Thianaphthene–Annulated Tetrapyrazinoporphyrazines⊗

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Tetrapyrazinoporphyrazine with fused thianaphthene fragments, i.e. tetra(benzo[4',5']thieno[2',3':5,6]pyrazino[2,3-b,g,l,q]porphyrazine, [H_2TSNpPyzPA], and its tetra-tert-butyl-substituted derivative, [H_2TSNpPyzPA^{t}Bu$_4$], having enhanced solubility in organic solvents, have been prepared by cyclotetramerization in a melt of corresponding benzo[4,5]thieno[2,3-b]pyrazine-2,3-dicarbonitriles obtained by condensation of diaminomaleodinitrile with 2,3-thianaphthenquinones [2,3-dihydrobenzo[b]thiophene-2,3-diones] easily available by acylation of thiophenols with oxalylchloride.

Keywords: Porphyrazines, tetrapyrazinoporphyrazines, thianaphthene, benzo[*b*]thiophene, spectral properties.

Porphyrazines (PA) with annulated aromatic heterocycles are widely investigated in different areas of practical application and for this reason a steady interest is observed in the synthesis and study of their representatives.[1] Among them a family of peripherally substituted tetra(pyrazino)porphyrazines (TPyzPA, see Chart 1) attract an increased attention in recent years. Thus, tetrapyrazinoporphyrazines bearing eight α-pyridyl groups (R = α-Py)[2] exhibit a remarkable electron deficient properties of the macrocyclic ligand and ability to peripheral coordination of palladium.[2d] These species as well as TPyzPA substituted with eight phenyl, 2-thienyl, 2-furyl, alkoxy, dialkylamino and alkylthio groups are actively investigated for their use in photodynamic therapy.[3]

The eight peripheral substituents in these TPyzPA derivatives are only partly involved in conjugation with the macrocyclic chromophore. Annulation of aromatic rings to the pyrazine fragments is another way of structural modification of TPyzPA leading to π-extended macrocyclic systems. Few reports on such π-extended TPyzPA includes benzohomologues, *i.e.* octa(2,3-quinoxalino)porphyrazines [MQxPA],[4-7] octa(naphtho)pyrazinoporphyrazines [MTNpPyzPA],[5,6,8] octa(9,10-phenanthro)-pyrazinoporphyrazines [MTPnPyzPA][9] and species with fused *N*-heterocycles – tetra(2,3-pyrrolo)-,[10] tetra(2,3-indolo)-,[11] and tetra(2,3-pyrazino)-[12] annulated TPyzPA (Chart 1). We have succeded in preparation of the novel TPyzPA derivatives with fused *S*-containing heterocycle and report here the synthesis of the first representative of 2,3-thianaphtheno-annulated species [MTSNpPyzPA], obtained as the free base [H_2TSNpPyzPA] (**6a**) and its *tert*-butyl substituted derivative [H_2TSNpPyzPA^{t}Bu$_4$] (**6b**).

Easily available commercial chemicals – thiophenol (**1**), oxalylchloride (**2**) and diaminomaleodinitrile (**4**) have been used for the two-step preparation of the dinitrile precursor **5** which can be then used directly for the synthesis of tetra(2,3-thianaphtheno)-annulated TPyzPA derivatives (Scheme 1). Treatment of thiophenol **1** (0.144 mol) with equimolar amount of oxalylchloride **2** (14.6 ml, 0.144 mol) under vigorous stirring leads to acylation of the thiol group and solidification of the

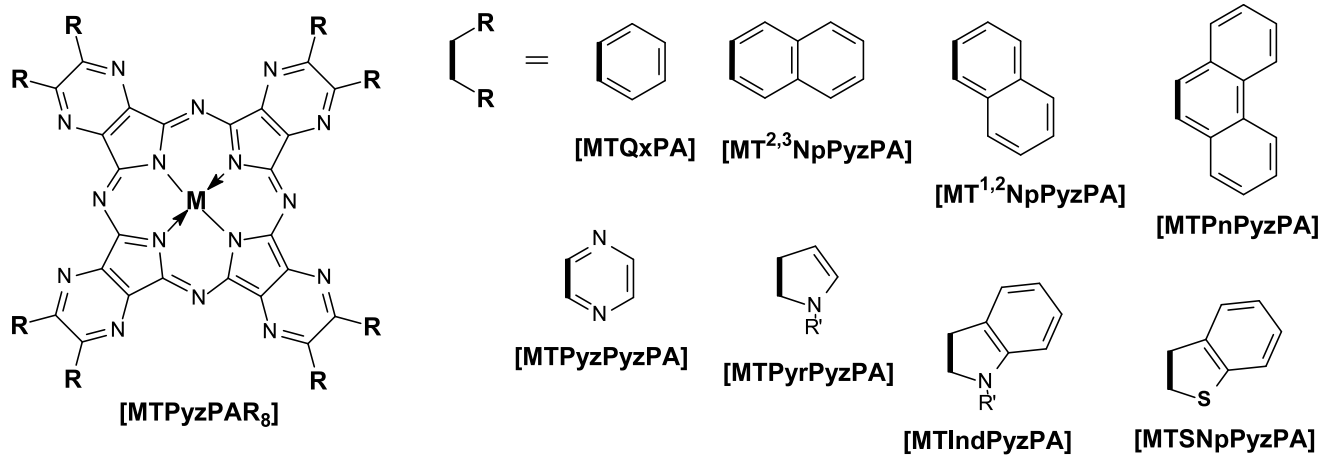
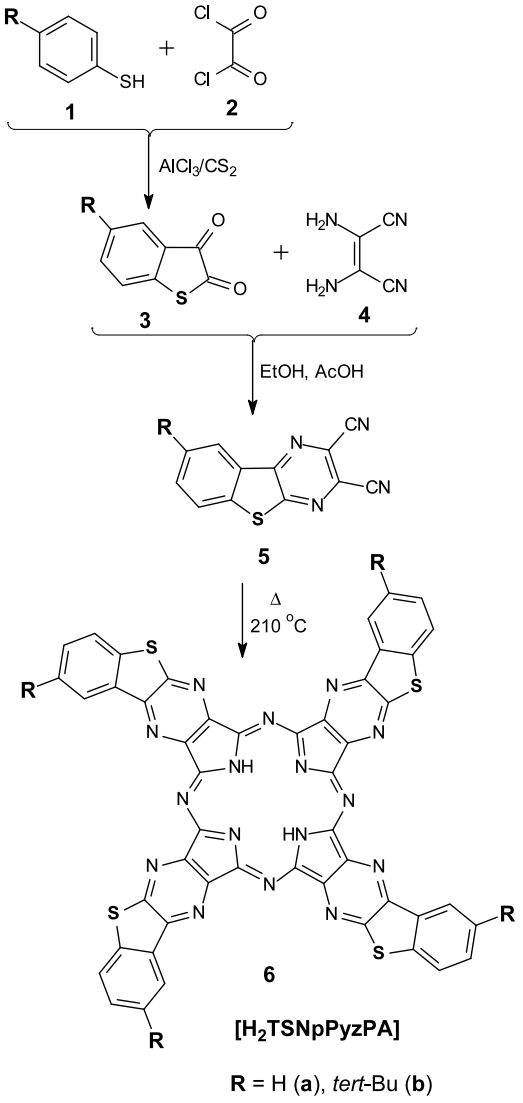


Chart 1. Peripherally substituted and annulated tetrapyrazinoporphyrazines (TPyzPA).

⊗ This contribution is dedicated to professor Vasilij Fedorovich Borodkin on the occasion of his 100th Anniversary.



Scheme 1. Synthesis of thianaphthene annulated TPyzPA.

reaction mixture. After its dissolution in carbon disulfide and cooling till 0-5 ºC anhydrous $AlCl_3$ (38.5 g, 0.288 mol) was added cautiously in portions under stirring (30 min) to perform the intramolecular acylation with formation of 2,3-thianaphthenequinone (**3**). The crude orange product obtained after evaporation of the solvent at 45-50 ºC and overnight treatment of the residue with ice was separated by filtration and purified by dissolution in 10% aqueous $NaHCO_3$ solution with following acidification with conc. HCl leading to precipitation of 2,3-thianaphthoquinones [2,3-dihydrobenzo[*b*]thiophene-2,3-diones] **3** as bright orange products.[#]

On the second stage quinone **3** (0.03 mol) was condensed with diaminomaleodinitrile **4** (3.3 g, 0.03 mol)

[#] **3a**. Yield 53 %. M.p.= 121-122 ˚C. Calc. for $C_8H_4SO_2$ (%): C, 58.54; H, 2.41; S, 19.51; O, 19.51. Found (%): C, 58.03; H, 2.27; S, 19.95; O, 19.81. ν_{max} (KBr)/cm^{-1} 1731s (ν(C=O)), 1714s (ν(C=O)), 1589s, 1573m, 1467s, 1452s, 1359s, 1342s, 1282s, 1241s, 1147s, 1108vs, 1060s, 962s, 842s, 748m.

3b. Yield 63%. M.p.=103 ˚C. Calc for $C_{12}H_{12}SO_2$ (%): C, 65.43; H, 5.49; S, 14.56; O, 14.53. Found (%): C, 64.58; H, 4.88; S, 13.39; O, 13.48. ν_{max} (KBr)/cm^{-1} 3072m (ν$(CH)_{arom}$), 2964s, 2871m, 1708vs (ν(C=O)), 1596s, 1562m, 1477s, 1365m, 1288m, 1257m, 1201m, 1110m, 1004m, 919m, 850m. ^{1}H NMR ($CDCl_3$): δ, ppm 7.84 (1H, m, Ar-*H*), 7.69 (1H, m, Ar-*H*), 7.39 (1H, m, Ar-*H*), 1.33 (9H, s, *tert*-Bu).

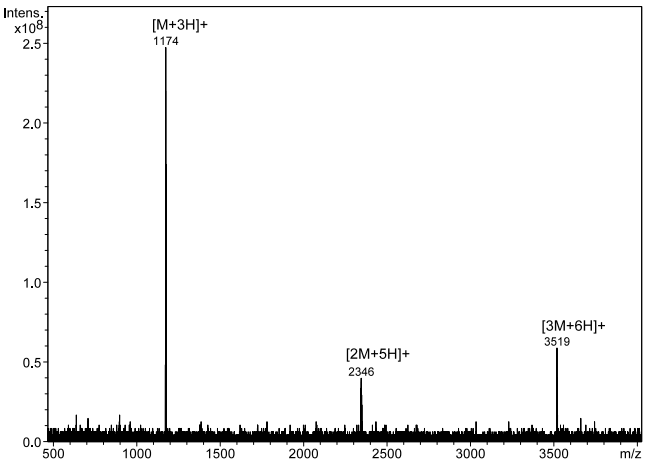


Figure 1. MALDI-TOF mass spectrum of [H_2TSNpPyzPA^{t}Bu$_4$] (**6b**) (matrix - 3,5-dihydroxybenzoic acid).

by heating under reflux in ethanol (30 ml) containing acetic acid (0.8 ml) for 40 min. After evaporation of the solvent and purification by column chromatography on silica (eluent - chloroform) benzo[4,5]thieno[2,3-*b*]pyrazine-2,3-dicarbonitriles **5** were obtained.[§]

Dinitriles **5** appeared to be very reactive in cyclotetramerization and formation of the free base porphyrazine macrocycle occurs spontaneously when they are heated above melting point at 210-220 °C for 10-15 min. Usually cyclotetramerization of dinitriles (*e.g.* phthalodinitriles) with formation of free base porphyrazines require higher temperatures and/or presence of sterically hindered *N*-bases[1] (*N*,*N*-dimethylaminoethanol, 1,8-diazabicyclo-[5.4.0]undecene) as a basic catalyst. Cyclotetramerization of dinitriles **5** upon melting seems to be a self-catalytic reaction. Due to low solubility of the unsubstituted porphyrazine **6a**, its purification is troublesome. The *tert*-butyl substituted derivative [H_2TSNpPyzPA^{t}Bu$_4$] (**6b**) which is well soluble in organic solvents can be easily purified by column chromatography on alumina using chloroform as an eluent.[¶]

The structure of **6b** was confirmed by the MALDI-TOF mass-spectrum (Figure 1), which contains the cluster peak at *m/z* = 1171 (100%) corresponding to molecular ions

[§] **5a**. Yield 64%. M.p.=214 ºC. Calc. for $C_{12}H_4N_4S$ (%): C, 61.01; H, 1.71; N, 23.71; S, 13.57. Found (%): C, 60.59; H, 1.23; N, 23.09; S, 13.56. ν_{max} (KBr)/cm^{-1} 3076w, 3056w, 3018w, 2239s (ν(CN)), 1641m, 1592s, 1513s, 1438s, 1407m, 1332vs, 1311s, 1255m, 1211vs, 1160s, 1103s, 798m, 765s, 736m, 694m, 453m, 426m.

5b. Yield 67%. M.p.=210 ºC. Calc. for $C_{16}H_{12}N_4S$ (%): C, 65.73; H, 4.14; N, 19.16; S, 10.97. Found (%): C, 64.68; H, 3.84; N, 17.83; S, 10.63. IR (KBr): ν, cm^{-1} 3085w, 3033w, 2962s, 2865m, 2239s (ν(C≡N)), 1606m, 1519m, 1477m, 1465m, 1363m, 1313vs, 1295m, 1268m, 1253m, 1211s, 1160m, 1093m, 977m, 829m, 698m, 464m.^{1}H NMR ($CDCl_3$): δ, ppm 8.59 (1H, m, Ar-*H*), 7.96 (2H, m, Ar-*H*), 1.49 (9H, s, *tert*-Bu).

[¶] **6a**. Yield 25%. Calc. for $C_{48}H_{18}N_{16}S_4$ (%): C, 60.88; H, 1.92; N, 23.66 ; S, 13.54. Found (%): C, 54.28; H, 1.39; N, 18.46; S, 14.63. λ_{max} (DMF) (relative intensity)/nm 635 (0.84), 674 (1).

6b. Yield 30%. Calc. for $C_{64}H_{50}N_{16}S_4$ (%): C, 65.62; H, 4.30; N, 19.13; S, 10.95. Found (%): C, 65.90; H, 4.95; N, 18.80; S, 10.17. UV-vis λ_{max} (CH_2Cl_2) (lgε)/nm 307 (4.24), 360 (4.41), 418 (4.10), 460sh, 613sh, 635 (3.92), 668 (4.41), 691 (4.48). δ_H ($CDCl_3$, 298 K) 9.2-9.4 (4H, m, Ar-*H*), 7.8-8.0 (8H, m, Ar-*H*), 1.61 (36H, s, *tert*-Bu), -1.6 (2H, br, N*H*).

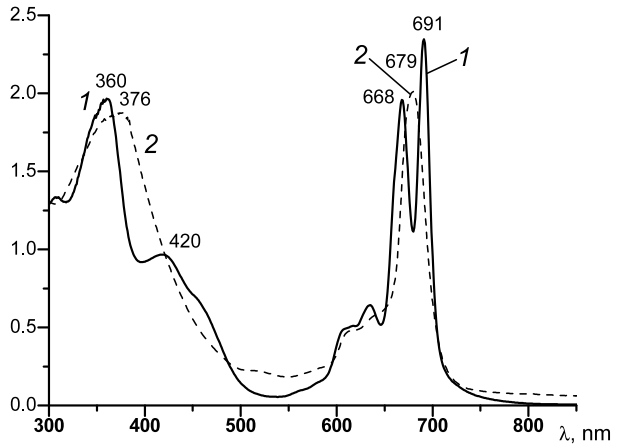


Figure 2. UV-vis spectrum of [H_2TSNpPyzPA^{t}Bu$_4$] (**6b**) in CH_2Cl_2 (*1*) and its changes after addition of tbaOH (*2*).

$[M+nH]^+$ (n = 1-3) accompanied by peaks of the dimer $[2M+nH]^+$ at m/z = 2346 (16%, n = 2-5) and trimer at m/z = 3519 $[3M+nH]^+$ (24%, n = 3-6).

The UV-vis spectrum of [H_2TSNpPyzPA^{t}Bu$_4$] (**6b**) is typical for porphyrazine free bases having the effective D_{2h} symmetry of the π-chromophore (Figure 2, spectrum *1*). It contains the intense absorption bands arising from the π-π* transitions of the porphyrazine π-chromophore: the split *Q*-band in the visible region (668 and 691 nm) and broad Soret band at 360 nm in the UV region. The maxima of the *Q*- and Soret bands for tetrapyrazinoporphyrazines **6a** and **6b** with fused thianaphthene fragments are shifted bathochromically as compared to non-annulated tetrapyrazinoporphyrazines. Thus, for [H_2TPyzPA^{t}Bu$_4$] in $CHCl_3$ solution the *Q*-bands were observed at 617 and 653 and Soret band at 340 nm.[13] This bathochromic shift is caused mainly by destabilization of HOMOs due to interaction of the thianaphthene fragments with the TPyzPA π-chromophore. However, the observed effect is much less than in the case of formally isoelectronic 2,3-annulation of naphthalene fragments (λ_Q = 803 nm for [H_2T^{2,3}NpPyzPA] in 1-chloronaphthalene[8b]), and even less than in the case of benzo annulation (λ_Q = 712 nm for [H_2TQxPA^{t}Bu$_4$] in $CHCl_3$[7]). It means that the 10π-electron system of thianaphthene is not involved as a whole in conjugation with the macrocyclic TPyzPA π-chromophore. Evidently the S atom exhibits an "insulating" effect and the interaction can be better described as *+C* effect of phenyl group. Similar situation was observed[11] for the isoelectronic indole annulated TPyzPA, [H_2TIndPyzPA^{t}Bu$_4$] (the Soret band at 364 nm and the double *Q*-band at 688 and 708 nm in $CHCl_3$ for *N*-amyl substituted species).

The splitting of the *Q*-band in the UV-vis spectrum of **6b** disappears and it is merged in a single band with maximum at 679 nm after addition of tetrabutylammonium hydroxide (tbaOH, Figure 2, spectrum *2*). This is due to deprotonation of the internal pyrrolic NH groups with formation of an anionic form with effective D_{4h} symmetry of the π-chromophore. Deprotonation leads also to disappearance of the absorption in 400-460 nm region which can be very likely assigned to the intramolecular charge transfer transition from thianaphthene fragments to the electron-deficient TPyzPA chromophore.

In conclusion, we have prepared and characterised the first representatives of a new family of S-containing porphyrazine derivatives – tetrapyrazinoporphyrazines with fused thianaphthene fragments, isolated as free bases. They are formed by self-catalytic cyclotetramerization of benzo[4.5]thieno[2.3:5.6]pyrazino-2,3-dicarbonitriles occurring upon their melting. Metal complexes, which are available by template condensation of these dinitriles in the presence of metal salts, are currently investigated.

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