

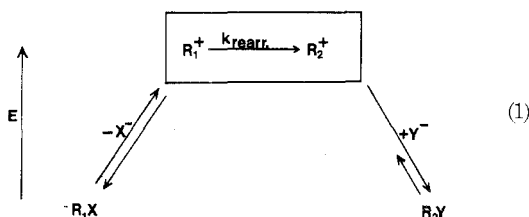
Terpene Rearrangements from a Superacid Perspective

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Organic molecular rearrangements occur by a variety of mechanisms, but for hydrocarbons, probably the most important class involves the intermediacy of carbocations with the actual molecular rearrangement taking place in the carbocation intermediate (eq 1).



This mechanism was first postulated over 50 years ago (1922) by Meerwein and Van Emster¹ but not universally accepted at the time.² The subsequent work of Whitmore³ and Ingold,⁴ in particular, eventually helped to confirm the generality of the Meerwein postulate. Today the concept is universally accepted.

The cationic intermediates in eq 1 are normally produced as a result of an SN1 reaction (solvolysis), as shown, or by protonation of an alkene, cyclopropane, etc. In media of low acidity very little of the reactant exists as a carbocation at any time, and one has true acid catalysis.

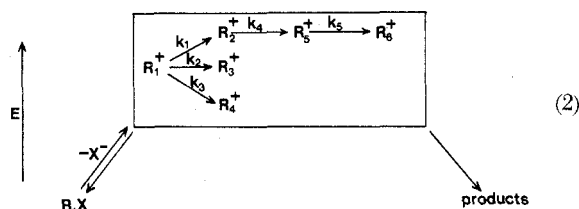
What we hope to show in this Account is that knowing the *absolute* rate (or activation barrier, ΔG^\ddagger) of the $R_1^+ \rightarrow R_2^+$ process is of importance for full understanding of the mechanism of the $R_1X \rightarrow R_2Y$ reaction and that this rate *dictates* the choice of experimental conditions used in carrying out these reactions under "normal" solvolysis or acid-catalysis conditions. The actual determination of such rates, where the carbocations have a fleeting existence (treated kinetically as steady-state intermediates), is nearly impossible. In favorable cases, where the rearrangement competes with nucleophilic capture of the unrearranged R_1^+ , one can obtain an approximate estimate of the cation rearrangement rate from a knowledge of nucleophile-carbocation recombination rates. For example, in alkaline media, the latter are often assumed to be ionic diffusion rates⁵ with pseudo-first order rate constants typically about 10^9 s^{-1} . The rate constant for a competing $R_1^+ \rightarrow R_2^+$ rearrangement would be of the same order of magnitude.

Superacid Studies

Working in very strong (super) acids, one can now prepare many of these carbocation "intermediates" and *directly* measure the rate (or activation barrier) of the

critical $R_1^+ \rightarrow R_2^+$ step. However, it may be difficult to convince anyone that reaction rates measured in such solvents (e.g., FSO_3H or SbF_5) bear any close relationship to those of a steady-state intermediate in a "normal" organic or aqueous solvent. It is perhaps fortunate for us that the latter rates cannot be accurately measured, since we shall subsequently assert that these superacid direct rate measurements are indeed valid for "normal conditions".

Let us momentarily return to eq 1. Most chemists will recognize that, if R is an organic molecule of reasonable complexity, then one will not be restricted to a single mode of rearrangement, as depicted there. A more chemically realistic representation is that in eq 2, where



k_1 , k_2 and k_3 indicate the possibility of competitive cationic rearrangements and k_4 and k_5 indicate that one might also have multiple rearrangements occurring sequentially. The competition may refer to carbocation rearrangements differing in stereochemistry or they may refer to various structural isomerizations, such as alkyl vs. hydrogen shifts.

Naturally occurring monoterpenes, with a C_9 or C_{10} skeleton, are organic molecules of at least some complexity. Furthermore, they are known from many previous studies to undergo both competitive and multiple cationic rearrangements under acid-catalysis as well as solvolysis conditions. As explained earlier, direct comparison of the rates of a single cationic rearrangement rate process in superacid media and in "normal" organic or aqueous media is not possible, but one can at least measure the ratio of two or more superacid rates and compare the rate ratio to the product ratios obtained in the organic or aqueous media. This situation is shown schematically in Figure 1. If these ratios are similar, one has an indication either that medium effects on rates are relatively unimportant or that fortuitously both rates are quantitatively affected by the medium in the same way. Secondly, it is of interest to consider the actual experimental conditions necessary for bringing

(1) H. Meerwein and K. Van Emster, *Ber.*, **55**, 2500 (1922).

(2) For example, in the well-known series "The Terpenes", Vol. II, 2d ed, Cambridge University Press, New York, N.Y., 1949, p 159, Simonsen writes in 1932 "Meerwein considers that the isomerization [isoborneol to camphene] is preceded by ionisation, the actual molecular rearrangement occurring in the cation . . .". However, Simonsen then goes on to favor a partial valence symbolism credited to Robinson and Lapworth, in which a dotted line formulation was used.

(3) F. C. Whitmore, *J. Am. Chem. Soc.*, **54**, 3274 (1932).

(4) H. Burton and C. K. Ingold, *J. Chem. Soc.*, 904 (1928).

(5) P. S. Skell and R. J. Maxwell, *J. Am. Chem. Soc.*, **84**, 3963 (1962).

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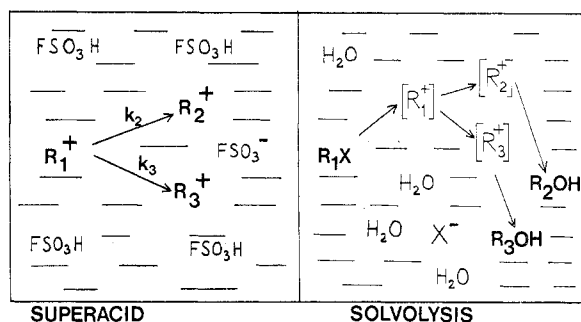


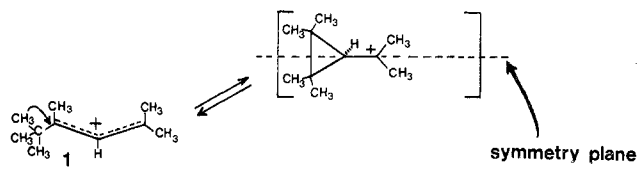
Figure 1.

about these overall terpene rearrangements with attention to estimates of the absolute rates (or activation barriers) for cation \rightarrow cation rearrangements in superacid media.

Uphill and Downhill Rearrangements

Also by way of introduction, let us look briefly at the energetics of carbocation rearrangements. Under solvolysis conditions, it is perfectly possible for the terpene $R_1^+ \rightarrow R_2^+$ step, in eq 1, to go uphill in energy, as long as the ultimate product is thermodynamically more stable than the reactant. Under the observable, superacid conditions, this uphill process cannot occur to any substantial extent and direct determination of its rate is impossible. Nevertheless, if the ion R_1^+ can form R_2^+ under solvolysis conditions, then a high-energy R_2^+ should also exist, albeit in very low population, under the observable ion conditions. If this intermediate has any element of symmetry not present in R_1^+ , one can observe the forward rearrangement rate $R_1^+ \rightarrow [R_2^+]$ using NMR spectroscopy, either by an isotope scrambling measurement or by noting NMR line-broadening in R_1^+ .

As a simple though nonterpene example, the allyl cation 1 can form a cyclopropylcarbinyl cation *intermediate* by methyl migration. If one takes appropriate



note of the statistical and symmetry factors involved, the rate of this "uphill" process can be determined, and in this example, both $\text{CH}_3\text{-CD}_3$ isotope scrambling⁶ and NMR line broadening⁷ have been used. Note, however, that one has only indirect evidence concerning the existence and structure of this intermediate cyclopropylcarbinyl cation. In more complex cases involving multiple rearrangements, the actual intermediates may not be uniquely defined by the NMR line broadening.

Comparison of the Absolute Rates for Terpene Carbocation Rearrangements in Superacid and "Normal" Experimental Conditions

The Fenchyl System. α -Fenchol (2), found in turpentine, has been the object of many solvolysis and acid-catalysis rearrangement-dehydration studies.⁸⁻¹² What made this terpene system perplexing to the early

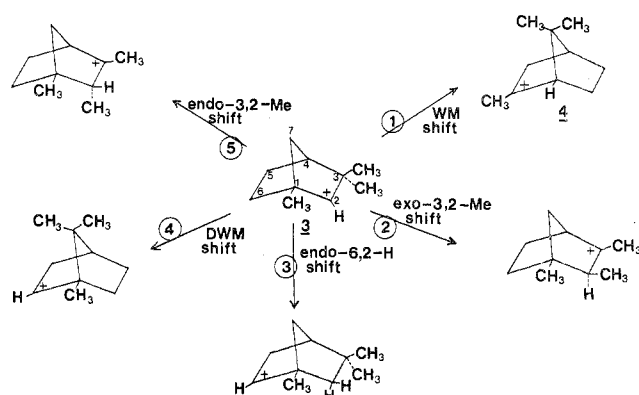


Figure 2. WM \equiv Wagner-Meerwein rearrangement, 6,1-bond \rightarrow 6,2-bond; DWM \equiv double Wagner-Meerwein rearrangement, 7,1 \rightarrow 7,2; 3,2 \rightarrow 3,1.

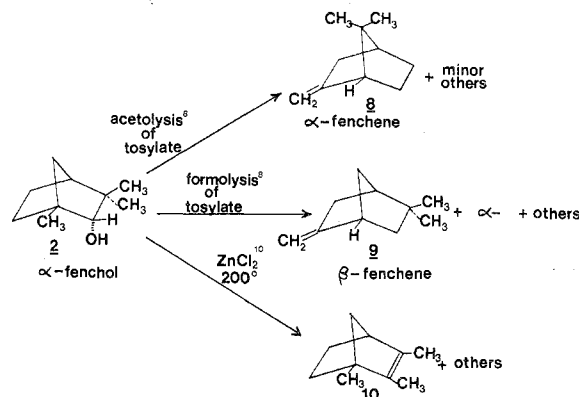
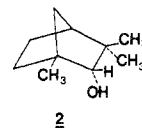


Figure 3.

workers was the multiplicity of rearrangement possibilities, once the carbocation has formed. There are at



least five chemically reasonable ways in which the first-formed fenchyl cation, 3, might proceed. These are shown in Figure 2.

One can quickly get a feeling for which of these processes has the lowest barrier by noting the products formed under varying experimental conditions. These are summarized in Figure 3 (although at least ten "fenchenes" are known, some of them are derived from the same cation, depending on the direction of proton elimination). Clearly, the severity of the reaction conditions increases from top to bottom in Figure 3. It should be noted that α -fenchene formation requires *only* the WM shift of Figure 2, β -fenchene requires a 6,2-hydride shift followed by a WM shift, and ϵ -fenchene formation requires a 3,2-methyl shift.

When one attempts to prepare the observable fenchyl cation 3, one quickly runs into trouble. Not only is one unable to slow down the WM shift leading from 3 to the

(8) (a) W. Hüchel, *Bull. Soc. Chim. Belg.*, **71**, 473 (1962); (b) W. Hüchel and D. Volkman, *Justus Liebigs Ann. Chem.*, **664**, 31 (1963); (c) W. Hüchel and H.-J. Kern, *ibid.*, **687**, 40 (1965); (d) W. Hüchel and E. N. Gabali, *Chem. Ber.*, **2766** (1967).

(9) W. von E. Doering and A. P. Wolf, *Perfum. Essent. Oil Rec.*, **42**, 414 (1951).

(10) E. Pulkkinen, *Suom. Kemistil. A*, **30**, 239 (1957).

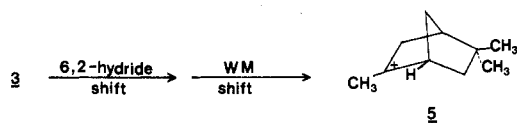
(11) N. J. Toivonen, *Suom. Kemistil. A*, **9**, 75 (1936), and preceding papers.

(12) (a) G. Komppa and R. H. Roschier, *Ann. Acad. Sci. Fenn.*, **Ser. A**, **7**, 1 (1915); (b) G. Komppa and G. A. Nyman, *Justus Liebigs Ann. Chem.*, **535**, 252 (1938).

(6) T. S. Sorensen and K. Ranganayakulu, *Tetrahedron Lett.*, 659 (1970).

(7) C. D. Poulter and S. Winstein, *J. Am. Chem. Soc.*, **91**, 3649-3650 (1969); C. D. Poulter and S. Winstein, *ibid.*, **94**, 2297 (1972).

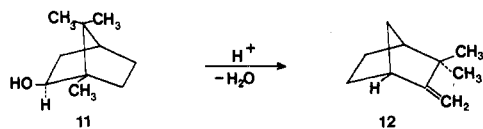
more stable tertiary ion 4 (see Figure 2), but even the combination 6,2-hydride shift–WM shift, giving the β -fenchene hydro cation 5, is too rapid to measure at



$-120\text{ }^{\circ}\text{C}$.^{13–15} However, at $-92\text{ }^{\circ}\text{C}$, the equilibrium mixture of 4 and 5 rearranges to an ϵ -fenchene cation, 6, in a process which involves an initial 3,2-methyl shift. One can therefore directly measure at least the slowest of the three cation rearrangement processes giving products (see Figure 3). Subsequently, two further rearrangements are observed as the temperature continues to warm up. These are shown in Figure 4, and the activation barriers are noted. The order of ion appearances in Figure 4 does not imply a consecutive rearrangement sequence since all of the reactions are reversible. The activation energies for $3 \rightarrow 4$ and $4 \rightarrow 5$ have been inferred from related work.¹⁴

From comparison of the superacid results with the acid-catalysis results, one can make three observations: (1) The order of increasing ΔG^{\ddagger} for the ion-to-ion rearrangement barriers seems to be the same under both sets of conditions. (2) Since there is no ΔG^{\ddagger} barrier for the direct observation (superacid) studies, these reactions are enormously faster. For example, the barrier from α -fenchol to ϵ -fenchene under the conditions of Figure 3 is about 35–40 kcal/mol, while the actual ion-to-ion barrier is only 13.1 kcal/mol. Since one can raise the temperature of superacid solutions to at least $100\text{ }^{\circ}\text{C}$, one can observe cation \rightarrow cation barriers of as high as 30 kcal/mol. Such rearrangements should *have no acid-catalysis equivalent*. Even a barrier of 18.5 kcal/mol, as in $6 \rightarrow 7$, appears to be too high, since fenchenes related to 7 have never been isolated from what one must regard as fairly rugged acid-catalysis conditions. (3) The thermodynamic factors which determine that carbocation 6 should be more stable than 4 or 5 seem to apply also to the acid-catalysis results, since ϵ -fenchene (10) must be thermodynamically more stable than α - or β -fenchene (8 and 9). Indeed, observable cation stabilities appear to *parallel the stability order of the corresponding alkenes*.

The Camphene–Isoborneol System. The isoborneol (11)–camphene (12) rearrangement was mentioned



earlier as the first example of a postulated carbocation rearrangement. Starting with optically active isoborneol, early workers¹⁷ sometimes observed considerable

(13) E. Huang, K. Ranganayakulu, and T. S. Sorensen, *J. Am. Chem. Soc.*, **94**, 1779 (1972).

(14) R. Haseltine, E. Huang, K. Ranganayakulu, T. S. Sorensen, and N. Wong, *Can. J. Chem.*, **53**, 1876 (1975).

(15) The preparation and NMR spectrum measurement time for observing carbocations cannot be accomplished in less than about 10 s, and a lower limit for the temperature is about -120 to $-150\text{ }^{\circ}\text{C}$, meaning that the activation barrier, ΔG^{\ddagger} , needs to be about 10–12 kcal/mol or greater in order to detect the rearrangement rate.

(16) The final allyl cation product was first observed by N. C. Deno and J. J. Houser, *J. Am. Chem. Soc.*, **86**, 1741 (1964).

(17) P. Lipp and G. Stutzinger, *Ber.*, **65**, 241 (1932).

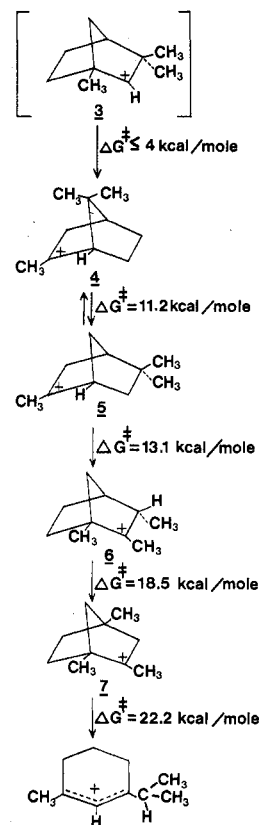
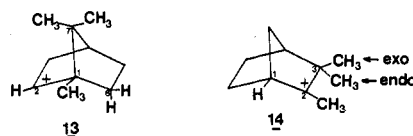


Figure 4. Order of appearance of observable cations starting with the fenchyl system 3.¹⁶

racemization in the camphene product (which itself is derived from the intermediate isobornyl cation 13 by a Wagner–Meerwein shift). This racemization was first attributed to a 3,2-methyl shift in the camphene hydro cation 14 (called the Nametkin rearrangement). Later



Meerwein¹⁸ suggested that a 6,2-hydride shift in the secondary isobornyl cation could also lead to racemization. Classical ¹⁴C camphene labeling experiments by Roberts¹⁹ and Vaughan and Perry²⁰ showed in fact that both mechanisms were operative. Vaughan²¹ has subsequently refined the measurements in this area and has recently concluded that no less than three competitive cationic racemization pathways are involved: (1) an exo 3,2-methyl shift in the camphene hydro cation 14; (2) an endo 6,2-hydride shift in the isobornyl cation 13 (starting from 14, this will therefore be preceded and followed by a Wagner–Meerwein 6,1 \rightarrow 6,2 shift, abbreviated as a WM-6,2-WM rearrangement); (3) an endo 3,2-methyl shift in the camphene hydro cation 14.

The observable camphene hydro cation 14 is easily prepared^{22,23} from isoborneol, camphene, or tricyclene,

(18) H. Meerwein and F. Montfort, *Justus Liebigs Ann. Chem.*, **435**, 207 (1924).

(19) J. D. Roberts and J. A. Yancey, *J. Am. Chem. Soc.*, **75**, 3165 (1953).

(20) W. R. Vaughan and R. Perry, *J. Am. Chem. Soc.*, **75**, 3168 (1953).

(21) (a) W. R. Vaughan, C. T. Goetschel, M. H. Goodrow, and C. L. Warren, *J. Am. Chem. Soc.*, **85**, 2282 (1963); (b) C. W. David, B. W. Everling, R. J. Kilian, J. B. Stothers, and W. R. Vaughan, *ibid.*, **95**, 1265 (1973).

(22) E. Huang, K. Ranganayakulu, and T. S. Sorensen, *J. Am. Chem. Soc.*, **94**, 1780 (1972).

(23) R. Haseltine, E. Huang, K. Ranganayakulu, and T. S. Sorensen, *Can. J. Chem.*, **53**, 1056 (1975).

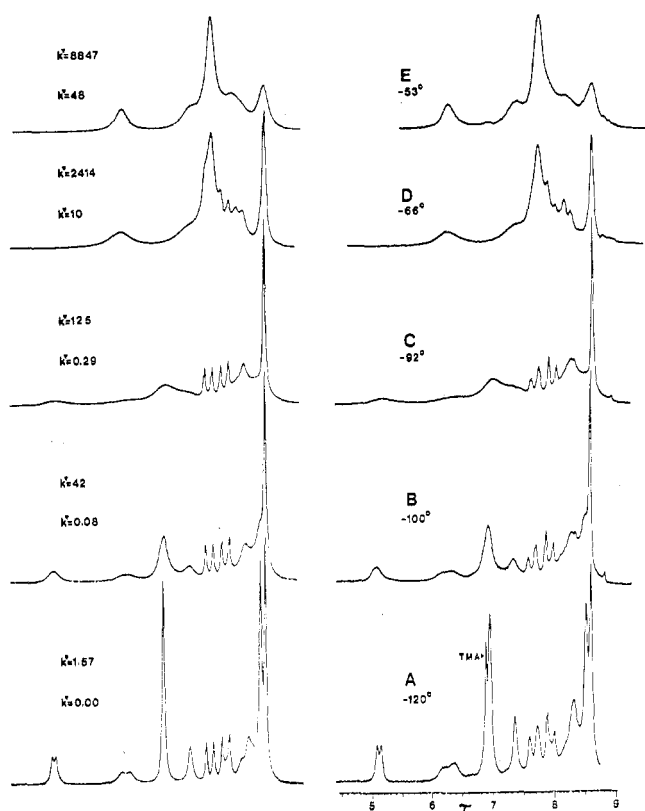


Figure 5. Right, experimental ^1H NMR spectra of the camphene hydro cation at various temperatures. Left, calculated ^1H NMR spectra, k^∇ = the *exo*-3,2-methyl shift rates in s^{-1} , k^∇ = the WM-6,2-WM rearrangement rate in s^{-1} .

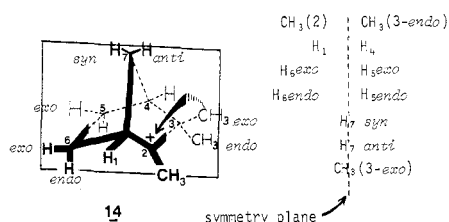


Figure 6.

in any of several superacid solvents. As an illustration of how one determines degenerate rearrangement rates in carbocations, we show the NMR spectrum of 14 at several temperatures (Figure 5). At -120°C , the NMR spectrum of this cation is "normal", showing all three nonequivalent methyls as sharp separate peaks. In the range -120 to -70°C , all peaks broaden except one methyl group and a four-line portion. This broadening pattern can be unequivocally attributed to a *stereospecific* 3,2-methyl shift. The groups becoming identical in the NMR spectrum by this migration can be easily seen if one moves the migrating methyl half way (suspended in the plane) to give a "structure" with C_s symmetry (Figure 6). The group identities are shown to the right of the structure. Those groups in the plane are not broadened. One notes that an *endo*-methyl shift would lead to the *same* set of identities as an *exo*-methyl shift, except for the migrating methyl itself. In the camphene hydro cation, it is impossible to specifically assign the two high-field methyl groups and therefore to decide which migration is occurring. However, using specifically deuterated analogs,²⁴ one can show that this *first* broadening process is in fact due to the *exo*-methyl migration.

(24) R. P. Haseltine and T. S. Sorensen, *Can. J. Chem.*, **53**, 1067 (1975).

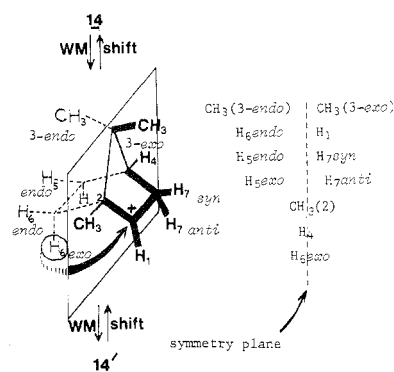


Figure 7.

Starting at about -70°C , the remaining sharp methyl peak broadens (Figure 5). The nature of this second, slower rearrangement is more difficult to ascertain since most NMR peaks are still broad as a result of the *exo*-methyl shift. From Vaughan's acid-catalysis results one would anticipate either the 6,2-hydride shift in the isobornyl cation 13 or an *endo*-methyl shift in 14. NMR line-broadening and double-resonance techniques yield results which are similar to those of a complete isotopic labeling experiment, and one can discriminate between these choices. This second rearrangement is in fact the one involving the 6,2-hydride shift; the corresponding C_s symmetry and the symmetry-derived group equivalences are shown in Figure 7. We cannot detect any *endo*-methyl shift in the observable camphene hydro cation.

Rearrangement rates for both processes can be derived from the NMR line-broadening data (see matching curves in Figure 5). One can now *quantitatively* compare the ratio under both superacid and acid-catalysis conditions; the following data pertain to 137°C , the superacid values being extrapolated from lower temperatures:

Acid catalysis²¹

$$\frac{k(\text{camphene racem. via } \textit{exo}\text{-methyl shift})}{k(\text{camphene racem. via WM-6,2-WM shift})} = \frac{2.8 \times 10^{-5} \text{ s}^{-1}}{2.2 \times 10^{-5} \text{ s}^{-1}} = 1.3$$

Superacid-observable ions²⁵

$$\frac{k(\textit{exo}\text{-methyl shift})}{k(\text{WM-6,2-WM shift})} = \frac{6 \times 10^7 \text{ s}^{-1}}{2 \times 10^6 \text{ s}^{-1}} = \text{ca. } 30$$

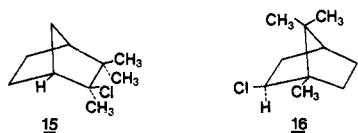
In both cases, the *exo*-methyl shift is faster, but under superacid conditions, the ratio is somewhat higher.

There are several further points of interest. One is that the rates derived for the actual ion \rightarrow ion rearrangements at a temperature (137°C) where the overall acid-catalysis reactions occur on a conveniently measured time scale are extremely rapid.

Furthermore, with the help of related data,¹⁴ one can calculate that the observable tertiary camphene hydro cation (14) is more stable than the secondary isobornyl cation (13) by 5.5 kcal/mol and that the WM barrier for the isobornyl (13) \rightarrow camphene hydro cation (14) conversion is <4 kcal/mol. At 100°C , this translates very approximately to a rate constant of $>10^{10} \text{ s}^{-1}$. If these

(25) The ΔG^\ddagger barriers are 8.3 kcal/mol for the methyl shift and 10.7 kcal/mol for the WM-6,2-WM shift. In the temperature extrapolation, there is a considerable error propagation.

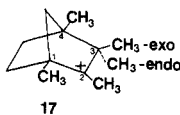
rates are applicable to "normal" organic or aqueous solvents, one would conclude from this that it would be extremely difficult to carry out a nucleophilic substitution on the isobornyl system, under irreversible conditions, *without* rearrangement of the intermediate isobornyl cation to the camphene hydro cation (as is found). On the other hand, camphene hydrochloride (15) can be converted to the thermodynamically more stable isobornyl chloride (16) under reversible condi-



tions, since the camphene hydro cation (14) \rightarrow isobornyl cation (13) rearrangement is "only" uphill by 5.5 kcal/mol plus the <4 kcal/mol "barrier", for a total barrier of <9.5 kcal/mol. In the fenchyl system, such a cation \rightarrow cation barrier was seen to be readily overcome in formic acid as the solvolysis medium (Figure 3).

A Comparison of Exo and Endo 3,2-Methyl Shifts

Using somewhat unnatural terpene analogs of the camphene hydro cation, with "extra" methyl groups at the 1 and 4 position, for example, 17, we have been able



to quantitatively examine the ratio of the exo and endo 3,2-methyl shifts under both acid-catalysis (using H-D exchange) and superacid-observable ion conditions.²⁴ The results are summarized below.

Acid catalysis (1% H₂SO₄-acetic acid at 25 °C)

$$\frac{k(\text{exo shift})}{k(\text{endo shift})} = \frac{1 \times 10^{-4} \text{ s}^{-1}}{5 \times 10^{-8} \text{ s}^{-1}} = 2 \times 10^3$$

Superacid-observable ions (extrapolated rates to 25 °C)

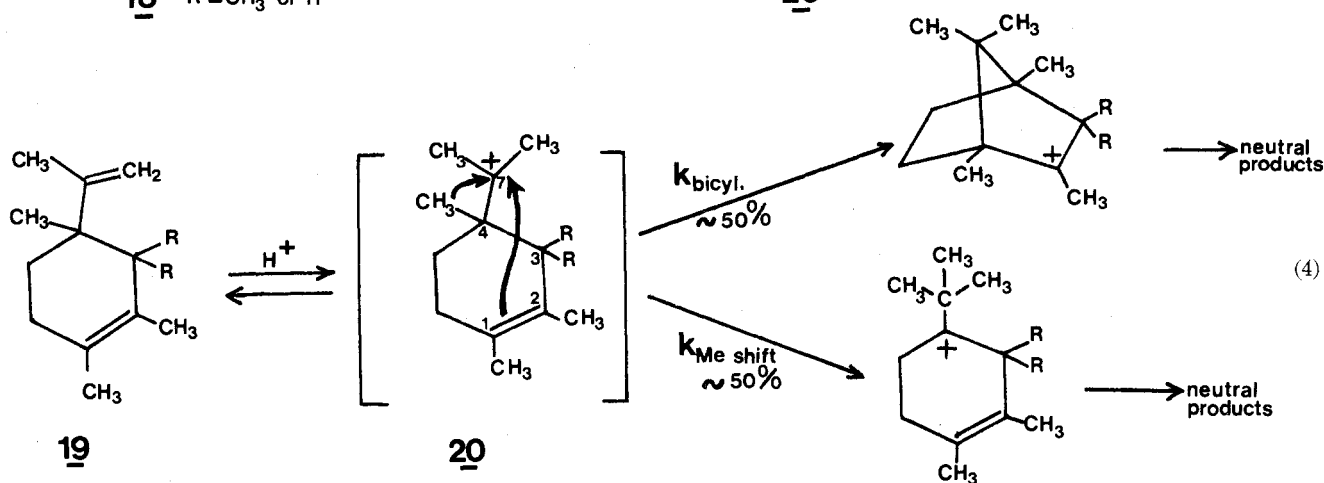
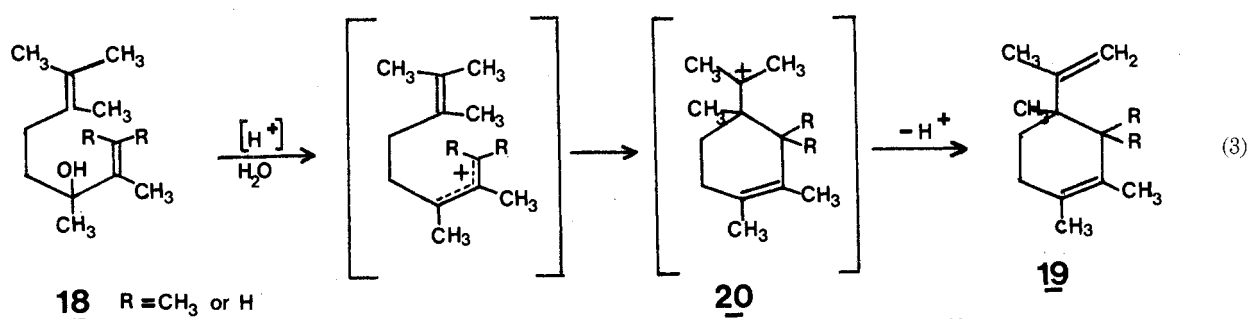
$$\frac{k(\text{exo shift})}{k(\text{endo shift})} = \frac{10^6 \text{ s}^{-1}}{10^{-2} \text{ s}^{-1}} = 10^8$$

Thus we see that, as for the camphene comparison of exo 3,2-methyl shift *vs.* WM-6,2-WM shift, there appears to be a directional correlation of the superacid chemistry and the acid-catalysis results, but the quantitative ratios are somewhat different. In order to provide a different comparison and still retain relevance to terpene chemistry, the competition between a cationic π ring closure and a methyl migration was examined.

Cationic Terpene Bicyclization Reactions

Competition between 1,7 π ring closure and methyl migration, in terpene-related systems, was first noted when we carried out biogenetic-like cyclizations, under acid-catalysis conditions, starting with precursors of the linalool (18) type.²⁶ The first cyclization (eq 3) to form the six-membered monocycle 19 involves no competition amongst cationic rearrangement processes, and this is consistent with the biogenetic results. However, in the further rearrangement of 19, there appears to be a fine dividing line between methyl migration and π bicyclization in the cationic intermediate 20 (eq 4). Both the methyl migration and bicyclization are irreversible under our particular experimental conditions, so that the product ratios are a true indication of the rate split in the cationic intermediates. Under these conditions, the split is about 50:50.

When one adds the diene 19 to superacids, no cation 20 is observed, only the further rearrangement ions. In this case, one observes about 50% of bicyclic ions and 50% of a monocyclic cation derived from the methyl shift route (actually an allylic cyclohexenyl cation). In this case also, the reaction is irreversible at the low



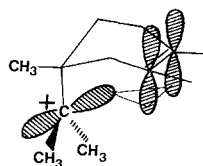
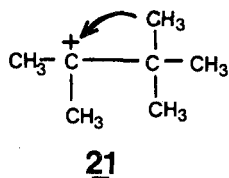


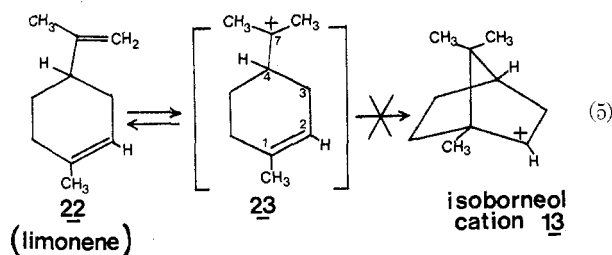
Figure 8.

temperatures involved. Note that here one does not know the actual rate of either the methyl migration or the bicyclization reaction in the observable ion case because the activation energy ΔG^\ddagger for either reaction must be less than about 10–12 kcal/mol.¹⁵ In actual fact, one suspects by comparison to rates observed in simple systems like the observable 2,3,3-trimethyl-2-butyl cation **21**²⁷ that methyl migration in **20** would probably



have a barrier of less than 3.5 kcal/mol. This then puts the same upper limit on the barrier for the bicyclization reaction in **20**.

This preoccupation with numbers may not be entirely frivolous. A postulated biosynthetic route to the isoborneol terpene system involves this carbocation bicyclization reaction. The natural terpene monocyclic skeleton **22**, in contrast to our synthetic analogs with a methyl group at C-4, cannot (or has not) been made to bicyclize under acid-catalysis conditions²⁸ (eq 5). We



suggest that the C-4 methyl group functions by allowing the cationic center to exist in the ground state as the desired pseudoaxial conformation (Figure 8) and that, from this energy base level, the ΔG^\ddagger barrier for bicyclization is <3.5 kcal/mol. With a C-4 hydrogen, as in **23**, the axial conformation of the cationic group will surely be several kilocalories per mole less stable than the unreactive equatorial conformation, thus making the overall barrier for bicyclization this much higher. This therefore tips the cationic rearrangement balance in favor of the C-4 migration route.

The rate comparisons in this section involve two quite different cationic rearrangement processes (π bicyclization vs. a methyl shift). Moreover, they both have very fast rearrangement rates and yet, once again, one finds excellent correlation between the acid catalysis and the superacid results. Our actual barriers estimated for the π bicyclization and the methyl migration processes

(26) T. S. Sorensen, unpublished results.

(27) M. Saunders, private communication to H. C. Brown and circulated by Brown.

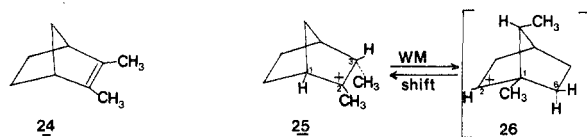
(28) R. S. Bly and H. L. Dryden, *Chem. Ind. (London)*, 1287 (1959); C. F. Wilcox and S. S. Chibber, *J. Org. Chem.*, **27**, 2332 (1962); F. Cramer and W. Rittersdorf, *Tetrahedron*, **23**, 3015 (1967); G. Le Ny, *C.R. Hebd. Seances Acad. Sci.*, **251**, 1526 (1960).

($\Delta G^\ddagger < 3.5$ kcal/mol, $k \sim 10^9$ – 10^{10} s⁻¹ at 25 °C) would perhaps indicate that proton loss from the cation **20** would be competitive with both rearrangements. Indeed there is some evidence that some of the rearranged products are formed “directly” from the acyclic material **18**.

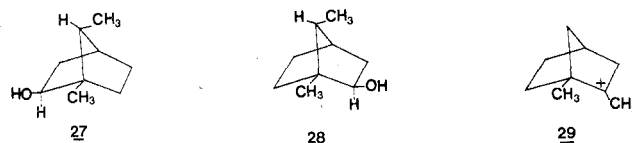
The Santene Cation System vis-à-vis the Complete Dimethyl-2-norbornyl Cation Graph

In concluding this Account, let us explore some the possibilities for carrying out cation \rightarrow cation terpene rearrangements which have no previously known solvolysis or acid-catalysis counterpart. Such reactions were seen in the fenchene rearrangements, where the rearrangement barrier (18.5 kcal/mol) leading to cation **7** appears to be too high for acid-catalysis conditions, but where the rearrangement occurs readily at -15 °C under superacid-observable ion conditions.

Cationic rearrangements involving santene **24**, a C₉ sandalwood oil terpene, are well known.^{29,30} In acid-catalyzed hydrations of **24**, under reversible conditions, this molecule is protonated from the exo side to yield the intermediate 2,3-endo-dimethyl-2-norbornyl cation (**25**), which, like the camphene hydro cation (**14**), is able to undergo an “uphill” Wagner–Meerwein shift (predicted $\Delta G^\ddagger < 9.5$ kcal/mol) to yield a very low population of the secondary 1,anti-7-dimethyl isomer **26**.



Nucleophile capture by **26** leads to the known rearrangement product **27**.



One would also predict, from the fenchene and camphene results, that under slightly more strenuous conditions one would get a 6,2-hydride shift in **26** (predicted $\Delta G^\ddagger_{\text{overall}} \sim 11$ kcal/mol), thereby leading upon nucleophile capture to some of the 1, syn-7-dimethyl alcohol **28**, as is indeed the case.

In observable ion studies, the superacid protonation of santene at low temperature yields cation **25**, but at -40 °C this ion rearranges to the 1,2-dimethyl-2-norbornyl cation **29**, $\Delta G^\ddagger = 17.4$ kcal/mol. This rearrangement has never been reported in acid-catalysis studies. It is apparent that even a 17.4 kcal/mol cation \rightarrow cation barrier is quite formidable under acid-catalysis conditions. However, before the irreversible transformation of **25** to **29** occurs, one can deduce from NMR line broadening in **25** that the cation undergoes the previously mentioned three-step sequence, WM shift–6,2-hydride shift–WM shift, with $\Delta G^\ddagger \sim 12$ kcal/mol,³¹ this process accounting for all the known acid-catalyzed rearrangements of this system.

This three-step WM shift–6,2-hydride shift–WM

(29) F. W. Semmler and K. Bartelt, *Ber.*, **41**, 128 (1908).(30) O. Aschan, *Ber.*, **40**, 4923 (1907).(31) A. J. Jones, E. Huang, R. Haseltine, and T. S. Sorensen, *J. Am. Chem. Soc.*, **97**, 1133 (1975).

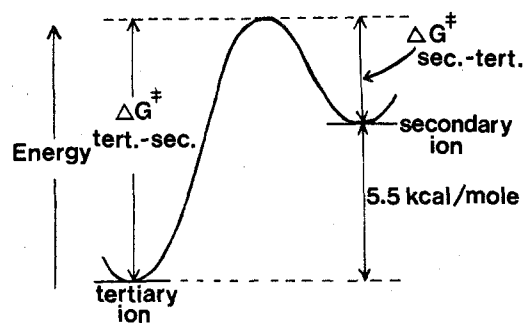


Figure 9.

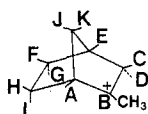
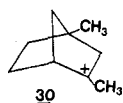


Figure 10. The ten positions A, C, D, E, F, G, H, I, J, and K include one CH_3 and nine protons. There are therefore a total of ten isomeric possibilities, including the santene cation (25) (BD) and the 1,2-dimethyl isomer 29 (AB).

shift process has an almost constant overall barrier in all the norbornyl systems which we have studied, thus 11.3 for the 2-methyl-2-norbornyl cation, 11.1 for 2,4-dimethyl-2-norbornyl cation, 10.7 for camphene hydro cation, ca. 11.2 for α -fenchene hydro- β -fenchene hydro cation interconversion, and 11.9 kcal/mol in the santene cation case. This suggests the possibility that one might be able to assign ΔG^\ddagger parameters (or constants) for all the various possible cationic rearrangements in these norbornyl terpene systems (see Figure 2 for the various possible rearrangement types). Most of these ΔG^\ddagger barriers can be estimated from data obtained from various observable norbornyl cation rearrangements,¹⁴ and a compilation is presented in Table I.

One key parameter is the energy difference between tertiary (methyl) and secondary 2-norbornyl cations, estimated as 5.5 kcal/mol.¹⁴ Thus, if one knows the barrier for a tertiary-secondary process of some kind, then the reverse reaction barrier can also be estimated. This is shown schematically in Figure 9.

Having set up this ΔG^\ddagger parameter list, one then needs an independent assessment of these, hopefully an assessment using previously uninvestigated systems for which one can make predictions before actually carrying out the experimental observations. In this regard, the other tertiary dimethyl-2-norbornyl cation isomers of the santene cation seemed a logical choice (Figure 10). All of the isomers in Figure 10 were synthesized³² and, as it turned out, all these eventually rearranged in superacids to the 1,2-dimethyl isomer 29, including the santene system 25, as already mentioned. The 1,2-dimethyl isomer 29 is therefore the thermodynamically most stable of all these, but the 2,4-dimethyl isomer 30



was found to exist in a metastable situation. It is more stable than all the remaining eight isomers, including the santene cation. Furthermore, the barrier from the 2,4-dimethyl isomer 30 to the 1,2-dimethyl isomer 29

Table I

Major rearrangement process	Operator symbol	Subdivision considered	Assigned ΔG^\ddagger value, kcal/mol
Wagner-Meerwein (WM) shift	1	1TT ^a	<4
		1TS	<9.5
		1ST	<4 (<9.5) ^b
		1SS	<4 (<9.5)
Exo 3,2-substituent shift	2H ^c	2HTT ^c	7.2
		2HTS	15.2
	2M ^c	2HST	9.7 (15.2)
		2HSS	11.4 (16.9)
		2MTT ^c	8.9
		2MTS	13.1
		2MST	7.6 (13.1)
		2MSS	14.5 (20) ^d
Endo 6,2-hydride shift	3	3TT	7.2
		3TS	11.3
		3ST	5.8 (11.3)
		3SS	5.8 (11.3)
Double Wagner-Meerwein shift ^e	4	4TT	18.0
		4SS	12.5 (18.0)
Endo 3,2-substituted shift ^f	5	5HTT	14.0

^a T = tertiary, S = secondary, the first letter refers to reactant ion, the second to product. ^b The bracketed figures are relative to a tertiary cation energy base, and these figures were used in the computer treatment. ^c H = hydrogen, M = methyl. ^d This figure has been drastically revised upward from the 13.1 used in the original paper.³² ^e A shift of the 1,7 bond to become 2,7, followed by a shift of the original 2,3 bond to become 1,3. ^f All other subdivisions are thought to have $\Delta G^\ddagger > 20$ kcal/mol.¹⁴

is the highest of all the mutual interconversion barriers. One can therefore examine the fate of the remaining eight isomers (in terms of the ΔG^\ddagger barriers in Table I) and ask two questions: (1) Will a given cation X of these remaining eight isomers rearrange to 29, or to 30? (2) Does the observed rearrangement rate for whatever process we find, i.e., cation X \rightarrow 29 or X \rightarrow 30, tally with that calculated from the ΔG^\ddagger parameters? These questions relate to the predictive use of these ΔG^\ddagger parameters in actually deciding which pathway has the lowest overall rearrangement barrier, starting from a given cation and ending with either 29 or 30.

In order to answer these questions, one must know all of the possible routes from a given isomer X to either 29 or 30 and then have a method for quickly determining which of these routes has the lowest overall barrier. The problem of doing this by hand is rather like that of an explorer standing at the junction of two mountain valleys in a sea of mountains and trying to decide which route will eventually offer the lowest overall barrier out to the plains. One solution is to do a complete mapping of the area, showing all allowable passes (or individual rearrangement steps). The ΔG^\ddagger barriers can then be equated with the heights of each particular pass. One can then use a computer to search out that route with the lowest barrier. An easier approach from a cartographer's point of view, but which is more restrictive, is to focus on where one is and where one wants to get to, and ask the computer to perform random walk pro-

(32) R. Haseltine, K. Ranganayakulu, N. Wong, and T. S. Sorensen, *Can. J. Chem.*, **53**, 1901 (1975).

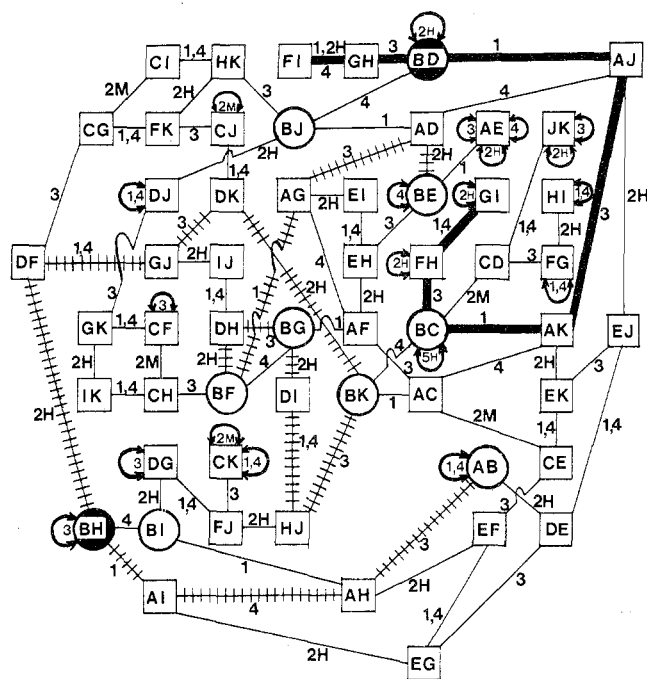


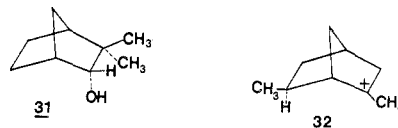
Figure 11. The dimethyl-2-norbornyl cation graph.

cesses until the goal is attained. In practice, one allows a restricted total number of steps (or random walks) and within this total, looks at all of those routes which were successful. For the case in hand, both procedures have been used.^{32,33}

The complete racemic map³⁴ for the dimethyl-2-norbornyl cation system contains 45 secondary cations, which will appear only as very low population intermediates and which we can regard as high valleys, together with the 10 tertiary cations, regarded as low valleys (Figure 11). We can equate valley height differences with the ca. 5.5-kcal/mol energy difference between the secondary and tertiary cations. In Figure 11, the tertiary ions are shown as circles and the secondary ions as squares, with the letters in these describing the positions of the two methyl groups, using the Figure 10 designations. The numbers on the interconnecting lines refer to the coding of the rearrangement types, given in Table I.³⁵ To translate these numbers into barriers, one refers to this table and also makes appropriate note of whether one is *starting* with a secondary or tertiary cation and also whether one is *ending* with a secondary or tertiary species.

Like most maps, these chemical examples become rather cluttered,³⁷ but we want to show two examples of how they can be used. Firstly, the santene cation (25) is identified as BD (on the top line of Figure 11), and the

explorations possible from this odoriferous valley under "normal" acid-catalysis conditions are indicated by heavy lines. We have made the assumption here that acid-catalysis conditions will surmount ΔG^\ddagger barriers of 11 kcal/mol or less, based on previous experience. One notes that the known rearrangement products derive from cations AJ and AK, but there appears to be no kinetic reason why one should not have obtained alcohol products related to ions GH, FI, FH, and GI, and one can surmise that alcohol thermodynamic factors must be important in this case. Incidentally, the terpene-derived compound, camphenilol (31), has been dehydrated and rearranged in acid to give santene.³⁸ This transformation, $CD \rightarrow BC$, is easily accessible in this direction, with ΔG^\ddagger estimated to be 7.6 kcal/mol, but presumably the reverse reaction is not, since ΔG^\ddagger for $BC \rightarrow CD$ is estimated to be 13.1 kcal/mol.



The second point to be made, concerning the Figure 11 map, is that all valleys (or cations) are kinetically accessible and populated under superacid-observable ion conditions at temperatures below 0 °C. With 10^{23} cation molecules in solution, all possible routes between any two cations will be followed by at least some molecules, but one can describe pathways which >99% of the molecules will follow. This lowest barrier pathway is often calculated to *not* be, by any means, the shortest pathway (in terms of the number of individual steps). For example, the 2,exo-6-dimethyl-2-norbornyl cation (32) (BH in Figure 11) is predicted to rearrange to BE, the 2,4-dimethyl isomer 30, rather than directly to AB (cation 29), and the preferred route contains 12 steps³⁹ (overall calculated $\Delta G^\ddagger = 15.2$ kcal/mol). In contrast, the shortest route to AB is only three steps, but ΔG^\ddagger (calculated) is 18.0 kcal/mol. Both routes are shown in the Figure 11 map using a hatched "railroad line". Experimentally, one does observe that BH (cation 32) rearranges first to BE (cation 30), with the experimental ΔG^\ddagger barrier being 15.3 kcal/mol. The calculated-observed agreement in the case of the other isomer interconversions in Figure 11 was also quite good.

Epilogue

If we can make one concluding plea in this Account, it would be to the effect that superacid chemistry results seem in fact to be relevant to what goes on in the ordinary chemical laboratory. Thus we hope that a con-

(33) We thank Professor C. J. Collins for a copy of his computer-derived graph for the dimethyl-2-norbornyl system: C. K. Johnson and C. J. Collins, *J. Am. Chem. Soc.*, **96**, 2514 (1974); C. J. Collins, C. K. Johnson, and V. F. Raaen, *ibid.*, **96**, 2524 (1974).

(34) The norbornyl cation is chiral, and a consideration of this would have led to a total of 110 separate cations. Berson has made elegant use of this fact in studying the rearrangements of monomethyl norbornyl cations: J. A. Berson, R. G. Bergman, J. H. Hammons, and A. W. McRowe, *J. Am. Chem. Soc.*, **89**, 2581 (1967).

(35) All the degenerate rearrangement processes are shown with curved lines, and a number of these have been detected by NMR line broadening.³⁶ In Table I, the only endo 3,2-shift process considered was where one starts and ends with a tertiary ion (5HTT). The only possible process of this type in a dimethyl ion is the degenerate shift in BC.

(36) R. Haseltine, N. Wong, T. S. Sorensen, and A. J. Jones, *Can. J. Chem.*, **53**, 1891 (1975).

(37) The trick in setting out these graphs is to initially ignore all nodes with a valence of one or two and concentrate on getting an arrangement of the remaining nodes having the fewest crossing lines. There is no mathematical theorem to calculate the fewest number of crossing lines in a system of our complexity, and it may even be desirable to compromise on this point (as is done in Figure 11) in the interests of minimizing two other variables of practical interest, the total area of the graph and the total length of all connections. There is also a theorem stating that points can always be connected by straight lines, but there may be occasions when this is unwieldy.

(38) H. Meerwein, *Justus Liebigs Ann. Chem.*, **504**, 134 (1914); S. V. Hinitikka and G. Komppe, *Bull. Soc. Chim. Fr.*, **21**, 14 (1917).

(39) To give an idea of why a computer is useful in finding all the possible paths, consider that, in the transformation of 32 to 30, there are, in addition to the preferred 12-step route, 3 routes of 7 steps, 8 of 8 steps, 30 of 9 steps and 34 of 10 steps. There are, in fact, 2 12-step routes with equal (calculated) barriers, the one shown in Figure 11 and a variant of this whereby $BK \rightarrow AC \rightarrow AF \rightarrow BG$ instead of $BK \rightarrow HJ \rightarrow DI \rightarrow BG$.

nection has been established between reactions that occur under the "normal" conditions of acid catalysis and solvolysis on the one hand and in superacid solutions on the other.

I wish to thank my co-workers K. Ranganayakulu, Rollin Haseltine, Alan Jones, Normal Wong, and Eileen and Lucy Huang. I am grateful to the National Research Council of Canada for financial support.

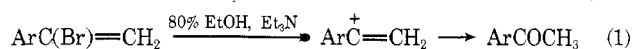
Solvolysis of α -Arylvinyl Derivatives

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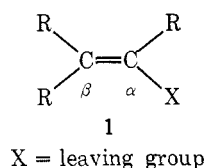
Following the pioneering work of Grob and Cseh, who showed that α -bromo-para-substituted styrenes solvolyze via the SN1 route¹ (eq 1), the solvolysis of vinylic



compounds has flourished in recent years. Work in the field has been extensively reviewed.²

Although it is recognized that solvolyses of vinylic and saturated compounds show qualitative similarities, there are differences between the two systems, especially in regard to aryl-substituted substrates in hybridization, conjugation, and steric effects, in stereochemistry and in the presence of potentially alternative reaction centers. Either of these factors alone, or their interaction, gives vinylic solvolysis some special characteristics.

The sp^2 hybridization of the vinylic carbon of a vinyl compound (1) increases its electronegativity,



strengthens the bond to the leaving group, and infers a lower inherent solvolytic reactivity for vinylic than for saturated systems. A compensation is that highly activating substituents may be used, enabling observation of phenomena which may escape observation in the solvolysis of highly reactive sp^3 derivatives.

The double bond can transmit electronic effects of β substituents, and it is also a potential reaction center by itself. These features, as well as the acidity of the vinylic hydrogens, may favor competing reaction routes such as E2 elimination and electrophilic and nucleophilic addition-elimination pathways over the SN1 route.

Depending on structure, the double bond conceivably may conjugate with any or all the four substituents on the vinylic carbons. Conjugation with the leaving group

or with an α -aryl group will reduce the ground-state energy, and the solvolytic reactivity will be lower than that of saturated compounds. Conjugation with β -aryl groups may be important in their rearrangement across the double bond. Obviously, any conjugation with aryl groups is highly dependent on the planarity of the system and hence on the steric interactions of the double bond substituents.

The double bond is shorter than a single bond and all the vinylic substituents are in the same plane. Both effects increase the crowding of the substituents compared with the saturated analogues. This should be reflected in phenomena which are sensitive to steric effects, such as steric acceleration and steric inhibition of solvation.

A stereochemical difference exists between the vinylic and the saturated systems. The *R* and *S* enantiomers of an sp^3 -substituted system solvolyze at identical rates and the derived sp^2 cation captures nucleophiles from both sides of the vacant orbital at identical rates. The *E* and *Z* sp^2 isomers solvolyze at different rates, and the vinyl cation captures nucleophiles from the two sides of the vacant orbital at different rates.

One purpose of this Account is to show that these facts lead to quantitative differences between the solvolysis of saturated and α -arylvinyl derivatives, especially in those substituted by bulky β substituents. Consequently, the use of criteria for assigning the detailed mechanism and for estimating the polarity of the transition state, which are applicable to saturated systems, may give the wrong answer in vinylic systems. This is demonstrated by the ambiguity of several mechanistic criteria when applied to solvolysis of the trianisylvinyl system $\text{An}_2\text{C}=\text{C}(\text{X})\text{An}$, where An represents a *p*-methoxyphenyl group. The low sensitivity to solvent and leaving group effects, as reflected by the Winstein-Grunwald *m* value of 0.34 when X = Br,^{3a} and a $k_{\text{OTs}}/k_{\text{Br}}$ ratio of 32,⁴ suggest a solvent assisted (k_s)⁵ or a neighboring group assisted (k_{Δ})⁵ solvolysis. How-

(1) C. A. Grob and G. Cseh, *Helv. Chim. Acta*, **47**, 194 (1964).

(2) (a) M. Hanack, *Acc. Chem. Res.*, **3**, 209 (1970); (b) C. A. Grob, *Chimia*, **25**, 87 (1971); (c) G. Modena and U. Tonellato, *Adv. Phys. Org. Chem.*, **9**, 185 (1971); (d) P. J. Stang, *Prog. Phys. Org. Chem.*, **10**, 205 (1973); (e) L. R. Subramanian and M. Hanack, *J. Chem. Educ.*, **52**, 80 (1975).

(3) Z. Rappoport and A. Gal: (a) *J. Am. Chem. Soc.*, **91**, 5246 (1969); (b) *J. Org. Chem.*, **37**, 1174 (1972).

(4) Z. Rappoport and J. Kaspi: (a) *J. Am. Chem. Soc.*, **92**, 3220 (1970); (b) *J. Chem. Soc., Perkin Trans. 2*, 1102 (1972).

(5) P. v. R. Schleyer, J. L. Fry, L. K. M. Lam, and C. J. Lancelot, *J. Am. Chem. Soc.*, **92**, 2542 (1970).

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