

Pd-catalysed direct dehydrogenative carboxylation of alkenes: facile synthesis of vinyl esters†

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A novel Pd-catalysed oxidative coupling reaction methodology using readily available carboxylic acids and alkenes for the preparation of vinyl esters has been developed. A broad range of vinyl esters were successfully synthesised. The reactions have demonstrated good efficiency as well as excellent chemo- and regio-selectivity.

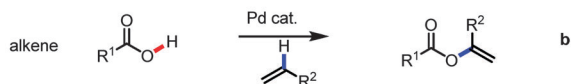
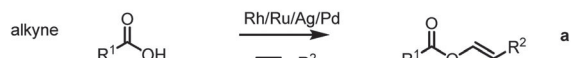
Vinyl esters present a class of useful organic building blocks which have been utilized in polymer chemistry, chemical industry and pharmaceutical sciences.¹ Various traditional processes for the synthesis of these motifs have been established. Only recently, with the development of modern organometallic chemistry, transition metal-catalysed reactions of carboxylic acids addition onto alkynes for the synthesis of unsaturated esters have entered the chemical world. In hydrocarboxylation under Rh,² Ru,³ Ag⁴ and Pd⁵-catalysed conditions, carboxylic acids can be introduced onto alkynes to form vinyl esters in an anti-Markovnikov's fashion (Scheme 1a). In addition, the Stambuli group observed the oxidative coupling of alkenes with carboxylic acids in a Markovnikov's manner (Scheme 1b).⁶ However, only a few transition metal-catalysed

direct intra- and intermolecular dehydrogenative coupling reactions of carboxylic acids and alkenes have been reported.⁷

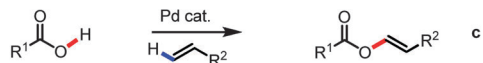
Herein, we report our latest discovery of Pd-catalysed oxidative coupling of carboxylic acids and alkenes for the synthesis of vinyl esters (Scheme 1c).

Our reaction condition optimization began with the reaction of benzoic acid with butyl acrylate in the presence of 10 mol% of Pd catalyst. MeCN showed to be the best solvent when compared with other solvents such as DMA, dioxane, butanol, toluene and H₂O during the solvent screening. The addition of halogen salts^{8,9} did not change the reactivity and the reaction conversions are rather low (Table 1, entries 2–4). When Cu salts were used as additives, our desired product was only obtained in poor yield. We pleasingly found that under an O₂ atmosphere¹⁰ when Ag₂CO₃ was employed the reaction speed increased rapidly and under these conditions, the reaction gave our desired vinyl ester **3a** in an excellent 91% yield. The reaction in the absence of O₂ was sluggish, only resulting in 50% of conversion after 24 hours. While the combination of O₂ and K₂CO₃ instead of Ag₂CO₃ gave rise to total

Previous work:



This work:



Scheme 1 The synthesis of vinyl esters.

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Table 1 Reaction conditions screening

Entry	Catalyst	Additive	Yield (%)	Ratio (E : Z)
1	Pd(OAc) ₂	—	12	92 : 8
2	Pd(OAc) ₂	NaCl	11	93 : 7
3	Pd(OAc) ₂	NaBr	5	93 : 7
4	Pd(OAc) ₂	NaI·2H ₂ O	0	—
5	Pd(OAc) ₂	Cu(OAc) ₂	6	92 : 8
6	Pd(OAc) ₂	CuBr ₂	0	—
7	Pd(OAc) ₂	Ag ₂ CO ₃	91	92 : 8
8	PdCl ₂	Ag ₂ CO ₃	75	92 : 8
9	Pd(MeCN) ₂ Cl ₂	Ag ₂ CO ₃	73	92 : 8
10	Pd(PPh ₃) ₂ Cl ₂	Ag ₂ CO ₃	56	92 : 8
11	Pd ₂ dba ₃	Ag ₂ CO ₃	34	85 : 15

Reaction conditions: benzoic acid **1a** (37 mg, 0.3 mmol), butyl acrylate **2a** (192 mg, 1.5 mmol), Pd catalyst (10 mol%), additive (2.0 equiv.) at reflux in MeCN (1.5 mL, 0.2 M), 7–36 h.

Table 2 Unsaturated ester synthesis

$ \begin{array}{c} \text{R}^1\text{CO}_2\text{H} \\ \text{1} \end{array} \xrightarrow[\text{Pd(OAc)}_2, \text{Ag}_2\text{CO}_3, \text{O}_2, \text{MeCN, reflux.}]{\text{CH}_2=\text{CH-R}^2 \text{ (2)}} \begin{array}{c} \text{R}^1\text{CO}_2\text{CH=CH-R}^2 \\ \text{3} \end{array} $							
Entry	Carboxylic acid 1	Unsaturated ester 3	Yield (E : Z)	Entry	Carboxylic acid 1	Unsaturated ester 3	Yield (E : Z)
1			91% (92 : 8)	9			65% (>98 : 2)
2			93% ^a (93 : 7)	10			83% (93 : 7)
3			92% ^a (91 : 9)	11			68% ^a (94 : 6)
4			78% (92 : 8)	12			42% (>98 : 2)
5			53% (94 : 6)	13			47% ^a (93 : 7)
6			88% (91 : 9)	14			64% (96 : 4)
7			80% (92 : 8)	15			41% (>98 : 2)
8			52% ^a (93 : 7)	16			42% (94 : 6)

Standard reaction conditions: benzoic acid **1** (0.3 mmol), butyl acrylate **2a** (192 mg, 1.5 mmol), Pd(OAc)₂ (10 mol%), Ag₂CO₃ (2.0 equiv.) at reflux under 1 atm O₂, in MeCN (1.5 mL, 0.2 M), 7–36 h. ^a When 10 mol% was used, reactions did not go to completion, 20 mol% of Pd(OAc)₂ was used instead.

decarboxylation of benzoic acid. These results suggest that the Ag salt acted as both base and co-oxidant where O₂ is the terminal oxidant in the reaction. Other Pd sources, PdCl₂, Pd(PPh₃)₂Cl₂ and Pd(MeCN)₂Cl₂, for instance, facilitated vinyl ester **3a** in moderate to good yields (entries 8–10). Interestingly, however, a Pd(0) source, Pd₂dba₃, also provided our desired product in 34% yield albeit with slightly lower (85 : 15) selectivity. In most of the cases, there is only a trace amount of branched alkene detected in the ¹H NMR spectra of the crude reaction mixture.

With the optimal conditions in hand, a wide range of carboxylic acids as well as terminal alkenes were evaluated. When benzoic acid reacted with butyl acrylate, our desired vinyl ester **3a** was isolated in an excellent 91% yield with a good 92 : 8 E/Z ratio. Good reactivity and regioselectivity were also observed for electron deficient substituted benzoic acids although 20 mol% Pd(OAc)₂ was used in terms of pushing the reaction into high conversion. When electron rich benzoic acids **1d** and **1e** were subjected to the reaction, the corresponding vinyl esters **3d** and **3e** were isolated in good 78% and 53% yields respectively. *meta*-Substituted benzoic acids were also tolerated well in this type of transformation (Table 2, entries 5–8).

Sterically hindered *ortho*-substituted benzoic acids are also demonstrated to be efficient substrates for the synthesis of corresponding vinyl esters **3j** and **3k**. In addition, the attempts on heteroaromatic and alkenyl carboxylic acids were all successful which gave rise to the desired corresponding vinyl esters in good yields with excellent selectivity (entries 11–14). Moreover, aliphatic carboxylic acids were also tolerated in this reaction and secondary as well as tertiary substituted carboxylic acids were both working well to give the corresponding vinyl esters **3o** and **3p** in useful 41% and 42% yields respectively.

On the other hand, a group of alkenes were also investigated. We were pleased to find that when benzoic acid reacts with acrylamide **2b**, our desired amide **3q** was isolated exclusively as the *E* alkene in a good 76% yield (Table 3, entry 2). The reaction with unsaturated ketones also worked and the vinyl ester **3r** was isolated in 33% yield with greater than 98 : 2 E/Z selectivity. The low yield was due to the rapid polymerization of reactive alkene **2c** under these reaction conditions. Unactivated alkene **2d** reacts fluently to provide vinyl esters in a good 58% yield with 36% of a mixture of C–H activation products **4** and **5**^{11,12}

Table 3 Reactions with various alkenes

Entry	2	3	Yield (E/Z)
1			91% (92 : 8)
2			76% (>98 : 2)
3			33% (>98 : 2)
4			58% (67 : 33)
5			65% (>98 : 2)
6			72% (>95 : 5)

with only 4% of *Z*-stilbene.¹³ Alkene **2e** with an adjacent sp³ hybridized carbon gave the corresponding allyl ester **3t** in a good 65% yield (>98 : 2 *E/Z*) with the double bond migration. This is consistently in agreement with White's discovery of the allylic ester synthesis.^{6,14} Compared to Stambuli's results with AcOH (60% yield with >95% *E/Z* selectivity), reaction of benzoic acid with 4-phenyl-1-butene **2f** under our conditions gave ester **3u** in 72% yield with similar (>95 : 5 *E/Z*) selectivity (Table 3, entry 6).

A catalytic reaction pathway was then proposed. Similar to Wacker oxidation,^{15,16} is the deprotonation of benzoic acid by Ag₂CO₃ to facilitate the Ag salt **A** which can be added onto the terminal side of the alkene without decarboxylation in the

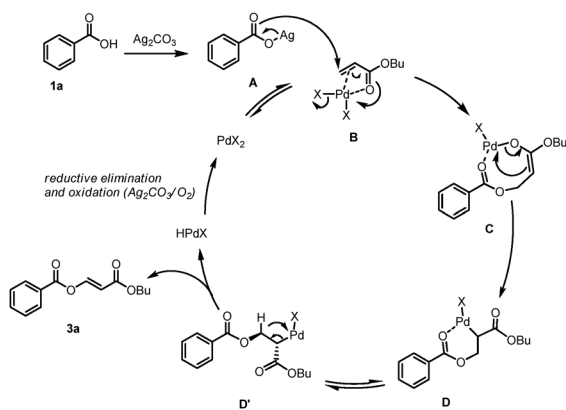
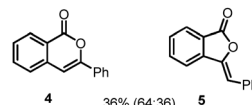
presence of a Pd(II) catalyst as a Lewis acid. The resulting 8-membered palladacycle **C** was then tautomerized to give a 6-membered intermediate **D** where a Pd–C bond formed instead of a Pd–O bond. After further bond rotation and β-hydride elimination, the desired product **3a** favouring a thermodynamically stable *E*-isomer was formed with the elimination of HPdX. Further reductive elimination and reoxidation of HPdX would give rise to active Pd(II) species which can be used for the next catalytic cycle (Fig. 1).

In conclusion, we have developed an efficient Pd-catalysed dehydrogenative coupling approach for the synthesis of vinyl esters from carboxylic acids and alkenes. As a good alternative to hydrocarboxylation of terminal alkynes, this methodology is suitable for the synthesis of a broad range of di-substituted vinyl esters with good yields and excellent chemo- and regio-selectivity.

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- A 64 : 36 mixture of compounds **4** and **5** was isolated in 36% yield.

**Fig. 1** Proposed catalytic cycle.

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