

Survival of the Weakest

Ligand Selection Using Mass Spectrometry in the Pd-catalyzed Allylic Substitution

Eveline Jansen, Jeroen Wassenaar and Joost N.H. Reek

Homogeneous and Supramolecular Catalysis, van 't Hoff Institute of Molecular Sciences, Universiteit van Amsterdam
Nieuwe Achtergracht 166, 1018 WV Amsterdam
jansen@science.uva.nl



1. Introduction

The success of combinatorial approaches in catalysis relies to a great extent on efficient screening technologies of catalyst libraries. Several high-throughput screening techniques have been reported, including the application of electrospray ionization mass spectrometry (ESI-MS), and generally the efficiency of all catalysts is measured.¹ Pfaltz recently showed that by labelling the relative rate of oxidative addition of pseudo enantiomers can be measured by MS, using mixtures of catalysts.²

We are interested in *selection* as an alternative for *screening*, which theoretically should be possible if there is a correlation between the stability of a intermediate and catalyst activity (figure 1). Here we report our first results, using the Pd-catalyzed allylic substitution as model reaction and ESI-MS as analytical tool.

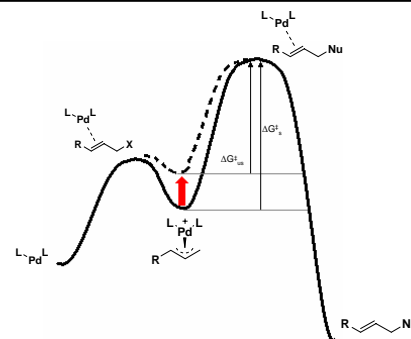
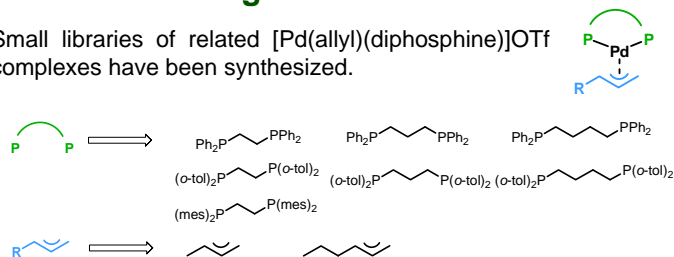


Figure 1. Energy Diagram

2. Investigation of Pd-libraries

Small libraries of related [Pd(allyl)(diphosphine)]OTf complexes have been synthesized.



A mixed library was created from a starting complex of one of the [Pd(allyl)(diphosphine)] complexes to which ligands were added. The equilibrium mixture analyzed with ESI-MS showed a non-statistical mixture (figure 2).

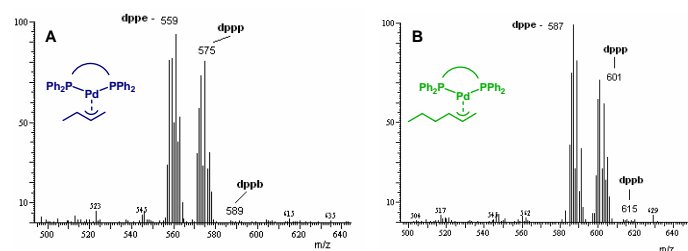
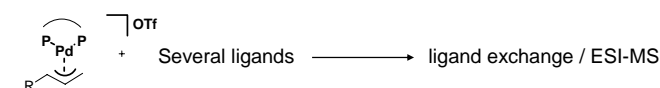


Figure 2. ESI-MS spectra of the A) Pd(crotyl)(diphosphine) and B) Pd(hexenyl)(diphosphine) library.

The ESI-MS signal was calibrated for all synthesized complexes.

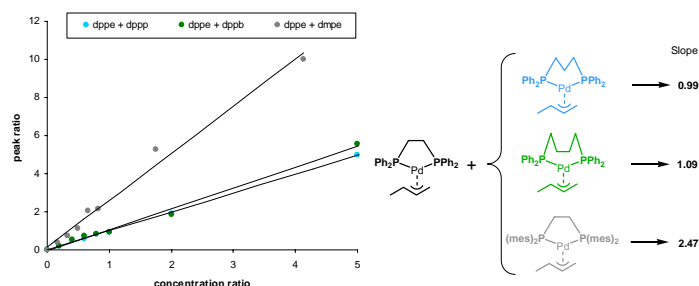
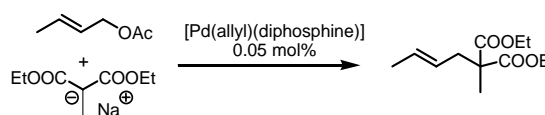


Figure 3. Plot of peak ratio in the mass spectrum as a function of the ratio of the concentration for three examples of the performed calibration.

3. Catalysis: Allylic Alkylation

Table 1. Allylic Alkylation³ of crotyl acetate by [Pd(allyl)(diphosphine)]



Entry	Complex	m/z	TOF (mol.mol ⁻¹ .h ⁻¹)
1.	Pd(crotyl)(dppe)	559	2000
2.	Pd(crotyl)(dppp)	573	2900
3.	Pd(crotyl)(dppb)	589	8900
4.	Pd(hexenyl)(dppe)	587	82
5.	Pd(hexenyl)(dppp)	601	111
6.	Pd(hexenyl)(dppb)	615	393

Good correlation between TOF and the intensity of the signals in the mass spectrum is observed: the more active catalyst is less present in the ESI-MS spectra (figure 4).

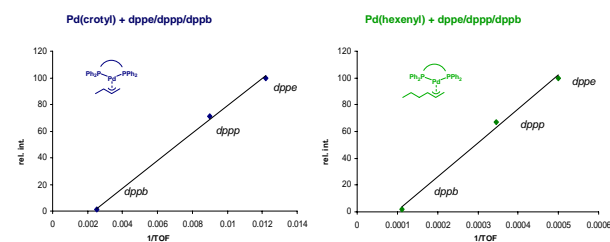


Figure 4. Plot of the relative intensity of complex peaks in the mass spectrum as a function of 1/TOF for palladium complexes in a homologue series.

4. Conclusion

A semi-quantitative correlation was observed between catalytic activity displayed by a catalyst and the intensity of its peak in the mass spectrum. These preliminary data demonstrate that selection procedures based on stability-activity correlation are feasible, which opens fundamentally new ways to find active catalysts from certain conversions.

5. References

- 1 a) M.T. Reetz, *Angew. Chem. Int. Ed.* **2001**, *40*, 284-310; b) M. T. Reetz, *Angew. Chem. Int. Ed.* **2002**, *41*, 1335-1338
- 2 C. Markert, A. Pfaltz, *Angew. Chem. Int. Ed.* **2004**, *43*, 2498
- 3 Results taken from the thesis of R.van Haaren and *Chem.Rev.* **2000**, *100*, 2741-2769