Electron Impact Mass Spectrometry of 3-Cyclohexen-1-ol and Related Compounds

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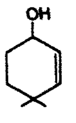
The electron impact mass spectrum of 3-cyclohexen-1-ol has been studied, especially with regard to the retro Diels-Alder reaction. Six deuterium labelled analogues and two dimethyl substituted homologues were synthesized. Contrary to what we have observed with 2-cyclohexen-1-ol, the double bond migration which precedes the retro Diels-Alder reaction plays a minor role.

INTRODUCTION

In a previous study[1] we showed that 2-cyclohexen-1-ol expels the elements of C_2H_4 via two competitive retro Diels-Alder (RDA) reactions. Besides the expected elimination of a C_2H_4 moiety containing the C-5 and C-6 atoms, another mechanism operates on a rearranged molecular ion, as is illustrated in Scheme 1 (ii). We also observed that substitution of the ring with methyl radicals affects the ratio of the two processes i and ii (Scheme 1), the elimination of the larger olefinic neutral fragment always being strongly favoured. By comparing the collision induced dissociation spectrum of **1** with the spectra of **2** and **3**, we later confirmed[2] that it is a 1,3 allylic hydrogen shift (ii, Scheme 1) which is responsible for the elimination of the olefin containing the C-4 and C-5 atoms and not a shift of the OH substituent (iii, Scheme 1). Our results have recently been confirmed by Terlouw *et al.*,[3] to whom we had sent two of our samples. However, there is a difference between their results and ours with regard to the kinetic energy release values ($T_{0.5}$) which are associated with the loss of $CH_3^{\cdot}$ from the metastable C_4H_6O ions at m/z 70. We found the same value of $T_{0.5} = 23.5$ meV with **1** and **3** as precursors, compared with 38.5 meV when **2** is the precursor of the metastable C_6H_6O ions. Terlouw and his co-workers did not find any difference with **1**, **2** and with hex-1-en-3-one as precursors, the latter being used to generate the same ionic structure as that of ion *a* in Scheme 1, instead of **3** which is the precursor we used.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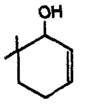
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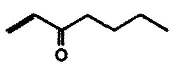
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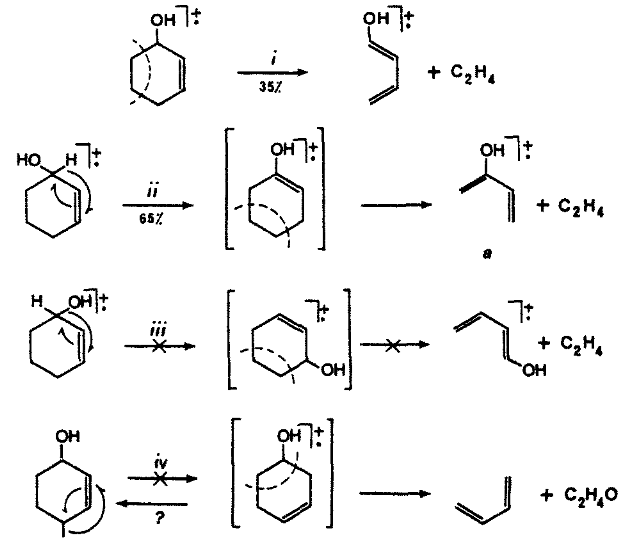
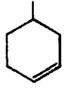


Scheme 1

Since we did not observe the isomerization of 2-cyclohexen-1-ol to 3-cyclohexen-1-ol with the subsequent loss of C_2H_4O (iv, Scheme 1), we concluded that it was the enhanced lability of the hydrogen atom attached to C-1 which was responsible for the 1,3 shift. The fact that reaction iv of Scheme 1 is not observed does not rule out the existence of the reverse transformation. Consecutive 1,3 allylic rearrangement reactions have been postulated in cyclohexene itself[4] in order to explain the partial randomization of the H atoms which precedes the RDA reaction, as well as in various methylcyclohexenes.[5] Since such 1,3 shifts would transform at least part of the molecular ions of 3-cyclohexene-1-ol into the isomeric 2-cyclohexen-1-ol molecular ions, we studied the electron impact mass spectra of 3-cyclohexen-1-ol (**4**) with the aid of the series of labelled compounds **4a**–**4f** and the two dimethyl substituted compounds **5** and **6**. We also inves-



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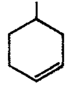
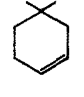


4a



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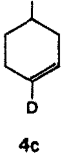

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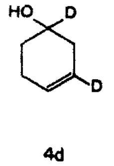
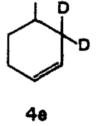
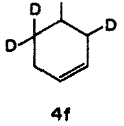


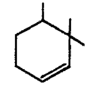
4d



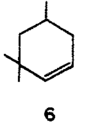
4e



4f



5



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tigated the elimination of H_2O and $CH_3^{\cdot}$ from the molecular ion of **4**.

RESULTS AND DISCUSSION

Figure 1 displays the 70 eV and the 12 eV mass spectra of the title compound. The 70 eV spectra of the labelled compounds **4a–4f** and those of the methyl substituted homologues **5** and **6** are listed in Table 1.

The retro Diels-Alder reaction

The RDA reaction yields the base peak in the 70 eV spectrum of **4**. High resolution shows that the peak is a singlet consisting of $[C_4H_6]^{+\cdot}$ ions only. Since the $[C_4H_6O]^{+\cdot}$ ions at m/z 70 represent only 7% of the base peak, it is obvious that the isomerization of **4** to the molecular ion of 2-cyclohexen-1-ol (hhh, Scheme 2) is a minor process. It should be noted that 20% of the m/z 70 ions have C_5H_{10} as elemental composition, which indicates the elimination of CO from the molecular ion. The $[C_4H_6O]^{+\cdot}$ ion of **4** appears almost completely as $[C_4H_5DO]^{+\cdot}$ in the high resolution spectra of **4a, 4b, 4c** and **4f**, and as $[C_4H_4D_2O]^{+\cdot}$ in the high resolution spectrum of **4d**. These mass shifts show that the few molecular ions which rearrange to 2-cyclohexen-1-ol then decompose via reaction i of Scheme 2 only.

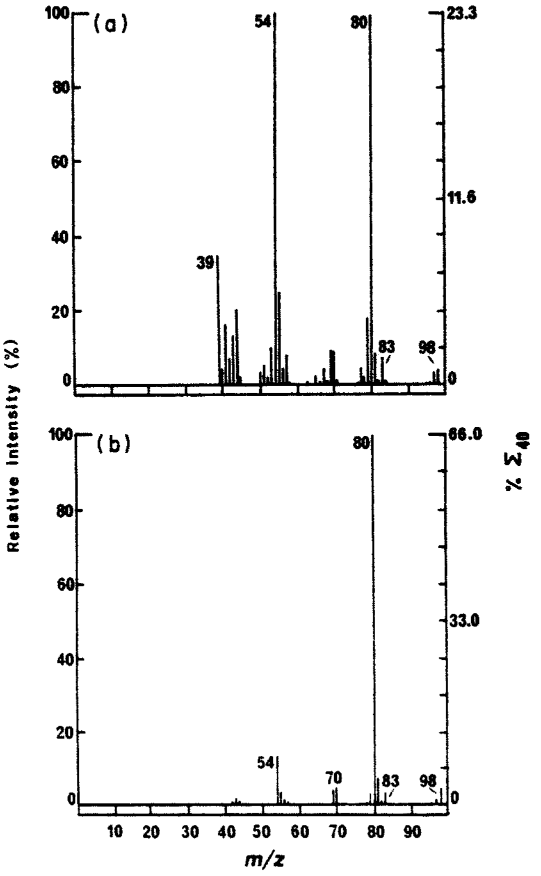
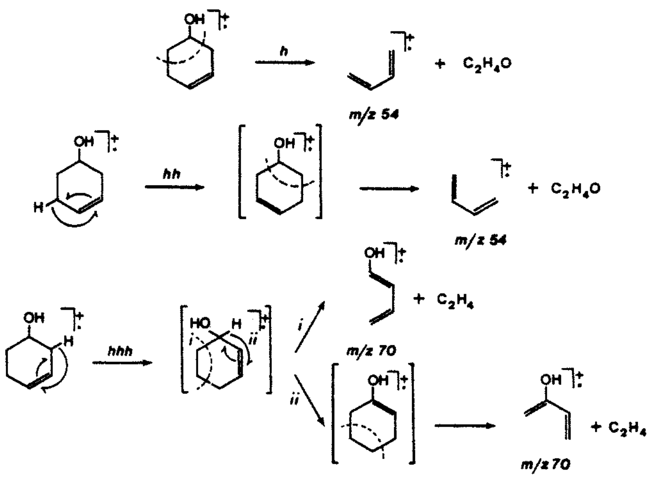


Figure 1. Electron impact spectra of 3-cyclohexen-1-ol (**4**): (a) 70 eV; (b) 12 eV.



Scheme 2

The double bond migration to C-4 (hh, Scheme 2) is also a minor process. Taking into account the incomplete labelling of **4f** one can estimate from the high resolution spectrum that only about 10% of the m/z 54 ions are displaced to m/z 56. This is supported by the high resolution spectrum of **4e** in which about 10% of the m/z 54 ions are not displaced.

The spectra of **5** and **6** show that the possibility of expelling a larger olefinic moiety does not promote isomerization, contrary to what is observed with methyl substituted 2-cyclohexen-1-ol.[1] In compound **5**, a double bond migration from C-3—C-4 to C-4—C-5 analogous to reaction hh of Scheme 2 would result in the elimination of C_4H_8O instead of C_2H_4O when there is no migration. The relative abundance of the m/z 54 ion which would result from the elimination of C_4H_8O is less than 1%, while the normal RDA reaction (h, Scheme 2) leads to the base peak at m/z 82. Compound **6** does not isomerize either; the m/z 82 ion which results from a classical RDA reaction shows a relative abundance of 93% compared with only 3% for m/z 70, the $[C_4H_6O]^{+\cdot}$ ion which would be formed after isomerization to 2-cyclohexen-1-ol. Thus, 1, 3 allylic rearrangement reactions are unimportant with 3-cyclohexen-1-ol and with its methyl substituted derivatives **5** and **6**, contrary to what is observed with 2-cyclohexen-1-ol and its substituted homologues. Although double bond shifts have been observed with cyclohexene,[4] methyl substituted cyclohexenes[5] and tetralines,[6] allylic activation of hydrogen atoms is not sufficient to initiate such rearrangement reactions in 3-cyclohexen-1-ol. As we have already suggested,[1] the fact that 2-cyclohexen-1-ol rearranges so easily shows that the concomitant activation of the allylic hydrogen atom by the OH substituent attached to the same carbon atom plays a key role in promoting the 1, 3 shift.

Elimination of H_2O from the molecular ions

The elimination of H_2O from the molecular ions of **4** leads to the very abundant m/z 80 ions and to a metastable peak (m^* 98 → 80, calc. 65.31, obs. 65.3). The behaviour of **4** with respect to this reaction is

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Table 1. 70 eV mass spectra of compounds 4a–4f normalized to base peak = 100.0

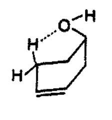
	Compound							
m/z	4a[a]	4b	4c	4d	4e[a]	4f	5	6
39	29.0	33.8	20.8	15.9	14.1	20.8	—	—
40	6.3	7.8	19.5	17.7	16.8	24.0	—	—
41	6.4	12.5	8.9	7.0	11.1	11.2	—	—
42	8.6	9.4	13.5	11.0	10.0	12.8	—	—
43	10.2	8.6	15.4	9.5	12.5	52.0	—	—
44	—	9.4	23.7	9.1	24.4	28.0	—	—
45	31.7	18.8	2.9	18.7	5.2	19.2	—	4.6
46	1.4	1.2	—	1.2	2.6	16.8	—	0.6
47	—	—	—	—	—	—	1.6	—
48	—	—	—	—	0.5	—	—	—
49	0.5	—	—	0.5	0.6	—	—	—
50	2.2	2.8	1.9	1.1	1.3	2.0	—	5.1
51	4.2	5.0	3.7	2.8	2.0	3.6	1.2	10.5
52	2.5	3.7	3.4	3.2	2.0	4.0	—	6.0
53	7.7	11.0	4.1	3.6	2.4	4.8	5.2	24.0
54	100.0	100.0	11.8	9.3	15.4	16.0	1.4	9.5
55	7.1	20.4	100.0	99.6	16.8	100.0	36.7	88.7
56	18.2	7.8	21.6	19.3	95.3	36.4	7.6	36.2
57	0.5	2.5	7.9	5.6	19.1	10.8	38.1	100.0
58	8.8	6.4	1.6	4.6	3.1	7.2	1.8	7.7
59	0.5	0.6	2.1	2.8	2.5	3.6	—	1.2
60	—	—	—	—	—	1.8	1.9	—
61	—	—	—	—	—	—	—	—
62	—	—	—	—	—	—	—	0.8
63	0.7	0.9	0.6	0.5	0.5	—	—	1.8
64	—	—	0.5	0.5	0.5	—	0.5	—
65	1.7	1.7	0.8	0.6	0.7	—	1.1	7.5
66	1.6	1.5	1.7	1.4	1.3	1.3	0.9	3.6
67	1.9	4.0	1.3	1.4	1.9	2.2	20.2	76.1
68	3.3	2.2	4.1	3.7	2.2	2.6	2.1	5.8
69	—	4.8	2.9	2.7	4.4	5.2	19.6	17.2
70	8.4	6.6	10.4	6.1	3.2	10.8	16.5	3.7
71	9.8	7.8	5.8	5.3	10.4	8.8	4.9	2.9
72	0.7	0.6	—	7.8	4.6	6.0	6.5	—
73	—	—	—	0.7	—	3.6	13.0	2.2
74	0.5	—	1.4	—	—	—	—	0.6
75	—	—	—	—	—	—	8.1	0.6
76	—	—	—	—	—	—	0.5	—
77	4.0	1.8	1.6	0.6	—	—	1.4	6.1
78	1.9	3.3	3.4	2.3	2.0	2.6	—	1.3
79	17.0	4.8	4.3	2.3	2.5	6.0	1.0	7.6
80	97.3	20.4	19.1	5.7	7.5	4.8	0.6	1.1
81	10.6	88.2	94.8	18.0	20.4	14.0	1.6	9.9
82	0.6	7.8	8.1	100.0	100.0	36.8	100.0	93.0
83	—	2.2	1.2	9.1	8.5	84.0	15.9	57.7
84	6.1	6.1	6.3	1.3	1.6	16.8	1.2	9.5
85	—	—	—	5.4	1.6	4.4	1.7	81.8
86	—	—	—	—	—	1.8	1.0	5.9
87	—	—	—	—	—	—	—	—
88	—	—	—	—	—	—	—	—
89	—	—	—	—	—	—	—	—
90	—	—	—	—	—	—	—	—
91	—	—	—	—	—	—	0.8	3.5
92	—	—	—	—	—	—	—	0.6
93	—	—	—	—	—	—	1.7	19.7
94	—	—	—	—	—	—	—	1.6
95	—	—	—	—	—	—	0.5	0.6
96	1.2	0.6	0.6	—	—	—	—	—
97	—	0.7	0.6	0.5	—	—	0.9	1.5
98	2.4	2.2	2.0	0.7	1.4	—	1.1	2.7
99	4.0	3.3	2.8	2.2	3.4	2.2	0.7	—
100	—	—	—	4.2	2.5	2.8	—	—
101	—	—	—	—	—	2.0	1.3	—
102	—	—	—	—	—	1.0	—	—
103	—	—	—	—	—	—	—	—
104	—	—	—	—	—	—	—	—
105	—	—	—	—	—	—	—	0.5
106	—	—	—	—	—	—	—	—
107	—	—	—	—	—	—	—	—
108	—	—	—	—	—	—	0.9	3.8
109	—	—	—	—	—	—	—	1.6
110	—	—	—	—	—	—	—	—
111	—	—	—	—	—	—	36.0	13.4
112	—	—	—	—	—	—	2.0	1.1
113	—	—	—	—	—	—	—	—
114	—	—	—	—	—	—	—	—
124	—	—	—	—	—	—	—	—
125	—	—	—	—	—	—	—	—
126	—	—	—	—	—	—	3.7	—

[a] Spectrum corrected to 100% deuteration.

totally different from that of its isomer 2-cyclohexen-1-ol. In the 12 eV spectrum of **4** (Fig. 1) *m/z* 80 represents 66% of the total ion current compared with only 2.5% in the spectrum of 2-cyclohexen-1-ol.[1] The mass shifts of *m/z* 80 which are observed in the 70 eV high resolution mass spectra of the labelled compounds are listed in Table 2. They unambiguously demonstrate that the water elimination is highly specific, involving the OH substituent and one of the hydrogen atoms attached to C-5. This 1, 3 elimination is similar to what occurs in 2-tetralol.[7] A 5-membered ring transition state can be envisaged to bring one of the allylic hydrogen atoms attached to C-5 into the vicinity of the OH group, as is illustrated with structure *b*. The importance of the $[M-H_2O]^{+\cdot}$ ion is drastically reduced in the spectra of **5** and **6**.

Table 2. Shifts of *m/z* 80 in the 70 eV high resolution partial mass spectra of the labelled compounds 4a–4f

Compound	m/z 83	84	85	86
4a		100		
4b	25	75		
4c		100		
4d	20	8	72	
4e	67	17	16	
4f	6	51	41	2



b

Loss of a methyl radical

The loss of $CH_3^{\cdot}$ from the molecular ion of **4** leads to *m/z* 83 and to a metastable peak at $m^* = 70.3$

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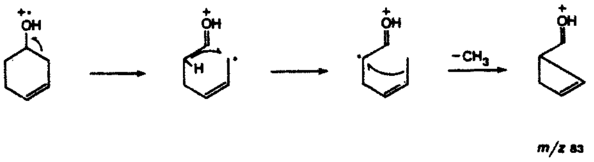
Table 3. Shifts of m/z 83 in the 70 eV high resolution partial mass spectra of the labelled compounds 4a–4f

Compound	m/z 80	81	82	83
4a	97	3		
4b		100		
4c		100		
4d		2	98	
4e		2	98	
4f			6	94

(98 → 83, calc. 70.30). This fragmentation is much more pronounced with 2-cyclohexen-1-ol. An examination of the mass shifts observed in the high resolution 70 eV mass spectra (Table 3) does not point to the existence of a single mechanism. However, since 67% of the molecular ions of compound **4e** and 51% of those of compound **4f** expel $CHD_2^{\cdot}$, the main mechanism involves the elimination of the C-2 methylene atoms, the third H atom originating from C-6 as is proposed in Scheme 3. If one takes into account the existence of a probable isotope effect during the elimination of $CHD_2^{\cdot}$ from **4f**, one can conclude that more than half but less than two-thirds of the molecular ions of **4** eliminate a methyl radical containing both C-2 hydrogen atoms and a C-6 hydrogen atom. The mass shifts in the high resolution spectra of **4b, 4c** and **4d** also show that other minor mechanisms eliminate the H atoms attached to C-1 and C-3, but not the one attached to C-4.



Scheme 3

EXPERIMENTAL

Low resolution mass spectra were recorded on a Varian MAT CH-4 instrument. The temperature of the inlet system was kept at 100 °C and that of the ion source at 150 °C. High resolution data were obtained on a Varian MAT SM1-B mass spectrometer. The ion source temperature was 150 °C and that of the inlet system 120 °C. The isotopic content of the labelled compounds has been determined, except in the case of **4a**, from the isobutane chemical ionization mass spectra of their benzoate esters, which exhibit negligible $[M-H]^+$ ions. All the compounds except **4f** were purified by vacuum distillation followed by preparative gas chromatography.

3-Cyclohexen-1-ol (4). 4-Tosyloxycyclohexanol was prepared from 1,4-cyclohexanediol and was then converted to **4** according to a procedure described by Owen and Robins.[8]

3-Cyclohexen-1-ol-0-*d* (4a). The mass spectrum of this compound was recorded after simultaneous introduction of **4** and D_2O in the inlet system which had previously been equilibrated with D_2O. The isotopic composition was 54% d_1 and 46% d_0; the mass spectrum was corrected to 100% d_1.

3-Cyclohexen-1-ol-1-d_1 (4b). 1,4-Cyclohexanedione monoethylene acetal was prepared according to a procedure described by Courtot.[9] It was reduced to 4-hydroxycyclohexanone ethylene acetal which was then converted to 4-tosyloxycyclohexanone ethylene acetal. This derivative was transformed into 3-cyclohexen-1-one ethylene acetal by the method of Owen and Robins.[8] Hydrolysis of this acetal in dilute acetic acid during 2 h at 25 °C yielded 3-cyclohexene-1-one which was reduced to **4b** with $LiAlD_4$ (98% d_2, 2% d_1).

3-Cyclohexen-1-ol-4d_1 (4c). The method was similar to that described for the synthesis of **4b** except that the first reduction was performed with $LiAlD_4$ and the second with $LiAlH_4$ (90% d_1, 10% d_0).

3-Cyclohexen-1-ol-1,3-d_2 (4d). 2-Cyclohexen-1-ol-1,3-d_2, which has been described in a previous publication,[1] was transformed into 1,3-cyclohexanediol-1,3-d_2 according to a method which has been used by Brown and Geoghegan[10] with 1-hexene. The labelled diol was then converted into 3-tosyloxycyclohexanol-1,3-d_2 which yielded **4d** by a procedure described by Clarke and Owen[11] (98% d_2, 2% d_1).

3-Cyclohexen-1-ol-2,2-d_2 (4e). 2-Cyclohexen-1-ol-2-d_1 whose synthesis has been described previously[1] was transformed into 1,3-cyclohexanediol-2,2-d_2 by the method of Brown and Geoghegan,[10] using $NaBD_4$. This diol was then converted into its monotosylate which gave **4e** by the method of Clarke and Owen[11] (67% d_2, 33% d_1).

3-Cyclohexen-1-ol-2,6,6-d_3 (4f). 2-Cyclohexen-1-one (1 g) was exchanged once with 20 cm^3 of CH_3OD containing 1 cm^3 of D_2O and 10 mg of CH_3ONa at 30 °C for 30 min in an ultrasonic bath. The labelled ketone was extracted and purified by chromatography on a silica gel column, using gradient elution by hexane containing increasing amounts of ethylacetate (from 0% to 25%). The purified ketone was then transformed into its 4-bromo derivative with *N*-bromosuccinimide in the presence of benzoylperoxide[12] and reduced to **4f** with $LiAlH_4$.[13] The final compound was purified by column chromatography as described for the labelled ketone. The isotopic content was 73% d_3, 17% d_2 and 10% d_4. A 360 MHz nuclear magnetic resonance spectrum showed that 8% of the d_2 compound is 3-cyclohexen-1-ol-2,6-d_2 and 9% the 6,6-d_2 analogue, the tetradeuterated compound being the 2,4,6,6-d_4 derivative.

2,2-Dimethyl-3-cyclohexen-1-ol (5). 2,2-Dimethyl-1,3-cyclohexanedione was prepared according to a method described by Majahan[14] using 2-methyl-1,3-cyclohexanedione and methyl iodide and reduced to 2,2-dimethyl-1,3-cyclohexanediol by the method of

Andersen and Ladner.[15] The diol was then converted into its monotosylate to yield **5** by the procedure described by Clarke and Owen.[11]

5,5-Dimethyl-3-cyclohexen-1-ol (6). 5,5-Dimethyl-1,3-cyclohexanediol prepared according to Zelinsky and Uspensky[16] was transformed into its monotosylate and then into **6** by the method of Clarke and Owen.[11]

Acknowledgement

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REFERENCES

1. D. Braem, F. O. Gülacar, U. Burger and A. Buchs, *Org. Mass Spectrom.* **14**, 509 (1979).
2. Unpublished results.
3. J. K. Terlouw, W. Heerma, J. L. Holmes and P. C. Burgers, *Org. Mass Spectrom.* **15**, 582 (1980).
4. P. J. Derrick, A. M. Falick and A. L. Burlingame, *J. Am. Chem. Soc.* **94**, 6794 (1972).
5. T. H. Kinstle and R. E. Stark, *J. Org. Chem.* **32**, 1318 (1967).
6. M. L. Gross and F. L. DeRoos, *J. Am. Chem. Soc.* **98**, 7128 (1976).
7. M. L. Gross, E. Chiu, D. Pokorny and F. L. DeRoss, *Org. Mass Spectrom.* **12**, 55 (1977).
8. L. N. Owen and P. A. Robins, *J. Chem. Soc.* 320 (1949).
9. P. Courtot, *Ann. Chim. (Fr.)* **8**, 197 (1963).
10. H. C. Brown and P. Geoghegan Jr, *J. Am. Chem. Soc.* **89**, 1522 (1967).
11. H. F. Clarke and L. N. Owen, *J. Chem. Soc.* 2103 (1950).
12. T. Toru, S. Kurozumi, T. Tanaka, S. Miura, M. Kobayashi and S. Ishimoto, *Synthesis* 867 (1974).
13. F. F. Knapp Jr and G. J. Schoepfer Jr, *J. Org. Chem.* **39**, 3247 (1974).
14. J. R. Majahan, *Synthesis* 110 (1976).
15. N. H. Andersen and D. W. Ladner, *Synth. Commun.* **8**, 499 (1978).
16. N. D. Zelinsky and A. E. Uspensky, *Chem. Ber.* **46**, 1466 (1913).

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