The Journal of Physical Chemistry

VOLUME 87, NUMBER 18 SEPTEMBER 1, 1983

LETTERS

The Liquid Chromatographic Reactor for Kinetic Studies

Mark W. Bolme and Stanley H. Langer*

Chemical Engineering Department, University of Wisconsin, Madison, Wisconsin 53706 *(Received: April 6, 1983)*

It is shown that a liquid chromatographic column can be used to generate a reactor chromatogram. The data of the chromatogram can then be utilized to calculate kinetic rate constants if the composition of the stationary phase is considered. Further study should make it possible to obtain accurate kinetic data as well as information about the composition and nature of the stationary phase.

Studies of reaction kinetics using the chromatographic reactor generally have been limited to gas chromatographic systems.[1-3] The advantages of the liquid–solid chromatographic reactor for exceeding equilibrium yields in hydrolysis and esterifications reaction, however, have been recognized.[4-6] This work is the result of efforts directed toward expanding applications of chromatographic reactors to the study of reaction kinetics with a liquid mobile phase. In addition to the concerted separation and reaction feature, a number of advantages over gas chromatographic reactors are readily recognizable.[1-3,7] These include the following: (a) substantial elimination of the need to correct for mobile phase expansion (a dilution effect) in the course of passage through the column, a factor which tends to limit gas chromatographic studies to first-order or pseudo-first-order reaction; (b) the possibility of dissolving reactants rather than vaporizing them so that heat-sensitive reactants and those of limited volatility can be studied in efficient columns; (c) the possible extension of chromatographic reactor studies to volatile liquid solvents (mobile phases) of a conventional type; and (d) the availability of a variety of detectors with different characteristics so that specific molecular features can be utilized to follow the kinetic study at hand.

We chose to investigate the base-catalyzed esterification of tetrachloroterephthaloyl dichloride (I) with alcohol because of our earlier familiarity with this compound and its chemistry.[8,9] We have found it to react initially by

---

(1) Conder, J. R.; Young, C. L. "Physiochemical Methods by Gas Chromatography"; Wiley: New York, 1979.

(2) Laub, R. J.; Pecsok, R. L. "Physiochemical Applications of Gas Chromatography"; Wiley: New York, 1978.

(3) Langer, S. H.; Patton, J. E. In "New Developments in Gas Chromatography"; Purnell, J. H., Ed.; Wiley: New York, 1973; pp 297–373.

(4) Wetherhold, R. G.; Wissler, E. H.; Bischoff, K. B. *Adv. Chem. Ser.* **1974**, *No. 133*, 181–90.

(5) Cho, B. K.; Carr, R. W.; Aris, R. *Chem. Eng. Sci.* **1980**, *35*, 74–81.

(6) Schweich, D.; Villermaux, J. *Am. Inst. Chem. Eng.* **1980**, *26*, 477–86.

(7) Langer, S. H.; Yurchak, J. Y.; Patton, J. E. *Ind. Eng. Chem.* **1969**, *61*, 10–21.

(8) Langer, S. H.; Mollinger, P.; Johnson, B. M.; Rubin, J. *J. Chem. Eng. Data* **1972**, *17*, 509–11.

(9) Langer, S. H. *Anal. Chem.* **1972**, *44*, 1915–6.

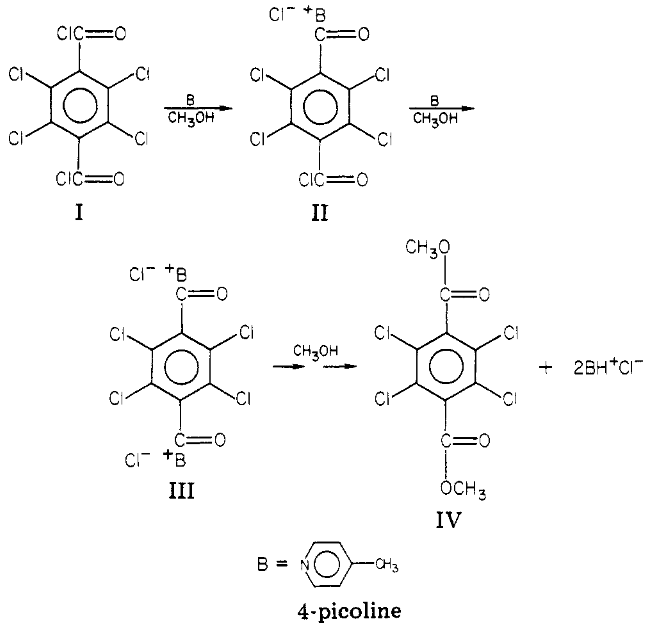
0022-3654/83/2087-3363$01.50/0 © 1983 American Chemical Society

TABLE I: Pertinent Retention Volumes[a] on the Liquid Chromatograph of This Study

compd	retention volume,[b] cm^3
tetrachloroterephthaloyl chloride (I)	9.1
[at 35 °C]	[8.6]
4-picolinium salt of I (II)	7.1
$CH_3O_2CC_6Cl_4COCl$ (methyl half-ester of I)	7.9
4-picoline	5.4
[at 35 °C]	[5.2]
1-phenyloctane (inert standard)	11.4
void volume	4.6

[a] Methanol mobile phase is 0.25 M in tetrahydrofuran and 0.0082 M in 4-picoline. At 25 °C except where otherwise noted. [b] Measured from injection.

pseudo-first-order kinetics with an excess of 4-picoline in methanol. Our work indicates that the course of the reaction proceeds with one aroyl chloride group reacting to form a quaternary salt (II), followed by a slower formation of a dipicolinium (III) ion, which eventually reacts to form dimethyl ester (IV) as follows:



Since absorbed immobilized liquid stationary phases have limited stability in a liquid chromatography apparatus in the presence of constant solvent flow,[10] a C_{18}-bonded silica stationary phase was selected for this investigation. Retention volumes of the compounds of this study with a mobile phase of methanol are presented in Table I.

Two illustrative liquid chromatographic reactor chromatograms for the first step of the reaction sequence obtained at different mobile phase flow rates are shown in Figure 1. The injections were 20 μL of a methanol solution approximately 0.0006 M in reactant ((tetrachloroterephthaloyl dichloride, I), 0.01 M in inert (1-phenyloctane), and 0.25 M in tetrahydrofuran (used as an aid in dissolving the reactant). The mobile phase was a methanol solution 0.0082 M in catalyst (4-picoline) and 0.25 M in tetrahydrofuran; the column temperature for these runs was 25.0 °C. Other experiments were conducted at 35 °C. The solvent was passed through a 10-μm inlet filter during removal from the reservoir with a Waters Model 6000A solvent delivery pump. The solvent then passed through a Beckman Model 210 bypass delivery valve before being introduced to the two series-connected Altex-ODS columns followed by a Perkin-Elmer LC-55 variable wavelength detector.

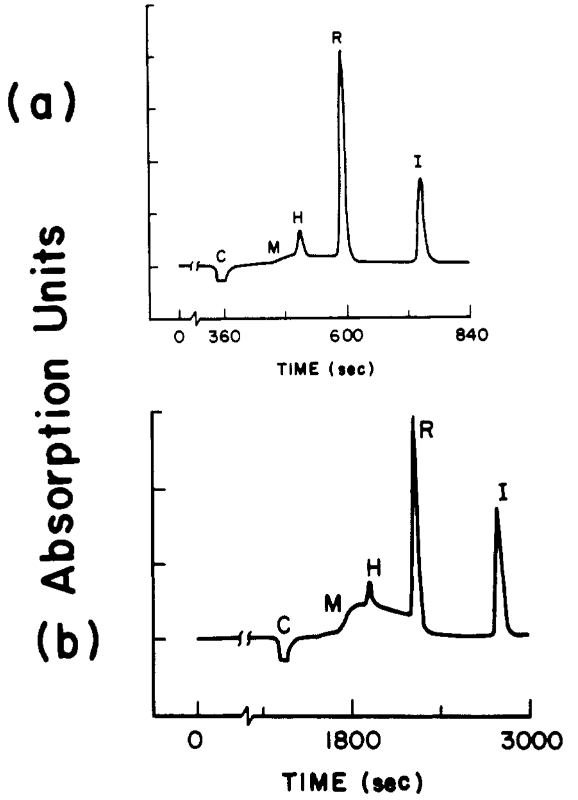


Figure 1. Illustrative liquid chromatographic reactor chromatograms with inert standard. Peaks: R = reactant tetrachloroterephthaloyl chloride; M = product quaternary salt (II); H = methyl half-ester impurity in original reaction mixture ($CH_3OCOC_6Cl_4COCl$); I = inert standard; C = vacancy peak for 4-picoline (not present in injected reaction mixture). T = 25 °C. Mobile phase is methanol with tetrahydrofuran (0.25 M) and 4-picoline (0.0082 M). Flow rate: (a) 0.90, (b) 0.23 mL/min. Note that as the flow rate decreases (and retention time of R increases) the conversion of R to M increases.

The 25-cm columns, 4.6 mm id, each contained 3.2 g of 5-μm silica particles with a surface area of 200 m^2/g and an average pore diameter of 80 Å.[11] The stationary phase was a monomolecular layer of octadecyldimethylsilane (ODS) bonded to a silica support which was orginally end-capped with trimethylsilane. The ODS surface coverage was reported to be 3.0 $\mu mol/m^2$ giving a packing material that was 12 wt % carbon.[12] The void volume of each column was about 2.2 cm^3 with the total void volume, V_m, of the apparatus measured as 4.6 cm^3 (by the homologous series method and with uracil).[13,14]

To obtain rate constants from the reactor chromatogram, we analyzed the kinetic data using an inert standard (1-phenyloctane) method[3,7,15] with the area of the reactant peak. Some iterative correction was made for the initial reactant peak area to account for the formation of a small amount of monomethyl ester (H) in the reaction mixture on standing (see Figure 1 caption) before injection.

---

(10) Locke, D. C. *Adv. Chromatogr.* **1976**, *14*, 87–198.

(11) Cooke, N. H. Altex Instrument Co., Berkeley, CA, personal communication to Alex Chu, 1981.

(12) Grushka, E.; Kita, E. J. *Anal. Chem.* **1977**, *49*, 1004A–1014A.

(13) Al-Thamir, W. K.; Purnell, J. H.; Wellington, C. A.; Laub, R. J. *J. Chromatogr.* **1979**, *173*, 388–91.

(14) Berendsen, G. E.; Schoenmakers, P. J.; de Galan L.; Vigh, G.; Varga-Puchony, Z.; Inczedy, J. *J. Liq. Chromatogr.* **1980**, *3*, 1669–86.

(15) Langer, S. H.; Patton, J. E. *J. Phys. Chem.* **1972**, *76*, 2159–69.

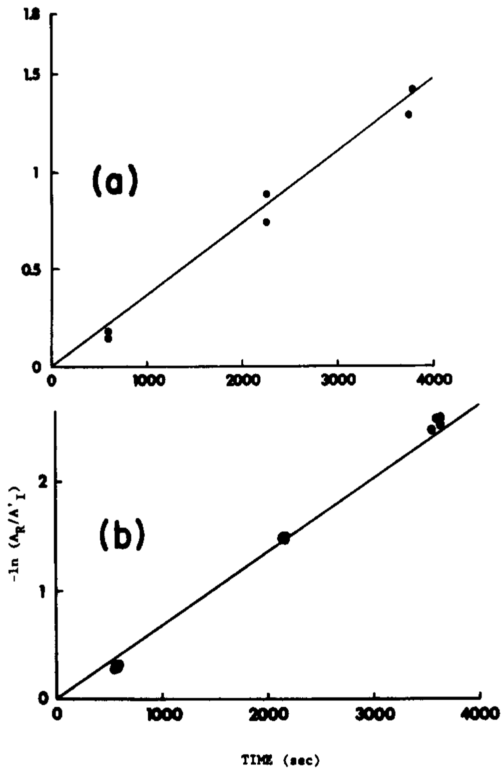


Figure 2. (a) Representative inert standard plot for data of a typical run at 25 °C. (See caption for Figure 1.) Superimposed on the data is the line representing the least-squares fit of eq 1 to seven runs. Plot adjusted so that the least-squares fit passes through the origin. (b) Plot for data of two runs at 35 °C according to eq 1. Least-squares fit of four runs superimposed. (See captions on Figures 1 and 2a and text for further explanation.)

The area of the reactant peak on the reactor chromatogram A_R is related to the apparent pseudo-first-order rate constant k_a[3,15] by

$$+\ln \frac{A_R}{A_{I'}} = -k_a t + \ln \left(\frac{A_R}{A_{I'}}\right)_{t=0} \quad (1)$$

where t is the total residence time of the reactant in the column and $A_{I'}$ is the area of the inert standard peak after adjustment for the reaction occurring prior to injection. Figure 2 shows plots of data from a number of runs.

The slopes of these lines give values of k_a where

$$k_a = k_m \frac{t_m}{t} + k_s \frac{t_s}{t} \quad (2)$$

and where k_m and k_s are the rate constants in the mobile phase and the stationary phase, respectively, and t_m and t_s are the residence times in the mobile and stationary phases. A value of t_m was obtained with the homologous series method or from the flow rate and retention volume of nonadsorbed uracil; t_s was obtained from the retention volume of TCTPCl$_2$ (I), dividing by the flow rate and subtracting the value of t_m.

Values of k_a are presented in Table II together with calculated values of the liquid-phase rate constant, k_m', and an assumption that no solvolysis takes place in the stationary phase ($k_s = 0$, eq 2). The homogeneous pseudo-first-order rate constants from conventional batch reactor studies are also presented in Table II. The k_m' values are approximately 30% higher than those obtained with the batch reactor. However, the calculated activation energy for the k_m' values is in good agreement with the batch reactor study. This would suggest that the difference in rate constants results from some consistent error in assumptions or techniques. The possibility of reaction in the stationary phase is a reasonable explanation for much of the discrepancy in rate constants.

TABLE II: Comparison of the Pseudo-First-Order Rate Constants[a] Determined by the Inert Standard Method with the Liquid Chromatographic Reactor

temp, °C	$10^4 k_a$,[b] s^{-1}	$10^4 k_m'$,[c] s^{-1}	$10^4 k_m$,[d] s^{-1}	$10^4 k_m''$,[e] s^{-1}
25.0	3.53	7.0 ± 0.4	5.4 ± 0.1	5.99
35.0	6.8	12.5 ± 0.6	9.7 ± 0.1	11.45[f]
activation energy, cal/mol		+10600	+10500	

[a] Second-order rate constant $k_2 = k_m$/(4-picoline concentration). Methanol with 0.25 M tetrahydrofuran; 4-picoline, 0.0082 M. [b] See text. [c] k_s assumed zero. LCR. The rate constant is reported plus or minus a standard deviation. Each rate constant is a result of seven different series of runs containing a total of 43 data points. [d] Batch reactor. [e] k_s considered. This value is based on the product of k_m, the calculated value of 4-picoline concentration in the stationary phase from chromatography and the calculated value of the volume fraction of methanol in the stationary phase. [f] For this calculation, bound methanol at 35 °C was assumed to be the same as at 25 °C (see text).

The correction for reaction in the stationary phase, which contains associated methanol, is dependent on the nature of the model selected to represent its reactive character. From available models, an approach suggested by the results of Burke and his co-workers for C_{18} chains[16,17] and other earlier work[15,18-22] is attractive (in terms of simplicity), as a first approximation. Burke et al. worked with a silica packing (150 m^2/g) containing 19.8% carbon by wt or 5.5 μmol of bonded $C_{18}H_{39}Si(CH_3)_2O$– groups (ODS)/m^2. They found that 11.16 mol of methanol per mol of ODS associated with the stationary phase at 25 °C.

The bonded phase in this work contained 12% carbon by wt or 3.0 μmol of ODS[12]/m^2. Assuming a methanol association comparable to Burke et al. we can calculate 33.48 μmol/m^2 of methanol associated with the ODS groups.[16,17] The two columns in series contain 6.4 g of packing. With the surface area, one can calculate that 1.74 cm^3 of methanol (V_{CH_3OH}) is associated with the stationary phase, assuming that methanol maintains its bulk density in the stationary phase. The volume of ODS groups would be 1.12 cm^3 from a bulk density estimate of 0.9 for these groups. Thus, the total volume of the stationary phase is estimated to be 2.86 cm^3. If we use the retention volume relationship for, V_R

$$V_R = V_m + KV_s \quad (3)$$

where V_m is the volume of mobile phase (dead volume) and V_s is the volume of the stationary phase, the distribution coefficient K can be calculated for I (1.57) and 4-picoline (0.28) from the data of Table I. Here K is C_s/C_m, the ratio of the concentration in the stationary phase to the ratio of the concentration in the mobile phase.

---

(16) Yonker, C. R.; Zwier, T. A.; Burke, M. F. *J. Chromatogr.* **1982**, *241*, 257–68, and references therein.

(17) Yonker, C. R.; Zwier, T. A.; Burke, M. F. *J. Chromatogr.* **1982**, *241*, 269–80, and references therein.

(18) Knox, J. H.; Pryde, A. *J. Chromatogr.* **1975**, *112*, 171–88.

(19) Scott, R. P. W.; Kucera, P. *J. Chromatogr.* **1977**, *142*, 213–32.

(20) McCormick, R. M.; Karger, B. L. *Anal. Chem.* **1980**, *52*, 2249–57.

(21) Melander, W.; Stoveken, J.; Horvath G. *J. Chromatogr.* **1980**, *199*, 111–27.

(22) Slaats, E. H.; Markovski, W.; Fekete, J.; Poppe, H. *J. Chromatogr.* **1981**, *207*, 299–323.

Thus the rate constant in the mobile phase k_m'' can be calculated from eq 2 by using the ratio of V_m/V_R for t_m/t and KV_s/V_R for t_s/t for the reactant compound I and by assuming the rate constant in the composite stationary phase is proportional to methanol concentration. If the value $K_{\text{picoline}}\,k_m''(V_{CH_3OH}/V_{\text{stationary phase}})$ is used for k_s, eq 2 becomes

$$3.53 \times 10^{-4} = k_m''(0.505) + (0.28)k_m''(0.61)(0.495) \qquad (4)$$

This gives a calculated value of k_m'' within 11% of the batch value (see Table II). When a similar approach is used for experiments at 35 °C, the calculated value of k_m'' is within 18% of the batch value. The use of the data of Burke et al. obtained at 25 °C for the methanol associated with the bonded phase makes the latter calculation less reliable.

With other models for the stationary phase and parameter adjustment, agreement could be improved. However, these require more investigation for justification. The effect of residual hydroxyl groups on the silica surface also has not been considered. However, the important conclusion is that with some consideration of stationary phase composition it is possible to obtain quite reasonable estimates of reaction rate data by using the liquid chromatographic reactor, validating the general approach presented here. Furthermore, it appears that a comparison of bulk kinetic data with those in the stationary phase of the liquid chromatographic reactor eventually should provide further insight into the nature of this phase and the reactive liquids (methanol here) associated with this phase. With these incentives we are carrying out further investigations of the study of kinetics in the liquid chromatographic reactor.

Acknowledgment. We thank the National Science Foundation and the University of Wisconsin for support of this work and Mr. Alex Chu and Mr. Joseph Powell for helpful discussion and suggestions.

Registry No. I, 719-32-4; I half methyl ester, 13376-62-0; II, 86633-42-3; 4-picoline, 108-89-4; methanol, 67-56-1.

Structure of $VO(H_2O)_5^{2+}$ in Cross-Linked Poly(vinyl alcohol)

Hans van Willigen

Department of Chemistry, University of Massachusetts at Boston, Boston, Massachusetts 02125 *(Received: April 15, 1983)*

In a recent paper on an electron spin echo study of VO^{2+}–water complexes in poly(vinyl alcohol) cages, structural and hyperfine data are given for the pentahydrate $VO(D_2O)_5^{2+}$. The data differ considerably from those derived from electron nuclear double resonance spectra. This paper addresses the question of the origin of the discrepancies. It is concluded that they must be attributed to shortcomings in the method of analysis of the spin echo modulation spectra.

In a recent paper[1] Kevan and co-workers report on a study of the structure of VO^{2+}–water complexes present in poly(vinyl alcohol) (PVA) cages of various size. The authors have derived detailed information on the structure of the pentahydrate present in large PVA cages by analysis of electron spin echo modulation (ESEM) spectra from $VO(D_2O)_5^{2+}$. Values for the distance between vanadium nucleus and deuterons of the axial and equatorial water molecules and for the isotropic hyperfine coupling constants given in this paper are summarized in Table I. The authors do not discuss the fact that the data differ markedly from those given in earlier papers[2-4] dealing with electron nuclear double resonance (ENDOR) studies of $VO(H_2O)_5^{2+}$. Evidently, the discrepancy deserves careful consideration. It may reflect the effect of solvent–polymer interactions on metal ion solvation structure, which would be an interesting finding. Alternatively, it may illustrate the shortcomings of the method of analysis of the spectra. In this Letter the probable origin of the differences between the two sets of values will be discussed.

TABLE I: Summary of Data on V-H Distances (r, nm) and Isotropic Couplings (a, MHz) in $VO(H_2O)_5^{2+}$

proton		ESEM[1]	ENDOR[2]
equatorial	r	0.29 ± 0.01	0.252 to 0.266[a]
	a	2.6 ± 0.3	−0.05 to 8.67[a]
axial	r	0.35 ± 0.01	0.29
	a	0	+0.01 and −0.04

[a] ENDOR shows that the eight equatorial protons are not equivalent. The range of r and a values is given.
[b] ESEM measurements were performed on $VO(D_2O)_5^{2+}$. It is assumed that isotopic substitution does not alter the structure significantly. The deuteron isotropic coupling constant (0.4 MHz) is multiplied by 6.5 to give the proton a value.

Table I gives a comparison of the data derived from the ESEM spectra of $VO(D_2O)_5^{2+}$ with those from a single-crystal ENDOR study of $VO(H_2O)_5^{2+}$ in $Mg(NH_4)_2(SO_4)_2\cdot 6H_2O$ (tutton salt) by Atherton and Shackleton.[2] It should be noted that values of vanadium–proton (deuteron) distances are derived on the assumption that the electron spin is confined to the vanadium nucleus (point-dipole model). Proton positions derived from the traceless components of the hyperfine tensors determined with ENDOR[2] agree quite well with those found in X-ray and neutron diffraction studies of tutton salts.[5] This indicates that the point-dipole model is a reasonable approximation. Table I shows that the two sets of data differ significantly. Particularly noteworthy is the fact that the

---

(1) D. Suryanarayana, P. A. Narayana, and L. Kevan, *J. Phys. Chem.*, **86**, 4579 (1982).

(2) N. M. Atherton and J. F. Shackleton, *Mol. Phys.*, **39**, 1471 (1980).

(3) H. van Willigen, *J. Magn. Reson.*, **39**, 37 (1980).

(4) H. van Willigen, C. F. Mulks, and N. M. Atherton, *Inorg. Chem.*, **21**, 1708 (1982).

(5) H. Montgomery and E. C. Lingafelter, *Acta Crystallogr.*, **17**, 1478 (1964); G. M. Brown and R. Chidambaram, *Acta Crystallogr., Sect. B*, **25**, 676 (1969).

0022-3654/83/2087-3366$01.50/0