Synthesis of Functionalized Unsymmetrical Thiophene Diols and Their Use in the Synthesis of *cis*-21-Monothia- and *cis*-21,23-Dithiaporphyrin Building Blocks with Two Different Functional Groups

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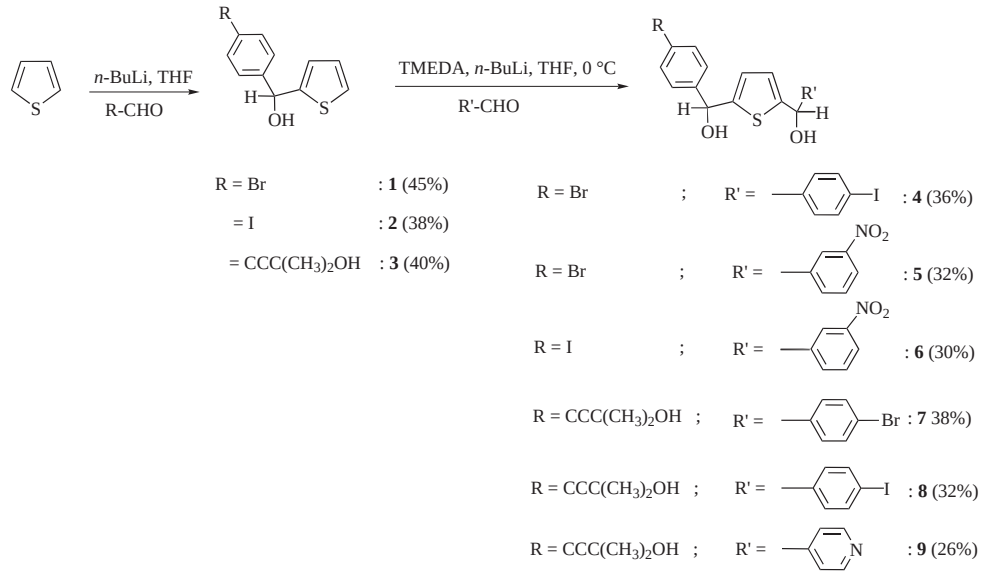
Abstract: A series of functionalized unsymmetrical thiophene diols were synthesized and used for the synthesis of *cis*-21-monothia and *cis*-21,23-dithiaporphyrin building blocks having two different functional groups at *meso*-positions. To show the use of the *cis*-thiaporphyrin building blocks with two different functional groups, a porphyrin trimer comprised of N_4, N_3S and N_2S_2 porphyrin sub-units was synthesized by using both covalent and non-covalent interactions.

Key words: functionalized unsymmetrical diols, *cis*-thiaporphyrin, porphyrin trimer, covalent, non-covalent interactions

Porphyrin arrays containing two or more porphyrin sub-units with different porphyrin cores connected covalently or non-covalently are very interesting systems which may have several applications in bioorganic and materials chemistry.[1] Recently we synthesized a series of unsymmetrical porphyrin arrays containing two different porphyrin sub-units such as N_2S_2–N_4, N_3S–N_4, N_3O–N_4, N_3S–N_3O, etc. and observed an efficient energy transfer in some of these systems from one porphyrin unit to another porphyrin unit on selective excitation of one porphyrin unit.[2] Interestingly, to the best of our knowledge, there is no report on porphyrin arrays containing more than two different types of porphyrin cores assembled by covalent or non-covalent interactions. This may be due to the inaccessibility of the suitable porphyrin building blocks. In this paper, we report the synthesis of a series of new functionalized unsymmetrical thiophene diols and their use in the synthesis of 21-monothia-and 21,23-dithiaporphyrin building blocks containing two different functional groups in a *cis* fashion. The use of *cis*-thiaporphyrin building blocks was demonstrated by synthesizing the first porphyrin trimer comprised of three different porphyrin cores (N_2S_2, N_3S and N_4 cores) assembled by using both covalent and non-covalent bonds.

The thiophene mono-ols **1**–**3** were obtained[2e] by treating one equivalent of thiophene with 1.2 equivalents of *n*-BuLi followed by addition of 1.2 equivalents of functionalized aryl aldehyde in THF at 0 °C (Scheme 1). The crude compounds were purified by silica gel column chromatography using petroleum ether–ethyl acetate (8–10%) and afforded **1**–**3** as white solids in 38–45% yields. To prepare the unsymmetrical thiophene diols **4**–**9**, the mono-



Scheme 1 Synthetic scheme for the preparation of functionalized unsymmetrical thiophene diols **4**–**9**

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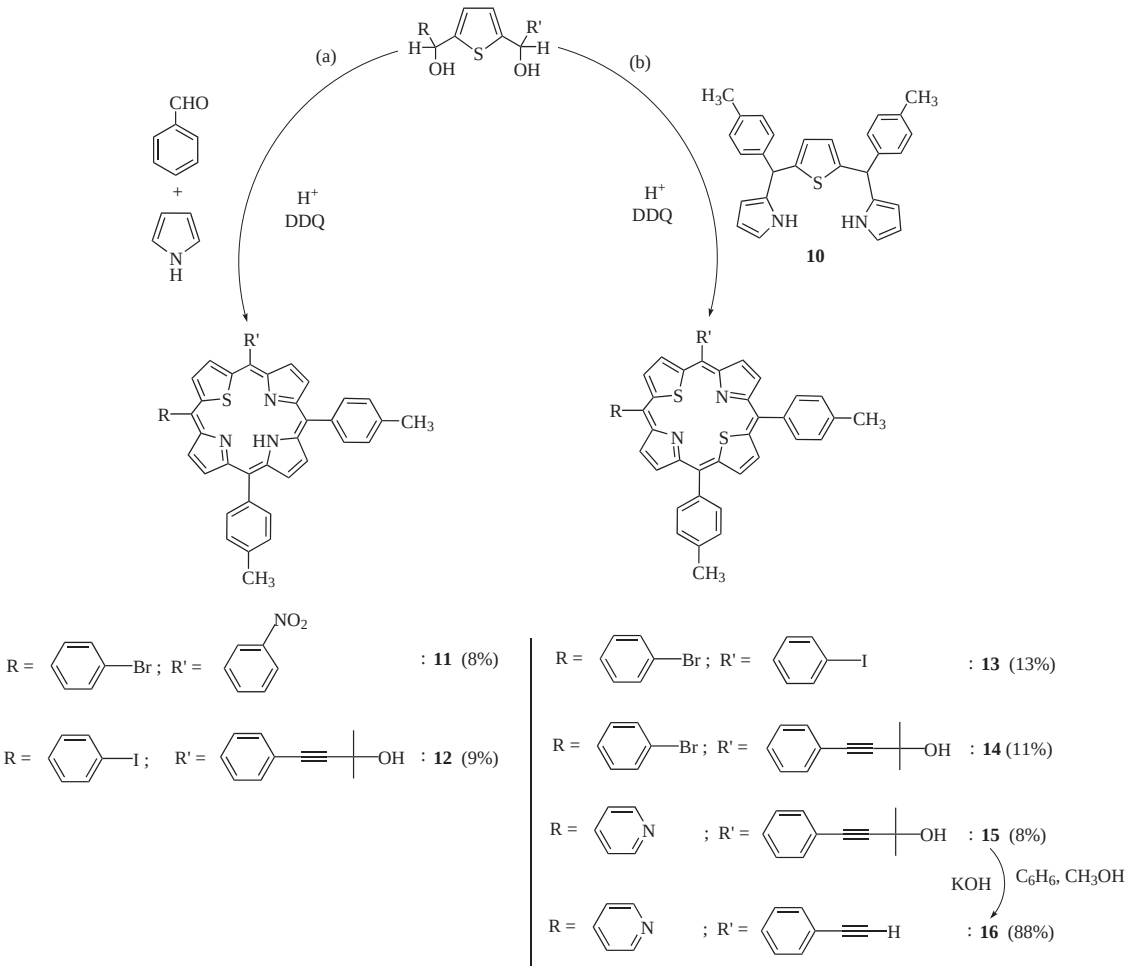
ols **1**–**3** were treated with 2.5 equivalents of corresponding functionalized aryl aldehyde in THF at 0 °C under similar reaction conditions[2f] (Scheme 1). Purification by silica gel column gave **4**–**9** in 26–36% yields. The other precursor 16-thiatripyrrane **10** was synthesized by following the literature procedure.[3]

The required *cis*-21-monothiaporphyrins **11**, **12** and *cis*-21,23-dithiaporphyrins **13**–**15** containing two different functional groups at the *meso*-positions were synthesized as shown in Scheme 2. The *cis*-21-monothiaporphyrins **11** and **12** were synthesized by condensing one equivalent of **5** and **8**, respectively, with two equivalents of *p*-tolualdehyde and three equivalents of pyrrole under standard porphyrin-forming conditions.[4] The crude porphyrinic mixture was subjected twice to silica gel column chromatography and afforded pure **11** and **12** in 8–9% yields. The *cis*-21,23-dithiaporphyrins **13**, **14** and **15** were synthesized by condensing one equivalent of diol **4**, **7** and **9**, respectively, with known 16-thiatripyrrane[3] **10** under similar acid-catalyzed porphyrin-forming conditions. Purification by column chromatography on silica afforded pure **13**–**15** in 8–13% yields. The deprotection of ethyne group of **15** to afford **16** was carried out by treating **15** with KOH in benzene–methanol at 80 °C. The *cis*-thiaporphyrin building blocks **11**–**16** were characterized by all spectroscopic techniques.[5]

To show the applicability of *cis*-thiaporphyrin building blocks, we synthesized the first example of porphyrin trimer **20** having three different porphyrin cores (N_4, N_3S and N_2S_2) using porphyrin building block **16** containing 4-ethynylphenyl and 4-pyridyl functional groups at the *meso*-positions (Scheme 3). The other required porphyrins, N_3S porphyrin having mono iodophenyl functional group at the *meso*-position **17** and RuTPP(CO)(EtOH) (**19**) were synthesized by following the literature methods.[2e,6] The N_2S_2–N_3S porphyrin dimer **18** was synthesized by following the coupling conditions developed by Lindsey and co-workers.[7] Coupling of **16** and **17** in toluene–triethylamine at 35 °C in the presence of catalytic amount of $Pd_2(dba)_3/AsPh_3$ followed by silica gel column chromatographic purification afforded pure dimer **18** in 62% yield (Scheme 3). The dimer **18** was characterized by all spectroscopic techniques. In the ^1H NMR spectrum of dimer **18**, the resonances corresponding to both the porphyrinic sub-units and the bridging group are present with minor differences in the chemical shift positions of the protons compared to their respective monomeric porphyrins **16** and **17**, respectively, indicating that the porphyrin



Scheme 2 Synthetic scheme for the preparation of *cis*-21-monothia (a) and *cis*-21,23-dithiaporphyrin (b) building blocks with different functional groups **11**–**16**

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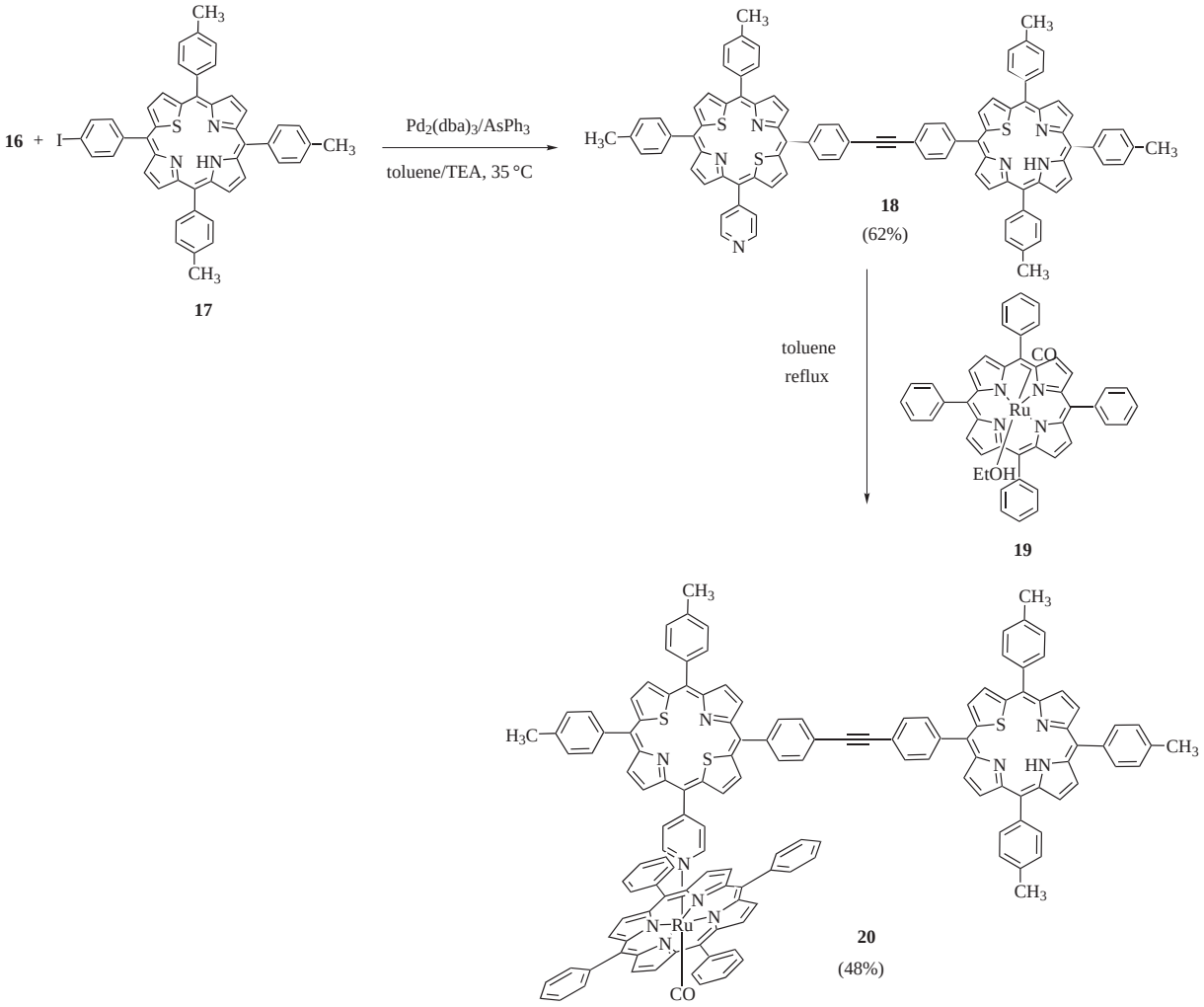

Scheme 3 Synthetic scheme for the preparation of porphyrin trimer **20** comprised of three different porphyrin sub-units

sub-units in the dimer **18** interact very weakly. The ES-MS mass spectrum of dimer **18** showed a strong M^+ ion peak. The absorption spectrum of **18** showed absorption peaks corresponds to both N_2S_2 and N_3S porphyrin sub-units and exhibited five Q-bands and a single broad Soret band.

The dimer **18** was treated with 1.2 equivalents of RuTPP(CO)(EtOH) (**19**) in toluene at refluxing temperature for four hours.[2d] The TLC analysis indicated the disappearance of starting materials and the formation of the required trimer **20**. The crude compound was purified by simple silica gel column chromatography and afforded the pure trimer **20** in 48% yield. The trimer **20** was highly soluble in most of the organic solvents and was characterized by NMR, ES-MS, and absorption spectroscopy. In the ^1H NMR spectrum, the trimer **20** showed signals corresponding to all three porphyrin sub-units. The N_3S porphyrin and RuTPP porphyrin sub-units showed minor changes in the chemical shifts of various protons compared to their corresponding monomers **17** and **19**, respectively. However, the protons of N_2S_2 porphyrin sub-unit experienced large upfield shifts compared to corresponding monomeric porphyrin **16** because of RuTPP ring current. The maximum upfield shifts were observed for the 2,6- and 3,5-pyridyl protons of N_2S_2 porphyrin sub-unit of trimer **20** implying the coordination of pyridyl group with central ruthenium ion of RuTPP unit. The absorption spectrum of **20** also showed very interesting features compared to dimer **18** and also as compared to the corresponding monomeric porphyrins.

In conclusion, we synthesized a series of functionalized unsymmetrical thiophene diols and used them for the synthesis of *cis*-21-monothia-and *cis*-21,23-dithiaporphyrin building blocks containing two different functional groups. The application of *cis*-thiaporphyrin building blocks was demonstrated by synthesizing the first example of novel trimer composed of three different porphyrin sub-units assembled via covalent and non-covalent interactions. The synthetic strategy presented in this paper will be extended in our laboratory to synthesize several novel heteroporphyrins based systems.

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(5) **Experimental Procedure and Spectroscopic Data for Selected Compounds.**

Diol **9**: the thiophene mono-ol **3** (1.00 g, 3.67 mmol), tetramethylethylenediamine (1.39 mL, 9.18 mmol) and *n*-BuLi (5.74 mL of ca. 15% solution in hexane) were added successively to freshly distilled dry Et_2O (30 mL) in a 250-mL three-necked round-bottomed flask and stirred for 15 min under nitrogen atmosphere at 0 °C. An ice-cold solution of 4-pyridine carboxaldehyde (0.87 mL, 9.18 mmol) in dry THF (30 mL) was added to it. The mixture was stirred for 15 min and ice-cold NH_4Cl (50 mL, ca. 1 M) was added to quench the reaction. After standard work up, the crude compound was purified by silica gel column chromatography using CH_2Cl_2–MeOH (95:5) and diol **4** obtained as a yellow oily liquid (0.40 g, 29%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (6 H, s, CH_3), 4.00 (3 H, br s, OH), 5.99–6.15 (2 H, m, CHOH), 6.82–6.86 (2 H, m, thiophene), 7.42–7.44 (2 H, m, aryl), 7.70 (2 H, d, *J* = 7.8 Hz, pyridyl), 8.03–8.06 (2 H, m, aryl), 8.30 (2 H, br s, pyridyl) ppm. ES-MS: *m/z* calcd for $C_{22}H_{21}NO_3S$: 379.48; found: 378.09 (100%) [M^+ – H]. Anal. Calcd: C, 69.63; H, 5.58; N, 3.69. Found: C, 69.74; H, 5.51; N, 3.74.

Porphyrin **15**: condensation of diol **9** (0.45 g, 1.19 mmol) with **10** (0.50 g, 1.19 mmol) in propionic acid (125 mL) at refluxing temperature for 2 h followed by standard work up and chromatography on silica using CH_2Cl_2–MeOH (96:4) gave the desired porphyrin **15** as a purple solid (0.07 g, 8%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (6 H, s, CH_3), 2.69 (6 H, s, CH_3), 7.52 (2 H, d, *J* = 7.8 Hz, aryl), 7.62 (4 H, d, *J* = 8.0 Hz, aryl), 7.98 (2 H, d, *J* = 7.8 Hz, aryl), 8.11 (4 H, d, *J* = 8.0 Hz, aryl), 8.20 (2 H, d, *J* = 7.8 Hz, 3,5-pyridyl), 8.54 (1 H, m, β-pyrrole), 8.64 (1 H, d, *J* = 4.6 Hz, β-pyrrole), 8.72 (1 H, d, *J* = 4.6 Hz, β-pyrrole), 8.78–8.81 (1 H, m, β-pyrrole), 9.14 (2 H, br s, 2,6-pyridyl), 9.54 (1 H, d, *J* = 4.4 Hz, β-thiophene), 9.72 (1 H, d, *J* = 4.4 Hz, β-thiophene), 9.76 (2 H, s, β-thiophene) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.56, 22.68, 31.06, 31.49, 128.03, 129.49, 133.61, 134.71, 134.93, 135.14, 135.73, 136.13, 138.02, 146.90, 147.61, 148.53, 148.68, 149.75, 150.87, 155.11, 156.63, 157.01 ppm. ES-MS: *m/z* calcd for $C_{50}H_{37}N_3OS_2$: 759.96; found: 760.31 (100%) [M^+]. UV/Vis (in toluene, λ_{max}/nm, ε/mol^{-1} dm^3 cm^{-1}): 437 (292652), 515 (26193), 549 (9062), 634 (2073), 697 (5030).

Porphyrin **16**: sample of porphyrin **15** (0.05 g, 0.07 mmol) was dissolved in benzene–MeOH (3:1, 40 mL) taken in a 100-mL round-bottomed flask and excess KOH (0.20 g) was added to it. The reaction mixture was refluxed at 80 °C using a Dean–Stark apparatus. The excess solvent was removed under vacuum and the crude compound was subjected to silica gel column chromatography using PE–CH_2Cl_2 (5:95) to afford the pure desired porphyrin **16** as a purple solid (0.04 g, 88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.70 (6 H, s, CH_3), 3.32 (1 H, s, CH), 7.50 (2 H, d, *J* = 7.8 Hz, aryl), 7.62 (4 H, d, *J* = 8.0 Hz, aryl), 7.96 (2 H, d, *J* = 7.8 Hz, aryl), 8.14 (4 H, d, *J* = 8.0 Hz, aryl), 8.20 (2 H, d, *J* = 7.8 Hz, 3,5-pyridyl), 8.56 (1 H, d, *J* = 4.5 Hz, β-pyrrole), 8.64 (1 H, d, *J* = 4.6 Hz, β-pyrrole), 8.72 (1 H, d, *J* = 4.6 Hz, β-pyrrole), 8.80 (1 H, d, *J* = 4.5 Hz, β-pyrrole), 9.11 (2 H, br s, 2,6-pyridyl), 9.58 (1 H, d, *J* = 4.4 Hz, β-thiophene), 9.68 (1 H, d, *J* = 4.4 Hz, β-thiophene), 9.76 (2 H, s, β-thiophene) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.61, 31.07, 31.49, 121.95, 128.31, 131.29, 132.54, 134.18, 134.55, 134.92, 135.75, 135.93, 138.32, 141.98, 147.52, 147.80, 148.92, 150.98, 155.95, 156.54, 156.60, 160.02 ppm. ES-MS: *m/z* calcd for $C_{47}H_{31}N_3S_2$: 701.90; found: 702.22 (100%) [M^+]. UV/Vis (in toluene, λ_{max}/nm, ε/mol^{-1} dm^3 cm^{-1}): 436 (262893), 515 (24005), 549 (8393), 634 (1845), 697 (4601).

Dimer **18**: A solution of **16** (0.02 g, 0.03 mmol) and **17** (0.02 g, 0.03 mmol) in dry toluene–Et_3N (3:1, 30 mL) was purged with nitrogen for 10 min. The coupling was initiated by adding $AsPh_3$ (0.01 g, 0.03 mmol) followed by $Pd_2(dba)_3$ (0.01 g, 0.01 mmol) and the reaction mixture was then stirred at 40 °C for 12 h. After work-up, the crude compound was subjected to silica gel column chromatography and the desired dimer **18** was collected with PE–CH_2Cl_2 (15:85) mixture as a violet solid (0.02 g, 64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = –2.71 (1 H, br s, NH), 2.70 (9 H, s, CH_3), 2.73 (6 H, s, CH_3), 7.53 (4 H, d, *J* = 7.6 Hz, aryl), 7.61 (8 H, d, *J* = 7.6 Hz, aryl), 7.96 (2 H, d, *J* = 8.0 Hz, aryl), 8.06 (4 H, d, *J* = 7.6 Hz, aryl), 8.12 (10 H, m, aryl), 8.17 (2 H, m, 3,5-pyridyl), 8.62 (4 H, m, β-pyrrole), 8.68 (3 H, m, β-pyrrole), 8.73 (1 H, d, *J* = 5.6 Hz, β-pyrrole), 8.94 (2 H, m, β-pyrrole), 9.03 (2 H, br m, 2,6-pyridyl), 9.58 (1 H, d, *J* = 5.2 Hz, β-thiophene), 9.67 (1 H, d, *J* = 5.2 Hz, β-thiophene), 9.72 (3 H, m, β-thiophene), 9.76 (1 H, d, *J* = 5.2 Hz, β-thiophene) ppm. ES-MS: *m/z* calcd for $C_{94}H_{63}N_6S_3$: 1373.76; found: 1373.57 (52%) [M^+]. UV/Vis (in toluene, λ_{max}/nm, ε/mol^{-1} dm^3 cm^{-1}): 433 (484803), 515 (41725), 549 (13604), 624 (3694), 680 (5357), 696 (4918).

Trimer **20**: The dimer **18** (0.02 g, 0.02 mmol) was dissolved in 30 mL of toluene in a two-necked 100-mL round-bottomed flask and was purged with N_2 for 10 min. RuTPP(CO)(EtOH) (**19**; 0.019 g, 0.02 mmol) was then added and the solution was refluxed with stirring for 4 h. The crude compound was purified by silica gel column

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chromatography using PE–CH_2Cl_2 (50:50) mixture as an eluent and afforded trimer **20** as a purple solid (0.01 g, 35%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = –2.61 (1 H, br s, NH), 1.64 (2 H, d, *J* = 3.2 Hz, 2,6-pyridyl), 2.68 (6 H, s, CH_3), 2.70 (9 H, s, CH_3), 6.08 (2 H, d, *J* = 3.2 Hz, 3,5-pyridyl), 7.10 (1 H, d, *J* = 4.4 Hz, β-pyrrole), 7.56 (18 H, m, aryl), 7.63 (4 H, d, *J* = 7.8 Hz, aryl), 7.71 (10 H, m, aryl), 7.91 (4 H, t, *J* = 7.4 Hz, aryl), 8.04 (8 H, m, aryl), 8.14 (4 H, d, *J* = 7.8 Hz, aryl), 8.19 (1 H, m, β-pyrrole), 8.33 (1 H, m, β-thiophene), 8.57 (2 H, m, β-pyrrole), 8.63 (2 H, m, β-pyrrole), 8.74 (8 H, s, β-pyrrole of TPP), 8.90 (4 H, m, β-pyrrole), 9.29 (2 H, m, β-thiophene), 9.57 (1 H, dd, *J* = 5.2 Hz, β-thiophene), 9.83 (2 H, m, β-thiophene) ppm. ES-MS: *m/z* calcd for $C_{139}H_{92}N_{10}OS_3Ru$: 2115.57; found: 2115.79 (23%). UV/Vis (in toluene, λ_{max}/nm, ε/mol^{-1} dm^3 cm^{-1}): 412 (302417), 432 (527038), 516 (35230), 549 (17975), 626 (bs), 683 (6228), 698 (5204).

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