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COMPUTER MODELLING OF MULTI-STEP CARBONIUM ION REARRANGEMENTS

APPLICATIONS TO METHYLCYCLOPENTYL AND *t*-AMYL

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Abstract—A general Monte-Carlo method computer program is described which simulates carbonium ion rearrangements via 1,2-hydride shifts and protonated-cyclopropanes. Its application in examining possible overall rearrangement mechanisms in *t*-amyl cation is discussed. Results from an earlier version of the program for the case of methylcyclopentyl cation are also presented.

INTRODUCTION

Carbonium ion intermediates have long been invoked in explaining rearrangements in organic reactions. Techniques developed in the last 15 years[1-3] have made possible the preparation of stable solutions of a variety of carbonium ions,[3-6] enabling direct studies of rearrangements by means of proton and ^{13}C NMR spectroscopy.

A process which interchanges nuclei, if it occurs rapidly enough, causes the corresponding lines in the NMR spectrum to broaden. As the rate of interchange increases, broadening continues, eventually leading to coalescence of the lines; further increases in the rate then cause these coalesced lines to sharpen. The general theory derived by Anderson and Kubo[7] provides a quantitative relation between the rate constant and detailed mechanism of the interchange process, and the resulting NMR lineshape. A previously described computer program[8] which applies this theory can be used to calculate lineshape as a function of rate constant for any given mechanism; the results may then be compared with the experimental lineshape to obtain a value for the rate constant. From spectra taken at a series of temperatures, the relation of rate constant to temperature may be determined, and thus the parameters log A and E_a of the Arrhenius equation.

The interchange mechanism is represented in the Anderson–Kubo theory by a matrix of transition probabilities. For simple mechanisms it is usually possible to write down the matrix by inspection; for example, the mechanism in Fig. 1 which interchanges α- and β-protons in methylcyclopentyl cation leads to the transition probability matrix:

$$|1/2 \backslash 1/2|.$$

The matrix is by no means intuitive, though, for more complex mechanisms.

This became clear when we discovered that the rate of *carbon* scrambling in methylcyclopentyl (obtained from the temperature-dependent ^{13}C spectrum, Table 1) was inconsistent with the simple mechanism of Fig. 1 and the previously determined rate of proton scrambling.[6] A mechanism involving a random series of methide and hydride shifts was then postulated (Fig. 2); this mechanism is complicated by the presence of two competing processes (methide and hydride shifts) and by there being no fixed number of steps which lead back to a tertiary ion.

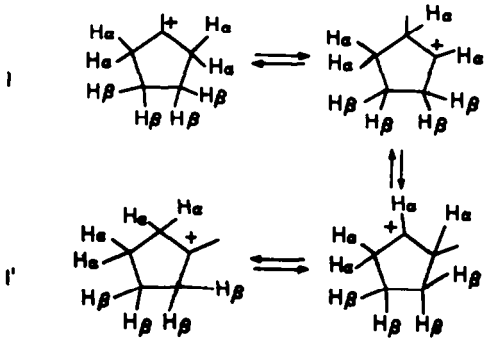

Fig. 1.

Table 1.

T (°C)	Half-height width α-methylene (Hz)	Half-height width methyl (Hz)	k (sec^{-1})
44.0	20.4	12.3	64.0
48.0	19.7	15.0	62.0
51.8	28.2	16.9	88.5
56.5	33.5	14.3	105.2
60.0	52.8	11.4	166.0

The problem of establishing the transition probability matrix for this mechanism was solved through the use of a Monte-Carlo method computer program—a program which simulates a random process an large number of times in order to obtain an average overall probability. In this case, the program performed "random walks" starting from the tertiary ion 1, and ending whenever another tertiary ion was reached. Included in the program was a map of all possible intermediates (secondary ions) and rearranged products (tertiary ions), and the pathways

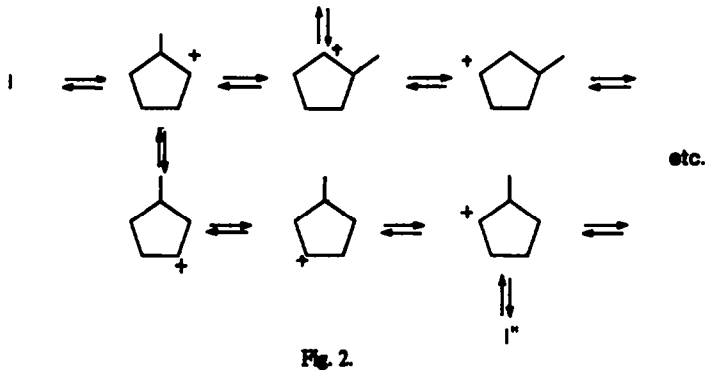

Fig. 2.

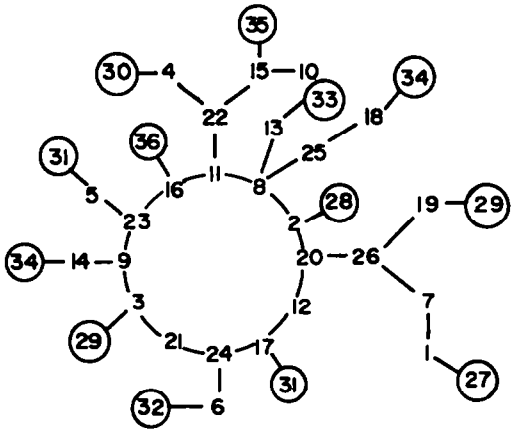

Fig. 3. "Random walk" map for rearrangements in methylcyclopentyl via 1,2-hydride shifts. Each walk begins at 32 and ends when a tertiary ion (indicated by the circled numbers) is reached. 1,2-methide shifts connect a second such map to this one at various points.

connecting them (Fig. 3). By recording *which* rearranged product was reached at the end of each random walk, the average α/β interchange for this mechanism could be determined. Adjusting the relative probability of methide to hydride shift assumed in the calculation made it possible to obtain a relative rate of carbon scrambling to proton scrambling which agreed with the experimental value. The ratio of methide to hydride shift rates for this case was found to be 1:17 at 20°, corresponding to a difference of ~1.5 kcal in activation energies.

General program

In attempting to extend the program to systems other than methylcyclopentyl, some serious drawbacks with this approach became apparent. The most serious was the need for the programmer to work out the entire rearrangement scheme, a task which quickly becomes unmanageable as the system becomes much larger than methylcyclopentyl or begins to involve more complex mechanisms (such as protonated-cyclopropane intermediates). An examination of Fig. 3 should confirm this statement. Another disadvantage inherent in this approach was the need to rewrite the program almost completely for every new system to be studied.

The program described here overcomes these limitations through the use of connection matrices to specify chemical structure, and a set of completely general rules for rearrangement steps which act on these matrices.

Method. The connection matrix is one of a number of computer representations of chemical structures which may be made both unique and unambiguous.[12,13] For the carbon skeleton, the connection matrix is a square of dimensions equal to the number of carbons. An element *m,n* of the matrix has the value *one* if there is a bond connecting carbons *m* and *n*, *zero* if there is not. Hydrogen substituents are represented in a compressed connection matrix of three columns and as many rows as there are carbons; here the elements of each row *m* are the *identifying numbers* of the hydrogens which are attached to carbon *m*. A number of carbon-skeleton connection matrices representing different chemical structures may be stored in memory in anticipation of the possible rearrangement products. One of these matrices is in addition designated to be the *starting matrix* which begins each random walk. The program then proceeds as follows:

(1) *Place entered matrices in canonical form.* The permutation of any two rows and the corresponding two columns of a connection matrix results in a rearranged matrix, differing in appearance, but representing the same *chemical* structure; what in effect has been done is to change the *numbering* of the C atoms. For a structure of *n* carbons there are thus *n*! possible connection matrices, corresponding to the *n*! different ways in which the carbons may be numbered. In order to identify the chemical structure of the rearrangement product and to identify any proton or carbon interchanges which have occurred, it is necessary to compare the final matrix with those originally entered; this is only possible if a unique *canonical form* for connection matrices can be defined. As follows from the above discussion, this is equivalent to establishing rules for uniquely numbering the carbon atoms of any chemical structure. The totally arbitrary and computer-oriented definition used here is as follows: A connection matrix is in canonical form if and only if (1) the number of C atoms follows the order

(i) charge-carrying carbon
(ii) primary carbons
(iii) secondary carbons
(iv) tertiary carbons
(v) quaternary carbons

and (2) within the above groups, the order of numbering results in a minimum value for the number formed by linearizing the half of the matrix to the right of the diagonal. An example appears in Fig. 4.

(2) *Perform rearrangement.* The general carbonium ion site

$$\overset{+}{C}_1—C_2—C_3$$

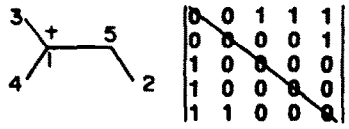

Fig. 4. Canonical-form numbering of carbon atoms in *t*-amyl, the corresponding carbon connection matrix, and the number formed by linearizing its right half.

can undergo two rearrangements: (1) a hydride shift from C_2 to C_1, and (2) the formation of a C_3–C_1 bond resulting in a protonated-cyclopropane structure.[9,10] The program first locates the C_2 carbons by checking the connection matrix for all carbons attached to C_1. All C_3 carbons and hydrogens on C_2 carbons are similarly located and placed in a list of possible rearrangements. A random selection from the list is made, using probabilities weighted according to the sort of rearrangement involved in each case, and the connection matrix altered to reflect the rearrangement.

Protonated-cyclopropane formation may be followed by any number of corner-to-corner migrations, the process terminating when a ring opening occurs. Selection among possible migrations and ring openings is carried out in a manner similar to that just described.

(3) *Check for tertiary ion.* If the rearrangement product is not a tertiary ion, step 2 is repeated. If it is tertiary, the random walk is over, and changes which have occurred may be identified and recorded as follows.

(4) *Place rearranged matrix in canonical form.* The final matrix is placed in canonical form and compared with the originally entered canonical-form matrices to identify its chemical structure.

(5) *Record carbon and hydrogen interchanges.* The position (i.e. carbon number) of each carbon and attached hydrogen in a canonical-form matrix is significant of its chemical position in the corresponding molecule. By keeping track throughout steps 2, 3 and 4 of the numbers assigned to the carbons in the canonical-form *starting matrix*, and by comparing these with the numbering in the canonical-form *final matrix*, it is thus possible to determine interchanges which have taken place. A frequency matrix, one for each chemical struc-

Table 2. Number of random walks: 250000
P-CP/HYD:[a] 0.120; H_+/OPEN:[b] 0.001; C_+/OPEN:[c] 0.000

$(H(3)_2C(4))_2\overset{+}{C}(1)C(2)H(1)_2C(3)H(2)_3$

	C(1)	C(2)	C(3)	C(4)
C(1)	0.91003	0.08972	0.00007	0.00018
C(2)	0.08971	0.90964	0.00056	0.00009
C(3)	0.00008	0.00056	0.90486	0.09449
C(4)	0.00009	0.00004	0.04725	0.95262
	H(1)	H(2)	H(3)	
H(1)	0.99905	0.00056	0.00039	
H(2)	0.00036	0.90501	0.09463	
H(3)	0.00014	0.04731	0.95255	

[a]Specified probability of protonated-cyclopropane formation relative to a 1,2hydride shift.
[b]Specified probability of an H_+ corner-to-corner migration relative to opening of the protonated-cyclopropane.
[c]Specified relative probability of a CH_3+ corner-to-corner migration.

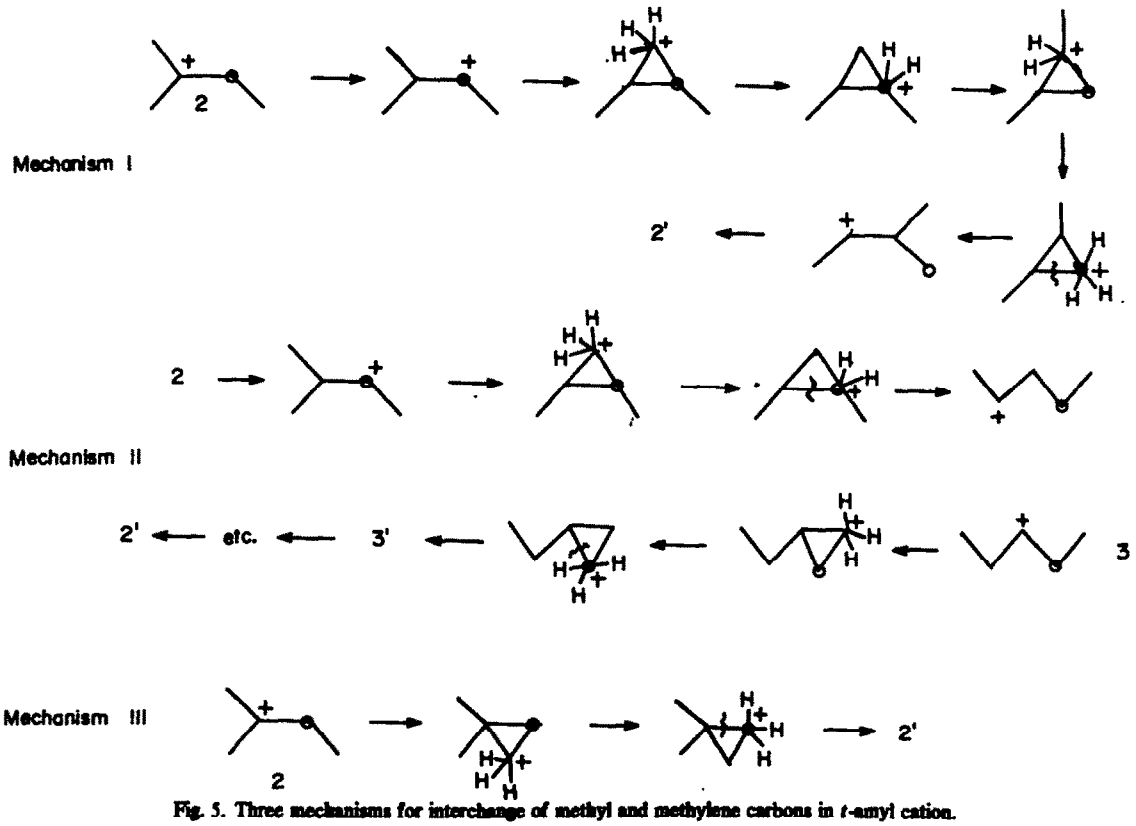

Fig. 5. Three mechanisms for interchange of methyl and methylene carbons in *t*-amyl cation.

ture, is used to record the number of times each carbon and hydrogen of the starting matrix (rows) ended up in each chemical position of the rearrangement product (columns).

Applications

t-Amyl cation. *t*-Amyl cation is of interest as a simple system in which CH_3^+ corner-to-corner migration could occur in the protonated-cyclopropane intermediate. As shown in mechanism I (Fig. 5), this process results in the scrambling of methylene carbons with methyl carbons. The results of the computer run which appears in Table 2, however, imply another mechanism for methyl/methylene carbon scrambling which does not involve CH_3+ migration (mechanism II); the higher probability of C_2/C_3 scrambling over the other methyl/methylene scramblings implies in addition mechanism III.

Adjustment of the relative probabilities of H^+ and CH_3^+ corner-to-corner migrations assumed in the calculation in order to fit the results to experimental data should provide an indication of the degree to which these steps occur in the overall rearrangement process, and the activation energies of these steps.

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