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Palladium(II)/Lewis Acid Synergistically Catalyzed Allylic C−H Olefination

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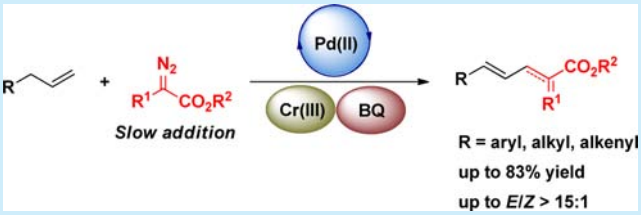
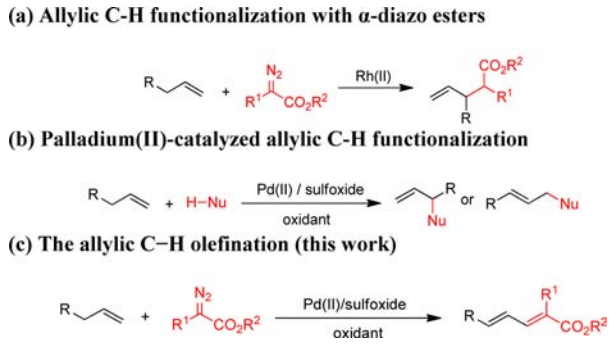
Supporting Information

ABSTRACT: The first allylic C−H olefination with α-diazo esters synergistically catalyzed by a palladium(II) complex and (salen)CrCl has been established to directly generate conjugated polyene derivatives in moderate to high yields and with excellent stereoselectivities.



The allylic C−H functionalization has sparked great interest in the development of new synthetic methods widely applicable to the construction of structurally complex architectures.[1] Metal−carbenoids have been an active species for the functionalization of allylic C−H bonds.[2] In particular, the C−H insertion reaction of rhodium carbenoid intermediates[2a] generated from α-diazo esters has rendered homoallylic esters to be regiospecifically yielded (Scheme 1a). Recently,

Scheme 1. General Strategies for the Allylic C−H Functionalization



[a]Allylic C−H functionalization with α-diazo esters. [b]Palladium(II)-catalyzed allylic C−H functionalization. [c]The allylic C−H olefination (this work).

White and co-workers established that Pd(II) complexes of sulfoxides could efficiently accelerate allylic C−H oxidation of terminal alkenes[3] and, more significantly, had been general catalyst systems for allylic C−H functionalizations, including allylic esterification, amination, dehydrogenation, fluorination, and alkylation as well[4] (Scheme 1b). However, a direct allylic C−H olefination,[5] basically giving rise to polyenes, which have been found in numerous natural products (Figure 1) and therefore hold great potential in organic synthesis,[6] has not been described. Herein, we report a palladium-catalyzed allylic

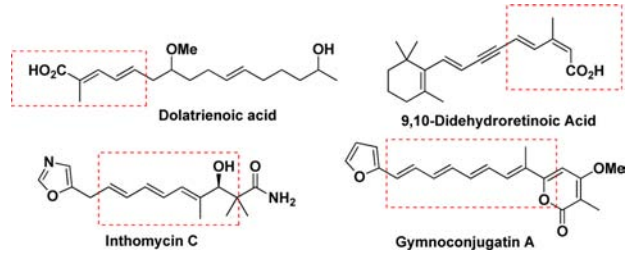


Figure 1. Selected natural products containing a dienyl carboxylate or carbinol moiety.

C−H olefination with α-diazo esters to directly produce conjugated polyenes in excellent stereoselectivity (Scheme 1c).

Previously, Wang and co-workers established a palladium(0)-catalyzed olefination of allylic halides with α-diazo esters,[7] wherein π-allylic palladium complexes generated from oxidative addition of Pd(0) onto allylic halides turned out to be key intermediates participating in the carbon−carbon double bond formation. Thus, we envisaged that a π-allylic palladium intermediate **A** generated from the cleavage of allylic C−H bond with Pd(II), would also be able to undergo a carbene insertion reaction with diazo compounds to form a π-allylpalladium carbenoid species **B**, which would undergo a migratory insertion to afford intermediate **C** (Scheme 2).[7] After a subsequent β-H elimination occurs in the intermediate **C**, the conjugated diene would be generated and the corresponding palladium(0) would be released. Afterward, the oxidation of Pd(0) with BQ in the presence of HOAc regenerated the Pd(II) catalyst (Scheme 2). As such, an allylic C−H activation based olefination would be accessed. On the other hand, an alternative pathway involving allylic substitution and subsequent elimination (E1-type) of intermediate **D** to afford the diene product is also possible.

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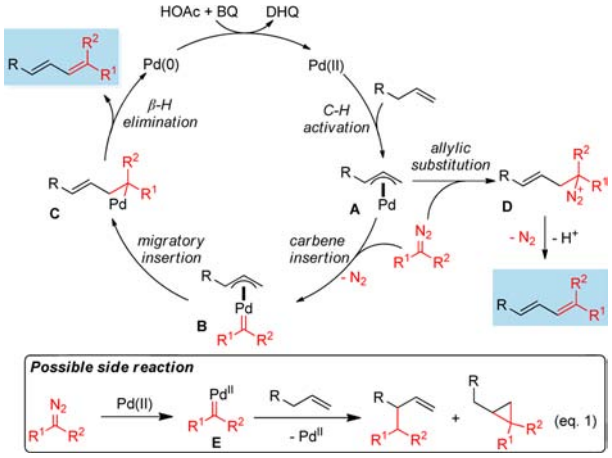
Scheme 2. Pd(II)-Catalyzed Allylic C−H Olefination with Diazo Compounds

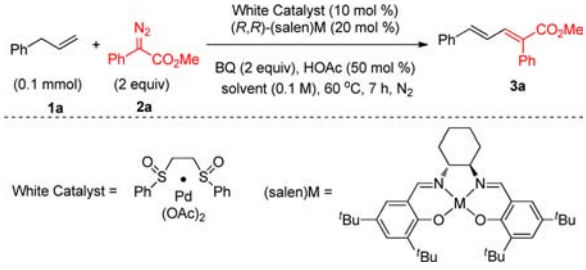


However, the proposed reaction was much more challenging than anticipated because the Pd−carbenoid species **E** generated rapidly from Pd(II) with the diazo compound, would undergo allylic C−H insertion[8] or cyclopropanation[9] based on the metal−carbenoid (Scheme 2, eq 1), either of which would compete with the formation of π-allylic palladium intermediate A via the allylic C−H activation by palladium(II). Indeed, the initial experiment on the reaction of allylbenzene (**1a**) with methyl phenyldiazoacetate (**2a**) in the presence of White catalyst mostly gave C−H insertion based allylic alkylation and cyclopropanation products, together with some other unidentified molecules, whereas the desired olefination product was isolated in a trace amount.[10]

The proposed reaction pathway (Scheme 2) indicates that if the palladium(II) catalyzed allylic C−H activation is complete to generate π-allylic palladium intermediate **A** prior to the formation of palladium carbenoid **E** the desired catalytic cycle might be realized. Thus, the allylic C−H olefination of allylbenzene (**1a**) was examined using the White catalyst and BQ/HOAc as an oxidant by slow addition of methyl phenyldiazoacetate (**2a**) with syringe pump with a purpose to diminish the side reaction promoted by palladium(0) (Table 1). Disappointingly, only trace amount of diene **3a** was detected (entry 1). We believed that the desired reaction failed to occur probably because the π-allylic palladium carbene intermediate **B** (Scheme 2) was unable to be efficiently generated. Inspired by findings from White and co-workers that the addition of Lewis acids as co-catalysts could facilitate the functionalization of allylic C−H bonds,[4a,11] we evaluated a variety of metal−salen complexes (entries 2−4). To our delight, the addition of 20 mol % of (salen)CrCl gave the desired diene product **3a** in a much enhanced 36% yield (entry 4). An evaluation of solvents suggested that ether-based solvents were beneficial to the conversion of allylbenzene and led to a considerable improvement in the yield (entries 5−7). The diene **3a** was isolated in a 54% yield in the presence of 15 mol % the White catalyst (entry 8). Importantly, the protocol was scalable with maintained results (entry 9).

Under the optimized conditions, structurally different olefin substrates were examined to demonstrate the generality (Scheme 3). A wide scope of either commercially available or easily accessible terminal olefins was able to be tolerated and smoothly underwent the allylic C−H olefination reaction to generate conjugated olefins in moderate to high yields.

Table 1. Evaluation of Lewis Acids and Optimization of Reaction Conditions[a]



entry	solvent	M	conv[a] (%)	yield[b] (%)	E/Z[c]
1	toluene		47	1	
2	toluene	MnCl	65	22	>15:1
3	toluene	FeCl	53	28	>15:1
4	toluene	CrCl	65	36	>15:1
5	THF	CrCl	97	41	>15:1
6	DCE	CrCl	87	47	>15:1
7	dioxane	CrCl	92	50	>15:1
8[d]	dioxane	CrCl	99	68 (54[e])	>15:1
9[d,f]	dioxane	CrCl	91	77 (56[e])	>15:1

[a]Determined by GC using benzophenone as an internal standard for reactions carried out on a 0.1 mmol scale. **2a** was dissolved in 0.5 mL of solvent and added by syringe pump over 5 h, and then the reaction was conducted for an additional 2 h. [b]Combined GC yields of E and Z isomers. [c]Based on GC analysis of the crude reaction mixture, and small response variations were uncorrected. [d]15 mol % of Pd of catalyst was used. [e]Isolated yield. [f]The reaction was carried out on a 0.3 mmol scale.

Although the reaction was seemingly sensitive to the electron feature of the aryl moiety of the olefin substrates, the presence of either an electronically donating (**3b−d**) or withdrawing (**3e−f**) substituent was allowed to give the desired products in high yields (up to 83%). Notably, even simple alkyl olefins also participated in the reaction to afford aliphatic conjugated dienes in acceptable yield (**3k−l**). However, an alkyl bromide-containing olefin was not well tolerated under the optimized conditions but resulted in a debromination product (**3m**). More significantly, for 1,4-diene-based allylic substrates, the C−H olefination chemoselectively occurred to give triene derivatives in good yields (**3n−p**). Moreover, the variation in the steric and electronic elements of aryldiazoacetates **2** was also well tolerated (**3q−s**). Interestingly, the subjection of ethyl 2-diazopropanoate to the identical conditions resulted in the formation of a 1,4-diene **3t**, a Hofmann-elimination like product, rather than a 1,3-diene, suggesting that the E1-type reaction is much less possible than β−H elimination (Scheme 2).

To understand the mechanism for this direct allylic C−H olefination, we investigated the π-allylic palladium intermediate forming step in the proposed catalytic cycle. The π-allyl palladium dimer **4** was prepared in a good yield from allylic C−H bond cleavage reaction between the palladium acetate and the allylbenzene **1a**.[4h] Then, we explored the effect of either ligand or Lewis acid on the olefination reaction of π-allyl Pd intermediate **4** with methyl phenyldiazoacetate **2a** (Table 2). As indicated previously, the allylic substitution of π-allyl palladium acetate dimer with nucleophiles could be accelerated by sulfoxide ligand and BQ.[4f,h,12] However, neither the sulfoxide ligand nor BQ was able to exert apparent impact on the performance of olefination reaction, which implied that this

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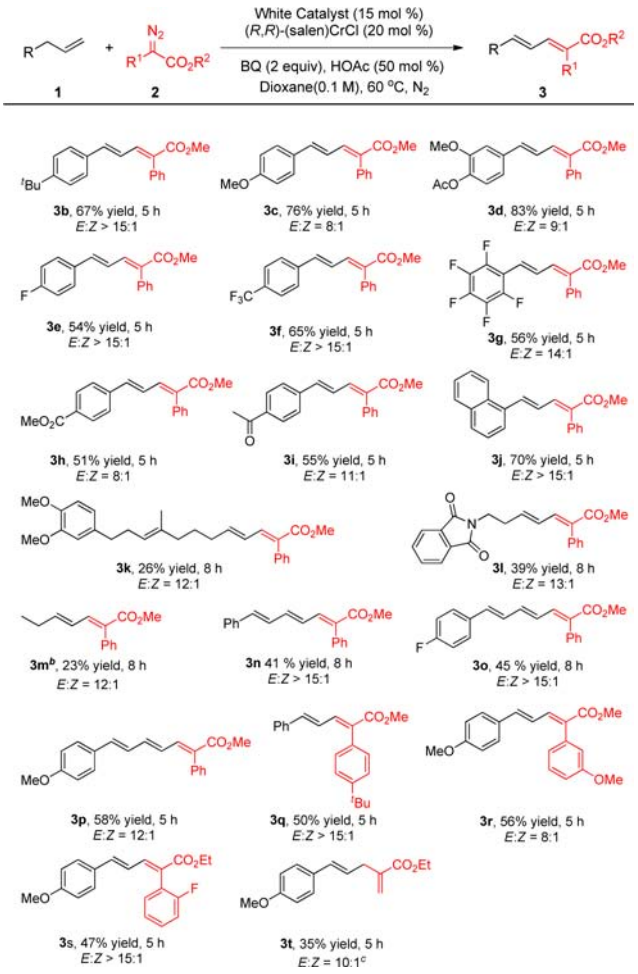
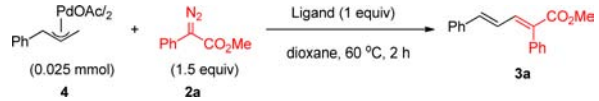
Scheme 3. Substrate Scope[a]



[a]The reactions was carried out on a 0.3 mmol scale. **2** was dissolved in 1 mL of solvent and added by a syringe pump over 5 or 8 h, and then the reaction was conducted for additional 2 h. The isolated yields were obtained after flash chromatography. In some cases, the products were mixed with byproducts and isolable after the reduction of $NaBH_4$. [b]The starting terminal olefin was 5-bromopent-1-ene. [c]The *E*/*Z* ratio points to the double bond adjacent to the aryl group

Table 2. Effects of Ligand and Lewis Acid on the Olefination of a π-Allyl Palladium Dimer

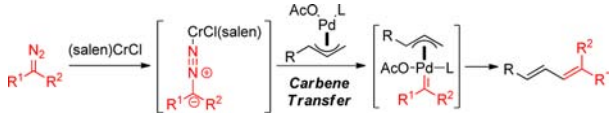


entry	ligand	yield[a] (%)	*E*/*Z*[b]
1		9	
2	1,2-bis(phenylsulfinyl)ethane	11	
3	BQ	7	
4	BQ + (*R*,*R*)-(Salen)CrCl	46	1.6:1
5	(*R*,*R*)-(Salen)CrCl	93	1.3:1
6	1,2-bis(phenylsulfinyl)ethane + (*R*,*R*)-(Salen)CrCl	85	2.7:1

[a]Determined by GC using 1,3,5-tri-*tert*-butylbenzene as an internal standard for reactions. [b]Based on GC analysis of the crude reaction mixture, and small response variations were uncorrected.

transformation was unlikely to go through an allylic substitution and followed by β–H elimination process because no ligand-accelerated effect was observed (entries 1–3). This conclusion was also indicated by the fact that a 4-diene **3t** rather than 1,3-diene product was formed as shown in Scheme 3. A much-enhanced yield was obtained when the olefination was conducted in the presence of BQ and (salen)CrCl, but with a poor stereoselectivity (entry 4). Interestingly, the use of (salen)CrCl alone as the cocatalyst rendered the reaction to give an excellent conversion, but still with a poor stereoselectivity (entry 5). In addition, the addition of disulfoxide ligand led to an enhanced stereoselectivity (entry 6). On the basis of these preliminary results, we identified that disulfoxide ligand not only served as a promoter to the allylic C–H cleavage, but also contributed to the control of stereoselectivity. The (salen)CrCl might act as a Lewis acid to enhance the nucleophility of the α-diazo esters by coordinating to the nitrogen and thereby would facilitate the formation of π-allylic palladium carbenoid (Scheme 4),[13] rather than the activation of the π-allylPd species by coordination to BQ.[12]

Scheme 4. Proposed Pathway for the Chromium(III) Lewis Acid Accelerated Carbenoid Transfer



In conclusion, we have developed the first C–H activation based olefination reaction between allyl hydrocarbons and α-diazo esters. The use of the palladium(II) complex and (salen)CrCl as a binary catalyst system efficiently promoted the olefination reaction for a wide scope of allyl compounds and α-diazo esters to directly generate conjugated polyene derivatives in moderate to high yields and with excellent stereoselectivities. An obvious synergistic effect between palladium(II) and [(salen)CrCl] was observed in the catalysis, probably because the [(salen)CrCl] acted as a Lewis acid to facilitate the formation of π-allylic palladium carbenoid. This finding might be amenable to improve the efficiency of other reactions involving metal carbene intermediates.

■ ASSOCIATED CONTENT

Supporting Information

Complete experimental procedures and characterization data for the prepared compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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