spectra of the methyl derivatives. Considering that these peaks differ by 2 amu, it may be supposed that the substituent attached to the nitrogen atom (CH@-R) is retained in the fragments. Consequently, these fragments are formed as a result of detachment of a methyl group from ion e ($[M - 2CO]^{+\cdot}$).

## EXPERIMENTAL

Compounds I-IX were obtained by a known method [6] and were purified as described in [1].

The mass spectra were recorded with an MKh-1303 spectrometer equipped with a glass system for direct introduction of the samples. The vaporization temperature in the inlet tube was 95-120°, the ionization chamber temperature was 150°, the ionizing voltage was 70 V, and the emission current was 1.0 mA. The reproducibility of the mass spectra during recording over a long time (14-60 days) was 8-10 rel.%.

## LITERATURE CITED


1. Kh. Sh. Khariton, G. I. Zhungietu, M. A. Rekhter, B. T. Oloi, and N. I. Chmykhova, Khim. Geterotsikl. Soedin., No. 7, 957 (1975).
2. M. Butcher, Org. Mass. Spectrom., 5, 759 (1971).
3. J. A. Ballantine, R. G. Fenwick, and M. Alam, Org. Mass. Spectrom., 1, 467 (1968).
4. C. Bogentoft and B. Danielsson, Acta Pharm. Suecica, 7, 257 (1969).
5. C. Bogentoft, Org. Mass Spectrom., 3, 1527 (1970).
6. G. Tacconi, P. P. Righetti, and G. Desimoni, J. Prakt. Chem., 315, 339 (1970).


# MASS SPECTROMETRIC STUDY OF ISATINS.

# III.* ISATIN AND N-METHYLISATIN KETALS


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UDC 543.51+547.756



In contrast to isatin and N-methylisatin, their ethylene-, propylene-, and 2,3-butyleneketals undergo fragmentation via several pathways. In addition to the principal fragmentation pathway — successive loss by the molecular ion ($M^+$) of a CO group and a dioxolane ring or its fragment, the $M^+$ ions of the ketals are also fragmented with elimination of a dioxolane fragment or the substituent attached to the nitrogen atom and, subsequently, a fragment of the dioxolane ring. The fragmentations of some of the fragment ions were investigated by means of the mass spectra of N-trideuteromethyl analogs.


In the course of a systematic study of the mechanism of the dissociative ionization of various isatin derivatives [1, 2], we studied the mass spectrometric behavior of ethylene-, propylene-, and 2,3-butyleneketals of isatin and N-methylisatin (A).

The selectivities ($S_{1/2}$) of the fragmentation of isatin β-ketals II and II and N-methylisatin β-ketals III-V differ considerably. The $S_{1/2}$ values in the mass spectra of I and II range from two to three and those of III-V range from six to seven, whereas $S_{1/2}$ is two in the mass spectrum of isatin and three in the mass spectrum of N-methylisatin [1]. Consequently, replacement of the β-keto group by a dioxolane ring has a considerably greater effect on the character of the fragmentation of N-methylisatin derivatives than on that of isatin derivatives.

*See [2] for communication II.


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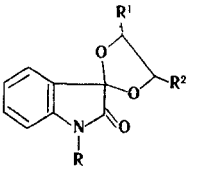


A

I $R=R^1=R^2=H$; II $R=H$, $R^1=R^2=CH_3$; III $R=CH_3$, $R^1=R^2=H$; IV $R=R^1=CH_3$, $R^2=H$; V $R=R^1=R^2=CH_3$; VI $R=CD_3$, $R^1=R^2=H$; VII $R=CD_3$, $R^1=R^2=CH_3$

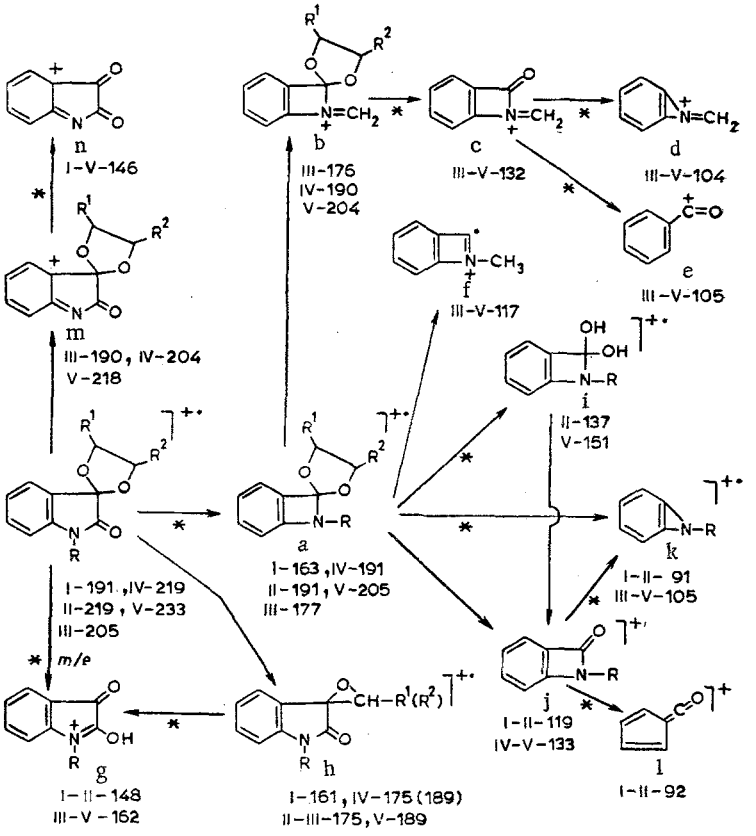
The stabilities ($W_M$) of the molecular ions of the N-methylisatin β-ketals are higher by a factor of approximately two than the stabilities of the corresponding isatin derivatives. The $W_M$ values of III-V are 0.08, 0.05, and 0.04, as compared with 0.04 and 0.02, respectively, for I and II. In the series of ketals, $W_M$ decreases on passing from the ethyleneketals to the 2,3-butyleneketals, and it is lower in all cases than the values for isatin (0.2) and N-methylisatin (0.21).

In contrast to isatin and N-methylisatin [1-3], the molecular ions of I-V undergo fragmentation via several pathways. The principal pathways of mass spectrometric fragmentation of the investigated ketals are given in the general scheme below. The fragmentation pathways confirmed by the observed metastable transitions are designated by asterisks. The molecular ions ($M^+$) of I and II successively eliminate a CO molecule, an $R^1CHCHR^2O$ dioxolane fragment, and an HCN molecule ($M \rightarrow a \rightarrow j \rightarrow l$). Fragmentation via the $M \rightarrow a \rightarrow j$ pathway is also characteristic for the N-methylisatin β-ketals, but, whereas 48 and 52%, respectively, of the total ion current goes into the fraction of peaks corresponding to the $M^+$, a, and j ions in the mass spectra of I and II, 21, 21, and 25% of the total ion current, respectively, are involved in the case of III-V. This means that replacement of the hydrogen atom attached to nitrogen by a methyl group has a substantial effect on the character of the fragmentation and the stabilities of the resulting ions. It should be noted that the ratios of the intensities of the peaks of the $[M - CO]^+$ (a) and ($M^+$) ions are considerably higher in the case of the ketals of the corresponding isatins than in the case of the isatins themselves [1-3]. The $I_{M-CO}/I_M$ values of I and II are 6.6 and 11.0 (as compared with 3.2 for isatin), whereas the values for III-V are 1.5, 2.5, and 3.7, respectively (as compared with 0.3 for N-methylisatin). These data make it possible to conclude that the dioxolane ring has a stronger stabilizing effect on ion a than does a keto group on the analogous ion in the mass spectra of isatin and N-methyl isatin [1].

Depending on substituent R, ion a may undergo fragmentation via several pathways. A common pathway for all I-V is detachment of a dioxolane ring from ion a to give ion k; this is confirmed by the metastable peaks. In addition, when $R = CH_3$, as a result of β cleavage ion a loses a hydrogen atom (a deuterium atom when $R = CD_3$) to give ion b. The relative intensity of the peak of ion b decreases in the order III > IV > V. The number of methyl groups in the dioxolane ring increases in the same order.

TABLE 1. Mass Spectra of I-V

| Compound | m/e values (rel. intensity, %) |
|---|---|
| I | 191 (15), 163 (100), 161 (3), 148 (2), 146 (3,5), 119 (64), 104(7), 103 (4), 93 (4), 92 (27), 91 (8), 90 (11), 77 (4), 76 (10), 75 (3,5), 65 (5), 64 (14), 63 (12), 62 (3), 52 (6), 51 (4), 50 (9) |
| II | 219 (5), 191 (54), 175 (8), 148 (11), 146 (4), 137 (4), 119 (100), 104 (3), 103 (2), 92 (18), 91 (4), 90 (6), 77 (2), 76 (5,5), 75 (2), 65 (3), 64 (7), 63 (4), 52 (1,5), 51 (1,5), 50 (3,5) |
| III | 205 (64), 190 (0,5), 177 (100), 176 (61), 175 (5), ,162 (5,5), 146 (17), 133 (5), 132 (32), 117 (7), 105 (44), 104 (37), 92 (8), 91 (6), 90 (17), 78 (19), 77 (28), 76 (14), 65 (4), 64 (11), 63 (13), 62 (5), 52 (5), 51 (16), 50 (14) |
| IV | 219 (39), 204 (0,2), 191 (97), 190 (19), 189 (3), 175 (5), 162 (21), 146 (16), 134 (17), 133 (23), 132 (56), 117 (7), 105 (100), 104 (53), 92 (9), 91 (6), 90 (16), 78 (23), 77 (33), 76 (14), 65 (4), 64 (9), 63 (12), 52 (4), 51 (15), 50 (11) |
| V | 233 (27), 218 (0.05), 205 (100), 204 (16), 189 (14), 162 (37), 151 (9), 146 (11), 133 (31), 132 (27), 117 (7), 105 (92), 104 (42), 92 (6), 91 (4), 90 (13), 78 (18), 77 (22), 76 (9), 65 (3), 64 (6), 63 (8), 52 (2), 51 (9), 50 (7) |




Ion b undergoes subsequent fragmentation with the loss of a fragment of the dioxolane ring (similar to pathway a → j) to give ion c, which in turn may lose both a CO group (c → d) and an HCN molecule with migration of a hydrogen (deuterium) atom to the aromatic ring (c → e).

The 105 peak* in the mass spectra of III-V should be a composite peak due to the contribution of the current of ions e and k. Peaks of ions with m/e 106 (ions e and d, respectively, with one and two deuterium atoms) and 108 (ion k with three deuterium atoms), the intensity ratios of which differ only slightly from the intensity ratios of the peaks of their analogs in the mass spectra of the unlabeled compounds, are recorded in the mass spectra of N-trideuteromethyl derivatives VI and VII. This fact provides a basis for the assertion that ion c primarily undergoes fragmentation with the ejection of CO and that fragmentation via the c → e pathway is less characteristic. Consequently, the ion with m/e 105 reflects mainly the fraction of ion k, which in the case of II, IV, and V is also formed by fragmentation via pathway a → j → k.

The mass spectra of III-V also contain peaks with m/e 117 (120 in the mass spectra of deutero derivatives VI and VII), which may be formed as a result of cleavage of two of the C-O bonds of the dioxolane ring (a → f).

The specific peaks of ions observed only in the mass spectra of 2,3-butyleneketals — 137 (II), 151 (V), and 154 (VII) — must be separately noted. Their formation is most likely connected with detachment of a butadiene molecule from ion a with simultaneous migration of two hydrogen atoms to the oxygen atoms of the dioxolane ring (a → i). Ion j is formed by splitting out of a water molecule from ion i. The subsequent fragmentation of ions d, e, and k is characteristic for all of the isatins and has been previously described [1, 3, 4].

In addition to the above-described principal fragmentation pathway, losses of a dioxolane ring fragment to give ion h are also characteristic; in this case two types of h ions are observed in the mass spectrum of IV (where $R^1 \neq R^2$): 175, corresponding to detachment of an acetaldehyde molecule from the molecular ion (the more intense peak), and 189, corresponding to detachment of a formaldehyde molecule (the less intense peak). Ion h may undergo further fragmentation to give ion g; this is confirmed by the metastable peaks in the mass spectra of

*Here and subsequently, the numbers characterizing the ion are the ratio of the mass of the ion to its charge (m/e).

V and VII. Ion g is also formed as a result of detachment of a dioxolane fragment from the molecular ion with migration of a hydrogen atom to the charged portion of the molecule. This fragmentation pathway was confirmed by the metastable peaks in the mass spectra of all of the investigated compounds. The most probable structure of ion g is presented in the scheme above.

The mechanism of the formation of ion n is of particular interest. Low-intensity (up to 0.5% of the maximum) peaks of $[M-R]^+$ (m) ions and metastable peaks that indicate further fragmentation of ion m to give ion n are observed in the mass spectra of I-VII. In addition, the peaks of ions m and n in the mass spectra of N-trideuteromethyl derivatives VI and VII have the same m/e values as in the mass spectra of the undeuterated compounds. Consequently, the formation of ion n occurs through detachment of the substituent attached to the nitrogen atom with subsequent ejection of a dioxolane fragment ($M \rightarrow m \rightarrow n$).

Thus the fragmentation of isatin β-ketals to a certain extent repeats the fragmentation of the corresponding isatins, but the presence of a dioxolane ring in the molecules gives rise to a number of specific pathways of fragmentation under electron impact; this can be used for the mass spectrometric identification of these compounds.

## EXPERIMENTAL

Compounds I-V were obtained by condensation of isatin and N-methylisatin with ethylene, propylene, and 2,3-butylene glycols (with p-toluenesulfonic acid as the catalyst) and were purified by column chromatography on silica gel.* The individuality of the compounds was monitored by thin-layer chromatography on Silufol in a benzene–acetone system (3.5:1). The melting points of I-V, respectively, were 134-136, 123-124, 93, 100, and 63°. The mass spectra were recorded with an MKh-1303 spectrometer. The conditions for recording of the spectra and the reproducibility of the mass spectra were as described in [1, 2].

## LITERATURE CITED


1. Kh. Sh. Khariton, G. I. Zhungietu, M. A. Rekhter, B. T. Oloi, and N. I. Chmykhova, Khim. Geterotsikl. Soedin., No. 7, 957 (1975).
2. G. I. Zhungietu, N. I. Chmykhova, M. A. Rekhter, Kh. Sh. Khariton, B. T. Oloi, and N.P. Dormidontova, Khim. Geterotsikl. Soedin., No. 5, 629 (1977).
3. J. A. Ballantine, R. J. Fenwick, and M. Alam, Org. Mass. Spectrom., 1, 467 (1968).
4. K. Yamada, T. Konakahara, and H. Iida, Kogyo Kagaku Zasshi, 73, 980 (1970); Chem. Abstr., 74, 23,628 (1971).


*The results of the elementary analyses were in agreement with the calculated values.