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Regioselective Pyridination of *m*-Benziporphyrin

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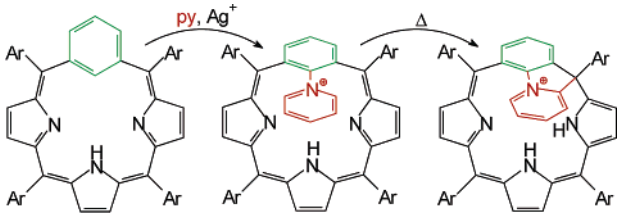
ABSTRACT



Reaction of tetraaryl-*m*-benziporphyrin with pyridine and silver tetrafluoroborate yields 22-pyridiniumyl-*m*-benziporphyrin as the only substitution product. This compound is further rearranged to a fused *m*-benziphlorin containing a 4a-azafluorene fragment. A mechanism involving a high-valent silver complex is proposed for the pyridination reaction.

Carbaporphyrinoids are porphyrin analogues containing a CH fragment instead of one of the pyrrolic nitrogens.[1] This so-called "internal carbon" is often found susceptible to substitution reactions. Examples reported to date include alkylations,[2−5] halogenations,[6,7] nitration,[8] internal fusion,[6] acetoxylation,[9] cyanation,[10] oxygen insertion,[11] and formation of a ketal.[12] Internal reactivity plays an important role in the chemistry of other porphyrinoids, notably 21-tellurapor-phyrin,[13] and regular porphyrins as well.[14−20] The products possess substantially modified coordination cores, and in many instances, new donor atoms are actually introduced.

Some of the above reactions are simple electrophilic substitutions, whereas in other cases an auxiliary oxidant is required.[9−12] A puzzling case of the latter type of reactivity was provided by the internal acetoxylation recently discovered for *m*-benziporphyrin.[9] This reaction, which is formally a benzene substitution, takes place under surprisingly mild conditions and is regioselective.

We now report on the pyridination of tetraaryl-*m*-benziporphyrin, which also takes place at the inner carbon atom (22-C), yielding the respective 22-pyridiniumyl-*m*-benzipor-

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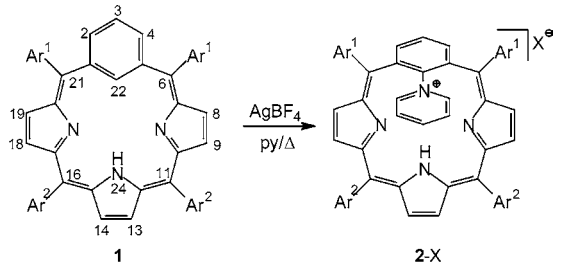
Scheme 1



Ar^1 = *p*-Tol, Ar^2 = *p*-$C_6H_4NO_2$

phyrin. This compound undergoes an unusual isomerization to form a *meso*-fused benziphlorin.

Treatment of 11,16-di(*p*-nitrophenyl)-6,21-di(*p*-tolyl)-*m*-benziporphyrin (**1**) with excess silver tetrafluoroborate in refluxing pyridine produced 11,16-di(*p*-nitrophenyl)-6,21-di(*p*-tolyl)-22-pyridiniumyl-*m*-benziporphyrin (**2**-X, where X denotes the counteranion). The synthetic work is summarized in Scheme 1. The overall reaction may be written as

$$\mathbf{1} + \text{py} + 2\text{AgBF}_4 \rightarrow \mathbf{2}\text{-BF}_4 + 2\text{Ag} + \text{HBF}_4$$

The ^{1}H NMR spectrum of **2** confirms the internal substitution of the benziporphyrin ring (Figure 1). The signal pattern

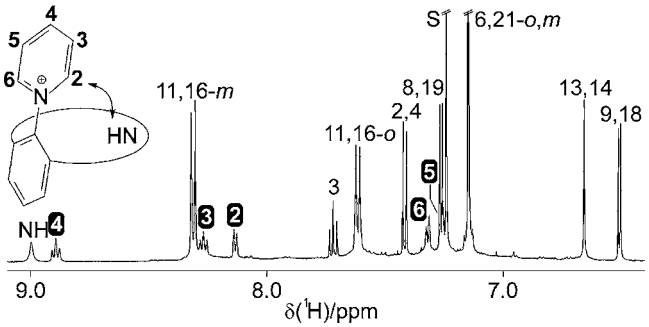
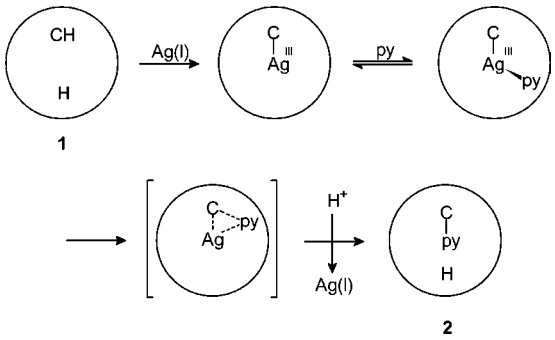


Figure 1. ^{1}H NMR spectra (500 MHz, 298 K, $CDCl_3$) of **2**-Cl. Resonance assignments (obtained from COSY and NOESY maps) follow the numbering scheme given in Scheme 1. White-on-black labels correspond to the pyridinium signals. The upfield region containing methyl signals is omitted.

of the peripheral protons (three β-pyrrole and two *m*-phenylene signals) found in **1** is preserved in **2**. However, the signal of proton 22 is replaced by a set of five resonances corresponding to the 22-pyridiniumyl substituent. The number of signals indicates that the pyridinium group is held perpendicular to the phenylene ring. This is further confirmed by the presence of a NOE contact between protons 2-py and 24-NH, which is crucial for unambiguous assignment of all of the pyridinum resonances. No exchange cross-peaks among the pyridinium signals were detected in the NOESY spectrum, suggesting that rotation of the substituent is slow on the NMR time scale or completely restricted.

The reaction of **1** with pyridine apparently resembles the substitutions observed for radical cations of regular porphyrins.[21−29] In the case of porphyrin radicals, however, only peripheral substitution is observed, which contrasts with the behavior of **1**, which is exclusively pyridinated on the internal 22-C. This selectivity is unlikely for a radical intermediate but can be accounted for by assuming that the substitution proceeds through a highly oxidized silver complex. Indeed, a silver(III) benziporphyrin has been observed in a THF solution, and its properties are currently under investigation. Stable Ag(III) complexes were observed earlier both for regular porphyrins[30,31] and carbaporphyrinoids.[32−34] A mechanism of pyridination can be envisaged (Scheme 2),

Scheme 2



in which an Ag(III) species undergoes reversible axial coordination of pyridine followed by a reductive elimination step to yield, after extrusion of Ag(I), the pyridiniumyl species **2**. 22-Acetoxy-*m*-benziporphyrin[9] would form on a similar route. The pyridination mechanism is related to the elimination reactions observed for high-valent metalloporphyrins with axially bound alkyls,[20] aryls,[35] and carbenes.[18] In those cases, however, the reacting carbon and nitrogen

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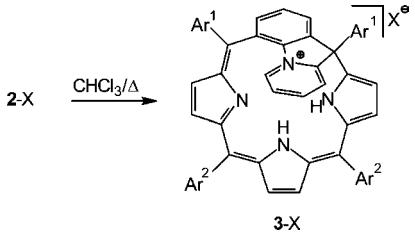
Scheme 3



donors occupy axial and equatorial sites, respectively, whereas in Ag(III) benziporphyrin their positions are reversed.

Alternatively, the formation of **2** may be viewed as N-arylation of pyridine, which produces a phenylpyridinium salt. Such reactions normally require highly activated aryl halides as substrates[36] or are performed using electrochemical oxidation.[37] *N*-Arylpyridinium ions were also generated by electron ionization of aryl halides followed by a reaction of the resulting radical cation with 3-fluoropyridine.[38]

The placement of a pyridinium moiety in the center of *m*-benziporphyrin seems to be a reason for an unusual reaction discovered for **2**. When a solution of **2** in chloroform was refluxed for 12 h in a tightly closed NMR tube the pyridinium species underwent quantitative isomerization to **3**, as shown in Scheme 3. Compound **3** was only characterized in solution.

The structure of compound **3** was determined by careful analysis of ^{1}H and ^{13}C NMR data. The completely assigned ^{1}H NMR spectrum is shown in Figure 2. The greater number of signals in the spectrum reflects the lowering of molecular symmetry in **3**. There are two NH signals at ca. 9.6 and 6.3 ppm. The number of pyridinum signals is now reduced to four, and the topology of the spin system confirms that the ring has been substituted in one of the ortho positions. A ^{1}H−^{13}C HMBC spectrum shows that carbon 6-C has a shift of 60.9 ppm, which corresponds to tetrahedral geometry. Strong differentiation of the 17-C and 20-C shifts (161.2 and 148.2 ppm, respectively) suggests that nitrogen 25 is not

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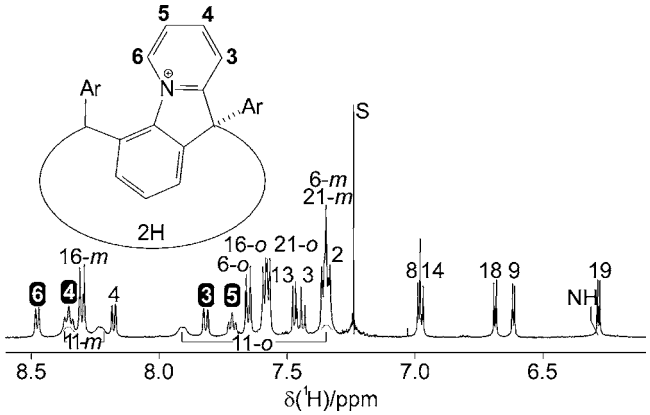

Figure 2. ^{1}H NMR spectrum (500 MHz, 298 K, $CDCl_3$) of **3**. Resonance assignments (obtained from COSY and NOESY maps) follow the numbering scheme given in Scheme 1. The upfield region containing methyl signals and the downfield NH signal (ca. 9.6 ppm) are omitted.

protonated, and **3** exists preferentially as the tautomer shown in Scheme 3.

Compound **3** is conveniently described as a *m*-benziphlorin[9] with the 22-pyridiniumyl ring fused to the adjacent meso position. This leads to the formation of a new heterocyclic unit, 4a-azafluorene. In addition, a chiral center forms at 6-C so that **3** is in fact a racemic mixture of enantiomers. Regardless of the reaction mechanism, the isomerization **2** → **3** is an intramolecular redox process, involving formal reduction of the benziporphyrin ring and oxidation of the pyridinium moiety.

The formation of 22-pyridiniumyl-*m*-benziporphyrin, presented in this letter, shows that the inner substitution of *m*-benziporphyrin induced by silver salts is not restricted to formation of 22-acetoxy-*m*-benziporphyrin. Further aspects of this reactivity are currently explored in our laboratory.

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Supporting Information Available: Synthetic procedures and spectral data for **2** and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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