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Synthesis of *meso*-tetraphenyl porphyrins via condensation of dipyrromethanes with *N*-tosyl imines

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ABSTRACT

A new synthetic route for the synthesis of 5,10,15,20-tetraphenyl porphyrins has been developed based on the reaction of 5-substituted dipyrromethanes with *N*-tosyl imines in the presence of a metal triflate catalyst. *meso*-Substituted tetraphenyl porphyrins were synthesized in a two-step process. The first step of the method is the metal triflate-catalyzed condensation of 5-substituted dipyrromethanes with *N*-tosyl imines to form a porphyrinogen intermediate and the second step is the oxidation of the porphyrinogen to porphyrin. The method was applied to the synthesis of *trans*-A_2B_2-tetraarylporphyrins and the products were obtained with only a trace amount of one scrambling product. The synthesis of two important building blocks for porphyrin synthesis, mono and di-sulfonamide alkylated 5-substituted dipyrromethanes, was achieved by the addition of 5-substituted dipyrromethane to *N*-tosyl imine. The application of mono and di-sulfonamide alkylated 5-substituted dipyrromethanes in '2+2' porphyrin formation reactions is presented.

1. Introduction

Porphyrins are a class of naturally occurring macrocyclic compounds, which play a very important role in the metabolism of living organisms.[1] Porphyrins and their metal complexes have been the subject of various studies and find application as photosensitizers in photodynamic therapy and boron neutron capture therapy,[2] catalysts,[3] sensors[4] and molecular electronic devices.[5]

Among the great variation of porphyrins with a specific pattern of substituents, the most widely studied synthetic porphyrin group encompasses the symmetrical 5,10,15,20-tetraarylporphyrins like 5,10,15,20-tetraphenylporphyrin (TPP) (A_4-type porphyrin), because of their potential applications in materials chemistry.[6] This type of porphyrin was first synthesized by the condensation of benzaldehyde and pyrrole in pyridine at high temperatures by Rothemund.[7] Adler later developed this method by using propionic acid or acetic acid as solvent,[8] however, the method fails with aldehydes bearing acid sensitive functional groups. This problem was solved with a new method developed by Lindsey who used BF_3-etherate as a catalyst in the synthesis of porphyrinogen and oxidized it to porphyrin with DDQ.[9] Although some improvements have been reported for the synthesis of *meso*-tetraarylporphyrins such as using clays[10] and transition metal salts as catalyst,[11] the yields are low and there are still some purification problems.

meso-Substituted *trans*-A_2B_2-tetraarylporphyrins are also important components found in many applications of biomimetic and materials chemistry.[12] The synthetic methods for *trans*-A_2B_2-tetraarylporphyrins suffer from rearrangement of substituents on porphyrins, the so-called 'scrambling', and the need for extensive chromatography to isolate *trans*-A_2B_2-tetraarylporphyrins from the mixture of porphyrins. Steric and electronic factors, reagent concentration and type of acid catalyst influence the formation of scrambled products.[13] Therefore, porphyrin synthesis without scrambling is a challenge for synthetic chemists.

Aminomethylpyrrole and aminomethyl-dipyrromethane derivatives have been used in porphyrin synthesis as in the self-condensation of aminomethylpyrroles[14] or in the condensation of bis(aminomethyl)dipyrromethanes or bis(aminomethyl)pyrroles with pyrrole derivatives.[15] The synthesis of *meso*-substituted porphyrins has been restricted to *trans*-AB and *trans*-A_2 porphyrins when Mannich reagents ($CH_2{=}NR_2X$) are used for the synthesis of aminomethylpyrrole and aminomethyl-dipyrromethane derivatives. This limitation has directed us to investigate a new reaction route allowing a possibility for the synthesis of *meso*-tetraarylporphyrins through the reaction of 5-substituted dipyrromethanes with *N*-tosyl imines. According to our knowledge, the only example of aminomethylation reaction in A_4-porphyrin synthesis is the preparation of *meso*-tetraalkyl porphyrin derivatives in low yields and very long reaction time by the reaction of pyrrole with Schiff bases.[16]

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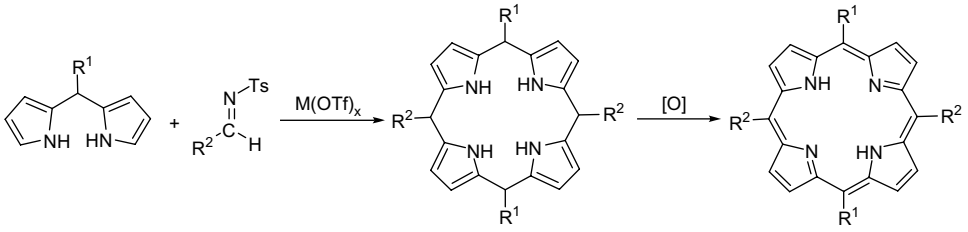
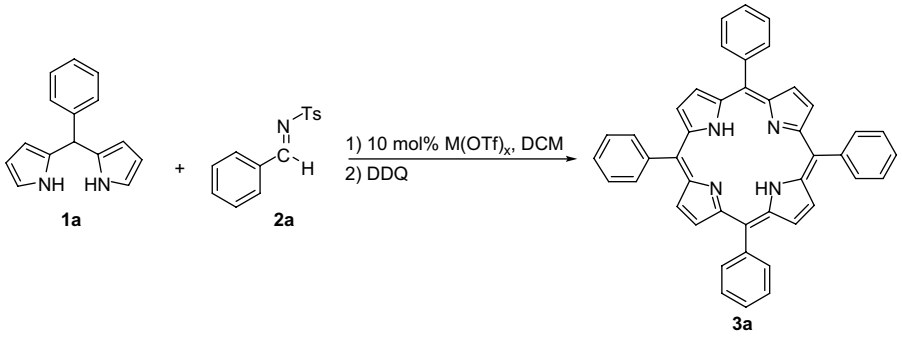
Recently, our studies on the alkylation of pyrrole[17] and synthesis of 5-substituted dipyrromethanes[18] by using *N*-tosyl imines showed that metal triflates are attractive Lewis acid catalysts for the preparation of porphyrinic macrocyles. Although several types of metal triflate-catalyzed organic reactions have been published so far,[19] only a few examples in porphyrin synthesis have been reported.[20,21]

Herein, we report a new route for the synthesis of 5,10,15,20-tetraphenyl porphyrins and *trans*-A_2B_2-tetraarylporphyrins by the reaction of 5-substituted dipyrromethanes with *N*-tosyl imines in the presence of a metal triflate catalyst. A one-flask, two-step reaction was chosen for the reaction protocol as in the Lindsey method. The first step of the method is the metal triflate-catalyzed condensation of 5-substituted dipyrromethanes with *N*-tosyl imines to form porphyrinogen intermediate and the second step is the oxidation of porphyrinogen to porphyrin (Scheme 1). The study involves the determination of favourable reaction conditions for condensation and oxidation steps by investigating the effects of various parameters.



Scheme 1.



Scheme 2.

It is known that 5-substituted dipyrromethanes have been used as important building blocks in the synthesis of porphyrins in '2+2' MacDonald synthesis, which is a useful strategy for preparing less symmetrical porphyrins by the condensation of dissimilar dipyrromethanes.[22] In this work, we also present the metal triflate-catalyzed preparation of mono and di-sulfonamide alkylated 5-substituted dipyrromethane intermediates and their application in '2+2' porphyrin formation.

2. Results and discussion

We attempted to synthesize *meso*-substituted porphyrins by the reaction of 5-phenyldipyrromethane (**1a**) with *N*-benzylidene-4-methylbenzenesulfonamide (**2a**) in the presence of metal triflate catalysts. The catalytic activity of metal triflates was first tested on a model reaction (Scheme 2). The synthesis of *meso*-substituted porphyrins from the reaction of 5-phenyldipyrromethane (**1a**) and *N*-benzylidene-4-methylbenzenesulfonamide (**2a**) was examined by taking 10 mM concentration of each reactant in the presence of 10 mol % of metal triflate catalyst in CH_2Cl_2 at room temperature. The reaction was monitored with TLC and 5,10,15,20-tetraphenylporphyrin (TPP) (**3a**) was purified by flash column chromatography after work-up. Gd, Yb and Zn-triflates were found inefficient, while Y, La and Nd-triflates catalyzed the reaction but with low yield (Table 1, entries 1–6). The highest yield of TPP was obtained with $Cu(OTf)_2$ catalyst as 44% (Table 1, entry 9). The effect of the amount of $Cu(OTf)_2$ (2–20 mol %) on the yield was then examined. The yield was increased up to 44% with 10 mol % of the catalyst (Table 1, entries 7–9). Higher amounts of $Cu(OTf)_2$ resulted in lower yields (Table 1, entries 10 and 11).

The effect of solvent was examined by performing the reaction in different organic solvents, like CH_3CN, acetone, THF, Et_2O, DCM, $CHCl_3$ and toluene, in the presence of 10 mol % $Cu(OTf)_2$ at room

Table 1
Effects of metal triflates type and the amount of catalyst on the synthesis of **3a**[a]

Entry	Catalyst	Amount of Catalyst (mol %)	Yield[b] (%) of **3a**
1	$Gd(OTf)_3$	10	—
2	$Yb(OTf)_3$	10	—
3	$Y(OTf)_3$	10	30
4	$La(OTf)_3$	10	2
5	$Zn(OTf)_2$	10	—
6	$Nd(OTf)_3$	10	4
7	$Cu(OTf)_2$	2	11
8	$Cu(OTf)_2$	5	20
9	$Cu(OTf)_2$	10	44
10	$Cu(OTf)_2$	15	25
11	$Cu(OTf)_2$	20	10

[a] Reaction conditions: (1) 10 mM of **1a** and **2a**, CH_2Cl_2, rt, 2 h; (2) DDQ.
[b] Yield refers to pure product after column chromatography.

temperature. The yield was highest (44%) in DCM among all the solvents. To investigate the effect of oxidant, the oxidation step of the reaction was repeated by using *p*-chloranil and *o*-chloranil as oxidants, and by refluxing the reaction mixture in open air without oxidant, however, high TPP yields could not be obtained as with DDQ.

One of the most important reaction parameters of the porphyrin formation reactions is the reactant concentrations. The reactant concentrations were examined over the range from 1 mM to 100 mM (Table 2, entries 1–7). TPP yield increased with the increasing concentration of reactants up to 10 mM and no formation was observed at 1 mM. The maximum yield of TPP (44%) was obtained when 10 mM of each reactants was used (Table 2, entry 4).

According to the literature knowledge, porphyrinogen forms with a reversible process in the first step of the reaction.[9a,b,23] Therefore, we next optimized the reaction time to reach the maximum amount of porphyrinogen for subsequent oxidation to porphyrin (Table 2, entries 8–12). The maximum chemical yield (45%) was obtained in 1.5 h (Table 2, entry 10).

On the basis of these studies, the best conditions for porphyrin formation have been determined as the condensation of 10 mM of dipyrromethane and *N*-tosyl imine with 10 mol % $Cu(OTf)_2$ in dichloromethane for 1.5 h and then oxidation with DDQ at room temperature. The critical role of the catalyst in porphyrin synthesis prompted us to examine other well-known Lewis acids or protic acids in our model reaction and compare their activities with metal triflates (Table 3, entries 1–9). Four of the examined acids listed in Table 3 ($CuCl_2$, $SnCl_4$, $TiCl_4$ and BF_3-etherate) did not provide TPP at all. Trichloroacetic acid, HCl, $AlCl_3$ and *p*-toluenesulfonic acid yielded the product with low yield (3–13%). Only trifluorosulfonic acid among the examined acids catalyzed the reaction by providing 39% yield of TPP (Table 3, entry 5).

Applying the optimum reaction conditions, various *N*-tosyl imines and 5-substituted dipyrromethanes were reacted to give the corresponding A_4-type *meso*-substituted porphyrins as summarized in Table 4. The yield of porphyrin was considerably affected by the nature and position of the substituents. Higher yields were obtained with electron donating 4-methoxy or 4-methyl substituents present at *para* positions to phenyl groups than with electron withdrawing trifluoromethyl and halogens (Table 4, entries 1, 2, 4 and 7–10). 2-Methoxy, 2-hydroxy and 4-nitro substituted dipyrromethanes did not yield the expected porphyrin product. The products were purified by flash column chromatography and characterized by NMR, FTIR and UV–vis spectroscopy. All the spectroscopic data for **3a**,**b**,**d**,**h**–**j** are in full agreement with the structures of the porphyrin compounds.[24]

We also examined whether the condensation of dipyrromethanes and *N*-tosyl imines could be applied to unsymmetrical porphyrins. Therefore, we extended our work to the synthesis of *trans*-A_2B_2-tetraarylporphyrins. 5-Phenyldipyrromethane (**1a**) was reacted with different *N*-tosyl imines in the presence of 10 mol % $Cu(OTf)_2$ and *trans*-A_2B_2-tetraarylporphyrins (**4a**–**e**) were obtained in 18–30% yield (Table 5). The compounds were characterized by NMR, FTIR and UV spectroscopy. MALDI-TOF experiments have been performed to detect the presence of scrambled porphyrins in the condensation reactions. Trace quantity of *meso*-A_3B-type porphyrin was detected while no other scrambled porphyrins were observed. MALDI-TOF spectrum of 5,15-bis-(4-chlorophenyl)-10,20-diphenylporphyrin (**4d**) is shown as a representative in Figure 1.

Table 2
Effect of concentrations of reactants and reaction time on the synthesis of **3a**[a]

Entry	Molarity [mM] of reactants	Reaction time (h)	Yield[b] (%) of **3a**
1	1	2	0
2	3.2	2	23
3	5.6	2	30
4	10	2	44
5	17.8	2	29
6	31.6	2	23
7	100	2	11
8	10	0.5	24
9	10	1	32
10	10	1.5	45
11	10	2.5	38
12	10	3	26

[a] Reaction conditions: (1) 10% $Cu(OTf)_2$, CH_2Cl_2, rt; (2) DDQ.
[b] Yield refers to pure product after column chromatography.

Table 3
The synthesis of **3a** by using different catalysts[a]

Entry	Catalyst	Yield[b] (%) of **3a**
1	*p*-$CH_3C_6H_4SO_3H$	13
2	$CuCl_2$	—
3	$AlCl_3$	11
4	HCl	5
5	CF_3SO_3H	39
6	Cl_3CCOOH	3
7	$SnCl_4$	—
8	$TiCl_4$	—
9	BF_3-etherate	—

[a] Reaction conditions: (1)10 mM of **1a** and **2a**, catalyst (10 mol %), CH_2Cl_2, rt, 1.5 h; (2) DDQ.
[b] Yield refers to pure product after column chromatography.

After the synthesis of *meso*-substituted tetraarylporphyrins by direct condensation of 5-substituted dipyrromethanes with *N*-tosyl imines (Scheme 3, route A), we applied MacDonald's-type '2+2' approaches to our system using routes B and C (Scheme 3).

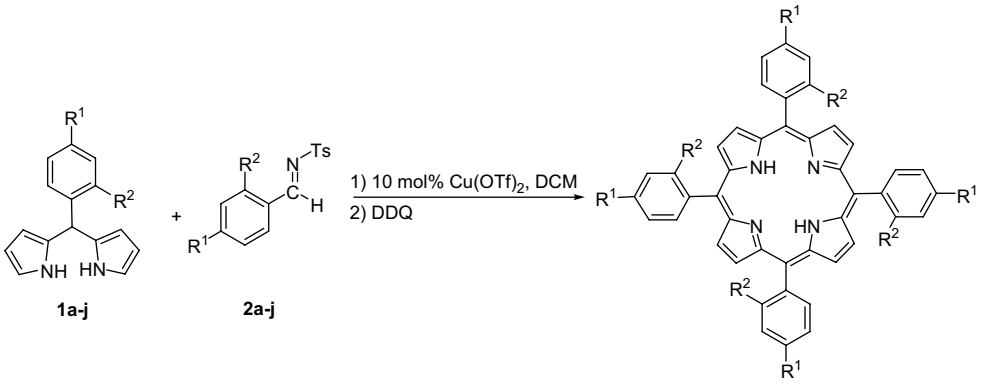
For this purpose sulfonamidealkyldipyrromethane and bis(sulfonamidealkyl)dipyrromethane, **5** and **6**, were synthesized by changing the ratio of reactants in the addition reaction of 5-phenyldipyrromethane (**1a**) to *N*-benzylidene-4-methylbenzenesulfonamide (**2a**) in the presence of 10 mol % of $Cu(OTf)_2$ (Scheme 4). When an excess amount of dipyrromethane was used at 0 °C, sulfonamidealkyldipyrromethane product **5** was obtained in 60% yield. Besides the main product, a side product was isolated in 10% yield and identified as *meso*-substituted bilane **7**. A similar reaction was performed with excess amount of *N*-tosyl imine at −20 °C and the reaction afforded bis(sulfonamidealkyl)dipyrromethane and sulfonamidealkyldipyrromethane, **6** and **5**, in 68% and 10% yields, respectively.

The synthesized compounds **5** and **6** were subjected to condensation reactions under optimized reaction conditions (Scheme 3). TPP (**3a**) was obtained in 42% yield by self-condensation reaction of sulfonamidealkyldipyrromethane **5** (Scheme 3, route B) and in 18% yield by the condensation of bis(sulfonamidealkyl)dipyrromethane **6** with 5-phenyldipyrromethane (Scheme 3, route C). These results have directed us to suggest that the porphyrin formation mechanism in the reaction of dipyrromethanes with *N*-tosyl imines proceeds through the formation of sulfonamidealkyldipyrromethane and its self-condensation in the reaction medium.

3. Conclusion

In conclusion, a new metal triflate-catalyzed, one-flask two-step *meso*-substituted porphyrin synthesis has been achieved by the reaction of 5-substituted dipyrromethanes and *N*-tosyl imines. This method introduces an alternative route to the existing methodologies by offering several advantages including (i) mild reaction conditions, (ii) reasonably good yields and (iii) only trace amount of scrambling product in *trans*-A_2B_2-tetraarylporphyrins. In addition, two important building blocks, mono and dialkylated 5-substituted dipyrromethanes, were also synthesized and used in different MacDonald-type '2+2' condensation reactions. The convenient availability of these intermediates makes possible to extend this methodology also to the synthesis of tetraarylporphyrins with different aryl groups for further studies.

Table 4
Effect of the substituents on the synthesis of *meso*-tetraphenyl porphyrins[a]



1a-j **2a-j** **3a-j**

Entry	Compound	R^1	R^2	Yield[b] (%)
1	**3a**	H	H	45
2	**3b**	OCH_3	H	44
3	**3c**	H	OCH_3	—
4	**3d**	CH_3	H	35
5	**3e**	H	OH	—
6	**3f**	NO_2	H	—
7	**3g**	CF_3	H	25
8	**3h**	F	H	13
9	**3i**	Cl	H	31
10	**3j**	Br	H	29

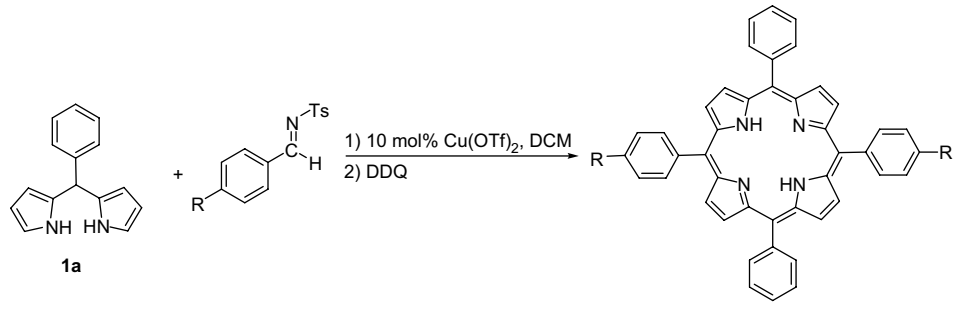
[a] Reaction conditions: (1) 10 mM of reactants, 10% $Cu(OTf)_2$, CH_2Cl_2, rt, 1.5 h; (2) DDQ.
[b] Yield refers to pure product after column chromatography.

4. Experimental

4.1. General

Commercially available reagents and solvents were used without further purification. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded using $SiMe_4$ as an internal reference with Bruker Ultrashield FT NMR spectrometer. Coupling constants are expressed as *J* values in hertz. Infrared spectra were taken by Unicam Mattson 1000 FTIR Spectrophotometer. Electronic absorption spectra were measured using a Jasco V-530 UV–vis spectrophotometer. Elemental analysis experiments were performed by LECO CHNS. Melting points were recorded on Gallenkamp melting-point apparatus. Reactions were monitored by thin-layer chromatography using 60F silica gel plates. Flash column chromatography was performed on silica gel 60 F_{254} (230–400 mesh). The spots were visualized with UV light (λ=254 nm). *N*-Tosyl imines (**2a**–**j**) are synthesized in high yields by the reaction of *p*-toluenesulfonamide and aldehydes in the presence of *p*-toluenesulfonic acid. 5-Substituted dipyrromethanes are synthesized

Table 5
The synthesis of *meso*-substituted-*trans*-A_2B_2-tetraarylporphyrins[a]



1a **4a-e**

Entry	Compound	R	Yield[b] (%)
1	**4a**	OCH_3	22
2	**4b**	CH_3	30
3	**4c**	NO_2	18
4	**4d**	Cl	27
5	**4e**	Br	30

[a] Reaction conditions: (1) 10 mM of reactants, 10% $Cu(OTf)_2$, CH_2Cl_2, rt, 1.5 h; (2) DDQ.
[b] Yield refers to pure product after column chromatography.

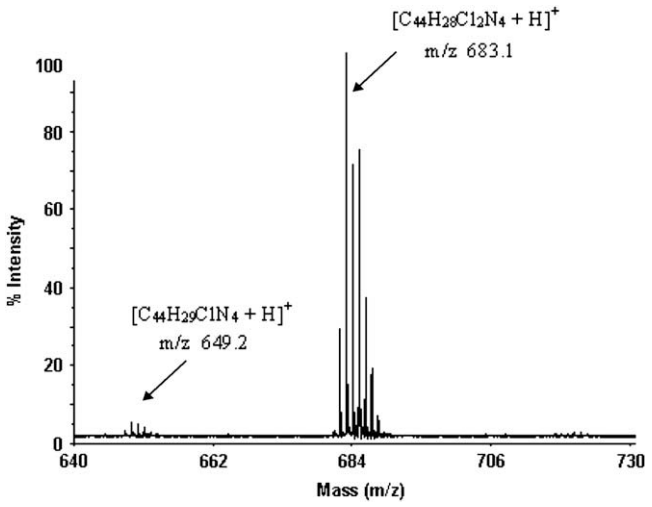


Figure 1. MALDI-TOF spectrum of 5,15-bis-(4-chlorophenyl)-10,20-diphenyl-porphyrin (**4d**).

according to the literature procedure.[18] MALDI-TOF spectra were recorded on Applied Biosystems Voyager DE Pro by using 2,5-dihydroxybenzoic acid matrix.

4.2. General procedure for the synthesis of *meso*-substituted porphyrins 3a–j and 4a–e

A solution of *N*-tosyl imine (1 mmol) and metal triflate (0.1 mmol) in dichloromethane (50 mL) was stirred for 30 min at room temperature under nitrogen atmosphere. A solution (50 mL) of dipyrromethane (1 mmol) in dichloromethane was added dropwise into the reaction mixture shielded from light with aluminium foil. After 1.5 h, DDQ (1.5 mmol) was added and the reaction mixture was further stirred for 2 h. Water (10 mL) was added to the mixture and aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phases were dried over magnesium sulfate and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography with dichloromethane.

*4.2.1. 5,10,15,20-Tetraphenylporphyrin (**3a**)*

Purple crystals; mp >300 °C; yield: 138 mg, 45%; spectroscopic data are identical to that reported in the literature.[24a]

*4.2.2. 5,10,15,20-Tetrakis(4-methoxyphenyl)porphyrin (**3b**)*

Purple crystals; mp >300 °C; yield: 162 mg, 44%; spectroscopic data are identical to that reported in the literature.[24a]

*4.2.3. 5,10,15,20-Tetrakis(4-methylphenyl)porphyrin (**3d**)*

Purple crystals; mp >300 °C; yield: 117 mg, 35%; spectroscopic data are identical to that reported in the literature.[24a]

*4.2.4. 5,10,15,20-Tetrakis(4-trifluoromethylphenyl)porphyrin (**3g**)*

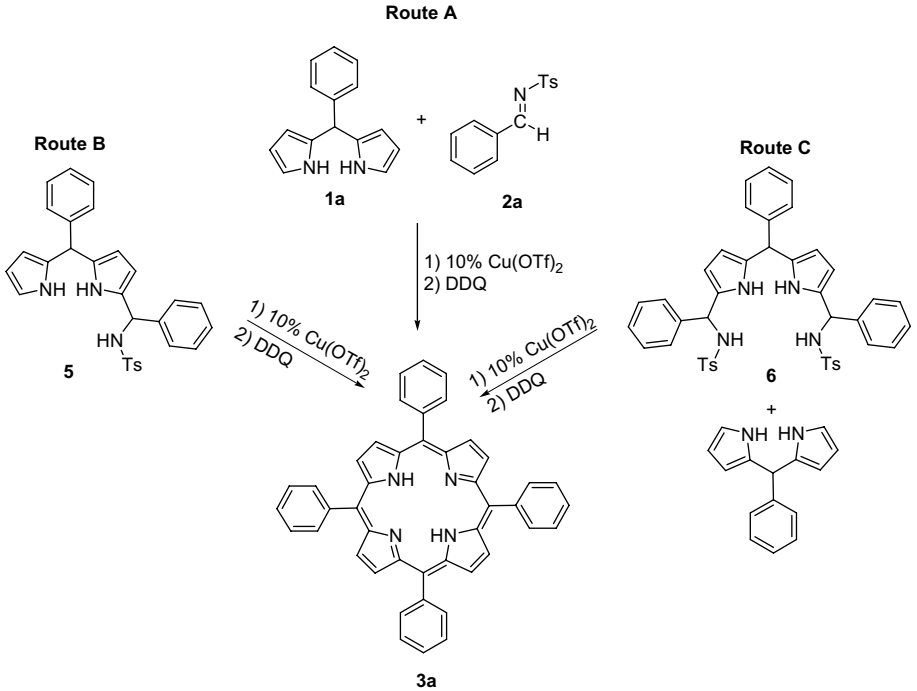
Purple crystals; mp >300 °C; yield: 111 mg, 25%; R_f 0.95 (CH_2Cl_2); UV–vis λ_{max} (CH_2Cl_2) (log ε): 416 (3.9), 512 (4.4), 546 (3.9), 588 (3.8), 644 (3.6); IR (KBr): 3312, 3044, 2929, 1614, 1557, 1477, 1405, 1322, 1165, 1125, 1067, 1019, 967, 854, 796, 727, 680, 605 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ −2.70 (br s, 2H, NH), 8.08 (d, J=8.2, 8H, *m*-PhH), 8.37 (d, J=8.0, 8H, *o*-PhH), 8.85 (s, 8H, pyrrole-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 119.0, 123.8 (q, $^3J_{C-F}$=3.6), 124.5 (q, $^1J_{C-F}$=270.5), 130.4 (q, $^2J_{C-F}$=32.5), 131.3 (br s), 134.6, 145.5. Anal. Calcd for $C_{44}H_{30}N_4$: C, 65.02; H, 2.96; N, 6.32. Found: C, 65.38; H, 2.75; N, 6.43.

*4.2.5. 5,10,15,20-Tetrakis(4-fluorophenyl)porphyrin (**3h**)*

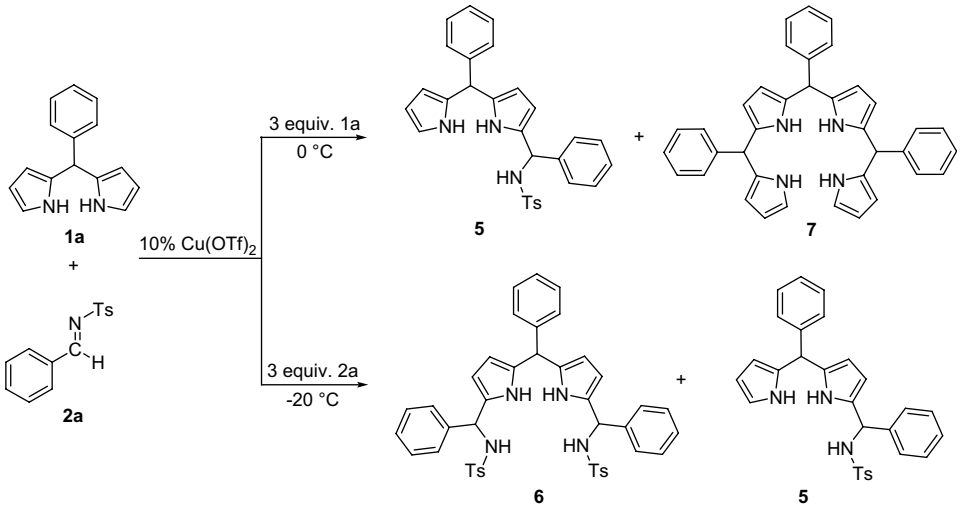
Purple crystals; mp >300 °C; yield: 45 mg, 13%; spectroscopic data are identical to that reported in the literature.[24a]

*4.2.6. 5,10,15,20-Tetrakis(4-chlorophenyl)porphyrin (**3i**)*

Purple crystals; mp >300 °C; yield: 117 mg, 31%; spectroscopic data are identical to that reported in the literature.[24a]



Scheme 3.



Scheme 4.

*4.2.7. 5,10,15,20-Tetrakis(4-bromophenyl)porphyrin (**3j**)*

Purple crystals; mp >300 °C; yield: 135 mg, 29%; spectroscopic data are identical to that reported in the literature.[24b]

*4.2.8. 5,15-Bis-(4-methoxyphenyl)-10,20-diphenyl-porphyrin (**4a**)*

Purple crystals; mp >300 °C; yield: 74 mg, 22%; R_f 0.80 (CH_2Cl_2); UV–vis λ_{max} (CH_2Cl_2) (log ε): 420 (4.0), 516 (4.4), 552 (4.1), 592 (3.9), 647 (3.8); IR (KBr): 3305, 3047, 2924, 2851, 1702, 1596, 1503, 1465, 1345, 1215, 1155, 966, 792, 726, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ −2.73 (br s, 2H, NH), 4.02 (s, 6H, OCH_3), 7.21 (d, J=8.5, 4H), 7.64–7.69 (m, 6H), 8.05 (d, J=8.4, 4H), 8.14 (m, 8H, pyrrole-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.5, 117.6, 119.4, 121.4, 125.7, 126.8, 128.9, 129.9 (br s), 133.5, 134.8, 140.0, 140.9. MALDI-TOF-MS m/z $[M+H]^+$ calcd for $C_{44}H_{30}N_4$: 675.3, found: 675.0.

*4.2.9. 5,15-Bis-(4-methylphenyl)-10,20-diphenyl-porphyrin (**4b**)*

Purple crystals; mp >300 °C; yield: 96 mg, 30%; R_f 0.94 (CH_2Cl_2); UV–vis λ_{max} (CH_2Cl_2) (log ε): 418 (3.5), 515 (4.0), 550 (3.6), 590 (3.4), 646 (3.3); IR (KBr): 3321, 3008, 2689, 2605, 1814, 1591, 1558, 1471, 1347, 1214, 1182, 964, 800, 787, 735, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ −2.66 (br s, 2H, NH), 2.60 (s, 6H, CH_3), 7.45 (d, J=7.6, 4H), 7.65–7.70 (m, 6H), 8.01 (d, J=8.1, 4H), 8.12 (d, J=7.5, 4H), 8.74–8.79 (m, 8H, pyrrole-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6, 120.0, 120.3, 126.7, 127.5, 127.7, 131.1 (br s), 134.6, 137.4, 139.3, 142.3. MALDI-TOF-MS m/z $[M+H]^+$ calcd for $C_{46}H_{34}N_4$: 643.3, found: 643.2.

*4.2.10. 5,15-Bis-(4-nitrophenyl)-10,20-diphenyl-porphyrin (**4c**)*

Purple crystals; mp >300 °C; yield: 63 mg, 18%; R_f 0.83 (CH_2Cl_2); UV–vis λ_{max} (CH_2Cl_2) (log ε): 420 (5.0), 516 (4.2), 551 (3.9), 590 (3.7), 646 (3.6); IR (KBr): 3450, 3316, 2957, 2918, 1594, 1515, 1344, 1261, 1104, 1015, 965, 844, 799, 724, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ −2.87 (br s, 2H, NH), 7.59–7.72 (m, 6H), 8.14 (d, J=7.2, 4H), 8.32 (d, J=8.2, 4H), 8.57 (d, J=8.3, 4H), 8.68 (d, J=4.7, 4H, pyrrole-H), 8.84 (d, J=4.6, 4H, pyrrole-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.1, 120.9, 121.0, 123.3, 125.8, 127.0, 129.4, 133.5, 134.1, 140.6, 146.8, 147.9. MALDI-TOF-MS m/z $[M+H]^+$ calcd for $C_{44}H_{28}N_6O_4$: 705.2, found: 705.1.

*4.2.11. 5,15-Bis-(4-chlorophenyl)-10,20-diphenyl-porphyrin (**4d**)*

Purple crystals; mp >300 °C; yield: 92 mg, 27%; R_f 0.94 (CH_2Cl_2); UV–vis λ_{max} (CH_2Cl_2) (log ε): 415 (3.8), 514 (4.3), 549 (3.9), 589 (3.8), 645 (3.6); IR (KBr): 3441, 3310, 3025, 1555, 1470, 1440, 1347, 1092, 1017, 965, 799, 715, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ −2.90 (br s, 2H, NH), 7.61–7.70 (m, 10H), 8.03 (d, J=8.1, 4H), 8.12 (d, J=7.2, 4H), 8.72 (d, J=4.4, 4H, pyrrole H), 8.77 (d, J=4.4, 4H, pyrrole-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.6, 119.4, 125.7, 125.9, 126.8, 129.8 (br s), 133.5, 134.5, 139.5, 140.9. MALDI-TOF-MS m/z $[M+H]^+$ calcd for $C_{44}H_{28}Cl_2N_4$: 683.2, found: 683.1.

*4.2.12. 5,15-Bis-(4-bromophenyl)-10,20-diphenyl-porphyrin (**4e**)*

Purple crystals; mp >300 °C; yield: 116 mg, 30%; R_f 0.94 (CH_2Cl_2); UV–vis λ_{max} (CH_2Cl_2) (log ε): 418 (4.6), 514 (4.4), 549 (4.0), 590 (3.8), 645 (3.7); IR (KBr): 3440, 2924, 2851, 1633, 1594, 1552, 1472, 1345, 1172, 1068, 1011, 965, 796, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ −2.90 (br s, 2H, NH), 7.61–7.72 (m, 6H), 7.78 (d, J=8.1, 4H), 7.98 (d, J=8.1, 4H), 8.12 (d, J=6.4, 4H), 8.73 (d, J=4.6, 4H, pyrrole-H), 8.78 (d, J=4.6, 4H, pyrrole-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 117.6, 119.4, 121.4, 125.7, 126.8, 128.9, 129.9 (br s), 133.5, 134.8, 140.0, 140.9. MALDI-TOF-MS m/z $[M+H]^+$ calcd for $C_{44}H_{28}Br_2N_4$: 771.1, found: 771.9.

4.3. The synthesis of 4-methyl-*N*-(phenyl(5-(phenyl(1*H*-pyrrol-2-yl)methyl)-1*H*-pyrrol-2-yl)methyl)benzene sulfonamide (5) and 5,5′-(phenylmethylene)bis(2-(phenyl(1*H*-pyrrol-2-yl)methyl)-1*H*-pyrrole) (7)

N-Benzylidene-4-methylbenzenesulfonamide (0.5 mmol) and $Cu(OTf)_2$ (0.05 mmol) were dissolved in THF (10 mL) at 0 °C and 5 mL solution of 5-phenyldipyrromethane (1.5 mmol) in THF was added dropwise after 30 min. The reaction was monitored with TLC and 5 mL of H_2O was added to the reaction mixture when the reaction completed. The aqueous layer was extracted with 2×10 mL of ether. The organic phase was dried over anhydrous $MgSO_4$. The solvent was then removed under reduced pressure and crude product was purified by flash column chromatography (1:6 EtOAc/hexane).

*4.3.1. 4-Methyl-N-(phenyl(5-(phenyl(1H-pyrrol-2-yl)methyl)-1H-pyrrol-2-yl)methyl) benzene sulfonamide (**5**)*

Brown viscous oil; yield: 144 mg, 60%; R_f 0.24 (1:3 EtOAc/hexane); IR (KBr): 3429, 2924, 2845, 1720, 1645, 1488, 1452, 1322, 1281, 1156, 1085, 1023, 808, 769, 699, 666, 561 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.39 (br s, 3H, CH_3), 5.36 (d, J=6.68, 1H, $HNSO_2$), 5.53–5.58 (m, 3H, 2×CH, pyrrole-H), 5.70 (br s, 1H, pyrrole-H), 5.89 (br s, 1H, pyrrole-H), 6.13 (br s, 1H, pyrrole-H), 6.64 (br s, 1H, pyrrole-H), 7.12–7.57 (m, 10H, Ar–H), 8.03 (br s, 1H, NH), 8.36 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 44.0, 55.9, 107.2, 107.3, 108.3, 108.4, 117.3, 126.9, 127.3, 127.7, 128.4, 128.6, 129.5, 130.1, 132.5, 133.8, 137.1,

138.8, 142.1, 143.3. Anal. Calcd for $C_{29}H_{27}N_3O_2S$: C, 72.32; H, 5.65; N, 8.72; S, 6.66. Found: C, 71.97; H, 5.72; N, 8.53; S, 6.81.

*4.3.2. 5,5′-(Phenylmethylene)bis(2-(phenyl(1H-pyrrol-2-yl)methyl)-1H-pyrrole) (**7**)*

Brown viscous oil; yield: 27 mg, 10%; R_f 0.36 (1:3 EtOAc/hexane); IR (KBr): 3429, 2924, 2857, 1695, 1627, 1488, 1451, 1286, 1158, 1113, 1068, 875, 769, 716, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.31 (br s, 1H, CH), 5.38 (br s, 2H, CH), 5.73–5.75 (m, 4H, pyrrole-H), 5.88 (br s, 2H, pyrrole-H), 6.16 (br s, 2H, pyrrole-H), 6.69 (br s, 2H, pyrrole-H), 7.17–7.52 (m, 11H, Ar–H), 7.74 (br s, 2H, NH), 7.92 (br s, 2H, NH), 8.11–8.15 (m, 4H, Ar–H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.1, 44.2, 107.3, 107.4, 108.4, 117.2, 126.5, 126.8, 126.9, 128.3, 128.4, 128.5, 128.6, 129.4, 129.7, 130.2, 132.2, 132.3, 132.5, 133.7, 142.1.

4.4. The synthesis of *N,N′*-(5,5′-(phenylmethylene)bis(1*H*-pyrrole-5,2-diyl)bis(phenylmethylene))bis(4-methylbenzenesulfonamide) (6)

N-Benzylidene-4-methylbenzenesulfonamide (1.5 mmol) and $Cu(OTf)_2$ (0.15 mmol) were dissolved in THF (10 mL) at −20 °C. A solution (5 mL) of dipyrromethane (0.5 mmol) in THF was added dropwise into the reaction mixture after 30 min. The reaction was monitored with TLC and 5 mL of H_2O was added when the reaction completed. The aqueous layer was extracted with 2×10 mL of ether. Combined organic phase was dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure. The product was purified by flash column chromatography (1:4 EtOAc/hexane) and was obtained as a diastereoisomeric mixture.

*4.4.1. N,N′-(5,5′-(Phenylmethylene)bis(1H-pyrrole-5,2-diyl)bis(phenylmethylene))bis(4-methylbenzenesulfonamide) (**6**)*

Brown viscous oil; yield: 252 mg, 68%; R_f 0.23 (1:3 EtOAc/hexane); IR (KBr): 3379, 3269, 2922, 2851, 1598, 1493, 1453, 1426, 1323, 1157, 1092, 1026, 909, 809, 731, 699, 664, 563 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 6H, CH_3), 2.25 (s, 6H, CH_3), 5.18 (s, 1H), 5.23 (s, 1H), 5.24 (br s, 1H), 5.31 (br s, 1H), 5.35–5.41 (m, 5H), 5.46–5.59 (m, 6H), 5.78 (br s, 1H), 6.37 (d, J=9.6, 1H), 6.44 (d, J=9.6, 1H), 7.00–7.23 (m, 38H, Ar–H), 7.23–7.50 (m, 8H, Ar–H), 8.25 (br s, 2H, 2×NH), 8.42 (br s, 1H, NH), 8.47 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.4, 20.5, 43.0, 43.1, 54.9, 55.0, 55.1, 106.2, 106.3, 106.4, 106.7, 107.2, 107.5, 107.6, 107.7, 125.7, 125.8, 125.9, 126.1, 126.2, 126.3, 126.4, 126.6, 126.7, 126.8, 127.2, 127.3, 127.4, 127.5, 128.3, 128.4, 128.5, 129.0, 129.2, 129.9, 130.3, 132.3, 132.5, 133.3, 135.9, 136.0, 136.2, 136.3, 136.8, 136.9, 137.5, 137.6, 140.6, 140.7, 140.8, 142.2, 142.3, 142.4. Anal. Calcd for $C_{43}H_{40}N_4O_4S_2$: C, 69.70; H, 5.44; N, 7.56; S, 8.66. Found: C, 69.45; H, 5.47; N, 7.91; S, 8.37.

4.5. The synthesis of 5,10,15,20-tetraphenylporphyrin (3a) via self-condensation of sulfonamidealkyldipyrromethane 5

$Cu(OTf)_2$ (0.02 mmol) was added to the solution of compound **5** (0.2 mmol) in 20 mL of dichloromethane under N_2 atmosphere. The mixture was stirred for 1.5 h and the solution of 0.3 mmol DDQ in dichloromethane was added to the reaction mixture. After 2 h, water (5 mL) was added to the mixture and aqueous phase was extracted with dichloromethane (3×10 mL). After removing the solvent under reduced pressure, the crude product was purified by flash column chromatography (CH_2Cl_2).

4.6. The synthesis of 5,10,15,20-tetraphenylporphyrin (3a) via condensation of bis(sulfonamidealkyl)dipyrromethane 6 with 5-phenyldipyrromethane (1a)

5-Phenyldipyrromethane (**1a**) (0.1 mmol) and $Cu(OTf)_2$ (0.01 mmol) were dissolved in 5 mL of dichloromethane at room temperature under N_2 atmosphere. The solution of compound **6** (0.1 mmol) in 5 mL of dichloromethane was added to the mixture. DDQ was added to this solution after 1.5 h. Water (5 mL) was added to the mixture after 2 h and the aqueous phase was extracted with dichloromethane (3×10 mL). After removing the solvent under reduced pressure, the crude product was purified by flash column chromatography (CH_2Cl_2).

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