Reaction Sequences Involving the Mutual Interconversion of All 10 Tertiary Dimethyl-2-norbornyl Cations. A Comparison of Predicted Products and Rates with Experiment

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All 10 tertiary dimethyl-2-norbornyl cations have been prepared. There are sequences of individual steps which will in theory interconvert any given two of these cations, a total of 45 permutations. All of the possible sequences (within a defined limit on the allowable total number of steps) for performing these interconversions were determined using a digital computer. Each step used in the computer generated sequence had previously been assigned a trial activation free energy value and a comparison is made in this paper between the actual experimental rearrangement results (in terms of both the kinetics of disappearance for the cation and what product is in fact formed) and the predicted results.

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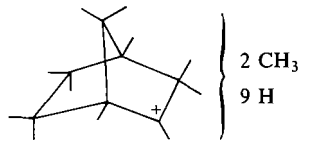
On a préparé les dix cations tertiaires diméthylnorbornyl-2. Il y a des séquences d'étapes individuelles qui transformeront en théorie n'importe quelle paire de ces cations et il y a en tout 45 permutations possibles. Toutes les séquences possibles, (à l'intérieur de limites définies pour un nombre total permissible d'étapes) pour effectuer ces transformations ont été déterminées en faisant appel à un ordinateur digital. Pour chaque étape utilisée dans la séquence générée par l'ordinateur, on avait auparavant assigné une valeur d'essai pour l'énergie d'activation et une comparaison est faite dans cet article entre les valeurs expérimentales trouvées pour ces réarrangements (en terme de cinétique de disparition de ces cations et en terme de quel produit est de fait formé) et les résultats qui sont prédits. [Traduit par le journal]

Introduction

In a previous paper (1), a trial set of activation free energy parameters were deduced for all of the low energy rearrangement processes which occur in 2-norbornyl cations, using data from the rearrangements experimentally observed in the parent 2-norbornyl cation, the 2-methyl-2-norbornyl cation, and in several trimethyl and higher methylated analogs. It is now the intention to test the predictive value of these parameters using the rearrangements involved in interconversions among the complete set of tertiary dimethyl-2-norbornyl cations.

Results

There exist 55 (isomeric) dimethyl-2-norbornyl cations, **I**, if one does not differentiate *R* and *S* enantiomers. Of this total, only 10 are tertiary, **II**, *i.e.* one methyl group always at C2.



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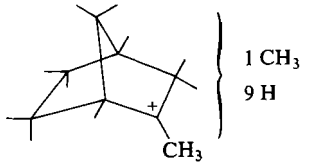


II

However, in constructing a diagram showing the rearrangements possible between any 2 of the 10 tertiary cations, the 45 secondary cation intermediates would have to be shown. Since this becomes extremely messy to depict, we have used an alternative approach, which is a modification

of the procedure described recently by Johnson and co-workers (2) and which simply consists of a computer print-out listing the combination of single steps which would bring about any given rearrangement.

Let us say one wishes to find the routes between two tertiary dimethyl-2-norbornyl cations **A** and **D** using a number of individual steps (which each result in certain permutations of the atoms). The first problem consists in delineating the various possible individual rearrangement steps; this was reported in a previous paper (1) and is historically based, of course, on the experimental results of many previous workers. The second problem consists in deciding how many steps one will allow since with 55 nodal points, it is perhaps possible that one could find a loop-free route of 50 steps or more connecting **A** and **D**. Johnson and co-workers (2) have used a weighting factor for each individual step in deciding sequence length but since we have introduced an activation energy for each step, we have simply made an arbitrary cut-off, based largely on the cost of computing time, on the number of steps considered. Any routes which regenerate starting material or in fact any other loops, are redundant and were not printed by the computer. Furthermore, certain rearrangement categories have been excluded in the computerized treatment for reasons discussed previously (1). These include process *4* steps where the two substituents on C1 and C2 are the same and also most of the *endo*-3,2-substituent shifts (process *5*). Besides printing out all the possible sequences, the computer prints out the highest activation energy for each sequence using the set of activation free energy parameters previously deduced (1).

In practice, there turn out to be thousands of predicted routes interconnecting any given tertiary dimethyl-2-norbornyl cation with any other one. When one comes to consider which route may be the one experimentally followed, one finds that one has done the absolute minimum amount of labelling, *i.e.* no isotopic substitution or enantiomeric labelling. The computerized treatment is ideally suited for telling one how many specific labels would be required to yield an unique answer regarding any particular interconversion. As an example, simply using as starting ion a single enantiomer of known absolute configuration and determining the absolute configuration of the product ion (assuming no symmetrical intermediates) would rule out approximately one-half of the computer predicted routes since it can be shown that an even number of steps keeps the same absolute configuration for the cation and an odd number reverses it (2). In solvolysis work, this sort of approach has been elegantly used by Berson *et al.* (3) in studying the much faster and much shorter overall routes involving secondary cation (intermediates) rearrangements.

Our intention is not necessarily to unequivocally decide which particular route experimentally interconnects any given pair of cations (clearly not possible nor could the required work be justified). By assigning activation energies to each step, one will find that the barrier for some routes is much smaller than for others. Therefore, one wishes to see whether the computed route showing the lowest activation energy *correlates* with the *experimentally determined* activation energy for the process.

The overall kinetic equation for multistep reactions is only simplified where one barrier is much larger than any other (a rate-determining step). Where several highest barriers of equal height are predicted, one can readily take this into account in comparing theory and experiment. In the worst cases, where nearly equal barriers might exist, it may be impossible to obtain a meaningful comparison. Such problems will be discussed in each specific case but turn out in practice not to be as bad as one might anticipate.

The activation energy parameters used in the computer print-out are listed in Table 1. Two sets of computations were carried out: (*a*) calculations using only processes *1*, *2*, and *3* (13 steps maximum) and (*b*) calculations using processes *1*, *2*, *3*, and *4* (10 steps maximum). The process 5TT can only be degenerate (corresponding to a loop) in a dimethyl-2-norbornyl cation and therefore never appears in a sequence. The two sets were computed because it is possible to bring about any overall transformation using only the first three processes (2). From this computation, one can see what the shortest sequences excluding a *4* step will be. For each set, one needs a total of 45 separate calculations to obtain all possible interconversions. Fortunately, all of these interconversions are not experimentally measurable since this might have resulted in carbocation solutions containing in the end up to ten different cations. The success of this study,

TABLE 1. Activation energies assigned to the major rearrangement categories

Major rearrangement	Abbreviated symbol used for this operator	Subdivisions considered	Assigned activation energy parameter $\Delta G^{\ddagger}$ (kcal/mol)
Wagner–Meerwein shift	1	1TT	<4
		1TS	<9.5
		1ST	<4 (<9.5)[a]
		1SS	<4 (<9.5)
exo-3,2-Substituent shift	2	2HTT	7.2
		2HTS	15.2
		2HST	9.7 (15.2)
		2HSS	11.4 (16.9)
		2MTT	8.9
		2MTS	13.1
		2MST	7.6 (13.1)
		2MSS	≥7.6 (≥13.1)
endo-6,2-Hydride shift	3	3TT	11.3
		3TS	11.3
		3ST	5.8 (11.3)
		3SS	5.8 (11.3)
Double Wagner–Meerwein shift	4	4TT	18.0
		4SS	12.5 (18.0)
endo-3,2-Substituent shift	5	5HTT	≥14.0

[a]The bracketed values refer to the barrier starting from a tertiary cation energy base and these were used in the computer treatment.

in this regard, was by no means assured at the start and we were extremely lucky in that there were never more than three different observable ions present at any one time in a particular reaction sequence (at least within the limits of experimental detection).

The Thermodynamic Stability of Tertiary Dimethyl-2-norbornyl Cations

The reason that one does not eventually see all 10 cations after all possible interconversions have occurred is that two in particular represent distinct energy minima. The end product of starting with any of the other nine tertiary dimethyl-2-norbornyl cations is the eventual formation of the 1,2-dimethyl isomer. The 2,4-dimethyl isomer however represents a distinct secondary minimum. It appears to be much more stable than any of the other eight remaining cations and indeed at higher temperatures can just be detected in equilibrium with the 1,2-dimethyl isomer, although the latter is considerably more stable. Furthermore, the barrier connecting the 1,2- and 2,4-dimethyl cations is predicted, and is found experimentally (see following), to be higher than any other observed process, *i.e.* the 2,4-dimethyl isomer is in part a minimum because of its thermodynamic stability relative to the eight other cations and partly because it is walled off from the actual true minimum by the highest barrier. The fortuitous end result of this is that if any of the other eight cations can rearrange to the 1,2- or 2,4-dimethyl isomers more easily than to any other in this group, the rearrangement sequence is essentially quenched at that stage (the billiard ball drops). Even so, it is remarkable that the observed sequences never involve more than three cations.

The Overall Rearrangement Sequences

The observed behavior of all 10 tertiary dimethyl-2-norbornyl cations is shown in Fig. 1, where only those interconversions with connecting lines shown could be experimentally measured (or verified). There are two ways in which the trial parameters used in the computed sequences can be checked against experiment: (*a*) One can directly compare the rates of the experimentally observed processes against the computed rate for this process and (*b*) one can verify in a qualitative sense whether the observed product is in fact the one expected, *i.e.* connected by the lowest barrier to the reactant ion. For example, if one experimentally observes the transformation of the 2-*endo*-6-dimethyl isomer into the 1,2-dimethyl isomer, one can compare this rate with

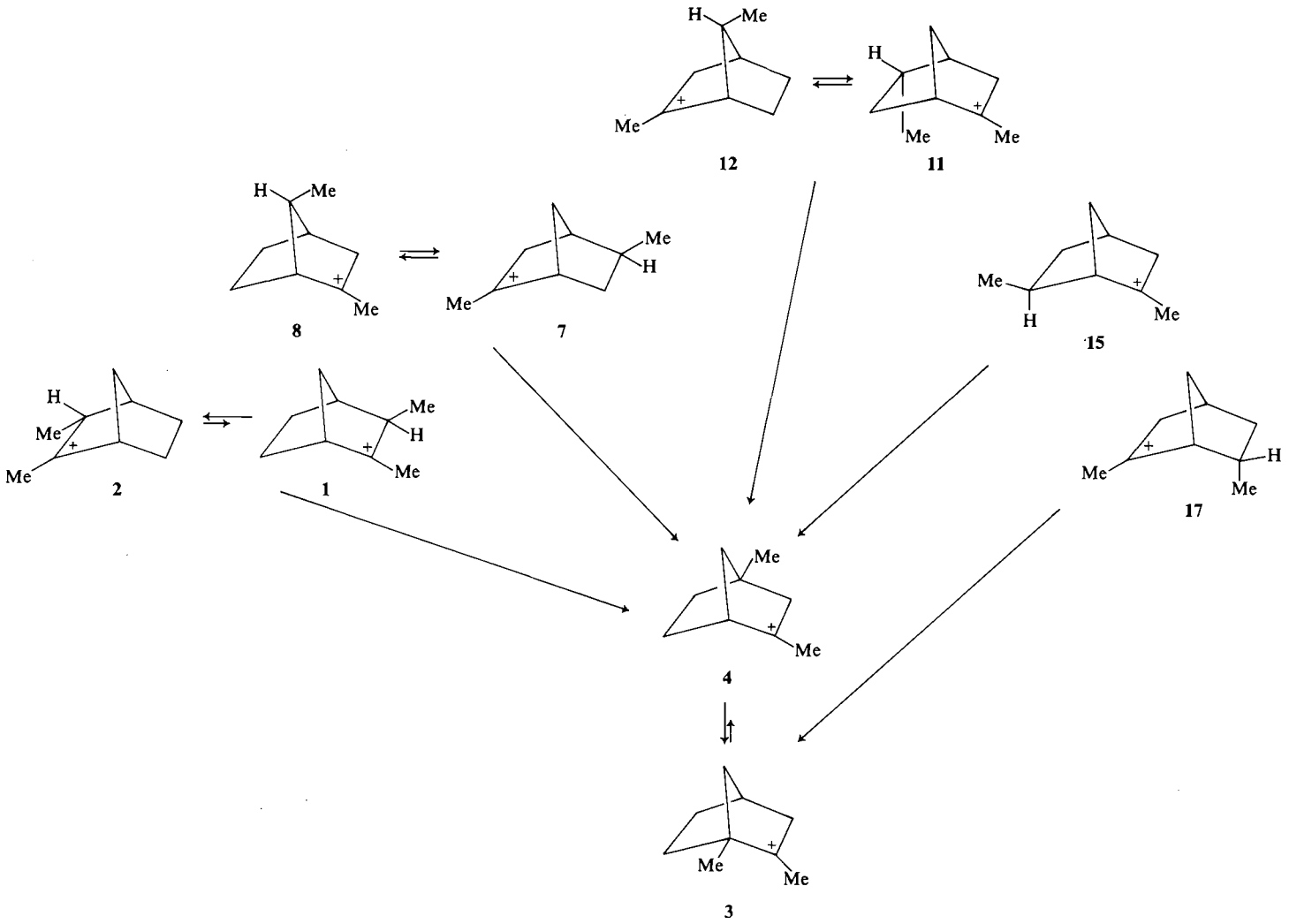
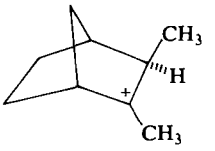


FIG. 1. The 10 possible tertiary dimethyl-2-norbornyl cations. Arrows indicate those conversions or interconversions which could be measured or at least verified.

the lowest computed rate for this process. Then one can check the computer outputs to see whether there are predicted to be any still lower energy pathways leading from the 2-*endo*-6-dimethyl isomer to any of the other eight.

2-exo-3-Dimethyl-2-norbornyl Cation 1 and 2-endo-3-Dimethyl-2-norbornyl Cation 2

The preparation of these cations has been reported in a previous publication (4). One predicts the 2-*exo*-3-dimethyl **1** and 2-*endo*-3-dimethyl isomer **2** to be interconnected by a three-step sequence 1TS,3SS,1ST with a predicted barrier of 11.3 kcal/mol. The experimentally



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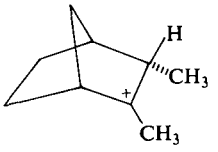

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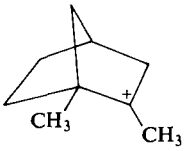
observed value, obtained both by n.m.r. line-broadening studies and probably by direct observation, was $\Delta G^{\ddagger} = 11.9$ kcal/mol (for **2** → **1**). The 2-*endo*-3-dimethyl cation **2** undergoes a degenerate *exo*-3,2-hydride shift (2HTT) for which $\Delta G^{\ddagger} = 6.6$ kcal/mol at -117 °C, in good agreement with the trial value for this parameter. The equilibrium constant for **2**/**1** was *ca.* 35 at -44 °C.

What else may be formed from either of these ions? Since they are interconverted by the low energy barrier of only 11.9 kcal/mol, both can be treated together, *i.e.* if another path of say $\Delta G^{\ddagger} = 15$ kcal/mol is somehow predicted for only one of the two, the other will have the same route open but the total sequence will be preceded by the three-step sequence 1TS,3SS,1ST. Unless excluded because of sequence length, this route will show up on the computer output anyhow. Equilibrium energy differences can be added to the kinetic $\Delta G^{\ddagger}$ value. It is obviously impractical to reproduce here the large number of routes interconnecting the cations **1** and **2** with all the others. It is even impractical to reproduce, in most cases, all the "lowest energy" routes. With 3 processes and 13 steps, the highest activation energy barrier mostly involves the 2HSS step (16.9 kcal/mol) or occasionally the 2HTS (or 2HST) step (15.2 kcal/mol). With the addition of process *4*, the only different routes will automatically involve the 18.0 kcal/mol barrier assigned to this. Simply for illustrative purposes, we show just one example of the fact that any one tertiary dimethyl-2-norbornyl cation, in this case **2**, can be rearranged into any one of the other nine. This is depicted in Table 2. Using only the first three processes, the shortest sequence is arbitrarily shown. If there is a still shorter sequence using process *4*, this is also shown. The highest barriers are listed together with the number of times they occur. An overall kinetic equation is very complex if two or more steps are competitive in rate. However, the higher barriers, *i.e.*, 18.0, 16.9, and 15.2 kcal/mol, are reasonably spread out and multiple steps with the same rate simply increase $\Delta G^{\ddagger}$ by the factor $RT \ln 2^{n-1}$, where n = number of like barriers. At the temperatures involved here, this will involve multiples of *ca.* 0.3 kcal/mol.

The sequences listed in Table 2 are illustrative only, since the shortest path need not involve the lowest barrier(s). However, an overall perusal of the computer output shows that one cannot do any better than shown in Table 2 except for the 2-*anti*-7-, 2-*exo*-6-, and 2,4-dimethyl isomers, where one can find single 16.9 barrier routes. If one looks at routes from the 2-*exo*-3-dimethyl isomer **1**, one finds, as expected, that the number and kind of high barriers is the same.

The actual "predicted product" results in the case of **1** and **2** are only marginally interpretable. The experimental result is the formation of the 1,2-dimethyl-2-norbornyl cation **3** with a rate constant, $k = 3 \times 10^{-4}$ s^{-1} at -39 °C, $\Delta G^{\ddagger} = 17.4$ kcal/mol. This is marginally higher than the predicted barrier for **2** → **3** of 16.9 kcal/mol.



3

Of the routes with this barrier, we prefer the shortest route shown in Table 2. That one should have formed **3** is not so obvious since the predicted barrier to any of the other cations also need involve no more than a single 2HSS step (16.9 kcal/mol). However, the 2-*endo*-6-dimethyl sequences all have **3** formed in the sequence and this route would be excluded. It may be significant in the other cases that all transformations involving a single 2HSS step also require the doubtful 2MSS step *except* for the transformation to **3**. Although the 2MSS barrier (from a tertiary base) is assigned a minimum 13.1 kcal/mol value, one can rationalize an upper

TABLE 2. Summary of the shortest sequences for **2** giving any of the other nine isomeric cations

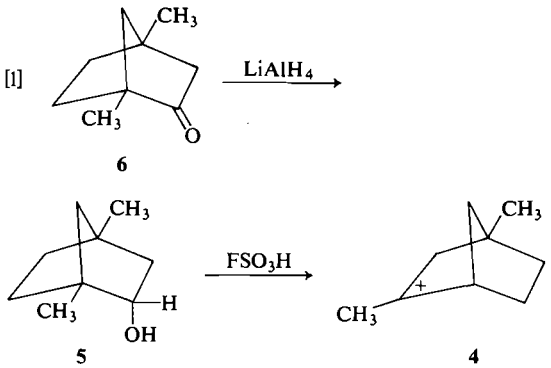
Product ion	Reaction sequences involving processes *1*, *2*, and *3*	Shorter alternative sequences involving process *4*	$\Delta G^{\ddagger}$ barrier (kcal/mol)
2-*exo*-3-Dimethyl **1**	1TS,3SS,1ST	—	11.3
2,4-Dimethyl **4**	1TS,3SS,2HSS,1SS,2MSS,3SS,2HSS,3ST	1TS,3SS,4SS,2HST	16.9(twice)
2-*exo*-5-Dimethyl **7**	1TS,2HSS,3SS,1SS,2MSS,3SS,1ST,3TS,2HST[a]	1TS,4SS,3SS,1ST[b]	16.9
2-*endo*-5-Dimethyl **11**	1TS,2HSS,3SS,1SS,2MSS,3SS,1ST	1TS,3SS,4SS,3SS,1ST[c]	16.9
2-*exo*-6-Dimethyl **15**	1TS,2HSS,1SS,3SS,2HSS,1ST	—	16.9(twice)
2-*endo*-6-Dimethyl **17**	1TS,2HSS,1SS,2HST,3TS,1ST	—	16.9
2-*anti*-7-Dimethyl **12**	1TS,3SS,2HSS,1SS,2MSS,3SS,2HSS,3ST,2HTS,1ST	4TT	16.9(twice)
2-*syn*-7-Dimethyl **8**	1TS,3SS,2HSS,1SS,2MSS,1ST	1TS,3SS,4SS,1ST	16.9
1,2-Dimethyl **3**	1TS,2HSS,1SS,2HST	—	16.9

[a]The symbol ⟲ implies that the operations can be carried out in either order (commute).
[b]The symbol ⟲R⟳ implies that the operations can be carried out in either order but that a secondary–tertiary designation has to be changed.

value of perhaps 20 kcal/mol. For example, the 2MSS barrier is 11.4 kcal/mol. The 2HTT and 2MTT barriers are 7.2 and 8.9, respectively. Therefore, the 2MSS barrier could be as high as $11.4 \times 8.9/7.2 = 14$ and from a tertiary base $14 + 5.5 = 19.5$ kcal/mol. The lower limit value (13.1) will rarely be even rate determining while the upper limit value would rule out any sequences containing the 2MSS step. We will therefore keep this in mind in the subsequent discussion.

2,4-Dimethyl-2-norbornyl Cation 4

The title cation was prepared from the alcohol **5**, which was in turn obtained by hydride reduction of the ketone **6** (eq. 1). On adding **5** to the



acid, one first obtains the protonated alcohol which solvolyzes at -45 °C to give **4** ($k = ca.$ 1.5×10^{-4} s^{-1}). The chemical shifts observed for **4** are reported in Table 3. Two degenerate rearrangement processes can be observed in **4**; the faster is a 1TS,3SS,1ST sequence and the slower is an unknown sequence which interconverts the two methyl groups. The 1TS,3SS,1ST sequence is quantitatively evaluated in another paper (5) and has also been briefly communicated previously (6).

Since the ion **4** is thermodynamically more stable than all others except the 1,2-dimethyl isomer **3**, one can only observe the transformation **4** → **3**. This process is experimentally observed, $k = 1.2 \pm 0.2 \times 10^{-4}$ s^{-1} at -19 °C, $\Delta G^{\ddagger} = 18.9$ kcal/mol. A measurable equilibrium exists at 25 °C between **4** and **3**, $K = \mathbf{3}/\mathbf{4} = 13 \pm 3$, $\Delta G = 1.5 \pm 0.2$ kcal/mol. The lowest calculated barrier for **4** → **3** is $16.9 + 0.3 = 17.2$ kcal/mol (two 2HSS steps) which occurs in numerous routes. However, all are long and the shortest is 3TS,2HSS,3SS,2MSS,3SS,2HSS,3ST. If one avoids the questionable 2MSS step, the best is ten steps, one of two possibilities is

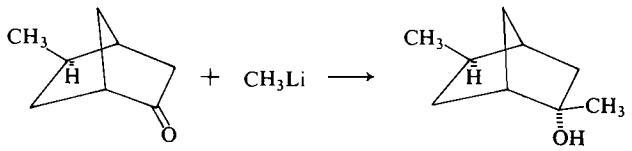
TABLE 3. Summary of observed and calculated activation energy ($\Delta G^{\ddagger}$) barriers for all of the measurable rearrangements

Rearrangement	Observed barrier (kcal/mol)	Calculated barrier (kcal/mol)
2 → **1**	11.9	11.3
2 → **3**	17.4	16.9
4 → **3**	18.9	16.9 + 0.3
7 ⇄ **8**	≤11.0	11.3
7,8 → **4**	12.1	15.2
11 ⇄ **12**	≤11.9	11.3
11,12 → **4**	13.9	15.2 + 0.3
15 → **4**	15.3	15.2 + 0.3 × 4
17 → **3**	≲11.2	11.3

3TS,2HSS,3SS,1ST,3TS,2HSS,1SS,2HST,1TS,3ST. Using a *4* process, there is a shorter path involving 2HTS,4SS,2HSS,1SS,2HST. Looking at the observed rate, we would not rule out the process *4* sequence nor can one really rule out the 10 step sequence involving two 2HSS barriers. In any case, since the barrier is nearly 2 kcal/mol higher than predicted for the two 2HSS barriers we would tentatively conclude that our trial parameter for the 2HSS process may be too low.

2-exo-5-Dimethyl-2-norbornyl Cation 7 and 2-anti-7-Dimethyl-2-norbornyl Cation 8

There is predicted to be a low energy barrier, 1TS,3SS,1ST, $\Delta G^{\ddagger} = 11.3$ kcal/mol, separating **7** and **8**. Experimentally, this is found to be the case. Cation solutions prepared from the chloride(s) of alcohol **9**, which should yield **7**, or from chlorides of the alcohol **10**, which should yield **8**, have identical n.m.r. spectra. The synthetic sequences start from known ketones and are shown in eq. 2. There are slight differences in the proton chemical shifts observed for **7** and **8** (listed in Table 3) so that one can clearly establish that two ions are present; however, it is not possible to assign which peaks are due to which particular ion. The equilibrium (close to unity) is established within 0.5 h at -120 °C (the Cl protons in **7** and **8** are separated enough so that one can clearly see both **7** and **8** at this temperature). One can estimate that the interconversion **7** ⇄ **8** must have a rate constant of greater than $ca.$ 1×10^{-3} s^{-1} at -120 °C, $\Delta G^{\ddagger} \lesssim 11.0$ kcal/mol, in agreement with the predicted barrier. Since all other barriers for **7** and **8** to rearrange to anything else involve energies of 15.2 or 16.9 kcal/mol, one can treat the two

[2] 

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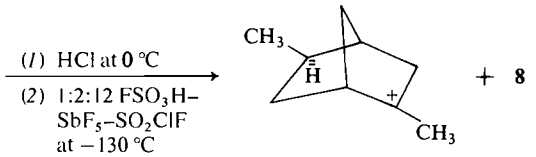

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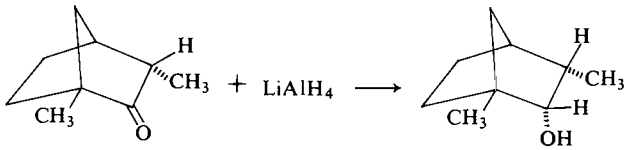

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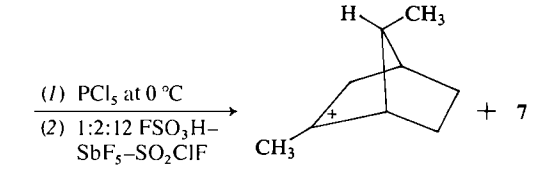

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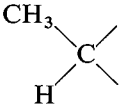
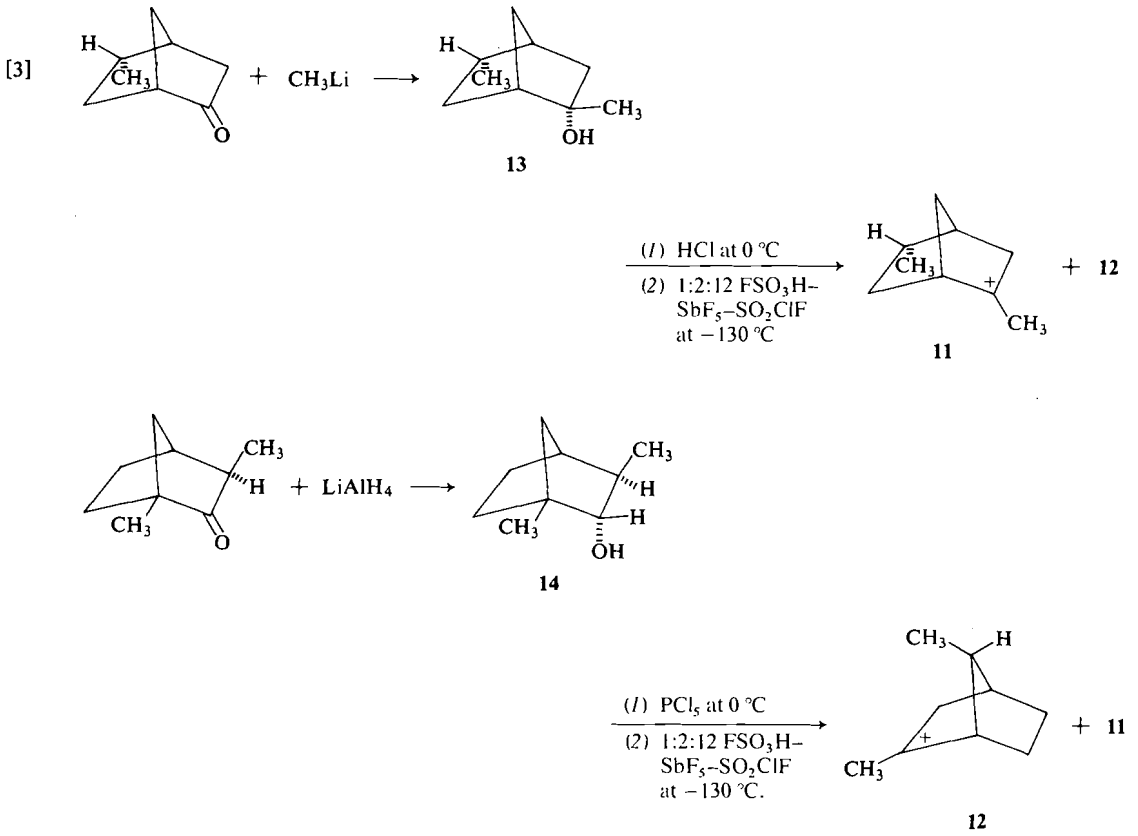
together (as was done with the two 3-methyl isomers).

Experimentally, **7** and **8** rearrange to the 2,4-dimethyl-2-norbornyl cation very rapidly, $k_{combined} = 1.35 \pm 0.5 \times 10^{-4}$ s^{-1} at -111 °C, $\Delta G^{\ddagger} = 12.1 \pm 0.1$ kcal/mol. Rather than looking at all possible interconversions, we will simply compare the barriers for these ions giving either the 1,2- or 2,4-dimethyl isomers. The shortest path to the 2,4-dimethyl isomer is from **8**, a two-step 1TS,2HST sequence involving a calculated 15.2 kcal/mol barrier. The shortest path to the 1,2-dimethyl isomer is again from **8** and involves the sequence 4TT,1TS,2HSS,1SS, 2HST, with a calculated high barrier of 18.0 kcal/mol. One can avoid this process *4* barrier by a number of much longer routes, the shortest being eight steps from **7**, 2HTS,3ST,1TS,3SS, 2MSS,3SS,2HSS,3ST, and a 16.9 kcal/mol barrier. Whichever one considers, the route to the 2,4-dimethyl isomer is clearly predicted but the predicted barrier is over 3 kcal/mol too high.

2-endo-5-Dimethyl-2-norbornyl Cation 11 and 2-syn-7-Dimethyl-2-norbornyl Cation 12

This pair are also predicted to be separated by the 11.3 kcal/mol barrier for the 1TS,3SS,1ST sequence and experimentally this is found to be the case. Cation solutions prepared from the chloride(s) of alcohol **13**, which should yield **11** or from chloride(s) of the alcohol **14**, which should yield **12**, have identical spectra. The synthetic sequences start from known ketones and are shown in eq. 3. The n.m.r. peaks of **11** and **12** overlap more than in the case of **7** and **8** and one has to warm the solution to -110 °C before the resolution is sufficiently good to be able to see two sets of  peaks. At still higher temperatures, the ratio of these does not change and therefore an equilibrium concentration of **11** and **12** has been established. It is not possible to assign the observed n.m.r. peaks to a given isomer, **11** or **12**, but in any case, the equilibrium



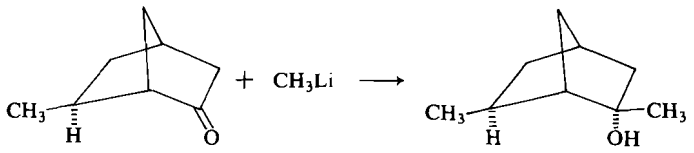
constant is near unity. The chemical shifts are listed in Table 3. One can estimate that the interconversion rate must be larger than 5×10^{-4} s^{-1} at -110 °C, $\Delta G^{\ddagger} \gtrsim 11.9$ kcal/mol, in agreement with the calculated 11.3 kcal/mol. Since all other barriers involve values of 16.9 or 15.2 kcal/mol, one can again treat the two ions together.

Experimentally, cations **11** and **12** rearrange to the 2,4-dimethyl isomers **4** with a combined rate of $4.8 \pm 0.15 \times 10^{-4}$ s^{-1} at -83 °C, $\Delta G^{\ddagger} = 13.9$ kcal/mol. Once again, we will simply look at the barriers for these ions giving either **4** or the 1,2-dimethyl isomer **3**. The shortest sequence for giving **4** starts from **11** and involves 1TS,2HSS,3ST and a barrier of 16.9 kcal/mol. The shortest sequence giving the 1,2-dimethyl isomer **3** is five steps from **12**, 1TS, 2MSS,3SS,2HSS,3ST, and once again a barrier of 16.9 kcal/mol. There are four 15.2 kcal/mol barrier routes to **3** but all involve the questionable 2MSS step.

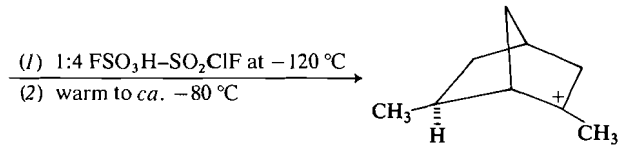
The actual route to the 2,4-dimethyl isomer **4** is predicted to *not* be the shortest sequence in this case but to involve, starting from **11**, the sequence 3TS,2HST,1TS,3SS,2HST, with two barriers of 15.2 kcal/mol. This sequence yields the 2-*exo*-5-dimethyl cation **7** after only two steps and then follows the same route to **4** as does **7**. Experimentally, the overall barrier is about 1 kcal/mol smaller than predicted. The rate-determining step must be the first 2HST step since experimentally the 2-*exo*-5-dimethyl cation **7** rearranges to **4** even faster than **11**–**12**.

2-exo-6-Dimethyl-2-norbornyl Cation 15

Carbocation **15** was prepared according to the sequence shown in eq. 4, starting from a known ketone. On addition of the alcohol **16** to the acid, one initially obtains the protonated alcohol and on warming, this gradually solvolyzes to **15**. Cation **15** undergoes a rapid, degenerate *endo*-6,2-hydride shift (see following paper) (5) which is not of interest here except that it gives one

[4] 

16



15

a definite value for the 3TT process, $\Delta G^{\ddagger} = 7.2$ kcal/mol. This had been only estimated previously as <11.3 kcal/mol.

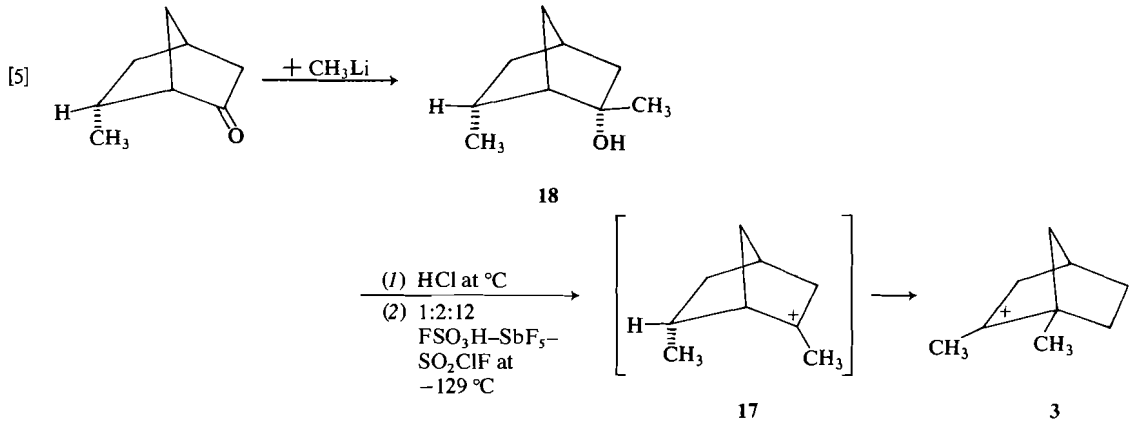
Experimentally, cation **15** is found to rearrange to the 2,4-dimethyl isomer **4**, $k = 1.3 \pm 0.05 \times 10^{-4}$ s^{-1} at -57 °C, $\Delta G^{\ddagger} = 15.3$ kcal/mol.[1] As before, we will check to see what the predicted product would be by looking at the calculated barrier for **15** giving either the 2,4-dimethyl isomer **4** or the 1,2-dimethyl isomer **3**. The shortest sequence giving the 1,2-dimethyl isomer is three steps involving 4TT,1TS,3ST. There is, however, a sequence bypassing process *4* involving only four steps, 1TS,2HSS,3SS, 2HST, with a calculated 16.9 kcal/mol barrier. There are in fact four sequences for **15** → **3** which involve the 15.2 kcal/mol barrier (three of these barriers) but all require the doubtful 2MSS step. The shortest sequence from **15** to **4** and involving the lowest calculated barrier is the seven-step sequence 2HTS,3SS,2MSS,1SS, 3ST,1TS,2HST with two 15.2 kcal/mol barriers. Avoiding the questionable 2MSS step, one finds that there are only two sequences involving 15.2 kcal/mol barriers, both 12 steps. They actually differ only in the fifth, sixth, and seventh steps, involving 3TS,1SS,2HST in one case and 1TS,3SS,1ST in the other. The preferred sequence is (2HTS,1SS,3SS,2HST)(1TS,3SS,1ST) (3TS,2HST)(1TS,3SS,2HST). (For convenience, parentheses have been added to enclose sequences leading from one tertiary ion to another.) The sequence converts the 2-*exo*-6-dimethyl ion **15** first to the 2-*syn*-7-dimethyl isomer **12**, then to the 2-*endo*-5-dimethyl **11**, to the 2-*exo*-5-dimethyl isomer **7**, and finally to **4**. There is excellent experimental support for this sequence since we already know that the rate from the 2-*syn*-7-dimethyl isomer **12** to **4** is faster than the experimental barrier from **15**, *i.e.* the barrier involves the first five-step sequence. This involves two 2HTS steps, 15.2 + 0.3 = 15.5 kcal/mol, in good agreement with the observed 15.3 kcal/mol.

This case neatly points out the tremendous advantages of having activation energy parameters assigned to the individual steps. Without these, one might have been tempted incorrectly to predict as product the 1,2-dimethyl isomer with the short, five-step, 16.9 kcal/mol barrier. The activation energies are also indispensible in sorting out the large number of predicted routes for a given interconversion. What we believe to be the correct sequence (above) for **15** → **4** is actually well "buried" in the computer output, *i.e.* without considering barriers and using only the "three process" routes, there are 2 7-step sequences, 4 of 8 steps, 2 of 9 steps, 5 of 10 steps, 5 of 11 steps, 13 of 12 steps, and 17 of 13 steps.

2-endo-6-Dimethyl-2-norbornyl Cation 17

Carbocation **17** was not directly observed, as in fact expected. The sequence which should have generated cation **17** is shown in eq. 5, starting from a known ketone. Addition of the alcohol **18** to FSO_3H–SO_2ClF (1:4) at -130 °C yields predominantly the protonated alcohol and some **3**. The protonated alcohol solvolyzes fairly rapidly and has disappeared within 0.5 h at -90 °C. Carbocation **3** is the only observed product. Addition of the chloride at -129 °C to SbF_5–FSO_3H–SO_2ClF and running the n.m.r. spectrum at -120 °C shows only the cation **3**. The rate constant for **17** → **3** can be conservatively estimated as $> 5 \times 10^{-4}$ s^{-1} at -120 °C,

[1]At -60 °C, there appears to be an equilibrium, where $K = ca.$ 65 for **4**/**15**.



$\Delta G^{\neq} \lesssim 11.2$ kcal/mol. The predicted lowest barrier for **17** to rearrange to anything else is the 1TS,3ST sequence leading to **3**, with a predicted barrier of 11.3 kcal/mol.

Discussion

The use of a computer to enable one to look at all of the allowed paths (up to at least a predetermined number of steps) in a sense shows one too much. It would be gratifying to have one clearcut path which could be safely separated from the less likely ones. In fact, this probably occurs in pencil and paper type elucidations of the overall transformations since the writer may have a bias toward certain steps and will almost certainly be biased toward the shorter sequences. It is completely unmanageable to work out many of the numerous multistep sequences by hand.

In looking at the success of the trial parameters, which is the real point of this work, the critical ones are the highest barriers. Numerical errors in the low barriers will not affect the calculated overall rate of a process involving at some point a much higher barrier. In practice, the three critical values for the "three process" sequences are for 2HST (or 2HTS), 2HSS, and 2MSS. A comparison of calculated and observed behavior for all of the rearrangements are summarized in Table 3 and a perusal of this shows that some sizeable $\Delta G^{\neq}$ deviations exist. We believe at this time that the major error factor is probably a thermodynamic one, due to a neglect of the "special" effect of a C1 methyl group, *i.e.* just as we have clearly separated the secondary C2 H and tertiary C2 CH_3 cations, we should probably take into account the increased stability of a secondary *or* tertiary cation resulting from a C1 methyl *vs.* hydrogen substitution. To make this distinction in the computerized treatment of activation energies seems too restrictive; there is already enough subdivision of steps for a general treatment. Such subtle thermodynamic factors are relevant to questions about the molecular structure of 2-norbornyl cations and this point is explored in an accompanying paper (5). Basically, the results of this analysis suggest that the 2HSS value used in this work (16.9) is appropriate only to a C1 methyl-substituted secondary ion and that the 2HTS value of 15.2 is only appropriate to a C1 hydrogen-substituted secondary ion. Consideration of this brings both the **4** → **3** and **7,8** → **4** barriers closer to the experimental values. Furthermore, we can better rationalize our overall observations by assuming a 2MSS value near our previously derived upper limit so that sequences involving this barrier are discounted.

We have been rather surprised in this work to note the large thermodynamic ground state energy differences between some of the dimethyl cations, *i.e.* **1** and **2** or **4** and **15**. This complicates the use of trial activation energy parameters and suggests that one should be cautious about trying to make too fine a comparison between calculated and experimental rates. We implicitly recognize this in the transformations of **7** and **8** to **4**, or **11** and **12** to **4**, where we have not evaluated the few tenths of a kcal/mol associated with the fact that the concentration of the reactive member of the pair has less than unit concentration. Similar small effects were

TABLE 4. Chemical shift values[a]

Ion	Positions										
	1	2(CH_3)	3-*exo*	3-*endo*	4	5-*exo*	5-*endo*	6-*exo*	6-*endo*	7-*syn*	7-*anti*
1	*ca.*5.0[b]	6.9	—[c]	—	—	—	—	6.3	—	—	—
2	*ca.*5.1[b]	*ca.*7.0 (7.70)[d]	7.10	*ca.*8.5 (CH_3)	*ca.*7.1[e]	(7.31)[f]	(8.46)[f]	(7.31)[f]	(8.46)[f]	8.13[g]	7.99[g]
3[h]	(7.58) (CH_3)	(7.58)	(7.63)[j]	(7.49)[j]	7.07	(8.37)[k]	(8.37)[k]	(7.15)[l]	(7.15)[l]	(7.49)[j]	(7.63)[j]
4	5.11[m]	6.76	6.94[n]	7.13[n]	8.51 (CH_3)	8–8.5	8–8.5	6.32	8–8.5	8.05	8.05
7	5.33[p] or *ca.*5.14[q]	6.70	—[r]	—	7.15?	8.73[b] (CH_3)	—	6.3	—	—	—
8	*ca.*5.14[q] or 5.33[p]	6.70	—	—	7.15?	—	—	6.3	—	—	8.73[b] (CH_3)
11	5.18[s]	6.73	—	—	—	—	8.94[t] or 8.99[t]	6.08–6.41[u]	—	—	—
12	5.18[s]	6.73	—[q]	—	—	—	—	6.08–6.41[u]	—	8.94[t] or 8.99[t]	—
17	5.44	6.64 (7.44)	(7.72 or 7.62)[v]	(7.72 or 7.62)[v]	6.92	(7.72 or 7.62)[v]	(7.72 or 7.62)[v]	8.24[h] (CH_3) (7.44)	8.02[w]	(7.86)	(7.86)

[a]Relative to tetramethylammonium cation (TMA^+) = τ 6.90.
[b]These values have been obtained at extremely low temperatures and are poorly resolved. There is also some evidence that chemical shifts change slightly with temperature.
[c]The assignments for **1** are somewhat tentative. Complete assignments were not made because the higher field region is obscured by cation **2** peaks.
[d]Values in parentheses represent averaged chemical shifts caused by a particular rearrangement (see text for these).
[e]Obtained by interpolation, knowing an averaged value and one of the "frozen out" peak values (see, however, [b]).
[f]A doublet, $J_{average} = 11$.
[g]An AB quartet, $J = 11$.
[h]The spectrum of **3** has been published (14) but several small peaks have been chopped off. Above 25 °C, this cation undergoes a second degenerate rearrangement shown from DISST experiments to be identical to the second degenerate rearrangement occurring in the 2-methyl-2-norbornyl cation (1).
[j]A 2(AB) quartet, $J = 15$.
[k]Triplet, $J = 6$.
[l]Poorly resolved triplet, $J = 6$.
[m]Doublet, $J = 6.5$.
[n]This assignment may be reversed.
[p]Doublet, $J = 5$.
[q]Partially obscured by HI of **4**.
[r]Assignments for **7** ⇄ **8** and **11** ⇄ **12** are incomplete because with two ions present, one has a very complex spectrum in the 7.5–8.5 region.
[s]Doublet, $J = 7$.
[t]Doublet, $J = 6.5$.
[u]Curiously shaped with two humps on the ends and nearly flat between these.
[v]The two peaks are not equal and are somewhat broad, possibly part of an AB quartet.
[w]This peak is broad and the assignment is somewhat uncertain.

also ignored, in general, in deriving the trial activation energy parameters.

In closing, perhaps the most valuable aspect of this study is to show how incredibly fast are many of these long rearrangement sequences. We have recently studied a pentamethyl-2-norbornyl cation rearrangement occuring at −40 °C where 15 steps (three processes) were needed to produce a single predicted sequence.

Experimental

Product purity was determined in each case by i.r., g.l.c., and n.m.r. Cation n.m.r. chemical shifts are reported relative to $TMA^+ = \tau$ 6.90 and were obtained on a Varian Associates HA-100.

1,4-Dimethylbicyclo[2.2.1]heptan-endo-2-ol **5**

Small quantities of the g.l.c. pure ketone, 1,4-dimethylbicyclo[2.2.1]heptan-2-one (**6**) were available from the ozonolysis of a 2-exomethylene hydrocarbon related to **6** (1). Reduction of this with lithium aluminum hydride gave the corresponding alcohol, which almost certainly has mainly the *endo* configuration; n.m.r. (CCl_4), 8.935 and 8.950 (both 3H, the C1 and C4 methyl groups), 6.155 and 6.250, (d, J = 10.5, each peak is further split into a doublet of doublets, J = 3.5 and 1.5, the C2 proton). Addition of the alcohol to FSO_3H or 1:4 FSO_3H–SO_2ClF at −80 °C yields only the protonated alcohol, peaks at 8.84 and 8.72 (3H each, the C1 and C4 methyl groups), 4.87 (d, J = 9, the C2 proton). Solvolysis becomes fairly rapid about −45 °C to yield the pure cation **4**. Secondary 2-norbornyl alcohols with an *exo* configuration cleave much more readily (7).

2-exo-5-Dimethylbicyclo[2.2.1]heptan-2-ol **9**

A commercial mixture of *exo*-5- and *endo*-5-methylbicyclo[2.2.1]hept-2-ene was converted to a mixture of the *exo*-5-, *endo*-5-, *exo*-6-, and *endo*-6-methylbicyclo-[2.2.1]heptan-2-ones using a literature procedure (8). Using a 20 ft × 3/8 in. column of 30% Carbowax 20M, it was possible to separate preparatively, without difficulty, the *endo*-6- and *endo*-5-methyl ketones, the shortest and longest retention peaks, respectively. Just the opposite g.l.c. behavior is reported (8) and the assignments in this paper may be in error. The *exo*-6- and the *exo*-5-methyl ketones have very similar retention times, the former marginally shorter. By cutting the longer retention side of the combined peak twice it was possible to obtain a sample of the *exo*-5-methyl ketone which was pure enough for our purposes (the same cations, **7** and **8**, in a pure form, are obtained from alcohol **10** and the *exo*-6-methyl cation impurity also produced from the impure **9** does not interfere with either our characterization of cations **7** and **8**, nor with the measurement of their rate of rearrangement). The split methyl peak in all four ketones is at a different chemical shift, in CCl_4, *endo*-6-methyl, τ 9.02; *exo*-5-methyl, 8.91; *exo*-6-methyl, 8.92; *endo*-5-methyl, 8.96; and based on this, the ketone fraction was about 75% *exo*-5-methyl and 25% *exo*-6-methyl. The pure *exo*-6-methyl ketone can be obtained by another route. The *exo*-5-methyl ketone (75.6 mg, 0.61 mmol) was treated with 1.2 mmol of methyl lithium in ether to yield 47.9 mg of alcohol. This was stirred with 1 ml of concentrated HCl at 0 °C for 30 min, the cold solution extracted with pentane, and the pentane dried and neutralized with anhydrous K_2CO_3. After pentane removal, the chloride residue (no —OH in i.r.) was used directly. From Berson's results (3), the alcohol–chloride transformation should proceed without appreciable rearrangement involving 6,2-hydride shifts.

1-exo-3-Dimethylbicyclo[2.2.1]heptan-2-ol **10**

The ketone, 1-*exo*-3-dimethylbicyclo[2.2.1]heptan-2-one, was prepared as previously described. The ketone (186.3 mg, 1.35 mmol) in 2 ml of ether was added dropwise to a solution of lithium aluminum hydride (102 mg) in 10 ml of ether. On work-up, 172.5 mg of alcohol **10** was obtained as a liquid at 25 °C; n.m.r. (CCl_4), τ 9.18 (d, J = 6.5, 3H, the C3 methyl), 8.945 (3H, the Cl methyl), 6.43 (d, J = 10, 1H, each peak is further split into a doublet, J = 1.5, the C2 proton). Judging from the n.m.r. spectrum, the alcohol is essentially a single isomer at C2, almost certainly the *endo*-2 alcohol. Using the phosphorus pentachloride – pentane procedure of Brown *et al.* (9), the alcohol was converted to the chloride, which is likely a mixture of the secondary and tertiary chlorides (*cf.* α-fenchol result (10) indicating that no 6,2-hydride shift is expected under these conditions).

2-endo-5-Dimethylbicyclo[2.2.1]heptan-2-ol **13**

The alcohol **13** was prepared as described for **9**. From 210 mg, 1.5 mmol, of ketone there was obtained 193 mg of **13** as a solid, m.p. 28–30 °C; n.m.r. (CCl_4), 9.02 (d, J = 6.5, 3H, the *endo*-5 methyl group), 8.78 (3H, the C2 methyl group).

Anal. Calcd. for $C_9H_{16}O$: C, 77.08; H, 11.5. Found: C, 77.02; H, 11.4.

Judging from the n.m.r. spectrum, the alcohol is mainly a single isomer at C2, almost certainly the *endo* alcohol. The alcohol was converted to the chloride (i.r.) by the same procedure described for **9**.

1-endo-3-Dimethylbicyclo[2.2.1]heptan-2-ol **14**

This alcohol was prepared by the same procedure used to prepare alcohol **10**, starting with the *endo*-3-methyl ketone (1). The alcohol has been reported (11). From g.l.c. and n.m.r., the alcohol is a mixture of the *exo*-2 and *endo*-2 alcohols. The major isomer (a solid) can be isolated by preparative g.l.c. The alcohol was converted to the chlorides by the same procedure described for **10**.

2-exo-6-Dimethylbicyclo[2.2.1]heptan-2-ol **16**

The ketone, *exo*-6-methylbicyclo[2.2.1]heptan-2-one was obtained using a procedure partially described by Beckmann *et al.* (12), starting with *exo*-2-methylbicyclo-[2.2.1]heptan-2-ol, converting this to the *endo*-2-methyl alcohol, heating this with formic acid and then saponifying. At this stage, the crude alcohol was oxidized with Jones' reagent to give a crude ketone mixture consisting mainly, as expected, of the 1-methyl ketone together with about 15% of the *exo*-6-methyl ketone and small amounts of others. Spinning band distillation (Nestor Faust Autoannular 30 in. column) at 14 mm effected the separation of most of the 1-methyl ketone, b.p. 57–58 °C. From the residue, a fraction consisting mainly of the *exo*-6-methyl ketone was separated by preparative g.l.c. (see **9**). This was further purified through the crystalline semicarbazone and hydrolysis of this in aqueous oxalic acid. The alcohol **14** was prepared as for **9** and after sublimation had

m.p. 38–41 °C; n.m.r. (CCl_4), τ 9.13 (d, J = 7, 3H, the *exo*-6-methyl peak), 8.79 (3H, the C2 methyl peak). The alcohol appears to be, from n.m.r. and g.l.c., a single isomer at C2, in all probability, the *endo* alcohol.

Anal. Calcd. for $C_9H_{16}O$: C, 77.08; H, 11.5. Found: C, 76.85; H, 11.98.

2-endo-6-Dimethylbicyclo[2.2.1]heptan-2-ol ***18***

The alcohol **18** was prepared as described for **9**. From 270 mg, 1.93 mmol, of the ketone, there was obtained 260 mg of alcohol, which after sublimation had a m.p. of 56–59 °C; n.m.r. (CCl_4), τ 8.77 (d, J *ca.* 6.5, 3H, the *endo*-6 methyl), 8.79 (3H, the C2 methyl). Judging from the g.l.c. and n.m.r. evidence, the alcohol is a single isomer at C2, in all probability the *endo* alcohol.

Anal. Calcd. for $C_9H_{16}O$: C, 77.08; H, 11.5. Found: C, 76.07; H, 11.2.

The alcohol was converted to the chloride (i.r.) by the same procedure described for **9**.

Rate Measurements

The preparation of the cations followed previously described procedures (13). The particular solvent system used is given under Results. Chemical shifts are given in Table 4. Plots involved a standard first-order kinetic treatment and were subject to standard least-squares analysis. The error limits represent the 90% confidence level. A given rate was run from two to five times. In the case of the lower temperatures, it was not possible to duplicate the exact temperature each time. In these cases, the best fit line is reported and the corresponding $\Delta G^{\ddagger}$ values for all runs are averaged and the deviation reported. A thermocouple was inserted directly into the n.m.r. tube and a temperature reading accompanied each time reading. The temperatures over a complete run were averaged. The specific procedures followed in each case were as follows.

Cation ***4*** → *Cation* ***3:*** (peak height of coalesced C1—C2 methyls of **3**)/2 (*a*) + C4 methyl peak height of **4** (*b*) = constant peak height (*c*). Plotted increase of (*a*)/(*c*) with time. The half-widths of (*a*) and (*b*) are nearly identical at the temperatures involved here.

Cation ***2*** → *Cation* ***3:*** followed increased peak height of coalesced C1—C2 methyls of **3** with time. The peak was standardized against a reference TMA^+ peak height.

Cations ***7*** ⇄ ***8*** → ***4:*** at the low temperatures involved, the H1 proton region shows two broad multiplet peaks. The lower field belongs to either **7** or **8** and **4**. The higher field one belongs to only one ion, either **8** or **7**. The total area of H1 protons was determined by tracing, cutting, and weighing and taken as constant. The rate was determined by plotting the decrease in the higher field H1 peak area (standardized) with time.

Cations ***11*** ⇄ ***12*** → *Cation* ***4:*** followed increased peak area of C4 methyl of **4** with time. The peak area was standardized against a reference TMA^+ peak area.

Cation ***15*** → *Cation* ***4:*** peak area of coalesced (C2—C6 methyl of **15**)/2 (*d*) + area of C4 methyl of **4** (*e*) = constant peak area (*f*). Plotted increase of (*e*)/(*f*) with time using the appropriate form of a first-order rate expression.

Program Transform

The purpose of the program is to find all possible pathways of getting from one norbornyl cation to another in N steps or less and with K different processes. A reaction sequence is represented by an integer with N digits with each digit representing a certain process and the arrangement of the digits representing the order in which they are performed. An integer is generated and the transformations are carried out, checking after each transformation to see if the product was formed. If it has been formed, then further checks are made to eliminate sequences which contain internal cycles and if the overall transformation requires less than N steps, a check is performed to eliminate identical sequences which were found previously. Finally, the sequence is printed along with complementary information concerning the nature of the intermediates, *i.e.* tertiary or secondary ions, and the energy barriers which the sequence must hurdle. The integer is incremented by one unit and the process starts over. The principle advantage of this over the elegant procedure of Johnson and co-worker (2) is that only a very limited amount of central memory is required, although our program does not execute as fast and never generates or contains the information necessary to construct a complete graph.

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