An Efficient and Concise Synthesis of Heteroaryldipyrromethanes, Tetrapyrazolylporphyrins and Metalloporphyrins

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Abstract: One pot synthesis of terpyrromethanes (**3a**) and [di(1*H*-pyrrol-2-yl)methyl]heteroarenes (**3b-m**) has been delineated by Amberlyst 15 catalyzed condensation of pyrrole and heterocyclic aldehydes (**2**), not reported earlier. The compounds **3a** and **3b** have been formylated to 5-[di(5-formyl-1*H*-pyrrol-2-yl)methyl]-1*H*-pyrrole-2-carbaldehyde (**4a**) and 5-[(5-formyl-1*H*-pyrrol-2-yl)(3-pyridinyl)methyl]-1*H*-pyrrole-2-carbaldehyde (**4b**), by using a mixture of $POCl_3$ and DMF as formylating agent. Similarly, 5-alkyl-1*H*-pyrrole-2-carbaldehyde (**8**) has also been prepared from 2-alkyl-1*H*-pyrroles (**6**), obtainable by acylation followed by Wolf-Kishner reduction. Amberlyst 15 / TFA catalyzed the condensation of **8** with pyrrole which gave **3a** instead of expected product **10**, due to an unusual cleavage of alkyl substituent at position 5 in **8**. CS_2 addition to **6** followed by methylation provided methyl 5-alkyl-1*H*-pyrrole-2-carbodithioates (**7**), which on reaction with hydrazine hydrate yielded 5-alkyl-1*H*-pyrrole-2-carbothiohydrazide (**9**). Tetrapyrazolylporphyrins (**12**) have been synthesized directly by condensation of pyrrole with 3-aryl-4-formyl-1-phenylpyrazole (**11**) in propionic acid. These porphyrins were transformed to metalloporphyrins (**13**) from reaction with zinc and copper acetate separately.

INTRODUCTION

Porphyrins represent one of the most fascinating classes of compounds because of their presence in nature and their unique physical and chemical properties. They play significant role in numerous biological systems [1] due to their coordinating ability with various transition metals to form metalloporphyrins. These compounds are currently in focus for their applications in supramolecular and material chemistry [2] owing to electrochemical, magnetic, catalytic, photochemical and photo-physical properties [3, 4]. Over the past two decades, the preparation of substituted porphyrins has attracted much attention, as they provide useful platform to introduce various functional groups with precise locations and orientations near the porphyrin backbone. The ability to anchor various groups on heterocyclic systems offers many exciting opportunities for engineering porphyrin platforms. These simple molecules have potential of useful building blocks for the preparation of heteronuclear porphyrins and the development of redox switchable tetrapyrrolic macrocycles. In the past years, numerous advances in porphyrin synthetic methodology have been realized [5]. These developments have been advanced systematically through monopyrrole tetramerization and dipyrromethane self-condensation in organic acid. The importance of photosensitizing properties [6] of these heterocycles made them useful for photodynamic therapy of tumors. This led to the synthesis of 5-heteroaryldipyrromethane as new building blocks for the synthesis of porphyrins [7], expanded porphyrins and porphyrin analogs [8].

Earlier, 5-aryldipyrromethanes, used as a precursor for the synthesis of porphyrins have been synthesized [9-14] by the reaction of aldehydes with excess of pyrrole in the presence of catalytic amount of acid to suppress the side reaction of polymerization. Nagarkatti and Ashley [9] reported first the synthesis of 4-pyridyldipyrromethane by condensation of 4-pyridylcarboxaldehyde and pyrrole in acidified methanol. Later on Casiraghi *et al*. [10] prepared dipyrromethanes from reaction of aliphatic aldehydes with Grignard reagent, derived from pyrrole in the presence of $TiCl_4$. Recently, a direct synthesis of substituted dipyrromethanes has been reported [15] through condensation of pyrrole with aromatic aldehydes in THF/acetic acid. In addition to the direct syntheses, two stepwise syntheses of meso substituted, β-unsubstituted dipyrromethanes have been developed [16,17]. We now report one pot synthesis of 5-heteroaryldipyrromethanes and terpyrromethane from Amberlyst 15 catalyzed condensation of pyrrole with 2-formylpyrrole, 3-pyridylcarboxaldehyde, 1,3-diaryl-4-formylpyrazole, and 3-aryl-5-formylisoxazole separately. The [di(1*H*-pyrrol-2-yl)methyl]heteroarenes have been quite often used as precursor for the synthesis of porphyrins. Most of the porphyrin syntheses proceed by tetramerization of monopyrrole. In the classical Adler-Longo porphyrin synthesis [18], a solution of aldehyde and pyrrole in high boiling acid solvent is refluxed with air condenser so that condensation-oxidation could occur simultaneously. Lindsey *et al*. [19] reported the improved methodology for the preparation of compounds of this ring system. In this manuscript, we report a direct method for the preparation of porphyrins by heating a mixture of pyrrole and heterocyclic aldehydes in propionic acid without using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) as an oxidant.

RESULTS AND DISCUSSION

5-Heteroaryldipyrromethanes have been obtained through Amberlyst 15 or TFA catalyzed condensation of heterocyclic aldehydes with pyrrole. Thus, stirring an equimolar mixture of heteroarylaldehyde (**2**) and pyrrole (**1**) using either Amberlyst 15 or catalytic amount of trifluoroacetic

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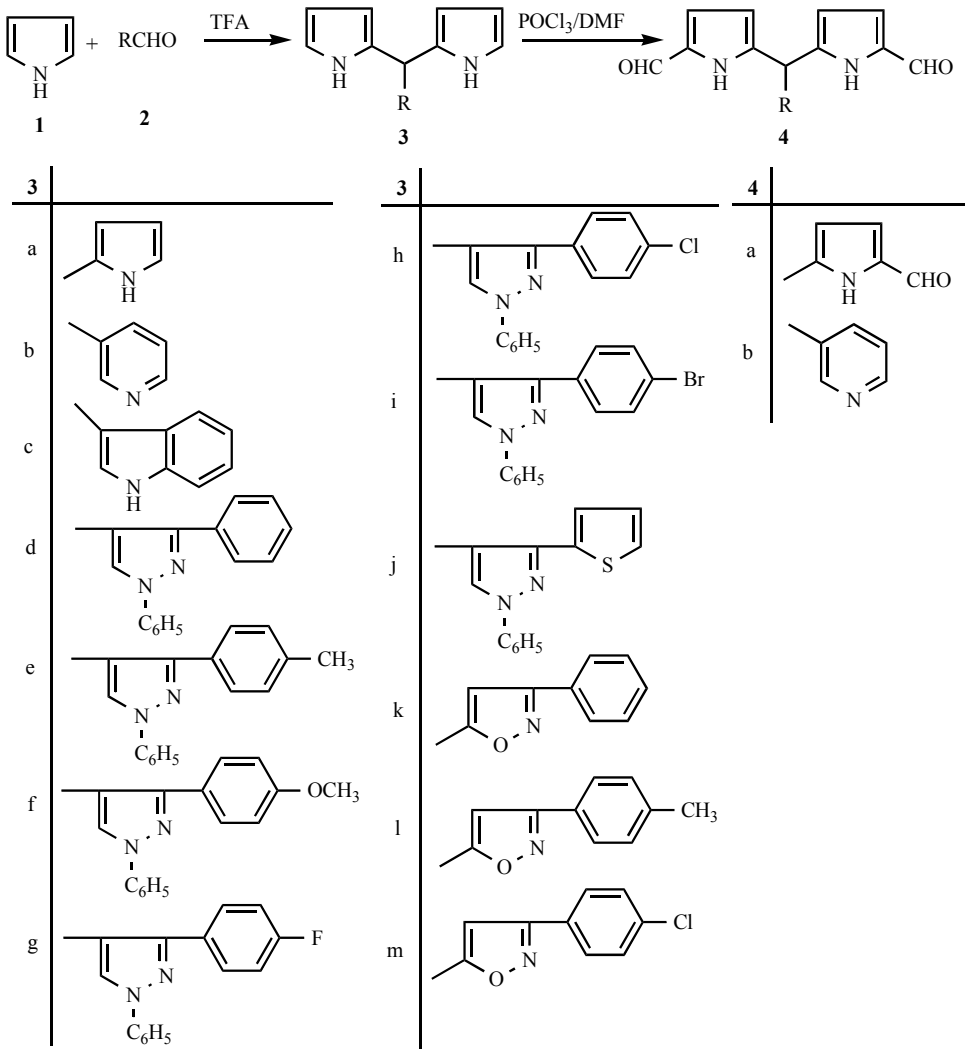


Scheme 1.

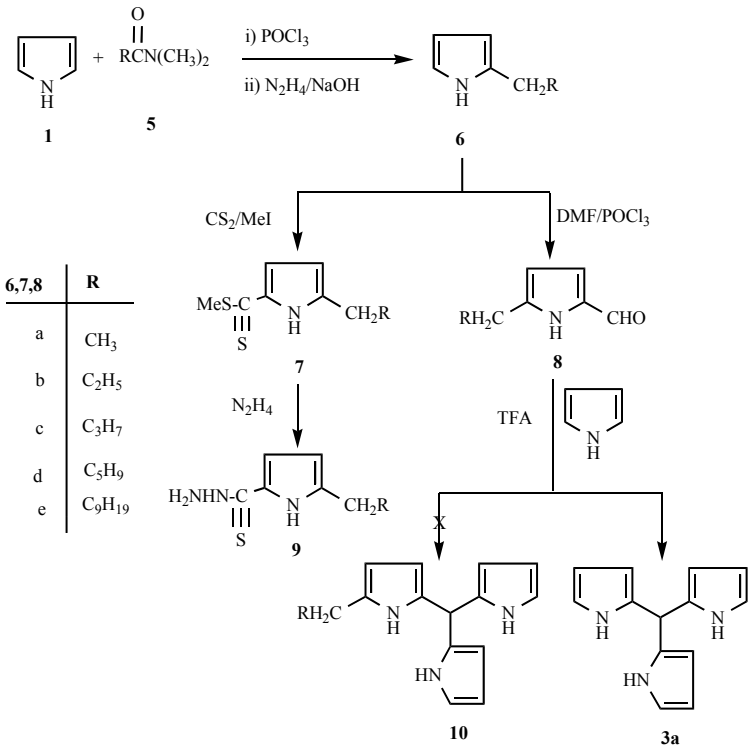
acid at room temperature for 30 minutes afforded crude [di(1*H*-pyrrol-2-yl)methyl]hetroarenes (**3**) after usual workup (Scheme **1**).

The crude product obtained was purified through silica gel column using a mixture of hexane: ethyl acetate (39:1) as eluent. The Amberlyst 15 was used as a catalyst because it is environment friendly, reusable, economically viable, commercially available and convenient to handle during the reaction. These points make Amberlyst 15 superior to the other reported acid catalysts. The isolated 2-[di(1*H*-pyrrol-2-yl)methyl]-1*H*-pyrrole (**3a**) and 3-[di(1*H*-pyrrol-2-yl)methyl] pyridine (**3b**) were formylated to 5-[di(5-formyl-1*H*-pyrrol-2-yl)methyl]-1*H*-pyrrole-2-carbaldehyde (**4a**) and 5-[(5-formyl-1*H*-pyrrol-2-yl)(3-pyridinyl)methyl]-1*H*-pyrrole-2-carbaldehyde (**4b**) by Vilsmeier-Haack reaction. 2-Alkyl-1*H*-pyrroles (**6**), used as precursors for the synthesis of various pyrrole derivatives were synthesized [20] by acylation followed by Wolf-Kishner reduction. Further, a reaction of **6** with carbon disulfide in the presence of super base system KOH-DMSO, regioselectively, yielded pyrroldithiocarboxylic acid, which on methylation with methyl iodide produced methyl 5-alkyl-1*H*-pyrrole-2-carbodithioate (**7**). Compound **7** on reaction with hydrazine hydrate provided 5-alkyl-1*H*-pyrrole-2-carbothiohydrazide (**9**).

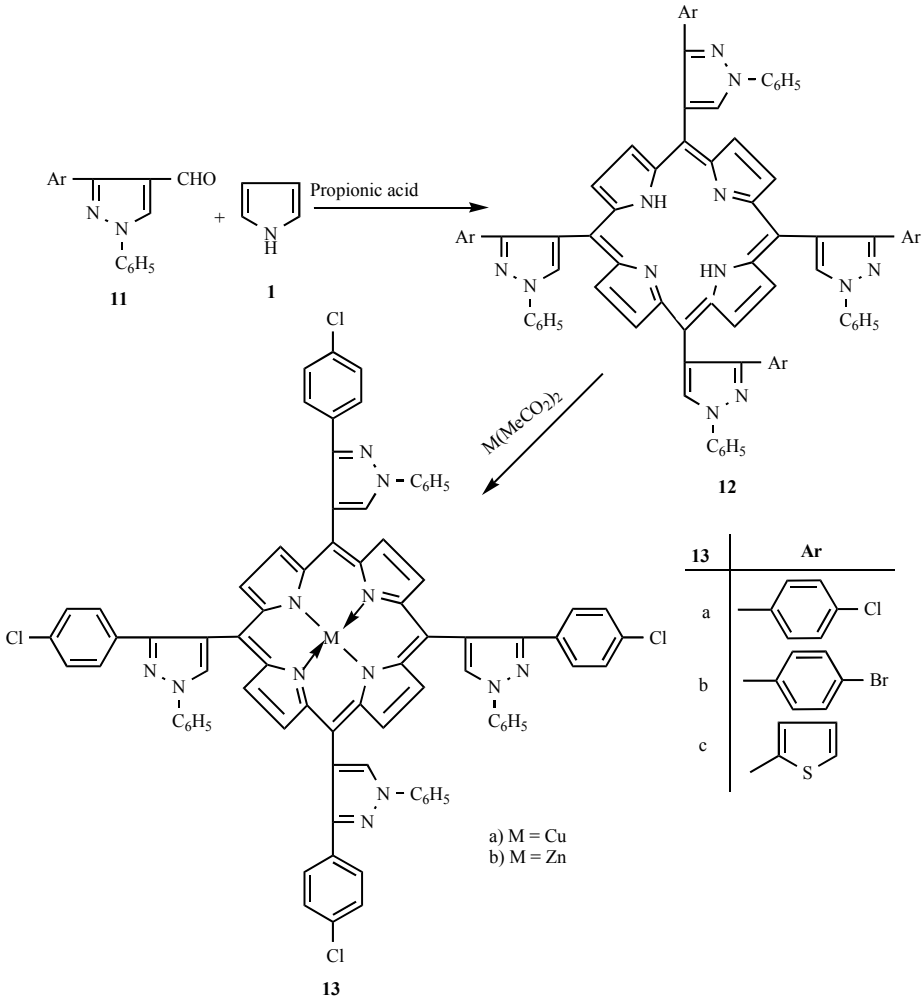
The acid-catalyzed condensation of pyrrole and 5-alkyl-1*H*-pyrrole-2-carbaldehyde (**8**) obtained by formylation of **6** led to yield **3a** instead of monoalkylterpyrromethane (**10**).

It was conspicuous that a reaction of **8a-e** with pyrrole in the presence of TFA always produced **3a** due to an unusual cleavage of alkyl chain present at position 5 of the pyrrole ring in **8** (Scheme **2**). Porphyrins with four 1,3-diaryl-4-pyrazolyl groups present at methylene junction of two pyrrole units are not reported so far. These compounds were prepared with the consideration that the presence of therapeutically important pyrazole moiety in the porphyrins unit would possibly enhance its pharmacological profiles. Attempts to prepare tetrapyrazolylporphyrin by acid-catalyzed condensation of 1,3-diaryl-4-formylpyrazole [21] and 5-(1,3-diaryl-4-pyrazolyl) dipyrromethane in the presence of DDQ as an oxidant failed.

To simplify this procedure [17] an equimolar mixture of 1,3-diaryl-4-formylpyrazole **11** and pyrrole **1** in propionic acid was heated to 135-140^{0}C for 5-6 h and thereafter the solution was left overnight at room temperature under nitrogen blanket. The reaction mixture was diluted with water and filtered. The solid obtained was purified on neutral alumina



Scheme 2.



Scheme 3.

column using a mixture of chloroform-hexane (1:2) as eluent and characterized as **12**. The heterometallic system **13**, which involves different metal ions in the chromophoric backbone of the porphyrin was prepared by mixing an equimolar mixture of porphyrin **12** in dichloromethane and a solution of zinc or copper acetate separately in methanol at room temperature (Scheme **3**).

All the synthesized compounds were characterized by their spectroscopic and elemental analyses.

EXPERIMENTAL SECTION

General Information

Melting points were determined in an open capillary with a Büchi-530 melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a 200 MHz spectrometer using TMS as internal reference compound (chemical shifts in ppm). IR spectra were obtained in KBr discs. EI-MS were accomplished at 70 eV on a mass spectrometer. Microanalyses (C, H, N) were carried out on a Carlo Erba EA-1108 elemental analyzer. TLC was performed on 7x3 cm precoated silica gel/ neutral alumina plastic plate.

[Di(1H-pyrrol-2-yl)methyl]heteroarenes (3a-m), General Procedure

To a stirred solution of an aldehyde (2, 1.2 mmol) and pyrrole (51.6 mmol), Amberlyst 15 or TFA (0.38 mmol) was added carefully. The reaction mixture was stirred at room temperature for 30 min. Chloroform (15 mL) was added and the resulting reaction mixture washed with aqueous sodium hydroxide solution (5%) followed by water. Chloroform layer was collected, dried over Na_2SO_4 and evaporated under reduced pressure. Oily crude product obtained was purified by silica gel column chromatography using hexane/ethyl acetate (39:1) as eluent.

2-[Di(1H-pyrrol-2-yl)methyl]-1H-pyrrole (3a)

White amorphous solid; Mp 128-129^{0}C [Lit [22]. 128^{0}C]; yield 75.3%.

3-[Di(1H-pyrrol-2-yl) methyl] pyridine (3b)

White crystalline solid; Mp 158-160^{0}C; yield 77.8%; ν_{max} (KBr) 3354 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.49 (s, 1H, CH), 5.87 (dd, J=2.64 Hz, 2H, pyrrolyl), 6.14-6.18 (m, 2H, pyrrolyl), 6.73 (dd, J=2.64 Hz, 2H, pyrrolyl), 7.27 (m, 1H, pyridinyl), 7.66 (d, J=8.02 Hz, 1H, pyridinyl), 8.02 (brs, 2H, NH), 8.51 (m, 2H, pyridinyl); m/z (EI) 223 (M^+). Anal.Calcd for $C_{14}H_{13}N_3$: C, 75.3; H, 5.86; N, 18.81 Found: C, 75.27; H, 5.97; N, 18.95.

3-[Di(1H-pyrrol-2-yl)methyl]-1H-indole (3c)

White crystalline solid; Mp 128-129^{0}C; yield 26.6%; ν_{max} (KBr) 3360 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.56 (s, 1H, CH), 5.84-5.89 (m, 1H, indolyl), 6.02-6.05 (m, 3H, indolyl, pyrrolyl), 6.15-6.22 (m, 3H, indolyl, pyrrolyl), 6.25-6.26 (m, 3H, indolyl, pyrrolyl), 6.81-6.85 (m, 1H, indolyl), 7.95 (brs, 1H, NH), 8.02 (brs, 2H, NH); m/z (EI) 261 (M^+). Anal.Calcd for $C_{17}H_{15}N_3$: C, 78.13; H, 5.78; N, 16.07 Found: C, 78.20; H, 5.87; N, 16.21.

4-[Di(1H-pyrrol-2-yl)methyl]-1,3-diphenyl-1H-pyrazole (3d)

White solid, Mp 130-131^{o}C; yield 82.7%; ν_{max} (KBr) 3372 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.57 (s, 1H, CH), 5.59-6.0 (m, 2H, pyrrolyl), 6.10-6.19 (m, 2H, pyrrolyl), 6.69-6.70 (m, 2H, pyrrolyl), 7.29-7.38 (m, 4H, Rah), 7.57-7.61 (m, 3H, ArH), 7.66–7.73 (m, 4H, ArH), 8.0 (brs, 2H, NH); m/z (FAB) 365 (M^++1). Anal.Calcd for $C_{24}H_{20}N_4$: C, 79.10; H, 5.53; N, 15.37 Found: C, 79.21; H, 5.62; N, 15.49.

4-[Di(1H-pyrrol-2-yl)methyl]-3-(4-methylphenyl)-1-phenyl-1H-pyrazole (3e)

White powder; Mp 158-159^{o}C; yield 80%; ν_{max} (KBr) 3390 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.36 (s, 3H, CH_3), 5.56 (s, 1H, CH), 5.59-6.0 (m, 2H, pyrrolyl), 6.14-6.18 (m, 2H, pyrrolyl), 6.68-6.71 (m, 2H, pyrrolyl), 7.16-7.28 (m, 3H, ArH), 7.38-7.50 (m, 4H, ArH), 7.68–7.73 (m, 3H, ArH), 7.99 (brs, 2H, NH); m/z (FAB) 379 (M^++1). Anal.Calcd for $C_{25}H_{22}N_4$: C, 79.34; H, 5.86; N, 14.80 Found: C, 79.47; H, 5.95; N, 15.02.

4-[Di(1H-pyrrol-2-yl)methyl]-3-[4-methoxyphenyl]-1-phenyl-1H-pyrazole (3f)

White amorphous solid; Mp 168-169^{o}C; yield 88%; ν_{max} (KBr) 3381 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 3.82 (s, 3H, OCH_3), 5.54 (s, 1H, CH), 5.59-6.0 (m, 2H, pyrrolyl), 6.15-6.19 (m, 2H, pyrrolyl), 6.69-6.70 (m, 2H, pyrrolyl), 6.98 (d, J=8.8 Hz, 2H, ArH), 7.28-7.53 (m, 5H, ArH), 7.68–7.72 (m, 3H, ArH), 7.98 (brs, 2H, NH); m/z (FAB) 395 (M^++1). Anal.Calcd for $C_{25}H_{22}N_4O$: C, 76.12; H, 5.62; N, 14.20 Found: C, 76.25; H, 5.68; N, 14.12.

4-[Di(1H-pyrrol-2-yl)methyl]-3-[4-fluorophenyl]-1-phenyl-1H-pyrazole (3g)

White crystalline solid; Mp 138-139^{o}C; yield 85%; ν_{max} (KBr) 3361 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.51 (s, 1H, CH), 5.59-6.0 (m, 2H, pyrrolyl), 6.16-6.18 (m, 2H, pyrrolyl), 6.70-6.71 (m, 2H, pyrrolyl), 7.01-7.09 (m, 2H, ArH), 7.25-7.58 (m, 5H, ArH), 7.68–7.72 (m, 3H, ArH), 7.98 (brs, 2H, NH); m/z (FAB) 383 M^++1). Anal. Calcd for $C_{25}H_{19}FN_4$: C, 75.37; H, 5.01; N, 14.65 Found: C, 75.55; H, 5.20; N, 14.56.

3-[4-Chlorophenyl]-4-[di(1H-pyrrol-2-yl)methyl]-1-phenyl-1H-pyrazole (3h)

White powdered solid; Mp 146-147^{o}C; yield 84%; ν_{max} (KBr) 3370 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.52 (s, 1H, CH), 5.58-6.04 (m, 2H, pyrrolyl), 6.14-6.19 (m, 2H, pyrrolyl), 6.70-6.71 (m, 2H, pyrrolyl), 7.23-7.59 (m, 7H, ArH), 7.68-7.71 (m, 3H, ArH), 7.98 (brs, 2H, NH); m/z (FAB) 399 (M^++1). Anal.Calcd for $C_{25}H_{19}ClN_4$: C, 72.27; H, 4.80; N, 14.05 Found: C, 72.34; H, 4.95; N, 14.16

3-[4-Bromophenyl]-4-[di(1H-pyrrol-2-yl)methyl]-1-phenyl-1H-pyrazole (3i)

White crystalline solid; Mp 148-149^{o}C; yield 84%; ν_{max} (KBr) 3382 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.51 (s, 1H, CH), 5.99-6.0 (m, 2H, pyrrolyl), 6.14-6.19 (m, 2H, pyrrolyl), 6.70-6.71 (m, 2H, pyrrolyl), 7.24-7.30 (m, 2H, ArH), 7.39-7.52 (m, 5H, ArH), 7.67–7.71 (m, 3H, ArH), 7.97 (brs, 2H, NH). m/z (FAB) 444 (M^++1). Anal.Calcd for $C_{25}H_{19}BrN_4$:C, 65.02; H, 4.32; N, 12.62 Found: C, 65.23; H, 4.39; N, 12.76.

4-[Di(1H-pyrrol-2-yl)methyl]-3-(2-thienyl)-1H-pyrazole (3j)

White crystalline solid; Mp 150-152°C; yield 89%; ν_{max} (KBr) 3386 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.64 (s, 1H, CH), 6.01-6.02 (m, 2H, pyrrolyl), 6.15-6.20 (m, 2H, pyrrolyl), 6.70-6.71 (m, 2H, pyrrolyl), 6.69-7.0 (m, 2H, ArH), 7.15-7.50 (m, 4H, ArH), 7.56–7.75 (m, 3H, ArH), 8.0 (brs, 2H, NH); m/z (FAB) 371 (M^++1). Anal.Calcd for $C_{22}H_{18}N_4S$: C, 71.32; H, 4.90; N, 15.12 Found: C, 71.40; H, 5.15; N, 15.22.

5-[Di(1H-pyrrol-2-yl)methyl]-3-phenylisoxazole (3k)

White amorphous solid, Mp 120-121°C, yield 86%; ν_{max} (KBr) 3355 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.56 (s, 1H, CH), 6.09-6.20 (m, 4H, pyrrolyl), 6.34 (s, 1H, isoxazolyl), 6.71-6.74 (m, 2H, pyrrolyl), 7.41-7.44 (m, 3H, ArH), 7.73-7.77 (m, 2H, ArH), 8.20 (brs, 2H, NH); m/z (FAB) 290 (M^++1). Anal.Calcd for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23; N, 14.52 Found: C, 74.75; H, 5.30; N, 14.76.

5-[Di(1H-pyrrol-2-yl)methyl]-3-(4-methylphenyl)isoxazole (3l)

White powdered solid; Mp 126-127°C; yield 88%; ν_{max} (KBr) 3360 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 2.34 (s, 3H, CH_3), 5.69 (s, 1H, CH), 6.08-6.19 (m, 4H, pyrrolyl), 6.32 (s, 1H, isoxazolyl), 6.72-6.75 (m, 2H, pyrrolyl), 7.23 (d, J=8.10 Hz, 2H, ArH), 7.63 (d, J=8.10 Hz, 2H, ArH), 8.21 (brs, 2H, NH); m/z (FAB) 304 (M^++1). Anal.Calcd for $C_{19}H_{17}N_3O$: C, 75.23; H, 5.65; N, 13.85 Found: C, 75.34; H, 5.51; N, 13.93.

3-(4-Chlorophenyl)-5-[di(1H-pyrrol-2-yl)methyl]isoxazole (3m)

White crystalline solid; Mp 75-76°C; yield 88%; ν_{max} (KBr) 3385 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.52 (s, 1H, CH), 6.09-6.19 (m, 4H, pyrrolyl), 6.32 (s, 1H, isoxazolyl), 6.64-6.74 (m, 2H, pyrrolyl), 7.42 (d, J=8.10 Hz, 2H, ArH), 7.72 (d, J=8.10 Hz, 2H, ArH), 8.21 (brs, 2H, NH); m/z (FAB) 324 (M^++1). Anal.Calcd for $C_{18}H_{14}ClN_3O$: C, 66.77; H, 4.36; N, 12.98 Found: C, 66.85; H, 4.54; N, 12.83.

5-[Di-(5-formyl-1H-pyrrol-2-yl)methyl]-1H-pyrrole-2-carbaldehyde (4a)

A solution of phosphorous oxychloride (6.6 mL) in dichloroethane (3.5 mL) was slowly added to a solution of *N,N*-dimethylformamide in dichloroethane (2.5 mL) at 0°C. The solution was allowed to stir at room temperature for half an hour followed by addition of a solution of **3** (1.9 mmol) in dichloroethane at 0°C with continued stirring for an additional 2 h. at room temperature. Sodium acetate (22.6 mmol in 10 mL water) was added to the reaction mixture and then refluxed for 20 min. Dichlorethane layer was separated and aqueous layer extracted with $CHCl_3$ (3x12 mL). The combined organic layer was dried over Na_2SO_4, evaporated under reduced pressure. Crude product thus obtained was purified on silica gel column using hexane/ethyl acetate (3:2) as eluent. Brown powdered solid; Mp > 250°C; yield 45%; ν_{max} (KBr) 1655, 3336 cm^{-1}; δ_H (200 MHz, $CDCl_3$+DMSO-d_6) 5.74 (s, 1H, CH), 6.18 (dd, J=2.64 Hz, 3H, pyrrolyl), 6.85 (dd, J=2.64 Hz, 3H, pyrrolyl), 9.41 (s, 3H, CHO), 10.64 (brs, 3H, NH); m/z (EI) 295 (M^+). Anal. Calcd $C_{16}H_{13}N_3O_3$: C, 65.08; H, 4.43; N, 14.24 Found: C, 65.04; H, 4.40; N, 14.22.

5-[(5-formyl-1H-pyrrol-2-yl)(3-pyridinyl) methyl]-1H-pyrrole-2-carbaldehyde (4b)

It was prepared by following the procedure of **4a**. Oil; yield 48%; ν_{max} (neat) 1651, 3346 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 5.61 (s, 1H, CH), 6.05 (dd, J=2.64 Hz, 2H, pyrrolyl), 6.88 (dd, J=2.64 Hz, 2H, pyrrolyl), 7.28-7.32 (m, 1H, pyridinyl), 7.66 (d, J=8.02 Hz, 1H, pyridinyl), 8.53-8.56 (m, 2H, pyridinyl), 9.40 (brs, 2H, CHO), 10.60 (s, 2H, NH); m/z (EI) 279 (M^+).Anal.Calcd for $C_{16}H_{13}N_3O_2$: C, 68.80; H, 4.79; N, 15.14 Found: C, 68.77; H, 4.68; N, 15.03.

Methyl 5-alkyl-1H-pyrrole-2-carbodithioate (7a-e), General procedure

Powdered KOH (21.05 mmol) was stirred in dimethyl sulphoxide (20 mL) at room temperature for 20 min. Alkylpyrrole (6, 10.52 mmol) was added slowly and allowed the reaction mixture to stir at room temperature for 45 min. Carbon disulphide (21.05 mmol) was charged into reaction mixture and again allowed to stir for 3 h. At the end, reaction mixture was diluted with water and extracted with diethyl ether, dried over $CaCl_2$. The crude product obtained was purified on silica gel column using hexane/CH_2Cl_2 (9:1) eluent.

Methyl 5-ethyl-1H-pyrrole-2-carbodithioate (7a)

Oil; yield 42.5%; ν_{max} (neat) 3349 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.28 (t, J=7.60 Hz, 3H, CH_3), 2.70 (q, J=7.60 Hz, 2H, CH_2), 2.72 (s, 3H, SCH_3), 6.08 (dd, J=2.54 Hz, 1H, pyrrolyl), 7.04 (dd, J=2.54 Hz, 1H, pyrrolyl), 9.40 (brs, 1H, NH); m/z (EI) 185 (M^+). Anal.Calcd for $C_8H_{11}NS_2$: C, 51.85; H, 5.98; N, 7.55 Found: C, 51.88; H, 5.84; N, 7.46.

Methyl 5-n-propyl-1H-pyrrole-2-carbodithioate (7b)

Oil; yield 48.3%; ν_{max} (neat) 3348 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.97 (t, J=7.40 Hz, 3H, CH_3), 1.68 (m, 2H, CH_2), 2.58 (t, J=7.60 Hz, 2H, CH_2), 2.72 (s, 3H, SCH_3), 6.07 (dd, J=2.54 Hz, 1H, pyrrolyl), 7.03 (dd, J=2.54 Hz, 1H, pyrrolyl), 9.55 (brs, 1H, NH); m/z (EI) 199 (M^+). Anal.Calcd for $C_9H_{13}NS_2$: C, 54.22; H, 6.57; N, 7.02 Found: C, 54.35; H, 6.67; N, 7.12.

Methyl 5-n-butyl-1H-pyrrole-2-carbodithioate (7c)

Oil; yield 46.3%; ν_{max} (neat) 3340 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.93 (t, J=7.24 Hz, 3H, CH_3), 1.33-1.44 (m, 2H, CH_2), 1.56-1.68 (m, 2H, CH2), 2.60 (t, J=7.36 Hz, 2H, CH_2), 2.72 (s, 3H, SCH_3), 6.07 (dd, J=2.54 Hz, 1H, pyrrolyl), 7.04 (dd, J=2.54 Hz, 1H, pyrrolyl), 9.55 (brs H, NH); m/z (EI) 213 (M^+). Anal.Calcd for $C_{10}H_{15}NS_2$: C, 56.29; H, 7.08; N, 6.56 Found: C, 56.30; H, 7.17; N, 6.70.

Methyl 5-n-hexyl-1H-pyrrole-2-carbodithioate (7d)

Oil; yield 49.2%; ν_{max} (neat) 3348 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.86 (t, J=6.54 Hz, 3H, CH_3), 1.30-1.34 (m, 4H, CH_2), 1.56-1.62 (m, 4H, CH2), 2.60 (t, J=7.36 Hz, 2H, CH_2), 2.72 (s, 3H, SCH_3), 6.07 (dd, J=2.54 Hz, 1H, pyrrolyl), 7.04 (dd, J=2.54 Hz, 1H, pyrrolyl), 9.55 (brs, 1H, NH); m/z (EI) 241 (M^+). Anal.Calcd for $C_{12}H_{19}NS_2$: C, 59.70; H, 7.93; N, 5.80 Found: C, 59.68; H, 7.81; N, 5.82.

Methyl 5-n-decyl-1H-pyrrole-2-carbodithioate (7e)

Oil; yield 52%; ν_{max} (neat) 3340 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.87 (t, J=7.24 Hz, 3H, CH_3), 1.23-1.26 (m, 14H,

CH_2), 1.64-1.68 (m, 2H, CH_2), 2.59 (t, J=6.06 Hz, 2H, CH_2), 2.72 (s, 3H, SCH_3), 6.06 (dd, J=2.54 Hz, 1H, pyrrolyl), 7.03 (dd, J=2.54 Hz, 1H, pyrrolyl), 9.54 (brs, 1H, NH); m/z (EI) 279 (M^+). Anal.Calcd for $C_{16}H_{27}NS_2$: C, 64.59; H, 9.14; N, 4.70 Found: C, 64.69; H, 9.25; N, 4.78.

5-Alkyl-1H-pyrrole-2-carbaldehyde (8a-e), General Procedure

A solution of phosphorous oxychloride (2.92 mmol) in dry benzene (5 mL) was added to a solution of *N,N*-dimethylformamide (2.68 mmol) in dry benzene (4 mL) at 0^0C for 30 min. and thereafter stirred at 20^0C for half an hour. Alkylpyrroles (**6**, 2.43 mmol) in dry benzene (5 mL) was added slowly at 0^0C and further stirred for 18 h at room temperature. The reaction mixture was diluted with ice cold water (15 mL) neutralized with sodium bicarbonate and NaOH solution (40%) added to adjust pH 12. The alkaline solution was stirred at room temperature for 1.5 h. Benzene phase was separated and aqueous layer extracted with $CHCl_3$ (3x30 mL). The combined extract was dried over Na_2SO_4, evaporated to dryness. The crude product was finally purified on silica gel column using CH_2Cl_2/ Hexane (1:1) as eluent.

5-Ethyl-1H-pyrrole-2-carbaldehyde (8a)

White semi solid; yield 77.2%; ν_{max} (neat) 1643, 3440 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 1.28 (t, J=7.60 Hz, 3H, CH_3), 2.70 (q, J=7.60 Hz, 2H, CH_2), 6.89 (dd, J=2.64 Hz, 1H, pyrrolyl), 7.04 (dd, J=2.64 Hz, 1H, pyrrolyl), 9.37 (s, 1H, CHO), 9.72 (brs, 1H, NH); m/z (EI) 123 (M^+). Anal.Clacd for C_7H_9NO: C, 68.26; H, 7.37; N, 11.37. Found: C, 68.34; H, 7.45; N, 11.48.

5-n-Propyl-1H-pyrrole-2-carbaldehyde (8b)

White semi solid; yield 72%; ν_{max} (neat) 1643, 3350 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.97 (t, J=7.40 Hz, 3H, CH_3), 1.58-164 (m, 2H, CH_2), 2.64 (t, J=7.60 Hz, 2H, CH_2), 6.07 (dd, J=2.64Hz, 1H, pyrrolyl), 6.89 (dd, J=2.60 Hz, 1H, pyrrolyl), 9.36 (s, 1H, CHO), 9.72 (brs, 1H, NH); m/z (EI) 137 (M^+). Anal.Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.23; H, 8.14; N, 10.13.

5-n-Butyl-1H-pyrrole-2-carbaldehyde (8c)

White semi solid; yield 69.7%; ν_{max} (neat) 1642, 3345 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.92 (t, J=7.24 Hz, 3H, CH_3), 1.28-1.46 (m, 2H,CH_2), 1.57-1.72 (m, 2H, CH_2), 2.65 (t, J=7.36 Hz, 2H, CH_2), 6.07 (dd, J=2.64 Hz, 1H, pyrrolyl), 6.88 (dd, J=2.64 Hz, 1H, pyrrolyl), 9.37 (s, 1H, CHO), 9.70 (brs, 1H, NH); m/z (EI) 151 (M^+). Anal.Calcd for $C_9H_{13}NO$: C, 71.48; H, 8.66; N, 9.26 Found: C, 71.38; H, 8.60; N, 9.35.

5-n-Hexyl-1H-pyrrole-2-carbaldehyde (8d)

White semi solid; yield 63.3%; ν_{max} (neat) 1643, 3348 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, J=6.54 Hz, 3H, CH_3), 1.25-1.38 (m, 6H, CH_2), 1.57-1.65 (m, 2H, CH_2), 2.65 (t, J=7.60 Hz, 2H, CH_2), 6.07 (dd, J=2.64 Hz, 1H, pyrrolyl), 6.88 (dd, J=2.64 Hz, 1H, pyrrolyl), 9.36 (s, 1H, CHO), 9.56 (brs, 1H, NH); m/z (EI) 179 (M^+). Anal.Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.55; N, 7.81 Found: C, 73.82; H, 9.63; N, 7.87.

5-n-Decyl-1H-pyrrole-2-carbaldehyde (8e)

White crystalline solid; Mp 40-41^0C; yield 71%; ν_{max} (KBr) 1642, 3341 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.87 (t, J=7.24 Hz, 3H, CH_3), 1.23-1.26 (m, 12H, CH_2), 1.62-1.68 (m, 4H, CH_2) 2.64 (t, J=7.46 Hz, 2H, CH_2), 6.06 (dd, J=2.64 Hz, 1H, pyrrolyl), 6.87 (dd, J=2.64 Hz, 1H, pyrrolyl), 9.30 (s, 1H, CHO), 9.54 (brs, 1H, NH); m/z (EI) 235 (M^+). Anal.Calcd for $C_{15}H_{25}NO$: C, 76.54; H, 10.70; N, 5.95 Found: C, 76.48; H, 10.83; N, 6.01.

5-Hexyl-1H-pyrrole-2-carbothiohydrazide (9)

White crystalline solid; Mp >250^0C; yield 45.5%; ν_{max} (KBr) 3402 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 0.88 (t, J=6.72 Hz, 3H, CH_3), 1.30-1.31 (m, 4H, CH_2), 1.57-1.59 (m, 4H, CH_2), 2.59 (t, J=7.38 Hz, 2H, CH_2), 5.99 (dd, J=2.50 Hz, 1H, pyrrolyl), 6.48 (dd, J=2.50 Hz, 1H, pyrrolyl), 8.32 (brs, 2H, NH), 9.45 (brs, 1H, NH); m/z (EI) 225 (M^+). Anal.Calcd $C_{11}H_{19}N_3S$: C, 58.63; H, 8.50; N, 18.65 Found: C, 58.49; H, 8.62; N, 18.72.

5,10,15,20-Tetra-(1,3-diaryl-1H-pyrazol-4-yl)-porphyrin (12a-c), General Procedure

A mixture of 1,3-diaryl-4-formylpyrazoles (**12**, 3.53 mmol) and pyrrole (**1**, 4.48 mmol) was stirred in propionic acid (15 mL) at 135-140^oC under nitrogen atmosphere for 5 h. Reaction mixture was diluted with distilled water, solid product separated was filtered, washed with excess of water and purified on neutral alumina column using hexane/$CHCl_3$ (3:2) as eluent.

5,10,15,20-Tetrakis-[3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl] porphyrin (12a)

Brown amorphous solid; Mp >250^0C; yield 38%; ν_{max} (KBr) 3422 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.67-6.80 (m, 8H, ArH), 7.09-7.29 (m, 4H, ArH), 7.33-7.44 (m, 8H, ArH), 7.51-7.63 (m, 8H, ArH), 8.08 (d, J=7.46H, 8H, ArH), 8.51-8.62 (m, 4H, ArH), 8.65 (brs, 2H, NH), 8.99-9.03 (m, 8H, ArH); m/z (FAB) 1319 (M^++1), 1320 (M^++2), 1321 (M^++3). Anal.Calcd for $C_{80}H_{50}Cl_4N_{12}$: C, 72.73; H, 3.81; N, 12.72 Found: C, 72.67; H, 3.97; N, 12.69.

5,10,15,20-Tetrakis-[3-(4-bromophenyl)-1-phenyl-1H-pyrazol-4-yl] porphyrin (12b)

Brown amorphous powder; Mp >250^0C; yield 35%; ν_{max} (KBr) 3427 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.85-6.96 (m, 8H, ArH), 7.17-7.31 (m, 4H, ArH), 7.35-7.7.41 (m, 8H, ArH), 7.55-7.59 (m, 8H, ArH), 8.02-8.10 (m, 8H, ArH), 8.68-8.76 (m, 4H, ArH), 8.79 (brs, 2H, NH), 8.98-9.04 (m, 8H, ArH); m/z (FAB) 1499 (M^++1), 1500 (M^++2), 1501 (M^++3). Anal.Calcd for $C_{80}H_{50}Br_4N_{12}$: C, 64.10; H, 3.36; N, 11.21 Found: C, 64.17; H, 3.50; N, 11.10.

5,10,15,20-Tetrakis-[3-(2-thienyl)-1-phenyl-1H-pyrazol-4-yl] porphyrin (12c)

Gray amorphous solid; Mp >250^0C; yield 29%; ν_{max} (KBr) 3423 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.05-6.42 (m, 12H, ArH), 6.80-6.87 (m, 8H, ArH), 7.36-7.43 (m, 4H, ArH), 7.55-7.62 (m, 4H, ArH), 8.00-8.09 (m, 4H, ArH), 8.44 (brs, 2H, NH), 8.51-8.53 (m, 2H, ArH), 8.64-8.67 (m, 4H, ArH), 8.83-8.85 (m, 2H, NH), 9.07 (s, 4H, ArH); m/z (FAB) 1207 (M^++1), 1208 (M^++2). Anal.Calcd $C_{72}H_{46}N_{12}S_4$: C, 71.62; H, 3.84; N, 13.92 Found: C, 71.58; H, 3.98; N, 13.83.

Cu(II)-5,10,15,20-Tetrakis-[3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl] porphyrin (13a)

A solution of (**12a** 0.05 mmol) in CH_2Cl_2 (6 mL) was added slowly to a solution of cupric acetate monohydrate (0.27 mmol) in methanol (10 mL) at room temperature. The solution was stirred for 1h. The precipitate obtained was filtered, washed with excess of methanol. Brown amorphous solid; mp >250^{0}C; yield 91%; ν_{max} (KBr) 3422 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.71-6.90 (m, 8H, ArH), 7.26-7.37 (m, 12H, ArH), 7.54-7.60 (m, 8H, ArH), 7.96-8.05 (m, 8H, ArH), 8.43-8.57 (m, 4H, ArH), 8.63-8.68 (m, 4H, ArH), 8.99-9.04 (m, 4H, ArH); m/z (FAB) 1382 (M^++1), 1383 (M^++2). Anal.Calcd for $C_{80}H_{48}Cl_4N_{12}Cu$: C, 69.49; H, 3.50; N, 11.63 Found: C, 69.68; H, 3.69; N, 12.16.

Zn(II)-5,10,15,20-Tetrakis-[3-(4-chlorophenyl)-1-phenyl-1H-pyrazol-4-yl] porphyrin (13b)

To a solution of zinc chloride (0.0906 mmol) and sodium acetate (0.0906 mmol) in methanol (15 mL), a solution of porphyrin (**12a**, 0.015 mmol) in CH_2Cl_2 (5 mL) was added at room temperature. The reaction mixture was stirred for 1 h. and filtered the precipitated solid, washed with methanol.

Brown amorphous solid; Mp >250^{0}C; yield 93%; ν_{max} (KBr) 3422 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.64-6.80 (m, 8H, ArH), 7.18-7.29 (m, 4H, ArH), 7.33-7.44 (m, 8H, ArH), 7.56-7.63 (t, J=7.76 Hz, 8H, ArH), 8.09 (d, J=9.03 Hz, 8H, ArH), 8.62-8.74 (m, 4H, ArH), 8.99-9.09 (m, 4H, ArH), 9.12 (s, 4H, ArH); m/z (FAB) 1384 (M^++1), 1385 (M^++2). Anal.Calcd for $C_{80}H_{48}Cl_4N_{12}Zn$: C, 69.40; H, 3.49; N, 12.14 Found: C, 69.52; H, 3.66; N, 12.25.

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