

Alkylation of Active Methylene Compounds by Allylic Alcohols using Tetrakis(triphenylphosphine)palladium(0) Catalysts

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We have found that active methylene compounds can be alkylated by allylic alcohols using $(PPh_3)_4Pd$ as a catalyst at 100 °C without prior activation of the allylic hydroxy group.

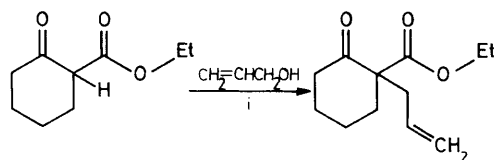
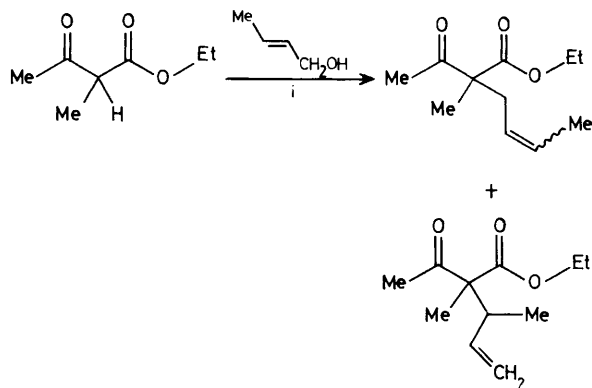
Palladium(0) catalysts are widely used in synthetic organic chemistry and a common class of reactions catalysed by these compounds is nucleophilic substitution of activated allylic alcohols.¹⁻⁴ In such reactions, allylic alcohols are often converted into esters which can then oxidatively add to the palladium(0) to form complexes susceptible to nucleophilic

attack. Many nucleophiles have been used for such reactions including carbanions derived from active methylene compounds. Decarboxylation-allylations of allylic esters of β -ketoacids and related compounds are other similar Pd⁰-catalysed reactions used to form carbon-carbon bonds.^{5,6} However, while activated allylic alcohols such as allyl acetate

Table 1. Alkylation of active methylene compounds using allylic alcohols and $[(C_6H_5)_3P]_4Pd^a$

Alcohol	Substrate	Time (h)	Yield (%) ^{b,c}	Products
Allyl alcohol	Ethyl acetoacetate	4	96 (91)	Ethyl 2-allylacetoacetate
Allyl alcohol	Ethyl 2-methylacetoacetate	9	100 (93)	Ethyl 2-allyl-2-methylacetoacetate
Allyl alcohol	Ethyl 2-cyanoacetate	3.5	100 (96)	Ethyl 2,2-diallyl-2-cyanoacetate
Allyl alcohol	Ethyl 2-cyclohexanonecarboxylate ^d	22	76 (67)	Ethyl 2-allyl-2-cyclohexanonecarboxylate
Allyl alcohol	Methyl 2-cyclohexanonecarboxylate ^d	22	84 (67) ^e	Methyl 2-allyl-2-cyclohexanonecarboxylate
<i>E</i> -But-2-en-1-ol	Ethyl acetoacetate	72	91	Ethyl 2-(<i>E</i> -but-2-enyl)acetoacetate (55) ^f Ethyl 2-(but-3-enyl)acetoacetate (45) ^f Ethyl 2,2-bis(<i>E</i> -but-2-enyl)acetate (3) ^f Ethyl 2-(<i>E</i> -but-2-enyl)-2-(but-3-enyl)acetoacetate (2) ^f
But-1-en-3-ol	Ethyl acetoacetate	72	85	— ^g
<i>E</i> -But-2-en-1-ol	Ethyl 2-methylacetoacetate	96	90 (79) ^h	Ethyl 2-(<i>E</i> -but-2-enyl)-2-methylacetoacetate (75) ^f Ethyl 2-(but-3-enyl)-2-methylacetoacetate (25) ^f

^a The allylation reactions were carried out at 100 °C in toluene using 5 mol% catalyst. ^b The yields are based on g.c. analysis of the conversion of starting material, except for the values in parentheses which are isolated yields from 10 mmol scale reactions. ^c Products were identified by ¹H n.m.r., ¹³C n.m.r. and g.c./mass spectroscopy and co-injected on g.c. with authentic samples. ^d This reaction was carried out using a commercially available mixture of 60% ethyl and 40% methyl esters of the starting material. ^e On a 10 mmol scale, this methyl ester yielded 48% isolated product which contained some decarboxylated 2-allylcyclohexanone. ^f Percentage composition in product mixture. ^g G.c. analysis showed that the products in this reaction were identical to those in the reaction of ethyl acetoacetate and *E*-but-2-enol. ^h Traces of decarboxylated product were detected by g.c. after 48 h.

**Scheme 1.** Reagents and conditions: i, $(PPh_3)_4Pd$, 100 °C, toluene.**Scheme 2.** Reagents and conditions: i, $(PPh_3)_4Pd$, 100 °C, toluene.

are generally useful, allyl alcohol itself is less reactive. Prior examples where unactivated allylic alcohols are used as substrates for this Pd^0 chemistry typically yield products in low or modest yields, or mixtures of products.^{1,3,7–10} Here we describe a simple procedure which produces high yields of *C*-allylated products from active methylene compounds and simple allylic alcohols using $(PPh_3)_4Pd$ as a catalyst at 100 °C in dry toluene.

The allylation reaction shown in Scheme 1 occurs without loss of CO_2 and without hydrolysis of the ethyl ester of the starting β -ketoacid. We have found that this reaction is applicable to a variety of β -ketoacid esters and to similar active methylene compounds, and that both primary and secondary allylic alcohols can be used. As shown by the data in Table 1, the consumption of starting β -ketoacid ester to allylated product is quantitative and the yields of *C*-allylated product are excellent. The principle limitation to the reaction

appears to be the possible diallylation seen in cases where the starting active methylene compound contains more than one acidic hydrogen; this is not a problem in most of the examples cited which have only one acidic C–H.

While we have not yet explored possible mechanisms for this reaction, some of our results together with prior literature provide an insight into the mechanism of this process. It was recently reported that allylic alcohols could serve as substrates for allylation of nitroalkanes catalysed by $(PPh_3)_4Pd$ as long as some substrate was present to act as a dehydrating agent.¹¹ While the β -ketoacid ester could conceivably have served the same purpose in these reactions, the fact that we were unable to detect allylated or diallylated decarboxylated β -ketoesters by gas chromatographic analysis and the high yields of ethyl ester products seen in several examples show that hydrolysis of either the starting β -ketoester or the product β -ketoesters is not occurring under our reaction conditions. In addition, we were also able to show that isomeric allylic alcohols such as but-1-en-3-ol and an *E/Z* mixture of but-2-en-1-ol form the same product mixture (Scheme 2). This suggests that there is a common intermediate from these isomeric allylic alcohols.

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