Synthesis, spectroscopic and crystallographic analysis of the Zn-complex of a di(β,β'-sulfoleno)pyrrin: model for Zn-complexes of bilirubin and of phylloxanthobilins

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Abstract A high yield preparation, spectroscopic and crystallographic investigation of the crystalline Zn-complex of a di(β,β'-sulfoleno)pyrrin are reported here. In the brightly green fluorescent Zn-complex of the hardly luminescent di((β,β'-sulfoleno)pyrrin, the metal ion is bound by two di(β,β'-sulfoleno)pyrrin ligands, as revealed first by its mass spectra. The crystal structure of this Zn-complex of the di((β,β'-sulfoleno)pyrrin confirmed a regular 2:1 composition of the bidentate di((β,β'-sulfoleno)pyrrin ligand and the metal ion. The latter was coordinated in a distorted tetrahedral fashion, as found in other dipyrrin Zn-complexes. The here studied Zn-complex of a designed di((β,β'-sulfoleno)pyrrin ligand provides insights into the coordination properties of the proposed (2:1)- and (2:2)-complexes of phylloxanthobilin and bilirubin, respectively, which are two abundant natural bilin-type tetrapyrroles.

Keywords Crystal structure · Dipyrrin · Fluorescence spectroscopy · Coordination chemistry · Zn-complex

Introduction

Dipyrrins (or dipyromethenes) feature two conjugated pyrrole rings and represent (formal) dipyrrolic building blocks for the construction of porphyrins and related tetrapyrrolic macrocycles [1]. The complexes of the bidentate dipyrrins with boron (the ‘BODIPY’-complexes) [2] or with transition metal ions [3, 4] have attracted particular attention due to the ‘predictable’ coordination properties of dipyrrins, and the tunable emission and absorption properties of their metal complexes [5–9]. Hence, the design of dipyrrin ligands has been attractive, and dipyrrin chemistry has taken advantage of the development of a broad range of strategies for their construction [2–5, 7, 8]. In one approach (used here), dipyrrins are prepared by dehydrogenation of easily accessible corresponding dipyrromethanes [3, 4].

In the context of our recent interest in the metal coordination properties of yellow chlorophyll catabolites
(phylloxanthobilins) [10], and of other natural linear tetrapyroles derived from chlorophyll [11, 12], we report here on our investigations of a model dipyrrrole, the di(β,β'-sulfoleno)pyrrin 2.

**Results and discussion**

Our synthetic route to di(β,β'-sulfoleno)pyrrin 2 relied on the earlier made corresponding di(β,β'-sulfoleno)pyrromethane (1), available, in turn, from condensation of 3,5-di-tert-butylbenzaldehyde and β,β'-sulfolenopyrrole [13]. Dipyrrromethane 1 was oxidized with dicyanodichlorobenzocinone (DDQ) to furnish bright yellow 2 in 76% yield, after crystallization in CH2Cl2/n-C6H14 (see Scheme 1). The UV/Vis spectrum of the dipyrrin 2, displayed in Fig. 1, exhibits characteristic maxima at 436.5 and 327 nm, comparable to the one of bilirubin [14, 15], or of a recently described yellow chlorophyll catabolite (YCC, a phylloxanthobilin) [16, 17]. A FAB-mass spectrum featured a strong pseudo-molecular ion at m/z = 513.1 [M - H]−, confirming its molecular formula as C27H32N2O4S2. Fragments at m/z = 448.2 and 384.2 indicated consecutive loss of the two SO2-groups. The 1H NMR spectrum of 2 exhibited two singlets at intermediate field of the two pairs of symmetry equivalent β-methylene groups, a singlet at 7.58 ppm of the pyrrole-α positions, the signals of aryl α- and β-protons at low field, and a broad signal of an NH at 12.76 ppm (see Fig. 2, bottom).

For the preparation of 3, a solution of 15 mg of Zn(OAc)2 2H2O (68.4 μmol, 18 eq) in 0.3 cm3 MeOH was mixed into a solution of 2 mg 2 (3.8 μmol) in 2.7 cm3 of CH2Cl2 at room temperature. After 5 min, the reaction mixture was worked up by extraction and evaporation of the solvent (see “Experimental” part). The Zn-complex 3 crystallized from CH2Cl2/n-C6H14 as pink-red crystals (2.0 mg, 94% yield).

The molecular formula of the dipyrrin Zn-complex 3 was indicated as C54H62N4O8S4Zn from analysis of its pseudo-molecular ion [M - H]− at m/z = 1087.2. Corresponding significant fragments occurred at m/z = 1023.3, 894.4, and 830.4, due to consecutive loss of the one, three, and four SO2-groups, respectively. The derived molecular formula of the Zn-complex 3 suggested the presence of two dipyrrin ligands 2 and one Zn(II)-ion, i.e. to represent Zn-(2)2 (see Scheme 2).

The pink-red Zn-complex 3 displayed a UV/Vis-spectrum in CH2Cl2 that featured a maximum at 487 nm (and a shoulder at 463 nm), corresponding to a 51 nm bathochromic shift, when compared with the spectrum of the dipyrrin 2 (see above). Similar bathochromic shifts of the absorption spectrum upon coordination of a Zn(II) ion were observed in Zn-complexes of bilirubin [18], or of phylloxanthobilins [10, 12]. Analysis of the Zn-complex 3 by fluorescence spectroscopy showed an intense emission band at 505 nm, whereas the metal-free dipyrrin 2 displayed little luminescence with a maximum around 530 nm (see Fig. 3). The excitation spectrum of dipyrrin Zn-complex 3, observed at 505 nm, fitted the absorption spectrum of 3. As, in contrast, the dipyrrin 2 was essentially non-luminescent in CH2Cl2, the rapid coordination of Zn ions and formation of 3 lightened up an intense green luminescence with about 200–300-fold higher intensity (see Fig. 3).

In the 1H NMR spectrum (in CDCl3, see Fig. 2) of the Zn-complex 3 [Zn-(2)2], a signal of an HN was lacking (which was found at 12.76 ppm in the spectrum of the dipyrrin 2), consistent with bidentate binding of the dipyrrin ligand 2 to the coordinated Zn(II) ion. Signals of aryl-α hydrogens and aryl-β hydrogen are slightly shifted to lower field while signals of β-methylene groups and pyrrole-α hydrogens are slightly moved to higher field.

X-ray diffraction quality crystals of the Zn-complex 3 grew from a solution of 3 in CH2Cl2 when n-C6H14 was
mixed in slowly at 4 °C. The Zn-complex 3 crystallized in the triclinic system with space group P-1 (no. 2). A unit-cell contained four molecules of 3. The crystal structure of 3 showed two bidentate dipyrrin moieties wrapped around one Zn(II) center leading to coordination in a distorted tetrahedral fashion with N–Zn–N angles of about 94, 113, and 121° (Fig. 4). The bonds of the four N atoms to the coordinated Zn ion are 1.98 Å long, consistent with crystallographic data from other Zn-dipyrrin complexes [19–21]. The structure of 3 in the triclinic crystal deviates slightly from the symmetric model reported for crystals of other bis(dipyrrinato) Zn-complexes [19]. The planes of the two dipyrrin ligands are roughly vertical to each other (82° dihedral angle), as are the aryl groups at the 5-position with respect to the conjugated pyrrole system in the same ligand moiety (85°). Thus, the plane defined by one aryl group at the meso-position is observed at 3.8° with respect to the plane of the conjugated pyrrole system in the other ligand. In contrast, the other aryl group at 5-position is inclined by 17.1° with respect to the conjugated pyrrole system in the second dipyrrin unit. Probably, these small symmetry-deviations are consequences of the packing in the triclinic crystal. The bond lengths and bond angles within the dipyrrin ligands in 3 are similar to those of other bis(dipyrrinato) Zn-complexes [19–21]. The crystal structure of 3 reflects the symmetric, bidentate coordination behavior of the dipyrrin 2. Thus, the Zn-complex 3 may represent a valuable model for the chelation pattern in non-crystalline Zn(II)-complexes of natural oligopyrroles with similar chromophores, e.g. of bilirubin [18] or of the phylooxanthobilin YCC [10].
Conclusion

Dipyrrin 2 is a yellow dipyrrole that possesses two conjugated pyrrolic rings and shows negligible luminescence. It may be considered a simple model compound for the chromophore part of some natural tetrapyrroles, such as the heme-derived bilirubin (BR) [14, 15] and phylloxanthobilins [17] or yellow chlorophyll catabolites (YCCs) [10, 16]. Binding of Zn(II) ions to the bidentate furnishes the 2:1 complex, the crystal structure of which exhibited a distorted tetrahedral structure. This type of coordination pattern was derived for the (2:1)-complex of a YCC with Zn(II) ions [10]. Similar, furthermore, to observation with the Zn(II)-complex of the YCC [10], the bis(dipyrrinato) Zn-complex displays intensive green luminescence.

Hence, the present study helps to model the coordination behavior of Zn-complexes of natural oligopyrroles with similar conjugated chromophores, e.g. of BR [18] or of YCC [10, 12], and to gain basic insights into their luminescence properties. Bis(dipyrrinato) Zn-complexes, and related boron complexes of dipyrrins (BODIPYs) [2], exhibit intensive and tunable absorption and emission properties, which make them useful in various optical applications [5–7, 9]. In contrast to BODIPYs, bis(dipyrrinato) Zn-complexes exhibit a tetrahedral coordination pattern in 2:1 assemblies (ligand: Zn), giving them considerable potential in supramolecular structuring [21, 22]. The sulfoleno-units of the dipyrrin 2 and of the bis(dipyrrinato) Zn-complex 3 are, furthermore, ‘programmed’ for introduction of covalent modifications at the pyrrole β-positions by [4+2]-cycloaddition reactions. As was recently developed with porphyrinoids, such as tetra-sulfolenoporphyrins [23–25] and a tetra-sulfolenocorrole [13], the dipyrrinato-units of 2 and 3 could, thus, also open up efficient access to further designed functionalized supramolecular assemblies.

Experimental

Dichlorodicyano-p-benzoquinone (DDQ) and zinc acetate dihydrate [Zn(OAc)2 2H2O] were reagent grade commercial chemicals from Fluka and were used as received; EtOAc, dichloromethane, methanol (MeOH), and n-C6H14 were from Acros and were distilled before use. Column chromatography (CC): Fluka silica gel 60 (230–400 mesh). Thin layer chromatography (TLC): Merck 0.25 mm silica gel 60 plates. Equipment: UV/Vis: Agilent Cary 60 UV–Visible, \( \lambda_{\text{max}} \) in nm (log ε). Fluorescence (FL): Varian Cary Eclipse, \( \lambda \) in nm (rel. intensity); Nuclear magnetic resonance (1H) spectra: Bruker 300 at 298K, chemical shifts (\( \delta \)) in ppm, with \( \delta \) (CHCl3) = 7.26 ppm, signal assignment follows the X-ray numbering scheme. FAB-MS: Finnigan MAT-95, positive ion mode, NOBA matrix; X-ray analyses: data collection on a Nonius Kappa CCD, equipped with graphite mono-chromatized Mo-K\( \alpha \)-radiation (\( \lambda = 0.71073 \) Å) at 233K. Melting point: Büchi 535.

5-(3,5-Di-tert-butylphenyl)-di(b, b'-sulfoleno)pyrrin (2, C23H32N2O4S4)

To the solution of 2 mg dipyrromethane 1 (3.8 μmol) [13] in 1 cm³ CH2Cl2 1.4 mg DDQ (6.2 μmol, 1.6 equiv) was added. After 20 h at room temperature, the reaction mixture was diluted to 20 cm³ with CH2Cl2 and washed with saturated aq. NaHCO3 (3 × 15 cm³). The organic phase was filtered through a plug of dry cotton-wool and evaporated to dryness under reduced pressure to give a brown residue. The residue was dissolved in 1.5 cm³ CH2Cl2 and loaded on a silica gel column (1.5 × 10 cm). The product was washed down with CH2Cl2/EtOAc 10/1 (v/v). The collected product fractions were combined and concentrated to dryness under reduced pressure to furnish 2.

Fig. 3 Fluorescence spectra of 2 and 3 in CH2Cl2 (top: 2, \( 4 \times 10^{-6} \) mol/dm³, EM: excited at 436 nm, EX: observed for 530 nm; bottom: 3, \( 4 \times 10^{-6} \) mol/dm³, EM: excited at 487 nm, EX: observed for 505 nm)
as a yellow residue. Dipyrrin 2 was isolated after crystallization from CH$_2$Cl$_2$/n-C$_6$H$_{14}$ (1/4 cm$^3$) at 4°C as 1.5 mg of yellow crystals (yield 76%). M.p.: 178°C; UV/Vis (CH$_2$Cl$_2$): $\lambda_{max}$ (log $\varepsilon$) = 327 (3.72), 436.5 (4.42) nm; fluorescence emission (CH$_2$Cl$_2$, $c = 4 \times 10^{-6}$ mol/dm$^3$, excited at 436 nm, rel. intensity): 530 nm (1.00); fluorescence excitation (obs. for 530 nm, rel. intensity): 437 (1.00), 330 (0.40) nm; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 1.35$ (s, CH$_3$ of t-Bu), 3.17 (s, H$_2$C$_3^1$, H$_2$C$_7^1$), 4.10 (s, H$_2$C$_2^1$, H$_2$C$_8^1$), 7.06 (d, $J = 1.7$ Hz, HC$_5^1$, HC$_5^2$), 7.58 (s, HC$_1$, HC$_9$), 7.61 (t, $J = 1.7$ Hz, HC$_5^4$), 12.76 (br s, HN$_{11}$) ppm; FAB-MS: m/z (%) = 515.2 (14), 514.2 (33), 513.1 (100), [M+H]$^+$, calcd. for C$_{27}$H$_{33}$N$_2$O$_8$S$_2$ (512.18), 450.1 (10), 449.2 (27), 448.2 (32, [M−SO$_2$]$^+$), 386.2 (15), 385.2 (52), 384.2 (75, [M−2SO$_2$]$^+$).

Bis(5-(3,5-di-tert-butylphenyl)-di(bis(5,5-sulfoleno)pyrrinato) Zn-complex (3, C$_{54}$H$_{62}$N$_4$O$_8$S$_4$Zn)

Dipyrrin 2 (2 mg, 3.8 μmol) was dissolved in 2.7 cm$^3$ CH$_2$Cl$_2$ and the solution of 15 mg Zn(OAc)$_2$·2H$_2$O (68.4 μmol, 18 eq.) in 0.3 cm$^3$ MeOH was added. After 5 min, the reaction mixture was diluted to 15 cm$^3$ with CH$_2$Cl$_2$ and washed with saturated aq. NaHCO$_3$ (3 cm$^3$). The organic layer was filtered through a plug of dry cotton wool and evaporated to dryness under reduced pressure to give a red residue. After crystallization in CH$_2$Cl$_2$/n-C$_6$H$_{14}$ (1.5/4 cm$^3$) at 4°C, 2 mg of 3 were obtained as pink-red crystals, yield is 94%. M.p.: > 195°C (decomp.); UV/Vis (CH$_2$Cl$_2$): $\lambda_{max}$ (log $\varepsilon$) = 242 (4.07), 357.5 (3.81), 385sh (3.66), 463sh (4.51), 487 (4.82) nm; fluorescence emission (CH$_2$Cl$_2$, $c = 4 \times 10^{-6}$ mol/dm$^3$, 2.895 Å, N(3) 2.912 Å, N(4) 3.301 Å, Zn(1) 2.172 Å, Zn(2) 2.172 Å, H atoms and tert-butyl substituents at meso-aryl groups are omitted).

Model of the distorted tetrahedral core of 3, with specified lengths Zn-N bonds and distances between the N’s (left part) and N-Zn-N bond angles of the Zn–N$_4$ core (right part). e Bond lengths (left) and bond angles (right) in the dipyrrin cores of 3.

Bis(5-(3,5-di-tert-butylphenyl)-di(bis(5,5-sulfoleno)pyrrinato) Zn-complex 3, C$_{54}$H$_{62}$N$_4$O$_8$S$_4$Zn

Zn-complex (3, C$_{54}$H$_{62}$N$_4$O$_8$S$_4$Zn)

Dipyrrin 2 (2 mg, 3.8 μmol) was dissolved in 2.7 cm$^3$ CH$_2$Cl$_2$ and the solution of 15 mg Zn(OAc)$_2$·2H$_2$O (68.4 μmol, 18 eq.) in 0.3 cm$^3$ MeOH was added. After 5 min, the reaction mixture was diluted to 15 cm$^3$ with CH$_2$Cl$_2$ and washed with saturated aq. NaHCO$_3$ (3 × 10 cm$^3$). The organic layer was filtered through a plug of dry cotton wool and evaporated to dryness under reduced pressure to give a red residue. After crystallization in CH$_2$Cl$_2$/n-C$_6$H$_{14}$ (1.5/4 cm$^3$) at 4°C, 2 mg of 3 were obtained as pink-red crystals, yield is 94%. M.p.: >195°C (decomp.); UV/Vis (CH$_2$Cl$_2$): $\lambda_{max}$ (log $\varepsilon$) = 242 (4.07), 357.5 (3.81), 385sh (3.66), 463sh (4.51), 487 (4.82) nm; fluorescence emission (CH$_2$Cl$_2$, $c = 4 \times 10^{-6}$ mol/dm$^3$, 2.895 Å, N(3) 2.912 Å, N(4) 3.301 Å, Zn(1) 2.172 Å, Zn(2) 2.172 Å, H atoms and tert-butyl substituents at meso-aryl groups are omitted).

Model of the distorted tetrahedral core of 3, with specified lengths Zn-N bonds and distances between the N’s (left part) and N-Zn-N bond angles of the Zn–N$_4$ core (right part). e Bond lengths (left) and bond angles (right) in the dipyrrin cores of 3.
excited at 487 nm, rel. intensity): 505 nm (1.00); fluorescence excitation (obs. for 505 nm, rel. intensity): 486 (1.00), 461sh (0.49), 355 (0.10) nm; 1H NMR (300 MHz, CDCl3): \( \delta = 1.40 \) (s, CH3 of t-Bu), 3.11 (s, H3C31, H3C71), 4.09 (s, H2C21, H2C81), 7.11 (d, \( J = 1.7 \) Hz, HC52, HC522), 7.54 (s, HC11, HC9), 7.66 (t, \( J = 1.7 \) Hz, HC54) ppm (due to the symmetric structure, only half molecular chemical shifts were labeled here); FAB-MS: \( m/z = 1087.2 \) ([M+H]+), calcld. for Cs5H62N4O8S4Zn 1086.27), 1023.3 ([M–SO2]+), 894.4 ([M–3SO2]+), 830.4 ([M–4SO2]+).

Crystalllographic data: Cs5H62N4O8S4Zn × CH2Cl2 × 0.75 C6H14, formula weight: 1238.24; temperature 233(2) K; radiation wavelength 0.71073 Å; crystal system triclinic; space group P-1 (no. 2); unit cell dimensions \( a = 18.5998(4) \) Å, \( b = 18.9173(3) \) Å, \( c = 21.6741(5) \) Å, \( \alpha = 98.771(1)^\circ \), \( \beta = 104.394(1)^\circ \), \( \gamma = 109.204(1)^\circ \); volume 6743.1(4) Å³; \( Z = 4; \) density (calculated) 1.220 g/cm³; absorption coefficient 0.618 mm⁻¹; crystal size 0.25 × 0.25 × 0.03 mm³; \( F(000) = 2606 \) \( \theta \) theta range for data collection 1.335°–24.145°; index ranges \(-21 \leq h \leq 21, -21 \leq k \leq 21, -24 \leq l \leq 24 \); reflections collected 36397; independent reflections 21231 \( R(int) = 0.0379 \); completeness to theta (24.145°) 98.5%; absorption correction none; refinement correction none; refinement Full-matrix least-squares on \( F^2 \); data/restraints/parameters 21231/29/1; crystal size 0.45 × 0.45 × 0.03 mm³; \( R_w = 0.0769, wR_2 = 0.1998, R_1 = 0.1148, wR_2 = 0.2209 \). Crystalllographic data of 3 (Zn(2)) (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC no. 1453954. Copies of the data can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://summary.ccdc.cam.ac.uk/structure-summary-form.

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