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 \(\pi\)-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 \(\pi\)-systems. This attempt to broaden the Huckel 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 \(\pi\)-electrons are negligible. Pyraceheptylene 1 is an example of a successful application of this rule (ref. 2).

There are, however, exceptions where the influence of internal \(\pi\)-electrons cannot 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 \(12^-\).

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 unaffected. 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)diazapyraceheptlenes (ref. 3) confirms these predictions.

Key intermediates of our approach to diazapyraceheptlenes 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-nitrides 5a which could be dehydrogenated under acetylationing conditions to give the first fully conjugated derivatives 6 (ref. 4).
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.

The antibonding relation in the bridge of the HOMO of 12- 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=OTs) 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.

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 olefinic 9.
A poorly reproducible reduction of the ketoesters 5b with sodium borohydride 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.

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 occurred upon treatment with potassium tert.-butylate in toluene, 15h 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 x-system, which is in agreement with the symmetry of 2 as reflected in the eigenvector of the HOMO of 15.

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.

Recently we were successful in synthesizing the parent compound 2 by thermoflash dehydrogeriation of the dihydro derivative 9. Using PtO2 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. 1H n.m.r. spectra of bridged (14)annulenes

<table>
<thead>
<tr>
<th>Compound</th>
<th>H-1</th>
<th>H-3</th>
<th>H-4</th>
<th>solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>8.60</td>
<td>8.31</td>
<td>8.10</td>
<td>d-acetone</td>
</tr>
<tr>
<td>10a</td>
<td>7.75</td>
<td>8.23</td>
<td>7.79</td>
<td>C6H6</td>
</tr>
<tr>
<td>1 (ref. 7)</td>
<td>8.43</td>
<td>8.72</td>
<td>7.38</td>
<td>CDCl3</td>
</tr>
<tr>
<td>20 (ref. 8)</td>
<td>8.74</td>
<td>8.77</td>
<td>8.04</td>
<td>CDCl3</td>
</tr>
</tbody>
</table>

N.m.r. spectra of related (14)annulenes are given in the table. A strong
influence of the 14α-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 12 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 20α-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 1.34–1.36 Å and C=C = 1.44–1.47 Å. These bond lengths closely resemble those in butadiene.

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.

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.
N-Bridged annulenes

Partially hydrogenated porphins have been investigated mainly by Eschenmoser 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 \( \pi \)-system from being planar.

Many derivatives of norporphins play important roles in biochemistry. A particularly striking example of a diminution of the porphin \( \pi \)-system is indicated in the following scheme which outlines some aspects of the biosynthesis of vitamin B12 (ref. 13).

![Chemical diagram](image)

We have obtained the bisnorporphins isobacteriophin 29 and bacteriophin 30.

![Chemical diagram](image)

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 \( \text{PtO}_2 \) as a catalyst. A dehydrogenation of the Cu-complex of 34 proved possible—even in solution—yielding 12% of Cu-isobacteriophin 30a.
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.

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.
Comparing the n.m.r. spectra of isobacteriophin 29 and octaethyl isobacteriochlorin 39 (ref. 17) one can observe a low field shift of the peripheral protons in the former compound which corroborates the conclusions about the planarity of 29 drawn from the UV-spectra. Two NH-signals in 29 indicate that these protons are in opposite, non-equivalent positions. The coupling constant $J_{15.16} = 7.6$ 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 obtained 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$^+$ 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 regiospecificity of the reaction (ref. 19).

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.

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REFERENCES