NIR spectroscopy for reaction monitoring and reaction mixture identification of cycloaliphatic epoxides

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Abstract
The industrially relevant cycloaliphatic epoxides do not have a directly distinguishable band in the NIR spectrum and their polymerisation conversion has so far typically been estimated via the simultaneous polymerisation of vinyl ethers. Here, an analytical procedure is presented for the quantitative inline analysis of 4-epoxycyclohexyl methyl-3,4-epoxycyclohexane carboxylate without the need to mix cycloaliphatic epoxides with vinyl ethers. By employing multivariate data analysis on the reaction spectra, the conversion could be analysed spectroscopically. This resulted in a mean uncertainty of 3.38% conversion in the range between 0 and 40% conversion. In addition, a deviation from the initial monomer concentration of 5 w% over a temperature range of 100 °C can be detected and identified via principal component analysis.

Keywords NIR spectroscopy · Multivariate data analysis · Cycloaliphatic epoxides · Uvacure 1500 · EEC

Introduction
Polymer properties are not only defined by the reagents involved in the synthesis, but also to a large extent by all process parameters during synthesis [1]. Particularly in the chemical industry, the review, control and optimisation of process parameters therefore is crucial. Thus, polymer synthesis can and should not only be designed to be time- and cost-efficient, but should also be as uniform and reproducible as possible [2, 3]. Another important aspect here is the safety that has to be ensured, since with functioning monitoring of the reactor content, faulty dosing or also an accumulation of a monomer can be detected at an early stage in order to avoid a possible runaway reaction in the worst case [4]. Direct monitoring of the process parameters is therefore indispensible for quality and safety assurance of the process [2].

Vibrational spectroscopy, such as Raman, near-infrared (NIR) and mid-infrared (MIR) spectroscopy, provides methods to qualitatively and quantitatively monitor polymerisation reactions at a molecular level [2, 5]. With the help of inline process probes, ongoing reactions can be monitored without sampling or further human interaction. In general, the chemical information content from Raman and infrared spectroscopy complement each other. However, while Raman spectroscopy is preferred for inline reaction monitoring in aqueous media, NIR spectroscopy is otherwise the method of choice on an industrial scale due to its comparatively higher flexibility and possible length of optical fibres [5]. It is a widespread and established method and is used in numerous processes to follow polymerisation reactions in the chemical industry [6–9] and also in the field of research. Solvent, emulsion and bulk polymerisations of both radical and ionic nature have been successfully investigated with regard to the conversion, kinetic parameters or other polymer information [4, 10–13].

The interpretation and analysis of reaction spectra, regardless of the type of spectroscopy, is usually of a complex nature, which is why chemometric methods were often used for evaluation in the aforementioned references. For this purpose, calibration and validation models are usually created using suitable software, which correlate the spectral change in certain wavelength ranges with one or more response factors (e.g. monomer concentration). These correlations, based on principal component analysis, can be represented using regression methods such as partial least squares regression (PLS). The regression models from
the calibration and validation spectra can then be applied to unknown spectra to obtain the values for the calibrated response values [2].

The monomer 3,4-epoxycyclohexyl-methyl-3,4-epoxycyclohexane carboxylate (EEC), which is to be spectroscopically examined in this work, ranks among the cycloaliphatic epoxides. Epoxy monomers are cationically and radically photocurable [14, 15] and due to their reduced yellowness after UV curing, they find their application in laminating and pressure-sensitive adhesives, sealants and encapsulants for electronic and optoelectronic devices [16–18] or in stereolithography [15].

As early as 1958, it was shown that terminal epoxides exhibit sharp absorption bands in the NIR spectrum at 6060 cm\(^{-1}\) (First overtone of the C-H stretching vibration) and at 4545 cm\(^{-1}\) (combination vibration) and can thus be detected and quantified with high accuracy [19]. In the case of cycloaliphatic epoxides, there were no further investigations until 2007 by Scherzer et al. [20]. Likewise using EEC as an example, Scherzer’s group was not able to identify specific absorption bands that change in the course of the reaction conversion [20, 21]. Assuming that epoxide monomers and vinyl ethers as mixtures do not copolymerise, but do polymerise together at a similar rate, the conversion of EEC was monitored by the conversion of the vinyl double bond band [21]. This was done on the basis of their own experiments and the work of Rajamaran et al. [22, 23], in which it was postulated by a complex mechanism that the cationic epoxide ring opening is accelerated by the addition of vinyl ethers and, in turn, the vinyl ether polymerisation is slowed down. By using less reactive epoxides, simultaneous polymerisation should thus occur. In contrast, Decker et al. [24] and Kim et al. [25] discussed on the basis of experimental, kinetic data that within the framework of these complex interactions, there is a high probability that copolymerisation of epoxide and vinyl ether also is occurring.

In this work, it is shown that it is not necessary to mix cycloaliphatic epoxide monomers with vinyl ethers for successful in-line reaction monitoring. With the help of multivariate data analysis on the reaction spectra, the reaction conversion can be monitored spectroscopically.

Materials and methods

Reaction vessel setup

The reactions were carried out in a cylindrical glass reaction vessel from Rettberg with a round bottom (Fig. 1). The nominal volume of the vessel is 0.75 L, the diameter at the flat flange is 10 cm, the height is 12 cm. The vessel was closed over the flange with a glass lid that had standard taper joints. A magnetically coupled stirrer shaft with a perforated steel anchor stirrer (9.5 cm wide, 8.5 cm high) was guided into the reaction vessel via the central ground joint. The NIR probe was inserted at an angle, but close to the stirrer shaft. Via the other sections, nitrogen degassing, cooling by means of a 400 mm long Dimroth cooler and the temperature monitoring with a Pt100 temperature sensor could be carried out. The temperature of the reaction vessel was controlled via a hemispherical heating mantle. The temperature sensors of the reactor and the mantle were recorded using the LABView software.

Polymerisation procedure

A mixture of 250 g 3,4-epoxycyclohexyl-methyl-3,4-epoxycyclohexane carboxylate (EEC, Uvacure 1500) and 250 g toluene were added to the reaction vessel. To remove atmospheric and dissolved oxygen inside the reaction vessel, the reaction mixture was overflowed with a mild but detectable stream of nitrogen while heating and stirring at 80 rpm for 30 min. As soon as a stable reactor temperature of > 90 °C had been established, first the t = 0 sample was taken for MIR spectroscopy. The reaction was then thermally initiated by
means of a quarternary ammonium blocked super acid catalyst via a syringe. By the addition of 5 g pyridine, the reaction could be stopped after approx. 40% conversion.

**Mid-infrared (MIR) spectroscopy**

During the reaction, samples of approx. 5 mL were taken from the reaction vessel via syringes. The samples were transferred to pre-cooled vials at 0 °C, in which 0.5 mL pyridine was placed to prevent further polymerisation. The sample vials were closed with a lid, sealed with parafilm and stored at 0 °C until the time of measurement.

The absorbance was measured using the Bruker VERTEX 70 spectrometer equipped with the A225/Q Platinum ATR unit. The background measurement was performed with 128 scans and the sample measurements with 32 scans. The spectra were baseline corrected (interactive, 100 iterations) in the OPUS 7.5 measurement software before further evaluation.

**Near-infrared (NIR) spectroscopy**

The inline measurement of the NIR spectra during the reaction was carried out using the VECTOR 22/N-F spectrometer from Bruker via the Excalibur XP 20 transmission probe from Hellma. The background measurement was carried out with 50 scans before the start of the reaction in the empty reaction vessel. For the sample measurements every 60 s, the time for repeated scans was limited to 0.25 min in the measurement software OPUS 6.5. The interferogram was recorded with a 10 kHz low-pass filter in double-sided foward-backward mode.

**Results and discussion**

**Reaction conversion monitoring**

When initially examining the NIR spectra during the polymerisation of EEC in toluene, some spectral changes could be detected. A more detailed investigation was then carried out after Standard Normal Variate (SNV) normalisation in the range between 4700–9300 cm\(^{-1}\) with subsequent dynamic baseline correction (Fig. 2).

The evaluation of changes in spectral regions was always carried out first visually and then by means of principal component analysis. It was found that not all changing bands and regions were dependent on the conversion. Scherzer et al. [20] also found such changes in their recorded NIR spectra of EEC, which in their case were due to moisture. However, influences of humidity are negligible in our case with a reaction temperature > 90 °C, which was usually already set at least 30 min before initiation. According to the principal component analysis, the most intensive changes in Fig. 2, which occur between 5700–6000 cm\(^{-1}\), describe both increasing and decreasing influences, which are, however, severely noisy. The observation of the right shoulder of this larger band region shows an inflection point between 5515–5625 cm\(^{-1}\) (highlighted in Fig. 2), which has a change that correlates with the reaction conversion. In order to show this area more clearly as well as to enable a noise-free multivariate evaluation, the first derivative of the spectrum should be formed (Fig. 2).

With the help of the first derivative of the spectra, the monomer concentration of EEC and thus also the reaction conversion can be described and evaluated as a decrease of the band between 5515–5625 cm\(^{-1}\). The range is highlighted in Fig. 3.

Since it was first determined that, contrary to the expectations of the known literature, the spectra allowed for an analysis of the EEC conversion, a calibration series was then to be created. For this purpose, different approaches were tried. In order to achieve an optimal prediction quality of the calibration, the measured calibration solutions must be as similar as possible to the reaction spectra. In order to cover a conversion range of 0–40%, which is up to the point until strong gelation in this system occurs, the decrease of the monomer and the increase of the forming polymer must be considered in a calibration series. The polymer influences the NIR spectra chemically, as well as by changing the viscosity and the refractive index. For this reason, calibration solutions were prepared which consisted of defined amounts of EEC, toluene and the polymer according to the theoretical monomer conversion. The polymer originated from the reaction mass of the first reaction after 40% conversion and
was dried in a vacuum at 60 °C. Using a PLS regression, the spectra of the calibration solutions could then be correlated with the weighed concentrations. Even though a clear linear correlation was evident, this calibration could not be applied to the reaction in any meaningful way. Since it is also known that the temperature has a non-negligible influence on the band intensities [26] and calibration solutions are usually measured at room temperature, measurements of the previously created solutions at the reaction temperature followed. The resulting PLS calibration could not be applied to the reaction spectra with this method either. It is assumed that the added polymer could not be completely freed from EEC and pyridine (inhibitor) and thus reactions still occurred (yellow colouration of the polymer). Moreover, other effects that are recorded spectroscopically during an ongoing reaction can generally not be covered by simple calibration solutions. For this reason, the calibration of the EEC conversion should be made based on reaction spectra. However, since the concentrations of the reactants in the reaction solution are no longer known during the reaction, they must first be determined using an alternative, reliable analytical method. During a polymerisation reaction up to a conversion of 40%, up to 9 samples were taken at different times, which were then measured using MIR spectroscopy. In the MIR spectrum, the isolated bands of the constant C=O stretching vibration in the range between 1670–1770 cm⁻¹ and the C-H bending vibrations of the epoxide at 770–825 cm⁻¹ could be observed (see Fig. 4). The integrals of these bands were put into ratio to determine the reaction conversion.

Since a NIR spectrum is recorded every minute during the reaction, each MIR spectrum could be assigned to a NIR spectrum at the respective times of sample collection. From four reactions with a total of 36 training samples, a PLS regression with two ranks, an $R^2$ of 0.985 and an RMSECV (Root Mean Square Error of Cross Validation) of 1.68% (conversion, absolute value) could then be created (Fig. 5).

In Fig. 6, the PLS regression from Fig. 5 was applied to two different reactions with comparable reaction procedure.

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![Fig. 3](image_url)  
**Fig. 3** First derivative of SNV-normalised NIR spectra of the reaction of EEC (50 w%) in toluene, every minute up to a conversion of 40%. Highlighted is the band between 5515–5625 cm⁻¹ which decreases with increasing conversion.

![Fig. 4](image_url)  
**Fig. 4** MIR spectrum before the start of polymerisation of EEC in toluene. The C=O stretching vibration at 1670–1770 cm⁻¹ and the C-H bending vibration of the epoxide at 770–825 cm⁻¹ are marked in red.

![Fig. 5](image_url)  
**Fig. 5** PLS regression of the band range between 5515–5625 cm⁻¹ for the conversion determination of the polymerisation reaction of EEC in toluene. The PLS was performed using 2 ranks of 36 reaction spectra from a total of four reactions. The pretreatment of the reaction spectra included a SNV in the range between 4700–9300 cm⁻¹, the formation of the first derivative and a baseline correction.
The linear reaction course corresponding to the cationic polymerisation can be observed by means of the conversion values obtained from the NIR spectroscopy. A scattering is recognisable, which is due to the low intensity of the calibrated band and thus an average uncertainty of the conversion of 3.38% (absolute conversion value) can be obtained from the 95% confidence interval. The values correspond to the MIR measuring points measured at-line.

**Reaction mixture identification**

Since the reaction system bears a strong exothermic potential, a deviation of the starting reaction mixture may have a potentially fatal consequence. Based on the reaction monitoring, it was further checked whether small deviations of the reaction temperature and the EEC:toluene ratio at the time of the reaction start can also be distinguished by means of multivariate evaluation of the NIR spectra. For this purpose, solutions with EEC:toluene mass ratios of 40:60 up to 60:40 were measured in 5% steps. In addition, the temperature was increased from room temperature up to 120 °C. At a stable temperature plateau, 5 spectra each were then recorded before the temperature was increased further. The spectra were then SNV-normalised in the range between 9300–4700 cm\(^{-1}\) and examined using principal component analysis. The influences on the spectra change could be limited to two principal components. The scores of the two principal components are plotted in Fig. 7.

It is shown that along the first principal components (x-axis) the spectra of different monomer concentrations can be divided into clearly defined clusters. In particular, the desired target formulation used in the reaction with the ratio 50:50 is clearly separated. The only exception here are the spectra of the EEC:toluene ratio 40:60, which split once here along the first principal component presumably due to a measurement error. The clusters continue to separate along their second principal component (y-axis), which correlates with the temperature change. The temperature influence is perceptible as linear, but noisy and not clearly separated. This is illustrated in Figs. A1 and A2, where the linear curves of the score values of the respective principal components are plotted.

**Conclusion**

It was shown that, contrary to what has been stated in previous literature, cycloaliphatic epoxides such as EEC can also be monitored with regard to their reaction conversion by means of NIR spectroscopy. For this purpose, the spectrum had to be pretreated by determining the first derivative and baseline correction. It was possible to calibrate the conversion from 0 to 40% by means of a PLS regression with a
mean uncertainty of the conversion of 3.38% (absolute conversion value). Furthermore, by means of principal component analysis of uninitiated reaction mixtures, it was possible to distinguish deviations of the monomer or solvent content from the desired target EEC:toluene mass ratio of 50:50 in 5% steps. This was done over a wide temperature range of 100 °C. A deviation of the temperature could be approximately determined in the spectra with a fixed mass ratio.

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Declarations

Conflict of interest The authors declare that they have no conflicts of interest for the submitted work.

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