Kinetic Studies in CombiCat with On-line Spectroscopy

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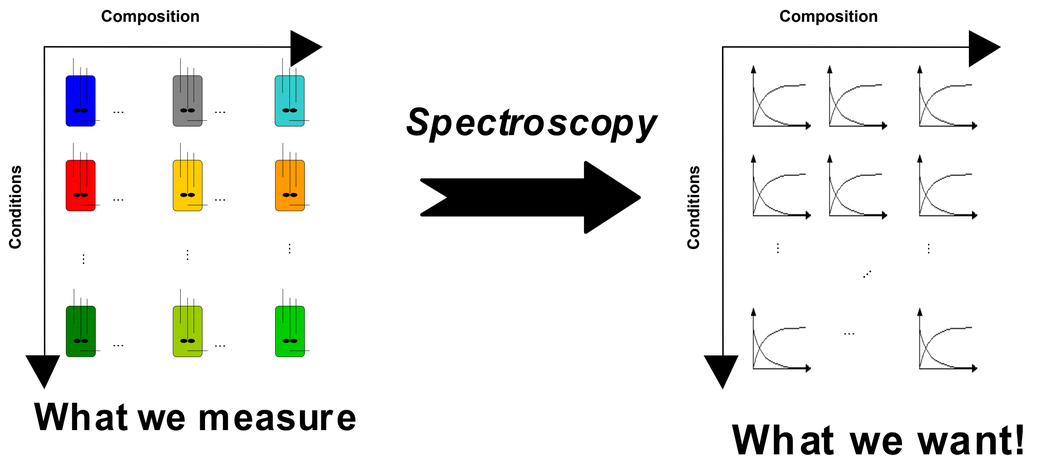
Introduction

Combinatorial catalysis is a new field that brings together rational catalyst design and high throughput experimentation. Much effort is focused on new methods for the synthesis and screening of catalyst libraries using novel techniques. These new methods should go hand-in-hand with data analysis development, since the amount of data generated in these systems is large.

Many high throughput systems are based on off-line chromatography methods (GC/HPLC) that are slow to tackle a large number of reactions simultaneously. Spectroscopy has some advantages over GC and HPLC:

- It is faster (sampling every *ca.* 5 seconds);
- It is non-invasive and non-destructive;
- Sample preparation is easier;
- Multiplexing.



We aim to develop chemometric methods to estimate **kinetic parameters** from spectroscopic data for multiple reaction sets. The underlying relationships within these sets will be the basis of the multiblock analysis methods.

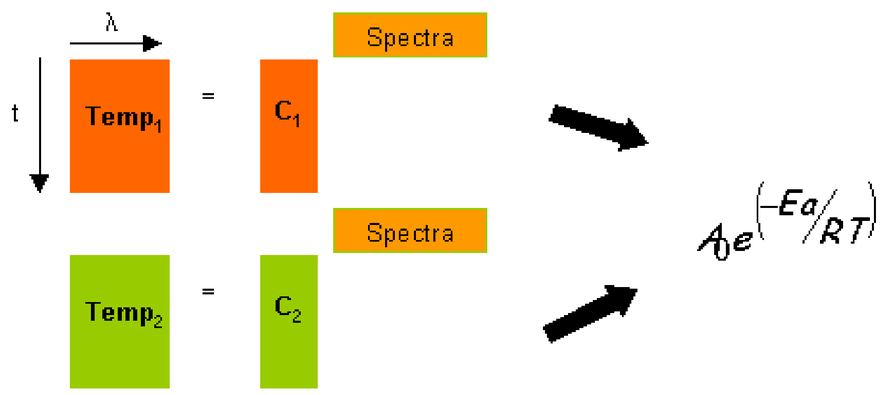
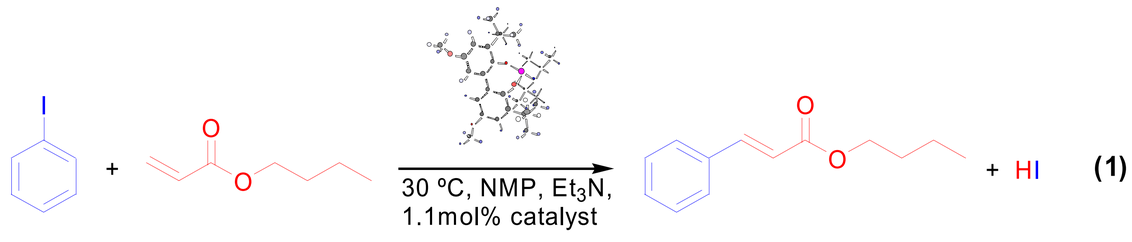


Figure 1:Multiblock Data Analysis.

For example, if a series of reactions is run using the same catalyst at different temperatures the Arrhenius equation, $k_{obs} = A_0.e^{(-Ea/RT)}$, could be used to analyse the effects of temperature changes on the reaction rate constant (Figure 1). The same equation can also be used to analyse the effects of small changes in catalyst structure on E_a and A_0 providing that the reaction mechanism does not change.

Results

The Heck coupling between Iodobenzene and *n*-butyl acrylate catalysed by a bulky monodentate phosphoamidite palladium complex was chosen as a model reaction. With monodentate ligands this reaction was reported to follow a first-order mechanism with the migratory insertion step being rate-determining[1]. We followed this reaction using GC, RAMAN, and FT-NIR until 40% conversion.



Quantitative GC analysis was performed using the internal standard method. For Raman, we used a univariate calibration model using test samples with concentrations ranging 0.05M to 0.3M. FT-NIR calibration was done using the Net Analyte Signal (NAS) approach[2].

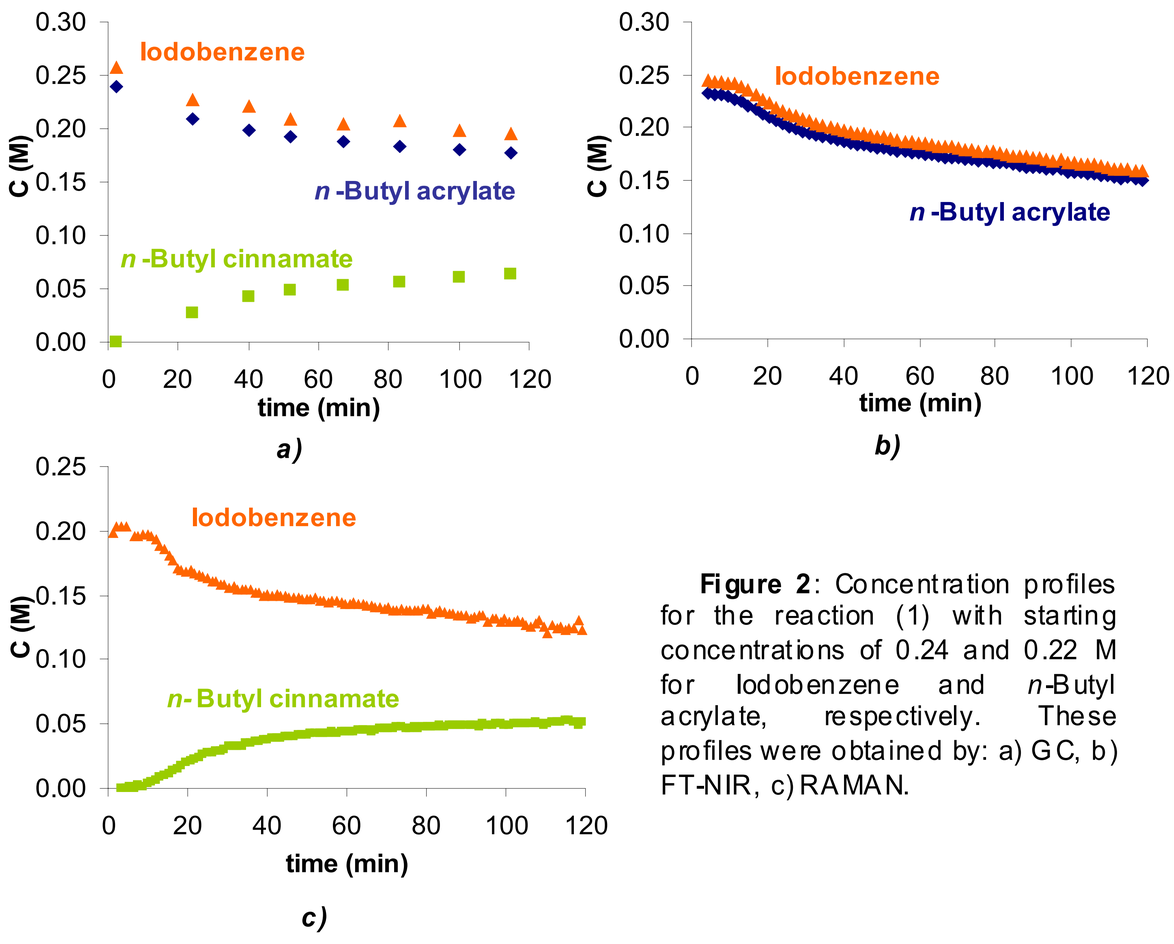


Figure 2: Concentration profiles for the reaction (1) with starting concentrations of 0.24 and 0.22 M for Iodobenzene and *n*-Butyl acrylate, respectively. These profiles were obtained by: a) GC, b) FT-NIR, c) RAMAN.

The profiles of all the compounds are consistent. However, actual concentration is somewhat lower in the case of Raman. The increasing coloring of the reaction and the fluorescence are problematic for the spectroscopic techniques. Going from GC to spectroscopy we observe a new phenomenon: the reaction starts slowly and only after *ca.* 10 minutes proceeds with approximately constant velocity. This activation period observed now at 30ºC, and not detected at higher temperatures[1], is thought to be caused by the equilibrium of the palladium complex with its dimer. Further exploration of kinetics for this system is in progress.

Conclusions

We have shown that fast spectroscopy has the advantage over chromatography as it allows one to obtain more information about the reaction over the same time period. However, the calibration of spectrocopic techniques is time-consuming and complex. We are now busy with optimising these calibrations.

Acknowledgments

We thank Gino van Strijdonck and Maarten Boele for a generous gift of the palladium catalyst complex.

[1]Van Strijdonck, G.P.F., *et al., Eur. J. Inorg. Chem.*, **1999**, 1073.

[2]Lorber, A., *et al.*, *Anal. Chem.*, **1997**, 1620.