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Reactivity of Pyrrole Pigments. Part 9 [1] MINDO/3 Calculations on Dipyrrolic Partial Models of Bile Pigments

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The applicability of the MINDO/3 method is evaluated for calculations on dipyrrolic partial structures of bile pigments. It is shown that this method cannot be used for an accurate conformational analysis. However, when applying the frontier orbital model for reactivity parameters, a good picture of the HOMO and the LUMO distribution can be obtained in this type of molecules.

(Keywords: Bile pigments; 3,4-Dihydro-5(1H)-pyrromethenones; Frontier orbital model; 5-⟨[2-Methylen-2(2H)-pyrrol-5-yl]methylene⟩pyrrolidin-2-one; 5-⟨[2-Methylen-2(2H)-pyrrol-5-yl]methylene⟩-3-pyrrolin-2-ones; MINDO/3; Pyrromethenes; 5(1H)-Pyrromethenones)

Reaktivität von Pyrrolpigmenten, 9. Mitt. MINDO/3-Rechnungen von dipyrrolischen Partialmodellen von Gallenpigmenten

Es werden die Einsatzmöglichkeiten von MINDO/3 für den Fall dipyrrolischer Partialstrukturen der Gallenpigmente aufgezeigt. Die Methode ist für eine genaue Konformationsanalyse nicht geeignet. Unter Verwendung der Reaktionsparameter des Frontier-Orbital-Modells läßt sich jedoch ein gutes Bild der HOMO- und LUMO-Verteilung für diesen Verbindungstyp gewinnen.

Introduction

More or less sophisticated semi-empirical methods have been used to study molecular energies and other structural features of bile pigment molecules, or of molecules representing partial models of linear bile pigments. CNDO/2 gives good information on the conformation and energies of pyrromethenes [2] and dipyrrylmethanes [3]. MINDO 3 has been used to obtain dipole moments and

some structural details of pyrroles and pyrrolinones [4]. MINDO/3 [5, 6] and MNDO [6] afford data on the relative energy of different tautomers and derivatives of pyrrolin-2-one, which represent partial models of the terminal rings of bile pigments. PCILO has been applied in the conformational study of azobilirubin dyes (i.e. pyrromethenone derivatives) [7]. We have recently published our first results on the reactivity of pyrromethenones [8], using the calculations obtained by MINDO/3 and a simple approach to the frontier orbital model.

Concerning the tetrapyrrolic linear systems, only π electron methods have been used, usually to correlate structure and electronic spectra [9]. The most recent example corresponds to the application to 2,3-dihydrobilatrienes-*abc* of a PPP method with CI [10], parametrized for dipyrrolic systems and also used on fully unsaturated bilatrienes-*abc* [9 e]. Predictions of reactivity obtained following the *Fukui* frontier orbital model [11] have been compared with empirical reactivity patterns of tetrapyrrolic pigments [12]. The same model has been used for bile pigments getting the atomic orbital coefficients from PPP calculations [9 e, 10]. We have already published our first results on pyrromethenones and 5-arylmethylene-3-pyrrolin-2-ones using atomic orbital coefficients obtained by the MINDO/3 method [8].

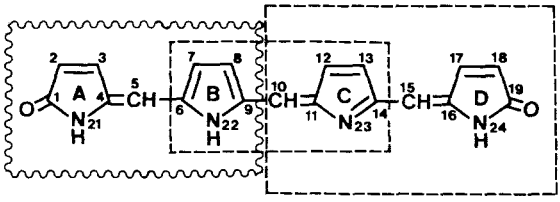
In this paper, we report our results on the MINDO/3 calculations performed on the dipyrrolic partial models of bilatrienes-*abc* and 2,3-dihydrobilatrienes-*abc*. In the following paper of the series we present the calculations performed on the corresponding tetrapyrrolic structures. Our aim is the evaluation of the applicability of the method to linear tetrapyrrolic systems. The features that we try to evaluate are molecular geometry, configurational and conformational relative energies, dipole moments and, through the reactivity parameters obtained using the frontier orbital method, chemical reactivity.

Methodology

5-(1*H*)-Pyrromethenone (**4**), pyrromethene (**5**), and 5-[2-methylene-(2*H*)-pyrrol-5-yl]methylene-3-pyrrolin-2-one (**6**) (see formula scheme) must be considered as dipyrrolic partial models of the fully unsaturated bilatrienes-abc (**1**). The atom numbering of the dipyrrolic systems corresponds to the tetrapyrrolic systems to enhance comparability. As partial models of 2,3-dihydrobilatrienes-abc and taking into account the tautomerism of the two central nitrogen atoms (see structures **2** and **3**), we have studied the 3,4-dihydro-5-(1*H*)-pyrromethenone (**7**) and the corresponding dihydro structure **8**. In the literature there is enough experimental data about pyrromethenones and pyromethenes to permit the evaluation of the MINDO/3 results on these compounds and to use it to predict properties of the chemically less studied structures (e.g. structure **8**).

In spite of the previously reported results from MNDO and MINDO/3 [6], one cannot clearly decide which method is more adequate to calculate the ΔH°_f of these type of compounds. However, owing to our interest in the reactivity, we have chosen the MINDO/3 method, because its reactivity parameters and its charge distribution were more in agreement with the experimental results than the MNDO ones [6 b].

All calculations have been carried out using the semi-empirical SCF-MO MINDO/3 method, with standard parameters [13]. Geometries have been optimized for the planar structures of **4–13** with the unique restriction of planarity in all the molecule: such a restriction was applied because former results using



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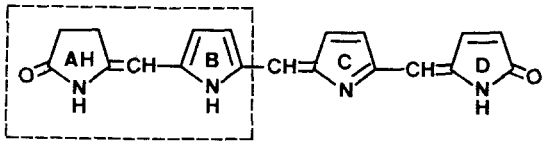

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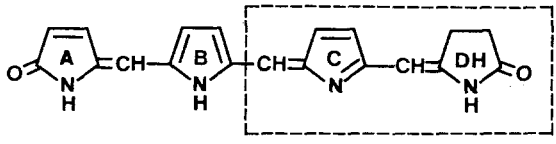

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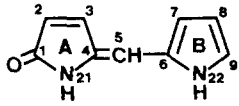
MINDO/3 on 5-methylenepyrrolidin-2-one and 5-methylene-3-pyrrolin-2-one, without any restriction, gave planar structures [6]. The non-planar conformations at the meso bridge-single bond have been calculated by keeping constant the remaining geometrical parameters. The theoretical reactivity parameters have been calculated using the *Fukui* frontier orbital model [11]: reactivity parameters for atom i, are calculated from $2\sum_k c_{ik}$, c_{ik} being the HOMO (for reactivity towards electrophiles) or LUMO (for reactivity towards nucleophiles) atomic orbital coefficient of the atomic valence orbital k of the atom i. Reactivity parameters towards radicals are calculated by the half sum of the electrophilic and nucleophilic parameters. The use of such a simple model is hold by the energy gap exists between HOMO and NHOMO, and LUMO and NLUMO orbitals ($\geqslant 0.4$ eV) for all these types of compounds.



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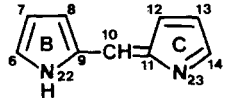

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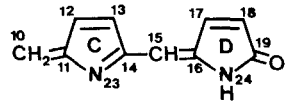

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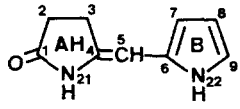

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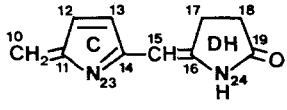

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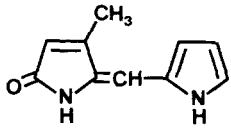

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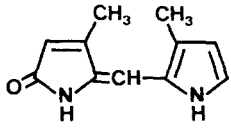

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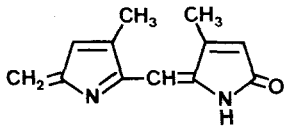

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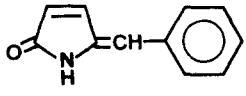

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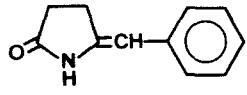

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Results and Discussion

Geometries

The calculated geometries are only in slight agreement with X-ray structural data described in the literature for similar compounds (see Ref. [14] for a review). Our calculated bond lengths show more single or double bond character (more in accordance with the localized bond representation) than the experimental ones. The most significant difference corresponds to the methine bridge angles (internal C—C—C bond angle),

Table 1. ΔH°_f *calculated by the MINDO/3 method for the Z- and E-isomers of the structures* **4–11** *at several conformational angles (for the sense of the conformational angle see Scheme 1; energy minima are underlined)*

Structure	Configuration	ΔH°_f(kJ mol^{-1})						
		Conformational angle						
		0°	30°	60°	90°	120°	150°	180°
4 (AB)	*Z*	9.1	8.4	**6.3**	6.8	6.5	7.4	8.5
	E	12.1	11.9	**11.1**	11.8	11.9	12.6	12.9
9 (AB)	*Z*	−20.9	−22.0	−24.4	**−25.5**	−24.7	−23.1	−21.3
	E	1.6	−7.8	−12.0	−13.2	**−13.7**	−9.4	−6.5
10 (AB)	*Z*	−54.6	−57.0	−61.8	**−62.4**	−53.5	−46.5	−38.8
	E	−31.1	−35.5	−45.2	**−60.4**	−32.7	−18.9	−4.0
5 (BC)	*Z*	**350.1**	350.3	353.2	355.3	354.7	355.1	355.0
	E	**359.0**	359.6	360.0	362.0	362.2	361.1	361.2
6 (CD)	*Z*	**155.0**	155.0	155.1	157.0	160.3	163.6	165.9
	E	160.6	**160.3**	160.6	163.1	166.5	168.8	170.9
11 (CD)	*Z*	90.0	88.8	**87.4**	89.5	99.3	119.9	126.7
	E	113.1	109.3	102.7	**101.7**	113.2	143.3	163.8
7 (AHB)	*Z*	−118.3	−119.8	−123.6	**−123.9**	−122.7	−121.7	−120.1
	E	−116.0	−116.7	−117.8	**−118.5**	−118.0	−116.8	−116.1
8 (CDH)	*Z*	**23.7**	23.8	24.3	26.4	29.9	35.1	35.6
	E	**29.4**	29.8	30.6	32.7	35.9	37.9	39.3

which are found to be wider (ca. 10°) in our calculations for all the structures. For structures **4** and **7**, the too wide calculated angle can be due to a MINDO/3 emphasis of the steric hindrance. However, in **5**, **6**, and **8**, this larger internal bond angle may be mainly attributed to the neglect by the MINDO/3 method of the intramolecular hydrogen bond. It is already known that the MINDO/3 method neglects hydrogen bonds [15] (see below).

Configurational and Conformational Energies

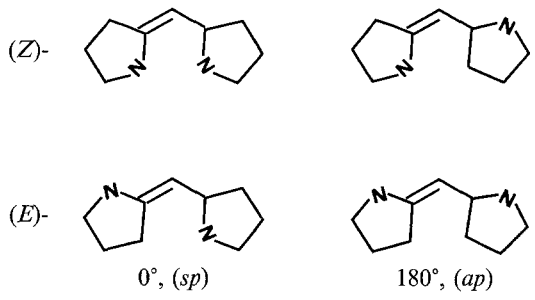
Table 1 shows the ΔH°_{f} calculated for several meso bridge single bond conformational angles of the *E*- and *Z*-isomers of the five studied dipyrrolic structures (**4–8**) and of some of the methyl and dimethyl derivatives of pyrromethenones and azafulvenylmethylene-pyrrolinones (**9–11**). The energies shown in Table 1 are given to illustrate the calculations but cannot be considered as representations of real energies, because of the restrictions applied in the calculation (see methodology) and the errors of the method. The calculations show that at the same meso-bridge conformational angle the *Z*-isomers are always more stable than the corresponding *E*-isomers. Although this trend is in agreement with all known experimental results [14, 16, 17], the calculated most stable dihedral angles are not always in good agreement with the experimental values, neither in solution nor in solid state. The experimental results indicate that in solution the conformational angle for (*Z*)-pyrromethenones [(*Z*)-**4**] lies at ca. 35° (*syn*) [18] and at 25° (*syn*) for the (*Z*)-3,4-dihydropyrromethenones [(*Z*)-**7**] [16]; in the case of *Z*-pyrromethenones [(*Z*)-**5**] a planar (*syn*) structure was found [19]; a 0° (*sp*) energy minimum (see Scheme 1 for the conformational angle definition) can also be inferred for structures (*Z*)-**6** and (*Z*)-**8** from the data of tetrapyrrolic systems [14, 17, 20]. Table 1 shows that the energy minima calculated for (*Z*)-**4** and (*Z*)-**7**, although *syn* as experimentally, have larger conformational angles than in solution (about 60°–90°). However for (*Z*)-**5**, (*Z*)-**6**, and (*Z*)-**8** a (*sp*) conformation is preferred, in agreement with experiments. The effect of methyl substitution at the p_0 positions flanking the meso-bridge determines, as found experimentally, an increase of the minimum conformational angle. But this effect is overestimated in the calculations: for the *Z*-isomers of the substituted derivatives of **4** and **6** (**9–11**) the minima calculated lie always at conformational angles near 90°. As discussed above, in the case of structures **4** and **7** whether substituted or unsubstituted, we attribute the large dihedral angle to an emphasis by MINDO/3 of the nonbonded interactions. However, although exaggerated, the calculated energies seems to undergo the same effects as experimentally detected: compare the flat energetic profile for (*Z*)-**4** with the "deep hole"

profile of (*Z*)-**9**, and the energetic effect of the methyl substitution at the positions flanking the meso bridge which is higher for the *E*-isomers than for the *Z*-isomers. For the structures of type **5**, **6**, and **8**, the underestimation of the stability of the (*sp*) conformation, with respect to that of the twisted conformations, must be attributed, in addition, to the neglect of the hydrogen bond by the MINDO/3 method [15]. Effectively, the analysis of the two centre energy terms [21] shows that for the *Z*-isomer of **5**, **6**, and **8** at 0° (*sp*) practically no interaction exists between the N—H hydrogen and the pyrroleninic nitrogen. The inclusion of the energetic effect of an intramolecular hydrogen bond would stabilize the *sp* conformations of the *Z*-isomers.

Dipole Moments

MINDO/3 has already been used to estimate the dipole moments of monocyclic pyrrolic partial models of bile pigments, giving a good estimation of the experimental values [4]. Table 2 compares, for the *E*- and *Z*-isomers of **4**–**8** at the conformation 0° (see Scheme 1), the MINDO/3

Scheme 1



calculated dipole moments with the dipole moments calculated from the vertical sum of the partial dipole moments of the corresponding two rings. These results indicate a correlation between these two types of calculated dipole moments, and corroborate the approximation to use the last ones in force field calculations of linear pyrrole pigments [4]. Although not indicated in Table 2, this correlation is also maintained for the conformation 180° (*ap*) and it is obviously improved for conformational angles near 90°.

The following values were used for the partial dipole moments: 1.960 D and an angle of 124.7° to the C—NH bond for the pyrrole ring; 3.765 D and an angle of 131.0° to the N—CO bond, for the 5-methylene-

3-pyrrolin-2-one system; 3.185 D and an angle of 125.1° to the N—CO bond, for the 3,4-dihydro-5-methylene-3-pyrrolin-2-one system; 1.484 D and an angle of 126.2° to the C=N bond, for the 2-methylene-(2*H*)-pyrrole: all these dipole moments were calculated by the MINDO/3 method.

Reactivity Parameters and HOMO and LUMO Distribution on the Molecule

Table 3 shows the reactivity parameters for the *Z*-isomers of **4–8** at the conformations 0° (*sp*) and 90°; at the same dihedral angle the *anti* conformations and also the *E*-configuration have practically the same values of reactivity parameters. In all structures calculated (*E*- and *Z*-isomers of **4–11**), the reactivity parameters are very similar for the both *E* and *Z* configurational isomers at the same conformational angle (calculations were performed between 0° and 180°, in steps of 30°; see methodology). This type of reactivity parameters represents the HOMO and LUMO distribution on the molecule. These results indicate that the two orbitals change only significantly with the angle between rings, and have a low dependence on the configuration at the exocyclic double bond. It has also been reported that in the case of the aryl analogues (**12**) the low energy band of the electronic absorption spectrum, i.e. the experimental energy gap between HOMO and LUMO depends only on the angle between rings [22], and it has been estimated from theoretical results that the tetrapyrrolic systems have the same behaviour [23]. Our results for structures **4–11**, showing the same HOMO and LUMO distribution for configurational isomers at the same angle between rings, agree with this general behaviour, in spite of not giving an accurate estimation of the HOMO—LUMO energy gap (owing to the low confidence of the LUMO energies).

5-(1*H*)-*Pyrromethenones* (**4**; AB): The results can be summarized (Scheme 2) as follows. The electrophilic reactivity of a pyrromethenone is fundamentally that of the 5-methylene-3-pyrrolin-2-one partial structure. At angles far from planarity this reactivity partition pattern is even more accentuated. Scheme 2 shows the reactivity coefficients of **4** at 0° and 90°. In case of the 5-arylmethylene-3-pyrrolin-2-one (**12**) both nucleophilic and electrophilic reactivity parameters are located on the 5-methylene-3-pyrrolin-2-one structure (see Scheme 2). These reactivity parameters agree with the experimental reactivity known. Thus, for 3,4-dialkyl substituted structures (positions 2 and 3 according to the denomination made in the formula scheme)—where the substitution obviously allows a better differentiation between the reactivities at positions 3 and 4 and the reactivities of the remaining positions of the molecule—has

Table 2. *Dipole moments calculated by the MINDO/3 method using the vectorial sum of partial dipole moments*[a] *for some dipyrrolic structures at the planar conformation [0° (sp) see Scheme 1]*

Structure	Configuration	MINDO/3 Dipole moment		Vectorial sum dipole moment[a]	
		D	Angle[b] (°)	D	Angle[b] (°)
4 (AB)	(*Z*)	2.5	143	1.8	122
	(*E*)	4.1	112	3.5	110
7 (AHB)	(*Z*)	1.6	117	1.4	102
	(*E*)	3.5	98	3.3	90
5 (BC)	(*Z*)	1.3	172	2.3	177
	(*E*)	2.8	127	3.3	148
6 (CD)	(*Z*)	4.8	129	5.2	133
	(*E*)	4.0	149	4.6	148
8 (CDH)	(*Z*)	4.2	120	4.6	131
	(*E*)	3.0	148	3.2	125

[a] For **4**, **6**, **7**, and **8**: lactam N, coordinate origin; N—Cl, *x* axis; ring on the *xy* plane. For **5**: C atom of C=N, coordinate origin; C=N, *x* axis; ring on the *xy* plane

[b] See Scheme 1

Table 3. *Reactivity parameters calculated from the HOMO and LUMO atomic at the 90°*

Atom Nr.[b]	**4** (AB)				**5** (AHB)			
	electroph.		nucleoph.		electroph.		nucleoph.	
	0°	90°	0°	90°	0°	90°	0°	90°
O—Cl	0.08	0.00	0.10	0.12	0.04	0.00	0.07	0.09
C1	0.02	0.00	0.18	0.21	0.01	0.00	0.17	0.24
C2	0.08	0.00	0.36	0.42	0.00	0.00	0.00	0.01
C3	0.00	0.00	0.39	0.47	0.00	0.00	0.02	0.03
C4	0.29	0.02	0.25	0.23	0.28	0.02	0.60	0.60
N21	0.17	0.01	0.00	0.00	0.19	0.01	0.01	0.01
C5	0.21	0.01	0.43	0.44	0.22	0.01	0.43	0.50
C6	0.40	0.70	0.03	0.02	0.41	0.69	0.13	0.09
C7	0.23	0.28	0.12	0.01	0.26	0.29	0.21	0.00
C8	0.13	0.25	0.00	0.00	0.13	0.24	0.00	0.01
C9	0.39	0.65	0.07	0.01	0.42	0.66	0.14	0.07
N22	0.01	0.00	0.07	0.04	0.01	0.00	0.15	0.14
C10								
C11								
C12								
C13								
C14								
N23								
C15								
C16								
C17								
C18								
C19								
N24								
O—C19								

[a] The differences observed between the reactivity indeces of the *E*- and *Z*-isomers at the same conformational angle are neglible

[b] For the atom numbering see the formula scheme

been reported that: aryl analogues as **12** undergo electrophilic substitution of the hydrogen at the bridge carbon atom while pyrromethenones (**4**) react at the α position of the pyrrole ring [8] (position 5′; C9 according to the denomination made in the formula scheme); nucleophilic addition of cyanide ion takes place at the bridge carbon in both cases (**4** and **12**) [6b, 24].

More experimental evidence corroborates also this frontier orbital location shown in Scheme 2. The chemical behaviour of pyrromethenones

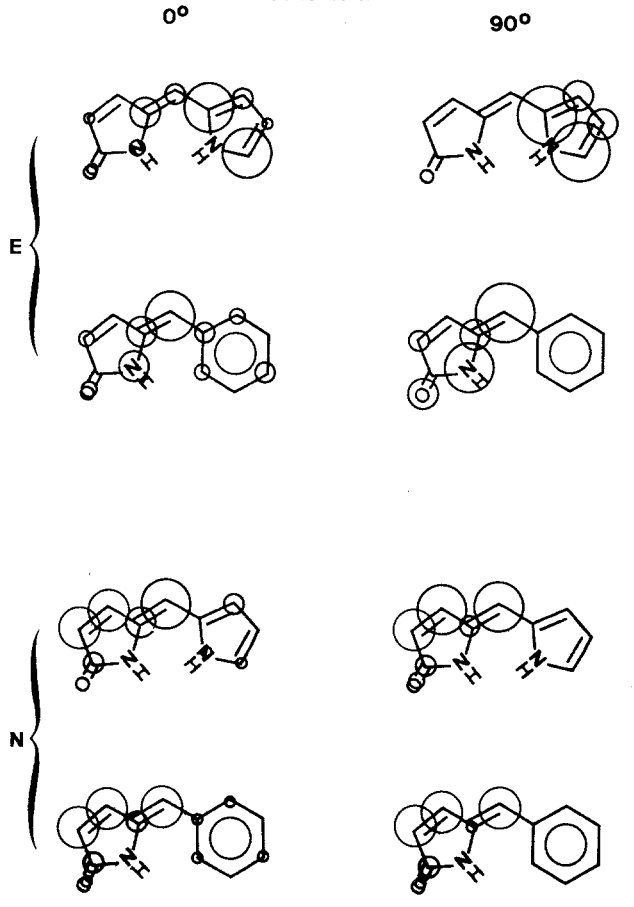
orbital coefficients obtained by MINDO/3 for the structures **4–8**[a] *at the planar and conformations*

Dipyrrolic ring system											
6 (BC)				**7** (CD)				**8** (CDH)			
electroph.		nucleoph.		electroph.		nucleoph.		electroph.		nucleoph.	
0°	90°	0°	90°	0°	90°	0°	90°	0°	90°	0°	90°
0.42	0.65	0.07	0.02								
0.16	0.21	0.00	0.00								
0.26	0.31	0.17	0.01								
0.46	0.68	0.03	0.02								
0.01	0.00	0.08	0.05								
0.14	0.02	0.53	0.57	0.21	0.00	0.19	0.00	0.23	0.00	0.42	0.57
0.35	0.03	0.53	0.57	0.08	0.02	0.03	0.01	0.09	0.03	0.10	0.17
0.00	0.00	0.27	0.33	0.02	0.04	0.07	0.00	0.02	0.05	0.21	0.35
0.09	0.00	0.21	0.25	0.00	0.18	0.03	0.02	0.00	0.21	0.12	0.25
0.11	0.00	0.26	0.30	0.13	0.09	0.15	0.00	0.14	0.10	0.31	0.35
0.00	0.02	0.16	0.20	0.34	0.48	0.22	0.02	0.37	0.57	0.30	0.25
				0.43	0.41	0.26	0.45	0.45	0.39	0.10	0.00
				0.27	0.22	0.28	0.22	0.26	0.21	0.32	0.01
				0.00	0.00	0.26	0.49	0.00	0.00	0.01	0.00
				0.08	0.07	0.28	0.43	0.00	0.00	0.00	0.00
				0.02	0.02	0.14	0.22	0.01	0.01	0.05	0.00
				0.30	0.31	0.00	0.00	0.32	0.31	0.02	0.00
				0.12	0.13	0.09	0.12	0.06	0.06	0.02	0.00

and their aryl analogous in the electrochemical reduction [25] indicates that the LUMO is located on the 5-methylene-3-pyrrolin-2-one structure. Furthermore, the study of the electrochemical mechanism in the formation of hydrodimers—bond through the bridge carbon atoms—in both types of compounds (**4** and **12**) gives also an indication about their different reactivity towards radicals [26]: according to the results reported here, in compounds of type **4** the meso bridge competes with the α-position of the pyrrole ring, while in aryl analogues such as **12** the meso

bridge carbon atom is clearly the most reactive: the electrolytic reductive hydrodimerization of pyrromethenones (**4**) and their aryl analogous (**12**) (meso bridge coupling) takes place only by the mechanism radical to substrate in the case of aryl analogues, but nucleophilic attack to substrate

Scheme 2

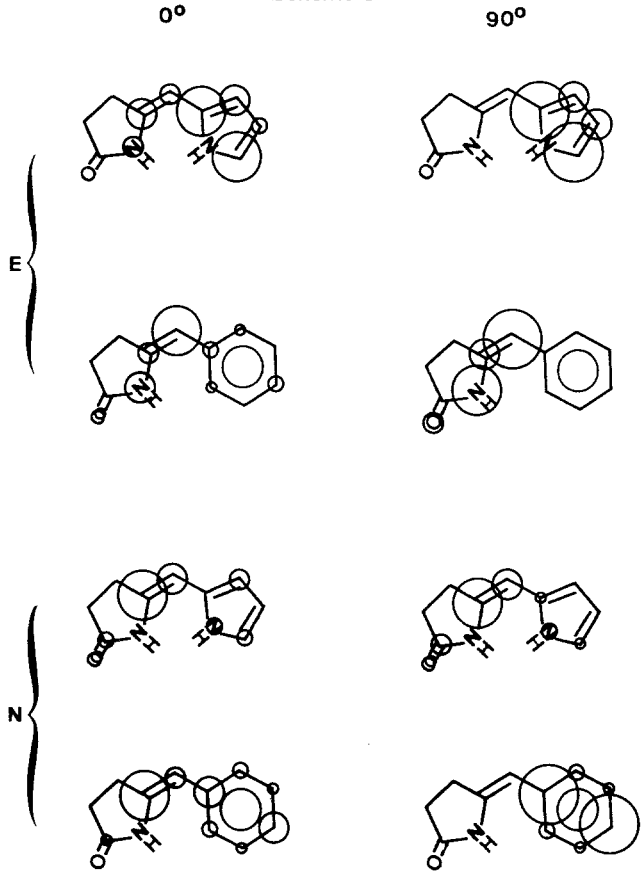


is the preferred reaction pathway for pyrromethenones [26]. Moreover, it has been described how in pyrromethenones the presence at the α position of the pyrrole ring of an electron withdrawing group, such as the ethoxycarbonyl group, determines a reactivity pattern similar to that of compounds of type **12** [8]. Such a result must be interpreted as due to the stabilizing effect of the alkyloxycarbonyl group on the original HOMO orbital located on the pyrrole ring, that determines the conversion

in HOMO of the molecular orbital located on the 5-methylene-3-pyrrolin-2-one structure.

On the other hand, linear polarization of the fundamental band of the electronic absorption spectra of 5(1*H*)-pyrromethenones [27], al-

Scheme 3



though in dimeric form, also accounts for this location of HOMO and LUMO in different halves of the molecule.

Taking into account that 5-(1*H*)-pyrromethenones are partial models of rubins, most of the typical reactivity of the last ones can be explained through the above described pyrromethenone reactivity pattern (e.g. "scrambling" reaction through electrophiles or radicals, reactivity of rubins towards diazonium salts, etc.) [28].

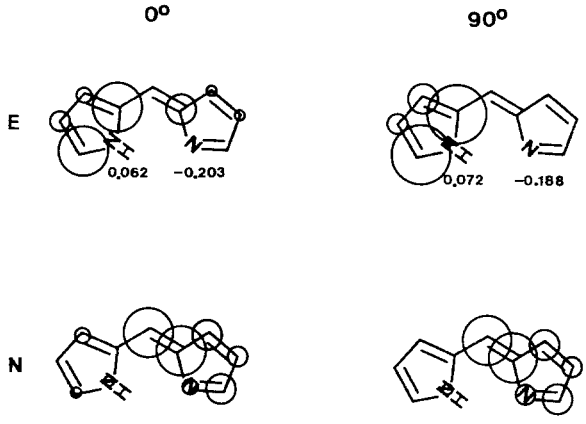
3,4-*Dihydro*-5-(1 *H*)-*pyrromethenones* (**7**; AHB): The reactivity parameters (Scheme 3) towards electrophiles are very similar to those obtained for the totally unsaturated system, i.e. the reactivity towards electrophiles is fundamentally that of the pyrrole ring. Non planar conformations give an even clearer location of the HOMO orbital on the pyrrole ring, as in the case of the unsaturated system. The LUMO is again located on the oxygenated ring, but it shows a different distribution compared to **4**: the more reactive position towards nucleophiles corresponds to the carbon atom at the position "4" (according to the numbering on formula scheme). An intramolecular lactonization of a 3,4-dihydropyrromethenone derivative [29] has been described which evidences the experimental nucleophilic reactivity of this carbon atom.

According to the reactivity parameters reported here the reactivity towards electrophiles of compounds of type **7** and their aryl analogues **13** must be different, in a similar manner to what occurs in the corresponding unsaturated systems (compare HOMOs of **4** and **12** in Scheme 2 with **7** and **13** in Scheme 3): to our knowledge it does not exist any experimental result about the reactivity towards electrophiles of basic structures of type **7**; however, a deuterium exchange at the meso bridge [29] of a derivative of **7** with an alkoxycarbonyl substituent at the position of the pyrrole ring has been reported. Such a reactivity could be related to the reactivity of **13**, indicating a similar effect of electron withdrawing groups on pyrromethenones (**4**) (see above) and on 3,4-dihydropyrromethenones (**7**). The comparison of the LUMO distribution on **12** and **13** at 90° gives a useful indication about the chemical differences between the lactam rings A and AH. In accord with that, both MINDO/3 and MNDO calculations show for AH a LUMO much less stable than for A [6 b].

Pyrromethenes (**5**; BC): See Scheme 4 to compare the relative reactivity parameters of the different atoms: the numbers on the nitrogen indicate the corresponding net atomic charges. A large number of nucleophiles add to the bridge carbon atom of pyrromethenes [30]: the high reactivity parameter of this carbon atom, compared to the remaining atoms of the molecule is in agreement with the experimental reactivity. Net atomic charges indicate that, for charge-controlled reactions towards electrophiles, the more reactive atom must be the pyrroleninic nitrogen. On the other hand, our results point to an orbital-controlled reactivity towards electrophiles typical of the pyrrole ring. Unfortunately, all the reactions of pyrromethenes towards electrophiles are described for their protonated forms (their salts are generally more stable than their free base forms). Many reactions of the protonated forms of pyrromethenes are used in the synthetic pathway to cyclic tetrapyrrolic pigments [31]: all these reactions can be interpreted as the electrophilic attack at the carbon atoms

6 or 14 (numbering in accord with formula scheme). In the case of the non protonated form (**5**) it is likely to expect high reactivity towards electrophiles at the α position of the pyrrole ring, in agreement with these reactivity parameters.

Scheme 4



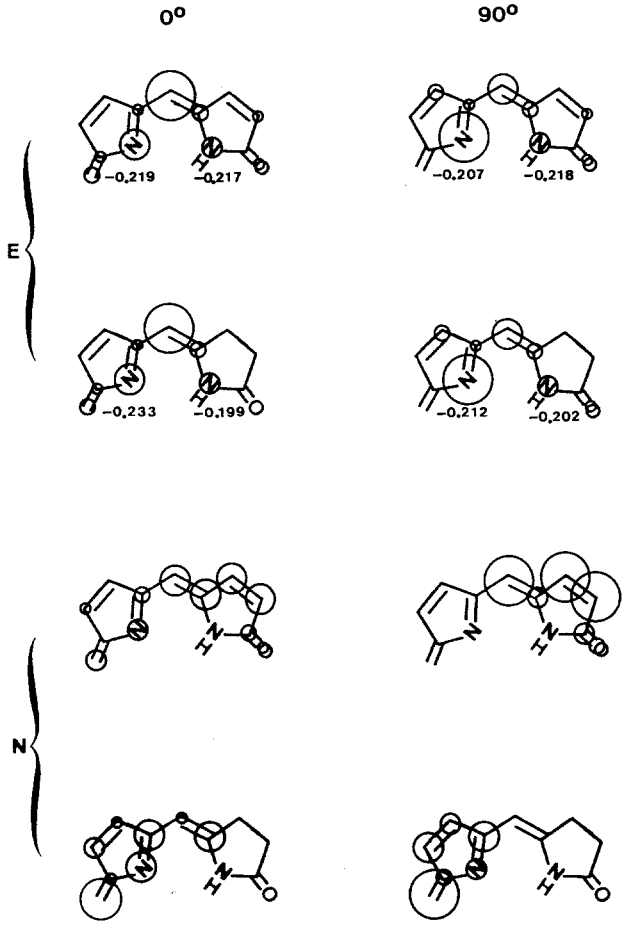
As shown in Scheme 4, HOMO and LUMO are each located preferentially on a different half of the molecule, this distribution being more accentuated for the out-of-plane conformations. This HOMO—LUMO distribution on the two halfs of the pyrromethene molecule also accounts for the polarization of the most important absorption bands of its electronic spectrum [32, 33], also in agreement with calculations performed by π-electron methods.

5-⟨[2-Methylene-(2H)-pyrrol-5-yl]methylene⟩-3-pyrrolin-2-one (**6**; CD) *and 5-⟨[2-methylene-(2H)-pyrrol-5-yl]methylene⟩pyrrolidin-2-one* (**8**; CDH): The electrophilic reactivity parameters are very similar for both type of structures (Scheme 5). Conformational changes also introduce similar changes in their reactivity towards electrophiles: these changes are not so important as those described above for other structures, and this must be attributed to the sigma character of the HOMO of **6** and **8**. The reactivity parameters towards nucleophiles are similar for the planar conformations of both types of structures (**6** and **8**), but they are different for the conformation at 90°. Thus at 90°, the HOMO is distributed in opposite halves of the molecule: at the 5-methylene-3-pyrrolin-2-one half for **6**, but at the azafulvenic part for **8**. Because of the low stability of this type of compounds, no experimental data on their reactivity were found. However, these structures have been proposed as reaction intermediates in a synthetic approach to bilatrienes-*abc*, the proposed

reaction pathway [34] being based on the reactivity towards nucleophiles at the methylene carbon atom of the exocyclic double bond at the pyrroleninic ring.

With respect to the net atomic charges at the pyrrolenin nitrogen (see numbers in Scheme 5), the results indicate that it is more negative in the

Scheme 5



dihydro structure CDH than in the corresponding unsaturated structure CD. Furthermore, such type of nitrogen is more negative in the structures CD or CDH (**6**, **8**), than in BC (**5**). A non planar conformation determines a decrease of the net atomic charge at that nitrogen in structures CD and CDH.

Final Remarks: The HOMO and LUMO of structures AB, AHB, BC, and the LUMO of CD, and CDH have a high π character: this π character determines in the conformations at 90° (obtained by rotation around the single exocyclic carbon-carbon bond which links the monocyclic partial models) the preferential distribution of the frontier molecular orbital on one or on the other half of the molecule, i.e. in only one of the two monocyclic partial models. Obviously, the favored location in one half, even the other can be estimated by the first ionization potential energy (for HOMO) or the electronic affinity (for LUMO) of the implicate monocyclic partial systems.

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