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Use of π-Allylpalladium as a Nucleophile via an Alkyl-Allyl Exchange Reaction with Alkylzinc

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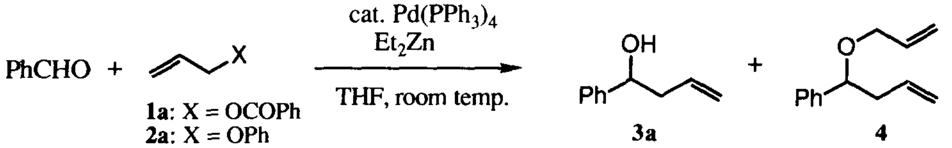
Summary: Allylation of carbonyl compounds (aldehydes, ketones, esters, lactones, acid anhydrides) proceeds smoothly at room temperature by the reaction of a carbonyl compound, an allylic benzoate or allylic phenyl ether, diethylzinc, and a catalytic amount of Pd(0)-complex in THF under N_2.

π-Allylpalladium has been utilized as a versatile allylic electrophile.[1] Umpolung of π-allylpalladium as a nucleophile undoubtedly widens its scope in organic synthesis. Accordingly, considerable efforts have been devoted to this target. The umpolung methods hitherto developed are based on either (1) the reduction of π-allylpalladium with low valent metals[2] or by electrochemical means[3] or (2) the addition of hetero-nucleophiles (e.g., Sn) to π-allylpalladium.[4] Here we report an entirely new type of umpolung method that presumably proceeds via an alkyl-allyl exchange reaction between π-allylpalladium complexes and alkylzinc reagents.



(1)

When a mixture of allyl benzoate (**1a**, 1.2 mmol), benzaldehyde (1.0 mmol), and diethylzinc (1.2 mmol) in dry THF was stirred under N_2 in the presence of tetrakis(triphenylphosphine)palladium [$Pd(PPh_3)_4$, 0.05 mmol] (eq 1), a smooth allylation of benzaldehyde took place to furnish 1-phenyl-3-buten-1-ol (**3a**) in 88% isolated yield (run 2, Table 1). The similar reaction, using diethylzinc in a half amount (0.6 mmol), furnished an allyl homoallyl ether **4** (30%, based on benzaldehyde) in addition to **3a** (24%) (run 1, Table 1). The ether **4** may be formed via an electrophilic allylation with π-allylpalladium toward a zinc salt of **3a**, which in turn is formed by a nucleophilic allylation of benzaldehyde. The correspondence of the combined amount of **3a** and **4** (0.54 mmol) and the amount of diethylzinc employed (0.6 mmol) suggests that diethylzinc produces an equimolar amount of an allylating agent.

The similar but less efficient allylation can be performed with either allyl acetate, allyl methyl carbonate, or allyl bromide (runs 3-5, Table 1). The reaction with allyl phenyl ether (**2a**) is rather reluctant under the similar conditions, however, proceeds smoothly to provide **3a** in good yield by increasing the amounts of diethylzinc (run 6, Table 1). Notably, even under such a condition, 1-phenyl-1-propanol is not formed in any detectable amounts.

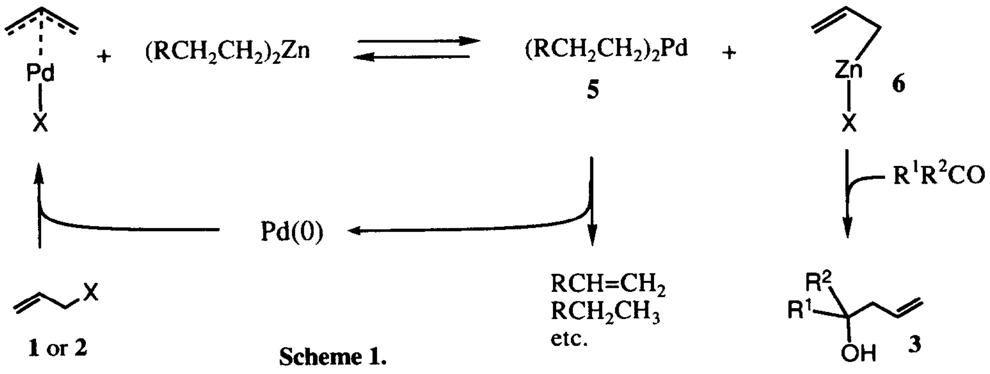
As a working hypothesis for the present allylation, we propose an allylzinc species **6** as an active allylating agent[5] that is generated by an alkyl-allyl exchange reaction between alkylzinc reagents and π-allylpalladium species (Scheme 1). Taking high thermodynamic stability of π-allylpalladium among the other components into consideration, the equilibrium shown in Scheme 1 is expected to lie to the left and may shift to the right either by prompt consumption of alkylpalladium species **5** and/or allylzinc species **6** or in the presence of excess amounts of alkylzinc. The effect of the excess amount of diethylzinc was noted already (run 6, Table 1 and *vide infra*). In the absence of benzaldehyde, the reaction of run 6 in Table 1 was very reluctant and **2a** was recovered. Under forcing conditions, e.g., **2a** (1 mmol), Et_2Zn (4 mmol), $Pd(PPh_3)_4$ (0.05 mmol) at 50 °C for 7 h, **2a** disappeared completely. Treatment of the resultant mixture with benzaldehyde (1 mmol) at - 35 °C for 10 min provided **3a** in 15% isolated yield (based on **2a**) (300% yield based on Pd).[6] The yield of **3a** (based on **2a**) indicates that the accumulated yield of **6** is as low as 15% and hence an application of Barbier-type procedure is essential for the satisfactory allylation. The yield of **3a** (based on Pd) suggests that palladium species such as $EtPdCH_2CH=CH_2$ and dialkylallylpalladate (e.g., $[Et_2PdCH_2CH=CH_2]^- ZnX^+$)[7] are not responsible for the present allylation.

Table 1. Pd-catalyzed Allylation of Benzaldehyde with Allyl-X and Et_2Zn[a]

run	$CH_2=CHCH_2X$	Et_2Zn (mmol)	time (h)	isolated yield[b]	
				3a	**4**
1	X = OCOPh (**1a**)	0.6	6	24%	30%
2	X = OCOPh (**1a**)	1.2	3	88%	0%
3	X = OCOMe	1.2	5	69%	8%
4	$X = OCO_2Me$	1.2	6	58%	6%
5	X = Br	1.2	4	78%	0%
6	X = OPh (**2a**)	2.4	4	87%	0%

a) Conditions: benzaldehyde (1.0 mmol), allylating agent (1.2 mmol), Et_2Zn (2M in hexane), $Pd(PPh_3)_4$ (0.05 mmol) in 3 mL of dry THF at room temperature.

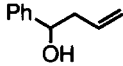
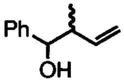
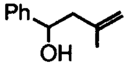
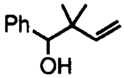
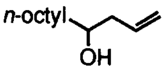
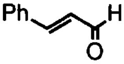
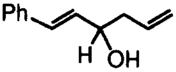
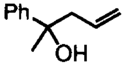
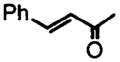
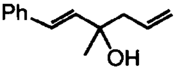
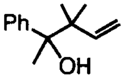
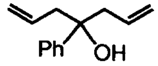
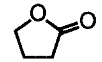
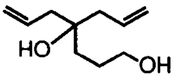
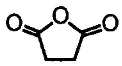
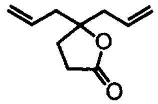
b) Yield based on benzaldehyde.



Scheme 1.

The formation of benzyl acrylate (69%) together with **3a** (58%) by the reaction of benzyl β-iodozinciopropionate (2.5 mmol), **1a** (1 mmol), benzaldehyde (1 mmol), and $Pd(PPh_3)_4$ (0.05 mmol) in THF at room temperature under N_2 (Scheme 1, $R = CO_2CH_2Ph$) supports an intermediacy of **5**. Furthermore, the similar reaction with ethyl β-iodozinciopropionate, under 1 atom of CO (a balloon), furnished a mixture of diethyl 4-oxopimelate (87%) and **3a** (58%).[8]

Table 2. **Pd^0-catalyzed Allylation of Carbonyl Compounds with Allylic Benzoates 1 (or Allylic Phenyl Ether 2) and Diethylzinc.**[a]

run	carbonyl compounds	allylating agents (mmol)	Et_2Zn (mmol)	time (h)	product (isolated yield)
1	PhCHO	allyl benzoate (**1a**, 1.2)	1.2	3	 **3a** (88%)[b]
2	PhCHO	*trans*-crotyl benzoate (**1b**, 1.2)	2.4	2	 **3b** (94%)[c]
3	PhCHO	α-methallyl benzoate (**1c**, 1.2)	2.4	2	**3b** (92%)[c]
4	PhCHO	β-methallyl benzoate (**1d**, 1.2)	1.2	5	 (82%)
5	PhCHO	prenyl benzoate (**1e**, 1.2)	2.4	2	 (95%)
6	n-$C_8H_{17}CHO$	**1a** (1.2)	2.4	6	 (89%)[d]
7		**1a** (1.2)	2.4	4	 (97%)
8	PhCOMe	**1a** (1.2)	2.4	6	 (92%)
9		**1a** (1.2)	2.4	5	 (94%)
10	PhCHO	allyl phenyl ether (**2a**, 1.2)	2.4	4	**3a** (87%)
11	PhCHO	*trans*-crotyl phenyl ether (**2b**, 1.2)	2.4	7	**3b** (74%)[c]
12	PhCOMe	prenyl phenyl ether (**2c**, 1.2)	2.4	22	 (83%)
13	$PhCO_2Et$	**2a** (2.4)	4.8	24	 (82%)
14		**2a** (2.4)	4.8	24	 (88%)
15		**2a** (4.8)	9.6	24	 (65%)

a) Conditions: carbonyl compound (1.0 mmol), allylating agent, Et_2Zn (2.0 M in hexane), $Pd(PPh_3)_4$ (0.05 mmol) in 3 ml THF at room temperature under N_2.

b) 84% with 1 mol% of $Pd(PPh_3)_4$ (room temp., 36 h).

c) *syn*/*anti* = ca. 3:7.

d) 73% with 1.2 mmol of Et_2Zn (room temp., 4 h).

As summarized in Table 2, the present allylation turned out widely applicable to the combinations of other allylating agents (**1a**-**e** and **2a**-**c**) and carbonyl compounds (aldehydes, ketones, esters, lactones, and acid anhydrides). For allylation of esters (runs 13 and 14), **2** are of choice to avoid an allylation of **1** themselves. Generally, better yields are obtained by using twofold excess or slightly more amounts of diethylzinc (run 6, footnote d).

The present reaction shows the following high regio- and chemoselectivities. Unsymmetrically substituted allylic nucleophiles react selectively at the allylic termini with the higher number of substituents (runs 2, 3, 5, 11, and 12, Table 2).[9] α,β-Unsaturated aldehydes and ketones undergo an 1,2-addition exclusively (runs 7 and 9). By competition experiments, benzaldehyde is found to be ca. 70 times more reactive than acetophenone, while only acetophenone undergoes an allylation even when methyl benzoate is used as a solvent (acetophenone/methyl benzoate = 1/100 mol).

Experimental Procedure: (*E*)-1-phenyl-1,5-hexadien-3-ol (run 7, Table 2) : To a solution of $Pd(PPh_3)_4$ (0.05 mmol) in 3 mL of dry THF under N_2 were successively added 1.2 mmol of **1a**, 1.0 mmol of cinnamaldehyde, and 2.4 mmol of diethylzinc [2M hexane solution]. Resulting pale-yellow solution was stirred at room temperature for 4 h, then diluted with ethyl acetate. The mixture was washed successively with 2*N* HCl and aqueous $NaHCO_3$, dried ($MgSO_4$), concentrated, and then chromatographed with benzene-ethyl acetate (20 x 1.5 cm, silica gel 60) to afford 0.169 g (97 %) of the title compound as a colorless oil: bp (decomp at 80 °C/0.5 mmHg). IR (neat) 3350, 1645, 1495, 1445, 965, 915, 745, 690 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ = 1.60 (br. s, 1H), 2.34-2.49 (m, 2H), 4.37 (ddt, J = 1.0, 6.6, 5.3 Hz, 1H), 5.15-5.22 (m, 2H), 5.86 (dddd, J = 7.0, 7.3, 10.1, 17.1 Hz, 1H), 6.25 (dd, J = 6.6, 15.9 Hz, 1H), 6.61 (dd, J = 1.0, 15.9 Hz, 1H), 7.21-7.41 (m, 5H). Anal. Calcd for $C_{12}H_{14}O$: C, 82.71; H, 8.10. Found: C, 82.47; H, 8.24.

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References and Notes

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5) The other allylzincs, e.g., $CH_2{=}CHCH_2ZnCH_2CH_2R$, may also participate in the allylation.

6) The similar reaction with cinnamyl phenyl ether (**2d**) provided a mixture of 1,2-diphenyl-3-buten-1-ol and 1,4-diphenyl-1,5-hexadiene in 5 and 50% yields (based on **2d**), respectively. For the related allylation of π-allylpalladium, see: a) H. Ochiai, Y. Tamaru, K. Tsubaki, Z. Yoshida, *J. Org. Chem.* **1987**, *52*, 4418-4420; b) J. van der Louw, J. L. van der Baan, F. Bickelhaupt, G. W. Klumpp, *Tetrahedron Lett.* **1987**, *28*, 2889-2892.

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8) Under the similar conditions, in the presence of HMPA and in the absence of benzaldehyde, was obtained ethyl 4-oxo-6-heptenoate: Y. Tamaru, K. Yasui, H. Takanabe, S. Tanaka, K. Fugami, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 645-646. For the formation of 4-oxopimelates, see: S. Aoki, E. Nakamura, *Tetrahedron*, **1991**, *47*, 3935-3946.

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