Determination of Rate Constants of Consecutive First Order Reactions Occurring on Chromatographic Columns

R. Thede[a]; D. Haberland[a]; E. Below[b]; J. A. Jönsson[c]
[a] Institute of Physical Chemistry, University of Greifswald Soldtmannstraße, Greifswald, Germany [b] Institute of Forensic Medicine, University of Greifswald Soldtmannstraße, Greifswald, Germany [c] Department of Analytical Chemistry, University of Lund Lund, Sweden

PLEASE SCROLL DOWN FOR ARTICLE

DETERMINATION OF RATE CONSTANTS OF CONSECUTIVE FIRST ORDER REACTIONS OCCURRING ON CHROMATOGRAPHIC COLUMNS

R. THEDE[1], D. HABERLAND[1],
E. BELOW[2], AND J. A. JÖNSSON[3]
[1]Institute of Physical Chemistry
[2]Institute of Forensic Medicine
University of Greifswald
Soldtmannstraße 23
D-17489 Greifswald, Germany
[3]Department of Analytical Chemistry
University of Lund
Lund, Sweden

ABSTRACT

Approximate analytical equations were developed for the products of consecutive reactions occurring on a chromatographic column. The equations were tested both by numerically evaluated chromatograms and the acid catalyzed hydrolysis of phthalic dichloride in a liquid chromatographic reactor.

INTRODUCTION

The determination of rate constants from chromato-grams of on-column reacting substances has been reported

1137

several times by different authors /1 /, /2 /.

Mostly, however, the papers are focused on simple first

order reactions or do not pay attention to the possibi-

lity of the occurrence of complex reactions.

The present paper deals with first order consecutive

reactions: $A_1 \xrightarrow{k_1} A_2 \xrightarrow{k_2} A_3$.

It is characteristic for a chromatographic reactor that

the separation of reactants and products is incomplete,

since the reactions occur from the beginning until the

end of the columns, and there is no possibility of a

separation of the products formed near the end of the

column. Therefore, in consecutive reactions always a

mixture of the intermediate product and the final pro-

duct is observed, and the evaluation of peak shape equa-

tions for both substances becomes necessary.

PULSE SHAPE EQUATIONS

Mathematical derivation and semi-analytical solution

     The mathematical derivation of the pulse shape

equations will be based on the following idea:

While passing a cross-section of the chromatographic

column the reactant produces a differential product

pulse having the initial shape of the reactant pulse at

this cross-section and an amount of substance due to the kinetics of its formation. This differential product pulse is then eluted in a normal chromatographic way, i. e. the moments of the pulse shape equation are altered in the same way as for an injected substance.

The product pulse at the end of the column is then derived by adding (integrating) all the concentration elements of all differential product pulses, which pass simultaneously at the end of the column. However, in case of an intermediate product of a consecutive reaction one must consider the loss of substance due to its transformation to the final product. Therefore, the amount of a differential pulse from the intermediate product at the end of the column is given by the product of the amount produced at x, which is $m_{10}k_{1a} \exp(-k_{1a} x/l)$ dx, and a factor for the part not converted to the final product, which is $\exp(- k_{2a}(1-x)/l)$:

$$dm_2(l) = m_{10}k_{1a}e^{-k_{1a}\frac{x}{l}}e^{-k_{2a}\frac{(1-x)}{l}}dx \qquad (1)$$

Hence, a concentration element of the product pulse is given by multiplication of the amount of the product pulse and a pulse shape equation (for a summary of suitable pulse shape equations see /3/):

$$dc_2(x,l,t) = dm_2(x,l)\,\psi(\mu_i,t)\,dx \qquad (2)$$

The intermediate product pulse shape equation was found
by transformation of Eqn.(2) to time coordinates using
the equation

$$\frac{x}{l} = \frac{(\mu - \mu_2)}{(\mu_1 - \mu_2)} \tag{3}$$

and integration:

$$c_2 = m_{10} \acute{K}_1 e^{-\acute{K}_2 (\mu_1 - \mu_2)} e^{-(\acute{K}_1 - \acute{K}_2)(t - \mu_2)} \int_{\mu_1}^{\mu_2} e^{-(\acute{K}_1 - \acute{K}_2)(\mu - t)} \psi \, d\mu \tag{4}$$

The derivation of a pulse shape equation for the final
product is still more complicated:

First, a differential amount of the final product pulse
is considered, which is formed by a differential inter-
mediate product pulse at position y in the column. The
differential intermediate product itself was formed
before at the position x (with x < y):

$$ddm_3 = k_{2a} dm_{20}(x, x) e^{-k_{2a}(\frac{y}{l} - \frac{x}{l})} dy \tag{5}$$
$$= m_{10} k_{1a} k_{2a} e^{-(k_{1a} - k_{2a})\frac{x}{l}} e^{-k_{2a}\frac{y}{l}}$$

Then, multiplication with the pulse shape equation,
transformation to time coordinates and integration leads
to the final product pulse shape equation:

$$c_3 = m_{10} \acute{k}_1 k''_2 e^{-\Delta k(t-\mu_2)} e^{-k''_2(t-\mu_3)}$$

$$\int_{\mu_2}^{\mu_1} e^{-\Delta k(\mu-t)} \int_{\mu_g}^{\mu} e^{-k''_2(\acute{\mu}-t)} \psi \, d\acute{\mu} \, d\mu \qquad (6)$$

Even in case of the probably simplest single pulse shape equation, the Gaussian, a numerical solution of both the product pulse equations (Eqn. 4 and Eqn. 6)is necessary, since the standard deviation of the differential pulse shapes depends on μ and μ ', respectively.

However, if the standard deviations of the pulses do not differ in order of magnitudes one can apply approximate equations for the standard deviations, in which these do not depend on the μ or μ', but on the time. In the evaluation of the standard deviation of the final product its dependence on the standard deviation of the intermediate product is completely neglected.

$$\sigma^2 = \sigma^2_{\ i} + \frac{t-\mu_i}{\mu_1-\mu_i} (\sigma^2_{\ 1} - \sigma^2_{\ i}) \qquad (7)$$

intermediate product: $i=2$

final product: $i=3$

Moreover, the approximate formulae developed here lead to slight "losses" or "gains" of mass due to an additional skewness of the product peaks, which is produced by the approximation.

Then, some partial integrations with the final product functions (Eqn.6) are possible, leading to:

$$
c_3 = m_{10} \frac{\acute{K}_1 k''_2}{\Delta k} e^{-\Delta k (t - \mu_2)} e^{-k''_2 (t - \mu_3)}
$$

$$
[PI(\mu_2, \mu_1, (\Delta k + k''_2))
$$
$$
+ e^{-\Delta k (\mu_2 - t)} (PI(\mu_3, \mu_2, (k''_2))
$$
$$
- e^{-\Delta k (\mu_2 - t)} e^{-\Delta k \frac{\Delta \mu_{12}}{\Delta \mu_{13}} (t - \mu_3)} PI(\mu_3, \mu_1, (\Delta k \frac{\Delta \mu_{12}}{\Delta \mu_{13}} + k''_2))]
$$

(8)

Similar, Eqn. 3 for the intermediate product can be rewritten:

$$
c_2 = m_{10} \acute{K}_1 e^{(-\acute{K}_2 (\mu_1 - \mu_2))}
$$
$$
e^{-\acute{K}_2 (t - \mu_2)} PI(\mu_1, \mu_2, (\acute{K}_1 - \acute{K}_2))
$$

(9)

The product integral PI in Eqn. 8 and Eqn. 9 is defined by:

$$
PI(\mu_A, \mu_B, k, \sigma) = e^{\frac{k}{2} \sigma^2}
$$
$$
(\int_{-\infty}^{\mu_B} \frac{1}{\sqrt{2\pi} \sigma} e^{-(\frac{t - \mu}{2\sigma})^2} d\mu - \int_{-\infty}^{\mu_A} \frac{1}{\sqrt{2\pi} \sigma} e^{-(\frac{t - \mu}{2\sigma})^2} d\mu)
$$

(10)

The main advantage of the approximation is that it becomes possible to evaluate approximate product pulses in very short time (using polynomial approximations for the Gaussian integrals /6/), which is favorable for curve fitting procedures - in our opinion the only one possibility to calculate rate constants from reaction chromatograms of complex reactions.

Discussion of the product pulse shapes

First of all it should be pointed out, that the PI-functions in the product pulse equations become one or at least constant between the moments forming the boundaries of the integral.

Therefore, similar to the product pulse in a simple irreversible reaction the intermediate product pulse is an exponential function between μ_1 and μ_2. However, while in a simple reaction there is always a decay from μ_1 to μ_2, the intermediate pulse can increase, decrease or even become constant, depending on the sign of the difference between the rate constants (Fig. 1). If there was a possibility to observe the pure intermediate, the difference of the rate constants could be evaluated by the so-called product curve method /4/,/5/.

For the final product pulse there are two different parts (Fig.2). First, the part between the retention time of the final product and the retention time of the intermediate, in which the final product curve has a convex curved shape:

$$c_3 = m_{10} \frac{k_1' k_2''}{\Delta k} e^{-k_2''(t-\mu_3)} (1 - e^{\Delta k \frac{\Delta \mu_{12}}{\Delta \mu_{13}}(t-\mu_3)}) \quad (11)$$

Second, the part between the retention time of the intermediate and the retention time of the reactant, in

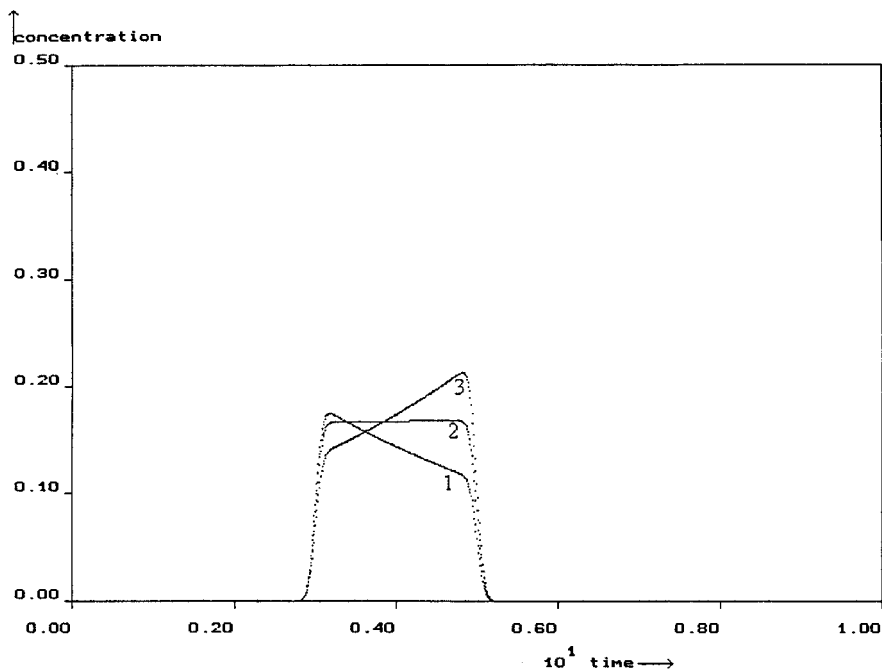FIGURE 1:   INTERMEDIATE PRODUCT PULSE OF A CONSECUTIVE
              REACTION
              (1: $k_1'-k_2'<0$, 2: $k_1'-k_2'=0$, 3: $k_1'-k_2'>0$)

which the final product curve has a concave (almost
exponentially decaying) curved shape:

$$c_3 = m_{10}\frac{k_1 k''_2}{\Delta k}\, e^{-k''(\mu_2-\mu_3)}\, e^{-(k_1-k_2)(t-\mu_2)} \left(1 - e^{-\Delta k(\mu_2-\mu_3)}\, e^{\Delta k \frac{\Delta \mu_{23}}{\Delta \mu_{13}}(t-\mu_3)}\right)$$

(12)

Also, from these equations it can be concluded that the
concentration of the final product disappears at μ_1 and
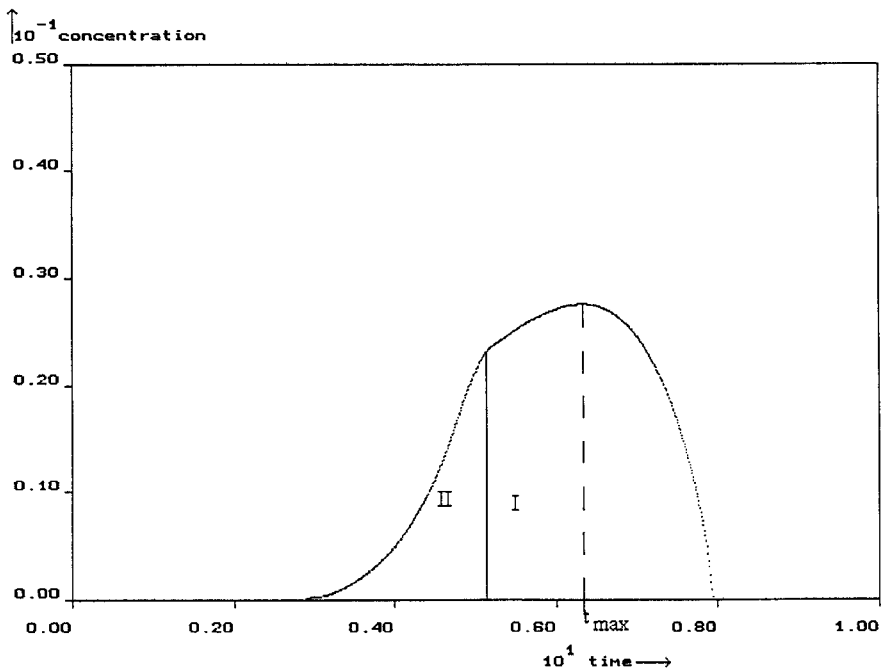
FIGURE   2:   FINAL PRODUCT PULSE OF A CONSECUTIVE REACTION
                 (I: CONVEX PART, II: CONCAVE PART)

μ_3, which is completely in contrast to the intermediate
product.

There is a local maximum between μ_3 and μ_2 for the final
product. The maximum concentration can be evaluated
(diffusion neglected):

$$c_3 (t_{max}) = m_{10} \acute{k}_1 \frac{\Delta \mu_{12}}{\Delta \mu_{13}} e^{-\Delta k \frac{\Delta \mu_{12}}{\Delta \mu_{13}} (t_{max}-\mu_3)} \tag{13}$$

It can be seen from Fig.1 and 2 that there is a marked
difference between the shape of the final product pulse

and the shape of the intermediate product pulse or the shape of a simple product pulse. As was indicated in a previous publication /5/ there is no marked difference in the shapes of product pulses of parallel reactions, moreover, their shapes are similar to the shape of a simple product pulse. Therefore, the investigation of product pulse shapes might be helpful in investigations of reaction mechanisms.

Results of numerical evaluations

In order to test the possibility to obtain rate constants from reaction chromatograms by fitting the sum of Equations (8) and (9) to the corresponding part of the chromatogram a reaction chromatogram was calculated by an explicit difference method.

Since there are eight parameters in the fitting equation leading to numerous side maxima, the initial values have to be chosen carefully. Fortunately, first approximations for the moments and the standard deviations can be taken from the chromatogram (Fig.3): For the retention times for the reactant and the products from the chromatogram at the maximum of the reactant, the steep flank of the intermediate and the breakthrough point of the final product.
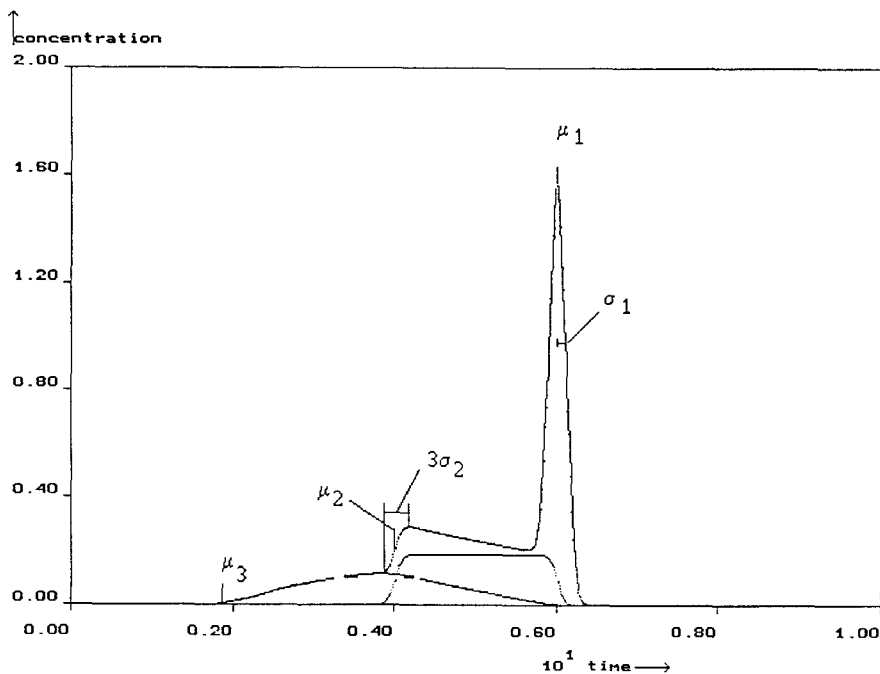
FIGURE 3: INITIAL VALUES FOR THE FITTING CALCULATIONS IN A TYPICAL REACTION CHROMATOGRAM FOR A CONSECUTIVE REACTION

The initial values for the rate constants were established by their systematic variation at the beginning of the fitting procedure.

Fig. 4 shows the excellent agreement between best fit and numerical chromatogram.

Also ,as can be seen from Table 1, the parameters from the fitting are in accordance with the parameters given for the numerical calculation of the chromatogram.

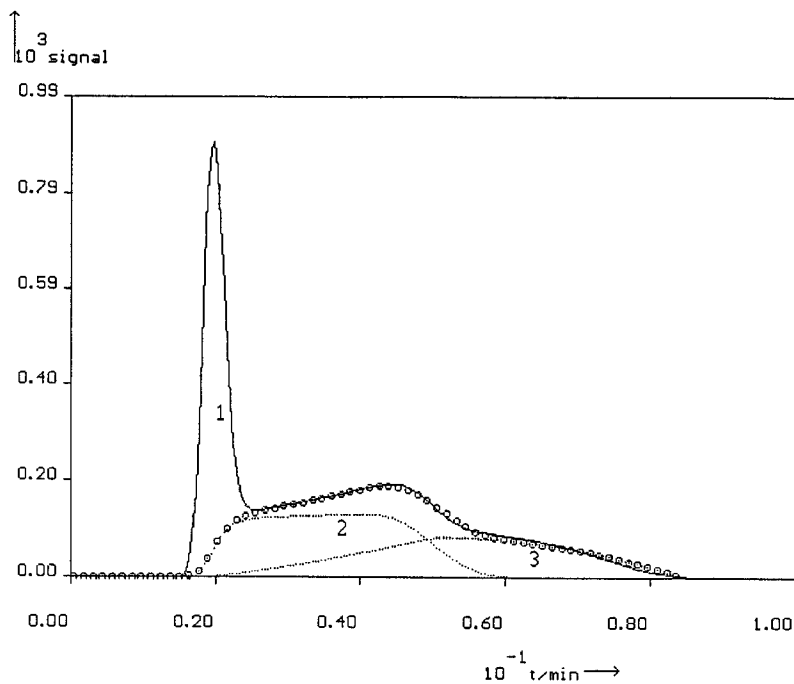FIGURE   4:   PRODUCT CURVE FUNCTIONS (EQN. 8 and EQN. 9)
                   FITTED TO A NUMERICALLY EVALUATED CHROMATO-
                   GRAM
                   (LINE: NUMERICAL EVALUATION, CIRCLES: SUM OF
                   EQN. 8 and EQN. 9 ; 1=REACTANT, 2=INTERMEDI-
                   ATE, 3=PRODUCT)

TABLE 1

Results of the Recalculation of the Parame-
ters of a Numerical Chromatogram

	k_1	k_2	μ_1	μ_2	μ_3
num.	1.20	1.20	3.00	5.00	8.00
fitting	1.20	1.17	2.98	4.98	8.02

EXPERIMENTAL

The acid-catalyzed hydrolysis of phthalic dichloride
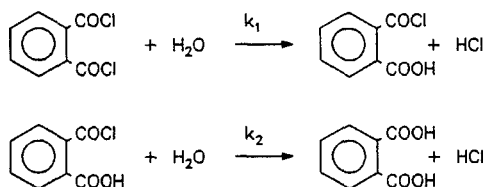
was investigated using the following liquid chromatographic equipment: A modular HPLC system from Gamma Analysentechnik Berlin, Germany (Kortec K35D HPLC pump, GAT-PHD 601 rapid scan UV-VIS detector with computer interface) with an EnCaPharm 100 RP 18 column from Molnar-Institut Berlin, Germany, which is persistent to high and low pH-ranges /6/ .

Acetonitrile/water (50:50) was the eluent, containing 10^{-2} mol/l HCl as acidic catalyst.

Experiments were carried out at 25°C with flow rates of 1.0 ml/min, 0.5 ml/min, 0.25 ml/min and 0.12 ml/min.

The chromatograms were recorded in the rapid scanning mode of the detector from 200 nm to 320 nm in steps of 1 nm. 0.5 μl of a 0.07 mol/l solution from phthalic dichloride in acetonitrile were injected.
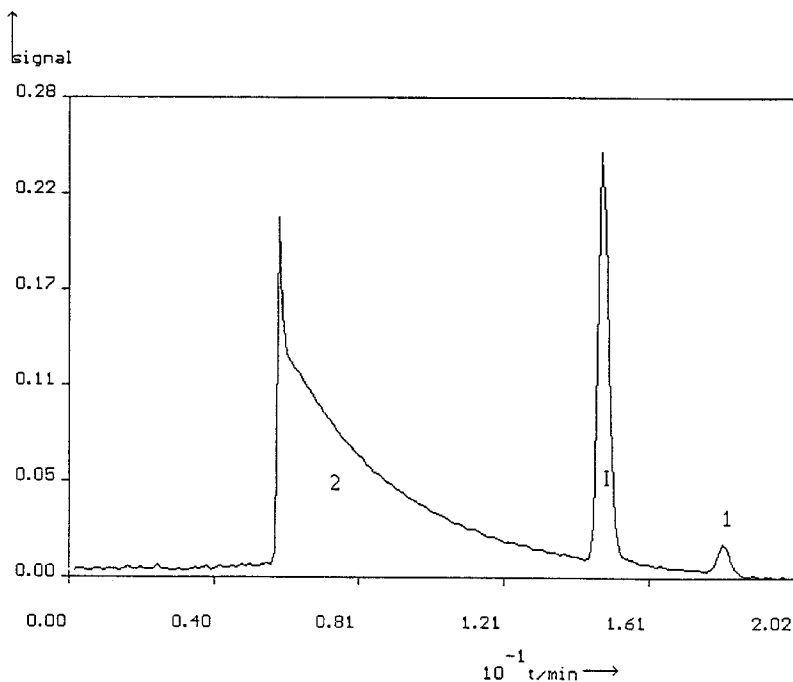
FIGURE   5:   REACTION   CHROMATOGRAM   OF   THE   HYDROLYSIS   OF
                   PHTHALIC DICHLORIDE AT A FLOW RATE OF 1ml/min
                   (1:   PHTHALIC   DICHLORIDE,   2:   PHTHALIC   CHLO-
                   RIDE, I: IMPURITY)

RESULTS AND DISCUSSION

The experimental product curves were fitted by the
functions (8) and (9) as shown in Fig. 5 - Fig. 8, con-
sidering a different molar detector response:

$$D = f * (c_3 + f_{23} c_2) \tag{14}$$

The detector response ratio of the products f_{23} was ex-

FIGURE   6:   BEST FIT OF EQN. 14 TO A REACTION CHROMATO-
                GRAM OF THE HYDROLYSIS OF PHTHALIC DICHLORIDE
                AT A FLOW RATE OF 0.5ml/min
                (LINE: EXPERIMENT, CIRCLES: EQN. 14, 2:PHTHA-
                LIC CHLORIDE, 3: PHTHALIC ACID , I: IMPURITY)

perimentally determined. In the investigations discussed

here there was the problem that conversion for the reac-

tant was already nearly complete, while there was still

little final product formed. However, the phthalic chlo-

ride contained an inert impurity, the peak of which

could be used to establish the reaction duration.

As can be seen from Figures 5-8 there is a good agree-
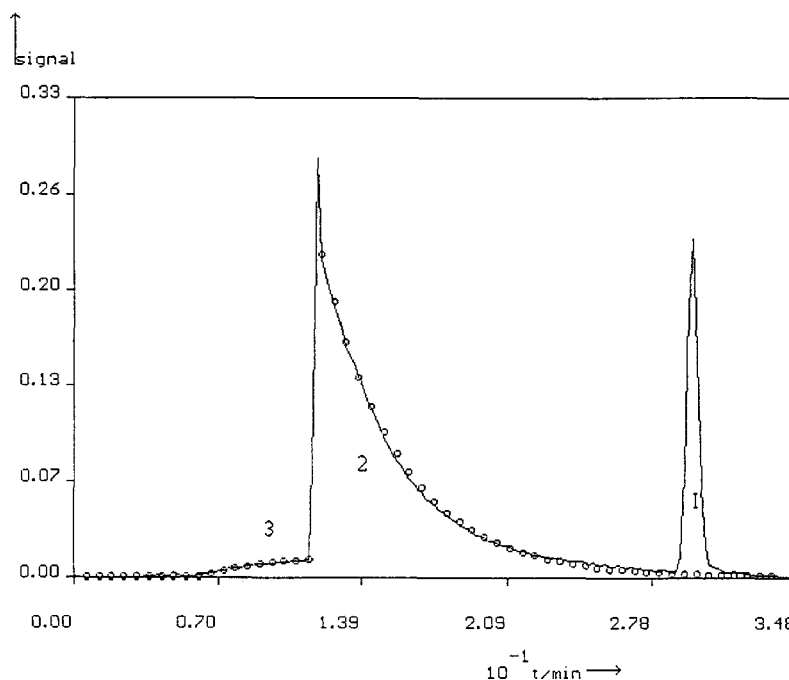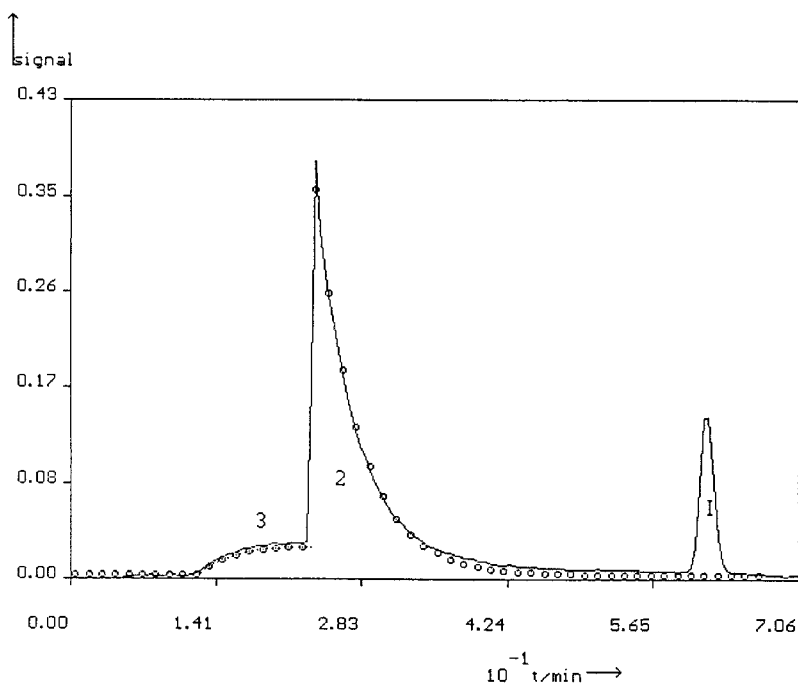
FIGURE   7:   BEST FIT OF EQN. 14 TO A REACTION CHROMATO-
                 GRAM OF THE HYDROLYSIS OF PHTHALIC DICHLORIDE
                 AT A FLOW RATE OF 0.25ml/min
                 (LINE: EXPERIMENT, CIRCLES: EQN. 14, 2:PHTHA-
                 LIC CHLORIDE, 3: PHTHALIC ACID , I: IMPURITY)

ment between the experimental results and the product

curves calculated from Eqn. (14).

Apparent rate constants were calculated with respect to

the retention time of the reactant. These are shown in

Table 2.

There is a sufficient agreement between the rate con-

stants of the different runs.

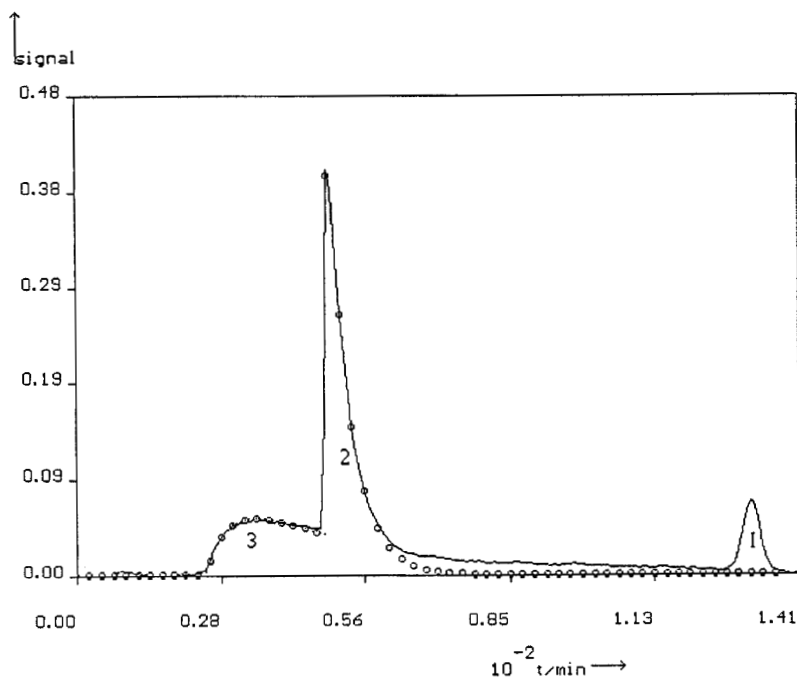FIGURE   8:   BEST FIT OF EQN. 14 TO A REACTION CHROMATO-
                  GRAM OF THE HYDROLYSIS OF PHTHALIC DICHLORIDE
                  AT A FLOW RATE OF 0.12ml/min
                  (LINE: EXPERIMENT, CIRCLES: EQN. 14, 2:PHTHA-
                  LIC CHLORIDE, 3: PHTHALIC ACID , I: IMPURITY)

TABLE 2

Apparent Rate Constants for the Hydrolysis of
Phthalic Dichloride as Evaluated from Fitting of
Eqn. 14 to Experimental Chromatograms

flow rate	0.5 ml/min	0.25ml/min	0.12ml/min
k_1	0.19/min	0.18/min	0.18/min
k_2	0.0057/min	0.0054/min	0.0053/min

CONCLUSIONS

Especially Equations (8) and (9) show that the intermediate and the final product are eluted together during a considerable time.

The product pulse shape of the intermediate is closely related to the pulse shape of a simple product pulse (exponential decay function). The product pulse shape of the final product consists of a concave and a convex part, and no useful linearization can be found for these parts. Therefore, the determination of rate constants from those reaction chromatograms requires a fitting procedure.

It was found that the sum of equations (8) and (9) can be fitted to numerical chromatograms as well as to experimental chromatograms, and both rate constants were established by this procedure.

SYMBOLS

D   :detector signal

f   :response factor

f_{23} :detector response ratio of intermediate and final
        product

c   :concentration

k_1' :virtual rate constant, defined by $k_1'=k_{1a} \, t_0/(\mu_1-\mu_2)$

k_2' :virtual rate constant, defined by $k_2'=k_{1a} \, t_0/(\mu_1-\mu_2)$

k_2'' :virtual rate constant, defined by $k_2''=k_{2a} \, t_0/(\mu_2-\mu_3)$

k_{ia} :apparent rate constant $k_{ia}=k_{i\,mobile} + q_i*k_{i\,stationary}$

l :length of the column

m_i :zeroth moment

m_{10} :initial zeroth moment of first reactant

q_i :retention capacity

t :time

t_0 :dead time

x :length coordinate

y :length coordinate

Δk :$k_1'-k_2'-k_2''$

$\Delta\mu_{ij}$:$\mu_i-\mu_j$

μ_1 :retention time of the reactant

μ_2 :retention time of the intermediate

μ_3 :retention time of the final product

μ_E :$\mu_3+(\mu-\mu_2)(\mu_1-\mu_3)/(\mu_1-\mu_2)$

μ :integration variable in Eqn. 4

μ' :integration variable in Eqn. 6

σ_i :standard deviation

ψ :pulse shape equation (i.e. Gaussian distribution)

REFERENCES

[1]   Coca,J.,Langer,S.H.:   Chemtech   13:682-689
         (1983)

[2]   Jeng,C.Y.,Langer,S.H.: J. Chromatogr. <u>589</u>:1-30
           (1992)

[3]   Jönsson,J.A.:Chromatography:Theory and Basic
           Principles, Marcel Dekker,New York 1985

[4]   Thede,R.,Below,E.,   Haberland,D.:   J.
           Chromatogr. <u>660</u>:25-31 (1994)

[5]   Langer,S.H., Patton,J.E.: in J.H. Purnell
           (Ed.), New Developments in Gas Chromatography,
           Wiley,New York 293-373 (1973)

[6]   Abramovitz, M., Stegun, A. : Handbook of
           Mathematical Functions, US Government Printing
           Office, Washington, DC, 1966

[7]   Dietrich, P.G.,Falkenhagen, J. ,Molnar, I.:
           GIT Fachz.Lab. 23-27 (1993)