** was first established as a very general catalyst for the nonasymmetric version of the reaction, operating under unusually mild reaction conditions.[5a,6,7] Subsequently, highly enantioselective variants of this reaction using prochiral 3,3-disubstituted allylic alcohols and catalyst-controlled diastereoselective isomerizations of stereochemically complex steroid derivatives have been developed using chiral catalysts such as **2** (Figure 1).[5]

Isotopic labeling experiments have shed light on an unconventional intermolecular hydride-type mechanism involving migratory insertion of the in situ generated [Ir−H] intermediates across the C=C bond of the substrate. Productive isomerization proceeds via insertion of iridium at C2, followed by β-hydride elimination and tautomerization to deliver the carbonyl compound. The collective results gathered over several years of investigation indicate that substrate

Received: November 28, 2016
Revised: January 13, 2017
Published: January 17, 2017

DOI: 10.1021/acscatal.6b03376
ACS Catal. 2017, 7, 1554−1562

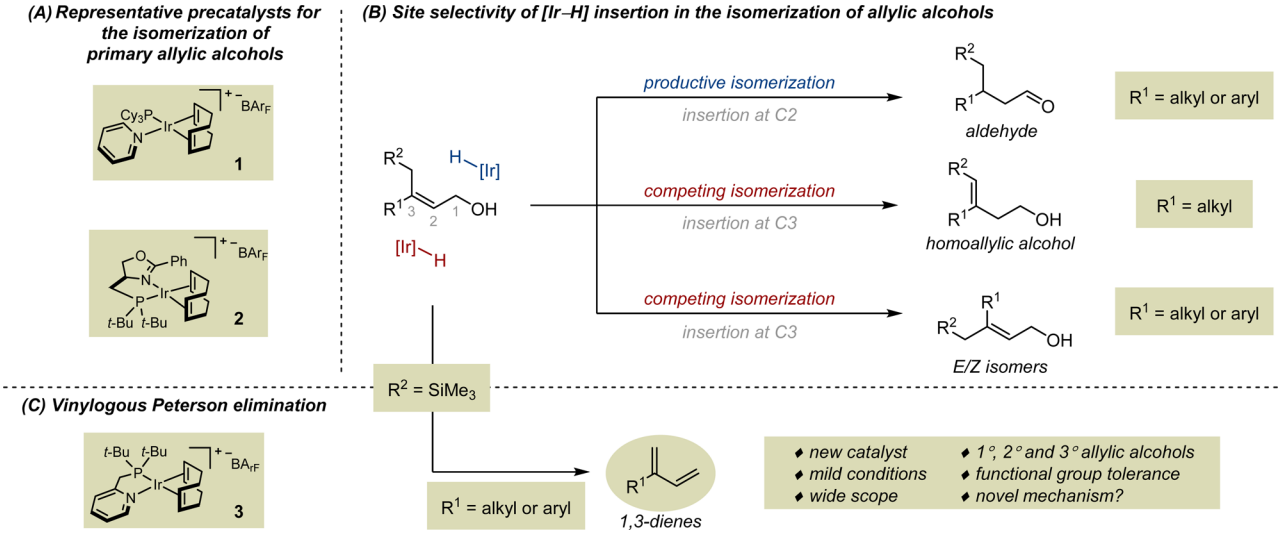


Figure 1. (A) Prototypical iridium precatalysts for the selective isomerization of primary allylic alcohols. (B) Influence of site selectivity of [Ir–H] insertion in allylic alcohol isomerizations. (C) Vinylogous Peterson elimination.

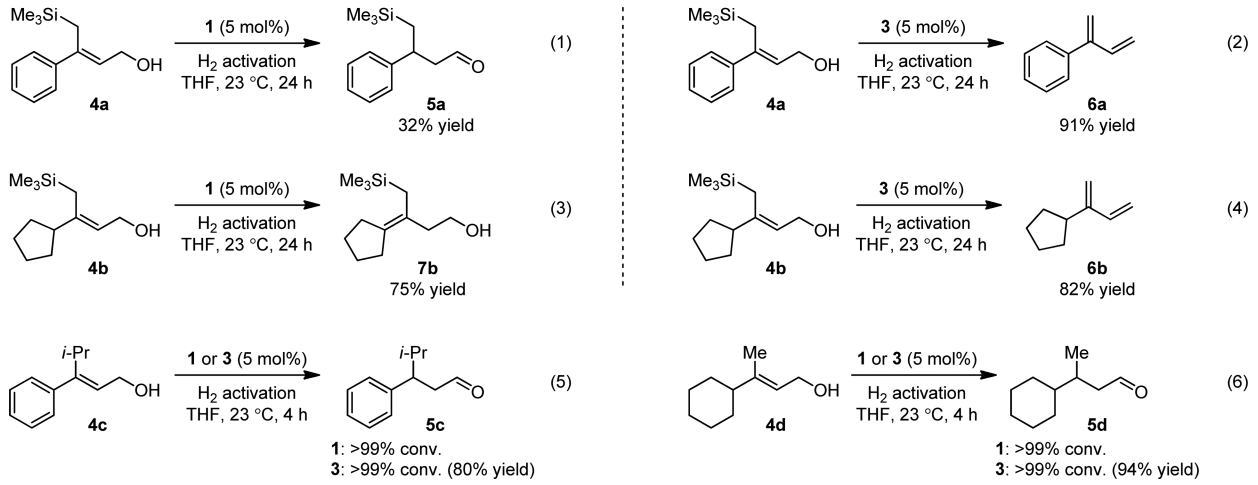


Figure 2. Comparative reactivity of achiral catalysts **1** and **3** for the isomerization of aryl- and alkyl-containing silylated primary allylic alcohols (eqs 1–4) and a comparison between **1** and **3** for the isomerization of model aryl- and alkyl-containing primary allylic alcohols (eqs 5 and 6).

polarity clearly influences site selectivity of migratory insertion.[2g,5] Formation of homoallylic alcohols—which implies iridium insertion at C3—has been observed only with alkyl/alkyl 3,3-disubstituted allylic alcohols and not with aryl/alkyl 3,3-disubstituted substrates. Adventitious traces of water were also found to potentially influence the site selectivity of migratory insertion and lead to the formation of homoallylic alcohols. Finally, competing *E*/*Z* isomerization—which also operates by insertion at C3—has been observed in several occasions (Figure 1B).

In this report, we describe how attempts to tune the site selectivity of migratory insertion by introduction of a silyl substituent in the vicinity of the C=C bond of the allylic alcohol led to the serendipitous discovery of a cationic iridium catalyst for a vinylogous Peterson elimination (Figure 1C). In addition, control experiments also showed that $[H(OEt_2)_2]$-BAr_F (noted $HBAr_F$), a Brønsted acid, effects this transformation in a complementary manner.[8] Optimization of this rather underdeveloped reaction was pursued with both catalytic systems to furnish a variety of 1,3-dienes in excellent yields under particularly mild reaction conditions.[9] Overall, olefinic substitution patterns that would be otherwise difficult to prepare and compatibility with functional groups that would not be tolerated by the more conventional reagents used for this transformation are important assets of these methods. Finally, preliminary investigations suggest that the iridium catalyst operates via an unorthodox mechanism, distinct from those previously reported for Peterson 1,4-elimination, while $HBAr_F$ likely functions via a more traditional carbocationic pathway.[9b,e,10]

RESULTS AND DISCUSSION

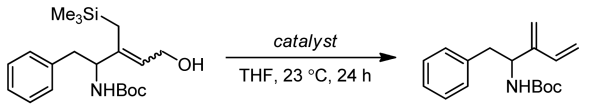
Exploring Site Selectivity of [Ir–H] Insertion in the Isomerization of Allylic Alcohols. The *β*-silicon effect refers to the ability of a silyl group to stabilize a developing positive charge at a carbon atom in the *β* position by hyperconjugation, a property that has been judiciously employed in a variety of transformations in organic synthesis.[10,11] At the outset of our investigations, we were intrigued by the potential influence a *β*-silyl group may exert on the site selectivity of [Ir–H] insertion in the C=C bond of allylic alcohols. Therefore, the representative silylated substrates **4a**,**b** (which possess an aryl

DOI: 10.1021/acscatal.6b03376
ACS Catal. 2017, 7, 1554–1562

and an alkyl group at C3, respectively) were subjected to the typical reaction conditions for isomerization of allylic alcohols using achiral complexes **1** and **3**.[5a,12,13] While isomerization of **4a** with **1** produced aldehyde **5a** exclusively (32% yield), isomerization of (*Z*)-3-cyclopentyl-4-(trimethylsilyl)but-2-enol (**4b**) afforded homoallylic alcohol **7b** as the sole product of the reaction (eqs 1 and 3, Figure 2). Unexpectedly, when **4a**,**b** were subjected to the same experimental protocol using **3**, exclusive formation of 1,3-dienes **6a**,**b** by a formal 1,4-Peterson elimination was observed (>99% conversion, 91% and 82% yields, respectively) (eqs 2 and 4, Figure 2). Consistent with our previous investigations, isomerization of **4c**,**d**—two closely related allylic alcohols devoid of a β-silyl group—furnished quasi-quantitatively aldehydes **5c**,**d**—with both complexes **1** and **3** (eqs 5 and 6, Figure 2). Collectively, these results indicate that, if indeed the presence of a silyl group in the vicinity of the C=C bond of the substrate strongly influences site selectivity of [Ir−H] insertion, the outcome of the reaction is also heavily dependent on the structure of the catalyst employed. This latter observation is more surprising, as both **1** and **3** behave similarly for nonsilylated 3,3-disubstituted alkyl/alkyl and alkyl/aryl primary allylic alcohols.

Interrogating the Specificity of 3 for the Vinylogous Peterson Elimination. Intrigued by the mildness of the reaction conditions and the selectivity with which **3** converted **4a**,**b** into **6a**,**b**, we set out to test the potential of this precatalyst with a substrate that in principle should not be compatible with the typical Brønsted and Lewis acid catalysts/reagents known to effect Peterson 1,4-eliminations. Therefore, both geometrical isomers of an *N*-Boc-protected phenylalanine derived silylated primary allylic alcohol, (*E*)-**4e** and (*Z*)-**4e**, were evaluated with a set of representative catalysts and reagents (Table 1). When they were used in catalytic amounts, $ZnCl_2$, HCl, and HOTs did not display any reactivity (entries 1−5). A stoichiometric amount of $ZnCl_2$ only led to decomposition of (*E*)-**4e**, while 100 mol % of HCl gave ca. 35% of **6e** along with an intractable mixture of side products. A commercially available cationic iridium source ($[Ir(cod)_2]BAr_F$) was also tested. Product formation was observed with (*E*)-**4e** (ca. 40% along with degradation products), and only decomposition of the substrate was noted with (*Z*)-**4e** (entries 6 and 7). Much to our satisfaction, with complex **3**, both geometrical isomers of allylic alcohol **4e** were quantitatively converted into **6e**, thus underlying the unique character of this catalyst to effect a 1,4-Peterson elimination on a sensitive substrate. Noticeably, while the use of only 5 mol % of **3** afforded **6e** in 92% yield, 10 mol % was required to observe a similar outcome (81% yield). This different reactivity between (*E*)-**4e** and (*Z*)-**4e** highlights the stereospecific nature of the elimination reaction on catalysis by complex **3** (entries 8−12).

Table 1. Reaction Optimization[a]



rac-(E)-**4e**
rac-(Z)-**4e**

rac-**6e**

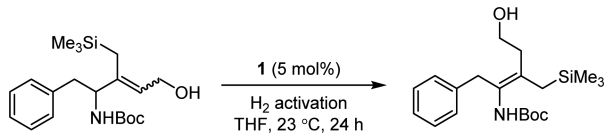
entry	catalyst	substrate	mol %	conv (%)[b]
1	$ZnCl_2$	*rac*-(*E*)-**4e**	5	nr
2	$ZnCl_2$	*rac*-(*E*)-**4e**	100	dec[c]
3	HCl	*rac*-(*E*)-**4e**	5	nr
4	HOTs	*rac*-(*E*)-**4e**	5	nr
5	HCl	*rac*-(*E*)-**4e**	100	~35[d]
6	$[Ir(cod)_2]BAr_F$	*rac*-(*E*)-**4e**	5	~40[d]
7	$[Ir(cod)_2]BAr_F$	*rac*-(*Z*)-**4e**	5	dec[c]
8	**3**	*rac*-(*E*)-**4e**	5	>99 (92)
9	**3**	*rac*-(*E*)-**4e**	5	nr[e]
10	**3**	*rac*-(*Z*)-**4e**	5	12
11	**3**	*rac*-(*Z*)-**4e**	10	>99 (81)
12	$[H(OEt_2)_2BAr_F]$	*rac*-(*E*)-**4e**	5	>99 (82)[f]
13	$[H(OEt_2)_2BAr_F]$	*rac*-(*Z*)-**4e**	5	>99 (82)[f]

[a]Reaction conditions: **4e** (0.1 mmol). Catalyst **3** was activated by molecular hydrogen unless otherwise noted. [b]Conversion into **6e** determined by ^{1}H NMR of the crude reaction mixture. Yield of isolated product after purification by column chromatography are given in parentheses. [c]Decomposition of the substrate. [d]Along with an intractable mixture of degradation products. [e]Without activation by molecular hydrogen. [f]After 4 h.

The decomposition of the catalytically competent iridium hydrides $[(P,N)Ir(H)_2(solv)_2]BAr_F$ generated upon activation of **1** (or related structures) by molecular hydrogen has been studied in detail over the last 40 years.[14,15] Typically, di-, tri-, and tetranuclear polyhydrido-iridium clusters are generated upon aggregation of the coordinatively unsaturated cationic dihydride intermediates. As this process is formally accompanied by the liberation of 1 equiv of $HBAr_F$, the behavior of a catalytic amount (5 mol %) of this peculiar Brønsted acid was also evaluated using allylic alcohol **4e** (Table 1, entries 12 and 13).[16]

In contrast not only to HCl or HOTs but also to **3**, after only 4 h quantitative conversion into **6e** was observed starting indifferently from (*E*)-**4e** or (*Z*)-**4e** (82% yield in both cases).

Of important note, at this stage of our studies, the distinct behaviors of **3** and $HBAr_F$ toward both geometrical isomers of substrate **4e** already point to potential mechanistic differences between the two catalytic systems. Our study also suggests that liberated $HBAr_F$ upon catalyst decomposition is not responsible for the catalytic activity observed with **3** (vide infra) and clearly eliminates the possibility of hidden Brønsted acid catalysis.[16] In line with the isomerization of **4b** (Figure 2, eq 3), when *rac*-(*E*)-**4e** was subjected to catalysis with **1** after activation by molecular hydrogen, homoallylic alcohol (*Z*)-**7e** was isolated as the sole product of the reaction. No reaction was observed with *rac*-(*Z*)-**4e** (Figure 3). These results further underscore the distinct reactivity profile of both iridium catalysts with silylated allylic alcohols despite their seemingly related structures.



rac-(E)-**4e**
rac-(Z)-**4e**

(*Z*)-**7e**
>99% conv.; 55% yield
nr

Figure 3. Isomerization of silylated allylic alcohol **4e** catalyzed by **1**.

Modular Synthesis of Silylated Allylic Alcohols. Having established the ability of **3** and $HBAr_F$ in effecting vinylogous Peterson elimination on a particularly sensitive substrate, we sought to explore and delineate the scope and limitations of both catalysts in a systematic comparative study. To ensure maximum efficiency and modularity for substrate synthesis, we adopted a strategy similar to that recently followed in our

DOI: 10.1021/acscatal.6b03376
ACS Catal. 2017, 7, 1554−1562

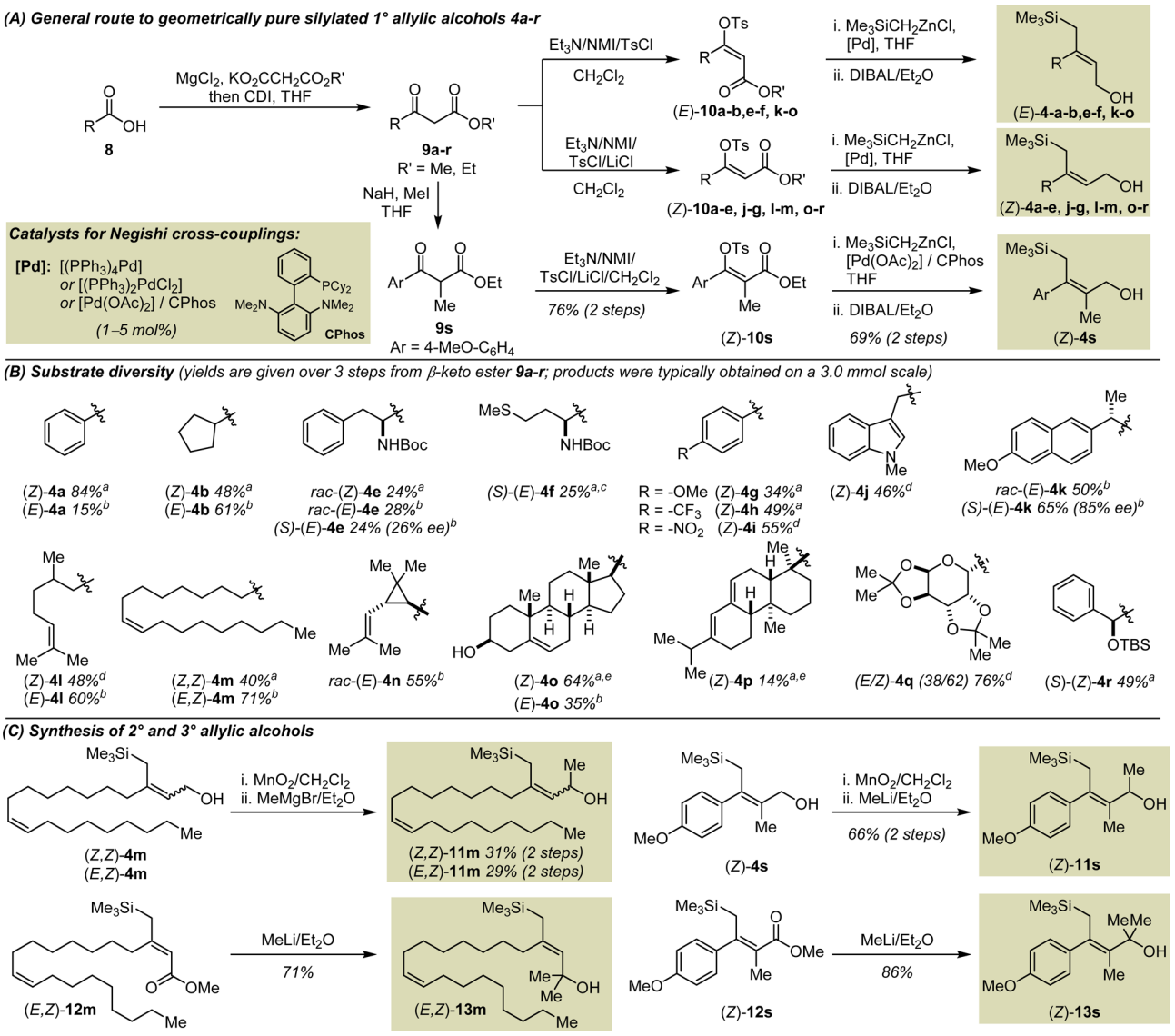


Figure 4. Substrate syntheses. (A) general route to geometrically pure silylated primary allylic alcohols; (B) substrate diversity for primary allylic alcohols; (C) synthesis of silylated secondary and tertiary allylic alcohols. Legend: (*a*) catalyst used for the Negishi cross-coupling $[(PPh_3)_4Pd]$ (1−5 mol %); (*b*) catalyst used for the Negishi cross-coupling $[(PPh_3)_2PdCl_2]$ (1−5 mol %); (*c*) enantiopurity not determined; (*d*) catalytic system used for the Negishi cross-coupling: $[Pd(OAc)_2]$ (5 mol %)/CPhos (10 mol %); (*e*) prepared via the corresponding enol triflate according to Frantz's protocol (see ref 19).

laboratories for the preparation of steroidal allylic alcohols which takes inspiration from protocols developed by Tanabe and co-workers on simple precursors (Figure 4).[5h,17] The pivotal 1,3-keto esters **9a−r** were either commercially available or were prepared in one step from the corresponding carboxylic acid.[18] The *E*-configured enol tosylates (*E*)-**10a,b,e,f,k−o** were obtained after treatment with triethylamine, *N*-methylimidazole, and tosyl chloride (1.5 equiv each). Keto esters **9a−e,g−j,l,m,o−r** were stereoselectively converted to (*Z*)-**10a−e,g−j,l,m,o−r** in moderate to good yields using 5.0 equiv of LiCl and otherwise identical reaction conditions. Pd-catalyzed stereoretentive Negishi cross-couplings using in situ generated (trimethylsilyl)methylzinc chloride followed by enoate reduction with diisobutyl aluminum hydride delivered the primary allylic alcohols in geometrically pure form and good yields over these two steps.[19] Overall, our synthetic strategy enabled the rapid assembly of a collection of 24 different silylated primary allylic alcohols with a high level of structural diversity and molecular complexity (polycyclic, tertiary, and quaternary α stereocenters) along with an array of functional groups (aryl, perfluoroaryl, alcohol, ether, thioether, silyl ether, acetal, N-heterocycles, protected amine, alkene). Substrate **4s**, which features a tetrasubstituted C═C bond, was prepared according to the same sequence after simple C-alkylation of **9g** into **9s**. Both geometrical isomers of secondary allylic alcohol **11m** were obtained starting from (*E*)-**4m** and (*Z*)-**4m** by oxidation to the corresponding α,β-unsaturated aldehydes followed by 1,2-addition of methylmagnesium bromide. The corresponding tertiary allylic alcohol (*E*)-**13m** was obtained in 71% yield by treatment of enoate (*E*)-**12m** with 3 equiv of MeLi. Similar sequences gave access to (*Z*)-**11s** and (*Z*)-**13s**, a secondary and a tertiary allylic alcohol, respectively, both featuring a tetrasubstituted C═C bond.

Comparative Study between 3 and $HBAr_F$ for the Vinylogous Peterson Elimination. The complete collection of primary, secondary, and tertiary allylic alcohols was

DOI: 10.1021/acscatal.6b03376
ACS Catal. 2017, 7, 1554−1562

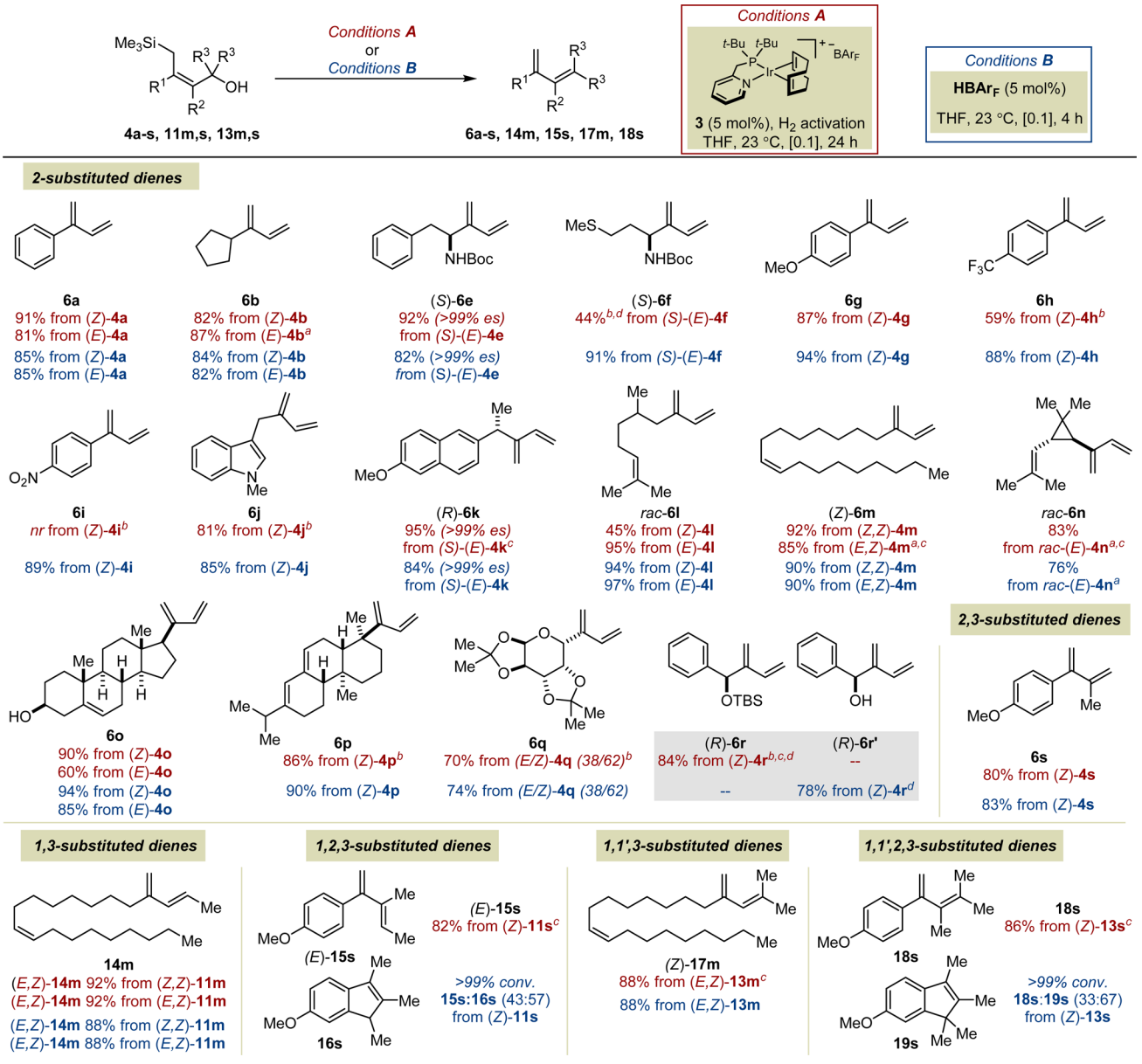


Figure 5. Substrate scope (0.1−0.2 mmol scale). Isolated yields after column chromatography. Legend: (*a*) 1 mol % of **3**; (*b*) 10 mol % of **3**; (*c*) 4 h; (*d*) enantiospecificity not determined.

subsequently subjected to the prototypical reaction conditions developed for the vinylogous Peterson elimination catalyzed by **3** (5 mol %, activation with molecular hydrogen, room temperature, 24 h) and $HBAr_F$ (5 mol %, room temperature, 4 h). The vast majority of silylated primary allylic alcohols tested proved competent in undergoing a 1,4-elimination reaction with catalyst **3** and $HBAr_F$, but some important differences were noted for several substrates (Figure 5). Specifically, substrates with electron-neutral (**4a**), electron-rich (**4g**), or electron-poor (**4h,i**) aryl substituents at C3 were converted quantitatively and isolated in excellent yield with $HBAr_F$. In contrast, **4h** required an increased catalyst loading of **3** (10 mol %) to isolate **6h** in an acceptable 59% yield, while no reaction was observed with **4i**. Similarly, **6j**, which is characterized by a *N*-methyl-protected indole motif, was isolated in 81% yield using 10 mol % of **3**, while no modifications of protocol B were necessary to achieve similar performances with $HBAr_F$ (5 mol %, 4 h). The stereospecific nature of the reaction with the iridium precatalyst was again noted in eliminations using (*Z*)- and (*E*)-**4b**, as the latter was reacted with a loading as low as 1 mol %. Interestingly, the optically active silylated allylic alcohols **4e,k**—which both possess a tertiary stereocenter adjacent to C3—underwent the 1,4-Peterson elimination with virtually perfect enantiospecificity and furnished the corresponding chiral products in excellent yields with both catalytic systems. The configurational stability of these stereocenters using **3** is particularly remarkable because isomerization of **4e,k** with catalyst **1** led to the exclusive formation of the corresponding tetrasubstituted homoallylic alcohols, implying migratory insertion at C3 and *β*-H elimination at C4.[20] Noticeably, a methionine-derived silylated allylic alcohol was successfully engaged in the elimination reaction, affording **6f** in 44% yield with **3** and 91% with the Brønsted catalyst.[21] The compatibility of both methods with isolated C=C bonds was demonstrated with substrates **4l−n**, leading to **6l−n** in satisfactory to excellent yields (45−95% with

DOI: 10.1021/acscatal.6b03376
ACS Catal. 2017, 7, 1554−1562

3; 76−97% with $HBAr_F$). Of note, no isomerization of the remote *Z*-configured 1,2-disubstituted double bond was noted in the reaction with (*Z*,*Z*)- and (*E*,*Z*)-**4m**.[22] The presence of a tertiary and—more remarkably—of a quaternary stereocenter adjacent to the allylic system does not affect the efficiency of both processes, as the stereochemically complex scaffolds **6o−q** were obtained in excellent yield upon vinylogous elimination of the appropriate allylic alcohols. These results also highlight the compatibility of the metal-based catalyst and the Brønsted acid catalyst with an endocyclic homoallylic alcohol (**4o**), an endocyclic diene system (**4p**), and a galactose acetonide derivative (**4q**).[23,24] The presence of a diene at these strategic positions of the terpene derivatives bodes well for rapid installation and diversification of heterocyclic ring systems via cycloaddition reactions. The ability of complex **3** to perform a high-yielding vinylogous Peterson elimination on a particularly acid sensitive silyl-protected derivative such as **4r** is simply remarkable (**6r**: 84% yield), especially because $HBAr_F$ led to the corresponding deprotected secondary alcohol **6r′** (78% yield). These contrasting outcomes reinforce the notion that **3** and $HBAr_F$ certainly operate via distinct reaction mechanisms and that the catalytic activity of **3** does not result from traces of acid that might have been generated upon catalyst decomposition.[14−16] It is also worth mentioning that a silyl-protected alcohol would certainly not be compatible with the classical basic fluorine reagents used for vinylogous Peterson eliminations.[9] Interestingly, (*Z*)-**4s**, a primary allylic alcohol with a tetrasubstituted C═C bond, delivered **6s** in 80−83% yield with **3** and $HBAr_F$, thus offering a potential complement to Heck-type cross-coupling with allenes or thermolysis of sulfones, two methods which typically deliver related 2,3-disubstituted diene motifs.[25]

The scope of 1,3-dienes accessible with both protocols was further explored by subjecting secondary and tertiary allylic alcohols (**11m,s** and **13m,s**) to the optimized reaction conditions for the two catalytic systems. All five substrates underwent vinylogous Peterson elimination with the iridium catalyst and afforded the corresponding dienes in excellent yields (82−92%). Noticeably, (*E*,*Z*)-**14m** was obtained in identical yields starting indifferently from (*Z*,*Z*)-**11m** or (*E*,*Z*)-**11m**, indicating that the metal-catalyzed process is stereoconvergent in nature. The elimination reactions of **11m** and **13m** led to comparable results when they were conducted with $HBAr_F$. The vinylogous Peterson elimination of **11s** and **13s** shed additional light on the striking differences between the organometallic and the organic catalysts. While with **3**, **15s** and **18s** were isolated in excellent yield (**15s**, 82%; **18s**, 86%), with $HBAr_F$ generation of these 1,2,3- and 1,1′,2,3-dienes was accompanied by the formation of the inseparable indenes **16s** and **19s.** Indene **19s** was obtained exclusively when the reaction time was extended, indicating that it is generated by a formal hydroarylation of transient diene **18s**.[16e,l]

Overall, from a synthetic point of view, the diversity of substitution patterns available with both protocols is simply remarkable, as it provides direct access to 2-, 2,3-, 1,3-, 1,2,3-, 1,1′,3-, and 1,1′,2,3-substituted dienes. Existing alternatives are at best scarce and limited in scope and often require harsh reaction conditions.[25−27]

Preliminary Mechanistic Insights. On the basis of the control experiments conducted on substrates (*E*)-**4e** and (*Z*)-**4e** (Table 1) and the results of the vinylogous Peterson elimination conducted on the silylated primary allylic alcohols (*E*)-**4f**, (*Z*)-**4h**, (*Z*)-**4i**, (*Z*)-**4l**, (*E*)-**4o**, (*E*/*Z*)-**4q**, and (*Z*)-**4r** and on the silylated secondary allylic alcohols (*Z*)-**11s** and (*Z*)-**13s** (Figure 5), it appears clearly that **3** and $HBAr_F$ operate via different mechanisms.

An intuitive proposal that accounts for diene formation when $HBAr_F$ is employed is depicted on Figure 6. It is represented using (*Z*)-**13s**, as it also allows us to propose a rationale for the obtention of indene **19s** resulting from the hydroarylation reaction.

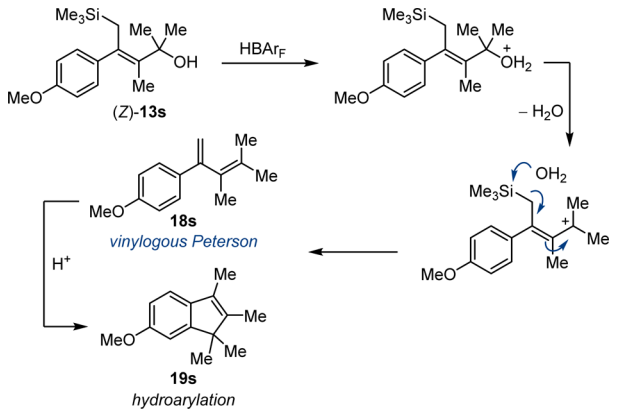
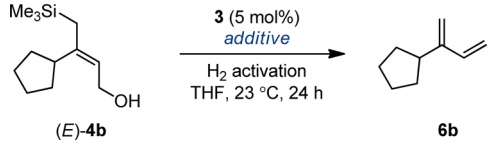


Figure 6. Proposed mechanism for the vinylogous Peterson elimination catalyzed by $HBAr_F$ exemplified with (*Z*)-**13s**.

In contrast, the mode of action of the dihydrido-iridium complexes generated upon activation of **3** by molecular hydrogen appears less obvious. In an effort to gather preliminary information on the mechanism by which catalyst **3** may operate to effect the vinylogous Peterson elimination, a series of additional control experiments was conducted using (*E*)-**4b** as a model substrate (Table 2).

Table 2. Control Experiments[a]



(*E*)-**4b** **6b**

entry	additive	conv (%)[b]
1	none	>99 (93)
2	DTBMP (10 mol %)[c]	>99
3	TEMPO (10 mol %)[d]	<5
4	4 Å MS (excess)	<5

[a]Reaction conditions: (*E*)-**4b** (0.1 mmol), 1 min activation with H_2 followed by degassing. [b]Conversion into **6b** determined by ^{1}H NMR of the crude reaction mixture. The yield of isolated product after purification by column chromatography is given in parentheses. [c]DTBMP = 2,6-di-*tert*-butyl-4-methylpyridine. [d]TEMPO = (2,2,6,6-tetramethylpiperidin-1-yl)oxyl.

When the reaction was run in the presence of 10 mol % of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP), a bulky non-coordinating base, quantitative formation of diene **6b** was observed after 24 h, suggesting that potential traces of acid that may be liberated upon decomposition of the iridium dihydride generated by activation with molecular hydrogen are not responsible for catalytic activity.[14−16] In contrast, in the presence of 10 mol % of TEMPO—a notorious trap for transition-metal hydrides—no product formation was observed,

DOI: 10.1021/acscatal.6b03376
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thus advocating the direct involvement of [Ir−H] intermediates in the operating mechanism for the vinylogous Peterson elimination.[4c,28] Of additional note, the absence of ring-opened product in the reaction with the cyclopropyl-containing substrate (*E*)-**4n** rules out a potential cage-escaped radical mechanism.[28] Finally, the complete loss of catalytic activity observed in the presence of 4 Å molecular sieves supports the notion that liberated water plays an important role in the overall catalytic process. Conversely, when (*E*)-**4b** was subjected to catalysis with $HBAr_F$ in the presence of TEMPO (10 mol %) or 4 Å molecular sieves, reactivity was still observed (33% conversion and >99% conversion respectively; see the Supporting Information for details).

Although additional experiments are needed, on the basis of these results and on observations made while investigating the scope of the reaction, we display in Figure 7 a tentative

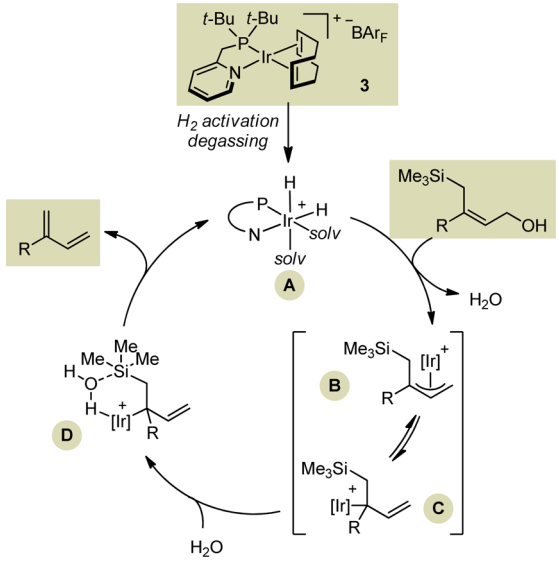

Figure 7. Tentative mechanism for the vinylogous Peterson elimination catalyzed by **3**.

rationale that may account for the vinylogous Peterson elimination catalyzed by **3**. Activation of complex **3** by molecular hydrogen generates the catalytically active cationic Ir(III) dihydride **A**.[12,13] Upon reaction with the silylated allylic alcohols, production of the cationic iridium-allyl complexes (**B** and/or **C**) accompanied by concomitant formation of one molecule of water seems reasonable. The decrease in or absence of reactivity for arylated substrates with a para-electron-withdrawing substituent at C3 may be explained by the difficulty in accessing or stabilizing intermediate **C**. Because of the stereospecific nature of the reaction, we believe that iridium-allyl formation is the rate-determining step of the catalytic process and that one of the hydride ligands is responsible for activation of the hydroxy functionality of the substrate. The water molecule generated (which may or may not leave the first coordination sphere of the iridium atom) subsequently participates in elimination of the silyl fragment. Intermediate **D** is postulated to precede a related six-membered pericyclic transition state leading to the formation of the diene and simultaneous regeneration of **A**.

CONCLUSION

In this article, we have reported the serendipitous discovery of two distinct catalysts for the vinylogous Peterson elimination of a variety of silylated allylic alcohols leading to valuable dienes. The first catalyst, a cationic iridium complex supported by a chelating (P,N) ligand, was identified while investigating the site selectivity of [Ir−H] insertion across the C═C bond of silylated allylic alcohols. The second catalytic system, a Brønsted acid ($HBAr_F$), was discovered when assessing whether traces of acid that might be generated upon decomposition of the active form of the iridium complex were responsible for catalytic activity. To delineate the synthetic potential of both entities, a systematic comparative study was pursued on a vast number of silylated allylic alcohols. This required the design of a modular sequence based on some of the most recent cross-coupling methods to access the substrates in geometrically pure form with the possibility to introduce up to four substituents on the C═C bond and a representative diversity of functional groups. Overall, both systems were found to react with a variety of primary silylated allylic alcohols to afford the expected 2- and 2,3-substituted dienes in usually good to excellent yields—independently of the extent of substitution of the olefinic moiety, the stereochemical complexity, and the congested nature of proximal stereocenters. The two catalysts were found to be both stereo- and enantiospecific. Several sensitive functional groups that would not be compatible with more conventional reagents were also perfectly tolerated by the organic and the organometallic catalyst. Nonetheless, for some specific substrates, clear reactivity differences were noted. For instance, the Brønsted acid catalyst appeared more appropriate to effect the elimination of a methionine-derived substrate but it proved to be incompatible with silyl-protected alcohol functionalities. In the latter case, the iridium catalyst led to the expected diene without cleavage of the acid-sensitive silicon−oxygen bond. While all substrates with an aromatic substituent at C3 were perfectly engaged in the elimination reaction with $HBAr_F$, a net decrease in reactivity was observed with the iridium complex upon para substitution with electron-withdrawing substituents. Alkyl-containing secondary and tertiary silylated allylic alcohols were equally reactive with both systems, and the corresponding 1,3- and 1,1′,3-substituted dienes were isolated in usually high yields. Analogues with an aromatic ring at C3 were converted smoothly to dienes with the organometallic species, while a competing hydroarylation leading to intractable mixtures of products occurred with the organic catalyst.

Overall, both synthetic methodologies give access to a broad set of dienes which would be otherwise difficult to prepare with a single and unified experimental protocol. From a practical point of view, the two catalysts effect the vinylogous Peterson elimination under mild reaction conditions and at relatively low loadings. The experimental setup with the Brønsted acid is simpler, but the use of the iridium catalyst is clearly preferred for some specific substrates and functional groups.

Aside from practical and synthetic considerations, collectively our results support the notion that both systems follow different catalytic manifolds. First, they clearly demonstrate that traces of acid that may be generated upon catalyst decomposition are not responsible for the activity observed with the iridium catalyst. Additional investigations underscored the key role of the in situ generated iridium-hydride and the liberated water. These control experiments, taken together with

DOI: 10.1021/acscatal.6b03376
ACS Catal. 2017, 7, 1554−1562

the stereospecific nature of the iridium-catalyzed reaction and the lack of reactivity toward substrates with electron-deficient aromatic substituents provided support for a mechanistic scenario involving iridium-allyl intermediates. A comparative study with other iridium catalysts clearly suggests that subtle variations in ligand design strongly influence site selectivity for [Ir−H] insertion across the C═C bond of silylated allylic alcohols. Further experimental and computational studies into the origin of the reactivity and selectivity of these different catalytic systems are underway in our laboratories.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.6b03376.

Experimental procedures, characterization of all new compounds, and spectral data (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the University of Geneva and the Swiss National Science Foundation (PP00P2_133482) for financial support and Johnson Matthey for a generous gift of iridium precursors. This article is dedicated to Prof. Alexandre Alexakis for his constant support and friendship.

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