amine pentaacetate, mp 182.5–183.5°, from Sigma Chemical Co.; α-D-galactopyranose pentaacetate, mp 94–98°, and β-D-galacto-pyranose pentaacetate, mp 144–147°, from Aldrich Chemical Co.

**B. Cyclitols.**[23]—*myo*-Inositol hexaacetate **26**, mp 217–218° (lit.[24] 216°), was prepared by acetylation of *myo*-inositol (General Biochemicals, Inc., Chagrin Falls, Ohio). *epi*-Inositol hexaacetate **27**, mp 183–184° (lit.[25] 188°), was prepared by acetylation of *epi*-inositol kindly supplied by Professor T. Posternak. Hexa-O-acetyl-*scyllo*-inositol (**28**), hexa-O-acetyllaminitol (**29**), penta-O-acetyl-*scyllo*-*ms*-inosose (**30**), penta-O-acetyl bornesitol (**31**), and penta-O-acetyl viburnitol (**32**) were gifts from Professor T. Posternak. Tetraacetates of DL-(1,2,3/4)-tetrol[26a] (**33**), mp 112.5–113.5°, and DL(1,2,4/5)-tetrol[26b] (**34**), mp 91.5–92.5° (lit.[27] 93°), were prepared by acetylation of the corresponding tetrols.[26–28] The azidotriol triacetate[26a] **35**, mp 84–85.5°, was prepared from the corresponding azidotriol, and the acetamido-

triol triacetate **36**, mp 157–159°, was prepared by catalytic hydrogenation of the corresponding cyclohexene compound, "conduramine C-4," previously reported by one of us.[29] Inosodiamines **37, 38, 39,** and **40** were described previously.[8,29]

(23) Trivial names are given for most of these compounds.

(24) E. G. Griffin and J. M. Nelson, *J. Amer. Chem. Soc.*, **37**, 1556 (1915).

(25) T. Posternak, *Helv. Chim. Acta*, **19**, 1333 (1936).

(26) Preparation and structure proof of these compounds will be described in subsequent papers in this series: (a) H. Z. Sable, H. Katchian, C. B. Niewoehner, and S. B. Kadlec, manuscript in preparation. (b) H. Z. Sable and A. L. Simonesen, manuscript in preparation.

(27) G. E. McCasland, S. Furuta, L. F. Johnson, and J. N. Shoolery, *J. Org. Chem.*, **28**, 894 (1963).

(28) N. D. Zelinski, Y. I. Denisenko, and M. S. Eventova, *Dokl. Akad. Nauk. USSR*, **1**, 313 (1935).

(29) (a) M. Nakajima, A. Hasegawa, and N. Kurihara, *Chem. Ber.*, **95**, 2708 (1962); (b) *Tetrahedron Lett.* 967 (1964); (c) *Ann. Chem.*, **689**, 235 (1965).

# Mass Spectrometry in Structural and Stereochemical Problems. CXLII.[1] Electron Impact Induced Analogies to Thermal Elimination Processes in S-Methyl Xanthates and Esters[2]

W. Scott Briggs and Carl Djerassi

*Department of Chemistry, Stanford University, Stanford, California*

The mass spectra of the epimeric 2-methylcyclohexyl-S-methyl xanthates, acetates, and higher esters have been examined. By a combination of deuterium-labeling techniques and high resolution mass spectrometry, the principal modes of fragmentation of members of these classes have been uncovered. Evidence has been found for the existence of an electron impact induced analog to the thermal Chugaev reaction and, although ring conformational mobility complicates the interpretation of the experimental data, some stereospecificity favoring *cis* elimination appears to exist. Ring conformational freedom obviates any sound stereochemical conclusions in the ester cases. The positional specificity of the analogous elimination processes in all 2-methylcyclohexyl-S-methyl xanthates and esters is found to be high (79–85% 1,2 elimination and independent of the energy of the ionizing electron beam). The corresponding pyrolytic processes have been studied in detail in the epimeric $d_0$- and 2-$d_1$-methylcyclohexyl-S-methyl xanthates and acetates and these results are contrasted with those from the electron impact studies. In terms of percentage of the total elimination process, values found for the portion of the electron impact induced elimination which proceeds toward the tertiary center (C-2) are found to be 47% in *cis*-2-methylcyclohexyl-S-methyl xanthate (**5**), 90% in *trans*-2-methylcyclohexyl-S-methyl xanthate (**6**), 42% in *cis*-2-methylcyclohexyl acetate (**7**), and 38% in *trans*-2-methylcyclohexyl acetate (**8**). The corresponding losses in the pyrolytic elimination mode are 29% in **5**, 65% in **6**, 9% in **7**, and 56% in **8**.

In the recent literature[3] have appeared numerous references to analogies existing between thermal and electron impact induced reactions of organic compounds.

It has been pointed out[4] that one of the most general mass spectrometric hydrogen-transfer processes,[5] the McLafferty rearrangement,[6] *i.e.*, electron impact induced β cleavage with concomitant transfer of a γ-hydrogen atom[7] (see a → b), may, in the case of certain esters (c → d),[8] be regarded as the mass spectrometric counterpart to the well-known ester

(1) For paper CXLI, see J. Diekman, J. B. Thomson, and C. Djerassi, *J. Org. Chem.*, **32**, 3904 (1967).

(2) Financial assistance (Grants No. CA-07195 and AM-04257) from the National Institutes of Health of the U. S. Public Health Service is gratefully acknowledged. The purchase of the Atlas CH-4 mass spectrometer was made possible through NASA Grant NsG 81-60.

(3) (a) F. W. McLafferty and R. J. Gohlke, *Anal. Chem.*, **31**, 2076 (1959); (b) E. K. Field and S. Meyerson, *Chem. Commun.*, 474 (1965); (c) S. Meyerson, *Rec. Chem. Progr.* (Kresge-Hooker Sci. Lib.), **26**, 257 (1965); (d) F. Weiss, A. Isard, and G. Bonnard, *Bull. Soc. Chim. Fr.*, 2332 (1965); (e) J. H. Beynon, R. F. Curtis, and A. E. Williams, *Chem. Commun.*, 237 (1966); (f) R. F. C. Brown, W. D. Crow, and R. K. Solly, *Chem. Ind.* (London), 343 (1966); (g) R. F. C. Brown, D. V. Gardner, J. F. W. McOmie, and R. K. Solly, *Chem. Commun.*, 407 (1966); (h) R. F. C. Brown and R. K. Solly, *Aust. J. Chem.*, **19**, 1045 (1966); (i) M. P. Cava, M. J. Mitchell, D. C. DeJongh, and R. Y. Van Fossen, *Tetrahedron Lett.*, 2947 (1966); (j) J. L. Cotter and G. J. Knight, *Chem. Commun.*, 336 (1966); (k) E. K. Field and S. Meyerson, *J. Amer. Chem. Soc.*, **88**, 21 (1966); (l) *ibid.*, **88**, 2836 (1966); (m) *ibid.*, **88**, 3388 (1966); (n) E. K. Field and S. Meyerson, *J. Org. Chem.*, **31**,

3307 (1966); (o) S. Meyerson and E. K. Field, *Chem. Commun.*, 275 (1966); (p) J. G. Pritchard and P. T. Funke, *J. Heterocycl. Chem.*, **3**, 209 (1966); (q) D. C. DeJongh, R. Y. Van Fossen, and C. F. Bourgeois, *Tetrahedron Lett.*, 271 (1967); (r) J. I. Jones and H. M. Paisley, *Chem. Commun.*, 128 (1967); (s) D. F. Lindow and L. Friedman, *J. Amer. Chem. Soc.*, **89**, 1271 (1967).

(4) G. Spiteller and M. Spiteller-Friedmann, *Monatsh.*, **95**, 257 (1964).

(5) *Cf.* C. Djerassi, *Pure Appl. Chem.*, **9**, 159 (1964).

(6) F. W. McLafferty, *Anal. Chem.*, **31**, 82 (1959).

(7) For a detailed review, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, Chapter 3.

(8) (a) W. Benz and K. Biemann, *J. Amer. Chem. Soc.*, **86**, 2375 (1964); (b) C. Djerassi and C. Fenselau, *ibid.*, **87**, 5756 (1965).

and Chugaev xanthate pyrolyses[9] (see 1 → 2 + 3). It should be noted that in ketones (a) the charge remains predominantly with the oxygen-containing moiety, while in esters (c) of higher alcohols, the olefin portion (d) retains most of the charge. In the thermally induced process the hydrogen abstraction is known to be *cis* cyclic in nature[9] and pyrolytic



$$X = S; \quad Y = O; \quad Z = -SCH_3$$
$$\text{or} \quad X = O; \quad Y = O; \quad Z = -CH_3$$
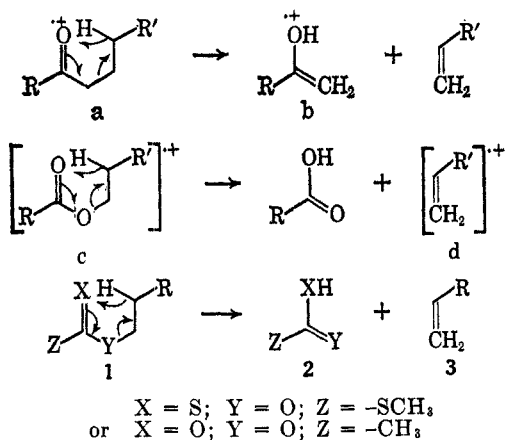
reactions have found wide synthetic utility as a result of their stereoselectivity. In esters, the acid fragment (2) produced is thermally stable, whereas that species produced in the xanthate case undergoes further decomposition to mercaptan (RSH) and carbonyl sulfide.

The over-all similarity in the behavior of esters with available β hydrogens in the electron impact (c → d) and pyrolytic (1 → 2 + 3) modes of breakdown prompted us to examine the stereochemical requirements of the radical-ion process, since nothing is known about it in contrast to the extensive body of knowledge existing for the thermal reaction.[9]

### Results and Discussion

As some steroidal xanthates were at hand in the course of another study,[10] the mass spectra of these were examined for the presence of peaks corresponding to the ionized olefin, the expected fragment if a process corresponding to c → d were operating. The low-resolution mass spectrum (12 eV) of 5α-cholestan-3β-ol S-methyl xanthate (4) is representative and the higher mass portion of it is reproduced in Figure 1. In fact, it will be noted that the two most important peaks correspond to the ionized olefin (e) and the even-electron ion (f) formed by C(3)–O bond cleav-
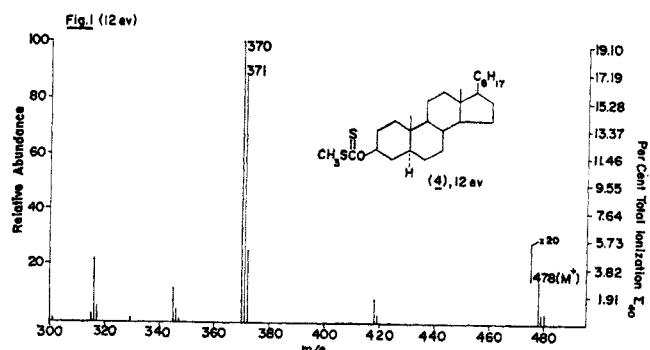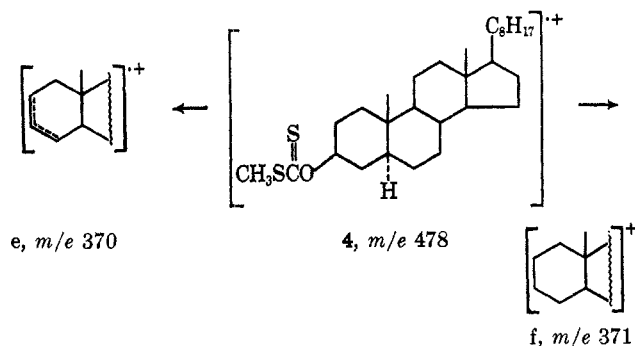


e, m/e 370      4, m/e 478

f, m/e 371



Figure 1.—Partial mass spectrum of 5α-cholestan-3β-ol S-methyl xanthate at 12 eV (A.E.I. MS-9 mass spectrometer).

age. Under the instrumental conditions employed for the measurements of the spectrum of this compound, it is conceivable that the peak at m/e 370 arose from ionization of olefin produced pyrolytically in the ion source of the mass spectrometer. However, the presence of a weak metastable ion at m/e 286.0 (calcd 286.1) corresponding to the process m/e 478 → m/e 370 established that at least a portion of the observed olefinic fragment e resulted by direct loss of the elements of xanthic acid from the molecular ion.

In the selection of a system in which to study the course and stereochemistry of the electron impact induced elimination reactions in esters and xanthates, primary consideration was given to the need for differentiation between *cis* and *trans* modes of elimination. Furthermore, sufficiently volatile S-methyl xanthates were required to allow introduction of the sample into the mass spectrometer at temperatures low enough to avoid complications in spectral interpretation arising by operation of competing thermal processes. The system chosen for this particular study was the 2-methylcyclohexyl moiety[11] in which the ring methyl may be disposed in either a *cis* or *trans* relationship to the ester or xanthate function. Compounds synthesized initially (see Experimental Section) were *cis*- (5) and *trans*-2-methylcyclohexyl-S-methyl xanthate (6) and the corresponding *cis* (7) and *trans* acetates (8).

At the outset it was hoped that the mass spectra of the two possible olefins formed by 1,2 elimination,



5, R = –CSCH₃ (∥S)    6, R = –CSCH₃ (∥S)    9

7, R = –CCH₃ (∥O)    8, R = –CCH₃ (∥O)
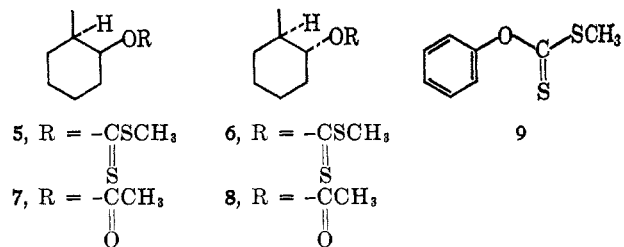
namely, 1-methyl-1-cyclohexene (Figure 2) and 3-methyl-1-cyclohexene, would differ significantly,[12]

---

(9) For leading references and an excellent review of such pyrolytic processes, see (a) C. H. DePuy and R. W. King, *Chem. Rev.*, **60**, 431 (1960); (b) H. R. Nace, *Org. Reactions*, **12**, 57 (1962).

(10) W. S. Briggs and C. Djerassi, *Tetrahedron*, **21**, 3455 (1965).

(11) However, as will be pointed out later, this system suffers from the disadvantage of ring conformational mobility which complicates the interpretation of the results. See also (a) J. Cason and K.-L. Liauw, *J. Org. Chem.*, **30**, 1763 (1965); (b) J. Cason and A. I. A. Khodair, *ibid.*, **32**, 575 (1967).

(12) Consideration of the differences in the retro-Diels-Alder fragments of menth-1-ene and menth-2-ene has recently allowed conclusions to be drawn regarding the direction of electron impact induced acetic acid elimination in carvomenthyl acetate [see A. F. Thomas and B. Willhalm, *J. Chem. Soc., Sect. B*, 219 (1966)].
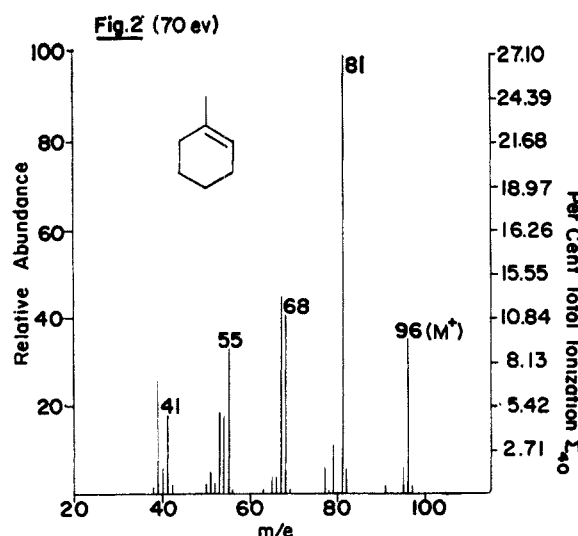
Figure 2.—Mass spectrum of 1-methyl-1-cyclohexene at 70 eV (Atlas CH-4 mass spectrometer).

thus allowing direct quantitative assessment of the preferred direction of elimination in **5–8**. However, the spectra of these two olefins were found to be virtually superimposable.[13] Thus, it was necessary to turn to deuterium-labeled substrates in order to determine unambiguously the course of these elimination processes. The syntheses of the required deuterated compounds are described later.

**2-Methylcyclohexyl Xanthates.**—The low resolution mass spectra of xanthates **5** and **6** determined at 70 and 14 eV by cold ion source techniques[14] are reproduced in Figures 3 and 4, and in Table I are reported

TABLE I

METASTABLE TRANSITIONS
AND ELEMENTAL COMPOSITIONS OF FRAGMENTS FROM
2-METHYLCYCLOHEXYL-S-METHYL XANTHATES

| Transition | | Calcd | Found for *cis*-xanthate (5) | Found for *trans*-xanthate (6) |
|---|---|---|---|---|
| $C_9H_{16}OS_2^{\cdot+}$ $^a$ → $C_7H_{12}^{\cdot+}$ + $C_2H_4OS_2$ | | 45.1 | 45.2 | 45.2 |
| (204$^+$ → 96$^+$ + 108) | | | | |
| $C_7H_{13}^+$ → $C_5H_9^+$ + $C_2H_4$ | | 49.1 | 49.1 | 49.1 |
| (97$^+$ → 69$^+$ + 28) | | | | |
| $C_7H_{13}^+$ → $C_4H_7^+$ + $C_3H_6$ | | 31.2 | 31.2 | 31.2 |
| (97$^+$ → 55$^+$ + 42) | | | | |
| $C_7H_{12}^{\cdot+}$ → $C_6H_9^+$ + $CH_3\cdot$ | | 68.4 | 68.4$^b$ | 68.4$^b$ |
| (96$^+$ → 81$^+$ + 15) | | | | |
| $C_6H_9^+$ → $C_4H_7^+$ + $C_2H_2$ | | 37.3 | 37.2 | 37.2 |
| (81$^+$ → 55$^+$ + 26) | | | | |
| $C_5H_9^+$ → $C_3H_5^+$ + $C_2H_4$ | | 24.3 | $c$ | 24.3 |
| (69$^+$ → 41$^+$ + 28) | | | | |

$^a$ This exact mass measurement was run by Dr. J. H. Beynon, Imperial Chemical Industries, Manchester, England. $^b$ This extremely strong metastable ion was visible in low-resolution mass spectra without logarithmic transfer recording. $^c$ Logarithmic transfer recording not run to low enough $m/e$ value to observe this metastable ion in xanthate **5**, but undoubtedly occurs by analogy to xanthate **6**.

the metastable ions[15] and the transitions to which they correspond[16] for these compounds. For comparison purposes, the cold ion source spectrum of the one aromatic S-methyl xanthate, phenyl-S-methyl xanthate (**9**), previously reported[17] from our laboratory, is shown in Figure 5.

Comparison of the 70-eV mass spectra of xanthates **5** and **6** with that (Figure 2) of 1-methyl- (or 3-methyl-) 1-cyclohexene (the expected products if a 1,2-hydrogen abstraction is operative) shows that there is a qualitative correspondence in the region $m/e$ 40–96 with the exception of heteroatom-containing fragments[16] at $m/e$ 91, 47, and 45 and a peak at $m/e$ 69 ($C_5H_9^+$).[18,19] The quantitative differences are those which would be predicted (see Table I) for ions known to arise through further breakdown of the $m/e$ 97 ion.

It is quite pertinent to the subsequent discussion of the mode of thermal *vs.* electron impact induced elimination to observe that, in the spectra (Figures 3 and 4) of xanthates **5** and **6**, no peaks appear at $m/e$ 48 and 60 corresponding to ionized methyl mercaptan and carbonyl sulfide, respectively. These are the two stable sulfur-containing moieties which are produced in the thermal Chugaev reaction and, while their absence by no means establishes rigorously the complete absence of thermal processes, it does indicate that pyrolysis in the ion source before passing through the ionizing electron beam does not occur. The mass spectrum of the *cis* xanthate (**5**) was also run under instrumental conditions[20] which should promote the pyrolytic process and was, in fact, virtually superimposable upon those (see Figure 2) of 1-methyl- and 3-methyl-1-cyclohexene, the expected pyrolytic products, with the exception of major fragments at $m/e$ 60 ($COS^{\cdot+}$), 48 ($CH_3SH^{\cdot+}$), 47 ($CH_3S^+$), and 45 ($CHS^{\cdot+}$). The latter two fragment ions are also evident in the cold-source mass spectrum (Figure 3) of xanthate **5**. It is clear, therefore, that Figures 3 and 4 represent true mass spectra of the ionized xanthates and not of some pyrolysis products.

The base peak in the 70-eV mass spectra of both xanthates **5** and **6** is due to the even-electron ion of mass 97 (28.1% $\Sigma_{40}$ in the former compound and 25.6% $\Sigma_{40}$ in the latter) having the composition $C_7H_{13}^+$ by high resolution mass spectrometry.[16]



o, $m/e$ 97     m, $m/e$ 204     n, $m/e$ 97

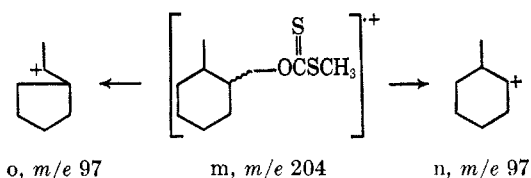(13) See also T. H. Kinstle and R. E. Stark, *J. Org. Chem.*, **32**, 1318 (1967).

(14) The compound was adsorbed on activated charcoal and introduced using the direct probe inlet into the TO-4 ion source (heated only by the filament current to ca. 70°) of the Atlas CH-4 mass spectrometer. A similar technique using molecular sieves has been employed by E. Schumacher and R. Taubenest, *Helv. Chim. Acta*, **49**, 1439 (1966).

(15) Metastable ions were detected with an Atlas CH-4 mass spectrometer in conjunction with a logarithmic transfer recorder. See R. T. Aplin, H. Budzikiewicz, H. S. Horn, and J. Lederberg, *Anal. Chem.*, **37**, 776 (1965).

(16) The composition of all relevant ions was established by high resolution measurements.

(17) J. B. Thomson, P. Brown, and C. Djerassi, *J. Amer. Chem. Soc.*, **88**, 4049 (1966).

(18) The complete mass spectra of the deuterated xanthates and acetates along with interpretations of the important fragmentation pathways will be presented in the dissertation submitted by W. S. B. to the Graduate School, Stanford University, 1967, in partial fulfillment of the requirements for a Ph.D. degree.

(19) Total ion current is reported as percentage of $\Sigma_{40}M^+$ (all peaks).

(20) This spectrum was run on a C.E.C. Model 21-103C mass spectrometer equipped with an all-glass heated inlet system (200°) and the isatron temperature maintained at 250°; ionizing voltage, 70 eV; ionizing current, 50 μA.
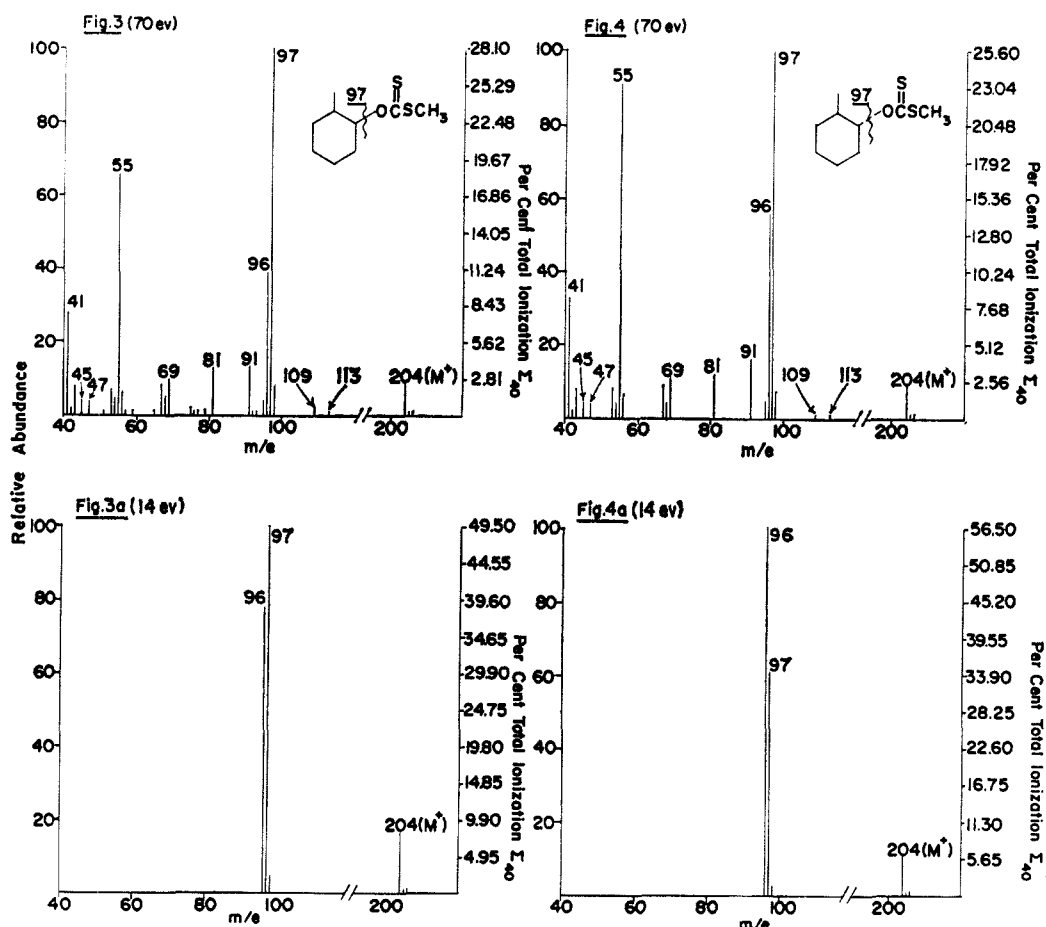
Figure 3.—Cold ion source mass spectrum of *cis*-2-methylcyclohexyl-S-methyl xanthate (5) at 70 and 14 eV (Atlas CH-4 mass spectrometer).

Figure 4.—Cold ion source mass spectrum of *trans*-2-methylcyclohexyl-S-methyl xanthate (6) at 70 and 14 eV (Atlas CH-4 mass spectrometer).

This species corresponds to direct loss of an xanthate radical from the molecular ion (m) and may be represented by the methylcyclohexyl cation n or a rearranged species such as o. In xanthate **9**, the corresponding even-electron species ($m/e$ 77) carries only 9.4% $\Sigma_{40}$ in the 70-eV mass spectrum (Figure 5).

Of particular interest is the fragment ion of mass 96 ($C_7H_{12}^+$) (11.0% $\Sigma_{40}$ in **5** and 14.3% $\Sigma_{40}$ in **6**). As will be noted in Table I, at least some of this species arises from expulsion of the elements of xanthic acid from the molecular ion m—the electron impact analog to the thermal Chugaev reaction. In the aromatic xanthate **9** (Figure 5) the analogous elimination process which yields, at least formally, ionized benzyne ($m/e$ 76) is much less important ($ca.$ 0.3% $\Sigma_{40}$).

The difference in the behavior of the two xanthate mass spectra (Figures 3 and 4) upon lowering the ionizing voltage is quite striking. Particularly notable in both is that at 14 eV only the molecular ion ($m/e$ 204) and the two cleavage ions ($m/e$ 96 and 97) remain. As the electron energy is lowered from 70 to 14 eV, the relative intensity of the $m/e$ 96 peak compared with that of the $m/e$ 97 fragment increases in both xanthate **5** and xanthate **6**; in the latter compound the $m/e$ 96 species becomes dominant at 14 eV. However, the differing behavior is more readily apparent if the ratios (1.3 in **5** and 4.8 in **6**) of the difference in the percentage total ion current carried by these two fragments at 70 and 14 eV are considered. The increased ratio is presumably due to the influence

of stereochemical factors and is in the direction to be expected for a preferential *cis* mode of hydrogen abstraction.

Before treating the results of deuterium-labeling studies, it is interesting to consider briefly the fate of the complementary "acid" fragment produced in the $m/e$ 96 yielding elimination process. In acetate and propionate esters of alcohols having available $\beta$ hydrogens in which McLafferty rearrangements of the type c → d may occur, the charge is only retained by the oxygenated fragment when a double hydrogen transfer occurs and an acyloxonium species of type p is generated.[8] In higher esters (see Table II), the

TABLE II

SUMMARY OF THE EFFECTS[a] OF THE ACYL SIDE CHAIN LENGTH ON THE VARIOUS CLEAVAGE MODES IN *trans*-2-METHYLCYCLOHEXYL ESTERS

| R | $RCO_2H^{·+}$ | $RCO_2H_2^+$ | $m/e$ 96 | $m/e$ 97 | Ratio of $m/e$ 96:$m/e$ 97 |
|---|---|---|---|---|---|
| $CH_3$ (8) | ... | ... | 17.5 | 0.8 | 21.9 |
| $C_2H_5$ (23) | ... | 0.5 | 14.1 | 2.9 | 4.9 |
| $n$-$C_3H_7$ (24) | ... | 1.1 | 14.8 | 4.0 | 3.7 |
| $n$-$C_4H_9$ (25) | 0.3 | 1.4 | 16.0[b] | 5.8 | 2.8 |
| $n$-$C_7H_{15}$ (26) | 0.6 | 1.5 | 18.4[b] | 7.4 | 2.5 |

[a] Data from 70 ev spectra, corrected for $^{13}C$ isotope contributions and reported as %$\Sigma_{29}$. [b] Denotes base peak of spectrum.
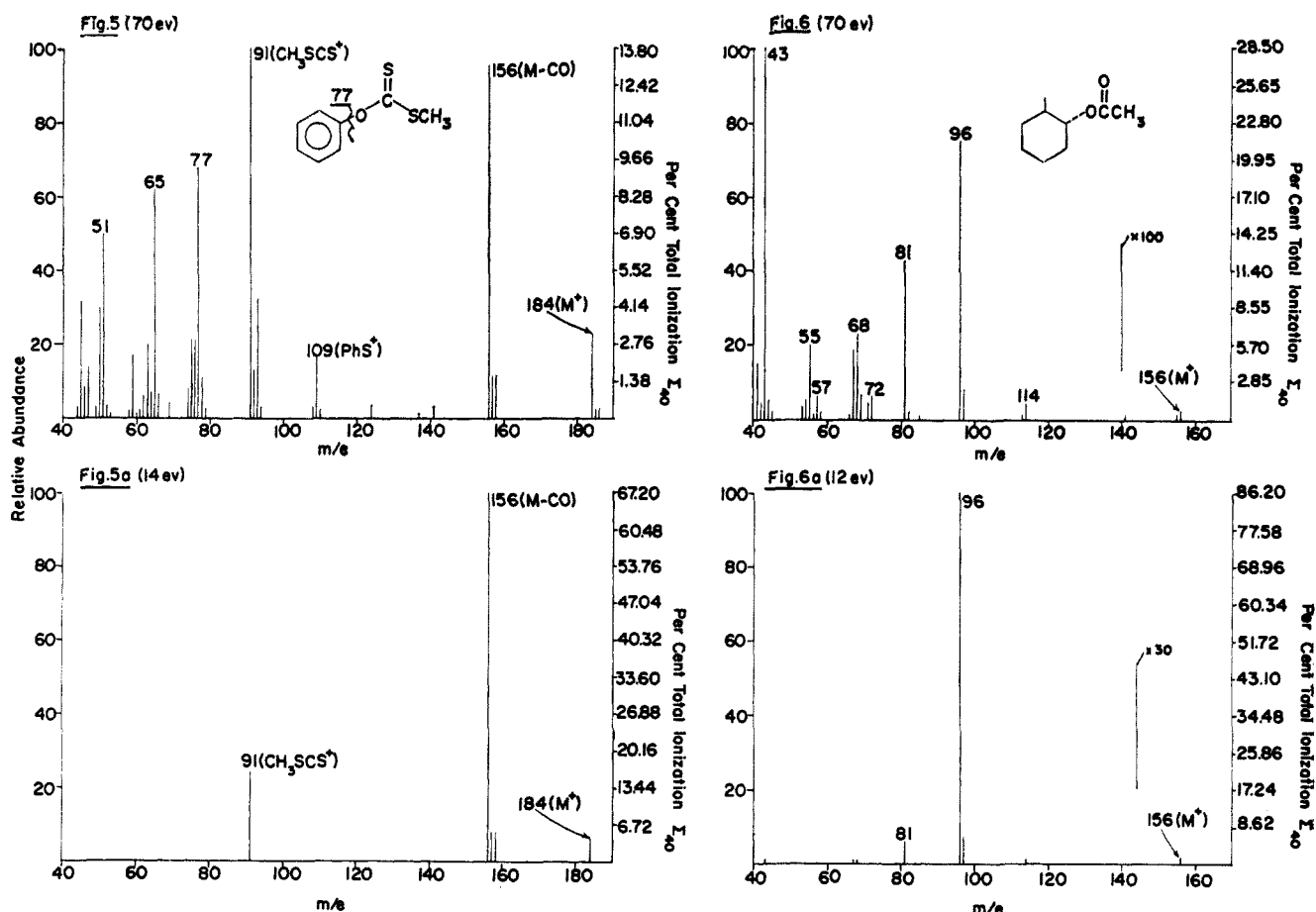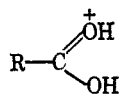
Figure 5.—Cold ion source of phenyl-S-methyl xanthate (9) at 70 and 14 eV (Atlas CH-4 mass spectrometer).
Figure 6.—Mass spectrum of *trans*-2-methylcyclohexyl acetate (8) at 70 and 12 eV (Atlas CH-4 mass spectrometer).

ionized acid itself bears an increasingly greater portion of the ion current; however, species of type p still carry the greater proportion.



p, R = CH$_3$ or C$_2$H$_5$

Likewise, in xanthates 5 and 6 no species corresponding to the ionized xanthic acid molecule (*m/e* 108) is to be found in the low-resolution mass spectra; however, a peak at *m/e* 109 ($\Sigma_{40}$ 0.3%) is visible in both spectra and presumably corresponds to the ionized protonated acid form (q) analogous to ion p. Shifts of this peak observed in the deuterated xanthates are consistent with this view; however, owing to the small magnitude of the peak, no precise quantitative calculations concerning the source of the second transferred hydrogen could be made. It appears, however, that most arises from C-3 and C-5 of the 2-methylcyclohexyl system, since little if any comes from compounds specifically labeled with deuterium at C-1, C-2, C-2 plus C-6, or C-4. This apparent loss of a γ-hydrogen atom is analogous to the similar process noted in open-chain esters[8b] in the formation of the protonated acid species (p, R = C$_2$H$_5$) and a mechanism of the type m → q may be operative.

In Table III are summarized the mass spectrometric data obtained for the specifically deuterated xanthates (10–19) synthesized to establish the stereochemical nature and course of the *m/e* 96 forming process and in Table IV the percentage of hydrogen loss from each
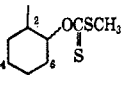


q, *m/e* 109
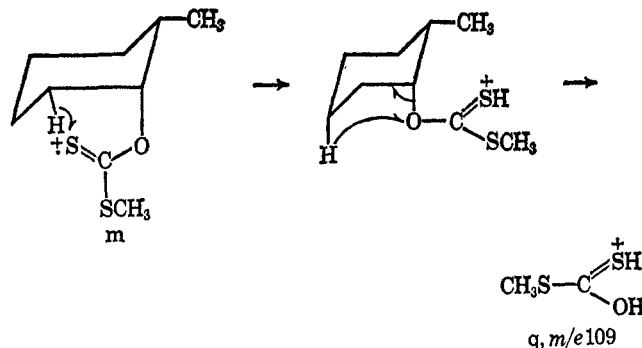
ring position is noted for xanthates 5 and 6. For comparison purposes, Table V presents an account of the pyrolytic results[21] obtained for the 2-*d*$_1$-labeled and unlabeled materials.

Inspection of the data summarized in Table IV reveals that the electron impact induced elimination proceeds primarily by the 1,2 mode, analogous to that previously found for cyclic acetates.[12,22] Particularly striking is the high specificity toward the tertiary center which leads to 90% abstraction of the tertiary hydrogen atom at C-2, whereas only 2% proceeds with elimination of the equally available (*cis*) secondary hydrogen at C-6. This is in contrast[21] to the thermal process (Table V) in which a combination of statistical and thermodynamic factors dictates the formation of the more highly substituted 1-methyl-1-

(21) W. S. Briggs and C. Djerassi, *J. Org. Chem.*, **33**, 1625 (1968).
(22) C. G. Macdonald, J. S. Shannon and G. Sugowdz, *Tetrahedron Lett.*, 807 (1963).

TABLE III

SUMMARY OF MASS SPECTROMETRIC DATA OBTAINED FOR DEUTERATED 2-METHYLCYCLOHEXYL-S-METHYL XANTHATES

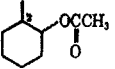| Compound[b] | Isotopic purity,[c] % | | | | Ionizing conditions[a] | Peaks in group m/e 95–100[d] | | | | | | Percentage of one deuterium loss in formation of M − 108 fragment[e] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $d_0$ | $d_1$ | $d_2$ | $d_3$ | | 95 | 96 | 97 | 98 | 99 | 100 | |
| trans-$d_0$ (6) | 100 | ... | ... | ... | A | 2.6 | 37.1 | 60.3 | ... | ... | ... | ... |
| | | | | | B | ... | 65.2 | 34.8 | ... | ... | ... | ... |
| | | | | | C | 3.0 | 49.8 | 47.2 | ... | ... | ... | ... |
| trans-1-$d_1$ (10) | 1 | 99 | ... | ... | C | 1.4 | 4.1 | 46.6 | 47.9 | ... | ... | 5 |
| trans-2-$d_1$ (11) | 2 | 98 | ... | ... | A | ... | 35.2 | 5.7 | 59.1 | ... | ... | 90 |
| | | | | | B | ... | 56.4 | 6.3 | 37.3 | ... | ... | 90 |
| trans-2,6,6-$d_3$ (12) | ... | ... | 3 | 97 | A | ... | ... | 0.9 | 33.6 | 2.7 | 62.8 | 92 |
| trans-ring Me-$d_3$ (13) | ... | 1 | 7 | 92 | C | ... | ... | ... | 3.4 | 52.5 | 44.1 | 0 |
| trans-S-Me-$d_3$ (14) | ... | ... | ... | 100 | C | 3.6 | 49.1 | 47.3 | ... | ... | ... | 100% loss of 3 |
| cis-$d_0$ (5) | 100 | ... | ... | ... | A | 2.8 | 28.2 | 69.0 | ... | ... | ... | ... |
| | | | | | D | ... | 33.4 | 66.6 | ... | ... | ... | ... |
| cis-1-$d_1$ (15) | 1 | 99 | ... | ... | A | 1.4 | 1.8 | 27.0 | 69.8 | ... | ... | 1 |
| cis-2-$d_1$ (16) | 5 | 95 | ... | ... | A | 0.5 | 11.2 | 18.6 | 69.7 | ... | ... | 32 |
| | | | | | D | ... | 12.4 | 25.4 | 62.2 | ... | ... | 37 |
| cis-4,4-$d_2$ (17) | ... | 3 | 97 | ... | A | ... | ... | 3.1 | 24.4 | 72.5 | ... | 2 |
| cis-6,6-$d_2$ (18) | 2 | 2 | 90 | 6 | A | 0.7 | 0.7 | 7.6 | 13.1 | 77.9 | ... | 32 |
| cis-2,6,6-$d_3$ (19) | 2 | 4 | 5 | 89 | A | ... | 1.0 | 2.6 | 21.8 | 4.2 | 70.4 | 84 |

[a] Ionizing conditions: A, cold source,[14] 70 eV; B, same as A, 14 eV; C, heated gas cartridge inlet system (70°), Atlas CH-4, ion source temperature, 145°, 70 eV; D, same as A, 16 eV.   [b] See Experimental Section.   [c] All isotopic purities calculated from molecular ion region of spectrum and considered reproducible to ±1%.   [d] These values have been corrected in the best manner possible for isotopic contaminants and for $^{13}C$ isotope contributions and are reported as $\%\Sigma_{95}^{100}$.   [e] Values are the average of five to twenty calculations and are considered reproducible to ±2%.

TABLE IV

SUMMARY OF POSITIONAL SPECIFICITY OF HYDROGEN LOSS IN FORMATION OF m/e 96 FRAGMENT IONS IN XANTHATE MASS SPECTRA

| Compound | Percentage[b] of hydrogen loss from various positions | | | | | |
|---|---|---|---|---|---|---|
| | Ring CH₃ | C-1 | C-2 | C-4 | C-6 | Unaccounted for[a] |
| cis (5) | a | 1 | 47 | 2 | 37 | 13 |
| trans (6) | 0 | a | 90 | a | 2 | 5 |

[a] See text.   [b] These figures are the weighted averages of results obtained at both high (70 eV) and low (16 and 14 eV) electron energies, since little change is noted in the per cent transfer from any given position with changing ionizing energy (see Table III).

TABLE V

SUMMARY OF PYROLYTIC STUDIES ON 2-METHYLCYCLOHEXYL-S-METHYL XANTHATES AND ACETATES[a]

| Compound | Percentage of olefin mixture[b] | |
|---|---|---|
| trans-$d_0$ (6) | 65 | 35 |
| cis-$d_0$ (5) | 29 | 71 |
| trans-2-$d_1$ (11) | 55 (>98% $d_0$) | 45 (>97% $d_1$) |
| cis-2-$d_1$ (16) | 28 (56% $d_0$, 44% $d_1$) | 72 (15% $d_0$, 85% $d_1$) |
| trans-$d_0$ (8) | 56 | 44 |
| cis-$d_0$ (7) | 9 | 91 |
| trans-2-$d_1$ (28) | 41 (>97% $d_0$) | 59 (100% $d_1$) |
| cis-2-$d_1$ (34) | 5 (22% $d_0$, 78% $d_1$) | 95 (100% $d_1$) |

[a] Values reported are those obtained from pyrolysis in seasoned stainless steel at 250° (xanthates) and 400° (acetates). For a full discussion of pyrolysis studies on these compounds, see ref 22.   [b] These values are corrected for the contribution of isotopic contaminants and any significant quantities of the isomeric materials present.

cyclohexene by tertiary hydrogen abstraction only 65–66% of the time.

From the mass spectral data for the labeled xanthates (Table III), values for the π and Γ deuterium isotope effects[23–25] may be calculated.[26] The π value of 0.64 found for the *cis* xanthate (5) is somewhat lower than the π value of 0.80 recently measured[24] in this laboratory for the McLafferty rearrangement process in the thione ester 20, as would be predicted

(23) F. H. Field and J. L. Franklin, "Electron Impact Phenomena and the Chemistry of Gaseous Ions," Academic Press Inc., New York, N. Y., 1957, pp 204–217.

(24) (a) J. K. MacLeod and C. Djerassi, *Tetrahedron Lett.*, 2183 (1966); and (b) J. K. MacLeod and C. Djerassi, *J. Amer. Chem. Soc.*, **89**, 5182 (1967).

(25) P. Natalis, *Bull. Soc. Chim. Belges*, **73**, 389 (1964).

(26) By making the initial reasonable assumptions that the elimination process is unimolecular and that the isotope effects (both primary and secondary) are "additive," expressions of the following type may be derived for *cis*-2-methylcyclohexyl-S-methyl xanthate **5** from data in Table III

$$0.84 = P\Gamma^2_\gamma[\% \text{ H}(2)] + P\Gamma_\alpha\Gamma_\gamma[\% \text{ H}(6)] \qquad (1)$$
$$0.35 = P[\% \text{ H}(2)] \qquad (2)$$
$$0.32 = P\Gamma_\alpha[\% \text{ H}(6)] \qquad (3)$$
$$P = \pi\Gamma \qquad (4)$$

where $P$ is the primary kinetic deuterium isotope effect defined as (probability of losing D in the deuterated compound)/(probability of losing H in the nondeuterated compound); $\Gamma_{\alpha(\text{or}\gamma)}$ is the secondary kinetic deuterium isotope effect defined as (probability of losing H in the deuterated compound)/(probability of losing H in the nondeuterated compound), with the deuterium atom at the same ($\alpha$) (C-6) or $\gamma$ position; $\%$ H(2) and $\%$ H(6) are the percentages of hydrogen loss from these two positions in the nondeuterated compound; and $\pi$ is defined[23] as (probability of losing D in the deuterated compound)/(probability of losing H in the deuterated compound). By contrast to solution chemistry where secondary isotope effects ($k_D/k_H$) [see E. A. Halevi, *Progr. Phys. Org. Chem.*, **1**, 109 (1963)] are generally less than unity, mass spectral processes exhibit $\Gamma$ effects from all positions[25] which are in the range 1.1–1.2. By combining eq 2 and 3 with eq 1, a quadratic expression (5) in terms of $\Gamma_\gamma$ results and this upon solution yields a value for $\Gamma_\gamma$ of 1.16, in good agreement with those found in other systems. Since $\Gamma_\alpha$ and

$$0.35\Gamma^2_\gamma + 0.32\Gamma_\gamma - 0.84 = 0 \qquad (5)$$
$$\Gamma_\gamma = 1.16$$

$\Gamma_\gamma$ are generally of approximately the same magnitude, a value of $\Gamma_\alpha = 1.16$ may be assumed. Assuming that the total hydrogen loss from the 2 and 6 positions is indeed 84%, values of $\%$ H(2), $\%$ H(6), $P$, and $\pi$ may be calculated from eq 2, 3, and 4.

$$\% \text{ H}(2) = 47\%$$
$$\% \text{ H}(6) = 37\%$$
$$P = 0.74$$
$$\pi = 0.64$$

by analogy[24] to other cases in which an ether oxygen was introduced into the rearranging side chain. By contrast, *trans* xanthate 6 yields a π effect of nearly unity. The possible mechanistic implications of these isotope effect data will be discussed below.
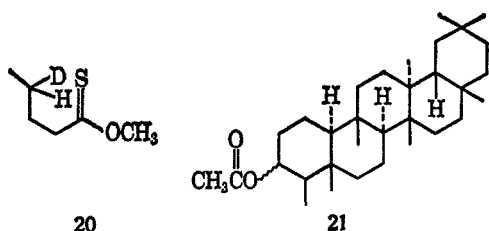


As opposed to the purely 1,2 mode of elimination in the pyrolytically induced reaction, the electron impact induced elimination of xanthates also proceeds to a small extent *via* 1,3 and 1,4 modes as is evidenced by the data in Table IV. Such processes have been previously noted in monocyclic[12,22] and triterpene[22] acetates and may be dominant when structural or stereochemical factors prevent the preferred 1,2-elimination process; thus in friedelan-3-ol acetate (21) deuterium labeling has shown[22] that none of the acetic acid produced originates from a 1,2-elimination process. While the mass spectra of the *cis*-ring-methyl-$d_3$ and *trans*-4,4-$d_2$ xanthates were not carried out, inspection of models gives no indication of reasons to expect increased elimination in these compounds compared with that of their C-2 epimers and in the subsequent discussion the percentage of hydrogen loss from each of these positions may be assumed to be equal to or less than that from the same position in the epimeric series. In Table IV, the last column presumably reflects the joint contribution of 1,3-elimination processes from C-3 and C-5 and isotope effects. Assuming the latter effects to be of approximately the same order of magnitude in both series, it is apparent that the amount of 1,3-elimination process in the *cis* xanthate (5) is at least twice as great as in isomer 6. This elimination may be visualized as proceeding through a five- or seven-membered transition state of which m → t is representative.
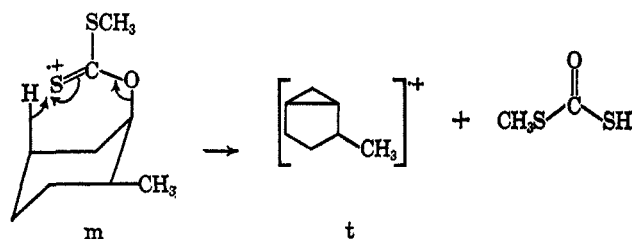


It is noteworthy that while ground-state conformational free-energy arguments[27] derived from solution chemistry are most certainly not directly applicable to the excited states of organic molecules in gas phase reactions, such as mass spectral fragmentations, the results obtained for the relative importance of the 1,3-elimination mode in the two 2-methylcyclohexyl-S-methyl xanthates correlate qualitatively with predictions made using ground-state "A" values.[27,28]

(27) See, for example, E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 234–239.

Such calculations predict that at 80° slightly over 80% of the *cis* xanthate should exist in chair conformer (5') with the xanthate function axial, the required orientation for 1,3 elimination to take place, whereas only 5% of xanthate 6 should exist in the corresponding chair conformer (6') at this temperature.
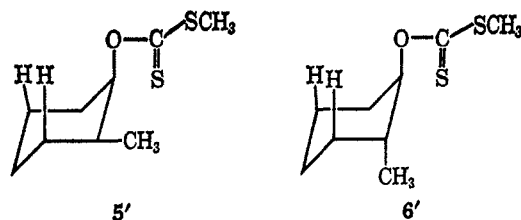


Consideration of the required boat forms gives qualitatively the same result. It would be predicted in the above manner that the 1,4-elimination process would also be favored in xanthate 5 over that in xanthate 6, but the required spectrum of 4,4-$d_2$-*trans* isomer was not available for comparison.

**2-Methylcyclohexyl Acetates and Higher Esters.—** Acetates, as one of the most common derivatives of alcohols employed in synthetic organic chemistry, have been examined previously in terms of mass spectrometric behavior.[8a,22,29,30] These studies indicated that major fragment ions result through initial expulsion of the elements of acetic acid from the molecular ion with charge retention on the resulting hydrocarbon fragment[8a,22,29] when the alcoholic side chain is greater than ethyl.

In straight-chain acetates[8a] and propionates,[8b] the course of this elimination was found by deuterium-labeling studies to be about equally divided between 1,3 (45%, clearly electron impact induced) and 1,2 (55%, either electron impact or possibly thermally induced) processes. In monocyclic acetates, by far the most predominant mode of elimination is 1,2 in nature.[12,22] In fact we found that in 1,2,2,6,6-$d_5$-cyclohexyl acetate (22) 83% of the elimination process
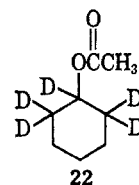


results in loss of $CH_3CO_2D$ (the result of the 1,2 mode) whereas 17% results in loss of $CH_3CO_2H$ (1,3 and 1,4 modes). This percentage loss is found to be virtually independent of the electron energy employed in the range 12–70 eV.

It was of interest, therefore, to examine this elimination process for the C-2 epimeric methylcyclohexyl acetates 7 and 8, in which the availability of specifically deuterated substrates might allow conclusions to be drawn regarding the sensitivity of this process to the *cis* or *trans* orientation of the eliminated β-

(28) Assuming that the conformational "A" value of the xanthate function is roughly equal to that of the acetate group ("A" = *ca.* 0.6 kcal/mol), the governing factor in determining this value being the *gauche* interaction with a C–O bond in both cases (see ref 27).

(29) For recent examples, see (a) ref 12; (b) E. v. Sydow, *Acta Chem. Scand.*, **19**, 2083 (1965); (c) V. I. Zaretskii, N. S. Wulfson, V. G. Zaikin, V. N. Leonov, S. N. Ananchenko, and I. V. Torgov, *Tetrahedron Lett.*, 347 (1966); and (d) S. J. Cristol, R. A. Sanchez, and T. C. Morrill, *J. Org. Chem.*, **32**, 2738 (1966).

(30) K. Biemann and J. Seibl, *J. Amer. Chem. Soc.*, **81**, 3149 (1959).

hydrogens with respect to the departing acetate function. Also, it was thought pertinent to examine the effect of lengthening the acid side chain upon the course of this elimination.

The low-resolution electron impact mass spectra of acetates **7** and **8** were run at 70 and 12 eV and, as the spectra of the two compounds are virtually superimposable at all electron energies, only those of the *trans* isomer (**8**) are shown (Figure 6). The photoionization[31] mass spectrum (Figure 7) of **8** was also available for comparison and corresponds well to the low-voltage electron impact spectrum. In Table VI are summarized the metastable ion transitions noted in the mass spectra of acetates **7** and **8**.



Figure 7.—Photoionization mass spectrum of *trans*-2-methylcyclohexyl acetate, 10.19 eV.

TABLE VI

METASTABLE TRANSITIONS AND ELEMENTAL COMPOSITIONS OF FRAGMENTS FROM 2-METHYLCYCLOHEXYL ACETATES

| Transition | | | Calcd | Found for *cis* acetate (7) | Found for *trans* acetate (8) |
|---|---|---|---|---|---|
| $C_9H_{16}O_2\cdot^+$ | $\rightarrow C_7H_{12}\cdot^+$ | $+ C_2H_4O_2$ | 59.0 | 59.0 | 59.0 |
| (156⁺ | → 96⁺ | 60) | | | |
| $C_7H_{14}O\cdot^+$ ᵃ | $\rightarrow C_4H_8O\cdot^+$ | $+ C_3H_6$ | 45.4 | 45.4 | 45.5 |
| (114⁺ | → 72⁺ | + 42) | | | |
| $C_7H_{14}O\cdot^+$ | $\rightarrow C_4H_7O^+$ | $+ C_3H_7$ | 44.2 | 44.3 | 44.2 |
| (114⁺ | → 71⁺ | + 43) | | | |
| $C_7H_{14}O\cdot^+$ | $\rightarrow C_3H_5O^+$ | $+ C_4H_9$ | 28.4 | 28.3 | 28.3 |
| (114⁺ | → 57⁺ | + 57) | | | |
| $C_7H_{13}^+$ | $\rightarrow C_5H_9^+$ | $+ C_2H_4$ | 49.1 | 49.2 | 49.1 |
| (97⁺ | → 69⁺ | + 28) | | | |
| $C_7H_{13}^+$ | $\rightarrow C_5H_8^+$ | $+ C_2H_5$ | 47.6 | 47.5 | 47.5 |
| (97⁺ | → 68⁺ | + 29) | | | |
| $C_7H_{13}^+$ | $\rightarrow C_4H_7^+$ | $+ C_3H_6$ | 31.2 | 31.3 | 31.2 |
| (97⁺ | → 55⁺ | + 42) | | | |
| $C_7H_{12}\cdot^+$ | $\rightarrow C_6H_9^+$ | $+ CH_3$ | 68.3ᵇ | 68.4 | 68.3 |
| (96⁺ | → 81⁺ | + 15) | | | |
| $C_7H_{12}\cdot^+$ | $\rightarrow C_5H_8\cdot^+$ | $+ C_2H_4$ | 48.2 | ... | 48.2ᶜ |
| (96⁺ | → 68⁺ | + 28) | | | |
| $C_7H_{12}\cdot^+$ | $\rightarrow C_5H_7^+$ | $+ C_2H_5$ | 46.7 | 46.8 | 46.8 |
| (96⁺ | → 67⁺ | + 29) | | | |
| $C_6H_9^+$ | $\rightarrow C_4H_7^+$ | $+ C_2H_2$ | 37.3 | 37.2 | 37.2 |
| (81⁺ | → 55⁺ | + 26) | | | |
| $C_5H_9^+$ | $\rightarrow C_3H_5^+$ | $+ C_2H_4$ | 24.3 | 24.4 | 24.4 |
| (69⁺ | → 41⁺ | + 28) | | | |
| $C_5H_7^+$ | $\rightarrow C_3H_5^+$ | $+ C_2H_2$ | 25.1 | 25.2 | 25.2 |
| (67⁺ | → 41⁺ | + 26) | | | |

ᵃ See footnote *a* in Table I.   ᵇ See footnote *b* in Table I. ᶜ This metastable ion was found in the photoionization mass spectrum of acetate **8** (see Table I, footnote *a*).

Just as previously noted for the xanthates **5** and **6**, there exists a qualitative correspondence of the fragment ion peaks below $m/e$ 100 in the 70-eV spectrum (Figure 6) of acetate **8** with those of the expected ionized olefinic products, 1-methyl- (or 3-methyl-) 1-cyclohexene (Figure 2), with additional peaks at $m/e$ 72, 71, 69, 58, 47, and 43. With the exception of the $m/e$ 69 fragment ($C_5H_9^+$) which arises through expulsion of ethylene from the even-electron species of mass 97 and whose genesis is supported by the appropriate metastable ion at $m/e$ 49.1 (Table VI), these latter ions are oxygen containing. Except for

(31) We wish to thank Dr. J. H. Beynon (Table I, footnote *a*) for the determination of this spectrum. Ionizing conditions are as follows: A.E.I. MS-9 mass spectrometer equipped with a glass inlet system and hydrogen discharge photon lamp; ion source temperature, 50°; ionizing energy, 10.19 eV (Lyman-α line of hydrogen). See J. H. Beynon, A. E. Fontaine, D. W. Turner, and A. E. Williams, *J. Sci. Instru.*, **44**, 283 (1967).
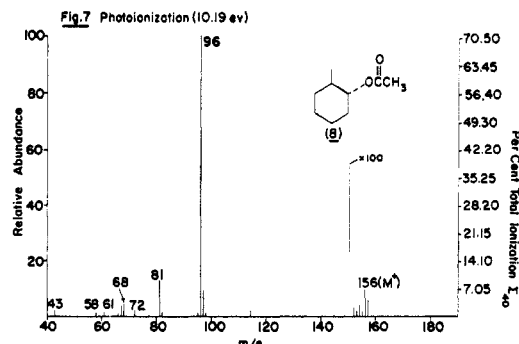
the well-known acetylium ion of mass 43, these arise from cleavages in the alcoholic grouping.[18]

The higher esters of *trans*-2-methylcyclohexanol, *viz.*, *trans*-2-methylcyclohexyl propionate (**23**), butyrate (**24**), valerate (**25**), and octanoate (**26**), behave in a qualitatively similar manner to the acetate (**8**) in respect to cleavages in the alcoholic grouping. Cleavages in the acyl side chain in such aliphatic esters have been well documented in the literature[8b,32] and suffice it to note that esters **23–26** behave in the expected manner. Of particular interest in the present study is the observation (Table II) that in the mass spectra of these esters the proportion of the total ion current carried by the even electron ion of mass 97 relative to that borne by that of mass 96 regularly increases as the acyl carbon chain is lengthened.
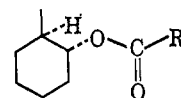
23, R = $-CH_2CH_3$
24, R = $-(CH_2)_2CH_3$
25, R = $-(CH_2)_3CH_3$
26, R = $-(CH_2)_6CH_3$

In Table VII are collected the mass spectral data in the $m/e$ 95–100 region for the deuterium-labeled esters, while in Table VIII are summarized the positional specificities of hydrogen loss in the formation of the $m/e$ 96 peak. It will be noted that the percentage hydrogen loss from any one position is virtually independent (Table VII) of the experimental conditions (hot or cold ion source, high or low energy electrons, photoionization, etc.) and this, coupled with the observed metastable ion at $m/e$ 59.0 in acetates **7** and **8** (Table VI) corresponding to the direct loss of acetic acid from the molecular ion, would suggest that in this case a purely electron impact induced elimination process is being observed. Also supporting this view are the differences to be noted in the site specificities of the pyrolytic[21] (Table V) and mass spectrometrically induced (Table VIII) elimination processes.

Most noteworthy are the small differences (Table VIII) in behavior exhibited by the *cis* and *trans* esters as compared with those of the corresponding xanthates. Also apparent is the independence of the specificity of elimination upon acyl chain length, as is evidenced by the nearly identical data obtained for the *trans* acetate (**8**) and the *trans* valerate (**25**).

(32) (a) Chapter 4 in ref 7; (b) R. Ryhage and E. Stenhagen in "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press Inc., New York, N. Y., 1963, Chapter 9.

TABLE VII

SUMMARY OF MASS SPECTROMETRIC DATA OBTAINED FOR DEUTERATED 2-METHYLCYCLOHEXYL ESTERS

| Compound[b] | Isotopic purity,[c] % | | | | Ionizing[a] conditions | Peaks in group m/e 95–100[d] | | | | | | Percentage of one deuterium loss in formation of M − RCO₂H fragment[e] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $d_0$ | $d_1$ | $d_2$ | $d_4$ | | 95 | 96 | 97 | 98 | 99 | 100 | |
| **R = CH₃** | | | | | | | | | | | | |
| *trans-d₀* (**8**) | 100 | ... | ... | ... | E | 11.1 | 84.4 | 4.5 | ... | ... | ... | ... |
| | | | | | C | 9.6 | 86.7 | 3.6 | ... | ... | ... | ... |
| | | | | | A | 9.3 | 83.7 | 7.0 | ... | ... | ... | ... |
| | | | | | F | 11.9 | 82.7 | 5.4 | ... | ... | ... | ... |
| | | | | | G | ... | 98.8 | 1.2 | ... | ... | ... | ... |
| | | | | | H | 1.0 | 96.8 | 2.2 | ... | ... | ... | ... |
| *trans-1-d₁* (**27**) | 1 | 99 | ... | ... | C | 1.6 | 11.7 | 83.9 | 2.8 | ... | ... | 5 |
| *trans-2-d₁* (**28**) | 2 | 98 | ... | ... | E | 2.1 | 38.5 | 53.9 | 5.5 | ... | ... | 35 |
| | | | | | C | 2.2 | 35.7 | 57.1 | 5.0 | ... | ... | 33 |
| | | | | | A | 5.8 | 33.2 | 55.3 | 5.7 | ... | ... | 36 |
| | | | | | F | 3.6 | 39.2 | 49.6 | 7.6 | ... | ... | 37 |
| | | | | | G | ... | 30.4 | 67.9 | 1.7 | ... | ... | 32 |
| | | | | | H | ... | 34.3 | 62.8 | 2.9 | ... | ... | 35 |
| *trans-4,4-d₂* (**29**) | ... | 3 | 97 | ... | C | ... | 3.2 | 9.9 | 83.3 | 3.6 | ... | 4 |
| *trans-6,6-d₂* (**30**) | ... | ... | 94 | 6 | E | ... | 3.0 | 45.4 | 48.3 | 3.3 | ... | 44 |
| *trans-2,6,6-d₃* (**31**) | ... | ... | 3 | 97 | C | ... | 0.7 | 2.3 | 79.1 | 13.7 | 4.2 | 84 |
| *trans-ring Me-d₃* (**32**) | ... | 1 | 7 | 92 | E | ... | ... | 0.9 | 9.9 | 84.9 | 4.3 | 0 |
| *cis-d₀* (**7**) | 100 | ... | ... | ... | E | 10.3 | 85.2 | 4.5 | ... | ... | ... | ... |
| | | | | | C | 8.8 | 87.4 | 3.8 | ... | ... | ... | ... |
| *cis-1-d₁* (**33**) | 1 | 99 | ... | ... | C | 1.4 | 15.2 | 79.9 | 3.5 | ... | ... | 9 |
| *cis-2-d₁* (**34**) | 5 | 95 | ... | ... | E | 2.2 | 43.6 | 50.8 | 3.4 | ... | ... | 38 |
| *cis-4,4-d₂* (**35**) | ... | 3 | 97 | ... | C | 0.7 | 3.1 | 10.5 | 81.4 | 4.3 | ... | 6 |
| *cis-6,6-d₂* (**36**) | 2 | 2 | 90 | 6 | C | ... | ... | 42.1 | 57.9 | ... | ... | 37 |
| *cis-2,6,6-d₃* (**37**) | 2 | 4 | 5 | 89 | C | ... | ... | ... | 78.2 | 18.3 | 3.5 | 80 |
| **R = -(CH₂)₃CH₃** | | | | | | | | | | | | |
| *trans-d₀* (**25**) | 100 | ... | ... | ... | E | 5.0 | 72.0 | 23.0 | ... | ... | ... | ... |
| *trans-1-d₁* (**38**) | 1 | 99 | ... | ... | E | 0.7 | 6.6 | 72.3 | 20.4 | ... | ... | 4 |
| *trans-2-d₁* (**39**) | 2 | 98 | ... | ... | E | 1.7 | 30.0 | 42.1 | 26.2 | ... | ... | 39 |
| *trans-6,6-d₂* (**40**) | ... | ... | 94 | 6 | E | ... | 2.0 | 36.3 | 37.8 | 23.9 | ... | 47 |
| *trans-2,6,6-d₃* (**41**) | ... | ... | 3 | 97 | E | ... | ... | 1.2 | 64.0 | 12.6 | 22.2 | 83 |

[a] A–D, see footnote *a*, Table III; E, same as C, ion source temperature, 175°; F, see ref 20; G, see ref 31; H, same as C, 12 eV. [b] See footnote *b*, Table III. [c] All isotopic contents were calculated from the molecular ion region of the corresponding S-methyl xanthates (Table III) and considered to be reproducible to ±1%. [d] See footnote *d* in Table III. [e] See footnote *e* in Table III.

TABLE VIII

SUMMARY OF POSITIONAL SPECIFICITY OF HYDROGEN LOSS IN THE FORMATION OF m/e 96 FRAGMENT IONS IN ESTER MASS SPECTRA

| Compound | Percentage[c] of hydrogen loss from various positions | | | | | |
|---|---|---|---|---|---|---|
| | Ring -CH₃ | C-1 | C-2 | C-4 | C-6 | Unaccounted for |
| **R = CH₃** | | | | | | |
| *cis* (**7**) | *a* | 9 | 42 | 5 | 37 | 7 |
| *trans* (**8**) | 0 | 5 | 38 | 3 | 47 | 7 |
| **R = -CH₂(CH₂)₂CH₃** | | | | | | |
| *trans* (**25**) | *b* | 4 | 38 | *b* | 45 | 10 |

[a] These labeled compounds were not available for comparison; however, inspection of models gives little reason to expect greater loss from the respective positions than recorded for the epimeric (*a*) or stereochemically identical (*b*) series. [b] Same as footnote *a*. [c] Reported values are the averages of numerous measurements at high and low electron energies. Minor (if any) changes were evident in the percentage loss of hydrogen from any given position in the range 12–70 eV.

The differences in positional specificity, albeit small, are interesting, since they are in the opposite direction to those expected for a preferential *cis* mode of elimination.

From the data in Table VII, π isotope effects[23–25] for the electron impact induced 1,2-elimination process may be calculated[26] in the acetates **7** (1.0) and **8** (0.84). These values are somewhat lower (greater isotope effect) than the π-effect value of 1.0 measured for the McLafferty rearrangement process[24] in 3-heptanone-6-d₁ (**42**), again in accord with expectations when an ether oxygen is introduced into the rearranging side chain.[24]



**42**
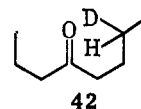
From the kinetic isotope effect and site specificity data (Tables IV and VIII) for compounds **5–8**, some information may be derived concerning the mechanism of the electron impact induced elimination process in 2-methylcyclohexyl-S-methyl xanthates and esters. First, it is important to note that in both the xanthate and acetate series, the calculated π-effect values are consistent with less complete hydrogen transfer (and resulting greater asymmetry in the activated complex[33]) when the tertiary hydrogen is in a *trans* relationship to the departing oxygenated function as compared to a *cis* relationship (see Figure 8), pro-

(33) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961).

vided that a more complete transfer of hydrogen to thione sulfur than to carbonyl oxygen is assumed. Second, the small magnitudes of the $\pi$ effects in all cases may be an indication of the low magnitude of the maximum isotope effect possible in such mass spectral processes, as it is difficult to imagine that two such closely related eliminations require both virtually complete (xanthates) and incomplete (acetates) transfer of hydrogen in the activated complex. The large proportion of the 1,2-elimination process which is directed toward the tertiary center in xanthate 6 is in accord with a mechanism which requires nearly complete transfer of hydrogen to thione sulfur, as the stability of tertiary *vs.* secondary radicals at carbon is well known[34] and the thermodynamic stability of the incipient ionized 1-methyl-1-cyclohexene should be slightly greater than that of incipient ionized 3-methyl-1-cyclohexene.

Thus, the observed isotope effect data for both xanthates **5** and **6** and acetates **7** and **8** appear consistent with a cyclic mechanism such as that previously suggested[21] for the mass spectral elimination process in monocyclic acetates and analogous to that currently accepted[9] in the pyrolysis of esters and xanthates. However, as opposed to the nearly symmetrical disposition of the itinerant hydrogen envisaged in the activated complex of the pyrolytic process,[9] the degree of hydrogen transfer appears to be much more strongly dependent on the nature of the receptor atom in the electron impact case, leading to unsymmetrical extremes (such as w‡ and x‡) of the activated complex (see also Figure 8).

w, *m/e* 204    w‡    $\xrightarrow[\mathrm{m^*}]{-C_2H_4O_2}$ *m/e* 96

x, *m/e* 156    x‡    $\xrightarrow[\mathrm{m^*}]{-C_2H_4O_2}$ *m/e* 96

Concerning the stereochemical course of the electron impact induced elimination process, very little can be said in the ester cases owing to the nearly identical amounts of elimination toward the tertiary center regardless of the stereochemical relationship of this hydrogen to the ester function. The failure to observe any specificity may be attributed to ring conformational freedom and is in accord with the observation that the amides[11a] and methyl esters[11b] of the *cis*- and *trans*-2,2,6-trimethylcyclohexylacetic acids (**43** and **44**) give nearly equal quantities of the respective McLafferty rearrangement ions (y and z) regardless of their stereochemical nature. The higher $\pi$ isotope effect (1.0) found for the *cis* acetate (**7**) compared with that (0.84) calculated for the *trans* isomer (**8**) and the greater percentage of the total elimination process (85 *vs.* 79%) which goes by the 1,2 mode in the latter compound do, however, tempt one to

(34) See, for example, J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 422, 423.
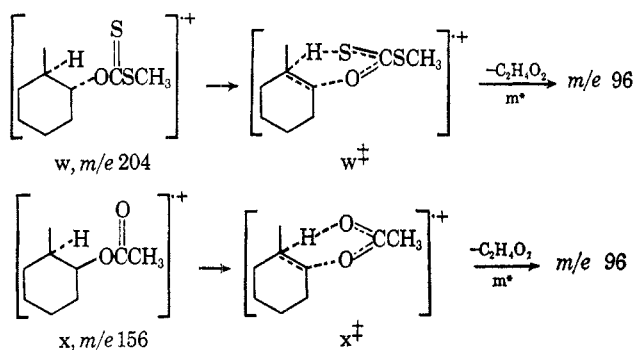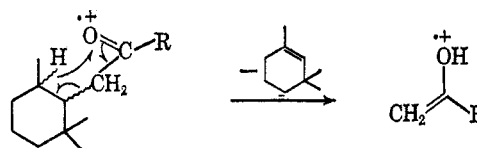
Figure 8.—Diagram relating position of migrating hydrogen in the activated complex to the expected $\pi$-isotope effect for 2-methylcyclohexyl-S-methyl xanthates and acetates.

speculate that the 1,2-elimination process is more favorable when the departing hydrogen and oxygenated function are in a *cis* relationship.

**43** (*cis*), R = $-NH_2$ or $-OCH_3$    y, R = $-NH_2$; *m/e* 74
**44** (*trans*), R = $-NH_2$ or $-OCH_3$    z, R = $-OCH_3$; *m/e* 59

In the xanthates, however, a greater degree of stereochemical specificity is evident. Site specificity data at the tertiary center (Table V) and $\pi$ isotope effect data [0.64 for **5** (*trans* hydrogen), 1.0 for **6** (*cis* hydrogen)] are consistent with a preferred *cis* mode of elimination in this series, analogous to that found[9] in the thermal case.

## Experimental Section[35]

*cis*-2-Methylcyclohexyl-S-methyl Xanthate (5). Procedure A.—Practical grade 2-methylcyclohexanol[36] was subjected to

preparative gas chromatography on a 20% glycerol column (20 ft × 0.25 in.) at 97° (conditions A). The isomer having the shorter retention time was collected and found to be identical in every respect with a sample of authentic *cis*-2-methylcyclohexanol prepared by the catalytic hydrogenation of 2-methylcyclohexanone using the procedure of Hückel and Hubele.[37] Utilizing the method of Djerassi, *et al.*,[38] 100 mg of this alcohol (45) was converted into the corresponding S-methyl xanthate in *ca.* 70% yield by treating the alcoholate salt in refluxing benzene sequentially with a slight excess of carbon disulfide and methyl iodide. The crude xanthate was purified by gas chromatography on a 15% Apiezon L column (5 ft × 0.25 in.) at 160° (conditions B): $\lambda_{max}^{liquid\ film}$ 7.7 (CH$_3$S), 8.2 (COC), and 9.5 μ (C=S).

*Anal.* Calcd for C$_9$H$_{16}$OS$_2$: mol wt, 204. Found: mol ion, 204.

*trans*-2-Methylcyclohexyl-S-methyl Xanthate (6).—1-Methyl 1-cyclohexene[39] (1.3 g) was hydroborated with oxidative work-up according to the *in situ* procedure of Sondheimer, *et al.*,[40] to produce, in *ca.* 70% yield, 2-methylcyclohexanol shown by gas chromatography (conditions A) to contain less than 2% of the *cis* isomer. This material was further purified by gas chromatography to yield *trans*-2-methylcyclohexanol (46) containing less than 1% of the *cis* compound. A portion (184 mg) of this material was converted into the S-methyl xanthate 6 according to procedure A. The crude xanthate was purified by gas chromatography (conditions B) to yield the mass spectral and analytical samples: $\lambda_{max}^{liquid\ film}$ 7.6, 8.2, and 9.5 μ.

*Anal.* Calcd for C$_9$H$_{16}$OS$_2$: C, 52.90; H, 7.89; mol wt, 204. Found: C, 52.73; H, 8.04; mol ion, 204 (by high resolution C$_9$H$_{16}$OS$_2$).

*cis*-2-Methylcyclohexyl Acetate (7).[41,42] Procedure B.— Alcohol 45 (330 mg, 2.9 mmol) was dissolved in 1.5 ml of reagent quality chloroform and 0.4 g (5.1 mmol) of reagent quality pyridine was added. The solution was cooled to 0° with stirring and *ca* a 1.2-fold *M* excess (3.5 mmol) of acetyl chloride added dropwise. The reaction flask was then stoppered and allowed to warm to 25° with continued stirring. After 12 hr, the mixture was poured into cold water, extracted with ether, washed twice with 10% hydrochloric acid, twice with 5% sodium hydroxide solution and twice with cold water, and dried for 4 hr over anhydrous magnesium sulfate. The ether was evaporated under reduced pressure (20°, 35 mm) and the crude ester purified by hot-box distillation (100–120°, 35 mm) and subsequent gas chromatography on a 15% Apiezon L column (10 ft × 0.25 in.) at 175° (conditions D): $\lambda_{max}^{liquid\ film}$ 5.7 (C=O), 7.3 (CH$_3$OC–), and 8.0 μ (COC).

*Anal.* Calcd for C$_9$H$_{16}$O$_2$: mol wt, 156. Found: mol ion, 156.

*trans*-2-Methylcyclohexyl Acetate (8).[41,42]—Alcohol 46 on a 20-mg scale yielded by a method identical with procedure B 15 mg of the desired *trans* acetate: $\lambda_{max}^{liquid\ film}$ 5.7, 7.3, and 8.0 μ.

*Anal.* Calcd for C$_9$H$_{16}$O$_2$: mol wt, 156. Found: mol ion, 156.

*trans*-2-Methylcyclohexyl propionate (23),[42] butyrate (24),[42] valerate (25),[42] and octanoate (26)[42] were all synthesized from alcohol 46 on a 20-mg scale by a method identical with procedure B, but employing the appropriate higher homolog in place of acetyl chloride. All were purified by gas chromatography employing conditions D, except for octanoate 26 for which column temperature was 200°: propionate, $\lambda_{max}^{liquid\ film}$ 5.7, 7.3, 7.4, and 8.4 μ (*Anal.* Calcd for C$_{10}$H$_{18}$O$_2$: mol wt, 170. Found: mol ion, 170); butyrate, $\lambda_{max}^{liquid\ film}$ 5.7, 7.3, 7.4, and 8.4 μ (*Anal.* Calcd for C$_{11}$H$_{20}$O$_2$: mol wt, 184. Found: mol

ion, 184); valerate, $\lambda_{max}^{liquid\ film}$ 5.7, 7.2, 8.0, and 8.5 μ (*Anal.* Calcd for C$_{12}$H$_{22}$O$_2$: mol wt, 198. Found: mol ion, 198); octanoate, $\lambda_{max}^{liquid\ film}$ 5.7, 7.2, 8.0, and 8.5 μ (*Anal.* Calcd for C$_{15}$H$_{28}$O$_2$: mol wt, 240. Found: mol ion, 240, (wk).

1-*d*$_1$-2-Methylcyclohexyl Esters and S-Methyl Xanthates.— 1-*d*$_1$-2-Methylcyclohexanol was prepared by the reduction[43] of 2-methylcyclohexanone[44] in dry ethereal solution with lithium aluminum deuteride.[45] The resulting alcoholic mixture (30% *cis*, 70% *trans*) was purified by preparative gas chromatography (conditions A) to give the pure (>99%) *cis*- (47) and *trans*- (48) 1-*d*$_1$-alcohols which were converted into the following requisite derivatives according to procedures A and B: *trans*-1-*d*$_1$-2-methylcyclohexyl-S-methyl xanthate (10), $\lambda_{max}^{liquid\ film}$ 7.6, 8.2, and 9.4 μ (*Anal.* Calcd for C$_9$H$_{15}$OS$_2$D: mol wt, 205. Found: mol ion, 205); *cis*-1-*d*$_1$-2-methylcyclohexyl-S-methyl xanthate (15) (*Anal.* Calcd for C$_9$H$_{15}$OS$_2$D: mol wt, 205. Found: mol ion, 205); *trans*-1-*d*$_1$-2-methylcyclohexyl acetate (27) (*Anal.* Calcd for C$_9$H$_{15}$O$_2$D: mol wt, 157. Found: mol ion, 157); *cis*-1-*d*$_1$-2-methylcyclohexyl acetate (33) (*Anal.* Calcd for C$_9$H$_{15}$O$_2$D: mol wt, 157. Found: mol ion, 157); *trans*-1-*d*$_1$-2-methylcyclohexyl valerate (38) (*Anal.* Calcd for C$_{12}$H$_{21}$O$_2$D: mol wt, 199. Found: mol ion, 199).

*trans*-2-*d*$_1$-2-Methylcyclohexyl Esters and S-Methyl Xanthate.—2-*d*$_1$-2-Methylcyclohexanol was prepared by the *in situ* deuterohydroboration of 1-methyl-1-cyclohexene following the general procedure of Sondheimer, *et al.*,[40] employing, however, lithium aluminum deuteride[45] instead of lithium aluminum hydride. The resulting alcoholic material (98% *trans*) was subjected to preparative gas chromatography (conditions A) and the resulting product (>99% *trans*) was employed both for the preparation of the required derivatives according to procedures A and B and for the subsequent preparation of *cis*-2-*d*$_1$-2-methylcyclohexanol. This purified *trans*-2-*d*$_1$-alcohol (49) exhibited in its nmr spectrum a sharp singlet at δ 1.00 ppm, whereas in the unlabeled *trans*-2-methylcyclohexanol this signal appears as a highly distorted doublet (*J* = 4 cps) centered *ca.* 1.02 ppm. The S-methyl xanthates exhibited the following properties: *trans*-2-*d*$_1$-2-methylcyclohexyl-S-methyl xanthate (11), $\lambda_{max}^{liquid\ film}$ 4.7 (CD), 7.6, 8.2, and 9.4 μ (*Anal.* Calcd for C$_9$H$_{15}$OS$_2$D: mol wt, 205. Found: mol ion, 205); *trans*-2-*d*$_1$-2-methylcyclohexyl acetate (28); $\lambda_{max}^{liquid\ film}$ 4.7 (CD), 5.8 (C=O), 7.3, and 8.1 μ (*Anal.* Calcd for C$_9$H$_{15}$O$_2$D: mol wt, 157. Found: mol ion, 157); *trans*-2-*d*$_1$-2-methylcyclohexyl valerate (39), $\lambda_{max}^{liquid\ film}$ 4.7, 5.8, 7.3, 7.5, 8.0, and 8.5 μ (*Anal.* Calcd for C$_{12}$H$_{21}$O$_2$D: mol wt, 199. Found: mol ion, 199).

*cis*-2-*d*$_1$-2-Methylcyclohexanol (50). Procedure C.—Greater than 99% *trans*-2-*d*$_1$-2-methylcyclohexanol (49, 1.4 g, 2% *d*$_0$ and 98% *d*$_1$ by calculation from the low-resolution mass spectrum of S-methyl xanthate 11) was oxidized under Jones conditions[46,47] to yield 2-*d*$_1$-2-methylcyclohexanone. This material was then reduced with lithium aluminum hydride in dry ether to yield a crude alcoholic mixture (0.9 g, 30% *cis*, 70% *trans*) which was separated by gas chromatographic conditions A to yield the pure *cis* isomer (50). This carbinol was subsequently converted into the required xanthate and acetate by application of procedures A and B. The S-methyl xanthates exhibited the following properties: *cis*-2-*d*$_1$-2-methylcyclohexyl-S-methyl xanthate (16), $\lambda_{max}^{liquid\ film}$ 4.7, 7.6, 8.2, 9.4, and 9.5 μ (*Anal.* Calcd for C$_9$H$_{15}$OS$_2$D: mol wt, 205. Found: mol ion, 205); *cis*-2-*d*$_1$-2-methylcyclohexyl acetate (34), $\lambda_{max}^{liquid\ film}$ 4.7, 5.7, and 8.1 μ (*Anal.* Calcd for C$_9$H$_{15}$O$_2$D: mol wt, 157. Found: mol ion, 157).

*trans*-Methyl-*d*$_3$-2-methylcyclohexyl Acetate (37) and S-Methyl Xanthate (13).—Methyl-*d*$_3$-1-methylcyclohexene,[48] pre-

(37) W. Hückel and A. Hubele, *Ann.*, **613**, 36 (1958).

(38) C. Djerassi, I. T. Harrison, O. Zagneetko, and A. L. Nussbaum, *J. Org. Chem.*, **27**, 1173 (1962).

(39) Purchased from Aldrich Chemical Co., Inc., Milwaukee, Wis., and freed of a small amount of contaminating 3- and/or 4-methyl isomers by preparative gas chromatography on a 15% Apiezon L column (10 ft × 0.25 in.) at 100° (conditions C).

(40) M. Nussim, Y. Mazur, and F. Sondheimer, *ibid.*, **29**, 1120 (1964).

(41) See also (a) G. A. C. Gough, H. Hunter, and J. Kenyon, *J. Chem. Soc.*, 2065 (1926); (b) W. Hückel and K. Hagenguth, *Chem. Ber.*, **64**, 2892, 2894 (1931); (c) R. T. Arnold, G. G. Smith, and R. M. Dodson, *J. Org. Chem.*, **15**, 1256 (1950); (d) W. J. Bailey and L. Nicholas, *ibid.*, **21**, 854 (1956).

(42) (a) M. Murat, *Ann. Chim. Phys.*, **16**, 108 (1909); (b) J. B. Senderens and J. Aboulenc, *Ann. Chim.*, **18**, 176 (1922).

(43) *Cf.* D. S. Noyce and D. B. Denney, *J. Amer. Chem. Soc.*, **72**, 5743 (1950).

(44) Purchased from Eastman Organic Chemicals, Distillation Products Industries, Rochester, N. Y.

(45) Lithium aluminum deuteride (>99.5%) was purchased from Ventron Corp., Metal Hydrides Division, Beverley, Mass.

(46) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

(47) Jones oxidation, even though some acid is present, does not cause significant back exchange at the enolizable α positions during the normal oxidation period (10 min). See, also, J. Fishman, *J. Amer. Chem. Soc.*, **87**, 3456 (1965).

(48) We thank Dr. Peter Brown of this laboratory for a sample of this material. See, also, R. A. Cotton, J. H. Fassnacht, W. D. Horrocks, Jr., and N. A. Nelson, *J. Chem. Soc.*, 4138 (1959).

pared by sequential addition of $d_3$-methylmagnesium iodide[49] to cyclohexanone,[44] xanthation,[50] and pyrolysis, was hydroborated by the *in situ* method of Sondheimer, *et al.*,[40] and gave, after oxidative work-up, an alcoholic mixture containing 80% of the desired *trans*-methyl-$d_3$-2-methylcyclohexanol. This material was purified by gas chromatography (conditions A) to give *trans* alcohol (>99%) (51) which was then treated according to procedures A and B to yield the required derivatives: *trans*-methyl-$d_3$-2-methylcyclohexyl-S-methyl xanthate (13), $\lambda_{max}^{liquid\ film}$ 4.5, 7.6, 8.2, and 9.5 $\mu$ (*Anal.* Calcd for $C_9H_{13}$-$OS_2D_3$: mol wt, 207. Found: mol ion, 207); *trans*-methyl-$d_3$-2-methylcyclohexyl acetate (32), $\lambda_{max}^{liquid\ film}$ 4.5, 5.7 (C=O), 7.3, and 8.1 $\mu$ (*Anal.* Calcd for $C_9H_{13}O_2D_3$: mol wt, 159. Found: mol ion, 159).

**2,6,6-$d_3$-2-Methylcyclohexyl Esters and S-Methyl Xanthates.**—2-Methylcyclohexanone was exchanged three times with 10% deuteriohydrochloric acid–deuteriophosphoric acid solution according to the procedure of Seibl and Gäumann.[51] This exchanged ketone (52) was reduced with lithium tri-*t*-butoxyaluminohydride in dry tetrahydrofuran solution according to the procedure of Brown[52] to give an alcoholic mixture containing 60% of the *trans* and 40% of the *cis* isomer. These components were separated by preparative gas chromatography (conditions A) and converted by application of procedures A and B into the xanthates and esters: *trans*-2,6,6-$d_3$-2-methylcyclohexyl-S-methyl xanthate (12), $\lambda_{max}^{liquid\ film}$ 4.5, 4.7, 7.6, 8.1, 9.3, and 9.4 $\mu$ (*Anal.* Calcd for $C_9H_{13}OS_2D_3$: mol wt, 207. Found: mol ion, 207); *trans*-2,6,6-$d_3$-2-methylcyclohexyl acetate (31), $\lambda_{max}^{liquid\ film}$ 4.6, 4.7, 5.8, 7.3, and 8.1 $\mu$ (*Anal.* Calcd for $C_9H_{13}O_2D_3$: mol wt, 159. Found: mol ion, 159); *trans*-2,6,6-$d_3$-2-methylcyclohexyl valerate (41), $\lambda_{max}^{liquid\ film}$ 4.5, 4.7, 5.7, 7.3, 8.0, and 8.5 $\mu$ (*Anal.* Calcd for $C_{12}H_{19}O_2D_3$: mol wt, 201. Found: mol ion, 201); *cis*-2,6,6-$d_3$-2-methylcyclohexyl-S-methyl xanthate (19) (*Anal.* Calcd for $C_9H_{13}OS_2D_3$: mol wt, 207. Found: mol ion, 207); *cis*-2,6,6-$d_3$-2-methylcyclohexyl acetate (37), $\lambda_{max}^{liquid\ film}$ 4.7, 5.7, 7.3, and 8.0 $\mu$ (*Anal.* Calcd for $C_9H_{13}$-$O_2D_3$: mol wt, 159. Found: mol ion, 159).

*trans*-2-**Methylcyclohexyl-S-methyl-$d_3$ Xanthate (14).**—*trans*-2-Methylcyclohexanol (46) was converted on a 30-mg scale into the S-methyl xanthate by the use of procedure A. However, instead of methyl iodide in the final step, $d_3$-methyl iodide[49] was employed: $\lambda_{max}^{liquid\ film}$ 8.1, 9.4, and 9.9 $\mu$ (SCD₃).

*Anal.* Calcd for $C_9H_{13}OS_2D_3$: mol wt, 207. Found: mol ion, 207.

**3,3-$d_2$-1-Methyl-1-cyclohexene.**—2,6,6-$d_3$-Methylcyclohexanone (52) was reduced in dry ethereal solution with a fourfold excess of lithium aluminum hydride[43] and the crude alcoholic mixture (30% *cis*, 70% *trans*) converted directly without further purification into the S-methyl xanthate by the procedure of Djerassi, *et al.*[38]

The crude xanthate thus obtained (containing a large amount of dimethyl trithiocarbonate,[53] as an impurity) was pyrolyzed over powdered soft glass in a flask equipped with a Vigreux column and a nitrogen inlet tube by heating in a Wood's metal bath at 200–210°. The pyrolysate was collected in a Dry Ice–isopropyl alcohol cooled trap. After the pyrolysis was complete (0.5 hr), the trap was removed and warmed slowly to ambient temperature allowing the slow ebullition of most of the methyl mercaptan and carbonyl sulfide which were collected in addition to the desired olefins. The olefinic fraction (*ca.* 50% 1-methyl-1-cyclohexene and 50% 3-methyl-1-cyclohexene[54] by comparative gas chromatography) was purified by gas chromatography (conditions D) to yield the 1-methyl-1-

cyclohexene fraction containing less than 1% of the isomeric olefin.

This material was examined by infrared, nmr, and mass spectral measurements. The low-resolution mass spectrum of this material on comparison with that of the unlabeled compound gave the isotopic content 94% $d_2$ and 6% $d_3$.[55] The infrared spectrum showed $\lambda_{max}^{liquid\ film}$ 4.6 (CD), 4.8 (CD), and 6.0 $\mu$ (C=C, wk). The nmr spectrum of the labeled compound showed the same three main structural features as did that of the unlabeled olefin: broadened signals centered at $\delta$ 5.4 ppm (1 H) (C=CH), 1.92 ppm (4 H) (C=CH–), and that for the remaining seven hydrogens at $\delta$ 1.63 ppm (CH₃C=C and –CH₂–); however, in the $d_2$ compound, the signal originally at $\delta$ 1.92 ppm is now centered at 1.85 ppm and integrates to only two hydrogens, thus establishing the site of deuteration.

*trans*-6,6-$d_2$-2-**Methylcyclohexanol and Derivatives.**—3,3-$d_2$-1-Methyl-1-cyclohexene (230 mg) was hydroborated according to the *in situ* conditions of Sondheimer, *et al.*,[40] and yielded, after oxidative work-up, a crude alcoholic mixture (*ca.* 150 mg) containing 90% of the desired *trans*-ol. This material was subjected to preparative gas chromatography (conditions A) to give *trans*-6,6-$d_2$-2-methylcyclohexanol (53) of greater than 99% purity: $\lambda_{max}^{liquid\ film}$ 2.9 (OH), 4.5, 4.7, 9–10 $\mu$ multiplet (CO). One portion of this deuterated alcohol was converted into the required derivatives (on a 10-mg scale) by procedures A and B, while a second portion was treated to yield the *cis* isomer. The derivatives and properties follow: *trans*-6,6-$d_2$-2-methylcyclohexyl acetate (30), $\lambda_{max}^{liquid\ film}$ 4.5, 4.7, 5.7, 7.3, and 8.1 $\mu$ (*Anal.* Calcd for $C_9H_{14}O_2D_2$: mol wt, 158. Found: mol ion, 158); *trans*-6,6-$d_2$-2-methylcyclohexyl valerate (40), $\lambda_{max}^{liquid\ film}$ 4.5, 4.7, 5.75, 7.3, and 8.5 $\mu$ (*Anal.* Calcd for $C_{12}H_{20}O_2D_2$: mol wt, 200. Found: mol ion, 200).

*cis*-6,6-$d_2$-2-**Methylcyclohexanol and Derivatives.**—On a 100-mg scale, *trans*-6,6-$d_2$-methylcyclohexanol was oxidized by the Jones procedure[46,47] and back reduced (procedure C) employing lithium tri-*t*-butoxyaluminohydride[52] in place of lithium aluminum hydride in the reduction step. The crude alcoholic mixture (40% of the desired *cis* isomer) was separated by preparative gas chromatography (conditions A) to yield the desired *cis*-6,6-$d_2$-2-methylcyclohexanol (20 mg) (54), containing less than 1% impurities. This material was then converted into the desired xanthate and acetate by application of procedures A and B: *cis*-6,6-$d_2$-2-methylcyclohexyl-S-methyl xanthate (18) (*Anal.* Calcd for $C_9H_{14}OS_2D_2$: mol wt, 206. Found: mol ion, 206); *cis*-6,6-$d_2$-2-methylcyclohexyl acetate (36) (*Anal.* Calcd for $C_9H_{14}O_2D_2$: mol wt, 158. Found: mol ion, 158).

**4-$d_1$-4-Hydroxycyclohexanone Ethylene Ketal (55).**—Cyclohexane-1,4-dione 4-monoethylene ketal (2.28 g), prepared according to the methods of Jones[56] and Plieninger[57] and containing less than 1% of 4-hydroxycyclohexanone ethylene ketal, was reduced in dry tetrahydrofuran solution with a slight excess of lithium aluminum deuteride.[43] The crude product [$\lambda_{max}^{liquid\ film}$ 2.9 (OH) and 4.7 $\mu$ (CD)] was used directly in the subsequent step.

**4-$d_1$-4-Tosyloxycyclohexanone Ethylene Ketal (56).**—Ketal 55 (2.4 g) was treated with *p*-toluenesulfonyl chloride in dry pyridine according to the procedure of Mićović and Stojiljković[58] to yield the crude ketal tosylate (4.0 g; mp 77–78°; $\lambda_{max}^{liquid\ film}$ 4.6 (CD), 5.2 and 6.3 (arom), 6.9 (SO₂), 7.4 (CO), 8.5 (SO₂), and 8.4–13.5 $\mu$ (ketal CO bands)). This material was used directly without purification in the ensuing displacement reaction.

**Displacement Reaction on 4-$d_1$-4-Tosyloxycyclohexanone Ethylene Ketal.**[47,59]—Tosylate 56 (3.9 g, 0.01 mmol) was dis-

(49) $d_3$-Methyl iodide (>99 % $d_3$) was purchased from Merck Sharpe and Dohme of Canada, Ltd., Montreal, Quebec.

(50) R. A. Benkeser and J. J. Hazdra, *J. Amer. Chem. Soc.*, **81**, 228 (1959).

(51) J. Seibl and T. Gäumann, *Helv. Chim. Acta*, **46**, 2857 (1963).

(52) H. C. Brown and R. F. McFarlin, *J. Amer. Chem. Soc.*, **78**, 252 (1956).

(53) This yellow, highly odiferous oil was present to a varying extent in all S-methyl xanthate preparations connected with this study and presumably arises through an alcoholate-initiated condensation process with excess carbon disulfide. Very little was formed in a blank experiment in which the alcohol was omitted. It was readily separable by gas chromatography (conditions B) and was identified in its infrared ($\lambda_{max}^{liquid\ film}$ 7.1 and 7.6 (CH₃S), 9.2 (C=S), 10.4, 11.4, 11.6, and 12.2 $\mu$) and high resolution mass spectra [mol ion, 138 ($C_3H_6S_3^+$); base peak $m/e$ 91 ($C_2H_3S_2^+$, M − 47)].

(54) Under gas chromatographic conditions D, 3-methyl-1-cyclohexene, 4-methyl-1-cyclohexene, and methylenecyclohexane had nearly equal retention times; hence this fraction may contain minor portions of the latter isomers, if they are formed under the pyrolytic conditions.

(55) The formation of $d_3$-1-methyl-1-cyclohexene in this pyrolytic process is most intriguing, since a deuterium rearrangement is required for the generation of this product. An analogous behavior was noted by Thomas and Willhalm[12] in the pyrolysis of an isomer mixture of 1,3,3-$d_3$-carvomenthyl acetate to yield as one of the products 3,3-$d_2$-menth-2-ene having the isotopic content 19.5 % $d_3$, 71 % $d_2$, and 9.5 % $d_1$; however, no comment on this anomalous result was offered by these authors. The explanation offered by us[22] to explain the retention of deuterium label in the 1-methyl-1-cyclohexene fraction from pyrolysis of *cis*-2-$d_1$-2-methylcyclohexyl-S-methyl xanthate (16) should also apply here.

(56) E. R. H. Jones and F. Sondheimer, *J. Chem. Soc.*, 615 (1949).

(57) H. Plieninger and H. J. Grasshoff, *Chem. Ber.*, **90**, 1973 (1957).

(58) V. M. Mićović and A. Stojiljković, *Tetrahedron*, **4**, 186 (1958).

(59) See (a) W. A. Sanderson and H. S. Mosher, *J. Amer. Chem. Soc.*, **88**, 4185 (1966); (b) ref 46.

solved in 35 ml of sodium-dried ether and added slowly (under nitrogen and with the exclusion of moisture) to a stirred suspension of 849 mg (0.02 mmol) of lithium aluminum deuteride in 10 ml of dried ether. After the addition was complete (0.5 hr), the reaction was heated to reflux with continued stirring and this condition maintained for 14 hr. After this time, the white suspension was cooled and the mixture decomposed with saturated sodium sulfate solution followed by solid sodium sulfate. The crystalline complex was removed by suction filtration through a layer of Celite and washed well with dry ether, and the organic layers were stripped under reduced pressure (20°, 35 mm) using a rotary evaporator.

The crude oil (2.3 g) was hot-box distilled (80–140°, 35 mm) and then subjected to preparative gas chromatography on a 15% Apiezon L column (5 ft × 0.25 in.) at 130°. Three components were found to be present in the approximate ratio 2:1:4; the first two of these were virtually inseparable under these conditions and were collected as a single fraction (523 mg) for subsequent treatment. The major component (ca. 1.0 g) was shown to be 2-(1',4',4'-$d_3$-cyclohexyloxy)ethanol (57) by a combination of mass spectrometric, infrared spectral,



**57**
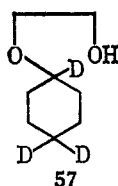
and gas chromatographic comparison with authentic unlabeled material synthesized according to the procedure of Eliel:[60,61] M+ = $m/e$ 147 (2% $d_2$, 98% $d_3$); $\lambda_{max}^{liquid\ film}$ 3.0 (OH), 4.6 and 4.8 (CD), and 8.7–10.0 $\mu$ (CO).

**4,4-$d_2$-Cyclohexanone.**[62]—The crude ketal fraction (523 mg) from the displacement reaction (containing 66% of the desired cyclohexanone ethylene ketal by gas chromatographic comparison with authentic material) was hydrolyzed according to the procedure or Magerlein and Levin[63] to give a ketonic mix-

(60) E. L. Eliel, V. G. Badding, and M. N. Rerick, *J. Amer. Chem. Soc.,* **84**, 2371 (1962).

(61) A similar 1,4 participation has recently been reported by R. A. LeMahieu (Abstracts of Papers, 153rd Meeting of the American Chemical Society, Miami Beach, Fla., April 1967, p 0-24), who noted that in the attempted conversion of ketal acid chloride or mixed anhydride of type **58** to the butyl ketone with di-*n*-butylcadmium, the only product isolated on acid work-up was the five-membered lactone (**59**). Evidence for the intermediacy of the eight-membered 1,4-cyclic diether has been obtained according to this report. In the present case, the ketal-opening process might be



**58**



**59**
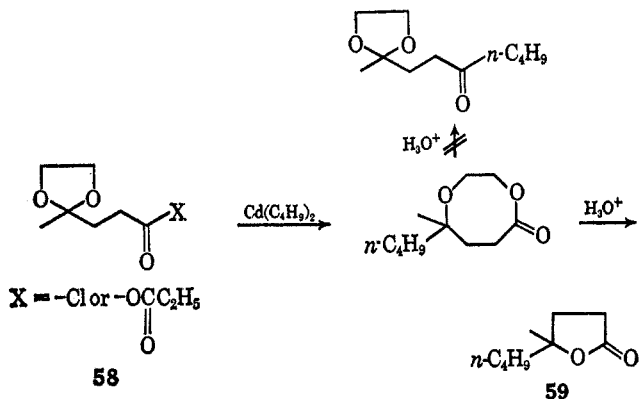
envisioned as proceeding through the analogous eight-membered cyclic intermediate (**60**) which is then attacked by deuteride at one of the bridge-



**60**
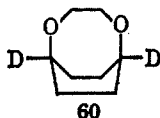
head positions yielding the ethylene glycol monoether (**57**); however, this hypothesis has not yet been confirmed.

(62) 4,4-$d_2$-Cyclohexanone has previously been synthesized by other routes: *cf.* (a) ref 51; (b) J. B. Lambert, *J. Amer. Chem. Soc.*, **89**, 1836 (1967). However, the present synthesis gives the best isotopic content in the final product of any reported to date.

(63) B. J. Magerlein and R. H. Levin, *ibid.*, **77**, 1904 (1955).

ture ($d_2$-cyclohexanone plus $\Delta^2$- and $\Delta^3$-cyclohexenones) which was separable by gas chromatography on a 20% Carbowax 20M column (10 ft × 0.25 in.) at 130° (conditions E). The cyclohexanone fraction was recycled until it contained less than 1% impurities: yield, 133 mg.

The $d_3$-ethylene glycol monether (**57**, 833 mg) was cleaved by the method of Johnson[64] to yield 1,4,4-$d_3$-cyclohexanol (400 mg) which was purified by gas chromatography on a 15% Apiezon L column (5 ft × 0.25 in.) at 110° (conditions E). This material was oxidized under Jones conditions[46] to yield the crude ketone (216 mg) which was purified by gas chromatography employing conditions E above: from both routes, $\lambda_{max}^{liquid\ film}$ 4.5 and 4.7 (CD) and 5.8 $\mu$ (C=O). *Anal.* Calcd for $C_6H_8OD_2$: mol wt, 100. Found: mol ion, 100 (97% $d_2$, 3% $d_1$).

**4,4-$d_2$-2-Methylcyclohexanols and Derivatives.**—4,4-$d_2$-Cyclohexanone (**61**, 216 mg) was methylated in dry toluene with sodium *t*-amylate and dimethyl sulfate according to the procedure of Seibl and Gäumann.[51] The products from this reaction [4,4-$d_2$-cyclohexanone (40%), 4,4-$d_2$-2-methylcyclohexanone (50%), and 4,4-$d_2$-2,2-dimethylcyclohexanone (10%)] were separated by gas chromatography on a 20% Apiezon L column (10 ft × 0.25 in.) at 120°. The resulting pure 4,4-$d_2$-2-methylcyclohexanone (**62**, ca. 50 mg; $\lambda_{max}^{liquid\ film}$ 4.6, 4.8, and 5.8 $\mu$) was reduced with lithium aluminum hydride in dry ether to yield the crude alcoholic mixture (30% *cis*, 70% *trans*) which was in turn separated into the pure components (**63** and **64**) by gas chromatography (conditions A). Procedures A and B were applied to obtain the required xanthates and acetates on a 4–10-mg scale: *trans*-4,4-$d_2$-2-methylcyclohexanol (**63**), $\lambda_{max}^{liquid\ film}$ 3.0, 4.6, and 4.8 $\mu$ (*Anal.* Calcd for $C_7H_{12}OD_2$: mol wt, 116. Found: mol ion, 116); *trans*-4,4-$d_2$-2-methylcyclohexyl acetate (**29**), $\lambda_{max}^{liquid\ film}$ 4.6, 4.8, 7.3, and 8.1 $\mu$ (*Anal.* Calcd for $C_9H_{14}$-$O_2D_2$: mol wt, 158. Found: mol ion, 158); *cis*-4,4-$d_2$-2-**Methylcyclohexanol** (**64**), $\lambda_{max}^{liquid\ film}$ 2.9, 4.6, and 4.8 $\mu$ (*Anal.* Calcd for $C_7H_{12}OD_2$: mol wt, 116. Found: mol ion, 116); *cis*-4,4-$d_2$-2-methylcyclohexyl-S-methyl xanthate (**17**) (*Anal.* Calcd for $C_9H_{14}OS_2D_2$: mol wt, 206. Found: mol ion, 206); *cis*-4,4-$d_2$-2-methylcyclohexyl acetate (**35**), $\lambda_{max}^{liquid\ film}$ 2.6, 2.8, 5.8, 7.3, and 8.0 $\mu$ (*Anal.* Calcd for $C_9H_{14}O_2D_2$: mol wt, 158. Found: mol ion, 158).

**1,2,2,6,6-$d_5$-Cyclohexyl Acetate (22) and S-Methyl Xanthate (65).**—Cyclohexanone was exchanged three times with 10% deuteriohydrochloric acid–deuteriophosphoric acid according to the procedure of Seibl and Gäumann,[51] then reduced with lithium aluminum deuteride in dry ether to yield the crude alcohol. This material was purified by preparative gas chromatography (conditions E) and converted by procedures A and B into the two requisite derivatives: 1,2,2,6,6-$d_5$-cyclohexyl-S-methyl xanthate (**65**) [*Anal.* Calcd for $C_8H_9OS_2D_5$: mol wt, 195. Found: mol ion, 195 (1% $d_1$, 3% $d_2$, 5% $d_3$, 8% $d_4$, 83% $d_5$)]; 1,2,2,6,6-$d_5$-cyclohexyl acetate (**22**), $\lambda_{max}^{liquid\ film}$ 4.5, 4.7, 5.7, 7.3, and 7.9 $\mu$ (*Anal.* Calcd for $C_8H_9O_2D_5$: mol wt, 147. Found: mol ion, 147).

(64) W. S. Johnson and R. B. Kinnel, *ibid.*, **88**, 3861 (1966). We wish to express our sincerest appreciation to Dr. Arne van der Gen of Professor Johnson's laboratory for informing us of his recent improvements on the method.