Vinyl Ether Hydrolysis. VI. Electrostatic Effects on Acid Catalysis[1]

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Abstract: The catalytic coefficients for the hydrolysis of ethyl vinyl ether catalyzed by seven amino acids, five other charged acids, and H_3PO_4 and HF deviate from a Brønsted relation based upon seven neutral carboxylic acid catalysts. The directions as well as the relative magnitudes of these deviations are understandable in terms of electrostatic interaction between the catalysts and the cationic center developing on the substrate in the rate-determining proton-transfer transition state of the hydrolysis reaction. This hypothesis also successfully explains similar dispersion according to catalyst charge type observed in the Brønsted relation for base-catalyzed decomposition of nitramide, and it suggests that the strong negative deviations generally shown by H_3O^+ in Brønsted correlations for rate-determining proton transfer may be largely electrostatic in origin.

In a recent study of the hydrolysis of a number of vinyl ethers catalyzed by neutral carboxylic acids,[2] we observed that acids bearing dipolar substituents showed small, but consistent, deviations from correlations (Brønsted relations) based upon all of the data. We attributed these deviations to electrostatic interaction between the dipolar groups and the positive charge being developed on the substrates in the rate-determining step of this reaction (eq 1).

$$CH_2{=}CHOR + HA \longrightarrow CH_3CHOR^+ + A^- \qquad (1)$$

It follows from this explanation that charged catalysts should show even greater systematic deviations from such correlations. We have therefore examined the hydrolysis of one of the original substrates, ethyl vinyl ether, in solutions of a number of charged acids. The results support our original hypothesis. They suggest, moreover, that such effects may be general and, if not taken into account, may upset Brønsted correlations. They also provide insight into the large deviations usually shown by the hydronium ion in Brønsted relations for rate-determining proton transfer from catalyst to substrate.

Experimental Section

Materials. All materials were obtained commercially and were used as received except for sulfamic acid and sulfoacetic acid. The former was purified by fractional crystallization according to the recipe given by Butler, Smith, and Audrieth,[3] and the latter was recrystallized from water as its dipotassium salt.[4]

Solutions were prepared using deionized water which had been further purified by distillation from alkaline permanganate in glass apparatus.

Kinetics. Rates were measured spectroscopically using the strong end-absorption of ethyl vinyl ether at 200–220 nm;[5] the spectrometer (Cary 11 or 15) cell compartment was thermostated at 26.0 ± 0.1°. Absorbance was recorded continuously as a function of time for 3–4 half-lives and infinite-time readings were made after 8–10 half-lives. First-order rate constants were evaluated as slopes of plots of ln $(A - A_\infty)$ *vs.* time; in some of the slower runs infinity readings were not taken and the data were treated by the method of Guggenheim[6] and/or Swinbourne.[7] In all cases the hydrolysis obeyed first-order kinetics exactly within the precision of the measurement over the entire course of the reaction.

Results

First-order rate constants were measured in series of buffer solutions of 12 catalyst acids at constant buffer ratio but different buffer concentration; the results are summarized in Table I.[8] These data were fitted to the rate law of eq 2, which the hydrolysis of ethyl vinyl

$$k_1 = k_{\rm H} + [{\rm H}^+] + k_{\rm HA}[{\rm HA}] \qquad (2)$$

ether obeys under these conditions,[2,5] by linear least-squares analysis. The resulting expressions, with error limits (standard deviations) of the slope ($k_{\rm HA}$) and intercept ($k_{\rm H^+}[{\rm H}^+]$) parameters, are also given in Table I.[8]

In this treatment, corrections were made wherever necessary for changes in the extent of dissociation of a buffer acid as its concentration varied along a series of solutions. Such changes occur, and produce undesirable differences in hydrogen ion levels, even at constant stoichiometric buffer ratio whenever strong buffer acids are used at low concentration. Buffer failure of this kind was compensated for here, as previously,[1b,2] by calculating hydrogen ion concentrations of all buffer solutions and then adjusting observed rate constants as necessary. The value of $k_{\rm H^+}$ used for this purpose, 1.95 M^{-1} sec^{-1}, was measured directly and is in good agreement with $k_{\rm H^+}$ = 1.93 M^{-1} sec^{-1} predicted for 26° from the known[9] temperature dependence of this reaction.

Ionic strength effects on the dissociation of neutral and negatively charged acids were allowed for using activity coefficients of ionic species calculated with the Debye–Hückel equation. An ion-size parameter of 4 Å was used except in the case of sulfamate ion (6 Å) and bioxalate ion (5 Å); the latter is the value recommended

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[1] (a) This research was supported by grants from the National Science Foundation (GP 9253 and GP 23578) and the Petroleum Research Fund of the American Chemical Society (5215-AC4). (b) Part V: A. J. Kresge and H. J. Chen, *J. Amer. Chem. Soc.*, **94**, 2818 (1972).

[2] A. J. Kresge, H. L. Chen, Y. Chiang, E. Murrill, M. A. Payne, and D. S. Sagatys, *ibid.*, **93**, 413 (1971).

[3] M. J. Butler, G. F. Smith, and L. F. Audrieth, *Anal. Chem.*, **10**, 690 (1938).

[4] F. L. Hahn and H. Wolf, *Z. Anorg. Chem.*, **144**, 122 (1925).

[5] A. J. Kresge and Y. Chiang, *J. Chem. Soc. B*, 53 (1967).

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

[7] E. S. Swinbourne, *J. Chem. Soc.*, 2371 (1960).

[8] Table I appears following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth Street N.W., Washington, D. C. 20036, by referring to code number JACS-73-803. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

[9] A. J. Kresge and Y. Chiang, *J. Chem. Soc. B*, 58 (1967).

Table II. Summary of Catalytic Coefficients for the Hydrolysis of Ethyl Vinyl Ether in Aqueous Solution[a]

Catalyst	pK_a	p	q	k_{HA}, M^{-1} sec^{-1}	Log deviation[b]
Neutral carboxylic acids[c]					
$CNCH_2CO_2H$	2.47[d]	1	2	0.0442	−0.08
$ClCH_2CO_2H$	2.87[e]	1	2	0.0324	+0.06
$CH_3OCH_2CO_2H$	3.57[f]	1	2	0.0111	+0.09
HCO_2H	3.75[g]	1	2	0.00672	−0.01
$HOCH_2CO_2H$	3.83[h]	1	2	0.00553	−0.04
CH_3CO_2H	4.76[i]	1	2	0.00138	+0.01
$CH_3CH_2CO_2H$	4.88[j]	1	2	0.00104	−0.03
Amino acids					
$CH_2[N(CH_3)_3{}^+]CO_2H$	1.82[k]	1	2	0.0487	−0.49
$CH_3CH_2CH(NH_3{}^+)CO_2H$	2.28[l]	1	2	0.0363	−0.29
$CH_2(NH_3{}^+)CO_2H$	2.35[m]	1	2	0.0335	−0.28
$CH_3CH(NH_3{}^+)CO_2H$	2.35[l]	1	2	0.0334	−0.28
$CH_3C(CH_3)(NH_3{}^+)CO_2H$	2.36[n]	1	2	0.0308	−0.31
$CH_2(NH_3{}^+)CH_2CO_2H$	3.55[o]	1	2	0.00527	−0.25
$CH_2(NH_3{}^+)CH_2CH_2CO_2H$	4.03[p]	1	2	0.00214	−0.10
Other acids					
H_3O^+	−1.74	3	1	1.75[c]	−1.35
$SO_3{}^-NH_3$	0.99[q]	3	1	0.284	−0.24
$HSO_4{}^-$	1.92[r]	1	4	1.41	+0.88
H_3PO_4	2.12[s]	3	2	0.339	+0.43
HF	3.17[t]	1	1	0.0671[u]	+0.80
$CH_2(SO_3{}^-)CO_2H$	4.20[v]	1	2	0.0156	+0.67
$CO_2{}^-CO_2H$	4.27[w]	1	4	0.0117	+0.38

[a] Neutral carboxylic acids, H_3O^+, and HF at 25.0°; others at 26.0°. [b] Deviation from Brønsted relation based on seven neutral carboxylic acids: $\log k/p = 0.235 + 0.696 \log qK_a/p$. [c] A. J. Kresge, H. L. Chen, Y. Chiang, E. Murrill, M. A. Payne, and D. S. Sagatys, *J. Amer. Chem. Soc.*, **93,** 413 (1971). [d] F. S. Feates and D. J. G. Ives, *J. Chem. Soc.*, 2798 (1956); D. J. G. Ives and P. D. Marsden, *ibid.*, 649 (1965). [e] D. J. G. Ives and J. H. Pryor, *ibid.*, 2104 (1955). [f] E. J. King, *J. Amer. Chem. Soc.*, **82,** 3575 (1960). [g] H. S. Harned and N. D. Embree, *ibid.*, **56,** 1042 (1934). [h] L. F. Nims, *ibid.*, **58,** 987 (1936). [i] H. S. Harned and R. W. Ehlers, *ibid.*, **55,** 652 (1933). [j] D. H. Everett, D. A. Landsman, and B. R. W. Pinsent, *Proc. Roy. Soc., Ser. A*, **215,** 403 (1952). [k] J. C. Ahluwalia, F. J. Millero, R. N. Goldberg, and L. G. Hepler, *J. Phys. Chem.*, **70,** 319 (1966). [l] P. K. Smith, A. C. Taylor, and E. R. B. Smith, *J. Biol. Chem.*, **122,** 109 (1937). [m] E. J. King, *J. Amer. Chem. Soc.*, **73,** 155 (1951). [n] R. M. Izatt, J. J. Christesen, and V. Kothari, *Inorg. Chem.*, **3,** 1565 (1964). [o] M. May and W. A. Felsing, *J. Amer. Chem. Soc.*, **73,** 406 (1951). [p] E. J. King, *ibid.*, **76,** 1006 (1954). [q] E. J. King and G. W. King, *ibid.*, **74,** 1212 (1952). [r] M. H. Leitzke, R. W. Stoughton, and T. F. Young, *J. Phys. Chem.*, **65,** 2247 (1961). [s] R. G. Bates, *J. Res. Nat. Bur. Stand.*, **47,** 127 (1951). [t] H. H. Broene and T. deVries, *J. Amer. Chem. Soc.*, **69,** 1644 (1947). [u] A. J. Kresge and Y. Chiang, *ibid.*, **94,** 2814 (1972). [v] R. P. Bell and G. A. Wright, *Trans. Faraday Soc.*, **57,** 1377 (1961). [w] G. D. Pinching and R. G. Bates, *J. Res. Nat. Bur. Stand.*, **40,** 405 (1948).

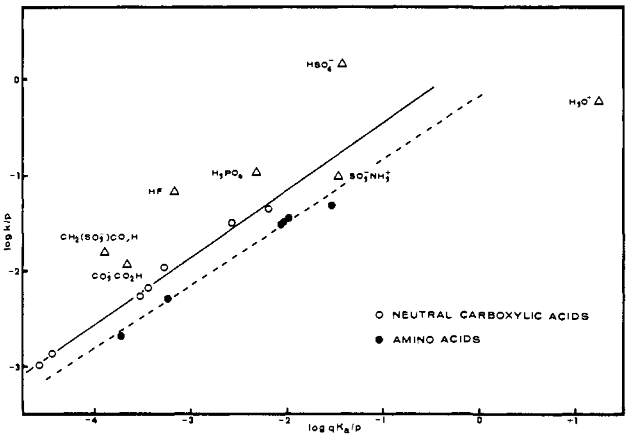

Figure 1. Brønsted plot for the hydrolysis of ethyl vinyl ether: solid line, least-squares correlation of data for seven neutral carboxylic acids; broken line, least-squares correlation of data for seven amino acids.

by Pinching and Bates[10] on the basis of their determination of the ionization constant of this acid.

The extent of dissociation of positively charged acids was taken to be independent of ionic strength at the low value (0.04 *M*) used for these acids. This assumption was checked for *N,N,N*-trimethylglycine and α-aminoisobutyric acid buffers by measuring hydrogen ion concentrations with a pH meter (Beckman Research, Model 1019) calibrated against dilute hydrochloric acid of the appropriate ionic strength; in all cases, calculated and measured values agreed to within 3%. The fact that identical kinetic results were obtained in glycine buffers when ionic strength was and was not held constant (Table I)[8] also implies that ionic strength effects were absent in the dissociation of these positively charged acids.

Calculated hydrogen ion concentrations were also used to evaluate k_{H^+} from the intercept of the least-squares relationship between k_1 and [HA] for each series of buffer solutions. The results, listed in Table I,[8] give 1.97 ± 0.08 $^{-1}$ sec^{-1} as the average value for all buffers; this is in excellent agreement with the directly measured value (1.95) and attests to the essential validity of this method of treating the experimental data.

The catalytic coefficients determined here together with all other available values for the hydrolysis of ethyl vinyl ether are summarized in Table II.

Discussion

Figure 1, in which the available catalytic coefficients for the hydrolysis of ethyl vinyl ether are presented in the form of a Brønsted plot, shows that the data clearly do not conform to a single Brønsted relation. The

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(10) G. D. Pinching and R. G. Bates, *J. Res. Nat. Bur. Stand.*, **40,** 405 (1948).

catalysts do, however, fall into groups according to charge type: all negatively charged acids lie above a correlation line based upon neutral carboxylic acids, and all positively charged acids lie below this line. The positively charged amino acids themselves give a good Brønsted relation with $\alpha = 0.65 \pm 0.04$, r (correlation coefficient) = 0.991, which is nearly parallel to and roughly a factor of 2 in rate below that provided by the neutral carboxylic acids ($\alpha = 0.70 \pm 0.03$, $r = 0.996$). The negatively charged acids seem to show greater variability in their deviation from the neutral-acid correlation, but the number of negatively charged catalysts examined was small, and it is difficult to say whether a larger sample would not give a Brønsted relation of its own.

Dispersion such as this according to charge type is not uncommon in Brønsted relations. Perhaps the best known example occurs in the base-catalyzed decomposition of nitramide, where dipositive, neutral, negative, and dinegative catalysts define four parallel lines separated by more than two orders of magnitude in reactivity.[11a]

An explanation of this phenomenon on the molecular level seems not to have been offered. It is significant, therefore, that these effects can be accounted for in terms of transition state interactions such as those recently advanced to explain the occurrence of Brønsted exponents greater than one and less than zero.[12]

It is convenient for this purpose to convert the usual expression for a Brønsted relation, which contains catalyst ionization constants, K_{HA} (eq 3), to an equivalent form involving rate, k_{HA}, and equilibrium, K, constants of the same, *i.e.*, the catalyzed, reaction (eq 4).[2]

$$\log k_{\mathrm{HA}} = \log G + \alpha \log K_{\mathrm{HA}} \qquad (3)$$

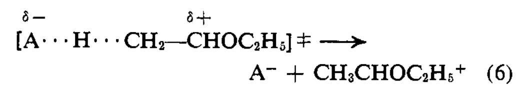
$$\log k_{\mathrm{HA}} = \log G + \alpha(\log k_{\mathrm{SH^+}} + \log K) \qquad (4)$$

A linear Brønsted relation may then be seen to require a linear relationship between the free energy of activation of the catalyzed process, $\Delta F^{\ddagger}$, and its overall free energy of reaction, ΔF° (eq 5). It is also evident that

$$\Delta F^{\ddagger} = \text{constant} + \alpha \Delta F^{\circ} \qquad (5)$$

any change in the system which affects one of these free energy quantities without producing the corresponding change in the other required by eq 5 will result in a deviation from the linear relationship.

Polar substituents introduced into the catalyst are capable of producing such deviations. In the hydrolysis of ethyl vinyl ether, for example, the substrate is taking on positive charge in the rate-determining transition state (eq 6), and this charge will interact with



$$\mathrm{AH} + \mathrm{CH_2{=}CHOC_2H_5} \longrightarrow [\overset{\delta-}{\mathrm{A}}\cdots\mathrm{H}\cdots\mathrm{CH_2}{-}\overset{\delta+}{\mathrm{C}}\mathrm{HOC_2H_5}]^{\ddagger} \longrightarrow \mathrm{A^-} + \mathrm{CH_3CHOC_2H_5^+} \qquad (6)$$

polar groups situated nearby in the catalyst. This interaction, however, will be absent from the final state of the process, for there the reaction partners are no longer in close proximity. This interaction will therefore affect $\Delta F^{\ddagger}$ and not ΔF°, and will produce deviations from a Brønsted relation based upon neutral catalysts possessing no polar groups. The direction of these deviations, moreover, should be energy lowering and therefore rate accelerating for negatively charged catalysts, and energy raising and rate retarding for positively charged catalysts, as is observed. In a base-catalyzed reaction such as nitramide decomposition, on the other hand, a proton is being transferred away from the substrate and negative charge is being generated; the direction of the polar substituent effect here should therefore be reversed, again as observed.

It follows from this explanation that positive, *i.e.*, rate accelerating, deviations may on the whole be greater than negative deviations. The former are the result of attractive interactions which, in flexible systems, will tend to bring the interacting groups closer together and thus augment the energy-lowering effect. Negative deviations, on the other hand, are produced by repulsive interactions which will tend to push the interacting groups apart minimizing the energy-raising effect. It is significant therefore that the average of the seven amino acid deviations listed in Table II is −0.32 log unit whereas the average for the three negatively charged catalysts is +0.54 log unit. In the decomposition of nitramide, moreover, the line correlating dipositive catalysts lies a factor of 46 in reactivity above the relation based on neutral catalysts, whereas the correlation using dinegative catalysts is only a factor of 8 below the neutral line.[11a] The larger positive deviations, being the result of shorter range interactions, should also be the more specific and therefore more variable, again as observed both here (Table II) and in nitramide decomposition.[11a]

These considerations can be extended to rationalize some of the differences in deviations shown in Table II or Figure 1. In bisulfate ion, for example, the negative charge is three atoms removed from the acidic proton, whereas in bioxalate ion it is four atoms away; bisulfate therefore shows a greater positive deviation than bioxalate. Removing the charge one atom more, as in sulfoacetic acid, reverses this trend and seems to deny a relationship between distance and deviation magnitude. The longer chain, however, allows more flexibility, and, with an attractive interaction such as this, the distance between the charged group and the cationic center on the substrate may well be shorter in the case of sulfoacetic acid than in bioxalate ion.

The large positive deviation shown by hydrogen fluoride has already been attributed to a lack of charge delocalization in the fluoride ion; electrostatic considerations show that less energy is required to move a proton a short distance away from an anion in which the charge is localized on a single atom than from an anion in which the same amount of charge is spread over several atomic centers.[13] It may seem paradoxical that charge delocalization, which makes, *e.g.*, carboxylic acids more acidic than they would be otherwise, should also lower their catalytic effectiveness, but this too can be understood as the result of an interaction which affects $\Delta F^{\ddagger}$ but not ΔF°. Delocalization of negative charge in the proton transfer transition state must occur at the expense of some electrostatic stabilization, for it requires shifting part of the negative charge away from the positive center developing nearby on the substrate and on the proton being transferred. In the final state, on the

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[11] R. P. Bell, "Acid-Base Catalysis," Oxford University Press, London, 1941: (a) p 85; (b) p 91.

[12] A. J. Kresge, *J. Amer. Chem. Soc.*, 92, 3210 (1970).

[13] R. P. Bell and J. C. McCoubrey, *Proc. Roy. Soc., Ser. A*, 234, 192 (1956); A. J. Kresge and Y. Chiang, *J. Amer. Chem. Soc.*, 94, 2814 (1972).

other hand, delocalization can occur without similar electrostatic destabilization, for here the reaction partners are no longer together and the opposite charges are not in close proximity. Thus, this effect raises the free energy of the transition state without having a corresponding influence on the free energy of reaction.

Phosphoric acid also shows a positive deviation despite the fact that it resembles the neutral carboxylic acids in being uncharged and having a charge-delocalized anion. The rate acceleration here may be the result of a particularly favorable disposition of solvent molecules about the hydroxylic H_3PO_4 species, which reduces the amount of solvent reorganization that must take place upon proton transfer. A similar argument has been advanced to explain the positive deviations generally observed for bisulfate ion in reactions of this kind.[14] It is not at all clear, however, that the catalytic effectiveness of bisulfate ion cannot be accounted for in terms of the electrostatic influence of the negative charge alone.

It is interesting that sulfamic acid gives a negative deviation. This is consistent with a zwitterionic structure, $SO_3^-NH_3^+$, for this substance, which makes its acidic end positive and puts it into the category of positively charged catalysts. Sulfamic acid is known to exist in this and not the neutral form, HSO_3NH_2, in the crystal,[15] but there has been some uncertainty about its structure in solution.[16]

The sulfamic acid deviation is smaller than expected for a catalyst with its positive charge so near the seat of reaction, but this is undoubtedly due to the close proximity of the negatively charged sulfonate group. The structural situation is not unlike that in the bisulfate ion, and approximating the effect of the negative charge by the positive deviation shown by bisulfate gives 1.1 log units as the negative deviation of $-NH_3^+$ alone; this comes to within a factor of 2 in rate to the strong negative deviation shown by the structurally similar hydronium ion. The hydronium ion is consistently a very poor catalyst in reactions such as this,[11b,17] and it has been suggested that this may be the result of an improperly assessed acidity constant.[18] The present results indicate that a good portion of the effect could be electrostatic in origin.

Apart from being interesting in their own right, these electrostatic effects on acid catalysis illustrate rather dramatically the dangers inherent in basing Brønsted correlations on structurally inhomogeneous groups of catalysts. For example, the present data for phosphoric and cyanoacetic acids give a Brønsted exponent of -2.7, whereas the data for bisulfate ion and sulfamic acid provide a value of nearly $+15$! On the other hand, the seven neutral carboxylic acids and the seven amino acids, taken as two separate groups, give exponents which are very similar: $\alpha = 0.70 \pm 0.03$ and 0.65 ± 0.04, respectively. This suggests that Brønsted exponents based upon different homogeneous groups of catalysts which cover the same pK_a range may in general be similar and therefore independent of the structure of the catalysts.

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(14) M. M. Kreevoy, T. S. Straub, W. V. Kayser, and J. L. Melquist, *J. Amer. Chem. Soc.*, **89**, 1201 (1967).

(15) F. A. Kanada and A. J. King, *ibid.*, 73, 2315 (1951).; K. Osaki, H. Tadokoro, and I. Nitta, *Bull. Chem. Soc. Jap.*, **28**, 529 (1955).

(16) P. Baumgarten, *Ber.*, **62B**, 820 (1929); E, J. King and G. W. King, *J. Amer. Chem. Soc.*, 74, 1212 (1952); M. K. Hargreaves, E. A. Stevenson, and J. Evans, *J. Chem. Soc.*, 4582 (1965); H. P. Hopkins, Jr., C. H. Wu, and L. G. Hepler, *J. Phys. Chem.*, **69**, 2344 (1965).

(17) J. M. Williams, Jr., and M. M. Kreevoy, *Advan. Phys. Org. Chem.*, **6**, 63 (1968).

(18) R. P. Bell, *Trans. Faraday Soc.*, **39**, 253 (1943).

Determination of Intermediate Ion Structure in the Mass Spectrometry of Heteroaromatic Compounds[1]

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Abstract: A quantum chemical method for the determination of ion structure in the course of the fragmentation of cyclic compounds is proposed. Using this method, the fragmentation mechanisms of pyridine and pyrimidine are examined. Electronic structures of some ions are calculated by the open-shell CNDO/2 method to give bases for their organic chemical expressions. It is shown that the first bond scission of a heteroaromatic ring generally occurs at the bond β to the heteroatom with an unpaired electron.

Many papers on the mass spectrometry of heteroaromatic compounds have been published.[2] In spite of the efforts of many authors, the mechanism of the fragmentation has not been so systematically established as with aliphatic compounds. The difficulty is considered to be caused by the uncertainty of our knowledge of the ion structures in the course of fragmentation. Besides, there seems to be no direct experimental technique available for determination of structures. In this paper we will deal with general cyclic ions and will propose a quantum chemical method based on three hypotheses: (1) the fracture of a ring proceeds stepwise; (2) the velocity of the first

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(1) A Molecular Orbital Approach to the Interpretation of Organic Mass Spectra. III. Part II: H. Ichikawa and M. Ogata, *Bull. Chem. Soc. Jap.*, submitted for publication.

(2) See, *e.g.*, Q. N. Porter and J. Baldas, "Mass Spectrometry of Heterocyclic Compounds," Wiley-Interscience, New York, N. Y., 1971.