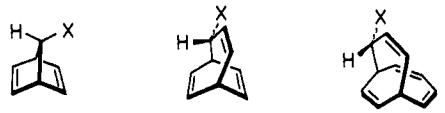
Chart I. S_N1 Rate Constants (10^6k, s^{-1}, 80 °C, *p*-Nitrobenzoates in 70% Aqueous Acetone)



13	14	2
6.3[a]	11.1[b]	<0.16

[a] C. L. Deyrup, Ph.D. Dissertation, Boston University, 1970, as cited in ref 18; extrapolated from higher temperatures (E_a = 25.5 kcal/mol). [b] Extrapolated from higher temperatures (E_a = 25.0 kcal/mol)[17] and from 80% aqueous acetone assuming m = 1,[19] whence $k_{70\%}/k_{80\%}$ = 6.35.

the cationic product. This view neglects many other factors, especially the differing stabilities of the reactants.

The remaining rate constants of Figure 1 were best determined indirectly. The kinetic parameters that govern cationic processes were extracted from an independent hydrolytic study of tetracyclic ester (**3**).[8] Independent thermal rearrangement of authentic bicyclic alcohol (**6**) provided the rate constant of this irreversible and uniquely simple first-order process. All of these parameters were next incorporated into an exact solution of the full kinetic network. Only then were the remaining two parameters—the rate constants for basic hydrolysis and for thermal rearrangement of the starting bicyclic ester (**2**)—fitted by a nonlinear least-squares program to the chromatographic area ratios observed during hydrolysis of **2**.

Acknowledgment. Financial support was provided by U.S. Public Health Service Grant No. 10495 from the National Cancer Institute.

Supplementary Material Available: ^{1}H NMR structural analysis of **4** and **5** (2 pages). Ordering information is given on any current masthead page.

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(1) M. J. Goldstein and R. Hoffmann, *J. Am. Chem. Soc.*, **93**, 6193, (1971).
(2) Syn and anti define the epimeric relationship between the functional group and the *closer* of two olefinic bridges or, as in **4**, the *longer* of two olefinic bridges. Cf. T. S. Cantrell and H. Shechter, *J. Am. Chem. Soc.*, **89**, 5868 (1967), footnote 11. Results obtained from the *anti-p*-nitrobenzoate will be reported separately.
(3) (a) Epimeric 9-chlorobicyclo[6.1.0]nonatrienes: J. C. Barborak, T.-M. Su, P. v. R. Schleyer, G. Boche, and G. Schneider, *J. Am. Chem. Soc.*, **93**, 279 (1971). (b) Epimeric 9-bicyclo[4.2.1]nonatriene derivatives: W. Kirmse and G. Voigt, *ibid.*, **96**, 7598 (1974); A. F. Diaz, J. Fulcher, M. Sakai, and S. Winstein, *ibid.*, **96**, 1264 (1974); A. Diaz and J. Fulcher, *ibid.*, **98**, 798 (1976); Y. Nomura, Y. Takeuchi, and S. Tomoda, *Tetrahedron Lett.*, 911 (1978).
(4) J. T. Groves and B. S. Packard, *J. Am. Chem. Soc.*, **94**, 3252 (1972); J. T. Groves and K. W. Ma, *Tetrahedron Lett.*, 5225 (1973); K. W. Ma and J. T. Groves, *ibid.*, 1141 (1975); J. T. Groves and C. A. Bernhardt, *J. Org. Chem.*, **40**, 2806 (1975); J. T. Groves and K. W. Ma, *J. Am. Chem. Soc.*, **97**, 4434 (1975); J. T. Groves and K. W. Ma., *Ibid.*, **99**, 4076 (1977).
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(6) ^{1}H NMR and chromatographic analysis of the crude product (105% isolated yield) revealed significantly less than 5% contamination by **6**, by its epimer, or by the epimers of **4** and **5**. Recovered internal chromatographic standard (borneol) was equally uncontaminated.
(7) (a) Elemental analyses of reactants and products agreed with expectation to ±0.3%. (b) *anti*-Tetracyclo[5.4.0.0^{2,11}.0^{4,10}]undeca-5,8-dien-3-ol,[5d] stereochemistry required by Pr(fod)$_3$-shifting slopes and by $^3J_{3,4}$ < 0.5 Hz. (c) *anti*-Pentacyclo[5.4.0.0^{2,11}.0^{4,10}]undec-8-en-6-ol, mp 166 °C, structure and stereochemistry assigned by analysis of the completely resolved Pr(fod)$_3$-shifted spectrum.
(8) M. J. Goldstein and D. P. Warren, *J. Am. Chem. Soc.*, following paper in this issue.
(9) (a) Few kinetic studies of solvolytic rearrangements have ever measured the concentrations of organic reactants and products.[9b] We did so using a modified Waters ALC-100 instrument, eluting with hexane–acetone (200:1 for esters, 95:5 for alcohols) through a 12 × 0.25 in. μ-Porasil column. Refractive index detector response was calibrated with authentic mixtures. (b) R. S. Bly, R. K. Bly, A. O. Bedenbauch, and O. R. Vail, *J. Am. Chem. Soc.*, **89**, 880 (1967); R. S. Bly, R. K. Bly, J. B. Hamilton, and S. P. Jindal, *Ibid.*, **99**, 204 (1977); R. S. Bly, R. K. Bly, J. B. Hamilton, J. N. C. Hsu, and P. K. Lillis, *ibid.*, **99**, 216 (1977).
(10) (a) Analogy[10b,c] would suggest that the second of these steps is the more rate limiting. (b) S. Masamune, R. T. Seidner, H. Zenda, M. Wiesel, N. Nakatsuka, and G. Bigam, *J. Am. Chem. Soc.*, **90**, 5286 (1968); R. T. Seidner, N. Nakatsuka, and S. Masamune, *Can. J. Chem.*, **48**, 187 (1970). (c) M. J. Goldstein and S. A. Kline, *Tetrahedron Lett.*, 1089 (1973).
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(15) (a) Tertiary aliphatic amines (p$K_a \approx$ 11) have occasionally been used to buffer nitrobenzoate hydrolyses, perhaps for similar reasons.[12,15b] (b) K. B. Wiberg and T. Nakahira, *J. Am. Chem. Soc.*, **93**, 5193 (1971); M. Geisel, C. A. Grob, W. Santl, and W. Tschudi, *Helv. Chim. Acta*, **56**, 1055 (1973).
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(19) A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, **78**, 2770 (1956).
(20) Presented in part at the 26th International Conference of Pure and Applied Chemistry, Tokyo, Sept 4–10, 1977.
(21) Taken in part from the Ph.D. Thesis of D. P. Warren, Cornell University, 1978.

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Quantitative Analysis of Two $C_{11}H_{11}$ Homoallyl Cationic Rearrangements

Sir:

A long anticipated experimental characteristic of the "nonclassical homoallyl" hypothesis[1] has only recently been reported. The identical mixture of solvolytic products was obtained from stereochemically appropriate allylcarbinyl and cyclopropylcarbinyl precursors, apparently via a common cation.[2] Previous discrepancies from product-mixture identity were admittedly minor,[3] and the experiments that provided them were less sophisticated in technology and design. Such discrepancies are easily attributed to minor deviations from ideal experimental prerequisites (kinetic control under precisely identical conditions, absence of competing mechanisms, etc.). The more recent report[2] strengthens this view and, with it, the reliability of the original hypothesis.

We now must report the observation of a *non*identical product composition, obtained in comparably well-controlled experiments. We analyze the necessary mechanistic consequences of this observation and test them by isotopic labeling. Finally, we indicate some of the more general conclusions that can and cannot be drawn from a realistic kinetic analysis of such data.

The preceding communication[4a] introduced the anti-tetracyclic ester (**4E**, Figure 1). It was the thermal rearrangement product of its syn-bicyclic isomer as well as the ionic precursor of tetracyclic and pentacyclic alcohol products (**4A, 5A**). Here we begin with separate hydrolytic studies of anti-tetracyclic and anti-pentacyclic esters (**4E, 5E**). Under identical conditions, each ester provided the other as a transient intermediate whose concentration rose, and then fell, during hydrolysis. Esters other than these could not be detected, nor could any alcohol other than **4A** and **5A**.[4b,5] The data consisted of 48 chromatographic area ratios: three different ratios[6] for each of 16 aliquot samples, eight samples from each of the two reactants.

Six of the seven independent mechanistic parameters of Figure 1 were fitted to these data by a nonlinear least-squares program (R factor = 0.042).[7] The seven include the two S_N1 rate constants that govern formation of each cation (**4C, 5C**)

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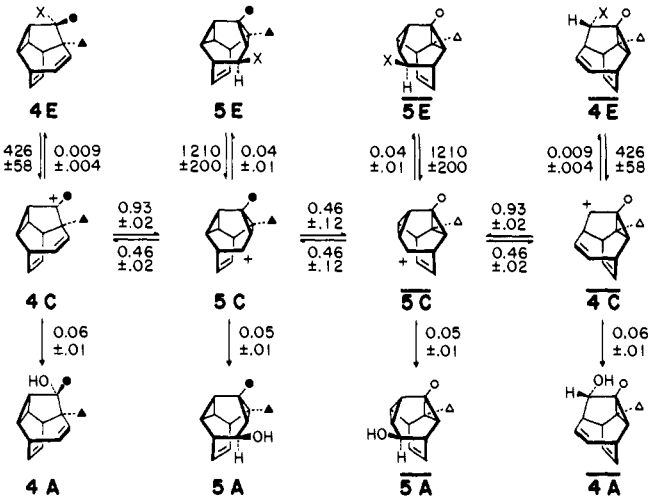
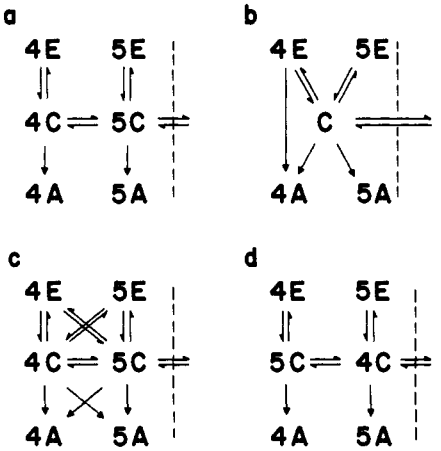


Figure 1. A cationic mechanism. The kinetic parameters less than unity are partitioning factors; those greater than unity are unimolecular rate constants in units of 10^{-6} s^{-1} (X = *p*-nitrobenzoate; ●, ▲, ○, △ = D; 1,8-bis(dimethylamino)naphthalene-buffered 70% aqueous acetone at 80 °C).

Scheme I



from its precursor as well as the five partitioning factors ($kji/\Sigma kji$) that describe subsequent transformations of the cations. The missing parameter, the fraction of **5C** that isomerizes to **5C̄** (and vice versa) was then fitted to the deuterium distribution in **4E**, **4A**, and **5A**, all of which were isolated from the hydrolysis of a single sample of α-deuterated (●) **4E** (*R* factor = 0.064).

Tables I and II reveal the consistency of experimental facts with hypothesis (Figure 1). The mechanism requires that the alcohol, isolated from pentacyclic ester (**5E**), be at least as rich in pentacyclic isomer (**5A**) as the alcohol isolated from tetracyclic ester (**4E**). The hydrolytic path—**4E** → **4C** → **5C** → **5A**—requires an additional cationic intermediate, hence an additional risk of solvent capture. Also for this reason, hydrolysis of deuterium-labeled tetracyclic ester (**4E**) must lead to isotopic scrambling which is at least as great in isolated pentacyclic alcohol (**5A**) as in isolated tetracyclic alcohol (**4A**). Note too that the deuterium-label distribution is both independent of its location, α (●) or β (▲), and of its origin, the tetracyclic ester (**4E**) or its thermal bicyclic precursor.

The calculated values in Tables I and II are derived from the best-fit parameters of Figure 1. Those of Table I illustrate that the time independence of product distribution is only apparent and not mechanistically required. The parameter set of this particular system has merely compressed the range of each of the two different product distributions below the limits of analytical uncertainty. Contrasting reports of apparently

Table I. Isomeric Composition of Alcohol Products

precursor	5A/(5A + 4A) obsd	5A/(5A + 4A) calcd[a]
tetracyclic ester (**4E**)[b]	0.570[c] ± 0.008	0.567-0.579
pentacyclic ester (**5E**)[d]	0.619[c] ± 0.003	0.621-0.619
equilibrium	0.52[e] ± 0.01	

[a] See text. [b] Eight samples; 5-63% hydrolysis. [c] Mean and standard deviation. [d] Eight samples; 13-98% hydrolysis. [e] Estimated graphically, with a plausible estimate of uncertainty, from data obtained using lutidine buffering.

Table II. Deuterium Distribution in Alcohol Products

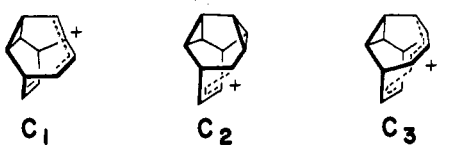
sample analyzed	*f*	Obsd[a] ○/(○ + ●)	Obsd[a] △/(△ + ▲)	Calcd[b]
tetracyclic alcohol (**4A**)	0.18[c]	0.36 ± 0.02	0.36 ± 0.03	
	0.28[c]		0.38 ± 0.01	
	0.36[d]	0.37 ± 0.03		0.37
pentacyclic alcohol (**5A**)	0.18[c]	0.42 ± 0.03	0.42 ± 0.02	
	0.28[c]		0.45 ± 0.03	
	0.36[d]	0.46 ± 0.03		0.45

[a] Mean and standard deviation of five $Pr(fod)_3$-shifted ^1H NMR scans. [b] See text. [c] Fractional extent of bicyclic ester hydrolysis. [d] Fractional extent of tetracyclic ester hydrolysis.

identical product distributions in other systems[2,3] can be understood in a similar way. There, the particular parameter set has compressed the difference between the two product distributions below the limits of analytical uncertainty. Different mechanisms are not required.

Next, there is an important distinction to be made between a sufficient hypothesis and a necessary one. Can the hypothesis of Figure 1 be somehow revised and yet fit the data equally well? Such revision cannot include direct equilibration of either esters (**4E** ⇌ **5E**) or alcohols (**4A** ⇌ **5A**); both processes were experimentally excluded.[4a]

Scheme I includes the hypothesis of Figure 1, abbreviated as a, and three of its revisions. Of these, b reduces the number of cationic intermediates from two to one.[5] The common cation (C) may be represented as either of the homoallylic cations, (C_1 or C_2), or as the homopentadienyl cation (C_3). To accommodate the discrepancy in product distribution, b must include the direct path **4E** → **4A**. To accommodate the discrepancy in label distribution, this path must conserve the original deuterium distribution of **4E**. Despite its fewer intermediates, b generates as many independent mechanistic parameters as a; these could be fitted equally well.



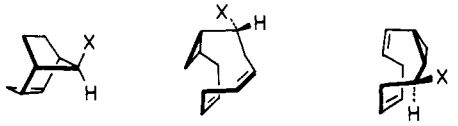
To choose between these hypotheses, we first identify the direct path, **4E** → **4A**, as hydrolysis by acyl-oxygen fission. Such a reaction would conserve both the epimeric purity and the deuterium-label distribution of **4E**. (Adequate precedent for its appearance in these solutions is already available.[4]) A necessary consequence is that hydrolysis of tetracyclic ester (**4E**) in $H_2{}^{18}O$ provides tetracyclic alcohol (**4A**) with less than the full complement of oxygen label. More precisely, the best-fit parameters of b require that the tetracyclic ester (**4A**) contain 84.6% of the maximum ^{18}O incorporation. Experimentally, **4A** incorporated 103 ± 3% of the maximum, a result that was indistinguishable from the ^{18}O incorporation of either **4A**, isolated from hydrolysis of **5E**, or **5A**, isolated from hy-

drolysis of either ester. Mechanism b must therefore be rejected in favor of a.

Might there not also be a direct path from tetracyclic cation (**4C**) to pentacyclic alcohol (**5A**)? One can at least imagine solvent attack to be concerted with bond shifting.[2c] Hypothesis c illustrates the ultimate logical extension of this idea. The additional parameters needed to define c, however, are not independent ones, assuming that **4C** and **5C** remain steady-state intermediates. An infinity of numerical values could then fit the data equally well. This criticism applies also to the many extensions of a that would increase the number of steady-state intermediates beyond two.[5,8]

Hypothesis d illustrates another generalization. This hypothesis is as well defined algebraically as a and fits the data equally well. Nevertheless, it must clearly be rejected on grounds of chemical simplicity. Kinetic labeling experiments can reveal, at best, only the number of necessary steady-state intermediates and the symmetry properties of each one. Finer details of structure cannot thus be obtained. The reader who wishes to do so may therefore replace the structural representations, **4C** and **5C**, either by any two of C_1, C_2, and C_3, or by two structurally distinct ion-pair representations of any one of them.[9] He must, however, choose only two. And both must be chiral.

The partitioning factors of Figure 1 deserve some comment, if only because comparable data are rare.[10] It is apparent that the two carbocations greatly prefer rearrangement to anything else. Solvent capture is only slightly less unfavorable than capture by the *p*-nitrobenzoate anion. Since the concentration of this anion ($<5 \times 10^{-2}$ M) is somewhat less than that of hydroxide ($\sim 10^{-2}$ M) and far less than that of water, it is clear that **4C** and **5C** represent the cationic parts of ion pairs, rather than free cations. The specialist may also wish to note that the two *p*-nitrobenzoate S_N1 rate constants of Figure 1 are significantly greater than those reported for 7-norbornadienyl[11] and **1**[12]—or for the more structurally analogous **2**[13] and **3**[13] (10^6k = 6.3, 43, 11, and 3.5, respectively).



1 **2** **3**

S_N1 reactivities, whether unusually high as in this communication or unusually low as in the preceding one, are still a puzzle. The mechanisms that reveal them need not be. The kinetic parameters, required by the necessary mechanism a, are both numerous and flexible. With appropriate adjustment, they can account not only for the quantitative behavior of this particular homoallylic system, but for all previously reported ones as well.

Acknowledgment. Financial support was provided by U.S. Public Health Service Grant No. 10495 from the National Cancer Institute. We are grateful also to C. A. Grob for helpful criticism.

Supplementary Material Available: Chromatographic, deuterium, and ^{18}O data analyses, relevant to both the preceding communication and to this one (20 pages). Ordering information is given on any current masthead page.

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(4) (a) M. J. Goldstein and D. P. Warren, *J. Am. Chem. Soc.*, preceding paper in this issue. (b) The criteria of purity are those that were cited in notes 6 and 7a; chromatographic conditions were described in note 9.

(5) Neglecting enantiomeric species whose isotopic labeling makes them diastereomeric.

(6) (i) (**4A** + **5A**)/(borneol standard), (ii) **4A**/(**4A** + **5A**), (iii) isomeric ester/total ester. Each such ratio, the mean of three–five analyses, was weighted inversely as its standard deviation.

(7) *R* factor $\equiv [\Sigma w_i^2(y_i^{obsd} - y_i^{calcd})^2/\Sigma(w_i y_i^{obsd})^2]^{1/2}$; y_i represents area ratios and w_i the corresponding weighting factors. W. C. Hamilton, "Statistics in Physical Science", Ronald Press, New York, 1964, p 157.

(8) (a) Most previous investigators in this area have felt little obligation to fit their hypotheses to their data.[8b] The resulting proliferation of hypothetical cationic intermediates seems to have been limited principally by the impact of unremitting criticism.[1e] (b) This tradition can be traced to the important classic paper which first recognized reversibly formed ion pairs (in addition to dissociated ions) as potential intermediates in cationic rearrangements.[8c] The associated kinetic analysis has since often been cited as a model. Paradoxically, this analysis entirely ignored carbocations of any kind as reactive intermediates. It also ignored the potentially reversible formation of those covalent species which it did consider. More realistic kinetic analyses of carbocationic rearrangements have since appeared,[8d] albeit much less often than those of carbanionic[8e] or thermal rearrangements.[8f] (c) W. G. Young, S. Winstein, and H. L. Goering. *J. Am. Chem. Soc.*, **73**, 1958 (1951). (d) R. S. Bly, R. K. Bly, J. B. Hamilton, and S. P. Jindal, *J. Am. Chem. Soc.*, 99, 204 (1977); R. S. Bly, R. K. Bly, J. B. Hamilton, and P. K. Lillis, *J. Am. Chem. Soc.*, **99**, 216 (1977). (e) L. Meurling and G. Bergson, *Chem. Scr.*, **6**, 104 (1974), and references there cited. (f) A. P. ter Borg, H. Kloosterziel, and N. Van Meurs, *Recl. Trav. Chim. Pays-Bas*, **82**, 717 (1963); M. J. Goldstein and H. A. Judson, *J. Am. Chem. Soc.*, **92**, 4119 (1970); M. J. Goldstein and M. S. Benzon, *ibid.*, **94**, 5119, 7147, 7149 (1972); M. J. Goldstein, M. S. Benzon, W. A. Haiby, and H. A. Judson in "Mechanisms of Hydrocarbon Reactions", F. Márta and D. Kalló, Ed., Akademiai Kiado, Budapest, 1975, p 779.

(9) C. J. Collins, *Chem. Soc. Rev.*, **4**, 251 (1975), has convincingly argued that an epimerically distinguishable pair of nonclassical cations can be replaced by two structurally distinguishable ion pairs whose cationic part is classical. They may equally well be replaced by two ion pairs whose cationic part is not.

(10) Only the fractional extent of return from ion pair to precursor has hitherto been evaluated. Cf. J. M. Harris, *Prog. Phys. Org. Chem.*, **11**, 89 (1974).

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(12) (a) Extrapolated from higher temperatures (E_a = 26.7 kcal/mol) and from 70% dioxane assuming m = 1,[12b] whence $k_{acetone}/k_{dioxane}$ = 1.31: J. S. Haywood-Farmer and R. E. Pincock, *J. Am. Chem. Soc.*, **91**, 3020 (1969). (b) A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, **78**, 2770 (1956).

(13) Extrapolated from lower temperatures (E_a = 25.0 kcal/mol) and from 80% acetone assuming m = 1,[12b] whence $k_{70\%}/k_{80\%}$ = 6.35; D. Whalen, M. Gašić, B. Johnson, H. Jones, and S. Winstein, *J. Am. Chem. Soc.*, **89**, 6384 (1967).

(14) Taken in part from the Ph.D. Thesis of D. P. Warren, Cornell University, 1978.

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Received June 22, 1978