ORGANIC
LETTERS

2007
Vol. 9, No. 22
4595−4598

Solvent-Controlled Highly Selective Bis- and Monoallylation of Active Methylene Compounds by Allyl Acetate with Palladium(0) Nanoparticle

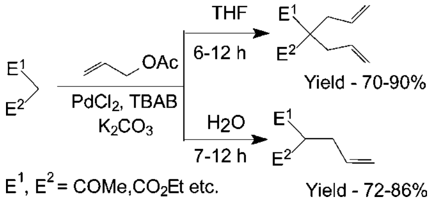
Brindaban C. Ranu,* Kalicharan Chattopadhyay, and Laksmikanta Adak

*Department of Organic Chemistry, Indian Association for the Cultivation of Science,
Jadavpur, Kolkata, 700 032, India*

ocbcr@iacs.res.in

Received August 27, 2007

ABSTRACT



Palladium(0) nanoparticle has been used as an efficient catalyst for the allylation of active methylene compounds. Very efficient bisallylation is achieved for a variety of active methylene compounds by allyl acetate and its derivatives in one stroke in THF solvent. The reaction in water provides monoallylated product selectively by allyl acetate only. The recovered Pd(0) nanoparticle is recycled. A probable mechanism is suggested.

Allylic substitution is a very useful reaction as it adds a moiety that has much potential for further elaboration. The palladium-catalyzed allylation by allylic alcohols or preferably its derivatives like acetate and carbonate is one of the most efficient protocols for constructing C−C bonds in organic synthesis.[1] Usually a palladium derivative in combination with a ligand is used.[2] These procedures involved $Pd_2(dba)_3/PPh_3$,[2a] $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/tetraphosphine ligand,[2b] $Pd(0)/P(C_6H_4\text{-}m\text{-}SO_3Na)_3$ [trisodium salt of tris(*m*-sulfonatophenyl)phosphine (tppts)],[2c] $Pd\text{-}P(OC_6H_5)_3$,[2d] $Pd(dba)_2/PPh_3/Al_2O_3$,[2e] $PdCl_2(CH_3CN)_2/[(HOCH_2CH_2NHCOCH_2)_2\text{-}NCH_2]_2$,[2f] and $Pd[PPh_3]_4$.[2g] A few procedures with other non-palladium catalysts such as [CpRuCl(cod)][3a,b] and Ni^o/dppp[3c] were also reported. In recent times, interest in nanoparticle-catalysis has increased considerably because of its improved efficiency under mild and environmentally benign conditions in the context of Green Chemistry.[4,5] Palladium nanoparticles have been found to be active species in various C−C bond formation, namely Heck, Sonogashira, and Suzuki, coupling reactions and thus showed great promise for further applications.[5] However, the Tsuji−Trost reaction, i.e., allylic substitution of active methylene compounds, has been less studied and only recently, palladium and cobalt nanoparticles immobilized on silica,[6a] montmorillonite entrapped sub-

---

(1) (a) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (b) Tsuji, J. *Transition Metal Reagents and Catalysts*; Wiley: New York, 2000.

(2) (a) Giambastiani, G.; Poli, G. *J. Org. Chem.* **1998**, *63*, 9608. (b) Laurenti, D.; Feuerstein, M.; Pepe, G.; Doucet, H.; Santelli, M. *J. Org. Chem.* **2001**, *66*, 1633. (c) Kinoshita, H.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2004**, *6*, 4085. (d) Kayaki, Y.; Koda, T.; Ikariya, T. *J. Org. Chem.* **2004**, *69*, 2595. (e) Ferroud, D.; Genet, J. P.; Muzart, J. *Tetrahedron Lett.* **1984**, *25*, 4379. (f) Chevrin, C.; Le Bras, J.; Henin, F.; Muzart, J.; Pla-Quintana, A.; Roglans, A.; Pleixats, R. *Organometallics* **2004**, *23*, 4796. (g) Schwartz, C. E.; Curran, D. P. *J. Am. Chem. Soc.* **1990**, *112*, 9272.

(3) (a) Yamamoto, Y.; Nakagai, Y.-i.; Itoh, K. *Chem. Eur. J.* **2004**, *10*, 231. (b) Renaud, J.-L.; Bruneau, C.; Demerseman, B. *Synlett* **2003**, 408. (c) Bricout, H.; Carpentier, J.-F.; Mortreux, A. *Chem. Commun.* **1997**, 1393.

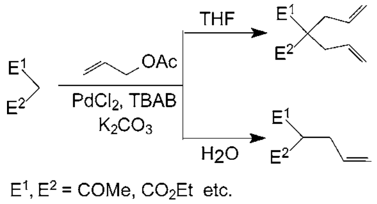
(4) (a) Lu, F.; Ruiz Aranzaes, J.; Astruc, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 7399. (b) Moreno-Manas, M.; Pleixats, R. *Acc. Chem. Res.* **2003**, *36*, 638. (c) Crooks, R. M.; Zhao, M.; Sun, L.; Chechik, V.; Yeung, L. K. *Acc. Chem. Res.* **2001**, *34*, 181.

(5) (a) Astruc, D. *Inorg. Chem.* **2007**, *46*, 1884. (b) Astruc, D.; Lu, F.; Aranzaes, J. R. *Angew. Chem., Int. Ed.* **2005**, *44*, 7852. (c) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.

10.1021/ol702099v CCC: $37.00

nanoordered Pd clusters,[6b] and palladium nanoparticle stabilized by an asymmetric diphosphite[6c] were reported. Allylation of amines[6d] and phenols[6e] by Pd nanoparticles was also demonstrated. We report here a novel ligand-free protocol for allylic substitution of active methylene compounds by allyl acetate and its derivatives (Tsuji−Trost reaction), catalyzed by palladium(0) nanoparticles. The reaction in THF leads to bisallylation in one stroke, whereas highly selective monoallylation by allyl acetate takes place in H_2O (Scheme 1).

Scheme 1



The experimental procedure is very convenient.[7] A one-pot reaction of active methylene compound and allyl acetate in the presence of the $PdCl_2/TBAB/K_2CO_3$ system in refluxing THF provided the product. The formation of Pd(0) nanoparticles in situ from this reagent system was detected by us from the analysis of the reaction mixture by transmission electron microscope (TEM) and Energy Dispersive X-ray spectroscopy (EDS) (Figures 1 and 2). The size of Pd nanoparticles was found to be 5−8 nm. In absence of Pd nanoparticle no reaction was initiated.

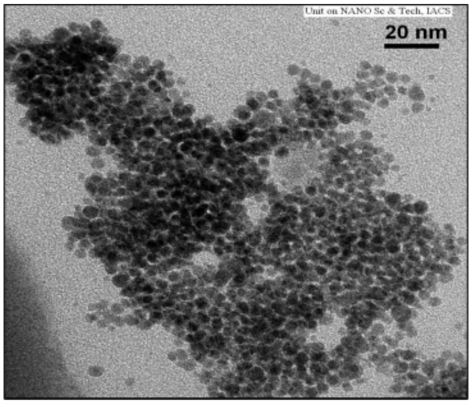


Figure 1. TEM image of Pd nanoparticles formed in the reaction mixture.

Several structurally diverse active methylene compounds underwent allylation by allyl acetate or its derivatives by in situ generated palladium(0) nanoparticles in THF to produce the corresponding allylated products in high yields. The results are summarized in Table 1.

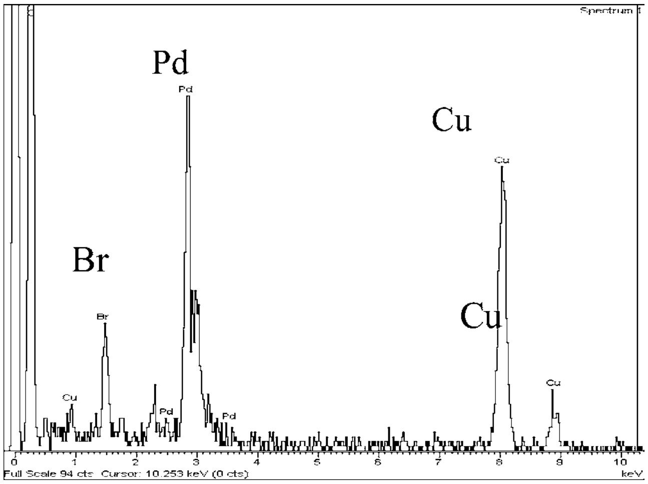


Figure 2. Energy dispersive X-ray spectra with the use of a Cu-grid.

As evident from the results all the substrates produced bisallylated products under these conditions. The participating active methylene compounds were acyclic and cyclic 1,3-diketones, 1,3-keto esters, and 1,3-diester, and allylic agents used were allyl acetate, crotyl acetate, and cinnamyl acetate and its derivatives. The careful monitoring of the progress of the reaction by TLC and ^1H NMR at intermediate stages indicated the presence of monoallylated compound in the range of 5−7% together with the starting material and bisallylated compound. It was also found that allylation of monoallyl ethyl acetoacetate by this procedure was complete within 1.5 h (entry 4, Table 1) compared to 7 h required for

---

(6) (a) Park, K. H.; Son, S. U.; Chung, Y. K. *Org. Lett*. **2002**, *4*, 4361. (b) Mitsudome, T.; Nose, K.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kitsukawa, K.; Kaneda, K. *Angew. Chem., Int. Ed*. **2007**, *46*, 3288. (c) Jansat, S.; Gomez, M.; Philippot, K.; Muller, G.; Guiu, E.; Claver, C.; Castillon, S.; Chaudret, B. *J. Am. Chem. Soc.* **2004**, *126*, 1592. (d) Cortial, G.; Siutkowski, M.; Goettmann, F.; Moores, A.; Boissiere, C.; Grosso, D.; Le Floch, P.; Sanchez, C. *Small* **2006**, *2*, 1042. (e) Park, C. M.; Kwon, M. S.; Park, J. *Synthesis* **2006**, 3790.

(7) **Representative Experimental Procedure for Allylation of Active Methylene Compound (entry 1, Table 1)**. To a stirred mixture of tetrabutylammonium bromide (323 mg, 1 mmol) and $PdCl_2$ (7 mg, 0.04 mmol) in THF (4 mL) were added allyl acetate (250 mg, 2.5 mmol), acetylacetone (100 mg, 1 mmol), and K_2CO_3 (414 mg, 3 mmol). The mixture was then heated at reflux for 6 h (TLC). After being cooled THF was evaporated and the residue was extracted with Et_2O (3×10 mL). The ether extract was washed with brine, dried (Na_2SO_4), and evaporated to leave the crude product, which was purified by column chromatography over silica gel (ether−hexane 10:90) to afford the pure product, 3,3-diallylpentane-2,4-dione, as a yellow oil (150 mg, 82%); IR (neat) 2979, 1739, 1697, 1639 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.06 (s, 6H), 2.61 (d, $J = 7.3$ Hz, 4H), 5.04−5.11 (m, 4H), 5.42−5.53 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.2 (2C), 35.0 (2C), 70.3, 119.3 (2C), 132.0 (2C), 205.7 (2C). These data were in agreement with the reported values.[2c] The solid residue after organic extract containing Pd(0) nanoparticles was reused for subsequent reactions (no loss of efficiency up to three runs).

(8) Muthusamy, S.; Gnanaprakasam, B. *Tetrahedron Lett.* **2005**, *46*, 635.

(9) Conrad, J. C.; Eelman, M. D.; Duarte Silva, J. A.; Monfette, S.; Parnas, H. H.; Snelgrove, J. L.; Fogg, D. E. *J. Am. Chem. Soc*. **2007**, *129*, 1024.

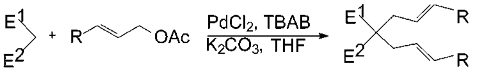
(10) Bhar, S.; Chaudhuri, S. K.; Sahu, S. G.; Panja, C. *Tetrahedron* **2001**, *57*, 9011.

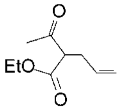
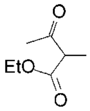
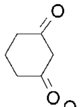
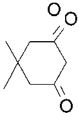
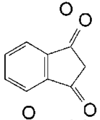
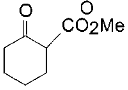
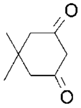
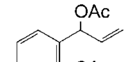
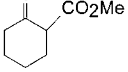
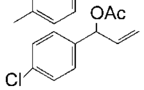
(11) Kondo, J.; Someya, H.; Kinoshita, H.; Shinokubo, H.; Yorimitsu, H.; Oshima, K. *Org. Lett*. **2005**, *7*, 5713.

(12) Matlin, A. R.; McGarvey, D. J.; Leckta, T. C.; Jacob, P. W.; Picken, H. A. *Tetrahedron Lett.* **1987**, *28*, 5087.

(13) Sigismondi, S.; Sinou, D. *J. Mol. Catal. A*: *Chem*. **1997**, *116*, 289.

Table 1. Allylation of Active Methylene Compounds by Allyl Acetate Catalyzed by Pd(0) Nanoparticle in THF



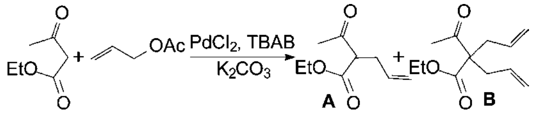
entry	E^1, E^2	R	time (h)	yield (%)[a]	ref
1	COMe, COMe	H	6	82	2c
2	COMe, CO_2Et	H	7	88	8
3	CO_2Et, CO_2Et	H	12	75	9
4		H	1.5	85	8
5		H	1.5	90	8
6		H	7	87	2d
7		H	6	88	2c
8		H	6.5	85	2c
9		H	5	70	2b
10	COMe, COMe	Me	9	75[b]	10
11	COMe, CO_2Me	Me	9.5	72[b]	
12	COMe, COMe	Ph	10	85	10
13	COMe, CO_2Et	Ph	11	81	10
14		Ph	9	76	13
15	COMe, COMe		11	72	
16			7	78	

[a] Yields refer to those of purified products characterized by IR, ^1H, and ^{13}C NMR spectroscopic data. [b] Mixture of *E* and *Z* isomers (90:10 by ^1H NMR).

bisallylation starting from ethyl acetoacetate (entry 2, Table 1). This indicates that bisallylation is much faster than the monoallylation step, restricting accumulation of monoallylated compound in the reaction mixture.

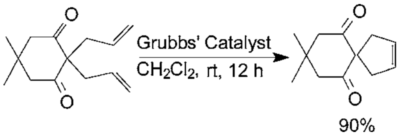
The reactions were very clean and bisallylated products were the only isolable compounds. The bisallylated compounds are very useful synthons, and we showed a representative example of the conversion of this compound to spiro annulated product by Grubbs' catalyst (eq 1). THF was found to be the solvent of choice for the formation of bisallylated product in high yields based on comparison of reaction results with other solvents (Table 2). Palladium(0) nanoparticle was formed from the reduction of $PdCl_2$ by the alkene moiety of allyl acetate.[5c] The slurry of palladium nanoparticles remaining after extraction of product was evaporated under vacuum to leave a dust of residue, which showed the presence of metallic Pd by XRD (Figure 3). This solid was equally effective for three subsequent runs without any loss of efficiency (Figure 4).

Table 2. Comparative Results of Allylation in Different Solvents



solvent	**A**:**B**[a]	time (h)	yield (%)
THF	00:100	7	88
CH_3CN	30:70	5	55
toluene	00:100	9	82
DMF	25:75	7	70
H_2O	80:20	8	72
DCM	00:100	9	80

[a] The ratio of **A** and **B** was determined by integration of peaks in the ^1H NMR spectra.



(1)

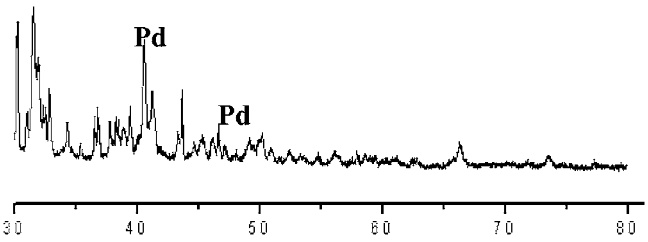


Figure 3. Powder XRD pattern with characteristic dihedral angles at 40.119° and 46.65° corresponding to Pd stabilized by TBAB in the recovered Pd residue.

Interestingly, when the reaction was carried out in H_2O monoallylation took place selectively. The results are reported in Table 3. However, this reaction was not very general. The reaction proceeded successfully only with allyl acetate; cinnamyl acetate and crotyl acetate failed to produce any allylated product. However, the selectivity was quite high; only in one example (entry 2, Table 3) was 20% of the bisallylated product formed out of four types of substrates.

The analysis of results of allylation of all substrates included in Tables 1 and 3 revealed that the additions were highly regioselective. When allyl acetate was used terminal

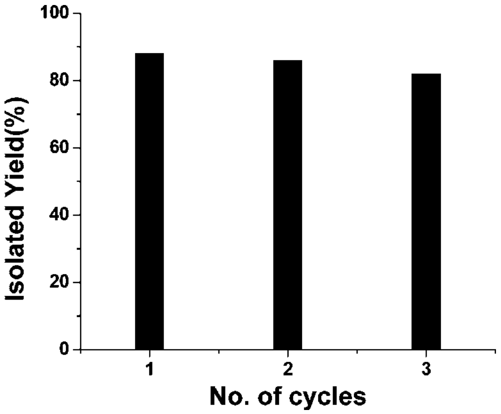
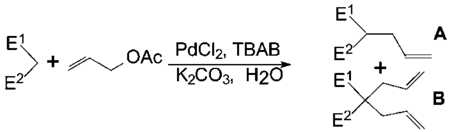
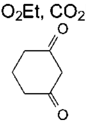


Figure 4. Recyclability Chart.

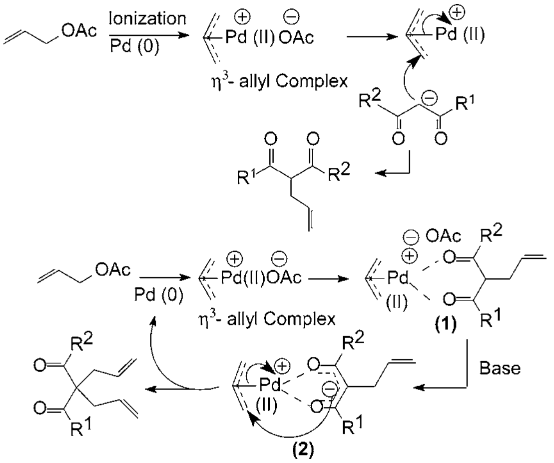
Table 3. Allylation of Active Methylene Compounds by Allyl Acetate Catalyzed by Pd(0) Nanoparticle in H_2O



entry	E^1, E^2	time (h)	A:B	yield (%)[a]	ref
1	COMe, COMe	9	100:00	86	2c
2	COMe, CO_2Et	8	80:20	72	2c
3	CO_2Et, CO_2Et	12	100:00	75	11
4		7	100:00	70	12

[a] Yields refer to those of purified products characterized by IR, ^1H, and ^{13}C NMR spectroscopic data.

Scheme 2. Possible Mechanism of Monoallylation in Water and Bisallylation in THF



alkenes were produced (entries 1−9, Table 1 and entries 1−4, Table 3), whereas substituted allyl acetates provided internal alkenes (entries 10−16, Table 1). We speculate that Pd(0) nanoparticle combines with allyl acetate to form an η^3-allyl-Pd(II)-complex **1** which then reacts with an active methylene compound to give an intermediate **2**, which provides the corresponding product by addition to the less-substituted carbon end (Scheme 2).[1a] The difference in reactivity of active methylene compounds in H_2O and THF leading to monoallylation and bisallylation, respectively, may be explained by the fact that H_2O hydrates[2c] the Pd(II) in complex **1**, weakening the coordination of Pd with C=O, thereby decreasing the acidity at the methine center to go for further allylation. However, in nonaqueous medium having no such effect bisallylation is favored. THF was found to be the best solvent toward bisallylation as mentioned earlier (Table 2). However, it is not clear to us why the monoallylation in water is successful only for allyl acetate and fails for other acetates. The steric factor may have a role.

The present procedure has its own distinction from others. The reaction is carried out in one pot including preparation of nano Pd(0) by a very simple and convenient means. The selective monoallylation and bisallylation were achieved by using H_2O and THF, respectively, and thus pure mono- and bisallylated products were obtained. Usually either monoallylated product or a mixture of mono- and bisallylated products was obtained with other reagents except [Cp*RuCl(cod)],[3a,b] which provide bisallylated products.

In conclusion, the present protocol using an in situ prepared palladium(0) nanoparticle provides a convenient and efficient procedure for allylation of active methylene compounds by allyl acetate. The significant improvements offered by this procedure are operational simplicity, achievement of selective mono- or bisallylation in H_2O or THF, respectively, high regioselectivity in the formation of products, high isolated yields, and reusibility of catalyst. To the best of our knowledge, this strategy for the solvent controlled selective allylation of active methylene compounds by allyl acetate involving Pd(0) nanoparticles is novel and not reported earlier.

Acknowledgment. We are pleased to acknowledge the financial support from DST [Grant No. SR/S5/GC-02/2006] for this investigation. K.C. and L.A. are thankful to CSIR for their fellowship.

Supporting Information Available: Characterization (IR, ^1H, and ^{13}C NMR spectroscopic data and elemental analysis) for the new compounds reported in Table 1 (listed in entries 11, 15, and 16) and ^1H NMR and ^{13}C NMR spectra of all compounds listed in Tables 1 and 3. This material is available free of charge via the Internet at http://pubs.acs.org.

OL702099V