Monatshefte für Chemie 115, 357—373 (1984)

Monatshefte für Chemie
Chemical Monthly

Reactivity of Pyrrole Pigments. Part 5[1]: Electrophilic Substitution—Nitration and Bromination— of Some Pyrromethenones and 5-Arylmethylene-3,4-dimethyl-3-pyrrolin-2-ones

Agustin Daroca, Ramón Mercè, Josep M. Ribó*, Francesc Trull, and **Asunción Vallès**

Departament de Química Orgànica, Facultat de Química, Universitat de Barcelona, Barcelona-28-(Catalunya), Spain

(Received 13 July 1983. Accepted 19 September 1983)

Some 5-arylmethylene-3,4-dimethyl-3-pyrrolin-2-ones react with both bromine and nitronium tetrafluoroborate (NO_2BF_4) to give 5-(aryl)nitromethylene-3-pyrrolin-2-ones and 5-(aryl)bromomethylene-3-pyrrolin-2-ones, respectively. The use of bromine in methanol affords 5-(aryl)bromomethyl-3,4-dimethyl-5-methoxy-3-pyrrolin-2-ones. Whereas pyrromethenones react mainly on the pyrrole ring, ethyl 3,4-demethyl-5-[(3,4-dimethyl-5-oxo-3-pyrrolin-2-yl)methylene]-1*H*-pyrrole-2-carboxylate reacts as the aryl derivatives, however, with bromine in methanol the addition of two methoxy groups at the exocyclic double bond takes place. 3,4-Dimethyl-5-(2-pyridylmethylene)-3-pyrrolin-2-one does not react with bromine or NO_2BF_4, but reacts as the aryl derivatives with bromine in methanol. The reactivity patterns are in agreement with the theoretical ones obtained from MINDO/3 calculations, using the *Fukui* frontier orbital model. The obtained results are used to explain the reactivity of rubins (biladienes-*a,c*) and verdins (bilatrienes-*a,b,c*) in front of electrophiles.

(Keywords: Bile pigments; Bromination; Electrophilic attack; Frontier orbital model; Nitration; Pyrromethenones)

Reaktivität der Pyrrolpigmente, 5. Mitt.:
Elektrophile Substituierung (Nitrierung und Bromierung) von einigen Pyrromethenonen und 5-Arylmethylen-3,4-dimethyl-3-pyrrolin-2-onen

Einige 5-Arylmethylen-3,4-dimethyl-3-pyrrolin-2-one reagieren sowohl mit Brom als auch mit Nitroniumtetrafloroborat (NO_2BF_4). Man erhält 5-(aryl)bromomethylen- oder 5-(aryl)nitromethylen-3-pyrrolin-2-one. Bei Verwendung einer methanolischen Bromlösung werden 5-(aryl)bromomethyl-3,4-dimethyl-5-methoxy-3-pyrrolin-2-one gebildet. Pyrromethenone reagieren hauptsächlich am Pyrrolring, Ethyl 3,4-dimethyl-5-[(3,4-dimethyl)-5-oxo-3-

pyrrolin-2-yl)methylen]-1*H*-pyrrol-2-carboxylat hingegen verhält sich wie ein Arylderivat, mit methanolischen Bromlösung jedoch erfolgt Eintritt zweier Methoxygruppen an der exocyclischen Doppelbindung.

5-(2-Pyridyl)methylen-3,4-dimethyl-3-pyrrolin-2-on reagiert nicht mit Brom oder NO_2BF_4, wohl aber mit einer methanolischen Bromlösung und verhält sich unter diesen Bedingungen wie ein Arylderivat; 3- und 4-Pyridylderivate verhalten sich analog. Die Reaktivität ist in Übereinstimmung mit theoretischen Werten aus MINDO/3-Rechnungen unter Verwendung des „*Fukui* frontier orbital model". Die Reaktivität von Rubinen (Biladiene-*a, c*) und Verdinen (Bilatriene-*a,b,c*) gegenüber Elektrophilen werden im Zusammenhang mit den erhaltenen Resultaten diskutiert.

Introduction

Pyrromethenones, 5-[(5-oxo-3-pyrrolin-2-yl)methylene]-1*H*-pyrroles, have been used as partial models for the study of tautomerism, configuration and conformation of bile pigments[2]. This approach can also be used to study the reactivity of bile pigments, e.g. *D. A. Lightner* has used pyrromethenones as models in the study of bilirubin reactivity with singlet oxygen[3], then, obviously, the pyrromethenone structure is a partial model of rubins (biladienes-*a,c*). Some well know examples of bile pigments (1,19-bilindiones) reactivity against electrophiles are reported in the literature; e.g. isomerization in acidic media[4] of bilirubin IXα to bilirubin IIIα and XIIIα; reaction of rubins with diazonium salts of aromatic amines to give dipyrrolic azo derivatives (diazo reaction)[5]; reaction of verdins (bilatrienes-*a,b,c*) with nitrous acid[6,7] to afford the 5-nitro substitution derivatives; deuteration of verdins[6a]; or the reaction of verdins with bromine in methanol to yield the 4,5-dimethoxy addition derivative[6b,7].

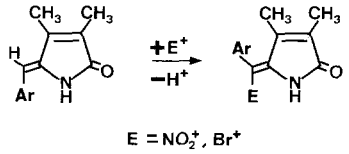
We have already reported that the pyrromethenone **Ig** and some aryl analogues (5-arylmethylene-3-pyrrolin-2-ones) react with nitrous acid to give 5-(aryl)nitromethylene-3-pyrrolin-2-ones[8] (e.g. **IIg** from **Ig**). Two possible mechanisms have been proposed to explain this reaction[9]; either by electrophilic attack of NO^+ (or a related electrophilic species) to give the nitroso substituted compound, followed by an oxidation to the nitro compound, or by a mechanism through radicals. Nevertheless, the already reported[1] substitution reaction of 5-arylmethylene-3-pyrrolin-2-ones with deuteriotrifluoroacetic acid favors the electrophilic mechanism. Furthermore, for the reaction of bile pigments with bromine in methanol, it is not clear whether the mechanism goes through radicals or through an electrophilic attack[6b].

In the present work we report the reactivity of some pyrromethenones and 5-arylmethylene-3,4-dimethyl-3-pyrrolin-2-ones in front of some electrophiles (NO_2^+ and Br^+) in order to correlate their reactivity to the reactivity of the bile pigments towards electrophiles.

Results and Discussion

The title compounds **Ia**, **Ib**, **Ie–g**, and *N*-CH_3-**Ia** react with bromine in methylene chloride (Br_2/CH_2Cl_2) to give the bromo substituted derivatives, **IIIa**, **IIIb**, **IIIe–g**, and *N*-CH_3-**IIIa**, at the bridge carbon atom. **Ia** and **Ig** with NO_2BF_4 afford also the corresponding nitro substituted derivatives **IIa** and **IIg**.

Scheme 1



Studies about the configuration of these substituted derivatives will be reported in a next paper.

A non-fully substituted pyrromethenone as **Ii** or a fully alkylated pyrromethenone without a α-ethoxycarbonyl group as **Ih** show distinct behaviour in front of bromine. In such cases, the reaction products indicate a preferent reactivity of the pyrrole ring towards electrophiles, but in contrast, the α-ethoxycarbonylpyrromethenone **Ig** reacts like the aryl derivatives (e.g. **Ia**). The 2-pyridyl analogue **Id**, which may be considered as a partial model of the pyrrolonenine (azafulvene) moiety of a verdin[10], presents, too, different behaviour in front of NO_2BF_4 and Br_2; **Id** does not give the substitution derivative, however, with bromine in methanol (Br_2/CH_3OH), **Id** gives the regiospecific addition to **IVd**. Such adducts are also obtained from the other tested compounds (**Ia**, *N*-CH_3-**Ia**, **Ie**, **If**). With the same reagent, **Ig** gives the dimethoxy adduct **VIIg**.

These results are analysed in detail in the following three sections: nitration, bromination and theoretical model.

Nitration

We have always encountered a great difficulty in the nitration of pyrromethenones with NO_2BF_4 because of their instability in acidic media. Thus, the pyrromethenone **Ii**, unsubstituted at the pyrrole ring, with NO_2BF_4, as well as with nitrous acid, gives a mixture of unidentified compounds. However in the case of nitrous acid, the nitro substituted derivative at the free α position of the pyrrole ring was detected by MS and ^{1}H-NMR. The fully alkylated pyrromethenone **Ih**

with NO_2BF_4, as it does with nitrous acid, yields a mixture of compounds. However, the pyrromethenenone **I g** with nitrous acid[8], likewise with NO_2BF_4, yields the same nitro derivative **II g**, but since **I a** does not react with nitrosyl tetrafluoroborate ($NOBF_4$; see experimental part), the electrophilic attack in the nitration mechanism with nitrous acid[9] seems to be excluded. NO_2BF_4 appears as a more reactive agent than nitrous acid, thus whereas **I c** does not react with nitrous acid (steric hindrance?), with NO_2BF_4 it yields a mixture of dinitro and trinitro substituted derivatives (one on the bridge carbon atom and the rest on one or two of the free carbon atoms of the aromatic ring).

A verdin system as the etiobiliverdin IV γ (**VIII**) reacts with NO_2BF_4 to give a mixture of polynitro derivatives (whereas its reaction with nitrous acid yields the 5-nitro derivative) and their fragmentation products. This fragmentation may be explained through the reactivity of the nitro derivatives in acidic media[8].

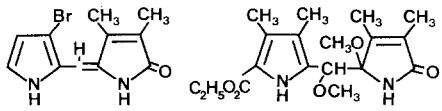
Surprisingly, the 2-pyridyl analogue **I d** with NO_2BF_4 does not afford the nitro substituted derivative; besides the initial compound **I d**, a mixture of products is formed, none of them being identified as the expected one. The behaviour of **I d** in front of electrophiles could be better understood taking account of its reactivity in front of bromine.

Bromination

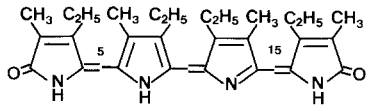
The reaction of the aryl analogues **I a**, **I b**, *N*-CH_3-**I a**, **I e** and **I f** and of the pyrromethenone **I g** affords, with equimolecular amounts of Br_2/CH_2Cl_2 in good yield, as the unique reaction product, the bromine substituted derivative at the methine bridge (**III a**, **III b**, **III e**, **III f**, **III g** and *N*-CH_3-**III a**). With the same reagent, the pyrromethenone **I i** (unsubstituted on the pyrrole ring) affords the α-bromine substituted derivative **V i** (82% yield) and small amounts of the β-brominated derivative **VI i**. The fully alkylated pyrromethenone **I h** affords with Br_2/CH_2Cl_2 a mixture of coloured compounds besides the ones corresponding to the bromination on the methyl group at the α-position of the pyrrole ring. The formation of the coloured compounds can be explained through a reaction similar to that described for the preparation of verdins from pyrromethenones[11]. These results, in accord with earlier experiments[12], point to a similar chemical behaviour of 5′-alkoxycarbonylpyrromethenones, having either an unsubstituted or a fully alkylated pyrrole ring (e.g. **I g**), and the 5-arylmethylene-3-pyrrolin-2-ones (e.g. **I a**), in contrast with the pyrromethenones having an unsubstituted or a fully alkylated pyrrole ring.

I
Ar
a 4-CH3C6H4
b 4-CH3OC6H4
c 2,4,6-(CH3)3C6H2
d 2-pyridyl
e 3-pyridyl
f 4-pyridyl
Ig
Ih
Ii
N-CH3-Ia
IIa
IIg
III
III g
(4-CH3C6H4)BrC
N-CH3-III a
IV
Ar BrCH
(4-CH3C6H4)BrCH
N-CH3-IV a
Vi

As in the attempted nitration, the 2-pyridyl analogue **I d** with Br_2/CH_2Cl_2 does not afford any traces of type **III** derivative; in the crude reaction mixture there is the starting compound **I d** together with small amounts of several compounds which may be explained (by analogy with the results obtained in the reaction with Br_2/CH_3OH) as the addition derivatives of type **IV**, due to the presence of traces of nucleophiles in the reaction medium (e. g. ethanol, as stabilizing agent, or traces of water, etc.).



VI i VII g

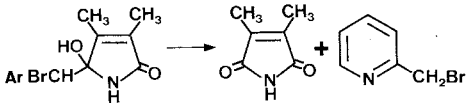


VIII

The presence of traces of reaction products, besides N-CH_3-**III a** found in the reaction of N-CH_3-**I a** with Br_2/CH_2Cl_2 may be explained in a similar way.

Fragmentation compounds were detected in those cases in which water was present; e.g. for **I d**, dimethylmaleimide and 2-bromomethylpyridine were detected (MS and ^{1}H-NMR).

Scheme 2



We interpret that such addition and fragmentation derivatives were also present in small amounts together with the starting material in the attempted nitration of **I d** with NO_2BF_4 and also with nitrous acid.

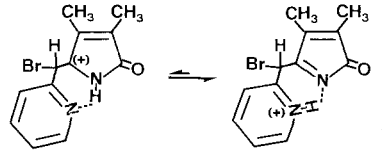
Nevertheless, **I d** gives with Br_2/CH_3OH the regiospecific addition of Br and CH_3O to the exocyclic double bond (**IV d**). In such case (Br_2/CH_3OH), no difference is observed between the chemical behaviour of **I d** and the other aryl analogues (**I a**, N-CH_3-**I a**, **I e**, **I f**), thus the addition derivatives of this type (**IV a**, N-CH_3-**IV a**, **IV e**, **IV f**) being obtained for anyone of them. Only in the case of **I a** and N-CH_3-**I a** small

amounts of the substitution derivatives of type **III** were detected. The absence of type **III** derivatives for **Ie** and **If** may be attributed to the basic character of these compounds. Thus, it was verified for **Ia** that traces of the bromhydric acid formed in the reaction determine the exclusive isolation of **IIIa** in good yield. In the case of Br_2/CH_2Cl_2 type **III** derivatives were always obtained whether a neutralization process was performed or not.

The reaction of **Ig** with Br_2/CH_3OH affords the dimethoxy addition derivative **VIIg**. This reactivity pattern is identical with the one observed in the verdin systems[6b,7] and may be explained through the formation of a compound of type **IV**, followed by a nucleophilic substitution of the Br (it is extensively reported that α-bromoalkylpyrroles are easily substituted by a wide range of nucleophiles[13]).

The different behaviour of **Id** in front of electrophiles may be explained through the stabilization of the initial cation, obtained by the electrophilic attack of bromine. As indicated in the following scheme, this stabilization is due to the formation of a pyridinium cation *B*, more stable than the pyrrolinyl cation *A*, that has the relatively stable structure of 2-oxo-2*H*-pyrrole (calculated by the MINDO/3 method[14]). This effect is clearly one of neighbouring group participation, the reactivity of **Ie** and **If** being not the same as that of **Id**. This neighbouring group effect determines also a higher stereospecificity for the CH_3OH group attack on the cation *B*; accordingly, only one of the two possible diastereomers was detected in the case of of **IVd**, but for **IVe** and **IVf** the other diastereomer appears in concentration ratios of 3 : 1 and 5 : 1 respectively. **IVa** and *N*-CH_3-**IVa** show even higher concentrations of this second diastereomer (see experimental part).

Scheme 3



An attack of the methoxy group trans to the Br atom would determine the *R,S* or *S,R* configuration of the isolated isomer of **IVd**. Comparison of the chemical shifts of the two methyl groups of the pyrrolinone ring allows to assign the configuration *R,S* (or *S, R*) to **IVd** taking into account the most probable conformers and the effect of the phenyl group upon the methyl groups of the pyrrolinone structure.

2-Pyridyl derivatives like **I d** have been proposed as partial models of the azafulvene moiety of verdins[10], consequently these results would indicate that an electrophilic attack on the exocyclic double bond of the pyrromethenone moiety is chemically distinguishable, and that it must be taken into account in the description of mechanisms for the biological role of bile pigments. However, pyrromethenone reactivity with

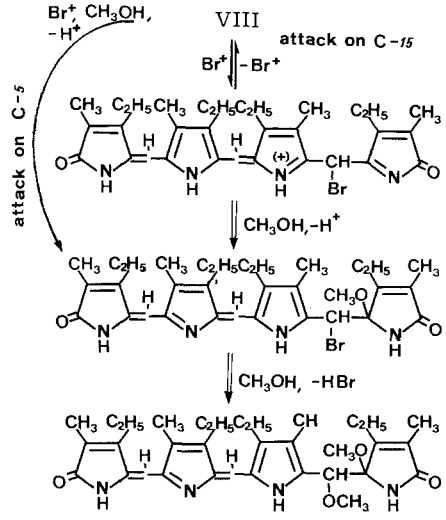


Fig. 1. Reaction path of the addition of two methoxy groups to a (*Z*,*Z*,*Z*)-verdin with Br_2/CH_3OH

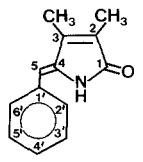
electrophiles is the typical one of a pyrrole ring (see the reactivity of **I i** and **I h** reported here) and this reactivity is effectively related to that of rubins (e.g. diazo reaction[5]). We believe that a fully conjugated bile pigment, e.g. a verdin, is chemically related to a pyrromethene (see the reactivity of verdins with nucleophiles[16]) with two methylene-3-pyrrolin-2-ones structures as substituents. The results reported here would indicate that it is possible to distinguish chemically between the last two structures. All these results allow us to describe the reaction path of the addition of two methoxy groups to a (*Z*,*Z*,*Z*)-verdin skeleton (with Br_2/CH_3OH) as it is shown in Fig. 1.

Theoretical Model

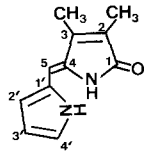
Theoretical predictions obtained by *Fukui*'s frontier orbital model have been compared with empirical reactivity patterns of tetrapyrrolic pigments[17]. This simple model has been used for bile pigments[18] and

their partial models[18,19]. Here, we apply it to the case of an aryl analogue *C*[(*Z*)-3,4-dimethyl-5-(phenylmethylene)-3-pyrrolin-2-one] (see Table 1) and the pyrromethenone **Ii**. The atomic orbital coefficients were calculated by the MINDO/3 method and the reactivity parameters as indicated in Table 1. This table shows the reactivity parameters in front of electrophiles, nucleophiles and radicals obtained for the limiting conformations (0° and 90°, but other conformations—30°, 60° and also 120°, 150°, 180° in the case of **Ii**—were calculated as well).

Scheme 4



(*c*)



Ii

The theoretical results for the preferential attack of a reagent agree with the experimental ones. The most reactive atom in front of electrophiles in the aryl analogue *C* is the bridge carbon atom (at 0° and also at 90°), but in the pyrromethenone **Ii** the most reactive position is the unsubstituted α-carbon atom of the pyrrole ring (this position becomes more reactive towards electrophiles as the dihedral angle is increased). It is known that the most stable conformation of **Ii** is about 40°[20], and the calculated reactivity parameters show that at about 50° the atom 2′ (see Table 1) is the second more reactive unsubstituted position of **Ii**, in accord with the results of the bromination of **Ii**.

The reactivity parameters towards radicals come from the electrophile *plus* the nucleophile ones (Table 1); for the aryl analogue this reactivity parameter shows that the bridge carbon atom is the most reactive position at any angle, but for the pyrromethenone at 0° it is the bridge carbon atom and at 90° the unsubstituted α-carbon atom of the pyrrole ring.

However, this simple model seems to be more suited for its application at 0° than at 90° because the energy differences between HOMO and subHOMO orbitals are rather different for the two angles (greater than 1.2 eV at 0° and about 0.4 eV at 90°) and may be that at 90° other orbitals than HOMO and LUMO must be used in the calculations.

The HOMO and LUMO orbitals of the aryl analogue *C*, at 90°, correspond to an orbital practically fully localized in the 5-methylene-3-

Table 1. *Reactivity parameters*[a] *calculated for the structures C and* **I i** *at 0° and 90° of the conformational angle about the bond between the atoms 1′ and 5′ (see Scheme 4)*

	C						**I i**[b]					
	electrophil[c]		nucleophil[c]		radical[d]		electrophil[c]		nucleophil[c]		radical[d]	
Atom	0°	90°	0°	90°	0°	90°	0°	90°	0°	90°	0°	90°
N	0.29	0.46	0.00	0.00	0.15	0.24	0.17	0.01	0.00	0.00	0.09	0.01
O	0.14	0.22	0.09	0.10	0.11	0.16	0.08	0.00	0.09	0.10	0.09	0.05
1	0.02	0.02	0.15	0.17	0.09	0.10	0.02	0.00	0.16	0.17	0.09	0.08
2	0.12	0.15	0.40	0.49	0.26	0.32	0.09	0.00	0.44	0.17	0.26	0.24
3	0.01	0.02	0.42	0.56	0.22	0.30	0.00	0.00	0.48	0.53	0.24	0.27
4	0.29	0.30	0.19	0.13	0.24	0.21	0.27	0.02	0.17	0.15	0.22	0.09
5	0.44	0.65	0.32	0.37	0.38	0.51	0.23	0.01	0.36	0.36	0.30	0.19
N′	—	—	—	—	—	—	0.01	0.01	0.04	0.03	0.03	0.02
1′	0.17	0.03	0.07	0.00	0.12	0.01	0.37	0.65	0.02	0.01	0.19	0.33
2′	0.12	0.04	0.07	0.01	0.09	0.02	0.22	0.22	0.08	0.01	0.15	0.11
3′	0.03	0.01	0.01	0.00	0.02	0.01	0.15	0.32	0.00	0.00	0.07	0.16
4′	0.21	0.00	0.10	0.00	0.15	0.00	0.39	0.68	0.04	0.01	0.22	0.34
5′	0.02	0.01	0.01	0.00	0.02	0.01	—	—	—	—	—	—
6′	0.13	0.04	0.07	0.01	0.10	0.03	—	—	—	—	—	—

[a] Calculated from the HOMO and LUMO atomic orbital coefficients obtained by the MINDO/3 method (see the experimental part).

[b] Angles higher than 90° (corresponding to the *anti* conformation) give atomic orbital coefficients very similar to the respective *syn* angles.

[c] $2\sum_{k} c_i^2$; where c_i are the HOMO (or LUMO) atomic orbital coefficients in the atom i, and k the four atomic valence orbitals of the atom i.

[d] Half addition of the electrophile and nucleophile parameters.

pyrrolin-2-one residue. Nevertheless, in the pyrromethenone **Ii**, at 90°, the HOMO is on the pyrrole ring (corresponding to the $1A_2$ orbital of 1*H*-pyrrole) and the LUMO on the 5-methylene-3-pyrrolin-2-one side.

The graphical representation of the reactivity parameters—or of the HOMO or LUMO atomic coefficients—shows a sharp increment or disminution at about 50°.

This HOMO localization at 90° depending on the kind of the aromatic residue (benzene or pyrrole) explains the different reactivity of the pyrromethenone **Ig** in front of electrophiles. The α-ethoxycarbonyl group increases the oxidation potential of the pyrrole ring making it similar to the phenyl ring and consequently this pyrromethenone shall have a HOMO similar to its aryl analogues.

This model indicates that the conformational angle between the 5-methylene-3-pyrrolin-2-one side and the rest of the bile pigment must be taken into account in the study of bile pigment reactivity. For rubins, the "pyrrole reactivity" would increase with the conformational angle. For the case of verdins it would be necessary to know whether the pyrrolinone units have a reactivity similar to pyrromethenones or to their aryl analogues. However, it is known that the experimental reactivity pattern of the verdin skeleton corresponds to the LUMO (see the reactions in front of nucleophiles[16]) of the pyrromethenone residue and, according to the results reported here, seems to have the HOMO reactivity of the 5-methylene-3-pyrrolin-2-one residue. However, other factors must be considered in the reactivity, the substituents on the rings (e.g. the vinyl group[21]) and the role of the intramolecular tautomerism due to the nitrogen atoms (e.g. as may be here infered from the results reported for **Id** in front of electrophiles).

We have performed the same calculations for the dihydro derivatives as model systems closer to the phytochrome chromophor, i.e. on the pyrrolinone ring of *C* and **Ii**. The dihydro (*C*) system has at 0° reactivity parameters similar to an enamide, but for the dihydro **Ii** system at 0° the higher parameters in front of electrophiles are on the α positions of the pyrrole ring. The dihydro derivative of **Ii** at 90° for the conformational angle gives a HOMO and LUMO "separated localization"—one on the pyrrole ring and one on the other moiety of the molecule—as for **Ii**. Also the dihydro derivative of *C* has this character (but not *C*!).

Experimental

Melting points were determined on a *Kofler*-Reichert microhot stage apparatus. Preparative thin layer chromatography (PTLC) was carried out on 20 × 20 cm plates using Merck 60 HF_{254} silica (1 mm thickness). All products separated by PTLC were subsequently purified by chromatography on a small

column of Merck 60 silica. High pressure liquid chromatography (HPLC) was carried out on Radial Pak silica columns with a Waters double pump using a variable wavelenght detector 5 FA 339. UV/VIS spectra were recorded on a Hitachi-Perkin-Elmer 124 instrument or on a Perkin-Elmer Lambda 5 instrument. Infrared spectra (IR) were recorded on a Pye Unicam SP 1 100 spectrometer or on a Perkin-Elmer 681 instrument. Mass spectra (MS) on a Hewlett Packard 5 700-A spectrometer. Proton magnetic resonance spectra (^{1}H-NMR) were determined on a Perkin-Elmer R 12 A instrument (60 MHz).

Pre-optimized geometries of 5-methylene-3,4-dimethyl-3-pyrrolin-2-one[14] as well as those of benzene or pyrrole were used for the MINDO/3 calculations[22]: only the optimization of the C—C bond lenght between the bridge carbon atom and the benzene or pyrrole ring and of the bond angles surrounding the exocyclic double bond were performed.

The preparation and properties of the following compounds are described in the literature; **Ia**[23], **Ib**[8], **Ic**[1], **Id**[10], **Ig**[8], **Ih**[24], **Ii**[20], *N*-CH_3-**Ia**[25].

(Z)-3,4-Dimethyl-5-(3-pyridylmethylene)-3-pyrrolin-2-one (**Ie**, $C_{12}H_{12}N_2O$)

The condensation of 3,4-dimethyl-3-pyrrolin-2-one with 3-formylpyridine following the general procedure described in the literature[23,26] yielded **Ie** (69%); m.p. 199–200°.

^{1}H-NMR (δ, $CDCl_3$): 8.7 (m; 2 aromatic H and NH), 7.8 (m; 1 aromatic H), 7,3 (d d; 1 aromatic H), 6.0 (sl. broad s; =CH—), 2.10 (sl. broad s; CH_3-4), 1.92 (sl. broad s; CH_3-3).

MS (*m/e*, 70 eV): 200 (M^+, 100%), 185 (8), 172 (38), 171 (38), 157 (48), 145 (40), 144 (37), 91 (59).

(Z)-3,4-Dimethyl-5-(4-pyridylmethylene)-3-pyrrolin-2-one (**If**, $C_{12}H_{12}N_2O$)

The condensation of 3,4-dimethyl-3-pyrrolin-2-one with 4-formylpyridine following the general procedure described in the literature[23,26] yielded **If** (78%); m.p. 241–242°.

^{1}H-NMR (δ, $CDCl_3$): 8.4 and 7.3 (AA'BB' system; 4 aromatic H), 5.90 (sl. broad s; =CH—), 2.10 (sl. broad s; CH_3-4), 1.90 (sl. broad s; CH_3-3).

MS (*m/e*, 70 eV): 200 (M^+, 100%), 185 (8), 172 (41), 171 (37), 157 (72), 145 (14), 144 (12), 130 (17), 118 (18), 91 (22).

General procedure for the reaction with nitronium tetrafluoroborate (NO_2BF_4).

A solution of 200 mg (1.5 mmol) of NO_2BF_4 in nitromethane (5 ml) was added to a stirred solution of 1 mmol of the substrate in nitromethane (5 ml) at 5° under argon atmosphere. The reaction mixture was kept 45 min under these conditions. The mixture was then neutralized with a saturated sodium carbonate solution and extracted with ether. The organic phase was separated, washed with water, dried with sodium sulfate and evaporated. PTLC of the crude eluted with $CHCl_3/CH_3CN$ (50 : 1) allowed the isolation of the corresponding nitromethylene derivative.

(Z)-3,4-Dimethyl-5-[(4-methylphenyl)nitromethylene]-3-pyrrolin-2-one (**IIa**) was obtained with this procedure in 57% yield and had the same properties as described in the literature[8].

Ethyl (Z)-3,4-dimethyl-5-[(3,4-dimethyl-5-oxo-3-pyrrolin-2-yl)-nitromethylene]-1H-pyrrole-2-carboxylate (**IIg**) was obtained with this procedure in 8% yield (the same properties as described in the literature[8]).

Nitration of (Z)-3,4-dimethyl-5-[(2,4,6-trimethylphenyl)methylene]-3-pyrrolin-2-one (**Ic**) using the general procedure afforded a mixture of dinitro and trinitro derivatives, identified as the products of substitution at the bridge carbon atom and at one or two non alkylated carbon atoms of the aromatic ring. The identification was based on the MS and on the total absence of ethylenic proton signals and the partial absence of aromatic proton signals on the ^{1}H-NMR spectra.

Attempted nitration of (Z)-3,4-dimethyl-5-(2-pyridylmethylene)-3-pyrrolin-2-one (**Id**) with the general procedure afforded the isolation of the initial product and of small amounts of 3,4-dimethylmaleimide.

Attempted nitration of (Z,Z,Z)-3,8,12,17-tetraethyl-2,7,13,18-tetramethyl-15H-bilin-1,19(22H,24H)-dione[11] using the general procedure afforded a mixture of compounds. The ^{1}H-NMR spectra of the reaction crude did not show any signal corresponding to ethylenic protons and 2-ethyl-3-methylmaleimide was identified by MS and analytical chromatography.

Attempted nitration of (Z)-3,4-dimethyl-5-(4-pyridylmethylene)-3-pyrrolin-2-one (**If**) was not possible due to the low solubility of **If**.

Attempted nitrosation with nitrosyl tetrafluoroborate ($NOBF_4$) *of* **Ia**: Using the general procedure described for NO_2BF_4, **Ia** was recovered unchanged.

Nitration with nitrous acid: For some nitration tests with this reagent the method described in Ref.[7] was used.

General procedure for the reaction with bromine in methylene chloride (Br_2/CH_2Cl_2).

To a solution of 1 mmol of the substrate in 1 l CH_2Cl_2 was added, under stirring and argon atmosphere, 1.1 mmol of Br_2 as a methylene chloride solution (0.2 *M*). After neutralization with a hydrogen sodium carbonate solution, the organic phase was separated, washed with water, dried over sodium sulfate and evaporated at room temperature in vacuo. Separation by PTLC afforded the corresponding bromomethylene derivative.

General procedure for the reaction with bromine in methanol (Br_2/CH_3OH).

To a solution of 1 mmol of the substrate in 1 l methylene chloride was added, under stirring and argon atmosphere, a solution of 1.1 mmol Br_2 as a methanol solution (0.02 *M*). After neutralization with sodium hydrogen carbonate solution, the organic phase was separated, washed with water and dried over sodium sulfate. The crude reaction mixture was obtained by vacuum evaporation at room temperature. Separation by PTLC afforded the corresponding derivatives.

(Z)-3,4-Dimethyl-5-[(4-methylphenyl)bromomethylen]-3-pyrrolin-2-one (**IIIa**, $C_{14}H_{14}BrNO$)

Prepared from **Ia** following the general procedure with Br_2 in CH_2Cl_2 in 75% yield (the reaction crude contains **IIIa** as unique reaction product); m.p. 170–173°.

^{1}H-NMR (δ, $CDCl_3$): 7.44 (broad s; NH), 7.22 (broad s; aromatic H), 2.35 (s; aromatic CH_3), 1.80 (broad s; CH_3-3), 1.44 (broad s; CH_3-4).

IR (cm^{-1}, KBr): 1700 (C=O), 1625–1600 (C=C), 580 (C–Br).

UV/VIS (λ_{max} nm (ε), CH_3OH): 302 (17600).

MS (*m/e*, 70 eV): 293/291 (M^+, 72%), 212 (100), 184 (72), 169 (69), 157 (78).

1,3,4-Trimethyl-5-[(4-methylphenyl)bromomethylene]-3-pyrrolin-2-one (*N*-CH_3-**IIIa**, $C_{15}H_{16}BrNO$)

Prepared from *N*-CH_3-**Ia** following the general procedure with Br_2/CH_2Cl_2 and isolated by HPLC in 45% yield. *N*-CH_3-**IIIa** was isolated as a mixture of (*E*) and (*Z*) isomers (1 : 2 approximately).

^{1}H-NMR (δ, $CDCl_3$): 7.20 (s; aromatic H), 3.52 [s; (*Z*), *N*-CH_3], 2.51 [s; (*E*), *N*-CH_3], 2.37 (s; aromatic CH_3), 2.36 [s; (*E*), CH_3-4], 1.91 [s; (*E*), CH_3-3], 1.80 [s; (*Z*), CH_3-3], 1.31 [s; (*Z*), CH_3-4].

IR (cm^{-1}, KBr): 1695.

MS (*m*/e, 70 eV): 307/305 (M^+, 36%), 226 (86), 211 (100), 198 (58), 183 (49).

(Z)-3,4-Dimethyl-5-[(4-methoxyphenyl)bromomethylene]-3-pyrrolin-2-one (**III b**, $C_{14}H_{14}BrNO_2$)

Prepared from **I b** following the general procedure with Br_2/CH_2Cl_2 in 99% yield; m.p. 170–173°.

^{1}H-NMR (δ, $CDCl_3$): 7.45 (broad s; NH), 7.04 (center of a AA'BB' system; aromatic H), 3.82 (s; CH_3O), 1.83 (broad s; CH_3-3), 1.45 (broad s; CH_3-4).

IR (cm^{-1}, KBr): 1695 (C=O), 1610 (C=C), 575 (C—Br).

UV/VIS [λ_{max} nm (ε), CH_3OH]: 313 (15700), 270 (12200), 232 (10300).

MS (*m*/e, 70 eV): 309/307 (M^+, 28%), 228 (100).

(Z)-3,4-Dimethyl-5-[(3-pyridyl)bromomethylene]-3-pyrrolin-2-one (**III e**, $C_{12}H_{11}BrN_2O$)

Prepared from **I e** following the general procedure with Br_2/CH_2Cl_2 in 20% yield as unique reaction product; m.p. 212–213°.

^{1}H-NMR (δ, $CDCl_3$): 8.60 (m; 2 aromatic H), 7.70 (m; 2 aromatic H), 7.35 (broad s; NH), 1.81 (broad s; CH_3-3), 1.45 (broad s; CH_3-4).

IR (cm^{-1}, KBr): 1750, 1630.

UV/VIS [λ_{max} nm (ε), CH_3OH]: 308 (13300), 281 (14100), 203 (9400).

MS (*m*/e, 70 eV): 280/278 (M^+, 35%), 199 (19), 184 (15), 63 (100).

(Z)-3,4-Dimethyl-5-[(4-pyridyl)bromomethylene]-3-pyrrolin-2-one (**III f**, $C_{12}H_{11}BrN_2O$)

Prepared from **I f** following the general procedure with Br_2/CH_2Cl_2 in 35% yield as unique reaction product; m.p. 228–230°.

^{1}H-NMR (δ, $CDCl_3$): 8.65 (m; 2 aromatic H), 7.39 (broad s; NH), 7.35 (m; 2 aromatic H), 1.81 (broad s; CH_3-3), 1.49 (broad s; CH_3-4).

IR (cm^{-1}, KBr): 1690 (C=O), 1590 (C=C).

UV/VIS [λ_{max} nm (ε)]: 308 (11620), 275 (15230), 203 (12360).

MS (*m*/e, 70 eV): 280/278 (M^+, 16%), 199 (37), 184 (17), 156 (44), 44 (100).

Ethyl (Z)-3,4-dimethyl-5-[(3,4-dimethyl-5-oxo-3-pyrrolin-2-yl)bromomethylene]-1H-pyrrole-2-carboxylate (**III g**, $C_{16}H_{19}BrN_2O_3$)

Prepared from **I g** following the general procedure with Br_2 in CH_2Cl_2 in 85% yield; m.p. 185–189°.

^{1}H-NMR (δ, $CDCl_3$): 9.42 (broad s; NH), 7.63 (broad s; NH), 4.26 (q; O—CH_2—), 2.26 (s; CH_3-4), 1.96 (s; CH_3-3), 1.82 (broad s; CH_3-3'), 1.48 (broad s; CH_3-4'), 1.29 (t; CH_3—CH_2—O).

IR (cm^{-1}, KBr): 1715, 1690.

UV/VIS [λ_{max} nm (ε), CH_3OH]: 325 (18500), 272 (14600).

MS (*m*/e, 70 eV): 368/366 (M^+, 32%), 287 (100), 213 (65).

3,4-Dimethyl-5-methoxy-5-[(4-methylphenyl)bromomethyl]-3-pyrrolin-2-one (**IV a**, $C_{15}H_{18}BrNO_2$)

Obtained from **I a**, as unique reaction product (45% yield), following the general procedure with Br_2/CH_3OH. Small amounts of the bromo substitution

compound **III a** were detected. When the reaction mixture was not neutralized with a sodium hydrogen carbonate solution, **III a** was isolated instead of **IV a**. **IV a** was isolated as a mixture of the two possible diastereoisomers (1 : 2 approximately). The ^{1}H-NMR for the diastereoisomer in higher concentration is:

^{1}H-NMR (δ, $CDCl_3$): 7.4–7.0 (m; aromatic H), 5.10 (s; —CHBr—), 3.08 (s; CH_3O—), 2.25 (s; aromatic CH_3), 1.71 (s; CH_3-3), 1.53 (s; CH_3-4); and for the diastereoisomer in lower concentration:

^{1}H-NMR (δ, $CDCl_3$): 7.4–7.0 (m; aromatic H), 4.95 (s; —CHBr—), 2.98 (s; CH_3O—), 2.32 (s; aromatic CH_3), 1.81 (s; CH-3 or -4), 1.71 (s; CH_3-4 or -3).

The MS for the diastereoisomer mixture is:

MS (*m*/e, 70 eV): 326/324 (M^+, 0.2%), 294/292 (0.5), 140 (100), 108 (35).

1,3,4-Trimethyl-5-methoxy-5(4-methylphenyl)bromomethyl-3-pyrrolin-2-one (*N*-CH_3-**IV a**, $C_{16}H_{20}BrNO_2$)

Obtained from *N*-CH_3-**I a** following the general procedure with Br_2/CH_3OH in 85% yield. Small amounts of the bromo derivative *N*-CH_3-**III a** were detected. *N*-CH_3-**IV a** was obtained as a mixture of the possible diastereoisomers in a 0.8 : 1 ratio. The ^{1}H-NMR spectrum for the isomer in higher concentration is:

^{1}H-NMR (δ, $CDCl_3$): 7.08 (broad s; aromatic H), 5.13 (s; —CHBr—), 2.64 (s; CH_3—N), 2.92 (s; CH_3O—), 2.37 (s; aromatic CH_3), 2.10 (broad s; CH_3-3 or -4), 1.77 (broad s; CH_3-4 or -3); and for the diastereoisomer in lower concentration:

^{1}H-NMR (δ, $CDCl_3$): 7.10 (broad s; aromatic H), 5.11 (s; —CHBr—), 3.14 (s; CH_3—N), 2.94 (s; CH_3O—), 2.37 (s; aromatic CH_3), 1.71 (s; CH_3-4 or -3), 1.61 (s; CH_3-3 or -4).

The MS for the diastereoisomeric mixture is:

MS (*m*/e, 70 eV): 340/338 (M^+, 0.5%), 258 (0.8), 185/183 (2), 154 (100).

3,4-Dimethyl-5-methoxy-5-[(3-pyridyl)bromomethyl]-3-pyrrolin-2-one (**IV e**, $C_{13}H_{15}BrN_2O_2$)

Prepared from **I e** by the general procedure for Br_2 in CH_3OH in 74% yield. **IV e** was isolated by PTLC as a mixture of the two possible diastereoisomers (1 : 3 ratio).

The ^{1}H-NMR spectrum for the isomer in higher concentration is:

^{1}H-NMR (δ, $CDCl_3$): 8.50 (m; 1 aromatic H), 7.90 (m; 1 aromatic H), 7.25 (m; 1 aromatic H), 6.3 (m; 1 aromatic H), 4.98 (s; —CHBr—), 3.02 (s; CH_3O—), 1.85 (broad s; CH_3-4 or -3), 1.74 (broad s; CH_3-3 or -4); and for the diastereoisomer in lower concentration:

^{1}H-NMR (δ, $CDCl_3$): 8.5–6.8 (m; aromatic H), 5.13 (s; —CHBr—), 3.14 (s; CH_3O—), 1.74 (broad s; CH_3-4 or -3), 1.54 (broad s; CH_3-3 or -4).

For the diastereoisomeric mixture:

IR (cm^{-1}, KBr): 1715, 1600, 1065 (C—O—C).

UV/VIS [λ_{max} nm (ε), CH_3OH]: 262 (2700), 201 (16500).

MS (*m*/e, 70 eV): 313/311 ($M^+ + 1$, 0.5%), 281/279 (2), 173/171 (20), 140 (100).

3,4-Dimethyl-5-methoxy-5-[(2-pyridyl)bromomethyl]-3-pyrrolin-2-one (**IV d**, $C_{13}H_{15}BrN_2O_2$)

Obtained from **I d** following the general procedure for Br_2 in CH_3OH as unique reaction product in 63%; m.p. 142–145°.

^{1}H-NMR (δ, $CDCl_3$): 8.52 (m; α aromatic H), 8.05 (broad s; NH), 7.56 (m; γ aromatic H), 7.25 (m; 2 β aromatic H), 4.96 (s; —CHBr—), 2.96 (s; CH_3O—), 1.87 (s; CH_3-3 and CH_3-4).

IR (cm^{-1}, KBr): 1690, 1070 (C—O—C).

UV/VIS [λ_{max} nm (ε), CH_3OH]: 264 (5700), 205 (22300).

MS (*m/e*, 70 eV): 312/310 (M^+, 1%), 281/279 (3), 231 (2), 200 (24), 199 (40), 185 (13), 173/171 (96), 140 (100).

3,4-Dimethyl-5-methoxy-5-[(4-pyridyl)bromomethyl]-3-pyrrolin-2-one (**IV f**, $C_{13}H_{15}BrN_2O_2$)

Prepared from **I f** by the general procedure for Br_2 in CH_3OH in 75% yield beside small amounts of **III f**. **IV f** was isolated by PTLC as a mixture of the two possible diastereoisomers (1 : 5 ratio).

The ^{1}H-NMR spectrum for the isomer in higher concentration is:

^{1}H-NMR (δ, $CDCl_3$): 8.45 and 7.45 (AA'BB' system; aromatic H), 4.99 (s; —CHBr—), 3.02 (s; CH_3O—), 1.85 (s; CH_3-4 and CH_3-3) and for the diastereoisomer in lower concentration:

^{1}H-NMR (δ, $CDCl_3$): 8.45 and 7.45 (AA'BB' system; aromatic H), 5.12 (s; —CHBr—), 3.13 (s; CH_3O—), 1.78 (sl. broad s; CH_3-4 or -3), 1.52 (s; CH_3-3 or -4).

UV/VIS [λ_{max} nm (ε), CH_3OH]: 262 (3800), 204 (21800).

IR (cm^{-1}, KBr): 1715 (C=O), 1600 (C=C), 1070 (C—O—C).

MS (*m/e*, 70 eV): 313/311 ($M^+ + 1$, 0.5%), 281/279 (1.5), 173/171 (30), 140 (100).

(Z)-2-Bromo-5-(3,4-dimethyl-5-oxo-3-pyrrolin-2-yl)-1H-pyrrole (**V i**, $C_{11}H_{11}BrN_2O$)

Prepared from **I i** following the general procedure with Br_2/CH_2Cl_2 and isolated by cristallization in 82% yield; m.p. 155–159°.

^{1}H-NMR (δ, $CDCl_3$): 11.62 (broad s; NH), 9.70 (broad s; NH), 6.67 (d; H-3), 6.17 (d; H-4), 5.94 (s; =CH—), 2.00 (broad s; CH_3-4'), 1.77 (broad s; CH_3-3').

IR (cm^{-1}, KBr): 1685 (C=O), 600 (C—Br).

UV/VIS [λ_{max} nm (ε), $CHCl_3$]: 389 (19800), 374 (21600).

MS (*m/e*, 70 eV): 268/266 (M^+, 13%), 188 (100), 187 (52), 159 (63), 154 (44).

From the mother liquor of cristallization of **V i** was identified (only by MS and ^{1}H-NMR: 200 MHz, Varian XL 200): *3-bromo-2-(3,4-dimethyl-5-oxo-3-pyrrolin-2-yl)-1H-pyrrole* (**VI i**) (5% yield approximately of the crude reaction mixture).

^{1}H-NMR (δ, $CDCl_3$): 7.07 (m; H-5), 6.29 m; H-4), 5.91 (sl. broad s; =CH—), 2.05 (sl. broad s; CH_3-4'), 1.77 (sl. broad s; CH_3-3').

Ethyl 3,4-dimethyl-5-[(3,4-dimethyl-2-methoxy-5-oxo-3-pyrrolin-2-yl)methoxymethyl]-1H-pyrrole-2-carboxylate (**VII g**, $C_{18}H_{26}N_2O_5$)

Prepared from **I g** following the general procedure for Br_2 in CH_3OH in 65% yield besides the initial product **I g** and small amounts of the bromosubstituted derivative **III g**. Separation by PTLC and HPLC did not allow to isolate **VII g**; a mixture of the possible diastereoisomers (1 : 3.5 ratio) of **VII g** and the initial product **I g** was always obtained. **VII g** was identified by MS and ^{1}H-NMR (200 MHz, Varian XL 200).

The ^{1}H-NMR spectrum for the diastereoisomer in higher concentration is:

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 9.30 (broad s; NH), 6.40 (broad s; NH), 4.32 (q, J = 7.2 Hz; CH_3—CH_2—O—), 4.18 (s; —CHBr—), 3.19 (s; CH_3—O—), 3.10 (s; CH_3—O—), 2.28 (s; CH_3-3 or -4), 1.95 (s; CH_3-4 or -3), 1.82 (q, J = 1.2 Hz; CH_3-3' or -4'), 1.43 (q, J = 1.2 Hz; CH_3-4' or -3'), 1.36 (t, J = 7.2 Hz; CH_3—CH_2—O—); and for the isomer in lower concentration:

^{1}H-NMR (δ, $CDCl_3$, 200 MHz): 9.30 (broad s; NH), 6.40 (broad s; NH), 4.29 (q, $J = 7.2$ Hz; $CH_3-C\mathbf{H}_2-O-$), 3.22 (s; CH_3-O-), 3.13 (s; CH_3-O-), 1.82 (s; CH_3-4 or -3), 1.97 (s; CH_3-3 or -4), 1.96 (q, $J = 1.2$ Hz; CH_3-4′ or -3′), 1.79 (q, $J = 1.2$ Hz; CH_3-3′ or -4′), 1.32 (t; $J = 7.2$ Hz; $C\mathbf{H}_3CH_2-O-$).

The most significative peaks of the MS of **VII g** are:

MS (*m*/e, 70 eV): 350 (M^+, 1%), 318 (1), 210 (100), 140 (9).

References

[1] Part 4: *Ribó J. M., Trull F. R.*, Monatsh. Chem., in press.

[2] *Falk H., Grubmayr K., Höllbacher G., Hofer O., Leodolter A., Neufingerl F., Ribó J. M.*, Monatsh. Chem. **108**, 1113 (1977); and related papers.

[3] *Lightner D. A., Park Y.-T.*, Tetrahedron **35**, 463 (1979).

[4] a) *McDonagh A. F., Assisi F.*, J. C. S. Chem. Comm. **1972**, 2149; b) *Manitto P., Monti D.*, Synth. Comm. **11**, 811 (1981); c) *Lightner D. A., Trull F. R.*, J. Amer. Chem. Soc. **104**, 6865 (1982).

[5] *McDonagh A. F.*, in: The Porphyrins, Vol. VI, part A, p. 293 (*Dolphin D.*, ed.). New York: Academic Press. 1979.

[6] a) *Bonfiglio J. V., Bonnett R., Hursthouse M. B., Abdul Malik K. M., Naithani S. C.*, J. C. S. Chem. Comm. **1977**, 829; b) *Bonfiglio J. V., Bonnett R., Buckley D. G., Hamzetash D., Hursthouse M. B., Malik K. M., Naithani S., Trotter J.*, J. C. S. Perkin I **1982**, 1291.

[7] *Dobeneck H. von, Sommer U., Brunner E., Lippacher E., Schnierle F.*, Ann. Chem. **1973**, 1934.

[8] *Ribó J. M., Trull F. R.*, Ann. Chem. **1983**, 1.

[9] *Bonnett R., Charalambides A. A., Martin R. A.*, J. C. S. Perkin I **1977**, 974.

[10] *Falk H., Grubmayr K.*, Monatsh. Chem. **108**, 625 (1977).

[11] *Falk H., Schlederer T.*, Monatsh. Chem. **112**, 501 (1981).

[12] *Trull F. R.*, Doctoral Thesis; F. de Química, Universitat de Barcelona, 1981.

[13] *Jones R. A.*, The Chemistry of Pyrroles, p. 556. London: Academic Press. 1977.

[14] *Ribó J. M., Vallès A.*, J. Chem. Res., in press.

[15] *Falk H., Grubmayr K., Hofer O., Neufingerl F.*, Monatsh. Chem. **106**, 991 (1975).

[16] a) *Falk H., Muller N., Schlederer T.*, Monatsh. Chem. **111**, 159 (1980); b) *Manitto P., Monti D.*, J. C. S. Chem. Comm. **1980**, 178.

[17] *Fuhrhop J.-H., Subramanian J.*, Phil. Trans. R. Soc. London **B 273**, 335 (1976).

[18] *Falk H., Höllbacher G.*, Monatsh. Chem. **109**, 1429 (1978).

[19] *Ribó J. M., Trull F. R.*, Monatsh. Chem. **110**, 201 (1978).

[20] *Falk H., Grubmayr K., Herzig U., Hofer H.*, Tetrahedron Lett. **1975**, 565.

[21] *Manitto P., Monti D.*, Experientia **29**, 137 (1973).

[22] *Bingham R. C., Dewar M. J. S., Lo D. H.*, J. Amer. Chem. Soc. **97**, 1302 (1975).

[23] *Falk H., Grubmayr K., Hofer O.*, Monatsh. Chem. **106**, 301 (1975).

[24] *Falk H., Grubmayr K., Höllbacher G., Hofer O., Leodolter A., Neufingerl F., Ribó J. M.*, Monatsh. Chem. **108**, 1113 (1977).

[25] *Falk H., Gergely S., Grubmayr K., Hofer O.*, Ann. Chem. **1977**, 565.

[26] *Plieninger H., Bauer H., Katritzky A. R.*, Ann. Chem. **654**, 165 (1962).