

## On-line NMR reaction monitoring

A new, innovative and powerful analytical system for the lab bench

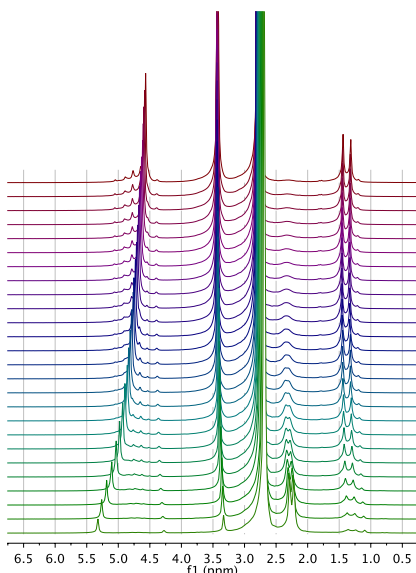
The Spinsolve high-resolution benchtop NMR spectrometer can be installed directly under the fume hood of a chemistry lab to monitor the progress of chemical reactions on-line. Reactants can be pumped in continuous mode from the reactor to the magnet and back using standard PTFE tubing.

### Why on-line?

- Determine reaction end points
- Identify intermediates and by-products
- Determine reaction kinetics
- Maximise yields
- Terminate failing reactions early
- Avoid sample preparation and isolation
- Real time information
- Save time and cost

### Why Spinsolve NMR?

- Chemically specific
- Quantitative for all species
- Provides structural information
- Solvent-independent calibration
- No deuterated solvents needed
- High spectral resolution
- Excellent time resolution
- High stability with external lock



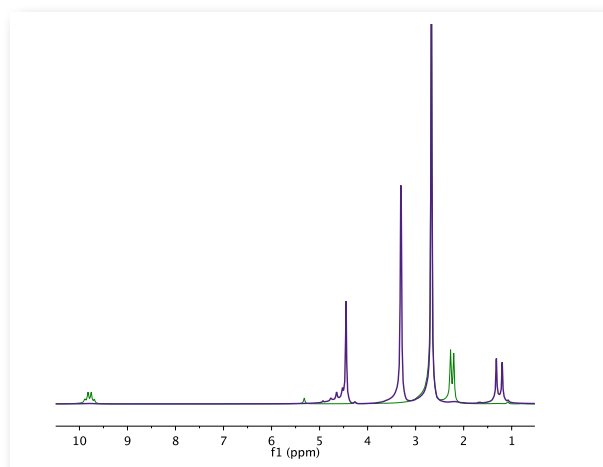
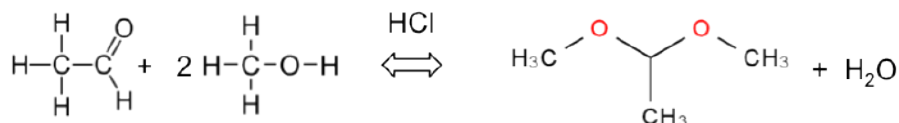
Waterfall plot showing NMR spectra acquired as a function of time during the reaction



Spinsolve NMR spectrometer set up in a fume hood to monitor a batch reaction

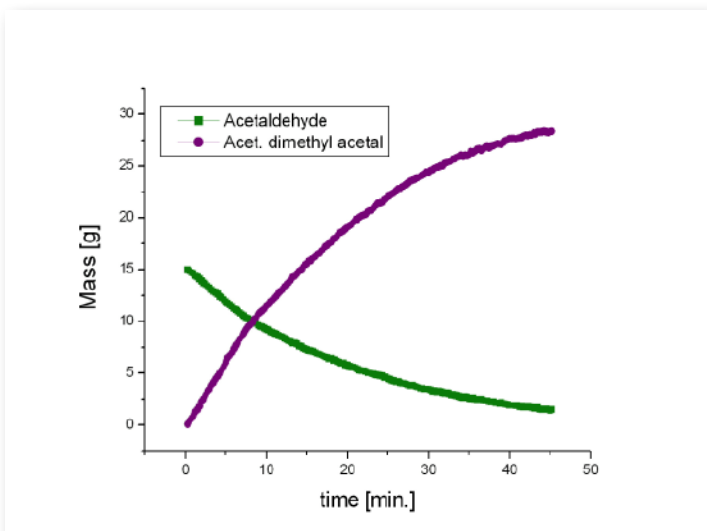
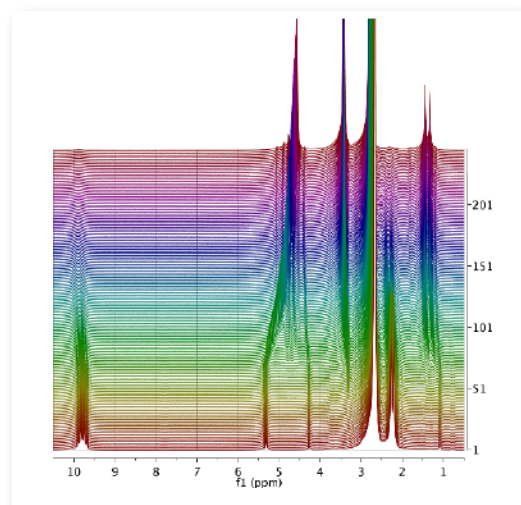
# Acetalisation of acetaldehyde

Acetalisation is a typical reaction in organic synthesis where an acetal is produced from an aldehyde and an alcohol. It is acid catalysed and eliminates water as by-product. Below the reaction equation is shown for acetaldehyde reacting with methanol to produce acetaldehyde dimethyl acetal.



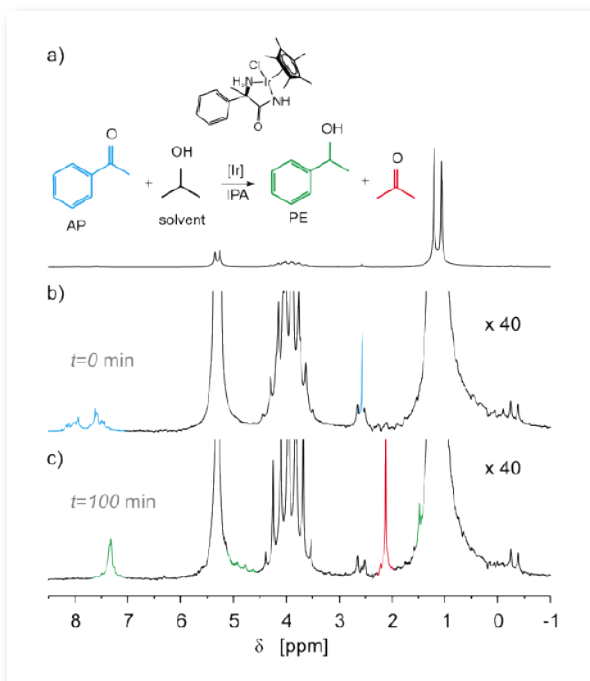
The reaction is carried out in DMSO

The spectrum of the initial mixture (brown) shows the signal of acetaldehyde (carbonyl at 9.7 ppm and methyl at 2.25 ppm). At the end of the reaction (green) the signals of acetaldehyde dimethyl acetal (CH at 4.8 ppm, CH<sub>3</sub> at 1.4 ppm, and -O-CH<sub>3</sub> at 3.5 ppm) and water at 4.7 ppm can be seen. There is a signal from DMSO at 2.7 ppm, but this does not interfere with the signal of either the reactants or the products. There is no need to use deuterated DMSO.

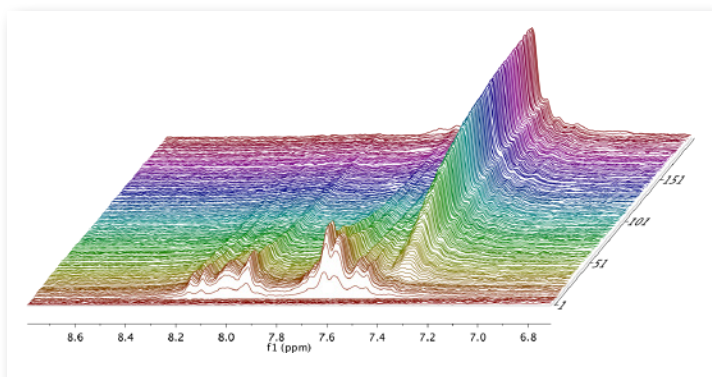


A reaction was carried out in a flask where 20 mL of acetaldehyde was dissolved in 30 mL of DMSO (to avoid evaporation) and 0.5 mL of hydrochloric acid (catalyst). 35 mL of methanol were added in drops to the reactor at a rate of about 1 mL min<sup>-1</sup>. The reaction was monitored for 1 hour with spectra acquired every 15 seconds, as shown in the waterfall plot. By integrating the regions marked in green and purple the total mass of aldehyde (green) and acetaldehyde dimethyl acetal in the reactor can be easily determined.

# Reduction of acetophenone to 1-phenylethanol

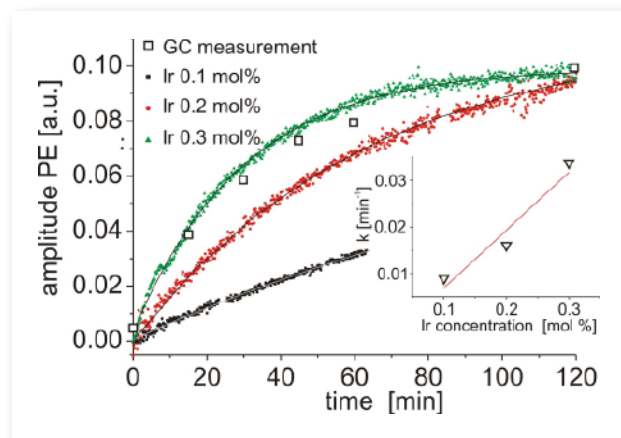


As a second example we monitored the reduction of acetophenone (AP) to 1-phenylethanol (PE) via the transfer hydrogenation with isopropanol. The experiments started with only isopropanol in the reactor. After turning the pump on, 2% of AP was added to the reactor with the NMR spectrometer set to acquire NMR spectra at regular intervals of 10 seconds. The main peaks in (a) correspond to the three different chemical groups of isopropanol and the AP signals (blue) can be seen only after zooming in the spectrum by more than one order of magnitude (b). Then the iridium catalyst was added to the solution and the reaction was monitored for some hours. The final spectrum is shown in (c). It can be seen that the signals from AP have been replaced by the peaks of acetone (red) and 1-phenylethanol (green).



Concentration of PE as a function of time measured for three different concentrations of catalyst. The results are compared with GC and show excellent agreement.

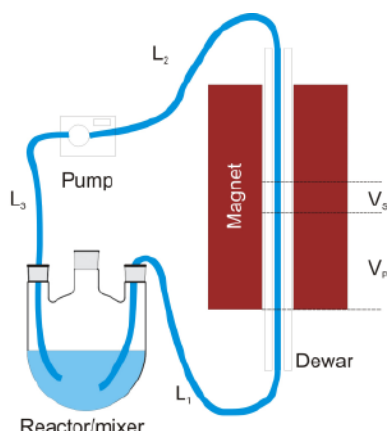
Zoom of the aromatic region of the spectrum. This region is not affected by the large solvent peaks and the signals can be integrated to measure the concentration of both AP (from 7.85 to 8.3 ppm) and PE (from 7.1 to 7.45 ppm).



These results show that reactants diluted in protonated solvents at concentrations less than 1% can be quantified on-line with high accuracy with the Spinsolve spectrometer set inside the fume hood.

## Typical flow setup

A typical setup for on-line monitoring is shown below. A dewar of 5 mm o.d. and 2.25 mm i.d. is mounted in the bore of the spinsolve to reduce the heat exchange between the flowing sample and the magnet. The reaction mixture is pumped through the bore of the magnet using a 2 mm o.d. PTFE tubing. To reduce the tubing length L1 that goes from the reactor to the sensitive volume of the Spinsolve the pump is placed after the magnet. The pump can be set to work in continuous mode or in stop flow mode to acquire points with a time resolution of about 15 seconds. To avoid affecting the stability of the spectrometer the temperature of the reaction mixture entering the magnet needs to be not higher than 30 °C. However, the reaction can be carried out at temperatures of about 100 °C. The reaction mixture naturally cools down under 30 °C as it flows along the L1 length of the tubing at room temperature.



- Tubing type: PTFE
- Maximum OD: 2 mm
- Typical ID: 1.5 mm
- Typical Length: 3 m (L1+L2+L3)
- Volume L1: 1.5 ml
- Total volume: 5 ml
- Tmax reactor: 100 °C
- Tmax magnet: 30 °C

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about this incredible  
**NEW** innovation in  
reaction monitoring  
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## Specifications

- Frequency: 42.5 MHz Proton, 10.8 MHz Carbon
- Resolution: 50% linewidth < 0.7 Hz (16 ppb)
- Lineshape: 0.55% linewidth < 20 Hz
- Dimensions: 58 x 43 x 40 cm
- Weight: 55 kg
- Magnet: Permanent and cryogen free
- Stray field: < 2 G all around system



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