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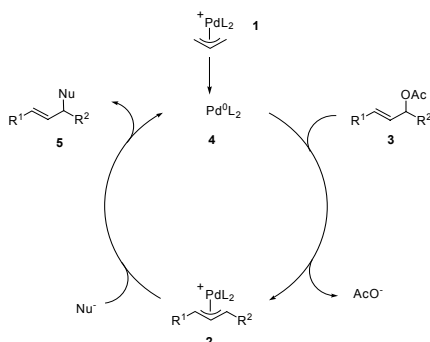
Allylic substitution reactions were investigated by Electrospray Ionisation Mass Spectrometry (ESI-MS). Furthermore, a microreactor system on-line coupled to ESI mass spectrometer was used for directly detecting intermediates in solution.

Introduction

Electrospray ionization mass spectrometry allows the observation of intermediates involved in catalytic reactions. Here, we report the first results of our investigations into palladium-catalyzed allylic substitution reactions.

Results and Discussion

Palladium-catalyzed reactions of allylic compounds via the formation of π -allylpalladium complexes offer many synthetically useful methods.^[1] The first step of the catalytic cycle is the formation of palladium-allyl complex **2** by oxidative addition of the allylic ester **3** to the Pd(0) species **4**, and the second step is the reaction of **2** with the nucleophile to give product **5** (Scheme 1).



Scheme 1. Pd-catalyzed allylic substitution reaction. L = ligand $P^{\wedge}P$, $P^{\wedge}P$ (Fig. 1); $Nu^- = ^-CEt(CO_2Et)_2$; a: $R^1 = R^2 = Ph$, b: $R^1 = Me$, $R^2 = H$, c: $R^1 = R^2 = Me$.

We used the chiral ligand $P^{\wedge}P$ **6** (Fig. 1) and the anion of diethyl ethylmalonate as the nucleophile.^[2]

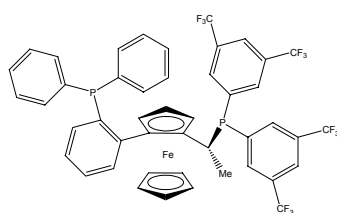


Fig. 1. Ligand $P^{\wedge}P$ **6**: (R)-(-)-1-[(R)-2-(2'-Diphenylphosphinophenyl)ferrocenyl]ethyl-di(bis-3,5-trifluoromethylphenyl)phosphane.

The allylation of diethyl ethylmalonate with methyl-, dimethyl- and diphenyl allyl acetates was studied by ESI-MS. Palladium complex $[Pd(C_3H_5)(P^{\wedge}P)OTf]$ (**1**) was used as precatalyst. The data being directly acquired from the reaction mixture. The formation of Pd-bond allyl intermediate $[Pd(PhC_3H_3Ph)(P^{\wedge}P)OTf]$ (**2a**) from the Pd precatalyst $[Pd(C_3H_5)(P^{\wedge}P)OTf]$ (**1**) is presented in Fig. 2. Comparison of the intensity of the signals of Pd allyl intermediates $[Pd(MeC_3H_4)(P^{\wedge}P)OTf]$ (**2b**) and $[Pd(MeC_3H_3Me)(P^{\wedge}P)OTf]$ (**2c**) in ESI mass spectrum (Fig. 3) shows, that in the competition reaction, obviously the methyl allyl acetate (**3b**) is more reactive than dimethyl allyl acetate (**3c**).

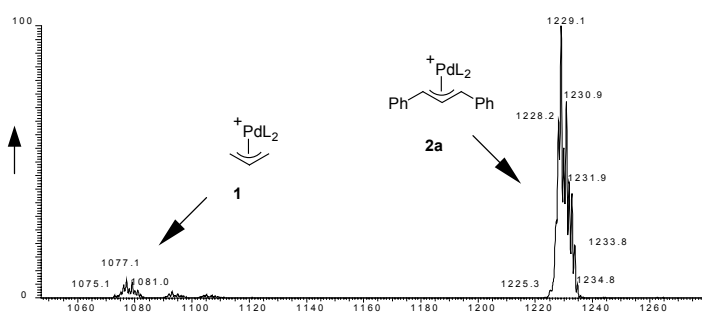


Fig. 2. Positive mode ESI mass spectrum of the reacting solution of diphenyl allyl acetate (**3a**), palladium complex $[Pd(C_3H_5)(P^{\wedge}P)OTf]$ (**1**) and diethyl ethyl malonate in CH_2Cl_2 (10^{-5} M) (ratio 50:1:2).

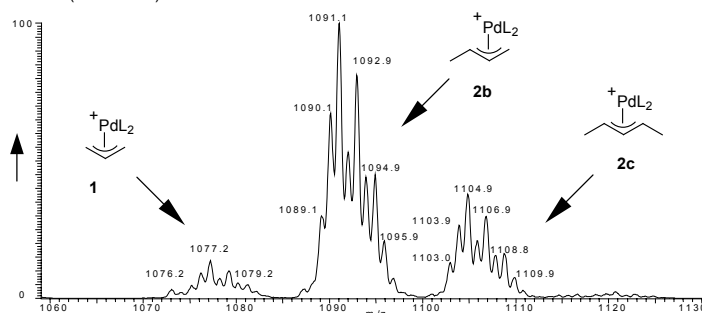


Fig. 3. Positive mode ESI mass spectrum of the reacting solution of methyl allyl acetate (**3b**), dimethyl allyl acetate (**3c**), palladium complex $[Pd(C_3H_5)(P^{\wedge}P)OTf]$ (**1**) and diethyl ethyl malonate in CH_2Cl_2 (10^{-5} M) (ratio 25:25:1:2).

The solution of diphenyl allyl acetate (**3a**) and palladium catalyst precursor $[Pd(C_3H_5)(P^{\wedge}P)OTf]$ **1** in MeCN (10^{-5} M) and of nucleophil (diethyl ethylmalonate), respectively, in MeCN (10^{-5} M) were mixed by using an effective micro reactor which was directly coupled to the ESI mass spectrometer. It was clearly detected the increasing of the signal of the Pd-allyl intermediate (m/z 1229) in the spectrum of the reacting solution after reaction time ca. 30 sec (Fig. 4).

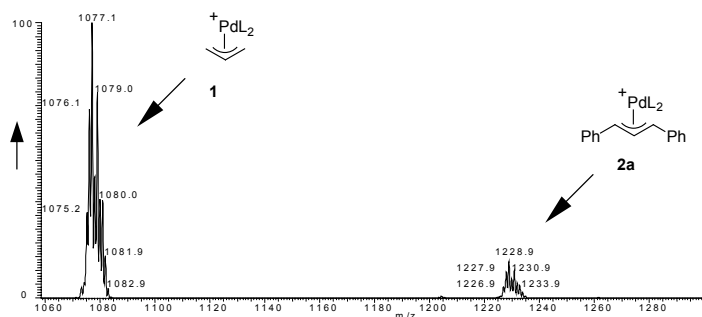


Fig. 4. Positive mode ESI mass spectrum of the reacting solution of diphenyl allyl acetate (**3a**), palladium catalyst precursor $[Pd(C_3H_5)(P^{\wedge}P)OTf]$ (**1**) in MeCN (10^{-5} M) and diethyl ethyl malonate in MeCN (10^{-5} M) (ratio 50:1:2, reaction time ca. 30 sec).

Acknowledgment

We thank the German Research Association (DFG) for financial support.

[1] J. Tsuji, *Palladium Reagents and Catalysts-New Perspectives for the 21st Century*, 2nd ed, John Wiley&Sons Ltd, 2004, pp. 431-517.
[2] C. Markert, A. Pfaltz, *Angew. Chem., Int. Ed.* **2004**, 43, 2498.