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Acylsilanes as Weakly Coordinating Directing Groups for Metal-Catalyzed C−H Functionalization

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Cite This: ACS Catal. 2025, 15, 6881−6894 Read Online

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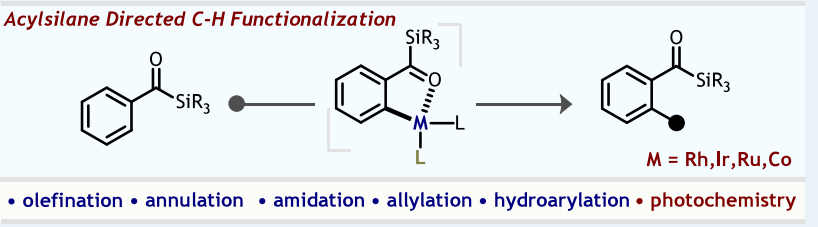


ABSTRACT: The capacity to engage acylsilanes as carbene precursors, electrophiles, and acyl radical precursors offers significant synthetic potential. However, harnessing the versatility of acylsilanes in chemical synthesis has been somewhat hampered to date by a lack of available methods to access complex scaffolds containing the acylsilane functionality. To address this challenge, catalytic synthetic methods that employ acylsilanes as weakly coordinating directing groups to direct the site-selective functionalization of proximal C−H bonds have recently been explored. Herein we review the discoveries in metal-catalyzed acylsilane-directed C−H functionalization strategies over the past decade that enable access to more complex acylsilane derivatives. Subsequent photochemical transformations of some of the acylsilane derivatives accessed via C−H functionalization are also presented to further showcase the unique reactivity profile of acylsilanes.

KEYWORDS: *acylsilane, C−H functionalization, directing group, carbocycle, heterocycle*

The directed functionalization of C−H bonds using transition-metal catalysis has emerged as a practical means to access a diversity of valuable molecular building blocks.[1−3] C−H functionalization strategies have been widely employed in the construction of synthetically mature frameworks across both natural product synthesis[4−6] and drug discovery (for example, the late-stage diversification of pharmaceutical agents).[7−10] The site-selective C−H functionalization of arenes, alkenes, and alkanes typically requires a Lewis basic functional group to coordinate a metal catalyst and direct the C−H bond insertion event via concerted metalation deprotonation (CMD) or analogous mechanistic processes including ambiphilic metal ligand activation (AMLA) or base-assisted internal electrophilic substitution (BIES).[11]

To date, a wide range of directing groups have been explored for this purpose, with many derived from strongly chelating N-donor pyridyl, pyrimidinyl, quinoline, and imino motifs (BF_3 affinity scale: BFA = >100 kJ/mol).[12,13] More weakly coordinating O-donor carbonyl-based directing groups such as ketones and esters have also been exploited in a range of transformations (BFA = 60−75 kJ/mol). Through dative σ-donor interactions, weakly coordinating carbonyl-based directing groups generate transient cyclometalated substrates that are less thermodynamically stable than their strongly chelating counterparts and are thus more reactive in subsequent coupling steps with a functionalization partner.[14,15] In addition, such metallacycles can deliver divergent reaction selectivity as they are less rigid and can undergo reorganization to attain transition states that might be otherwise geometrically disfavored.[16,17] Weakly coordinating carbonyl-based directing groups have hence attracted much attention in the catalysis community as they can undergo various downstream diversification processes and are often native within molecular scaffolds, which avoids the extraneous installation and removal of a chelating scaffold that often contradicts the step economy gained via a C−H activation strategy.[15,18,19]

Acylsilanes, considered the silicon analogues of ketones, are intriguing functional groups that possess a number of unique properties (Figure 1).[20−26] For example, the silicon atom polarizes the carbonyl group via inductive effects leading to absorption at lower frequencies in the infrared and ultraviolet spectra than for analogous ketones.[20] When analyzed by ^{13}C NMR spectroscopy, the chemical shift of the carbonyl group in a benzoyltrialkylsilane ($\delta \approx 230-240$ ppm) is significantly shifted downfield relative to the analogous carbonyl resonances

Received: January 30, 2025
Revised: April 5, 2025
Accepted: April 7, 2025

https://doi.org/10.1021/acscatal.5c00794
ACS Catal. 2025, 15, 6881−6894

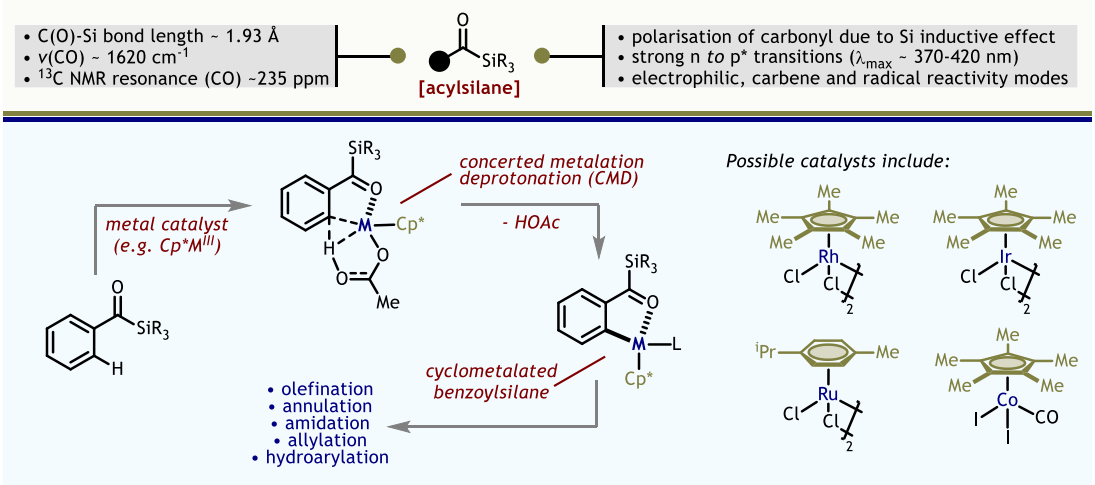


Figure 1. Acylsilanes can be engaged as weakly coordinating directing groups in the site-selective functionalization of benzoylsilanes.

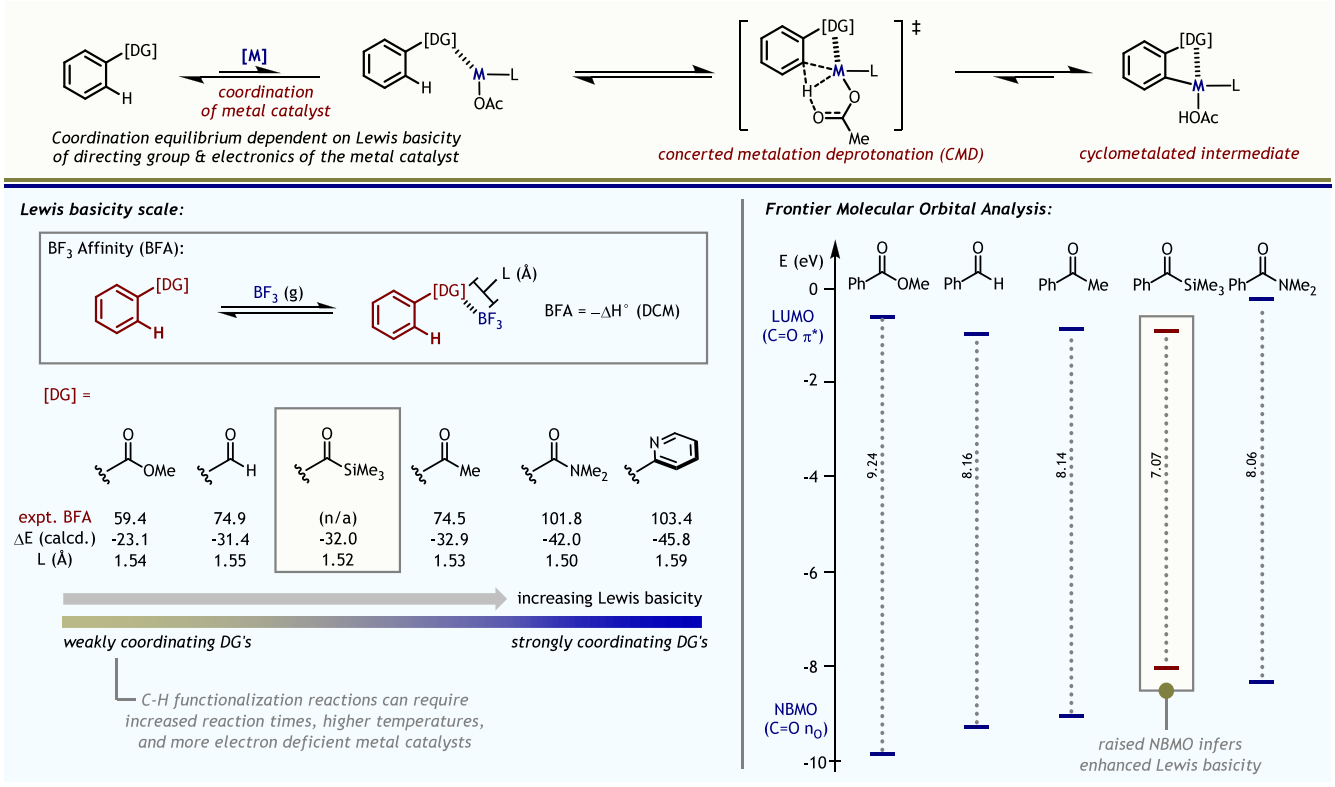


Figure 2. Acylsilanes are intrinsically Lewis basic and can coordinate cationic transition-metal catalysts. Experimental BFA values (kJ/mol) were obtained from literature reports. ΔE (calcd) values (kcal/mol) are the calculated energy difference upon binding of Ph-[DG] to BF_3 to afford the associated Ph-[DG]-BF_3 adduct. Bond lengths were determined following geometry optimization using M06-2x/6-311++G, scrf = CPCM (dichloromethane). FMO energies (eV) were obtained following geometry optimization at the M06-2x/6-311++G level and correspond to the relevant frontier molecular orbitals.

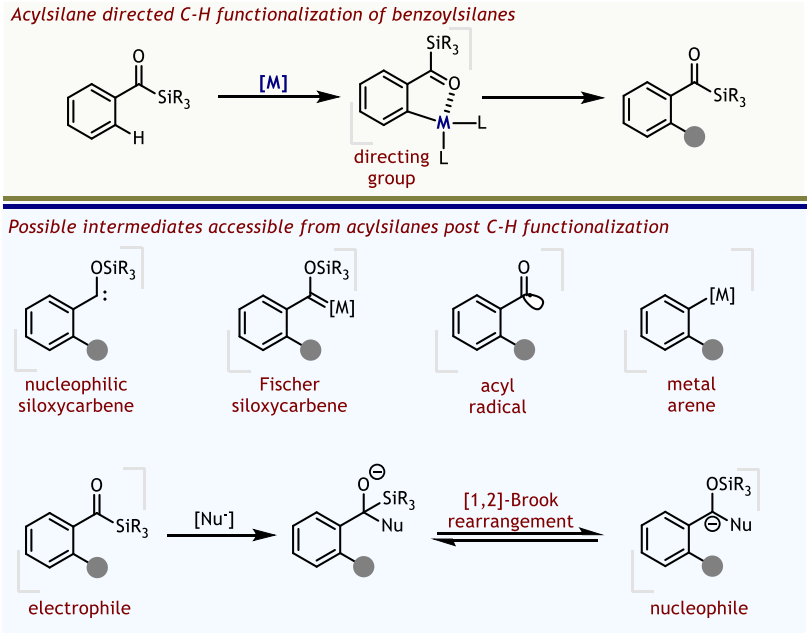
for acetophenones ($\delta \approx 190–200$ ppm). Acylsilanes possess an atypically long Si–C(O) bond (1.93 Å) relative to the analogous R–C(O) bond in ketones (1.51 Å), in addition to steric tunability via modifications to the bulky trialkylsilicon substituent.[20]

Acylsilanes possess significant σ-donor capacity, owing to polarization of the acylsilane carbonyl group. Indeed, an inspection of the relevant frontier molecular orbitals (FMOs) obtained by DFT analysis reveals that the nonbonding electron pairs situated on the carbonyl oxygen in benzoyl(trimethyl)-silane possess the highest energy when compared to that for the corresponding ester, aldehyde, ketone, and tertiary amide, suggesting enhanced Lewis basicity for the benzoylsilane (Figure 2). The low-lying LUMO level of the benzoylsilane (C=O π^* orbital) and thus narrowed band gap also give rise to its electrophilic properties and characteristic photonic transitions in the visible light range.

To the best of our knowledge, BF_3 affinity scale (BFA) data for benzoylsilanes is not available; however, calculations comparing the relative stability of carbonyl-BF_3 adducts

https://doi.org/10.1021/acscatal.5c00794
ACS Catal. 2025, 15, 6881–6894

Scheme 1. Acylsilanes Initially Harnessed as Directing Groups for C−H Functionalization Reactions Are Primed to Undergo a Range of Subsequent Transformations via the Acylsilane Functional Group, Which Enables Access to a Diverse Range of Reactive Intermediates



(M06-2x/6-311++G solvation in the conductor-like polarizable continuum model for DCM) imply that the benzoyl(trimethyl)silane would form a BF_3 complex thermodynamically analogous to that derived from acetophenone and benzaldehyde. Further comparison of the computed dative bond lengths to BF_3 within the carbonyl series reveals a similar trend, with the acylsilane·BF_3 adduct possessing a shorter O−B bond than the benzaldehyde·BF_3 or acetophenone·BF_3 adduct yet a longer bond than the corresponding amide·BF_3 adduct.

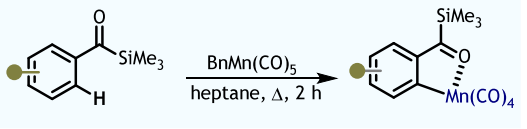
Chemical building blocks containing acylsilane functional groups have been increasingly utilized in chemical synthesis.[21,24,26] For example, acylsilanes can be reacted with organometallic nucleophiles to generate stereodefined and densely substituted frameworks (Scheme 1).[27−29] Under photoredox catalysis, acylsilanes can be engaged as radical precursors,[30−32] and in the presence of transition-metal catalysts, acylsilanes undergo decarbonylation or form reactive Fischer-carbene-type intermediates.[33−37] Most extraordinarily, when activated photochemically via direct irradiation or energy-transfer catalysis, acylsilanes undergo the 1,2-Brook rearrangement to generate singlet siloxycarbene intermediates that participate in a wide variety of insertion transformations dominated by their nucleophilic properties.[25,26,38−47] Remarkably, excited-state acylsilanes can even function as triplet photosensitizers.[46,48]

Despite their synthetic utility, limited methods exist to prepare densely functionalized molecules possessing an acylsilane linchpin.[22] Current methods for preparing acylsilane derivatives typically demand the use of carbon monoxide, organolithium, organomagnesium reagents, or strong oxidants, which limits broad functional group compatibility. To access more complex acylsilane derivatives, recent efforts within the field have focused on harnessing the intrinsic Lewis basic properties of acylsilanes as weakly coordinating directing groups in site-selective C−H functionalization transformations. Cyclometalation using Co^{III}, Ir^{III}, Rh^{III}, and Ru^{II} catalysts in the presence of various coupling partners has been exploited to access a series of previously inaccessible scaffolds containing the acylsilane functional group.

If considered in isolation, many of the site-selective C−H functionalization reactions that can be envisaged using acylsilane directing groups are achievable using the more prevalent ketone or amide directing groups. However, the versatility of acylsilane chemistry that can be envisaged post-C−H functionalization presents a myriad of opportunities for synthesis beyond that possible for ketones, esters, or amides. Thus, acylsilanes represent "transformative" directing groups that can be harnessed to enable further elaboration as uniquely reactive synthetic lynchpins. To this end, we herein highlight the advances that have been made in acylsilane-directed C−H functionalization since the first report just over a decade ago.

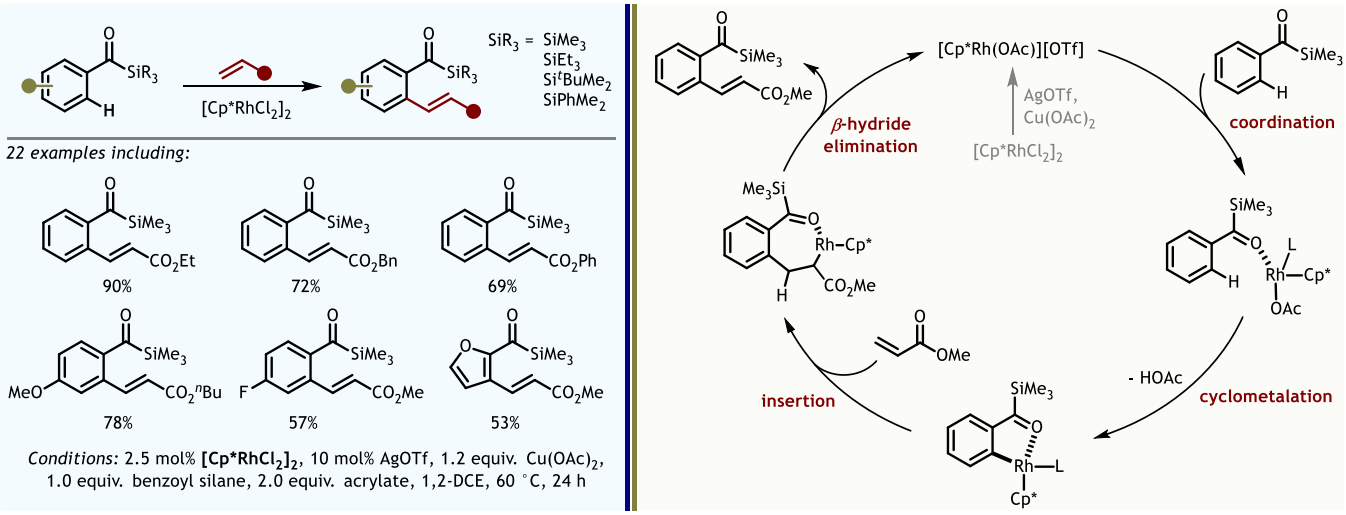
In 1994, Cambie and co-workers first reported the use of acylsilane derivatives as suitable ligands in organometallic complexes following the reaction of a stoichiometric amount of benzylpentacarbonylmanganese [$BnMn(CO)_5$] with benzoylsilanes to generate cyclometalated species in high yield (Scheme 2).[49] This cyclometalated reagent could then be reacted with alkenes and alkynes to afford a variety of cyclic products, including indanes. It should be noted that while manganese-catalyzed C−H activation has emerged as a useful strategy for chemical synthesis,[50−55] the Mn-catalyzed C−H functionalization of benzoylsilanes is yet to be reported.

Scheme 2. Cyclometalated Benzoyl Silane Reagents Can Be Prepared via Reaction with Manganese Complexes

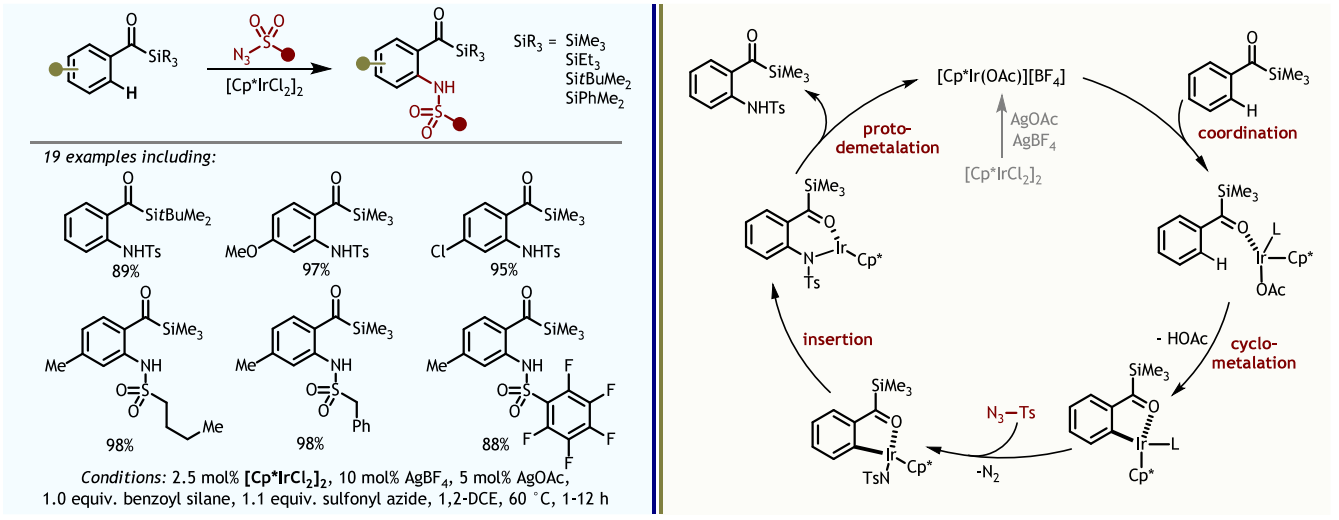


https://doi.org/10.1021/acscatal.5c00794
ACS Catal. 2025, 15, 6881−6894

Scheme 3. Cp*Rh^{III}-Catalyzed *ortho*-Olefination of Benzoylsilanes with Acrylates



Scheme 4. Cp*Ir^{III}-Catalyzed Sulfonamidation of Benzoylsilanes Employing Sulfonyl Azides as Nitrene Precursors



Cyclopentadienyl-derived Rh^{III} complexes have proven to be highly effective catalysts for a range of useful synthetic transformations.[56,57] Inspired by Cambie's early work, in 2014 Bolm and co-workers reported the first catalytic example of C−H functionalization harnessing the acylsilane functional group as a weakly coordinating directing group in the Cp*Rh^{III}-catalyzed *ortho*-olefination of benzoylsilanes with acrylates (Scheme 3).[58] Optimization of the acylsilane-directed olefination process revealed that 2.5 mol % $[Cp^*RhCl_2]_2$ in combination with 10 mol % AgOTf or $AgBF_4$ gave the best results, although other silver salts also proved effective. A slight excess of $Cu(OAc)_2$ was employed as an oxidant and a source of acetate ions. The reaction was ideally conducted at 60 °C, which afforded high yields of the desired product, whereas bis-olefination at both the 2- and 6-positions was encountered when higher temperatures were used. 1,2-DCE was the optimal solvent with the reaction failing to proceed when conducted in tetrahydrofuran or toluene, and when conducted in *tert*-amyl alcohol, the olefinated benzaldehyde adduct was the major product inferring instability of the acylsilane functional group in this solvent at elevated temperature. Initial attempts using other catalysts that are commonly used across C−H functionalization programs such as the more available $[(p\text{-cymene})RuCl_2]_2$ proved relatively unsuccessful.

A range of acrylates demonstrated good to excellent reactivity in the acylsilane-directed olefination process (Scheme 3). Substituents on the aryl ring within the benzoylsilanes appeared to have little influence on overall reactivity, and the variation in the acylsilane group was also tolerated whereby trimethyl, triethyl, and *tert*-butyldimethyl and phenyldimethyl silyl groups all delivered the olefinated product in good yield. Key mechanistic steps include directed activation of the *ortho*-C−H site followed by cyclometalation. The cyclometalated species then coordinates the alkene coupling partner (in this case, an acrylate), which initiates migratory insertion, followed by *β*-hydride elimination to generate the olefinated acylsilane adduct and release the catalyst which is deprotonated and oxidized to Cp*Rh^{III} to re-enter the catalytic cycle.

Cyclopentadienyl-derived Ir^{III} complexes are also exceptionally versatile catalysts that have enabled the discovery of a diversity of novel C−H functionalization strategies.[59] In 2015, Bolm and co-workers reported the Cp*Ir^{III} catalyzed acylsilane directed *ortho*-sulfonamidation of benzoylsilanes (Scheme 4).[60]

https://doi.org/10.1021/acscatal.5c00794
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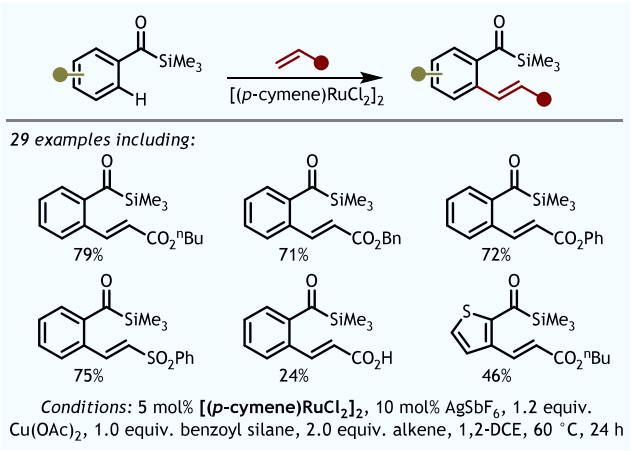
p-Toluenesulfonyl azide, which has been widely employed as a nitrene precursor,[61,62] was initially employed in combination with $[(p\text{-cymene})RuCl_2]_2$ to afford moderate yields of the sulfonamidated product. It was subsequently discovered that improved yields could be obtained using $[Cp^*IrCl_2]_2$ as a catalyst. Reaction optimization revealed that $AgBF_4$ was the best silver salt for catalyst activation, and AgOAc was also required as an acetate source. The reaction performed most effectively in 1,2-DCE as solvent at 60 °C with reaction times varying from 1 to 12 h.

A range of functionalized alkyl and aryl sulfonyl azides demonstrated excellent reactivity in the acylsilane directed sulfonamidation (Scheme 4). Within the acylsilane directing group, trimethyl, triethyl, *tert*-butyldimethyl and phenyldimethyl silyl derivatives all delivered the sulfonamidated product in high yield. Variation in the arene substituent on the benzoyl silane was also possible, affording a library of derivatized 2-sulfonamido benzoylsilanes. Mechanistically, following coordination and C−H activation of the benzoyl silane, interaction of the cyclometalated species with the sulfonyl azide promotes liberation of N_2. The resulting iridium-nitrenoid species can undergo insertion (nitrene transfer) via the nucleophilic attack of the Ir−C bond on the electrophilic nitrenoid. Finally, protodemetalation occurs to afford the sulfonamidated product and release the catalyst (Scheme 3).

Half-sandwich Ru^{II} complexes have also been successfully utilized in C−H functionalization chemistry to drive a diversity of transformations.[63−65] In 2019, Zhong, Zhang, and co-workers reported the first example of acylsilane-directed ruthenium-catalyzed C−H activation utilizing alkenes as coupling partners (Scheme 5).[66] Optimization of the reaction

Scheme 5. (p-Cymene)Ru^{II}-Catalyzed *ortho*-Olefination of Benzoylsilanes



process revealed that 5.0 mol % $[(p\text{-cymene})RuCl_2]_2$ in combination with 10 mol % $AgSbF_6$ delivered the highest yields. 1.2 equiv of $Cu(OAc)_2$ was used as both the oxidant and acetate source. The reaction was best conducted at 60 °C, and 1,2-DCE was the optimal solvent ,with significant reductions in yield observed when conducted in THF, DCM, DME, MeCN, DMF, or toluene.

With regard to the scope, a wide range of functionalized benzoylsilanes were amenable to this olefination reaction employing *n*-butyl acrylate (including heterocyclic thiophenyl and furanoyl acylsilanes), delivering excellent yields. The possible variation in the olefin component was exceptionally broad, where acrylates, styrenes, vinyl sulfones, vinyl phosphonates, and acrylic acid all reacted well to afford a range of 2-alkenyl benzoylsilanes. Fast and reversible C−H cyclometalation of the Ru^{II} catalyst was confirmed by deuteration experiments, and KIE studies suggested that the C−H activation process was not the rate-determining step. Mechanistically, this transformation proposedly proceeds in a fashion analogous to that outlined in Scheme 3.

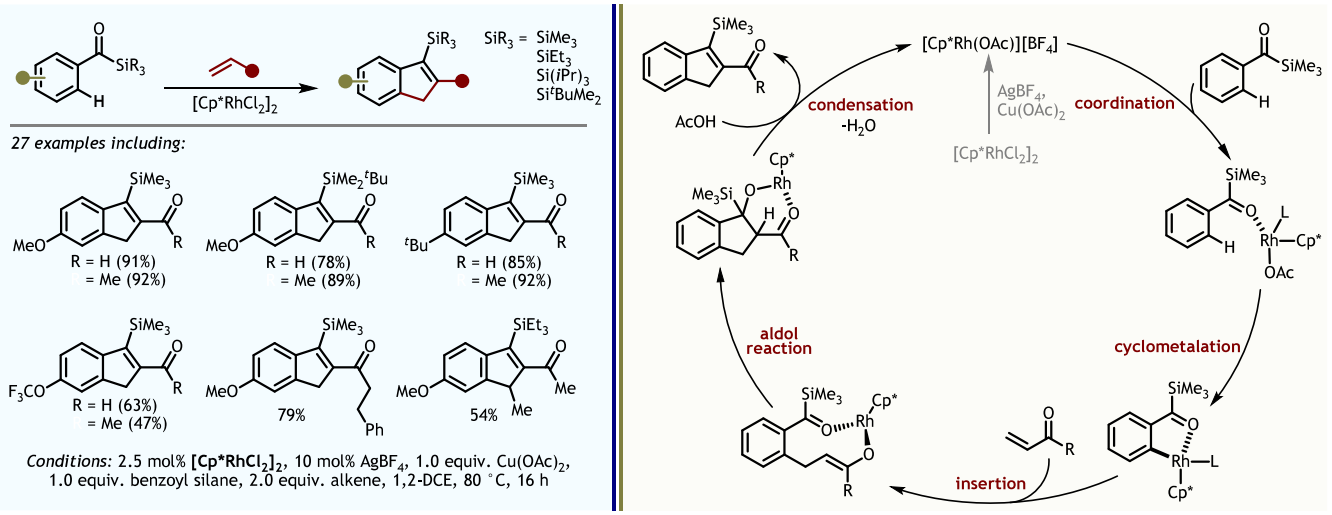
In 2021, Priebbenow and co-workers reported the $[Cp^*RhCl_2]_2$-catalyzed alkylation/annulation reaction between benzoylsilanes and vinyl ketones or acrolein to afford silyl indenes (Scheme 6).[67] Optimization of the reaction revealed that 2.5 mol % $[Cp^*RhCl_2]_2$ in combination with 10 mol % $AgBF_4$ delivered the highest yields. Although 1.0 equiv of $Cu(OAc)_2$ was identified as the optimal source of acetate ions, AcOH and AgOAc were also relatively effective, whereas alternative additives including NaOAc, KOAc, and KOPiv afforded reduced yields. The reaction was best conducted at 80 °C in 1,2-DCE with reduced yields, or no reaction was observed when conducting the reaction in THF, 1,4-dioxane, $CHCl_3$, or toluene. The commercially available complex $[Cp^*Rh(MeCN)_3](SbF_6)_2$ afforded lower yields relative to the analogous catalyst formed *in situ* while the use of other catalysts such as $Cp^*CoI_2(CO)$ led to poor conversion.

A range of substituted benzoylsilanes were suitably applied, affording good to excellent yields of the corresponding silyl indenes (Scheme 6). Typically, however, benzoylsilanes containing electron-donating substituents afforded higher yields than unsubstituted benzoylsilanes or those possessing electron-withdrawing substituents. Variation to the silyl component within the acylsilane directing group was also tolerated whereby trimethyl-, triethyl-, and *tert*-butyldimethyl silyl groups all delivered the annulated product in good yield, while reduced yields were observed for the bulky triisopropylsilyl derivative. Some variation in the structure of the vinyl ketone was tolerated. Mechanistically, coordination and cyclometalation proceed as described previously. Then, following migratory insertion of the vinyl ketone, formation of the silyl indene proceeds via an intramolecular aldol condensation between the metal enolate formed following olefin insertion and the acylsilane functional group.[68] Within this mechanistic cycle, the acylsilane functional group plays an important role as both a weakly coordinating directing group and an electrophile to ultimately afford silicon-furnished carbocyclic scaffolds.

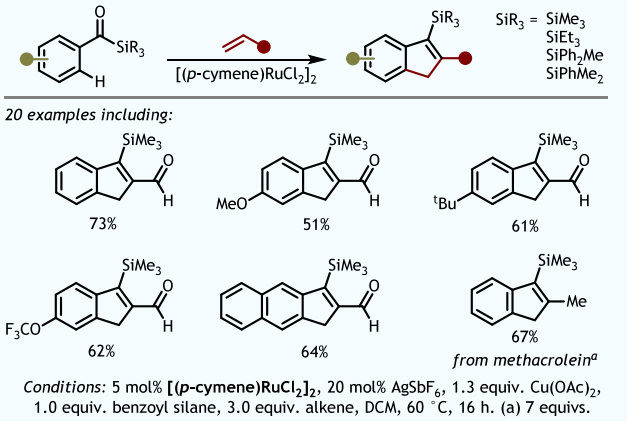
A transformation similar to that outlined in Scheme 6 was recently reported by Zhang and co-workers involving silyl indene formation via the reaction of benzoylsilanes with acrolein under (p-cymene)Ru^{II} catalysis (Scheme 7).[69] Optimization revealed that 5.0 mol % $[(p\text{-cymene})RuCl_2]_2$ in combination with 20 mol % $AgSbF_6$ delivered the highest yields of silyl indene. A slight excess of $Cu(OAc)_2$ was required, and the reaction was conducted at 60 °C in CH_2Cl_2. Reaction attempts using $[Cp^*RhCl_2]_2$ afforded lower yields in this case while $[Cp^*IrCl_2]_2$ was ineffective. Alternative olefins including vinyl sulfones, vinyl phosphonates, and styrenes all afforded the *ortho*-olefinated adducts rather than the cyclic silyl indene product. With regard to the scope of the reaction, a range of substituted benzoylsilanes were compatible, affording good to excellent yields of the corresponding silyl indenes. Where excess 2-alkyl acroleins were used as the reaction partner, decarbonylated silyl indene products were obtained instead (Scheme 7).

https://doi.org/10.1021/acscatal.5c00794
ACS Catal. 2025, 15, 6881−6894

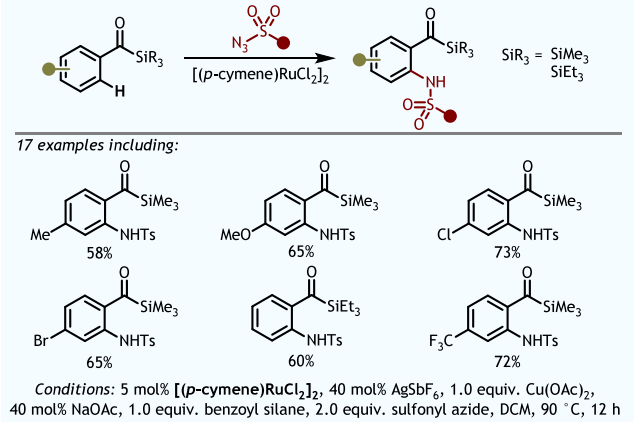
Scheme 6. Cp*Rh^{III}-Catalyzed Annulation of Benzoylsilanes with Acrolein and Vinyl Ketones Proceeds to Generate Silyl Indene Adducts



Scheme 7. (*p*-Cymene)Ru^{II}-Catalyzed Annulation of Benzoylsilanes with Acrolein Proceeds to Form Silyl Indene Frameworks



Scheme 8. (*p*-Cymene)Ru^{II}-Catalyzed Sulfonamidation of Benzoylsilanes Employing Sulfonyl Azides as Nitrene Precursors



It is noteworthy that an analogous Cp*Rh-$(CH_3CN)_3(SbF_6)_2$-catalyzed annulative olefination reaction was reported using a ketone directing group, rather than an acylsilane, to give alkylated indene products.[70,71] However, under Cp*Rh^{III} catalysis, much higher temperatures (130 °C) were required to mediate the reaction, reflecting the comparatively enhanced ability of the acylsilane directing group to recruit the metal catalyst and promote C−H insertion and annulation reactions.

In 2021, Zhang and co-workers reported that (*p*-cymene)-Ru^{II} efficiently catalyzed an *ortho*-amidation reaction of benzoylsilanes using sulfonyl azides (Scheme 8).[72] Compared to the 2015 report by Bolm which utilized Cp*Ir^{III},[60] (*p*-cymene)Ru^{II} is advantageously a relatively more available and less expensive catalyst. After optimization, the highest yields were delivered by a catalyst system of 5.0 mol % $[(p\text{-cymene})RuCl_2]_2$ in combination with 40 mol % $AgSbF_6$ activator. Equimolar $Cu(OAc)_2$ in addition to 40 mol % NaOAc was required, and the reaction performed best when conducted at 90 °C in CH_2Cl_2. Employing $[(C_6H_6)RuCl_2]_2$ and $[Cp^*RhCl_2]_2$ catalysts afforded lower yields while $[Cp^*IrCl_2]_2$ was identified as effective. A range of substituted benzoylsilanes were compatible in the amidation protocol affording good to excellent yields of the corresponding *ortho*-sulfonamidated benzoylsilanes (Scheme 8). Mechanistically, this process is proposed to proceed in a fashion analogous to that outlined in Scheme 3.

In the same paper, Zhang and co-workers reported the (*p*-cymene)Ru^{II}-catalyzed *ortho*-amidation reaction of benzoylsilanes using *N*-tosyloxyphthalimide as a coupling partner to afford *N*-phthalimido-derived benzoylsilanes (Scheme 9).[72] *N*-Tosyloxyphthalimides, activated via heterolytic cleavage of the *N*−*O* bond, have been widely employed as an amination reagent whereby the phthalimide protecting group can be subsequently cleaved to reveal the free aniline.[73−75] Optimization of the reaction revealed that 5.0 mol % $[(p\text{-cymene})RuCl_2]_2$ in combination with 20 mol % $AgNTf_2$ and 0.5 equiv of Ag_2O at 90 °C in CH_2Cl_2 delivered the highest yields. Significantly reduced reactivity was observed when the reaction was conducted in THF, 1,4-dioxane, MeOH, 1,2-DCE, CH_3Cl, or toluene. Substitution of $[(p\text{-cymene})RuCl_2]_2$ by $[(C_6H_6)RuCl_2]_2$ or $[Cp^*RhCl_2]_2$ afforded reduced yields while $[Cp^*IrCl_2]_2$ was ineffective. A range of substituted benzoylsilanes were compatible, affording good to excellent

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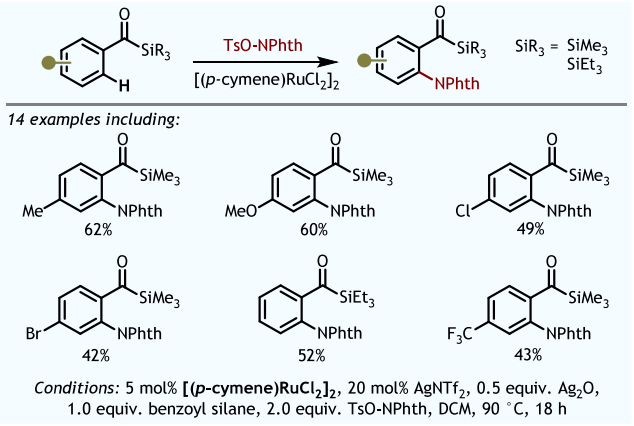
Scheme 9. (p-Cymene)Ru^{II}-Catalyzed Amidation of Benzoylsilanes Employing Activated *N*-Tosyloxyphthalimides as Amination Reagents



yields of the corresponding *ortho*-amidated benzoylsilanes (Scheme 9). Again, additional mechanistic studies involving deuterated species revealed that the C−H cyclometalation of the Ru^{II} catalyst is reversible, implying that cyclometalation is not the rate-determining step.

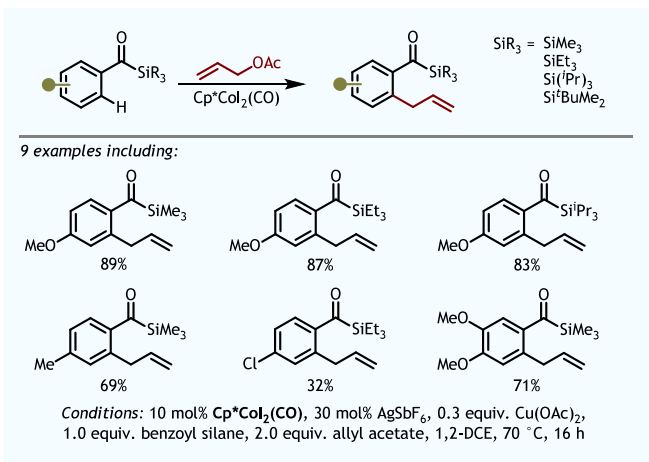
Half-sandwich Co^{III} complexes have become widely utilized in C−H functionalization, affording access to a variety of valuable chemotypes.[76,77] Moreover, the utilization of earth abundant metals in contemporary C−H activation chemistries is of particular interest due to obvious economic advantages in cost and sustainability.[78,79] In 2022, Priebbenow and co-workers reported the first example of acylsilane-directed Cp^*Co^{III}-catalyzed C−H functionalization using $Cp^*CoI_2(CO)$ as a catalyst to drive the allylation reaction between benzoylsilanes and allyl acetate (Scheme 10).[80] Attentive optimization revealed that 10 mol % $Cp^*CoI_2(CO)$ in combination with 30 mol % $AgSbF_6$ and 30 mol % $Cu(OAc)_2$ delivered the highest yields. The additive Ag_2CO_3 was also relatively effective; however, alternative additives including AgOAc, NaOAc, or KOAc afforded reduced yields. The reaction was best conducted at 70 °C and 1,2-DCE was determined to be the optimal solvent while reduced yields or no reaction was observed in tetrahydrofuran, 1,4-dioxane, $CHCl_3$, acetonitrile, or methanol. Notably, catalysts such as $[Cp^*RhCl_2]_2$ and $[(p\text{-cymene})RuCl_2]_2$ could also be employed to afford the allyl product in reasonable yields.

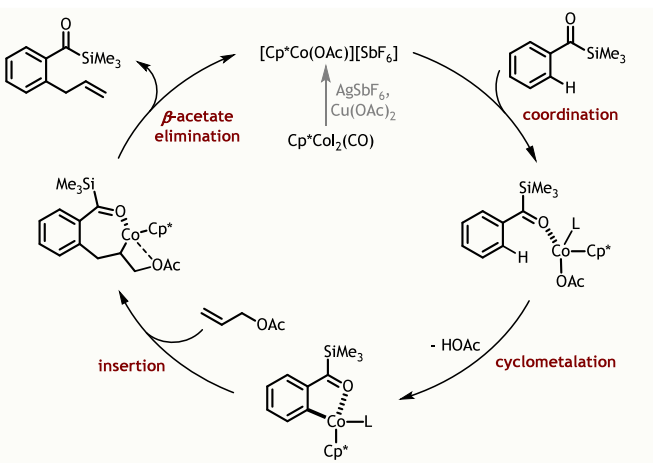
Benzoylsilanes furnished with various substituents (alkyl, alkoxy, and halogen) were compatible in the reaction, affording good to excellent yields of the corresponding *ortho*-allyl benzoyl silane (Scheme 10). Electron-rich benzoylsilanes were favored and underwent allylation in higher yields than unsubstituted benzoylsilanes or those containing electron-withdrawing substituents. Acylsilanes containing various (trialkyl)silicon groups were well tolerated largely irrespective of steric bulk, and all delivered the allyl benzoylsilanes in good yield (Scheme 10).

Priebbenow and co-workers also discovered that identical conditions enabled the $Cp^*CoI_2(CO)$-catalyzed annulation of benzoylsilanes with internal alkynes (Scheme 11), occurring via C−H alkenylation and concomitant annulative desilylation of the acylsilane directing group.[80] A range of substituted benzoylsilanes were compatible in the reaction, affording good to excellent yields of the corresponding indenones (Scheme 11). Again, unsubstituted benzoylsilanes or those containing electron-withdrawing substituents reacted with reduced rates compared to electron-rich examples. Trimethyl, triethyl, triisopropyl, and *tert*-butyldimethyl silyl groups in the acylsilane all translated to the desilylated indenone in good yields, and internal alkynes bearing aryl or alkyl substituents were applicable to the annulation process. Notably, $Cp^*CoI_2(CO)$ has also been utilized to direct the annulation of internal alkynes using benzoate esters as directing groups to afford identical products, although such processes required much high temperatures (120−130 °C).[81,82]

Inspired by previous work from the Cheng group,[83,84] Priebbenow and co-workers also explored acylsilane-directed C−H functionalization using 1,6-enyne reagents to afford the *ortho*-alkylated benzoyl silane in 59% yield under $Co^{I/III}$ catalysis.[80] Mechanistically, this transformation proceeds via initial zinc-mediated *in situ* reduction of the Co^{II}/phosphine catalyst to afford a Co^{I} species which promotes oxidative cyclization of 1,6-enyne to generate a cyclometalated Co^{III} species. This Co^{III} species then engages the acylsilane carbonyl which initiates *ortho* C−H metalation to afford an intermediate that can then undergo reductive elimination to afford unique benzoyl silane derivatives and regenerate the catalytically active Co^{I} species (Scheme 12).

Scheme 10. Cp^*Co^{III}-Catalyzed Reaction of Allyl Acetate with Benzoylsilanes





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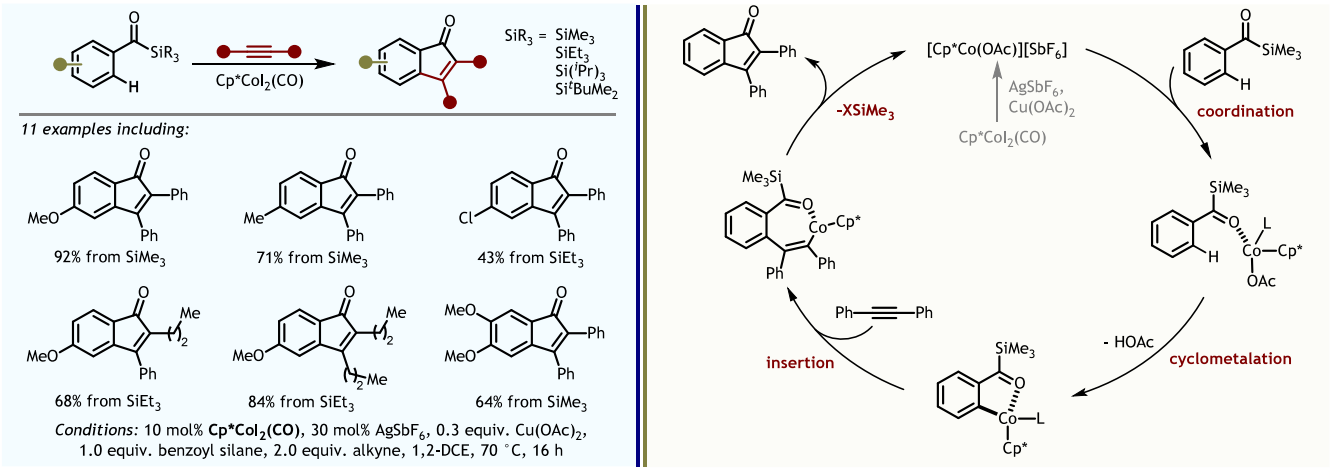
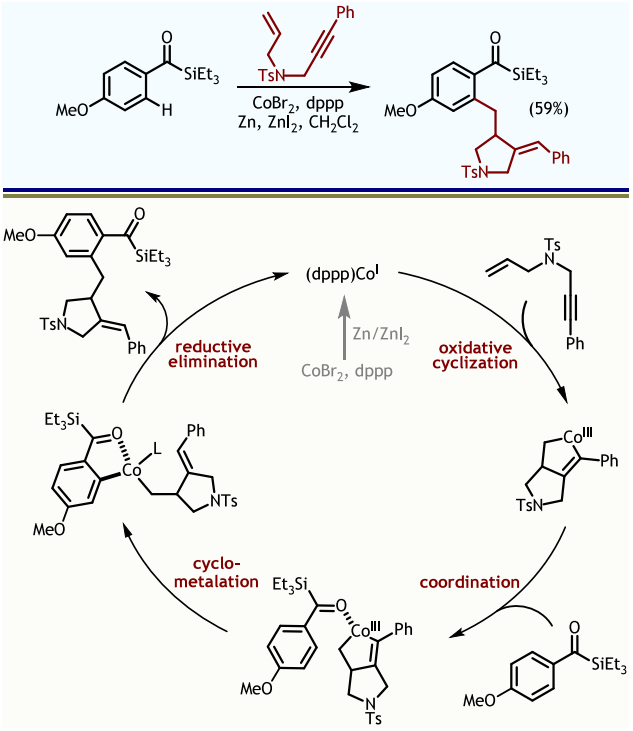
Scheme 11. Cp*Co^{III}-Catalyzed Annulation of Benzoylsilanes and Alkynes to Access Indenones



Scheme 12. Cobalt-Catalyzed Acylsilane-Directed C−H Functionalization of Benzoylsilanes Using 1,6-Enyne Reagents



Maleimides are interesting heterocyclic cross-coupling partners for C−H functionalization that can be used to access a range of products.[85] In 2023, Das and co-workers reported the Cp*Rh^{III}-catalyzed hydroarylation reaction between benzoylsilanes and maleimides (Scheme 13).[86] Optimization of the reaction concluded that 5.0 mol % $[Cp^*RhCl_2]_2$ in combination with 10 mol % $AgSbF_6$ provided the highest yields of the C−H activation product. $Cu(OAc)_2{\cdot}H_2O$ was identified as the optimal source of acetate ions with alternatives including $Zn(OAc)_2$, CsOAc, or AcOH affording reduced yields. The reaction was conducted at 70 °C, and 1,2-DCE was determined to be the uniquely optimal solvent with reduced or no reactivity observed in other solvents. A range of substituted benzoylsilanes were compatible, affording good to excellent yields of the corresponding alkylated products, and *N*-aryl, *N*-alkyl and unprotected maleimides could be effectively employed (Scheme 13).

By switching the catalyst to (*p*-cymene)Ru^{II}, a divergent system for the [3 + 2] carboannulation of benzoylsilanes and maleimides was discovered (Scheme 14).[86] An optimal catalytic triad consisting of 5.0 mol % $[(p\text{-cymene})RuCl_2]_2$ in combination with 10 mol % $AgSbF_6$ and $Cu(OAc)_2{\cdot}H_2O$ (1.2 equiv) afforded fused indano-succinimide products in good yields. Structurally diverse maleimides were observed to react with benzoylsilanes in good yields. In the case of 2,3-dimethoxy-substituted benzoyl silane, the indanol product was formed as a result of methoxy-group coordination which promoted a 1,2-Brook and proto-demetalation process. This fused indanol was recognized as a precursor molecule to an antihypertensive agent (Scheme 14). The observed catalyst-dependent divergency in these systems proposedly arises from the greater propensity of carbon−rhodium-bound intermediates to undergo protodemetalation compared to the less acidic carbon−ruthenium bond which favors 1,2-carbonyl addition.

In 2023, Priebbenow reported the acylsilane-directed amidation of benzoylsilanes using 1,4,2-dioxazol-5-ones as nitrene precursors (Scheme 15).[87] Dioxazolones are accessible in two steps from parent carboxylic acids and represent convenient acyl nitrene precursors due to their ease of synthesis and favorable energetic profile compared to acyl azides.[88,89] Comprehensive investigations into this process revealed that C−H amidation could be catalyzed by either Cp*Co^{III} or Cp*Rh^{III} complexes. The Cp*Co^{III}-catalyzed reaction performed best using 10 mol % $Cp^*CoI_2(CO)$ in combination with 30 mol % $AgSbF_6$ and 30 mol % NaOAc in 1,2-DCE at 80 °C. The Cp*Rh^{III}-catalyzed reaction required reduced catalyst and additive loading and operated at milder temperature, using 2.5 mol % $[Cp^*RhCl_2]_2$ in combination with 10 mol % $AgSbF_6$ and 15 mol % NaOAc in 1,2-DCE at 60 °C. Higher yields were typically obtained under Cp*Rh^{III} catalysis; however, in certain cases where bulkier substituents were present in either the acylsilane or 1,4,2-dioxazol-5-one reagent, the Cp*Co^{III} catalyst performed best (Scheme 15).

During the course of their investigations, Priebbenow and co-workers investigated a series of modified Cp^{x}Rh^{III} complexes containing various substituents designed to vary the steric and electronic properties of the cyclopentadienyl ligands.[87] These studies were guided by computational

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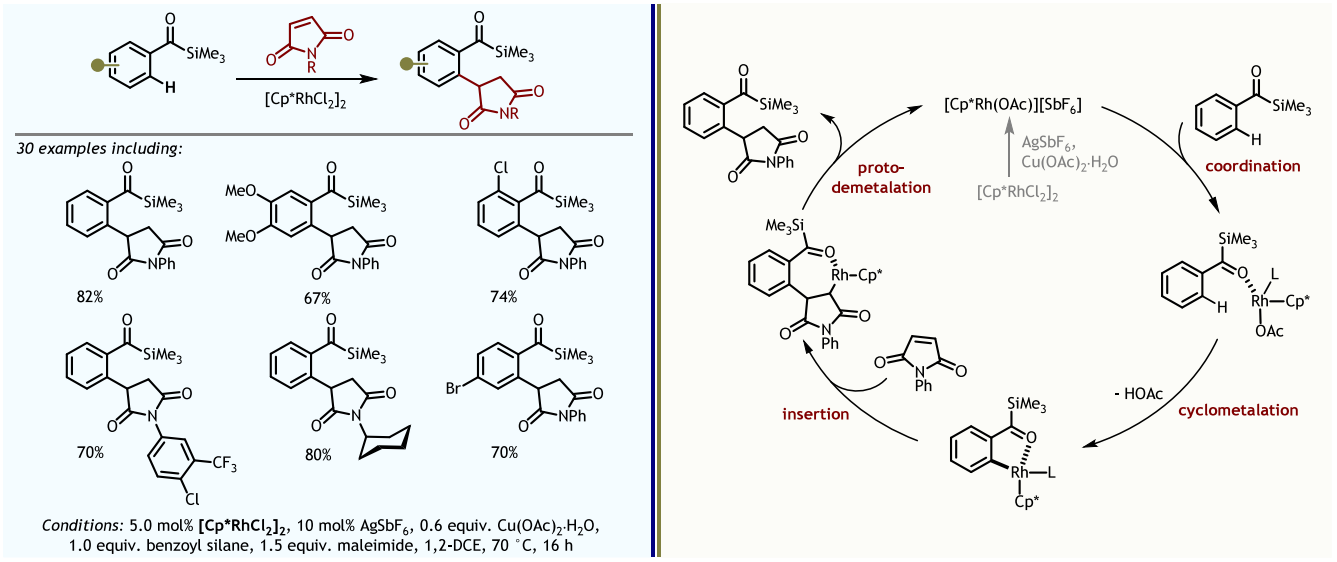
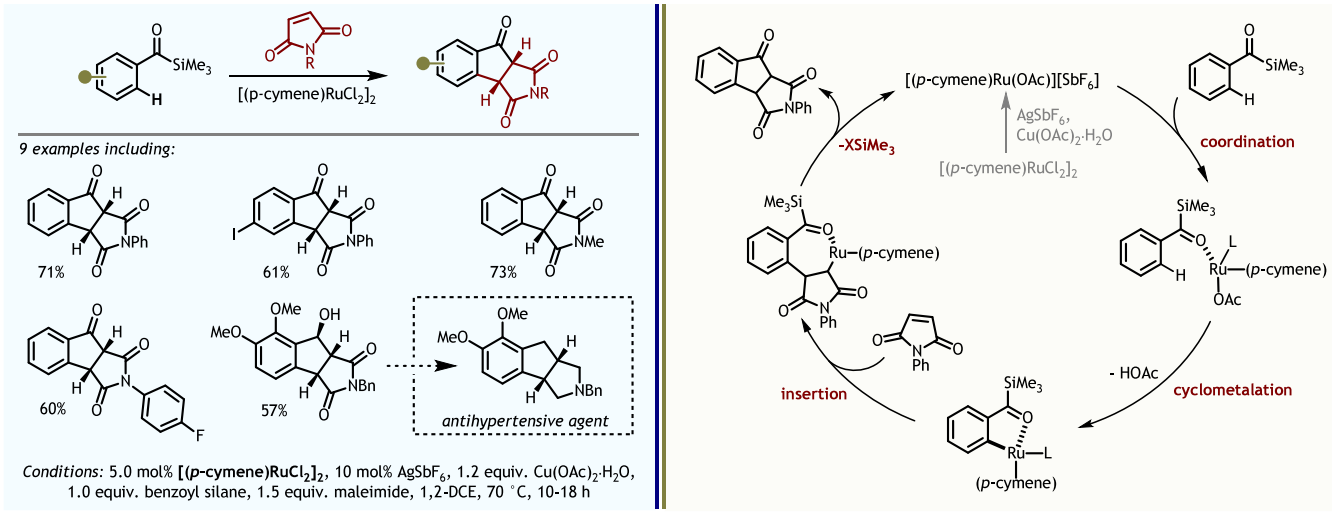
Scheme 13. Acylsilane-Directed Cp*Rh^{III}-Catalyzed Hydroarylation of Maleimides



Scheme 14. (*p*-Cymene)Ru^{II}-Catalyzed Carboannulation Reaction between Benzoylsilanes and Maleimides



analysis, which indicated that increasing the electron deficiency of both Cp^{x}Rh^{III} and Cp^{x}Co^{III} complexes might reduce the transition-state energy barrier for the concerted metalation deprotonation step relative to the parent Cp* complex. Insertion of the metal complex into the C−H bond also appeared to be more thermodynamically favorable for several of the electron-deficient cyclometalated intermediates relative to Cp*. The combined computational and experimental studies ultimately resulted in the discovery that a heptamethylindenyl-ligated Rh^{III} complex [Ind*RhCl$_2$]$_2$ significantly accelerated the acylsilane-directed nitrene-transfer process (Scheme 16).[87] This acceleration is purportedly due to the indenyl effect, which involves ring slippage of the indenyl ligand from an η^5 to η^3 binding mode. This ring slippage affords a new coordination site on the metal center, which enables the catalytic process to proceed via an associative rather than a dissociative mechanism, delivering increased rates and yields for several substrates (Scheme 16). Intriguingly, this acceleration process was observed only in reactions employing weakly coordinating acylsilane and ketone directing groups, whereas for analogous reactions using more strongly coordinating heteroaryl directing groups, including pyridine and pyrimidine, no accelerated catalysis was observed (Scheme 16).[87]

Previous attempts to access *ortho*-olefinated benzoylsilanes using vinyl ketones as the alkenyl coupling partner were either low yielding (using [(*p*-cymene)RuCl$_2$]$_2$ catalysis)[66] or resulted in carboannulation products (using [Cp*RhCl$_2$]$_2$ catalysis, see Scheme 6).[67] In 2024, the Priebbenow group reported acylsilane-directed ruthenium-catalyzed C−H olefination using vinyl ketones where the use of trifluoroethanol as a cosolvent proved critical for obtaining high yields (Scheme 17).[90] Fluorinated alcohols have been recognized as important solvents for C−H activation reactions, with beneficial effects arising from their unique properties as non-nucleophilic strong hydrogen bond donors with low acidity, which proposedly assists in reactant solvation and transition-state stabilization.[91−93] Optimization of the reaction process revealed that 5.0 mol % [(*p*-cymene)RuCl$_2$]$_2$ in combination with 10 mol % AgSbF$_6$ delivered the highest yields. 2.0 equiv of Cu(OAc)$_2$·H$_2$O was used as both the oxidant and acetate source. The reaction was best conducted at 60 °C, and the use of 1,2-DCE/

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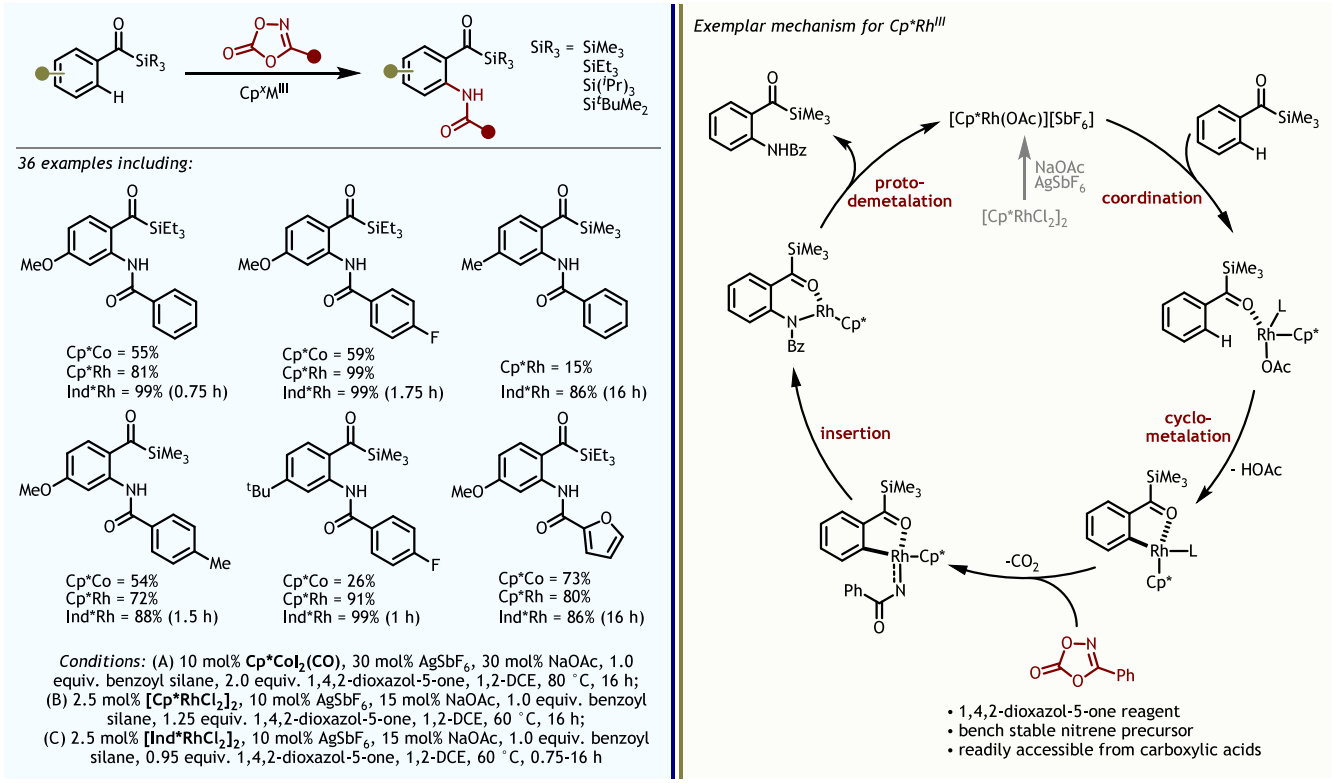
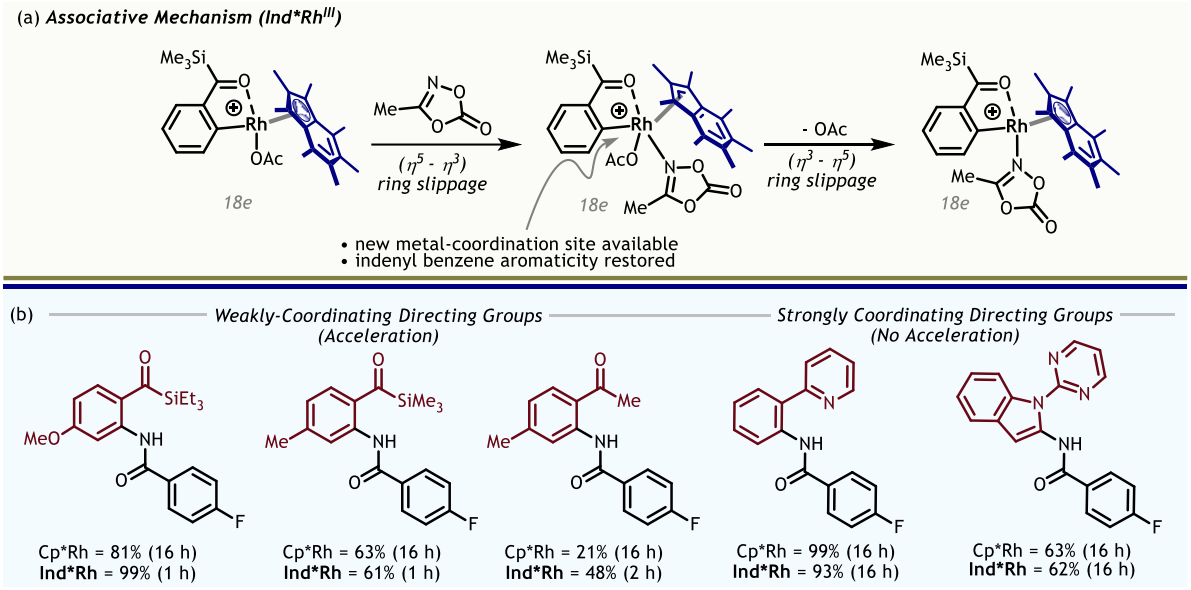
Scheme 15. Co^{III}- or Rh^{III}-Catalyzed Amidation of Benzoylsilanes Employing 1,4,2-Dioxazol-5-ones as Acyl Nitrene Precursors



Scheme 16. Accelerated Nitrene-Transfer Catalysis and Acceleration Observed for Weakly Coordinating Directing Groups[a]



[a](a) Accelerated nitrene-transfer catalysis was achieved in the Ind*Rh^{III}-catalyzed acylsilane-directed C−H amidation due to the indenyl effect which enables the mechanism to proceed via an associative rather than a dissociative mechanism. (b) Interestingly, acceleration was observed only for weakly coordinating directing groups, not strongly coordinating heteroaryl directing groups.

TFE (9:1) as a solvent proved crucial for accelerating the C−H olefination process (increasing yields and reducing reaction times), particularly for electron neutral or deficient benzoylsilanes. With regard to the scope, a wide range of functionalized benzoylsilanes were amenable to this olefination reaction employing methyl vinyl ketone (including thiophenyl and furanoyl acylsilanes) delivering excellent yields. Variation in the olefin component was also tolerated where a collection of vinyl ketones all reacted well to afford a range of 2-alkenyl benzoylsilanes (Scheme 17).[90]

As outlined above, a series of novel C−H functionalization strategies to access more complex scaffolds containing acylsilane functionality have been developed in recent years exploiting acylsilanes as weakly coordinating directing groups.

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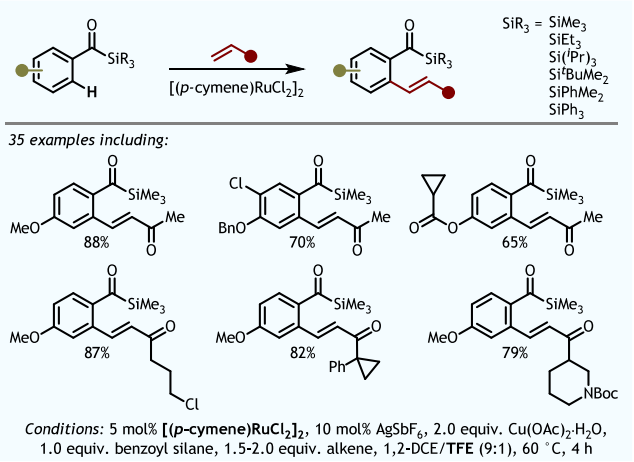
Scheme 17. (p-Cymene)Ru^{II}-Catalyzed Olefination of Benzoylsilanes Using Vinyl Ketones as Coupling Partners



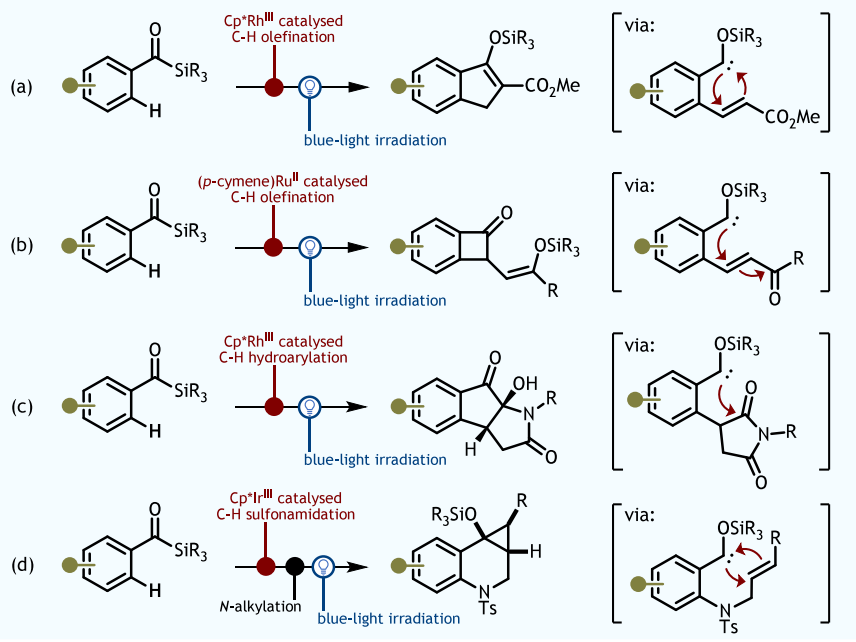
One key advantage of using the acylsilane as a directing group is the diverse range of reactive intermediates that can be accessed post−C-H functionalization, which facilitates rapid access to molecular complexity (see Scheme 1). In recent years, the photolytic conversion of the acylsilane directing group to a siloxycarbene warhead via the 1,2-Brook rearrangement has attracted much attention.[21,24,26] To this end, acylsilanes can be considered "photofunctional directing groups" that can first be harnessed as weakly coordinating directing groups and then readily converted using visible light photochemistry (via direct irradiation or energy-transfer catalysis) to reactive carbene intermediates that participate in secondary transformations. For example, the visible-light irradiation of vinyl ester-tethered benzoylsilanes (accessed via Cp^*Rh^{III}-catalyzed olefination) generates transient siloxycarbene intermediates that drive a rearrangement to afford siloxy indenes (Scheme 18a).[58] Intriguingly, the visible light irradiation of the corresponding vinyl ketone-tethered benzoylsilanes (accessed via (p-cymene)Ru^{II}-catalyzed olefination) affords benzocyclobutenone scaffolds following a photochemical 1,4-conjugate addition process (Scheme 18b).[90]

Visible-light irradiation of the benzoyl silane-derived maleimides (accessed via Cp^*Rh^{III}-catalyzed hydroarylation) generates transient siloxycarbene intermediates that undergo nucleophilic 1,2-carbonyl addition to the proximal amide to afford the corresponding tetrahydroindeno[2,1-b]pyrrole-2,8-diones (Scheme 18c).[86] Finally, a process involving N-alkylation of the *ortho*-sulfonamido benzoylsilanes (accessed via Cp^*Ir^{III}-catalyzed sulfonamidation) to install an olefin tether followed by photochemical irradiation to promote the [2 + 1]-cycloaddition of siloxycarbene intermediates was reported to access a series of unique heterobicyclic frameworks (Scheme 18d).[38]

In summary, acylsilanes possess significant synthetic utility as versatile linchpins that can be engaged as carbene precursors, electrophiles, or acyl radical precursors. Historically, however, access to diversely functionalized acylsilane derivatives has been limited by the harsh nature of the methods needed to install the acylsilane functional group. To address this limitation, a series of catalytic methods for the acylsilane-directed site-selective C−H functionalization of benzoylsilanes have emerged that deliver concise access to previously inaccessible elaborated acylsilane derivatives bearing an *ortho* functionality.

While the discoveries described herein represent useful advances in strategies to access a diversity of novel substrates, to date the use of acylsilane directing groups has been limited to the C−H functionalization of arenes. As such, there now exists the exciting opportunity to expand the utility of acylsilane directing groups to facilitate the site-selective functionalization of proximal alkenyl C(sp^2)−H bonds[94] and alkyl C(sp^3)−H bonds,[95,96] enabling the unique properties and reactivity of acylsilanes to be more widely exploited in the

Scheme 18. Benzoylsilanes Derivatized via Acylsilane-Directed C−H Functionalization Are Amenable to a Range of Subsequent Transformations to Access Carbo- and Heterocyclic Scaffolds under Visible Light Irradiation



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ACS Catal. 2025, 15, 6881−6894

construction of C(sp^3)-rich frameworks. In addition, the potential use of modified acylsilane directing groups to achieve the activation and functionalization of the *meta*- and *para*-positions of benzoylsilanes warrants investigation.[2,97,98] Additional studies into the use of more earth-abundant metals including manganese[50−55] and iron[99−103] complexes to catalyze acylsilane-directed C−H functionalization processes would also be of significant utility.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.5c00794.

Computational details; computational analysis of BF_3 affinity; and Cartesian coordinates of the optimized geometries; (PDF)

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Funding

Australian Research Council (DE200100949 and DP240100102).

Notes

The authors declare no competing financial interest.

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