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RESEARCH ARTICLE

Synthesis and Characterization of New *Meso*-Substituted and β-Substituted Unsymmetrical Metalloporphyrins

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Abstract: The synthesis and characterization of new *meso*-substituted and β-substituted unsymmetrical metallorphyrins has been described. A new modified Alder method was used for the synthesis of unsymmetrical porphyrins. Reaction of these unsymmetrical porphyrins with metal chlorides and nitrates afforded the corresponding metalloporphyrins in high yields with excellent purity. These porphyrins and their metal derivatives were characterized by spectroscopic methods.

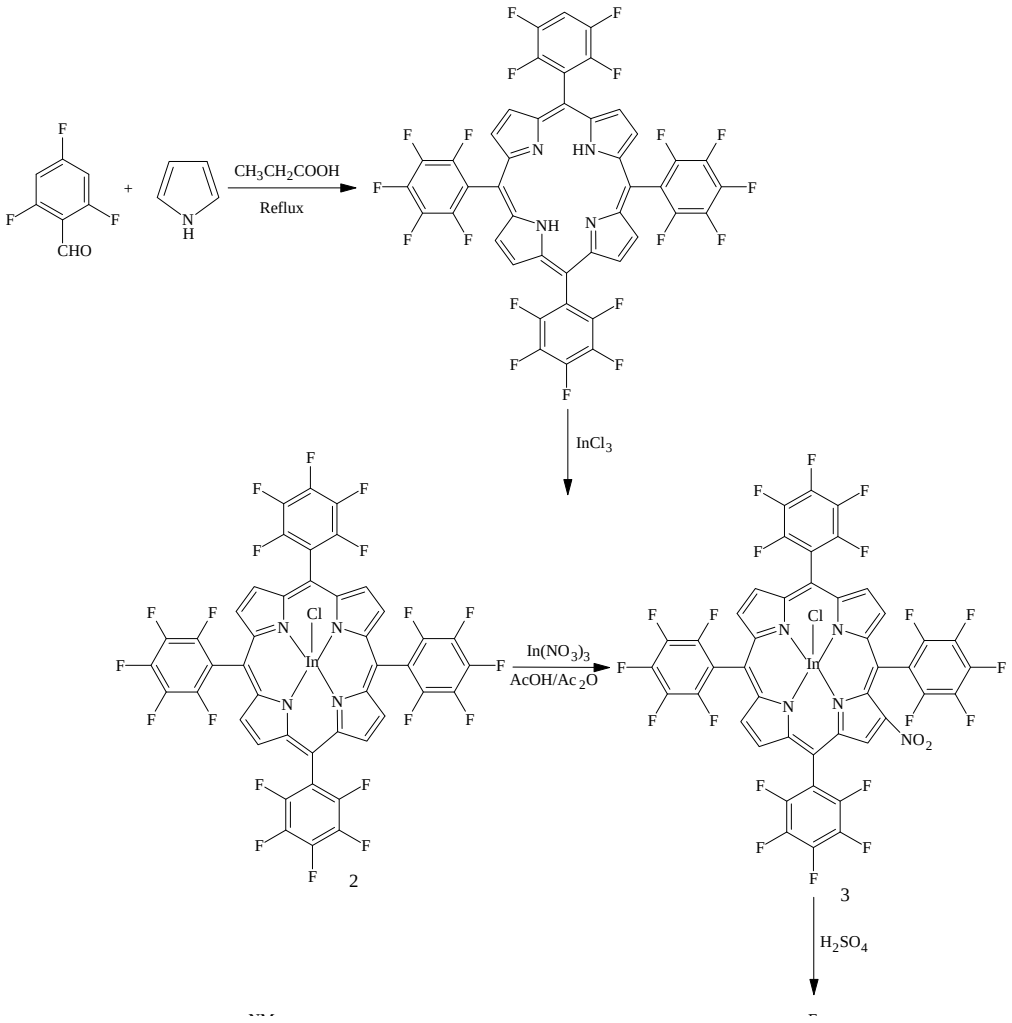
Keywords: *Meso*-functionalization, Unsymmetrical metalloporphyrins, Metal ligand interaction

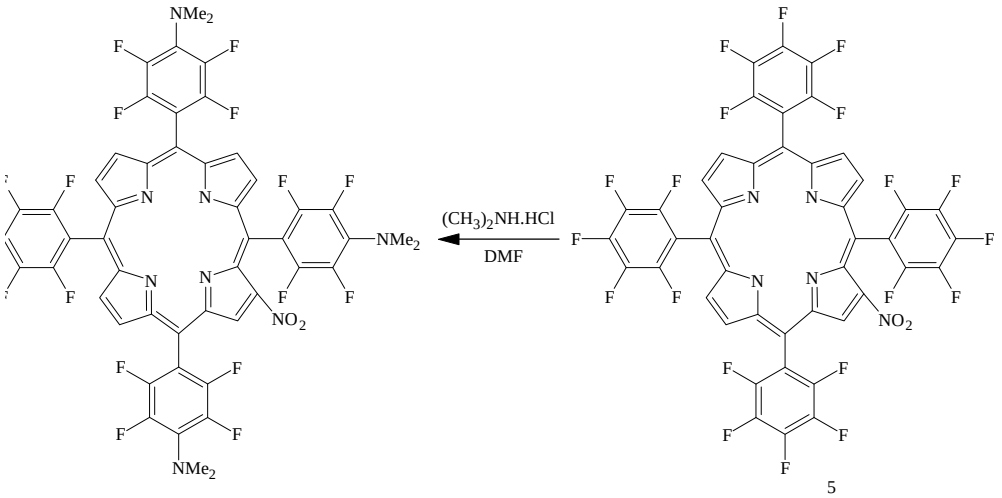
Introduction

Porphyrins are unique class of compounds with potential applications in all disciplines of Science, including medicine[1]. The electronic properties of porphyrins can be changed by introducing suitable substituents at the *meso*-position or β-position. Porphyrins and metallophyrins are essential to the life of bacteria, fungi, plants and animals and have received considerable attention from many investigators in various fields. Synthetic porphyrins, especially *meso*-tetraphenyl porphyrin derivatives substituted in the *para*-position with soluble acidic, basic and neutral groups are of potential interest in medicinal chemistry because they can form chelates either with some toxic heavy metals or with a gamma-ray emitting radioisotopes[2-4].

Although some degree of control may be achieved by altering the substitutents on the aryl rings of *meso*-tetraarylporphyrins[5], large changes in redox properties may be achieved by direct substitution on the porphyrin macrocycle[6]. The position and the nature of the substituents on the porphyrins considerably alter the planar structure of these entities and confer certain unique spectroscopic properties[7]. Among various peripheral substituents, nitro group was shown to have major effect in spectral and electrochemical behaviour of the porphyrins[8]. Although substitution at this position is impossible for *meso*-tetraaryl porphyrins, nitration of tetraphenylporphyrin at the pyrrole β-position is facile[9] and the resulting mono nitro product is a better electron acceptor than *meso*-tetraphenylporphyrin itself by ~350 mV. Several interesting studies of porphyrins endowed with nitro groups either

at the β-pyrrole positions or directly attached at the meso carbon atoms[10] or on the *meso*-aryl rings[11] have been reported in the literature. A systematic spectroscopic studies of the *meso*-fluoroarylporphyrins with different peripheral substituents would be of great interest to elucidate the effect of substituents on the display of many spectral properties. The better solubility of these porphyrins in a wide variety of solvents, higher chemical stability owing to the steric effect of the fluorine atoms and non-aggregation properties of tetra(pentafluoro) phenylporphyrin make them an attractive system to study[12]. These porphyrins exhibit catalytic activity towards hydrocarbon oxygenation reactions[13]. Metal complexes of tetrapyrrolic macrocycles play a key role with respect to life on earth because of their implications in a variety of enzymatic systems[14]. Their ability to carry out the reactions rather unusual in organic chemistry has been the object of intensive investigations aiming to utilize them as a model compounds for biological systems and as catalyst[15]. Therefore the synthesis of well defined *meso*-substituted unsymmetrical porphyrin derivatives is of great interest for development of new unsymmetrical porphyrins were synthesized using modified Alder method[16].





Scheme 1. Synthetic route for substituted porphyrin and metalloporphyrin

We report here convenient synthesis of some metalloporphyrins using *meso*-substituted unsymmetrical porphyrins.

Experimental

The pyrrole and propionic acid were distilled before use. The IR spectra were recorded on Shimadzu infrared spectrophotometer (FT-IR-8400). The NMR spectra were recorded on using tetramethyl silane as internal standard. UV-Visible spectra were obtained on Shimadzu UV-spectrometer using chloroform. Mass spectra were obtained on micromass (Q-T of micro YA-105) using chloroform Elemental analysis was carried out on Perkin Elmer elemental analyzer. Synthesis of tetrakis(pentafluoro)phenyl porphyrin (H_2TFPPa) were prepared using modified Alder method[16].

Synthesis of tetrakis (2,3,5,6-tetrafluoro-4-dimethylamino) phenylprophyrin (H_2TFPPb)

In a 100 mL round bottom flask 130 mg (0.13 mmol) of H_2TFPPa was dissolved in 40 mL of distilled DMF and 3.2 g of dimethylammonium chloride 39 (mmol) was added to it. The resulting solution was refluxed under N_2 for 15 hours. The solvent was removed under reduced pressure the crude solid product was dissolved in $CHCl_3$ and washed several times with distilled water to remove excess amine. The chloroform extract was purified by silica gel column chromatography with $CHCl_3$:pet. ether (1:1, v/v) mixture as eluant. The first fraction was discarded and the second reddish brown colour fraction was collected as the desired product. The yield of the product was 90% based on starting porphyrin (H_2TFPPa). The compound was characterized by ^{1}H and ^{19}F NMR spectroscopies. FAB-MS showed molecular ion peak (*m/z*) at 1075 $(M+H)^+$ (Calc. $M^{+\cdot}$ for $C_{52}H_{34}N_8F_{16}$ = 1074).

Synthesis of 2-nitro (5,10,15,20) tetrakis (pentafluoro)phenylporphyrin (H_2TFPPc)

In 160 mL of $CHCl_3$ InTFPPa (250 mg) was dissolved and $In(NO_3)_3.H_2O$ (116 mg) in 25 mL mixture of acetic anhydride and acetic acid (4:1, v/v) was added to it. The reaction mixture was stirred at 40 °C for 30 hours. At the end of the reaction, the solution was neutralized with aqueous Na_2CO_3 solution and the $CHCl_3$ was subjected to silica gel column chromatorgrphy to obtain the pure product.

Initially eluant used was (3:1, v/v) mixture of pet.ether and chloroform to remove all unreacted InTFPPa and then eluant was changed to (3:2, v/v) product. Increasing the $HCCl_3$ in the eluant mixture helps in the separation of higher nitro derivatives. The free base porphyrin (H_2TFPPc) was obtained by acid demetallation of InTFPPc with H_2SO_4 following standard procedure. The overall yield of the desired product was 50% based on starting porphyrin (InTFPPc). The compound was characterized by UV-Vis. ^{1}H and ^{19}F-NMR spectroscopies. FAB-MS showed molecular ion peak (*m/z*) at 1020 $(M+H)^+$. (Calc. M+. for $C_{44}H_9F_{20}O_2$ = 1019).

Synthesis of 2-nitro (5,10,15,20) tetrakis (2,3,5,6-tetrafluoro-4-dimethylamino)phenyl porphyrin (H_2TFPPd)

In a 100 mL round bottom flask H_2TFPPc (120 mg, 0.12 mmol) was dissolved in distilled DMF (40 mL) and dimethyl ammonium chloride (3.0 g, 37 mmol) was added to it. The resulting solution was refluxed under N_2 for 15 h. At the end of the reaction, the solvent was removed under reduced pressure, the solid crude product was dissolved in $CHCl_3$ and washed several times with distilled water to remove the excess amine. The $CHCl_3$ extract was dried over anhydrous Na_2SO_4 and the solution was then concentrated and passed through silica gel column. On elution with $CHCl_3$, the most intense brown band after yellowish orange fraction was collected as the desired product. The yield of the product was 75% based on starting porphyrin (H_2TFPPc).The compound was characterized by UV-Visible, ^{1}H and ^{19}F NMR spectroscopies. FAB-MS showed molecular ion peak (*m/z*) at 1120 $(M+H)^+$ (calc. M+. for $C_{44}H_9N_5F_{20}O_2$-1119).

Synthesis of In(III) derivatives of the porphyrins

The In(III) derivatives of the unsubstituted and substituted fluoroarylporphyrin were prepared using the In(III)chloride as the carrier. A typical procedure for the synthesis of InTFPPd is as follows; To a solution of free-base (H_2TFPPd) porphyrin (100 mg, 0.09 mmol) in 25 mL of $CHCl_3$ excess of In(III)chloride (200 mg) in 15 mL of methanol was added and the reaction mixture was refluxed for a period of 30 min. Then the solvent was evaporated under reduced pressure and the residue thus obtained was washed with water and extracted in $CHCl_3$ and dried over anhydrous Na_2SO_4. The resultant $CHCl_3$ solution was chromatographed on a silica gel column using $CHCl_3$ as the eluant. The yield of the product was found to be greater than 90%. In all the cases compounds were characterized by UV-Vis, ^{1}H and ^{19}F NMR spectroscopies and purity of the samples were verified by thin layer chromatography.

Results and Discussion

Nitration of the H_2TFPP can in principle lead to polynitrated products. We achieved the preparation of β-mononitro tetrakis (pentafluorophenyl)porphyrin (InTFPPc) by nitration of the In(III) derivative of tetrakis (pentafluorophenyl) porphyrin (InTFPPa) by $In(NO_3)_3.H_2O$. The isolated yield of mono nitro substituted product compared to other higher nitro derivatives are highly dependent on the ratio of the porphyrinato $In(NO_3)_3$ and the reaction time at a given temperature. In general a mixture of mono, di and tri nitro compounds were obtained in such reactions. We obtained InTFPP(NO_2) (InTFPPc) in 50% yield by using optimum conditions. The *N,N*-dimethylamino groups were introduced into the *meso*-fluoroaryl rings by nucleophilic substitution of para fluorine atoms by -NMe_2 group.

^{1}H and ^{19}F NMR spectroscopy

The NMR spectra of the free-base porphyrins and their In(III) derivatives are highly characteristic and provides structural information of these compounds in solution. The ^{1}H NMR data is given the Table 1. The integrated intensity of the resonance agree well with the number

of protons. The assignment of various resonances were carried out by comparison with the ^{1}H NMR spectra of H_2TFPP and InTFPP. The inner imino proton resonance of the unsubstituted porphyrin, H_2TFPPa undergo a downfield shift on incorporation of electron donating/withdrawing groups -N$(CH_3)_2$ and nitrogroup in the mesofluoraryl rings and one of the pyrrole carbons of the tetrapyrrole moiety respectively. The shift is found to be maximum when both donor and acceptor groups are present in the porphyrin (H_2TFPPd). This suggests a change in the electron density on the inner imino nitrogens as a consequence of substitution of the different groups in the peripheral positions of the porphyrins. However, the presence of –NMe_2 groups in the *meso*-fluoroaryl rings appear to have less influence in the shift of the imino proton resonances compared to that produced by the –NMe_2 groups on the *meso*-tetraphenyl porphyrin. Interestingly, the proton resonance of –N$(CH_3)_2$ groups in H_2TFPPb appear as a triplet in contrast to a singlet resonance in the corresponding *meso*-tetraphenyl porphyrins. The occurrence of a triplet resonance is ascribed to the coupling between the m-fluorine atoms of *meso*-fluoroaryl ring and the protons of –N$(CH_3)_2$ group. The major effect of nitro group substitutions in the exhibition of a multiplet resonance for pyrrole protons. The seven β-pyrrole proton resonances of H_2TFPPc are classified easily from the integrated intensity pattern. Thus the singlet at 9.15 ppm is assigned to the proton juxtapositioned to the nitro group of the same pyrrole ring (ring I) and the broad signal at 9.02 ppm is assigned to the four protons belonging to the two pyrrole rings positioned on either side of the pyrrole ring bearing the nitro group (ring II and IV). The relatively higher upfield shifted resonance centred at 8.79 ppm is assigned to the protons of the pyrrole ring positioned diagonally opposite to the pyrrole ring bearing the nitro group (ring III). The presence of -N$(CH_3)_2$ groups in the *meso*-fluoroaryl rings of the porphyrin,H_2TFPPd retains the pattern of the pyrrole proton resonances as in H_2TFPPc. The proton resonances of –N(CH_3) groups in H_2TFPPd, However, appear as a multiplet (instead of a triplet as in H_2TFPPb) indicating partial rotation of the fluoroaryl rings to different extent. The presence of In(III) in the porphyrins result in the shift of the resonances to low field accompanied by the change in splitting pattern of the resonances indicating conformational change of the porphyrin core.

Table 1. ^{1}H NMR[a] data (δ in ppm) of the porphyrins in $CDCl_3$ at 300 K

Compound	β-H	-NMe_2-H	-NH
H_2TFPPa	8.92(s)	-	-2.92(s)
H_2TFPPb	8.94(s)	3.28(t)	-2.86(s)
H_2TFPPc	9.15(s) 9.02(b) 8.79(d/d)	-	-2.83(s)
H_2TFPPd	9.17(s) 9.03(q) 8.80(s)	3.28(m)	-2.75(s)
InTFPPa	9.01(s)	-	-
InTFPPb	9.03(s)	3.28(t)	-
InTFPPc	9.25(s) 8.94(m)	-	-
InTFPPd	9.28(s) 8.95(m)	3.28(m)	

a ^{1}H NMR values are versus TMS at 0 ppm; d/d = doublet of doublet, d = doublet; S = singlet; q = quartet; m = multiple; t = triplet

Fluorine -19 NMR ha been extremely helpful in ascertaining both the identity and purity of the compound. The 100% natural abundance of spin ½ ^{19}F and its high gyromagnetic ratio allow ^{19}F NMR spectra to be obtained readily. The ^{19}F NMR spectra are usually first order in their multiplicities and this permits detailed structural analysis to be made from the observed splitting patterns. The fluorine atoms of all four phenyl groups appear equivalent in ^{19}F-NMR spectrum as *o*-, *m*- and *p*-fluorine atoms. The four *meso*-fluoroaryl rings on the porphyrin are related to high degree of symmetry. The chemical shift of the fluorine atoms on the meso fluoroaryl rings are extremely sensitive to the metal centres its *meso*-aryl and the pyrrole carbon atom substituents. The resonances of fluorine atoms of the *meso*-aryl rings occur at characteristic frequencies and are easily distinguishable from the position and nature of the multiplet of the resonance and their integrated intensities. The incorporation of $–N(CH_3)_2$ group in the *p*-position of the *meso*-fluoroaryl rings shift the *o*-and *m*- fluorine resonances up field and downfiled respectively by about 4.0 and 9.0 ppm while the $–NO_2$ group substitution at the β-pyrrole carbon doesnot shift the ^{19}F resonances significantly. Interestingly, the fluorine atoms in the nitroporphyrins are easily distinguishable depending upon the location of $–NO_2$ group in the pyrrole ring. The *o*-fluorine atom resonances in H_2TFPPc appear as three closely spaced doubled of doublets while these resonances appear unresolved in H_2TFPPa and H_2TFPPb. The resonances at -137.5 ppm, arise from the *o*-fluorine atoms of the fluoroaryl ring at C_{15} and the peak centred at -136.7 ppm was ascribed to the fluorine atoms of the fluoroaryl rings adjacent to the pyrrole ring bearing the nitro group (at C_{10} and C_{20}). The most downfield shifted peak at -136.4 ppm was assigned to the fluorine atoms of the phenyl ring adjacent to the nitro group (at C_5). A similar splitting pattern was also observed for the m-fluorine atoms. The single set of triplet that appeared for the p-fluorine atoms of *meso*-fluoroaryl rings of the porphyrin (H_2TFPPa), split into two multiplets in nitro substituted porphyrin (H_2TFPPc) due to the p-fluorine atoms of neighbouring and distant *meso*-fluoroaryl rings. A marginal change was observed in the ^{19}F NMR spectra of the porphyrins upon In(III) ion incorporation.

Table 2. ^{19}F-NMR[a] data (δ in ppm) of the porphyrin in $CDCl_3$ at 300 K

Compound	ortho	meta	Para
H_2TFPPa	-136.8(d)	-161.5(t)	-151.5(t)
H_2TFPPb	-140.4(d/d)	-152.5(d)	-
H_2TFPPc	-136.4(d/d) -136.7(d/d) -137.5(d/d)	-160.6(m) -160.9(m) -161.2(m)	-149.7(m) -150.5(m)
H_2TFPPd	-140.2(d/d) -140.4(d/d) -141.3(d/d)	-151.9(bd) -152.2(bd) -152.7(bd)	- - -
InTFPPa	-138.5(d)	-163.7(m)	-154.8(t)
InTFPPb	-140.4(d/d)	-152.5d	-
InTFPPc	-136.7(d/d) -136.9(d/d) -137.7(d/d)	-161.1(m) -161.5(m) -161.9(m)	-150.7(m) -151.4(t)
InTFPPd	-140.5(d) -141.3(d)	-152.1(d) -153.4(d) -152.9(d)	- - -

[a]^{19}F NMR values are versus $CFCl_3$ at 0 ppm. d/d = doublet; d = doublet; s = singlet q = quartet; m = multiplet; t = triplet

Electrochemical redox properties

The electrochemical redox properties of the porphyrins and their metallated derivatives arise primarily from the π-electron system of the macrocycle. Cyclic voltametric and differential pulse voltammetric studies have been carried out for all the synthesized free-base fluoroarylporphyrins and their metal derivatives [Indium(III)] to elucidate the effect of peripheral substitutents at pyrrole position and *meso*-fluoroaryl rings on the electrochemical redox potentials. The electrochemical redox date of the synthesized compounds in CH_2Cl_2 solution are given in Table 3. In most of the cases only first oxidation process was observed because the second ring oxidation occurs at a potential too close to the solvent oxidation. It is seen that the presence of fluoroaryl groups at the *meso*-position of the porphyrin shifts the ring oxidation and reductions to a more anodic potential relative to that found for tetraphenyl porphyrins. The free-base fluoroarylporphyrins (H_2TFPPa) and its Indium (III) derivatives exhibit one electron ring oxidation to a more anodic potential relative to that found for *meso*-tetraphenylporphyrin and its metal(III) derivatives. This suggests the highly electron deficient nature of pentafluoroaryl porphyrins relative to the corresponding *meso*-tetraphenylporphyrins.

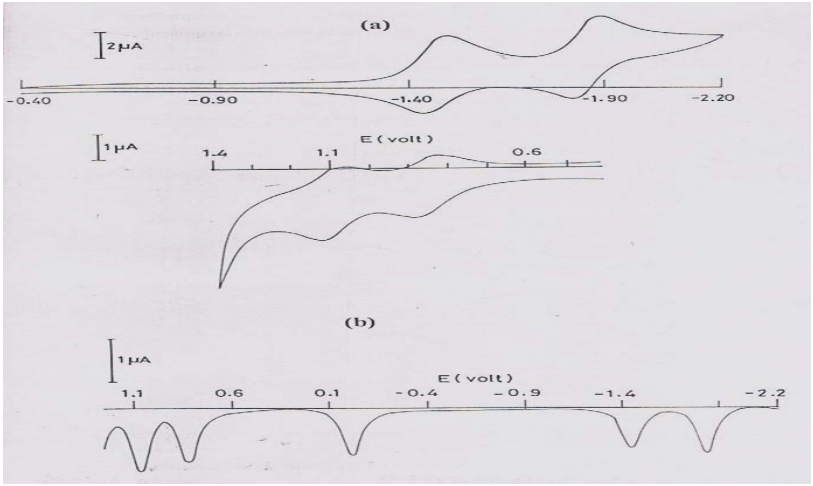


Figure 1 (a). Cyclic voltammogram (b) differential pulse voltammogram of InTPFa in CH_2Cl_2 solution containing 0.1 M $TBAPF_6$ at 300 K

Table 3. One electron redox potential data (in mV) the fluoroaryl porphyrins in CH_2Cl_2 at 300 K

Compound	Oxidation	Reduction	
	OX1	RED 1	RED2
H_2TFPPa	1055	-1265	-1655
H_2TFPPb	840	-1360	-1795
H_2TFPPc	1210	-965	-1225
H_2TFPPd	895	-1095	-1345
InTFPPa	830	-1450	-1840
InTFPPb	685	-1555	-1950
InTFPPc	980	-1150	-1410
InTFPPd	765	-1280	-1525

It is of interest to note that the effect of electron withdrawing group on the reduction potential was more pronounced in the second ring reduction process than the first one in all the *β*-nitro substituted (porphyrins c and d). The shift in the ring reduction potentials induced by the presence of electron donating $–N(CH_3)_2$ groups in the *p*-position of *meso*- fluoroaryl rings of the free-base porphyrins and its metal(III) derivatives was not significant compared to the shift induced by the introduction of a $–NO_2$ group in the *β*-pyrrole position of the porphyrins.

Fluorescence spectra

Fluorescence emission spectra of In(III) derivatives of the porphyrins are shown in Figure 2. The S_1 fluoresence spectra of InTFPPc exhibits two emission maxima with Q(0,0) band being more intense than Q(0,1) band. Interestingly, 2-nitrotetra(pentafluoro) phenyl porphyrinato Indium(III) (InTFPPc) shows two fluorescence bands in CH_2Cl_2 solvent with vibrational fine structure unlike to that observed for indium-2-nitrotetra(phenyl/tolyl) porphyrin in the same solvent. It has been observed that Intensity of emission band (InTFPPd) was drastically reduced with the appearance of a featureless emission band. Thus, the In(III) derivative of nitroamino porphyrin undergoes strong fluorescence quenching relative to either amino or nitro substituted porphyrins. These observations suggest that the face-base porphyrin and In(III) derivatives of amino-nitro substituted porphyrins must possess a considerable fraction of charge transfer in the excited state.

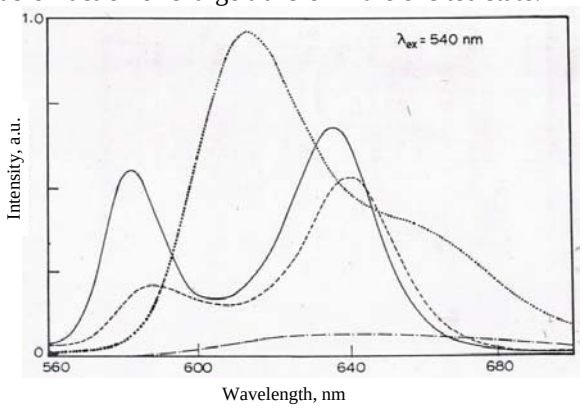


Figure 2. Fluorescene spectra of the In (III) derivatives of the fluoroarylporphyrins in CH_2Cl_2 solution at 300 K, a) InTFPPa, ——— (b) In TFPPb,------ (c) In TFPPc, ……. (d) InTFPPd, —·—·—·

Table 4. Fluorescene a properties of the porphyrins in CH_2Cl_2 at 300 K

Compound	λ_{em}, nm	Relative Q. yield (ϕ)
H_2TFPPa	638, 702	1.0
H_2TFPPb	654, 710	0.85
H_2TFPPc	664, 718	0.83
H_2TFPPd	694	0.35
InTFPPa	584, 638	1.0
InTFPPb	588, 642	0.79
InTFPPc	612, 652	1.2
InTFPPd	638	0.30

[a] *λ_{em} for free-base and Indium(III) derivatives were 510 and 540 nm respectively*

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