Tetrahedron. Vol. 29, pp. 4077 to 4082. Pergamon Press 1973. Printed in Great Britain

MASS SPECTRAL STUDIES OF SOME CARBOHYDRATE ENONES[a]

N. L. HOLDER[b] and B. FRASER-REID*
Department of Chemistry, University of Waterloo, Waterloo, Ontario.

(*Received in the USA* 21 *February* 1973; *Received in the UK for publication* 30 *August* 1973)

Abstract—A study of the mass spectra of ethyl 2,3-dideoxy-α-D-*glycero*-hex-2-enopyranosid-4-ulose **1a**, its 6-O-acetyl derivative **1b**, and methyl 3,4-dideoxy-α-D-*glycero*-hex-3-enopyranosidulose **2a** indicates that the main fragmentation of these compounds occurs by a retro-Diels-Alder type cleavage. Recognition of the ions produced by this cleavage provides a means of allocating the position of the α,β-unsaturated chromophore in carbohydrate enones. Fragmentation of molecular ions of **1a** and **1b** also occurred by direct loss of individual ring substituents to give ions which retain the pyranoid nucleus. The fragmentation pathways suggested are supported by accurate mass measurements of the salient fragment ions of **1a**.

INTRODUCTION

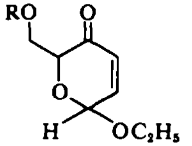
The usefulness of mass spectrometry in the field of carbohydrate chemistry[1,2] for the analysis of acetylated glycosides,[3,4] determination of ring size[5] and location of site of unsaturation[6] is well established. Carbohydrate enones have recently become readily available in large quantities,[7] and they have been employed in a variety of studies at the ground and excited states.[7f,8] In view of these developments, we undertook a mass-spectral study of enones 1 and 2 to determine whether the fragmentation patterns are of any diagnostic value.

A considerable body of data has been amassed from the electron impact induced mass spectra of cyclic α,β-unsaturated ketones.[9] From these data, the more significant fragmentation processes have been determined to be (a) elimination of ketene from the structural unit $\rangle C{=}CH{-}CO{-}CH_2{-}$, and (b) one which may formally be regarded as a retro-Diels-Alder reaction. Dauben *et al.*[9b] showed that ketene is lost readily, only if the enone has at least one Me substituent at the γ-position. This observation has been extended by other workers who, in a study of steroidal systems, found that the importance of ketene-loss varies not only with the nature of the functional group,[10] but also with the stereochemistry of the molecule.[11] In the absence of the γ-substituents, the major fragmentation is of the retro-Diels-Alder type.[9]

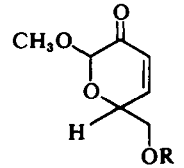
RESULTS AND DISCUSSION

As model compounds for our studies, the readily available enones **1**[7d,e] and **2**[7h] were chosen. The mass spectra obtained are shown in Figs 1–3 and the accurate masses and elemental composition of selected ions of **1a** are presented in Table 1.

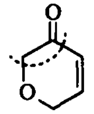
As in the case with most alkyl hexopyranosides,[2] the enones **1** and **2** show very weak molecular ions.



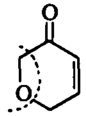
1a: R=H
1b: R=Ac



2a: R=H
2b: R=*p*-nitrobenzoate

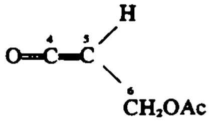


ketene elimination



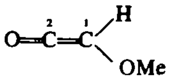
retro Diels–Alder cleavage

Despite the fact that the enones all have γ-substituents,[9b] loss of the ketenes



$$O{=}\overset{4}{C}{=}\overset{5}{C}\begin{matrix}H\\ \overset{6}{C}H_2OAc\end{matrix}$$

from **1b** (*m/e* 214-*m/e* 114) and



$$O{=}\overset{2}{C}{=}\overset{1}{C}\begin{matrix}H\\ OMe\end{matrix}$$

from **2a** (*m/e* 158-*m/e* 72) is not observed. How-

---

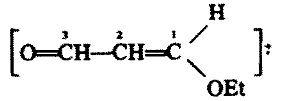
[a] Pyranosiduloses Part VI. For Part V see N. L. Holder and B. Fraser-Reid, *Canad. J. Chem.* in Press

[b] Taken from the Ph.D. Thesis of N. L.H.; University of Waterloo, Waterloo, Ontario, Canada 1972. Present address: Gillette Research Institute, Rockville, Maryland 20850, U.S.A.

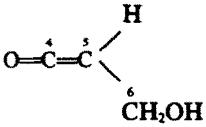
Table 1. High resolution mass spectral data of **1a**

Observed	Calculated	Elemental composition
29·0027	29·0027	CHO(62·5%)
29·0396	29·0391	C_2H_5(37·5%)
55·0183	55·0184	C_3H_3O
84·0203	84·0211	$C_4H_4O_2$(31·5%)
84·0565	84·0575	C_5H_8O(68·5%)
112·0531	112·0524	$C_6H_8O_2$
172·0736	172·0735	$C_8H_{12}O_4(M^+)$

ever, the related alcohol, **1a**, does give a peak *m/e* 100 (2%) consistent with the radical ion



which would be formed upon the expulsion of the ketene



(*cf* 9*b*). The major pathway of enones **1a**, **1b** and **2a** appears to be the retro-Diels-Alder type cleavage illustrated in Scheme 1.

Retro-Diels-Alder type fragmentation (*Scheme* 1)

The proposed major fragmentation pathways for **1a**, **1b** and **2a** leading to ions *m/e* 112 and *m/e* 98 follow closely those proposed by Bowie[12] and Dauben,[9b] for cyclohexenone and its 2-Me analogue.* From the high resolution mass spectrum of **1a**, the accurate mass measurement of the ion *m/e* 112 (Obs. 112·0531, Calc 112·0524) shows that it has the appropriate elemental composition of $C_6H_8O_2$ (Table 1).

The charged-radicals *m/e* 112, obtained from **1a** or **1b** and *m/e* 98 $(C_5H_6O_2)^{+\cdot}$ from **2a**, being similar in structure can undergo analogous fragmentations. Three fragmentation pathways are possible, two of which involve (i) McLafferty rearrangements[13] and (ii) loss of carbon monoxide giving rise to cyclopropenes. With regard to (i), the ions *m/e* 112 and *m/e* 98 can lose acetaldehyde and formaldehyde respectively *via* the rearrangements shown below.

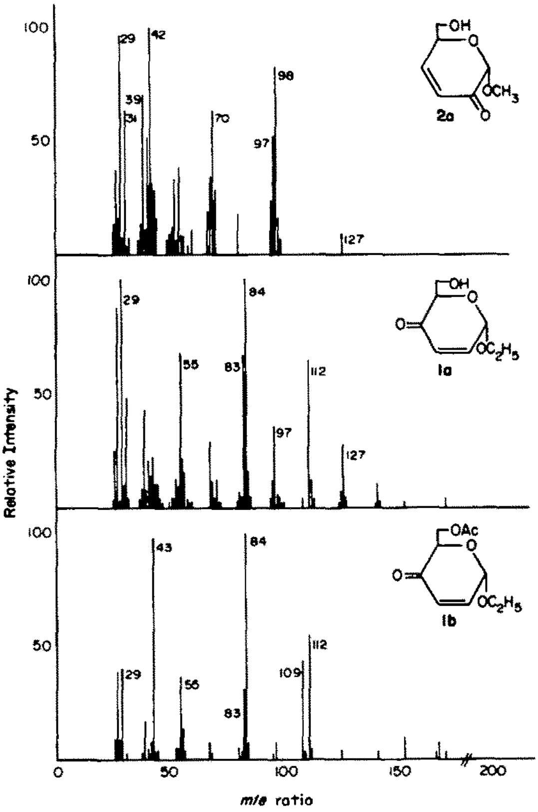
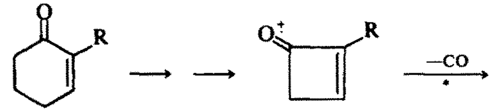
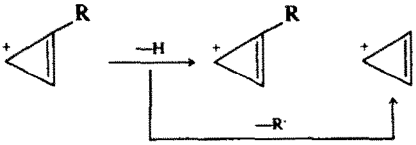


Fig 1.



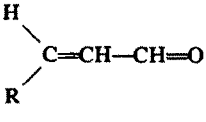
R = Me, Ref. 9*b*
R = H, Ref. 12

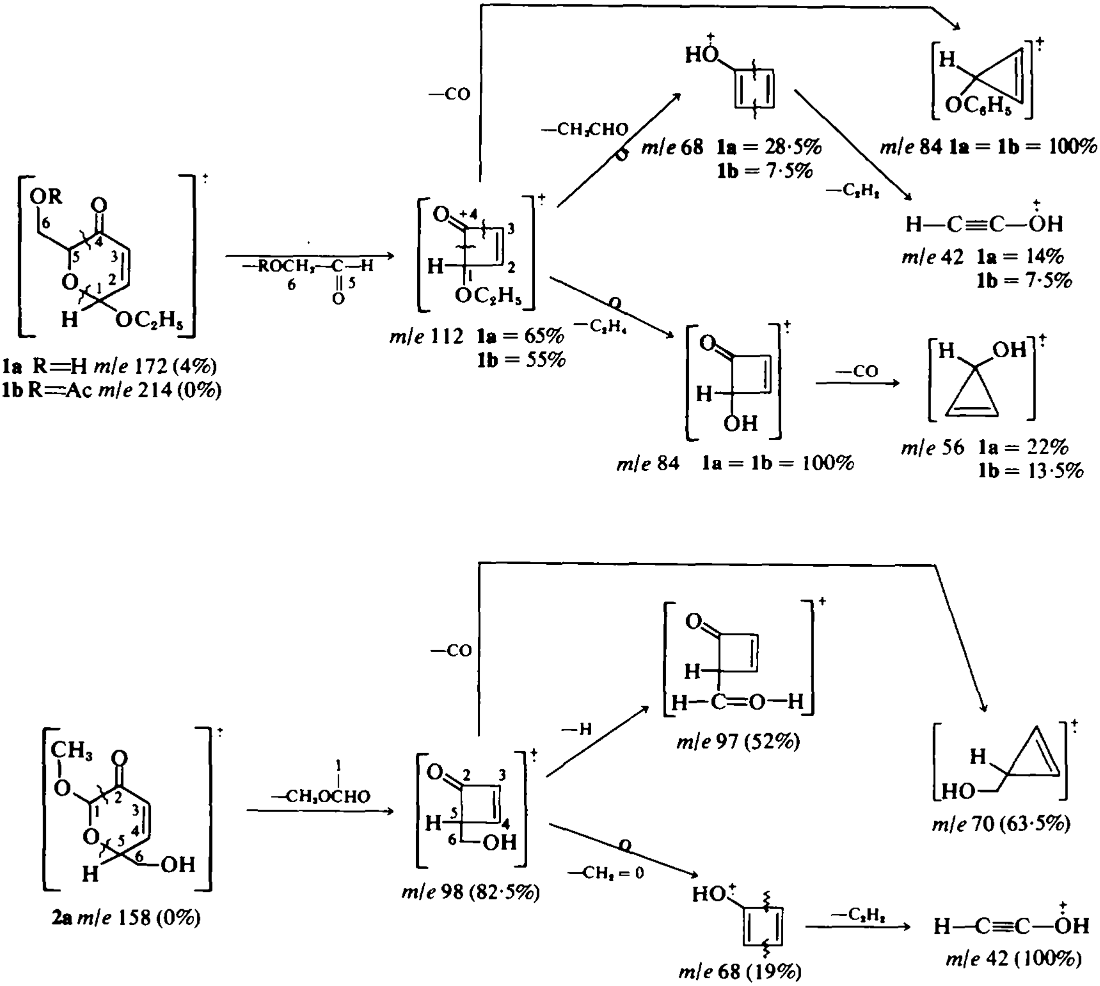


In the absence of labelled experiments, the hydroxycyclobutadiene structure proposed for ion *m/e* 68 must be regarded as tentative. However this species has been written in its cyclobutenone form by Bowie,[12] and Hiraoka has recently found that cyclobutenone is converted to furan and, by an alternate route, to acetylene and ketene as outlined in the drawing.[14] Further loss of acetylene from the diene structure generates the species *m/e* 42. This species gives the most intense peak in the spectrum

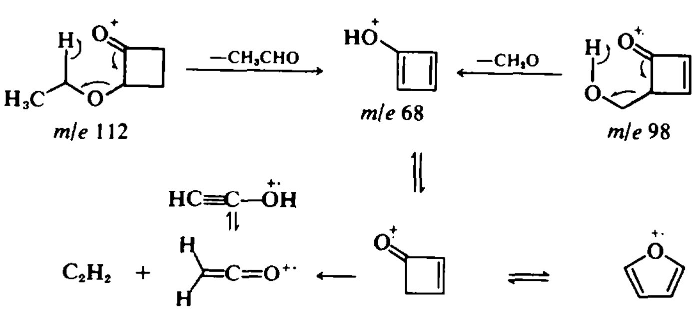
---

*The ions *m/e* 112 and *m/e* 98 are written in their cyclic forms following the format of Bowie[12] and Dauben;[9b] however it is conceivable that these may exist in their open chain forms





SCHEME 1



of **2a** (Fig 1), but in the spectra of **1a** and **1b** (Figs 2 and 3), its intensity is only 14% and 7·5% respectively.

Concerning the second proposed pathway (ii), loss of carbon monoxide from *m/e* 112 gives the cyclopropene radical-ion $[C_5H_8O]^{+\cdot}$ *m/e* 84 as the most abundant peak (Figs 2 and 3).

Similarly, loss of carbon monoxide from the cyclobutenone *m/e* 98 gives the hydroxymethyl cyclopropene *m/e* 70 (63·5% relative intensity Fig 1). Fragmentations similar to these, occur as the second stage in the fragmentation pathway* proposed for cyclohexenones.[9b,12]

---

*See footnote on previous page.

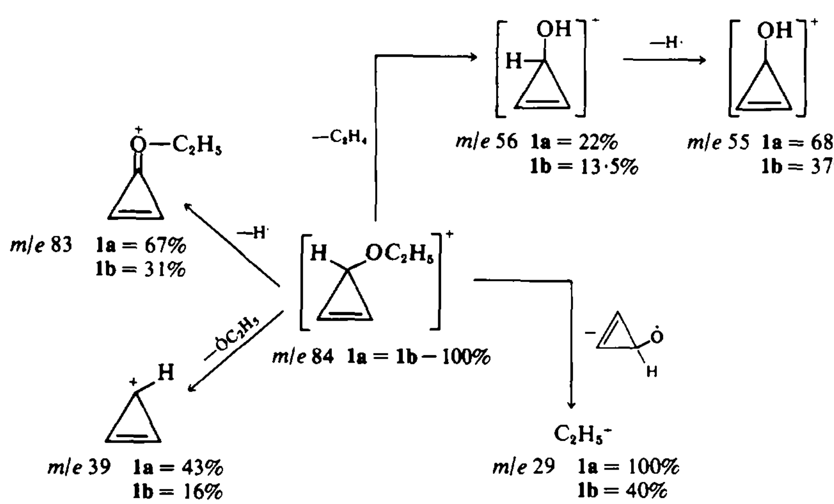
The third course of decomposition for ion *m/e* 112 finds precedent in the proposed fragmentation of allylic ethers.† On this basis, ethylene is lost from the ethoxy group with the formation of 4-hydroxycyclobut-2-enone $[C_4H_4O_2]^{+}$ *m/e* 84.

The implication of the analyses in the two foregoing paragraphs is that the peak *m/e* 84 ought to be a doublet. High resolution studies of **1a** summarized in Table 1 verify that this is the case, with the $[C_5H_8O]^{+}$ (Obs. 84·0565, Calc 84·0575) component being 68·5% and the species $[C_4H_4O_2]^{+}$ (Obs. 84·0203, Calc 84·0211) being 31·5% of the total peak.

Further support for the analyses in Scheme 1 is given by the observation of metastable peaks for the transitions 112→84, 84→56, 98→70, 68→42 (Table 2).

Table 2. Metastable peaks of some transitions in the mass spectra of the carbohydrate enones **1a**, **1a** and **2a**

Transition	Compound	Metastable peak Observed	Metastable peak Calculated
112→84	**1a**	63·2	63
	1b	63·2	63
84→45	**1a**	37·1	37·33
	1b	37·1	37·33
98→70	**2a**	50	50
68→42	**2a**	25·7	25·9
172→142	**1a**	117	117·23
127→97	**1a**	74	74·08
169→109	**1b**	70	70·3
154→109	**1b**	77	77·14



SCHEME 2

The ethyl cyclopropenyl ether $[C_5H_8O]^{+}$ *m/e* 84, can undergo the typical fragmentation of allylic ethers† by losing ethylene to form cyclopropenol, *m/e* 56 (Scheme 2) which, by loss of hydrogen, forms the protonated cyclopropenone *m/e* 55. Alternatively, direct loss of hydorgen from *m/e* 84 leads to the alkylated cyclopropenone *m/e* 83. These cyclopropenones are highly stabilised aromatic species.[16] A third alternative course of fragmentation for the ether, *m/e* 84, is that in which rupture occurs on either side of the oxygen, the charge being retained by the hydrocarbon moiety[15] (Scheme 2). Appropriately, high resolution of **1a** (Table 1), shows that the peak at *m/e* 29 (Obs 29·0396; Calc 29·0391, 37·5%) has the elemental composition C_2H_5.

The intermediacy of the cyclopropenyl carbinol *m/e* 70 (Scheme 1) finds support in the presence of a strong peak at *m/e* 39 (70%). This is ascribed to the cyclopropenyl cation, which would be formed together with the hydroxymethyl radical upon fragmentation of *m/e* 70. Absorptions corresponding to these ions are found in Fig 1.

Retention of the pyranosidulose ring

Fragmentation of the molecular ion may also occur by direct loss of individual ring substituents to give ions which retain the pyranoid ring. This is illustrated in Schemes 3 and 4 for **1a** and **1b** respectively. For each of the enones, ions were produced

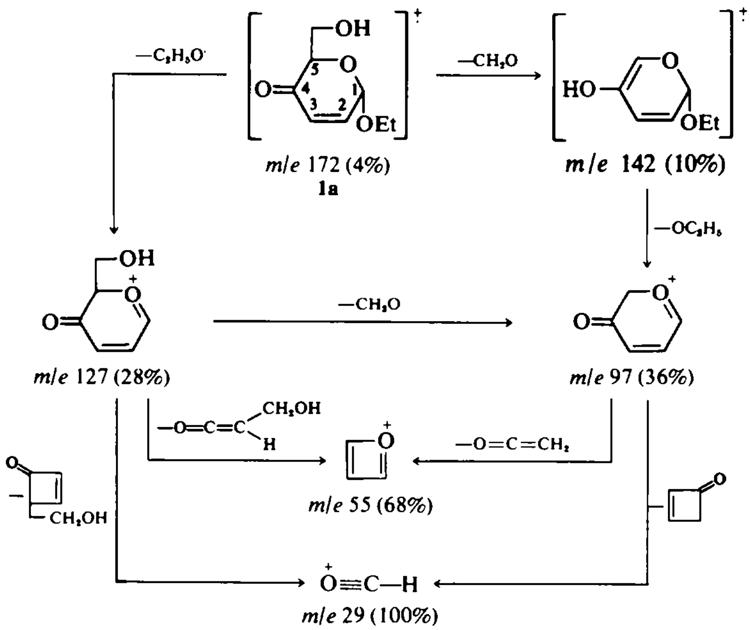
---

†Allyl n-propyl ether, **ka**, decomposes to give allyl alcohol and propene; similarly crotyl ethyl ether, **kb**, gives crotyl alcohol and ethylene. The process involves cleavage of the O—C$_\alpha$ bond with synchronous migration of a β-hydrogen.[15]

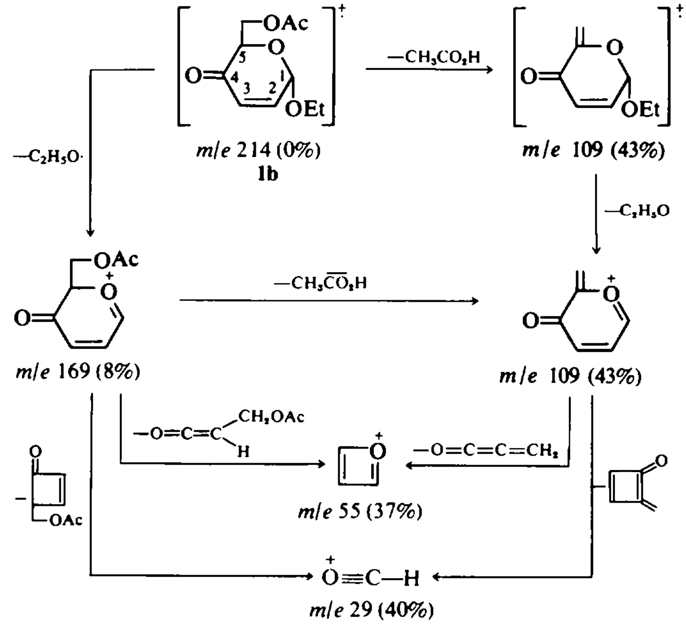
$$\mathrm{R{-}CH{=}CHCH_2{-}O\underset{\alpha}{C}H_2\underset{\beta}{C}H_2R'} \xrightarrow{-\bullet} \mathrm{R{-}CH{=}CH{-}CH_2\overset{+}{\dot{O}}H + CH_2{=}CHR'}$$

k

a: R = H, R′ = Me
b: R = Me, R′ = H



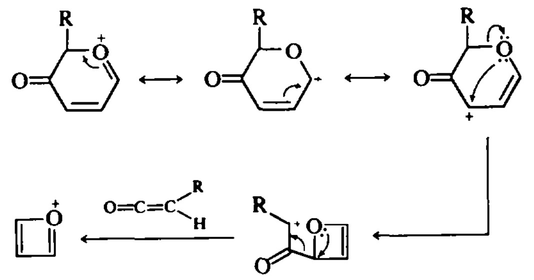
SCHEME 3



SCHEME 4

by loss of the aglycon, and either CH_2O from **1a** or CH_3COOH from **1b**. These ions and those from their subsequent degradation, were observed at *m/e* 127, 142, 95, 55 and 29 in the spectrum of **1a** and *m/e* 169, 154, 109, 55 and 29 in the spectrum of **1b**. Accurate mass measurements (Table 1) of the ions *m/e* 55 (*Obs.* 55·0183, *Calc* 55·0184) and *m/e* 29 (Obs. 29·0027, Calc 29·0027, 62·5%) show that they have the elemental compositions C_3H_3O and CHO respectively. It is interesting to note that the species *m/e* 169 and 109 were proposed as intermediates in the fragmentation of β-D-glucopyranose pentaacetate.[17] Metastable peaks (Table 2) were observed for the transitions *m/e* 172-*m/e* 142 and *m/e* 127-*m/e* 97 in **1a**, and for *m/e* 154-*m/e* 109 and *m/e* 169→*m/e* 109 in **1b**.

Formation of m/e 55 by direct cleavage of C-3—C-4 and C-5—O bonds in m/e 127 and m/e 97 on the one hand (Scheme 3), and in m/e 169 and m/e 109 on the other (Scheme 4), necessitates cleavage of a vinylic bond. It has been shown in a number of cases, that cleavage of such a bond is severely repressed or inoperative when compared to scission of the corresponding σ bond in saturated analogues.[18-20] Since ketene elimination is rarely seen in the fragmentation of saturated 6-ring ketones,[21] it seems unlikely that the loss of ketene observed in the α,β-unsaturated ketones involves direct scission of the vinyl bond. One probable pathway by which the ketene could be lost is illustrated in Scheme 5.



SCHEME 5

The mass spectrum of **2b** not surprisingly[6,22] is dominated by peaks arising from fragmentation of p-nitrobenzoic acid. Thus in comparison with **2a** the only recognizable fragment is m/e 127 observed in 9% relative intensity, representing the pyran ring residue.

From this study of the mass spectra of the enones **1a**, **1b** and **2a**, it is concluded that the main directions of fragmentation are (a) direct loss of the ring substituents retaining the pyranosidulose ring, and (b) the retro-Diels-Alder type cleavage. In the latter case, the primary fragments contain the substituents that were in the γ-position in the molecular ion, therefore, recognition of these ions could provide a means of allocating the position of the α,β-unsaturated keto chromophore in carbohydrate enones.

EXPERIMENTAL

The low resolution mass spectra of **1a**, **1b** and **2a** (Figs 1–3) were measured on a RMU 6A single-focusing instrument at an ionization potential of 70 eV, and 50 μA voltage. Samples were introduced through a direct inlet system at 200°. Spectra are plotted in terms of relative abundance, with the most intense peak (base peak) taken as 100%.

High resolution mass spectrum of **1a** was determined on a C.E.C. 21-110B double-focusing mass spectrometer. Samples were introduced through a direct inlet system. The high resolution mass spectrum was recorded on Ilford Q-2 photographic plates, which were developed in the usual way.

Acknowledgements—Financial support from the National Research Council and Bristol Laboratories is gratefully acknowledged. We express our gratitude to Dr. D. B. MacLean of McMaster University for making available to us the spectrometers, and for helpful suggestions regarding interpretation, and to Mr. F. A. Ramelan for recording the spectra.

REFERENCES

[1] P. A. Finan, R. I. Reed and W. Snedden, *Chem. Ind.* 1172 (1958)

[2] N. K. Kochetkov and O. S. Chizhov. *Advan. Carbohyd. Chem.* **21**, 39 (1966)

[3] K. Biemann, D. C. DeJongh and H. K. Schnoes. *J. Am. Chem. Soc.* **85**, 1763 (1963)

[4] I. A. Pearland and S. F. Darling, *Phytochemistry* **7**, 831 (1968)

[5a] D. C. DeJongh, T. Radford, J. D. Hribar, S. Hanessian, M. Bieber, G. Dawson and C. C. Sweeley, *J. Am. Chem. Soc.* **91**, 1728 (1969); [b] O. S. Chizhov, L. S. Golovkina and N. S. Wulfson, *Carbohyd. Res.* **6**, 138 (1968); [c] S. Karady and S. H. Pines, *Tetrahedron* **26**, 4527 (1970)

[6] R. J. Ferrier, N. Vethaviyasar, O. S. Chizhov, V. I. Kadentsev and B. M. Zolotarev. *Carbohyd. Res.* **13**, 269 (1970)

[7a] E. F. L. J. Anet. *Ibid.* **1**, 348 (1969); [b] K. Bock and C. Pedersen. *Tetrahedron Letters* 2983 (1969); [c] P. M. Collins, *Carbohyd. Res.* **11**, 125 (1969); [d] B. Fraser-Reid, A. McLean and E. W. Usherwood, *J. Am. Chem. Soc.* **91**, 5392 (1969); [e] B. Fraser-Reid, A. McLean, E. W. Usherwood and M. Yunker, *Canad. J. Chem.* **48**, 2877 (1970); [f] E. H. Williams, W. A. Szreck and J. K. N. Jones, *Carbohyd. Res.* **20**, 49 (1971); [g] O. Achmatowicz Jr., P. Bukowski, B. Szechner, Z. Zwiezchowska, and A. Zamojski, *Tetrahedron* **22**, 1973 (1971); [h] B. Fraser-Reid and N. L. Holder, *J.C.S. Chem. Comm.* 31 (1972); [i] N. L. Holder and B. Fraser-Reid, *Canad J. Chem.* in press

[8a] B. Fraser-Reid, N. L. Holder and M. Yunker, *J.C.S. Chem. Comm.* 1286 (1972); [b] P. M. Collins and B. Whitton, *Carbohyd. Res.* **21**, 487 (1972)

[9a] For general discussion and leading references, see H. Budzikiewicz, C. Djerassi and D. H. Williams, *Mass Spectrometry of Organic Compounds*, pp. 151–155. Holden-Day, San Francisco, Calif. (1967); [b] C. Fenselau, W. G. Dauben, G. W. Shaffer and N. D. Vietmeyer. *J. Am. Chem. Soc.* **91**, 112 (1969)

[10] S. H. Eggers, *Tetrahedron Letters*. 733 (1965)

[11] H. Egger, *Monatsh.* **97**, 1290 (1966)

[12] J. H. Bowie, *Austral. J. Chem.* **19**, 1619 (1966)

[13] Ref 9a, Pages 152–162

[14] H. Hiraoka, *Abstracts 166th ACS Nat'l Meeting.* Org # 46. Chicago, Illinois, Aug. 27–31, (1973)

[15a] S. Meyerson and J. D. McCollum (Edited by C. N. Reilly), *Advances in Analytical Chemistry and Instrumentation* Vol. 2, pp. 202–213. Interscience, New York (1963); [b] Ref 9a, p. 232

[16] R. Breslow, G. Ryan and J. T. Groves, *J. Am. Chem. Soc.* **92**, 988 (1970)

[17] H. Budzikiewicz, C. Djerassi and D. H. Williams, *Structure Elucidation of Natural Products by Mass Spectrometry*, Vol. 2, p. 206–207. Holden-Day, San Francisco, Calif. (1964)

[18] K. Biemann, *Mass Spectrometry Organic Chemical Applications*, pp. 98–99, 328–330. McGraw-Hill, N.Y. (1962)

[19] G. P. Hopp and D. W. Stewart, *J. Am. Chem. Soc.* **74**, 4404 (1952)

[20] L. Friedman and F. A. Long. *Ibid.* **75**, 2832 (1953)

[21] Ref 9a, pp. 64–91

[22] Ref 9a, pp. 219 and 515