The Mass Spectrometric Fragmentation of 2-Isopropenyl-2,5-dimethylcyclohexanone and 2-Isopropyl-2,5-dimethylcyclohexanone

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The mass spectra of six polyalkylcyclohexanones (2a, 2b, 3a, 3b, 4, and 5) related to menthone are described. The fragmentation patterns have been substantiated by deuterium labeling, exact mass measurements, and metastable ions. The McLafferty rearrangement is observed for 3a, 3b, and 5, as expected, with the formation of an odd-electron ion peak at M − 42. However, for the unsaturated compounds (2a, 2b, and 4), α cleavage predominates to give an even-electron ion peak at M − 43.

The synthesis and degradation of (−)-2-isopropenyl-2,5-dimethylcyclohexanone (2a) (4-methylisopulegone)[3,4] provided a series of alkylated cyclohexanones for mass spectrometric fragmentation study. Mass spectra of deuterated analogs were used to study the various fragmentation schemes presented. The mass spectra of menthones alkylated at C-4 have not previously been reported, although the spectra of menthone and related molecules are known.[5,6] Our ketones are shown in Scheme I. These were prepared as de-

SCHEME I

2a, R = CH₃
b, R = CD₃

3a
b

4

5
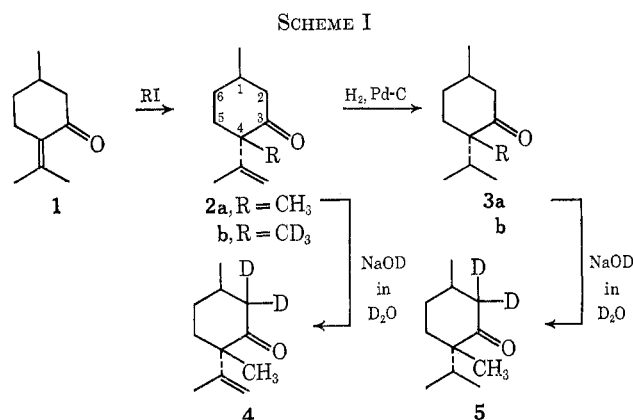
scribed[7] except the deuterium-containing ketones, which were obtained as noted in the Experimental Section. Catalytic hydrogenation of 2a and 2b in the presence of Pd–C catalyst gave 3a and 3b. Both 2a and 3a were treated with deuterium oxide containing sodium deuterioxide to give 4 and 5. The presence of deuterium in 2b and 3b was confirmed by absorption at 2220–2230 cm⁻¹ and by nmr studies. The partial mass spectra of all ketones are shown in Tables I and II, respectively. The bar graph spectra for 2a and 3a are shown in Figure 1.

(1) Taken in part from the Ph.D. thesis of M. V. Kulkarni, Oklahoma State University, May 1967.

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(3) M. V. Kulkarni, E. J. Eisenbraun, and M. M. Marsh, *J. Org. Chem.*, 33, 1661 (1968).

(4) C. Djerassi, J. Osiecki, and E. J. Eisenbraun, *J. Amer. Chem. Soc.*, 83, 4433 (1961).

(5) (a) B. Willhalm and A. F. Thomas, *J. Chem. Soc.*, 6478 (1965); (b) J. Seibl and T. Gaumann, *Z. Anal. Chem.*, 197, 33 (1963); (c) T. Sato, T. Tsuchiya, and N. Wasada, *J. Org. Chem.*, 33, 1249 (1968).

(6) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, pp 143–159.
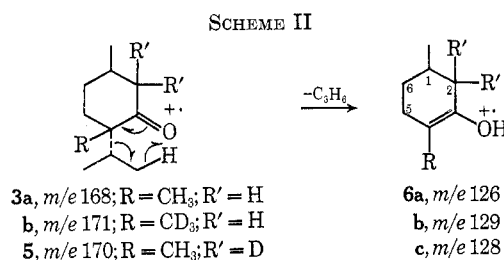
(7) E. J. Eisenbraun, F. Burian, J. Osiecki, and C. Djerassi, *J. Amer. Chem. Soc.*, 82, 3476 (1960).

TABLE I

PARTIAL MASS SPECTRA[a] OF SATURATED KETONES 3a, 3b, AND 5

m/e	Intensities in % of total ionization		
	3a	3b	5
55	10.0	3.5	7.1
56	1.9	2.9	3.2
58		3.9	0.7
69	6.8	3.1	4.8
70	1.8	0.9	3.2
72		3.1	0.2
84	2.6	0.8	1.6
86		2.0	1.3
87		2.3	0.2
97	4.6	0.6	1.9
100		2.9	0.4
111	1.4	1.5	0.2
113		0.3	1.3
114		0.3	0.2
124	3.5		3.8
127		3.9	1.9
126	8.2 (M − C₃H₆)		0.4[b]
128		1.0	7.9 (M − C₃H₆)
129		9.8 (M − C₃H₆)	0.7
153	1.3 (M − CH₃)	0.9 (M − CD₃)	0.1
155			1.3 (M − CH₃)
156		1.0 (M − CH₃)	0.2
168	0.7 (M⁺)		
170			0.6 (M⁺)
171		0.7 (M⁺)	

[a] Obtained from a Consolidated Electrodynamics Corp. mass spectrometer, Model 21-103C, operating at 70 eV. [b] Possibly due to 3a.

Mass spectra of the saturated ketones (3a, 3b, and 5) all show intense peaks at M − 42 attributed to the loss of a C₃H₆ fragment resulting from the McLafferty rearrangement.[3] While specific ketones deuterated at the γ carbon were not prepared, this fragmentation is well known for other saturated cyclic ketones.[5a] This cleavage as shown in Scheme II is supported by a meta-

SCHEME II

3a, m/e 168; R = CH₃; R′ = H
b, m/e 171; R = CD₃; R′ = H
5, m/e 170; R = CH₃; R′ = D

6a, m/e 126
b, m/e 129
c, m/e 128

(8) (a) F. W. McLafferty, *Anal. Chem.*, 28, 306 (1956); (b) F. W. McLafferty, *ibid.*, 31, 82 (1959).

Table II

Partial Mass Spectra[a] of Unsaturated Ketones
2a, 2b, and 4

	Intensities in % of total ionization		
m/e	2a	2b	4
67	5.4	1.7	5.3
69	1.9	3.4	1.6
70	0.7	2.4	1.7
82	3.4	1.6	3.3
85		2.1	0.3
96	1.7	0.6	0.9
99		1.1	0.1
123	7.7 (M − C₃H₇)	0.5	6.5 (M − C₃H₅D₂)
126		7.1 (M − C₃H₇)	0.2
137	3.0		0.1
138	0.4	0.1	3.1
140		4.9	
151	1.6 (M − CH₃)	1.3 (M − CD₃)	
153			1.7 (M − CH₃)
154		0.7	0.2
166	2.0 (M⁺)		
168			1.0 (M⁺)
169		1.3 (M⁺)	

[a] Obtained from a Consolidated Electrodynamics Corp. mass spectrometer, Model 21-103C, operating at 70 eV.

stable transition in each case as well as through high-resolution mass spectrometry, which shows that the fragments **6a**, **6b**, and **6c** contain oxygen as cited in Table III. High-resolution mass measurements also

Table III

High-Resolution Data for Principal Mass Fragments

m/e	Principal source of ion	Calcd	Exptl	Ref	Empirical formula
171	3b	171.1702	171.1691	168.9888[a]	C₁₁H₁₇D₃O
170	5	170.1639	170.1631	168.9888[a]	C₁₁H₁₈D₂O
169	2b	169.1545	169.1549	168.9888[b]	C₁₁H₁₅D₃O
168	3a	168.1514	168.1514	168.9888[a]	C₁₁H₂₀O
168	4	168.1483	168.1480	168.9888[a]	C₁₁H₁₆D₂O
166	2a	166.1359	166.1346	168.9888[a]	C₁₁H₁₈O
129	3b	129.1233	129.1223	130.9920[b]	C₈H₁₁D₃O
128	5	128.1170	128.1183	130.9920[b]	C₈H₁₂D₂O
127	3b	127.1440	127.1437	129.1233	C₉H₁₃D₃
126	2b	126.0999	126.1003	118.9920[c]	C₈H₈D₃O
126	3a	126.1045	126.1062	124.1252[d]	C₈H₁₄O
124	3a	124.1252	124.1258	118.9920[c]	C₉H₁₆
124	5	124.1236	124.1240	118.9920[c]	C₉H₁₄D
123	2a	123.0809	123.0819	118.9920[c]	C₈H₁₁O
123	4	123.0809	123.0824	118.9920[c]	C₈H₁₁O
110	2b	110.1048	110.1059	106.0782[e]	C₈H₈D₃
107	2a	107.0860	107.0867	106.0783[e]	C₈H₁₁
107	4	107.0860	107.0865	106.0783[e]	C₈H₁₁
69	3a[f]	69.0349	69.0344	68.9954[g]	C₄H₅O
69	3a[f]	69.0904	69.0905	68.9954[g]	C₅H₉

[a] C₃F₇. [b] C₃F₅. [c] C₂F₅. [d] C₉H₁₆. [e] C₈H₁₀. [f] Also derived from 2a. [g] CF₃.

show that the rearrangement does not involve the deuterium atoms of **3b** and **5**.

A second fragmentation sequence for **3a**, **3b**, and **5** resulting from 1,2 or "α" cleavage[6] is shown in Scheme III. An important conclusion from the high-resolution mass spectrometric study is that fragment *m/e* 69 from **3a** or **3b** or *m/e* 70 from **5** is made up of ¹/₃ C₄H₅O (*e.g.*, **8a**) and ²/₃ C₅H₉ (*e.g.*, **11a**). These results clearly establish that more than one cleavage route is operating in the fragmentation of **3a**, **3b**, and **5**.
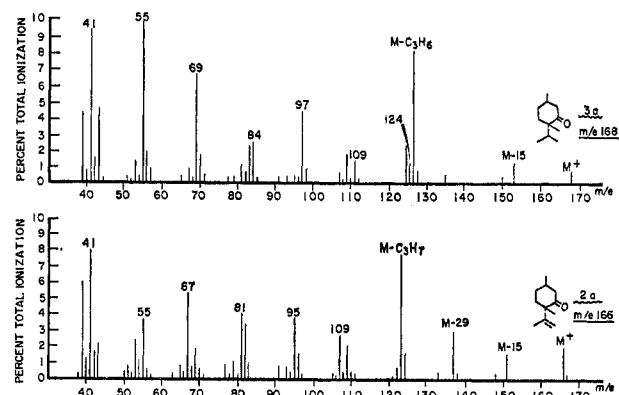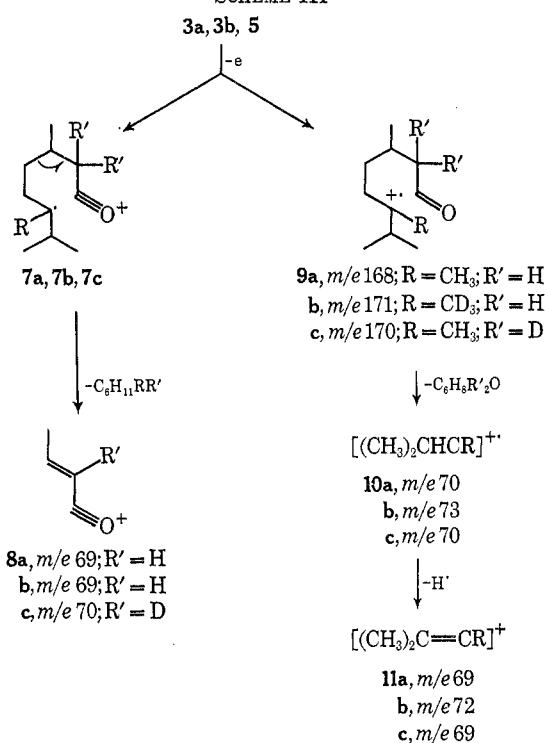

Figure 1.—Mass spectrum of 2-isopropenyl-2,5-dimethyl-cyclohexanone (top) and 2-isopropyl-2,5-dimethylcyclohexanone (bottom).

Scheme III

3a, 3b, 5

9a, *m/e* 168; R = CH₃; R' = H
b, *m/e* 171; R = CD₃; R' = H
c, *m/e* 170; R = CH₃; R' = D

[(CH₃)₂CHCR]⁺·

10a, *m/e* 70
b, *m/e* 73
c, *m/e* 70

[(CH₃)₂C=CR]⁺

11a, *m/e* 69
b, *m/e* 72
c, *m/e* 69

7a, 7b, 7c
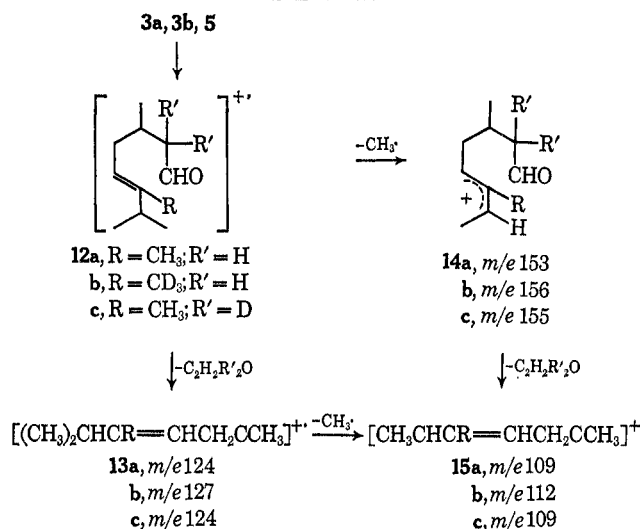
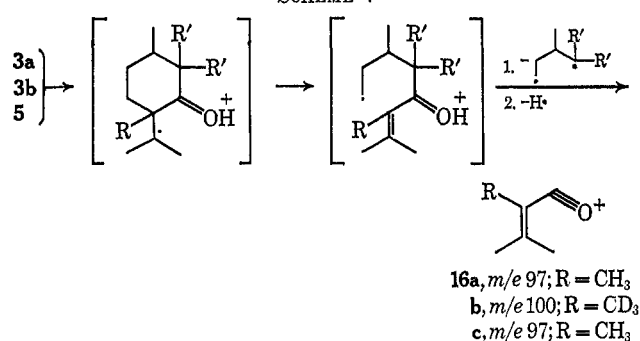8a, *m/e* 69; R' = H
b, *m/e* 69; R' = H
c, *m/e* 70; R' = D

The fragmentation of **3a**, shown in Scheme IV, resulting in loss of methyl group, may be due to cleavage at C-1 or C-4 or from the isopropyl group. The mass spectrum of **3b** shows even-electron ions *m/e* 153 and *m/e* 156 of about equal intensity (Table I). These ions must arise by loss of both CD₃ and CH₃ groups, which implies that methyl cleavage other than at C-4 is taking place. The formation of hydrocarbon fragments **15a**, **15b**, and **15c** may be rationalized as shown, but, at present, there is no evidence which distinguishes the routes. Willhalm and Thomas[5a] clearly demonstrated that methyl group cleavage from menthone removes methyl groups from the isopropyl group rather than from C-1.

The ions **16a**, **16b**, and **16c**, shown in Scheme V, are proposed to account for a major shift in intensity of the peak at *m/e* 97 of **3a** to *m/e* 100 for **3b** (the CH₃ group at C-4 is replaced by a CD₃ group for **3b**), as recorded in Table I.
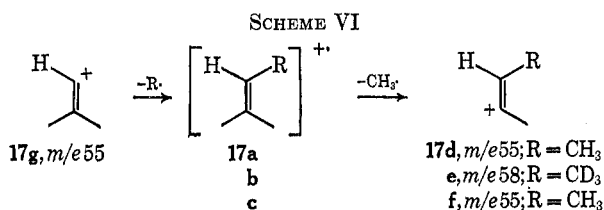
SCHEME IV

3a, 3b, 5

12a, R = CH$_3$; R' = H
b, R = CD$_3$; R' = H
c, R = CH$_3$; R' = D

14a, m/e 153
b, m/e 156
c, m/e 155

$-CH_3$

$-C_2H_2R'_2O$

$[(CH_3)_2CHCR=CHCH_2CCH_3]^{+\cdot} \xrightarrow{-CH_3\cdot} [CH_3CHCR=CHCH_2CCH_3]^+$

13a, m/e 124
b, m/e 127
c, m/e 124

15a, m/e 109
b, m/e 112
c, m/e 109

SCHEME V

3a
3b
5

1. $-$
2. $-H\cdot$

16a, m/e 97; R = CH$_3$
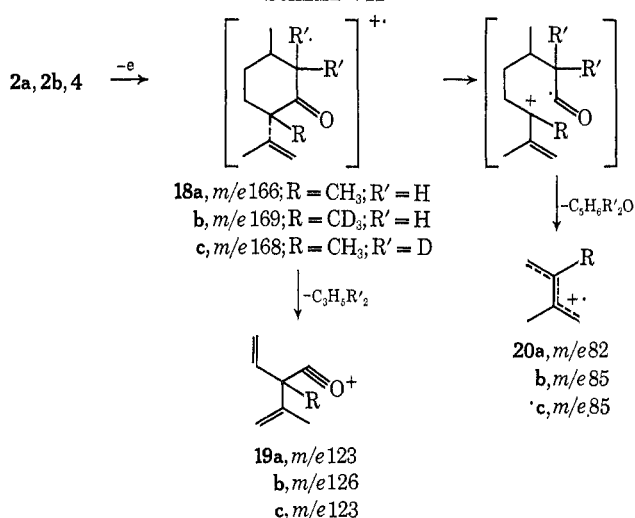b, m/e 100; R = CD$_3$
c, m/e 97; R = CH$_3$

The m/e 55 fragment from **3a** requires comment. The slow-scan high-resolution spectrum of **3a** shows absence of oxygen for this fragment; and, therefore, it is most likely **17d** or **17g**, derived from **17a** as shown in Scheme VI. The even-electron ions **17a**, **17b**, and **17c**

SCHEME VI

17g, m/e 55

$-R\cdot$

17a
b
c

$-CH_3\cdot$

17d, m/e 55; R = CH$_3$
e, m/e 58; R = CD$_3$
f, m/e 55; R = CH$_3$

are derived from **9a**, **9b**, and **9c**, as previously shown in Scheme III. The low-resolution data are shown in Table I.

The mass spectra of the unsaturated ketones, **2a**, **2b**, and **4**, are strikingly different from those of the corresponding saturated ketones **3a**, **3b**, and **5**. The McLafferty rearrangement[8] for the latter ketones is not observed but instead both α and α' cleavages as shown in Scheme VII occur. Cleavage of the bond between C-2 and C-3 (α cleavage) predominates over α' cleavage between C-3 and C-4 as evidenced by the higher abundance of the peak at m/e 123 for **19a** compared with m/e 82 for **20a** derived from **2a** and **4** (see Table II and Figure 1). The peak appearing at m/e 123 (**19a** and **19c**) is shifted to m/e 126 (**19b**) in the spectrum of **2b**, clearly showing that the C-4 methyl group remains with the ion at m/e 82 (**20a**), as shown by a major shift of

SCHEME VII

2a, 2b, 4 $\xrightarrow{-e}$

18a, m/e 166; R = CH$_3$; R' = H
b, m/e 169; R = CD$_3$; R' = H
c, m/e 168; R = CH$_3$; R' = D

$-C_3H_5R'_2$

$-C_3H_6R'_2O$

19a, m/e 123
b, m/e 126
c, m/e 123

20a, m/e 82
b, m/e 85
c, m/e 85

intensity of the m/e 82 peak to m/e 85 (**20b**), when comparison of spectra from **2a** and **2b** are made (about a $^2/_3$ shift in intensity; see Table II). Since there are no shifts in peak intensities for m/e 123 (**19c**) or m/e 82 (**20c**) in the spectrum of **4**, α cleavage between C-2 and C-3 is assumed. High-resolution mass measurements show that ions **19a**, **19b**, and **19c** contain oxygen and thus support the fragmentation shown in Scheme VII.

The peak at m/e 107 of compounds **2a** and **4** is shown by the high-resolution mass measurements in Table III to be a hydrocarbon ion rather than a hydroxytropylium ion. This peak is shifted to m/e 110 in the spectrum of **2b**, which indicates that the m/e 110 peak contains the three deuterium atoms of the C-4 methyl group. The m/e 110 peak is shown to be free of oxygen by high-resolution measurements. A scheme for the formation of these ions has not been devised.

The loss of the methyl group from the unsaturated ketones **2a**, **2b**, and **4** is due primarily to removal of the methyl group at C-4, since there is a shift of the greater part of the intensity of the M $-$ 15 peaks from **2a** and **4** to M $-$ 18 of **2b** (Figure 1, Table II). The presence of the double bond in **2a**, **2b**, and **4** is adequate to account for differences in methyl group cleavage of the unsaturated and saturated ketones.
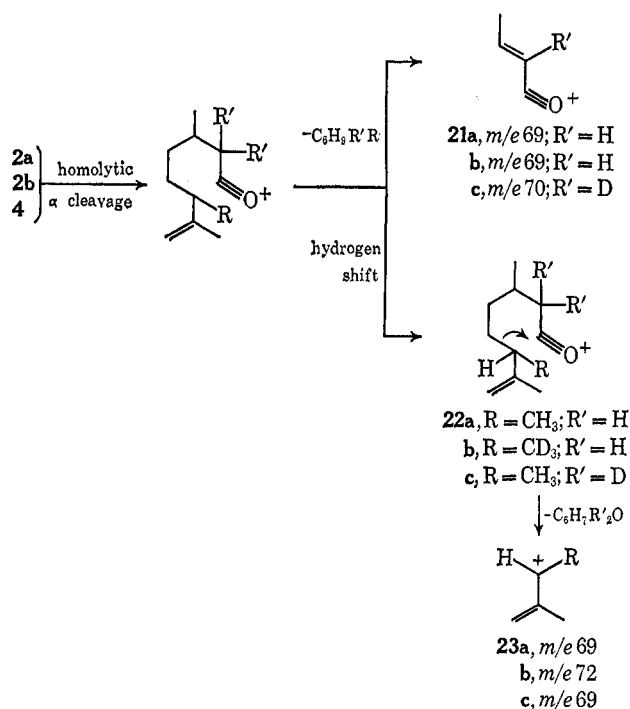
The formation of m/e 69 fragment is shown through homolytic cleavage in Scheme VIII. The fragments represented by m/e 69 have been shown to be composed of 0.5 C$_4$H$_5$O (**21a**) and 0.5 C$_5$H$_9$ (**23a**).

The high-resolution mass spectra of the saturated ketones **3a**, **3b**, and **5** show m/e 69 is due to $^2/_3$ C$_5$H$_9$ and $^1/_3$ C$_4$H$_5$O.
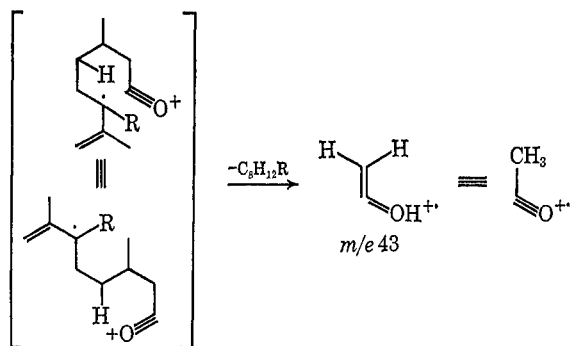
Some additional differences in the fragmentation pattern of the unsaturated ketones **2a**, **3b**, and **4** as compared with the saturated ketones **3a**, **3b**, and **5** are to be expected; these appear prominently in the fragment m/e 43. While m/e 43 from **3a** consists mainly of C$_3$H$_7$, for the unsaturated ketone **2a** it is made up of $^1/_3$ C$_3$H$_7$ and $^2/_3$ C$_2$H$_3$O. The formation of the oxygen-containing fragment may be explained as shown in Scheme IX, while hydrocarbon fragment C$_3$H$_7$ may be formed via **23a**.

The rigidity of bicyclic ketones has been used to explain loss of oxygen through expulsion of ketene.[5a] However, several flexible cyclic ketones are known that do not lose ketene during fragmentation.[5c] The high-

SCHEME VIII

21a, m/e 69; R' = H
b, m/e 69; R' = H
c, m/e 70; R' = D

22a, R = CH₃; R' = H
b, R = CD₃; R' = H
c, R = CH₃; R' = D

23a, m/e 69
b, m/e 72
c, m/e 69

SCHEME IX

m/e 43

resolution mass spectra of the ketones in both the saturated and unsaturated series show important fragments containing oxygen, and, therefore, the major fragmentation course appears to follow the previously reported suggestion.[5c]

Experimental Section

For the gas chromatography (glpc) studies, a Beckman GC-2A or an F & M Model 700 apparatus was used. The columns used for analytical glpc were 10 ft by $^1/_4$ in. and were packed with acid-washed Chromosorb W 60-80 mesh coated with LAC 886 or

Carbowax 20M. The column temperature was usually 180–190°. Ir spectra were obtained with a Beckman IR-5A spectrometer and nmr spectra with a Varian A-60 spectrometer, using tetramethylsilane as the internal standard (τ 10).

The low-resolution mass spectra were obtained at 70 ev on a CEC 21-103C mass spectrometer of 10.0 μA, and a collector slit width of 30 mils; a field of 2398 G was used for recording peaks from m/e 12 to 90. A collector slit width of 7 mils and a field of 4138 G were used for recording peaks greater than m/e 90. Samples were loaded in a heated inlet system operated at 320°, while the source temperature was controlled at 230°. The 226/57 ratio for n-C₁₆ was 3.9. Accurate mass measurements were made on a CEC 21-110B mass spectrometer for selected peaks using the mass-matching technique to a reference peak.

Preparation of (−)-C₄-(Deuteriomethyl)isopulegone (2b).— The deuteriomethylation of 1 was carried out in the same way as the previously described methylation of 1.[3,7] Thus, reaction of 11 g of 1 with 4.4 g of deuteriomethyl iodide gave 10 g of crude product. After purification by distillation [6 g, bp 64° (1.1 mm)]; preparation of the semicarbazone, two recrystallizations of the semicarbazone to 2 g of material melting at 210–212°,[9] and its regeneration by steam distillation in the presence of 5 g of oxalic acid hydrate yielded 0.8 g of 2b [bath temperature of the distillation was 81° (0.5 mm)]: $[\alpha]^{23}$D −67.4° (c 0.83, CHCl₃); $\nu_{max}^{CCl_3}$ 2950, 2240, 1712, 1645, 1250, and 1100 cm⁻¹; nmr (CCl₄) τ 9.2 (3 H, s), 8.7 (1 H, m), 8.2 (2 H, s), 7.9 (3 H, s), between 7.2 and 7.8 (4 H, m), and 4.8 (2 H, m).

Preparation of (+)-C₄-(Deuteriomethyl)dihydroisopulegone (3b).—Catalytic hydrogenation of 0.4 g of 2b in the presence of 0.3 g of 5% Pd-C catalyst in 25 ml of 95% ethanol resulted in the uptake of 1 equiv of hydrogen in 90 min. The catalyst was filtered out, the solution was concentrated, and the product was distilled [bath temperature 88° (0.4 mm)] to give 0.45 g of 3b: $[\alpha]^{23}$D +11.3° (c 0.9, CHCl₃); $\nu_{max}^{CCl_4}$ 2950, 2225, 1702, 1450, 1390, 1250, and 1110 cm⁻¹; nmr (CCl₄), τ 9.2 (3 H, d), 9.1 (6 H, m), between 8.6 and 8.8 (2 H, m), and between 7.8 and 8.5 (6 H, m).

Preparation of 2,2-d₂-Methylisopulegone (4).—A mixture of deuterium oxide (30 ml) and sodium (50 mg) was allowed to react, after which (−)-methylisopulegone (2a) (25 mg) was added to the solution and the mixture heated for 20 hr. The reaction mixture was cooled and extracted with ether; the ether layer was dried, evaporated, and distilled to give 18 mg of 4 [bath temperature 98° (1.9 mm)].

Preparation of 2,2-d₂-Dihydromethylisopulegone (5).—Preparation of 5 was analogous to that described for 4 above. Thus, 50 mg of 3a gave 35 mg of 5 [bath temperature 115° (2.1 mm)].

(9) Melting point not corrected.