N-Bridged annulenes

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Abstract – The labile [10b,10c]diazapyraceheptylene **2** was obtained
by thermoflash dehydrogenation of olefinic precursors. Pyrazino-
[2,1,6-cd:5,4,3-c'd']dipyrrolizine **11** is a by-product of this
synthesis. A frontier orbital model has been used to demonstrate
that the chemical properties of diazapyraceheptylene derivatives
depend to a great extent on the internal nitrogen lone pairs.

The consequences of a diminution of the porphin π-system have been
studied synthesizing bacteriophin **29** and isobacteriophin **30**. These
parent compounds of hydrophorphins were compared with porphin
derivatives.

INTRODUCTION

A periphery model proposed by J.R. Platt (ref. 1) has proven to be useful
for a description of many polycyclic π-systems. This attempt to broaden the
Hückel rule is based on the assumption that the properties under discussion
depend mainly on a privileged, i.e., peripheral conjugation circle and that
interactions between internal and external π-electrons are negligible.
Pyraceheptylene **1** is an example of a successful application of this rule
(ref. 2).

$$1 \qquad\qquad 2 \qquad\qquad \text{HOMO of } 1^{2-}$$
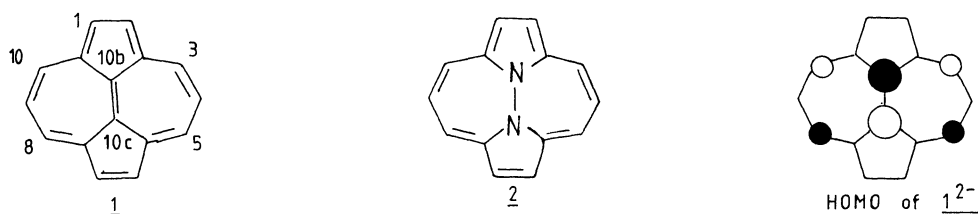
There are, however, exceptions where the influence of internal π-electrons
can not be neglected, or the periphery of the molecule does not represent
the relevant conjugation pathway. Examples of both types of a 'violation'
of the periphery rule are presented in this lecture.

(10b, 10c)DIAZAPYRACEHEPTYLENES

We intend to show that properties of the heterocyclic system **2** depend to
a fairly large extent on the internal lone pairs of the nitrogen atoms.
This is demonstrated by considering the eigenvector of the HOMO of the
isoelectronic pyraceheptylene dianion 1^{2-}.

It is easily seen that an enhancement of the electronegativity in positions
10b and 10c as well as a cleavage of the bridge between these positions
results in a stabilization of the HOMO, leaving the LUMO uneffected.
Increasing electronegativity in the active peripheral positions 3,5,8 and
10, however, lowers the energy of both frontier orbitals by equal amounts.
The chemistry of (10b,10c)diazapyraceheptylenes (ref. 3) confirms these
predictions.

Key intermediates of our approach to diazapyraceheptylenes are the N.N-
bipyrryls **4** which were obtained from N.N-bissuccinimid **3** by a one-pot
Wittig olefination. Thorpe-Ziegler condensation of **4a** gave the enamino-
nitriles **5a** which could be dehydrogenated under acetylating conditions to
give the first fully conjugated derivatives **6** (ref. 4).

|	
3	
4a	X=CH₂CN
b	X=CH₂CO₂Et
5a	X=CN, Y=NH₂
b	X=CO₂Et, Y=O
6a	8-CN
b	10-CN
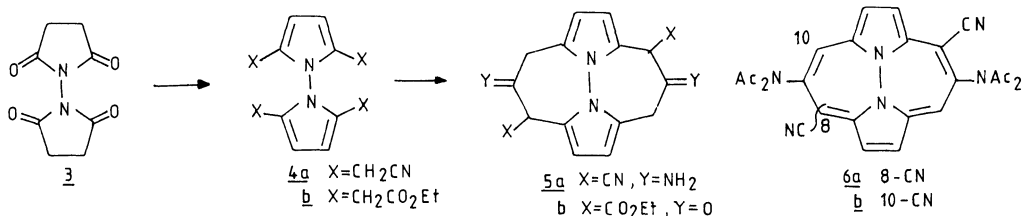
The first attempts of a synthesis of the parent compound 2 started from the ketoesters 5b which were transformed into the diketone 7. The products 8 and 9 were obtained by conventional routes. Despite many experiments a dehydrogenation of 9 could not be effected in solution. Upon a treatment with potassium tert.-butylate in dimethylsulfoxide, however, the bisimino-bridged (14)annulene 10a was obtained and could be monoacetylated to 10b.


7	
8	X=OH,Cl,OTs
9a	Δ 8,9
b	Δ 9,10
10a	R=H
b	R=COCH₃
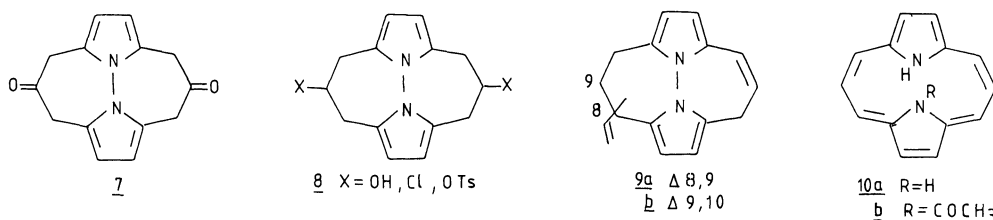
The antibonding relation in the bridge of the HOMO of 1^{2-} reflects the ease of cleavage of the (N-N)-bond.

Shifts of external (7.6-8.4 ppm) and internal protons (10a: -2.1 ppm, 10b: NH=3.1, CH₂=-1.34 ppm) point to a diatropicity of 10. The coupling constants of the 7-membered ring, however, indicate deviations from planarity: 10a ^3J = 9.6 and 13 Hz.

The formation of 10a may be initiated by a deprotonation of 9:
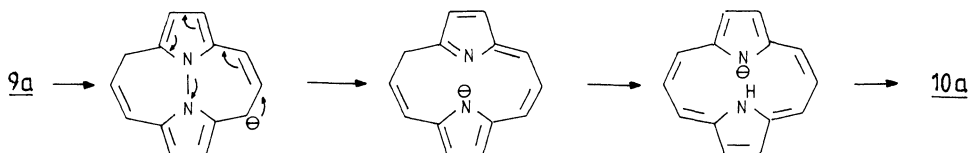

The elimination reaction leading from 8 (X=OTs1) to 9 yielded 1% of the bisimino(14)annulene 11 as a by-product (ref. 5), the structure of which could be confirmed by a comparison with an authentic sample (ref. 6). It is conceivable that the mechanism is frontier orbital controlled, starting from the diazapyraceheptylene 2 to give the dihydro derivative 11a, which is finally dehydrogenated to the stabilized heterocycle.

11a	11
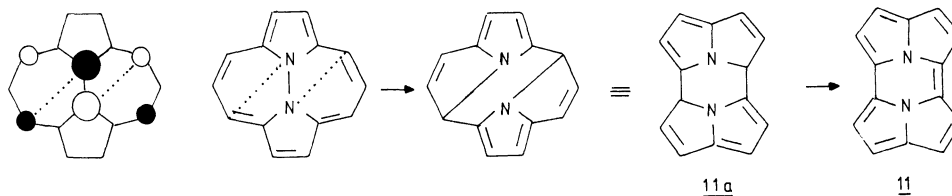
From our investigations we concluded that a cleavage of the hydrazine bridge should be avoided if the diazapyraceheptylene received additional stabilization from electron withdrawing groups in the active peripheral positions 3,5,8 and/or 10 (ref. 4). We therefore aimed at dihydro-derivatives 14 to compare their behaviour with that of the olefines 9.

12	
E = CO₂Et	
13	
14a	8-E; Δ 8,9
b	10-E; Δ 9,10
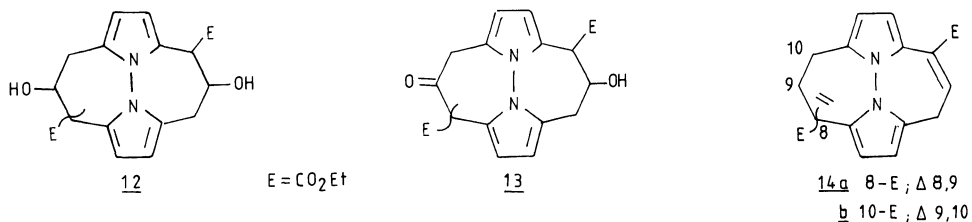
A poorly reproducible reduction of the ketoesters 5b with sodium boro-
hydride at -9°C gave a mixture of the alcohols 12 and 13. In the presence
of bis(triphenylphosphane)palladium chloride, however, 12 was the sole
product and the yield was 60%. Dehydration to 14 was carried out with
sodium carbonate in ethanol.

9 R=H
14 R=CO₂Et = E

10a

15a R=8-E
b R=10-E
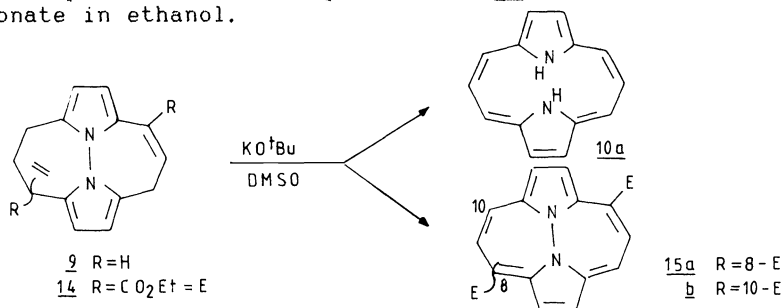
Under the same conditions as for the rearrangement of 9 to 10 a reaction
of the dihydroderivatives 14 yielded the fully conjugated heterocycles 15
containing the unchanged (N-N)-bond. A direct conversion of 12 into 15
occured upon treatment with potassium tert.-butylate in toluene, 15b being
formed more easily than 15a.

The diazapyraceheptylenesters 15 are stable diatropic compounds. The n.m.r.
spectra of the isomers show that the shifts are not influenced by the
change of the substitution pattern of the π-system, which is in agreement
with the symmetry of 2 as reflected in the eigenvector of the HOMO of 1^{2-}.

A reaction of the monoester 16 with bases should be revealing since a
cleavage of the (N-N)-bridge is to be expected besides a dehydrogenation
reaction. Attempts to obtain this compound have so far been unsuccessful.
Precursors 18 were obtained by conventional routes. Treatment with bases,
however, led to an extremely unstable highly coloured compound, the
spectra of which point to structure 19. A mechanism similar to that
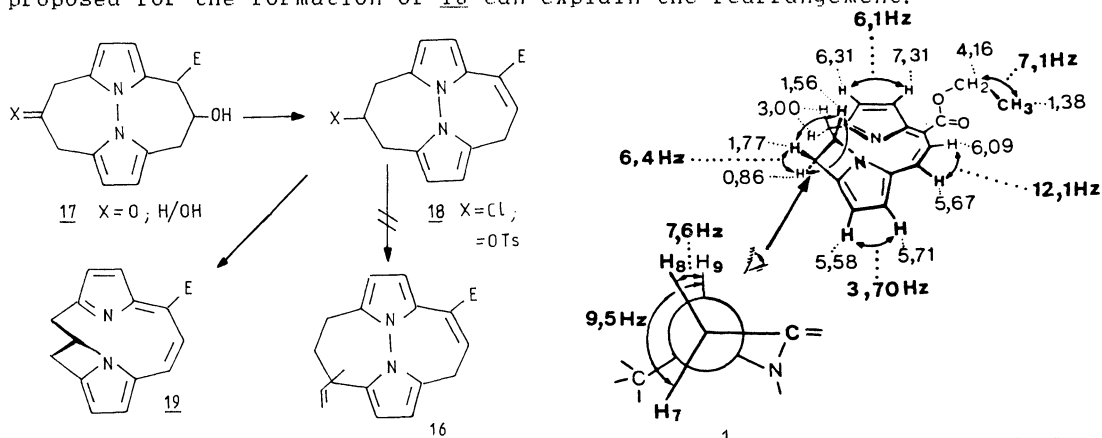proposed for the formation of 10 can explain the rearrangement.

17 X=O; H/OH

18 X=Cl;
=OTs

19

16

Fig. 1. ^{1}H n.m.r. spectrum of 19

Recently we were successful in synthesizing the parent compound 2 by
thermoflash dehydrogenation of the dihydro derivative 9. Using PtO_2 as a
catalyst we obtained at 250°C and 0.01 Torr 13% of a red coloured
compound which is stable in the crystalline state but decomposes quickly
in solution. 2 is diatropic. A small difference in the coupling constants
of the protons of the 7-membered ring (J=9.75, 9.25 Hz) points to a
deviation from planarity, though it is modest compared to the N-bridged
(14)annulene 10a mentioned above.

Table. ^{1}H n.m.r. spectra of bridged (14)annulenes

| Compound	H-1	H-3	H-4	solvent
2	8.60	8.31	8.10	d₆-acetone
10a	7.75	8.23	7.79	CS₂
1 (ref. 7)	8.43	8.72	7.38	CDCl₃
20 (ref. 8)	8.74	8.77	8.04	CDCl₃

20
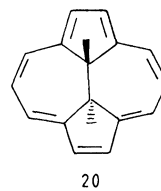
N.m.r. spectra of related (14)annulenes are given in the table. A strong

influence of the 14π-periphery on the chemical shifts is obvious since even differences of shifts of compounds which are not isoelectronic, e.g. 2 compared with 20, are small. Unfortunately solvent effects which are difficult to evaluate may strongly influence the shifts.

Periphery influences on the n.m.r. spectra may be explained using the eigenvector of the HOMO of 1^{2-} which shows that a filling of the HOMO of 2 leaves the periphery fairly unchanged since these electrons are mainly located in the bridge.
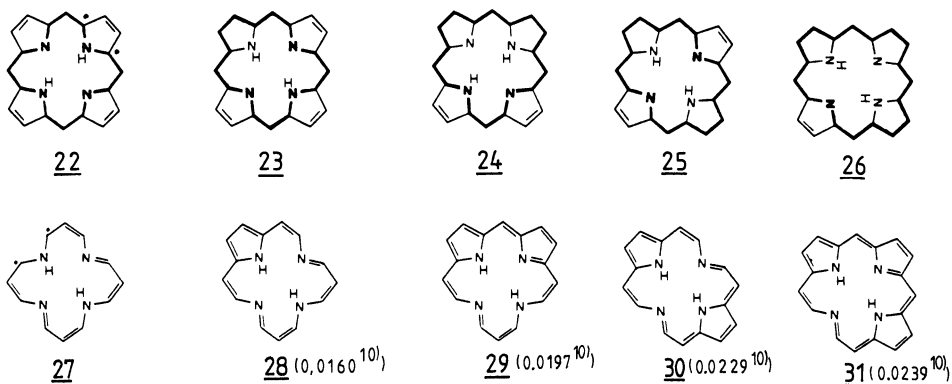
NORPORPHINS

Aromatic porphyrins are endowed with a 20π-electron periphery and therefore do not fit Platt's periphery model. The existence of an internal delocalized conjugation pathway 22 has been deduced mainly from X-ray structure determinations of porphyrins, yielding bond distances of $C_{\beta\beta}$ = 1.34-1.36 A and $C_{\alpha}C_{\beta}$ = 1.44-1.47 A. These bond lengths closely resemble those in butadiene.

21   22   22a
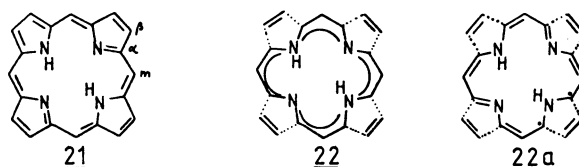
There is additional chemical evidence in favour of this view: electrophilic substitutions occur at the meso positions even in the presence of free β-positions, external double bonds may participate in cycloaddition reactions, oxidations etc. (ref. 9).

It is, however, difficult to imagine that a stabilization should result from structure 22 since it represents an open shell system. This may be deduced from structure 22a as well as from a MO-calculation indicating two degenerate singly occupied HOMO's. Additional structures, which may be useful for a description of the porphin π-system are given below together with the pertinent parent compounds described here. REPE-values of the norporphins are included which may reflect the importance of a particular structure for a description of the porphin π-system. The names which we propose demonstrate the relation of norporphins to the first member of the series, i.e. porphin, as well as to the pertinent partially hydrogenated porphins as indicated


22   23   24   25   26

27   28 (0,0160[10])   29 (0,0197[10])   30(0,0229[10])   31(0,0239[10])

| Name proposed:	Pyrrophin	Isobacteriophin	Bacteriophin	Chlorophin
Related to:	Pyrrocorphin	Isobacteriochlorin	Bacteriochlorin	Chlorin

Investigating the properties of norporphins we try to transform the question for the "most relevant conjugation pathway" of porphin (ref. 11) into a comparison of model compounds 28 - 31, because this seems to be easier to settle experimentally.

Partially hydrogenated porphins have been investigated mainly by Eschen-
moser et al. (ref. 12). Differences to norporphins are due to perturbations
by alkyl substituents which may sum up remarkably in case of several
substituents in equivalent positions. Steric interactions may be expected
from substituents and, more aggravating, from the hydrogenated bridges
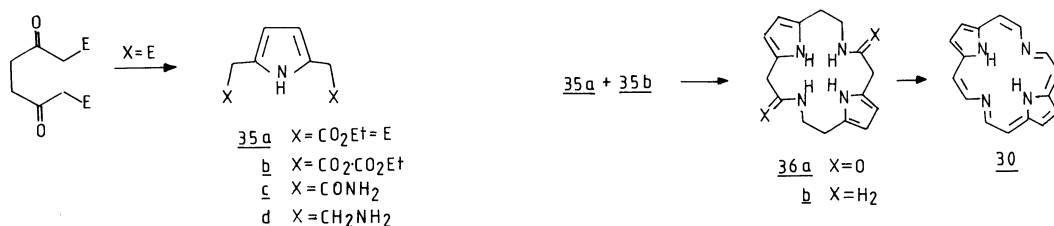restricting conformations and even preventing the π-system from being
planar.

Many derivatives of norporphins play important roles in biochemistry. A
particulary striking example of a diminution of the porphin π-system is
indicated in the following scheme which outlines some aspects of the
biosynthesis of vitamin B_{12} (ref. 13).

R = CH₂CO₂H or CH₃
M = H,H or Co'''

R = CH$_2$CO$_2$H or CH$_3$
M = H,H or Co^{III}

Vit. B$_{12}$
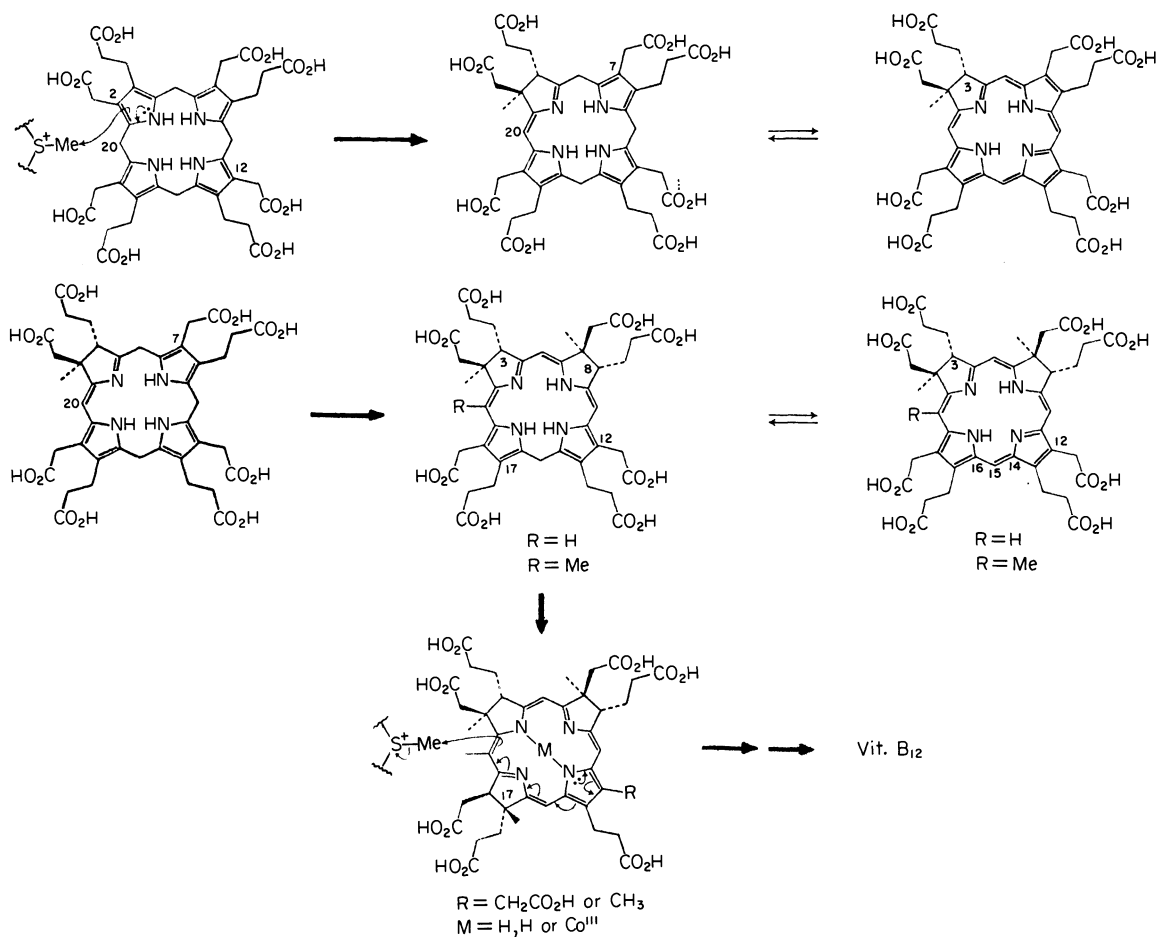
We have obtained the bisnorporphins isobacteriophin **29** and bacteriophin **30**.
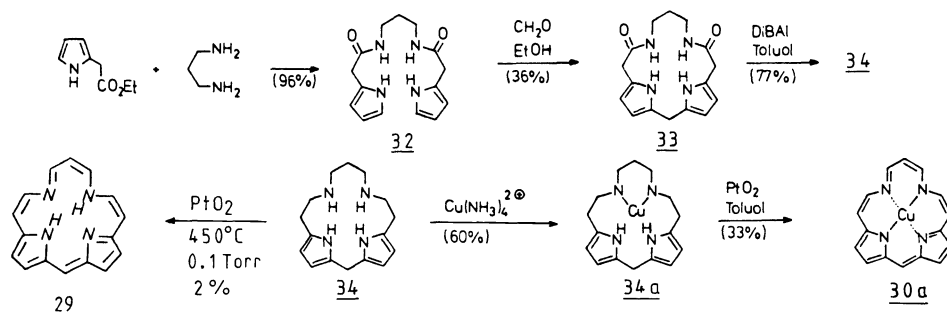
The crucial step of the synthesis of isobacteriophin **29**, i.e. the
cyclization of **32** with formaldehyde, did surprisingly not require high
dilution technique. Dehydrogenation of the amine **34** was effected under
thermoflash conditions using PtO$_2$ as a catalyst. A dehydrogenation of the
Cu-complex of **34** proved possible even in solution yielding 12% of Cu-
isobacteriophin **30a**.

$$35a \quad X = CO_2Et = E$$
$$\underline{b} \quad X = CO_2 \cdot CO_2Et$$
$$\underline{c} \quad X = CONH_2$$
$$\underline{d} \quad X = CH_2NH_2$$

$$\underline{36a} \quad X = O$$
$$\underline{b} \quad X = H_2$$

$$\underline{30}$$

The macrocycle 36 containing the topology of bacteriophin was obtained using high dilution technique. A painstaking control of the reaction conditions afforded a yield of 33% 36a avoiding side reactions originating from an attack of the anhydride function at the free β-positions of the pyrrole ring. The thermoflash dehydrogenation of the amine 36b turned out to be impossible since the compound is not volatile and decomposes before going into the gas phase. Thus the reaction had to be carried out in solution and the yield was very low.
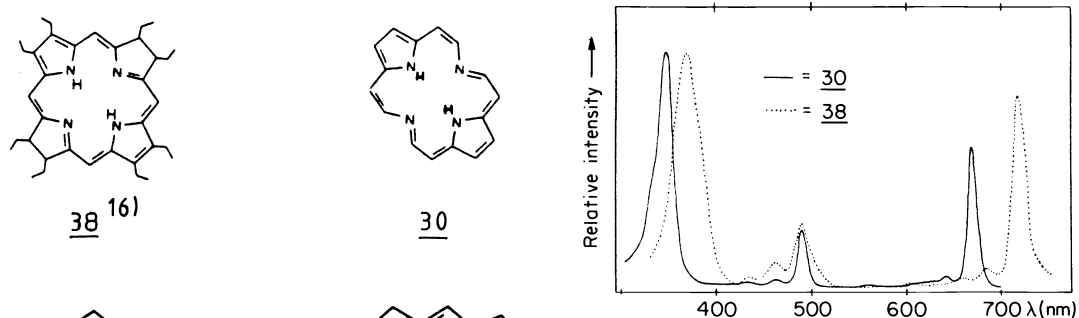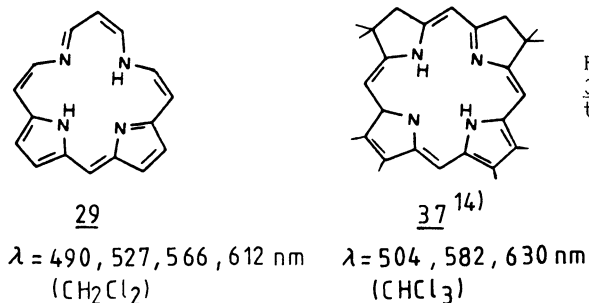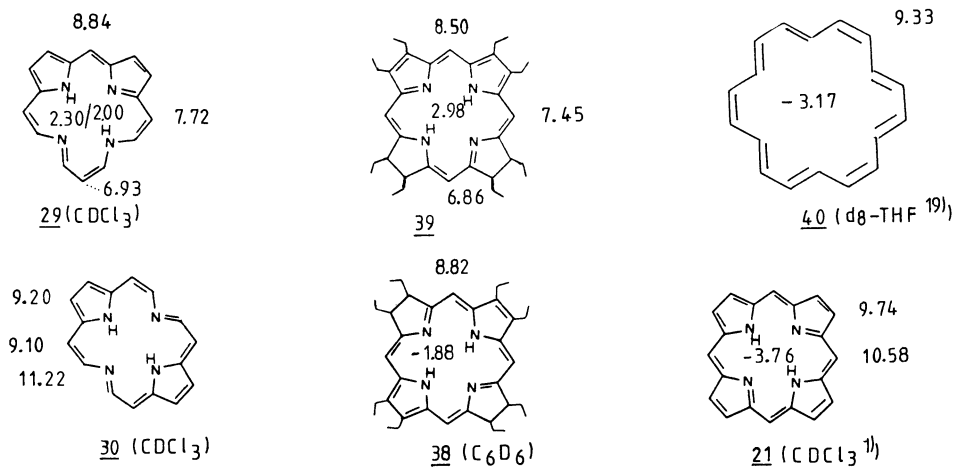

38 [16]

30

29

λ = 490, 527, 566, 612 nm
(CH₂Cl₂)

37 [14]

λ = 504, 582, 630 nm
(CHCl₃)

Fig. 2. UV-spectra of bacteriophin 30 (in CHCl₃) and octaethyl bacteriochlorin 38 (in C₆H₆, ref. 16).

First informations about the π-systems can be obtained from a comparison of UV-spectra. A 14-18 nm hypsochromic shift compared to octamethyl isobacteriochlorin 37 (ref. 14) points to a deviation from planarity in compound 37. Similar effects have been observed for bridged porphins where the deviation from planarity was dependant on the length of the bridge (ref. 15). An even more pronounced influence of a deviation from planarity on UV spectra of the bacteriophin π-system is shown in Fig. 2.


8.84
2.30/2.00   7.72
6.93
29 (CDCl₃)

8.50
2.98   7.45
6.86
39

9.33
-3.17
40 (d8-THF [19])

9.20
9.10
11.22
30 (CDCl₃)

8.82
-1.88
38 (C₆D₆)

9.74
-3.76   10.58
21 (CDCl₃ [1])

Comparing the n.m.r. spectra of isobacteriophin 29 and octaethyl iso-
bacteriochlorin 39 (ref. 17) one can observe a low field shift of the
peripheral protons in the former compound which corroborates the conclu-
sions about the planarity of 29 drawn from the UV-spectra. Two NH-signals
in 29 indicate that these protons are in opposite, non equivalent posi-
tions. The coupling constant $^3J_{15,16}$ = 7.6 Hz is in agreement with a
planar conformation equivalent to that of porphin.

More marked differences of chemical shifts originating from deviations in
planarity (for 38) were observed comparing bacteriophin 30 and octaethyl
bacteriochlorin 38 (ref. 16,18). One NH-signal points to a symmetric
structure of the parent compound 30.

A marked difference in diatropicity of bacteriophin 30 and isobacteriophin
29 can be observed. This may mean that a conjugation pathway resembling
bacteriophin 24 could be more important for a rationalization of the
properties of porphin than that of isobacteriophin 25.

CONCLUDING REMARKS

Simple models are not infrequently suited to answer questions arising in
the laboratories of experimental chemists. First informations may be ob-
tained from a periphery model the requirements of which can be scrutinized
by MO considerations. Alternatively a frontier orbital model may be useful
as well as a discussion of a particular structure. Diazapyraceheptylene may
serve again as an example. A Vilsmeier formylation of 2 gave the expected
3-aldehyde 41a together with the 3,6-diformyl derivative 41b which was the
only diformylated product formed. The HOMO of 1^{2-} allows no differentiation
between the active positions 3,5,8 and 10. The intermediate 42 which reacts
with the second molecule of the Vilsmeier reagent may contain a delocalized
bridged 14π-system loosely connected with a dienamine thus explaining the
regiospecifity of the reaction (ref. 19).

41a R=H
  b R=CHO

42
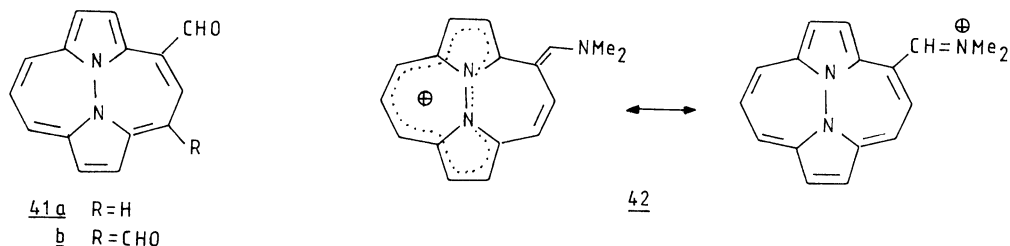
Despite a successful application of these models, however, one should
always remember the limits of these proceedings, since they consider only a
part of possible correlations.

ACKNOWLEDGEMENT

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