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Preparation of Functionalized Polyhalogenated Tetraarylporphyrins by Selective Substitution of the p-Fluorines of meso-Tetra-(pentafluorophenyl)porphyrins

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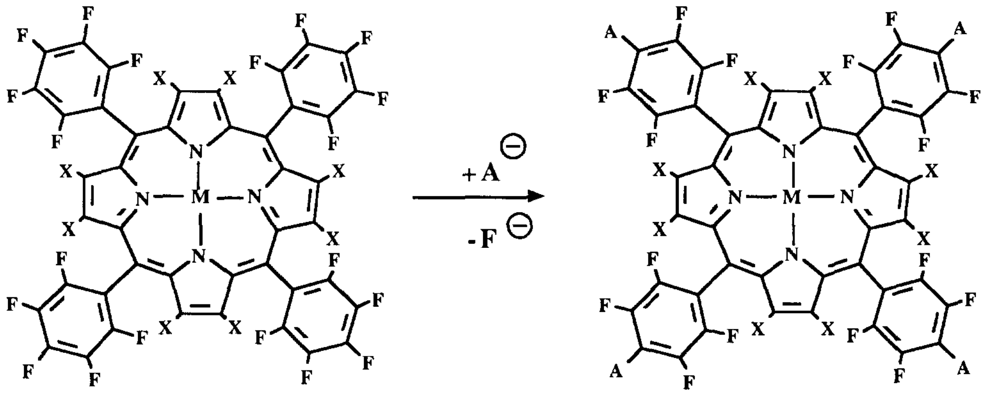
__Abstract__ : *Reaction of various nucleophiles, such as primary and secondary amines in refluxing DMF, alkoxides in alcohol or THF and thiols in the presence of NEt_3 in DMF, with meso-tetra-(pentafluorophenyl)porphyrin (or its Zn(II) and Fe(III) complexes) led to the selective replacement of the p-fluorine substituents of the starting porphyrin by NR_2 , OR or SR groups, in yields between 70 and 90%. The same regioselectivity was obtained by reaction of meso-tetra-(pentafluorophenyl) octabromoporphyrin with n-propylamine. Reaction with KCN gave a more complex reaction mixture.*

Transition metal complexes of polyhalogenated meso-tetraarylporphyrins are particularly stable and interesting oxidation catalysts[1]. In that context, it would be very important to have a general and easy access to functionalized polyhalogenated tetraarylporphyrins from a commercially available and simple porphyrin. Selective nucleophilic substitutions on the C_6F_5 groups of meso-tetra-(pentafluorophenyl)porphyrin, TF_5PPH_2, appeared as an attractive solution to this problem, since nucleophilic substitutions on some pentafluoroarenes were known to selectively occur with replacement of the p-F atoms[2]. First data very recently published about the formation of $T(p\text{-}Me_2N)F_4PPH_2$ [for meso-tetra-(2,3,5,6-tetrafluoro-4-dimethylamino)phenylporphyrin] from TF_5PPH_2 in refluxing DMF[3] indicated that this kind of substitution, presumably by dimethylamine formed by decomposition of DMF was possible. However, the authors indicated that the direct reaction of $(CH_3)_2NH$ with TF_5PPH_2 gave a mixture of products[3]. The present paper describes proper conditions for the preparation of functionalized polyhalogenated porphyrins in __one step__ and __high yields__ by selective substitution of the p-F substituents of the C_6F_5 groups of TF_5PPH_2 by various nucleophiles. Moreover, it gives a first idea of the scope of this reaction, since it shows that (i) the introduction of electron-donating substituents (from amine, alcohol or thiol nucleophiles) occurs with high yields and selectivity whereas that of electron-withdrawing substituents (from CN^- for instance) gives complex mixtures, and (ii) the substitution of p-F atoms by amines is successful not only with

TF_5PPH_2 but also with various polyfluorinated metalloporphyrins including one which bears Br substituents on its pyrrole rings (Fig.1).

Reaction of Zn(TF_5PP) (200 mg) with diethylamine in a 10 ml refluxing $NHEt_2$-DMF(1:1) mixture overnight led, after removal of DMF under vacuum and a single column chromatography (neutral Al_2O_3), to almost only one crystalline product (86% yield). The elemental analysis (C,H,N) and mass spectrum (table 1) of this product indicated that it was derived from the substitution of four F atoms of Zn(TF_5PP) by NEt_2 groups. Its ^1H and ^{19}F NMR spectra clearly showed it to be the Zn(II) complex of porphyrin 3a, Zn(3a), with a singlet for the 8 pyrrole protons at 9.01 ppm and only two sets of ^{19}F signals for the ortho and meta fluorine atoms (table 1). In a very similar manner, the Zn complexes of porphyrins 3b, 3c, 3d and 3e were obtained by reaction of Zn(TF_5PP) respectively with $nPrNH_2$ in DMF, 5 eq. of EtO^- in EtOH, 100 eq. of PhOH in the presence of 30 eq. of Na in THF, and 8 eq. of nBuSH in a DMF-NEt_3 mixture (2:1) (all reactions in refluxing solvent), in yields between 80 and 90% after a single column chromatography. ^1H and ^{19}F NMR spectra of the corresponding reaction mixtures showed in each case the almost exclusive formation of the product deriving from the substitution of the four p-F atoms of the starting porphyrin by the nucleophile.



A=NEt$_2$,NHPr,OEt,OPh,SBu

X = H 1 X = H 3 a b c d e

X = Br 2 X = Br 4 b

Fig.1. Reaction of polyfluorinated porphyrins with various nucleophiles (free base porphyrins : 1 - 4(M = 2H), their metal complexes : M(1 - 4)).

Substitution of the four p-F atoms of the TF_5PP moiety was also accomplished upon reaction of $NHEt_2$ with TF_5PPH_2 itself or with other metal complexes such as Fe(TF_5PP)Cl (table 1). Interestingly enough, this substitution of the four p-F atoms was also the only reaction observed between $nPrNH_2$ and the Zn complex of meso-tetra-(pentafluorophenyl)-octabromoporphyrin, 2,[4] in refluxing DMF, the Zn complex of 4b being obtained in a 80% yield (table 1).

However, it is noteworthy that no reaction was observed between Zn(TF_5PP) and the tertiary amine NEt_3 in refluxing DMF and that the reaction of Zn(TF_5PP) with excess EtOH or EtO^- in DMF at 80°C led to complex mixtures. Moreover, reaction of KCN (4 eq. relative to the porphyrin) with Zn(TF_5PP) in DMF led to a mixture

Table 1 : Spectral Characteristics and Yields of Formation of Porphyrins 3 and 4 or of their Metal Complexes.

Complex	U.V.-visible [a]		^{1}H NMR [b]		^{19}F NMR [b]		Mass [d]	Yield[e]
	Soret	Q bands	pyr	A	ortho [c]	meta [c]		
Zn(3a)	419	505(sh)545 576(sh)	9.01	3.53(q,16H) 1.36(t,24H)	-140.5	-150.0	1250	86
3a	419	511 543 586 655	8.92[f]	3.55(q,16H) 1.35(t,24H)	-140.2	-150.2	1187	82
Fe(3a)Cl	418	507 570 637 740	80.21	4.52(s,16H) 2.00(s,24H)			1276	50
Zn(3b)	422	510(sh)548 577(sh)	8.99	3.75(sb,4H)3.23(t,8H) 1.65(h,8H)1.00(t,12H)	-141.0	-161.5	1194	83
Zn(3c)	416	505(sh)548 577(sh)	9.20	4.66(q,8H) 1.62(t,12H)	-141.5	-159.4	1141	85
Zn(3d)	416	505(sh) 545 579(sh)	9.06	7.52(m,8H) 7.3(m,12H)	-137.7	-154.5	1333	90
Zn(3e)	417	505(sh) 545 579(sh)	9.00	3.25(t,8H) 1.85(qt,8H) 1.65(h,8H 1.05(t,12H)	-134.8	-137.7	1317	85
Zn(4b)	478	598 656	none	4.23(sb,4H) 3.6(t,8H) 1.80(h,8H) 1.10(t,12H)	-141.8	-162.1		80

a) in CH_2Cl_2 except for Zn(3c) in acetone ; λ in nm. b) in $CDCl_3$ except for Zn(3c) in CD_3COCD_3 ; δ in ppm relative to $SiMe_4$ for ^{1}H and to $CFCl_3$ for ^{19}F. In all cases, pyrrole (pyr) H appeared as a singlet (8H), s = singlet, t = triplet, q = quadruplet, qt = quintuplet, h = hextuplet, sb = broad singlet. c) ortho and meta F as doublets of doublets (8F each). d) chemical ionization by NH_3 ; isotopic cluster corresponding to $[M + 1]^+$ always observed (the indicated figures correspond to the highest peak of this cluster) together with that of $[M + NH_4]^+$ in some cases. e) yield of purified product. f) pyrrole NH at -2.85(s,2H).

of products. The ^1H and ^{19}F NMR and mass spectra of a major product[7] indicated that it was derived from the substitution of four fluorine atoms of the same C_6F_5 group by CN^- and thus had a structure very different from those of the Zn complex of porphyrins **3**.

Altogether these data show that the reaction of a nucleophile with Zn(TF5PP) begins by a substitution of the more reactive p-F atom of an electron-deficient C_6F_5 group[2]. The following of the reaction depends on the nature of the introduced group. After introduction of an NR_2 , OR or SR substituent, the corresponding meso-$C_6F_4NR_2$ (OR or SR) group becomes less reactive than the 3 other C_6F_5 groups towards nucleophiles. Therefore, further substitutions occur on the C_6F_5 groups leading to symmetric porphyrins **3**. On the contrary, after a first introduction of an electron-withdrawing substituent like CN, the obtained C_6F_4CN group is much more reactive than the C_6F_5 groups toward the nucleophile[8] and further substitutions occur on the same meso-aryl group.

Thus, reaction of proper nucleophiles with TF5PP derivatives provides a simple and general access to functionalized meso-tetraarylporphyrins containing various electron-donating substituents (OR, NR_2, SR) in p-position of their meso-aryl groups. High yields of these functionalized polyhalogenated porphyrins are obtained in one step from a commercially available porphyrin. This nucleophilic aromatic substitution remains highly regioselective if various metal complexes of TF_5PPH_2 and even tetra-(pentafluorophenyl) porphyrins bearing eight Br substituents on the tetrapyrrole ring are used. Application of this reaction to the preparation of various biomimetic oxidation catalysts is underway.

References and Notes

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7. We did not try to obtain it in a completely pure state. However, its mass spectrum with a molecular ion at 1064, its ^1H NMR spectrum in CD_3COCD_3 with 3 broad pyrrole signals (9.23, 9.28 and 9.3 ppm) and its ^{19}F NMR spectrum with 3 sets of signals as in C_6F_5 groups (-165, -156.4 and -139.6 ppm) indicated a structure with three C_6F_5 and one $C_6F(CN)_4$ meso-aryl groups.
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