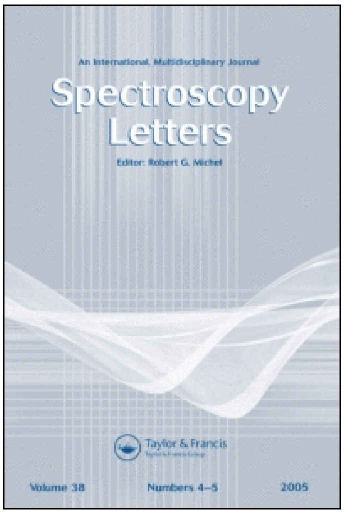

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CNDO/S Method Interpretation of Ultraviolet Spectra of 4-Nitro and 5-Nitroimidazoles

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CNDO/S METHOD INTERPRETATION OF ULTRAVIOLET SPECTRA OF 4-NITRO AND 5-NITROIMIDAZOLES

Key Words: CNDO/S, UV Spectra, Nitroimidazole.

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ABSTRACT

The uv spectra of several nitroimidazoles are reported. These experimental results are interpreted using CNDO/S method (Complete Neglect of Differential Overlap for Spectroscopy). Calculations show that observed transitions are $\pi \rightarrow \pi^*$ type transitions.

INTRODUCTION

Ultraviolet spectroscopy has been applied to studies of 1,2-dimethyl-5-nitroimidazole (I), 1-methyl-2-(2,2-dimethyl-vinyl)-5-nitroimidazole (II) and 1-methyl-2-(2-methyl-2-phenyl-vinyl)-5-nitroimidazole (III) (1). The nitroimidazoles as a class of compounds have attracted much attention and are widely used in

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different fields of pharmalogical interest which include anaerobic infections, hypoxic cell radiosensitizers in radiotherapy and possibly as adjuncts with various other anticancer drugs (2). These compounds show two absorption bands at 310-355 nm and at 230-270 nm. The uv spectra of these compounds have been computed using the CNDO/S method to identify the different parts of the molecule related to the transitions. In order to confirm the suitability of the CNDO/S method for the characterization of the uv spectra of this class of compounds, we have also computed 1-methyl-5-nitroimidazole (IV) and two 4-nitroimidazoles: 1-methyl-4-nitroimidazole (V) and 1,2-dimethyl-4 nitroimidazole (VI).

METHOD OF CALCULATION

The method of calculation used in this work is the CNDO/S method following DEL BENE and JAFFE (3) except that the parameter β selected for oxygen atom is that used in the CNDO/2 method with the value -31 e.v. (4).

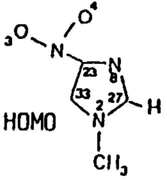
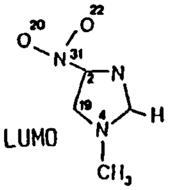
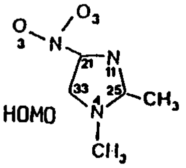
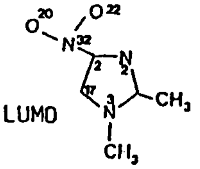
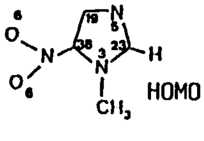
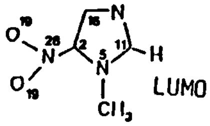
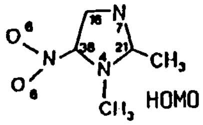
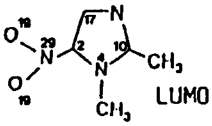
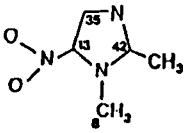
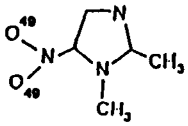
The configuration interaction was limited to the 30 monoexcited lower energy configurations. We have observed that a more complete configuration interaction with 60 configurations did not change significantly the results.

The geometry used for imidazole cycle has been described by ROCHE (5). The substituents have been placed on the bisectrix of the corresponding bond angles. The different bond-lengths and angles are given in Appendix.

RESULTS AND DISCUSSION

The results show (Tables 1,2 and 3) that the first transition results from a configuration corresponding to the transition of one of the electrons of the highiest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) for all studied molecules. This transition is a $\pi \rightarrow \pi^*$ type transition. It is noteworthy, from the comparison of the theoretical

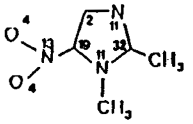
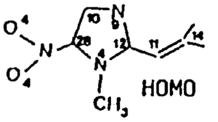
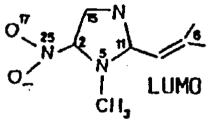
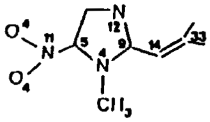
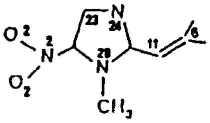
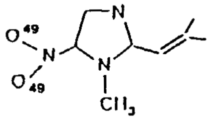
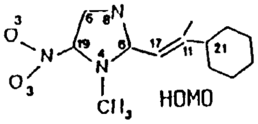
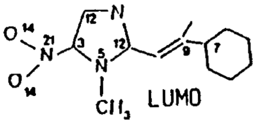
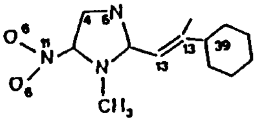
TABLE 1

Compound λ Oscillator strength Main configuration squared coefficient	Occupied Molecular Orbital	Unoccupied Molecular Orbital
(V) 290 nm 0.2315 0.96	 HOMO	 LUMO
(VI) 302 nm 0.2168 0.97	 HOMO	 LUMO
(IV) 301 nm 0.4683 0.97	 HOMO	 LUMO
(I) 310 nm 0.4927 0.98	 HOMO	 LUMO
(I) 238 nm 0.0215 0.81		LUMO
(I) 222 nm 0.3093 0.96		LUMO

The numbers adjoined to the figures of the molecules are the squared coefficients of the atomic orbitals involved in the corresponding molecular orbital multiplied by 100 .

values for the LUMO energy in the different 5-nitroimidazoles, that few variations of the energy levels are found. Even when the configuration in the molecules increases the delocalization of

TABLE 2

Compound λ Oscillator strength Main configuration squared coefficient	Occupied Molecular Orbital	Unoccupied Molecular Orbital
(I) 220 nm 0.0961 0.93	HOMO	
(II) 334 nm 0.702 0.95	 HOMO	 LUMO
(II) 252 nm 0.1511 0.83	HOMO	
(II) 241 nm 0.0848 0.69		LUMO
(II) 223 nm 0.2795 0.95		LUMO
(III) 350 nm 1.005 0.90	 HOMO	 LUMO
(III) 280 nm 0.230 0.79	HOMO	

The numbers adjoined to the figures of the molecules are the squared coefficients of the atomic orbitals involved in the corresponding molecular orbital multiplied by 100 except for phenyl group whese the number is the sum of the numbers for the six carbon atoms.

this orbital changes very little. If we consider the squared coefficients (for which the total values are equal to one), of the molecular orbital in the different atoms, it is possible to

TABLE 3

Compound	I		II		III		IV	V	VI
Experimental λ (nm)	310	230	340	235	355	270	296	289	301
							(2)	(2)	(2)
log ϵ	3.95	(s)	4.04	4.05	4.17	4.05	3.90	3.84	3.84
Theoretical λ (nm)	310	238	334	252	350	280	301	290	302
		222		241					
		220		223					
Oscillator strength	0.49	0.02	0.70	0.15	1.00	0.23	0.47	0.23	0.22
		0.31		0.08					
		0.10		0.28					

(s)=shoulder

find that only 6% of this orbital on the extra cyclic double bond of compound II (with two methyl groups) and 16% in the case of compound III (with a methyl and a phenyl groups on the double bond). The situation is dramatically different for the HOMO whose energy changes significantly and for the delocalization in fonction of the substituents on the double bond which varies between 25 and 49%. The change in the HOMO energy level (Table 4) is consequently the essential reason for the bathochromic effect observed with an increase in conjugation.

The second transition observed for I and II is more difficult to explain. This transition is observed at 230 nm as a shoulder for the first compound and a band at 235 nm for the second.

TABLE 4

Compound	I	II	III	IV	V	VI
HOMO energy (e.v.)	-9.54	-9.00	-8.77	-9.82	-9.78	-9.47
LUMO energy (e.v.)	-2.20	-2.17	-2.25	-2.35	-2.16	-2.08

Calculation gives a first transition relative to an oscillator strength with a value different to zero at 238 nm, a second transition at 222 nm which finds its origin in electronic transition from an orbital centered on oxygen atoms of nitro group to LUMO, and a third transition at 220 nm. For the compound II, the observed transition is at 235 nm, and the calculations give three transitions in this region of absorption at 252 nm, 241 nm and 223 nm, this last transition involving oxygen atoms of nitro group in the occupied orbital. All these transitions are $\pi \rightarrow \pi^*$ type transition.

For the compound III with a phenyl group on the double bond the second transition is found experimentally at 270 nm and computed at 280 nm. Its origin is essentially in a configuration relative to an electronic transition from the HOMO to a completely delocalized orbital with 39% of electronic density in phenyl group, 26% in the extracyclic double bond and 20% in the nitro group. This transition is also a $\pi \rightarrow \pi^*$type transition.

The uv absorption spectra of isomeric 1-methyl-4- and 5-nitroimidazole IV and V show experimentally a small bathochromic effect which is also found by calculations. This bathochromic effect results primarily from a lowering in LUMO energy level. The energy level of the HOMO decreases also but less markedly.

The bathochromic effect resulting from the substitution of a hydrogen atom by a methyl group in position 2 agrees satisfactorily with calculations.

Calculations for all these molecules give n→π^* type transition, whose transition moment is zero at about 500 nm, which means that these transitions are forbidden transitions and are not observed experimentally. It should be pointed out that the selection rules are not absolute and that perturbation of the molecular states by intermolecular vibration, by collision, and by association with other particles tend to relax these rules. The nitroimidazoles are always yellow or pale yellow in solid state and this colour may possibly be caused by these transitions.

CONCLUSION

The results of calculations agree very well with experimental results for two 4-nitroimidazoles V and VI or for the 5-nitro imidazole (I). Compatible results are also obtained for other 5-nitroimidazoles II, III and V.

The bathochromic effect observed experimentally for the first transition with the extension of conjugate system corresponds closely to the results obtained by calculations.

These calculations will be completed by further work in this field with a view to studying more complex molecules.

ACKNOWLEDGMENTS

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(5) M.ROCHE, Thesis (Marseille) 1969.

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APPENDIX

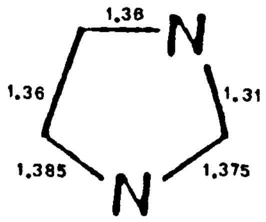
Distances (Angstroms)

$\underset{1.08}{C\text{-}H}$ except CH_3: 1.09

$\underset{1.25}{N\text{-}O}$ $\underset{1.40}{C\text{-}NO_2}$ $\underset{1.41}{N\text{-}CH_3}$ $\underset{1.53}{C\text{-}CH_3}$

$\underset{1.39}{C\text{-}C}$ in phenyl group

$C\underset{1.50}{-}C\underset{1.35}{=}C\underset{1.50}{-}C_6H_5$



Angles (degrees)

For sp^2 carbon atom and nitrogen atom all valence angles are 120 except for imidazole cycle.

For methyl group all valence directions are equivalent.