

MASS-SPECTROMETER STUDY OF HETEROCYCLIC COMPOUNDS

IV. Study of Modes of Fragmentation of Formyl- and Carbalkoxyindoles*

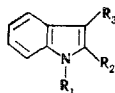
N. S. Vul'fson, V. I. Zaretskii, A. V. Kisin, N. N. Suvorov, and Zh. D. Ovchinnikova

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 3, No. 3, pp. 502-506, 1957

UDC 543.51+547.757

A study is made of mass-spectra of aldehydes and carboxylic acid esters of indoles. It is shown that the mass-spectra can be used to differentiate α -carbonyl derivatives of indole from the β -analogs.

Of recent years the mass-spectrometer has been widely used to determine the structures of a large number of alkaloids with molecules containing the indole system [4]. However, with the exception of the work of Beynon and Williams [5] on alkylindoles, the literature does not contain any systematic mass-spectrometer work on the simplest indole derivatives. Using as examples β -indole aldehyde (I), esters of β -indole (II) and α -indole carboxylic acids (III, IV) and a number of analogs of these (V-XII), it was decided to study the mode of splitting of compounds of this class under electron impact.



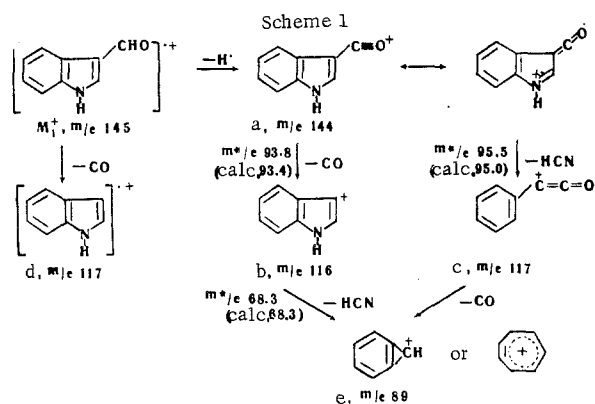
| | R ₁ | R ₂ | R ₃ |
|-----|-----------------|----------------------------------|--------------------|
| I | H | H | CHO |
| II | H | H | COOCH ₃ |
| III | H | COOCH ₃ | H |
| IV | H | COOC ₂ H ₅ | H |
| V | CH ₃ | COOC ₂ H ₅ | H |
| VI | CH ₃ | COOH | H |

| | R ₁ | R ₂ | R ₃ |
|------|-------------------|----------------------------------|----------------------------|
| VII | H | COOCH ₃ | CHO |
| VIII | H | COOC ₂ H ₅ | CHO |
| IX | CH ₃ | COOC ₂ H ₅ | CHO |
| X | H | H | COCH ₃ |
| XI | COCH ₃ | H | COCH ₃ |
| XII | H | H | COCH(OH)CH ₂ OH |

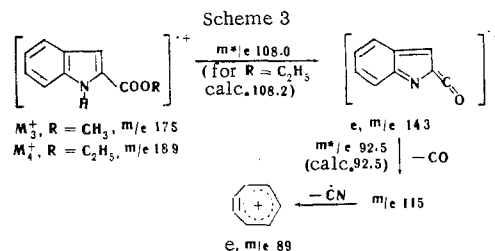
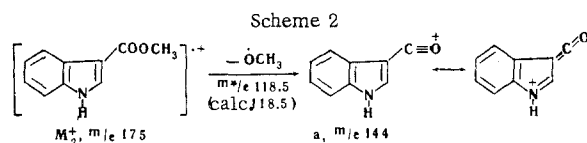
The results obtained made it possible to deduce that fragmentation with formation of a type *a* ion is obviously general with indole compounds having a carbonyl group at the β -position (I, II, X, XI, XII).

Like aromatic aldehydes [6], the molecular ion of β -indole aldehydes (M_1^+ , see scheme 1 and Fig. 1) readily loses a hydrogen atom to give ion a, whose further splitting proceeds in two ways. One is accompanied by ejection of a CO molecule and gives ion b (m/e 116) which, like indole, splits off a molecule of HCN, giving fragment e (m/e 89). The second mode of decomposition of ion a is characterized by subsequent losses of HCN and CO molecules and formation of the corresponding fragments c (m/e 117) and e (m/e 89). The fragment having m/e 117 can

also have an indole ion structure (d), confirmed by the spectrum of indole aldehyde, like that of indole [7], showing the peak of a double-charged ion with m/e 58.5 (cf [8]), and a peak with m/e 90.



Esters of β - and α -indole carboxylic acids (II-IV) undergo fragmentation in different ways. A m/e 144 peak (fragment a) predominates in the mass-spectrum of II (see scheme 2, and Fig. 2a), while decomposition of α -esters III and IV (see scheme 3 and Figs. 2b, 3a) is accompanied by splitting off of the corresponding alcohol, and formation of fragment f (m/e 143).



The fact that when a molecule of alcohol is split off, a hydrogen of NH is lost, is confirmed by the mass-spectrum of the N-deutero analog of IV, where the mass number of the peak of ion f remains the same. It should be noted that unlike esters of α -pyrrole carboxylic acid, whose mass-spectra show for example equal-intensity peaks of fragments $M^+ - OR$ and $M^+ - ROH$ [9], the indole analogs (III, IV) do not show a peak for the fragment $M^+ - OR$.

*For Parts I-III see [1-3].

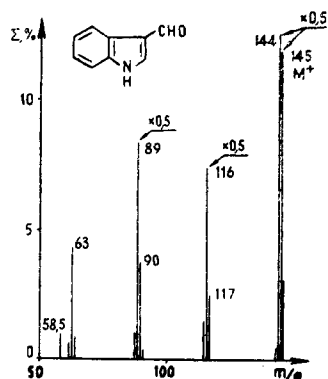


Fig. 1. Mass-spectrum of β -indole aldehyde (I).

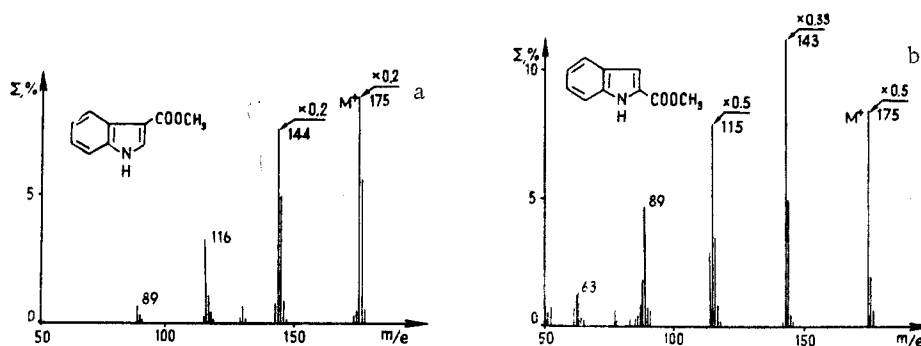


Fig. 2. Mass spectra. a) β -Methoxycarbonylindole (II); b) α -methoxycarbonylindole (III).

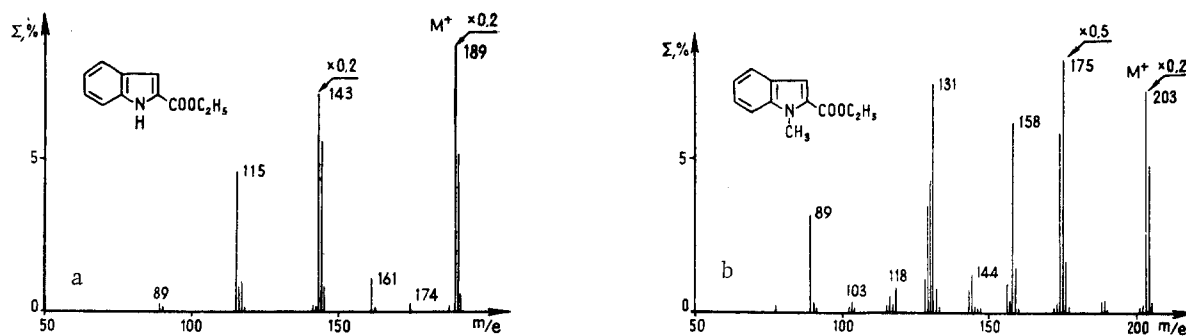


Fig. 3. Mass spectra. a) α -Ethoxycarbonylindole (IV); b) N-methyl- α -ethoxycarbonylindole (V).

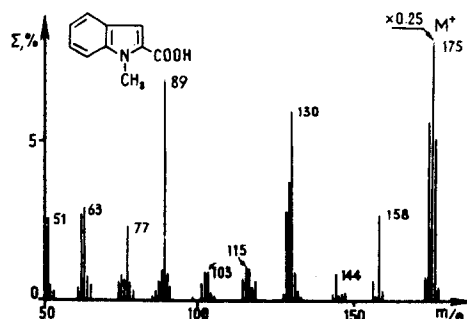
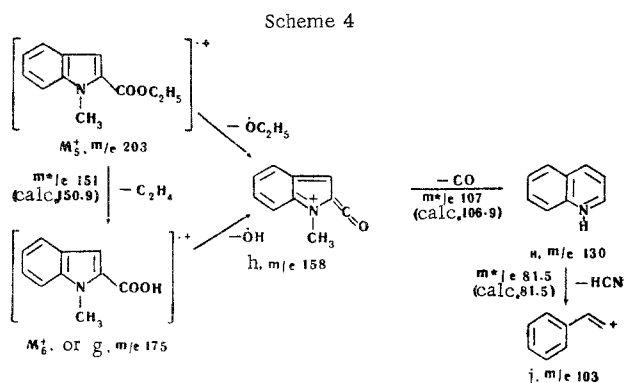


Fig. 4. Mass-spectrum of N-methyl- α -indole carboxylic acid (VI).

Further disruption of ion *f* proceeds similarly to decomposition of ion *a*, and ejection of a molecule of CO and of a $\dot{C}N$ radical gives fragment *e* (m/e 89). The fragmentation scheme for esters **III** and **IV** given above is in agreement with results in the literature [10]. In the case of *N*-methyl- α -ethoxycarbonylindole (**V**), the main direction of splitting of the molecular ion (M_5^+ , see scheme 4 and Fig. 3b) was splitting off of a molecule of ethylene and formation of fragment *g* (m/e 175), further splitting of which is accompanied by loss of a hydroxyl group, giving fragment *h* (m/e 158). Ion *h* can also be formed directly from the molecular ion by elimination of a $C_2H_5\dot{O}$ radical. Subsequent loss of CO and HCN by ion *h* gives fragments *i* (m/e 130) and *j* (m/e 103). The mechanism proposed



for the decomposition of compound **V** is confirmed by the mass spectrum of *N*-methyl- α -indole carboxylic acid (**VI**) (Fig. 4), where the mass numbers of the peaks of the fragments *h*, *i*, *k*, are unchanged.

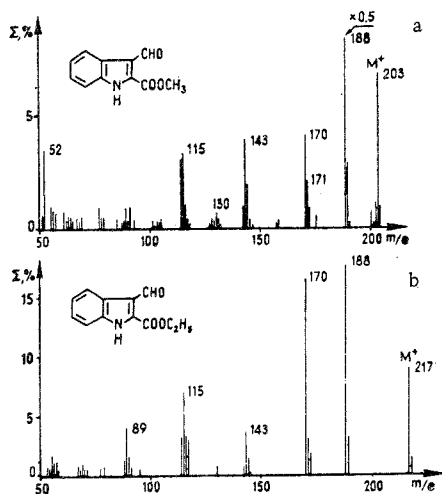


Fig. 5. Mass-spectra. a) β -formyl- α -methoxycarbonylindole (**VII**); b) β -formyl- α -ethoxycarbonylindole (**VIII**).

Splitting of the molecular ion (M_8^+) of α -ethoxycarbonyl- β -formylindole (**VIII**) follows two paths (see scheme 5 and Fig. 5b). One of them leads to elimination of an ethyl group from $COOC_2H_5$ and formation of fragment *k* (m/e 188). The fact that here loss of 29 mass units corresponds to ejection of the \dot{C}_2H_5 radical, and not to the CHO group, is

confirmed by the mass-spectrum of α -methoxycarbonyl- β -formylindole (**VII**, Fig. 5a), where there is also a peak m/e 188, while the peak $M_7^+ - 29$ is

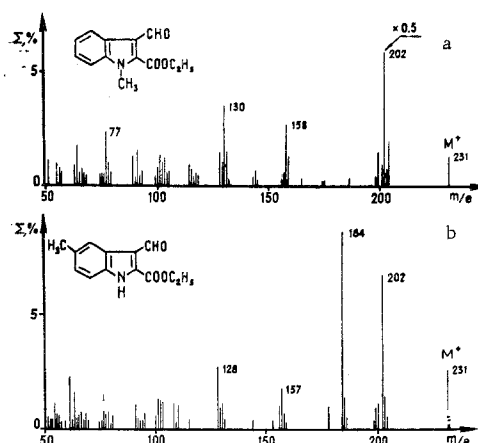
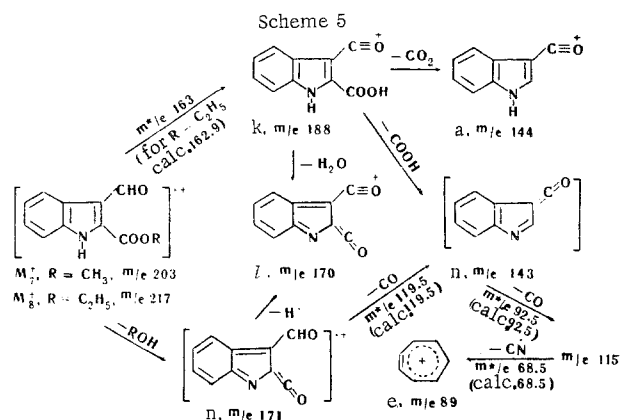


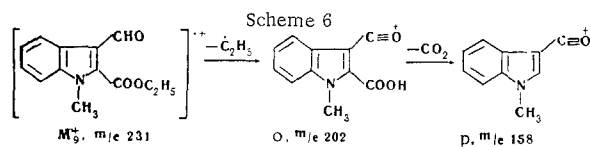
Fig. 6. Mass-spectra. a) *N*-Methyl- β -formyl- α -ethoxycarbonylindole; b) 5-methyl- β -formyl- α -ethoxycarbonylindole (**XIII**).

absent. Further decomposition of fragment *k* is accompanied by loss of H_2O and CO molecules or of radical $\dot{C}OOH$, giving respectively ions *l* (m/e 170), *a* (m/e 144), and *m* (m/e 143). The second path for the decomposition of molecular ions M_7^+ and M_8^+ , is, analogous to the esters of α -indole carboxylic acids, accompanied by elimination of a molecule of alcohol, and subsequent splitting off of a hydrogen atom or molecule of CO, to give fragments *n* (m/e 171), *l* and *m*. Like the ion *f*, ion *m* splits further to give fragments with m/e 115 and 89.



The fragmentation mechanism suggested for α -alkoxycarbonyl- β -formylindoles (**VII**, **VIII**), is confirmed by the mass-spectra of 5-methyl- α -ethoxycarbonyl- β -formylindole (**XIII**) and *N*-methyl- α -ethoxycarbonyl- β -formylindole (**IX**, see Fig. 6). In the spectrum of the 5-methyl derivative (**XIII**), the main peaks are shifted by 14 mass units each. In the case of the *N*-methyl derivative (**IX**), the peaks $M_9^+ - 46$ and $M_9^+ - 47$ are lacking. This shows that elimination of a molecule of alcohol when esters **VII** and **VIII** decompose, and also loss of a molecule of water from ion *k* involves the hydrogen atom of the

>NH group. At the same time fragmentation of the molecular ion of the ester IX, with formation of ions o (m/2 202) and p (m/e 158) prevails (see scheme 6).



The mass-spectra of all the compounds except I, VI, and XII, were determined with a series mass-spectrometer MKh-1303, fitted with a heated glass admission system (30–40 eV, 125°–200° C). The mass spectra of compounds I, VI, and XII were determined with a MKh-1303 instrument, where the specimen was introduced directly into the ion source (30–40 eV, 100°–160° C).

REFERENCES

1. N. S. Vul'fson, V. I. Zaretskii, and V. G. Zaikin, *Izv. AN SSSR, ser. khim.*, 2215, 1963.
2. N. S. Vul'fson, V. I. Zaretskii, and V. G. Zaikin, *DAN*, **155**, 1104, 1964.
3. V. I. Zaretskii, N. S. Vul'fson, L. S. Chetverikova, and V. G. Zaikin, *ZhOKh*, **34**, 3655, 1964.

4. H. Budzikiewicz, C. Djerassi, and D. H. Williams. "Structure elucidation of natural products by mass spectrometry," *Alkaloids*, Vol. 1, San Francisco, 1964.

5. J. H. Beynon and A. E. Williams, *Appl. Spectroscopy*, **13**, 101, 1959; **14**, 27, 1960.

6. H. Budzikiewicz, C. Djerassi, and D. H. Williams *Interpretation of Mass-Spectra of Organic Compounds*, [Russian translation], 234, 1966.

7. *Catalog of Mass Spectral Data*, American Petroleum Institute Research Project 44, Carnegie Institute of Technology, Pittsburgh, Pa., Spectrum No. 623.

8. J. H. Beynon, *Mass-Spectrometry and its Application in Organic Chemistry* [Russian translation], *Mir, Moscow*, 289, 413, 1964.

9. H. Budzikiewicz, C. Djerassi, A. H. Kenner, and D. J. Newman, and J. M. Wilson, *J. Chem. Soc.* 1949, 1964.

10. U. K. Pandit, H. J. Hofman, and H. O. Huisman, *Tetrahedron*, **20**, 1679, 1964.

20 July 1965 Institute of the Chemistry of Naturally occurring Compounds AS USSR, Moscow

Ordzhonikidze All-Union Scientific Research Chemical and Pharmaceutical Institute, Moscow