

Screening Carbonylation Reactions Sampling at Elevated Pressure



Based on studies by **Theresa Makowski** and **David Place**, Pfizer

Automated sampling enables researchers to gain insight into reactions at elevated pressure. This improves productivity and reaction understanding, and reduces costs.

Sampling reactions at elevated pressure, without breaking pressure and affecting reaction progression, is very tedious. It is common that only two samples are taken, providing information on the reaction at just the beginning and end of the experiment. No information on what happens during the reaction is available, and researchers are left with large blind spots in their data. In this Palladium-Catalyzed Carbonylation reaction, the effects of solvent-dependent degradation of the chiral center were studied by taking advantage of the automated sampling abilities of EasySampler. The reaction was sampled throughout the duration of the experiment, without affecting the reaction progression and thus providing (immediate and in-depth) insight to this reaction at elevated pressure.

The reaction was at a concentration of approximately 116 mg/mL, and run in the presence of palladium catalyst. The reaction temperature was 80 °C and the reactor pressure 50 psi. The two solvents screened were methanol and 2-MeTHF. To sample the reactions continuously, EasySampler was programmed to take 13 and 12 samples, respectively, and samples were analyzed by UPLC.



Figure 1. EasySampler probe in a pressure reactor

Results

The data gathered throughout the entire course of the reactions provided insight to the solvent-dependent degradation of the chiral center. The data shows that methanol degraded the chiral center (Figure 2), while switching solvent to 2-MeTHF provided consistent conversion without the degradation of the chiral center (Figure 3).

Conclusions

The application of EasySampler for sampling reactions at elevated pressure enables the acquisition of high quality samples throughout the duration of the reaction, providing more information from a single experiment. The analytical data gained from these high quality samples provides complete and accurate reaction information for improved reaction understanding, thus enabling better decisions at an earlier stage. Overall, EasySampler improves productivity and decreases costs by reducing the number of experiments required, and enabling better experiment planning and scheduling.

"EasySampler provides a method to sample without breaking pressure – this is pretty huge"

Dr. David Place, Pfizer

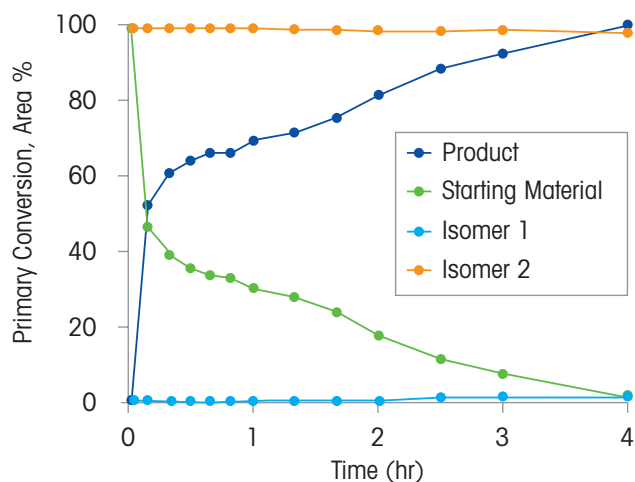


Figure 2. Pd-catalyzed Carbonylation in Methanol

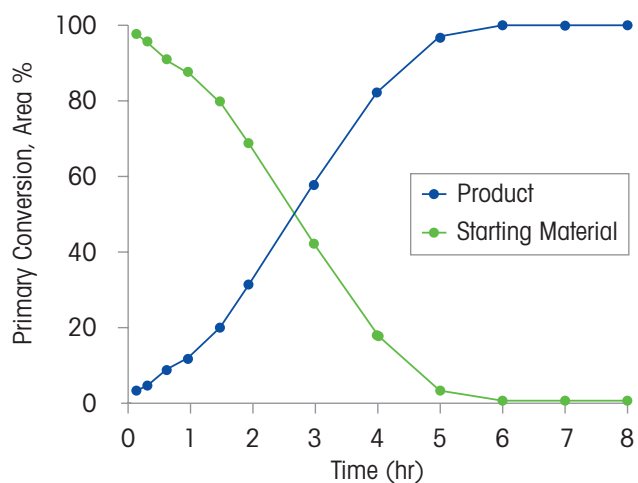


Figure 3. Pd-catalyzed Carbonylation in 2-MeTHF

EasySampler: Unattended, Representative Sampling



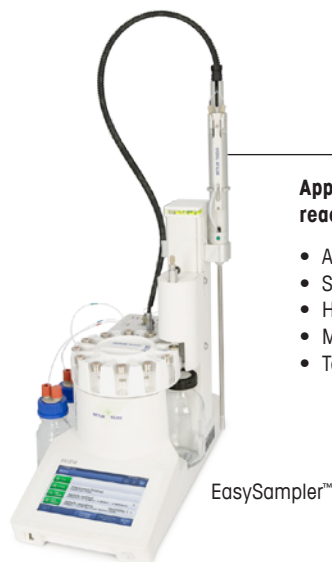
Difficult to Sample Reactions

The *in situ* sampling probe eliminates tedious manual sampling steps of reactions at elevated pressure.



Automated and Unattended

Samples are taken as scheduled by the user to provide high quality samples for complete reaction information and understanding.



Application of EasySampler in other reactions that are difficult to sample:

- Air and moisture sensitive reactions
- Sub-ambient temperature reactions
- Heterogeneous reactions
- Multi-phase reactions
- Toxic reactions

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