POTENTIAL APPLICATIONS OF PROCESS ANALYSIS BY NMR SPECTROMETRY

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To date, there have been very few successful attempts to perform at-line or on-line analysis of a chemical process using NMR spectrometry. However, NMR possesses a number of features that make the technique ideally suited for such a task. These include the ability to analyze solids, liquids, and gases in a non-destructive manner. Clearly, the high-field NMR spectrometer found in most analytical laboratories is not suitable for the rigors of a plant environment. However, low-field NMR spectrometers employing a permanent magnet are better suited due to their smaller size and robustness. Instruments based around this technology have been used to measure moisture, fat and solids content, and refinery applications. Magnetic resonance imaging has also been used to determine the ripeness of fruit. In this work, the use of a low-field NMR spectrometer manufactured by Resonance Instruments has been assessed for at-line and on-line process analysis.

The resolution achievable on a low-field NMR spectrometer is inferior to that obtained on a high-field instrument. However, the resolution of a low-field ^{1}H NMR spectrum is still sufficient to obtain qualitative information. For example, ^{1}H NMR spectra have been acquired of samples taken at various stages from a benzene production plant. It is possible to observe spectral changes that arise from the removal of toluene or olefins from the process stream. From comparison of ^{1}H NMR spectra of 4-methyl pent-1-ene and -----dimethyl but-1-ene (Figure 1), it is feasible that NMR spectrometry could be used to distinguish between two C6 isomers.

Four different blends of two types of polyether polyols have been analyzed using low-field ^{1}H NMR spectrometry. Polyether polyols are made from propylene oxide and ethylene oxide. The ^{1}H NMR spectrum of a typical sample contains two signals; one arising from CH_2 and CH and the other arising from CH_3. It is possible to relate the difference in the two signal intensities to the percentage of ethylene oxide in the sample. It was found that where the signal intensities differed by between 2.3 and 2.5 intensity units, the sample could be identified as one type of polyol. In comparison, when the signal intensities differed by between 2.7 and 3.0 intensity units the sample could be identified as the second of the two types of polyols. Investigation of additional samples is planned to see if it is possible to distinguish between different blends of the same polyol and also to quantify the percentage of ethylene oxide in samples.

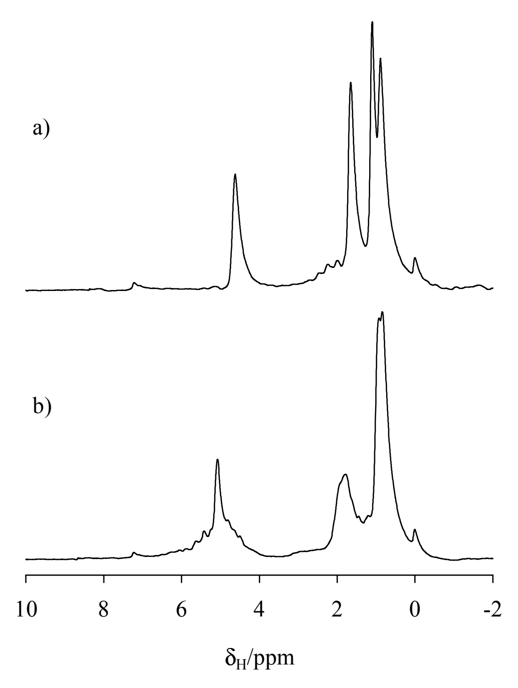

Figure 1. ^{1}H NMR spectra of: a) 2,3-dimethyl but-1-ene and b) 4-methyl pent-1-ene.

Where quantitative information is required, chemometric techniques such as partial least squares (PLS) can be used to analyze spectra. PLS was used to analyze low-field ^{1}H NMR spectra of samples taken from two different stages of a methacrylamide plant. The samples are viscous and/or solid at room temperature and are also in concentrated sulfuric acid. However, samples were heated in a water bath to 80°C for analysis. The predicted concentration of methacrylamide was in good agreement with the results obtained by off-line HPLC. However, the precision of the results was relatively poor (1–8%), as the physical state of the sample changed during analysis. Hence, on-line analysis at the reaction temperature (150°C) would be preferred.

Both temperature and flow affect the NMR signal. The NMR signal area is inversely proportional to temperature (Boltzman equation) and thus decreases with an increase in temperature. This is illustrated in Figure 2 by the variation in the ^{1}H NMR signal area of water with temperature. For on-line analysis, the sample will be continually flowing through the NMR spectrometer. When increasing the flow rate, the NMR signal linewidth increases while the signal area decreases. This is illustrated in Figure 3 using the ^{1}H NMR spectra of a mixture of cyclohexane and toluene under both static (b) and flowing (a) conditions. It can be seen that on-line analysis of flowing streams at elevated temperatures will result in a decrease in signal area and resolution. From analysis of simulated data, it has been shown that of the two effects, a deterioration of the signal-to-noise ratio has a far greater influence on the predictive accuracy of PLS than resolution. The decrease in signal area observed with an increase in flow rate can be reduced through the use of a flow cell incorporating a pre-magnetization region. However, the decrease in NMR signal area observed at elevated temperatures is likely to be preferable for analytes where cooling the stream will compromise the integrity of the sample. Making measurements over a longer time can compensate for the effects of reduced sensitivity, provided that during the measurement period, the composition of the flowing liquid is reasonably consistent. For example, the detection limit of cyclohexane is improved from 0.45% v/v to 0.08% v/v when the analysis time is increased from 12 seconds to 6.4 minutes.

To allow further investigations of the effects of flow and temperature, an esterification reaction, involving butanol and crotonic acid, has been chosen as a model process. Through PLS analysis of ^{1}H NMR spectra acquired off-line of simulate reaction mixtures, it has been shown that the extent of reaction can be deduced from the predicted concentrations of butanol, crotonic acid, water, and butyl crotonate. At the start of the reaction, lower percentage errors (Figure 4) can be obtained by monitoring the change in butanol and/or crotonic acid concentration. However, as the reaction progresses the ester concentration increases and its concentration can be determined with a higher degree of accuracy. Thus, determination of the ester concentration could be used to monitor the end-point of a reaction. Samples taken during the esterification of crotonic acid in a five liter batch reactor have been analysed using low-field ^{1}H NMR. The predicted concentrations of butyl crotonate were in good agreement with those predicted by GC and NIR spectrometry. Having completed the off-line study, further investigation of the batch reaction is currently underway using on-line analysis.

In appropriate cases, ^{19}F NMR spectrometry can yield simpler spectra than ^{1}H NMR spectrometry, particularly if the solvent is non-fluorinated. A model reaction involving the mono-dehydroxylation of tetrafluorohydroquinone has been examined using ^{19}F NMR spectrometry. Simulate reaction mixtures were made up containing tetrafluorohydroquinone (starting material), tetrafluorophenol (product) and tetrafluorobenzene (by-product). Prior to the analysis of the data, line broadening and a variable selection technique were applied. Line broadening is a commonly used data pre-processing technique in NMR, which can result in a beneficial increase in the signal-to-noise ratio, but also causes a detrimental decrease in spectral resolution. Variable selection involves the selection of the “most important” variables according to some criteria; in this case the variables with the maximum standard deviation were selected. Application of line broadening and variable selection gave a marginal improvement in the accuracy of the results, but the precision was typically improved by a factor of 2. Table I indicates that the results obtained for the three components using PLS calibration are in good agreement with the actual concentrations for all three components.

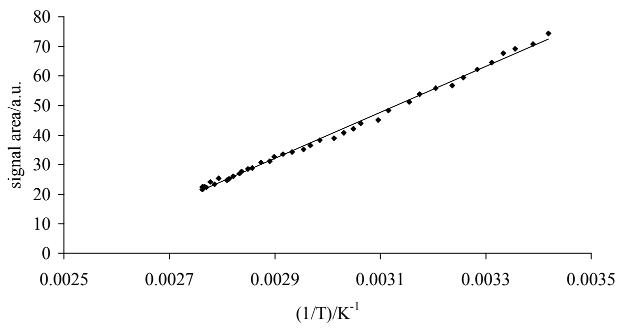

Figure 2. Variation in the ^{1}H NMR signal area of water with 1/T.

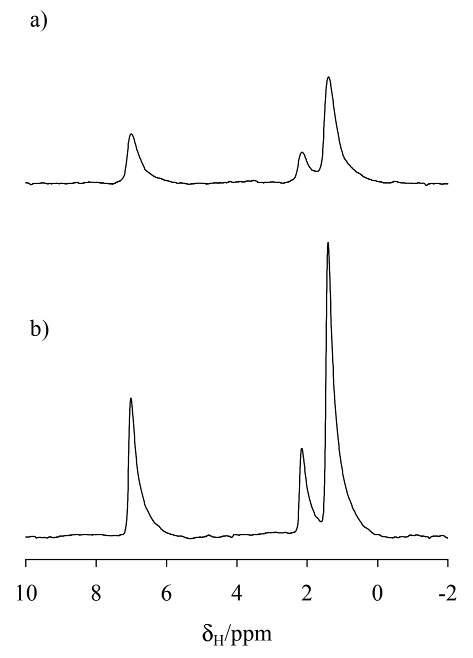

Figure 3. ^{1}H NMR spectra of toluene and cyclohexane at: a) 25 mL min^{-1} and b) 0 mL min^{-1} using a standard flow cell.

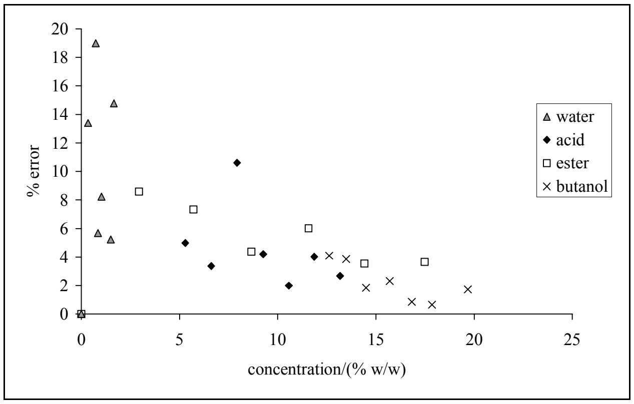

Figure 4. Error of prediction (%) for butanol, crotonic acid, butyl crotonate, and water as a function of concentration.

It has been demonstrated that low-field NMR could be used for a wide range of applications. In some cases, qualitative information can be extracted from spectra and where required, chemometric techniques such as PLS can be used to analyze data quantitatively. Detection limits in the region of 0.01–0.5% v/v or m/v can be obtained with NMR, although the detection limit is dependent on the analysis time. Although both flow and temperature affect the NMR signal, with an increase in the magnitude of both parameters resulting in a decrease in signal area, steps can be taken to compensate for the effects. The study has shown the potential of ^{1}H and ^{19}F low-field NMR spectrometry for process analysis. Further investigations will include at-line and on-line analysis using ^{31}P NMR measurements.

Table I Comparison of Actual and Predicted Concentration of Each Component

Sample	**Actual Concentrations / (% m/v)**			**Predicted Concentrations ± Standard Deviation / (% m/v)**		
	Tetrafluoro-hydroquinone	**Tetrafluoro-benzene**	**Tetrafluoro-phenol**	**Tetrafluoro-hydroquinone**	**Tetrafluoro-benzene**	**Tetrafluoro-phenol**
1	1.1	6.9	2.1	1.1 ± 0.02	7.0 ± 0.11	2.1 ± 0.03
2	5.0	3.3	2.1	5.1 ± 0.09	3.3 ± 0.07	1.9 ± 0.07
3	4.2	2.0	3.8	4.2 ± 0.09	2.1 ± 0.06	3.8 ± 0.03
4	4.0	3.1	3.1	4.0 ± 0.08	3.1 ± 0.07	3.1 ± 0.02
5	2.4	5.1	4.0	2.4 ± 0.05	5.1 ± 0.09	3.6 ± 0.02

Note: Prediction made from PLS analysis of NMR spectra pre-processed using 10 Hz. line broadening and variable selection.