

Novel Synthetic Methodology for Metalloporphyrins in Ionic Liquid

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5,10,15,20-Tetraarylporfirinas reagem com sais metálicos na presença do solvente brometo de 1-hexil-3-metilimidazol ([hmim][Br]) em temperatura ambiente, fornecendo as metaloporfirinas correspondentes, com rendimento entre 80-98%.

5,10,15,20-Tetraarylporphyrins undergo metalation with metal salts in the presence of reusable 1-hexyl-3-methylimidazolium bromide ([hmim][Br]) as solvent at room temperature to afford the corresponding metalloporphyrins in 80-98% yields.

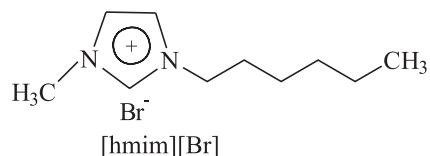
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Introduction

Heme proteins (which contain iron porphyrins) are ubiquitous in nature and serve many roles, including O₂ storage and transport (myoglobin and hemoglobin), electron transport (cytochromes b and c), and O₂ activation and utilization (cytochrome P450 and cytochrome oxidase).¹ The metalloporphyrins with various transition metals have been used as synthetic chemical model systems to mimic heme proteins and other natural oxidation and oxygenation reactions.^{2,3} The synthesis of metalloporphyrins from free-base porphyrins and metal salts have been reported in different solvents and reaction conditions.⁴⁻⁸ Metalation is usually carried out in a carefully chosen solvent which can offer mutual solubility to both the metal salt and free-base porphyrin. However, these methods suffer from certain disadvantages such as rates of reactions are slow, yields are low and workup of the product for purification is troublesome. Further, chlorinated hydrocarbons, pyridine, acetonitrile, tetrahydrofuran or dimethylformamide (DMF), that have their limitations towards environment,⁹ have been used as solvents to metalate different free-base 5,10,15,20-tetraarylporphyrins.⁴⁻⁶ DMF as a solvent is known to decompose during reflux and results in the formation of dimethylamine during metalation which acts as a nucleophile and gives side products during metalation of porphyrins having

electron withdrawing groups such as H₂F₂₀TPP.⁷ The use of pyridine as solvent in the metalation reaction is discouraged as it forms complexes with metals of high charge and retards the metalation process.⁸ Hence, the environmental friendly synthesis of iron porphyrins and related metalloporphyrins has its importance in agrochemical, chemical and pharmaceutical industries.

Room-temperature ionic liquids especially those based on the 1,3-dialkylimidazolium cation provide an eco-friendly reaction medium for a variety of chemical and biochemical transformations, as they lack significant vapor pressure, have ease of reuse, absence of flammability and tolerance for large temperature variations.¹⁰⁻¹³ Herein, we report for the first time the synthesis of metalloporphyrins in reusable 1-hexyl-3-methylimidazolium bromide [hmim][Br] ionic liquid (Scheme 1).



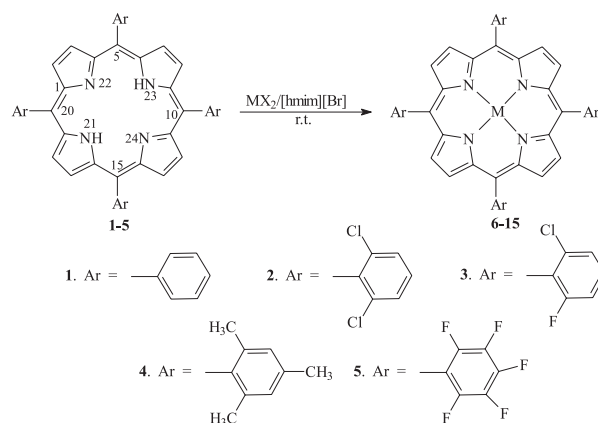
Results and Discussion

The free-base 5,10,15,20-tetraarylporphyrins (**1-5**) used in this study were prepared according to the reported procedure.^{14,15} The metalloporphyrins (**6-15**) have been prepared by simple stirring of the porphyrins with metal

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salts in [hmim][Br] ionic liquid (Table 1, Scheme 1). The metalation of free base porphyrins **1-5** was studied with different metal salts in [hmim][Br]. The separation of metalloporphyrins from the reaction mixture was easy and the recovered ionic liquid was further used for other reactions. It has been observed that the ionic liquid was found to be active even after eight runs. Hence, this metalation process offers less health and environmental hazards than the traditional used solvents such as chlorinated solvents and DMF. The formation of metalloporphyrins has been confirmed spectrophotometrically and on comparison with authentic samples, prepared by conventional methods.⁴⁻⁶ On the formation of a metalloporphyrin, in most of the cases, the four banded spectrum collapses into an essentially two-banded one in visible region, whereas the Soret may remain in the usual range or shifted to higher or lower energy depending upon the metal used.¹⁶ Interestingly, the bromide ion present in

the reaction mixture does not get exchanged with the axial chloride of the metallated porphyrins (**6-15**) as confirmed by the far IR spectra. The presence of peak at 294 cm⁻¹ in



Scheme 1.

Table 1. Yields and UV-Visible spectroscopic data of metalloporphyrins prepared

Free-base Porphyrins	MX ₂	Product	Yield ^a (%)	UV-visible in CHCl ₃ λ _{max} nm (ε _{max} × 10 ⁻³ mol L ⁻¹)	C,H,N analysis
H ₂ TPP (1)	MnCl ₂ ·2H ₂ O	TPPMn(III)Cl (6)	98	402 (30.1), 479 (47.3), 528 (3.5), 618 (2.1)	For C ₄₄ H ₂₈ ClMnN ₄ ; calc. C, 75.16; H, 4.01; N, 7.97; found C, 75.23; H, 3.97; N, 7.85
	FeCl ₂ ·2H ₂ O	TPPFe(III)Cl (7)	97	416 (111.0), 510 (14.1), 576 (3.1), 657 (2.1)	For C ₄₄ H ₂₈ ClFeN ₄ ; calc. C, 75.05; H, 4.01; N, 7.96; found C, 74.96; H, 4.11; N, 7.83
	ZnCl ₂ ·2H ₂ O	TPPZn(II) (8)	92	419 (39.1), 555 (2.1), 644 (1.0)	For C ₄₄ H ₂₈ ZnN ₄ ; calc. C, 77.93; H, 4.16; N, 8.26; found C, 77.85; H, 4.11; N, 8.13
H ₂ Cl ₈ TPP (2)	FeCl ₂ ·2H ₂ O	Cl ₈ TPPFe(III)Cl (9)	95	418 (72.0), 509 (8.3), 584 (3.3), 642 (2.3)	For C ₄₄ H ₂₀ Cl ₉ FeN ₄ ; calc. C, 53.95; H, 2.06; N, 5.72; found C, 54.01; H, 1.99; N, 5.79
	MnCl ₂ ·2H ₂ O	Cl ₈ TPPMn(III)Cl (10)	96	478 (69.0), 522 (4.4), 580 (8.6), 616 (2.8)	For C ₄₄ H ₂₀ Cl ₉ MnN ₄ ; calc. C, 54.00; H, 2.06; N, 5.72; found C, 53.91; H, 2.14; N, 5.61
H ₂ Cl ₄ F ₄ TPP (3)	FeCl ₂ ·2H ₂ O	Cl ₄ F ₄ TPPFe(III)Cl (11)	95	419 (69.0), 503 (7.2), 581 (2.1), 644 (1.2)	For C ₄₄ H ₂₀ Cl ₅ F ₄ FeN ₄ ; calc. C, 57.84; H, 2.21; N, 6.13; found C, 57.91; H, 2.30; N, 5.99
	MnCl ₂ ·2H ₂ O	Cl ₄ F ₄ TPPMn(III)Cl (12)	97	479 (70.1), 525 (4.5), 588 (7.6), 618 (3.0)	For C ₄₄ H ₂₀ Cl ₅ F ₄ MnN ₄ ; calc. C, 57.89; H, 2.21; N, 6.14; found C, 57.79; H, 2.29; N, 6.05
H ₂ Me ₁₂ TPP (4)	FeCl ₂ ·2H ₂ O	Me ₁₂ TPPFe(III)Cl (13)	97	416 (42.4), 510 (5.5), 576 (1.3), 694 (1.1)	For C ₅₆ H ₅₂ ClFeN ₄ ; calc. C, 77.10; H, 6.01; N, 6.42; found C, 76.94; H, 5.91; N, 6.50
	MnCl ₂ ·2H ₂ O	Me ₁₂ TPPMn(III)Cl (14)	95	478 (68.0), 522 (4.4), 580 (8.7), 617 (2.0)	For C ₅₆ H ₅₂ ClMnN ₄ ; calc. C, 77.18; H, 6.01; N, 6.43; found C, 77.24; H, 5.93; N, 6.51
H ₂ F ₂₀ TPP (5)	MnCl ₂ ·2H ₂ O	F ₂₀ TPPMn(III)Cl (15)	80	476 (61.0), 562 (3.4), 589 (2.7)	For C ₄₄ H ₈ ClF ₂₀ MnN ₄ ; calc. C, 49.72; H, 0.76; N, 5.27; found C, 49.82; H, 0.81; N, 4.88

^aIsolated yield.

the far IR of manganese complex of H₂TPP with MnCl₂ indicated that the axial ligand is chloride.

In conclusion, we have developed a simple, convenient and eco-friendly method for the metallation of porphyrins in reusable ionic liquid in high yields. The method avoids the use of organic solvents, excess of metal salts and refluxing at high temperature. The ionic liquids have been used as alternative of organic solvents.

Experimental

The purities of the compounds were determined on silica-coated Al plates (Merck). The electronic spectra were recorded on a Shimadzu UV-260 UV-visible spectrophotometer and the absorption maxima are expressed in nanometers (nm).

Pyrrole, benzaldehyde and its derivatives, used for the synthesis of free-base 5,10,15,20-tetraarylporphyrins,^{14,15} are obtained from Fluka, Switzerland. Metal salts are obtained from s.d. Fine Chemicals, India.

The required ionic liquid has been prepared by the modification of literature procedure.¹⁰⁻¹³ In a round-bottom flask (100 mL), 1-methylimidazole (12.32 g, 0.15 mol, dried over MgSO₄) was mixed with *n*-hexyl bromide (41.25 g, 0.25 mol) and stirred for 12 h at 70-75 °C. The excess hexyl bromide was distilled off and the residue was extracted thoroughly 2-3 times (50 mL each) with diethyl ether to remove the unreacted starting materials. A clear oily liquid of 1-hexyl-3-methylimidazolium bromide [hmim][Br] was obtained in 95% yield. IR (thin film) $\nu_{\max}/\text{cm}^{-1}$: 3420, 3092, 3140, 2962, 2936, 2877, 2062, 1631, 1571, 1461, 1400, 1337, 1160, 1114, 1022, 741; ¹H NMR (CDCl₃, 60 MHz) δ ppm: 0.81 (t, 3H, CH₃), 1.11-1.93 (m, 8H, 4'CH₂), 3.66 (s, 3H, N-CH₃), 4.03 (t, 2H, N-CH₂), 7.33 (s, 1H, CH), 7.54 (s, 1H, CH), 8.41 (s, 1H, CH); ¹³C NMR (CDCl₃, 75 MHz) δ ppm: 12.21, 12.99, 13.41, 19.11, 30.52, 37.01, 46.43, 121.00, 123.81 and 137.03.

General procedure for the reaction of porphyrin with metal salt

The porphyrin (0.5 mmol) and metal salt (0.6 mmol) were stirred at room temperature in [hmim][Br] ionic liquid (15 mL) for one hour. After completion of the reaction as indicated by the TLC, the mixture was extracted with Et₂O (5×20 mL). The combined ether layers were washed with water (2×20 mL) and dried (Na₂SO₄), concentrated in vacuum to afford the metallated compound, which was

further purified by column chromatography using chloroform as eluting solvent. The rest of the viscous ionic liquid was further washed with Et₂O and dried under reduced pressure to retain its activity in subsequent runs.

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