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Photoelectron (PE) spectra of imidazole (1), 1-methylimidazole (2), 2-methylimidazole (3), 4(5)-nitroimidazole (4), 2-methyl-4(5)nitroimidazole (5), 1,2-dimethyl-5-nitroimidazole (6), 1-ethyl-2-methyl-5-nitroimidazole (7), 1-bromoethyl-2-methyl-5-nitroimidazole (8) and 1-hydroxyethyl-2-methyl-5-nitroimidazole (9) have been recorded using Hel excitation. The electronic structure of the potent antitrichomonal agent 9 is discussed in comparison with compounds 1-8 allowing for the study of the influence of substituents on the imidazole ring.

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### Introduction.

The discovery of the strong antitrichomonal activity of 5-nitroimidazoles (2) resulted in the effective therapy of trichomonitis in human and animal therapy. Positive clinical results obtained also with derivatives of 2- as well as 4-nitroimidazoles, stimulated, in the last 15 years, numerous investigations of physicochemical and biological properties of substituted nitroimidazoles intended to solve the problem of the mechanism of antitrichomonal activity (3). Much work has been done to find out the mode of action of these drugs in micro-organisms (4) and their binding to plasma proteins (5).

Recently, from PE spectra of imidazole and methylimidazoles (6) which were compared with results of *ab initio* calculations (7,8) the electronic structure of these compounds was determined. It is in agreement with earlier work on imidazole done by Cradock, *et al.*, (9). In the present study, the gas phase electronic structure of the potent antitrichomonal agent 9 is elucidated by comparison with the simpler compounds 1-8. Knowledge of this structure might be of some help in defining the structure-activity relationship in methylnitroimidazoles.

### EXPERIMENTAL

#### Compounds.

All compounds were of high purity and had been prepared in the laboratories of CRC.

#### Photoelectron Spectra.

The PE spectra were recorded with a low ( $\approx 35$  meV) and high ( $\approx 12$  meV) resolution on a Vacuum Generator UVG3 instrument (10) using small amounts of argon and xenon for calibration. Enhanced temperatures of the inlet system (105°, 80°, 80°, 220°, 215°, 100°, 90°, 150° and 170° for 1-9, respectively, were used to obtain satisfactory spectra. Decomposition did not take place under these conditions.

#### Results and Discussion.

The low resolution PE spectra of 3, 2 and 1 are repro-

duced from top to bottom in Figure 1., those of 6, 5 and 4 in Figure 2 and those of 7, 8 and 9 in Figure 3. Numbers above the observed band systems represent vertical ionization energies ( $\pm 0.02$  eV). As shown recently (6) by correlation of *ab initio* orbital energies with observed energies of band systems (Koopmans' theorem), the ionizations in the PE spectrum of 1 take place in the following order of ascending energy:  $\pi_2 < \pi_2$  and  $n_N < \text{three } \sigma$  and

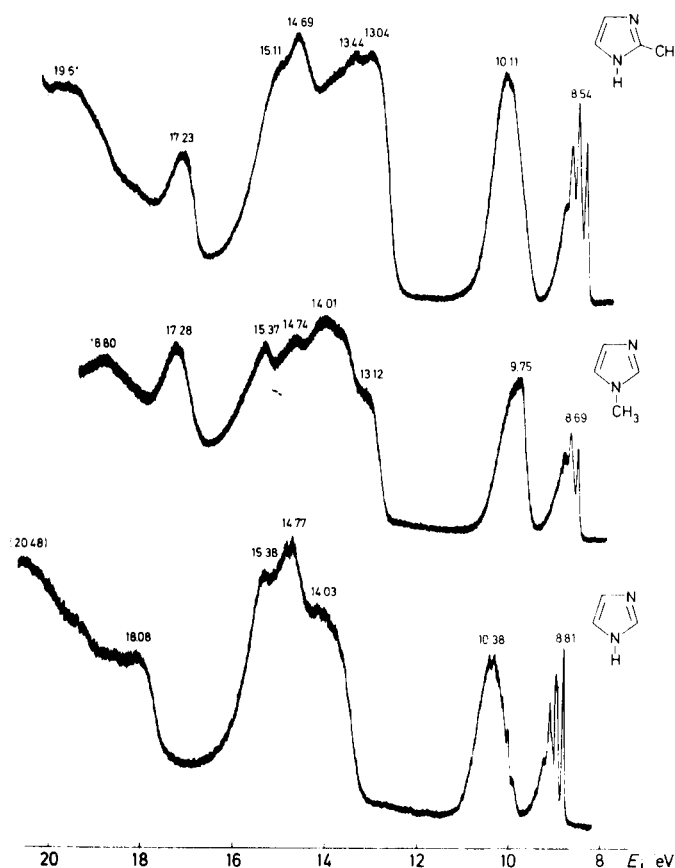


Figure 1. Hel PE Spectra of the compounds 1-3.

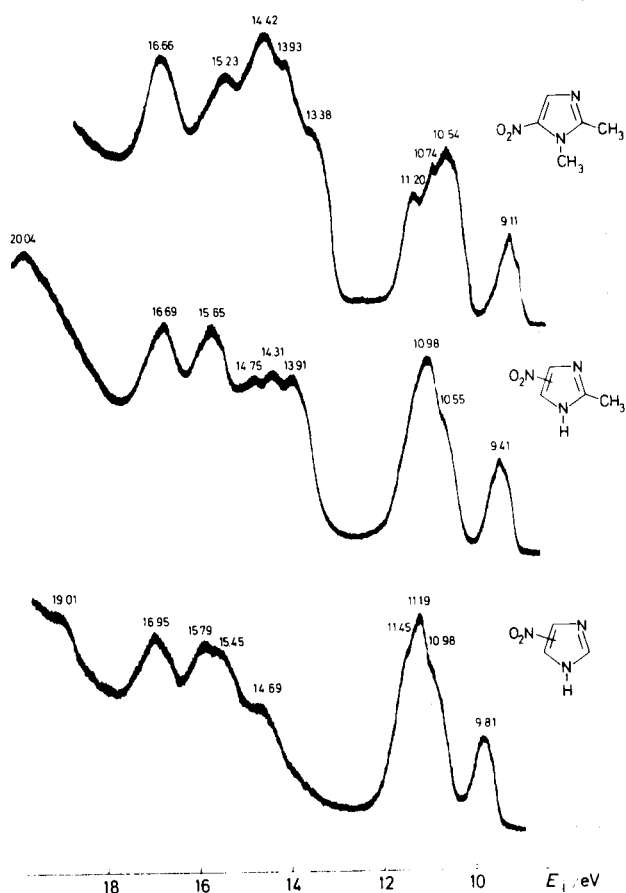


Figure 2. Hel PE Spectra of the compounds 4 - 6.

$\pi_1 < \sigma$  onset. The situation in the PE spectra of **2** and **3** is changed only to the extent that the first three systems are shifted by about 0.3 eV to lower energy on account of the inductive effect of the methyl group and that new  $\sigma$ -ionizations arising also from the methyl group are additionally observed in the range between 13 and 14 eV.

The effect of the nitro substituent is apparent from a comparison of the PE spectra in Figure 1 and Figure 2. The change in electronic structure from imidazole to nitroimidazole can be explained similarly to that from benzene to nitrobenzene as compared with nitromethane (11). Here, a strong stabilization of the low energy  $\pi$ -ionizations is observed with respect to benzene as well as with respect to nitromethane; a destabilization of the ionizations arising from the in-plane ( $n_O$ ) and out-of-plane ( $\pi_O$ ) combination of the oxygen p-electrons is also observed. In **4** the stabilization of the lowest energy  $\pi$ -ionization relative to **1** is 1 eV. The likewise stabilized  $n_N$  and  $\pi$ -systems already overlapping in **1**, yield in **4**, together with the additional  $n_O$  and  $\pi_O$  systems, a poorly resolved group of peaks between 10.5 and 11.5 eV, which are correlated to nitro-

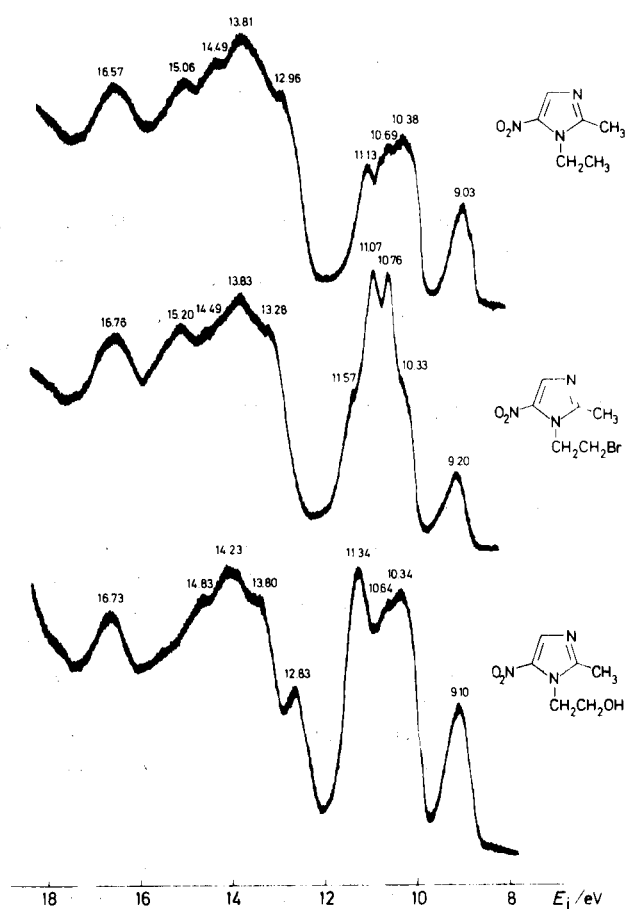


Figure 3. Hel PE Spectra of the compounds 7 - 9.

benzene tentatively assigned as  $n_N < \pi$  and  $n_O < \pi_O$ . The  $\pi$ -ionization, which predominantly arises from the electrons located on the nitro group, is expected to be  $\pi_1$  in the range  $E_i > 16$  eV (12), where also in the PE spectrum of **4** the new peak at 16.95 eV is observed, as compared with **1**. It should be pointed out that two tautomeric forms of **4** are possible with the nitro group in the 4- and 5-positions of the imidazole ring, respectively, and that the loss of fine structure in the first  $\pi$ -system and the overall smoothing of the PE spectrum of **4** could also be caused by the presence of both forms in the gas phase. Unfortunately, the already high inlet system temperature of 220°, which was necessary to record the PE spectrum of **4**, excluded temperature variation experiments. Fine structure in the first system and some resolution of the next four overlapping systems is gradually observed when going from **4** via **5** (which also has two tautomeric forms) to **6**, which appears only in one form. In **6**, the system at 11.20 eV corresponds with a high probability to the  $\pi_O$ -ionization, thus confirming the assignment of  $\pi_O$  in nitroimidazoles as the highest in energy in this range. Again, in the spectra

of **5** and **6** the inductive shift to lower energy of about 0.3 eV per methyl group is observed, and also the occurrence of new  $\sigma$ -ionizations at energies higher than 13 eV.

In comparison with **6**, compounds **7**, **8** and **9** only have a longer chain in the 1-position of the imidazole ring, *i.e.*, an ethyl, bromoethyl and hydroxyethyl group instead of a methyl. Thus, the spectre of **6** (Figure 2, top) and **7** (Figure 3, top) are extremely similar, especially in the range between 8 and 12 eV, the latter showing only a slight stabilization caused by the additional methylene link. However, in **8** and **9** ionizations from the lone pair of electrons of the bromo and oxygen atoms are expected within this range. In the spectrum of **8**, the two systems corresponding to the ionization electron from the bromo  $p$ -orbitals, split by spin-orbit interaction, are observed at 10.76 and 11.07 eV, respectively. The system at 11.57 eV corresponds to  $\pi_{\text{O}}$ -ionization and it indicates together with lowest  $\pi$ -ionization, shifted from 9.07 eV in **7** to 9.20 eV, the positive inductive effect of the bromo substituent. This effect is exhibited to a lesser extent also by the hydroxyethyl group of **9**, as compared with the ethyl substituent of **7**. In the PE spectrum of **9**, the oxygen lone pair ionizations of the hydroxy ( $n_{\text{O}}\text{H}$ ) and nitro ( $\pi_{\text{O}}$ ) group coincide in energy, thus raising the intensity of the peak at 11.34 eV. It is interesting to note that only in **9**, the following  $\sigma$ -ionization observed at 12.83 eV is well separated from the remaining systems, presumably by

interaction with the oxygen atom of the hydroxyl group.

## REFERENCES AND NOTES

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