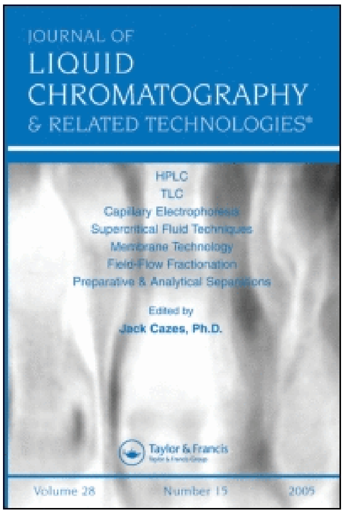

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DETERMINATION OF RATE CONSTANTS IN A LIQUID CHROMATOGRAPHIC REACTOR WITH SIMULATED RECYCLING, USING EMPIRICAL PEAK SHAPE EQUATIONS

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ABSTRACT

A new mathematical-analytical equation is derived for fitting purposes in the determination of mobile phase rate constants from liquid chromatographic reactor experiments, with a recycling of the internal chromatogram via an empty capillary. The equation was successfully tested with results from numerical calculations, as well as results from the on-column hydrolysis of ortho-phthalic dichloride.

INTRODUCTION

The determination of rate constants from reactions occurring in elution chromatographic experiments has been investigated, during three decades, as pointed out in reviews.[1–3] Methods were developed for irreversible, reversible,

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and consecutive first order reactions, as well as for second order reactions. However, only an apparent rate constant, being the weighted average from the rate constants in the mobile phase and the stationary phase, was usually obtained. Since the apparent rate constant largely depends on the actual geometry and packing of a column, Chu and Langer suggested a setup, in 1987, in which two columns of the same type (stationary phase, size) are connected via an empty capillary[4] (Fig. 1), and from which pure mobile (i.e., liquid) phase rate constants can be obtained. The first column produces a typical reaction chromatogram, due to the simultaneous occurrence of separation and chemical reaction (Fig. 2b). In the capillary (Fig. 2c), only the mobile phase reaction can proceed, producing an extra peak, and then the internal chromatogram is either really recycled into the same column, or a recycling is simulated by connecting a column of the same type (size, stationary phase). In this second column run (Fig. 2d), the on-column product formation, as well as the separation of the pre-column product and of impurities, is completed, and the extra peak is separated from the reactant.

The subject of the present paper is the development of a method for the determination of the mobile-phase rate constants, based on the derivation and application of a mathematical-analytical equation, which is used in a fitting procedure on experimental chromatograms from irreversible first-order reactions by home-made software. At least, in reactions with the eluent, poorly reproducible pre-column reactions (in the injection loop and in the capillary before the column) cannot generally be suppressed or ignored. Hence, an inert standard method will not be appropriate in such investigations, and the application of a fitting procedure becomes a requirement.

MATHEMATICAL MODELING

The mathematical model is based on the assumptions of isothermal columns, constant eluent flow rate, and linear chromatographic conditions

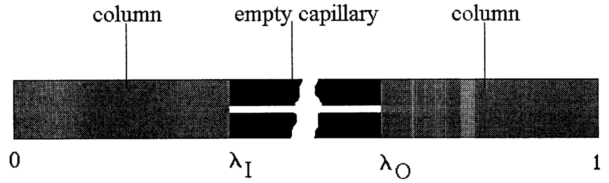

Figure 1. Development of the reaction chromatogram in a recycling setup (schematic). a: Sample; b: at the outlet of the first column; c: at the outlet of the capillary; d: at the outlet of the second column. (White: reactant, dark gray: product from pre-column reaction, gray: product from on-column-reaction, black: impurity).

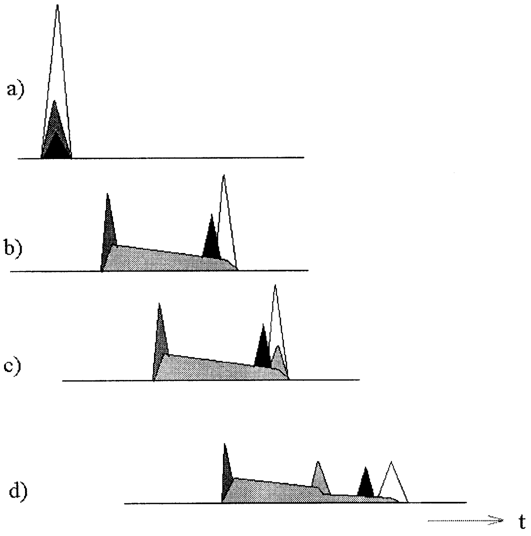

Figure 2. Chromatographic reactor with simulated recycling (schematic).

(retention times and peak variances depend linearly on the spatial coordinate). Furthermore,[5,6] it is assumed that the reactant peak produces differential product pulses at each cross-section of the column, which then move like differentially small product injections.

Introducing a reduced length coordinate, λ, specified to each part of the chromatographic reactor as shown in Fig. 1, the following balance equations are established.

Generally, it follows, for a differential product pulse:

$$\mathrm{d}c_P = -\frac{\mathrm{d}m_R}{\mathrm{d}\lambda}\Psi(\lambda, \mu_R, \mu_P, \sigma_R, \sigma_P, t)\,\mathrm{d}\lambda \tag{1}$$

i.e., the differential pulse area is given by the decrease of the reactant pulse while passing a cross-section, and the peak shape is given as a weighed result from the peak shape of the reactant and from the peak shape of the product.

Assuming a Gaussian differential pulse shape, the following is obtained: $0 \leq \lambda \leq \lambda_I$:

$$\mathrm{d}c_P = m_0 k_a t_0 \exp(-k_a t_0 \lambda) \frac{1}{\sqrt{2\pi\sigma^2}} \times \exp\left\{ - \frac{\begin{array}{r}[\mu_R \lambda + \mu_P(\lambda_I - \lambda) + t_0(\lambda_I - \lambda_O) \\ + \mu_P(1 - \lambda_O) - t]^2\end{array}}{2\sigma^2} \right\} \mathrm{d}\lambda \tag{2}$$

$\lambda_I \leq \lambda \leq \lambda_O$:

$$\mathrm{d}c_P = m_0 k_e t_0 \exp(-k_a t_0 \lambda_I) \exp[-k_e t_0(\lambda - \lambda_I)] \frac{1}{\sqrt{2\pi\sigma^2}} \times \exp\left\{ \frac{-[\mu_R \lambda_I + t_0(\lambda_I - \lambda_O) + \mu_P(1 - \lambda_O) - t]^2}{2\sigma^2} \right\} \mathrm{d}\lambda \tag{3}$$

$\lambda_O \leq \lambda \leq 1$:

$$\mathrm{d}c_P = m_0 k_a t_0 \exp(-k_a t_0 \lambda_I) \exp[-k_e t_0(\lambda_I - \lambda_O)] \exp(-k_a t_0 \lambda) \times \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left\{ - \frac{\begin{array}{r}[\mu_R \lambda_I + t_0(\lambda_I - \lambda_O) + \mu_R(\lambda - \lambda_O) \\ + \mu_P(1 - \lambda) - t]^2\end{array}}{2\sigma^2} \right\} \mathrm{d}\lambda \tag{4}$$

Obviously, these equations can only be integrated analytically by assuming spatially constant standard deviations. If the difference in the standard deviations is less than an order of magnitude, different standard deviations for product and reactant might be approximated via a weighted (time-dependent) average:

$$\sigma^2 \approx \frac{(t_R - t){\sigma_P}^2 + (t - t_P){\sigma_R}^2}{t_R - t_P} \tag{5}$$

where

$$t_R = \mu_R + t_E \tag{5a}$$

$$t_P = \mu_P + t_E \tag{5b}$$

$$t_E = t_0(\lambda_O - \lambda_I) \tag{5c}$$

The reactant-pulse is given by

$$c_R = m_0 \exp(-\kappa_a(t_R - t_E) \exp(-k_e t_E) \frac{1}{\sqrt{2\pi{\sigma_R}^2}} \exp\left(\frac{-(t - t_R)^2}{2{\sigma_R}^2} \right) \tag{6}$$

where

$$\kappa_a = k_a t_0 \frac{(1 - (\lambda_O - \lambda_I))}{t_R - t_E} \tag{7}$$

and the extra-pulse is given by

$$\begin{aligned} c_P = {} & m_0 \exp\left(-\kappa_a \frac{(t_R - t_E)}{2}\right)(1 - \exp(-k_e t_E)) \\ & \times \frac{1}{\sqrt{\pi({\sigma_R}^2 + {\sigma_P}^2)}} \left\{ - \frac{((t_R + t_P)/2 - t)^2}{{\sigma_R}^2 + {\sigma_P}^2} \right\} \end{aligned} \tag{8}$$

From Eqs. (6) and (8), it becomes clear that it is not necessary to measure the geometric parameters from the setup, but it is sufficient to observe the retention times and the residence time in the void capillary t_E. Unfortunately, the latter cannot be obtained from the extra-pulse, since its shape does not explicitly depend on t_E. The solutions for Eqs. (2) and (4) will not be given here, because they are rather voluminous and not instructive. They can be obtained from the authors.

EMG shapes could be used instead of Gaussian in Eqs. (2)–(4), as well as in Eq. (6), and different standard deviations and skewness factors for product, reactant, and impurities could be taken into account following the published method,[8] resulting in a better fit for tailed peaks. This calculation-oriented subject will not be discussed here, also considering the fact that the slight tailing due to linear processes can be covered by Gaussians, whereas a strong tailing is also a strong indication for a nonlinear sorption isotherm.

DETERMINATION OF RATE CONSTANTS

Based on the solutions of Eqs. (2)–(4) and Eq. (6), essentially the following fitting equation was used in a Delphi program (impurities c_I or product from pre-column reactions c_{PRE} are encountered as additional Gaussians):

$$\hat{h} = \varepsilon(c_P(0 \cdots \lambda_I) + c_P(\lambda_I \cdots \lambda_O) + c_P(\lambda_O \cdots 1) + f c_R + f_I c_I + c_{\mathrm{PRE}}) \tag{9}$$

From fitting calculations, primarily, the reduced rate constants $\kappa_a(t_R - t_E)$ and $k_e t_E$, respectively, are found. The fitting procedure includes adjustment of all retention times and variances and, in principle, also detector responses. Because of the multitude of parameters contained in the aforementioned analytical equations, numerous side minima are possible. The main problem is the weak influence of the detector response ratio from the product peak and the reactant peak (response factor f) on the fitting minimum. If the response factor f is treated as a variable in the fitting procedure, the outcome of the rate constants depends markedly on the initial values. Therefore, the response factor should be determined independently and, preferably, under the same solvent composition as in the experiments. Furthermore, the response factor determination should be accomplished in experiments without recycling in order to have fewer degrees of freedom in the chromatogram.

Two single-column experiments can be carried out, with a large difference in the flow rates, to obtain large differences in the conversions. For each experiment, the ratio of on-column product area to total area from on-column product and reactant must be evaluated (Eq. (10a)).

From Eq. (10b), the retention time-related apparent rate constant κ_a can be evaluated numerically and, finally, from Eq. (10c), the response-factor can be obtained.

$$y = \frac{A_P}{(A_R + A_P)} = \frac{m_0(1 - \exp(-\kappa_a \mu_R))}{m_0(1 - \exp(-\kappa_a \mu_R)) + f m_0 \exp(-\kappa_a \mu_R)} \tag{10a}$$

$$\frac{(1/y_1) - 1}{(1/y_2) - 1} = \frac{\exp(\kappa_a \mu_{R1}) - 1}{\exp(\kappa_a \mu_{R2}) - 1} \tag{10b}$$

$$f = \frac{1}{y}(\exp(\kappa_a \mu_R) - 1) \tag{10c}$$

The fitting program can be used to obtain the response factor. By choosing an initial value for f, first guesses of y_1 and y_2 can easily be obtained by the program, also excluding impurities and pre-column product. A refined value of f is then calculated from Eq. (10c) and the procedure is started over, following an iteration algorithm.

Another way to establish the response factor is to investigate the sum of the reduced residua

$$E = \sum \frac{\sqrt{\sum (h - \hat{h})^2}}{A_T} \tag{11}$$

from a number of experiments, as a function of the response factor (cf. Fig. 6), which is found at the minimum of this correspondence. This overall calculation has the advantage of being more reliable than a two-experiment calculation, but has the disadvantage of a much greater experimental and computational effort.

Finally, the residence time in the capillary t_E must be known to evaluate the rate constants explicitly. This can be done either by direct comparison of the retention times in a setup, with and without a capillary. However, exactly the same flow rate then must be applied. On the other hand, the retention time ratios from product and reactant can be used:

$$\tau = \frac{t_P}{t_R} = \frac{\mu_P + t_E}{\mu_R + t_E} = \frac{\tau_C + t_E/t_R}{1 + t_E/t_R} \tag{12a}$$

where

$$\tau_c = \frac{\mu_P}{\mu_R} \tag{12b}$$

Consequently:

$$t_E = t_R \frac{\tau - \tau_C}{1 - \tau_C} \tag{12c}$$

i.e., having once established the selectivity τ_C from a setup without capillary, the residence time within the capillary can be calculated from t_R and t_P, which are explicitly obtained in the fitting procedure.

RESULTS FROM NUMERICALLY CALCULATED REACTION CHROMATOGRAMS

To be sure that the aforementioned equations, as well as the program based on these equations, are correct, reaction chromatograms were calculated numerically, using a finite difference scheme similar to the one used by Czok and Guiochon,[7] and controlling the peak variances via the so-called numerical dispersion. As can be seen from Fig. 3, the original chromatograms and the fitted chromatograms are practically congruent.

However, there are slight systematic deviations in the recalculated rate constants, which amount to about 1% of the original values. On the other hand, some part of these errors stems from the numerical calculation procedure for the original chromatograms.

RESULTS FROM CHROMATOGRAMS OBTAINED EXPERIMENTAL

The hydrolysis of ortho-phthalic dichloride ($ClCOC_6H_4COCl$) to form ortho-phthalic chloride $HOOCC_6H_4COCl$ was used to obtain respective reaction chromatograms. Two Multospher 100 RP 18-5/FBS 125 × 4.6 columns (Chromatographie Service, Langerwehe, Germany) were applied, which were connected with a 25 m stainless steel HPLC capillary (0.25 mm i.d.).

The experiments were carried out with a modular HPLC from Knauer (Berlin, Germany), consisting of HPLC pump K-501, Knauer column oven and

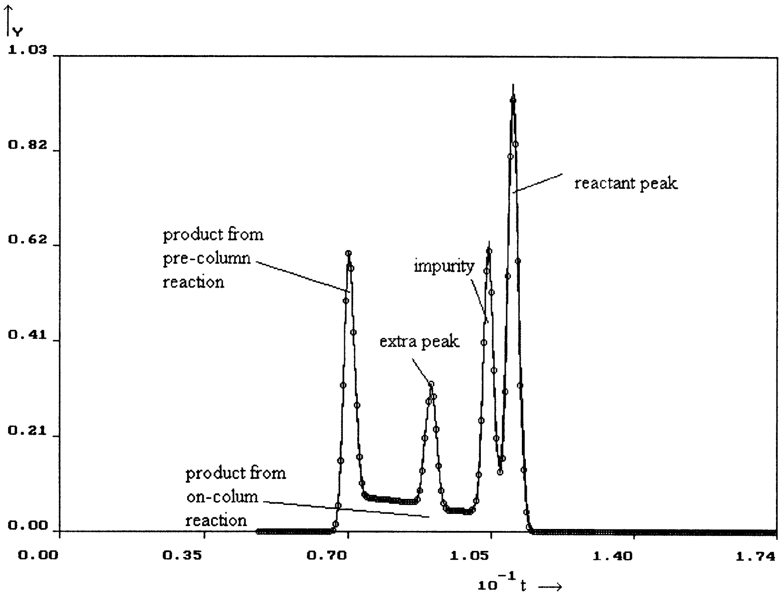

Figure 3. Comparison of a numerically calculated chromatogram (circles) with the best fit (line).

DAD K-2700 WellChrom. Measurements were obtained with acetonitrile/water (85 : 15,v/v) as eluent, flow rates from 0.4 to 0.7 mL/min, and chromatograms were recorded at 205 nm. Chromatograms and fitting result are shown in Fig. 4 for an experiment without recycling and, in Fig. 5, for an experiment with simulated recycling. In Fig. 6, the determination of the response factor can be seen.

Mobile phase rate constants of $0.046 \pm 0.007\,\mathrm{min}^{-1}$ (22°C), $0.052 \pm 0.009\,\mathrm{min}^{-1}$ (25°C) and $0.070 \pm 0.01\,\mathrm{min}^{-1}$ (28°C) were found. The experimental error, though being quite large, is comparable with that in Ref. (4) and illustrates the limits of commercially available equipment. Nevertheless, the data correspond quite well to the rate constant of $0.040 \pm 0.006\,\mathrm{min}^{-1}$ (22°C), $0.053 \pm 0.005\,\mathrm{min}^{-1}$ (25°C) and $0.063 \pm 0.008\,\mathrm{min}^{-1}$ (28°C) as obtained by conductimetric batch experiments.

CONCLUSIONS

The derived mathematical-analytical function is useful for the determination of mobile phase rate constants in chromatographic reactors with simulated

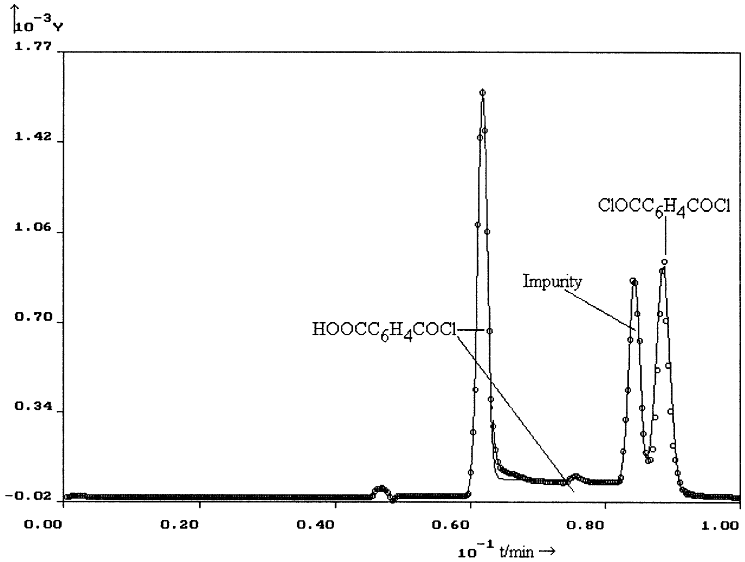

Figure 4. Comparison of an experimental chromatogram without recycling (circles) and the best fit (line).

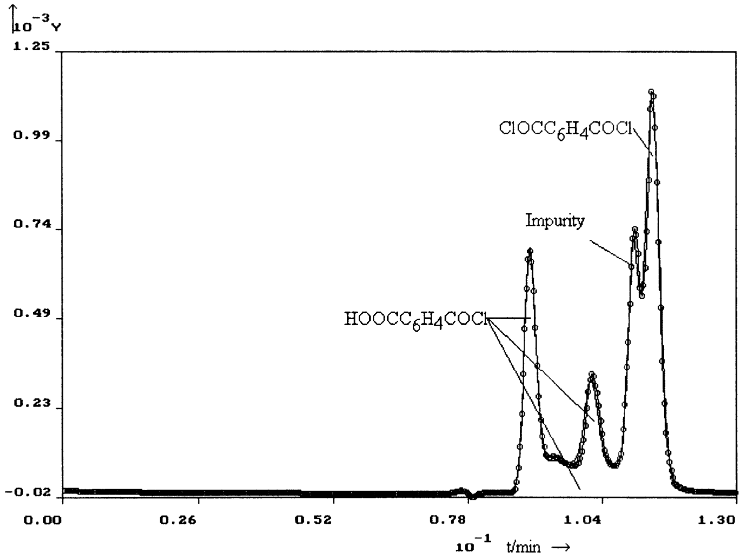

Figure 5. Comparison of an experimental chromatogram with recycling (circles) and the best fit (line).

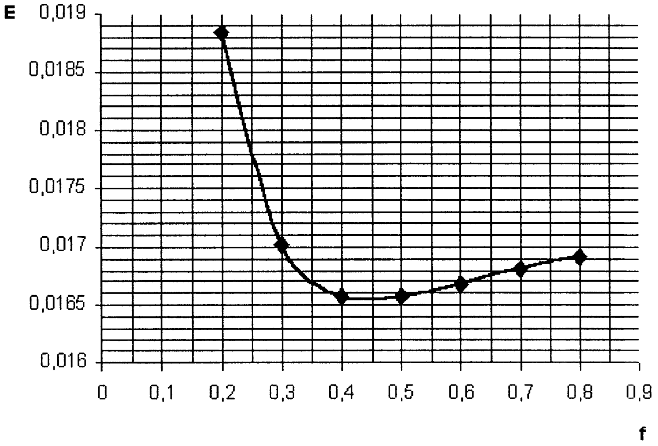

Figure 6. Dependence of the sum of the reduced residua E from 80 experiments, without recycling, on the response factor f. The experimental response factor is obtained from the minimum.

recycling. Since it is not possible to process reaction chromatograms by normal integration routines, such fitting functions are necessary for the computer-assisted evaluation of mobile phase rate constants from HPLC measurements. The rate constant can be evaluated from one chromatogram; however, the detector response ratio from reactant and product, as well as their retention ratio (selectivity), on a single column must be determined independently.

SYMBOLS

A_P:	peak area of product peak
A_R:	peak area of reactant peak
A_T:	total peak area
c_P:	concentration of the product
c_{PRE}:	concentration of the product from pre-column reactions
c_R:	concentration of the reactant
E:	sum of all reduced residua in a number of experiments
f:	response factor of the product
f_I:	response factor of an impurity
h:	experimental recorder signal
$\hat{h}$:	theoretical recorder signal (cf. Eq. (9))
k_a:	dead-time related apparent rate constant

k_e: rate constant (mobile phase)
m_0: concentration-time area of reactant at the column inlet
t: time
t_E: residence time in the capillary
t_R: maximum retention time of the reactant in a recycling setup
t_P: maximum retention time of the product in a recycling setup
t_0: dead time
ε: detector response of the product
κ_a: retention-time related apparent rate constant
λ: reduced spatial coordinate (cf. Fig. 2)
λ_I: reduced spatial coordinate of the capillary inlet
λ_O: reduced spatial coordinate of the capillary outlet
μ_R: maximum retention time of reactant (column)
μ_P: maximum retention time of product (column)
σ: standard deviation of differential product pulse as defined in Eq. (5)
σ_R: standard deviation of reactant peak
σ_P: standard deviation of product peak
τ: retention ratio product vs. reactant (recycling setup)
τ_C: retention ratio product vs. reactant (column), selectivity

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