A Damped Non-linear Least-squares Computer Program (DALSFRK) for the Evaluation of Reaction Rate Constants

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After consideration of the limitations of linear treatments for the analysis of kinetic data, a damped non-linear least-squares computer program (DALSFRK) is described. The program, which employs Marquardt's algorithm as the basis of minimisation, has been developed with the aid of synthetic data. The program is applied to an analysis of the kinetics of the halide-substitution reactions of $[Pt(3NH\text{-}pd)X]^+$ [X = halide, 3NH-pd = 3-azapentane-1,5-diamine (diethylenetriamine)]. It is shown that the present non-linear data treatment not only provides a very satisfactory overall analysis of the data but also enables an accurate evaluation of the first-order rate constants for the process (i). Such values have not previously been attainable directly by linear treatments.

$$[Pt(3NH\text{-}pd)X]^+ \xrightarrow{H_2O} [Pt(3NH\text{-}pd)(OH_2)]^{2+} + X^- \qquad \text{(i)}$$

THE study of reaction mechanisms usually involves a kinetic investigation of the factors that influence the rate of reaction. Such investigations have often been undertaken using a linear method of data analysis (*e.g.* the pseudo-first-order approach). Linearisation of the data treatment necessarily involves the incomplete use of that data and accordingly we have written a computer program that analyses the data by a non-linear approach in the belief that, in addition to making full use of the data, such a method will be particularly useful in the kinetic analysis of complex reaction networks. In the present paper we analyse the disadvantages of the linear pseudo-first-order treatment of data before describing a non-linear computer program for data treatment, DALSFRK. The application of this approach to the substitution reactions of (3-azapentane-1,5-diamine)halogenoplatinum(II) complexes, $[Pt(3NH\text{-}pd)X]^+$, is then described. This system was chosen because it has been widely investigated by linear treatments of the data and thus provides a good test of the value of the new computer program.

Limitations of Linear Data Treatment.—A great deal of success has been achieved in the study of reaction kinetics by linear data treatments. Most treatments are based on a pseudo-first-order approach in which a reaction is studied under conditions in which the concentrations of one or more of the reactants are kept constant or nearly constant during a run. Traditionally[1] the data are fitted to equation (1) which has the form $y = mx$ or equation (2) which has the form $y = mx + c$, where λ_0, λ_t, and λ_∞ are the values of the observable at zero time, t, and at the end of the reaction. Both

$$\ln[(\lambda_t - \lambda_\infty)/(\lambda_0 - \lambda_\infty)] = -kt \qquad (1)$$

$$\ln(\lambda_t - \lambda_\infty) = -kt + \ln(\lambda_0 - \lambda_\infty) \qquad (2)$$

equations (1) and (2) involve critical observables, errors in which will automatically lead to an error in the calculated rate constant. How critical are such errors? In order to determine the deviation of the true rate constant due to errors in λ_0 and λ_∞ a set of zero-error first-order data was generated with $\lambda_0 = 0.400$,‡ $\lambda_\infty = 0.880$, $k = 0.08$ min^{-1}, and a time interval between points of 1 min. A second set of data was then generated by introducing a random error of ± 0.005 units of λ. These data were then used to determine the percentage error in k consequent upon errors in λ_0 and λ_∞ for both equations (1) and (2) (Table 1).

It can be seen from the error matrices in Table 1 that the elements of the matrix for equation (2) are almost independent of λ_0 (as expected), but are strongly dependent on the value of λ_∞, an error of -1.71% in λ_∞ leading to one of $+13.6\%$ in k. Although these actual numerical values only pertain to the parameters originally chosen, it is clear that any data treatment using equation (2) is highly unsatisfactory because the calculated rate constant is so sensitive to one observable;

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‡ The λ values were typical of values of spectrophotometric absorbances.

[1] A. A. Frost and R. G. Pearson, 'Kinetics and Mechanism,' 2nd edn., Wiley, New York, 1961.

furthermore, it is this particular observable, λ_∞, that is likely to be subject to the most error.

The elements of the error matrix generated using equation (1) are also very dependent on the values of λ_0 and λ_∞; however, they are generally lower than those from equation (2) due to the possibility of some errors cancelling. Thus of the two equations (1) and (2), equation (1) is the preferred method of data treatment although it is clear that any method of data treatment that gives a 10.6% error in k due to a -1.71% deviation in λ_∞ and a -3.75% error in λ_0 is unsatisfactory. This high error in k consequent upon relatively small errors in λ_0 and λ_∞ arises from treating the data in a linear manner by the use of a logarithmic function in which certain combinations of observables (*e.g.* when λ_t approaches λ_0 or λ_∞) render the argument of the logarithm close to zero so that its value is not accurately obtained. This is the first reason for our investigating the use of non-linear methods of data treatment which enable the data to be used directly.

TABLE 1

Percentage error in k determined from equations (1) and (2) and consequent upon errors in λ_0 and λ_∞*

	Percentage error in λ_0						
(*i*) Equation (1) Percentage error in λ_∞	-3.75	-2.50	-1.25	0.0	$+1.25$	$+2.50$	$+3.75$
$+1.71$	-3.1	-4.1	-5.2	-6.3	-7.3	-8.4	-9.5
$+1.14$	-0.98	-2.0	-3.1	-4.2	-5.3	-6.4	-7.6
$+0.57$	$+1.2$	$+0.11$	-1.0	-2.2	-3.3	-4.4	-5.6
0	$+3.4$	$+2.3$	$+1.2$	0.0	-1.2	-2.3	-3.5
-0.57	$+5.8$	$+4.6$	$+3.4$	$+2.2$	$+1.0$	-0.2	-1.5
-1.14	$+8.2$	$+7.0$	$+5.7$	$+4.5$	$+3.2$	$+2.0$	$+0.7$
-1.71	$+10.6$	$+9.4$	$+8.1$	$+6.8$	$+5.5$	$+4.2$	$+2.8$
(*ii*) Equation (2)							
$+1.71$	-9.8	-9.9	-10.0	-10.0	-10.1	-10.2	-10.3
$+1.14$	-6.7	-6.8	-6.9	-7.0	-7.1	-7.2	-7.2
$+0.57$	-3.4	-3.5	-3.6	-3.6	-3.7	-3.8	-3.9
0	$+0.25$	$+0.16$	$+0.08$	0.0	$+0.08$	$+0.17$	$+0.25$
-0.57	$+4.3$	$+4.2$	$+4.2$	$+4.0$	$+3.9$	$+3.7$	$+3.8$
-1.14	$+8.8$	$+8.7$	$+8.6$	$+8.5$	$+8.4$	$+8.3$	$+8.3$
-1.71	$+13.8$	$+13.8$	$+13.7$	$+13.6$	$+13.5$	$+13.4$	$+13.4$

* True $\lambda_0 = 0.400$; true $\lambda_\infty = 0.880$.

So far it has been assumed that it is possible to determine λ_∞ directly, which in turn assumes that the reaction goes to completion. This assumption is frequently invalid for one of three reasons. (*i*) The reaction may go to equilibrium rather than to completion [*e.g.* reaction (3)].[2] (*ii*) The initially relatively fast reaction may be

$$[Pt(3NH\text{-}pd)(NO_2)]^+ + I^- \longrightarrow [Pt(3NH\text{-}pd)I]^+ + [NO_2]^- \qquad (3)$$

followed by a second somewhat slower reaction which prevents λ_∞ for the first being observed [*e.g.* reaction (4) is followed by the slower reaction (5)]. (*iii*) The initial

$$[RhCl(OH_2)_5]^{2+} + Cl^- \longrightarrow trans\text{-}[RhCl_2(OH_2)_4]^+ + H_2O \qquad (4)$$

$$trans\text{-}[RhCl_2(OH_2)_4]^+ + Cl^- \longrightarrow [RhCl_3(OH_2)_3] + H_2O \qquad (5)$$

reaction may be followed by a rapid decomposition reaction [*e.g.* reactions (6) and (7)].

$$[PdCl_4]^{2-} + C_2H_4 \xrightarrow{H_2O} [Pd(C_2H_4)Cl_3]^- + Cl^- \qquad (6)$$

$$[Pd(C_2H_4)Cl_3]^- + H_2O \xrightarrow{\text{fast}} Pd^0 + MeCHO + 2HCl + Cl^- \qquad (7)$$

When λ_∞ cannot be determined directly two approaches may be adopted: in certain cases λ_∞ can be calculated {*e.g.* if reaction (3) were being followed by spectrophotometry the final absorbance value could be calculated if the molar absorbance of the $[Pt(3NH\text{-}pd)I]^+$ species were determined}; where this is not possible, for example because the product cannot be isolated, the Kezdy–Mangelsdorf–Swinbourne method [3-5] can be used to calculate λ_∞. In this latter method observations are made at time t [equation (8)] and $t + \Delta$ [equation (9)], where Δ is a constant increment. Dividing equation (9)

$$(\lambda_t - \lambda_\infty) = (\lambda_0 - \lambda_\infty)e^{-kt} \qquad (8)$$

$$\lambda_{(t+\Delta)} - \lambda_\infty = (\lambda_0 - \lambda_\infty)e^{-k(t+\Delta)} \qquad (9)$$

by (8) we obtain (10) which may be rewritten in the

$$(\lambda_{(t+\Delta)} - \lambda_\infty) = (\lambda_t - \lambda_\infty)e^{-k\Delta} \qquad (10)$$

form (11) from which λ_∞ can be obtained either by

$$\lambda_{(t+\Delta)} = \lambda_t e^{-k\Delta} + \lambda_\infty(1 - e^{-k\Delta}) \qquad (11)$$

combining the gradient ($e^{-k\Delta}$) and intercept $\lambda_\infty(1 - e^{-k\Delta})$ of a plot of $\lambda_{(t+\Delta)}$ against λ_t, or better still from the co-ordinates of the point of intersection of equation (11) with the line $\lambda_{(t+\Delta)} = \lambda_t(\lambda_\infty,\lambda_\infty)$. The disadvantages of this method are: (*a*) if a large value of Δ is chosen then only the very early and very late values of λ_t are used, and by having too few points to define the

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[2] P. Haake, S. C. Chan, and V. Jonas, *Inorg. Chem.*, 1970, **9**, 1925.

[3] F. J. Kezdy, J. Jaz, and A. Bruylants, *Bull. Soc. chim. belges*, 1958, **67**, 687.

[4] P. C. Mangelsdorf, *J. Appl. Phys.*, 1959, **30**, 443.

[5] E. S. Swinbourne, *J. Chem. Soc.*, 1960, 2371.

gradient of the straight line the standard error becomes large; (*b*) if a small value of Δ is chosen the gradient becomes very small and the relative error in the rate constant becomes correspondingly large; and (*c*) the method is relatively insensitive to deviations from the strict first-order law, so that this must be checked independently.

An alternative logarithmic linear treatment is due to Guggenheim.[6] Equation (9) is subtracted from (8) to give (12) which can be reduced to (13), from which it is

$$\lambda_t - \lambda_{(t+\Delta)} = (\lambda_0 - \lambda_\infty)e^{-kt}(1 - e^{-k\Delta}) \qquad (12)$$

$$kt + \ln(\lambda_t - \lambda_{(t+\Delta)}) = \ln[(\lambda_0 - \lambda_\infty)(1 - e^{-k\Delta})] = \text{constant} \qquad (13)$$

apparent that a plot of $\ln(\lambda_t - \lambda_{(t+\Delta)})$ against time should have a gradient of $-k$. The disadvantages of this method are: (*i*) before the method can be used, the reaction must be known to be simple first order since some other more complex reactions also give apparent rate constants by this method; (*ii*) for accuracy the interval Δ should be two or three times as great as the half-life of the reaction, which means that a very large proportion of the reaction time must be used. (This necessitates using a very large excess of the species to be maintained at effectively constant concentration. In addition, of course, only the very early and very late values of λ_t are used, intermediate values being ignored.)

Clearly, there are very severe limitations to the precision with which λ_∞ can be evaluated by the Kezdy–Manglesdorf–Swinbourne method, and we have already noted the profound consequences of any errors in λ_∞ on the calculated rate constants. Neither this nor Guggenheim's method for linear data treatment make the most effective possible use of the available data. In addition, it is extremely difficult to use a linear data treatment to evaluate the relative merits of a number of complex reaction networks for describing a particular chemical system. These reasons led us to investigate thoroughly a non-linear approach to the treatment of kinetic data.

Non-linear Data Treatment using DALSFRK.—The computer program described herein, DALSFRK, analyses the time dependence of an observable in terms of an assumed reaction network (or model), in such a way as to minimise the difference between the calculated and experimental observable–time plots. That is to say the program will read in observable and time data for any number of mixtures (*i.e.* starting compositions) of a reaction system and fit the parameters of the assumed chemical model to all the data simultaneously. At present the program is available * only for spetrophotometric data, but it is structured in such a way that subroutines to deal with other types of observable can easily be added. (These would replace the existing OBSERV and VARIAN subroutines.) The program, which incorporates Marquardt's algorithm for locating the minimum, is a damped non-linear least-squares program that has been formed by the amalgamation, and suitable modification to enable time-dependent data to be handled, of two earlier programs: DALSFEK for evaluating equilibrium constants which we have recently described in detail,[7] and NETWORK, an earlier program written for the analysis of reaction networks.[8,9] A flow diagram of DALSFRK is available as Supplementary Publication No. SUP 22169 (7 pp.).†

The subroutines are as follows.

DALS. DALS is the master routine. It reads in the control parameters and the mechanism definition, and also the initial values of the rate constants. The mechanism definition involves assigning integer digits to each species, endeavouring to give products higher numbers than reactants. Also the rate constants for each step are assigned a number. Thus given the network shown in (14)—(16) the following mechanism

$$\mathrm{A} \xrightarrow{k_1} \mathrm{B} + \mathrm{C} \qquad (14)$$

$$\mathrm{B} + \mathrm{D} \xrightarrow{k_2} \mathrm{E} + \mathrm{F} \qquad (15)$$

$$\mathrm{E} + \mathrm{F} \xrightarrow{k_{-2}} \mathrm{B} + \mathrm{D} \qquad (16)$$

would be assigned:

1		1	2	3
2	4	2	5	6
5	6	3	2	4

The first two columns are the numbers assigned to the reactants (*i.e.* $\mathrm{A} \equiv 1$, $\mathrm{B} \equiv 2$, $\mathrm{C} \equiv 3$, *etc.*), the third column is the rate-constants number (*i.e.* $k_1 \equiv 1$, $k_2 \equiv 2$, and $k_{-2} \equiv 3$), and the last two columns are the numbers assigned to the products. Control then passes to CYCLE.

CYCLE. CYCLE defines the parameter arrays and assigns codes to the various 'types' of parameters. These codes are used later in the program to control the manner in which the differentials are calculated. This routine is structured so that up to three 'constant-parameter' arrays can be defined, enabling the parameters to be refined groupwise.

This routine then enters a loop over the number of experiments, this being the number of experimental runs for a kinetic problem or the number of samples prepared for an equilibrium problem. Within this loop the program reads a card that defines which OBSERV subroutine the program is to enter (at present the program is only equipped with a subroutine to deal with absorbance data), and the number of experimental times at which observations were made. A time-definition card is then read in and the program enters the OBSERV routine to read in the experimental data. Control then returns to CYCLE and thence to CONC to calculate the

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* Full details are available from Dr. D. E. Rogers at Southampton.

† For details see Notices to Authors No. 7, *J.C.S. Dalton*, 1977, Index issue.

[6] E. A. Guggenheim, *Phil. Mag.*, 1926, **2**, 538.

[7] R. M. Alcock, F. R. Hartley, and D. E. Rogers, preceding paper.

[8] D. E. Rogers and A. E. Warn, unpublished work.

[9] A. E. Warn, Ph.D. Thesis, Southampton University, 1971.

concentrations of the species at each time. The concentrations at each time must be stored in order to calculate the derivatives of the measured observables (*e.g.* absorbances) at each time, with respect to the parameters. These concentrations are stored on a scratch tape (Tape 2), thus saving unnecessary core store. CYCLE controls the rewinding of this tape.

A large loop is next entered which calculates the derivatives (*i.e.* **B**-matrix elements) [7] of the observables at each time with respect to the parameters. For the rate constants, these derivatives are found using the difference approximation given in equation (17) (O = observable and k = rate constants), a procedure which involves repeated calling of subroutine CONC. The fraction Δ by which k is incremented can be varied at will, but 0.001 (0.1%) has generally been found to be satisfactory. As they are calculated, the derivatives with respect to each parameter are also stored on Tape 2.

$$\frac{\partial O_i}{\partial k_i} = \frac{\Delta O_i}{\Delta k_i} \qquad (17)$$

The normal matrix $\widetilde{\boldsymbol{B}}\boldsymbol{W}\boldsymbol{B}$ is then calculated by a rather complicated manipulation of Tape 2, which enables the derivatives for each parameter to be read off in turn and correctly multiplied together.

As in the program DALSFEK,[7] this matrix is finally normalised and subroutine LEASTSQ called to calculate the corrections to the parameters. On convergence, subroutine ERROR is called which calculates the standard deviations of the parameters and also the correlation coefficients. These are printed along with the final values of the parameters.

CONC. This subroutine differs from its counterpart in the previous program DALSFEK,[7] in that it is now a controlling subroutine, determining how the concentrations are to be calculated. It is here that the initial concentrations are read in for each experiment and stored on a further scratch tape (Tape 1).

Subroutines FIRST or SECOND are called next depending on whether the chemical model is a first- or second-order network. The concentrations calculated for each time are written on Tape 2, or if derivatives are being calculated the changes in concentrations are determined. The appropriate OBSERV subroutine is then called to evaluate the observables from these concentrations. (At present this can only be OBSERV 1 to evaluate absorbances.) Control then returns to the calling routine.

FIRST. This subroutine was inserted, with only a few modifications, from the program NETWORK.[8,9] It calculates the concentrations of the species, at each experimental time, for a first-order network. The input data are the initial concentrations of the species and the initial estimates of the rate constants.*

The mathematical details of this routine are given in ref. 9, but briefly this calculation is achieved by setting up a real unsymmetric matrix of dimension NOS × NOS (where NOS = number of species), using the mechanism definition and the input rate constants. The eigenvectors and eigenvalues of this matrix are then found using a library subroutine. The eigenvectors are used with the initial-concentration vector to create a set of simultaneous linear equations which are again solved using a library subroutine. The species distribution for any specified time is finally created by matrix multiplication.

SECOND. This subroutine was also inserted, with rather more modification than subroutine FIRST, from the program NETWORK.[8-9] It calculates the concentrations of the species, at each experimental time, for a second-order network. The input data necessary to do this are the same as for subroutine FIRST.

It calculates the concentrations by solving a set of simultaneous first-order differential equations using a library subroutine [10] which uses a fourth-order Runga–Kutta method. The library subroutine must be interfaced with a small subroutine defining the equations. This uses the mechanism definition to create the equations. Concentrations at specified times are obtained by interpolation between points in the numerical-integration procedure.

OBSERV 1. OBSERV 1 reads in the experimental absorbances, for each time, and stores them on Tape 1. When the routine is first entered the initial estimates of the absorption coefficients are read in for each species, at each wavelength. When the routine is called from CONC, it calculates the absorbances, at each experimental time, using the species distribution as supplied by CONC. These calculated absorbances are subtracted from the observed values to obtain the error vector and also the sum of the squares of the errors. The absorbance errors for each time are stored on Tape 2, in a similar fashion to the concentrations.

LEASTSQ, HDIAG, *and* ERROR. These subroutines are virtually the same as those described previously for DALSFEK.[7]

The goodness of fit of the data is determined in subroutine ERROR by comparing the estimate of variance, σ^2, obtained by adjustment of the parameters with a prior estimate of variance,[7] σ_p^2, in an F test [equation (18)].[11] The appropriate value of F (at the significance level desired and with the degrees of freedom associated with σ^2 and σ_p^2) that would be obtained by chance is

$$F = \sigma^2/\sigma_p^2 \qquad (18)$$

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* A referee has pointed out that previous workers have found difficulties where there are great disparities in rate-constant values. In the present work no difficulties were experienced with three k values spanning a range of 10^6 ($k_1 = 5 \times 10^{-3}$, $k_2 = 4$, and $k_3 = 1\,500$). The initial guessed values of the rate constants were not found to be critical. Approximate rate constants obtained using pseudo-first-order data obtained at high ligand-to-substrate concentrations were adequate. For further discussion of the problem of obtaining these initial guessed values the reader is referred to J. R. Kittrell, R. Mezaki, and C. C. Watson, *Ind. and Eng. Chem.*, 1965, **57**(12), 19.

[10] FO2AGF, Document no. 623 in the ICL 1900 system, N.A.G. Library Manual.

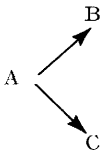
[11] W. E. Wentworth, *J. Chem. Educ.*, 1965, **42**, 96.

found from an F-distribution table.[12] If the value of F calculated from equation (18) is less than that from the table the fit can be assumed to be satisfactory.

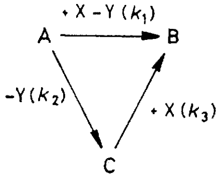
The program was tested by generating synthetic data for five types of reaction network:

Problem 1 $A \longrightarrow B + C$
Problem 2 $A \rightleftharpoons B$
Problem 3 $A \longrightarrow B \longrightarrow C$

Problem 4



Problem 5



These tests highlighted a number of important problems that had to be overcome in order to achieve an effective program.

One of the most significant problems we encountered in developing a non-linear approach to the analysis of kinetic data was that of determining the zero time of the reaction. This is not a problem in a linear approach where the 'zero' time as used in equation (1) can be taken at any moment to suit the experimenter. However, it is vital, in our non-linear treatment that the true zero time is accurately known. This is because it is essential to know the concentrations of all the species present in solution at zero time, in order to calculate their concentrations at each subsequent time and thus to evaluate the calculated absorbances. An error in the initial concentrations can be caused by errors in pipette or burette volumes or more usually because mixing the reactants and making up to volume takes a finite amount of time.

An error introduced as described in the initial concentrations will propagate a systematic error in the absorbance values. As has been emphasised elsewhere,[7,13-15] it is important to take systematic errors into account when using computer programs of this type as an aid to chemical model-building. In accordance with the procedure recommended by Sillén, provision was made to allow these systematic errors to be treated as extra parameters to be refined by the program. That is, the initial concentrations can be adjusted together with the kinetic parameters to obtain the best fit between the observed and calculated absorbances. This facility was tested with the synthetic data already described, but it should be noted that the initial concentrations can only be adjusted in this way if the molar absorption coefficients of one species are fixed at known values; otherwise parameter indeterminancy arises through correlation. Only small adjustments should arise from this procedure, which allows for any small 'zero-time error' due to mixing of reactants, *etc.* Implausible adjustments to the initial concentrations mean the model is probably incorrect, and other reactions are taking place.

The other program facility tested with the synthetic data from the above reaction networks was that of calculating the absorbance blanks. These parameters are the absorbances of the sample cuvette, at the experimental wavelengths, as compared to the reference when both contain only the solvent together with any background electrolyte that may have been added. These absorbances should be determined in any non-linear estimation method such as is described here, if bias is not to be introduced into the remaining parameters.[11] These experimental computer runs also showed that the absorbance blanks are perfectly correlated with the molar absorption coefficients of the species present. Again, therefore, the molar absorption coefficients of at least one of the species should be known and held at fixed values. Further experience with the program {see subsequent discussion on the $[Pt(3NH\text{-}pd)X]^+ + Y^-$ kinetic data} has shown that in fact the absorbance blanks are very sensitive to the 'correctness' of the chemical model. Thus, only if the program gives a good fit to the data with 'reasonable' absorbance blanks (*i.e.* no suspect trends in their magnitudes or sign) can the model under test be said to be satisfactory. One of the obvious problems associated with adjusting the absorbance blanks and initial concentrations is that the number of parameters has clearly been increased significantly and therefore the number of degrees of freedom has been decreased with the inevitable consequence that the opportunities for parameter correlation have been increased.

One possibility investigated for overcoming the problems of parameter correlation and the number of parameters that require refining in an average calculation was the adjustment of parameters in groups. The program was written so that up to three constant-parameter arrays could be defined. If two groups of parameters are to be refined, the following procedure is adopted. Keeping one set constant, the program iterates to the minimum with one set of parameters. These are then fixed at their new values, and the second set refined. This process is repeated until the adjustments to both sets, on successive iterations, are less than the specified criteria for convergence. In this fashion, it is possible, in theory, to refine more parameters than the dimension of the normal matrix, which is the limiting feature of the program, will allow. However, this groupwise refinement of parameters is not generally satisfactory because the program is forced on each iteration

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[12] N. R. Draper and H. Smith, 'Applied Regression Analysis,' Wiley, New York, 1966, p. 307.

[13] L. G. Sillén, *Acta Chem. Scand.*, 1964, **18**, 1085.

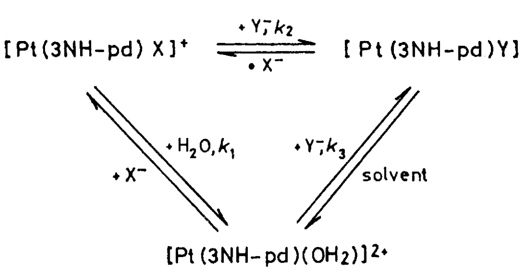
[14] P. Brauner, L. G. Sillén, and R. Whitekar, *Arkiv. Kemi*, 1969, **31**, 365.

[15] L. G. Sillén in 'Coordination Chemistry,' ed. A. E. Martell, Amer. Chem. Soc. Monograph 168, 1971, vol. 1, p. 520.

to find a compromise solution to two or more minima in multidimensional space. Furthermore, the shape and position of the minimum of the multidimensional parameter surface depends on the values of those parameters that have been fixed. Nevertheless, the groupwise adjustment facility is a useful feature because when a minimum-variance set of kinetic parameters has been found it is desirable to have the largest number of degrees of freedom available, so as to calculate the smallest reasonable set of standard deviations. The best strategy is therefore to refine only the kinetic parameters of interest as the first set of parameters, and print out the final values with standard deviations. These can then be taken as the true ' best-fit ' set of parameters for an acceptable chemical model if subsequent refinement of these parameters plus the systematic error parameters (assuming the normal matrix is of sufficient size) does not result in large adjustments or a significant reduction in the sum of the squares of the errors.

Experimental computer runs with synthetic data have shown that it is not possible to refine simultaneously both the initial concentrations of the species present and the absorbance blanks on the same data. Severe correlation problems are encountered which cannot be avoided by adjusting groupwise. The procedure for model testing with the program is therefore as follows. The kinetic parameters of interest and the absorbance blanks should be fitted to the data initially. This is particularly so if non-matched cuvettes are used. These absorbance blanks can then be examined for any unreasonably large (positive or negative) values, or for any suspect trends in their magnitudes (see subsequent discussion). In the event of unreasonable absorbance blanks being calculated, two options exist for the next step. Either (*a*) the data can be reprocessed, holding the absorbance blanks fixed at zero, and allowing the program to adjust the initial concentrations of the species to discover the extent of possible errors due to an incorrect model. Or (*b*) the model can first be changed to reduce the absorbance blanks to reasonable values, before fixing them at these values and allowing the program to adjust the initial concentrations of the species as a final check on the correctness of the model. Judgement and chemical knowledge concerning the likely possible chemical models should be used to aid decision.

Application of DALSFRK *to the* [Pt(3NH-pd)X]$^+$ *System*.—The program DALSFRK was tested by studying halide-substitution reactions of (3-azapentane-1,5-diamine)halogenoplatinum(II) complexes. This system was chosen first, because it is relatively simple due to the fact that the 3-azapentane-1,5-diamine (3NH-pd or dien) blocks three of the co-ordination sites around Pt^{II}; secondly, it has been well studied previously,[16-23] under pseudo-first-order conditions, and is believed to occur by reaction network (19). The reactions at 25 °C and ionic strength 1 mol dm^{-3} (Na[ClO$_4$]) were monitored simultaneously at four different wavelengths. These wavelengths were chosen to give a significant change in absorbance during the reaction and accordingly spanned the regions of greatest difference in molar absorption coefficient between the reactants and products. In addition, the ligand-to-substrate ratio was varied from 1 : 1 to 15 : 1, thus fulfilling the criteria for obtaining data to adequately test a chemical model.[24,25] Typically, therefore, the input to the program for each chemical system consisted of 24 curves of absorbance against time (four wavelengths for each of six concentration ratios of ligand to substrate) each consisting of $\geqslant$20 data points, *i.e. ca.* 500 absorbance readings. The program is able to take all this data and refine the parameters of interest to fit all its 24 curves simultaneously.



(19)

The literature mechanism for the reaction of [Pt(3NH-pd)X]$^+$ complexes with halide, notwithstanding the data for ligand substitution, were first analysed assuming a second-order path only. However, a good fit to the data could not be obtained and the observed and fitted curves of absorbance against time always crossed as in Figure 1. In addition, large negative absorbance blanks were calculated, for the replacement of chloride and bromide by iodide.

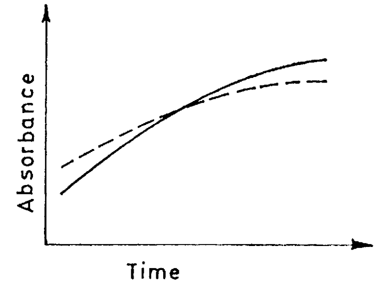


FIGURE 1 Typical observed (—) and computer-fitted plots (---) of absorbance against time obtained by analysis of the experimental data assuming a second-order path only

The next modification to the chemical model was to incorporate a first-order reaction step for the halogeno-complex to proceed to the product. With this chemical

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[16] F. Basolo, H. B. Gray, and R. G. Pearson, *J. Amer. Chem. Soc.*, 1960, **82**, 4200.

[17] H. B. Gray, *J. Amer. Chem. Soc.*, 1962, **84**, 1548.

[18] H. B. Gray and R. J. Olcott, *Inorg. Chem.*, 1962, **1**, 481.

[19] S. C. Chan, *J. Chem. Soc.* (*A*), 1966, 1000.

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[21] G. W. Watt and W. A. Cude, *Inorg. Chem.*, 1968, **7**, 335.

[22] S. C. Chan and F. T. Wong, *J. Chem. Soc.* (*A*), 1968, 2951.

[23] J. R. Paxson and D. S. Martin, *Inorg. Chem.*, 1971, **10**, 1551.

[24] G. E. P. Box and W. G. Hunter, *Technometrics*, 1965, **7**, 23.

[25] D. M. Himmelblau, C. R. Jones, and K. B. Bischoff, *Ind. and Eng. Chem.* (*Fundamentals*), 1967, **6**, 539.

model, a very good fit (as shown by an *F* test) was obtained. Typical experimental and computer-fitted plots of absorbance against time for the substitution of chloride by iodide are shown in Figure 2.

The intermediate by which the chloro- proceeds to the iodo-complex has been shown by other workers [18] to be $[Pt(3NH\text{-}pd)(OH_2)]^{2+}$. This complex was isolated and characterised by us [26] and its molar absorption coefficients were known. In addition the rate constants for the reaction of this complex with chloride and bromide [k_3 in network (19)] were measured. However, the reaction with iodide was too fast to measure under our conditions and an estimate from the literature was taken for the next enhancement of the chemical model. This was to modify the first-order reaction path to allow for it proceeding *via* the aqua-complex. For this computer run the molar absorption coefficients of the aqua-complex were fixed at their known values, as was the value of k_3. As expected, a very similar value of the sum of the squares of the errors was obtained as on the previous computer run. This is due to the very disparate values of k_1 and k_3 resulting from the fact that the aqua-complex does not build up to make a significant contribution to the absorbances. From a purely statistical viewpoint then, the two chemical models, one incorporating a first-order reaction path directly to the product and the other incorporating a first-order process *via* the aqua-complex, are indistinguishable.

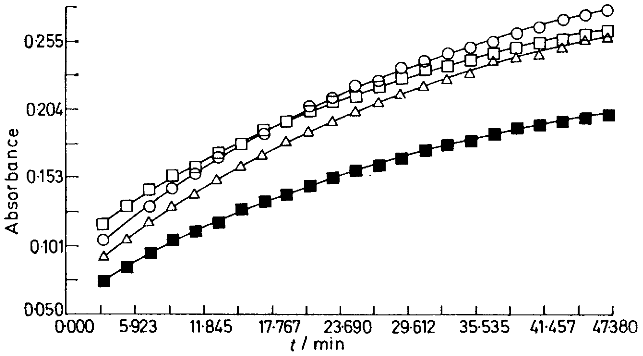

FIGURE 2 Profiles of absorbance against time for a 7 : 1 ratio of I^- : $[Pt(3NH\text{-}pd)Cl]^+$ (the points are experimental and the full lines link the computer-fitted values) at 295(□), 302(○), 310(△), and 320nm(■)

Despite the very good fits to the data, the problem of the large negative absorbance blanks calculated for the reaction of the bromo- and chloro-complexes with iodide remained to be resolved. Incorporation of further reaction steps and/or adjustment of the initial concentrations failed to significantly improve the situation. The phenomena eventually proved to be due to the reaction of the halogeno-complex with water [23] to produce a small amount of aqua-complex when the solid material was dissolved to make the stock solutions [equation (20)]. This reaction, combined with the simultaneous computer adjustment of data from a wide range of ligand-to-substrate ratios, resulted in the trends observed in the fitted absorbance blanks. Thus these parameters proved sensitive detectors of errors in the assumed set of initial concentrations. This observation leads to the important conclusion that, in order to use our non-linear data treatment, wherein it is very important to know the concentrations of each species at ' zero time ' as accurately as possible, it is essential to use solutions that have been allowed to come to equilibrium. This is in direct contrast to the linear approach where the use of ' fresh ' solutions is generally stressed. Fortunately, further computer experiments showed that the error in the initial concentrations caused by equation (20) resulted in a negligible error in the value of k_2 and an error of only *ca.* 5% in k_1, for these particular substitution reactions. Most of the error was carried by the molar absorption coefficients of the chloro- or bromo-complex.

$$[Pt(3NH\text{-}pd)Cl]^+ + H_2O \rightleftharpoons [Pt(3NH\text{-}pd)(OH_2)]^{2+} + Cl^- \qquad (20)$$

The final rate constants calculated for a variety of reaction systems involving $[Pt(3NH\text{-}pd)X]^+$ complexes are shown in Table 2. The *F* values given should be compared to an *F* value of 1.88 (corresponding to a standard deviation in absorbance of 0.002 6) for the results to be significant at the 95% level, so that it is apparent that the fit for all the data sets is very good. Particularly noteworthy are the results obtained from the competitive reactions of $[Pt(3NH\text{-}pd)Cl]^+$ and $[Pt(3NH\text{-}pd)Br]^+$ with iodide ions in the presence of hydroxide ions. These reactions give profiles of absorbance against time which exhibit maxima and, as such, are very difficult to deal with by conventional graphical methods. The values obtained are all consistent with those reported in the literature [19,20,23] bearing in mind the expected influence of ionic strength.[19] It is noteworthy that the present non-linear data treatment gives reliable values for k_1, in contrast to previous linear treatments. Thus plots of the observed pseudo-first-order rate constants against the concentration of entering ligand pass virtually through the origin because k_1 is negligible compared with $k_{obs.}$. The value of k_1 could, until now, only reliably be estimated from the reactions of these complexes with $[OH]^-$, which are first order and independent of hydroxide-ion concentration.[17-19] This is in contrast to the present method of data treatment, where good fits to the data could only be obtained if the k_1 step was included in the reaction model. The k_1 values show that, whilst chloride and bromide are replaced by water at comparable rates, iodide is replaced more slowly. This is similar to the replacement of these halide ions by pyridine [16] and is consistent with the higher position of iodide in the σ-*trans*-effect series which is a consequence of the bond between Pt^{II} and iodide being stronger than that between Pt^{II} and the other halides.

Conclusions.—A non-linear estimation program such as DALSFRK offers a very satisfactory and more rigorous method of testing a variety of kinetic models on large

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[26] R. M. Alcock, F. R. Hartley, and D. E. Rogers, *J.C.S. Dalton*, 1973, 1070.

volumes of data than previous linear approaches. Several types of data, and many kinetic runs, can, and indeed for maximum accuracy should, be refined simultaneously to provide precise estimates of the kinetic parameters. (Simultaneous refinement of several runs has not yet been achieved using linear data treatments.) In particular, it has been shown that the division of the overall rate of reaction into the rates of the component steps can be achieved more precisely by the present non-linear approach compared to previous linear treatments in the situation in which one step is very much slower (factor of 10^3) than another.

TABLE 2

Rate constants for the $[Pt(3NH\text{-}pd)X]^{n+} + Y^-$ system [network (19)] determined using DALSFRK from spectrophotometric data at four wavelengths in aqueous solution at 25 °C and $I = 1.0$ mol dm^{-3} (Na[ClO$_4$])

Reaction system	No. of experiments [a]	Entering group	Leaving group	$\frac{10^3 k_1}{\text{min}^{-1}}$	$\frac{k_2}{\text{dm}^3\ \text{mol}^{-1}\ \text{min}^{-1}}$	F [b]
$[Pt(3NH\text{-}pd)Cl]^+ + I^-$	6	I^-	Cl^-		$4.21 + 0.04$	0.284
		H_2O	Cl^-	5.15 ± 0.08		
$[Pt(3NH\text{-}pd)Br]^+ + I^-$	6	I^-	Br^-		10.64 ± 0.07	0.480
		H_2O	Br^-	6.71 ± 0.17		
$[Pt(3NH\text{-}pd)(OH_2)]^{2+} + Br^-$	6	Br^-	H_2O		88.79 ± 1.20	0.477
$[Pt(3NH\text{-}pd)(OH_2)]^{2+} + Cl^-$	6	Cl^-	H_2O		15.74 ± 0.19	0.343
$[Pt(3NH\text{-}pd)I]^+ + Cl^-$	4 [c]	I^-	Cl^-		4.38 ± 0.04	0.439
		Cl^-	I^-		0.041 ± 0.002	
		H_2O	Cl^-	5.38 ± 0.30		
$[Pt(3NH\text{-}pd)I]^+ + Br^-$	4 [c]	I^-	Br^-		8.59 ± 0.03	0.262
		Br^-	I^-		0.195 ± 0.005	
		H_2O	Br^-	7.97 ± 0.28		
$[Pt(3NH\text{-}pd)Cl]^+ + I^- + [OH]^-$	4	I^-	Cl^-		4.19 ± 0.02	0.217
		H_2O	I^-	2.38 ± 0.07		
		H_2O	Cl^-	7.35 ± 0.20		
$[Pt(3NH\text{-}pd)Br]^+ + I^- + [OH]^-$	4	I^-	Br^-		8.67 ± 0.09	0.391
		H_2O	I^-	3.86 ± 0.20		

[a] This is the number of runs, at varying substrate : entering group ratios in the range 1 : 1 to 1 : 15 that were fitted concurrently. [b] The prior estimate of variance for the spectrophotometer necessary for calculation of the F values was 6.76×10^{-6} which corresponds to a standard deviation in absorbance of 0.0026. This was determined by the method of G. Wernimont, *Analyt. Chem.*, 1967, **39**, 554. [c] Fitted in combination with data from two of the experimental runs of $[Pt(3NH\text{-}pd)Cl]^+ + I^-$ or $[Pt(3NH\text{-}pd)Br]^+ + I^-$ as appropriate.

With regard to fitting kinetic parameters to spectrophotometric data by non-linear regression the following points should be noted.

(*i*) In order to obtain precise estimates of the rate constants, the molar absorption coefficients of as many of the species believed to be present should be fixed at known values. At least one set of molar absorption coefficients must be held fixed if the absorbance blanks are to be refined.

(*ii*) In addition to a statistical measure of the reliability (DALSFRK uses an F test [11]) and an examination of the absorbance residuals, any chemical model should be tested by allowing the program to adjust the initial concentrations of the species present, after a minimum-variance set of parameters has been found.

(*iii*) Correlation problems generally become worse as the molar absorption coefficients of the species in solution approach each other. For this reason, it is again advisable to hold as many molar absorption coefficients as possible constant.

(*iv*) It is not possible to obtain estimates for rate constants which do not cause the concentration of a particular species to build up and make a significant contribution to the absorbance. Thus, if a fast reaction step follows a slow step, the rate constant for the fast step cannot be directly determined by a non-linear least-squares technique.

(*v*) The initial concentrations and the zero time should be known as accurately as possible. Thus rapid mixing of the reagents, preceded if necessary by equilibrium of the reactants to ensure that any equilibria (which will otherwise start to be set up whilst the reagents are being prepared) have become fully established at known values by zero time. Rapid mixing of reactants whose concentrations are known as accurately as possible clearly involves a practical dichotomy which must be resolved to the best of the experimentalist's ability.

EXPERIMENTAL

The complexes [Pt(3NH-pd)Cl][ClO$_4$] and [Pt(3NH-pd)(OH$_2$)][ClO$_4$]$_2$ were prepared as described previously; [26] [Pt(3NH-pd)Br]Br was prepared from [Pt(3NH-pd)I]I in a similar manner to that described previously [21] for [Pt(3NH-pd)Cl]Cl. Sodium perchlorate (Koch–Light, analytical reagent grade) was filtered to remove suspended organic material before use and analysed for chloride content, which was less than 10 p.p.m., using Ag[NO$_3$]. Kinetic runs were carried out in aqueous solution using equilibrated solutions of $[Pt(3NH\text{-}pd)X]^+$ having initial concentrations of 8×10^{-4} mol dm^{-3}. 10-mm silica cuvettes were used and were maintained at 25.0 ± 0.1 °C using a Tecam Tu-12 Tempunit water-circulating thermostat. Absorbances were determined at four wavelengths {295, 302, 310, and 320 nm for the reactions of $[Pt(3NH\text{-}pd)Cl]^+$ and $[Pt(3NH\text{-}pd)Br]^+$ with I^- and I^-–[OH] and also for the reverse reactions; 270, 278, 286, and 295 nm for the reaction of $[Pt(3NH\text{-}pd)(OH_2)]^{2+}$ with Br^-; 267, 275, 282, and 289 nm for the reaction of $[Pt(3NH\text{-}pd)(OH_2)]^{2+}$ with Cl^-} at 2-min intervals on the same sample using a Pye–Unicam SP 1700a spectrophotometer, fitted with electronic timer, automatic cell changer, and digital printer.

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