Online process monitoring of a batch distillation by medium field NMR spectroscopy

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Abstract

Medium field NMR spectrometers are attractive for online process monitoring. Therefore, in the present work, a single-stage laboratory batch distillation still was coupled online with a medium field NMR spectrometer. This enables quantitative non-invasive measurements without calibration. The technique was used for studying isobaric and isothermal residue curves in two ternary systems: (dimethyl sulfoxide + acetonitrile + ethyl formate) and (ethyl acetate + acetone + diethyl ether) and boiling curves and high-boiling azeotropes in two binary systems: (acetic acid + pyridine) and (methanol + diethylamine). The results of the online NMR spectroscopic analysis were compared to results from offline analysis as well as to results from thermodynamic modeling using NRTL parameters that were parametrized with literature data. The new method for online process monitoring gives reliable results and is well-suited for fast and robust measurements of residue curves.

Keywords: medium field NMR spectroscopy, Benchtop NMR spectrometer, online analysis with flow NMR, single-stage batch

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1. Introduction

Online process monitoring is important for process control and optimization. Recently, robust and small medium field nuclear magnetic resonance (NMR) spectrometers have become available. These instruments use permanent magnets but have a field that is high enough to yield a resolution that enables to distinguish component peaks in the spectrum, which is the prerequisite for quantitative spectroscopy. Medium field devices are particularly attractive for online process monitoring because, in contrast to conventional high field instruments, they do not require cryogenic media, climatized and vibration-free installation, and they are comparatively cheap. Despite the lower sensitivity and chemical resolution compared to high field NMR spectrometers, the spectra obtained by medium field spectroscopy can be evaluated quantitatively. The quantification is possible without calibration, which is an advantage over other spectroscopic methods e.g. IR spectroscopy. Furthermore, due to the high dispersion of NMR spectroscopy, peak overlaps are often no problem, and, if they occur, advanced techniques are available that enable a reliable quantification also in these cases [1, 2]. Because NMR spectroscopy is applicable to flowing liquid samples, the spectrometer can be coupled to the process by a sample loop. This allows a non-invasive measurement with high temporal resolution where pressure, temperature, and the composition of the mixture is not affected by the analysis.

A variety of applications of high field NMR spectroscopy for online process monitoring have been described in the literature [3–6], but they are limited

24 to laboratory conditions. The advent of commercially available medium field
 25 NMR spectrometers opened up new possibilities. Various publications de-
 26 scribe applications of medium field NMR spectrometers for monitoring of
 27 reactions [7–11] and processes [12–16] and for controlling the product quality
 28 during production [17–20]. To our knowledge, however, NMR spectroscopy
 29 (neither with medium nor with high magnetic fields) has not been used yet for
 30 online monitoring of fluid separation processes such as distillation. Therefore,
 31 in the present work, a single-stage batch distillation was coupled online with
 32 a medium field NMR spectrometer. This enables, e.g. determining residue
 33 curves and high-boiling azeotropes. More generally, pTx -data of vapor-liquid
 34 equilibria (VLE) can be determined, where p is the pressure, T is the tem-
 35 perature and x the liquid-phase composition. This is possible for systems
 36 with a many of components.

37 The setup that was used in the present work consists of a simple batch
 38 distillation still which was coupled online with a sample loop to a medium
 39 field NMR spectrometer. The sample is taken from the liquid phase and the
 40 NMR spectrometer is operated in flow-mode. The control is designed such
 41 that the distillation can be carried out at isobaric as well as at isothermal
 42 conditions. In preliminary investigations the setup was characterized and the
 43 residence time in the sample loop as well as the maximal volume flow rate
 44 for sufficient magnetization were determined [21, 22]. The setup was then
 45 used for studying isobaric and isothermal residue curves in two ternary test
 46 systems: (dimethyl sulfoxide (DMSO) + acetonitrile (ACN) + ethyl formate
 47 (EF)) and (ethyl acetate (EA) + acetone (ACT) + diethyl ether (DE)). It was
 48 also applied for measuring the isobaric boiling curve and for determining the

49 high-boiling azeotrope in two binary systems: (acetic acid (AA) + pyridine
50 (P)) and (methanol (M) + diethylamine (DEA)). For comparison, the system
51 (DMSO+ACN+EF) was investigated by offline gas chromatography (GC)
52 analysis as well. The experimental data from this work were compared to
53 results that were obtained from thermodynamic modeling, based on NRTL,
54 with model parameters that were determined from experimental data from
55 the literature.

56 **2. Experimental section**

57 *2.1. Chemicals*

58 Table 1 lists the chemicals that were used in the present work. All chem-
59 icals were used without further purification. No side components were de-
60 tected in the sample analysis. Figure 1 shows the chemical structures of all
61 components that were quantified by NMR spectroscopy together with the
62 nomenclature that is used for the peak assignment.

63 *2.2. Experimental setup*

64 Figure 2 shows the distillation setup. It consists of an electrically heated
65 glass batch distillation still (total volume 500 ml) that is connected to a
66 medium field NMR spectrometer by a sample loop in which the liquid phase
67 circulates. The setup can be operated at isobaric or at isothermal conditions.
68 In case of the isothermal measurement the pressure was manipulated in a
69 control loop to maintain the temperature in the still.

70 The liquid in the distillation still (about 210 ml at the beginning) was
71 continuously stirred during the experiment (RCT Basic with flask carrier,

72 IKA). The changing magnetic field of the magnetic stirrer was shielded with
73 a μ -metal foil. The ascending vapor was condensed in a water cooled Liebig
74 condenser and was collected in the distillate flask.

75 The temperature of the liquid phase was measured with a calibrated
76 PT100 thermometer connected to a multimeter (series 2700 Multimeter,
77 Keithley Instruments, accuracy: ± 0.1 °C). The pressure was measured with
78 piezo sensors (VSR53DL and VSC42MA4, Thyracont Vacuum Instruments,
79 accuracy: ± 0.3 %). Temperature and pressure were continuously recorded
80 with the software LabView. The control system that was realized using Lab-
81 View enables both isobaric and isothermal operation. In case of the isother-
82 mal measurement the pressure was adjusted in a control loop to maintain
83 constant temperature in the still.

84 The sample loop was realized with a PEEK capillary ($d_i = 1$ mm), which
85 was passed through the medium field NMR spectrometer (42.5 MHz, Spin-
86 solve Carbon, Magritek). The flow was maintained by a double piston high-
87 pressure pump with damping piston (WADose LITE HP, Flusys, accuracy:
88 ± 0.01 ml/min) and was measured with a Coriolis flow sensor (Mini Cori-
89 Flow, Bronkhorst, accuracy: ± 0.2 %). The flow sensor's signal was used to
90 control the pump. This set-up gave very good results and we would have liked
91 to keep it also for the isothermal measurements. However, in these measure-
92 ments, the pressures were sometimes so low that the Flusys pumps did not
93 work properly. Therefore, in the isothermal measurements a high precision
94 dosing pump (HPD3351, Bischoff Chromatography, accuracy: ± 2 %) was
95 used. To reduce pulsation, the flow was split. This pump gave acceptable
96 results but is not considered as an optimal system for the present application.

97 Discontinuities of the flow lead to a larger scattering of the analytical results.
98 Volume and mass flow in the sample loop were continuously recorded with
99 the software LabView.

100 2.3. Procedure

101 All chemicals were degassed before the experiment. The liquid feed mix-
102 tures were prepared gravimetrically using an analytical balance (XS603S
103 DeltaRange, Mettler Toledo, accuracy: ± 10 mg). Isobaric experiments were
104 performed at 970 mbar, isothermal experiments were performed at 303 K
105 and 323 K. The flow rate in the sample loop was set to $\dot{V} = 0.2$ ml/min.
106 It was shown in preliminary experiments that this flow rate is sufficient to
107 ensure complete magnetization of the components prior to entering the ac-
108 tive volume of the NMR spectrometer. More information on this is given in
109 the Supplementary Material. ^1H NMR spectra were recorded with intervals
110 of 1 min. As the sample loop was not thermostated, the circulating liquid
111 cooled down during analysis. The small reflux from the sample loop has no
112 significant influence on the temperature of the liquid in the still. For a com-
113 parative offline analysis, a syringe was used to withdraw samples (0.5 ml)
114 from the liquid phase in the still.

115 Because the fluid needs to be transported from the still to the active
116 volume of the NMR spectrometer, where the analysis takes place, there is a
117 time delay between the measurement of temperature and pressure and the
118 measurement of the composition. This was determined by residence time dis-
119 tribution measurements. The delay was found to be 455 s in the isobaric setup
120 and 209 s in the isothermal setup. By taking this time delay into account
121 each measured composition was assigned to the temperature and pressure in

122 the still. When we report concentrations in the still as a function of time, the
123 time refers always to the time at which the sample was withdrawn from the
124 still. It is calculated from the time of the analysis by subtracting the time
125 delay for transferring the sample to the NMR spectrometer. Details on the
126 residence time distribution measurements are reported in the Supplementary
127 Material.

128 *2.4. Analysis*

129 The composition of the liquid phase was analyzed online by medium field
130 NMR spectroscopy. The composition of the liquid samples that were taken
131 from the still in the studies of the system DMSO + ACN + EF were deter-
132 mined by GC.

133 The online NMR analysis was carried out with a medium field NMR
134 spectrometer (Spinsolve Carbon, Magritek) with a field strength of 1 T cor-
135 responding to a Larmor frequency of 42.5 MHz for ^1H . The optimization of
136 the magnetic field homogeneity (shimming) was performed with water in the
137 capillary using the standard procedure of the manufacturer. The ^1H NMR
138 spectra were measured with the following parameters: acquisition time: 3.2 s,
139 16k data points, one scan, 90° excitation pulse. Prior to integration, post
140 processing (baseline and phase correction) of the obtained NMR spectra was
141 carried out with the SINC method [23]. Because of fully overlapping peaks
142 in the system EA + ACT + DE, an indirect hard modeling (IHM) approach
143 was used to determine the peak areas of all components in this mixture using
144 the software PEAXACT S-Pact. For all other systems the MNova software
145 (MestReLabs) was used for integration.

146 Figure 3 shows examples of ^1H NMR spectra for all studied systems.

147 The mole fractions of the different components in the sample were calculated
 148 from the normalized peak area fractions of the corresponding peaks in the
 149 NMR spectrum. For each system, three reference samples were prepared
 150 gravimetrically to test the accuracy of the NMR analysis and to assign the
 151 peaks in the spectrum. The absolute error of the method for the reference
 152 samples was on average 0.006 mol/mol. Taking the reduced signal to noise
 153 ratio of a flowing sample into account the absolute error of the NMR method
 154 is 0.01 mol/mol. More information is given in the Supplementary Material.

155 The offline GC analysis was carried out with an Agilent gas chromato-
 156 graph with a flame ionization detector (FID) (7890A, Agilent Technologies).
 157 1,4-dioxane was used as internal standard. Each sample was analyzed three
 158 times and the results were averaged. The absolute error of the method for the
 159 reference samples was below 0.006 mol/mol. As the composition of the ref-
 160 erence samples is representative for the compositions investigated in the dis-
 161 tillation experiments, the absolute error of the GC method is 0.006 mol/mol.
 162 More details on the GC method and calibration are given in the Supplemen-
 163 tary Material.

164 2.5. Modeling and simulation

165 The batch distillation still was modeled as an equilibrium stage, i.e. it
 166 was assumed that the gas stream, that leaves the still is in equilibrium with
 167 the remaining liquid residue. The residue curves were obtained by solving
 168 the Rayleigh equation:

$$\frac{dx_i}{d\theta} = x_i - y_i \quad (1)$$

169 where x_i and y_i are the mole fractions of component i in the liquid and gas
 170 phase respectively and θ is a dimensionless time parameter. The vapor-liquid

171 equilibrium was calculated from:

$$p_i^s \cdot x_i \cdot \gamma_i = p \cdot y_i \quad (2)$$

172 where p_i^s is the vapor pressure of component i and γ_i is the liquid phase ac-
 173 tivity coefficient, which was calculated here using the NRTL model [24]. The
 174 NRTL parameters were determined as follows: for the system EA+ACT+DE,
 175 the parameters were adapted from the Aspen data base as the model pre-
 176 dictions were found to agree well with experimental literature data from the
 177 Dortmund Data Bank (DDB). For all other systems, the NRTL parameters
 178 were fitted to experimental literature data from the DDB. The vapor pressure
 179 correlations and NRTL parameters are given in the Supplementary Material.

180 3. Results and discussion

181 In this section, the results of the distillation experiments are presented.
 182 For the ternary systems (DMSO + ACN + EF) and (EA + ACT + DE)
 183 residue curves were measured in isobaric as well as in isothermal experiments
 184 (Figure 4 and Figure 5). For the binary systems (AA + P) and (M + DEA)
 185 the boiling curve and the high-boiling azeotrope were determined in isobaric
 186 experiments (Figure 6 and Figure 7). The numerical experimental online
 187 and offline data of the residue curves, the boiling curves and the high-boiling
 188 azeotropes are reported in the Supplementary Material.

189 3.1. System: Dimethyl sulfoxide + Acetonitrile + Ethyl formate

190 Figure 4 shows the residue curves of the distillation experiments of the
 191 ternary system DMSO + ACN + EF. Two feed compositions were used in
 192 isobaric measurements at 970 mbar as well as in isothermal measurements at

193 323 K. As expected, the component with the highest boiling point (dimethyl
194 sulfoxide) is enriched in the liquid phase during experiment. For the isobaric
195 measurement experimental online NMR data is compared to experimental
196 offline GC data. For both feeds, the NMR data is in fair agreement with
197 the GC data. There are some systematic deviations, but they rarely exceed
198 the cumulated analytical uncertainties of both methods. The deviations are
199 caused by imperfections of the setup (deviations in flow rate and in pressure
200 (isobaric measurement) and temperature (isothermal measurement)) and un-
201 certainties in the evaluation of NMR data. This comparison proves the appli-
202 cability of the online NMR setup for the monitoring of residue curves. The
203 NRTL model predicts the experimental data well, although not perfectly.
204 The scattering of the NMR data in the isothermal experiment is larger than
205 that of the isobaric experiment. This is due to the different pumps that
206 were used in the sample loop and the different control strategy, see section
207 2.2. The comparison shows that the isothermal set-up leaves room for im-
208 provements. There is no good reason why the scattering in the isothermal
209 experiments could not be as low as that in the isobaric experiments, had
210 a better pump been available. Hence, for future isothermal experiments,
211 pumps should be used that enable maintaining constant flow rates also at
212 low pressures. Nevertheless, the results show the general usefulness of the
213 method.

214 As an alternative to the presentation of the residue curves shown in Fig-
215 ure 4, also plots of the concentration of the liquid as a function of the tem-
216 perature (isobaric measurement) or the pressure (isothermal measurement)
217 can be used. Such plots are presented in the Supplementary Material. Again,

218 good agreement is observed.

219 3.2. System: Ethyl acetate + Acetone + Diethyl ether

220 Figure 5 shows the residue curves of the distillation experiments of the
221 ternary system EA + ACT + DE. Two feed compositions were used in iso-
222 baric measurements at 970 mbar as well as in isothermal measurements at
223 303 K. As expected, the component with the highest boiling point (ethyl ac-
224 etate) is enriched in the liquid phase during experiment. No offline samples
225 were taken because of the high volatility of the components which leads to
226 biased sample compositions. Experimental online NMR data is compared to
227 predictions with the NRTL model. For both feeds the NMR data agrees well
228 with the model. Again, the scattering of the NMR data in the isothermal
229 measurement is much higher than that of the isobaric data, for the reasons
230 discussed above.

231 Plots of the concentration of the liquid as a function of the temperature
232 (isobaric measurement) or the pressure (isothermal measurement) are pre-
233 sented in the Supplementary Material. Again, good agreement is observed.

234 3.3. System: Acetic acid + Pyridine

235 Figure 6 shows the results of the distillation experiments of the binary
236 system AA + P, which has an high-boiling azeotrope. Two feed compositions
237 were used in isobaric measurements at 970 mbar to measure the boiling
238 curve and the azeotropic point of the binary system. In Figure 6a) the
239 boiling curve is plotted as a function of mole fraction of pyridine in the
240 liquid phase. The experimental online NMR data is compared to the NRTL
241 model prediction. Both NMR data sets agree well with the model data. After

the heating up (points under the boiling curve), the boiling starts at slightly lower temperatures than predicted. This results from the fact, that right after the boiling sets in, there is still nitrogen in the gas phase of the still. At constant temperature, the presence of nitrogen would lead to an increased pressure. Vice versa, for constant pressure, as in the experiment shown in Figure 6, the presence of nitrogen leads to temperatures that are too low. The effect is present until all nitrogen is purged from the gas phase by the vaporized components.

Figures 6b) and c) show the experimental values of temperature and mole fraction of pyridine in the liquid phase as a function of time. By means of the online measurement a continuous monitoring of temperature and liquid phase composition is possible. The azeotropic point found in this work is in good agreement with the predicted one and with those published in literature, see Table 2. This comparison shows that the setup is well suited to investigate boiling curves and high-boiling azeotropes.

3.4. System: Methanol + Diethylamine

Figure 7 shows the results of the distillation experiments of the binary system M + DEA, which has an high-boiling azeotrope. Two feed compositions were used in isobaric measurements at 970 mbar to measure the boiling curve and the azeotropic point of the binary system. The representation of the results is the same as in Figure 6. The experimental online NMR data is well predicted by the NRTL model. As explained above, a kinetic effect occurs at the beginning of the boiling, which causes a slight discrepancy between experimental data and prediction. The azeotropic point measured with online NMR spectroscopy agrees well with the NRTL model prediction

267 and with data from literature, see Table 2.

268 4. Conclusions

269 In the present work, a laboratory batch distillation still was coupled on-
270 line with a medium field NMR spectrometer and was used for measuring
271 residue curves, boiling curves, and high-boiling azeotropes. The liquid phase
272 is continuously withdrawn from the still and circulates in the sample loop in
273 which it is analyzed with the online NMR spectrometer. The sample loop
274 is a simple PEEK capillary that passes through the spectrometer’s bore.
275 Isobaric and isothermal measurements were performed. The results from
276 isothermal experiments scatter more than those from the isobaric measure-
277 ments, as a consequence of a less favorable pump that had to be used in
278 the sample loop. The setup was tested using two ternary zeotropic and two
279 binary azeotropic mixtures. The residue curves obtained with the new setup
280 were found to agree well with offline GC sampling. All experimental results
281 were in good agreement with the predictions from a thermodynamic model
282 that was parametrized using literature VLE data of the studied systems.
283 The online NMR analysis of the liquid phase enables the determination of
284 residue curves and boiling curves with high resolution. The investigation of
285 high-boiling azeotropes is also feasible.

286 As the NMR measurement is non-invasive, the analysis in the sample loop
287 does not affect the thermodynamic conditions of the system (temperature,
288 pressure, composition of phases). This enables a simple analysis of systems
289 with volatile components, unstable intermediates and at pressure below at-
290 mospheric pressure. The compact and robust medium field NMR spectrom-

eters enable online monitoring of processes not only in the laboratory but also in pilot and production plants. The presented setup is simple and robust and extends the standard techniques for thermodynamic measurements. The easy access to residue curve data in multicomponent systems, that is provided by the present set-up, is particularly interesting for the validation of VLE models that were parametrized based on binary data.

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Figure 1: Chemical structures of the components that were analyzed by ^1H NMR spectroscopy and nomenclature used for the peak assignment.

Figure 2: Experimental setup for the batch distillation with online NMR analysis.

Figure 3: ^1H medium field NMR spectra of reference samples of the investigated systems. Peak assignment, see Figure 1.

Figure 4: Results from measurements of two isobaric ($p = 970 \text{ mbar}$) and two isothermal ($T = 323 \text{ K}$) residue curves in the system dimethyl sulfoxide (DMSO) + acetonitrile (ACN) + ethyl formate (EF). Experimental data this work: ($\diamond$) Offline GC, ($\blacklozenge$) Online NMR; Prediction: (—) NRTL.

Figure 5: Results from measurements of two isobaric ($p = 970 \text{ mbar}$) and two isothermal ($T = 303 \text{ K}$) residue curves in the system ethyl acetate (EA) + acetone (ACT) + diethyl ether (DE). Experimental data this work: ($\blacklozenge$) Online NMR; Prediction: (—) NRTL.

Figure 6: Results from isobaric ($p = 970$ mbar) distillation in the system acetic acid (AA) + pyridine (P). a) Boiling curve as a function of mole fraction of pyridine in the liquid phase, b) Temperature as a function of the time, c) Mole fraction of pyridine in the liquid phase as a function of the time. Experimental data this work: Online NMR: ($\blacklozenge$) boiling curve, ($\color{red}\blacklozenge$) azeotrope; Prediction: (—) NRTL.

Figure 7: Results from isobaric ($p = 970$ mbar) distillation in the system methanol (M) + diethylamine (DEA). a) Boiling curve as a function of mole fraction of diethylamine in the liquid phase, b) Temperature as a function of the time, c) Mole fraction of diethylamine in the liquid phase as a function of the time. Experimental data this work: Online NMR: ($\blacklozenge$) boiling curve, ($\color{red}\blacklozenge$) azeotrope; Prediction: (—) NRTL.

Table 1: List of chemicals used for the investigations.

Chemical name	Source	Grade	Purity *
Acetic acid	Carl Roth	Rotipuran	≥ 0.998 g/g
Acetone	Merck	Uvasolv	≥ 0.999 g/g
Acetonitrile	Carl Roth	Rotisolv	≥ 0.999 g/g
Diethylamine	Acros Organics	ExtraPure	≥ 0.990 g/g
Diethyl ether	Sigma-Aldrich	ACS reagent	≥ 0.995 g/g
Dimethyl sulfoxide	Merck	Reagent Plus	≥ 0.990 g/g
Ethyl acetate	Sigma-Aldrich	ACS reagent	≥ 0.995 g/g
Ethyl formate	Sigma-Aldrich	ACS reagent	≥ 0.970 g/g
Methanol	Carl Roth	Anhydrous	≥ 0.998 g/g
Pyridine	Fisher	Analytical reagent grade	≥ 0.999 g/g

*specification of the supplier

Table 2: High-boiling azeotrope in the systems AA+P and M+DEA. Experimental NMR data from isobaric measurements at 970 mbar is compared to predictions by the NRTL model and literature data.

acetic acid + pyridine			
	T / K	$x_{\text{P}} / \text{mol mol}^{-1}$	p / mbar
NMR experiment	411.8	0.421	970
NRTL model	411.0	0.428	970
Swearingen and Ross [25]	411.5	0.416	1013
Zieborak et al. [26]	411.3	0.422	1013
Holmberg [27]	411.2	0.410	1013
methanol + diethylamine			
	T / K	$x_{\text{DEA}} / \text{mol mol}^{-1}$	p / mbar
NMR experiment	340.1	0.268	970
NRTL model	339.8	0.260	970
Aucejo et al. [28]	339.8	0.245	1013
Yang et al. [29]	340.2	0.260	1013
Nakanishi et al. [30]	340.4	0.240	973

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