Dehydrative Allylation of 2-Alkylbenzophenones with Allylic Alcohols

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Herein reported is a dehydrative allylation reaction of 2alkylbenzophenones with allylic alcohols promoted by light and palladium. Photoirradiation of 2-alkylbenzophenones generates nucleophilic species which couple with allylic alcohols. Mechanistically, in-situ generated carboxylic acid is likely to activate allylic alcohols to facilitate the palladium-catalyzed allylation reaction.

Keywords: Dehydrative reaction | Photoreaction | Palladium

2-Alkylbenzophenones isomerize to o-quinodimethanes¹ upon photoirradiation.² The o-quinodimethanes are nucleophilic enough to react with various carbon electrophiles such as acrylates,³ aldehydes,⁴ and ketones⁵ (Figure 1a). We recently disclosed that even carbon dioxide was fixed on 2-alkylbenzophenones through a C–C bond formation.⁶

The *o*-quinodimethanes are also subject to transformations promoted by organo-⁷ and transition metal catalysts. For example, we have reported a palladium-catalyzed acylation reaction of 2-alkylbenzophenones with carboxylic anhydrides.⁸ We herein report a palladium-catalyzed allylation reaction of 2-alkylbenzophenones with allylic alcohols (Figure 1b). A carbon–carbon bond is formed on the benzylic carbon with elimination of water.

Allylic alcohol 1 was reacted with 2-methylbenzophenone (2, 3.0 equiv) under photoirradiation in the presence of a catalytic amount of palladium(II) benzoate $[Pd(OBz)_2]$ and 2-di-*tert*-butylphosphino-2',4',6'-triisopropylbiphenyl (*t*-BuXPhos) at room temperature. After 45 minutes, the reaction mixture was subjected to chromatographic purification to afford the allylated benzophenone 3 in 71% yield based on 1 together with the diallylated benzophenone 4 (Scheme 1). When the reaction was examined using 1.0 equiv of 2 to 1, the yield of the monoallylated product 3 decreased to 21%. Control experiments confirmed that both light and palladium were indispensable for the formation of the allylated products 3 and 4.⁹

We assumed that the mechanism involved a palladium(0)species, which was potentially generated in situ by the reaction of Pd(OBz)₂ with the phosphine ligand.¹⁰ Next examined were other precursors for palladium(0) (Table 1). When cyclopentadienyl π -allyl palladium [PdCp(π -allyl)], a typical precursor of palladium(0), was used in combination with t-BuXPhos, no allylated product 3 was obtained (Entry 1). Remarkably, the product 3 was found in 52% yield when the reaction was carried out in the presence of benzoic acid in addition to $PdCp(\pi-allyl)$ and t-BuXPhos (Entry 2). These contrasting results were suggestive that benzoic acid would activate the allylic alcohol to accelerate its oxidative addition onto a palladium center.¹¹ Whereas Pd(OAc)₂ afforded 3 in 68% yield, PdCl₂ failed to give 3 probably because a palladium(0) species was hardly generated from PdCl₂ and t-BuXPhos (Entry 3).¹⁰ Pd(TFA)₂ and Pd(OTs)₂(MeCN)₂ were inactive as well.

a) Reactions of photo-generated o-quinodimethane







Scheme 1. Dehydrative coupling reaction of allylic alcohol 1 with ketone 2.

Table 1. Effect of precursors for palladium(0).

1 +	2 2 UV light (365 nm) Pd precursor (5 mol %) <i>t</i> -BuXPhos (10 mol %) toluene, rt. 45 min	Ph OMe
	3.0 equiv	3
entry	Pd precursor	vield of 3
entry 1	Pd precursor PdCp(π-allyl)	yield of 3 not detected
entry 1 2	Pd precursorPdCp(π-allyl)PdCp(π-allyl) + BzOH (10 mol %)	yield of 3 not detected 52%

Scheme 2 shows a plausible reaction pathway for the formation of **3** from allylic alcohol **1** and 2-methylbenzophenone (**2**). Initially, palladium(II) benzoate reacts with the phosphine ligand to form palladium(0) species, phosphine oxide, and benzoic anhydride.¹⁰ Benzoic anhydride is hydrated by allylic alcohol **1** to generate benzoic acid. The acid catalyst thus generated accelerates oxidative addition of allylic alcohol **1** onto palladium(0) to furnish π -allyl(benzoato)palladium(II) (**A**) along with elimination of water. Finally, *o*-quinodimethane **B**¹² generated from **2** couples with the allyl ligand of **A** to give the



Scheme 2. Proposed reaction pathway.



Table 2. Scope with respect to 2-alkylbenzophenones.^{a,b}

(a) reaction contitions: 1 (0.20 mmol), ketone (0.00 mmol), Pd(OBZ)₂ (0.01 mmol t-BuXPhos (0.02 mmol), toluene (2 mL), UV light (365 nm), room temperature, 45 min.
 (b) Isolated yield.

(c) The product contains inseparable *t*-BuXPhos. (14%)

coupling product **3**. Palladium(0) species and benzoic acid are regenerated and enter into a next catalytic cycle.

Various 2-alkylbenzophenone derivatives were examined for the dehydrative coupling reaction (Table 2). Dimethyl substituted benzophenones such as **5** and **6** underwent the allylation reaction selectively at the benzylic C–H bond ortho to the carbonyl group, and the mono-allylated products were produced in 75% and 62% yields, respectively. 2-Methylphenyl ketones possessing electron-rich (7) and electron-deficient (**8**) benzene rings were suitable substrates for the present allylation reaction. Functional





groups such as fluoro (9), cyano (10), and methoxycarbonyl (11) groups were all tolerated on the aromatic rings. The secondary C–H bond of 2-ethylbenzophenone (12) was also allylated, and the corresponding product was obtained in 55% yield. In all cases, di-allylated products were also formed and the ratios of mono-/di-allylated products ranged from 86:14 to 72:28.

The substrate scope with respect to allylic alcohols was investigated (Table 3). Allyl alcohol (13) and β -methallyl alcohol (14) successfully participated in the reaction to afford the corresponding products in 55% and 65% yield, respectively. For the reactions of β -aryl-substituted allylic alcohols, 2-(dicyclohex-ylphosphino)-3,6-dimethoxy-2',4',6'-triisopropyl-1,1'-biphenyl (BrettPhos) was a superior ligand in terms of the product yield.¹³ 2-Phenyl-2-propenol (15) underwent the coupling reaction with 2 to furnish the allylated product in 61% yield by using BrettPhos. Substituents on the aromatic ring such as methoxy (16) and fluoro (17) were tolerated under the reaction conditions.

Next, α - and γ -substituted allylic alcohols were examined (Scheme 3). When the reaction was carried out with 1-buten-3ol (18), a mixture of allylated products 19 and 20 (56:44) was obtained. Essentially the same 19/20 ratio (55/45) was observed when 2-buten-1-ol (21) was used, being consistent with the proposed mechanism which involves a π -allyl palladium intermediate.

There are a number of palladium-catalyzed allylation reactions available for forming $C(sp^3)$ – $C(sp^3)$ bonds.¹⁴ Allylic esters are used as the allylating agent in most cases. The present method presents a unique example of dehydrative allylation reaction¹⁵ where the photo-generated *o*-quinodimethanes couple with allylic alcohols by the aid of benzoic acid. Such a dehydrative allylation reaction with allylic alcohols is beneficial for green chemistry because allylating agents are readily available and the byproduct is water.

In conclusion, we have disclosed that cooperation of light and palladium enables a dehydrative allylation reaction of 2alkylbenzophenones with allylic alcohols. An acid-promoted activation step of allylic alcohols is involved in the mechanistic pathway.



Scheme 3. Reactions with 1-buten-3-ol (18) and 2-buten-1-ol (21).

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