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ASSIGNMENTS OF THE CHEMICAL SHIFTS OF *MESO*-PHENYL PROTONS AND CARBONS OF TETRAKIS-5,10,15,20 (α,β,α,β–*ORTHO*-AMIDOPHENYL) PORPHYRINS

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Abstract: ^{1}H and ^{13}C NMR studies of "bis-strapped" porphyrins, namely meso-5,10,15,20-tetrakis-(α,β,α,β-ortho-amidophenyl)porphyrin derivatives, permitted to conclusively assign the chemical shifts relative to the meso-phenyl protons and carbons.

As part of a project directed towards the synthesis of chiral porphyrins, we have prepared a series of "amide-strapped" porphyrins, e.g. "gyroscope-like" porphyrins 1 and "basket-handle" porphyrins 2[1]. The hydrogen of the *meso*-phenyl group *ortho* to the porphyrin cycle, namely the H-6' proton of the bis-*ansa*-porphyrins 2, occupies a key position which allows it to observe everything that is happening at the active site of the porphyrin. Therefore, the chemical shift of this proton should provide fundamental information concerning the nature and the geometry of the ligand coordinated to iron of the corresponding iron(II)porphyrin (ligand = O_2, CO, nitrogen axial base in the case of an hemoglobin model[2], thiolate axial base in the case of a cytochrome P-450 model[3]).

Peaks of *meso*-phenyl protons of tetrakis-(*ortho*-amidophenyl)porphyrins have been previously assigned; in two reports[4], the H-6' proton was attributed to the most shielded *meso*-aryl proton and in four others to the least shielded proton[5]. More recently, Perlmutter[6] determined the chemical shifts of *meso*-phenyl protons of "amide-strapped" porphyrins by an elegant application of ^{1}H NMR Nuclear-Overhauser technique confirming the data described in the reference 4 and in contradiction with the data described in the reference 5. This prompts us to report our own results concerning the assignments of *meso*-phenyl protons and carbons in our porphyrinic derivatives 2 by ^{1}H and ^{13}C NMR techniques.

The effect of the acetamido group of acetanilide on the chemical shift of the *meta* hydrogen is known to be very small[7]. This fact has also been found to be true from our ^{1}H NMR studies of a series of related *ortho*-amido substituted arylporphyrins (see Table 1, entries 1,3-6)[8a,12]. This argument can be used to assign the signal for the hydrogen H-4' in 2 from the unambiguous assignment of H-4' in 1. Knowing the chemical shift of H-4' in each case, we can use the COSY technique to correlate each of the other protons, completing the assignments shown in Table 1, entries 7-11. We can thus observe that the H-3' protons resonate at the lowest field* and that the H-4' protons resonate at about the same field in the case of all the compounds 1 and 2.

We then studied our porphyrins by ^{13}C NMR techniques: selected ^{13}C chemical shifts are listed Table 2, entries 1-4 and 8. Knowing the chemical shifts of the carbons of N-BOC-Alanine-aniline 3 (Table 2, entry 5) relative to those of benzene (128.5ppm), the calculated *ortho, meta and para* substituent effects of this amido group were found to be respectively - 8.5, + 0.4 and - 4.3 ppm.The chemical shifts of the carbons of TPPH2 being known in the same solvent (Table 2, entry 6)[10], the calculated chemical shifts of tetrakis-5,10,15,20-(α,β,α,β-N-BOC-L-Ala-*ortho*-amidophenyl)porphyrin 2a should be those given Table 2, entry 7. The lowest field doublet resonance of the C-6' carbon at 134.9ppm (Table 2, entry 1) is in a good agreement with the measured value at 134.4ppm (Table 2, entry 7) and cannot be attributed to the C-3' highest field doublet resonance at 121.8ppm (Table 2, entry 1). Only ^{1}H-^{13}C selective decoupling at 1727Hz**(8.63ppm) transforms the ^{13}C off resonance doublet at 121.8ppm to a singlet thus proving that this carbon bears the H-3' proton.

This simple experiment permits us to assign definitively the controversial chemical shifts[4,5] of the *meso* -phenyl protons of *meso*-tetrakis-5,10,15,20-(α,β,α,β-*ortho*-amidophenyl)porphyrins.Thus the C-3' carbon signal occurs at the highest field and the H-3' proton signal at the lowest field. The remarkable difference between the chemical shift values of H-3' and the adjacent C-3' may arise from the shielding of the amide carbonyl[11] and held for all the porphyrins we synthesized (Tables 1 and 2).These arguments are significant in view of the growing body of hindered hemoprotein model compounds and the need to assign unambigously their ^{1}H NMR spectra.

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* In one case, the NH amido-2' phenyl proton is correlated by COSY ^{1}H NMR technique to a doublet phenyl proton of the hexacoordinated iron-porphyrin 2 (R-R = R'-R' = -(CH(CH$_2$Ph)NHCO)$_2$-m-C$_5$H$_5$N (L-Phe derivative). We can now definitively conclude that the correlated phenyl proton is the H3' proton.

**DP = 24L (200 MHz BRUKER spectrometer)

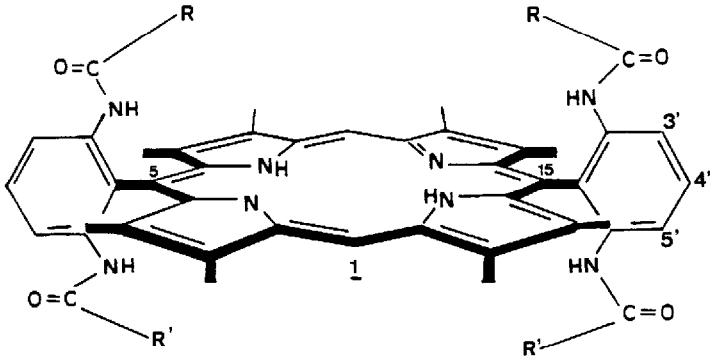
Table 1: ^{1}H NMR data of *meso*-phenyl protons of porphyrins 1 and 2

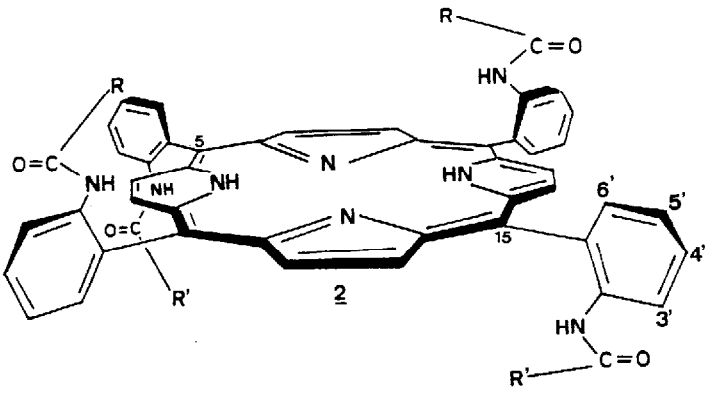
H3'	H4'	H5'	H6'	Compounds	Entry
8.50	7.90	8.50	-	1a R=R'=-CH_3 [8a]	1(a)
7.80	7.80	7.80	8.30	$TPPH_2$ [9]	2(a)
8.48	7.81	8.48	-	1b R=R'=-$CH(CH_3)_3$ [8a]	3(a)
8.51	7.85	8.51	-	1c R=R'=-$CH(CH_3)NHCO_2{}^tBu$*	4(a)
8.43	7.75	8.43	-	1d R=R'=-$CH(CH_3)NH_2$*	5(a)
8.47	7.86	8.47	-	1e R-R=R'-R'=-$(CH(CH_3)NHCO)_2$-p-C_6H_4*	6(a)
8.63	7.83	7.51	7.92	2a R=R'=-$CH(CH_3)NHCO_2{}^tBu$*	7(a)
9.13	7.79	7.78	7.83		7(b)
8.78	7.83	7.47	7.82	2b R=R'=-$CH(CH_3)NH_2$*	8(a)
9.18	7.86	7.49	7.91		8(b)
8.72	7.93	7.55	7.73	2c R-R=R'-R'=	9(a)
9.13	7.82	7.21	7.35	-$(CH(CH_3)NHCO)_2$-p-C_6H_4*	9(b)
8.76	7.83	7.41	7.63	2d R-R=R'-R'=	10(a)
9.03	7.78	7.27	7.49	-$CH(CH_3)NHCOCH_2)_2$-p-C_6H_4*	10(b)
8.75	7.88	7.51	7.68	2e R-R=R'-R'=	11(a)
8.87	7.82	7.26	7.38	-CHR"$NHCO)_2$-p-C_6H_4**(c)	11(b)

* L-Ala derivatives[8a,12];** L-Isoleu derivatives R"=-$CH(CH_3)C_2H_5$ (this work)
(a) $CDCl_3$; (b) C_5D_5N ; (c) In C_5D_5N, the Isoleucine residue creates a remarkable effect only on the H-3' proton if we compare the chemical shift of this proton: entry 11(b) to the corresponding proton of the alanine counterpart: entry 9(b)

Table 2: ^{13}C NMR data of *meso*-phenyl carbons of *meso*-phenyl porphyrin derivatives

C1'	C2'	C3'	C4'	C5'	C6'	Compounds($CDCl_3$)	Entry
131.6	138.4	121.8	130.0	123.3	134.9	2a	1
131.3	138.6	121.2	129.9	123.0	135.1	2b	2
132.0	137.4	121.6	129.6	123.5	134.6	2c	3
131.0	138.1	121.8	130;0	123.3	134.9	2d	4
138.1	120.0	128.9	124.2	128.9	120.0	3 $C_6H_5NHCOCH(CH_3)NHBOC$	5
141.7	134.0	126.1	127.5	126.1	134.0	$TPPH_2$ [10]	6
133.2	143.6	117.6	127.9	121.8	134.4	Calculated 2a	7
132.2	137.9	121.8	129.7	123.8	134.6	2e	8





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