Tetrahedron Vol 39, No. 19, pp. 3201 to 3206, 1983
Printed in Great Britain

0040-4020/83 $3.00 + .00

ELECTRON STRUCTURE INVESTIGATION OF 3-IODO-5-NITRO-4-HYDROXYBENZONITRILE AND SOME OF ITS DERIVATIVES

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(*Received in the UK* 24 *January* 1983)

Abstract—A new synthesis for Nitroxynil has been elaborated. The IR and UV spectra of Nitroxynil have been measured and the π-electron properties were calculated by the quantum chemical PPP and MIM methods. The UV bands have been assigned and the pK_a value was calculated from the pH dependence of the spectrum. Certain parameters needed for the calculation have been optimized with the aid of some subsystems of the Nitroxynil. The strong red shift occuring in alkaline media as well as in aqueous and dilute alcoholic solutions is interpreted by the ionization of hydroxy group and is justified by theoretical calculations.

3-Iodo-5-nitro-4-hydroxybenzonitrile (Nitroxynil) is a useful fasciolicide.[1,2] We have described[3] a new salt of the acidic Nitroxynil with 5-amino-imidazole-4-carboxamide. A new process was developed for the preparation of Nitroxynil.[4]

The IR spectra of compounds investigated were measured in solid state and in solution of CCl_4. The UV spectra were measured in solvents of various polarity and in Britton–Robinson buffers of various pH. The values of pK_a were calculated from the pH dependence of spectra.

The IR spectra were recorded on a Zeiss UR-20 spectrometer, the UV spectra on a Unicam SP8-100 spectrometer.

RESULTS AND DISCUSSION

The IR bands of the substituents at wavelengths characteristic of benzene derivatives show it to be planar, and the vibrations ν_{OH} (3180–3250 cm^{-1}), β_{OH} (1150–1160 cm^{-1}) and γ_{OH} (628–693 cm^{-1}) show intramolecular hydrogen-bond both in crystalline and in solution (CCl_4) phases. This is verified by the lower frequency (by 20–30 cm^{-1}) of symmetrical and antisymmetrical ν_{NO_2} frequencies. The splitting of two nitro bands caused by conjugation, is 190 cm^{-1}.[5]

The UV spectrum is very similar to that of o-nitrophenol. The spectrum consists of very strong π–π^* bands which cover the n–π^* transition. The other two substituents seem to have only a smaller influence on the spectrum. The first bands of p-hydroxybenzonitrile and σ-iodophenol have almost the same energy as the second band of o-nitrophenol(4.54, 4.48, and 4.59 eV respectively, see Table 2) but there is a significant difference between the energy of their second bands and third band of nitrophenol (5.02, 5.54 and 5.88 respectively). In the spectrum of Nitroxynil the third band has nearly the same energy than that of p-hydroxybenzonitrile and the energy of the fourth band is almost the same as for ortho-nitrophenol (see Table 2). Thus the iodine atom seems to have the smallest effect on the spectrum. This is supported also by the spectrum of 2-nitro-4-cyanophenol in which a weak blue shift of the two lowest energy π–π^* transitions occurs compared to o-nitrophenol. One halogen atom in position 6 causes a red shift in comparison with the former trisubstituted derivatives and as a result the band maxima of Nitroxynil differ from that of o-nitrophenol by only 5 nm and a new band appears at wavelength 250 nm which can be derived from the spectrum of para-hydroxybenzonitrile.

The solvent and pH dependence of the UV spectrum of Nitroxynil was investigated in detail. In ethanolic solution, below 10^{-3} mol dm^{-3} a new band appears near 400 nm besides the original band near 350 nm. This new band becomes gradually more intense under the influence of dilution while the band near 350 nm becomes weaker and below 2×10^{-4} mol dm^{-3} concentration disappears (Fig. 1).

In aqueous solution only the longest wavelength band appears at 400 nm independent of concentration, i.e. the band shift is very strong in this case. The order of band shift caused by dilution in different solvents is: acetonitrile < methanol < ethanol < water. In aqueous alcoholic solutions of acids the 400 nm band vanishes and the 350 nm band appears. In basic media the 400 nm band is present.

The form giving the 350 nm band present in hexane and HCl solutions presumably contains the OH and NO_2 groups bonded by intramolecular hydrogen bond. In aqueous, alcoholic, and alkaline solutions of low concentration the phenolic hydroxy group is in ionized form.

The spectrum changes between pH 0-6 (Fig. 2), shows isosbestic points. The calculated pK_a value of Nitroxynil is 2.75 showing a more acidic character

Table 1. Atomic and bond parameters

	I_μ /eV/	A_μ /eV/	$r_{C-\mu}$ /pm/	$\beta^{PPP}_{C-\mu}$ /eV/	$\beta^{MIM}_{C-\mu}$ /eV/
C /aromatic/	11.16	0.03	139.7	-2.39	
C /nitril/	11.19	0.10	145.5	-2.39	-2.5
N /nitril/	14.18	1.66	115.9$^{\times}$	-3.5 $^{\times}$	
N /nitro/	25.73	8.97	138	-2.1	-3.0
O /nitro/	17.70	2.47	121 $^{\times\times}$	-3.0 $^{\times\times}$	
I	18.35	9.55	205	-1.4	-1.0
O /hydroxy/	30.07	10.83	136	-2.5	-2.6
O^- /hydroxy/	24.28	9.0	140	-2.3	-3.0

$^{\times}$ r_{C-N} and β_{C-N} in nitril group

$^{\times\times}$ r_{N-O} and β_{N-O} in nitro group

Table 2. PPP results of neutral molecules

Compound	Calculated			Experimental /corrected/		
	E	f	α	E	f	Ref.
2-nitrophenol	3.916	0.172	139.1	3.573	0,089	present
	4.871	0.156	184.4	4,592	0.174	work
	5.516	0,104	21.4			
	5.805	0.360	196.1	5.876	0.348	
2-iodophenol	4.486	0.054	238.7	4.484	0.072	24
	5.317	0.168	291.6	5.535	0.199	
	6.062	0.853	200.2			
	6.276	0.478	98.3			
4-hydroxy-benzonitril	4.507	0.016	90	4.541	0.148	present
	5.027	0.749	0	5.019	0.379	work
	6.224	0.676	270			
	6.602	0.832	0			
3-iodo-4-hydroxy-benzonitril	4.326	0.046	198.1	4.366	0.196	present
	4.834	0.429	336.9	4.920	0.212	work
	5.569	1.031	218.5			
	5.921	0.155	145,4			
Nitroxynil	3.660	0.125	56,7	3.512	0.055	present
	4.588	0.078	302.6			work
	4.760	0.460	309.6	4.412*	0.060	
	5.109	0.211	162.0	5.081	0.063	
	5.504	0.366	237.4	5.767	0.093	

*sh.

than that of the ortho-nitrophenol ($pK_a = 7.23$).[6] The low pK_a value explains ionization in alkaline and in water solutions.

Calculations. The π-electron spectra and structure have been calculated by the Pariser, Parr, Pople (PPP)[7,8] and Molecules in Molecules (MIM)[9] methods. The PPP method of the form used in this work was described earlier.[10] The starting parameters were taken from our former papers: the parameters for the OH group from Ref. [10] for the I atom from Ref. [11] and for the NO_2 group from Ref. [12]. The parameters of the nitril group were determined as for carbonyl[11] and nitro[12] substituents. These parameters and the molecular geometries used[13] are given in Table 1 where I_μ and A_μ denote the valence state ionization potential and electron affinity respectively, $r_{C-\mu}$ is the distance between the ring carbon and μ atoms, $\beta_{\mu\nu}$ is the corresponding resonance integral.

The version of the MIM method was described in Ref. [11] and the starting parameters were adopted also in this case from our former works: parameters for the OH group from Ref. [4] for the I atom from

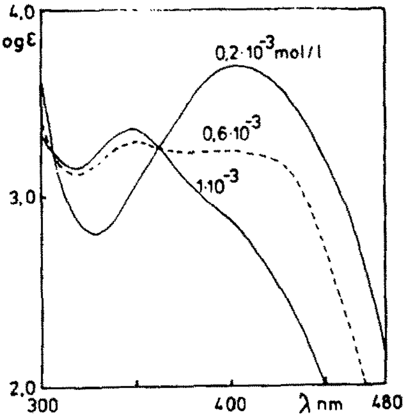

Fig. 1. Concentration dependence of Nitroxynil in ethanolic solution.

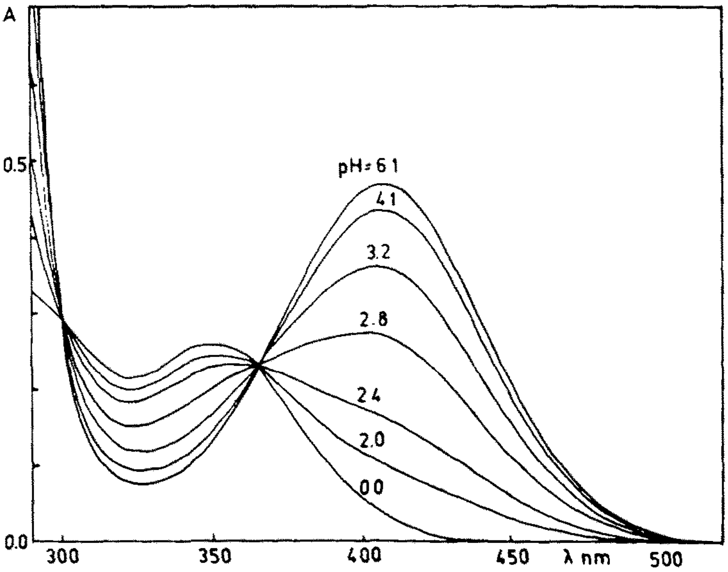

Fig. 2. pH dependence of the spectrum of Nitroxynil.

Ref.[11] and for the NO_2 and CN groups from Ref.[15]. These parameters can be found in Table1, oo. The Nitroxynil molecule was divided into five arts for the MIM calculation. The iodo and hydroxy roups were considered as electron donors and the nitro nd nitrile groups as electron acceptors compared to he benzene. The local transitions of subsystems and the harge transfer (CT) interactions between the benzene ing and one substituent were taken into consideration or the calculations. Of the direct charge transfer ransitions only the transition between the OH and NO_2 roups was taken into account and the other possible irect CT transitions were omitted because, according our calculations, the energies of these transitions are large that this neglect causes no significant error. On e other hand the interaction between the strong onor OH and acceptor NO_2 groups situated in ortho osition have had to be taken into account.

The hydrogen bond between the OH and NO_2 oups in ortho position was taken into consideration st as in Ref.[16]: the valence state ionization potenl of the oxygen atom of the OH group was reduced 3 eV and at the same time the valence state nization potential of one of the oxygen atoms of the acceptor NO_2 group was increased by the same value. However the calculated results are only slightly sensitive to these changes.

The optimized starting parameters of O^- ion needed for the PPP calculation of the supposed ionized molecule existing in basic solvents were determined by the reproduction of the spectrum of phenolate ion. The r_{CO^-} bond distance was taken somewhat longer than the corresponding value in phenol (Table 1). Two empirical electron affinities found in the literature were applied: 9.6[17] and 9.2 eV.[18] The corresponding ionization potentials are 28.84[17] and 23.2 eV.[15] To find the optimum an additional electron affinity value of 10.0 eV was investigated as well. With these parameters three different β_{CO^-} resonance integrals were tested. Because none of these calculations gave satisfactory results the calculation was carried out by $\gamma_{oo^-} = 15.28$ eV value calculated by Kwiatkowsky's method[20] using Hinze's tables[19] for O^- $(s^2p^2p^2p^2)$ state. Although the results using $A_{O^-} = 9.2$ eV and $\beta_{CO} = 2.3$ eV values produced better accordance in spectral data, the calculated charge densities refer to a weaker +M effect for O^- ion than for amino group in contrast to the expectation. For this reason the A_{O^-} electron affinity was slightly decreased for improving the agreement for the charge density. The rational lowest limit of this decreasing is the experimental first ionization potential of the CH_3NH_2 molecule (8.97 eV[21]). The best agreement for the first two bands was obtained with $A_{O^-} = 9.0$ eV. With this electron affinity the calculated charge densities are nearly the same as for aniline and better than expected. This electron affinity optimized for phenolate ion (giving satisfactory results for mono- and dinitrophenolates, too) was used for the PPP calculation of anionic form of Nitroxynil.

For the MIM calculations the electron affinity of 9 eV and the one centre repulsion integral of 15.28 eV proved to the best. The optimum value of resonance integral ($\beta_{CO^-} = -3.0$ eV) for MIM calculations was determined by variation, repreducing the transitions for ionized phenolate and nitrophenolate models. The calculated spectral data of some molecules used for parametrization are given in Table 5.

All two centre repulsion integrals were calculated by the method given by Mataga and Nishimoto.[22]

The spectral data of Nitroxynil calculated by the PPP and MIM methods are given in Tables 2 and 3. Both approximations reproduce the experimental transition energies satisfactorily and justify our earlier statements on transferability of MIM parameters as well. These parameters taken from our earlier works were optimized for a larger number of substituted benzenes and they are expected to be transferable. To control this transferability statement, calculations were made with modified resonance integrals but no significant improvement could be reached. The results of calculations justify the transferability of parameters. The parameters optimized for the composite molecules can be used with good results for calculations of complicated molecules.

The relative intensity of the first, fourth and fifth bands calculated by the PPP method correspond to the experimental values, the second band can be

Table 3. MIM results of neutral molecules

Compound	Calculated		Experimental	
	E	$E_{tri}-E_{tetra}$	E	$E_{tri}-E_{tetra}$
2-iodo-6-nitro-phenol	3.921	0.097	3.473	0.039
	5.092	0.204	4.196	0.216
	5.474	0.040	5.390	0.309
	5.747			
3-iodo-4-hydroxy-benzonitril	4.325	0.501	4.366	0.854
	5.141	0.253	4.920	0.508
	5.764			
	6.286			
3-iodo-5-nitro-benzonitril	4.261	0.437		
	5.212	0.324		
	5.478			
	5.730			
3-nitro-4-hydroxy-benzonitril	4.056	0.232	3.734	0.222
	4.682	0.206	4.492	0.080
	5.171			
	5.754			
Nitroxynil	3.824		3.512	
	4.888		4.412	
	4.952		5.081	
	5.434		5.767	

* present work /ethanolic solution/

Table 4. Net π charges of some characteristic atoms of Nitroxynil

Form	C_3	C_5	O_7	I_8	C_9	N_{10}	N_{11}	O_{12}	O_{13}
Neutral	+0.033	+0.048	+0.159	+0.052	+0.158	-0.195	-0.061	-0.523	-0.496
Ionized	+0.031	+0.049	+0.212	+0.053	+0.158	-0.199	-0.062	-0.530	-0.499

Table 5. PPP and MIM results of ionized molecules

Compound	Calculated				Experimental			
	PPP			MIM	Uncorrected		Corr.	
	E	f	α	E	E	f	E	Ref.
Phenolat	4.378	0.060	270	4.088	4.312	0.055	4.295	present work
	5.271	0.432	0	5.008	5.276	0.200	5.276	
	6.312	0.380	270	5.970				
	6.632	0.777	180	6.429				
2-nitro-phenolat	3.518	0.185	136.9	3.275	2.987	0.126	3.033	25
	4.731	0.032	169.4	4.765	4.396	0.115	4.528	
	5.277	0.044	351.0	5.050				
	5.414	0.678	208.3	5.506	5.498	0.338	5.498*	
3-nitro-phenolat	3.663	0.095	48.9	3.404	3.155	0.036	3.352	25
	4.814	0.050	227.9	4.446	4.253	0.100	4.550	
	5.213	0.580	160.2	5.534	4.939	0.252	4.939●	
	5.417	0.369	133.7	5.699	5.510	0.338	5.510●	
4-nitro-phenolat	4.176	0.634	180	3.974	3.107	0.468	3.534	25
	4.341	0.010	270	4.437				
	5.437	0.189	270	5.236	5.486	0.151	5.685	
	5.808	0.021	180	5.870				
Nitro-xynil anion	3.412	0.157	183.0	3.231	3.069	0.113	3.000	present work
	4.462	0.012	339.7	4.454	4.592	0.434	4.505	
	4.580	0.530	83.0	4.618				
	4.938	0.202	95.0	5.317				

* uncorrected /data for acidic solution is not avaible/

● uncorrected /data for hexane solution is not avaible/

considered as a forbidden one on the basis of its calculated intensity and the third band can be assigned to the 4.412 eV band that appears as a shoulder in the experimental spectrum. The results of the MIM calculations are in good accordance with that of the PPP calculations but the forbidden band of PPP calculation has no equivalent in the MIM result. According to the MIM calculation the CT contribution to the calculated eigenfunction of the first band is negligible. There is however a large contribution of the charge transfer between the benzene ring and the nitro group to the third and fourth transitions. The CT contribution in the wavefunction of second band is small and this is why the calculated energy is larger than the experimental one.

The spectra of some subsystems containing two or three of the substituents were calculated by the PPP method as well as to investigate the conjugation of the Nitroxynil molecule. The calculated and experimental transition energies and oscillator strengths are given in Table 2. The experimental oscillator strengths were calculated by the equation of $\epsilon = k \cdot f$[23] with the experimental ϵ_{max} [$dm^3 mol^{-1} cm^{-1}$] values ($k = 41{,}700$ cm). The calculated polarization directions are measured from the bond axis of OH substituent in clockwise direction. The calculated spectral data are in agreement with the conclusions obtained from the experimental spectra, that is the conjugation is the strongest between the OH and NO_2 as well as the OH and CN groups and the iodine atom has the smallest role in the conjugation in the Nitroxynil.

A different consideration was used for the investigation of the conjugation interaction in the case of the MIM method. The change in the spectrum caused by the omission of one substituent in Nitroxynil was examined. The calculated and experimental transition energies are given in Table 3. The difference between the excitation energies of the corresponding trisubstituted derivatives and the tetrasubstituted Nitroxynil ($E_{tri} - E_{tetr}$) are also given. According to these results the effect of nitro and hydroxy groups can be considered as dominant.

In the light of the results derived from the PPP and MIM calculations as well as from the the experimental data the conjugation between the hydroxy and nitro groups seems to be of greatest importance. According to the PPP calculation and experimental spectrum of trisubstituted derivatives containing nitrile group, however, the participation of the nitrile group in the conjugation is also considerable as shown by the band near 5 eV.

The spectrum of the ionized form of Nitroxynil was calculated to justify the supposed ionization of Nitroxynil in alkaline and diluted alcoholic solution. The atomic π-charges were calculated by the PPP method for the determination of the presumable position of the ionization. The net π-charges obtained for the substituents are given in Table 4. Accordingly the most likely position for ionization is the oxygen atom of the hydroxy group having the greatest positive charge. Although C-9 of the nitrile group has also positive charge, the basic ionization of the hydroxy group seems to be more probable. The results of the PPP and MIM calculations as well as the results obtained for the molecules used for parametrization were collected in Table 5. Although the calculated transition energies refer to isolated molecules (vapour, non-polar solvent), the spectrum of anion cannot be measured in apolar solvents. For this reason the solvent effect of water was taken into account in correcting the band maxima of the spectrum for basic solutions by the shift of $\Delta\lambda = \lambda_{max}(\text{acid}) - \lambda_{max}(\text{hexane})$. The correction was made for the acidic solution instead of the aqueous one because in acidic solution the totally undissociated form is present. The energies of the corrected and uncorrected band maxima are given in Table 5. The expected ortho > meta > para order of λ_{max} values is realized for the corrected values only and the calculated results are in better agreement with these corrected energies as well. The calculated spectra of nitrophenolate ions could be improved slightly with some modification of the parameters of nitro group but these modified parameters could not improve the results calculated for nitrobenzene, therefore no modification was performed. The calculation gives the band shifts caused by the phenolic oxygen in accordance with the experimental spectrum, that is the shift of the first band of nitrophenolate ions correspond to the experimental order.

The calculated spectrum of the Nitroxynil model having an ionized hydroxy group is in good agreement with the experimental measurement for alkaline solution. Thus it can be stated that the reason of the red shift found in alkaline media is the ionization of the hydroxy group of the Nitroxynil molecule. According to the MIM calculation the shift of the first calculated band is slightly greater than that of the experimental spectrum and according to the PPP calculation this shift is somewhat smaller. However the calculated results give unambiguous verification for the ionizations that occur in alkaline solution.

The net π-charges calculated for the ionic model are given in Table 4. It can be seen that apart from the hydroxy oxygen atom no significant change in charges occurs compared to the neutral molecule. In turn a greater positive π-charge appears on the oxygen atom due to the new σ lone-pair electrons.

CONCLUSION

It is verified that in neutral form of the Nitroxynil the substituent effect of the hydroxy and nitro groups is very strong but the appearance of the 5 eV band refers to the non-negligible role of the nitrile group, too. The results calculated by both theoretical methods used (PPP, MIM) are in accordance with the experimental ones. This confirms our earlier statements that the parameters used for the MIM calculations and optimized for the subsystems can be transferred to the MIM calculations of more complex molecules with good results.

The strong red shift of the Nitroxynil molecule occurring in alkaline solution can be interpreted by the ionization of the hydroxy group. A similar interpretation was given for the change of the spectrum occurring in aqueous and alcoholic solutions. Both calculations (PPP and MIM) carried out for the ionized form reproduce this experimental red shift very well. New parameters for O^- ion were elaborated for these calculations.

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