Heck-type Benzylation of Olefins with Benzyl Trifluoroacetates

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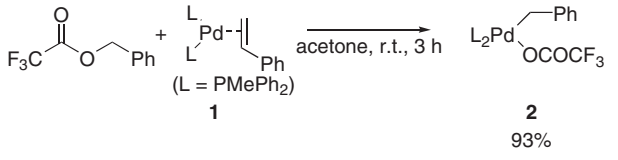
A new synthetic method for 1-aryl-2-alkenes from 1-olefins by benzylation treating with benzyl trifluoroacetates using palladium-catalyst is developed on the basis of oxidative addition of benzyl carboxylates to Pd(0) complexes to give benzyl(carboxylato)palladium(II) complexes with cleavage of benzyl–oxygen bond.

Over the last years, the Heck reaction has been widely used as a mild and efficient method for the regioselective attachment of side chains to aromatic rings or benzyl groups.[1] In general, a wide variety of organic halides such as aryl halides, aroyl halides, and benzyl halides[2] have been utilized. Besides organic halides aromatic triflates and alkenyl triflates obtained form phenols or enolates can be also used.[1] Goossen[3] and De Vries[4] utilized *p*-nitrophenyl benzoic acid esters and acid anhydride as non-halide aryl sources, respectively, which enable to avoid using stoichiometric amounts of base and the resulting salt production, providing a clean reaction. However, benzylation of olefins using non-halogen benzyl compounds was scarcely reported since oxidative addition of benzyl carboxylates hardly proceeds with normal benzyl esters.

Palladium-catalyzed allylation of nucleophiles utilizing the C–O bond cleavage in allylic carboxylates and carbonates has been extensively used in organic synthesis, on the other hand the utility of benzyl carboxylates has been much less explored despite the expected propensity benzyl compounds having the allylic nature to add oxidatively to Pd(0) complex.[5] We have been concerned with transition metal-catalyzed C–O bond cleavages in oxygen-containing organic compounds and their application to development of molecular catalysts for organic synthesis. So far with utilization of the C–O bond cleavage processes we have developed useful new processes to convert carboxylic anhydrides and carboxylic acids into aldehydes and ketones.[6–8] On the continuous efforts to develop possibility of C–O activation with transition metal complexes, we have found that oxidative addition of benzyl trifluoroacetates takes place with ease, which is applied to catalytic benzylation of olefins.

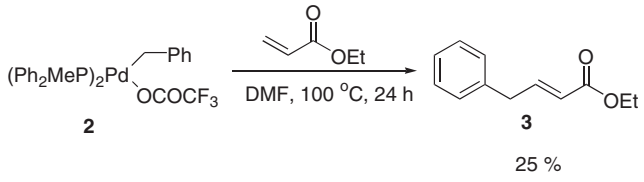
Cleavage benzyl C–O bond of benzyl trifluoroacetate on interaction with tertiary phosphine-coordinate Pd(0) has been reported (Scheme 1).[9]

Olefin insertion reaction from readily obtained benzyl (trifluoroacetato)palladium(II) complex was expected. In fact, the benzylpalladium complex **2**[10] reacted with ethyl acrylate to yield ethyl (*E*)-4-phenyl-2-butenoate (**3**) (Scheme 2).



Scheme 1.

Furthermore, the reaction using benzyl trifluoroacetates was developed to catalytic olefin benzylation.



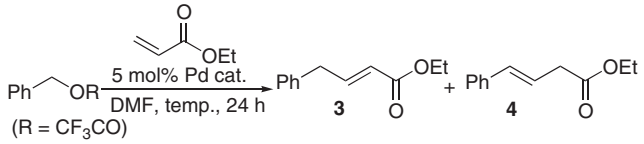
Scheme 2.

Table 1 shows the conversion of ethyl acylate on reaction with benzyl trifluoroacetate in the presence of Pd catalyst into **3** as the product of olefin benzylation process under various conditions.

The catalytic reaction at 100–120 °C afforded the benzylation product in good yields (Runs 3, 4, and 11). When the reaction was carried out at higher temperature, 120 and 140 °C, the double bond isomerization took place to give ethyl (*E*)-4-phenyl-3-butenoate (**4**) in addition to **3** (Runs 11 and 12). The thermal isomerizaion in the absence of palladium catalysts was observed in an experiment of heating **3** in DMF at 130 °C for 24 h to give the isomer **4** in 83% yield along with the starting **3** (16%).

The catalyst system composed $Pd(OAc)_2$ and 4 equiv. of PPh_3 and DMF as solvent was most effective, affording a variety

Table 1. Palladium-catalyzed benzylation of ethyl acrylate

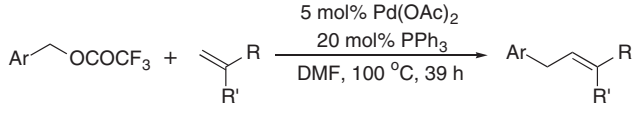


Entry	Pd cat.	temp/°C	yield (3 + 4)/%[a]	3/4[b]
1	$Pd(OAc)_2$	100	0	-
2	$Pd(OAc)_2$ + 2 PPh_3	100	45	1:0
3	$Pd(OAc)_2$ + 4 PPh_3	100	61	1:0
4[c]	$Pd(OAc)_2$ + 4 PPh_3	100	75	1:0
5	$Pd(OAc)_2$ + 4 P(*o*-tolyl)$_3$	100	0	-
6	$Pd(OAc)_2$ + 4 P(*n*-Bu)$_3$	100	55	1:0
7	$Pd(dba)_2$ + 4 PPh_3	100	60	1:0
8	$Pd(OAc)_2$ + dppp	100	0	-
9	$Pd(PPh_3)_4$	100	49	1:0
10	$Pd(OAc)_2$ + 4 PPh_3	80	31	1:0
11	$Pd(OAc)_2$ + 4 PPh_3	120	68	1:1
12	$Pd(OAc)_2$ + 2 PPh_3	140	48	1:5

[a] Isolated yield. [b] The distribution of isomers **3** and **4** was determined by ^{1}H NMR analysis of the mixture of **3** and **4**. [c] Reaction time was 39.5 h.

of benzylation products. The results by treating various olefins with benzyl trifluoroacetates in DMF at 100 °C for 39 h were summarized in Table 2.[11]

Table 2. The palladium-catalyzed benzylation of olefins with benzyl trifluoroacetates

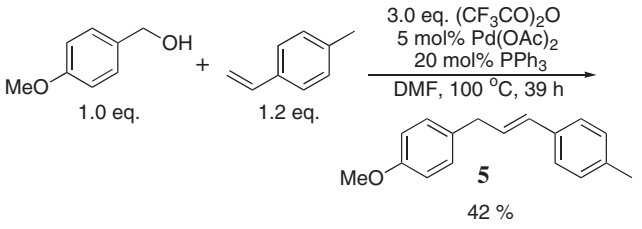


Entry	Ar	R	R′	Yield/%
1	Ph	COOEt	H	75
2	*p*-$MeOC_6H_4$	COOEt	H	59
3	Ph	*p*-MeC_6H_4	H	65
4	*p*-$MeOC_6H_4$	*p*-MeC_6H_4	H	42
5	*p*-ClC_6H_4	*p*-MeC_6H_4	H	81
6	*p*-FC_6H_4	*p*-MeC_6H_4	H	80
7	Ph	2-pryridine	H	27
8	*p*-$MeOC_6H_4$	Ph	Ph	21
9	*p*-$MeOC_6H_4$	*p*-ClC_6H_4	H	56
10	2,4,6-trimethyphenyl	*p*-MeC_6H_4	H	69
11	3,5,6-trimethoxyphenyl	*p*-MeC_6H_4	H	56

The present process is applicable to various benzyl trifluoroacetates with olefins and is tolerant to a variety of functional groups. Benzyl trifluoroacetates having functional groups such as methoxy, chloro, and fluoro groups at the *para* position can be catalytically converted into the corresponding compounds in good yields. The benzylation can be also preformed with olefins such as 2-vinylpyridine, 4-methyl, 4-chlorostyrene, and 1, 1-diphenylstyrene.

We have previously observed that treatment of carboxylic acids with less reactive carboxylic anhydride such as pivalic anhydride or dimethyl dicarbonate leads to the anhydride mixture, which can be subjected to the C–O bond cleavage process to yield aldehydes or ketones. Under a similar concept, we attempted the direct benzylation of olefins from benzyl alcohols. In fact, treatment of *p*-methoxybenzyl alcohol with *p*-methyl styrene at 100 °C in DMF in the presence of trifluoroacetic anhydride (3 equiv.) and Pd catalyst for 24 h gave **5** in 42% yield (Scheme 3).

In conclusion, a practical method to convert olefins into aryl-2-alkenes by treating benzyl trifluoroacetates with olefins is developed on the basis of oxidative addition of benzyl carboxylates to Pd(0) complexes to give benzyl(carboxylato)palladium(II) complexes with cleavage of benzyl–oxygen bond, which does not require the use of benzyl chlorides or any extra base.



Scheme 3.

The catalytic benzylation of olefins from benzyl alcohols was developed using trifluoroacetic anhydride. These methods provide a useful tool for preparation of various aromatic compounds as a non-halogen method.

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10 Synthesis of the complex **2** in this paper is as follows. To a mixture of acetone (5 mL) *trans*-[$PdEt_2(PMePh_2)_2$] (1.66 mmol) and styrene (5.24 mmol) were added at −20 °C. On standing the mixture at 50 °C for 2 h, the solution became a homogeneous yellow solution. After cooling this solution at room temperature, benzyl trifluoroacetate (2.02 mmol) was added to this solution and the solution was stirred at room temperature for 3 h. After the reaction mixture was concentrated, hexane was added to precipitate **2**, which was filtrated and collected. Subsequent washing with hexane and drying in vacuo gave a pale white powder of **2** (1.54 mmol, 93% yield).

11 General procedure for the reactions in Table 2 is as follows. A DMF solution (5 mL) of benzyl trifluoroacetate (1 mmol), olefin (1.2 mmol), $Pd(OAc)_2$ (0.05 mmol) and PPh_3 (0.20 mmol) was placed in a 25-mL-Schlenk tube. The solution was stirred at 100 °C for 39 h. On cooling the mixture, ethyl acetate and water were added and the aqueous layer was extracted with ethyl acetate. The organic layer was dried over $MgSO_4$ and the solvent was evaporated in vacuo. Purification of the residue by column chromatography (hexane/ethyl acetate) gave the benzylation compound.

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