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Palladium-catalyzed allylic substitution reaction: oxidative addition versus dissociation in an olefin–palladium(0) complex

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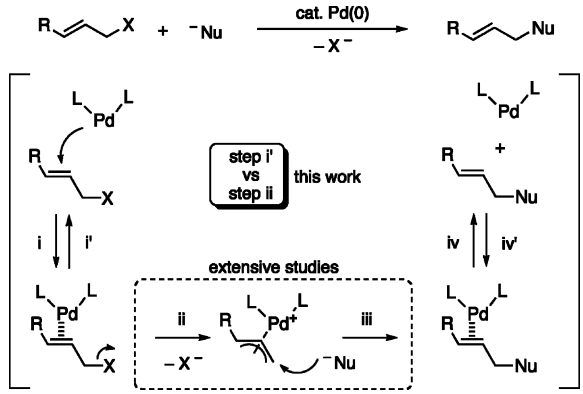
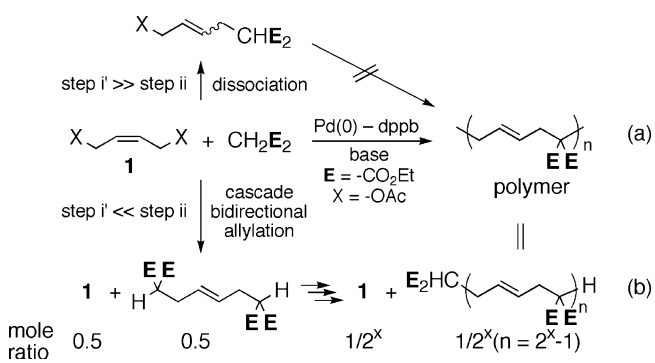
Abstract—The reaction behavior of a transient olefin–palladium(0) complex after the first allylation was studied. Highly efficient palladium-catalyzed cascade double alkylation of a diallylic substrate is achieved by tuning the ligands. As a result, bidentate ligands which could form cyclic catalysts with a four-methylene bridge between two phosphorus atoms were effective for high selectivity and catalytic activity. © 2002 Elsevier Science Ltd. All rights reserved.

Palladium-catalyzed allylic substitution reaction is an extremely versatile and powerful tool for C–C, C–O and C–N bond formation.[1] The general catalytic cycle is shown in Scheme 1: (i) olefin–metal complexation; (ii) ionization (oxidative addition); (iii) alkylation; (iv) dissociation. A number of studies have been reported on the ionization and alkylation steps (steps ii and iii) as well as allylpalladium complexes to reveal the origin of regio-, stereo- and enantioselectivity,[1] while much less effort has been devoted to the transient olefin–palladium(0) complex and its reaction behavior: ionization (step ii) and dissociation (step i′).[2,3]

We recently reported palladium-catalyzed allylic substitution polymerization[4] using a bifunctional substrate, (*Z*)-1,4-diacetoxybut-2-ene (**1**) and diethyl malonate (Scheme 2a), and found that the polymerization proceeded via a cascade bidirectional allylation mechanism[5] (Scheme 2b). We also referred to the possibility of C–C bond-forming *polycondensation out of stoichiometric control* according to its mechanistic rationale. In addition to the construction of a quantitative reaction system, exclusive selectivity of the cascade double alkylation of **1** is essential for development of this intriguing phenomenon to a practical level. Here, we focus on quantitative Pd-catalyzed cascade double alkylation of **1**, which is accessible via controlling the relative reaction rate between oxidative addition (step ii) and dissociation (step i′) in the olefin–palladium(0) complex. Although there had been many similar reports of the reaction between **1** and malonate esters,[6] the reaction conditions were not identical, and the ligand



Scheme 1. Catalytic cycle of palladium-catalyzed allylic alkylation.



Scheme 2. Mechanism of allylic substitution polymerization.

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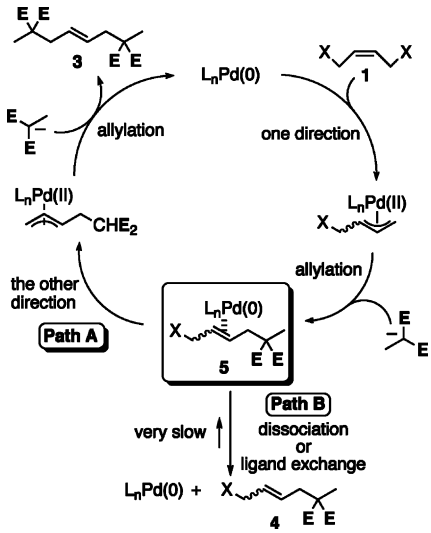
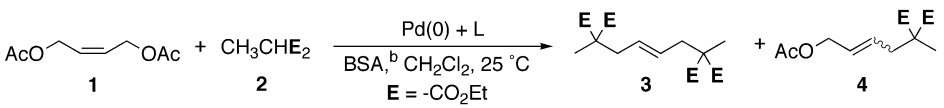
effects could not be assessed because of the sensitive selectivity of this reaction. We examined the reaction in detail using various ligands under the same reaction conditions (Table 1). Under the reaction conditions in Table 1, no regioisomers were detected at all, and regioselectivity turned out to be exclusive.[4] All of the reactions were monitored by TLC and quenched soon after either **1** or **2** was completely consumed, or after 24 h. Monoalkylated product **4** was preferentially obtained by use of PPh_3 (entry 1),[3,7] which indicated that dissociation of the olefin ligand from the olefin–palladium complex **5** after the first allylation readily occurred (path B, Scheme 3) before oxidative addition. Compound **4** reluctantly participated in further reactions, probably because of steric effects of the bulky malonic functionality.[8] Taking into consideration the poor reactivity of **4**, double-alkylated product **3** was mostly produced via successive formation of a π-allylpalladium complex from **5** (path A, Scheme 3).[9] ^{n}BuPPh$_2$, which was a more electron-rich ligand than PPh_3, induced a slightly higher selectivity of Path A than PPh_3 (entry 2), for electron-rich ligands of metals generally accelerate insertion reactions of metals to C–X bonds. Although the effects of the bridge lengths between two phosphorous atoms of bidentate ligands were unclear (entries 3–6), the reactions using dppe, dppp and dppb as ligands[10a] selectively proceeded via Path A to produce **3** (entries 4–6). Recently, van Leeuwen pointed out the importance of bite angles of bidentate ligands in some C–C bond-forming reactions,[11] where the bite angles greatly influenced both reactivity and selectivity. Although dppp effected an exclusive selectivity of the reaction pathways (entry 5), it was inappropriate for allylic substitution polymerization because of the slow reaction rate.[4,5] Dppb, which has a larger bite angle than those of dppe and dppp, accelerated the allylation reaction rate, but the selectivity of **3**/**4** slightly decreased (entry 6). We suspected that the bimetallic complex **6** (Fig. 1) or linear oligomeric complex **7** as well as the seven-membered cyclic monometallic complex **8** formed in situ, and that **6** or **7** gave **4** as the complex (^{n}BuPPh$_2$)$_2$Pd(0) (entry 2), while the cyclic complex **8** predominantly afforded **3**. When an equimolar amount of **2** to **1** was employed, the selectivity diminished (entry 7) because increasing the initial ratio of **1**/**2** accelerated the ligand exchange reaction between olefin–palladium(0) complex **5** and **1**. Interestingly, a



Scheme 3. Cascade bidirectional alkylation mechanism.

Table 1. Ligand effects on the reaction between **1** and **2**[a]



Entry	Ligand	Time (h)	Recovery of **1** (%)[c]	**3** (%)[c]	**4** (%)[c]	Total yield (%)[d]	**3**/**4**
1	2PPh$_3$	3	0	24	74	98	24/76
2	2^{n}BuPPh$_2$	1.3	2	38	58	98	39/61
3	dppm	24	89	<1	11	100	<5/95
4	dppe	9	0	89	11	100	89/11
5	dppp	16	0	99	<1	99	>99/1
6	dppb	0.7	0	93	3	96	97/3
7	dppb[e]	0.7	39	45	10	94	82/18
8	1.5 dppb[e]	0.3	20	28	43	91	39/61
9	dppxy	1.3	0	98	<1	98	>99/1
10	dppcyh	2	1	99	<1	>99	>99/1
11	dpppen	1	0	44	52	96	46/54
12	dpphex	0.7	0	30	66	96	31/69
13	Xantphos	1.3	0	16	65	81[f]	20/80

[a] Reaction conditions: **1**, 0.50 mmol; **2**, 1.5 mmol; BSA, 3.0 mmol; $Pd_2(dba)_3$, 5 μmol (1 mol%); bidentate ligand, 10 μmol (2 mol%) (monodentate ligand, 20 μmol (4 mol%)); CH_2Cl_2, 1 mL, 25°C.

[b] *N*,*O*-Bis(trimethylsilyl)acetamide.

[b] Isolated yield.

[b] Total yield = recovered **1**+**3**+**4**.

[b] 1 equiv. of **2** (0.50 mmol) was employed. Complete conversion of **2** was monitored by TLC and ^{1}H NMR analysis.

[b] Unidentified byproducts were also obtained.

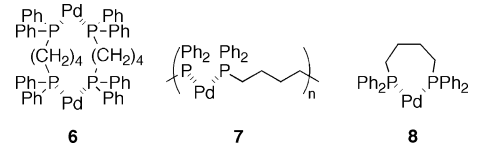


Figure 1. Plausible structures of Pd–dppb complexes.

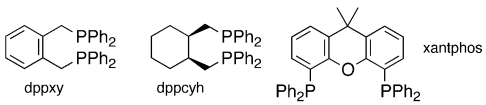


Figure 2. Some ligands.

slightly excess amount of the phosphine ligand to palladium (1.5 equiv. to Pd) reversed the selectivity (entry 8). Since tertiary phosphines strongly coordinate to the palladium center, the excess phosphine might also accelerate path B by the ligand exchange. The exclusive selectivity and high reactivity were obtained by use of 1,2-bis(diphenylphosphino)xylylene (dppxy, Fig. 2) and *cis*-1,2-bis(diphenylphosphinomethyl)cyclohexane (dppcyh),[10b] whose two phosphorous atoms were tethered by four carbons similar to dppb, and which tended to form a cyclic monometallic catalysts (entries 9 and 10). As expected, the ligands with five and six methylenes between two diphenylphosphino groups, gave the selectivities of path B (entries 11 and 12) similar to ^{n}BuPPh$_2$. Xantphos,[10c,11] which had been documented to be a useful ligand in several reactions, reversed the selectivity in spite of its larger bite angle (entry 13). To confirm the reaction pathway using dppb, dppxy and dppcyh, the ratios of **3**/**4** were also analyzed at several conversions of **1** under the same conditions. The ratio of **3**/**4** was always >99/1 in the dppxy[12] and dppcyh[13] systems, and the exclusive cascade double alkylation was proved. The path-selectivity of dppb[14] was not exclusive, while the ratio of **3**/**4** was maintained at 97/3 until 100% conversion of **1**.

In conclusion, the reaction behavior of transient olefin–palladium(0) complexes (oxidative addition versus dissociation) was systematically examined. It turned out that the fine tuning of ligands such as electronic and steric effects, structural flexibility, bite angles and amounts were extremely important for controlling the reaction pathways in this reaction. As a result, bidentate ligands which could form cyclic catalysts with a four-methylene bridge between two phosphorus atoms, were effective toward oxidative addition. In addition, the reaction pathway was changed by a slightly excess amount of the ligand to the palladium center. Since this reaction itself is a convenient system to assess the relative reaction rate between oxidative addition and dissociation, it is useful to reveal characteristics of various ligands in the state of olefin–Pd(0) complexes. We are now working on practical C–C bond-forming *polycondensation out of stoichiometric control* based on these results.

Acknowledgements

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12. Conversion of **1** (**3**/**4**) using dppxy: 12% (>99/1); 34% (>99/1); 48% (>99/1); 68% (>99/1).
13. Conversion of **1** (**3**/**4**) using dppcyh: 21% (>99/1); 45% (>99/1); 59% (>99/1); 78% (>99/1).
14. Conversion of **1** (**3**/**4**) using dppb: 22% (97/3); 43% (97/3); 80% (97/3); 96% (97/3).