Analysis of Mass Spectral Fragmentation Patterns in Various Bicyclic Alcohols

Harold Kwart and Thomas A. Blazer

Department of Chemistry, University of Delaware, Newark, Delaware 19711

Various bicyclo[2.2.1]heptyl, bicyclo[2.2.2]octyl, and bicyclo[3.2.1]octyl substrates, particularly alcohols and olefins, have been subjected to careful study of their fragment ions occurring in the high-resolution mass spectrometer. The olefins undergo retro-Diels–Alder cleavage as the principal mode of fragmentation. An internal retro-Diels–Alder[1a] fragmentation appears to take place in the [3.2.1]octene ion which does not accommodate a normal class D fragmentation. All the alcohols, including the bridgehead cases, undergo dehydration *via* the formation of an intermediate carbonium ion, which then experiences extensive scrambling of the hydrogen (and deuterium) atoms on the skeleton before completing elimination of the elements of water. The resulting olefin ion then suffers a retro-Diels–Alder fragmentation, but this route is shown to be vitiated as a means of locating the deuterium on the skeleton and tracing the course of rearrangement reactions in solution thereby. It is demonstrated, however, that the m/e 57 peak may be applied for this purpose since it is produced in all bicyclic alcohol cases without rearrangement of the skeleton in the mass spectrometer. The manner in which m/e 57 (and m/e 58 in deuterated cases) arises through fragmentation, the method of locating H and D in bicyclic models, and its use in tracing the course of solvolytic rearrangements are discussed in detail.

Recent studies of carbonium ion rearrangements of bicyclo[3.2.1]-2-octanol and bicyclo[2.2.2]-2-octanol sulfonate esters and analogous derivatives[1b] required application of the mass spectrometer as a means of following the course of reaction. Since more information was needed concerning the fragmentation patterns of bicyclic alcohols, a study was undertaken of the electron-impact fragmentation of **1**, **2**, and **3** alcohols, the olefins derivable therefrom, and related compounds.
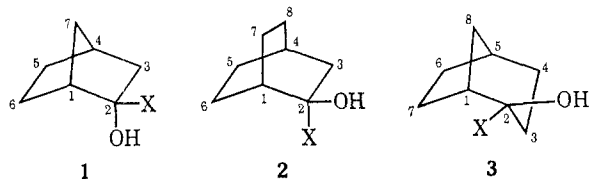
X = hydrogen (normal) or deuterium

In each instance the occurrence of H_2O elimination producing an olefin ion was confirmed by the observation of a metastable peak in the mass spectrum. Two general fragmentation paths were observable, one originating from the parent alcohol and directed by the oxygen containing fragment, the other stemming from the olefin and directed by the double bond.

Results and Discussion

Molecular ions.—The parent peaks of the alcohols (**1**, **2**, **3**) were always readily perceived. They ranged from a low of 1.7% for **1** to a high of 21.5% for **3**. As expected, the corresponding olefins exhibited more intense molecular ion peaks; *e.g.*, 14.7% for bicyclo[2.2.2]octene *vs.* 7.1% for the alcohol **2**. Other investigators have shown[2,3] that in the case of monocyclic alcohols the molecular ion is more intense in the case of equatorial hydroxyl than axial. Such differences, however, though significant in a relative sense, do not appear to be large on an absolute scale. From a practical viewpoint, this did not seem to offer a solution to our

problem and no attempt was made to study epimeric differences of this nature.

Retro-Diels–Alder Fragmentations.—This type of mechanism is know to operate in cyclohexenes. Biemann[4] refers to this as a "class D" mechanism and lists two requirements for the operation of the fragmentation mode: (1) the presence of a cyclic olefin or similar system, and (2) the absence of other bonds which might cleave with particular ease *via* certain stated mechanisms. Since bicyclo[2.2.1]-2-heptene (**4**) and bicyclo[2.2.2]-2-octene (**5**) could be prepared *via* Diels–Alder reactions, and since the normal (X = H) alcohols **1** and **2** could dehydrate under mass spectral circumstances to form these olefins, it was assumed that evidence for a retro-Diels–Alder reaction might be found in the mass spectra of **1**, **2**, **4**, and **5**.

The peaks corresponding to this "class D" mechanism actually constitute the major fragment ions of the mass spectra of **4** and **5** (see Figure 1). This observation holds for the spectra obtained at 15 V as well as those obtained at the conventional 70 V. Metastable transition peaks representing these fragmentations were observed at m/e 46.3 in the spectrum of **4** and at m/e 59.5 in the spectrum of **5**.

The (normal) alcohols **1** and **2** also show evidence of the retro-Diels–Alder fragmentation. The peaks analogous to those in the spectra of **4** and **5**, although not the major peaks of the spectra (see Figures 2 and 3), are still very intense, 20.1% for the m/e 66 peak in (normal) **1** and 79.0% for the m/e 80 peak in (normal) **2**. In addition, these alcohols also display metastable transition peaks at m/e 46.5 in the case of (normal) **1** and m/e 59.4 in the spectrum of (normal) **2**. A metastable peak at m/e 60.2 in the spectrum of the deuterated (X = D) **2** confirm this fragmentation. This results from the transition $109 \rightarrow 81 + 28$.

On the other hand, *no* metastable peak was detected in the mass spectrum of the [3.2.1] (normal) alcohol **3** (see Figure 4) which could be correlated with fragmentation *via* a "class D" pathway. This is attributable to the absence of structural accommodation for the retro-

(1) (a) H. Kwart and K. King, *Chem. Rev.*, **68**, 415 (1968). (b) H. Kwart and J. L. Irvine, *J. Amer. Chem. Soc.*, **91**, 541 (1969).

(2) K. Biemann and J. Seibl, *ibid.*, **81**, 3149 (1959).

(3) D. R. Dimmel and J. Wolinsky, *J. Org. Chem.*, **32**, 410, 2735 (1967).

(4) K. Biemann, "Mass Spectrometry, Organic Chemical Applications," McGraw-Hill Book Co., Inc., N. Y., 1962. See also, for further illustrations of the RDA fragmentation in bicyclic compounds, T. Gato, *et al.*, *Tetrahedron*, **22**, 2213 (1966), and W. C. Steele, B. H. Jennings, G. L. Botyos, and G. O. Dudek, *J. Org. Chem.*, **30**, 2886 (1965).
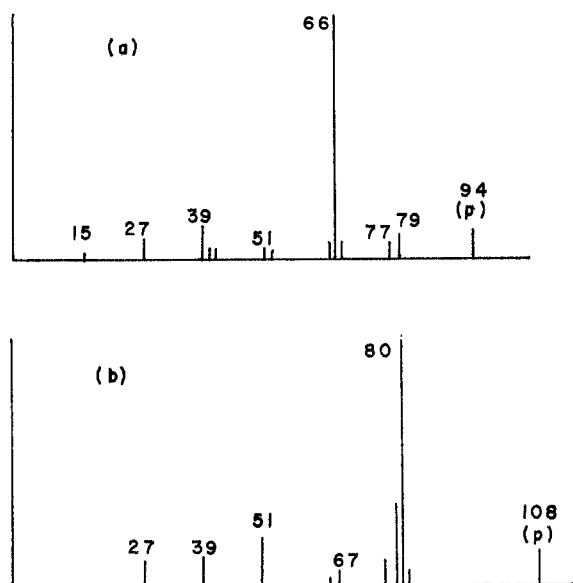
Figure 1.—Mass spectra: (a) bicyclo[2.2.1]-2-heptene (4), (b) bicyclo[2.2.2]-2-octene (5).
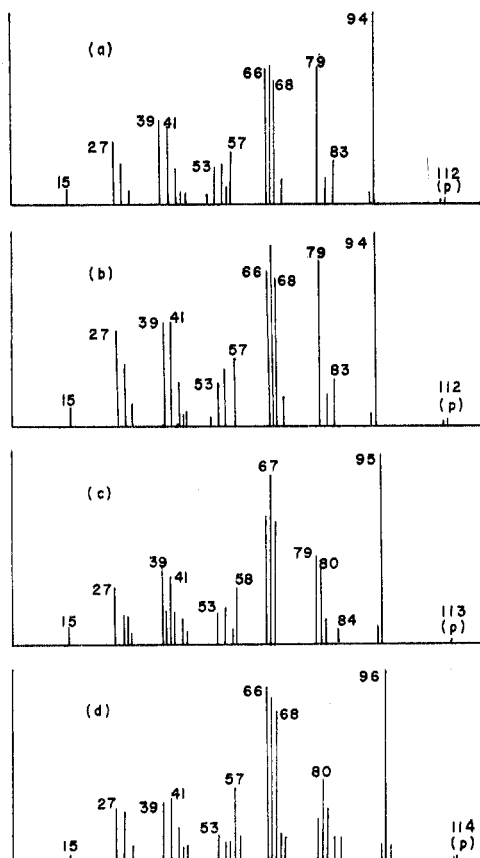

Figure 2.—Mass spectra: (a) bicyclo[2.2.1]-2-heptanol, *endo* (1, X = H); (b) bicyclo[2.2.1]-2-heptanol, *exo;* (c) bicyclo-[2.2.1]-2-heptanol-2-*d*, *endo* (1, X = D); (d) bicyclo[2.2.1]-2-heptanol-3,3-*d₂*, *endo* (6).

Figure 3.—Mass spectra: (a) bicyclo[2.2.2]-2-octanol (2, X = H); (b) bicyclo[2.2.2]-2-octanol-2-*d* (2, X = D); (c) bicyclo-[2.2.2]-2-octanol-3,3-*d₂* (7).

Figure 4.—Mass spectra: (a) bicyclo[3.2.1]-2-octanol (3); (b) bicyclo[2.2.2]-1,8-octadiol (10).

readily under far less energetic circumstances than prevail in the mass spectrometer (as illustrated below).

Dehydration.—The major peak in the spectra of the bicyclic alcohols 1 and 2 and their deuterated analogs is due to the loss of water. In the mass spectrum of the [3.2.1] alcohol, 3 (X = H), the peak due to the loss of a mole of H_2O, although not the major peak of the spectrum, is still very intense (32.6%). Metastable transition peaks establish this fragmentation as due to

Diels–Alder reactions.[5] However, a major peak (98.7%) was recorded at *m/e* 80 whose constitution was established to be $C_6H_8{}^+$ (through high-resolution mass determination). This could arise as a result of fragmentation *via* an internal retro-Diels–Alder,[5] a well characterized electrocyclic rearrangement proceeding

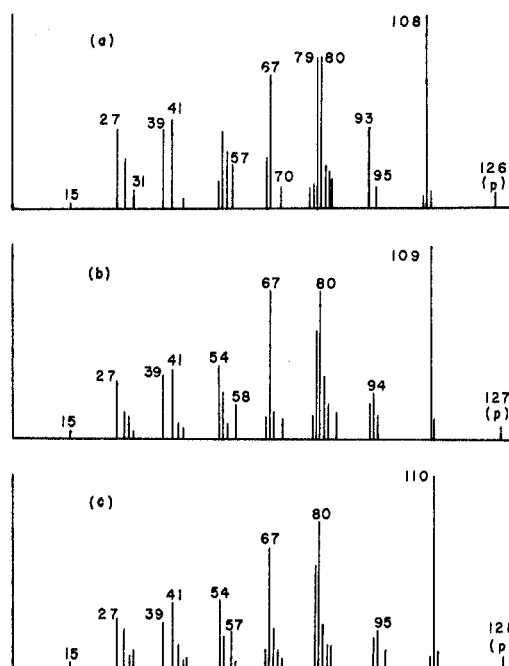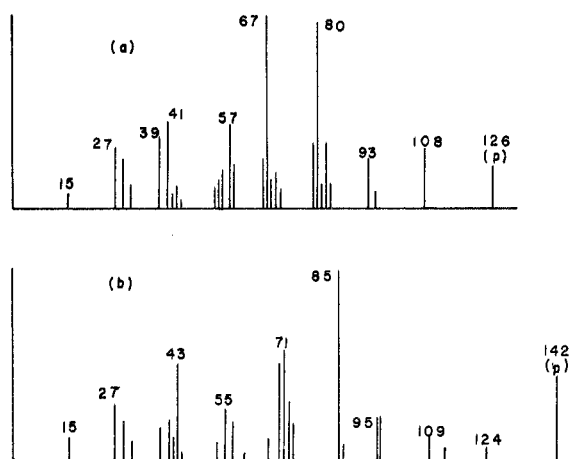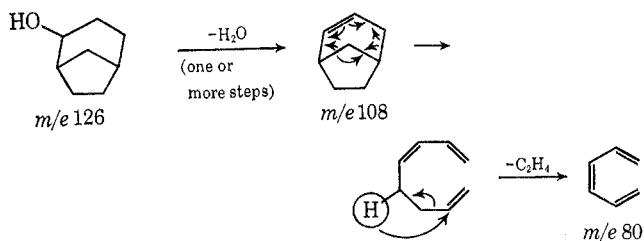(5) See, for a full discussion of this reaction, ref 1a.

dehydration, since the 18 mass units are lost as a single group.

The loss of water has been demonstrated to occur to varying extents in the spectra of monocyclic alcohols, ranging from approximately 10% in cyclopentanol to 50% in cyclohexanol. Dehydration by way of aldehyde intermediates, which have been shown to fragment with subsequent elimination of water, has been suggested[6] as one possible mechanistic course. However, this path is not functional in any of the bicyclic alcohols under study here. No evidence could be found to confirm the fragmentation of a formyl group from the parent ion.

In the case of cyclohexanol, the source of the hydrogen which coupled with the hydroxyl group (comprising the water eliminated) was proven[7] to be distributed around the ring with the exception of the C_1. The failure of the hydroxyl-bearing carbon to yield its other hydrogen to form the water eliminated has been confirmed by our studies. In the spectra (c), Figure 2, of alcohol 1 (X = D) and (b), Figure 3, of 2 (X = D) there is no evidence for the loss of 19 mass units, which could occur if this atom were involved, (HDO in these cases).

The source of the second hydrogen could have been the C_3 if the analogy to an α,β-elimination reaction in solution is fulfilled. The resulting olefin (for example, the bicyclo[2.2.1] heptene ion) could then give rise to a retro-Diels–Alder fragmentation route, as discussed in the previous section of this report.

However, when *endo* bicyclo[2.2.1]-2-heptanol-3,3-d_2, 6, suffers fragmentation, as is evident from the spectrum (d), Figure 2, the m/e 96 (the base peak) is more than ten times as intense as m/e 95, indicating


6   7
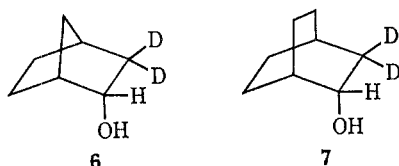
that little or no α,β elimination of deuterium has taken place. This confirms an observation briefly reported earlier.[8] Moreover, we have found a nearly identical result in the case of fragmentation of the corresponding [2.2.2]bicyclic alcohol 7, where the base peak (m/e 110) is actually more than twenty times as intense as the peak (m/e 109) corresponding to HDO elimination.

Clearly, the loss of hydroxyl from the parent ion in each case (6 and 7) has resulted in a carbonium ion in whose structure hydrogen and deuterium positions have become extensively scrambled. Presumably this has occurred through very rapid C—C bond shifting and hydride migrations such as are characteristic of the similarly structured carbonium ions in solution.[1] Ultimately these carbonium ions must lose hydrogen and be converted to the olefin ions 8 and 9. This is demanded by the retro-Diels–Alder products of fragmentation of 8 and 9, namely, the formation of cyclopentadiene (m/e 66) and cyclohexadiene (m/e 80) ions (respectively), through expulsion of a neutral ethylene fragment, which

(as pointed out earlier) are very evident in the spectra of the (normal) alcohols 1 and 2. In the case of 7, the m/e 80, representing the expulsion of CD_2=CH_2 from the base m/e 110, is significantly more intense than m/e 81 and 82 (corresponding, respectively, to the expulsion of CHD=CH_2 and CH_2=CH_2). Consequently, the structure 9 can be assigned as the preponderant olefin (ion) resulting from dehydration of 7. Its formation could be readily accomplished in two successive steps involving C—H bond breaking in the intermediate carbonium ion 7a (illustrated below).
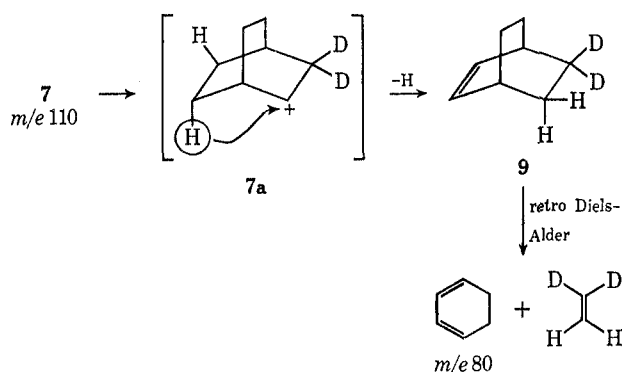
A concomitant path of more than equal likelihood producing expulsion of CD_2=CH_2 from the intermediate carbonium ion 7a is the result of very facile rearrangement to the [3.2.1] ion (or its nonclassical equivalent). As indicated earlier, the occurrence of an internal retro-Diels–Alder[5] is a highly probable fragmentation mode, which in the present instance can also account for the observed results (illustrated below).
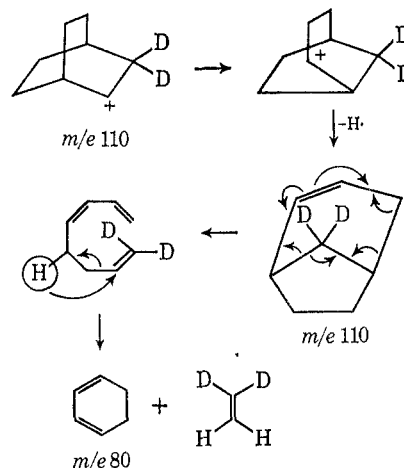
The mechanism is supported by the fragmentation pattern of the monodeuterio alcohol (2, X = D) (see spectrum b, Figure 3), where the ratio of m/e 109/80 is nearly identical with the ratio of m/e 110/80 in the spectrum of 7. Furthermore, the ratio of m/e 80/79 is almost the same for the deuterated alcohols 2 (X = D) and 7, but is significantly different for the undeuterated bicyclooctanol shown in spectrum a, Figure 3.

Unfortunately, it is not possible to trace with the same degree of confidence (as in 7) the course of rearrangement in the corresponding carbonium ion intermediate formed from 6. The cyclopentadiene ion ($C_5H_6{}^+$) derived from alcohols is accompanied by a strong (C_6H_7)$^+$ peak and both of these appear to experience extensive protonation (to m/e 67 and 68, re-

(6) J. A. Gilpin and F. W. McLafferty, *Anal. Chem.*, **29**, 990 (1957).

(7) P. Natalis, *Bull. Soc. Roy. Sci. Liege*, **31**, 790e (1962). See also C. G. MacDonald, J. S. Shannon, and G. Sugowdz, *Tetrahedron Lett.*, **13**, 807 (1963).

(8) W. Benz and K. Biemann, *J. Amer. Chem. Soc.*, **86**, 2375 (1964).

spectively; see Figure 2) in contrast to the same ion (m/e 66) arising from the bicycloheptene directly (see spectrum a, Figure 1). It will be seen, nevertheless, that the m/e 66 derived from **6** is of slightly greater intensity than m/e 67 and 68, whereas the converse is true of the undeuterated norborneols in Figure 2 (spectra a and c). This would suggest that hydride migration in the carbonium ion derived from **6** through loss of hydroxyl is somewhat more facile. That is to say, this carbonium has a sufficiently greater lifetime than that arising from **7**, allowing for a greater extent of hydride migrations and producing **8**, a more extensively scrambled structure than **9** (as is shown below in classical ion notation).
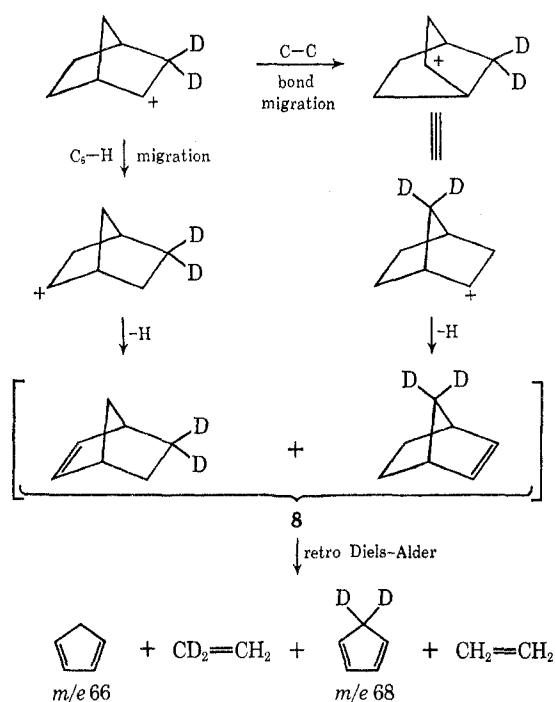
A parallel observation of the relative lifetimes of these carbonium ions in solution and the significance of this factor in determining the occurrence of C–C and C–H bond migrations have been previously discussed.[1]

Finally, the case of the bridgehead diol **10** will serve as an illustration of the generality of dehydration, even where α,β elimination of the elements of water is most unlikely because the resultant ion would possess the highly strained bridgehead double bond. Nonetheless,
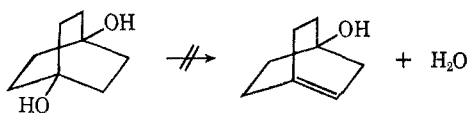
a prominent P − 18 peak is noted in the spectrum (b, Figure 4) of **10**. Similarly the ion product of subsequent retro-Diels–Alder cleavage in the form of the relatively intense peak (24%) at m/e 96 is identifiable by high resolution mass determination as $(C_6H_8O)^+$, and its deprotonated satellite (m/e 95, 21%). These data can (once again) be reconciled with the occurrence of hydride migration following the formation of the (unstable) bridgehead ion through loss of hydroxyl.
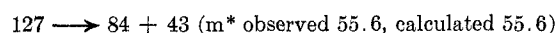
Formation of m/e 57 peak.—Another mode of stabilizing the odd-electron molecular ion of an alcohol (supposedly formed by expulsion of a nonbonding electron of an oxygen atom) is through rupture of the C_2–C_3 bond with subsequent decomposition to an m/e 57 ion and a hydrocarbon radical. High resolution mass measurements on the bicyclic alcohols studied in this investigation established that the fragment ion of mass 57 has the composition $(C_3H_5O)^+$, probably a resonance stabilized ion of the form $[CH_2=CHCHOH]^+$. This is in accord with a conclusion reported earlier[7,9] for cyclohexanol and cyclopentanol.

Although m/e 57 is not the major peak of any of the bicyclo alcohols studied here, it is quite intense, comprising 28.6% in **1**, 22.7% in **2**, and 43.9% in **3**. These are shifted to m/e 58 in the deuterated analogs with similar peak intensities for corresponding substrates, (*i.e.*, where W = D replaces X = H). Dimmel and Wolinsky[3] have reported m/e 57 as the ninth most intense peak in the spectra of both *endo*- and *exo*-norbornanol.

Appropriate labeling of the [2.2.1] and [2.2.2] alcohols established that the initial fragmentation steps in the formation of m/e 57 from these alcohols involves the rupture of the C_2–C_3 bond. Thus, deuteration of the hydroxyl-bearing carbon in each case shifted the peaks to m/e 58, but complete deuteration of the α (C_3) carbon produced *no shift* of m/e 57.

Additional evidence bearing on the course of fragmentation are the metastable peaks at m/e 38.9 (calculated 39.1) in the spectrum of the bicyclic alcohol **2** (X = H), and at m/e 39.9 (calculated 40.1) of deuterated **2** (X = D). Calculations indicate further that these could be the result of fragmentations which yield peaks at m/e 57 and 58, respectively (illustrated below).

$$83 \longrightarrow 57 + 26 \ (m^* -39.1)$$

$$84 \longrightarrow 58 + 26 \ (m^* -40.1)$$

This would require that there be a prior fragmentation splitting off 43 mass units. Evidence for this occurrence can be found in metastable peaks present in the spectra of **2** (both X = H and X = D).

$$126 \longrightarrow 84 + 43 \ (m^* \text{ observed } 54.7, \text{ calculated } 54.7)$$

$$127 \longrightarrow 84 + 43 \ (m^* \text{ observed } 55.6, \text{ calculated } 55.6)$$

On the basis of these lines of evidence the most likely fragmentation path (**2a** → **2f**) which can be proposed for the bicyclooctanols is that displayed in Scheme I where encircled H traces the hydrogen retained in m/e 57.

An analogous fragmentation route (**1a** → **1e**) can be plotted for formation of m/e 57 from the bicycloheptanol **1** (see Scheme II) where encircled H traces the hydrogen retained in m/e 57.

An alternative route leading from **1b** → **1g** (Scheme III) upon rupture of the C_2–C_3 bond is one of the

(9) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964.

SCHEME I

SCHEME II

SCHEME III
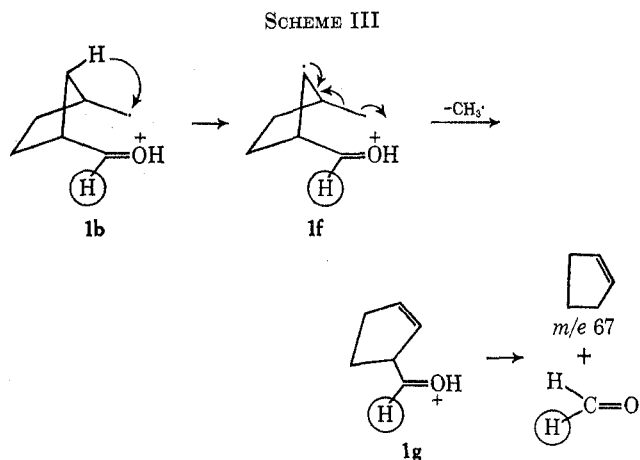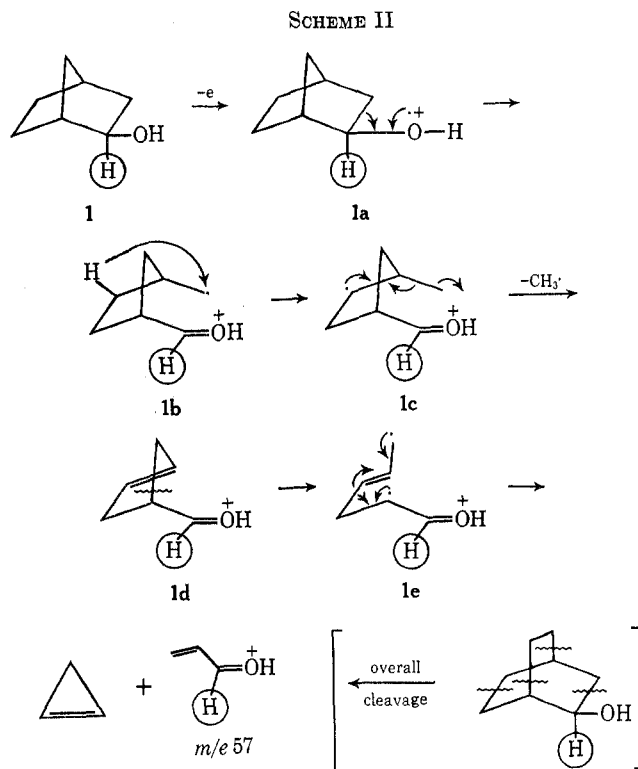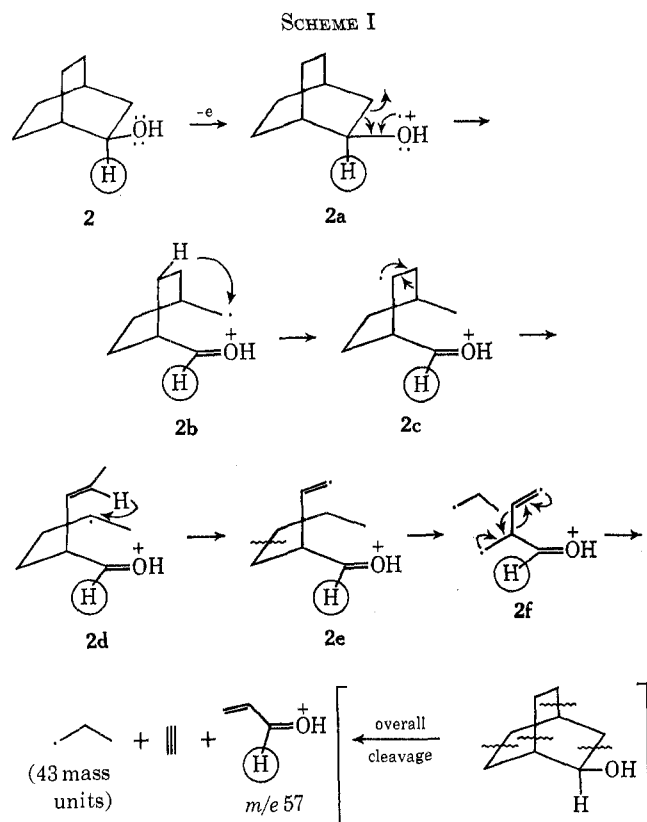
strongest competitors for fragmentation of the parent (along with the dehydration mechanism previously considered). The m/e 67, one of the most intense peaks aside from P − 18 in the spectra of all the alcohols in Figure 2, has been shown by high-resolution mass determination to be the pure hydrocarbon ion $(C_5H_7)^+$. The fact that this peak is equally intense in the spectra of all the bicyclo[2.2.1]heptanols, both deuterated and nondeuterated [1 (X = H), 1 (X = D), and 6] may be cited as strong evidence supporting this mechanistic proposal. It will also be recognized (see following section of this report) as one of the factors vitiating the application of the retro-Diels–Alder cleavage for locating deuterium on the norbornyl skeleton *via* the m/e ratio 66:67.

The complete generality of this overall cleavage course in bicyclic alcohol fragmentations leading to m/e 57 is to be perceived in the spectrum of the bridgehead diol 10. In all other (mono) alcohols studied the m/e 57 retains the charge [because it has the electronegative oxygen in its $(C_3H_5O)^+$ structure] while losing neutral hydrocarbon fragments in the final cleavage steps. In the diol 10, however, we observe that the second (hydroxyl) oxygen tends to stabilize the ionic charge, with the consequence that both cleavage fragments can be readily identified as intense peaks; the m/e 57 peak is 22% and the m/e 85, identified as $(C_5H_9O)^+$, is the most intense (base) peak in the mass spectrum (b), Figure 4. The following (Scheme IV) appears to be the most attractive way of accounting for this result, in consonance, as well, with the fragmentation patterns of the other bicyclic alcohols considered in these studies.

Applications to Deuterium Analysis in Atom-Bridged Compounds.—The migration of deuterium and rearrangement of the carbon skeleton which might be associated with Wagner–Meerwein rearrangements

can be followed in certain cases by examination of some of the fragment ions in the mass spectrum. For example, Cristol and coworkers[10] have demonstrated that the retro-Diels–Alder decomposition of dehydronorbornyl acetates provides a way of determining the location of deuterium on the skeleton of this class of bicyclic derivatives. Essentially the method consists of a comparison of the intensities of m/e 66 and 67 peaks for estimating the extent of deuterium migration into that part of the molecule which acquires the cyclopentadienyl ion structure in fragmentation of the parent ion.

We have attempted to apply this approach to (saturated bicyclic) norbornyl derivatives which would undergo elimination of HX in the spectrometer. Since fragmentation of the (P − HX) peak to retro-Diels–Alder products is a common occurrence, it seemed likely that a method of deuterium tracing analogous to that used for dehydronorbornyl derivatives could be ap-

(10) S. J. Cristol, R. A. Sánchez, and T. C. Merrill, *J. Org. Chem.*, **31**, 2738 (1966).

Scheme IV[a]
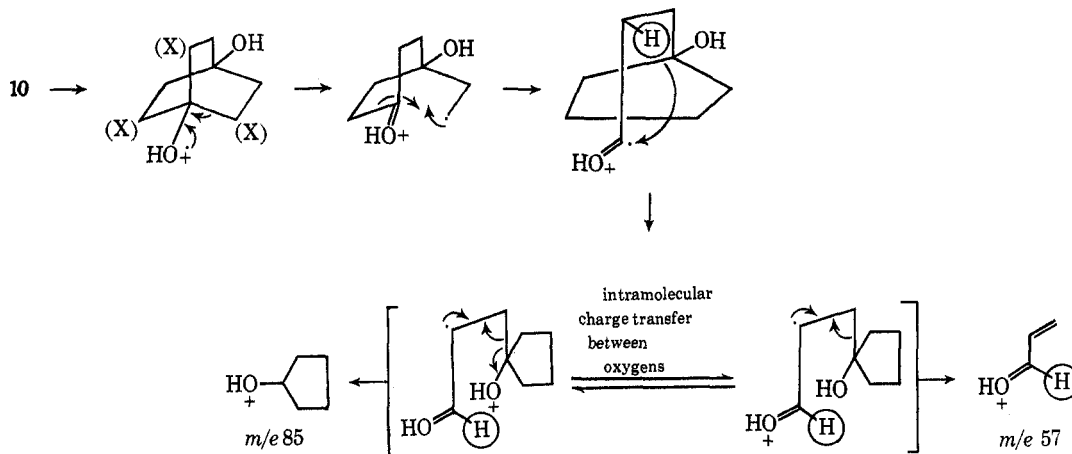
[a] (X) denotes three equivalent ways in which this fragmentation would occur.

plicable. However (as has been shown earlier in this article), the loss of HOH in the bicyclic alcohols studied was not a simple α,β elimination. Instead, a deep seated rearrangement (in the intermediate carbonium ion) of the hydrogen (and deuterium) atoms of the skeleton attended the loss of hydroxyl. This circumstance clearly obviated the use of any fragment ion which did not contain hydroxyl for purposes of locating deuterium atoms on the skeleton of any saturated bicyclic derivative, particularly the alcohols. Furthermore, as shown in the previous section of this report, the m/e 67 peak arises also from one of the most abundant ions in the spectra of norbornyl alcohols independently of deuteration in the C_2 and C_3 positions. This must surely be the most decisive reason why the retro-Diels–Alder cleavage cannot be applied for structure tracing in saturated norbornyl derivatives.

Clearly, then, the only fragment peak which could be used reliably for such trace analysis is one containing the hydroxyl (thereby avoiding the rearrangements stemming from loss of hydroxyl). The m/e 57:58 ratio fulfills this specification, both for the bicyclo[2.2.1] and -[2.2.2] alcohols. The substitution of deuterium for the hydrogen on C_2 in each case shifts the bulk of this peak to m/e 58. Thus, if, as a result of reaction, the D is "scrambled" out of the C_2 or C_6 positions, this event can be readily detected in all rearrangements of norbornanol derivatives (where the product can be converted to a norbornanol sample for mass spectral analysis).

However, in applying this analysis to rearrangements of bicyclo[2.2.2]octanol derivatives[1] a statistical correction of two must be made for the equivalence of the C_6 and C_7 positions in fragmentation. This can be readily seen in the following illustrative computation. Here the m/e 57:58 ratio in a nondeuterated sample corresponds to 100% migration of the deuterium from C_2 while the same measured ratio of 57:58 intensities in the known deuterated, alcohol would represent no deuterium migration from C_2. Thus, the nondeuterated sample of 2 (= 100% D loss) showed a 7.7 (m/e 57:58) ratio, while in a sample of 2, deuterated only at C_2 (= 0% D loss), the measured ratio was 0.22. In a typical acetolysis of the brosylate derivative of the

sample deuterated at C_2 the acetate product was purified by glc methods and saponified, and the pure [2.2.2] alcohol recovered in which some of the deuterium had migrated from C_2. The measured ratio of this product was 0.28. This result calculates as

$$2\left[\frac{0.28}{7.7 - 0.22}\right] = 6\% \text{ D migration}$$

Experimental Section

Technique.—The mass spectra of most of the compounds were obtained on a Consolidated Electrodynamics Corp. instrument, Model 21-103-C. Most of the high-resolution fragment ion mass determinations were carried out with a Model 110 instrument. Sample introduction was effected by means of a 350° capacity heated inlet accessory unit. Sufficient volatility of all samples used was realized at inlet temperatures in the range of 150°.

The spectra were obtained usually employing nominal 70-eV ionizing energies except as noted for low voltage spectra where 15-eV ionizing energies were used. The ionizing current could always be adjusted to yield spectra of satisfactory intensity.

Origin of Samples.—We are indebted to John L. Irvine for furnishing the bicyclo[2.2.2]octanol samples (2, X = H and X = D). The samples of 6 and 7, the bicyclic alcohols dideuterated at C_3, were kindly prepared by Dr. Norbert Kucharczyk from the corresponding ketones by three successive base-catalyzed exchanges in dioxane–D_2O media, followed by lithium aluminum hydride reduction to the alcohol, and purification of the product by familiar methods. The samples of 1 (X = H and X = D) were prepared by reduction of the norbornanone using lithium aluminum hydride or deuteride, respectively, adapting the procedures by Brown.[11] Gas chromatographic cuts were ordinarily used to obtain the appropriate mass spectra. The structures of the alcohols and the positions of deuteration, where possible, were always confirmed by nmr and ir analysis.

The samples of bicyclo[2.2.1]-2-heptene (4) and bicyclo[2.2.2]-2-octene (5) were obtained from Chemical Samples Co., Columbus, Ohio, and were recommended to be greater than 99% purity. The sample of bicyclo[2.2.2]-1,8-octanediol was kindly furnished (in pure form) by Dr. James Kauer. Mass spectra were taken on these samples as received.

(11) W. G. Brown, *Org. React.*, **6**, 469 (1951).