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Catalytic asymmetric synthesis of cyclopentenones from propargyl malonates and allylic acetate by successive action of homogeneous palladium(II) and cobalt on charcoal catalysts in a one-pot reaction†

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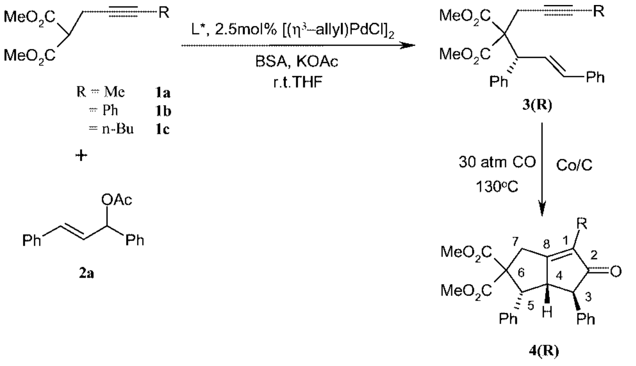
The tandem action of a homogeneous chiral Pd(II) catalyst and a heterogeneous Co/C catalyst leads to a two-step one-pot highly enantioselective Pauson–Khand-type reaction.

Much success has been achieved in the field of transition-metal-mediated (or catalyzed) synthesis of cyclopentenones from readily available substrates;[1] however, catalytic asymmetric synthesis is still surprisingly underdeveloped. The use of a chiral titanocene complex (EBTHI)Ti(CO)$_2$ (EBTHI = ethylene-1,2-bis(η^5-4,5,6,7-tetrahydroinden-1-yl)[2] and Co,[3] Rh,[4] and Ir[5] complexes with chiral diphosphines have been recently reported. Demand for the development of a catalytic and enantioselective Pauson–Khand type reaction remains high.

Recently, the tandem use of two kinds of homogeneous catalyst in a one-pot multistep transformation of substrates to products has been reported.[6] The report by Jeong's group has attracted our attention. They used a combination of Pd and Rh catalysts in the preparation of bicyclopentenones from propargyl malonates. The use of Pd-catalyzed asymmetric allylic alkylation[7] to generate enantioselective enynes appears to be quite promising. However, the use of *in situ* generated enantiomerically enriched enynes as substrates in the Pauson–Khand reaction has not been reported even though increasing efforts are being devoted to the development of practical enantioselective versions of the Pauson–Khand reaction.[8]

In this connection, we decided to use the Pd(II)-catalyzed asymmetric allylic alkylation in the synthesis of enantiomerically pure enynes. We report herein that the tandem action of homogeneous chiral Pd(II) catalyst and heterogeneous catalyst Co/C[9] leads to a 'two-step one-pot' highly enantioselective Pauson–Khand-type reaction. The efficiency of this two-step one-pot reaction was studied for **3(Me)** as shown in Scheme 1. Thus, we screened several chiral ligands (Chart 1) to find the best chiral ligand (Table 1).[10] The same reaction was conducted in the presence of dppe to obtain racemic products. All the chiral ligands were effective for Pd-catalyzed asymmetric allylic alkylation. The ee values of **4(Me)** ranged from 83 to 95% at room temperature. As expected, the best ligand was phosphinooxazoline ligand **b**. The best ee value of 96% was obtained when the reaction was conducted at 0 °C in the presence of **b** (entry 3 in Table 1). The absolute configuration of **3(Me)** was easily established by comparison of the observed [α] values with those of the known reactions. The absolute configuration (3*R*,4*S*,5*R*) of the bicyclic enone **4(Me)** was determined by an NMR study. When the reaction in Scheme 1 was carried out stepwise to determine whether the ee value was changed during the carbonylative cyclization, the ee value of the final product was the same as that of the first step and no other diastereomer was found in the second step. Thus, the ee value of the first asymmetric allylic alkylation reaction was maintained during the second cycloaddition reaction. This suggests that the first step is a stereoselective reaction and the second a stereospecific one. The enantioselectivity of this tandem cycloaddition was absolutely dependent on the Pd-catalyzed asymmetric allylic alkylation. This could be a good advantage of this combination of catalysts because the palladium-catalyzed allylic alkylation is one of the most thoroughly and intensively studied catalytic transformations. High yields were observed for all reactions. The yield of the second step was always quantitative. Thus, the turnover number was completely dependent upon the Pd-catalyzed allylic alkylation. For convenience, we used 2.5 mol% of Pd(II) catalyst for studying the reactions.

The success of this tandem catalytic reaction is primarily due to the use of Co/C. In the Pd(II)-catalyzed allylic alkylation reaction, acetic acid was generated. The acid would interact with cobalt species in the solution. When Co$_2$(CO)$_8$ (20 mol%) instead of Co/C was used as a catalyst, only 2% of the product



Scheme 1

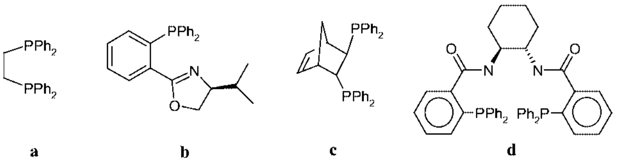


Chart 1

Table 1 Asymmetric one-pot synthesis of bicyclopentenone[a]

Entry	Chiral ligand	Time/h[b]	Yield (%)[c]	Ee (%)[d]
1	**a**	10	74	—
2	**b**	4	81	95
3[e]	**b**	18	95	96
4[f]	**b**	4	2	—
5	**c**	12	81	83

[a] **1a** and **2a** used as substrates. Conditions for the 2nd step: 130 °C, 18 h, 30 atm. CO. [b] Reaction time of the first step at rt. [c] Isolated yield. [d] Diacel OD column was used. [e] Reaction temperature of the first step is 0 °C. [f] 20 mol% Co$_2$(CO)$_8$ was used instead of Co/C.

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† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b1/b106836a/

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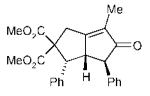
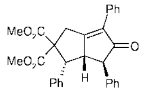
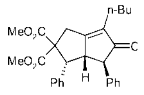
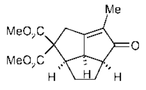
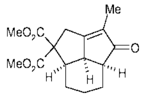
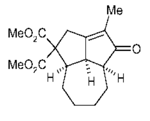
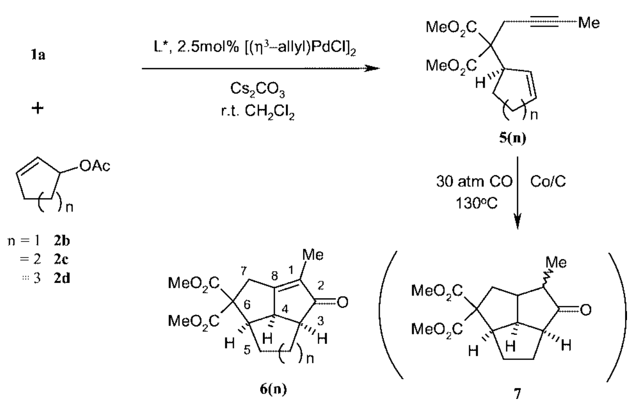
Table 2 Asymmetric one-pot synthesis of various cyclopentenones[a]

	Substrates	Product	L*	Base	Time/ h[b]	Yield (%)[c]	Ee (%)[d]
1	**1a 2a**	 **4(Me)**	**b**	BSA	4	81	95
2	**1b 2a**	 **4(Ph)**	**b**	BSA	6	95	84
3	**1c 2a**	 **4(Bu)**	**b**	BSA	4	84	93
4	**1a 2b**	 **6(1)**	**a** **d** **d**	BSA BSA CS_2CO_3[e]	10 24 12	95 85 92	— 33 94
5	**1a 2c**	 **6(2)**	**a** **d** **d**	BSA BSA Cs_2CO_3[e]	10 24 12	95 90 90	— 36 72
6	**1a 2d**	 **6(3)**	**a** **d** **d**	BSA BSA Cs_2CO_3[e]	10 24 12	89 93 97	— 4 31

[a] Reaction conditions: 6.0 mol% L* , 2.5 mol% [(η^3allyl)PdCl]$_2$, 0.2 g Co/C, and THF. Condtions for the 2nd step: 130 °C, 18 h, and 30 atm CO.[b] Reaction time of the first step at rt.[c] Isolated yield.[d] Diacel OD column was used.[e] CH_2Cl_2 as a solvent.

was isolated (entry 4 in Table 1). However, the Co/C was found to be insensitive to acid or base. Generally, for good enantioinduction, low temperatures are required. However, our reaction conditions in the second step seem to be quite harsh, nevertheless no racemization occurred under these reaction conditions. We also examined the catalytic asymmetric carbonylative cyclization of **3(R)** (R = Ph, *n*-Bu) (entries 2 and 3 in Table 2). Under our reaction conditions, **4(R)** were obtained in high yields (84–95%) with high ee values (84–95%). The usefulness of this combination catalyst is highlighted by the synthesis of various tricyclic enones **6(*n*)** (*n* = 1–3) (Scheme 2 and entries 4–6 in Table 2).



Scheme 2

The intramolecular Pauson–Khand reaction of cyclic enynes having cyclopentenes or cyclohexenes with pendant alkynes has been well studied.[11] Chiral ligand **d** developed by Trost[12] was selected since it is one of the best ligands in the Pd(II)-catalyzed asymmetric reaction of 2-cyclopentenyl, -hexenyl, or -hepenyl acetate with the anion of dimethyl malonate.[13] The reaction was quite sensitive to the base and the solvent used. The best results were obtained when Cs_2CO_3 and dichloromethane were used as a base and a solvent, respectively.[13] Interestingly, substrates **5(2)** and **5(3)** were known not to be cyclized with (EBTHI)-Ti(CO)$_2$.[1] However, fairly high yields (89–97%) were obtained in our case. In the cyclization of **5(1)**, the reduced **7** was obtained as a byproduct provided the generated acetic acid was not removed. In contrast to the high yields, the ee values (31–94%) were quite sensitive to the ring size. As the ring size increases, the ee values decrease. A fairly high ee value of 94% was obtained for **6(1)**. The absolute configuration (3*R*,4*R*,5*S*) of the tricyclic enone **6(*n*)** was determined by comparison with the known reactions.[13] The fused tricyclic systems such as **6(1)** and **6(2)** had been used in the synthesis of natural products.[14]

In summary, we have demonstrated that the tandem action of a homogeneous chiral Pd(II) catalyst and a heterogeneous Co/C catalyst leads to a two-step one-pot highly enantioselective Pauson–Khand-type reaction. The enantiomeric purity of the product depends upon the optical purity of the *in situ* generated enyne. Further synthetic applications of the tandem action of two different catalysts in other reactions are now in progress.

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Notes and references

1 For recent reviews, see: N. Jeong, in *Transition Metals in Organic Synthesis*, ed. M. Beller and C. Bolm, Wiley-VCH, Weinheim, 1998, vol. 1, p. 560; Y. K. Chung, *Coord. Chem. Rev.*, 1999, **188**, 297; K. M. Brummond and J. L. Kent, *Tetrahedron*, 2000, **56**, 3263.
2 F. A. Hicks and S. L. Buchwald, *J. Am. Chem. Soc.*, 1996, **118**, 11688.
3 K. Hirori, T. Watanabe, R. Kawagishi and I. Abe, *Tetrahedron Lett.*, 2000, **41**, 891.
4 N. Jeong, B. K. Sung and Y. K. Choi, *J. Am. Chem. Soc.*, 2000, **122**, 6771.
5 T. Shibata and K. Takagi, *J. Am. Chem. Soc.*, 2000, **122**, 9852.
6 R. W. Barnhart and G. C. Bazan, *J. Am. Chem. Soc.*, 1998, **120**, 1082; Z. J. A. Komon, X. Bu and G. C. Bazan, *J. Am. Chem. Soc.*, 2000, **122**, 1830; N. Jeong, S. D. Seo and J. Y. Shin, *J. Am. Chem. Soc.*, 2000, **122**, 10220; P. A. Evans and J. E. Robinson, *J. Am. Chem. Soc.*, 2001, **123**, 4609.
7 B. M. Trost and D. L. van Vranken, *Chem. Rev.*, 1996, **96**, 395.
8 X. Verdaguer, J. Vázquez, G. Fuster, V. Bernardes-Génisson, A. E. Greene, A. Moyano, M. A. Pericàsa and A. Riera, *J. Org. Chem.*, 1998, **63**, 7037; J. Castro, A. Moyano, M. A. Pericàsa, A. Riera, A. Alvarez-Larena and J. F. Piniella, *J. Am. Chem. Soc.*, 2000, **122**, 7944.
9 S. U. Son, S.-I. Lee and Y. K. Chung, *Angew. Chem., Int. Ed.*, 2000, **39**, 4158.
10 P. Von Matt and A. Pfaltz, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 566; J. Sprinz and G. Helmchen, *Tetrahedron Lett.*, 1993, **34**, 1769; G. J. Dawson, C. G. Frost, J. M. J. Williams and S. J. Coote, *Tetrahedron Lett.*, 1993, **34**, 3149.
11 C. Almansa, A. Moyano and F. Serratosa, *Tetrahedron*, 1988, **44**, 2657; J. Macro-Contelles and J. Ruiz, *Tetrahedron Lett.*, 1998, **39**, 6393; J. Cassayre and S. Z. Zard, *J. Organomet. Chem.*, 2001, **624**, 316.
12 B. M. Trost, D. L. van Vranken and C. Bingel, *J. Am. Chem. Soc.*, 1992, **114**, 9327.
13 B. M. Trost and R. C. Bunt, *J. Am. Chem. Soc.*, 1994, **116**, 4089; B. M. Trost and R. C. Bunt, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 99.
14 S. Takano, K. Inomata and K. Ogasawara, *Chem. Lett.*, 1992, 443; L. A. Paquette and S. Borrelly, *J. Org. Chem.*, 1995, **60**, 6912; J. Cassayre and S. Z. Zard, *J. Am. Chem. Soc.*, 1999, **121**, 6072.