ELECTRONIC SPECTRAL PROPERTIES OF REDOX COENZYME PYRROLOQUINOLINE QUINONE: A CNDO-CI STUDY

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Electronic absorption spectra of coenzyme PQQ and its reduced form, PQQH$_2$, were calculated by the CNDO/S-CI method. The use of 170 monoexcited configurations was found to be necessary in order to give the correct interpretation of observed UV absorption. Influence of the carboxylic group geometries on the spectra is discussed.

PQQ (pyrroloquinoline quinone) is the semi-systematic name given[1] to 4,5-dihydro--4,5-dioxo-1H-pyrrolo[2,3-*f*]quinoline-2,7,9-tricarboxylic acid (*I*) which can be also found under the name of "methoxatin" (ref.[2]). In the past few years it has become clear that in addition to the NAD(P)-dependent and flavoprotein dehydrogenases there is another class, the so-called quinoproteins, in which PQQ is involved as the coenzyme[3]. PQQH$_2$ (*II*), the reduced form of the coenzyme, is also involved in the


I *II*
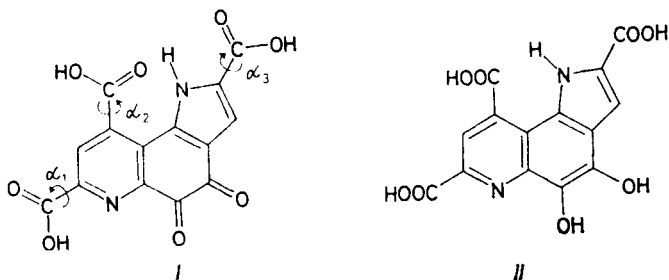
enzymatic catalysis[4]. Although a sufficient effort has been given to isolation, characterization and synthesis of the PQQ itself and its derivatives, no attention has been paid to its theoretical study. Since especially UV absorption spectra have frequently been utilized for the identification of compounds *I* and *II* in various biological materials, we have decided to examine the spectral properties by quantum chemical methods.

CALCULATIONS

All numerical calculations were carried out using the standard MNDO program[5] with automatic procedure searching minima on a potential hypersurface[6,7] in addition to standard CNDO/2 (ref.[8]), INDO (ref.[9]) and CNDO/S-CI (ref.[10]) programs, all adapted on an ICL-4-72 computer.

RESULTS AND DISCUSSION

The initial problem to solve was to assess the unknown molecular geometries of *III* and *IV*, the skeletons of PQQ and PQQH$_2$, respectively. In the first step the hetero-cyclic systems *III* and *IV* were approximated as planar molecules possessing standard bond lengths and bond angles[11]. Such geometries were then submitted to MNDO optimization with respect to all degrees of freedom. The calculated nuclear Cartesian
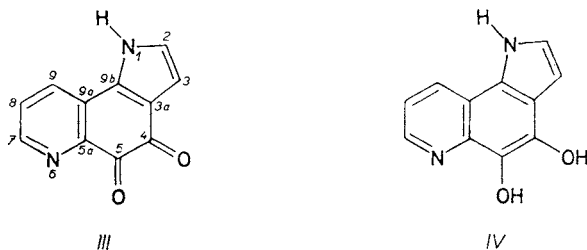
coordinates of *III* and *IV* are available on request. In the second step the complete PQQ (*I*) and PQQH$_2$ (*II*) molecules were constructed, exchanging hydrogen centres H(2), H(7) and H(9) for three carboxylic groups. Geometries of the carboxylic groups, chosen according to ref.[11] and the distance C—C(OOH) adjusted at 146 pm, were accepted.

Assuming molecule *I* to roughly planar, the occurence of eight rotational isomers *Ia* − *Ih*, having typical torsion angles α_{1-3}, may be expected. The relevant structures are summarized in Table I.

In the third step we have tried to perform the MDO calculation of planar molecules *Ia* − *Ih* but the method failed probably due to its incapability[12] to describe hydrogen bonds among carboxylic groups and heterocyclic nitrogens. Therefore, only CNDO/2 calculations of the above mentioned isomers *Ia* − *Ih* were accomplished. As follows from Table I, the corresponding CNDO/2 energies seem to be mainly influenced by the α_2 values, i.e. by the C(9) carboxylic group orientation. Any nuclear configuration in which the C=O bond points to the N(1) hydrogen leads to a decrease of CNDO/2 energy, evidently due to a hydrogen bond formation and differences between individual isomers *Ia* − *Id* are negligible. On the other hand, isomers *If* and *Ih* are energetically disfavoured because of the interaction between (H1) and the carboxylic hydrogen.

Table I summarizes the dipole moments of isomers $Ia-Ih$ calculated by the CNDO/2 and INDO methods. A comparison with available experimental values might help in the identification of individual conformers of I especially in apolar solvents.

The standard PPP method (ref.[13]) in the π-approximation was found to be quite incapable to interpret the UV absorption curves of Ia. Similarly, the CNDO/S-CI method (Del Bene–Jaffe's constant kappa established to 0·585) involving 16, 49 and 81 monoexcited configurations did not reproduce the experimental spectrum satisfactorily. Only its extension to 170 monoexcited configurations resulted in good agreement with the experiment[14] (see Fig. 1). The relatively large range of the configuration interaction does not seem to be surprising since system I has 18 free electron pairs. To establish the influence of carboxylic groups orientation on the absorption spectra we have performed analogous calculations involving 170 monoexcited configurations also for conformers $Ib-Id$, as well as for such a configuration Ii of molecule I, in which all three carboxylic groups are perpendicular to the plane of heterocyclic system III. From Table II follows that the position and character of the first five absorption bands is roughly conserved for all structures of $Ia-Id$. Relative participation of particular AOs in resulting MOs influence only its detailed values but lone pairs of C(2) carboxylic oxygen evidently play the most important role. Positions of the 1st and 4th absorption bands of the $n_{O(quinone)} \to \pi^*$ type vary according to α_1 value, while the other absorption bands ($n \to \pi^*$ and $\pi \to \pi^*$) are not so sensitive to α_1 and α_3 variations. In the case of conformation Ii any interaction of the carboxylic lone pairs with the heterocyclic system is eliminated and the character of the calculated spectrum is then completely changed. The new $\pi \to \pi^*$

TABLE I

Description of isomers $Ia-Ih$, their relative energies and dipole moments (1 D = 3·33564 . . 10^{-10} Cm)

	Torsion angle, °			Relative energy kJ mol^{-1}	Dipole moment, D	
	α_1	α_2	α_3		CNDO/2	INDO
Ia	0	0	0	0·0	3·764	4·056
Ib	0	0	180	5·5	9·083	9·630
Ic	180	0	0	2·1	5·746	6·324
Id	180	0	180	7·7	10·967	11·780
Ie	0	180	0	126·9	2·491	2·730
If	0	180	180	140·2	7·291	7·681
Ig	180	180	0	128·5	4·526	5·008
Ih	180	180	180	141·8	9·277	9·936

absorption band is now localized near 280 nm. A similar shift to lower wave lengths could be observed for other transitions, due to formal division of conformation Ii into two independent subsystems — the heterocyclic III and the carboxylic ones. However, confrontation with the experimental UV spectra suggests the negligible abundance of the perpendicular structure Ii under conditions of measurements.

Similarly as in the case of molecule I the spectral characteristic for II were also examined. Assuming that its spectrum will not be substantially influenced by the α_1 and α_3 variations, only rotational isomer IIa was examined. Again 170 mono-excited configurations were taken into account. Fig. 2 shows good agreement of the calculated electronic transitions with the experimental absorption curve[14].

The nature of calculated spectra of I and II differ substantially. While for I the most important transitions are of $n_{O(quinone)} \rightarrow \pi^*$ type, compound II exhibits important participation of carboxylic free electron pairs (see Table II). The first three transitions are of very low intensity and free electron pairs of centres N(1), carbonyl O(9), (333·1 nm band), carbonyl O(2) (322·1 nm band) and carbonyl C(7), N(6) (321·1 nm band), respectively, are responsible. All the excitations proceed into π^* antibonding MOs completely delocalized over the whole heterocyclic skeleton IV. Among those three transitions the first one bears another interesting feature. Due to the presumed hydrogen bond between nitrogen N(1) and carbonyl oxygen O(9) s-orbital of the respective H atom also participates somewhat in the 333·1 nm absorption band.
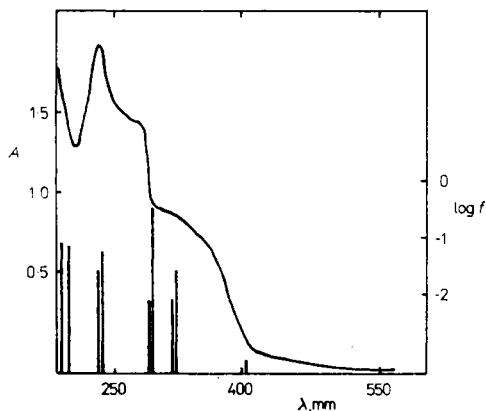

FIG. 1

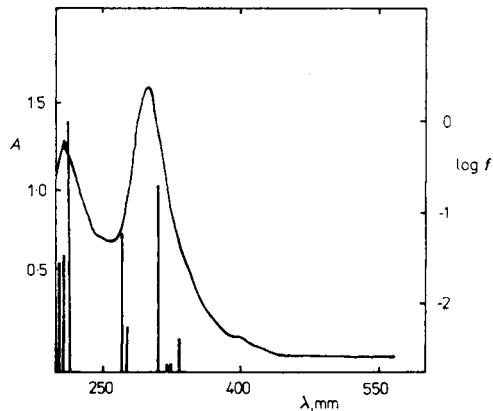Comparison of the absorption curve of compound I with the CNDO/S calculated spectrum

FIG. 2

Comparison of the absorption curve of compound II with the CNDO/S calculated spectrum

TABLE II

Characteristics of the first five absorption bands calculated for compounds $Ia—Id$, Ii and IIa

No.	Compound	λ_{max} nm	$\log f$	Type	Compound	λ_{max} nm	$\log f$	Type
1	Ia	405·2	−5·7499	$n_{O(quinone)} \to \pi^*$	Ib	405·2	−5·6518	$n_{O(quinone)} \to \pi^*$
2		328·8	−2·4170	$n_{O,N} \to \pi^*$		339·3	−2·4903	$n_O \to \pi^*$
3		325·9	−3·4438	$n_O \to \pi^*$		322·7	−3·4846	$n_{O,N} \to \pi^*$
4		303·3	−3·0099	$n_{O(quinone)} \to \pi^*$		309·4	−3·3457	$n_{O(quinone)} \to \pi^*$
5		302·0	−0·2349	$\pi \to \pi^*$		302·4	−0·1524	$\pi \to \pi^*$
1	Ic	371·6	−5·1985	$n_{O(quinone)} \to \pi^*$	Id	364·9	−5·1527	$n_{O(quinone)} \to \pi^*$
2		333·9	−3·3526	$n_O \to \pi^*$		341·9	−3·3651	$n_O \to \pi^*$
3		325·7	−2·6479	$n_O \to \pi^*$		325·8	−3·4751	$n_O \to \pi^*$
4		325·6	−2·6957	$n_{O(quinone)} \to \pi^*$		322·2	−2·3924	$n_{O(quinone)} \to \pi^*$
5		302·2	−0·2452	$\pi \to \pi^*$		302·8	−0·1690	$\pi \to \pi^*$
1	Ii	279·8	−0·2183	$\pi \to \pi^*$	IIa	333·1	−2·4714	$n_{N(1),O(7)} \to \pi^*$
2		250·7	−2·4801	$n_O \to \pi^*_{C(2)=O}$		322·1	−3·3800	$n_{O(2)} \to \pi^*$
3		247·6	−3·8227	$n_O \to \pi^*$		321·1	−3·3490	$n_{O(7)} \to \pi^*$
4		231·2	−1·6409	$\pi \to \pi^*$		313·6	−0·7161	$\pi \to \pi^*$
5		193·6	−0·9451	$\pi \to \pi^*$		274·4	−2·3623	$n_{N(6)} \to \pi^*$

The intensive fourth absorption band $(313 \cdot 6 \text{ nm})$ is exclusively of a $\pi \rightarrow \pi^*$ character with dominant HOMO $\rightarrow$ LUMO transition (78%). The last depicted transition of $n \rightarrow \pi^*$ type is similar to those of the first three.

CONCLUSIONS

Electronic transitions of complex heterocyclic dione *I* and diole *II*, having three carboxylic groups, have been found to be correctly calculated by CNDO/S-CI method provided by a large number of monoexcited configurations taken into account. The calculations enabled to attribute individual transitions to the respective absorption bands.

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