Mass Spectrometry in Structural and Stereochemical Problems. CLXXX.[1] Oxygen Rearrangement and Fragmentation Reactions after Electron Impact on 4-Hydroxy- and 4-Alkoxy-1-decalones[2]

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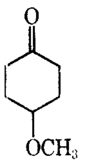
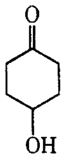
Received May 5, 1969

Electron impact induced oxygen rearrangement has been found to be an important fragmentation pathway in 4-hydroxy- and 4-alkoxy-1-decalones and their 9-methylated analogs. Charge retention is on a hydrocarbon fragment, and, although no evidence can therefore be obtained from high-resolution measurements concerning the mechanism of the fragmentation, the occurrence of such a rearrangement has been demonstrated by specific deuterium labeling. For a similar rearrangement in the monocyclic analogs, the charge remains on the oxygenated fragment, leading to possible erroneous structural conclusions. With charge retention on the hydrocarbon portion, no such errors are possible. The other major fragmentation paths for these bifunctionalized compounds, including loss of ROH (R = H, Me, or Et), have also been elucidated. In general, they do not involve transannular interaction, and are typical of the separate functionalities, as shown by comparison with their monofunctional analogs.

Since the advent of mass spectrometry in the field of organic chemistry, many electron impact induced rearrangements have been discovered.[4] Most of these rearrangements have involved transfer of a hydrogen atom or an alkyl radical, usually producing a more stable fragment ion.[5]

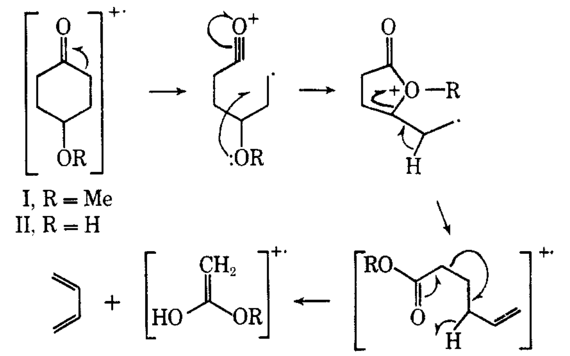
During the course of a systematic study of substituted cyclohexanones in this laboratory, it was reported that the base peak in the mass spectrum of 4-methoxycyclohexanone (I) occurs at *m/e* 74 and has an elemental composition of $C_3H_6O_2$.[6] Similarly, the intense fragment ion of mass 60 in the spectrum of 4-hydroxycyclohexanone (II) was shown to be composed only of $C_2H_4O_2$. It follows that these fragments must arise from a rearrangement process, in order that the two oxygen functions may be brought into closer proximity in the fragment ion than they were in the parent compound. Using the techniques of high-resolution analysis, deuterium labeling, and metastable analysis, the rearrangement mechanism was deduced to be as shown in Scheme I.[7] This study thus uncovered one of the first substantiated electron impact induced rearrangements involving migration of a hydroxyl or alkoxyl group.


I


II

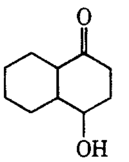
We now wish to report the discovery of a similar, important rearrangement process in the bicyclic analogs of I and II. It seemed a natural extension of our earlier study[6] to investigate the generality of such a rearrangement, especially since one basic approach[5] in this laboratory has been to concentrate on those fragmentations assisted by functional groups in the molecule. Also, when a molecule contains two or more functional groups, it has been of considerable interest to examine the effect of one group on another in order to see if they react independently or by interaction.

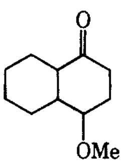
SCHEME I



An excellent example is afforded by the 4-hydroxy- and 4-alkoxy-1-decalones in question. Lund, *et al.*,[8] have already made an extensive mass spectral study of labeled and unlabeled 1-decalones and 9-methyl-1-decalones, and it was only necessary to examine the corresponding 1-hydroxy- and 1-alkoxydecalins, in order to secure the necessary basic information for evaluating functional group interaction in 4-hydroxy- and 4-alkoxy-1-decalones.

In contrast to the behavior[6] of 4-hydroxycyclohexanone (II), the mass spectrum[9] of 4-hydroxy-1-decalone (III) (Figure 1) shows only a minute peak at


III


IV

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[1] Paper CLXXIX by A. F. Gerrard and C. Djerassi, has been submitted for publication.

[2] Financial support by the National Institutes of Health (Grants GM 06840 and AM 04257) is gratefully acknowledged.

[3] (a) Postdoctoral Fellow, 1968–1969; (b) Postdoctoral Fellow, 1966–1968.

[4] For a recent review, see P. Brown and C. Djerassi, *Angew. Chem.*, **79**, 481 (1967); *Angew Chem. Intern. Ed. Engl.*, **6**, 477 (1967).

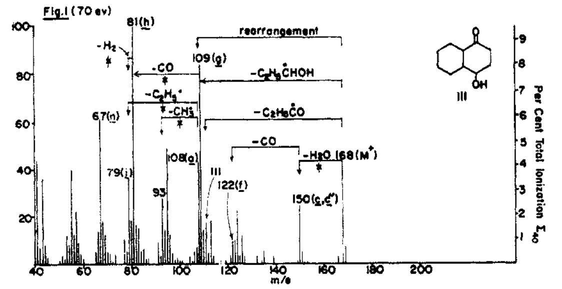
[5] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967.

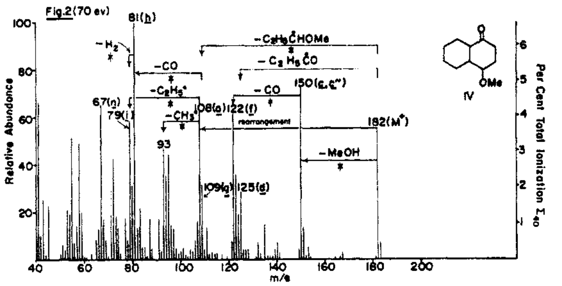
[6] M. M. Green, D. S. Weinberg, and C. Djerassi, *J. Amer. Chem. Soc.*, **88**, 3883 (1966); M. M. Green and C. Djerassi, *ibid.*, **89**, 5190 (1967).

[7] It is assumed that the rearrangement ions from the homologous series are formed from the molecular ion by the same mechanism.

[8] E. Lund, H. Budzikiewicz, J. M. Wilson, and C. Djerassi, *J. Amer. Chem. Soc.*, **85**, 941 (1963).

[9] All mass spectra were measured at 12 and 70 eV. Unless otherwise stated, however, the spectra discussed in the text are those obtained at 70 eV.





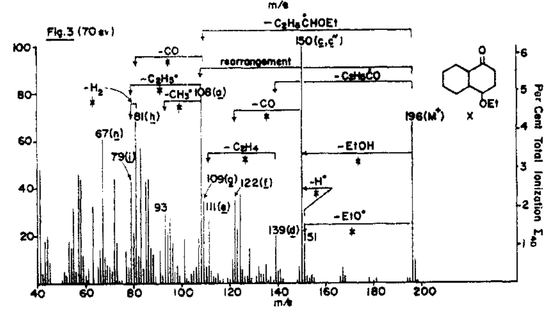
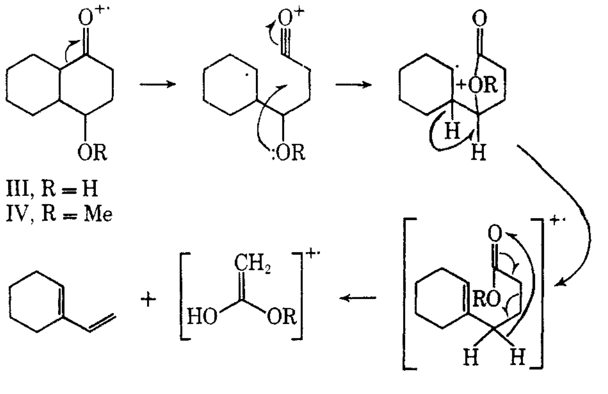


Figure 1.—Mass spectrum of 4-hydroxy-1-decalone (III).
Figure 2.—Mass spectrum of 4-methoxy-1-decalone (IV).
Figure 3.—Mass spectrum of 4-ethoxy-1-decalone (X).

m/e 60. Similarly, in the mass spectrum (Figure 2) of 4-methoxy-1-decalone (IV), the corresponding peak at *m/e* 74, as expected from the possible rearrangement (Scheme II[10]), is only 13% of the base peak. However,

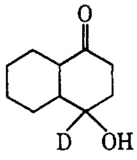
Scheme II


III, R = H
IV, R = Me

for both III and IV, a large peak is observed at *m/e* 108,[11] which may be associated with the same rearrangement, the charge in this case remaining on the hydrocarbon portion of the molecule. In contrast to the examples of I and II, in which the occurrence of a rearrangement will be demonstrated directly by the composition of the oxygen-containing fragments, the existence of a rearrangement in the genesis of the hydrocarbon fragment can only be demonstrated by isotopic labeling. To determine the specificity of bond cleavage and migration, a series of deuterium-labeled compounds was devised, in addition to the unlabeled analogs, whose mass spectra would give definitive information concerning the mechanism of this rearrangement.

Results and Discussion

To investigate the specificity of a possible electron impact induced hydroxyl and alkoxyl migration in 4-hydroxy- and 4-alkoxy-1-decalones, 11 deuterated and nondeuterated analogs of III were synthesized (III–XIII).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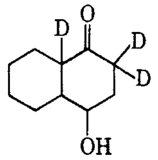
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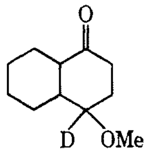
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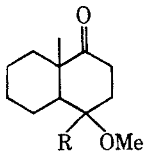
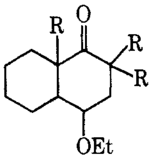
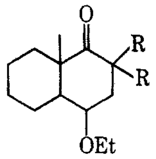
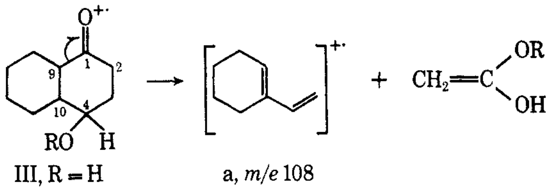

VIII, R = H
IX, R = D


X, R = H
XI, R = D


XII, R = H
XIII, R = D

The mass spectrum (Figure 1) of 4-hydroxy-1-decalone (III) shows a peak of 44% relative abundance at *m/e* 108. It is postulated that this fragment ion is formed by a hydroxyl transannular migration, to give *m/e* 108, of elemental composition C_8H_{12} (Scheme III). High-resolution measurements indeed indicate the major portion (87%) of this peak to correspond to a hydrocarbon. The remainder has composition C_7H_8O, of an unknown structure.

Scheme III


III, R = H
IV, R = Me
X, R = Et

a, *m/e* 108

This compound also exhibits a strong peak at *m/e* 109 (84% relative abundance), formed by another fragmentation pathway, and shown by high-resolution measurements to be composed of C_7H_9O (95%) and C_8H_{13} (5%). Upon introduction of a deuterium atom at C-4 in III, to give 4-d_1-4-hydroxy-1-decalone (V), the peak at *m/e* 108 in III decreases in intensity, with a concomitant increase of *m/e* 109. A similar trend is seen in the mass spectrum of 2,2,9-d_3-4-hydroxy-1-decalone (VI). High-resolution measurements show the *m/e* 109 peak from VI to be composed of C_7H_9O and $C_8H_{11}D$. Hence, it appears that carbons 4 and 9 are indeed involved in the formation of the hydrocarbon

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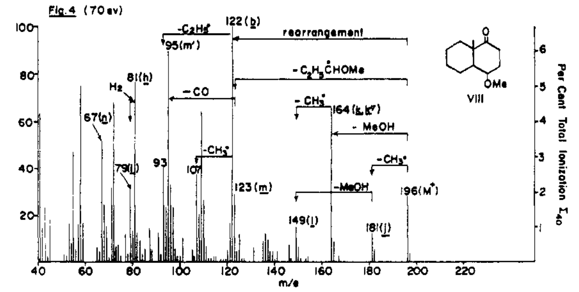
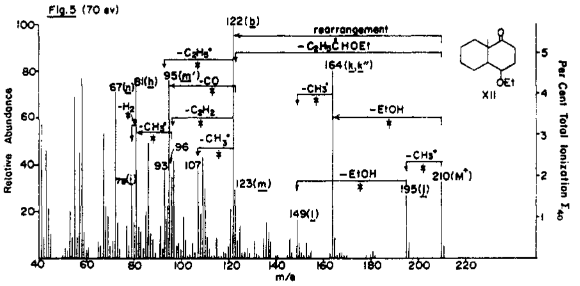
[10] There exist at least two obvious sites for charge localization. For purposes of clarity, in this paper the charge will be schematically localized at the functionality which appears to trigger each particular fragmentation sequence.

[11] The composition of all relevant peaks was determined by high-resolution measurements.





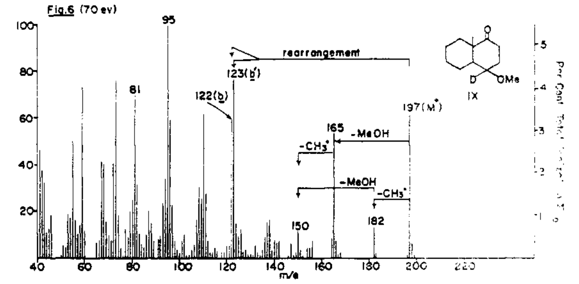


Figure 4.—Mass spectrum of 4-methoxy-9-methyl-1-decalone (VIII).

Figure 5.—Mass spectrum of 4-ethoxy-9-methyl-1-decalone (XII).

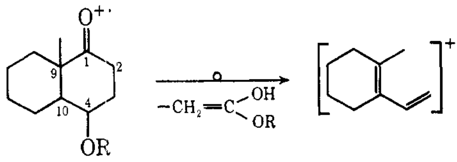
Figure 6.—Mass spectrum of 4-d_1-4-methoxy-9-methyl-1-decalone (IX).

portion of the fragment of mass 108, as suggested by Scheme III. However, owing to the presence of the intense oxygen-containing peak at m/e 109, and to the complexity of the composition of the one at m/e 108, no firm conclusion could be reached concerning the specificity of the rearrangement.

An equally ambiguous situation exists in the cases of 4-methoxy-1-decalone (IV) and 4-ethoxy-1-decalone (X). The mass spectra of both compounds (Figures 2 and 3) indeed exhibit an intense peak at m/e 108 (C_8H_{12}, 91%; C_7H_8O, 9%), consistent with the proposed rearrangement mechanism. However, a fragment ion of mass 109 is also observed in both spectra, thus complicating the possibility of quantitative interpretation of the mass spectra of any analogs specifically labeled with deuterium. For example, although a shift in the m/e 108 peak from IV and X was observed on labeling carbons 4 and 9 with deuterium (giving peaks at m/e 109 for VII and XI, respectively), no conclusive results could be obtained owing to the high population of this area with peaks derived from other fragmentation pathways.

This problem was circumvented by introduction of a methyl group at C-9 in IV and X to give VIII and XII, respectively. If the proposed mechanism for the rearrangement is correct, this should give the resulting charged species at m/e 122, in an area relatively unobscured by other fragment ions (Scheme IV). Also, introduction of an angular methyl group should increase α cleavage at C-9, giving a relatively more intense fragment ion (b) at m/e 122.

Scheme IV



VIII, R = Me
XII, R = Et

b, m/e 122

The mass spectra of VIII and XII are shown in Figures 4 and 5, respectively. As predicted, the fragment ion at m/e 122 is the base peak in both cases. Even at 12 eV, this fragment from XII carries 12.5% of the total ionizing current,[12] indicating a very facile fragmentation process. Also, a relatively much smaller fragment ion of mass 123 is observed in both cases. Thus, through consideration of the mass spectra of the angularly methylated compounds VIII and XII and the deuterated compounds VII and XI, the participation of carbons 4 and 9 in this fragmentation pathway has been unambiguously verified.

When C-2 in XII is deuterated (giving XIII), little change occurs in this area of the spectrum. Indeed, m/e 122 remains the base peak, indicating no transfer of the C-2 hydrogens from the molecular ion into the fragment under discussion.

If the proposed mechanism (Scheme III) is correct, the hydrogen atom at C-10 should migrate to C-4 with concomitant cleavage of the C-4 alkoxyl bond. Hence, in the final step in the formation of m/e 122, the McLafferty rearrangement would involve transfer of the hydrogen atoms originally situated at C-4 and C-10 in the parent molecule. Therefore, if a deuterium atom is incorporated at C-4 in VIII to give IX, the fragment ion of mass 122 for VIII should split equally between m/e 122 and 123 for IX. The mass spectrum (Figure 6) of 4-d_1-4-methoxy-9-methyl-1-decalone (IX) does indeed show the predicted splitting for this fragment. Although the relative abundances of the two fragment peaks (C_9H_{14} and $C_9H_{13}D$) are not equal (m/e 122, 59%; m/e 123, 76%), this difference can be entirely attributed to the residue of the peak at m/e 123 with elemental composition $C_8H_{11}O$. As described below, the position of this latter fragment would not be expected to change on deuteration at C-4.

From the above discussion, it is evident that in at least one major fragmentation pathway the two functional groups do, in fact, come together upon electron impact, and therefore it was of interest to examine the other major fragmentation pathways observed for this system. For those mass spectral fragmentation routes where no interaction is evident, it will be worthwhile to compare the mass spectra of these 4-substituted 1-decalones with those exhibited by the corresponding monofunctionalized compounds.[13]

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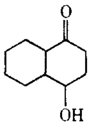
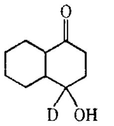
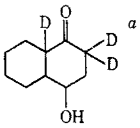
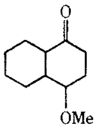
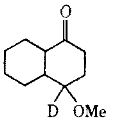
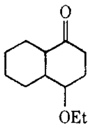
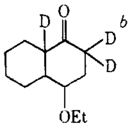
[12] This refers to that region of the spectrum above m/e 40.

[13] It has been demonstrated by Lund, *et al.*,[8] that *cis-* and *trans-*1-decalone exhibit different mass spectra. In this investigation, the stereochemistry of the bridgehead (in the nonmethylated compounds) is in the *trans* orientation unless otherwise stated; that of the 9-methylated compounds is probably a mixture of *cis* and *trans* orientations.

TABLE I

PRINCIPAL MASS SPECTRAL PEAKS IN THE SPECTRA OF 4-HYDROXY- AND 4-ALKOXY-1-DECALONES, *m/e* (% RELATIVE ABUNDANCE)

Compd	M − ROH	(M − ROH) − CO	M − $C_2H_3O_2R$	*m/e* 108 − $CH_3\cdot$	*m/e* 108 − $C_2H_5\cdot$	M − $C_2H_5\dot{C}HOR$	*m/e* 109 − CO	*m/e* 81 − H_2	M − $C_2H_5\dot{C}O$
 III	150 (24)	122 (9)	108 (44)	93 (28)	79 (36)	109 (84)	81 (100)	79 (36)	111 (17)
 V	151 (15)	123 (5)	109 (100)	93 (10) 94 (13)	79 (18)	109 (100)	81 (68)	79 (18)	112 (10)
 VI [a]	152 153	125	109	94	80	110	82	80	112
 IV	150 (72)	122 (61)	108 (62)	93 (47)	79 (59)	109 (31)	81 (100)	79 (59)	125 (28)
 VII	151 (80)	123 (41)	109 (80)	93 (24) 94 (42)	79 (43)	109 (80)	81 (100)	79 (43)	126 (40)
 X	150 (100)	122 (36)	108 (79)	93 (30)	79 (43)	109 (35)	81 (69)	79 (43)	139 (20)
 XI [b]	152 (53) 153 (73)	125 (68)	109 (67)	94 (40)	80 (45)	110 (35)	82 (80)	80 (45)	140 (60)

[a] Owing to the poor isotopic purity of this compound, relative abundances are not given. [b] The molecular ion is the base peak.

The mass spectra will be discussed in two distinct groups, first those of the compounds containing a hydrogen at C-9, followed by those exhibited by the compounds bearing a C-9 angular methyl group. The data indicate that it will be permissible and convenient to consider the spectra of 4-hydroxy-, 4-methoxy-, and 4-ethoxy-1-decalone together, since they all exhibit similar fragmentation patterns. Each proposed pathway will be supported where possible by deuterium labeling (Table I) and metastable ion peaks.

The Mass Spectra of 4-Hydroxy- and 4-Alkoxy-1-decalones. Peak at *m/e* 150.[14]—This fragment ion is prominent in all three series of compounds, and is due to loss of ROH (R = H, Me, or Et) from the molecular ion. It is interesting to note the trend in the relative abundance of this fragment from compounds III, IV, and X. Loss of ethanol from X seems to be much preferred over loss of water from III.

It has been pointed out[15] that such elimination reactions are frequently of thermal origin and it could be argued that a similar phenomenon is responsible for the observed behavior in the present examples. This is considered unlikely in view of the fact that samples of each compound, when subjected to gas chromatography under elevated temperature conditions, were recovered unchanged. Moreover, the compounds exhibited similar mass spectra when measured on two different spectrometers under different conditions. Finally, the presence of appropriate metastable peaks demonstrates that at least a portion of the elimination must proceed after ionization.

It is postulated that loss of ROH occurs by three different pathways (Scheme V). This is most evident from the spectrum of 2,2,9-d_3-X (XI), in which peaks at *m/e* 152 (53%) and 153 (73%) are observed for this transition. Thus, an appreciable portion of the fragmentation occurs by a 1,3-elimination process, as indicated by the substantial loss of ethanol-*d*. However, blockage of the C-9 position with a methyl group results in the disappearance of the corresponding M − EtOD

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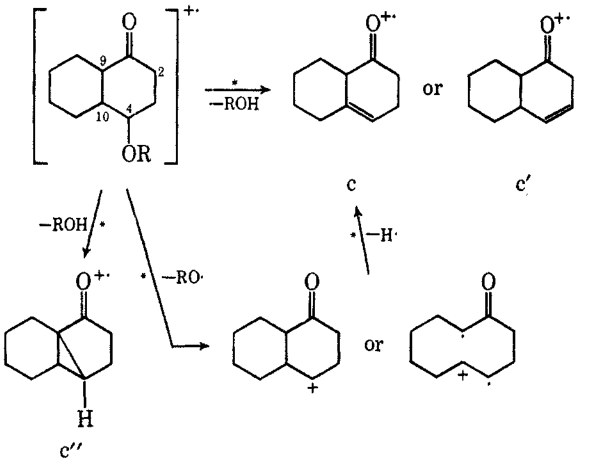
[14] The sample peak values will be taken from the mass spectra of compounds III, IV, and X. The corresponding *m/e* values for the deuterium-labeled analogs are shown in Table I.

[15] Reference 5, p 98.

SCHEME V

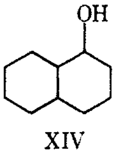


peak (*vide infra*), suggesting that 1,3 elimination in X only occurs between C-4 and C-9 (c″).

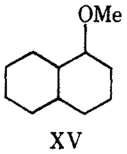
Loss of ROH also occurs in a 1,2 fashion, resulting in 4–10 (c) or 3–4 (c′) unsaturation. Although these would also be the positions of thermal elimination, the occurrence of a large metastable peak at *m/e* 117.6 (calcd *m/e* 117.6 for *m/e* 199 → 153) in the spectrum of XI indicates that at least a portion of the 1,2 elimination also occurs after ionization. It may be predicted that c, with a more highly substituted double bond, would be the preferred structure for this fragment, but further deuterium labeling would be needed to substantiate this assignment.

In the methoxy and ethoxy series, metastable ions were also observed for loss of an alkoxyl radical, followed by elimination of a hydrogen atom, again resulting in species c. This suggests that electron impact induced elimination of ROH is occurring by both a stepwise and a concerted mechanism.

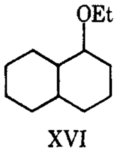
As may be expected, loss of ROH is also the dominating fragmentation in the mass spectra of 1-hydroxy- (XIV),[16] 1-methoxy-, (XV)[16] and 1-ethoxydecalin (XVI), the resulting ion of mass 136 being the base peak in each case (the mass spectrum of XVI is shown in Figure 7). Since metastable ion peaks are observed in each spectrum, it is suspected that elimination probably occurs predominantly in a 1,3[17,18] and 1,4 fashion,[17,18] as has been demonstrated for the corresponding monocyclic analogs. Deuterium labeling



XIV



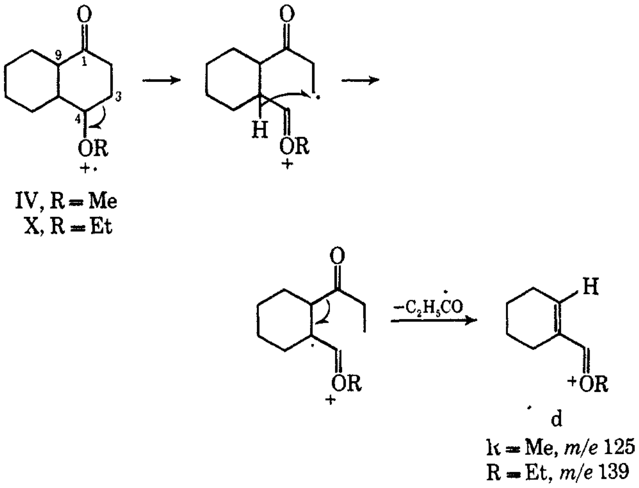
XV



XVI

experiments would be needed to substantiate this prediction. However, even in the absence of such labeling, it is easily possible to assign fragmentation paths to the principal ions, as shown in Scheme VI.

Peak at M − 57 (*m/e* 125 in IV, 139 in X).—This fragment ion is of less abundance in the mass spectrum (Figure 1) of 4-hydroxy-1-decalone than in those (Figures 2 and 3) of the corresponding alkoxy analogs. Loss of 57 mass units indicates cleavage of the 1–9 and 3–4 bonds, with concomitant transfer of a hydrogen atom from the nonfunctionalized ring. It is suggested that this fragmentation is triggered by ionization of the ether function, followed by loss of the $C_2H_5\dot{C}O$ moiety, to give the conjugated ion d. This fragment



would be expected to be more stable with R = Me or Et than when R = H.

This conclusion is in full accord with the results from the 1-alkoxydecalins. Metastable ion peaks for

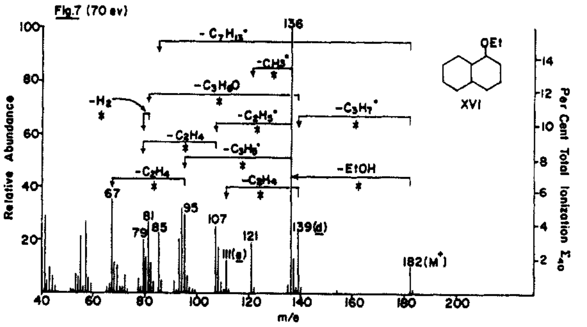
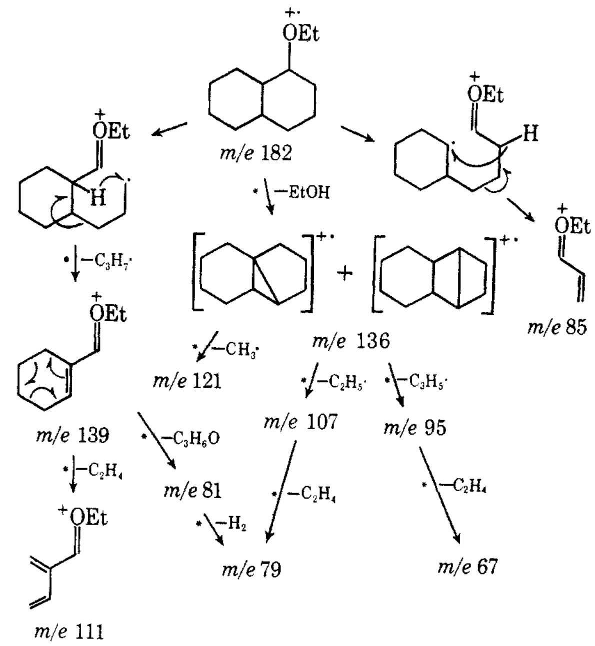


Figure 7.—Mass spectrum of 1-ethoxydecalin (XVI).

SCHEME VI



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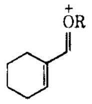
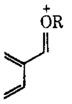
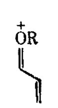
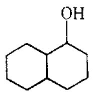
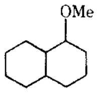
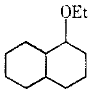
(16) The stereochemistry of the bridgehead is unknown.

(17) H. Budzikiewicz, Z. Pelah, and C. Djerassi, *Monatsh. Chem.*, **95**, 158 (1964).

(18) M. M. Green and J. Schwab, *Tetrahedron Lett.*, 2955 (1968).

TABLE II

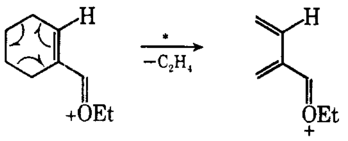
PRINCIPAL MASS SPECTRAL PEAKS IN THE SPECTRA OF 1-HYDROXY- AND 1-ALKOXYDECALINS, *m/e* (% RELATIVE ABUNDANCE)

Peak	M⁺			M − ROH		*m/e* 121	*m/e* 107	*m/e* 95	*m/e* 81	*m/e* 79	*m/e* 67
 XIV	2	15	6	100	24	32	32	45	50	31	60
 XV	16	34	2	100	49	20	27	27	25	22	23
 XVI	10	23	12	100	22	19	25	29	26	19	35

similar transitions are observed for both XV and XVI (Table II), and high-resolution measurements indicate the peak at *m/e* 139 from XVI to be comprised entirely of the species $C_9H_{15}O$, which would also be expected to have the conjugated structure d.

Fragmentation also occurs with initial cleavage between C-1 and C-9, and the intensity of the resulting ions (*e.g.*, *m/e* 85 in Scheme VI) is nearly equal to or greater than that of ion d (Table II).

Metastable ion peaks at *m/e* 88.7 (calcd *m/e* 88.6 for *m/e* 139 → 111) in the spectra of X and XVI correspond to the further decomposition of ion d. Since high-resolution measurements indicate the composition of the daughter ion to be predominantly oxygen-containing ($C_7H_{11}O$, 98%; C_8H_{15}, 2%), this may be explained by a retro Diels-Alder reaction, giving the high conjugated oxonium ion e.

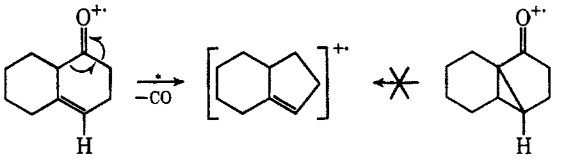


d e

This conclusion is supported by a corresponding metastable ion and peak shift of one mass unit for XI, suggesting that the hydrogen at C-9 in the parent ion remains in the charged species throughout the fragmentation pathway.

Peak at *m/e* **122.**—High-resolution measurements indicate this fragment ion to consist predominantly of a hydrocarbon moiety (C_9H_{14}, 80%; $C_8H_{10}O$, 20% for IV; C_9H_{14}, 73%; $C_8H_{10}O$, 27% for X). Metastable ions are observed for its formation through loss of carbon monoxide from the fragment ion of mass 150, to give a species of proposed structure f. This fragmentation pathway is confirmed by the relative shifts of the corresponding peaks derived from the labeled analogs. It seems to represent only a very minor fragmentation pathway in the 4-hydroxy-1-decalones.

Loss of carbon monoxide occurs only from the 1,2-elimination product ion c, since a significant peak at *m/e* 124, derivable by loss of CO from c″, is not observed in the mass spectrum of the 2,2,9-d_3 analog (XI).

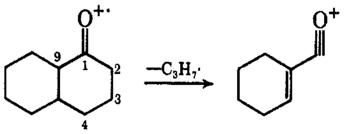


c f c″

The structure of the minor (oxygenated) component of this fragment ion is not readily apparent.

Peak at *m/e* **109.**—Although this represents a fairly significant peak in all the spectra (Table I), especially in that of 4-hydroxy-1-decalone (III), it is not so prominent here as in the spectrum of *trans*-1-decalone[8] or even that of cyclohexanone itself.[19] Since the first step in the fragmentation is undoubtedly cleavage of the 1–2 bond, it is probable that other fragmentations associated with the alkoxyl groups account for this decrease in the relative abundance of *m/e* 109.

Deuterium labeling in the *trans*-1-decalone series indicated[8] loss of carbons 2, 3, and 4, together with the hydrogen attached to C-9, resulting in the formation of fragment g.



g, *m/e* 109

A fragment of this structure may also be derived from III, IV, and X by a similar pathway. However, the corresponding peak at *m/e* 123 for the methylated analog XII also occurs, although not to such a large extent (*vide infra*). This suggests that a second pathway, such as that shown in Scheme VII, may be energetically navigable.

Although g′ is not anticipated to be as stable as g, loss of the more stable α-alkoxy radical, as contrasted to a propyl radical in 1-decalone, may favor the latter mechanism. A significant peak at *m/e* 110 in the spectrum of XI suggests that the hydrogen atom at C-9 in the molecular ion has, to some extent, been retained in the fragment ion of mass 109.

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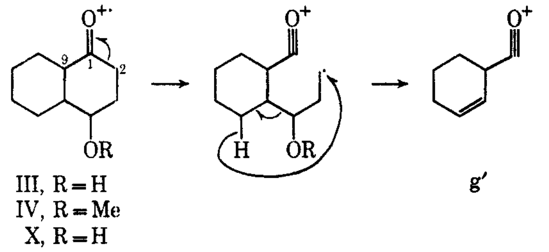
(19) D. H. Williams, H. Budzikiewicz, Z. Pelah, and C. Djerassi, *Monatsh. Chem.*, **95**, 166 (1964).

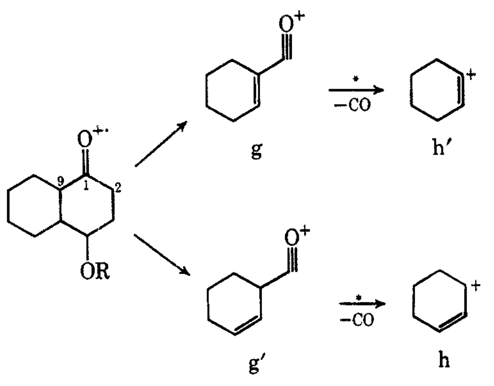
Scheme VII



Peak at ***m/e*** **108.**—This fragment is composed predominantly of a hydrocarbon moiety (C_8H_{12}, 91%; C_7H_8O, 9% for X), whose structure and mode of formation have been described above. A metastable analysis indicates that this fragment decomposes further, through loss of methyl and ethyl radicals, to give fragment ions of mass 93 and 79, respectively. Although the structures of these ions are not known, the mechanism of their genesis must involve extensive hydrogen migration.

Peak at ***m/e*** **81.**—Metastable ion peaks at *m/e* 60.2 (calcd *m/e* 60.2 for the transition *m/e* 109 → 81) and high-resolution measurements (C_6H_9, 100% for VII) indicate that this fragment is derived from the peak at *m/e* 109, by loss of carbon monoxide, with generation of a cyclohexenyl cation (h). This explanation is in accord with the observation that the *m/e* 81 peak in X shifts, at least in part, to *m/e* 82 in the 2,2,9-d_3 derivative, which suggests strongly that the hydrogen at C-9 in X is maintained in this fragment ion. However, high-resolution measurements on the peaks at *m/e* 81 (C_6H_9, 97%) and 82 (C_6H_8D, 96%) derived from the 2,2,9-d_3 analog of III (VI) may indicate a duality of mechanism (Scheme VIII).

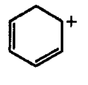
Scheme VIII



Loss of carbon monoxide from g′ would certainly be more facile than from g, but, as suggested by Lund,[8] the latter process may involve hydrogen transfer prior to fragmentation. This may again result in a fragment with structure h. Furthermore, it is conceivable that one or both of these species possess an open-chain structure.

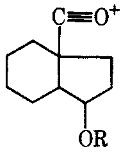
Peak at ***m/e*** **79.**—This peak is derived from at least two different pathways. As discussed above, metastable ions are observed for the transition *m/e* 108 → 79, which occurs with loss of an ethyl radical from ion a.

However, a large metastable peak at *m/e* 77.1 (calcd 77.05 for the transition *m/e* 81 → 79) indicates that this fragment originates to some extent from a precursor of mass 81. For 2,2,9-d_3-X, the corresponding metastable peak is observed at *m/e* 78.2, which is in accord with the results only if one deuterium atom is retained in the charged species.



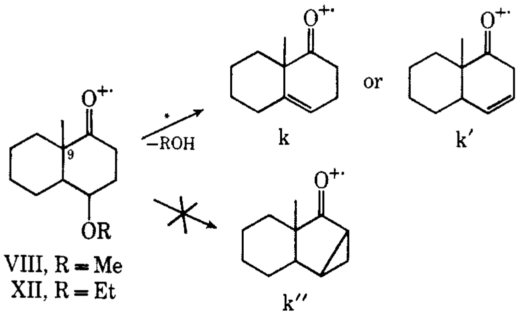
i, *m/e* 79

The Mass Spectra of 9-Methyl-4-alkoxy-1-decalones. Peak at M − 15.—The loss of a methyl radical is much more pronounced in the spectra (Figures 4 and 5, respectively, Table III) of the angularly substituted analogs VIII and XII as compared to those (Figures 2 and 3) of the parent ketones. It is likely, therefore, that the principal source of methyl is the angular substituent rather than the alkoxy function. Although formally the resulting species would possess an unfavorable structure (positive charge next to a carbonyl group),[20] a more effective representation might be j, which could be formed by a ring-contraction process.

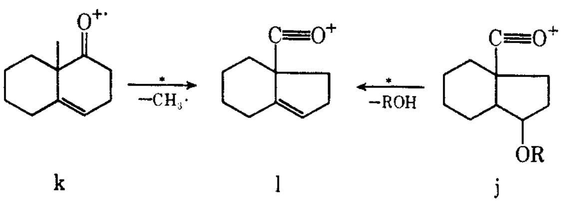


j

Peak at ***m/e*** **164.**—Prominent metastable ion peaks indicate this loss of ROH to be an electron impact induced process. Whereas in the absence of the angular methyl group (X) it was shown that a similar elimination occurred in both a 1,2 and a 1,3 manner, blockage of C-9 with a methyl group causes loss of the elements of ROH to take place exclusively in a 1,2 fashion. This is supported by complete deuterium retention in the corresponding fragment from the 2,2-d_2 analog (XIII), giving a fragment ion with structure k or k′.



Peak at ***m/e*** **149.**—This fragment ion is formed by two distinct mechanistic pathways. Metastable ion peaks are observed for its genesis by the loss of a methyl radical from the M − ROH peak k or k′ (at



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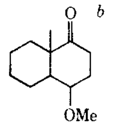
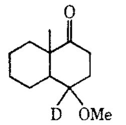
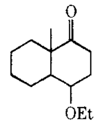
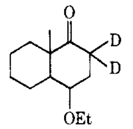
[20] The loss of a methyl radical from the corresponding angular position in 1-keto steroids has also been observed. See H. Powell, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, **86**, 2623 (1964).

TABLE III

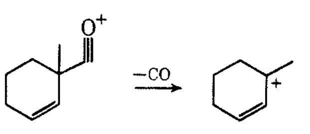
PRINCIPAL MASS SPECTRAL PEAKS IN THE SPECTRA OF 9-METHYL-4-ALKOXY-1-DECALONES, *m/e* (% RELATIVE ABUNDANCE)

Compd	M − CH_3	M − ROH	M − (ROH + CH_3)	M − $C_2H_3O_2R$	M − $C_2H_4\dot{C}HOR$[a]	M − (C_2H_4CHOR + CO)	*m/e* 81	*m/e* 79
 [b] VIII	181 (12)	164 (66)	149 (14)	122 (100)	123 (29)	95 (90)	81 (76)	79 (31)
 IX	182 (13)	165 (53)	150 (11)	122 (59) 123 (76)	123 (76)	95 (100)	81 (70)	79 (21)
 XII	195 (27)	164 (80)	149 (16)	122 (100)	123 (29)	95 (76)	81 (74)	79 (31)
 XIII	197 (27)	166 (74)	151 (12)	122 (100)	123 (36)	95 (64)	81 (55)	79 (31)

[a] These values have not been corrected for the natural abundance of the ^{13}C isotope from the fragment of mass 122. [b] Measured on the Atlas CH-4 mass spectrometer.

m/e 164 in VIII and XII) and by the loss of the elements of ROH from the M − 15 peak j (at *m/e* 195 in XII).

Peak at ***m/e*** **123.**—This peak corresponds to the *m/e* 109 fragment (g or g′) from the nonmethylated compounds (III, IV, and X), and probably has a structure such as m.



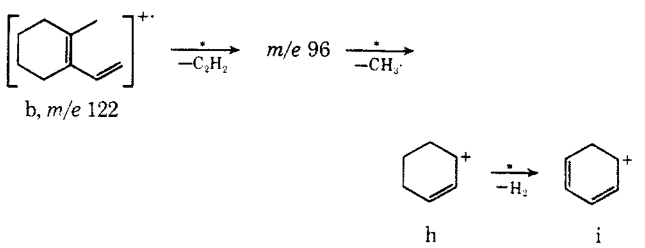
m m′, *m/e* 95

Ejection of carbon monoxide from m, giving the stable allylic tertiary cation m′, is expected to be very facile, and indeed the resulting peak at *m/e* 95 is prevalent in all of the spectra.

Peak at ***m/e*** **122.**—High-resolution measurements indicate the composition of this, the base peak in each spectrum, to be almost completely hydrocarbon in nature (C_9H_{14}, 96%; $C_8H_{10}O$, 4% for XII), and as described above it is formed by a rearrangement mechanism.

Metastable peaks are observed for further decomposition of this ion, with loss of methyl and ethyl radicals, to give fragments of masses 107 and 93, respectively.

Peak at ***m/e*** **81.**—Metastable peaks at *m/e* 68.3 (calcd 68.3 for the transition *m/e* 96 → 81) indicate that this abundant fragment is derived, at least in part, by loss of a methyl group from a fragment ion of mass 96. However, as discussed by Lund for a fragment of the same *m/e* value derived from 9-methyl-1-decalone,[8] no straightforward conclusion can be made as to its structure.



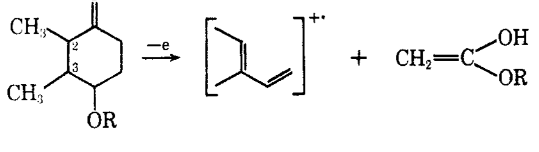
b, *m/e* 122 h i

It is convenient to write the structure of this fragment ion as h, because metastables at *m/e* 77.2 (calcd 77.2 for the transition *m/e* 81 → 79) indicate its further decomposition with loss of two mass units, as in the case of the nonmethylated ketones.

Summary.—In general, the presence of two functional groups in these bicyclic molecules is reflected by fragmentations which are typical of the separate functionalities, as typified in Scheme IX for *trans*-4-ethoxy-1-decalone (X). Only one rearrangement has been encountered which is uniquely associated with the close proximity and interaction of the two functionalities. This is the fragmentation leading to the hydrocarbon species a.

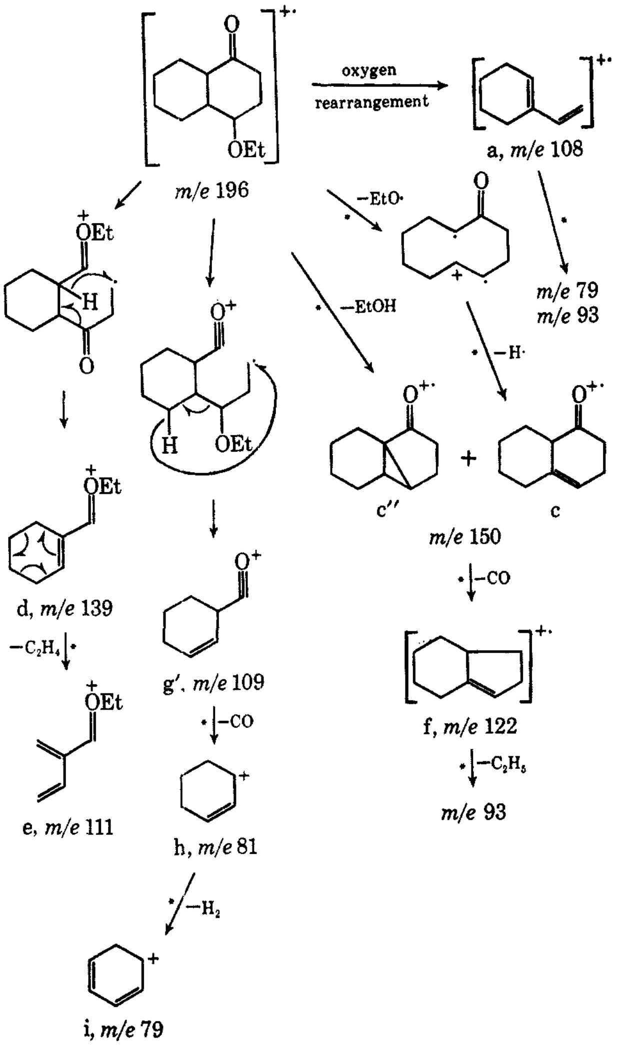
While very similar to the oxygen rearrangement (Scheme I) in the monocyclic analogs, it differs significantly in that the charge remains with the hydrocarbon fragment and hence does not lead to erroneous structural conclusions. As pointed out elsewhere,[6] charge retention on the oxygenated fragment can lead to misleading conclusions if one is unsure of the occurrence of an oxygen rearrangement.

Predominant charge retention on the hydrocarbon portion (a) in the bicyclic compounds is probably associated with the higher degree of substitution of



SCHEME IX

MAJOR FRAGMENTATION PATHWAYS OF *trans*-4 ETHOXY-1-DECALONE



the resulting diene (a), and it can be predicted that a similar change in charge retention would be encountered in the monocyclic series of methyl groups were introduced at positions 2 and 3.

Synthesis of Labeled Compounds.—For this investigation it was necessary to synthesize labeled compounds with deuterium at the activated C-2 and C-9 positions, and also at the "nonactivated" C-4 position.

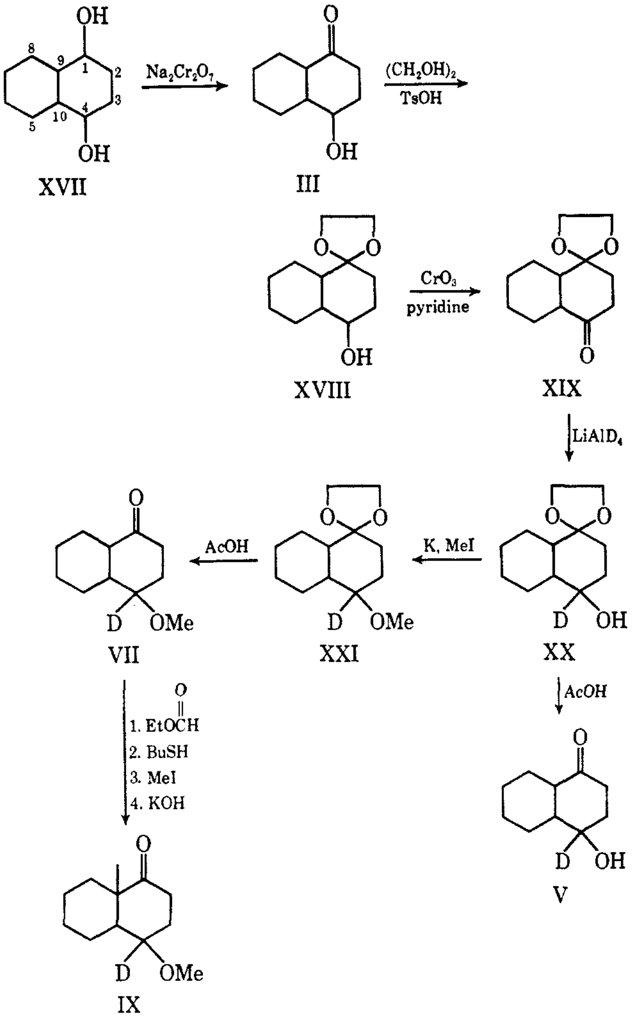
The former group of compounds (VI, XI, and XIII) were prepared by repeated equilibration of the parent ketone with sodium in a mixture of deuteriomethanol and deuterium oxide. The isotopic purities obtained using this technique are given in the Experimental Section.

A suitable precursor to 4-substituted 1-decalones with a label at the 4 position proved to be the commercially available *trans*-decaline-1,4-diol (XVII). The overall reaction pathway is shown in Scheme X.

Experimental Section

Low-resolution mass spectra were obtained by Mr. R. G. Ross, using an A. E. I. MS-9 double-focusing spectrometer, and by Mr. C. Carroll, using an Atlas CH-4 spectrometer. High-resolution measurements with the A. E. I. MS-9 instrument were secured by Mr. R. G. Ross. All compounds for mass spectral analysis were purified and checked for purity by vpc.

SCHEME X



Infrared spectral data were recorded with either a Perkin-Elmer Infracord or a Perkin-Elmer Model 700 spectrophotometer. Elemental analyses were done by Mr. E. Meier and Mr. J. Consul of the Stanford microanalytical laboratory. Melting points were obtained on a Kofler hot stage and are uncorrected.

***trans*-4-Hydroxy-1-decalone (III) and Its 2,2,9-d_3 Analog (VI).**—Using a modification of a previously described procedure,[21] 6.45 g (0.038 mol)of *trans*-1,4-decalinediol (Aldrich Chemical Co.) was oxidized with a solution of 3.76 g (0.013 mol) of $Na_2Cr_2O_7 \cdot 2H_2O$ in 25 ml of a 6:2:1 mixture of water–concentrated sulfuric acid–glacial acetic acid. Work-up yielded 4.0 g of a mixture of III and *trans*-1,4-decalinedione as a pale yellow oil. Separation of this mixture by tlc on silica gel H in 25% ethyl acetate–benzene gave 1.3 g (20%) of III as a colorless oil: ir (film) 1710 (C=O) and 3440 cm^{-1} (OH); mass spectrum *m/e* 168 (M$^+$).

Using a procedure described earlier,[8] three repeated equilibrations of a portion of III with 2 ml of a standard solution of sodium metal (75 mg) in deuteriomethanol (4.5 ml) and deuterium oxide (1.5 ml) gave a good return of VI. Mass spectral analysis indicated the presence of 70% the desired d_3 ketone accompanied by 21% d_2, 4% d_1, and 5% d_4 species (M$^+$ 171).

4-Hydroxy-1-decalone Ketal (XVIII).—A solution of 1.30 g (0.0078 mol) of III in 20 ml of dry benzene containing 50 mg of *p*-toluenesulfonic acid and 1.2 g (0.019 mol) of ethylene glycol was heated at reflux under a Dean–Stark trap for 22 hr. The solution was cooled, washed with water, and dried ($MgSO_4$). Distillation of the solvent under reduced pressure gave 1.60 g (97%) of XVIII as colorless needles. One recrystallization from petane–ether gave an analytical sample: mp 96–97°; ir ($CHCl_3$) 3450 cm^{-1} (OH), no carbonyl absorption; mass spectrum *m/e* 212 (M$^+$).

4-Methoxy-1-decalone (IV).—To a solution of 0.10 g (0.47 mmol) of XVIII in 10 ml of dry benzene was added 0.1 g of potas-

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[21] W. S. Johnson, C. D. Gutsche, and D. K. Banerjee, *J. Amer. Chem. Soc.*, **73**, 5464 (1951).

sium metal, and the mixture was heated at reflux for 3 hr. Methyl iodide (3 ml) was then added and the resulting solution was maintained at reflux for a further 12 hr. After cooling, the solution was washed with water, dried ($MgSO_4$), and evaporated, giving **4-methoxy-1-decalone ketal** as a pale yellow oil.

A solution of this methoxy ketal in 5 ml of 90% acetic acid was heated at 60° for 12 hr. Water was added and the mixture was extracted with ether. Work-up in the usual way gave IV as a pale yellow oil. Purification was effected by vpc,[22] giving IV as a colorless oil: ir (film) 1710 cm^{-1} (C=O); mass spectrum m/e 182 (M$^+$).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.64; H, 9.96.

4-Methoxy-9-methyl-1-decalone (VIII).—To a stirred, ice-cold suspension of 0.55 g (0.01 mol) of sodium methoxide in 15 ml of dry benzene was added 0.46 g (0.0025 mol) of IV and 0.74 g (0.01 mol) of ethyl formate.[23] The mixture was stirred at room temperature under nitrogen for 15 hr. Ice-water was then added, and the organic layer was separated and extracted with dilute sodium hydroxide solution. These extracts were combined with the main aqueous layer, acidified with concentrated hydrochloric acid, and extracted with ether. The combined ether extracts were washed with water and saturated NaCl solution, dried ($MgSO_4$), and evaporated, giving 0.23 g of **2-hydroxymethylene-4-methoxy-2-decalone** as a pale yellow oil.

A solution of this product, 0.12 g (0.003 mol) of *n*-butanethiol, and 10 mg of *p*-toluenesulfonic acid in 50 ml of dry benzene was heated at reflux under a Dean-Stark trap for 18 hr. The mixture was then cooled, washed with water, dried ($MgSO_4$), and evaporated, giving 0.30 g of **2-*n*-butylthiomethylene-4-methoxy-1-decalone** as a pale brown oil.

This total product was added to a solution of 0.50 g of potassium *t*-butoxide in 10 ml of *t*-butyl alcohol under nitrogen. The mixture was stirred in an ice bath for 10 min, methyl iodide (2 ml) was added, and the mixture was heated at reflux for 2 hr. After it had cooled, water was added and the mixture was extracted with ether. The extracts were thoroughly washed with water, dried ($MgSO_4$), and evaporated, giving 0.28 g of **2-butylthiomethylene-4-methoxy-9-methyl-1-decalone** as a pale brown oil.

Hydrolysis of this material with 5 ml of 25% potassium hydroxide in 5 ml of ethylene glycol for 12 hr, followed by steam distillation of the product, gave 0.10 g (20% from IV) of **4-methoxy-9-methyl-1-decalone** (VIII) as a brown oil. Purification of this oil with vpc gave VIII as a colorless oil: ir (film) 1710 cm^{-1} (C=O); mass spectrum m/e 196 (M$^+$).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.30; H, 10.25.

Decaline-1,4-dione Monoketal (XIX).—This material was obtained using a previously described[24] oxidation with chromium trioxide in pyridine. To a mixture of 12 g of chromium trioxide in 150 ml of pyridine at 10° was added a solution of 1.50 g (0.0071 mol) of XVIII in 15 ml of dry pyridine. The stirred mixture was kept at 10° for 2 hr, then allowed to stand at room temperature for a further 4 hr. A conventional work-up gave 1.24 g (85%) of XIX as colorless needles. Sublimation at 40° (2 mm) gave an analytical sample: mp 53–55°; ir ($CHCl_3$) 1720 cm^{-1} (C=O); mass spectrum m/e 210 (M$^+$).

4-d_1-4-Hydroxy-1-decalone (V).—To a mixture of 1 g of lithium aluminum deuteride in 30 ml of dry ether at 0° was added a solution of 0.85 g (0.0040 mol) of XIX in 25 ml of ether. The mixture was stirred at 0° for 30 min under nitrogen, then heated at reflux for a further 4 hr. The solution was cooled to 0°, and the excess deuteride was destroyed with saturated Na_2SO_4 solution. The ethereal solution was filtered, dried ($MgSO_4$), and evaporated, giving 0.85 g (99%) of **4-d_1-4-hydroxy-1-decalone ketal** (XX) as a white solid. Recrystallization of a small portion from pentane–ether gave XX as colorless needles: mp 97–98°; ir ($CHCl_3$) 3440 (OH) and 2110 cm^{-1} (C—D); mass spectrum m/e 213 (M$^+$).

A solution of 0.14 g (0.66 mmol) of XX in 25 ml of 90% acetic acid was heated on a steam bath for 1 hr. After cooling, water was added, and a usual work-up procedure gave a good return of **4-d_1-4-hydroxy-1-decalone** (V). Purification was effected on vpc, giving V as a colorless oil. Mass spectral analysis showed that the material consisted of 98% d_1 and 2% d_0 species (M$^+$ 1969).

4-d_1-4-Methoxy-1-decalone (VII).—Using the method described above for the synthesis of IV, methylation of 0.85 g (0.004 mol) of XX gave a good yield of **4-d_1-4-methoxy-1-decalone ketal** (XXI) as a pale yellow oil. A sample purified by vpc showed mass spectrum m/e 227 (M$^+$).

A solution of the crude reaction product in 10 ml of 90% acetic acid was heated at 60° for 18 hr. A conventional work-up followed by evaporation of the solvent gave 0.80 g of a pale yellow oil. By vpc analysis, this product consisted of 95% VII contaminated with 5% nonmethylated material. A pure sample of VII was obtained by vpc and consisted of 97% d_1 and 3% d_0 species by mass spectrometry (M$^+$ m/e 183).

4-d_1-4-Methoxy-9-methyl-1-decalone (IX).—Using the procedure described above for VIII, 0.19 g (0.0010 mol) of VII was converted toi ts 2-butylthiomethylene derivative. Methylation followed by hydrolysis with sodium hydroxide in water–ethylene glycol gave 60 mg of a brown oil, shown by vpc to be a mixture of VII and IX. Separation was accomplished by vpc, giving pure IX as a colorless oil, consisting of 97% d_1 and 3% d_0 species by mass spectrometry (M$^+$ m/e 197).

4-Ethoxy-1-decalone (X) and Its 2,2,9-d_3 Analog (XI).—This material was prepared from 5.1 g (0.026 mol) of *trans*-4-ethoxy-1-decalol (Aldrich Chemical Co.) by a standard chromic acid oxidation in acetone.[25] Distillation of the crude product (4.71 g) gave 4.06 g (81%) of X as a colorless oil: bp 94–96° (1 mm); ir (film) 1720 cm^{-1} (C=O); mass spectrum m/e 196 (M$^+$).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.37; H, 10.24.

Repeated equilibration of X with a standard solution of sodium metal in a deuteriomethanol–deuterium oxide mixture gave a good return of XI. The mass spectrum indicated the presence of 94% d_3 and 6% d_2 species (M$^+$ m/e 199).

4-Ethoxy-9-methyl-1-decalone (XII) and Its 2,2-d_2 Analog (XIII).—Using a similar procedure to that described above for the preparation of VIII, 2.32 g (0.012 mol) of X was converted into its 2-butylthiomethylene derivative.[23] Angular methylation, followed by hydrolysis and steam distillation, gave 0.36 g (14% from X) of a yellow oil, shown by vpc to consist of <95% XII. Final purification by vpc gave XII as a colorless oil: ir (film) 1720 cm^{-1} (C=O); mass spectrum m/e 210 (M$^+$).

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.05; H, 10.53.

Three repeated equilibrations of XII with a standard solution of sodium metal in deuteriomethanol–deuterium oxide gave a good return of XIII, shown by mass spectrometry to be composed of d_2 (87%) and d_1 (13%) species (M$^+$ m/e 212).

α-Decalol (XIV), bp 80–84° (1 mm) [lit.[26] bp 116–120° (7 mm)], was purified by vpc and was a mixture of *cis* and *trans* isomers (M$^+$ m/e 154).

1-Methoxydecalin (XV).—A mixture of 0.720 g (0.0047 mol) of α-decalol (XIV) and 0.62 g (0.05 g-atom) of potassium metal in 30 ml of dry benzene was heated at reflux under nitrogen for 15 hr. Methyl iodide (5 ml) was added and the mixture was maintained at reflux for a further 4 hr. Methanol was added to destroy the excess potassium metal, and a usual work-up procedure gave 0.780 g (99%) of XV as a pale yellow oil. Final purification by vpc gave XV as a colorless oil: ir (film) 2670 and 1110 cm^{-1} (OCH_3); mass spectrum m/e 168 (M$^+$).

1-Ethoxydecalin (XVI).—Using a previously described[27] modified Huang-Minlon reduction procedure, 0.120 g of ethoxyketone X was converted to XVI in 54% yield. Final purification by vpc gave XVI as a colorless oil: mass spectrum m/e 182 (M$^+$).

Registry No.—III, 21766-50-7; IV, 21727-79-7; V, 21727-80-0; VI, 21727-81-1; VII, 21727-82-2; VIII, 21720-85-4; IX, 21720-86-5; X, 21727-83-3; XI, 21727-84-4; XII, 21720-87-6; XIII, 21720-88-7; XIV, 529-32-8; XV, 21720-89-8; XVI, 21727-85-5; XVIII, 21727-86-6; XIX, 21727-93-5; XX, 21727-87-7.

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(22) The column used in each purification by vpc was 5% SE-30 on Chromosorb W (5 ft). The oven temperature was varied between 170 and 200°.

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