

Silica Sulfuric Acid/ $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$: An Efficient and Green Alternative for the Synthesis of Tetraarylporphyrins

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Porphyrins, as an important biomolecules, have some applications such as catalysts,¹⁻³ photosensitisers,⁴ non-linear optical materials,⁵ liquid crystal,⁶⁻⁷ photodynamic therapy of cancer,⁸ solar-energy conversion,⁹ molecular binding,¹⁰ energy and electron transfers,¹¹⁻¹² and light harvesting.¹³ This tetrapyrrole aromatic macrocycle compound exist in biological active materials such as hemoglobin, chlorophyll, vitamin B12, cytochromes and other enzymes.¹⁴ The best reported procedure for synthesis of porphyrins is tetramerization of monopyrrole.

In most cases, a solution of aldehyde and pyrrole in a high-boiling acid such as propionic acid as solvent is heated at reflux in air, so that condensation and oxidation occur simultaneously. This method gives low yields of sensitive porphyrins, reflecting rather vigorous conditions, and intractable purification problems arise for porphyrins which do not readily crystallize or precipitate from the tar-laden propionic acid and a high percentage of tarry by-products are also formed.¹ Recent modifications in the tetramerization of mono pyrrole are the use of K_10 ,¹⁶ CF_3COOH or BF_3 ,¹⁷ $\text{CF}_3\text{SO}_2\text{Cl}$,¹⁸ PCl_5 ,¹⁹ and silica chloride²⁰ as catalyst. In these methods, there are intrinsic disadvantages such as long reaction time, low yields, and costly reaction and purification procedure.

In continuation of our investigations on solid acids in organic synthesis,²¹⁻²⁶ we investigated the synthesis of tetraarylporphyrin in the presence of various solid acids. Herein, we report that mixture of silica sulfuric acid (SSA)²⁷ and $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ is an efficient catalyst for the synthesis of tetraarylporphyrinogen and is comparable with some other catalysts such as CF_3COOH , BF_3 , K_10 , PCl_5 , silica chloride and $\text{CF}_3\text{SO}_2\text{Cl}$. To optimize the reaction conditions, the reaction of benzaldehyde and pyrrole, was used as a model reaction (Table 1). Reactions at different conditions in the presence of SSA/ $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ revealed that the best conditions were mixing of reactants in dichloromethane at room temperature and a ratio of aldehyde (mmol) : pyrrole (mmol) : SSA (g) : $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ (mmol), 1 : 1 : 0.05 : 0.5. In our opinion, SSA, activates carbonyl group in aldehyde, and, $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$, aggregates the pyrrole and aldehyde molecules in non-template manner.

Next, various aldehydes and pyrrole were used as substrates for the synthesis of tetraaryl porphyrinogens (Scheme 1 and Table 2).

In this paper, we report a method for preparing porphyrins under mild conditions at room temperature. Pyrrole and

aldehyde in the presence of SSA and $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ react to form tetraarylporphyrinogen (1) as intermediate. This intermediate was oxidized to tetraarylporphyrin (2) by air or DDQ/SSA. Under these reaction conditions, tetraarylporphyrins were formed in 41 - 65% yields. All the products are known and were characterized by IR, UV-Visible and $^1\text{H-NMR}$ and by comparison of their physical properties with those reported in the literature.

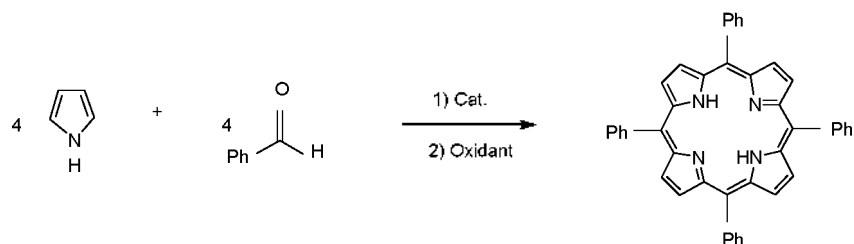
In conclusion, we have demonstrated a simple method for the synthesis of tetraarylporphyrin using SSA/ $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ as an eco-friendly, inexpensive and efficient catalyst. Short reaction times, high yield, simplicity of operation and easy work-up are some advantages of this method.

Experimental Section

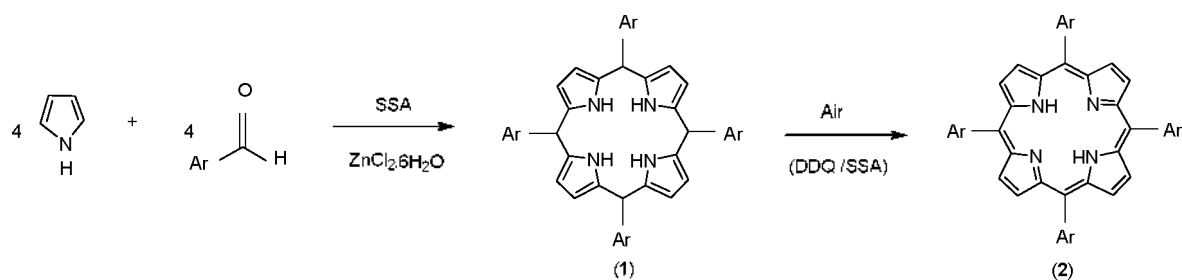
General. Melting points were measured with an Büchi melting point B-540 B.V.CHI apparatus and are uncorrected. IR spectra were recorded with a Bnker, Eqinox 55 spectrometer. ^1H NMR spectra were recorded with a BRUKER 400 MHz AVANCE spectrometer. NMR spectra were obtained on solutions in CDCl_3 . UV-Visible spectra of porphyrins were recorded with GBC UV-Visible Cintra 101. All the products are known compounds, which were characterized by UV-Visible, IR and ^1H NMR spectral data and their mp's compared with literature reports.

General procedure for synthesis of tetraarylporphyrin, pyrrole (3 mmol), aldehyde (3 mmol), $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ (0.3 g), SSA (0.15 g) and dichloromethane (20 mL) were placed in a 100 mL beaker. The mixture was stirred at room temperature for 2 hours. The progress of the reaction was followed by TLC. After 2 h, the maximum amount of porphyrinogens was obtained. Then, 0.3 g of DDQ and 0.2 g of SSA was added to mixture and stirred at room temperature for 10 min to oxidize the porphyrinogen to porphyrin. Aerating of toluene mixture under reflux for 48 h is another method for oxidation of porphyrinogen to porphyrin. The general workup involves concentration of the crude reaction mixture, followed by passing over a short chromatography column. Filtration of mixture, evaporation of solvent, washing the obtained crude solid with diethyl ether, hot water, and cold methanol, respectively, is alternative method for purification of porphyrin. The porphyrin products obtained in two manner are relatively pure.

Table 1. Reaction of pyrrole (1 mmol) and benzaldehyde (1 mmol) in the presence of various catalysts.



Entry	Catalyst	Solvent	Condition	Oxidant	Time (h): Yield ^a (%)	Ref.
1	-	CH ₂ Cl ₂	grinding	air	0.12:0	-
2	Oxalic acid	CH ₂ Cl ₂	grinding	air	0.12:0	-
3	NaHSO ₄	CH ₂ Cl ₂	grinding	air	0.12:5	-
4	Al(HSO ₄) ₃	CH ₂ Cl ₂	grinding	air	0.12:7	-
5	SiO ₂ -P ₂ O ₅	CH ₂ Cl ₂	grinding	air	0.12:0	-
6	Silica chloride	CH ₂ Cl ₂	reflux	air	4:45	20
7	PCl ₅	CH ₂ Cl ₂	reflux	air	4:62	19
8	CF ₃ SO ₂ Cl	CH ₂ Cl ₂	reflux	air	4:65	18
9	BF ₃	Et ₂ OH	reflux	P-Chloranil	1:46	17
10	CF ₃ COOH	Et ₂ OH	reflux	P-Chloranil	1:46	17
11	K10	CH ₂ Cl ₂	reflux	P-Chloranil	3:25	16
12	Propionic acid	Propionic acid	reflux	air	0.5:20	15
13	SiO ₂ -OSO ₃ H (0.05 g)	CH ₂ Cl ₂	r.t.	air	4:10	-
14	SiO ₂ -OSO ₃ H (0.05 g)	CH ₂ Cl ₂	reflux	DDQ	3:15	-
15	SiO ₂ -OSO ₃ H (0.05 g)	CH ₂ Cl ₂	grinding	CAN	0.12:5	-
16	SiO ₂ -OSO ₃ H (0.05 g)	CH ₂ Cl ₂	grinding	TCM	0.12:5	-
17	SiO ₂ -OSO ₃ H (0.05 g)	CH ₂ Cl ₂	grinding	DDQ	0.12:5	-
18	SiO ₂ -OSO ₃ H (0.05 g)	Toluene	reflux	air	3:8	-
19	SiO ₂ -OSO ₃ H (0.05 g)	benzene	reflux	air	3:6	-
20	SiO ₂ -OSO ₃ H (0.05 g)	<i>n</i> -Hexane	reflux	air	3:5	-
21	SiO ₂ -OSO ₃ H (0.05 g)	THF	reflux	air	3:5	-
22	SiO ₂ -OSO ₃ H (0.05 g)	Et ₂ O	reflux	air	3:4	-
23	SiO ₂ -OSO ₃ H (0.05 g)	CH ₃ COCH ₃	reflux	air	4:5	-
24	SiO ₂ -OSO ₃ H (0.05 g)	CH ₃ OH	reflux	DDQ	5:15	-
25	SiO ₂ -OSO ₃ H (0.05 g)	CH ₃ Cl	reflux	air	3:20	-
26	SiO ₂ -OSO ₃ H (0.05 g)	CH ₂ Cl ₂	MW	air	0.12:0	-
27	SiO ₂ -OSO ₃ H (0.025 g) + ZnCl ₂ (0.25 mmol)	CH ₂ Cl ₂	reflux	air	4:50	-
28	SiO ₂ -OSO ₃ H (0.025 g) + ZnCl ₂ (0.25 mmol)	CH ₃ OH	reflux	air	4.5:35	-
29	SiO ₂ -OSO ₃ H (0.025 g) + ZnCl ₂ (0.5 mmol)	CH ₂ Cl ₂	r.t.	air	4:55	-
30	SiO ₂ -OSO ₃ H (0.05 g) + ZnCl ₂ (0.5 mmol)	CH ₂ Cl ₂	r.t.	air	4:65	-
31	SiO ₂ -OSO ₃ H (0.075 g) + ZnCl ₂ (0.5 mmol)	CH ₂ Cl ₂	r.t.	air	4:65	-
32	SiO ₂ -OSO ₃ H (0.1 g) + ZnCl ₂ (0.5 mmol)	CH ₂ Cl ₂	r.t.	air	4:67	-



Scheme 1

Table 2. Synthesis of meso-tetraarylporphyrinogens (**1**) from pyrrole (1 mmol) and aryl aldehydes (1 mmol) in the presence of silica sulfuric acid (0.05 g) and ZnCl₂·6H₂O (0.5 mmol), at room temperature for 4 h.

Entry	Ar	Ref.	Yield (%)
1	Ph	18	65
2	4-CH ₃ -C ₆ H ₄	18	57
3	4-Cl-C ₆ H ₄	20	56
4	4-Br-C ₆ H ₄	20	55
5	4-OCH ₃ -C ₆ H ₄	18	60
6	4-NO ₂ -C ₆ H ₄	18	51
7	4-((CH ₃) ₂ CH)-C ₆ H ₄	18	64
8	4-CN-C ₆ H ₄	19	48
9	2-NO ₂ -C ₆ H ₄	19	41
10	2-Cl-C ₆ H ₄	19	65
11	2-CH ₃ -C ₆ H ₄	20	63
12	2-Cl-C ₆ H ₄	18	58
13	3-NO ₂ -C ₆ H ₄	19	46

^aAll the products are known and were characterized by IR, UV-Visible and ¹H-NMR and by comparison of their physical properties with those reported in the literature. ^bIsolated yield.

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