# Benchtop NMR Reaction Monitoring for Kinetic Profiling

The Spinsolve high-resolution NMR spectrometer has been used to study the hydrolysis of acetic anhydride by water. Rate constants can easily and reliably be obtained by plotting the peak height or integral of a characteristic peak as a function of reaction time. The activation energy of the process can be determined by carrying out the reaction at different temperatures.
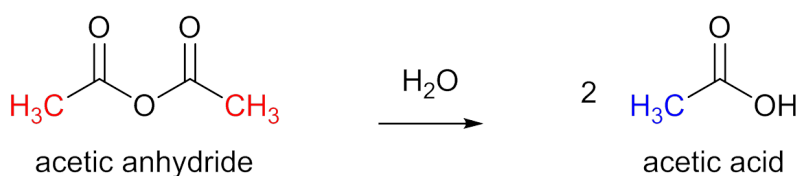
Reaction Scheme for Hydrolysis of Acetic Anhydride
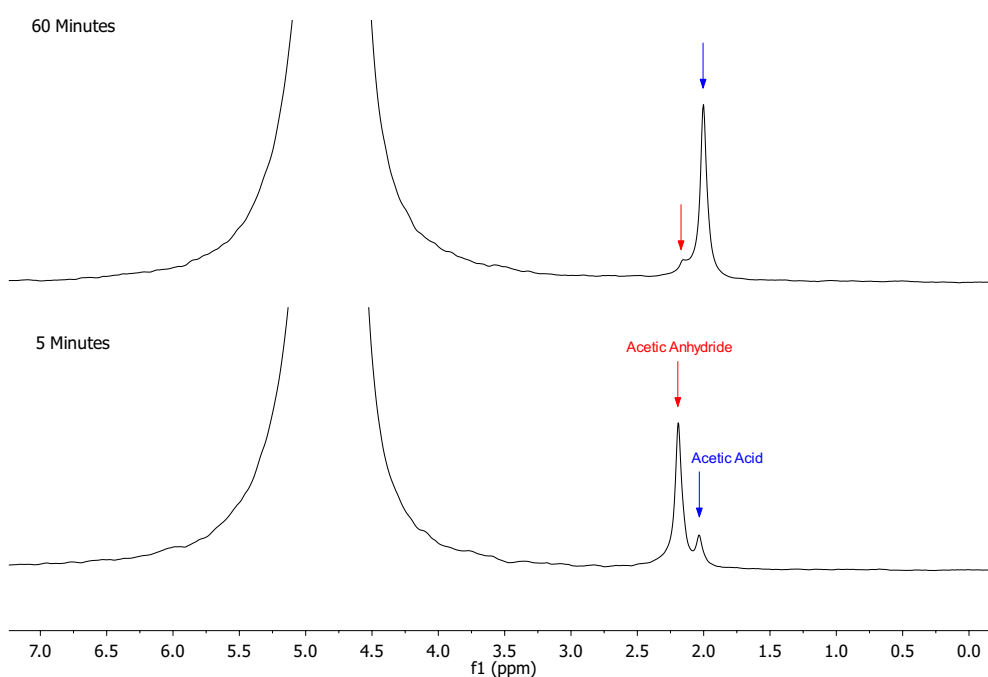
Experiment

Acetic anhydride (0.05 mL) and water (10 mL) were mixed in a 25 mL reaction flask to make a 0.05% v/v solution. The reaction was monitored in real time by connecting the reactor to the flow cell with PTFE tubing of 1 mm I.D. as shown in Figure 1. The reaction mixture was circulated through the PTFE tubing using a flow rate of 0.9 mL/min and spectra were acquired every 15 seconds. With this set-up the reaction mixture reached the sensitive volume in less than 50 seconds. Temperature variations in the reactor (5 - 50°C) were achieved using a hot plate and an ice bath. A mechanical stirrer was used to ensure that the mixture was homogeneous. It is important to note that these conditions are difficult and costly to achieve within conventional 5 mm NMR tubes typically used at high field.
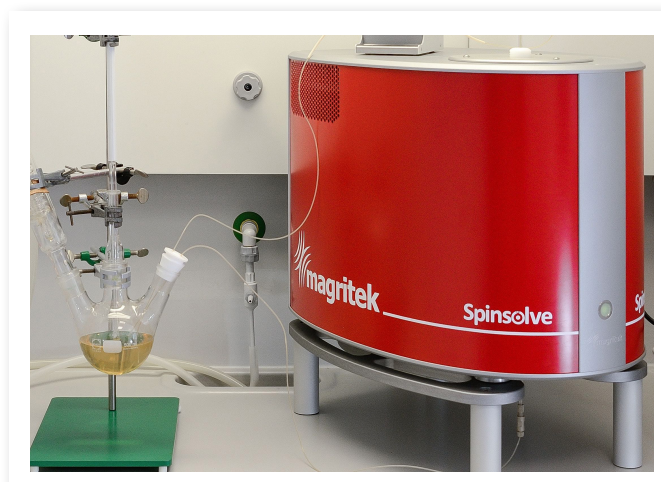

Figure 1. Spinsolve NMR spectrometer set in a fume hood to monitor the hydrolysis of acetic anhydride.

Hydrolysis of acetic anhydride

The area containing the peaks corresponding to the reactants and products in the stacked NMR spectrum and the corresponding kinetic curves acquired from the signal amplitude of the described peaks is shown in Figures 2A and 2B, respectively.
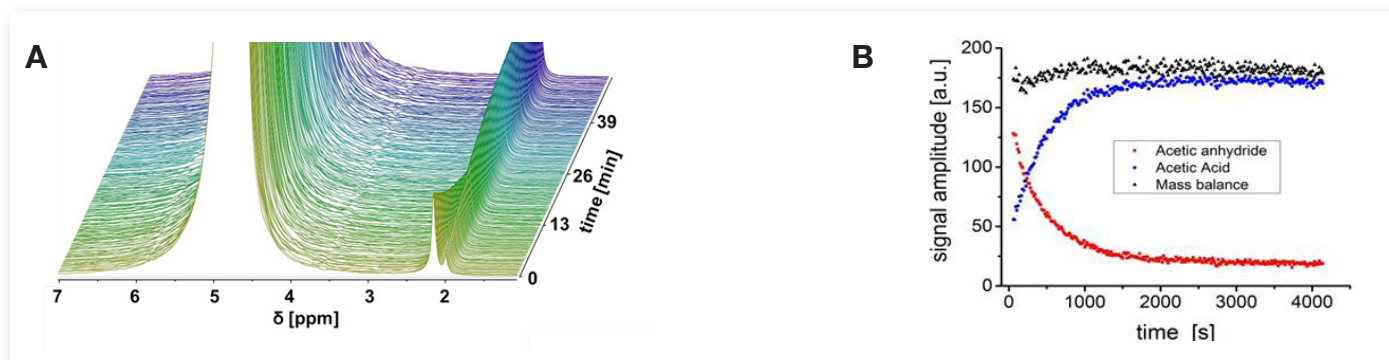

Figure 2. (A) Stacked spectrum from 1.0 ppm to 7.0 ppm. The growing peak near 2.04 ppm corresponds to acetic acid and the decreasing peak near 2.19 ppm corresponds to acetic anhydride. (B) Profile of the reaction, showing the mass balance and peak height of the reactant (red) and product (blue).

Kinetic model

The amount of H_2O is in excess compared to the concentration of the acetic anhydride, thus a pseudo-first order reaction is expected. Consequently, a first order kinetic model was used to fit the experimental data and to calculate the rate constant.

Equation 1: $[OAc_2] = [OAc_2]_0 \, e^{-kt}$

Where $[OAc_2]$ is the concentration of acetic anhydride, which is measured by the height of the methyl peak near 2.19 ppm in the ^1H NMR spectrum (Figure 3A), and *'k'* is the pseudo-first order rate constant of the reaction. The negative sign in Equation 1 indicates that the concentration of acetic anhydride is decreasing with elapsed time, as shown in the reaction scheme.

A plot of the peak height against time yields an exponential curve. The fit of the curve (red line, Figure 3B) has a decay constant of *k* according to Equation 1, hence the rate constant of the reaction at 296 K is 0.8 x 10^{-3} $s^{-1.}$ There is a strong correlation between the fit and experimental data (Figure 3C), thus the data is consistent with a pseudo-first order reaction mechanism.
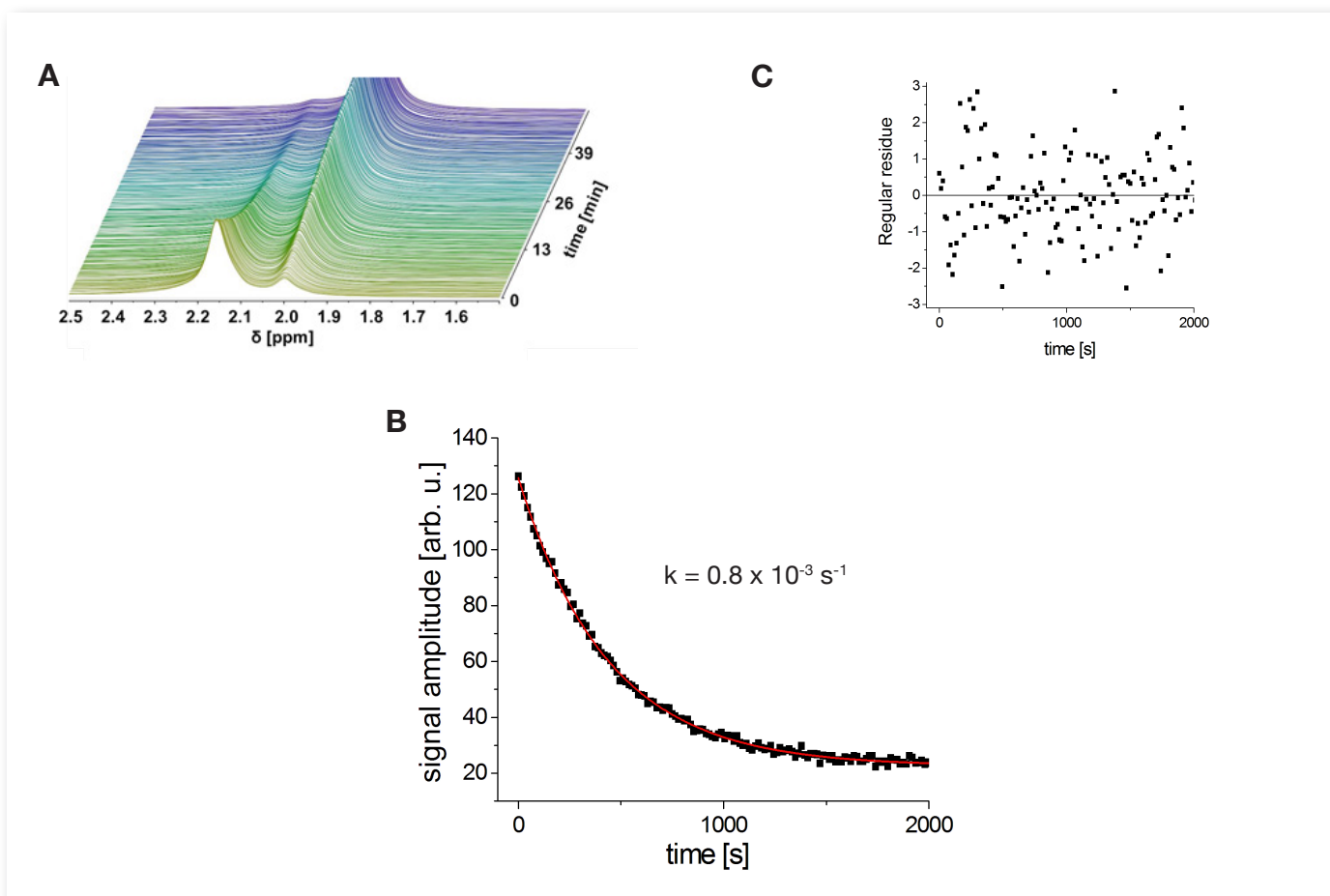

Figure 3. (A) Stacked spectrum showing decreasing acetic anhydride peak at 2.19 ppm that was measured. (B) Plot of acetic anhydride peak height against time, with the fit of the curve shown in red. (C) Residual plot of the fit showing the fit quality.

Effect of temperature

The reaction was performed at different temperatures and it was observed that the rate constant is temperature dependant (Figure 4A). The activation energy of the reaction was determined by the Arrhenius equation (Equation 2). A plot of the natural logarithm of the rate constant against $1/T$ yields a straight line, the gradient of which gives the activation energy according to Equation 2 (Figure 4B).

Equation 2: $\ln(k) = \ln(A) - \dfrac{E_a}{R}\left(\dfrac{1}{T}\right)$

Where A is a pre-exponential factor, E_a is the activation energy, R is the universal gas constant (1.98 kcal mol^{-1}) and T is the temperature.
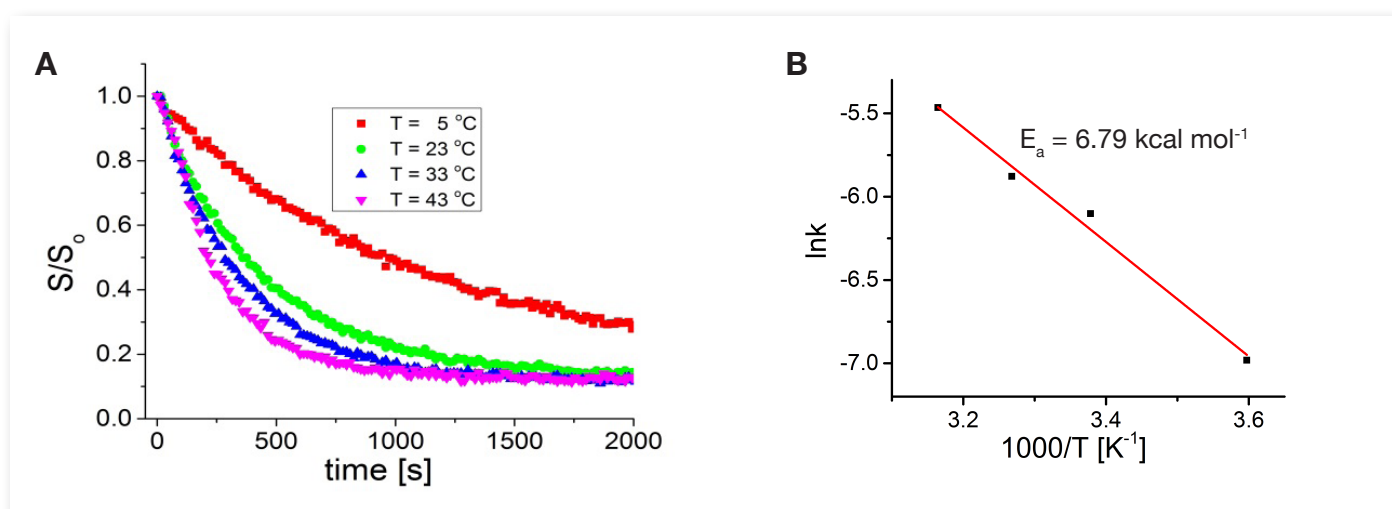

Figure 4. (A) Reaction profiles at various temperatures, showing the effect of temperature on the rate of the reaction (B) Arrhenius plot.

These results show that reactants diluted in protonated solvents at concentrations less than 1% can be measured with accuracy using the Spinsolve spectrometer set inside the fume hood. For reactions whose products do not precipitate at lower temperatures, it is possible to monitor the effect of temperature in the reactor provided that the sampling volume represents a small fraction of the reactor volume. This condition is met due to the small scale of the compact NMR system.

Spinsolve

Flow Setup Specifications

The setup required for on-line monitoring is shown below (Figure 5). A dewar (5 mm O.D. and 2.25 mm I.D., available from Magritek) is mounted in the bore of the Spinsolve to reduce the heat exchange between the flowing sample and the magnet which enables the monitoring of reactions at a range of temperatures. The reaction mixture was pumped through the bore of the magnet using 2 mm O.D. (1 mm I.D) PTFE tubing. To reduce the tubing length, L_1, 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.
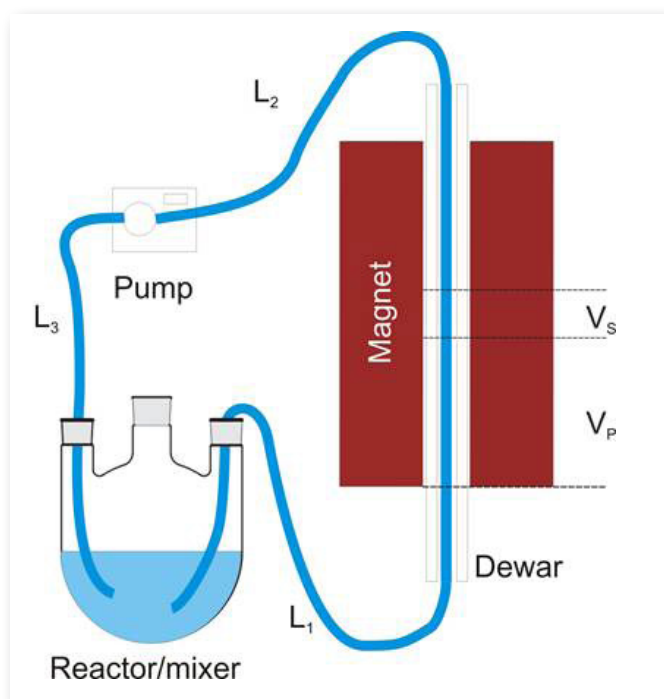
- Tubing type: PTFE
- Maximum OD: 2 mm
- Typical ID: 1.0-1.5 mm
- Typical Length: 3 m ($L_1+L_2+L_3$)
- Volume L1:   1.5 ml
- Total volume: 5 ml
- T_{max} reactor: 100°C
- T_{max} magnet: 30°C

Figure 5: Flow Setup. The reaction mixture is pumped from the reactor to the magnet via L_1, from the magnet to the pump via L_2 and from the pump back to the reactor via L_3.

Contact us now for a quote, to request a demo or to measure your samples

Email: sales@magritek.com

Website: www.magritek.com/contact-us

GERMANY	+49 241 9278 7270	**UNITED STATES**	+1 855 667 6835
UNITED KINGDOM	+44 7468 529 615	**NEW ZEALAND**	+64 4 477 7096

For a complete listing of our global offices and distributors visit: www.magritek.com/about-us/distributors/