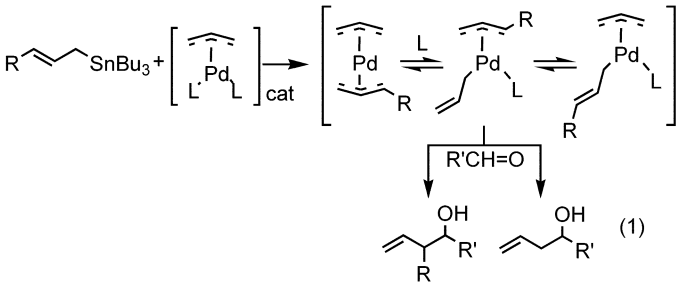
Pd-Catalyzed Allylation

Palladium-Catalyzed Electrophilic Substitution via Monoallylpalladium Intermediates

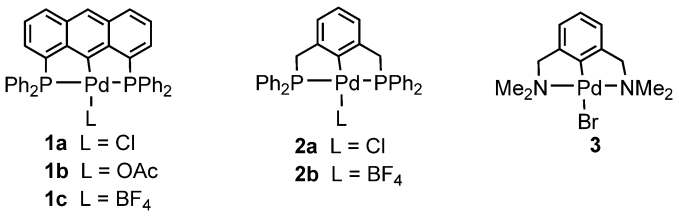
*Niclas Solin, Johan Kjellgren, and Kálmán J. Szabó**

Allylpalladium chemistry is one of the most successful areas in transition-metal catalysis. In the most common application of these complexes an allylpalladium intermediate is generated which subsequently reacts with nucleophiles.[1] The recent extension of the synthetic scope of these compounds to reactions with electrophilic substrates has attracted much attention. [2,3] It was shown that in order for the allyl moiety to have nucleophilic reactivity bisallylpalladium intermediates must be generated [Eq. (1)].[2a,3a] However, the diverse reactivity of the bisallylpalladium



(1)

intermediates imposes considerable synthetic limitations on the reaction. Controlling the regioselectivity is difficult when the two allylic moieties bear different substituents [cf. Eq. (1)].[3b,c] A further problem is that bisallylpalladium complexes may undergo allyl–allyl (Stille) coupling prior to the reaction with electrophiles.[2d] Because of these limitations it would be desirable to conduct the catalytic transformations with monoallylpalladium intermediates. This is a challenging task, since it is well known that monoallylpalladium complexes react with nucleophiles.[1] Nevertheless, our previous mechanistic studies showed that the electrophilic attack on a bisallylpalladium complex proceeds through the η^1-coordinated allyl moiety,[3a–b] while the other, η^3-coordinated allyl group acts as a strong π-donor spectator ligand [cf. Eq. (1)]. This model suggests that the catalytic generation of an (η^1-allyl)palladium intermediate coordinated to an electron-donating spectator ligand provides nucleophilic reactivity to the allyl moiety. We have now found that this type of reactivity occurs when so-called pincer complexes[4] (**1**–**3**, Scheme 1) are employed in palladium-catalyzed electrophilic substitution of allylstannanes **4a**–**c** [Eq. (2)].

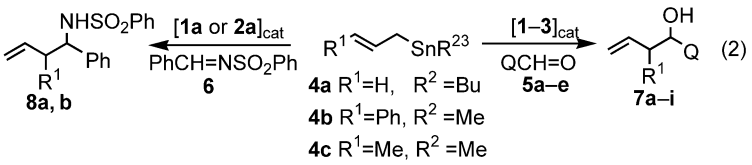


1a L = Cl
1b L = OAc
1c L = BF_4

2a L = Cl
2b L = BF_4

3

Scheme 1. Pincer complexes used as catalysts.



4a R^1=H, R^2 =Bu
4b R^1=Ph, R^2 =Me
4c R^1=Me, R^2 =Me

(2)

The reactions were performed with **4a**–**c** and various aldehydes **5** and imine **6** in the presence of catalytic amounts of **1**–**3** to obtain homoallylic alcohols **7** and amines **8**, respectively (Table 1). Complexes **1a**[4c] and **2a**[5a,c] showed high catalytic activity and very high stability under the reaction conditions. Although the reactions could be performed in many different solvents, the best results were obtained in DMF (for **1a**) and THF (for **2a**). Activated aldehydes **5b**–**e** reacted faster and usually with a higher yield than benzaldehyde (**5a**) itself (entries 1–9). The reactions proceed under neutral reaction conditions without added base or Lewis-acid catalyst, and therefore, many functionalities, such as NO_2, F, CN, and CH_3CO are tolerated (entries 3–9). Cinnamylstannane **4b** readily undergoes palladium-catalyzed allylic substitution providing exclusively the branched allylic products **7g**, **7h**, and **8b** with high diastereoselectivity (entries 13–15, 17). The corresponding reaction with crotylstannane **4c** also gives the branched allylic isomer **7i**, albeit without stereoselectivity (entry 16). The N-Pd-N type complex **3**[4a] was also tested in these reactions (entry 15); however, it showed lower catalytic activity than **1a** and **2a**. We attempted to increase the catalytic activity of **1a** and **2a** by replacing the chloride ligand with acetate (**1b**) and with tetrafluoroborate (**1c** and **2b**). These complexes displayed a very high initial catalytic activity even at room temperature; however, within a couple of hours these catalysts were completely deactivated. Nevertheless, complexes **1b** and **1c** were stable enough to achieve full conversion of **4a** with activated aldehyde **5e** (entries 7 and 8) at moderate temperature.

Transition-metal pincer complexes are widely used in organometallic chemistry and catalysis.[4] Complex **2** is known to readily undergo transmetalation with organometallic reagents.[5b,c] For example, Cotter and co-workers[5b] have shown that 2-furylstannane undergoes tin-to-palladium transmetalation with the triflate salt of **2**. It is reasonable to assume that the first step in the above reaction [Eq. (2)] is also transmetalation of the allylstannane **4** with the pincer

[*] Prof. Dr. K. J. Szabó, N. Solin, J. Kjellgren
Deparment of Organic Chemistry
Stockholm University
SE-10691 Stockholm (Sweden)
Fax: (+46) 8-154-908
E-mail: kalman@organ.su.se

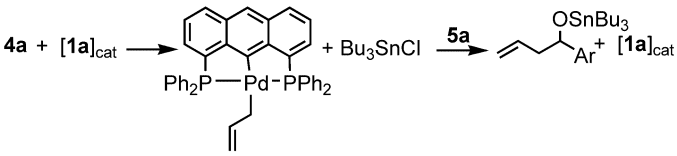
  DOI: 10.1002/anie.200351477

Table 1: Palladium-catalyzed[a] electrophilic substitution reactions [Eq. (2)].

Entry	Substrates		Cat.	Prod.	Q	R^1	Solv.	Cond. [b]	Yield [%][c]
1	**4a**	**5a**	**1a**	**7a**	C_6H_5	H	DMF	60/22	81
2	**4a**	**5a**	**2a**	**7a**	C_6H_5	H	THF	60/21	88
3	**4a**	**5b**	**1a**	**7b**	4-FC_6H_5	H	DMF	60/22	77
4	**4a**	**5c**	**1a**	**7c**	4-CNC_6H_5	H	DMF	60/17	88
5	**4a**	**5d**	**1a**	**7d**	4-$CH_3COC_6H_5$	H	DMF	60/17	82
6	**4a**	**5e**	**1a**	**7e**	4-$NO_2C_6H_5$	H	DMF	60/17	82
7	**4a**	**5e**	**1b**	**7e**	4-$NO_2C_6H_5$	H	$CHCl_3$	40/2	95
8	**4a**	**5e**	**1c**	**7e**	4-$NO_2C_6H_5$	H	$CHCl_3$	20/3	95
9	**4a**	**5e**	**2a**	**7e**	4-$NO_2C_6H_5$	H	THF	40/21	95
10	**4a**	**5f**	**2a**	**7f**	cinnamyl	H	THF	60/21	80
11	**4a**	**6**	**1a**	**8a**	–	H	DMF	60/17	66
12	**4a**	**6**	**2a**	**8a**	–	H	THF	60/21	69
13	**4b**	**5a**	**2a**	**7g**	C_6H_5	Ph	THF	60/21	61[d]
14	**4b**	**5e**	**2a**	**7h**	4-$NO_2C_6H_5$	Ph	THF	60/21	95[d]
15	**4b**	**5e**	**3**	**7h**	4-$NO_2C_6H_5$	Ph	THF	20/64	85[d]
16	**4c**[e]	**5e**	**1a**	**7i**	4-$NO_2C_6H_5$	Me	DMF	60/14	77[f]
17	**4b**	**6**	**2a**	**8b**	–	Ph	THF	60/21	65 [g]

[a] Catalyst amount: 5 mol%. [b] Temperature [°C]/time [h]. [c] Yield of isolated product. [d] Diastereomer ratio *anti*/*syn*[6a] = 10:1. [e] *Z*/*E* ratio = 2:1. [f] Diasteromer ratio *syn*/*anti*[6b] = 1:1. [g] Diastereomer ratio *syn*/*anti*[6c] = 12:1.

complex (**1**, **2**). Because of the strong η^3-coordination of the pincer ligands to palladium only one coordination site is available for the allyl moiety. Accordingly, an η^1-allyl complex is formed, in which the allyl moiety is *trans* to the strongly electron-donating phenyl group [Eq. (3)]. This structure lends nucleophilic character to the allyl moiety, which is similar to



(3)

that of the η^1 moiety in the bisallylpalladium intermediates [cf. Eq. (1)]. Subsequently, the η^1-allyl complex reacts with electrophiles (**5**, **6**) providing the final product of the reaction (**7**, **8**).

An alternative mechanism may involve Lewis-acid-type activation of the aldehydes by the pincer complexes.[4a,5d] However, **1c** and **2b** undergo rapid reaction with **4a** even in the absence of aldehydes. When this reaction was carried out with **1c** and **4a** or (allyl)trimethylstannane at −10 °C in $CDCl_3$, rapid formation of propene was observed by ^{1}H NMR spectroscopy. This process indicates transmetalation of the allylstannane with palladium [cf. Eq. (3)] followed by protonation of the η^1-allyl moiety by traces of water present in the reaction mixture. The high proton affinity of the η^1-allyl moiety is a characteristic feature of bisallylpalladium complexes.[3d,5e,5f] Further evidence for the transmetalation mechanism is provided by the high reactivity of sulfonimine **6** (Table 1, entries 11, 12, and 17), which cannot be activated by Lewis-acid catalysts.

In summary, we have found a new procedure for palladium-catalyzed electrophilic substitution of allylstannanes. In this procedure pincer complexes **1**–**3** serve as catalyst sources. In contrast to previous applications proceeding via bisallylpalladium intermediates this reaction is thought to involve monoallylpalladium intermediates. Application of this procedure eliminates the side reactions that occur in bisallylpalladium-catalyzed transformations, thus extending the synthetic scope of electrophilic reagents in allylpalladium chemistry.

Experimental Section

Representative procedure for palladium-catalyzed allylation of electrophiles: To a mixture of the aldehyde (0.15 mmol) and **1a** (5 mg, 0.007 mmol) in DMF (0.5 mL) was added **4a** (59.7 mg, 0.18 mmol). This solution was then heated at the designated temperature for the allotted time (Table 1). Subsequently, the reaction mixture was quenched by addition of water and extracted with ether. The collected organic phases were dried and concentrated to dryness, and then purified by chromatography with pentane/ethyl acetate as the eluent.

Received: March 25, 2003 [Z51477]

Keywords: aldehydes · allylation · electrophilic substitution · homogenous catalysis · palladium

[1] J. Tsuji in *Palladium Reagents and Catalysis: Innovations in Organic Synthesis*, Wiley, Chichester, **1995**.

[2] a) H. Nakamura, H. Iwama, Y. Yamamoto, *J. Am. Chem. Soc.* **1996**, *118*, 6641; b) H. Nakamura, J.-G. Shim, Y. Yamamoto, *J. Am. Chem. Soc.* **1997**, *119*, 8113; c) H. Nakamura, K. Aoyagi, J.-G. Shim, Y. Yamamoto, *J. Am. Chem. Soc.* **2001**, *123*, 372; d) H. Nakamura, M. Bao, Y. Yamamoto, *Angew. Chem.* **2001**, *113*, 3308; *Angew. Chem. Int. Ed.* **2001**,*40*, 3208.

[3] a) K. J. Szabó, *Chem. Eur. J.* **2000**, *6*, 4413; b) N. Solin, S. Narayan, K. J. Szabó, *J. Org. Chem.* **2001**, *66*, 1686; c) N. Solin, S. Narayan, K. J. Szabó, *Org. Lett.* **2001**, *3*, 909; d) O. A. Wallner, K. J. Szabó, *Org. Lett.* **2002**, *4*, 1563; e) O. A. Wallner, K. J. Szabó, *J. Org. Chem.* **2003**, *68*, 2934.

[4] a) M. Albrecht, G. van Koten, *Angew. Chem.* **2001**, *113*, 3866; *Angew. Chem. Int. Ed.* **2001**,*40*, 3751; b) J. T. Singleton, *Tetrahe-*

dron **2003**, *59*, 1837; c) M. W. Haenel, S. Oevers, J. Bruckmann, J. Kuhnigk, C. Krüger, *Synlett* **1998**, 301.
[5] a) H. Rimml, L. M. Venanzi, *J. Organomet. Chem.* **1983**, *259*, C6; b) W. D. Cotter, L. Barbour, K. L. McNamara, R. Hechter, R. J. Lachicotte, *J. Am. Chem. Soc.* **1998**, *120*, 11016; c) H. Rimml, Ph.D. Thesis, ETH Zürich, **1984**, d) Y. Motoyama, M. Okano, H. Narusawa, N. Makihara, K. Aoki, H. Nishiyama, *Organometallics* **2001**, *20*, 1580; e) P. W. Jolly, *Angew. Chem.* **1985**, *97*, 279; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 283; f) J. Kiji, T. Okano, T. Nomura, K. Saiki, T. Sai, J. Tsuji, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1939.
[6] The diastereomer ratios were established on the basis of NMR data: a) J. P. Takahara, Y. Masuyama, Y. Kurusu, *J. Am. Chem. Soc.* **1992**, *114*, 2577; b) R. A. Batey, A. N. Thadani, D. V. Smil, A. J. Lough, *Synthesis* **2000**, 990; c) W. Lu, T. H. Chan, *J. Org. Chem.* **2000**, *65*, 8589.

