[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY, STANFORD, CALIF.]

Mass Spectrometry in Structural and Stereochemical Problems. XVIII.[1] Fragmentation and Hydrogen Transfer Reactions after Electron Impact on α-Decalones. Synthesis of Polydeuterated α-Decalones[2]

BY E. LUND,[3] H. BUDZIKIEWICZ, J. M. WILSON AND CARL DJERASSI

RECEIVED NOVEMBER 10, 1962

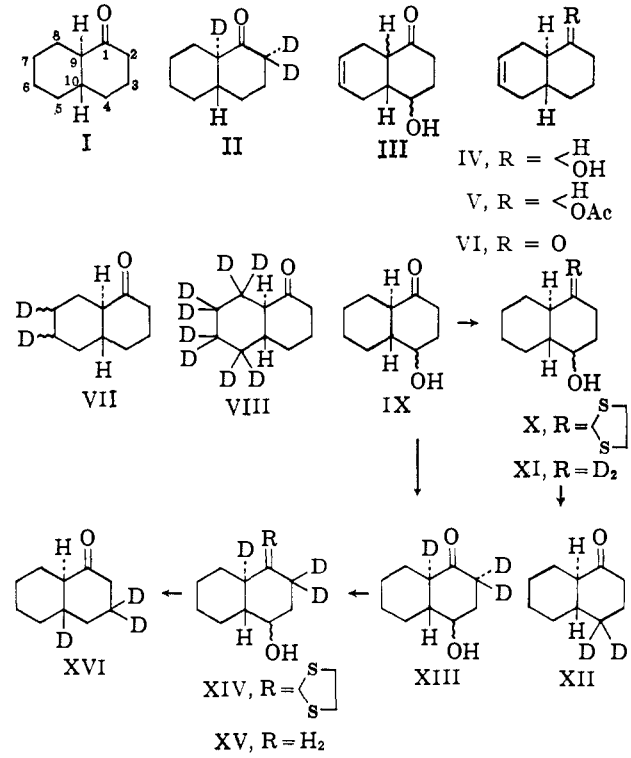
Seventeen deuterated analogs of *trans*-decalone-1 (I), *trans*-9-methyldecalone-1 (XVIIa) and *cis*-9-methyldecalone-1 (XVIIb) have been synthesized and their mass spectra investigated. By noting the occurrence or absence of shifts upon deuteration in any given mass spectral peak, plausible mechanisms could be proposed for most of the principal fragmentation processes. Furthermore, insight could be gained into the many hydrogen transfer reactions accompanying such fragmentation processes initiated by electron bombardment. Several of these processes are dependent upon the nature of the ring juncture and the stereochemical implications of these observations are pointed out.

As part of our program[4] on the correlation of mass spectral fragmentation patterns and structural features of polycyclic molecules, there have been studied the mass spectra of a variety of steroid ketones.[5-7] The over-all course of the principal fragmentation processes can usually be determined by "labeling" different portions of the molecule with substituents such as alkyl groups. However, in order to gain insight into the fragmentation mechanism and especially the hydrogen transfer reactions incident upon electron impact, it is necessary to have available deuterated analogs and an extensive synthetic program along these lines is currently under way in our laboratory. At the same time, synthetic and mass spectral studies were also initiated with simpler bicyclic model ketones, especially since the past literature is virtually devoid of relevant information in the field of cyclic ketones. In the present article we record the mass spectral results derived from an examination of various deuterated analogs of α-decalone.

Synthesis of Deuterated α-Decalones.—The only deuterated analog derivable from *trans*-α-decalone (I) itself is the 2,2,9-d_3-analog II, which can be obtained readily by equilibration with sodium in a mixture of deuteriomethanol and heavy water. Since it was also necessary to label all of the other "non-activated" positions with deuterium, a more versatile precursor had to be selected and this proved to be the 4-hydroxy-Δ^6-octalone-1 (III), a convenient preparation of which was recently described by Ireland and Marshall.[8]

Modified Wolff–Kishner reduction[8] of III followed by acetylation provided Δ^6-octalol-1-acetate (V),[9] which successively was reduced[10] with N-trideuterio-*p*-toluenesulfonylhydrazide, saponified and oxidized to provide 6,7-d_2-*trans*-decalone-1 (VII). The initial step in the synthesis[8] of the hydroxyoctalone III is the Diels–Alder addition[11] of butadiene to *p*-benzoquinone. By utilizing commercially available d_6-butadiene and otherwise following the Ireland–Marshall sequence,[8] there was obtained the 5,5,6,7,8,8-d_6 analog of *trans*-Δ^6-octalone-1 (VI), which upon catalytic deuteration[12] afforded the desired 5,5,6,6,7,7,8,8-d_8-*trans*-decalone-1 (VIII). Mass spectrometry demonstrated the presence of 89% of the d_8-ketone VIII, contaminated with 8% of the d_7- and 3% of the d_6-species.

In order to label positions 3, 4 and 10 in the oxygenated ring, *trans*-4-hydroxydecalone-1 (IX)[13] was transformed into its ethylenemercaptal X and desulfurized with deuterated W-7 Raney nickel catalyst.[14] In our experience, this represents the least satisfactory method of introducing deuterium selectively and oxidation of the chromatographically homogeneous desulfurization product led to 4,4-d_2-*trans*-decalone-1 (XII), accompanied by substantial amounts of d_1-, d_3- and non-



(1) Paper XVII, M. Plat, J. LeMen, M.-M. Janot, H. Budzikiewicz, J. M. Wilson, L. J. Durham and C. Djerassi, *Bull. soc. chim. France*, 2237 (1962).

(2) We are indebted to the National Institutes of Health of the U. S. Public Health Service for financial support (grants No. CRTY-5061 and No. A-4257).

(3) Taken from part II of the Ph.D. dissertation of E. Lund, Stanford University, 1963, where the mass spectra of the deuterated analogs (Tables 1–3) are reproduced.

(4) For review see C. Djerassi, *Pure Appl. Chem.*, **6**, No. 4 (1963).

(5) H. Budzikiewicz and C. Djerassi, *J. Am. Chem. Soc.*, **84**, 1430 (1962).

(6) C. Djerassi, J. M. Wilson, H. Budzikiewicz and J. W. Chamberlin, *ibid.*, **84**, 4544 (1962).

(7) C. Djerassi, H. Budzikiewicz and J. M. Wilson, "Recent Applications of Mass Spectrometry in Steroid Chemistry," Proc. Internat. Congress Hormonal Steroids, Milano, May, 1962, Academic Press, Inc., New York, N. Y., in press.

(8) R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1620 (1962).

(9) This material may still contain some *cis* fused isomer, but purification was always effected at the ketone stage to provide the *trans*-decalones.

(10) See R. S. Dewey and E. E. van Tamelen, *J. Am. Chem. Soc.*, **83**, 3729 (1961).

(11) As modified by L. F. Fieser, *ibid.*, **70**, 3165 (1948).

(12) As yet unpublished experiments by J. W. Chamberlin in this laboratory on the course of catalytic deuteration of steroidal cyclic olefins and dienes have shown that scrambling of deuterium is largely limited to the immediate environment of the double bond in contrast to the situation observed with aliphatic olefins (see Ng. Dinh-Nguyen and R. Ryhage, *Acta Chem. Scand.*, **13**, 1032 (1959), for catalytic deuteration of methyl oleate).

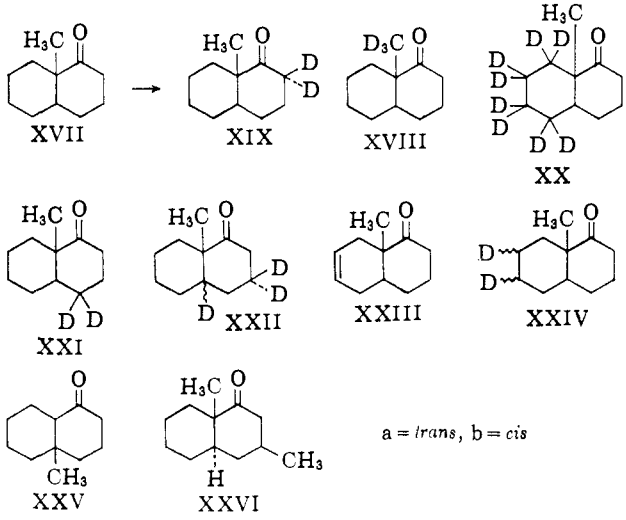
(13) W. Hückel and W. Kraus, *Ber.*, **95**, 233 (1962).

(14) Prepared essentially according to H. R. Billica and H. Adkins, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 176, but substituting heavy water for water in the digestion and washing steps.

deuterated *trans*-decalone-1. Alternatively, the ketol IX was first equilibrated with sodium in deuteriomethanol–heavy water and the trideuterated ketol XIII converted into the mercaptal XIV, shown by mass spectrometry to contain at least 95% of the desired d_3-species. Desulfurization with Raney nickel and hydrogen followed by oxidation gave 3,3,10-d_3-*trans*-decalone-1 (XVI) (62% d_3), contaminated by 30% of d_2- and 8% of d-species, thus indicating again the complications attending the use of Raney nickel catalyst in the synthesis of specifically labeled deuterated substances.

The above-described five polydeuterated ketones II, VII, VIII, XII and XVI all represent labeled analogs of *trans*-decalone-1 (I). Angular methylation of α-decalone utilizing the recently described[15] *n*-butylthiomethylene blocking group affords a chromatographically separable mixture of *cis*-(XVIIb) and *trans*-(XVIIa)-9-methyldecalone-1 and repetition of this sequence with trideuteriomethyl iodide led to *cis*-(XVIIIb) and *trans*-(XVIIIa)-9-trideuteriomethyldecalone-1, while the standard equilibration process applied to XVII gave *cis*-(XIXb) and *trans*-(XIXa)-2,2-d_2-decalone-1. Application of the methylation procedure to the polydeuterated α-decalones VIII, XII and XVI led to the stereochemically pure *cis*- and *trans*-5,5,6,6,-7,7,8,8-d_8 (XX), 4,4-d_2-(XXI) and 3,3,10-d_3-(XXII) analogs of 9-methyldecalone-1 (XVII).

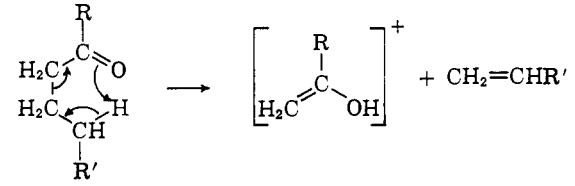
The *cis*- and *trans*-6,7-d_2-9-methyldecalones (XXIV) were not prepared by angular methylation of 6,7-d_2-decalone-1 (VII), but rather by methylation of the octalone VI as described by Ireland and Marshall.[8] The resulting inseparable mixture of *cis*-(XXIIIb) and *trans*-(XXIIIa)-9-methyl-Δ^6-octalone-1 was reduced with lithium aluminum hydride to the corresponding octalols, acetylated and the double bond saturated with N-trideuterio-*p*-toluenesulfonylhydrazide. Saponification followed by oxidation and gas phase chromatographic separation provided the required *cis*-(XXIVb) and *trans*-(XXIVa)-6,7-d_2-9-methyldecalone-1.



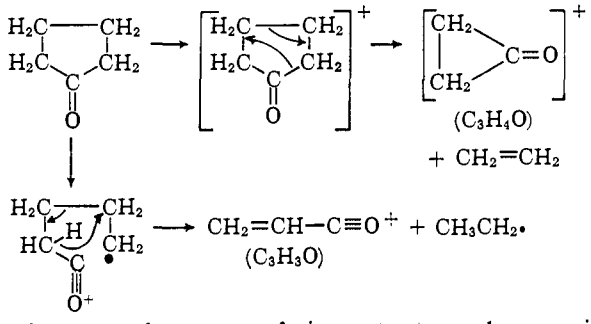
Discussion of Mass Spectra

In the preceding section, there has been described the preparation of six deuterated analogs each of *cis*- and of *trans*-9-methyldecalone-1 (XVII) as well as of five polydeuterated derivatives of *trans*-decalone-1 (I). The availability of these seventeen labeled substrates has permitted a reasonable interpretation of the principal mass spectral fragmentation peaks, but as background to this and forthcoming articles from this Laboratory, it is worthwhile first to discuss briefly earlier accumulated information on the behavior of ketones upon electron impact.

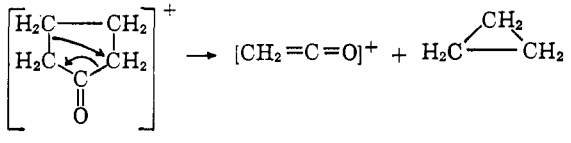
Aliphatic ketones[16] show a relatively simple pattern, principal cleavage occurring adjacent to the carbonyl group and the charge remaining with the oxygen-containing fragment, stabilization being achieved through participation of the electrons on oxygen. Thus in an unsymmetrical ketone RCOR′, important peaks will correspond to fragments of mass RCO^+ and $R'CO^+$, the alkyl fragment being lost as a radical. If a chain of three or more carbon atoms is attached to the carbonyl group, then a second type of fission accompanied by hydrogen transfer from the γ-carbon atom becomes important, the operation of a six-membered transition state first having been proposed by McLafferty.[17] A completely analogous process operates in fatty acid esters (R = OMe) and has been substantiated by deuterium labeling.[18] The only cyclic ketones for which mass spectra have been reported are



cyclopentanone,[16,19,20] cyclohexanone,[16,20] its 4-methyl derivative,[16] cycloheptanone[20] and *cis*- and *trans*-β-decalone.[20] In this group, cyclopentanone has been examined most thoroughly since data from the 2,2,4,4-d_4 derivative[19] and from double-focusing measurements[20] are available. In the high mass range, the two most important fragments correspond to C_3H_3O (base peak) and C_3H_4O for which the following mechanisms[17] are suggested



The second group of important peaks consists principally of the fragments C_3H_5, C_3H_6 and C_2H_2O, the latter probably arising from a fragmentation process giving rise to the ketene ion and to cyclopropane.



The $C_3H_5^+$ ion consists of two species, since the corresponding peak in the d_4-cyclopentanone spectrum is split into $C_3H_3D_2$ and $C_3H_2D_3$. Such shifts of hydrogen and deuterium atoms have also been observed in our

(15) R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1615 (1962).

(16) A. G. Sharkey, J. L. Shultz and R. A. Friedel, *Anal. Chem.*, **28**, 934 (1956).

(17) For leading references and discussion of hydrogen transfer reactions upon electron impact see F. W. McLafferty in "Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, N. Y., 1962, Vol. 2, pp. 129–149.

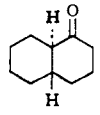
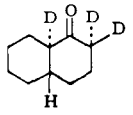
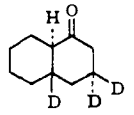
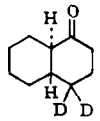
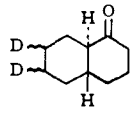
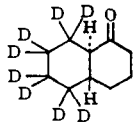
(18) Ng. Dinh-Nguyen, R. Ryhage, S. Ställberg-Stenhagen and E. Stenhagen, *Arkiv Kemi*, **18**, 393 (1961).

(19) P. Natalis, *Bull. soc. chim. Belges*, **67**, 599 (1958).

(20) J. H. Beynon, R. A. Saunders and A. E. Williams, *Appl. Spectry.*, **14**, 95 (1960).

TABLE I

MASS SPECTRA OF *trans*-DECALONE-1 (I) AND OF DEUTERATED ANALOGS

Peak (Fig. 1) *m/e*	 I (152)[a]	 II (155)[a]	 XVI (155)[a]	 XII (154)[a]	 VII (154)[a]	 VIII (160)[a]
110	M-42	42	42	42	44	47
109	M-43	46	45	45	43	43
97	M-55	55	55	55	56, 57	62
81	M-71	73, 74	73	73	71	71, 72
67	M-85	87, 88	87, 88[b]	87	85, 86	86, 87, 88

[a] Molecular ion peak. [b] Predominant.

studies with bicyclic ketones and will be discussed below. The principal fragments observed in the high resolution mass spectrum[20] of cyclohexanone can be rationalized in the same fashion as for cyclopentanone, the most notable additional features being the loss of methyl and especially of water. This last point will be covered in detail in the analysis of the *trans*-9-methyldecalone spectrum (Fig. 2).

Turning now to the mass spectra of bicyclic ketones, the only ones that have been recorded in the literature[20] are those of *cis*- and *trans*-decalone-2. As work in our laboratory has shown that the mass spectral behavior of β-decalones differs substantially from that of α-decalones, we shall defer comment on the former group for a later paper dealing with the synthesis and mass spectra of deuterated β-decalones. In Fig. 1 is reproduced the mass spectrum of *trans*-decalone-1 (I) and it will be noted that assignments have been made to most of the prominent peaks in the higher mass range. This was accomplished by comparing the shifts (or absence of shifts) of these peaks in the spectra of the deuterated analogs, the data being summarized in Table I. Before discussing these peak assignments and suggested modes of formation, the following potential difficulties in interpretation should be noted: (i) A single peak may consist of more than one species. These may be identical in mass but differ in elementary composition[21]—one containing only C and H and the other C, H and O—or, more seriously, may possess the identical empirical formula, but arise from different fragmentation processes. In such instances, deuterium labeling at a specific position will lead to splitting of such a peak; if the latter is surrounded by other intense peaks, then it may be very difficult to follow an appropriate shift in mass.

(ii) A second uncertainty may arise from the fact that introduction of more than one deuterium atom at times may make it impossible to predict how many mass units a given peak may shift, especially in complicated hydrogen transfer reactions. Thus a strong peak arising from incidental superimposition may be mistaken for a single, abundant fragment.

(iii) A limitation, largely peculiar to synthetic work of the type discussed in this and future papers from our laboratory, is introduced by the reactions utilized for deuteration, which at times lead to isotopically impure products.[22] A case in point is the use of Raney nickel catalyst and while qualitative conclusions are usually possible, quantitative statements about the fate and genesis of a given peak may at times be unwarranted.

The Mass Spectrum of *trans*-Decalone-1 (I) (Fig. 1). Peak M-18 (*m/e* 134 in Fig. 1).—Aside from a relatively small M-15 peak, due to the loss of methyl, the first significant peak below the molecular ion peak (*m/e* 152) of *trans*-decalone-1 (I) is the one at *m/e* 134 (M-H_2O). This loss of water has already been noted in the mass spectrum[20] of cyclohexanone and inspection of the mass spectra of the deuterated α-decalones II, XVI, XII, VII and VIII shows that the hydrogen

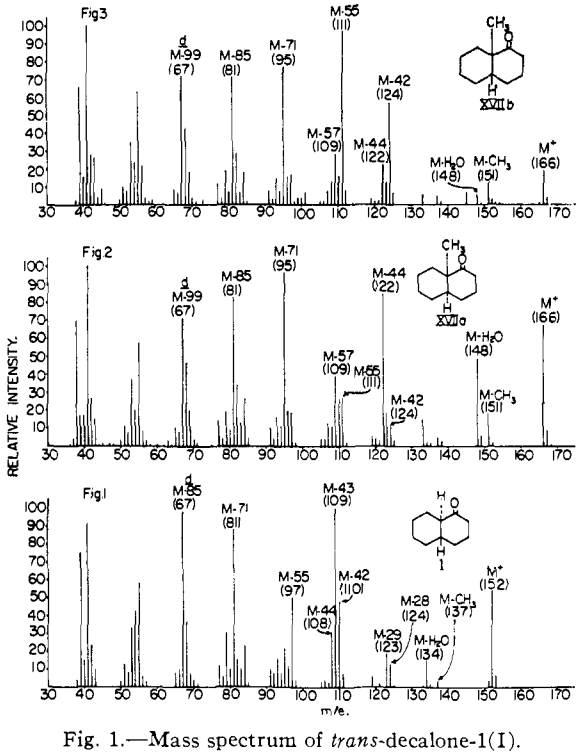


Fig. 1.—Mass spectrum of *trans*-decalone-1(I).
Fig. 2.—Mass spectrum of *trans*-9-methyldecalone-1 (XVIIa).
Fig. 3.—Mass spectrum of *cis*-9-methyldecalone-1 (XVIIb).

atoms of this water molecule are randomly picked from every position in the molecule. Since the five deuterated α-decalones cover all of the carbon atoms of the molecule and the total deuterium loss in the formation of this peak in the labeled compounds amounts to only about 80% of the loss of H_2O in I, a strong isotope effect must be operating (H_2O > HDO > D_2O). Such a M-18 peak becomes especially noticeable in the mass spectrum (Fig. 2) of *trans*-9-methyldecalone-1 (XVII).

Peaks M-28 and M-29 (*m/e* 124 and 123 in Fig. 1).—The high-resolution mass spectrum[20] of cyclohexanone has already demonstrated that the M-28 and M-29 peaks are formed by loss of CO and COH as well as of

(21) A differentiation can be made by the use of a double-focusing instrument, which, however, was not available to us. For pertinent discussion see J. H. Beynon, "Mass Spectrometry and Its Applications to Organic Chemistry," Elsevier, Amsterdam, 1960, chapters 1 and 2; R. D. Craig and G. A. Errock in J. D. Waldron (ed.), "Advances in Mass Spectrometry," Pergamon Press, London, 1959, pp. 66–85.

(22) Inspection of the mass spectral molecular ion peaks will, of course, give a quantitative indication of the composition of such mixtures.

C_2H_4 and C_2H_5. Some shifts of these two peaks are observed in all of the deuterated analogs of I and several different fragmentation processes must, therefore, be involved. A clear distinction, however, can only be made in the mass spectrum of the octadeuterio derivative VIII, where a separation into two groups of peaks can be noted. The M-28 and M-29 peaks in this spectrum evidently arise[21] from the loss of CO, CHO and C_2H_4, while a new group of peaks at M-32, M-33 and M-34 represents the loss of highly deuterated C_2-fragments from the non-oxygenated ring, the approximate ratio of the two groups being 1:1.

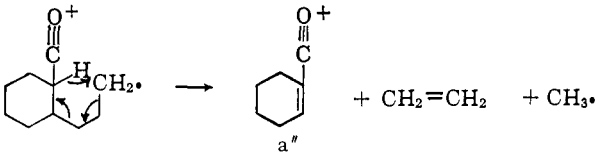
Peak M-42 (*m/e* **110 in Fig. 1**).—The shifts of this peak in the deuterated analogs are listed in Table I and clearly show that loss of a C_3H_6 fragment from the non-oxygenated ring has occurred. This peak becomes especially noticeable in the mass spectrum (Fig. 3) of *cis*-9-methyldecalone-1 (XVIIb), where a mechanism for the genesis of this ion is being proposed.

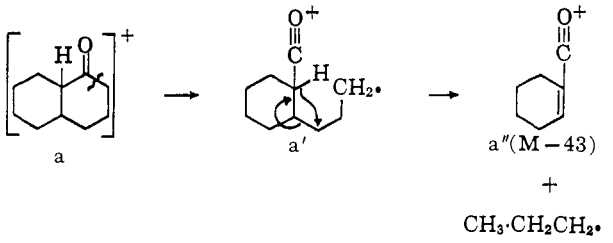
The shift (see Table I) of this M-42 peak in the mass spectrum of the octadeuterio derivative VIII to M-47 rather than M-48 demonstrates that a *double hydrogen transfer* must have occurred, one deuterium atom having moved to the ionized portion of the molecule and a hydrogen atom shifting to the neutral C_3-hydrocarbon fragment. As the mass spectrum of the 6,7-d_2-*trans*-decalone-1 (VII) shows a complete shift (Table I) of the M-42 peak to M-44, only hydrogen atoms in two positions, C-5 or C-8, can be implicated in the transfer to the ionized portion of the molecule. The back-transfer of hydrogen from the oxygen-containing fragment to the neutral C_3H_6 moiety appears to originate from several positions. Thus if the abundance of the M-42 peak in the spectra of II, XVI and XII is expressed in terms of the total ionization of this group of peaks (*m/e* 105–*m/e* 111), the results (I, 19%; II, 16%; XVI, 12%; XII, 13%) indicate an additional and perceptible shift to M-43.

Peak M-43 (*m/e* **109 in Fig. 1**).—This represents the most intense peak in the spectrum (Fig. 1) and it is interesting to note that this also applies to cyclohexanone[16,20] itself, where the use of a double-focusing instrument[20] has shown that the fragment lost consists principally of C_3H_7. This conclusion is in full accord with our results with the labeled α-decalones, the shifts of the M-43 peak in Table I demonstrating that only carbon atoms 2, 3 and 4 are lost, together with the hydrogen atom attached to C-9 (note M-46 loss in 2,2,9-d_3-*trans*-decalone-1 (II)). A plausible mechanism[23] for the formation of the important M-43 peak is shown and involves the common[16] cleavage of the bond adjacent to the carbonyl group (wavy line in a) followed by transfer of the C-9 hydrogen (a')[23] with generation of the stable conjugated ion a'' (*m/e* 109 in Fig. 1).

Peak M-44 (*m/e* **108 in Fig. 1**).—The movements of this peak cannot be observed easily due to the presence of its more abundant neighbors at *m/e* 109 and 110.

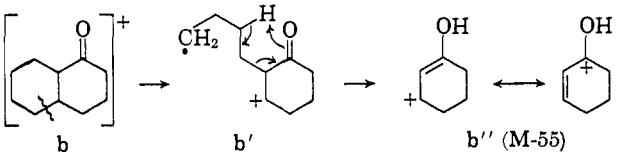
(23) Whenever mechanisms are proposed in the present article, they are expressed in terms of energetically plausible intermediates. Obviously, this does not mean that other representations are not equally feasible and particular care has to be exercised in assigning structures to the neutral particles of these fragmentation processes (for a recent pertinent paper see B. G. Hobrock and R. W. Kiser, *J. Phys. Chem.*, **66**, 1648 (1962)). Thus, the hydrogen transfer represented by a' could also be visualized as follows, the principal difference being the nature of the neutral fragment(s)



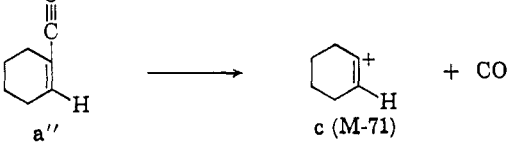


However this fragment becomes one of the most important ones in the spectrum (Fig. 2) of *trans*-9-methyldecalone-1 (XVIIa) and will be discussed there.

Peak M-55 (*m/e* **97 in Fig. 1**).—The shifts of this peak, summarized in Table I, point unambiguously toward the loss of a C_4H_7 fragment derived from the non-oxygenated ring. Migration of one hydrogen from that portion to the positively charged moiety is demonstrated by the spectra of VII and VIII, the split to M-56 and M-57 in the spectrum of the 6,7-d_2 derivative VII showing that hydrogen from one of these two positions is moved. A reasonable mechanism would involve initial rupture of the 5–10 bond (wavy line in b) followed by hydrogen transfer from C-7 by the usual[17] six-membered cyclic transition state b' to yield b'' (*m/e* 97 in Fig. 1).



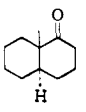
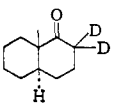
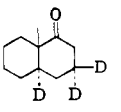
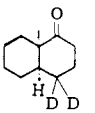
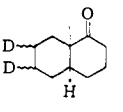
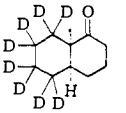
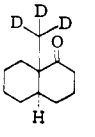
Peak M-71 (*m/e* **81 in Fig. 1**).—A metastable ion at *m/e* 60.5 (calculated 60.5 for transition *m/e* 109 → 81) indicates that this fragment is derived, at least in part, from the M-43 ion a'' by loss of carbon monoxide with generation of the cyclohexenyl cation c (*m/e* 81). This explanation is in accord with the observation (Table I) that the M-71 peak of I shifts to M-73 in the 3,3,10-d_3-(XVI) and 4,4-d_2-(XII) derivatives, but remains at M-71 in the 6,7-dideuterio analog VIII.



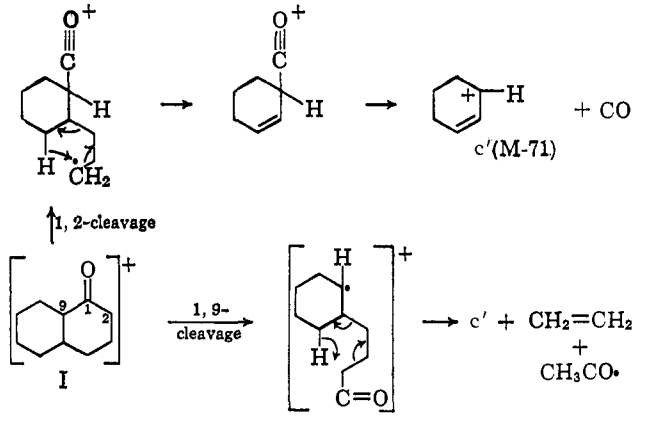
That the situation is more complicated is indicated by the appearance of two peaks, M-73 and M-74 (Table I), in the mass spectrum of the 2,2,9-d_3 derivative II, thus demonstrating that the M-71 peak of *trans*-decalone-1 (I) is actually made up of two species. The portion yielding the M-74 peak in the spectrum of II is in agreement with the mechanism a'' → c, while the production of the other moiety (M-73 in II), though still comprising carbon atoms 1, 2, 3 and 4 with their attached hydrogens, cannot involve the loss (see a' → a'') of the C-9 hydrogen atom. The source of this alternate hydrogen transfer can be learned from the mass spectrum of the d_8-derivative VIII, where the M-71 peak has shifted in part to M-72, while it remained at M-71 in the 6,7-d_2-(VII) spectrum. It follows that only hydrogen attached to C-5 or C-8 can be implicated, the former appearing much more plausible. Two alternate mechanisms (initiated either by cleavage of the 1–2 or the 1–9 bond) can be visualized in which the C-5 hydrogen is lost through a transfer in a six-membered intermediate.

TABLE II

MASS SPECTRA OF *trans*-9-METHYLDECALONE-1 (XVIIa) AND OF DEUTERATED ANALOGS

Peak (Fig. 2) *m/e*	 XVIIa (166)[a]	 XIXa (168)[a]	 XXIIa (169)[a]	 XXIa (168)[a]	 XXIVa (168)[a]	 XXa (174)[a]	 XVIIIa (169)[a]
151	M-15	15	15	15	15	15	18
148	M-18	18	18, 19 (10%)	18, 19 (30%)	18, 19 (40%)	19, 20 (15%)	18
122	M-44	46	45	45	44	44	44
111	M-55	55	55	55	56, 57	62	55
109	M-57	59	59	58(?)[26]	57	57	57
95	M-71	73	73	73	71	[c]	71
81	M-85	87	87[b]	86,[b] 87	85[b]	[d]	85, 88
67	M-99	101	100, 101	100[b]	99[b]	100, 101	102

[a] Molecular ion peak. [b] Predominant. [c] Peaks over the range *m/e* 101–105 are observed. [d] Peaks over the range *m/e* 82–89 are observed.



Peak M-85 (*m/e* **67 in Fig. 1**).—The representation of this peak as a C_5H_7 fragment derived from the non-oxygenated ring of *trans*-decalone-1 (I) is shown quite clearly in Table I by the observation that the peak remains at *m/e* 67 in the spectrum of the 4,4-d_2-(XII) and to a large extent also the 3,3,10-d_3-(XVI) derivatives, but has shifted to *m/e* 68 and 69 in the 6,7-d_2 analog VII and to *m/e* 72, 73 and 74 in the 5,5,6,6,7,7,-8,8-d_8 labeled α-decalone VIII. The spread of these peaks shows clearly that extensive scrambling of hydrogens has occurred and/or that several fragmentation processes are involved; it would, therefore, not be profitable to suggest a mechanism for its formation. The *m/e* 67 ion is probably best represented as either d or d', C-9 possibly being retained to a larger extent than C-10 (see shifts in II and XVI of M-85 peak in Table I).

d (M—85) d' (M—85)

The Mass Spectra of *trans*-(XVIIa) and *cis*-(XVIIb) 9-Methyldecalone-1 (Fig. 2 and 3).—The various peaks in the mass spectra (Fig. 2 and 3) of *trans*-(XVIIa) and *cis*-(XVIIb) 9-methyldecalone-1 will be discussed together in order to call attention to the effect of the stereochemical differences upon their fragmentation patterns.

Peak M-15 (*m/e* **151 in Fig. 2 and 3**).—The loss of the elements of CH_3 is much more pronounced in the spectra of the angularly substituted α-decalones XVIIa and XVIIb as compared to that (Fig. 1) of the parent ketone *trans*-decalone-1 (I). This is clearly associated with expulsion of the angular methyl function as demonstrated in Tables II and III by the shift to a M-18 peak in the spectra of the 9-trideuteriomethyl derivatives XVIIIa and XVIIIb.

Peak M-18 (*m/e* **148 in Fig. 2 and 3**).—This loss of water is extremely pronounced in the spectrum (Fig. 2) of *trans*-9-methyldecalone-1 (XVIIa), the M-18 peak representing nearly 50% of the base peak. As noted already in the discussion of this peak in the *trans*-decalone-1 (I) spectrum (Fig. 1 and Table I), the loss of water does not occur in a single fragmentation process, but rather by a random removal of protons from virtually every position of the molecule. It is interesting to note from Table II that a somewhat more selective "dehydration" process occurs in *trans*-9-methyldecalone-1 (XVIIa) since the 2,2-d_2-(XIXa) and trideuteriomethyl (XVIIIa) analogs show no detectable loss of deuterium, while the 4,4-d_2-(XXIa) and 6,7-d_2-(XXIVa) derivatives exhibit a 30–40% shift from M-18 to M-19. Especially noticeable is the virtually complete shift to M-19 in the spectrum of the d_8-labeled ketone XXa.

Peak M-42 (*m/e* **124 in Fig. 3**).—This fragment is one of the most important ones in the spectrum (Fig. 3) of *cis*-9-methyldecalone-1 (XVIIb), while it is virtually absent in that (Fig. 2) of the *trans* isomer XVIIa. The shifts of this peak in the deuterated analogs are summarized in Table III and just as observed above (Fig. 1 and Table I) for *trans*-decalone-1, they require the loss of a C_3H_6 fragment, which can only comprise carbon atoms 5, 6 and 7 or 6, 7 and 8. Since the labeled derivative XXb loses only five (rather than six) deuterium atoms in this fragmentation, a double hydrogen transfer (shift of deuterium from C-5 or C-8 to oxygen-containing charged fragment and back transfer of one hydrogen) must have occurred. The following, *a priori* very plausible[17] mechanisms, involving shifts of the hydrogen atoms attached to C-9 and C-7 (e → e' or e'' → e''') could be excluded by the mass spectrum of the 6,7-d_2 labeled derivative XXIVb which demonstrated (Table III) that hydrogens

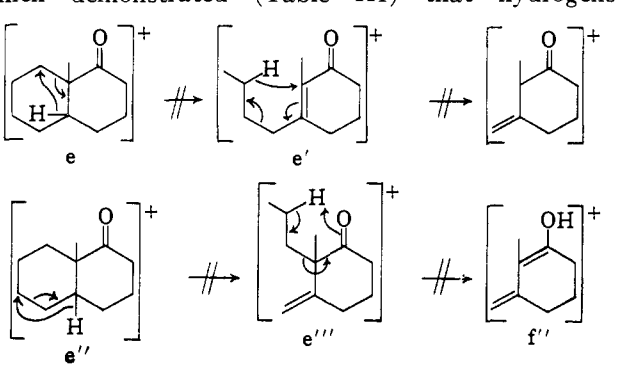
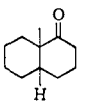
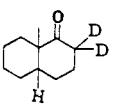
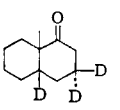
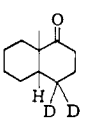
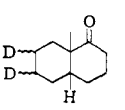
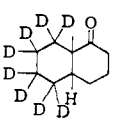
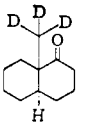


TABLE III

MASS SPECTRA OF *cis*-9-METHYLDECALONE-1 (XVIIb) AND OF DEUTERATED ANALOGS

Peak (Fig. 2) *m/e*							
	XVIIb (166)[a]	XIXb (168)[a]	XXIIb (169)[a]	XXIb (168)[a]	XXIVb (168)[a]	XXb (174)[a]	XVIIIb (169)[a]
151	M-15	15	15	15	15	15	18
148	M-18	18	18	18, 19	18, 19	19	18
124	M-42	42	43	42	44	47	42
122	M-44	46	45	45	44	44	44
111	M-55	55	55	55	56, 57	62	55
109	M-57	59	59	58(?)[26]	57	57	57
95	M-71	73	73	73	71	[c]	71
81	M-85	87	87[b]	86,[b] 87	85[b]	[d]	85, 88
67	M-99	101	100, 101	100[b]	99[b]	100, 101	102

[a] Molecular ion peak. [b] Predominant. [c] Peaks over the range *m/e* 95–105 are observed. [d] Peaks over the range *m/e* 82–89 are observed.

attached to positions 6 and 7 could not be implicated to the extent of more than 10%, thus leaving only C-5 or C-8 as the points of origin for the departing hydrogen (respectively, deuterium) atom.

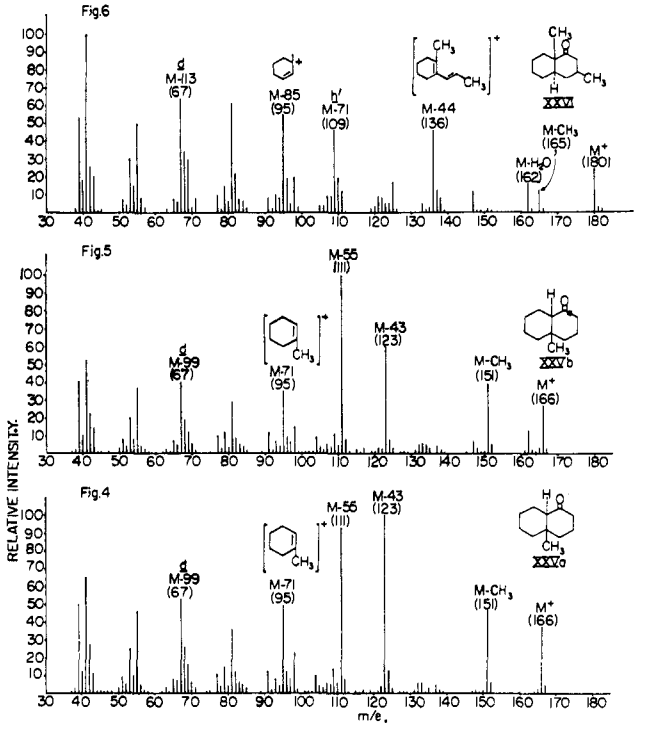
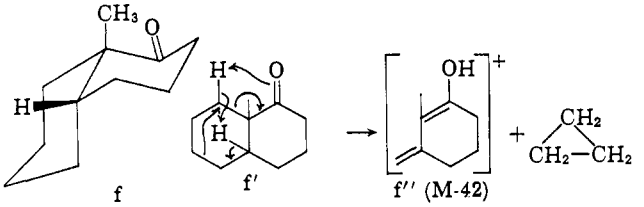


Fig. 4.—Mass spectrum of *trans*-10-methyldecalone-1 (XXVa).
Fig. 5.—Mass spectrum of *cis*-10-methyldecalone-1 (XXVb). (The *m/e* 162 peak is due to an impurity).
Fig. 6.—Mass spectrum of *trans*-3,9-dimethyldecalone-1 (XXVI).

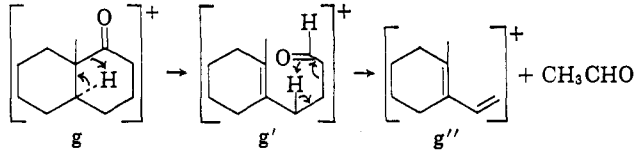
Turning now to the back transfer of the hydrogen atom from the oxygen-containing fragment, no particular location seemed to be favored in *trans*-decalone-1 (I) (see Table I). However in *cis*-9-methyldecalone-1 (XVIIb), the origin of this "returning" hydrogen could be defined, since a more selective rearrangement exists in this instance. The M-42 peak is shifted to M-43 in the 3,3,10-d_3-(XXIIb) spectrum (see Table III), thus pointing toward C-3 or C-10 as the locus, and since the mass spectra (Fig. 4, 5) of *trans*-(XXVa) and *cis*-(XXVb) 10-methyldecalone-1 do not show a M-42 peak, we consider it most reasonable that the C-10 hydrogen atom is back-transferred. A possible rationalization, reminiscent of the double hydrogen transfer mechanism suggested by McLafferty and Hamming[24] for *sec*-butyl acetate, is indicated by the arrows (no concerted mechanism implied) in f′, which lead to the very stable carbonium ion f″ (*m/e* 124 in Fig. 3). The driving force for this fragmentation must be largely steric in origin, since the intensity of this M-42 peak is very much reduced in the spectrum (Fig. 2) of the *trans* isomer. It is conceivable that the special relationship of the C-10 hydrogen (in one of the all-chair forms (f) of the *cis* isomer XVIIb) to the oxygen-free ring facilitates its transfer and thus triggers the remaining fragmentation process leading ultimately to the observed ion f″.



Peak M-44 (*m/e* **122 in Fig. 2 and 3**).—In the spectrum (Fig. 1) of *trans*-decalone-1 (I) itself, the most intense peak in this region of the spectrum was found at M-43, while such a peak is only very small in the spectra (Fig. 2 and 3) of the 9-methylated analogs XVIIa and b. This is in accord with our postulate that a C-9 hydrogen transfer is required for the genesis of the M-43 ion (a″) and is further supported by the reappearance of an intense M-43 peak in the mass spectra (Fig. 4 and 5) of the 10-methylated α-decalones (XXVa and XXVb). On the other hand, the hitherto unimportant M-44 peak in this mass range has now become one of the most important ones in the spectrum (Fig. 2) of *trans*-9-methyldecalone-1 (XVIIa). Indeed, the relative intensities of the M-42 and M-44 peaks can be used as excellent diagnostic means for the nature of the A/B ring juncture. While identical shifts in the M-44 peak were observed upon deuteration in both the *trans* (Table II) and *cis* (Table III) series, the peak is much more intense in the *trans*-9-methyldecalone-1 (XVIIa) spectrum (Fig. 2) and hence will be discussed in terms of this substance. The labeling experiments demonstrate (Table II) that a C_2H_4O fragment has been lost, which is in agreement with the high-resolution mass spectra[20] of cyclohexanone and of β-decalone, where such a M-44 peak has also been recorded.

(24) F. W. McLafferty and M. C. Hamming, *Chem. Ind.* (London), 1366 (1958).

The expelled C_2H_4O moiety must contain the carbonyl group C-2 with its attached hydrogen atoms (note M-46 peak in 2,2-d_2-XIXa spectrum—Table II) as well as two additional hydrogen atoms. One of these must come from C-4 (see M-45 peak in 4,4-d_2-XXIa) and the other either from C-3 or from C-10 (see M-45 peak in 3,3,10-d_3 analog XXIIa). We favor C-10 by assuming that this hydrogen atom is initially transferred to C-1 with rupture of the 1–9 bond (g), followed by a shift of the C-4 hydrogen atom *via* the six-membered intermediate g′ to produce the stable positively charged, conjugated diene fragment g″ (*m/e* 122 in Fig. 2) and acetaldehyde. Such a mechanism is supported by the absence of an M-44 peak in the mass spectra (Fig. 4 and 5) of the 10-methylated decalones XXVa and XXVb and in the greatly reduced intensity of this peak in the *cis*-9-methyldecalone-1 (XVIIb) spectrum (Fig. 3). This is reasonable in the "non-steroid" conformation (f)[25] of the *cis* isomer, where the C-10 hydrogen atom is unfavorably disposed for transfer to C-1.



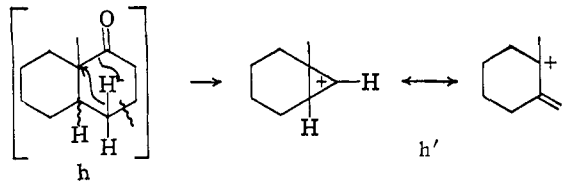
g g′ g″

Peak M-55 (*m/e* **111 in Fig. 2 and 3**).—The movements of this peak (see Tables II and III) are completely analogous to those observed earlier (Table I) in the spectrum (Fig. 1) of *trans*-decalone-1 (I) and the identical mechanism (b → b′ → b″ with angular methyl group) obtains here. This M-55 peak is much more intense in the *cis* (XVIIb) than in the *trans* (XVIIa) spectrum (Fig. 3 *vs.* Fig. 2) and it is pertinent to recall that a similar observation was made earlier[5] in comparing the mass spectra of *cis*- and *trans*-A/B fused 4- and 6-ketosteroids. The same relationship in the intensity of the M-55 peak, though not of such pronounced quantitative difference, is also noted in the mass spectra (Fig. 4 and 5) of *trans*-(XXVa) and *cis*-(XXVb) 10-methyldecalone-1.

According to the above-postulated mechanism, this fragmentation is initiated by fission of the 5–10 bond (b → b′), a process which evidently is preferred in the energetically less favored *cis*-α-decalone series.

Peak M-57 (*m/e* **109 in Fig. 2 and 3**).—This peak is present in both the *trans*-(XVIIa) and *cis*-(XVIIb) 9-methyldecalone-1 spectra (Fig. 2 and 3) and the shifts incurred upon deuteration (Tables II and III) demonstrate that its formation involves the loss of a C_3H_5O moiety derived from carbon atoms 1, 2 and 3 together with the transfer of one hydrogen. The latter appears to be derived from C-4,[26] thus suggesting rupture of type h with formation of the *m/e* 109 ion h′. The elementary composition of the peak h′ is confirmed by the presence of this ion (M-71) in the mass spectrum (Fig. 6) of *trans*-3,9-dimethyldecalone-1 (XXVI).

Peak M-71 (*m/e* **95 in Fig. 2 and 3**).—In the above discussion of the mass spectrum (Fig. 1) of *trans*-decalone-1 (I), it was pointed out that the M-71 peak



h h′

was made up of two species, c and c′, the former arising from the further loss of carbon monoxide from the ion a″ (and hence loss of the C-9 hydrogen atom), while formation of c′ involved the loss of the C-5 hydrogen. In the 9-methylated analogs XVIIa and XVIIb, only the latter mechanism is possible and all of the shifts of this peak in the mass spectra of the deuterated analogs (Tables II and III) are in accord with this conclusion.

Conversely, in the 10-methylated α-decalones XXVa and XXVb, the M-71 peak (Fig. 5 and 6) can again arise by both mechanisms (giving c or c′ with methyl group at C-10).

Peak M-85 (*m/e* **81 in Fig. 2 and 3**).—In contrast to the rather secure assignment of this *m/e* 81 peak to species c and c′ in the spectrum (Fig. 1) of *trans*-decalone-1 (I), no such straightforward conclusion can be reached in the 9-methylated analogs. This is illustrated in Tables II and III where the M-85 peak in the trideuteriomethyl derivatives XVIIIa and XVIIIb is now divided between M-85 and M-88, thus demonstrating the existence of at least two ions with and without the angular methyl group. Further complications are indicated by the rather extensive hydrogen rearrangements observed in the multiple shifts of this peak in the octadeuterio analogs XXa and XXb.

Peak M-99 (*m/e* **67 in Fig. 2 and 3**).—The shifts (Tables II and III) upon deuteration are again consistent with the formulation (see d and d′) of this peak as a $C_5H_7^+$ ion arising from the non-oxygenated ring and not containing the angular methyl group. The adjacent *m/e* 68 peak (see Fig. 2 and 3) consists of a different portion of the molecule since the spectrum of XVIIIa demonstrates (shift to *m/e* 71) that the angular methyl group is retained.

The Mass Spectra of *trans*-10-Methyldecalone-1 (XXVa) (Fig. 4), *cis*-10-Methyldecalone-1 (XXVb) (Fig. 5) and *trans*-3,9-Dimethyldecalone-1 (XXVI) (Fig. 6).—The principal peaks in the mass spectra of these three methylated α-decalones are indicated directly on the spectra (Fig. 4–6) and, where pertinent, they were discussed in connection with the mass spectra of the 9-methylated α-decalones XVIIa and XVIIb. Their mass spectral fragmentation behavior completely falls in line with the major fragmentation mechanisms outlined above and needs no further comment.

Stereochemical Considerations and General Conclusions

The results in this work and the earlier steroid studies[5] indicate that a fragment ion (*e.g.*, M-42 or M-55 in Fig. 3) will be more abundant in the *cis*-α-decalone series, when ring cleavage involved in its formation releases the greater strain (*vis-a-vis* the *trans* isomer) inherent in the *cis* ring juncture.[26a] Hydrogen transfer reactions (*e.g.*, M-44 peak in Fig. 2 and 3) may also be very dependent on stereochemistry, since the proper spatial relationship between the departing hydrogen and the "acceptor atom" is obviously of crucial importance. In any event, in the two pairs (XVIIa, b and XXVa, b) of stereoisomeric α-decalones

(25) Whether classical conformational analysis of such flexible molecules can be applied to high energy intermediates in electron impact phenomena is a moot point. Nevertheless, it is interesting to note that rotatory dispersion studies (W. Moffitt, R. B. Woodward, A. Moscowitz and C. Djerassi, *J. Am. Chem. Soc.*, **83**, 4013 (1961)) indicate that in solution it is this "non-steroid" conformer (f) of *cis*-9-methyldecalone-1 (XVIIb) which is the preferred one. This would be in agreement with the mass spectral results, since in the "steroid-like" conformation of the *cis*-decalone, the C-10 hydrogen atom would be just as close to C-1 as in the *trans* isomer.

(26) This conclusion is not unequivocal, because the 4,4-d_2 derivative is contaminated (see Experimental) by appreciable amounts of d_1- and d_3-species, thus complicating a precise search for peak shifts in this region of the spectrum.

(26a) NOTE ADDED IN PROOF.—P. Natalis (*Nature*, **197**, 284 (1963)) has discussed the effect of stereochemistry on the mass spectra of the parent hydrocarbons *cis*- and *trans*-decalin. For further comments see R. I. Reed, *Advan. Org. Chem.*, **3**, 36 (1963).

studied by us, the over-all fragmentation patterns are sufficiently distinct (Fig. 2–5) so that their mass spectra can be used as secure criteria for purposes of differentiation.

The present study of the mass spectra of α-decalones shows again[18,27] the advantages of labeling as many carbon atoms as possible with deuterium. Aside from aiding in the assignment of plausible species to the various mass spectral peaks, such labeled substrates are indispensable if information is going to be accumulated on the nature of hydrogen transfer reactions accompanying carbon–carbon bond fissions. As noted in the present work, virtually all of the principal fragmentations are accompanied by single or multiple hydrogen transfers. At times, these appear to be highly specific, while in other instances extensive scrambling of hydrogen occurs (*e.g.*, M-H_2O or *m/e* 67 peaks). The rather interesting conclusions derivable from the mass spectra of deuterated analogs have prompted us to undertake extensive synthetic studies of other deuterium-labeled bicyclic and polycyclic ketones, which will be described in future publications from this Laboratory.

Experimental[28]

2,2,9-d_3-*trans*-Decalone-1 (II).—A standard solution of 75 mg. of sodium in 4.5 cc. of deuteriomethanol and 1.5 cc. of heavy water was used for all exchange reactions. *trans*-Decalone 1 (I) (100 mg.) was dissolved in 2 cc. of the above solution and heated under reflux in a current of nitrogen for 10 min. The methanol was removed, dry ether was added to the residue and the aqueous layer was withdrawn by means of a pipet. The ether was distilled and the entire exchange process was repeated twice. The final ether solution was dried over magnesium sulfate, the solvent evaporated and the residue distilled at a bath temperature of 80° and 2 mm. Mass spectral analysis indicated the presence of 98% of the desired d_3-ketone accompanied by 2% of d_2-species.

6,7-d_2-*trans*-Decalone-1 (VII).—Δ^6-Octalol-1 (IV)[8] was acetylated with acetic anhydride and pyridine at room temperature (20 hr.) and the oily **acetate V**, which proved to be homogeneous in a thin-layer chromatogram (R_f 0.8 in 1:1 benzene-ether on silica gel), was distilled at a bath temperature of 80–90° (0.1 mm.), $\lambda_{max}^{CHCl_3}$ 5.80 μ.

Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.14; H, 9.51.

A solution of 103 mg. of the acetate IV and 680 mg. of N-trideuterio-*p*-toluenesulfonylhydrazide[29] in 4 cc. of diglyme (freshly distilled from lithium aluminum hydride) was heated under reflux for 1 hr. in a current of nitrogen. After cooling, 4 cc. of 2 *N* sodium hydroxide was added and the solution was heated for 1 hr. (nitrogen atmosphere) at 50–100°. The product was extracted with ether, washed with water and after removal of the ether and diglyme, the residue was completely saponified by heating under reflux for 1 hr. with 10% methanolic potassium hydroxide. The decalol was oxidized with sodium dichromate–sulfuric acid in ether solution[30] and the desired decalone VII was distilled at 0.1 mm. below 100°, a considerable quantity of higher-boiling material (b.p. above 140° (0.1 mm.)) being rejected. The homogeneity of the product was established by gas phase chromatography, while mass spectrometry showed that the product consisted of 61% of the d_2-ketone VII, accompanied by 33% of monodeuterated material and 6% of deuterium-free *trans*-decalone-1 (I).

5,5,6,6,7,7,8,8-d_8-*trans*-Decalone-1 (VIII).—The *trans*-Δ^6-octalone-1 (VI) synthesis of Ireland and Marshall[8] was repeated, except that in the first step d_6-butadiene (purchased from Merck Sharpe and Dohme of Canada, Ltd., Montreal) was substituted for butadiene. The resulting 5,5,6,7,8,8-d_6-*trans*-Δ^6-octalone-1 (150 mg.) was deuterated at room temperature and atmospheric pressure in cyclohexane solution with 100 mg. of degassed 5% palladized charcoal catalyst (degassing being effected by heating at 100° (0.1 mm.) for 5 hr.) and deuterium gas. The catalyst was removed by filtration and the product distilled prior to mass spectrometric analysis, which indicated the presence of 89% of the desired d_8-ketone VIII, accompanied by 8% of d_7- and 3% of d_6-species.

4,4-d_2-*trans*-Decalone-1 (XII).—A solution of 1.0 g. of *trans*-4-hydroxydecalone-1 (IX)[13] in 2 cc. of ethanedithiol was kept at room temperature for 2 days followed by shaking for 15 min. with a solution of 10 drops of boron trifluoride etherate in 1 cc. of ether.[31] All volatile material was removed at room temperature and 0.1 mm. (5 hr.) and the product was chromatographed on 50 g. of neutral alumina (activity II). Elution with methylene chloride–ether mixtures and recrystallization from hexane provided 1.4 g. of the **mercaptal X**, m.p. 109–110°, which lacked carbonyl absorption in the infrared.

Anal. Calcd. for $C_{12}H_{20}S_2O$: C, 58.97; H, 8.24; S, 26.24. Found: C, 59.00; H, 8.25; S, 25.83.

Deuterated W-7 Raney nickel[14] was prepared as follows: Raney nickel alloy (1.6 g.) was added in portions to a solution of 1.2 g. of sodium in 8.5 cc. of heavy water at such a rate that the temperature remained below 50° and after completion of addition, the reaction mixture was maintained at 50° for an additional 50 min. The catalyst was allowed to settle, the supernatant liquid was decanted and the nickel was washed six times by stirring each time with 3 cc. of heavy water followed by decantation.

The freshly prepared catalyst was washed 11 times with 1-cc. portions of dioxane and then heated under reflux for 20 hr. in dioxane solution with 163 mg. of the thioketal X, the reaction being conducted in an atmosphere of nitrogen. Filtration of the catalyst and evaporation of the solvent left 93 mg. of the oily 4,4-d_2-α-decalol XI (homogeneous on thin-layer chromatography), which was oxidized directly with sodium dichromate in ether solution[30] to afford, after distillation, 79 mg. of *trans*-decalone-1 (XII), the composition of the various isotopically labeled species being determined mass spectrometrically from the intensity of the various molecular ion peaks: d_0 17%, d_1 37%, d_2 (XII) 31%, d_3 13%, d_4 2%. A preliminary trial experiment in which the desulfurization step was performed with ordinary W-7 Raney nickel catalyst[14] gave pure *trans*-decalone-1 (I) as determined by infrared spectroscopy.[32]

3,3,10-d_3-*trans*-Decalone-1 (XVI).—*trans*-4-Hydroxydecalone-1 (IX) (200 mg.) was equilibrated in the above-described manner with sodium in deuteriomethanol and heavy water to afford the 2,2,9-d_3 analog XIII, consisting by mass spectrometry of 90% d_3, 5% d_2 and 5% d_1 species. The total product was transformed into the mercaptal XIV by the above-described (see X) procedure providing 173 mg. of the **2,2,9-d_3-mercaptal XIV** (90% d_3 by mass spectrometry), which was desulfurized with 1 g. of deuterated W-7 Raney nickel catalyst by heating under reflux in dioxane solution for 20 hr. The crude alcohol XV was immediately oxidized with sodium dichromate in ether solution[30] giving, after distillation at a bath temperature of 60–70° (0.1 mm.), 70 mg. of the desired ketone XVI, which by mass spectrometry consisted of 66% d_3, 27% d_2 and 7% d_1 species.

***trans*-(XVIIIa) and *cis*-(XVIIIb)-9-Trideuteriomethyldecalone.**—Methylation of 2-*n*-butylthiomethylenedecalone-1 with methyl iodide followed by removal of the butylthiomethylene blocking group as described by Ireland and Marshall[15] provided a 2:1 mixture of *cis*-(XVIIb) and *trans*-(XVIIa) 9-methyldecalone-1, which was readily separated by gas phase chromatography using a Beckman Megachrom instrument with a 6-ft. diethylene glycol succinate column operating at 180° with helium as the carrier gas. The component of 15-min. retention time was shown to be the *cis*-isomer XVIIb by conversion to the oxime of m.p. 114–115° (lit.[33] m.p. 114.5–115.5°), while the *trans* isomer (m.p. of oxime 141–142°, lit.[33] m.p. 141.5–142.5°) exhibited a retention time of 18 min.

Utilizing the identical procedure with trideuteriomethyl iodide, there were obtained the *trans*-(XVIII) and *cis*-(XVIII) 9-trideuteriomethyldecalones of 92% purity (determined mass spectrometrically).

The usual equilibration of *trans*-9-methyldecalone-1 (XVIIa) provided the **2,2-d_2 derivative XIXa** (95% d_2, 5% d_1 species),

(27) *Inter al.* P. N. Rylander, S. Meyerson and H. M. Grubb, *J. Am. Chem. Soc.*, **79**, 842 (1957).

(28) All mass spectra were determined with a Consolidated Electrodynamics Corp. mass spectrometer no. 21-103C using an all-glass inlet system heated to 200°, while the isatron temperature was maintained at 270° The ionizing voltage was kept at 70 e.v. and the ionizing current at 50 μa. The microanalyses were performed by Messrs. E. Meier and J. Consul of the Stanford University Microanalytical Laboratory.

(29) Hydrazine hydrochloride, prepared from 1 cc. of 95% hydrazine and 2.7 cc. of 12 *N* hydrochloric acid, was freed of excess water at 0.1 mm. Heavy water (2 cc.) was added, the mixture heated to dissolve the salt and the water was then removed by heating at 100° (25 mm.). This process was repeated nine times with 1 cc. each of heavy water and the final product was stirred vigorously for 1 hr. with 10 cc. of benzene, 4 cc. of heavy water and 4 g. of anhydrous sodium carbonate. A solution of 6.0 g. of *p*-toluenesulfonyl chloride in 20 cc. of dry benzene was added over a period of 3 hr., the mixture was filtered, the precipitate washed well with benzene and then discarded. The evaporated filtrate was extracted with 30 cc. of dry acetonitrile, the solvent removed and the residue dried at 25° (0.1 mm.); yield 2.8 g. of white, crystalline solid.

(30) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, **83**, 2952 (1961).

(31) The alternate procedure (L. F. Fieser, *ibid.*, **76**, 1945 (1954)) of adding immediately the boron trifluoride gave only a 30% yield of the desired mercaptal X accompanied by dehydrated material.

(32) See C. Djerassi and J. Staunton, *ibid.*, **83**, 734 (1961), Table II.

(33) W. S. Johnson, *ibid.*, **65**, 1317 (1943).

while similar treatment of the *cis*-decalone XVIIb led to the 2,2-d_2 analog XIXb of 100% purity.

trans-(**XXa**) **and** *cis*-(**XXb**)-**5,5,6,6,7,7,8,8-d$_8$-9-Methyldecalone-1.**—A sample (88 mg.) of the d_8-α-decalone VIII was transformed by the published procedure[15] to the butylthiomethylene derivative, methylated, the blocking group removed and the *trans* and *cis* isomers separated by gas phase chromatography. Mass spectrometry showed the presence of 9% d_9, 40% d_8, 23% d_7, 11% d_6 and less than 4% each of d_0, d_1, d_2, d_3, d_4, and d_5 species.

trans-(**XXIa**) **and** *cis*-(**XXIb**)-**4,4-d_2-9-Methyldecalone-1.**—Methylation[15] of XII and gas phase chromatographic separation gave the required ketones XXIa and XXIb, the composition of which was determined mass spectrometrically as: d_0 13%, d_1 38%, d_2 35%, d_3 14%.

trans-(**XXIIa**) **and** *cis*-(**XXIIb**)-**3,3,10-d_3-9-Methyldecalone-1.**—The identical procedure applied to XVI led to the ketones XXIIa and XXIIb of the isotope composition: d_3 61%, d_2 32% and d_1 7%.

trans-(**XXIVa**) **and** *cis*-(**XXIVb**)-**6,7-d_2-9-Methyldecalone-1.**—The mixture (267 mg.) of *trans*-(XXIIIa) and *cis*-(XXIIIb) 9-methyl-Δ^6-octalones[8] was reduced with lithium aluminum hydride in ether solution (20 hr., room temperature), the resulting alcohol acetylated, reduced with N-trideuterio-*p*-toluenesulfonyl hydrazide (see preparation of VII), saponified, oxidized and the mixture (over-all yield, 93 mg.) of *trans*-(XXIVa) and *cis*-(XXIVb) isomers separated by gas phase chromatography on a Craig succinate column, the products consisting of 57% d_2, 33% d_1 and 27% d_0 species.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY, WASHINGTON UNIVERSITY, ST. LOUIS, MO.; POLYTECHNIC INSTITUTE OF BROOKLYN, BROOKLYN, N. Y.; STANFORD UNIVERSITY, STANFORD, CALIF.]

Absolute Configuration and Optical Rotatory Dispersion of 3-Methylcycloheptanone and 4-Methylcycloheptanone

BY CARL DJERASSI,[1] B. F. BURROWS,[1] C. G. OVERBERGER,[2] T. TAKEKOSHI,[2] C. D. GUTSCHE[3] AND C. T. CHANG[3]

RECEIVED NOVEMBER 19, 1962

Ring enlargement of (+)-3-methylcyclohexanone, a compound of reliably established absolute configuration, is shown to yield (+)-3-methylcycloheptanone and (−)-4-methylcycloheptanone. The reassignment of the sign of rotation and the sign of the optical rotatory dispersion Cotton effect to the 3-methyl isomer eliminates the contradictions posed by the stereochemical outcome of the diazomethane ring enlargement of optically active 2-methylcyclohexanones and confirms the proposition that the diazoalkane–carbonyl reaction proceeds with retention of configuration.

A recent communication directed to the stereochemistry of the diazomethane ring enlargement of optically active 2-methylcyclohexanone[4] required the conclusion, based on the data contained therein and on the existing data in the literature, that the diazoalkane–carbonyl reaction proceeds with inversion of configuration. On the basis of other facts concerning such reactions, however, this appeared to be inadmissible and to call for a reinvestigation of some of the earlier experiments. One of the several critical points in the argument focused on the previously reported synthesis of (−)-3-methylcycloheptanone by diazomethane ring enlargement of (+)-3-methylcyclohexanone,[5] the absolute configuration of which had been established by methods generally accepted as reliable.[6] The work reported in the present communication demonstrates that the product of ring enlargement of (+)-3-methylcyclohexanone is actually the (+)-rotating rather than the (−)-rotating 3-methylcycloheptanone, the earlier reported[5] negative rotation (and negative Cotton effect) having been due to contamination with the strongly levorotatory 4-methylcycloheptanone which is also produced in the ring enlargement reaction. Thus the contradictions posed by the stereochemical outcome of the diazomethane ring enlargement of 2-methylcyclohexanone are resolved, and it is firmly established that the diazomethane–carbonyl reaction proceeds with *retention* of configuration.

Ring enlargement of (+)-3-methylcyclohexanone was carried out by the *in situ* diazomethane method according to the procedure previously employed by Djerassi and Krakower,[5,7] by the *ex situ* diazomethane method,[8] and by the Demjanow–Tiffeneau method[9]; in all cases the product consisted of approximately equal amounts of the 3- and 4-methylcycloheptanones. The two materials, however, are not easily separated, and it is this difficulty that obscured the earlier report[5] concerning their optical rotations. By subjecting the crude mixture to distillation through a very efficient spinning band column at a very high reflux ratio or by passing the crude mixture through a sufficiently long and efficient vapor phase chromatographic (v.p.c.) column it is possible to obtain one fraction with $[\alpha] + 64°$ and another fraction with $[\alpha] - 137°$. Although resembling each other in boiling point, refractive index and nuclear magnetic resonance spectra (n.m.r.), the two fractions showed significant differences in detail in the infrared spectrum, in the mass spectrum, in v.p.c. behavior and especially in optical rotatory dispersion (R.D.) (Fig. 1). Furthermore, derivatives of the two fractions showed them to be quite different compounds. Identification of the (+)-fraction as (+)-3-methylcycloheptanone (strong positive Cotton effect) was based on a comparison with material previously obtained[4] from the ring enlargement of 2-methylcyclohexanone; identification of the (−)-fraction as (−)-4-methylcycloheptanone (strong negative Cotton effect) was based on a comparison with material obtained from the ring enlargement of 4-methylcyclohexanone. Additional support for these structural assignments was adduced from the degradative reactions resulting in the conversion of the respective ketones to the corresponding dibasic acids followed by pyrolytic cyclization to a mixture of methylcyclohexanones which could be separated by v.p.c. As anticipated, application of this reaction sequence to (+)-3-methylcycloheptanone provided 2- and 3-methylcyclohexanone, while (−)-4-methylcycloheptanone afforded 3- and 4-methylcyclohexanone uncontaminated with 2-methylcyclohexanone.

(1) The work at Stanford University was supported by grant no. CRTY-5061 from the National Cancer Institute, U. S. Public Health Service.

(2) The work at the Polytechnic Institute of Brooklyn was supported by Chas. Pfizer, Co., Inc.

(3) The work at Washington University was supported by grant no. 628-A4 from the Petroleum Research Fund administered by the American Chemical Society and by grant no. G-21323 from the National Science Foundation.

(4) C. D. Gutsche and C. T. Chang, *J. Am. Chem. Soc.*, **84**, 2263 (1962).

(5) C. Djerassi and G. W. Krakower, *ibid.*, **81**, 237 (1959).

(6) A. Fredga, *Arkiv. Kemi Mineral. Geol.*, **24A**, No. 32 (1947); E. J. Eisenbraun and S. M. McElvain, *J. Am. Chem. Soc.*, **77**, 3383 (1955).

(7) T. J. DeBoer and H. J. Backer, *Org. Syntheses*, **34**, 24 (1954); G. W. Krakower, Ph.D. Thesis, Wayne State University, 1958.

(8) C. D. Gutsche, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, p. 364.

(9) P. A. S. Smith and D. R. Baer, "Organic Reactions," Vol. 11, John Wiley and Sons, Inc., New York, N. Y., 1960, p. 157.