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MASS SPECTROMETRIC EVIDENCE FOR FORMATION OF THE 2-CARBONYL-2H-INDOLE INTERMEDIATE

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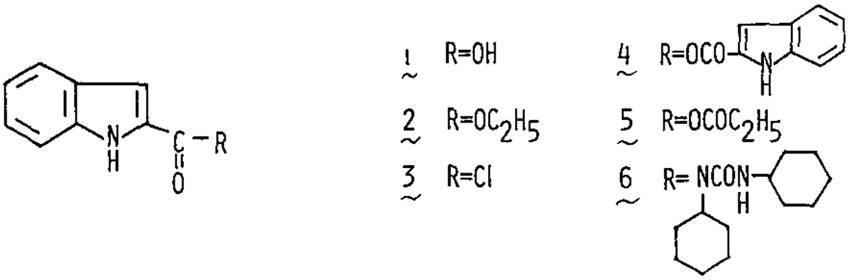
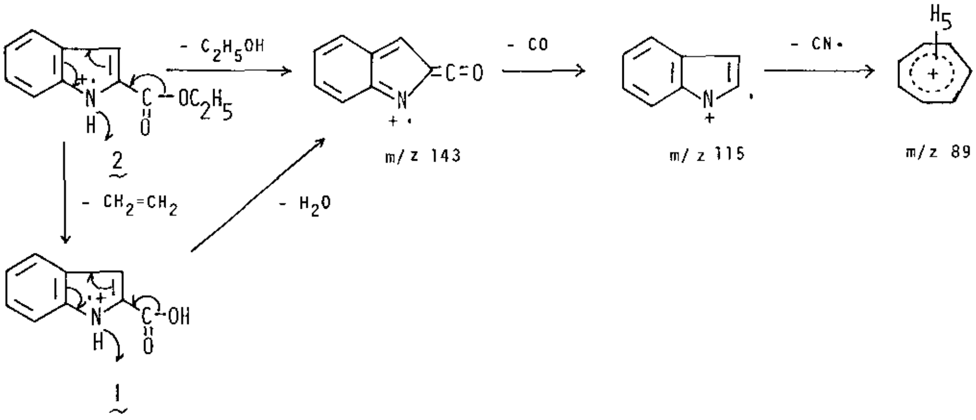
Abstract —— The mass spectra of indole-2-carboxylic acid derivatives were investigated. In particular, indole-2-carboxylic acids with good leaving groups were noted to undergo the thermal rearrangement in the ion source of the mass spectrometer to form a ketene and a ketene dimer.

2-Carbonyl-2H-pyrrole, 2-carbonyl-2H-indole and related analogoues are well-known chemical species and important reaction intermediates in heterocyclic processes. These ketenes can be formed by a) treatment of pyrrole- and indole-2-carboxylic acid chlorides with base[1], b) the Wolff rearrangement of diazopyridones[2] and c) the flash vacuum pyrolysis (650-850°C) of indole-2-carboxylic acid and related compounds[3]. We conducted a study of the thermal behavior of the various indole-2-carboxylic acid derivatives in the hope of obtaining such ketenes under neutral and mild conditions. Some of these indole-2-carboxylic acid derivatives were found to undergo the thermal rearrangement in the ion source of the mass spectrometer[4] to form a ketene. The present paper summarizes some of our observation in the mass spectra of these compounds. The compounds used in this study were indole-2-carboxylic acid (1) and its derivatives (2-6) possessing good leaving groups with relatively weak bonds to the carbonyl carbon, such as Cl^-.

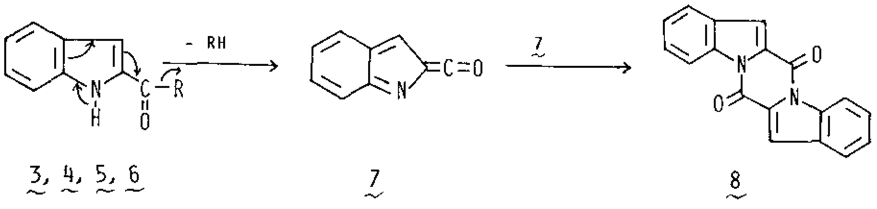


Compounds 4 and 6 were prepared by reactions of 1 with DCC in methylene chloride at 0-5°C. Compound 5 was obtained from 1 and ethyl chloroformate in the presence of triethylamine. The mass spectrum of compound 2 has been discussed in detail by Pandit et al.[5] (eq. 1). The fragmentation process indicated the loss of ethanol from the parent ion followed by that of carbon monoxide and then a cyanide radical. This process was proved by the presence of the metastable peaks. In the present study, we note the alternative minor fragmentation in the primary process in which ethylene and water were lost to lead to the ketene radical cation. This cation was also observed in the spectrum of 1.



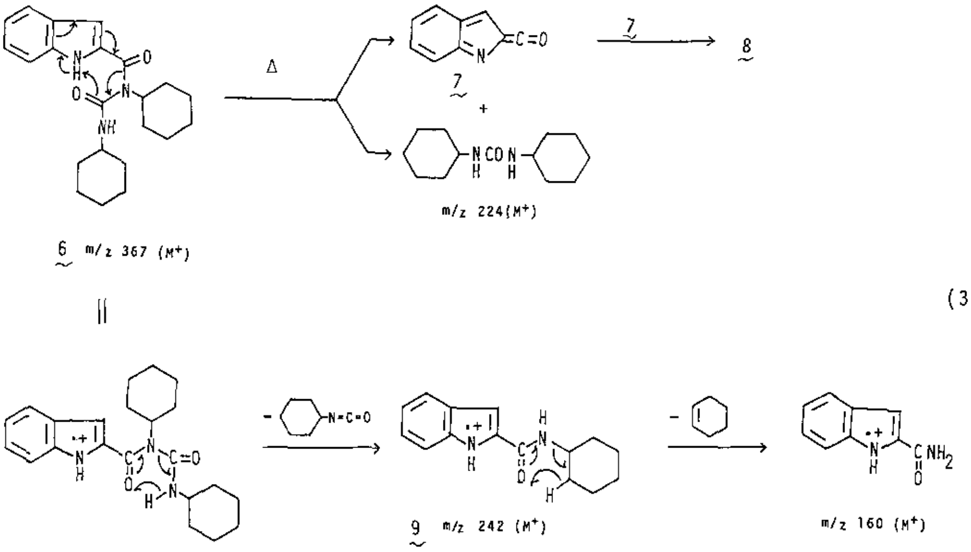
(1)

The spectra of 3, 4, 5, and 6 (Fig. 1, 2, 3, and 4) indicated a new peak at m/z 286 in addition to the conventional fragment peaks. This peak, not observed for 1 and 2, was noted to correspond to $C_{18}H_{10}N_2O_2$, identical to the molecular ion of the ketene dimer 8[1] (m/z 286.0767, Calcd for $C_{18}H_{10}N_2O_2$ 286.0742). It seems very likely that 7 is formed by a thermal elimination of RH at the temperature (200°C) in the ion source followed by dimerization to the ketene dimer 8 prior to electron-impact (eq. 2). It does not seem probable for compounds 1 and 2 to actually undergo thermal decomposition under the present condition rather, electron ionization may occur to produce the ketene radical cation as shown in equation 1. Compound 8, however, is not formed from this radical cation.



(2)

The spectrum of 4 in Fig. 2 shows a peak at m/z 161 corresponding to indole-2-carboxylic acid which is produced from the parent molecule by thermal decomposition in the ion source in a primary process. The peaks at m/z 161 and m/z 189 in the spectrum of 5 (Fig. 3) correspond to the molecular ions of compounds 1 and 2, respectively. It would thus follow that the thermal decomposition of 5 in the ion source may give rise to the ketene intermediate 7, with the loss of carbon dioxide and ethanol, which undergoes the recombination reaction to give 2. The spectrum of 6 (Fig. 4) indicates the formation of N,N'-dicyclohexylurea [(m/z 224 (M$^+$)] and 8 by thermal elimination and dimerization. The strong peaks at m/z 242 and m/z 160 in Fig. 4 indicate the loss of cyclohexyl isocyanate as well as cyclohexene. This process is supported by a comparison of the fragmentation patterns in the spectrum of 6 with those in compound 9 [6](eq. 3).



(3)

From the relative intensity ratio of the ketene dimer to the ketene adduct, the thermal decomposition in 4, 5, and 6 seems to be more favorable for ketene formation than in compound 3. This may be because the good leaving and proton abstraction groups are both present in the molecule. The results of thermolysis observed in the mass spectra of indole-2-carboxylic acid derivatives are summarized in Scheme 1. Although the thermolysis[7] of compounds 1 and 2 failed to produce any products, the ketene dimer 8 was obtained from compound 3, as is consistent with its mass spectrum, in 37% yield.

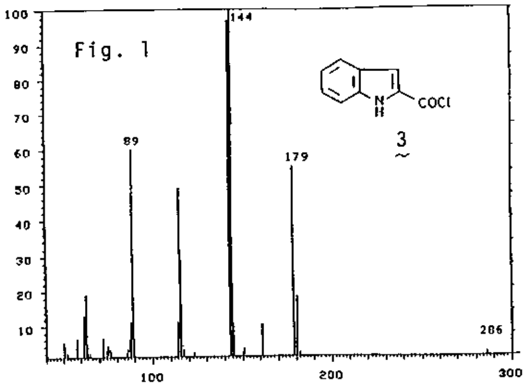


Fig. 1

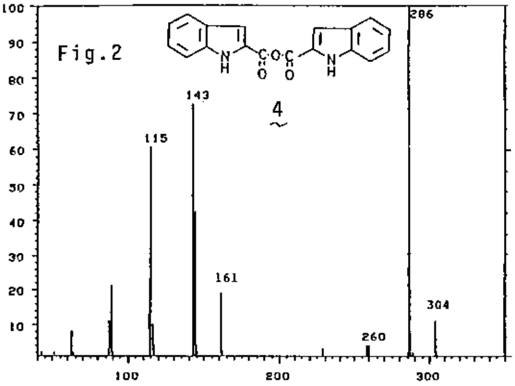


Fig.2

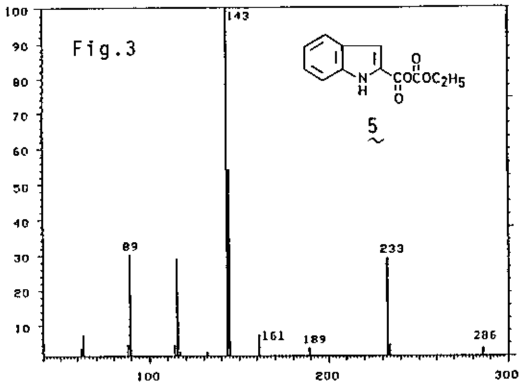


Fig.3

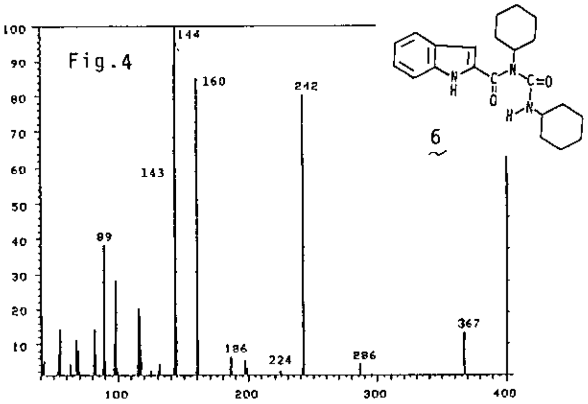


Fig.4

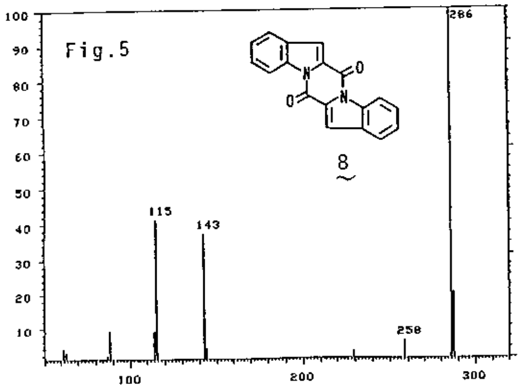
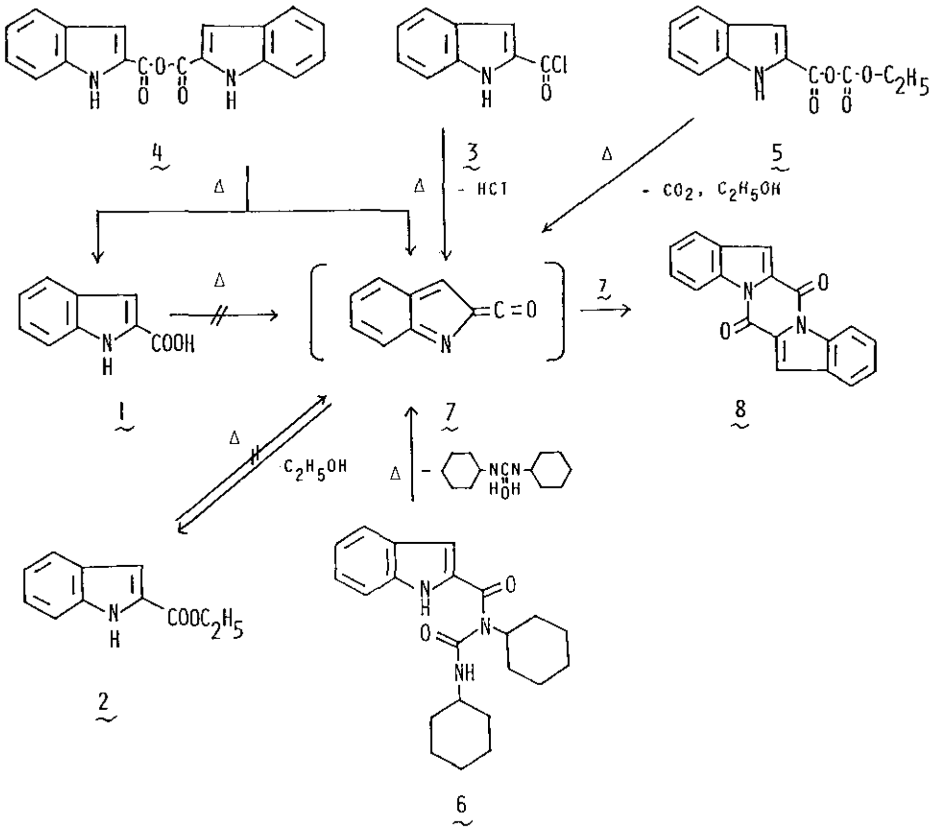


Fig.5



Scheme 1

REFERENCES AND NOTES

1. R.J. Boatman and H.W. Whitlock, J. Org. Chem., 1976, 41, 3050.
2. O. Sus and K. Moller, Liebigs Ann. Chem., 1955, 593, 91.
3. G. Gross and C. Wentrup, J. Chem. Soc., Chem. Commun., 1982, 360.
4. Mass spectral measurements were carried out on a Hitachi M-80 spectrometer with a direct inlet system. The ionizing potential used in all measurements was 70 ev. The temperature in the heat-attended inlet system was 200°C.
5. U.K. Pandit, H.J. Hofman, and H.O. Huisman, Tetrahedron., 1964, 20, 1679.

6. The amide (**9**, mp 198-200°C) was prepared by reaction of **1** with cyclohexylamine in methylene chloride at 5°C in the presence of DCC. The mass spectrum of **9** indicated the loss of a molecule of cyclohexene from the parent molecule (m/z 242).
7. Thermolysis was carried out at approximately the same temperature as that used in the heat-attended inlet system.

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