Journal of Molecular Structure 1130 (2017) 10–18

Contents lists available at ScienceDirect

Journal of Molecular Structure

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

Metallo-porphyrazines with eight [5-thiopentyl 3,4,5-tris(benzyloxy) benzoate] groups: Synthesis, characterization, aggregation, and solubility behavior

Ergün Gonca

Faculty of Engineering, Department of Chemical Engineering, Çanakkale Onsekiz Mart University, Terzioglu Campus, TR 17020, Çanakkale, Turkey

ARTICLE INFO

Article history:
Received 16 August 2016
Received in revised form
19 September 2016
Accepted 26 September 2016
Available online 28 September 2016

Keywords:
Porphyrazine
3,4,5-Tris(benzyloxy)benzoic acid
Esterification
Monomeric complex
Oligomeric complex

ABSTRACT

Metal-free and metallo-porphyrazines having eight 5-hydroxypentylthio units at the peripheral positions have been prepared from 2,3-bis(5-hydroxypentylthio)maleonitrile. By the esterification reaction of magnesium hydroxy-porphyrazine with 3,4,5-tris(benzyloxy)benzoic acid in dicyclohexylcarbodiimide and toluene-*p*-sulfonic acid, the reactivity of the hydroxypentyl units was indicated. On the other hand, iron porphyrazine derivatives with eight [5-thiopentyl 3,4,5-tris(benzyloxy)benzoate] groups attached to the periphery positions were synthesized. By the reaction of metal-free porphyrazine with iron (II) acetate and further processing with HCl solution, FePzCl was obtained. Finally, by reacting FePzCl with pyridine or pyrazine, $[FePz(py)_2]$ and $[FePz(pyz)]_n$ complexes were prepared, respectively. The characterizations of target complexes were carried out by utilizing different spectroscopic methods such as FT-IR, UV–vis, mass, ^1H NMR, and ^{13}C NMR together with elemental analysis.

1. Introduction

The porphyrins, porphyrazines, tetrabenzoporphyrins, and phthalocyanines are known as tetrapyrrolic structures. Heteroatomic substitutions directly fusing to the macrocyclic periphery have brought a raising increasing interest to the porphyrazine researches [1–5]. Comparing to the phthalocyanine counterparts, direct fusion of heteroatomic substituents onto the porphyrazine β-positions ends in an evident effect; moreover, there is no such attainable related derivatives for the porphyrins. The porphyrazines also often represent highly raised solubility in many organic solvents. Thus, they ensure a unique position among the tetrapyrrolic macrocycles, and their easy synthesis coupled with their tunable electronic and optical features, provides them interesting candidates for a whole series of application areas [6–10]. The tetrapyrrolic structures are of great complexity and may be very interesting as combining structural features typical to medicinal and technological relevant compounds (discotic liquid crystals). They look fascinating calling for further investigation, e.g. with small angle neutron scattering (SANS). Therefore, the provided information including synthetic receipts and essential spectral analysis is very important.

Porphyrazines have found various potential application area in novel fields such as bleachable dyes in laser technique, discotic liquid crystals, components of electrochromic and electrophotographic materials, gas sensors, radiation protectors, catalysts of different processes (in particular, electrochemical), antimicrobial drugs, in luminescent diagnostics and photodynamic therapy of cancer tumors [11–15]. For tetrapyrrolic compound, the solubility feature is very important and the most of their behaviors are the best identified in the soluble species. A couple of unsubstituted metal-free and metallo-porphyrazines and the most of the metallo-porphyrazines are a less soluble in extensive organic solvents. An extensive expressions for preparing very soluble porphyrazines is to append varied units such as 4-*tert*-buthylphenylthio [16], *o*-tolylthio and *p*-tolylthio [17], 1-naphthylmethylthio [18], 9-anthracenylmethylthio [19], 3,5-bis-trifluoromethyl-benzylthio [20], etc. at the peripheral positions of tetrapyrrolic compounds. Compared to unsubstituted metal-free and metallo-tetrapyrroles, ester-containing porphyrazines or phthalocyanines (e.g., triphenylphosphine [21], acetoxy [22], 9-anthroyl [23], tetra(acetoxyethylthio) [24], pentafluorobenzoate [25], 1-naphthoate [26], and etc.) are very soluble in chloro- organic solvents. In continuation of our researches on different species of porphyrazines, we have prepared several new soluble porphyrazines with 2-fluoro-5-

E-mail addresses: egonca@comu.edu.tr, egonca@gmail.com.

http://dx.doi.org/10.1016/j.molstruc.2016.09.073
0022-2860/

(trifluoromethyl)phenylacetate [27], 4-biphenylcarboxylate [28], [(4-biphenyl)-2-*seco*-2,3-dioxo] [29] units appended to the peripheral positions and related monomeric and oligomeric complexes.

Tetrapyrrolic compounds containing benzyloxy units have been broadly indicated for compound activity relationships since the antioxidant impact of benzyloxy units is widely known. Benzyloxy units could be equally potent to non-tumor human cell lines, able to obstruct the proliferation of normal human peripheral lymphocytes and able to affect in a similar way confluent and non-confluent (exponential growing) cells. The main aim of that type of synthesis is to investigate how this chromone affects microtubules and microfilament network of cells and research how it impresses the polymerization of tubulin in vitro [30]. It is biologically significant for cytotoxic factors and microtubule-binding agents utilized in cancer chemotherapy. The synthesis and in vitro cytotoxic efficiencies of different *cis*-restricted 1,4- and 1,5-disubstituted 1,2,3-triazole analogs of combretastatin, as well as the inhibition data of tubulin polymerization for the best effective analogs were identified [31]. New metallo tetrapyrrolic compounds with four peripheral 3,4,5-trimethoxybenzyloxy units were synthesized by the cyclotetramerization reaction of phthalonitrile derivatives. The antioxidant efficiencies of tetrapyrrolic compounds were indicated by in vitro antioxidant analysis such as free radical scavenging ability of 1,1-diphenyl-2-picrylhydrazyl and iron(II) ion chelating ability. The maximum DPPH activity and iron(II) ion chelating activity were achieved from tetrakis [(3,4,5-trimethoxybenzyloxy) phthalocyaninato] cobalt(II) and 4-(3,4,5-trimethoxybenzyloxy) phthalonitrile, respectively. 4-(3,4,5-trimethoxybenzyloxy) phthalonitrile was indicated to have an entirely iron(II) ion chelating activity [32].

We noticed herein the synthesis and characterization of metallo-porphyrazines with [5-thiopentyl 3,4,5-tris(benzyloxy) benzoate] having substituents on the peripheral position, and we also notice the effects of the substituents on the spectroscopic and aggregation features of the porphyrazine complexes in various solvents and at several amount of matters in dichloromethane. The characterizations of recently prepared structures were maintained by utilizing several spectroscopic techniques such as FT-IR, UV–vis, ^{1}H NMR, ^{13}C NMR, mass, and elemental analysis. In order to prevent aggregation, inclusion of large bulky groups on the periphery has been proposed. The aggregation studies performed in varied amount of matters demonstrated that 3,4,5-tris(benzyloxy)benzoate-substituted porphyrazine complexes did not show any aggregation feature in the concentration series of 5×10^{-6} mol dm^{-3} to 1×10^{-4} mol dm^{-3}. The solubility feature investigations were carried out in the organic solvents with different polarity (acetone, chloroform, THF, and dichloromethane) and there was nearly no difference due to the changes in the type of the organic solvent. When porphyrazines are combined with benzyloxy groups, these groups may show a strong antioxidant effect. There is a considerable interest in the development of the structure-activity relationships for new porphyrazine derivatives. As a part of these endeavours, here we report the synthesis of a new series of porphyrazines having eight 3,4,5-tris(benzyloxy)benzoate substituents groups.

2. Results and discussion

The reaction between **1** and 5-chloro-1-pentanol was occurred **2** which is appropriate for the cyclotetramerization reaction to produce **3** in the existence of magnesium alcoholate as published by Wöhrle et al. [33] with higher polymethylene chain lengths (Scheme 1).

To ensure high solubility, ester groups were chosen due to the ease of their synthesis [16–29]. The ideal reaction conditions for the condensation of carboxylic acid and hydroxy groups on porphyrazine complexes were to perform the reaction at room temperature in the being of a highly dehydrating reactant such as dicyclohexylcarbodiimide. By filtering the reaction mixture after proceeding with cold dichloromethane, the dicyclohexylurea which was by-product was eliminated. By utilizing the MS data, the usage of DCCI-mediated esterification system for **3** ensured that all of the valid –OH units reacted in the process. The choice of reaction time was attributed with classical TLC tests and altered with varied cases. Other purpose of that method was to observe various esterification states on the reaction output. DCCI:OH unit in 9:1 concentration ratio demonstrated the best data [16–29]. The yield of **4** was at adequate level (64%) (Scheme 1). The porphyrazines with eight ester units which has symmetrically functionalized feature were soluble in some organic solvents such as acetone, $CHCl_3$, THF, DMSO, CH_2Cl_2, and toluene and insoluble in *n*-hexane and water. **4** was a convenient intermediary for producing porphyrazines with different metal (II) ions in the core (Fig. 1). The classical way of treatment with trifluoroacetic acid gave the metal-free derivative (**5**) which was further reacted with cobalt(II), copper(II), or zinc(II) acetate to give products having the respective metal (II) ions in the porphyrazine core (M = Co, Cu, Zn) (**6**–**8**) (Fig. 1). The reaction yields of **4**–**11** porphyrazine complexes were enough amount and 67%, 71%, 75%, 72%, 81%, 62%, 57%, and 54%, respectively.

The supplementation of Fe(II) ion into **5** was carried out in glacial CH_3COOH by utilizing freshly synthesized anhydrous $Fe(OAc)_2$ acetate salt (Scheme 2) [34–36]. The reaction was performed under inert atmosphere, but a little amount of O_2 induced to Fe(III) derivatives. The derivative was reacted with dilute HCl solution to vary the whole of the trivalent iron derivatives into **9**.

Owing to various magnetic features of metal(II) ions, Co(II), Cu(II) and Zn(II) acetate salts were chosen for metal porphyrazine complexes. The NMR spectra for paramagnetic metal (II) porphyrazine complexes **6** and **7** were not gotten due to the peak broadening and shifting expected for these porphyrazine complexes. The NMR spectra were taken only for diamagnetic Zn(II) ion complexes. The NMR spectrum of **8** was in accordance with the target structure. All ^{1}H and ^{13}C NMR spectral results of **8** were shown in the manuscript.

By having many spectroscopic methods such as elemental analysis, FT-IR, UV–vis, MS, ^{1}H NMR, and ^{13}C NMR, the characterization of the newly synthesized products was ensured. Spectral investigations for all new products were coherent with the target structures.

Elemental analyses comply much the same with the values calculated for (**3**–**11**).

In the FT-IR spectrum of **2**, the C≡N stretching vibration appeared at about 2222 cm^{-1}. After conversion of **2** into **3**, the C≡N stretching vibration disappeared. In the FT-IR spectra of **4**–**11** with [5-thiopentyl 3,4,5-tris(benzyloxy)benzoate] units, the aromatic C–H stretching vibration peaks at around 3056–3035 cm^{-1}, the aliphatic C–H stretching vibration peaks at around 2985–2840 cm^{-1}, O–C=O peaks at around 1251–1268 cm^{-1}, the aromatic C=C peaks at around 1641–1675 cm^{-1} as strong absorptions and the C=O vibration of the ester group appeared at around 1715–1726 cm^{-1} for **4**–**11**. Furthermore, the disappearance of the O–H stretching vibration peaks at around 3330 cm^{-1} for **3** and the N–H stretching vibrations of the inner core of porphyrazine structure were measured at around 3285 cm^{-1} for **5**, withal good solubility in organic solvents such as acetone, chloroform, dichloroform, and tetrahydrofuran got after this reaction, are all demonstrations for the formation of **4**–**11**. In the FT-IR spectrum of **9**, the band at 1125 cm^{-1} may be referred to the additive of axial