Acta Chemica Scandinavica B 31 (1977) 671—678

The Electron Impact Mass Spectra of 4-Hydroxy and 4-Methoxy Derivatives of 5,6-Dihydro-2-pyrones

JØRGEN MØLLER, TORSTEN REFFSTRUP and PER M. BOLL

Department of Chemistry, Odense University, DK-5230 Odense M, Denmark

Dedicated to Professor K. A. Jensen on his 70th birthday

The electron impact mass spectra of twenty 6-substituted 5,6-dihydro-2-pyrones carrying either a 4-methoxy or a 4-hydroxy group have been recorded and discussed. The main fragmentation modes, inferred from metastable ion analyses (metastable refocusing and DADI technique) as well as from high resolution mass measurements, have been rationalized and compared. The decomposition depends strongly on the 6-substituent (alkyl, phenetyl, alkenyl, or cycloalkanespiro), and in most cases the 4-hydroxy substituted compounds give rise to more complex fragmentation patterns than the corresponding 4-methoxy derivatives. This is ascribed to contribution of the 4-oxo tautomers of the 4-hydroxy compounds.

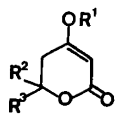
This paper reports on the electron-impact-induced fragmentation of a number of 6-substituted 4-hydroxy-5,6-dihydro-2-pyrones and their corresponding 4-methyl ethers. The behaviour of such compounds are of interest due to their structural similarity of the Kawa-lactones as well as to 2-pyrones and tetrahydro-2-pyrones (δ-lactones).

The mass spectra of substituted monocyclic 2-pyrones have been reported and reviewed.[1] An initial loss of the C^6-substituent together with expulsion of CO and the formation of substituted cyclopropenyl ions appear to be processes of general importance. Similarly, loss of the side chain from the molecular ions is a characteristic behaviour of tetrahydro-2-pyrones. No systematic study of the fragmentation of simple dihydro-2-pyrones has been reported so far, although a series of Kawa-lactones, some being dihydro-2-pyrones and others 2-pyrones, has been investigated in some detail.[2] It appears that the fragmentation upon electron impact depends highly on the presence of a styrylic double bond.

This investigation is centered around C^6-substituted 5,6-dihydro-2-pyrones, in which the C^6-substituents are characterized as being either alkyl/aralkyl, cycloalkanespiro, or *trans*-1-alkenyl.

6-Alkyl/aralkyl derivatives of 5,6-dihydro-2-pyrones. The compounds given in Table 1 have been investigated. Representative mass spectra are given in Fig. 1 together with the major decomposition modes. These are all verified by exact mass measurements and by metastable ions (metastable refocusing as well as the DADI technique have been applied).

Table 1. 6-Alkyl-aralkyl derivatives.



	R^1	R^2	R^3
1a	H	H	C_5H_{11}
1b	CH_3	H	C_5H_{11}
2a	H	C_2H_5	C_2H_5
2b	CH_3	C_2H_5	C_2H_5
3a	H	H	$CH_2CH_2C_6H_5$
3b	CH_3	H	$CH_2CH_2C_6H_5$

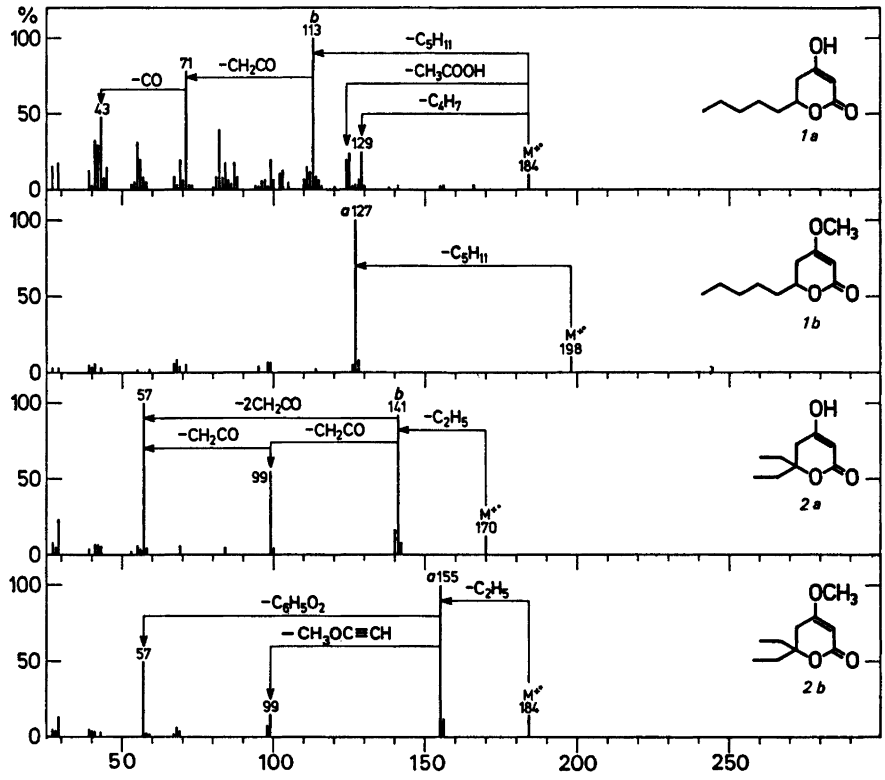
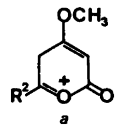


Fig. 1. Mass spectra of *1a*, *1b*, *2a* and *2b* recorded at 80, 15, 50, and 15 °C, respectively.

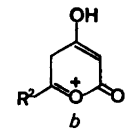
The typical α-cleavage reaction of 2-pyrones and tetrahydro-2-pyrones with loss of the C^6 side chain is also found to be an important process for the 6-mono- and 6,6-disubstituted dihydro-2-pyrones. For the 4-methoxy-substituted compounds, type b, this reaction is predominant and the corresponding $[M-R^3]^+$ ion,

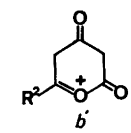


$R^3=H$: *m/e* 127; $R^3=C_2H_5$: *m/e* 155

a, possesses a considerable stability. It is carrying 42 % of the total ion current ($\sum_{25}$) of *1b* and in the case of *3b* it has a higher abundance than the tropylium ion (*m/e* 91).

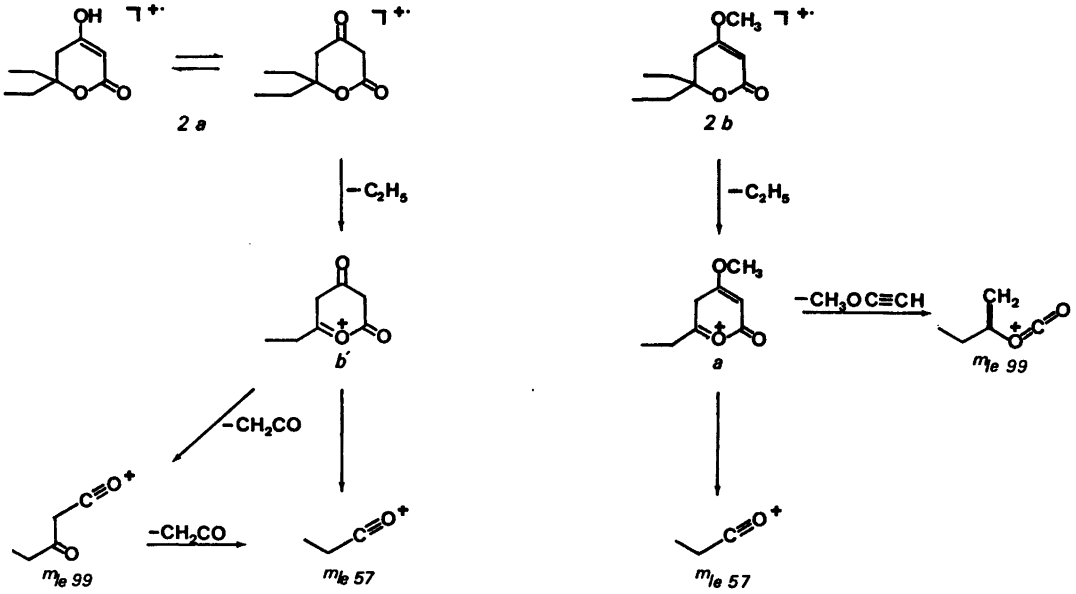
The corresponding ion, *b*, formed from the 4-hydroxy-substituted compounds (*1a*, *2b*, and *3a*) appears to be less stable than *a*. It has an





$R^3=H$: *m/e* 113; $R^3=C_2H_5$: *m/e* 141

abundance of 12.3 % of $\sum_{25}$ in *1a*. In the spectrum of *3a* the tropylium ion is the base peak and ion *a* amounts to a relative intensity of 7 % only. One reason for the observed decrease in stability of the $[M-R^3]^+$ ion may be that its structure preferentially corresponds to *b'*, as the further decomposition is elimination of $CH_2=CO$. In *1a* and *3a* this process is followed by a CO loss, in *2a* by another CH_2CO loss. In *2a* the $[b'-CH_2CO]^+$ ion appears at *m/e* 99. The spectrum of *2b* also exhibit a *m/e* 99 ion which corresponds to the loss of $CH_3OC{\equiv}CH$ from *a*, but in this case further loss of ketene cannot be detected. The $[C_2H_5CO]^+$ ion at *m/e* 57 is found only to have ion *a* as precursor.



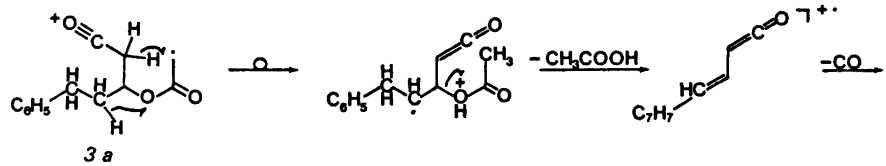
Scheme 1.

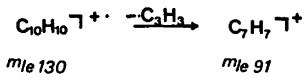
This latter process corresponds to a *retro*-Diels-Alder decomposition with charge retention on the C_2H_5CO species. Reversed charge retention leads to formation of the *m/e* 98 ion being an important key-fragment in the fragmentation of the 6-cycloalkanespiro and the 6-(*trans*-1-alkenyl) derivatives discussed below.

Possible structures for the various ions in question are shown in the rationale, Scheme 1.

The type a derivatives here discussed have been shown by NMR to exist more or less enolized depending on the solvent. In dimethyl sulfoxide they are fully enolized, but in less polar solvents the enolization is diminished.[3] A keto-form of *1a* and *3a* is supported by the formation of the $[M-C_2H_4O_2]^{+\cdot}$ ions. Such ions may according to the suggested rationale, Scheme 2 for *3a*, be generated by a double hydrogen rearrangement in the ring-opened molecular ion of the keto form with subsequent elimination of a molecule of acetic acid. In addition a stepwise formation of the *m/e* 158 ion is indicated to take place by elimination of H_2O and CH_2CO.

6-Cycloalkanespiro derivatives of 5,6-dihydro-2-pyrones. The compounds given in Table 2 have been investigated. As representative for this series the mass spectra of *6a* and *6b* are shown in Fig. 2.





Scheme 2.

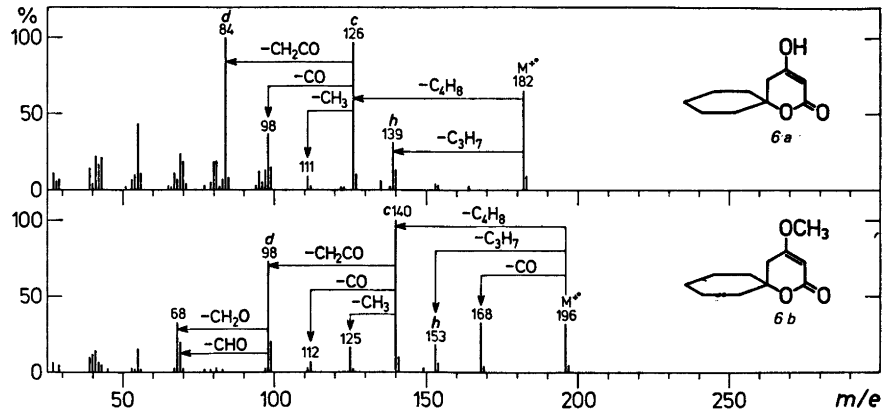


Fig. 2. Mass spectra of *6a* and *6b* recorded at 70 and 40 °C, respectively.

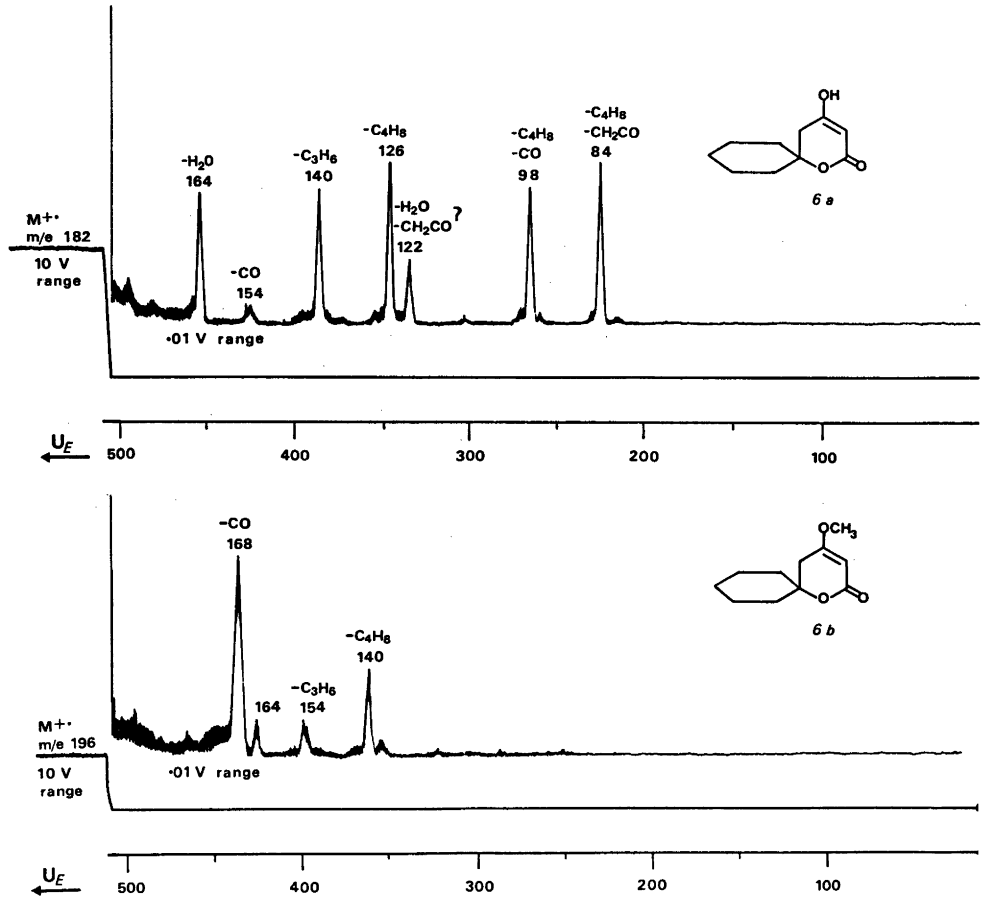
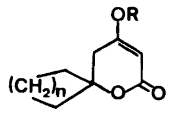


Fig. 3. DADI spectra [4] of *6a* and *6b*, showing the metastable transitions of the molecular ions. The calculated masses of the daughter ions – all formed directly from the molecular ions – as well as the compositions of the eliminated neutrals are indicated.

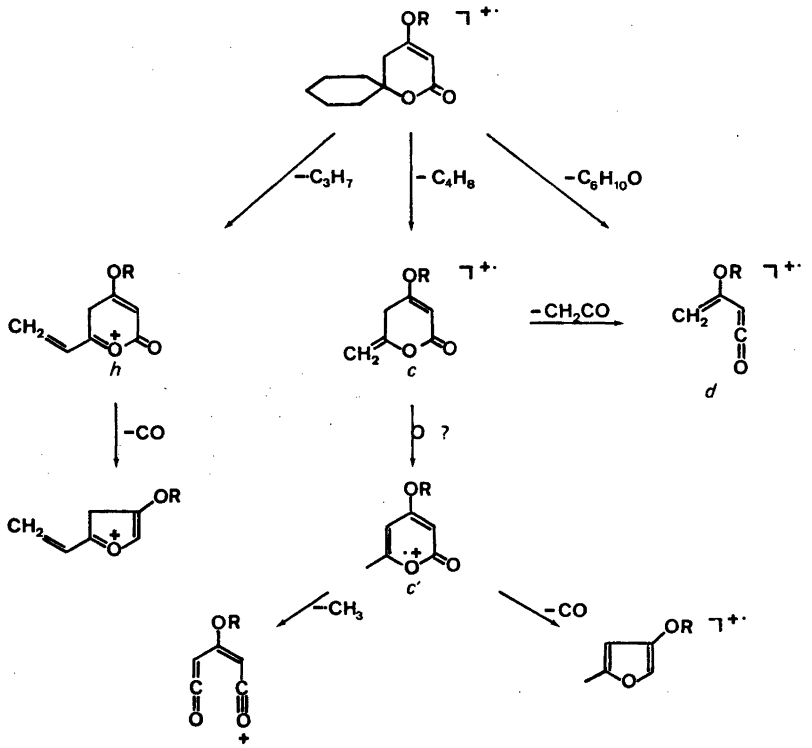
Table 2. 6-Cycloalkanespiro derivatives.



	R	*n*
4a	H	1
4b	CH_3	1
5a	H	2
5b	CH_3	2
6a	H	3
6b	CH_3	3
7a	H	4
7b	CH_3	4

The fragmentation patterns of this series are dominated by odd electron ions most of which are formed in several competing decompositions as demonstrated by the presence of numerous metastable ions. The DADI spectra of the molecular ions of *6a* and *6b* are given in Fig. 3, suggesting concerted losses of stable molecules such as cycloalkanes, CO, and CH_2CO. The varying abundances of the metastable ions in the DADI spectra [4] obtained from the molecular ions in this series suggest that the degree to which these processes are followed changes considerably. However, it appears that only few of these reactions contribute significantly to the ion abundances since the general appearance of the mass spectra is very much alike.

An important ion in all cases is brought forth by decomposition of the cycloalkanespiro ring, probably giving rise to elimination of a cycloalkane (ethene in *4a* and *4b*) as shown in the rationale, Scheme 3, for *6a* and *6b*. The resulting ion is formulated as *c*, from which the observed loss of CH_2CO, yielding *d*, would be a likely process. However, it is possible that the rearrangement $c \rightarrow c'$ occurs also to some extent. The mass spectrum of 4-methoxy-6-methyl-2-pyrone [5] exhibits abundant $[M-CH_3]^+$ and $[M-CO]^{+\cdot}$ ions, whereas elimination of CH_2CO from the molecular ion does not take place.



Scheme 3.

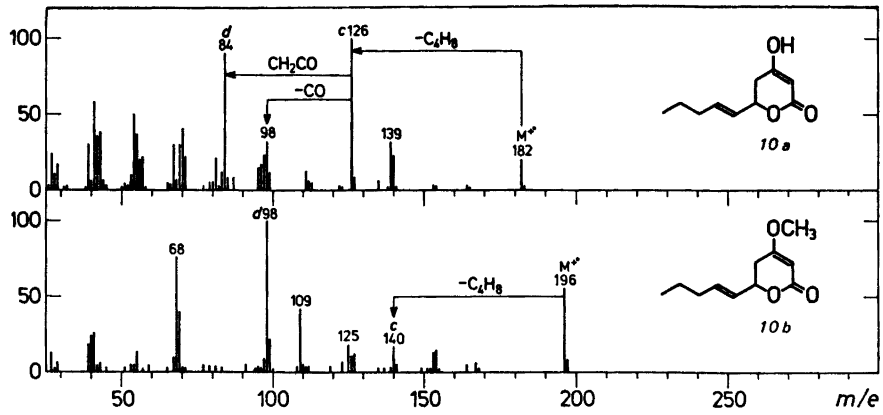


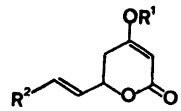
Fig. 4. Mass spectra of *10a* and *10b* recorded at 20 and 25 °C, respectively.

Ion *d* is additionally formed directly from the molecular ion, either by elimination of cyclohexanone (a *retro*-aldol reaction) or by concerted losses of cyclobutane and ketene. In the type b compounds ion *d* (*m/e* 98) eliminates CHO and CH_2O yielding *m/e* 69 and *m/e* 68.

The direct elimination of an alkyl group (C_3H_7 in Scheme 3), requiring a hydrogen rearrangement of the molecular ion, appears to be a general process (except for compounds *4a* and *4b*), yielding an even electron ion of relative high abundance, formulated as *h*. Also the initial CO loss is an often occurring process. However, the corresponding $[M-CO]^{+\cdot}$ peak appears with varying abundances and is insignificant in several spectra.

6-(trans-1-Alkenyl) derivatives of 5,6-dihydro-2-pyrones. The compounds given in Table 3 have been investigated. The mass spectra of *10a* and *10b* are given in Fig. 4.

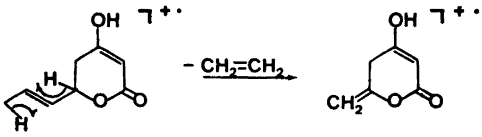
Table 3. 6-(*trans*-1-Alkenyl) derivatives.



	R^1	R^2
8a	H	CH_3
8b	CH_3	CH_3
9a	H	C_2H_5
9b	CH_3	C_2H_5
10a	H	C_3H_7
10b	CH_3	C_3H_7

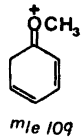
Introduction of the double bond has a marked effect upon the electron-impact-induced fragmentation, and inhibits completely formation of the pyronium ion by elimination of the C^6 side chain which is the most characteristic process of the compounds with saturated substituents. Instead a formal breakage of the double bond takes place with charge retention preferentially at the pyrone ring. This process may be rationalized if it is anticipated that the double bond introduces a new site for charge localization initiating a hydrogen rearrangement. This is illustrated in the mass spectrum of kawain having a styryl substituent at the C^6 position. In this case fission of the double bond accompanied by rearrangement of one hydrogen atom has been reported.[3] The origin of this hydrogen is C^6 and C^5 (1:1), as demonstrated by labelling experiments,[6] and the resulting ion is the highly stable tropylium ion. Formation of similar stable ions is not possible in the decomposition of compounds *8* to *10* all having aliphatic substituents. However, it is anticipated that the double bond also in these cases initiates hydrogen rearrangement, and subsequent rupture of that bond may then lead to the formation of stable neutral molecules (ethene, propene, and butene, respectively). The resulting ion, which constitutes the base peak (at *m/e* 126) in *8a*, *9a*, and *10a* is probably identical to the corresponding ion, *c*, in the spectra of the cycloalkanespiro compounds (the DADI spectra of *m/e* 126 in *10a*

and *6a*, showing degradation to *m/e* 98 and *m/e* 84, are virtually identical). To obtain this structure, rearrangement of two hydrogen atoms is required. Although other modes are possible and random rearrangements cannot be excluded a possible origin of these hydrogen atoms may be:



In *8b*, *9b*, and *10b* the alkene elimination is less prevalent and the corresponding ion (*m/e* 140) appears with significantly lower abundance. This may suggest that the double bond is a less favoured site for charge localization and thus restrains the possibility for hydrogen rearrangements. Such changes in charge distribution in the molecular ions can hardly be attributed to differences induced by the methoxy group as compared to the hydroxy group, but may be rationalized if the keto-form of the type a compounds is anticipated.

Characteristic for the type b compounds is the presence of the *m/e* 109 ion (C_7H_9O). Metastable data have revealed that besides a direct formation from the molecular ions this ion is also generated in a two-step process *via* the $[M-CO_2]^{+\cdot}$ ion. This indicates that loss of CO_2 takes place in all three cases although the abundance of the $[M-CO_2]^{+\cdot}$ ion is insignificant in *9b* and *10b*. A possible structure for the *m/e* 109 ion is



m/e 109

The presence of this ion as well as the relative low abundance of *m/e* 140 constitutes the major general difference between the spectra of type b compounds and those of the corresponding cycloalkanespiro isomers. Similar diagnostic differences are not encountered for corresponding 4-hydroxy substituted compounds.

SUMMARY

The fragmentation upon electron impact of 5,6-dihydro-2-pyrones is found to depend strongly on the nature of the 6-substituent. In most cases the fragmentation pattern for the 4-hydroxy derivatives (a) is more differentiated than for the corresponding 4-methoxy analogues (b). This is ascribed to the contribution of a 4-oxo form of a.

(a) 6-Alkyl derivatives show the general loss of the 6-substituent yielding the important pyronium ion *a* (with 4-methoxy) or *b* (with 4-hydroxy) in agreement with the behaviour of similarly substituted 2-pyrones and tetrahydro-2-pyrones. The 4-hydroxy group diminishes considerably the relative stability of *b* as compared to *a*.

(b) 6-Cycloalkanespiro derivatives exhibit a prevalent pyronium ion *c*, including a CH_2 group from the cycloalkanespiro ring, probably formed by elimination of a cycloalkane.

(c) 6-(1-Alkenyl) derivatives exhibit spectra resembling considerably those of the isomeric cycloalkanespiro compounds. This makes diagnostic differentiation between type a compounds of the two series ambigous. The formation of ion *c*, corresponding to formal rupture of the double bond in the side chain, is attributed to hydrogen rearrangements to the double bond and subsequent elimination of an alkene.

EXPERIMENTAL

Mass spectra were obtained on a Varian MAT 311A mass spectrometer using the direct sample insertion system with the lowest feasible sample temperature and ionization by electron impact (70 eV). Peaks corresponding to doubly charged ions appearing at half mass numbers as well as peaks of abundance lower than 2 % were omitted from the spectra shown. All the decompositions given are supported by appropriate metastable transitions detected by metastable refocusing or by the DADI technique.

Microanalyses were carried out at the Microanalytical Department of the University of Copenhagen by Mr. Preben Hansen. Melting points were determined on a Büchi melting point apparatus. ^1H NMR spectra were recorded on a Jeol JNM-PMX60 NMR spectrometer; chemical shifts are given in ppm relative to TMS.

The 4-hydroxy-5,6-dihydro-2-pyrones investigated were all prepared according to a

procedure earlier described.[7] In the following the aldehyde or ketone used for preparation is mentioned, and data for the primarily obtained compounds are given in parenthesis. For purification all compounds were triturated with ether and were all shown to be analytically pure by elemental analysis (C, H).

4-Hydroxy-6-pentyl-5,6-dihydro-2-pyrone (1a). Hexanal (yield 86 %, m.p. 65–70 °C), m.p. 72–74 °C. NMR (DMSO-d_6): 0.87 (t, 3 H), 1.33 (m, 8 H), 2.30 (s, 1 H), 2.46 (d, 1 H, J 3 Hz), *ca.* 4.2 (m, 1 H), 5.28 (s, 1 H).

4-Hydroxy-6,6-diethyl-5,6-dihydro-2-pyrone (2a). 3-Pentanone (yield 70 %, m.p. 82–93 °C), m.p. 98–100 °C. NMR (DMSO-d_6): 0.85 (d of t, 6 H), 1.65 (d of q, 4 H), 2.42 (s, 2 H), 4.92 (s, 1 H).

4-Hydroxy-6-cyclobutanespiro-5,6-dihydro-2-pyrone (4a). Cyclobutanone (yield 63 %, m.p. 110–116 °C), m.p. 125–129 °C. NMR (DMSO-d_6): 1.4–2.4 (complex, 6 H), 2.64 (s, 2 H), 4.94 (s, 1 H).

4-Hydroxy-6-cyclopentanespiro-5,6-dihydro-2-pyrone (5a). Cyclopentanone (yield 60 %, m.p. 95–125 °C), m.p. 131–133 °C. NMR (DMSO-d_6): 1.73 (s broad, 8 H), 2.56 (s, 2 H), 4.93 (s, 1 H).

4-Hydroxy-6-cyclohexanespiro-5,6-dihydro-2-pyrone (6a). Cyclohexanone (yield 60 %, m.p. 98–105 °C), m.p. 117–121 °C. NMR (DMSO-d_6): 1.2–2.0 (complex, 10 H), 2.45 (s, 2 H), 4.97 (s, 1 H).

4-Hydroxy-6-cyclooctanespiro-5,6-dihydro-2-pyrone (7a). Cyclooctanone (yield 45 % m.p. 128–130 °C), m.p. 129–130.5 °C. NMR (DMSO-d_6): 1.1–2.1 (broad, 14 H), 2.43 (s, 2 H), 4.42 (s, 1 H).

*4-Hydroxy-6-(*trans*-1-butenyl)-5,6-dihydro-2-pyrone* (9a). *trans*-2-Pentenal (yield 52 %, m.p. 90–92 °C), NMR (DMSO-d_6): 0.97 (t, 3 H J Hz), 2.04 (q, 2 H J 1 and 7 Hz), 2.40 (s, 1 H), 2.54 (d, 1 H J 2 Hz), 4.6–5.1 (m, 1 H), 4.95 (s, 1 H), 5.58 (q, 1 H J 5 and 15 Hz), 5.90 (q, 1 H J 5 and 15 Hz).

The preparation of compounds *3a*, *8a*, and *10a* has been described earlier.[7]

From the compounds *1a* to *10a* the corresponding 4-methoxy derivatives were prepared.

On reaction with dimethyl sulfate and potassium carbonate in acetone at room temperature [8] followed by purification on preparative TLC (silica gel, ether as eluent), the following compounds, all showing satisfactory NMR spectra, were obtained.

4-Methoxy-6-pentyl-5,6-dihydro-2-pyrone (1b). R_F 0.56, oil (Found for M+: 198.1250. Calc. for $C_{11}H_{16}O_3$: 198.1256).

4-Methoxy-6,6-diethyl-5,6-dihydro-2-pyrone (2b). R_F 0.62, oil (Found for M+: 184.1100. Calc. for $C_{10}H_{16}O_3$: 184.1099).

4-Methoxy-6-cyclobutanespiro-5,6-dihydro-2-pyrone (4b). R_F 0.50, crystals of m.p. 53–55 °C (Found for M+: 168.0782. Calc. for $C_9H_{12}O_3$: 168.0786).

4-Methoxy-6-cyclopentanespiro-5,6-dihydro-2-pyrone (5b). R_F 0.70, oil (Found for M+: 182.0943. Calc. for $C_{10}H_{14}O_3$: 182.0943).

4-Methoxy-6-cyclohexanespiro-5,6-dihydro-2-pyrone (6b). R_F 0.53, crystals of m.p. 74–77 °C (Found for M+: 196.1082. Calc. for $C_{11}H_{16}O_3$: 196.1099).

4-Methoxy-6-cyclooctanespiro-5,6-dihydro-2-pyrone (7b). R_F 0.70, viscous oil (Found for M+: 224.1410. Calc. for $C_{13}H_{20}O_3$: 224.1412).

The preparation of compounds *3b* and *8b* has been described earlier.[7]

4-Hydroxy-5,6-dihydro-2-pyrones gave when reacted with ethereal diazomethane the 4-methoxy-5,6-dihydro-2-pyrones as well as the 2-methoxy-5,6-dihydro-4-pyrones. The isomeric pyrones were easily separated on preparative TLC (silica gel, ether as eluent), the 5,6-dihydro-4-pyrones having the lower R_F-value. In this manner *9b* and *10b*, both giving satisfactory NMR spectra, were obtained.

*4-Methoxy-6-(*trans*-1-butenyl)-5,6-dihydro-2-pyrone* (9b). R_F 0.59, oil (Found for M+: 182.0941. Calc. for $C_{10}H_{14}O_3$: 182.0943).

*4-Methoxy-6-(*trans*-1-pentenyl)-5,6-dihydro-2-pyrone* (10b). R_F 0.62, oil (Found for M+: 196.1101. Calc. for $C_{11}H_{16}O_3$: 196.1099).

Acknowledgement. The authors are indebted to the Danish Natural Science Research Council for the MS facilities (grant No. 511-3809).

REFERENCES

1. Porter, Q. N. and Baldas, J. *Mass Spectrometry of Heterocyclic Compounds*, Wiley-Interscience, New York 1971, Chapters 5 and 6.
2. Pailer, M., Schaden, G. and Hänsel, R. *Monatsh. Chem. 96* (1965) 1842.
3. Reffstrup, T. and Boll, P. M. *Unpublished results.*
4. Schlunegger, U. P. *Angew. Chem. Int. Ed. Engl. 14* (1975) 679.
5. Nakata, H., Hirata, Y. and Tatematsu, A. *Tetrahedron Lett. 2* (1965) 123.
6. Achenbach, H., Wörth, J. and Raffelsberger, B. *Org. Mass Spectrom. 10* (1975) 850.
7. Reffstrup, T. and Boll, P. M. *Acta Chem. Scand. B 30* (1976) 613.
8. Seebach, D. and Meyer, H. *Ger. Offenlegungsschrift* P 2400429.3 of 17.7.75.

Received April 18, 1977.