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Rhodium(III)-catalyzed coupling of *N*-sulfonyl 2-aminobenzaldehydes with oxygenated allylic olefins through C–H activation†

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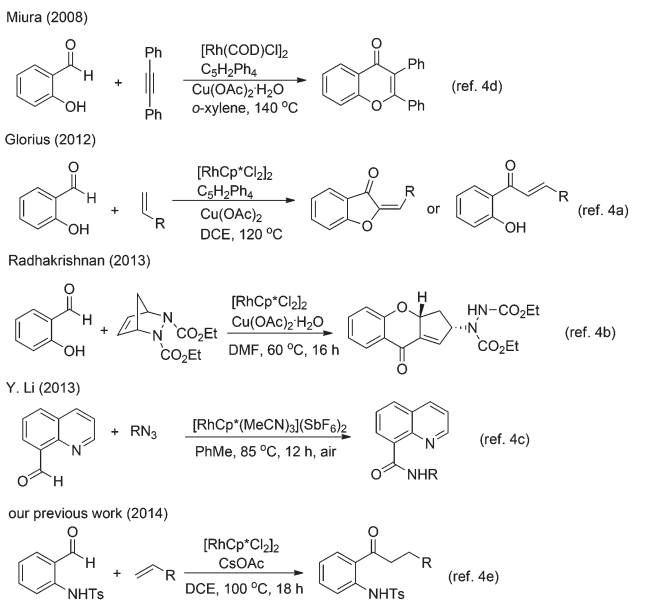
Rh(III)-catalyzed coupling of *N*-sulfonyl 2-aminobenzaldehydes with oxygenated allylic olefins *via* C–H bond activation is described. Diarylketones were obtained through coupling of *N*-sulfonyl 2-aminobenzaldehydes with 7-oxabenzonorbornadienes. On the other hand, the coupling with allyl carbonate yielded a six-membered sulfonyl lactam *via* a sequence of allylation–isomerization–Michael cyclization.

In the past several decades, the selective functionalization of C–H bonds catalyzed by transition metals has garnered considerable attention and represents one of the most efficient strategies to construct complex structures.[1] The advantage of this process stems from its step- and atom-economy and the abundance of C–H bonds in organic molecules. Thus it represents an attractive approach in synthetic chemistry, especially at low catalyst loading and with the low costs associated with the preparation of starting materials. In recent years, rhodium(III) complexes have been extensively explored in C–H activation and subsequent functionalization,[2] and Rh(III)Cp* complexes have stood out as attractive catalysts that render C–H activation with broad substrate scope, high catalytic efficiency and good functional group tolerance, and many elegant systems have been recently reported.[2,3]

Aldehydes are widely used as simple chemical feedstocks. The construction of ketones *via* C–H activation has been recognized as an important strategy to utilize the availability of aldehydes. Two categories of reactions have been developed in this regard. Aldehydes can undergo C–H activation at the formyl group,[4] followed by redox-neutral functionalization with alkenes or alkynes, leading to hydroacylation. Rh(I) catalysts are particularly well-known for serving this purpose, where the C–H activation is proposed to occur *via* an oxidative addition pathway. On the other hand, arenes can also undergo C–H activation followed by oxidative coupling with aldehydes to afford ketones *via* C–C coupling.[5] Despite the significance, reports on formyl C–H activation of aldehydes by Rh(III) catalysts are limited,[4] probably because the C–H oxidative addition pathway is unlikely. Assisted by chelating groups, Satoh and Miura,[4d] Glorius,[4a] Radhakrishnan,[4b] Li[4c] and we[4e] have successfully developed catalytic activation of aldehyde C–H bonds by subsequent functionalization with unsaturated molecules (Scheme 1). Despite the progress, the scope of aldehydes still needs expansion. We reasoned that coupling of aldehydes with olefins bearing built-in oxidizing groups should be a desirable redox-economic process for C–C coupling. We now report a Rh(III)-catalyzed redox-neutral coupling of *N*-sulfonyl 2-amino-



Scheme 1 Rhodium-catalyzed acyl C–H activation.

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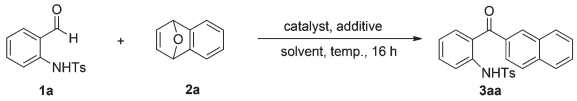
Table 1 Optimization studies[a]



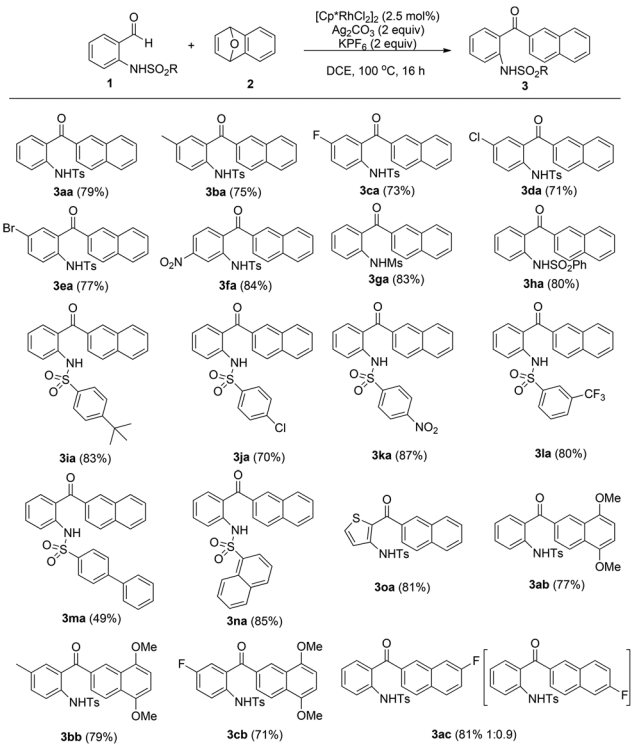
Entry	Catalyst[b] (mol%)	Base (equiv.)	Additive (equiv.)	Solvent	Temp. (°C)	Yield[c] (%)
1	**A** (2.5)	Ag_2CO_3 (2)	KPF_6 (2)	DCE	110	76
2	**A** (2.5)	Ag_2CO_3 (2)	KPF_6 (2)	DCE	100	79
3	**A** (2.5)	Ag_2CO_3 (2)	KPF_6 (2)	DCM	100	69
4	**A** (2.5)	Ag_2CO_3 (2)	KPF_6 (2)	Dioxane	100	61
5	—	Ag_2CO_3 (2)	KPF_6 (2)	DCE	100	nd
6	**B** (5)	Ag_2CO_3 (2)	KPF_6 (2)	DCE	100	nd
7	**C** (5)	Ag_2CO_3 (2)	KPF_6 (2)	DCE	100	nd
8	**A** (2.5)	—	KPF_6 (2)	DCE	100	47
9	**A** (2.5)	K_2CO_3 (2)	—	DCE	100	35
10	**A** (2.5)	Ag_2CO_3 (2)		DCE	100	71

[a] Reactions were carried out by using a catalyst, oxidant, additive, *N*-Ts 2-aminobenzaldehyde (0.2 mmol), and 7-oxabenzonorbornadiene (0.24 mmol) in DCE (2 mL) at 100 or 110 °C for 16 h. [b] Catalyst **A** = $[RhCp^*Cl_2]_2$, **B** = $[RhCp^*(MeCN)_3](SbF_6)_2$, **C** = $[Ru(p\text{-cymene})Cl_2]_2$. [c] Isolated yield after column chromatography.

benzaldehydes with oxygenated allylic olefins such as 7-oxabenzonorbornadienes and allyl carbonates.

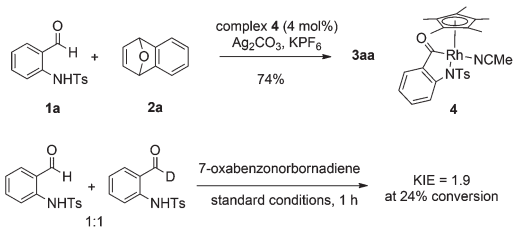
7-Oxabenzonorbornadienes and analogues have been well studied as a strained olefin to introduce a (dihydro)naphthalene ring.[6] However, integration of C–H activation with (ring-opening) coupling of strained olefins such as 7-oxabenzonorbornadienes has experienced limited precedence.[3a,7] With this in mind, we initiated our studies with the screening of reaction conditions for the coupling of *N*-Ts 2-aminobenzaldehyde (**1a**) with 7-oxabenzonorbornadiene (**2a**). We found that a dehydrative coupling reaction occurred when $[RhCp^*Cl_2]_2$ (2.5 mol%) was used as a catalyst and Ag_2CO_3 was used as a base in the presence of KPF_6 in DCE (110 °C, Table 1, entry 1). NMR analyses of the major product isolated pointed to a diaryl ketone **3aa** as a result of 2-naphthylation of the aldehyde C–H bond.[3a] When Ag_2CO_3 was omitted or switched to K_2CO_3, the coupling occurred with lower efficiency (entries 8 and 9), indicating that Ag_2CO_3 is playing a unique role as a base although it is a typical oxidant in coupling reactions. In addition, poor results were obtained when the solvent was switched to DCM or 1,4-dioxane (entries 3 and 4). To our delight, a slightly higher yield was isolated when the temperature was lowered to 100 °C (entry 2). In contrast, lower yield was isolated when the KPF_6 additive was omitted (entry 10) and no reaction occurred when the rhodium catalyst was omitted or when other catalysts were used (entries 5–7).

With these optimized conditions in hand, we set out to explore the scope and limitations of this coupling system. A broad scope of *N*-Ts 2-aminobenzaldehyde has also been defined (Scheme 2). Thus electron-withdrawing, -donating and halogen groups at different positions of the benzene ring are well tolerated, including a nitro substituent which is usually problematic in C–H activation reactions.[8] Variation of the sulfonyl group is also tolerated, and moderate to high yields were isolated when methyl and aryl-substituted sulfonyls were applied (**3ga–3na**). Importantly, when the benzaldehyde ring



Scheme 2 Substrate scope of the dehydrative naphthylation. Reaction conditions: *N*-sulfonyl 2-aminobenzaldehyde (0.2 mmol), 7-oxabenzonorbornadiene (0.24 mmol), $[RhCp^*Cl_2]_2$ (0.005 mmol), Ag_2CO_3 (0.4 mmol), KPF_6 (0.4 mmol) in DCE (2 mL) at 100 °C for 16 h. Isolated yield after column chromatography.

was extended to a 2-thiophenaldehyde, the coupling reaction still occurred to afford **3oa** in 81% yield. What is more, a series of 7-oxabenzonorbornadienes underwent smooth coupling with **1a** and the 2-naphthylation products were isolated in 71–81% yield. In the case of fluorine-substituted 7-oxabenzonorbornadiene, a regioisomeric mixture of naphthylation pro-



Scheme 3 Mechanistic studies.

ducts was obtained in a 1 : 0.9 ratio and in 81% total yield (**3ac**). The sulfonyl group in the product may serve as a useful handle for further chemical manipulations.

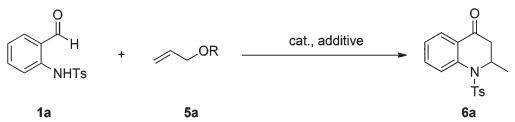
Several experiments have been carried out to explore the reaction mechanism. To demonstrate the relevancy of C–H activation, a rhodacyclic acyl complex **4** was prepared[4e] and was designated as a catalyst (Scheme 3). Indeed, complex **4** (5 mol%) proved active for the coupling of **1a** and **2a** to give **3aa** in 74% yield. Therefore C–H activation is involved. To further probe this C–H activation process, intermolecular kinetic isotope effect (KIE) has been measured in the competitive coupling of an equimolar mixture of **1a** and **1a**-*d* with 7-oxabenzonorbornadiene.[9] ^{1}H NMR analysis of the level of deuteration of the recovered (isotopically mixed) aldehydes gave KIE = 1.9 at 24% conversion (HPLC). This KIE value indicates that cleavage of the C–H bond may be involved in the rate-limiting step.

With the development of these dehydrative naphthylation reactions, we next extended the strained olefins to allyl esters. Recently, allyl esters have been applied to the allylation of arenes by rhodium catalysis *via* a C–H activation pathway.[10] Our initial finding revealed that the reaction of **1a** and allyl acetate under the standard conditions in Scheme 2 failed to give any conversion. Thus further screening has been performed. Using CsOAc as a base additive in the presence of the $[RhCp^*Cl_2]_2$ catalyst, a reaction occurred and, interestingly, a sulfonyl lactam **6a** was isolated in 41% yield (Table 2, entry 1). Product **6a** was proposed to be generated *via* allylation followed by isomerization to a conjugated ketone. Intramolecular aza-Michael addition of the NHT directing group furnished the final product.[11] Extensive screening gave allyl carbonate as a more efficient substrate and an optimal yield of 85% was isolated when $RhCp^*(OAc)_2$ was employed as a catalyst in the presence of CsOPiv (1.5 equiv.).

Under these optimized conditions, the scope of this reaction was next explored (Scheme 4). A series of *N*-sulfonyl-2-aminobenzaldehyde coupled smoothly with ally carbonate, and the cyclic sulfonamides (**6a–6m**) were isolated in good to high yield (57–85%). In line with the coupling of 7-oxabenzonorbornadiene, the scope of the *N*-sulfonyl-2-aminobenzaldehyde is broad in terms of the substitute in the benzene ring and in the sulfonyl group. Extension of the benzaldehyde substrate to a 2-thiophenaldehyde also gave the desired product **6n** in moderate yield (60%). Extension of the sulfonamide directing group to a hydroxyl group as in the coupling of salicylaldehyde **7**, however, only affords a conjugated enone **8** in moderate yield (eqn (1)), and no cyclization was involved, indicative of the differences in steric and electronic effects of the protic directing groups. The reaction is sensitive to the substituent at the allylic and olefinic positions of the allyl carbonate because poor conversion was observed for but-3-en-2-yl methyl carbonate and cinnamyl methyl carbonate. Desulfonylation of the product to give a protic amine has been reported[12] and this structural motif has been widely encountered in natural products and pharmaceuticals.[13]

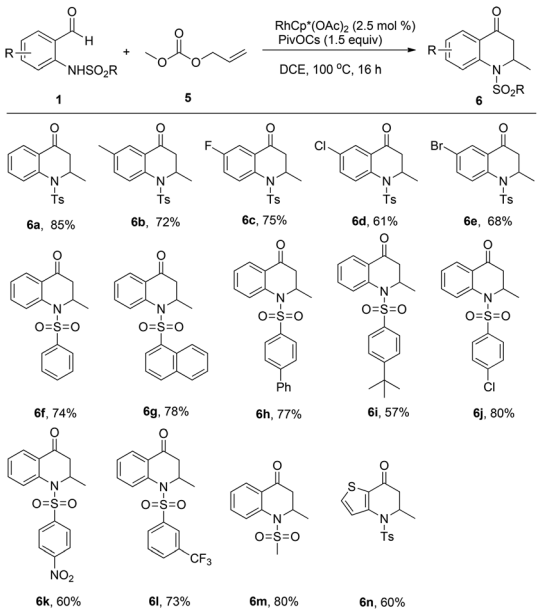
A plausible mechanism to account for the formation of lactam **6** is given in Scheme 5. Sulfonamide coordination and cyclometalation affords a rhodacycle. Subsequent olefin insertion into the Rh–C bond generates a Rh(III) alkyl intermediate,

Table 2 Optimization studies of the coupling with allyl esters[a]

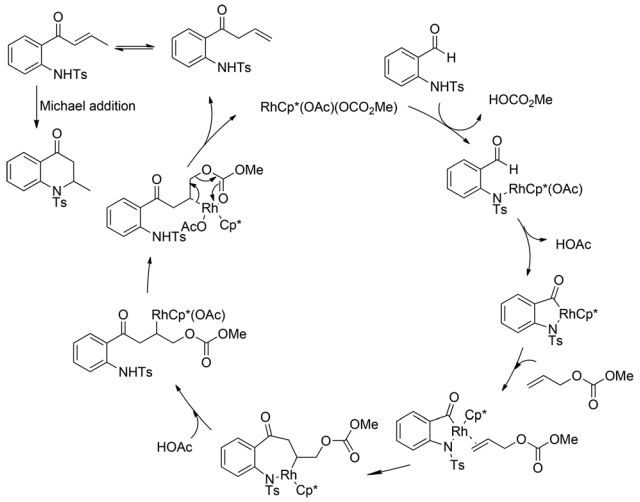


Entry	R	Catalyst[b] (mol%)	Solvent	Additive (equiv.)	Temp. (°C)	Yield[c] (%)
1	Ac	**A** (2.5)	DCE	CsOAc (1.0)	100	41
2	Ac	**A** (2.5)	DCE	PivOCs (1.0)	100	61
3	COOMe	**B** (2.5)	DCE	PivOCs (1.0)	100	75
4	COOMe	**B** (2.5)	DCE	PivOCs (1.0)	80	72
5	COOMe	**B** (2.5)	DCE	PivOCs (1.0)	120	75
6	COOMe	**B** (2.5)	DCE	PivOCs (1.5)	100	85
7	COOMe	**B** (2.5)	DCM	PivOCs (1.5)	100	10
8	COOMe	**B** (2.5)	THF	PivOCs (1.5)	100	71
9	COOMe	**B** (2.5)	Dioxane	PivOCs (1.5)	100	72
10	COOMe	**B** (2.5)	Acetone	PivOCs (1.5)	100	20
11	COOMe	**B** (2.5)	*t*-AmOH	PivOCs (1.5)	100	70

Conditions: [a] Reactions were carried out by using a catalyst, additive, *N*-Ts 2-aminobenzaldehyde (0.2 mmol), and allyl acetate or allyl methyl carbonate (0.6 mmol) in DCE (2 mL) at 100 °C for 16 h. [b] Catalyst **A** = $[RhCp^*Cl_2]_2$, **B** = $RhCp^*(OAc)_2$. [c] Isolated yield after column chromatography.

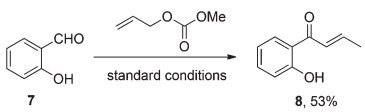


Scheme 4 Substrate scope of *N*-sulfonyl-2-aminobenzaldehydes. Reaction conditions: *N*-Ts 2-aminobenzaldehyde (0.2 mmol), allyl methyl carbonate (0.6 mmol), RhCp*$(OAc)_2$ (0.005 mmol), PivOCs (0.3 mmol) in DCE (2 mL) at 100 °C for 16 h. Isolated yield after column chromatography.



Scheme 5 Plausible mechanism.

which undergoes β-elimination of a methyl carbonate group to give the allylation intermediate. Isomerization of the double bond and intramolecular aza-Michael reaction furnish the final product.



(1)

Conclusions

In conclusion, we have demonstrated a rhodium(III)-catalyzed redox-neutral coupling of *N*-sulfonyl 2-aminobenzaldehydes with oxygenated allylic olefins such as 7-oxabenzonorbornadienes and allyl carbonate. The coupling of 7-oxabenzonorbornadienes resulted in 2-naphthylation of the aldehyde group, while the coupling of allyl carbonate yielded a six-membered sulfonamide *via* an allylation–isomerization–Michael cyclization sequence. These synthetic methods serve to broaden the scope of rhodium(III)-catalyzed C–H activation/functionalization reactions, particularly under redox-neutral conditions, and may find applications in synthetic chemistry. Further experimental and theoretical investigations are underway in our laboratory.

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