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#### **Graphical Abstract**





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### tetraarylporphyrins in presence of acidic ionic liquids catalyst

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#### ABSTRACT

The reaction of 2,5-bis-( $\alpha$ -arylhydroxymethyl)thiophenes with 5aryldipyrromethanes in the presence of acidic ionic liquid gives 21thia-5,10,15,20-tetraarylporphyrins in 30 % yield whereas the reaction of 2,5-bis-( $\alpha$ -arylhydroxymethyl)thiophenes with 5,10diaryltripyrromethane or pyrrole gives 21,23-dithia-5,10,15,20tetraarylporphyrins in 35 % yield. Acidic ionic liquids are better catalyst and reaction media than acid catalyzed reaction in organic solvents for the synthesis of core modified porphyrins.

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The replacement of one or two pyrrole NH group with O, S, Se and Te atoms in porphyrins forms 21heteroatom<sup>1,2</sup> and 21,23-heteroatom core modified porphyrins,<sup>3-5</sup> respectively. The core modified porphyrins result in an altered electronic structure with interesting  $optical^6$ , chemical, photochemical<sup>7</sup> and electrochemical<sup>8</sup> properties. The introduction of a heteroatom in place of "N" results in large red shift in both Soret and Q-bands. The maximum red shift was observed with "S", "Se" and "Te" containing heteroporphyrins and minimum for "O" containing heteroporphyrins.<sup>9</sup> Furthermore, the red of diheteroatom shift absorption bands of substituted porphyrins were greater than those

monoheteroatom<sup>10</sup> for observed substituted porphyrins. The heteroatom porphyrins are easy to reduce and difficult to oxidize compared to regular porphyrins.<sup>11</sup> The reaction of mono or bifunctionalized (2 or 5 position) five membered heterocycles aromatic aldehydes, with dipyrromethanes and tripyrromethane in presence of protic or Lewis acid in organic solvents gives core modified porphyrins in moderate yields. The synthesis of core modified porphyrins have been examined in the presence of strong acids such as BF<sub>3</sub>O(Et)<sub>2</sub>, TFA, methylsulfuric acid and propionic acid.<sup>12-14</sup> In order to avoid the use of corrosive acid and to minimize the amount of harmful organic

solvents, the development of a new method for the synthesis of core modified porphyrins catalyzed by acidic ionic liquids would be highly desirable.

The acidic ionic liquids have gained special attention as a catalyst in organic synthesis because of many advantages such as their outstanding flexibility, heat resistance, non-volatility, noncorrosiveness, negligible vapour pressure. tunable polarity, operationally simplicity and high reactivity with common organic solvents.<sup>15,16</sup> Acidic ionic liquids have been used in the synthesis of porphyrins in moderate yield<sup>17,18</sup> whereas, they are not been used as catalyst and solvents for the synthesis of core modified porphyrins. Herein, we report the high yield synthesis of core modified porphyrins in the condensation of 2,5-bis-(aarylhydroxymethyl)thiophenes 5with aryldipyrromethanes, tripyrromethanes<sup>19,20</sup> or pyrrole in different reaction conditions (Scheme 1, Figure 1).

The starting materials 5-arydipyrromethanes (2a-2h) and 2,5-bis-( $\alpha$ arylhydroxymethyl)thiophenes (3a-3d) were prepared by minor modification of known literature procedure.<sup>21-23</sup> The different acidic ionic liquids were used for the synthesis of core modified porphyrins and the better yields were obtained in the presence of 1-methyl-3-(4-sulfopropyl)-

imidazolium trifluoromethylacetate acidic ionic liquid as compared to that with longer alkyl chains in dichloromethane (Table 1). This is adroit to the short chain length of methylene groups, hence, drop off in hydrophobicity and +I effect of ionic liquid leading to an increase in acidic nature. Primarily 1a was screened under a variety of experimental conditions to optimize the product distribution at room temperature. The equivalent amount of 5arydipyrromethanes and 2.5-bis-( αarylhydroxymethyl)thiophenes were taken up in dichloromethane. Acidic ionic liquid 1a (0.1 mol equiv.) was added into the reaction mixture. The progress of the reaction was monitored by TLC (complete consumption of dipyrromethane). The core modified porphyrin was isolated in 21% yield. The formation of 21-heteroporphyrins was possible when the scrambling occurred in dipyrromethanes. The 21-heteroporphyrins (4) were formed in 28-30% yields, using 0.3-0.5 equivalents of acid catalyst. However, the core modified porphyrins (4) were formed in 20 % yields, using 1 equivalent of acid catalyst, the time required for the completion of reaction was comparatively more, which is attributed to different extent of acidolysis under different reaction conditions. The exclusive formation of 21thiaporphyrins under reaction conditions suggested 5-aryldipyrromethanes acidolysis that the of

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occurred in the presence of acidic ionic liquids.<sup>24,25</sup> This type of acidolysis of 5-aryldipyrromethane is also reported in literature.<sup>26</sup> Results obtained by the variation of catalyst concentration suggested that 0.5 mol equivalent concentration found to be rational concentration for the acidolysis of dipyrromethane and its conversion into 21thiaporphyrins.

With respect to the appealing results obtained from the catalyst concentrations screening, we framed the general protocol for the synthesis of 21thiaporphyrins by treating several 5-2,5-bis-(αaryldipyrromethanes and arylhydroxymethyl)thiophene using acidic ionic liquid **1a** (0.5 mol equiv.) followed by DDQ oxidation in dichloromethane (Table 2). The structure of 21-thia-5,10,15,20-tetraarylporphyrins was characterized by UV-Visible spectroscopy and confirmed by <sup>1</sup>H NMR spectroscopic and mass spectrometric techniques (data in the supplementary information). Nevertheless, the reaction of 5substituted dipyrromethanes (2) also showed similar behaviour in ionic liquids and the yields were

dependent upon the steric bulk of 5-substituent in dipyrromethane. Moreover, the yields of core modified porphyrins (4) were also dependent on the nature of dipyrromethane; dipyrromethane with electron donating groups at para position gave better yield as compared to electron withdrawing groups. The reactions of 5-(mesityl)dipyrromethane (2e) with 2,5-bis-( $\alpha$ -arylhydroxymethyl)thiophenes (3d) gave corresponding core modified 21-thiaporphyrin (12 % yield) and porphyrin at ambient temperature. The observed time required for the conversions was too long (Table 2, Entry 5). This could be ascribed to steric hindrance of bulky methyl substituents. The reaction of 5-aryldipyrromethane with 2,5-bis- $(\alpha$ -arylhydroxymethyl)thiophenes, in the presence 1-methyl-3-(4-sulfopropyl)-imidazolium of hydrogen sulphate, afforded core modified porphyrins and porphyrin in poorer yields. Apart from this, a black tarry third isomer was also observed; but due to less availability of sample and poor solubility in organic solvents a detailed structural characterization was not possible.



Scheme 1

Table 1:Synthesis		sis of 21-thia	porph	yrins in	
presence of different acidic ionic liquids <sup>a</sup>					
Entry	AILs	DPMs	DPMs 2,5-Bis-(α- arylhydrox ymethyl)thi ophenes		Yield (%) <sup>b</sup> 4
1	<b>1</b> a	2a	3a	40	30
2	1b	2a	<b>3</b> a	45	27
3	1c	2a	<b>3</b> a	40	22
4	1d	2a	3a	45	26
5	1e	2a	3a	40	25
6	1f	2a	3a	40	23
7	1g	2a	3a	40	24
8	1h	2a	3a	40	22
9	1i	2a	3a	40	25
10	1j	2a	<b>3</b> a	40	25
11	1k	2a	<b>3</b> a	40	25
12	11	2a	<b>3</b> a	40	25

<sup>a</sup> Reaction conditions: reaction temperature 25 °C, dipyrromethanes (0.45 mmol), Diols (0.45 mmol); acidic ILs (0.22 mmol); solvent (10 mL) dichloromethane; <sup>b</sup>Isolated yields

Table 2: Condensation of dipyrromethane and 2,5bis-(α-arylhydroxymethyl)thiophenes in presence of acidic ionic liquids 1a<sup>ab</sup>

Entry	1a (Mol equiv.)/Tim e (min)	DPMs	2,5-Bis-(α- arylhydrox ymethyl)th iophenes	Yield (%) <sup>c</sup> 4 /lit[1]
1	0.1/70	2a	3a	19/17
2	0.2/70	2a	<b>3</b> a	21/17
3	0.3/60	2a	-3a	28/17
4	0.5/40	2a	<b>3</b> a	30/17
5	1.0/90	<b>2</b> a	<b>3</b> a	20/17
6	0.5/40	2b	3d	25/15
7	0.5/40	2c	3d	27
8	0.5/40	2d	3d	20/14
9	0.5/40	2e	3d	12/8
10	0.5/40	2f	3d	16
11	0.5/40	2h	3d	18
12	0.5/40	2d	3b	20

<sup>ab</sup>Reaction conditions: reaction temperature 25 °C,
dipyrromethanes (0.45 mmol), Diols (0.45 mmol);
AILs (1a) (0.22 mmol); reaction time: 40 min.
dichloromethane (10 mL); <sup>c</sup>Isolated yields

The 21,23-dithia-5,10,15,20-tetraarylporphyrins were prepared and characterized as above. The 21,23-diheteroporphyrins (**5**) were isolated in 35% yield using 0.1equivalent of acid catalyst **1a**. Higher amounts of acid concentration did not improve the result to a greater extent. The equimolar amount of

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2,5-bis-( $\alpha$ -arylhydroxymethyl)thiophene and pyrrole were taken up in dry dichloromethane. Acidic ionic liquids (0.1 mol equiv.) was added into the reaction mixture for appropriate time (Table 3) followed by the oxidation with DDQ gave core modified 21,23-dithiaporphyrins in upto 35 % yields (Scheme 1b Table 3). The same reactions, performed in the presence of p-toluene sulfonic acid in dichloromethane gave the 9-20 % yield while in presence of BF<sub>3</sub>OEt<sub>2</sub> maximum yields of 10-13 % were obtained<sup>27</sup>. The yields of the products were observed to be increased upto  $\sim 10$  % by following [3+1] strategy. The reaction of 2,5-bis-(αarylhydroxymethyl)thiophenes with tripyrromethane in presence of acidic ionic liquid followed by DDQ oxidation in dichloromethane gave core modified porphyrins in upto ~45 % yields (Scheme 1c, Table 3, Entry 6-8)

#### Table 3: Synthesis of 21,23-dithiaporphyrins by

the reaction of 2,5-bis-(α-

#### arylhydroxymethyl)thiophenes<sup>a</sup>

Entry	2,5-Bis-(α- arylhydroxymethyl )thiophenes	TPM s	Yield (%) <sup>b</sup> 5
1	<b>3</b> a	-	32%
2	<b>3</b> b	-	35%
3	3c	-	33%

Entry	2,5-Bis-(α- arylhydroxymethyl	TPM s	Yield (%) <sup>b</sup> 5
	)thiophenes		
4	3d	-	30%
5	3d	6	45%
6	<b>3</b> b	6	42%
7	3с	6	40%

<sup>a</sup>Reaction conditions: reaction temperature 25 °C, pyrrole (0.45 mmol), diols (0.45 mmol); acidic ILs (0.11 mmol); dichloromethane (10 mL); reaction time: 30 min; <sup>b</sup>Isolated yield

# Acidolysis of dipyrromethane in acidic ionic liquids:

The synthesis of core modified porphyrinoids has been obtained by the acidolysis of at least one of the precursors, either dipyrromethanes or tripyrromethanes followed by the reaction of resulting species with other components leading to porphyrinogen, which on oxidation with DDQ gave the final product as core modified porphyrins. The acidolysis of 5-aryldipyrromethanes were observed in the presence of inorganic acid, organic acids and selected acidic ionic liquids depending upon their concentrations, temperatures and reaction conditions.<sup>28,29</sup> The reaction of two moles of 5aryldipyrromethanes forms scrambled tripyrromethanes catalyzed by acidic ionic liquids,

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which further reaction with 2,5on bis(arylhydroxymethyl)thiophene form 21thiaporphyrinogen (Figure 2). The oxidation of porphyrinogens or 21-thiaporphyrinogens by DDO or other oxidizing agent produced corresponding 21-heteroporphyrins. porphyrins and The condensation of dipyrromethane and 2,5-bis-( $\alpha$ arylhydroxymethyl)thiophenes is common а method for the synthesis of 21-thia porphyrins,<sup>30,31</sup> but it is often overwhelmed by scrambling processes leading to a mixture of porphyrins. The problem of scrambling is more prominent in 5unhindered dipyrromethanes (e.g., than that in hindered phenyldipyrromethane) dipyrromethanes (e.g., 5-mesityldipyrromethane). Scrambling can be suppressed by inhibiting the reaction of oligomer fragments generated by acidic ionic liquid-induced cleavage of dipyrromethane, rather than by inhibiting acidolysis itself. However, such reaction conditions were also found to inhibit the condensation, leading to low yields (<10%) of The modified porphyrin. absence of core scrambling in 5-mesityldipyrromethane and 2.5-bis-(a-arylhydroxymethyl)thiophenes condensations due to the resistance of 5was mesityldipyrromethane towards acidolysis. These

studies together provide an insight into the origin of scrambling with different types of substrates reaction under different conditions in the dipyrromethane with 2,5-bis-(αarylhydroxymethyl)thiophenes 21route to heteroatom-porphyrins.

product of 21-thia-5,10,15,20-The major tetraarylporphyrins (4) apparently formed as a result of the acidic ionic liquids-driven cleavage of dipyrromethane and subsequent recombination of the fragments with another equivalent of 2,5-bis-( $\alpha$ arylhydroxymethyl)thiophenes (3). This side reaction, leading to scrambling of substituents, is often observed in porphyrin synthesis.<sup>32,33</sup> In some cases, scrambling can be controlled to prepare the scrambled porphyrins<sup>34,35</sup> selectively. The easy availability of this catalyst and its superiority over the existing methods should make the present protocol an attractive addition to conventional procedures.

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Figure 2: Plausible mechanism for the synthesis of core modified porphyrins

We have developed a convenient, and clean protocol for the synthesis of 21-thiaporphyrins and 21,23-dithiaporphyrins. The high yield, operational simplicity, easy availability and low cost of the reagents make the procedure more attractive as compared to existing procedures.

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- 35.



a. R =  $-(CH_2)_3SO_3H$ , X = CF<sub>3</sub>COO b.  $R = -(CH_2)_3SO_3H$ ,  $X = CF_3SO_3$ c. R = -(CH<sub>2</sub>)<sub>3</sub>SO<sub>3</sub>H, X = CH<sub>3</sub>SO<sub>3</sub> d. R =  $-(CH_2)_3SO_3H$ , X = HSO<sub>4</sub>

e. R = -CH <sub>2</sub> COOH, X = CF <sub>3</sub> COO	i. $R = -(CH_2)_4SO_3H$ , $X = CF_3COO$
f. $R = -CH_2COOH$ , $X = CF_3SO_3$	j. R = $-(CH_2)_4SO_3H$ , X = $CF_3SO_3$
g. R = -CH <sub>2</sub> COOH, X = CH <sub>3</sub> SO <sub>3</sub>	$k.R = -(CH_2)_4SO_3H, X = CH_3SO_3$
h. R = -CH <sub>2</sub> COOH, X = HSO <sub>4</sub>	$I. R = -(CH_2)_4 SO_3 H, X = HSO_4$

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