Journal of Molecular Structure 1029 (2012) 92–97

Contents lists available at SciVerse ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc

One-pot synthesis and characterization of new cuprous pyrazinoporphyrazines containing peripherally functionalized units

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ARTICLE INFO

Article history:
Received 13 March 2012
Received in revised form 9 June 2012
Accepted 11 June 2012
Available online 10 July 2012

Keywords:
Porphyrazine
Pyrazinoporphyrazine
Phthalocyanine
Photosensitizer
Photodynamic therapy (PDT)

ABSTRACT

The synthesis and characterization of some new peripherally substituted Cu-pyrazinoporphyrazines (Cu-Pzs) is described. The prepared α-dicyano compounds in the presence of cuprous chloride produced porphyrazine counterparts via one-pot cyclotetramerization reaction. The resulted porphyrazines are useful photosensitizers and good reagent for photodynamic therapy of cancer.

1. Introduction

Recently, synthesis and application of phthalocyanines (Pcs), porphyrazines (Pzs) and related macrocycles modified by peripheral substituent attachments, have been reported as great interesting subjects because of their vast applications in diverse areas. For example photodynamic therapy (PDT) has been used as a potential treatment source for many forms of cancers, curing early or localized disease, improving the quality of life in advanced disease and increasing survival [1–3]. The photosensitizing compound (Pz), visible light and molecular oxygen are three main components of PDT wherein, photosensitizer absorbs the light and efficiently transfers the energy to ground state triplet oxygen forming highly reactive singlet oxygen that destroys the target tissues selectively [1,2,4–8]. Photodegradation of chlorophenol pollutants with singlet oxygen generated by irradiation of the supported phthalocyanine derivatives has also been reported successfully [9–11]. Therefore, improving the Pz as photocatalyst to be active in the visible or near-infrared region of light has been a highly active research topic in recent years. Some improved routes for example; immobilization of metal complexes onto solid supports [9,12], binuclear annulations of porphyrazines [13,14] and peripheral substitution of porphyrazines [4,15–18] have been quoted. The application of porphyrazines in switches, information storage, imaging devices, dyes, liquid crystals, semiconductor devices, non-linear optics, photosensitizers, anticancer, anti AIDS, DNA cleavers, photochromism, photocatalyst, optical filters, thermally stable polymers, degradation of organic pollutants, redox properties, solar cells, electron transfer, magnetic interactions and ionophoric activity have been reported too [4–7,9,13–22].

The cyclic-tetramerization of α-dicyano compounds is the most important synthetic route for producing porphyrazine derivatives. The importance of dicyanopyrazine derivatives has been mentioned mainly in the chemical industry, food, agricultural and medicinal chemistry [19]. The specific properties of 2,3-dicyanopyrazine derivatives are resulted from the two strong electron withdrawing cyano groups on the pyrazine ring. In the present work, we have carried out the premade 2,3-dicyanopyrazine derivatives for the one-pot synthesis of some novel Cu(II)-pyrazinoporphyrazines by direct cyclic-tetramerization.

2. Experimental section

2.1. General

The UV–Vis spectra were measured on a Shimadzu UV-2100 spectrometer. The ^{1}H NMR (500 MHz) spectra were obtained with a Bruker 500 DRX-Avance NMR and the others (400 MHz) were registered with a Bruker 400 Avance 3 spectrometer. The IR spectra were taken with a Shimadzu 470 spectrometer using KBr pellets. Melting points of crystalline dicyano compounds were measured with a Electrothermal melting point apparatus and have not been corrected. Mass spectra were recorded on a GC–MS Agilent

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http://dx.doi.org/10.1016/j.molstruc.2012.06.021

Technologies QP-5973 N MSD instrument. Typical reaction procedures and spectroscopic data for all products are described below.

2.2. Synthesis of α-dicyano derivatives (**1–5**): a general procedure

A solution of benzil (0.036 mol), DAMN (4.73 g, 0.044 mol) and *p*-toluenesulfonic acid (0.02 g) in EtOH (50 ml) was refluxed for 5 h. In the end of reaction a dark cream colored suspension was achieved. The crude mixture was filtered off and washed with MeOH. The crude product was recrystallized from mixture solution of $CCl_4/CHCl_3$; 1:1 to lead pure compound **1**. The other dicyano compounds **2**–**5** were synthesized via similar manner from phenanthraquinone, dinitrobenzil, dinitro phenanthraquinone and 1,4-benzodialdehyde respectively, the recrystallization solution for compound **2** was *o*-dichlorobenzene and for compounds **3**–**5** was 96% EtOH.

2.2.1. 5,6-Diphenylpyrazine-2,3-dicarbonitrile (**1**)

Cream needle crystals, yield 83.72%, 8.5 g, mp 255 °C; ^{1}H NMR (δ_H 500 MHz, DMSO-d_6/ppm) 7.48 (*d*, *J* = 7.85 Hz, 3H, 2 × ArH), 7.41 (*t*, *J* = 7.81 Hz, 2H, 2 × ArH); IR (ν_{max} KBr/cm^{-1}) 3058 (ArH), 2235 (CN), 1691 (C=N), 1512 (C=C); Exact mass (M$^+$): calcd. for $C_{18}H_{10}N_4$, 282.0905 found 282.0912.

2.2.2. Dibenzo[f,h]quinoxaline-2,3-dicarbonitrile (**2**)

Greenish brown powder, yield 70.46%, 7.11 g, mp $310_{dec.}$°C; ^{1}H NMR (δ_H 500 MHz, DMSO-d_6/ppm) 8.30 (*d*, *J* = 7.83 Hz, 1H, 2 × ArH), 8.01 (*d*, *J* = 7.41 Hz, 1H, 2 × ArH), 7.78 (*t*, *J* = 7.30 Hz, 1H, 2 × ArH), 7.53 (*t*, *J* = 7.17 Hz, 1H, 2 × ArH); IR (ν_{max} KBr/cm^{-1}) 3091 (ArH), 2228 (CN), 1604 (C=N), 1450 (C=C); Exact mass (M$^+$): calcd. for $C_{18}H_8N_4$, 280.0749 found 280.0742.

2.2.3. 5,6-Bis(3-nitrophenyl)pyrazine-2,3-dicarbonitrile (**3**)

Cream crystals, yield 76%, 9.6 g, mp 248 °C; ^{1}H NMR (δ_H 500 MHz, DMSO-d_6/ppm) 7.50–7.47 (m, 3H, 2 × ArH), 7.42–7.39 (m, 1H, 2 × ArH); IR (ν_{max} KBr/cm^{-1}) 3050 (ArH), 2240 (CN), 1690–1680 (C=N), 1585 (C=C), 1505 (NO_2), 1370 (NO_2); Exact mass (M$^+$): calcd. for $C_{18}H_8N_6O_4$, 372.0607 found 372.0615.

2.2.4. 6,9-Dinitrodibenzo[f,h]quinoxaline-2,3-dicarbonitrile (**4**)

Light green powder, yield 50.27%, 6.7 g, mp $300_{dec.}$°C; ^{1}H NMR (δ_H 500 MHz, DMSO-d_6/ppm) 9.07 (*d*, *J* = 8.28, 1H, Hz, ArH), 8.94 (*d*, *J* = 8.23 Hz, 1H, ArH), 8.05 (*t*, *J* = 7.51 Hz, 2H, ArH), 7.92 (*t*, *J* = 7.57 Hz, 1H, ArH); IR (ν_{max} KBr/cm^{-1}) 3050 (ArH), 2210 (CN), 1690 (C=N), 1500 (NO_2), 1440 (C=C), 1370 (NO_2); Exact mass (M$^+$): calcd. for $C_{18}H_6N_6O_4$, 370.0451 found 370.0446.

2.2.5. 2,3-Bis((Z)-(4-formylbenzylidene)amino)but-2-enedinitrile (**5**)

Yellow powder, yield 68.56%, 8.4 g, mp $200_{dec.}$°C; ^{1}H NMR (δ_H 500 MHz, DMSO-d_6/ppm) 10.05 (s, 1H, COH), 8.32–8.28 (m, 2H, ArH), 8.24 (*d*, *J* = 8.23 Hz, 4H, ArH), 8.11 (s, 3H, α-CH), 7.97 (d, *J* = 8.21 Hz, 2H, ArH); IR (ν_{max} KBr/cm^{-1}) 3193 (ArH), 2831–2742 (CH, aldehyde), 2233–2198 (CN), 1687 (C=N), 1610 (C=O), 1558 (C=C); Exact mass (M+): calcd. for $C_{20}H_{12}N_4O_2$, 340.0960 found 340.0968.

2.2.6. 5,7-Dimethyl-6H-1,4-diazepine-2,3-dicarbonitrile (**6**)

Colorless cubic crystals, yield 60%, 1.95 g, mp 199 °C; ^{1}H NMR (δ_H 500 MHz, DMSO-d_6/ppm) 4.47 (s, 1H, CH_2), 2.29 (s, 6H, CH_3), 2.08–2.23 (m, 1H, CH_2); IR (ν_{max} KBr/cm^{-1}) 3008 (Homo-arom, CH_2), 2956 (AliH), 2227 (CN), 1691 (C=N), 1512 (C=C); Exact mass (M$^+$): calcd. for $C_9H_8N_4$, 172.0749 found 172.0757.

2.3. Synthesis of tetrapyrazinoporphyrazines (**7–10**): a general procedure

A mixture of α-dicyano precursor (**1**–4) (5.5 mmol), an equivalent amount of Cu(I)Cl in 10 ml of *o*-dichlorobenzene was heated at 160–180 °C for 18 h. The deep greenish suspension product was cooled and allowed to stay for overnight in room temperature. The solution was filtered and washed with 5% HCl aqueous solution and ammonia solution. The precipitate was washed with EtOAc, $(CH_3)_2CO$ and MeOH repeatedly. The crude products were purified by column chromatography using the eluent solvents; CH_2Cl_2/DMF for compounds **7,10** and CH_2Cl_2/EtOH for compounds **8,9** in that order (The silica gel is the stationary phase for the chromatographic column).

2.3.1. Copper tetra (2,3-diphenylpyrazino) porphyrazine (**7**)

Green needle crystals, yield 30.54%, 0.51 g; ^{1}H NMR (δ_H 400 MHz, $CDCl_3$-d_6/ppm) 7.61–7.02 (m, ArH); IR (ν_{max} KBr/cm^{-1}) 2938 (ArH), 1666 (C=N), 1445 (C=C); UV–Vis (λ_{max} CH_2Cl_2/nm) 717 (log ε = 3.66), 495 (log ε = 3.57); Exact mass (M$^+$): calcd. for $C_{72}H_{40}CuN_{16}$, 1191.2918 found 1191.2923.

2.3.2. Copper tetra (2,3-dihydrodibenzo[f,h]quinoxalino)porphyrazine (**8**)

Green needle crystals, yield 35.57%, 0.59 g; ^{1}H NMR (δ_H 500 MHz, $CDCl_3$-d_6/ppm) 8.60 (b, 1H, 8 × ArH), 7.91–7.73 (b m, 3H, 8 × ArH); IR (ν_{max} KBr/cm^{-1}) 2950 (ArH), 1677 (C=N), 1575 (C=C); UV–Vis (λ_{max} CH_2Cl_2/nm) 705 (log ε = 2.06), 630 (log ε = 1.55); Exact mass (M$^+$): calcd. for $C_{72}H_{32}CuN_{16}$, 1183.2448 found 1183.2453.

2.3.3. Copper octanitrotetra (2,3-diphenylpyrazino) porphyrazine (**9**)

Green needle crystals, yield 27.16%, 0.58 g; ^{1}H NMR (δ_H 400 MHz, DMSO-d_6/ppm) 7.64–7.38 (m, 4H, 8 × ArH); IR (ν_{max} KBr/cm^{-1}) 3050 (ArH), 1590–1570 (C=N), 1540 (NO_2), 1480 (C=C), 1345 (NO_2); UV–Vis (λ_{max} CH_2Cl_2/nm) 735 (log ε = 3.75); Exact mass (M$^+$): calcd. for $C_{72}H_{32}CuN_{24}O_{16}$, 1551.1724 found 1551.1736.

2.3.4. Copper octanitrotetra (2,3-dihydrodibenzo[f,h]quinoxalino) porphyrazine (**10**)

Green needle crystals, yield 37.61%, 0.80 g; ^{1}H NMR (δ_H 400 MHz, DMSO-d_6/ppm) 9.24 (b m, 1H, 4 × ArH), 8.94 (d, *J* = 6.80 Hz, 1H, 4 × ArH), 8.00–7.91 (m, 3H, 4 × ArH); IR (ν_{max} KBr/cm^{-1}) 3050 (ArH), 1690 (C=N), 1610 (C=C), 1551 (NO_2), 1425 (C=C), 1371 (NO_2); UV–Vis (λ_{max} CH_2Cl_2/nm) 715 (log ε = 3.52), 660 (log ε = 3.50); Exact mass (M$^+$): calcd. for $C_{72}H_{24}CuN_{24}O_{16}$, 1543.1255 found 1543.1345.

2.4. Synthesis of porphyrazine complexes (**11, 12**): a general procedure

A mixture of 5,6-diphenylpyrazine-2,3-dicarbonitrile **1** (0.08 g, 0.29 mmol) and phthalonitrile (0.04 g, 0.29 mmol) for 1:1 mol ratio was dissolved in *o*-dichlorobenzene (7 cm^3) and anhydrous copper(I)chloride (0.04 g, 0.38 mmol) was added. The mixture was heated at 130 °C for 4 h. After cooling and remaining a nightlong in room temperature, a deep greenish suspension was achieved. The mixture was dissolved in toluene (20 cm^3) and filtered. The solid was dried, purified by TLC (eluent: toluene/ CH_2Cl_2) and resulted porphyrazine **11**. The compound **12** was synthesized from dibenzo[f,h]quinoxaline-2,3-dicarbonitrile **2** as starting material, via similar manner.