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Is a Proposed Reaction Mechanism Free from Unnecessary Assumptions? Occam's Razor Applied in a Mathematical Way To Complex First-Order Reaction Systems

Göran Bergson*,† and Jan Linderberg‡

Department of Biochemistry and Organic Chemistry, BMC/Biomedical Center, Box 576, University of Uppsala, SE-751 23 Uppsala, Sweden, and Department of Chemistry, Center for Theoretical Chemistry, University of Aarhus, DK-8000 Aarhus, Denmark

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Following Occam's principle, a proposed reaction mechanism should not contain assumptions about the existence of reactive intermediates and reaction paths that are unnecessary for a full description and interpretation of the available facts. A mechanism refers, in this paper, to a proposed reaction scheme or network that represents the reactions supposed to be going on in a complex reaction system with observable species as well as unobservable reactive intermediates. The scope is limited here to (pseudo) first-order reactions and the steady-state approximation is invoked in order to relate unknown mechanistic rate constants to experimentally determined ones, and, when available, theoretically calculated quantities. When the resulting, nonlinear system of equations admits a unique solution within a physically reasonable domain, it is concluded that the reaction mechanism fulfills Occam's principle. Otherwise, there are many or no solutions. No subjective or qualitative arguments enter the procedure and the outcome is not negotiable.

Introduction

Mechanisms that are proposed for complex reactions may imply unobservable intermediates and unwarranted steps. The present effort is designed to formulate a procedure to distinguish between alternative proposed reaction mechanisms by means of an objective criterion depending on Occam's razor. There follows a short review of the kinetic equations for (pseudo) first-order reactions in the next section, a matrix partitioning procedure and a steady-state approximation are the subjects for the third part, and the fourth is devoted to the discussion of possible solutions. Application to a base-catalyzed 1,3-proton-transfer reaction is then offered and Occam's principle serves, in the sixth section, to differentiate between the suggested options. Concluding remarks on the feasibility of a mathematical resolution of conflicts among suggested reaction mechanisms are submitted. The aim of our present study is restricted to general (pseudo) first-order systems because they allow a general and straightforward mathematical strategy with non-negotiable results.

General (Pseudo) First-Order Kinetics[1]

Considering N reacting species of a system, one represents its state by a vector $\mathbf{u}(t)$ composed of N elements $u_\mu(t)$ giving concentrations at time t. When first-order kinetics applies to all individual reactions in the system, the matrix eq 1 represents the rate equations where $\mathbf{K}$ is the rate constant matrix. Off-diagonal elements of $\mathbf{K}$ are the separate rate constants, whereas the diagonal ones are the negatives of the sums of the other elements in the same column. The rate constant matrix $\mathbf{K}$ is therefore a matrix representation of the reaction scheme, and it constitutes the final results obtained from kinetic experiments, because the ultimate goal of kinetic experiments on the system is to determine all the separate rate constants. This can be achieved as follows if all concentrations are determined as functions of time with sufficient accuracy.

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathbf{u}(t) = \mathbf{K}\mathbf{u}(t) \tag{1}$$

Initial values of the concentrations at $t = 0$ are propagated by means of the evolution operator according to the formal expression

$$\mathbf{u}(t) = e^{\mathbf{K}t}\mathbf{u}(0) \tag{2}$$

A more explicit expression is given by the spectral form

$$u_\mu(t) = \sum\nolimits_\nu C_{\mu\nu} \exp(\lambda_\nu t) \tag{3}$$

where the eigenvalues λ_ν of the matrix $\mathbf{K}$ appear. It follows that the matrix $\mathbf{C} = \{C_{\mu\nu}\}$ is formed by the right-hand eigenvectors of the matrix $\mathbf{K}$

$$\mathbf{KC} = \mathbf{C}\Lambda;\ \Lambda = \mathrm{diag}\{\lambda_1, \lambda_2, \ldots, \lambda_{N-1}, 0\} \tag{4}$$

From experimental observations of the N concentrations as functions of time and using suitable numerical procedures, it is possible to determine the parameters in eq 3 and therefore the matrices $\mathbf{C}$ and Λ. There will exist an inverse matrix $\mathbf{C}^{-1}$ unless there are degeneracies among the eigenvalues. Thus, one obtains the individual rate constants from

$$\mathbf{K} = \mathbf{C}\Lambda\mathbf{C}^{-1} \tag{5}$$

Partitioning and the Steady-State Approximation

There are reasons to assume the presence of unobservable reactive intermediates in addition to the observable species in many cases. Such a reaction system is represented by a mechanistic reaction scheme. The reactive intermediates occur with low concentrations that do not affect the mass balance within experimental error. Thus, their concentrations cannot be

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* Corresponding author. E-mail: goran.bergson@biorg.uu.se.

† University of Uppsala.

‡ University of Aarhus.

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determined and therefore, the full rate constant matrix evades recovery in the way described in the previous section. To proceed, we have to restrict the kinetic analysis to the observable species by elimination of the reactive intermediates from the rate equations. This is conveniently done by means of the steady-state approximation as applied to a partitioned form[2] 6 of the basic eq 1. The vector **u** is composed of the *n* observable concentrations in the vector $\mathbf{u}_a$ and *m* unobservable concentrations for the reactive intermediates in the vector $\mathbf{u}_b$, whereas the mechanistic rate constant matrix partitions into four blocks, eq 6. It follows that eq 6 is equivalent to eqs 7 and 8.

$$\frac{d}{dt}\begin{pmatrix}\mathbf{u}_a(t)\\ \mathbf{u}_b(t)\end{pmatrix} = \begin{pmatrix}\mathbf{K}_{aa} & \mathbf{K}_{ab}\\ \mathbf{K}_{ba} & \mathbf{K}_{bb}\end{pmatrix}\begin{pmatrix}\mathbf{u}_a(t)\\ \mathbf{u}_b(t)\end{pmatrix} \qquad (6)$$

$$\frac{d}{dt}\mathbf{u}_a(t) = \mathbf{K}_{aa}\mathbf{u}_a(t) + \mathbf{K}_{ab}\mathbf{u}_b(t) \qquad (7)$$

$$\frac{d}{dt}\mathbf{u}_b(t) = \mathbf{K}_{ba}\mathbf{u}_a(t) + \mathbf{K}_{bb}\mathbf{u}_b(t) \qquad (8)$$

The intermediates have low concentrations and their rate of change is set to zero in the steady-state approximation

$$\frac{d}{dt}\mathbf{u}_b(t) = 0 \qquad (9)$$

Using the steady state approximation 9, contraction of eqs 7 and 8 leads to the forms

$$\mathbf{u}_b(t) = -\mathbf{K}_{bb}^{-1}\mathbf{K}_{ba}\mathbf{u}_a(t) \qquad (10)$$

$$\frac{d}{dt}\mathbf{u}_a(t) = \mathbf{K}_{ss}\mathbf{u}_a(t) \qquad (11)$$

$$\mathbf{K}_{ss} = \mathbf{K}_{aa} - \mathbf{Q}\mathbf{K}_{ba}; \qquad \mathbf{Q} = \mathbf{K}_{ab}\mathbf{K}_{bb}^{-1} \qquad (12)$$

Because the concentrations in the vector $\mathbf{u}_a(t)$ can be observed experimentally, they are the components of the so-called phenomenological reaction scheme in contrast to the mechanistic reaction scheme, which contains the observable species as well as the unobservable reactive intermediates. The rate equations for phenomenological schemes in general are therefore written as

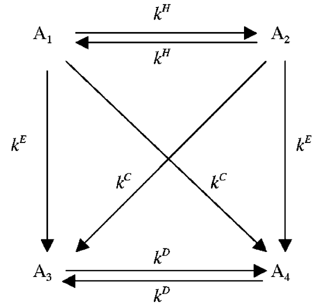
$$\frac{d}{dt}\mathbf{u}_a(t) = \mathbf{K}_{phen}\mathbf{u}_a(t) \qquad (13)$$

Both $\mathbf{K}_{phen}$ and $\mathbf{K}_{ss}$ are $n \times n$ matrices, so comparison of eqs 11 and 12 with eq 13 shows how the mechanistic and phenomenological rate constants are connected, thus

$$\mathbf{K}_{phen} = \mathbf{K}_{ss} \qquad (14)$$

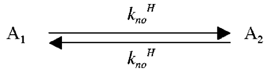
Were all elements in the $(n + m) \times (n + m)$ mechanistic rate constant matrix, eq 6, known, an easy calculation would yield the phenomenological rate constants from eqs 12 and 14. In practice, however, we are faced with the reverse problem. The phenomenological rate constants, i.e., the elements of the $n \times n$ matrix $\mathbf{K}_{phen}$, are determined experimentally as described above, cf. eq 5, and we want to extract information about the rate constants in the mechanistic reaction scheme. The matrix blocks $\mathbf{K}_{aa}$ and $\mathbf{K}_{ba}$ contain the rate constants for the slower reactions from the observable species, whereas $\mathbf{K}_{ab}$ and $\mathbf{K}_{bb}$ are built from the more rapid rates of the non-observable ones. Thus, the matrix **Q**, eq 12, expresses ratios between the rate constants for these faster reactions rather than their absolute values. This is a consequence of the steady-state approximation.

SCHEME 1: Phenomenological Reaction Scheme and Rate Constants for the "Degenerate" 1,3-Proton-Transfer Reaction in 1,3-Dimethylindene Competing with Irreversible H/D-Exchange[a]



[a] A_1 is 1-($^2H_3$)methyl-3-methylindene and A_2 is 1-methyl-3-($^2H_3$)methylindene. Corresponding species in which the mobile proton has been replaced by a deuteron are denoted A_3 and A_4. Thus, A_3 is 1-($^2H_3$)methyl-3-methyl(1-^{2}H)indene and A_4 is 1-methyl-3-($^2H_3$)methyl(1-^{2}H)indene.

SCHEME 2: Phenomenological Reaction Scheme and Rate Constant for a "Degenerate" 1,3-Proton-Transfer Reaction with No Competing H/D-Exchange[a]



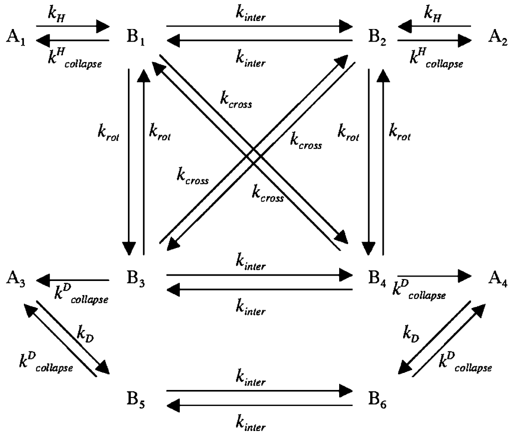
[a] A_1 is 1-($^2H_3$)methyl-3-methylindene and A_2 is 1-methyl-3-($^2H_3$)methylindene.

Unique Solution of a System of Nonlinear Equations as Criterion of Occam's Principle

Let p_o be the number of independent nonzero elements in $\mathbf{K}_{phen}$ and $\mathbf{K}_{ss}$. Thus, p_o is the number of phenomenological rate constants. The numerical values of these rate constants are obtained from experiments as explained above. According to eqs 6 and 12, the nonzero elements in $\mathbf{K}_{ss}$ will be functions of the *q* independent mechanistic rate constants and rate constant ratios, $\mathbf{x} = \{x_1 \quad x_2 \quad \cdots \quad x_q\}$, in $\mathbf{K}_{aa}$, $\mathbf{K}_{ba}$, and **Q**. Thus, eq 14 represents a system of p_o nonlinear equations with *q* unknowns, expressed more explicitly by the form 15 below. The ultimate goal of a mechanistic study is to determine the unknown mechanistic parameters **x**.

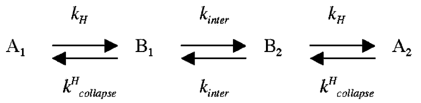
If the phenomenological rate constants represented by $\mathbf{K}_{phen}$ are the only facts available for the reaction system studied, there is obviously no imperative necessity to propose the existence of reactive intermediates. It is also well-known that an arbitrary number of hypothetical mechanisms consistent with $\mathbf{K}_{phen}$ can be found, if there are no restrictions on the number of mechanistic parameters in **x**. Such proposed mechanisms therefore contain unnecessary assumptions and remain speculative. Thus, mechanistic information can be achieved only if additional facts providing auxiliary equations can be found. An example is kinetic studies, under unchanged conditions, of a system in which some of the original reaction steps are decoupled from the others as exemplified by the mechanistic reaction Schemes 3 and 4. In analogy with the above treatment, this gives the equation system 16 where $\mathbf{K}'_{phen}$ has p' indepen-

SCHEME 3: Mechanistic Reaction Scheme and Rate Constants When H/D-Exchange Competes with Proton Transfer[a]



[a] Proposed reactive ion-pair intermediates to which the steady-state approximation is applied are denoted B_1,... B_6.

SCHEME 4: Mechanistic Reaction Scheme and Rate Constants for the Reaction without H/D-Exchange[a]



[a] Proposed reactive ion-pair intermediates to which the steady-state approximation is applied are denoted B_1 and B_2.

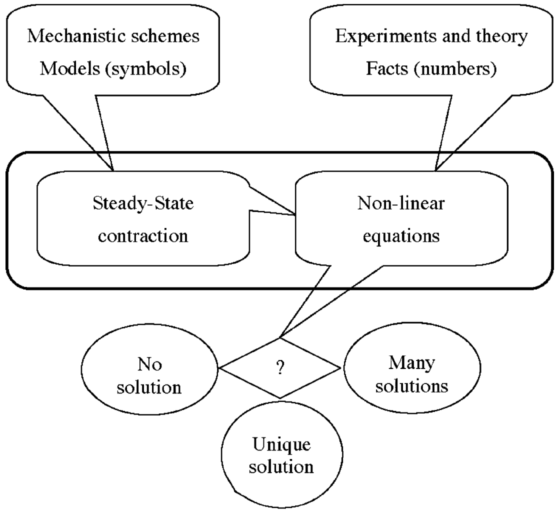


Figure 1. General strategy for testing a reaction mechanistic model with respect to Occam's principle.

dent nonzero elements. Thus, eqs 15 and 16 represent together a system with $(p_o + p')$ equations.

$$\mathbf{K}_{ss}(x) - \mathbf{K}_{phen} = 0; \qquad x = \{x_1, x_2, ..., x_q\} \tag{15}$$

$$\mathbf{K}'_{ss}(x') - \mathbf{K}'_{phen} = 0; \qquad x' \in x \tag{16}$$

$$\Gamma(x'') - \Gamma_{theor} = 0; \qquad x'' \in x \tag{17}$$

It may also be possible to extend the number of facts beyond what can be obtained by kinetics. In the examples given below, we use a theoretically calculated equilibrium isotope effect, which can be expressed as a function of (some of) the variables $\mathbf{x} = \{x_1 \; x_2 \; \cdots \; x_q\}$. This gives an additional equation symbolically written as eq 17 to include the general case with $p'' > 1$ auxiliary quantities collected in the vector Γ. Altogether, the forms 15, 16, and 17 now represent a system with $p = (p_o + p' + p'')$ nonlinear equations and q unknowns.

An equation system of this kind can have many solutions, one unique one, or none. Iterative numerical procedures are required in the search for solutions.[3] A situation with no solution implies that the proposed mechanistic model cannot account for the facts available. A mechanism that results in many solutions is unsatisfactory because it gives no unambiguous results concerning the mechanistic rate constants and rate constant ratios. (This ambiguity can be expected when $p < q$, i.e., when the number of unknowns is greater than the number of equations.) Thus, the only acceptable outcome is a unique solution within a physically reasonable domain.

We conclude that a proposed mechanistic scheme complies with Occam's principle vis-à-vis a set of given facts if there is a unique solution to the corresponding system of nonlinear equations. The mechanistic model is confronted only with available facts and no subjective or qualitative arguments enter the procedure. Figure 1 offers a general strategy to test a reaction mechanistic model with respect to unnecessary assumptions, given a number of phenomenological and (if necessary) theoretically calculated quantities. The steady-state contraction of the mechanistic rate constant matrix according to eq 12 is included as an option to a computer program for the numerical solution of systems of nonlinear equations. The output depends therefore only on the input and no subjective arguments enter the procedure. The statement that a mechanistic model complies with Occam's principle does not, of course, mean that it is the "true" mechanism. Eventually, additional facts may become available necessitating analysis of a new system of nonlinear eqs 15−17.

Phenomenology

The use of the present method to find a reaction mechanistic model in agreement with Occam's principle and to determine the mechanistic rate constants and rate constant rations will now be exemplified by a reaction system where an amine-catalyzed "degenerate" 1,3-proton transfer in the indene system competes with H/D-exchange.[4] Additional kinetic information was obtained by a study of the 1,3-proton transfer without competing H/D-exchange. The phenomenological reaction schemes and rate constants are given symbolically in Scheme 1 and Scheme 2 and the phenomenological rate constant matrices in eqs 18 and 19, respectively.

$$\mathbf{K}_{phen} = \begin{bmatrix} -(k^H + k^C + k^E) & k^H & 0 & 0 \\ k^H & -(k^H + k^C + k^E) & 0 & 0 \\ k^E & k^C & -k^D & k^D \\ k^C & k^E & k^D & -k^D \end{bmatrix} \tag{18}$$

$$\mathbf{K}'_{phen} = \begin{bmatrix} -k^H_{no} & k^H_{no} \\ k^H_{no} & -k^H_{no} \end{bmatrix} \tag{19}$$

One of the CH_3- groups in 1,3-dimethylindene had been replaced by a CD_3- group that made it possible to distinguish by NMR technique[4] the four dimethylindene species A_1-A_4. The 1,3-transfer reactions were catalyzed by an aliphatic amine. The irreversible H/D-exchange (Scheme 1) was effected by

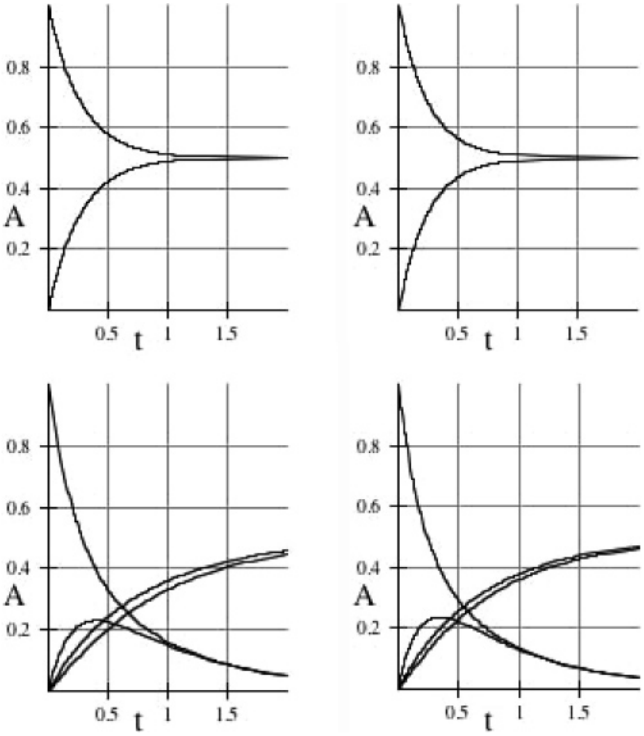


Figure 2. Graphical representations of the concentrations of the observable species A_1 and A_2 (upper panels) and A_1, A_2, A_3, and A_4 (lower panels) in Catalyst I (left panels) and Catalyst II (right panels). Numerical values are given in Appendix A.

using a large excess of deuterated catalyzing amine. The reactions were studied using two different amine catalysts called Catalyst I and Catalyst II. These can be imagined as secondary and primary amines, respectively. The expected small secondary isotope effects due to the methyl group labeling are neglected. Because of the lack of sufficient experimental data,[4] the analysis that follows is based on realistically simulated experiments, here presented graphically in Figure 2 where the time evolution of the concentrations of all the observable species, A_1, A_2, and A_1, A_2, A_3, A_4, respectively, are given. Treatment of the "experimental" data by standard numerical methods results in the matrices **C** and Λ, cf. eqs 3 and 4 and Appendix A. Numerical values for the phenomenological rate constant matrices were then calculated using eq 5, with the results given in Appendix A.

Mechanistic Models for Proton Transfer and H/D-Exchange

The base-catalyzed 1,3-proton-transfer reaction in the indene system has been supposed to proceed via two ion-pair intermediates[4] according to the mechanistic reaction Scheme 3. Of special importance was the determination of the ratio between collapse and interconversion of the indenyl-ammonium ion pair, i.e., $k^{\mathrm{H}}_{\mathrm{collapse}}/k_{\mathrm{inter}}$. Furthermore, knowledge about the competing pathways for H/D-exchange as represented in the mechanistic reaction Scheme 3 was essential. Finally, knowledge of the primary isotope effect for proton abstraction from the hydrocarbon to form the ion-pair, i.e., $k_{\mathrm{H}}/k_{\mathrm{D}}$, is of vital importance for understanding of the mechanistic details. Here we will show that complete mechanistic information in the Occam sense can be found for the "degenerate" rearrangement of 1,3-dimethylindene using the strategy described in the present report. Previously,[4] it was possible to draw only qualitative and incomplete conclusions from the experimental results. The species B represent hydrogen-bonded ion pairs between the dimethylindenyl anion and a substituted ammonium ion. B_1 and B_2 are H-bonded and B_3-B_6 are D-bonded. The mechanistic rate constants k_{H} and k_{D} characterize the slow reactions involving H− and D-abstraction respectively, from carbon to nitrogen. In addition, we have five rate constants representing the rapid reactions ($k^{\mathrm{H}}_{\mathrm{collapse}}$ $k^{\mathrm{D}}_{\mathrm{collapse}}$ k_{rot} k_{cross} k_{inter}). Secondary isotope effects are neglected.

As explained above, steady-state contraction of mechanistic rate constant matrices results in rate constant ratios for the rapid reactions. These ratios appear in the matrix **Q**, eq 12. Thus, there are altogether six mechanistic parameters involved after steady-state contraction of our reaction schemes. We choose k_{inter} as denominator in the ratios. Furthermore, and for convenience, we make use of the primary kinetic isotope effects z and β instead of k_{H} and $k^{\mathrm{H}}_{\mathrm{collapse}}$. The "complete" set of mechanistic parameters **x** is therefore defined by eq 20.

$$\mathbf{x} = \begin{bmatrix} k_{\mathrm{D}} \\ z \\ \beta \\ \xi \\ \eta \\ \theta \end{bmatrix} = \begin{bmatrix} k_{\mathrm{D}} \\ k_{\mathrm{H}}/k_{\mathrm{D}} \\ k^{\mathrm{H}}_{\mathrm{collapse}}/k^{\mathrm{D}}_{\mathrm{collapse}} \\ k^{\mathrm{D}}_{\mathrm{collapse}}/k_{\mathrm{inter}} \\ k_{\mathrm{rot}}/k_{\mathrm{inter}} \\ k_{\mathrm{cross}}/k_{\mathrm{inter}} \end{bmatrix} \tag{20}$$

The explicit matrix representations, in partitioned form according to eq 6, of the mechanistic schemes are given in Appendix B. The steady-state contracted rate constant matrices, obtained using the general procedure shown by eq 12, are given for the mechanistic reaction Scheme 3 by eq 21

$$\mathbf{K}_{\mathrm{ss}}(k_{\mathrm{D}}, z, \beta, \xi, \eta, \theta) = \mathbf{K}_{\mathrm{aa}}(k_{\mathrm{D}}, z) - \mathbf{Q}(\beta, \xi, \eta, \theta)\mathbf{K}_{\mathrm{ba}}(k_{\mathrm{D}}, z) \tag{21}$$

where

$$\mathbf{Q}(\beta, \xi, \eta, \theta) = \mathbf{K}_{\mathrm{ab}}(k_{\mathrm{inter}},\beta,\xi)\mathbf{K}_{\mathrm{bb}}{}^{-1}(k_{\mathrm{inter}}, \beta, \xi, \eta, \theta) \tag{22}$$

and by eq 23 for Scheme 4

$$\mathbf{K}'_{\mathrm{ss}}(k_{\mathrm{D}}, z, \beta, \xi) = \mathbf{K}'_{\mathrm{aa}}(k_{\mathrm{D}}, z) - \mathbf{Q}'(\beta, \xi)\mathbf{K}'_{\mathrm{ba}}(k_{D}, z) \tag{23}$$

with

$$\mathbf{Q}'(\beta, \xi) = \mathbf{K}'_{\mathrm{ab}}(k_{\mathrm{inter}}, \beta, \xi)\mathbf{K}'_{\mathrm{bb}}{}^{-1}(k_{\mathrm{inter}},\beta,\xi) \tag{24}$$

A complicated case as eq 21 presents a formidable − and unnecessary − task to try to evaluate the individual elements of the matrix $\mathbf{K}_{\mathrm{ss}}$ explicitly. Equation 23 can be readily evaluated explicitly but this is not required for the numerical applications to follow.

Facts versus Models Exposed to Occam's Razor

We will now match the experimental facts with the mechanistic models following the general strategy outlined in Figure 1. Demonstrating the basic idea, we first consider the simple case when a reaction with no exchange is the only one providing facts about proton transfer (Schemes 2 and 4). We have then a numerical value {eq (A4) or (A8)} for the phenomenological rate constant and there is only one equation, $k^{\mathrm{H}}_{\mathrm{no}} = k_{\mathrm{H}}/(2 + \varphi)$, involving the two unknown mechanistic parameters $k_{\mathrm{H}} = zk_{\mathrm{D}}$ and $\varphi = \beta\xi = k^{\mathrm{H}}_{\mathrm{collapse}}/k_{\mathrm{inter}}$. There are thus infinitely many

TABLE 1: Number of Solutions to the Equation Systems 15−17 for Mechanisms a, b, and c

experimental and theoretical facts from	no. p of facts = equations	mechanism a, $q = 5$ k_{rot}, $\equiv 0 \Rightarrow$ $\eta \equiv 0$	mechanism b, $q = 5$, $k_{\mathrm{cross}} \equiv 0 \Rightarrow$ $\theta \equiv 0$	mechanism c, $q = 6$ no constraints
$\mathbf{K}_{\mathrm{phen}}$	4	0 (0)	>1 (>1)	>1 (>1)
$\mathbf{K}_{\mathrm{phen}} + \mathbf{K}'_{\mathrm{phen}}$	5	0 (0)	$\mathbf{x}_{\mathrm{bI}}$ (0)	>1 (>1)
$\mathbf{K}_{\mathrm{phen}} + \mathbf{K}'_{\mathrm{phen}} + \Gamma_{\mathrm{theor}}$	6	0 (0)	$\mathbf{x}_{\mathrm{bI}}$ (0)	$\mathbf{x}_{\mathrm{cI}}(\mathbf{x}_{\mathrm{cII}})$

[a] Number of mechanistic parameters = q. Results are for Catalyst I with those for Catalyst II in parentheses. Unique solutions, i.e., those representing Occam mechanisms, are $\mathbf{x}_{bI}$, $\mathbf{x}_{cI}$, and $\mathbf{x}_{cII}$ (cf. eqs 20 and 26).

solutions to the equation in the two unknown mechanistic quantities k_{H} and φ. The conclusion is that the mechanistic model (Scheme 4) can account for the experimental data but does contain unnecessary assumptions because it gives ambiguous results that cannot be distinguished on the basis of here available facts. Put in a different way: A single phenomenological rate constant gives no mechanistic information.

Considering the proposed general mechanistic model where irreversible H/D-exchange competes with 1,3-transfer reactions (Scheme 3), three different cases can be imagined concerning how the H/D-exchange between the ion pairs occurs. They are denoted mechanism a, b, and c and defined in Table 1 with the notations given in Scheme 3 and eq 20. As explained above, $\mathbf{K}_{\mathrm{phen}}$ and $\mathbf{K}'_{\mathrm{phen}}$ represent the phenomenological rate constants obtained from experiments with and without exchange respectively (cf. Appendix A). It is admissible to assume that the equilibrium isotope effect for ion pair formation can be calculated with sufficient accuracy to provide an additional condition (cf. eq 17). This equilibrium isotope effect, Γ, is related to the mechanistic rate constants in Scheme 3 as

$$\Gamma(z,\beta) = \left(\frac{k_{\mathrm{H}}}{k^{\mathrm{H}}_{\mathrm{collapse}}}\right)\left(\frac{k^{\mathrm{D}}_{\mathrm{collapse}}}{k_{\mathrm{D}}}\right) = z/\beta \tag{25}$$

The possible outcomes, i.e., no solution, a unique solution and many solutions (Figure 1), which are obtained from the nonlinear system of eqs 15−17 with four, five, or six equations, are presented in Table 1.

$$\mathbf{x}_{\mathrm{bI}} = \begin{bmatrix} 1.25 \\ 5.82 \\ 4.21 \\ 0.45 \\ 1.90 \end{bmatrix}, \mathbf{x}_{\mathrm{cI}} = \begin{bmatrix} 1.25 \\ 5.82 \\ 4.21 \\ 0.45 \\ 1.90 \\ \theta = 0 \end{bmatrix}, \mathbf{x}_{\mathrm{cII}} = \begin{bmatrix} 1.33 \\ 5.77 \\ 4.18 \\ 0.41 \\ 2.67 \\ 0.32 \end{bmatrix} \tag{26}$$

Only a few comments on Table 1 seem necessary:

- The mechanistic model a with $k_{\mathrm{rot}} \equiv 0$ cannot account for the facts neither for Catalyst I nor for Catalyst II because no solution is obtained. This is expected already from qualitative inspection of the lower panels of Figure 2, which shows that A_3 is formed faster than A_4. (This fact also excludes, for symmetry reasons, a simpler mechanistic model with a single intermediate between the isomeric indenes.)
- No reaction mechanism in the Occam sense can be found from the results of an exchange experiment alone ($\mathbf{K}_{\mathrm{phen}}$), for neither Catalyst I nor Catalyst II.
- A unique solution ($\mathbf{x}_{\mathrm{bI}}$) was found for mechanism b using the combined results of experiments with and without exchange ($\mathbf{K}_{\mathrm{phen}} + \mathbf{K}'_{\mathrm{phen}}$) for Catalyst I (but not Catalyst II).

TABLE 2: Mechanistic Rate Constants and Ratios as Used in Schemes 3 and 4

rate constant (ratio)	Catalyst I	Catalyst II
$k_{\mathrm{H}}(zk_{\mathrm{D}})$	7.28	7.67
k_{D}	1.25	1.33
$k^{\mathrm{H}}_{\mathrm{collapse}}/k_{\mathrm{inter}}(\beta\xi)$	1.89	1.71
$k^{\mathrm{D}}_{\mathrm{collapse}}/k_{\mathrm{inter}}(\xi)$	0.45	0.41
$k_{\mathrm{rot}}/k_{\mathrm{inter}}(\eta)$	1.90	2.67
$k_{\mathrm{cross}}/k_{\mathrm{inter}}(\theta)$	0	0.32
$k_{\mathrm{H}}/k_{\mathrm{D}}(z)$	5.82	5.77
$k^{\mathrm{H}}_{\mathrm{collapse}}/k^{\mathrm{D}}_{\mathrm{collapse}}(\beta)$	4.21	4.18

TABLE 3: Phenomenological Kinetic Isotope Effects from Schemes 1and 2

KIE	Catalyst I	Catalyst II
no exchange: $k^{\mathrm{H}}_{\mathrm{no}}/k^{\mathrm{D}}_{\mathrm{no}}$	3.67	3.75
with exchange: $k^{\mathrm{H}}/k^{\mathrm{D}}$	3.26	3.65

- A unique solution ($\mathbf{x}_{\mathrm{cII}}$) for Catalyst II required the use of six equations and mechanism c.
- This essential difference between the two Catalysts can hardly be detected by qualitative inspection of the primary experimental results presented in Figure 2, and it is therefore a striking example of the usefulness of our mathematical approach.
- It is also consistent that in the unique solution $\mathbf{x}_{\mathrm{cI}}$ for Catalyst I, θ “automatically” becomes zero and that the calculated values of the other parameters are the same as in $\mathbf{x}_{\mathrm{bI}}$.

Numerically resolved mechanistic rate constants and ratios are listed in Table 2 for the two examples considered. Table 3 gives the phenomenological kinetic isotope effects as obtained directly from the phenomenological rate constants. These depend, as expected, on whether H/D-exchange is included or not. As forseen, they differ considerably from the mechanistic one, $k_{\mathrm{H}}/k_{\mathrm{D}} = z$, for the proton abstraction step, which is significant in structure−reactivity investigations.

Conclusions

Experimental and theoretical data, albeit simulated, have been used here to demonstrate that qualitative as well as quantitative results can be derived for a mechanistic model, such as offered by Scheme 4, by our proposed mathematical-numerical approach. It provides stronger evidence for the proposed model than qualitative arguments, and the presence of a unique solution to the nonlinear equations implies that the mechanistic model obeys Occam’s principle vis-à-vis given facts.

The mechanistic model(s) and facts available from experiments and (if necessary) theory are fused to form a system of nonlinear equations. The kinetic equations for the model are suitably partitioned in a matrix formulation and application of the steady-state approximation provides, as eq 12, forms that are added as an option to a computer program for the numerical solution of systems of nonlinear equations. We used the solve block routine in the Mathcad 8 Professional package. For a standard PC, the cpu time is <2 s for problems of the present size.

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Appendix A

Time evolution of the observable species (cf. eq 3) and numerical values for the corresponding rate constant matrices (cf. eqs 18 and 19) obtained using eq 5. Subscripts I and II refer to experiments using different catalysts. The time evolution is represented graphically in Figure 2.

$$\begin{pmatrix} \mathrm{A}_1(t) \\ \mathrm{A}_2(t) \\ \mathrm{A}_3(t) \\ \mathrm{A}_4(t) \end{pmatrix}_{\mathrm{I}} = \begin{pmatrix} 0.5 & 0.5 & 0 & 0 \\ -0.5 & 0.5 & 0 & 0 \\ -0.0414 & -0.5 & 0.0414 & 0.5 \\ 0.0414 & -0.5 & -0.0414 & 0.5 \end{pmatrix} \begin{pmatrix} \exp(-4.50t) \\ \exp(-1.17t) \\ \exp(-1.02t) \\ 1 \end{pmatrix} \tag{A1}$$

$$\mathbf{K}_{\mathrm{phenI}} = \begin{pmatrix} -2.835 & 1.663 & 0 & 0 \\ 1.663 & -2.835 & 0 & 0 \\ 0.730 & 0.442 & -0.510 & 0.510 \\ 0.442 & 0.730 & 0.510 & -0.510 \end{pmatrix} \tag{A2}$$

$$\begin{pmatrix} \mathrm{A}_1(t) \\ \mathrm{A}_2(t) \end{pmatrix}_{I} = \begin{pmatrix} 0.5 & 0.5 \\ -0.5 & 0.5 \end{pmatrix} \begin{pmatrix} \exp(-3.74t) \\ 1 \end{pmatrix} \tag{A3}$$

$$\mathbf{K}'_{\mathrm{phenI}} = \begin{pmatrix} -1.868 & 1.868 \\ 1.868 & -1.868 \end{pmatrix} \tag{A4}$$

$$\begin{pmatrix} A_1(t) \\ A_2(t) \\ A_3(t) \\ A_4(t) \end{pmatrix}_{II} = \begin{pmatrix} 0.5 & 0.5 & 0 & 0 \\ -0.5 & 0.5 & 0 & 0 \\ -0.0282 & -0.5 & 0.0282 & 0.5 \\ 0.0282 & -0.5 & -0.0282 & 0.5 \end{pmatrix} \begin{pmatrix} \exp(-5.35t) \\ \exp(-1.33t) \\ \exp(-1.10t) \\ 1 \end{pmatrix} \tag{A5}$$

$$\mathbf{K}_{\mathrm{phenII}} = \begin{pmatrix} -3.341 & 2.011 & 0 & 0 \\ 2.011 & -3.341 & 0 & 0 \\ 0.785 & 0.546 & -0.551 & 0.551 \\ 0.546 & 0.785 & 0.551 & -0.551 \end{pmatrix} \tag{A6}$$

$$\begin{pmatrix} \mathrm{A}_1(t) \\ \mathrm{A}_2(t) \end{pmatrix}_{\mathrm{II}} = \begin{pmatrix} 0.5 & 0.5 \\ -0.5 & 0.5 \end{pmatrix} \begin{pmatrix} \exp(-4.13t) \\ 1 \end{pmatrix} \tag{A7}$$

$$\mathbf{K}'_{\mathrm{phenII}} = \begin{pmatrix} -2.065 & 2.065 \\ 2.065 & -2.065 \end{pmatrix} \tag{A8}$$

Appendix B

Rate constant matrices partitioned according to eq 6 for the mechanistic reaction Schemes 3 (eqs B1−B4) and 4 (eqs B5−B8).

$$\mathbf{K}_{\mathrm{aa}}(k_{\mathrm{D}}, z) = -k_D \begin{pmatrix} z & 0 & 0 & 0 \\ 0 & z & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \tag{B1}$$

$$\mathbf{K}_{\mathrm{ba}}(k_{\mathrm{D}}, z) = k_{\mathrm{D}} \begin{pmatrix} z & 0 & 0 & 0 \\ 0 & z & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \tag{B2}$$

$$\mathbf{K}_{\mathrm{ab}}(k_{\mathrm{inter}}, \beta, \xi) = k_{\mathrm{inter}}\xi \begin{pmatrix} \beta & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 & 1 \end{pmatrix} \tag{B3}$$

$$\mathbf{K}_{\mathrm{bb}}(k_{\mathrm{inter}}, \beta, \xi, \eta, \theta) = k_{\mathrm{inter}} \begin{pmatrix} -\Delta & 1 & \eta & \theta & 0 & 0 \\ 1 & -\Delta & \theta & \eta & 0 & 0 \\ \eta & \theta & -\Delta' & 1 & 0 & 0 \\ \theta & \eta & 1 & -\Delta' & 0 & 0 \\ 0 & 0 & 0 & 0 & -1-\xi & 1 \\ 0 & 0 & 0 & 0 & 1 & -1-\xi \end{pmatrix} \tag{B4}$$

The notations $\Delta = 1 + \beta\xi + \eta + \theta$ and $\Delta' = 1 + \xi + \eta + \theta$ are used here.

$$\mathbf{K}'_{\mathrm{aa}}(k_{\mathrm{D}}, z) = -zk_{\mathrm{D}} \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \tag{B5}$$

$$\mathbf{K}'_{\mathrm{ba}}(k_{\mathrm{D}}, z) = zk_{\mathrm{D}} \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \tag{B6}$$

$$\mathbf{K}'_{\mathrm{ab}}(k_{\mathrm{inter}}, \beta, \xi) = k_{\mathrm{inter}}\beta\xi \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} \tag{B7}$$

$$\mathbf{K}'_{\mathrm{bb}}(k_{\mathrm{inter}}, \beta, \xi) = -\,k_{\mathrm{inter}} \begin{pmatrix} 1+\beta\xi & -1 \\ -1 & 1+\beta\xi \end{pmatrix} \tag{B8}$$

References and Notes

(1) . Bergson, G. *Chem. Scr.* **1975**, *8*, 145 and references therein. Carpenter, B. K. *Determination of Organic Reaction Mechanism*; John Wiley & Sons: New York, 1984; p 62.

(2) Löwdin, P.-O. *J. Chem. Phys.* **1951**, *19*, 1396. *J. Mol. Spectrosc.* **1963**, *10*, 12. Löwdin, P.-O. *J. Mol. Spectrosc.* **1964**, *14*, 119. Löwdin, P.-O. *Linear Algebra for Quantum Theory*; John Wiley & Sons: New York, 1998; p 65.

(3) See for example: Golub, G. H.; Ortega, J. M. *Scientific Computing and Differential Equations*; Academic Press: New York, 1992.

(4) Hussénius, A.; Matsson, O.; Bergson, G. *Chem. Commun.* **1998**, 2693 and references therein.