

# ACCOUNTS OF CHEMICAL RESEARCH®

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## IUPAC Recommendations for the Representation of Reaction Mechanisms<sup>1</sup>

ROBERT D. GUTHRIE\*

*Department of Chemistry, University of Kentucky, Lexington, Kentucky 40506*

WILLIAM P. JENCKS

*Graduate Department of Biochemistry, Brandeis University, Waltham, Massachusetts 02254*

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About 10 years ago, the IUPAC Commission on Physical Organic Chemistry set about the task of producing a set of recommendations for the naming of reaction mechanisms. Initially there was vigorous debate as to whether the well-established system designed by Ingold<sup>2</sup> should be revised or a new approach recommended. There followed an arduous effort by a working party dedicated to the retention of a revised Ingold-type system, but despite discussion over a period of about two years, the commission decided that revision of the Ingold system was impractical.

The Ingold system of nomenclature was designed to describe the observed properties of an organic reaction: A bimolecular nucleophilic substitution is an  $S_N2$  reaction. It was not designed to describe reaction mechanisms, although it has been widely used for that purpose even by Ingold himself. The Ingold code states the type of transformation and the observed molecu-

larity, but this does not necessarily specify the reaction mechanism. A significant fraction of the controversy about reaction mechanisms arises because of ambiguities in the definition of the reaction mechanisms. In some cases identical names refer to different mechanisms; in others, different names are used for the same mechanism. For example, the term  $S_N2$  does not indicate whether the substitution is concerted or stepwise; a stepwise " $S_N2$  intermediate" mechanism has been proposed,<sup>3</sup> although Ingold himself restricted the term to a one-step mechanism.<sup>4</sup> The term  $S_E2$  has been applied to both the two-step mechanism of electrophilic aromatic substitution<sup>5</sup> and the one-step, concerted process at aliphatic carbon.<sup>6</sup> Mechanistically,  $B_{AC}1 = S_N1$  but  $B_{AC}2 \neq S_N2$ .<sup>7</sup> There are at least three names that have been used to indicate the tetrahedral-intermediate mechanism of nucleophilic substitution.<sup>8</sup> This loose relationship between the Ingold nomenclature and the actual mechanism was largely responsible for the decision that the commission should undertake the development of a system that is designed specifically for the representation of reaction mechanisms.

Several alternatives to the Ingold system had been suggested: Mathieu, Ailis, and Valls (1960);<sup>9</sup> Langford

Robert D. Guthrie is Professor of Chemistry at the University of Kentucky. He was born in Bronxville, NY, and grew up in New Orleans, LA. He received his Ph.D. from the University of Rochester in 1963 working with Marshall Gates and did postdoctoral work with D. J. Cram at UCLA. He has been at the University of Kentucky since 1965 and was chairman of the Department of Chemistry from 1983 to 1987. His research has been in carbanion chemistry, electron transfer reactions, and radical anion chemistry. He was an associate member of the IUPAC Commission on Physical Organic Chemistry from 1977 to 1987.

William P. Jencks is Professor of Biochemistry at Brandeis University. He was born in Bar Harbor, ME, and received an M.D. degree from Harvard Medical School in 1951. After internship, he carried out postdoctoral work with F. Lipmann and R. Woodward and spent two years in the Army Medical Service Graduate School. He has been at Brandeis since 1957. His research is concerned mainly with the mechanism of carbonyl, acyl, and phosphoryl group reactions and their acceleration by chemical and enzymatic catalysts. He was a member of the IUPAC Commission on Physical Organic Chemistry from 1981 to 1985.

(1) We regret that we will be unable to supply reprints of this Account.  
(2) Ingold, C. K. *Structure and Mechanism in Organic Chemistry*, 2nd ed.; Cornell University Press: Ithaca, New York, 1969.

(3) Bentley, T. W.; Bowen, C. T.; Morten, D. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* 1981, 103, 5466-5475.

(4) Reference 2, p 423.

(5) March, J. *Advanced Organic Chemistry*, 3rd ed.; John Wiley and Sons, Inc.: New York, 1985; p 447, footnote 2.

(6) Reference 5, pp 513 and 678.

(7) Reference 2, pp 1129-1131.

(8) See ref 2, p 1128, and ref 5, pp 576 and 295.

and Gray (1965);<sup>10</sup> Guthrie (1975);<sup>11</sup> Roberts (1978);<sup>12</sup> Littler (1979).<sup>13</sup> With the exception of Roberts's approach, all suggested replacements for the Ingold system selected an indicator that describes the number and sequence of bond-making/bond-breaking steps as the primary delineator of reaction mechanism. It was apparent that chemists who had tried to deal with the problem found this to be the most fundamental distinction between reaction mechanisms. Accordingly, the commission followed the approach of Mathieu,<sup>9</sup> Guthrie,<sup>11</sup> and Littler,<sup>13</sup> which translates easily into that of Langford and Gray.<sup>10</sup>

After several years of debate over how much detail was to be encoded in the new system, the commission came to the conclusion that, to serve all needs, two systems would be required. There would be a simple version designed for rapid (speech/writing) transmission of the "essential" characteristics of a mechanism, which would place it in one of several broad categories. There would then be a more extensive set of rules, which would provide for registration of all conceivable detail that could eventually form the basis for a computerized information retrieval system. Accordingly two working parties were constituted to accomplish these separate tasks.<sup>14</sup> Descriptions of both systems have been published recently in *Pure and Applied Chemistry*.<sup>15</sup> The two systems are closely related, and translation is straightforward. This account will deal with only the simple version.

### Description of the System

We describe here some of the features of the IUPAC "System for Symbolic Representation of Reaction Mechanisms".<sup>15a</sup> The system lists the sequence of covalent-bond-making and -breaking steps and the apportionment of electrons in these processes. It indicates whether processes are concerted or occur in separate steps and, if they are separate, whether the intermediate species have a sufficient lifetime to diffuse freely through the solvent before reacting further. It is also possible to indicate the rate-limiting step of a reaction sequence and to describe intramolecular, cycloaddition, and chain reactions.

A new system for nomenclature is certain to stimulate controversy. Resistance to a new system will be strong, and perhaps overwhelming. However, we believe that this system deserves the attention of chemists. For one thing, a number of the controversies and uncertainties regarding mechanism arise from incomplete definitions of what is at issue. We believe that the system will be useful in defining these issues by clarifying the distinctions between reaction mechanisms. It will perform

a significant function even if it only serves to focus attention on the variety of distinctions that are possible. We also believe that it has the potential to systematize and simplify the teaching of chemistry, because the concept of bonds being made and broken in different sequences is easily grasped by students.

### Selected Examples

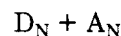
**Substitution Transformations.** The system is best illustrated by example. It follows inorganic nomenclature<sup>10</sup> by describing reactions in terms of associative, A, and dissociative, D, processes or *primitive changes*. Thus, a concerted "S<sub>N</sub>2" displacement is



in which the subscript N stands for nucleophilic or nucleofugic and means that the attacking and departing groups each have an unbonded electron pair. An electrophilic displacement is

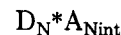


In an "S<sub>N</sub>1" process that forms a moderately stable intermediate, dissociation of the leaving group with its electron pair precedes nucleophilic attack and the reaction is



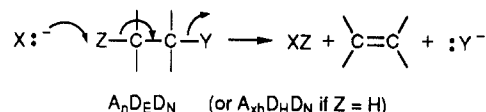
The separation of the terms indicates that the intermediate carbocation can diffuse through the solvent before it reacts with a nucleophilic reagent.

A less stable cation might react with a neighboring nucleophilic molecule faster than it diffuses away, through a "preassociation" mechanism,



in which the asterisk indicates a short-lived intermediate and the subscript indicates an intimate ion pair intermediate.

**Elimination Transformations.** The system is particularly useful for keeping track of the steps of more complex reactions, such as the different mechanisms of olefin-forming elimination transformations. A one-step "E2" elimination is



in which  $A_N D_E$  refers to removal of the electrofugic group, Z, and  $D_N$  refers to dissociation of the leaving group,  $:Y^-$ , with its electron pair. The use of lower-case subscripting indicates that the bond undergoing change is between non-"core atoms". Thus, attachment of  $X:$  to Z ( $A_N$ ) does not involve a core atom (the two C's becoming doubly bonded are *core* atoms in elimination or addition). For the common variation in which  $Z = H$ , the first term,  $A_{xh}$ , indicates that the hydron (the hydron is a proton, deuteron, or triton)<sup>16</sup> associates with another molecule, X, and the  $D_H$  indicates that it dissociates from one of the two core atoms. The three primitive changes,  $A_{xh}$ ,  $D_H$ , and  $D_N$ , will be common to all mechanisms for elimination of an H-nucleofuge pair. The absence of punctuation indicates a one-step, concerted reaction.

(16) Commission on Physical Organic Chemistry, *Pure Appl. Chem.* 1988, 60, 1115.

(9) Mathieu, J.; Ailis, A.; Valls, J. *Angew. Chem.* 1960, 72, 71.

(10) Langford, C. H.; Gray, H. B. *Ligand Substitution Processes*; W. A. Benjamin: Reading, MA, 1965; p 7.

(11) Guthrie, R. D. *J. Org. Chem.* 1975, 40, 402.

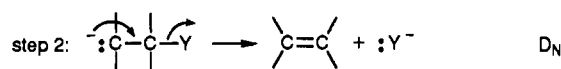
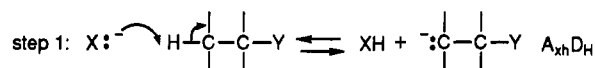
(12) Roberts, D. C. *J. Org. Chem.* 1978, 43, 1473.

(13) Littler, J. *J. Org. Chem.* 1979, 44, 4657.

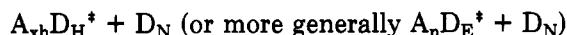
(14) The commission on Physical Organic Chemistry of the Organic Chemistry Division of IUPAC had as chairmen during the period in which this document was prepared H. Zollinger, J. F. Bunnett, and V. Gold; members and national representatives included P. Ahlberg, A. T. Balaban, A. R. H. Cole, M. P. Doyle, W. Drenth, R. D. Guthrie, E. A. Halevi, J. J. E. Hummeres-Allende, G. Illuminati, W. P. Jencks, X. Jiang, R. A. Y. Jones, J. S. Littler, J. March, D. J. McLennan, M. Lj. Mihailovic, P. Müller, O. M. Nefedov, M. Nógrádi, J. R. Penton, M. J. Perkins, J. Reedijk, K. Schwetlick, A. Streitwieser, J. Toullec, and J. Vaughn.

(15) (a) Commission on Physical Organic Chemistry, IUPAC. *Pure Appl. Chem.* 1989, 61, 23-56; (b) *Ibid.* 1989, 61, 57-81.

The "E1cB" mechanism for  $\beta$ -elimination of HY is illustrated below:

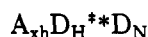


The "E1cB" elimination reaction might then be



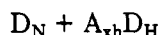
in which the punctuation shows that hydron removal gives a moderately stable carbanion intermediate and that this is followed by dissociation of the leaving group in a separate step. The \* in the first step of this example means that hydron removal is rate limiting; the reaction is E1cB (irreversible) in the Ingold nomenclature. Alternatively, a  $\text{D}_{\text{N}}^*$  term would indicate an "E1cB (reversible)" mechanism, in which departure of the leaving group is rate-limiting.

If the leaving group is expelled very rapidly, in the second step, before the hydronated base diffuses away, the reaction is



This corresponds to an "E1cB<sub>ip</sub> (irreversible)" mechanism, in which the leaving group dissociates from an initially formed ion pair before the hydronated base diffuses away.

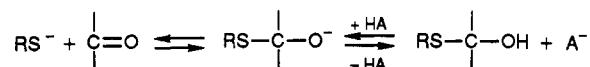
The reverse sequence of terms



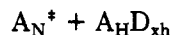
corresponds to an E1 elimination in which departure of the leaving group is followed by hydron abstraction from the carbocation.

Thus, the system describes the important properties of a mechanism, at a glance. By simply changing the punctuating symbols or the order of terms, it is easy to write down the different possible mechanisms. This may be helpful in deciding what experimental tests should be undertaken in order to distinguish the correct mechanism, as discussed later.

**Addition Transformations.** The addition of a thiol anion to a carbonyl group



may be described by



if rate-limiting addition of the thiol anion,  $\text{A}_{\text{N}}^*$ , is followed by rapid hydronation of the hemithioacetal anion in a separate step to give the hemithioacetal,  $\text{A}_{\text{H}}\text{D}_{\text{XH}}$ . Note that this is the reverse of an elimination transformation.

If the hemithioacetal anion is unstable, so that it breaks down to reactants very rapidly and hydron transfer from a buffer acid is rate limiting, the reaction is



In a reaction of this kind, the hydron transfer step is likely to be diffusion controlled. The reaction is then written

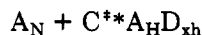
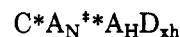


Table I  
Glossary of Symbols Used in the IUPAC System

symbol	placement	meaning
A	on the line	bond making (association)
D	on the line	bond breaking (dissociation)
+	on the line	stepwise process
*	on the line	same as +, but the intermediate is short lived
E	subscript	electrophilic or electrofugic (at core atom)
N	subscript	nucleophilic or nucleofugic (at core atom)
R	subscript	homolytic (at core atom)
e	subscript	same as E, at a peripheral atom
n	subscript	same as N, at a peripheral atom
r	subscript	same as R, at a peripheral atom
H	subscript	same as E, with hydron as electrophile or electrofuge
h	subscript	same as H, at a peripheral atom
xh	subscript	bond making or breaking between hydron and a hydron carrier reagent atom
C	on the line	diffusional combination
P	on the line	diffusional separation
int	subscript	molecules or ions weakly complexed; intimate ion pairs or equivalent pairs of uncharged molecules
ss	subscript	solvent-separated ion pairs or equivalent pairs of uncharged molecules
*	superscript	preceding step rate limiting
{ }	on the line	repeated sequence

in which the  $\text{C}^*$ , "combination", means that diffusion-controlled combination of the acid and the hemithioacetal anion is rate limiting; it is followed by rapid hydron transfer.

If nucleophilic attack on the carbonyl group to form an unstable addition intermediate is catalyzed by hydrogen bonding to the buffer acid, in a preassociation mechanism, the reaction is



When C appears in a mechanism, but is not designated as rate limiting ( $\text{C}^*$ ), its inclusion is understood to refer to arrival of an additional reagent. Thus the C preceding  $\text{A}_{\text{N}}$  in the case above indicates that the three reactants have assembled in an encounter complex (preassociation) before rate-limiting addition. Rapid hydron transfer then takes place.

A fully concerted addition reaction is



which is the reverse<sup>17</sup> of a concerted elimination reaction,  $\text{A}_{\text{XH}}\text{D}_{\text{H}}\text{D}_{\text{N}}$ .

## Summary of Terms

It may be useful at this point to summarize briefly some of the terms and conventions of the system. The complete report should be consulted for a full description; a glossary of symbols is given in Table I.

A reaction mechanism involves one or more *elementary reactions*. Each separate step of a mechanism is an elementary reaction. The elementary reactions involve *core atoms* (defined by the nature of the transformation: addition, elimination, substitution, rearrangement), *peripheral atoms* (noncore atoms within the substrate molecule), and *carrier atoms* (atoms that remain part of an external reagent molecule throughout the reaction. For example, in the hydroxide-promoted

(17) A convenience of the system is that it is usually possible to generate the code for the mechanism of the reverse reaction by first changing A's to D's and D's to A's, then changing the sequence of punctuation-separated terms, and then reversing the order of the primitive changes within each term.

elimination of HBr from a bromoalkane to produce an alkene, the oxygen is a carrier atom, the H and Br are peripheral atoms, and the two carbon atoms becoming doubly bonded are core atoms.<sup>18</sup>

The reacting atoms can undergo associative, A, or dissociative, D, changes. No explicit account is taken of the movement of  $\pi$  electrons, as in the formation or disappearance of double bonds in an elimination reaction, for example. These *primitive changes* are nucleophilic or nucleofugic, N, when the entering or leaving group carries the reacting electron pair; they are electrophilic or electrofugic, E, when the reacting electron pair remains with the core atom. By convention, reactions proceed with electron movement (curved arrows) from left to right. Homolytic reactions are designated by the subscript R.

The subscripts N, E, and R are capitalized if the bond being made or broken involves a core atom but lower case if it involves only carrier or peripheral atoms, making it easier to identify the primitive changes that take place at the core atoms. This allows immediate recognition of the type of transformation involved. With the exception of rearrangements, named mechanisms contain only two A and/or D terms (primitive changes) with upper-case subscripts. If both terms are A, the transformation is an addition. If both are D, it is an elimination. If one is A and one D, it is a substitution. Rearrangements have four such primitive changes.

Because of the ubiquity of the hydron (the hydron is a proton, deuteron, or triton),<sup>16</sup> a primitive change involving a hydron may be designated with the subscript H or h depending on whether or not a core atom is involved in the primitive change. If the hydron transfer involves a general acid or base, as in buffer-catalyzed reactions, the hydron carrier is identified by the subscript x, as in  $A_{xh}$  or  $D_{xh}$ . The subscript H or h always identifies the electrophilic or electrofugic partner in a primitive change as the hydron. It is the only chemical species that is given a unique symbol.

The separate steps of a multistep reaction are normally separated by a plus sign (+). However, if the steps occur faster than an intermediate reaches diffusional equilibrium with the bulk solvent, as in reactions of an ion pair, the steps can be separated by an asterisk (\*). A pericyclic reaction in which concerted bond reorganization takes place throughout a cyclic array of atoms is indicated by the prefix *cyclo-*, while simple intramolecular reactions are indicated by *intra-*.

The repetitive process in a chain reaction can be indicated by enclosing it in braces ({}).

Diffusional combination and separation, or parting, can be indicated by C or P. These processes are usually assumed to occur and are not noted explicitly. They are included when they can be kinetically or mechanistically significant.

The subscripts int and ss may be useful to designate ion pairs or other nonbonded complexes in which the

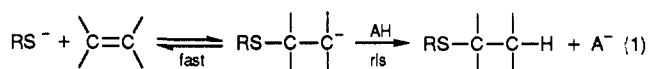
components are in contact or separated, respectively.

An electron transfer is designated by T.

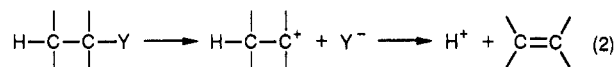
### More Examples

The application of the system to a variety of reactions of increasing complexity provides the best demonstration of its use.

Addition to an olefin with rate-limiting hydronation by an acid is termed  $A_N + A_H D_{xh}$  (eq 1; rls = rate-limiting step).

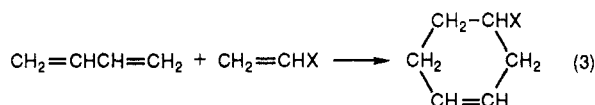


An "E1" elimination with rate-limiting expulsion of the electrofugic group is designated  $D_N^* + D_H$  (eq 2).

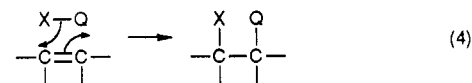


In the general case, or if the electrofuge is not a hydron, this is named  $D_N^* + D_E$ . The second term would be  $A_{xh} D_H$  if it is desired to take explicit note of the base that accepts the proton.

The simplest form of cycloaddition, such as that involved in a Diels-Alder reaction, eq 3, is designated



**cyclo-AA** if the process is concerted. No subscripts are affixed unless a polarized transition state is being suggested. No attempt is made to replace the well-established distinctions based on number and type of electrons involved. These are effectively subcategories of the IUPAC categories. In other words, a cyclo-AA reaction is considered to be mechanistically the same whether it is  $\pi_2s + \pi_4s$  or  $\pi_2s + \pi_2a$  because each involves making two connections in a synchronous fashion.<sup>19</sup> It would of course have a different designation,  $A_R + \text{intra-}A_R$ , if it occurred in two steps with a diradical intermediate. A different mechanistic designation would be required for a concerted  $\pi_2s + \sigma_2a$  process because an additional single bond disconnection is involved, cyclo-AAD (see eq 4). If the transition state is strongly polarized, the mechanism is designated **cyclo- $A_N A_E D_n$** .

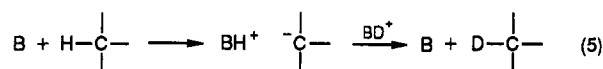


It may be pedagogically helpful that the various established categories of pericyclic reactions are nicely separated by using this nomenclature. Cycloadditions are cyclo-AA or cyclo-AAD, cycloreversions are cyclo-DD or cyclo-DDA, electrocyclic reactions are cyclo-A or cyclo-D, and sigmatropic reactions are cyclo-AD. The IUPAC system thus emphasizes the same distinctions that are used for the traditional subdivisions. The above analysis does suggest that a new name should be found for cyclo-AAD and cyclo-DDA reactions because, in the context of connections and disconnections, these are somewhere between cycloadditions and sigmatropic reactions or, perhaps, are combinations of cycloadditions and electrocyclic reactions.

(19) The commission decided not to include stereochemical designations in the initial version of the system. It would be possible to add an indicator of relative direction for bonds undergoing change in a future version if this would be useful.

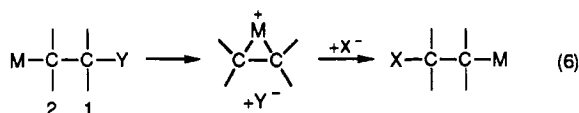
(18) Classification of a given transformation as substitution, elimination, or addition can be subjective. For example, it is possible to view hydroxide-promoted elimination of HBr as substitution at hydrogen rather than as elimination between carbons. If the former view were adopted, the name would be  $A_N D_N D_n$  rather than  $A_N D_E D_N$ . Both names are correct just as the transformation is both a substitution and an elimination. This does not cause ambiguity as long as the outcome of the transformation has been specified. Otherwise, a phrase such as "at hydrogen" may be employed.

Base-catalyzed hydrogen-deuterium exchange of a carbon acid, eq 5, is designated  $A_{xh}D_H + A_HD_{xh}$ . The



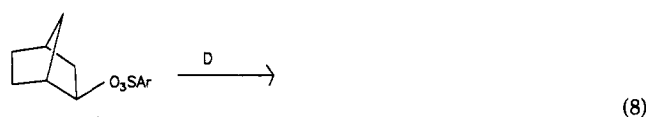
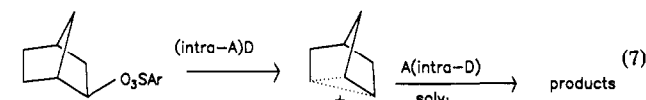
more general term for attack of a nucleophile on an electrofuge to give a carbanion is  $A_ND_E$ .

An example of an intramolecular reaction is



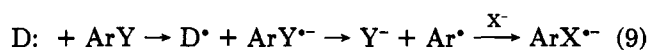
which is termed (intra-1/ $A_N$ )1/ $D_N$  + 2/ $A_N$ (intra-2/ $D_N$ ). Although these names may seem complicated, the numerical part of the code is mainly for the purpose of distinguishing 1,2-rearrangements from migrations between more remote sites. Numerical position indicators are separated from the primitive change to which they apply by a solidus (/). Basically, four bonding changes are involved: intra-A and intra-D take place within a single molecular unit, whereas the unprefix A and D indicate the association or dissociation of separate molecular entities.

The most famous mechanistic controversy in the history of organic chemistry,<sup>20</sup> translated into the IUPAC system, is whether there should be one or two asterisks in the code for the solvolytic rearrangement of *exo*-2-norbornyl arenesulfonates: (intra-A) $D^*A$ -(intra-D), eq 7, versus  $D^*$ intra-AD $^*A$ , eq 8.



Although it would be presumptuous of us to suggest that the new nomenclature would have added rationality to the debate, we do feel that it might have some value in explaining the dispute to nonexperts. For example, it facilitates separation of the question of whether there is a nonclassical ion intermediate (Are intra-A and intra-D separated by an asterisk?) from the question of anchimeric assistance (Are D and intra-A separated by an asterisk?).<sup>21</sup>

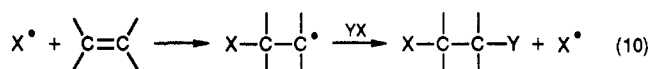
A radical-initiated substitution reaction occurs in the "S<sub>RN</sub>1" mechanism in which an electron is donated to the substrate to form a radical, followed by expulsion of the leaving group and combination with a nucleophile (eq 9). A stepwise reaction of this kind is completed



by another electron transfer, which is not shown. This mechanism is described by  $T + D_N + A_N$ .

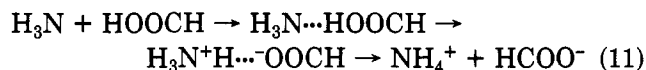
A common free radical addition mechanism involves the attachment of a radical to an unsaturated species, followed by attack of the intermediate radical to dis-

place the initial radical from a reagent molecule (eq 10).



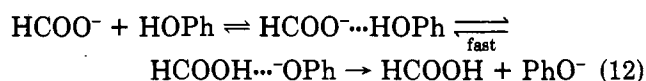
This is an  $A_R + A_RD_r$  mechanism. This pair of steps represents the propagation sequence of a radical chain reaction, which aspect can be emphasized with braces if desired:  $\{A_R + A_RD_r\}$ .

A diffusion-controlled hydron transfer that is thermodynamically favorable involves a rate-limiting encounter of the reactants followed by rapid hydron transfer and association (eq 11). This is designated



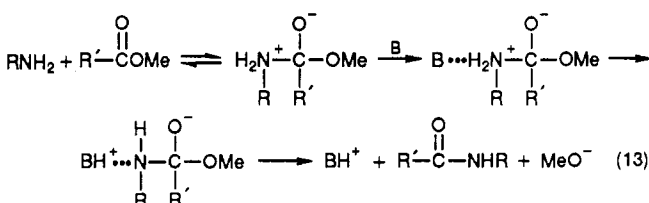
$C^*A_HD_H$ . The final separation step is not indicated unless it is kinetically significant.

For a thermodynamically unfavorable diffusion-controlled hydron transfer, the rate-limiting step is separation of the products, as shown in eq 12 (there is



rate-limiting diffusional combination in the reverse direction). This is described as  $A_HD_H^*P^*$ . Here the combination step is understood while the separation, or parting step, is indicated because it is rate limiting.

General base-catalyzed ester aminolysis that occurs with rate-limiting, diffusion-controlled hydron removal is shown in eq 13. This complicated mechanism is



described by  $A_N + C^*A_{xh}D_H^*D_N$ .

Consideration of the different routes by which a reaction can occur, as designated by this nomenclature, may well be useful in diagnosing the mechanism that is followed in a particular reaction. Consideration of these different possible mechanisms may lead to greater clarity in distinguishing and specifying these mechanisms.

An attempt to provide IUPAC equivalents for Ingold system names has been carried out and a table constructed as part of the commission's report.<sup>15a</sup> That table has been reproduced as Table II of the present paper and includes example numbers that refer to the original report. Users should be aware that in some cases the correspondence is inexact for reasons discussed in the beginning of this paper.

### Help in Diagnosing Mechanisms

Because the new system is based on the fundamental currency of molecular change, the making and breaking of bonds, it can be used to generate a comprehensive set of sequences for any transformation. With substitution, for example, the defining transformation is  $X + Z-Y \rightarrow X-Z + Y$ . A bond is made (A), and one is broken (D). At the simplest level, the possibilities are  $A + D$ ,  $D + A$ , and  $AD$ . With N, E, and R subscripts as options, the possibilities become more numerous (27

(20) For a summary and leading references, see ref 5, p 272.

(21) See ref 5, pp 273-274. See also: Cram, D. J. *J. Am. Chem. Soc.* 1964, 86, 3767.

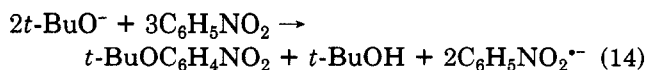
Table II<sup>a</sup>  
Comparison of Names Proposed in This Document with Corresponding Ingold System Names

Example Number	Ingold System Name	Proposed Name	Example Number	Ingold System Name	Proposed Name
SUBSTITUTION MECHANISMS			ADDITION MECHANISMS		
1.1a	S <sub>N</sub> 2	A <sub>N</sub> D <sub>N</sub>	2.1	Ad3	A <sub>N</sub> A <sub>E</sub>
1.1b	S <sub>N</sub> 2'	3/1/A <sub>N</sub> D <sub>N</sub>	2.2	none	cyclo-A <sub>N</sub> A <sub>E</sub> D <sub>N</sub>
1.2a	S <sub>E</sub> 2	D <sub>E</sub> A <sub>E</sub>	2.3	none	cyclo-AA
1.2b	S <sub>E</sub> 2'	1/3/A <sub>E</sub> D <sub>E</sub>	2.4	none	A <sub>N</sub> + A <sub>E</sub>
1.3	S <sub>N</sub> 2cA or A2	A <sub>e</sub> + A <sub>N</sub> D <sub>N</sub>	2.5	none	A <sub>E</sub> + A <sub>N</sub>
1.4	none	A <sub>n</sub> + D <sub>E</sub> A <sub>E</sub>	5.4	none	A <sub>R</sub> + A <sub>R</sub> D <sub>r</sub>
1.5	S <sub>E</sub> C or S <sub>E</sub> 2 coord	A <sub>n</sub> + cyclo-D <sub>E</sub> A <sub>E</sub> D <sub>N</sub>	ELIMINATION MECHANISMS		
1.6a	S <sub>E</sub> i or S <sub>F</sub> 2	cyclo-D <sub>E</sub> A <sub>E</sub> D <sub>N</sub> A <sub>n</sub>	3.1	none	D <sub>E</sub> D <sub>N</sub>
1.6b	S <sub>E</sub> i'	cyclo-1/3/D <sub>E</sub> A <sub>E</sub> D <sub>N</sub> A <sub>n</sub>	3.2	E2 or E2H	A <sub>n</sub> D <sub>E</sub> D <sub>N</sub> or A <sub>xh</sub> D <sub>H</sub> D <sub>N</sub>
1.7	S <sub>N</sub> Ar or Ad <sub>N</sub> -E or B <sub>AC</sub> 2	A <sub>N</sub> + D <sub>N</sub>	3.3	E <sub>i</sub>	cyclo-D <sub>E</sub> D <sub>N</sub> A <sub>n</sub>
1.8a	none	A <sub>N</sub> + A <sub>e</sub> + D <sub>N</sub>	3.4	E2cA?	A <sub>e</sub> + D <sub>E</sub> D <sub>N</sub> and A <sub>e</sub> + A <sub>n</sub> D <sub>E</sub> D <sub>N</sub>
1.8b	A <sub>AC</sub> 2	A <sub>n</sub> + A <sub>N</sub> + A <sub>h</sub> D <sub>H</sub> + D <sub>N</sub> + D <sub>h</sub>	3.5	E1	D <sub>N</sub> + D <sub>E</sub>
1.9	S <sub>E</sub> 2	A <sub>E</sub> + D <sub>E</sub>	3.6	E1	D <sub>N</sub> + A <sub>n</sub> D <sub>E</sub> (or D <sub>N</sub> + A <sub>xh</sub> D <sub>H</sub> )
1.10a	S <sub>N</sub> 1 or B <sub>AL</sub> 1	D <sub>N</sub> + A <sub>N</sub>	3.7	ElcA	A <sub>e</sub> + D <sub>N</sub> + A <sub>n</sub> D <sub>E</sub> (or A <sub>h</sub> + D <sub>N</sub> + A <sub>xh</sub> D <sub>H</sub> )
1.10b	S <sub>N</sub> 1'	1/D <sub>N</sub> + 3/A <sub>N</sub>	3.8	ElcB	A <sub>n</sub> D <sub>E</sub> + D <sub>N</sub> (or A <sub>xh</sub> D <sub>H</sub> + D <sub>N</sub> )
1.11	S <sub>E</sub> 1	D <sub>E</sub> + A <sub>E</sub>	REARRANGEMENT MECHANISMS		
1.12	S <sub>N</sub> 1cA or A1	A <sub>e</sub> + D <sub>N</sub> + A <sub>N</sub>	4.1	none	1/D <sub>N</sub> + intra-1/A <sub>N</sub> + intra-2/D <sub>N</sub> + 2/A <sub>N</sub>
1.13	none	A <sub>n</sub> + D <sub>E</sub> + A <sub>E</sub>	4.2	none	1/D <sub>N</sub> + intra-1/2/A <sub>N</sub> D <sub>N</sub> + 2/A <sub>N</sub>
1.14	S <sub>E</sub> 1(N) or S <sub>E</sub> 1-X <sup>+</sup>	A <sub>n</sub> D <sub>E</sub> + A <sub>E</sub>	4.3	none	(intra-1/A <sub>N</sub> )1/D <sub>N</sub> + 2/A <sub>N</sub> (intra-2/D <sub>N</sub> )
1.15	S <sub>N</sub> i	D <sub>N</sub> + D + A <sub>N</sub>	4.4	none	(intra-2/1/D <sub>N</sub> A <sub>N</sub> )1/D <sub>N</sub> + 2/A <sub>N</sub>
5.1	S <sub>H</sub> 2	A <sub>r</sub> D <sub>R</sub> + A <sub>R</sub> D <sub>r</sub>			
5.2	S <sub>H</sub> 1	D <sub>R</sub> + A <sub>R</sub> D <sub>r</sub>			
5.3	S <sub>RN</sub> 1	T + D <sub>N</sub> + A <sub>N</sub>			

<sup>a</sup>Reprinted with permission from ref 15a. Copyright 1989 IUPAC.

in all, if radical-ion and doubly charged ion mechanisms are included). Catalytic steps can be added, and ion pairing and solvation add the type of variations mentioned earlier, but, even so, the number of possibilities is finite. This large set of possibilities can then be reduced to manageable size by application of chemical precedent. Most importantly, the approach provides assurance that all reasonable sequences are considered.

For a realistic example, consider the following. Nitrobenzene reacts with potassium *tert*-butoxide in THF to produce 2- and 4-*tert*-butoxynitrobenzene with the stoichiometry shown in eq 14.<sup>22</sup> To accomplish a re-



action with this stoichiometry, it will be necessary to break a C-H bond (D[C-H]), make an O-C bond (A[O-C]), make an O-H bond (A[O-H]), and transfer two electrons (2T). The correct mechanism will, therefore, include a sequence of these five primitive changes.<sup>23</sup> The atomic symbols here placed in brackets are intended only to identify the bond involved and not to imply a specific mode of electron apportionment.

(22) Guthrie, R. D.; Nutter, D. E. *J. Am. Chem. Soc.* **1982**, *104*, 7478.

(23) It is possible that other steps are involved, but these must be negated by the corresponding reverse steps before completion of the sequence.

Initially *all* conceivable apportionment modes must be considered.

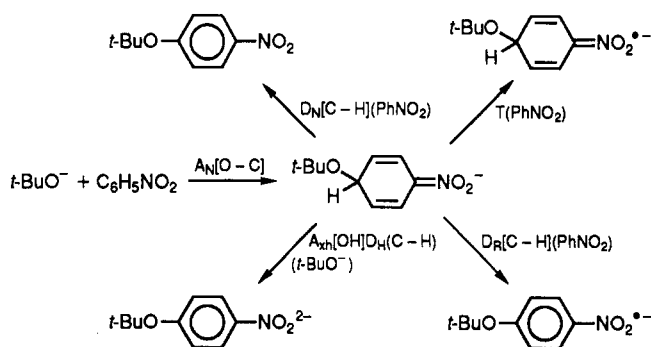
It is impractical, although not impossible, to evaluate all possible sequences of these five primitive changes in all possible electron apportionment modes with zero to four "+" symbols interspersed. A more efficient procedure is to consider the five essential primitive changes and possible combinations thereof as candidates for the first step. When this is done, various energy relationships and literature precedents eliminate all possibilities save A[O-C].<sup>22</sup> There is no possibility of *tert*-butoxide bonding to aromatic carbon as anything other than a nucleophile, so that the electron apportionment for A[O-C] can be specified as A<sub>N</sub>[O-C].

Having established that the first step can only be A<sub>N</sub>[O-C] leaves D[C-H], A[O-H], and T for possible use in the next step. With *tert*-butoxide as reagent, A[O-H] would have to appear as A<sub>xh</sub>[OH]D<sub>H</sub>[C-H]. D[C-H] could appear as part of this combination, but it could also be D<sub>N</sub>[C-H] or D<sub>R</sub>[C-H] (hydride or hydrogen atom loss, presumably to nitrobenzene).

Given these premises, Scheme I constitutes a comprehensive map of possible mechanisms for the initial steps of the reaction. Logical follow-up processes generate the observed products.

In this particular case, the various paths of Scheme I were distinguishable experimentally.<sup>22</sup> The loss of

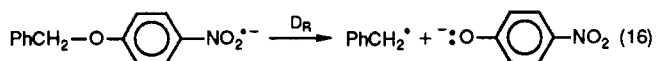
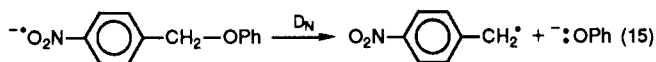
Scheme I



nitrobenzene was found to exhibit second-order dependence on *tert*-butoxide and an  $O_2$ -independent deuterium isotope effect which definitively showed the correct mechanism to be  $A_N + A_{xh}D_H + 2T$ . This is the path that proceeds via the lower left-hand structure in Scheme I. Transfer of two electrons to nitrobenzene completes the mechanism. The demonstrated combination of  $A_N$  and  $D_H$  in a substitution mechanism is unusual for a neutral substrate because it leads to a dianion. More obvious mechanisms which avoid the doubly charged intermediate such as  $A_N + T + A_{xh}D_H + T$  (upper right route in Scheme I) are apparently not utilized. Note that not only is diagnosis facilitated by the systematic evaluation of all reasonable sequences of symbolic primitive changes but the approach provides assurance that no other answer that is consistent with the experimental data has been overlooked.

### Suggesting New Interpretations

The exercise of categorizing mechanisms according to the IUPAC system can bring to light subtle differences that might otherwise go unnoticed. Consider for example the processes of eq 15 and 16. The rules of the system lead to the conclusion that eq 15 is  $D_N$  and eq 16 is  $D_R$ . Is this a meaningful distinction? The dif-



ferent names are required only because of the initial positioning of the extra electron. Experimentally, it is found that the reaction of eq 16 is a minimum of  $10^4$  times slower than that of eq 15,<sup>24</sup> despite what is arguably<sup>24</sup> a thermochemical advantage for eq 16. This suggests that the two processes *do* differ in some fundamental way. The nature of this difference is being investigated.

### Facilitating Learning

Although our experience in using this new terminology in teaching has been limited, one of us has tried introducing it to both undergraduates and beginning graduate students. Although the observations were made on a relatively small sample, it appeared that the ease of learning for the students was inversely proportional to years of prior exposure, i.e., beginning students learned it easily and found it more straightforward than the Ingold system; graduate students were more resistant, having already learned one system and not wanting the burden of the more precise specification demanded. This suggests that the place to start presenting the new approach may be in general chemistry textbooks. In this way, by the time the student is dealing with the mechanistic complexity that is almost certainly present in even the simplest of reactions, he or she will know the right questions to ask and will speak a language that expresses the answers clearly.

### Summary

The IUPAC is recommending a system for naming reaction mechanisms. The system simply lists the bonds made and broken, with punctuation to separate reaction steps and subscripts to indicate electron apportionment. It removes ambiguities of the traditional system and may stimulate disciplined thought about the nature of molecular change.

*R.D.G. thanks The Research Corporation for support from a Research Opportunity Award for the period during which this paper was being written.*

(24) Maslak, P.; Guthrie, R. D. *J. Am. Chem. Soc.* **1986**, *108*, 2628-2636.