Molecular Rearrangements. XXX. Applications of an Algebraic–Graphical Model for Analyzing Rearrangements of Bicyclo[2.2.1]heptyl Cations[1]

Clair J. Collins,* Carroll K. Johnson, and Vernon F. Raaen

Contribution from the Chemistry Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37830. *Received August 21, 1973*

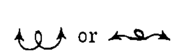
Abstract: The algebraic model, coset graphs, and computer program previously described[1b,2] have been applied to two specific chemical problems: (1) the rearrangements,[6,7] in sulfuric acid, of 1-methyl-7,2-carbolactone (**1**) and of 5-methyl-2-*endo*-norbornenecarboxylic acid (**4**), and (2) the rearrangements,[9] in SO_2ClF–FSO_3H, of the fenchyl cation. The use of coset graphs is illustrated. In each study described, important mechanistic information resulted from the use of the model and computer program. We also discuss how the method can be used in the design of isotopic tracer experiments.

In an accompanying paper[2] we described an algebraic model for the rearrangements of 2-bicyclo[2.2.1]-heptyl cations. We included only three of the several possible rearrangements these cations are known to undergo but indicated[2] that the model can easily accommodate additional processes. The three included are the Wagner–Meerwein rearrangement,[3a] the 6,2-hydride shift,[3b] and the 3,2-hydride shift.[3c] The model will accommodate both substituent and isotopic replacement of the 11 hydrogens of the parent norbornyl cation and, in additon, is applicable to isotopic substitution in the carbon skeleton. The part which relates to the substitution of the norbornyl hydrogens is based on permutations of the letters A–K, which designate specific positions in the two enantiomers shown in Figure 1. One enantiomer is arbitrarily designated the "right-handed" or (+) form, and its mirror image is then the "left-handed" or (−) form. If, for example, the substituents are methyl groups, the symbols A+, EI−, and BJK+ describe the appropriate enantiomers of the 1-methyl-2-norbornyl, 4-*exo*-6-dimethyl-2-norbornyl, and 2,7,7-trimethylnorbornyl-(fenchyl) cations shown in Figure 2. When the substituents are different, as in the 3-*exo*-hydroxy-2-methyl-2-norbornyl cation, one group is arbitrarily designated first, and if we give the hydroxyl group priority, the ion becomes DB+ (also shown in Figure 2). Just as different substituents are identified by the order in which the symbols are written, so are isotopic labels in like substituents. For example, consider protonated (+)-camphor, which becomes BAJK+, the hydroxyl group being designated first. The two forms of labeled, protonated (+)-camphor,[4] in which the 7-*syn*- and 7-*anti*-methyls are labeled with carbon-14, can also be designated BAJK+, J and K marking the two carbon-14 tags, which are distinguished (Figure 2) by (*) and (‡). When BAJK+ undergoes racemization by the generally accepted[1b,4,5] mechanism, the unlabeled methyl in the no. 1 bridgehead position (site A) of (+)-camphor goes to the 7-syn position, site J, of (−)-camphor, the 7-*syn*-methyl at site J goes to the no. 1 bridgehead position (site A), and the 7-*anti*-methyl on site K remains in the 7-anti position. Thus the notation BAJK+ ⇄ BJAK− and the declared ordering (OH, CH_3, $*CH_3$, $‡CH_3$) completely describe the isotopic and stereochemical transformations shown conventionally above each appropriate symbol (Figure 2).

We also discussed[2] the construction and use of coset graphs and the fact that the graphs can be derived with the aid of a computer by using the PL/I ORNOCARE program.[2] These graphs can be of two types: (1) a complete coset graph of all possible intermediates and the specific reactions which interconnect them, and (2) an abbreviated coset graph in which enantiomers (handedness) and "transposition" isomers[2] are superimposed. The complete coset graph of the disubstituted norbornyl cation contains 220 nodes for 220 intermediates; it is easy to use but too large and complicated to be duplicated here. We therefore show in Figure 3 the abbreviated coset graph for the disubstituted norbornyl cation in which Wagner–Meerwein rearrangement (*W*) and 3,2- (*3*) *exo*- and 6,2- (*6*) *endo*-hydride shifts are included[2,3] and which contains only 55 nodes but portrays all 220 intermediates. Some simple rules must be followed in using Figure 3, and these are (1) the "handedness" of an intermediate changes between each double arrow, *e.g.*

$$\text{AJ+} \xleftrightarrow{6} \text{AK−}$$

(2) the transpose sign



(1) (a) Research sponsored by the U. S. Atomic Energy Commission under contract with Union Carbide Corporation. (b) For a preliminary report of an application of the model, see C. J. Collins and C. K. Johnson, *J. Amer. Chem. Soc.*, **95**, 4766 (1973). (c) Paper XXIX in this series: C. J. Collins and B. M. Benjamin, *J. Org. Chem.*, 37, 4358 (1972).

(2) C. K. Johnson and C. J. Collins, *J. Amer. Chem. Soc.*, **96**, 2514 (1974).

(3) (a) G. Wagner, *J. Russ. Phys. Chem. Soc.*, 31, 680 (1899); H. Meerwein, *Justus Liebigs Ann. Chem.*, **405**, 129 (1914); (b) H. Meerwein and F. Montfort, *ibid.*, **435**, 213 (1924); N. J. Toivonen, *Suom. Kemistilehti B*, **24**, 62 (1951); W. E. Doering and A. P. Wolf, *Perfum. Essent. Oil Rec.*, **42**, 414 (1951); J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *J. Amer. Chem. Soc.*, **76**, 4501 (1954); (c) for key references to 3,2-hydride shift, see ref 2 and also J. Berson in "Molecular Rearrangements," Part 1, P. de Mayo, Ed., Wiley-Interscience, New York, N. Y., 1963, Chapter 3.

(4) O. R. Rodig and R. J. Sysko, *J. Amer. Chem. Soc.*, **94**, 6475 (1972).

(5) A. M. T. Finch, Jr., and W. R. Vaughan, *J. Amer. Chem. Soc.*, **91**, 1416 (1969); T. Miki, M. Nishikawa, and P. H. Hagiwara, *Proc. Jap. Acad.*, 31, 718 (1955).

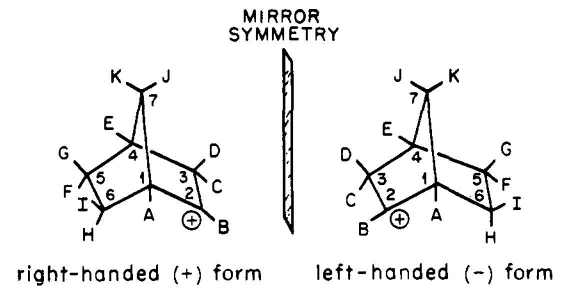


Figure 1. Notational convention used to designate positions on the enantiomers of the 2-norbornyl cation.

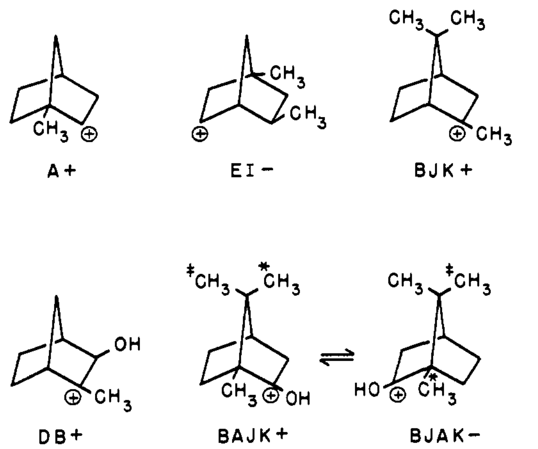


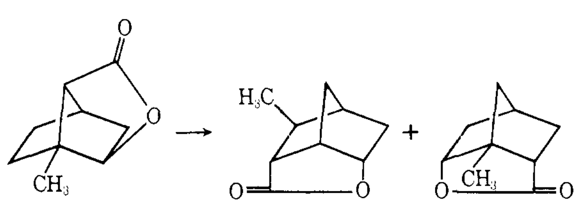
Figure 2. Several typical bicyclo[2.2.1]heptyl (norbornyl) cations and the symbols describing them.

requires transposition of the letters involved *e.g.*

(BC) 3 means (BC+) $\overset{3}{\longleftrightarrow}$ (CB−) or (CB+) $\overset{3}{\longleftrightarrow}$ (BC−)

and (3) the dotted lines connecting the nodes mean that the 3,2-exo shift might not occur if the 3-exo position contains other than hydrogen or one of its isotopes.

We will now illustrate how we used the model[2] in specific chemical problems. First, consider the rearrangements,[6,7] in sulfuric acid, of 1-methyl-7,2-carbolactone **1** to the two lactones **2** and **3**. The



1 **2** **3**

carbocation first formed directly from **1** (Figures 3 and 4) is AJ+, since we specify that the methyl is named before the carboxyl. (The node AJ is in row 6, column 8 of Figure 3.) All cations which can lactonize must have J or H as the second symbol, since the carboxyl group can undergo ring closure only from the 6-endo or 7-syn positions. In the lower right-hand portion of Figure 3 we have emphasized with heavy lines the most economical routes available for rearrangement of AJ

(6) S. Beckman, H. Geiger, and M. Schaber-Kiechle, *Chem. Ber.*, **92**, 2419 (1959); H. Geiger and S. Beckmann, *Justus Liebigs Ann. Chem.*, **722**, 219 (1969).

(7) J. A. Berson and P. W. Grubb, *J. Amer. Chem. Soc.*, **87**, 4016 (1965).

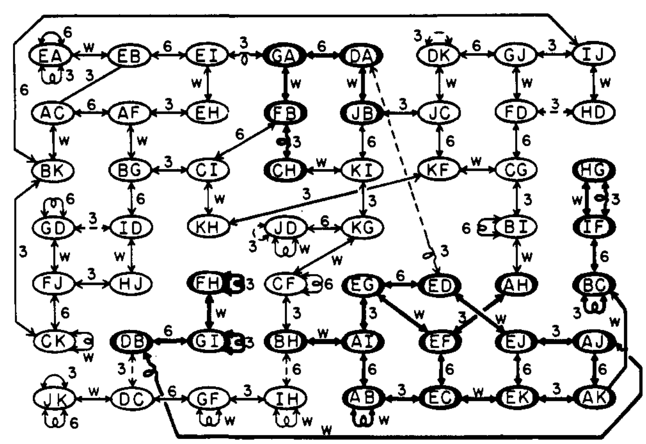


Figure 3. Coset graph for disubstituted norbornyl cations. (a) Handedness and transposition isomers are superimposed so that 55 rather than 220 nodes are required. (b) Only three processes (WM, 62H, 32H) are considered. (c) This graph differs from Figure 5 of ref 2 in that disallowed 6,2-Me or 6,2-COOH shifts have been removed.

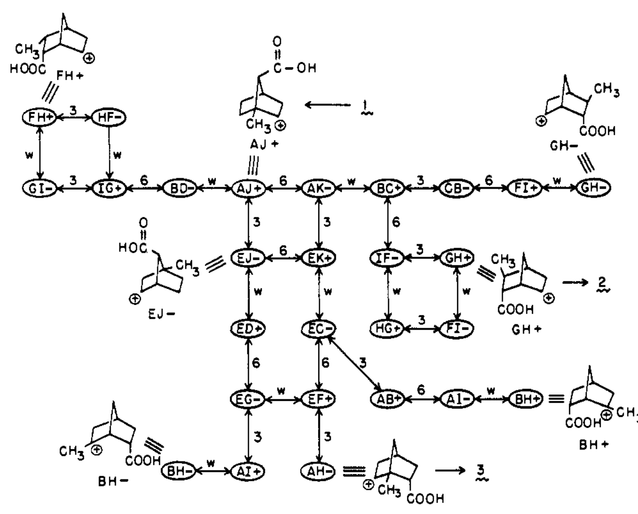
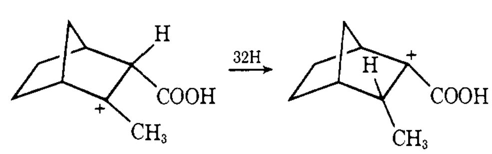


Figure 4. A portion of the coset graph of Figure 3 showing AJ+ and its relation to several nearby cations capable of lactonization.

to lactonizable cations, and these routes lead (in six steps or less) to AH, FH, EJ, BH, and GH. This relevant portion of Figure 3 is redrawn, in Figure 4, to show the chirality of each cation. If we presume, for steric reasons (two adjacent cis, endo groups), that cation FH+ is less stable than the other structures of Figure 4 and that the formation of GH− is improbable because it requires the highly unlikely (because of the strong polarization of the carbonyl group) 3,2-hydride shift BC+ → CB−, then only five possibilities remain,



BC+ CB−

namely the lactones from EJ−, GH+, AH−, and BH±. Two of these (GH+ and AH−) do, in fact, lactonize[6] to yield **2** and **3**, respectively. The results of Beckmann and Geiger[6] were obtained with racemic materials, so the configurational relationships of and

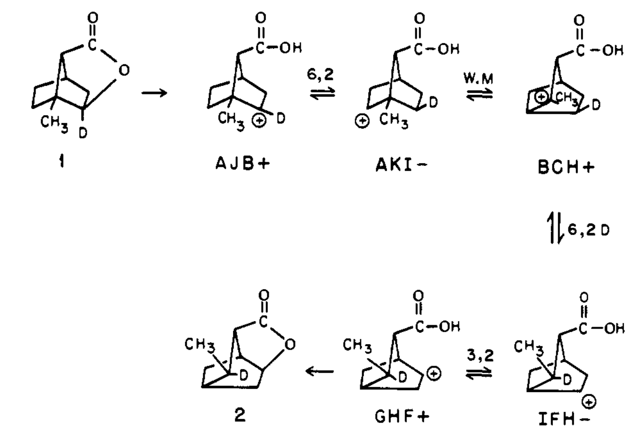


Figure 5. Deuterium label results and the most likely route from $1 \rightarrow 2$.

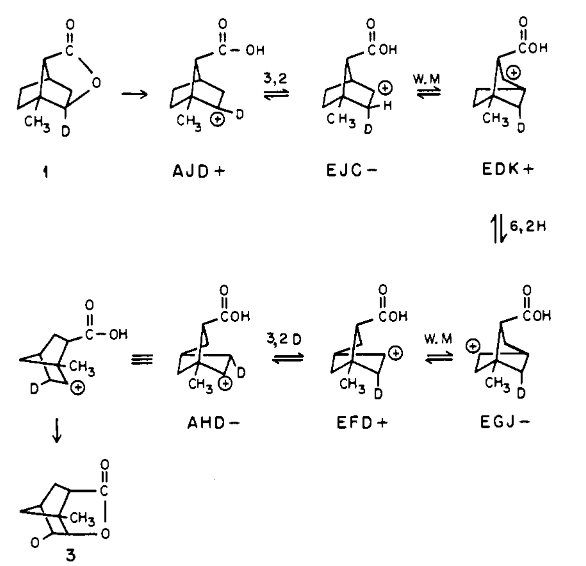


Figure 6. Deuterium label results and the most likely route from **1** → **3**.

the routes followed between **1**, **2**, and **3** are unknown. It is possible, however, to check the mechanistic pathways from **1** → **2** + **3** by means of a deuterium label in lactone **1**. The computer program ORNOCARE[2] can be helpful in the design of such an experiment by using the multiple-path option to produce an output summarized in Table I. From Figures 3 and 4 we can see that there are three reasonable pathways for **1** → AJ+ → AH− → **3**, and these are summarized in the first three rows of Table I. For **1** → AJ+ → GH+ → **2** there are two routes [5 and 6 of Table I], and for **1** → AJ+ → GH− → **2** there is one route (6). To illustrate how the information in Table I can be used, consider reaction sequence 3 and the symbols for that sequence which appear in the second column

Table I. Output from ORNOCARE[2] Program Showing the Cyclically Resolved Permutations for Several Alternate Paths[a]

	Reaction sequence	Overall rearrangement
	AJ+ → AH−	
(1)	32H, WM, 62H, WM, 32H	(BD)(EF)(HJ)(IK)(A)(C)(G) (45)(67)(1)(2)(3)(+−)
(2)	32H, 62H, WM, 62H, 32H	(BD)(CF)(EG)(HJ)(IK)(A) (45)(67)(1)(2)(3)(+−)
(3)	62H, 32H, WM, 62H, 32H	(DFEGKIJH)(A)(B)(C) (45)(67)(1)(2)(3)(+−)
	AJ+ → GH+	
(4)	62H, WM, 62H, 32H	(AGKIE)(BFJHCD) (15764)(23)(+)(−)
(5)	62H, WM, 62H, WM, 32H, WM	(BFJHE)(AG)(CD)(IK) (15)(24)(67)(3)(+)(−)
	AJ+ → GH−	
(6)	62H, WM, 32H, 62H, WM	(BKFDIE)(AGC)(HJ) (2764)(153)(+−)

[a] This information is used in choosing where to label **1** with deuterium to distinguish the mechanistic routes **1** → **2** + **3**.

(DFEGKIJH)(A)(B)(C)

(45)(67)(1)(2)(3)(+−)

The set (DFEGKIJH) means that the atom or group on site D is moved to site F ([D] → [F]), [F] → [E], [E] → [G], . . ., [H] → [D]. A one-character set such as (A) specifies that the substituent on site A is not moved (*i.e.*, [A] → [A]). In a similar fashion the numbers designate the skeletal atom sites, and (+−) means that handedness (Figure 1) is changed from (+) to (−).

Reaction sequences 1, 2, and 3 of Table I cannot be distinguished by skeletal labels, since each path produces the identical skeletal rearrangement (45)(67)(1)(2)(3). There are, however, nine possibilities for replacing the hydrogens of **1** (and thus AJ+) with deuterium, and certain of these allow unique distinctions to be made among the available routes. These possibilities and the result expected from each are summarized in Table II. From Table II it can be seen

Table II. An Illustration of the Fates of Deuterium Labels as **1** → **2** or **1** → **3** by the Three Routes Available for Each Reaction

Rearrangement route[a]	Site of label		
	BCDEFGHIK	(in AJ+)	Reactant cation
(1)	DCBFEGJKI	(in AH−)	Product cations
(2)	DFBGCEJKI	(in AH−)	
(3)	BCFGEKDJI	(in AH−)	
(4)	FDBAJKCEI	(in GH+)	
(5)	FDCBJAEKI	(in GH+)	
(6)	KAIBDCJEF	(in GH−)	

[a] From Table I.

that a label at site K would provide very little new information but that a label at site G would resolve all ambiguities about the routes from **1** to **2** and **3**. Single labels at any of the other sites would distinguish unambiguously only one of the first three pathways, although single labels at sites D, G, or K would tell us unambiguously how AJ+ proceeded to GH+ or GH−. It should be noted, however, that certain combinations of two experiments with labels at different sites could also give unambiguous answers.

Although a single deuterium label at site G in the reactant (**1**) would have allowed the optimum experiments, practical synthetic considerations dictated that we introduce the deuterium at site B. The results of the experiments are shown in Figures 5 and 6, in which the last symbol under each cationic structure denotes the position of deuterium. (See the Experimental

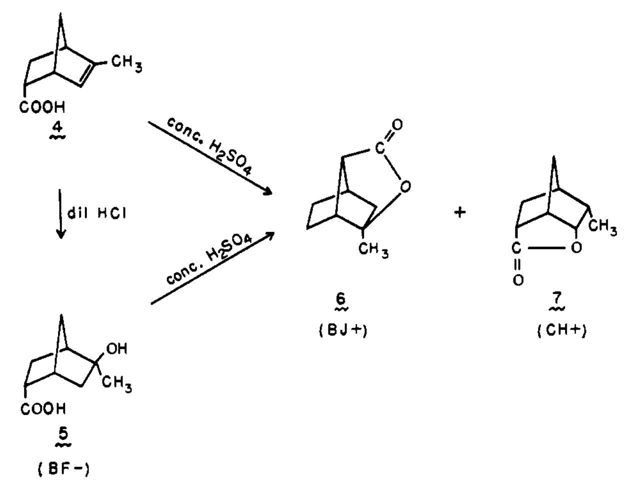
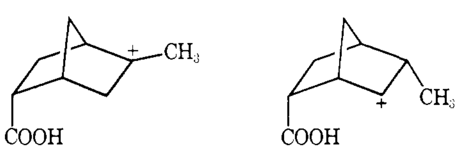


Figure 7. Results of the acid-catalyzed rearrangements of 5-methylnorbornenyl-2-*endo*-carboxylic acid (**4**). The symbols in parentheses indicate those cations which are the immediate precursors of or which are formed directly from the compounds to which they refer. For example, **6**(BJ+) means that cation BJ+ is the immediate precursor of compound **6**.

Section for details.) These results are consistent with routes 1 and 2 for the production of **3** and with routes 4 and 5 for the production of **2** and definitely exclude pathways 3 and 6. In Figures 5 and 6 we have shown routes 4 and 1, respectively; we prefer route 4 over route 5 because it is shorter. We believe route 1 is to be preferred over route 2 since it contains the sequence WM, 62H, WM, whereas route 2 contains 62H, WM, 62H (the first and last steps in both pathways being the same (3, 2H).

We tested the coset graph in another way, by preparing[8] the Diels–Alder adduct **4** (Figure 7) which, on protonation in H_2SO_4, should produce BF$\pm$ and CH$\mp$. As we can see from Figure 3, BF and CH are in a com-



BF− CH+

pletely different section of the graph, being seven and six steps removed from AH, and twelve and eleven steps removed from GH, the precursors respectively of lactones **3** and **2**. Unless there are more rearrangement mechanisms than the three (WM, 62H, 32H) we used to generate the graph, **4** should seek to lactonize from intermediates in the neighborhood of BF and CH and should not be converted into the same products as reactant **1**. The lactones (**6** and **7**) were produced when **4** was treated with concentrated sulfuric acid, and these were probably formed through the processes **4** $\rightarrow$ BF− (WM) $\rightarrow$ AG+ (62H) $\rightarrow$ AD− (WM) $\rightarrow$ BJ+ $\rightarrow$ **6**, and **4** $\rightarrow$ CH+ $\rightarrow$ **7**, respectively (also emphasized with heavy lines in the top center of Figure 3). Adduct **4**, when treated with dilute hydrochloric acid, yielded crystalline hydroxy acid **5**, which, when treated with concentrated H_2SO_4, also was converted to **6** and **7**.

(8) The procedure of J. D. Roberts, E. R. Trumbull, Jr., W. Bennett, and R. Armstrong, *J. Amer. Chem. Soc.*, **72**, 3116 (1950), for cyclopentadiene and methyl acrylate was followed.

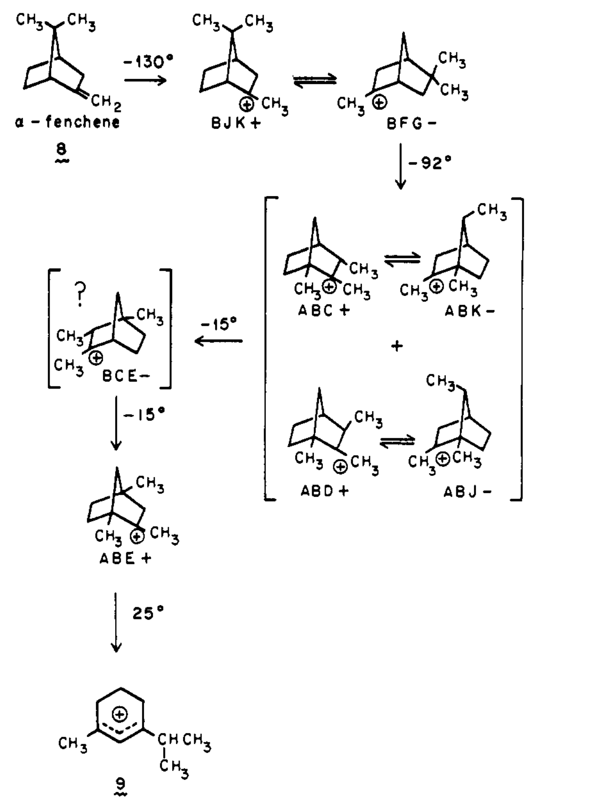


Figure 8. Summary of the results of Sorensen, *et al.*,[9] for the rearrangements of the α-fenchyl cation BJK+.

A second problem for which we found the model[2] useful was in interpreting the rearrangements, carried out[9] at temperatures between −130 and 25°, of the fenchyl cation in 4:1 $SO_2ClF–FSO_3H$. The essential experimental results are shown in Figure 8. Fenchene (**8**), when dissolved[9] in 4:1 $SO_2ClF–FSO_3H$ at −130°, forms a solution from which the nmr spectrum of BJK $\rightleftharpoons$ BFG was observed. At −92°, the nmr spectrum indicated the two equilibria ABC $\rightleftharpoons$ ABK and ABD $\rightleftharpoons$ ABJ (with the former predominating); at −15° the spectrum of ABE was observed. Finally, at 25° ring opening to **9** took place.

As Sorensen indicated, these results[9] raise some interesting questions. (1) Are the cations formed stepwise, in exactly their order of appearance, one from the other, in sequential processes? (2) Can the conversion ABC $\rightarrow$ ABE take place without the intervention of the type of process shown in Figure 9?

Before attempting to answer these questions we will discuss briefly the "double Wagner–Meerwein" (DWM) rearrangement, which is the sequence of two back-to-back shifts (AEK+ $\rightarrow$ ACE−) illustrated in Figure 9. This unique sequence was foreshadowed by the work of Aschan,[10] of Meerwein and van Emster,[11] and of Bertram and Helle;[12] Noyce[13] first suggested it might be

(9) E. Huang, K. Ranganayabulu, and T. S. Sorensen, *J. Amer. Chem. Soc.*, **94**, 1779, 1780 (1972).

(10) O. Aschan, *Justus Liebigs Ann. Chem.*, **388**, 1 (1911).

(11) H. Meerwein and K. van Emster, *Ber. Deut. Chem. Ges.*, **53**, 1825 (1920); **55**, 2521 (1922). Both Meerwein and van Emster and Aschan[10] converted (+)-α-pinene to (−)-camphene hydrate.

(12) J. Bertram and J. Helle, *J. Prakt. Chem.*, **62**, 293 (1900).

(13) D. S. Noyce, *J. Amer. Chem. Soc.*, **72**, 924 (1950); see also O. Wallach, *Justus Liebigs Ann. Chem.*, **362**, 181 (1908); W. Hückel and H. Wolwoski, *Ber. Deutschen. Chem. Ges.*, **80**, 39 (1947.)

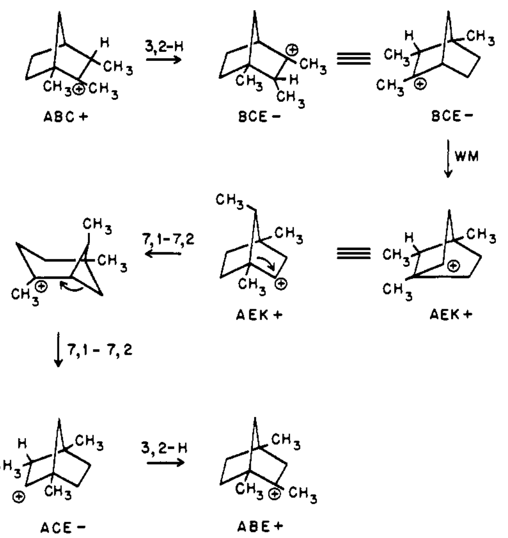
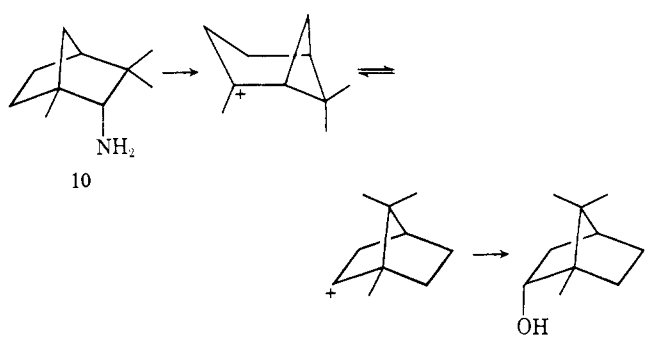


Figure 9. The "double Wagner-Meerwein" rearrangement[2,10-16] in the rearrangement ABC+ → ABE+.

important in the rearrangement of camphor.[14,15] The conversion of a bicyclo[2.2.1]heptyl cation to a bicyclo-[3.1.1]heptyl and back again was experimentally demonstrated by Hückel and Kern[16] when they isolated borneol (**11**) from deamination products of *endo*-fenchylamine (**10**).[17] Thus, the reaction rests on firm experimental ground.



10

11

In the rearrangement of the fenchyl cation BJK+ there are 330 theoretically distinguishable intermediates; these can be reduced,[2] in an abbreviated coset graph, to a minimum of 165 nodes by combining those intermediates of opposite chirality; *e.g.*, BJK+ and BJK− are combined to give just one node, BJK. Such a coset graph is too cumbersome to present here. We have given in Figure 10, however, a small segment (42

(14) P. Yates and R. J. Crawford, *J. Amer. Chem. Soc.*, **88**, 1561 (1966), first showed that a bicyclo[2.2.1]heptyl ring could rearrange to a [3.1.1] bicyclic system in their experiments on the decomposition of diazonorcamphor. For a recent and tidy confirmation of their contested [L. Friedman in "Carbonium Ions," G. A. Olah and P. v. R. Schleyer, Ed., Vol. II, Interscience, New York, N. Y., 1969, Chapter 16] structure proof, see D. S. Sethi and P. Yates, *J. Amer. Chem. Soc.*, **95**, 3820 (1973).

(15) See also C. J. Collins, B. M. Benjamin, V. F. Raaen, I. T. Glover, and M. D. Eckart, *Justus Liebigs Ann. Chem.*, **739**, 7 (1970); C. J. Collins, V. F. Raaen, B. M. Benjamin, and I. T. Glover, *J. Amer. Chem. Soc.*, **89**, 3940 (1967).

(16) W. Hückel and H.-J. Kern, *Justus Liebigs Ann. Chem.*, **728**, 49 (1969).

(17) There are, in fact, two other possible sequences of rearrangement (provided by the ORNOCARE program[2]) not involving DWM which will convert 10 to 11. The least complicated of these consists of the following 11-step sequence: WM, 62H, 32H, WM, 62H, 32H, WM, 32H, 62H, WM, 32H, which seems too long to be considered seriously, given the deaminating conditions used by Hückel and Kern.[16]

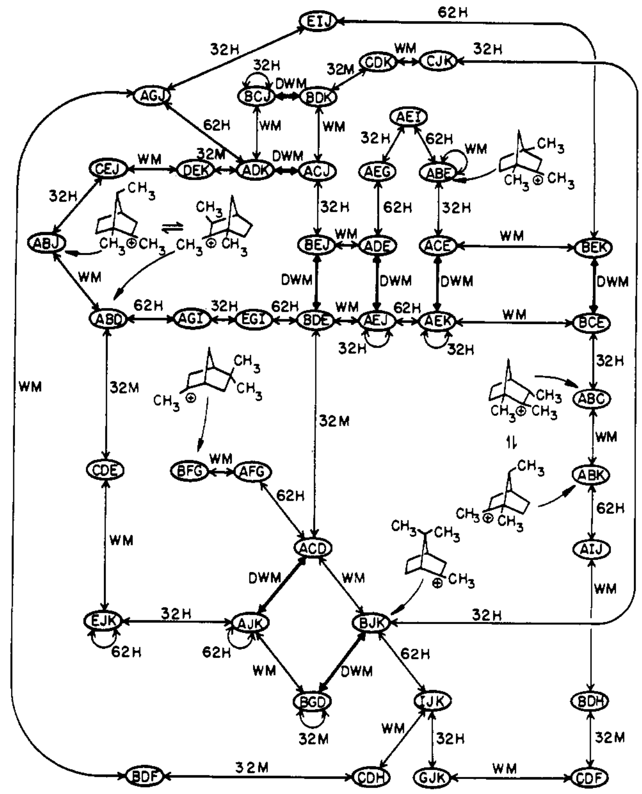


Figure 10. A section of the abbreviated coset graph for the rearrangement of the fenchyl cation BJK+.

nodes) of the abbreviated coset graph for BJK, showing the important pathways which interconvert the cations of interest (Figure 8) in the Sorensen study.[9] The transformations "allowed" were the Wagner–Meerwein rearrangement (WM);[3] 6,2-*endo*-hydride shift (62H);[3] 3,2-*exo*-hydride shift (32H),[3] 3,2-*exo*-methyl shift (32M),[18] and the "double Wagner-Meerwein" rearrangement (DWM).[1b,10] As discussed earlier, an odd number of steps changes the handedness (Figure 1) of the cation. From Figure 10 we are now in a position to answer some of the questions raised[9] assuming, always, that there are no further complicating factors than the five "allowed" reactions.

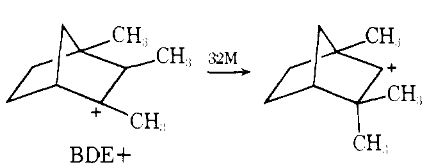
(1) As presumed by Sorensen,[9] the cations do not form sequentially. Instead the system appears to seek out those structures which are thermodynamically most stable at a given temperature.

(2) The double Wagner–Meerwein transformation[1b,10] certainly provides easy access between ABE and the other cations of Figure 8. (DWM is emphasized in Figure 8 by the heavy lines between nodes.) From Figure 10, however, we can determine that DWM is not essential to explain the results of Figure 8. Thus, ABC and ABE are connected by the 16-step process: 32H, WM, 62H, WM, 62H, 32H, 62H, WM, 32H, WM, 32M, 62H, 32H, 62H, WM, 32H. In addition, there are 14- and 15-step routes, also not involving DWM, which proceed through BJK. The latter two processes include the unlikely methyl shift BDE → ACD, in which a tertiary cation (BDE) is converted to a secondary (ACD). Such transformations would be highly improbable during solvolytic or deamination

(18) The "Nametkin" rearrangement: S. S. Nametkin and L. Brüssoff, *Justus Liebigs Ann. Chem.*, **459**, 144 (1927); *J. Prakt. Chem.*, [2] **135**, 155 (1932).

Table III. Computer Output Showing the 46 "Best" Pathways [Column (4)] between BJK+ and ABE±, Indicating the Fate, in the Product [Column (1)], of Each of the 11 Positions in BJK+ [Column (3)]

(1)	(2)	(3)	(4)									
ABE−	11	JBHIGFKCDAE1265734	WM	32M	WM	62H	DWM	32H	WM			
	12	HAKJDFCGIBE2173564	WM	32M	WM	DWM	62H	32H	62H			
	12	JAHIGFKCDBE2165734	WM	32M	WM	62H	DWM	32H	DWM			
	12	HAKJDFCGIBE2173564	WM	32M	DWM	WM	62H	32H	62H			
	13	DEGFHIKCJBA2456731	WM	32M	WM	62H	32H	DWM	32H			
	13	DEFHIKJGCBA2456731	WM	32M	WM	32H	62H	DWM	32H			
	13	JBHIGFKCDAE1265734	WM	32M	WM	62H	WM	DWM	WM	32H	WM	
	14	JECDIFHGKAB7431652	WM	32M	WM	DWM	32M	62H	32H	62H	WM	
	14	JAHIGFKCDBE2165734	WM	32M	WM	62H	WM	DWM	WM	32H	DWM	
	14	JECDIFHGKAB7431652	WM	32M	DWM	WM	32M	62H	32H	62H	WM	
	15	JBHIGFKCDAE1265734	WM	32M	WM	DWM	62H	DWM	62H	32H	WM	
	15	FEIHDKJGCBA5462731	WM	32M	WM	DWM	32M	DWM	62H	DWM	32H	
	15	FEIHDKJGCBA3462751	WM	32M	WM	DWM	32M	62H	DWM	62H	32H	
	15	JECDIFHGKBA7432651	WM	32M	WM	DWM	32M	62H	32H	62H	DWM	
	15	DEGFHIKCJBA2456731	WM	32M	WM	62H	32H	WM	DWM	WM	32H	
	15	DEFHIKJGCBA2456731	WM	32M	WM	32H	62H	WM	DWM	WM	32H	
	15	JBHIGFKCDAE1265734	WM	32M	DWM	WM	DWM	62H	DWM	32H	WM	
	15	JBHIGFKCDAE1267534	WM	32M	DWM	WM	62H	DWM	62H	32H	WM	
	15	FEIHDKJGCBA5462731	WM	32M	DWM	WM	32M	DWM	62H	DWM	32H	
	15	FEIHDKJGCBA3462751	WM	32M	DWM	WM	32M	62H	DWM	62H	32H	
	15	JECDIFHGKBA7432651	WM	32M	DWM	WM	32M	62H	32H	62H	DWM	
	15	JBHIGFKCDAE1265734	DWM	WM	DWM	32M	WM	62H	DWM	32H	WM	
	15	FEIHDKJGCBA5462731	DWM	32M	WM	DWM	32M	WM	62H	DWM	32H	
	15	FEIHDKJGCBA5462731	DWM	32M	DWM	WM	32M	WM	62H	DWM	32H	
	15	JECDHGIFKBA1436572	62H	WM	32M	WM	32H	62H	WM	32H	WM	
ABE+	10	DAIHFGCKJBE2165374	WM	32M	WM	62H	DWM	32H				
	12	DAIHFGCKJBE2165374	WM	32M	WM	62H	WM	DWM	WM	32H		
	13	IBCDJGKFHAE1237564	WM	32M	WM	DWM	62H	32H	62H	WM		
	13	DEKJHGIFCBA3472651	WM	32M	WM	DWM	32M	62H	32H	62H		
	13	IBCDJGKFHAE1237564	WM	32M	DWM	WM	62H	32H	62H	WM		
	13	DEKJHGIFCBA3472651	WM	32M	DWM	WM	32M	62H	32H	62H		
	14	DAIHFGCKJBE2163574	WM	32M	WM	DWM	62H	DWM	62H	32H		
	14	IACDJGKFHBE2137564	WM	32M	WM	DWM	62H	32H	62H	DWM		
	14	JEFGIHCKDAB1456372	WM	32M	WM	62H	32H	DWM	32H	WM		
	14	JEGIHCDFKAB1456372	WM	32M	WM	32H	62H	DWM	32H	WM		
	14	DAIHFGCKJBE2165374	WM	32M	DWM	WM	DWM	62H	DWM	32H		
	14	DAIHFGCKJBE2163574	WM	32M	DWM	WM	62H	DWM	62H	32H		
	14	IACDJGKFHBE2137564	WM	32M	DWM	WM	62H	32H	62H	DWM		
	14	DAIHFGCKJBE2165374	DWM	WM	DWM	32M	WM	62H	DWM	32H		
	*14	DEKJIFHGCAB2476531	62H	WM	32M	WM	32H	62H	WM	32H		
	15	JEFGIHCKDBA2456371	WM	32M	WM	62H	32H	DWM	32H	DWM		
	15	HEDJKGIFCBA2437651	WM	32M	WM	32H	DWM	62H	32H	62H		
	15	JEGIHCDFKBA2456371	WM	32M	WM	32H	62H	DWM	32H	DWM		
	15	CEKJIFHGDAB3476521	62H	DWM	32M	WM	32H	62H	WM	32H		
	15	CEKJDIHGFAB3472651	62H	WM	32M	WM	DWM	32M	WM	62H	WM	32H
	15	CEKJDIHGFAB3472651	62H	WM	32M	DWM	WM	32M	WM	62H	WM	32H



BDE+ ACD−

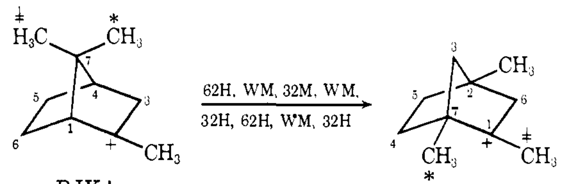
reactions but certainly not impossible during rearrangements which take place in superacid solutions. In fact, the formation [9] of **9** at 25° (Figure 8) implies that ABE returns to BJK before ring opening to **9** can take place, which strongly implicates the reaction BDE → ACD. It is likely that ^{13}Cmr studies of the rearrangements of methyl- and methylene-labeled fenchenes would be helpful in determining which of these alternate pathways is most important. Consequently, we show in Table III an excerpt from one of the several possible forms of output from the multiple-path printout of the ORNOCARE[2] program.

In column 4, reading from left to right, are given all the routes [based on an arbitrary weighting system[2] with l(WM) = l(32M) = 1; l(DWM) = l(62H) = 2; l(32H) = 3, and cut off at a total weight of 15] between the fenchyl cation, BJK+, and the ions shown in column 1 (ABE− and ABE+). The number in column 2 is the total weighting factor, and the letters and digits of column 3 tell us the new locations for each of the 11 substituents originally on sites A–K, respectively, and the 7 carbon atoms originally at sites 1–7, respectively, of the original cation BJK+. The use of column 3 can be illustrated as follows. Consider the 15th line, designated by (*), for ABE+ of Table III, which shows the easiest path BJK+ → ABE+ not requiring DWM. This may be written as the permutation

$$\begin{Bmatrix} \text{ABCDEFGHIJK1234567} \\ \text{DEKJIFHGCAB2476531} \end{Bmatrix}$$

which is read "[A] → [D] (*i.e.*, the substituent on site A of the reactant goes to site D of the product), [B] → [E], . . . , [K] → [B], [1] → [2] (*i.e.*, the carbon atom on site 1 of the reactant goes to skeletal site 2 of the product), ..., and [7] → [1]."

We know, therefore, that if ABE+ is formed from BJK+ by the indicated route, then the methyl groups and carbon atoms of the two cations are related as follows.



BJK+ ABE+

The relationship of each hydrogen is also apparent from column 3, but this has not been shown in the above equation.

The type of information available from the output illustrated in Table III allows us to decide immediately whether one given pathway can be distinguished from another by deuterium or ^{13}C-labeling techniques (explained below). In addition, it indicates what information can be gained from labeling any given position and can even tell us the minimum number of labels necessary to resolve alternate routes (compare with the example given previously in connection with Tables I and II). Certain routes (*e.g.*, the first two for ABE+ in Table III) give the same permutations and cannot be distinguished through labeling experiments. Even in these cases, however, the possibility exists that certain key intermediates in one or the other of the hypothetical routes could be isolated or their spectra could be observed, thus allowing alternate routes to be distinguished. The cases which are completely indeterminate on the basis of identical permutations in the final products always involve relators.[2] For example, the two pathways noted above (the first two for ABE+) are related through the equation

$$\mathrm{WM} = (\mathrm{DWM})(\mathrm{WM})(\mathrm{DWM})$$

which arises from the relators

$$(\mathrm{WM})^2 = (\mathrm{DWM})^2 = [(\mathrm{WM})(\mathrm{DWM})]^2 = 1$$

described by eq 7 and 23 of ref 2.

In conclusion, we believe the use of the algebraic model[2] and coset graphs can be of invaluable help (1) in determining likely pathways for rearrangement of substituted norbornyl compounds and (2) in designing tracer experiments which will allow us to establish which of the several pathways is (or are) followed as reactant proceeds to product. We shall turn our attention next to the possibility of generalizing the methods described in the present and preceding[2] paper with the hope that they might be adapted to other chemical systems

Experimental Section

Preparation of 1-Methyl-2-*endo*-*d*-bicyclo[2.2.1]heptyl-7,2-carbolactone (1-*d*). The diene synthesis of 3-*endo*-methyl-3-*exo*-*d*-norbornene-2-*exo*-carboxylic acid was carried out as described by Komppa and Beckmann[19] except that β-deuteriocrotonic acid was employed. The β-deuteriocrotonic acid was synthesized as follows: 15 g of $CH_3CH_2NO_2$ (Aldrich Chemical Co.), 20 g of D_2O (96% enriched), and 10 mg of sodium acetate were sealed in a 0.5-in. Pyrex pipe with a clamp and gasket fitting, and the pipe was immersed in an oil bath (120°) so that the D_2O layer boiled through the nitroethane and condensed on the upper section of pipe. The exchange was complete after 3 hr, and from the nmr spectrum of the nitroethane it was calculated that about 78% of the α hydrogens had been replaced with deuterium. The exchange procedure was then repeated with fresh batches of 96%-enriched D_2O until approximately 25 such exchanges had been completed, and 97% of the exchangeable hydrogens were replaced with deuterium. The α-deuterionitroethane was converted to acetaldehyde-*d* by the method of Leitch,[20] and thence to crotonic-β-*d* acid.[21] The product contained more than 99% deuterium in the β position, probably a result of favorable isotope effects during the synthesis. The adducts (exo and endo acids) were separated by the iodolactone procedure,[6] 100 g of cyclopentadiene and 100 g of crotonic-β-*d* acid yielding 40 g of pure 3-*endo*-methyl-3-*exo*-*d*-norbornene-2-*exo*-carboxylic acid, mp 55°, a portion of which was converted to 1-methyl-2-*endo*-*d*-bicyclo[2.2.1]heptyl-7,2-carbolactone (**1**-*d*), mp 121–123°, by the method of Beckmann, Geiger, and Schaber-Kiechle.[6] The nmr spectrum of **1** (CCl_4) was as follows: 2-*endo*-hydrogen, broad, 4.03 ppm; bridgehead (no. 4) hydrogen, broad, 2.42 ppm; 7-*anti*-hydrogen, broad, 2.24 ppm; methyl hydrogens, singlet, 1.25 ppm; remaining hydrogens, unresolved between 1.4 and 1.9 ppm. The signal at 4.03 ppm (3-*endo*-hydrogen) was totally absent.

Rearrangement of 1-*d*. The procedure of Geiger and Beckmann[6] was followed. The lactone (3.1 g, 0.022 mol) was dissolved in 20 ml of concentrated sulfuric acid and the mixture was stirred (room temperature) for 3 days before it was poured onto 100 g of ice. The combined lactones were then extracted with eight 15-ml portions of ether. The combined ether extracts were washed with dilute sodium bicarbonate solution and were dried over $MgSO_4$. The lactones were dissolved in 8 ml of hot 5 *N* sodium hydroxide solution and cooled to precipitate the sodium salt. The salt was washed with a little cold 5 *N* sodium hydroxide before acidifying with cold, dilute hydrochloric acid to form the lactone **2**-*d*, which was extracted with ether and checked by glc on a 3% Carbowax column. Measurement of peak areas showed 83% of the above lactone in addition to 15% of **3**-*d* and a small amount of an unidentified substance. The filtrate from the precipitation of the sodium salt was treated with excess dilute hydrochloric acid. The lactone (**3**) was extracted with ether and dried and a small portion analyzed by glc on a 3% Carbowax (SD Anakrom support) column. Measurement of peak areas showed 75% of **3** was present along with a small amount of **2** and unidentified products. Both lactones **2**-*d* and **3**-*d* were purified:[6] **2**-*d*, bp 136–137° (15 mm); **3**-*d*, mp 142–144°.

Nmr Spectral Analyses of 2-*d* and 3-*d*. A sample of pure **2**, undeuterated, in carbon tetrachloride solvent, showed a doublet for the methyl group centered at 1.06 ppm, 3 H. The signal for the no. 1 bridgehead hydrogen was a broadened triplet at 3.10 ppm, 1 H, and the signal for the 6-exo hydrogen was a broadened triplet at 4.68 ppm, 1 H. The signals for the other seven hydrogens appeared between 1.17 and 2.20 ppm and could not be assigned. When **3**, in carbon tetrachloride, was mixed with $Eu(dpm)_3$ in the weight ratio of 1.3:1, most of the signals could be assigned as follows: 6-exo H, broadened quartet at 5.73 ppm; no. 1 bridgehead H, broadened triplet at 4.13 ppm; 2-exo H, broadened doublet at 3.89 ppm; 3-endo H, broadened quartet at 3.48 ppm; no. 4 bridgehead H, broad singlet at 2.65 ppm; 5-exo H and 5-endo H, multiplet at 2.47 ppm; 7-syn H, broad doublet at 2.39 ppm; 7-anti-H, broad doublet at 2.01 ppm; methyl H, doublet at 1.34 ppm. Compound **2**-*d*, derived from **1**-*d*, showed a signal for the methyl group which was mostly collapsed to a single line. The signal for the 3-endo hydrogen at 3.48 ppm was reduced in intensity to 30% of its expected integrated value. From the integrated intensities no deuterium was found in the other positions. That some hydrogen exchange takes place during the sulfuric acid treatment of **1** was demonstrated by carrying out the rearrangement **1** → **2** + **3** in tritiated sulfuric acid and finding uptake of tritium (3–4 equiv) in the products.

Lactone **3**, undeuterated, gave a singlet for the methyl group at 1.35 ppm. The signal for the 6-exo hydrogen was a broadened doublet at 4.37 ppm. All other signals were unresolved between 1.44 and 2.42 ppm. When **3** was mixed with $Eu(dpm)_3$ in the weight ratio of 1.35:1 in carbon tetrachloride solvent, the 6-exo

(19) G. Komppa and S. Beckmann, *Justus Liebigs Ann. Chem.*, **523**, 68 (1936).

(20) L. C. Leitch, *Can. J. Chem.*, **33**, 400 (1955).

(21) W. J. Hickinbottom, "Reactions of Organic Compounds," 3rd ed, Longmans, Green and Co., New York, N. Y., 1957, p 222.

hydrogen doublet appeared at 5.63 ppm. The 3-endo hydrogen gave a broadened doublet at 4.57 ppm, and the 7-syn hydrogen gave a broadened doublet at 3.46 ppm. The signal for the methyl hydrogen was now at 2.30 ppm. The signals for the other six hydrogens appeared between 2.58 and 3.17 ppm. In the spectrum for **3**-*d* from **1**-*d*, the signal for the 6-exo hydrogen was collapsed to a single broad resonance, because of the deuterium atom in the 5-exo position. The intensity of the signals between 2.58 and 3.17 ppm was reduced to about 5.3 hydrogens. The appearance of the remaining signals was unchanged.

5-Methylnorbornene-2-*endo*-carboxylic Acid (4). Freshly distilled methylcyclopentadiene (100 g, 1.25 mol) was added dropwise with stirring to a cooled (−40°) solution of 130 g (1.51 mol) of methyl acrylate and 1 g of hydroquinone in 100 ml of ether. The addition required 2 hr. The bath temperature was permitted to rise to 0° and stirring was continued for an additional 4 hr, after which the reaction mixture was stored in the refrigerator for an additional 5 days. The ether was then removed and a fraction which distilled in the range 66–68° (5 mm) was collected. Glc with Carbowax 20M showed that five compounds were present, four in amounts greater than 15%. The esters were hydrolyzed in excess warm 10% aqueous sodium hydroxide solution. The alkaline layer was extracted twice with ether to remove minor neutral components. The solution was acidified with cold 6 *N* hydrochloric acid solution, the acids were extracted with ether, and the ether extract was dried over magnesium sulfate. Most of the ether was removed by partial vacuum distillation. The mixture of five acids was triturated with an equal volume of light petroleum ether and cooled on Dry Ice. Scratching induced the slow precipitation of one component. After 2 days about 40 g of crystalline acid, mp 77–79°, was obtained from the starting mixture of 200 g of esters. The acid was recrystallized from light petroleum ether, and a portion of it was sublimed at 78° (1 mm) to produce the pure 5-methylnorbornene-2-*endo*-carboxylic acid (**4**), mp 81–82°.

Anal. Calcd for $C_9H_{12}O_2$: C, 71.00; H, 7.95. Found: C, 70.83; H, 7.85.

The structure **4** was established from the nmr spectrum (CCl_4): methyl H, closely spaced doublet, 1.77 ppm; no. 4 bridgehead H, broad, 2.65 ppm; 2-exo H, quartet, 2.97 ppm; no. 1 bridgehead H, broad, 3.13 ppm; 6-olefin H, broad, 5.55 ppm; carboxylic H, 12 ppm.

5-*endo*-Methyl-5-hydroxy-2-*endo*-norbornanecarboxylic Acid (5). Ten grams of the Diels–Alder adduct **4**, mp 81–82°, was added to 100 ml of 1.0 *N* HCl. After 16 hr the solution was extracted with ether, the ether extract was concentrated to dryness, and the residue (11.2 g) had a mp of 156–157°. Recrystallization from ethanol–hexane raised the mp to 158–159°.

Anal. Calcd for $C_9H_{14}O_3$: C, 63.48; H, 8.29. Found: C, 63.56; H, 8.20.

The hydroxy acid **5** was identified from the following characteristics of its nmr spectrum.

Because compound **5** is insoluble in CCl_4 the spectrum was taken in pyridine solvent. Two groups of signals appeared, one group with intensity of 2 between 2.65 and 3.17 ppm and the second group with intensity 10 between 1.23 and 2.55 ppm. The methyl signal appeared as a single resonance at 1.65 ppm. The exchanging hydroxylic and carboxylic hydrogens appeared at 9.5 ppm. When **5** was prepared using dilute DCl, the high field group of signals had a relative intensity of 9 and a signal at 1.83 ppm (presumably the 6-exo hydrogen) was reduced in amplitude.

Lactonization of 4 in Sulfuric Acid to 6 and 7. A solution of 4 g of **4** in 40 ml of cold concentrated sulfuric acid was permitted to stand at 0° for a week. The solution was then poured on 200 g of ice, the organic layer was extracted with three 30-ml portions of ether, and the combined ether layers were washed with saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. Evaporation of the ether left 2.1 g of almost colorless oil. Glc on 3% Carbowax 20M showed two principal (>98%) products, in equal quantities, later identified as **6** and **7**. The lactone mixture was dissolved in the minimum necessary volume of 2 *N* NaOH solution, clarified, and chilled. The sodium salt consisting mainly of saponified **7** precipitated. The salt was recrystallized from water, collected on a filter, and washed with methanol to which ice had been added. The sodium salt was added to cold, dilute HCl, and the resulting oily suspension was extracted with ether. The hydroxy acid lactonized during the work-up, and crystallization of the concentrated extract from 1:5 (by volume) petroleum ether–diethyl ether yielded crystals of **7**, mp 112–114°. The yield was low (less than 5%). The carbon analyses for **7** were consistently low (about 0.5–0.6%), probably because of small fractions of hydrolysis to the hydroxy acid. The lactone **7** was therefore reduced with lithium aluminum hydride to 3-*endo*-methyl-6-*endo*-hydroxymethyl-2-*endo*-norborneol, which was crystallized from ether–petroleum ether (twice) and alcohol–hexane (three times), mp 130–131°.

Anal. Calcd for $C_9H_{16}O_2$: C, 69.17; H, 10.33. Found: C, 69.34; H, 10.15.

The ether extract of the above acidified sodium salts left an oily, partially solid residue which was collected on a funnel and allowed to stand at room temperature for 24 hr. At that time the hydroxy acid must have completely lactonized, as the solid was then readily soluble in ether and could be crystallized readily from ether–petroleum ether (1:4 by volume). After two crystallizations the lactone **6** was better than 98% pure (gc on 3% Carbowax on S. D. Anachrom), mp 39–41° (capillary). The overall yield of pure material was low (less than 5%). As with lactone **7**, carbon analyses for lactone **6** were consistently about 0.5% low. Reduction of **6** with lithium aluminum hydride afforded 2-*endo*-methyl-7-*anti*-hydroxymethyl-2-norborneol, mp 109–110° (from ethanol–hexane).

Anal. Calcd for $C_9H_{16}O_2$: C, 69.17; H, 10.33. Found: C, 69.23; H, 10.31.

The structures of **7** and **6** were established by interpretation of their nmr spectra as follows. Lactone **7** gave an nmr spectrum containing a doublet for the methyl hydrogens at 0.89 ppm showing that the methyl group is attached to a carbon containing one hydrogen. The signal for the HCO group (6-exo-H) was a broadened quartet centered at 4.56 ppm. The line separations were about 7.2 and 5 Hz from coupling with the 5-exo hydrogen and the no. 1 bridgehead hydrogen, respectively. If the 5 position contained an *exo*-methyl (rather than endo) the adjacent HCO signal would be expected to exhibit two smaller coupling constants. If the methyl group were in some other position the HCO coupling should be more complex. The no. 1 bridgehead hydrogen appeared as a broadened triplet at 3.18 ppm, downfield from the expected position of about 2.5 ppm because of deshielding by the carbonyl oxygen. All remaining signals were unresolved between 1.5 and 2.6 ppm.

Compound **6** (in carbon tetrachloride) showed an nmr signal for the methyl group as a singlet (no neighboring hydrogens) at 1.42 ppm. The 7-anti hydrogen and the two bridgehead hydrogens appeared as a single signal at 2.5 ppm. All the remaining signals were unresolved between 1.3 and 1.9 ppm. Further assignment of the spectrum was accomplished by using the shift reagent $Eu(dpm)_3$ in approximately 0.5 molar ratio. As a result four signals were distinctly resolved as follows: the 7-anti hydrogen now appeared as a slightly broadened singlet at 3.90 ppm and the no. 1 bridgehead hydrogen appeared as a broad signal at 3.50 ppm. The no. 4 bridgehead signal was a doublet (separation 5.5 Hz) at 3.19 ppm and it was coupled to the 3-exo hydrogen which appeared as a quartet (separations 5.5 and 13.0 Hz) centered at 2.70 ppm. The remaining signals were complex and overlapped the methyl signal at 2.0 ppm.

Action of Concentrated Sulfuric Acid on 5. The hydroxy acid **5** (6.0 g, 0.033 mol) was dissolved in 40 ml of cold (0°) concentrated sulfuric acid and the mixture was stirred at 0° for 15 min. The solution was allowed to stand 20 hr at −2° before pouring onto ice and extracting with ether. A sample was analyzed by glc (3% Carbowax on S. D. Anakrom), and it was shown that **6** and **7** were present in equal amounts.

Acknowledgment. We thank Mr. David J. Houser, De Pauw University, Greencastle, Ind., for technical assistance in the synthesis of **1**-*d*. Mr. Houser was a participant in the Great Lake Colleges Association Summer Semester Program in 1970. We also thank Dr. B. M. Benjamin for the nmr spectra and for their interpretation.