Syntheses of Thiazole-Containing Macroheterocycles Related to Porphycene

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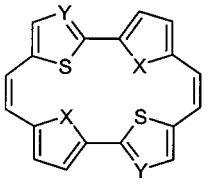
Dedicated to Prof. Dr. Dr. *h.c. mult. Albert Eschenmoser* on the occasion of his 75th birthday

The syntheses of 2,2′-bithiazole-containing and related expanded macrocycles **13**–**16** were accomplished by the *McMurry* coupling reaction of the corresponding [2,2′-bithiazole]-5,5′-dicarbaldehyde **6c** and 2,2′-(1,4-phenylene)bis[thiazole-5-carbaldehyde] **7**, readily available by a two-step reaction sequence. The success of the dimerization strongly depends on the steric repulsion of the substituents vicinal to the CHO group.

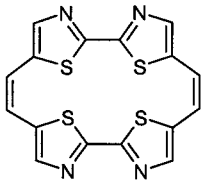
1. Introduction. – In recent years, a number of studies have been conducted concerning the use of porphyrinoids for biomedical applications such as fluorescence detection, viral inhibition, and photodynamic tumor therapy (PDT) [1]. Thus, the synthesis of structurally modified porphyrins, porphycenes and related conjugated macrocycles is of particular interest due to their potential use as photosensitizers for biomedical applications [1], as well as to their aromatic properties as annulene derivatives [2]. In this context, many attempts have been made to modify the porphyrin ring system to generate more effective chromophores for PDT as well as to get insights into the fundamental criteria defining aromaticity [3].

Since a strong absorption at long wavelengths is desirable for application in PDT [1] [4], we investigated the synthesis of S-containing porphycene analogous like **1** and **2**, and observed remarkable changes in the structural and chemical properties of these compounds [4].

Recently, we introduced additional N-atoms at the peripheral positions of the porphycene analogue **2** and described the syntheses of a new family of dihydro-3,13-diaza-21,23-dithiaporphycenes **3** [5]. After oxidation of **3**, the resulting aromatic macroheterocycles show a strong bathochromic shift of the long-wavelength absorption band in the UV/VIS absorption spectra, and thus might be interesting compounds for PDT [5].



1 X = S, Y = CH
2 X = NH, Y = CH
3 X = NH, Y = N



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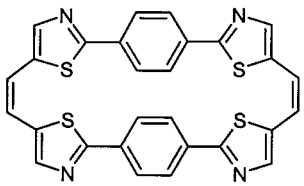

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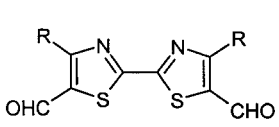
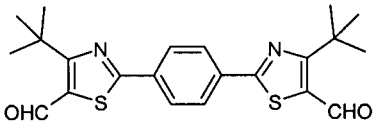
The 2,2′-bithiazole moieties, the major structural component of **4**, have been reported as a class of heterocycles possessing interesting biological activities like luminescence, DNA-cleaving activity, and inhibition of platelet aggregation [6]. As part of our studies on the use of thiazole as a building block for the syntheses of macrocycles related to porphycene, we became interested in the synthesis of the porphyrinoid **4**, which would combine the properties found in **3** and those found in 2,2′-bithiazoles. We also were interested in the synthesis of expanded thiazole-containing macrocycles **5** and in the investigation of the properties of this new core-modified porphyrinoid[1]).

Results and Discussion. – The most efficient route to porphycenes and analogous macrocycles involves the intermolecular dimerization of dicarbonyl compounds with low-valent titanium under *McMurry* conditions [7] [8]. Thus, the 2,2′-bithiazole-dicarbaldehydes **6a–c** [9] and the 2,2′-(1,4-phenylene)bis[4′-(*tert*-butyl)-thiazole-5-carbaldehyde] (**7**) should be suitable precursors for the preparation of macrocycles such as **4** and **5**.



6a R = H
b R = Br
c R = ^{t}Bu



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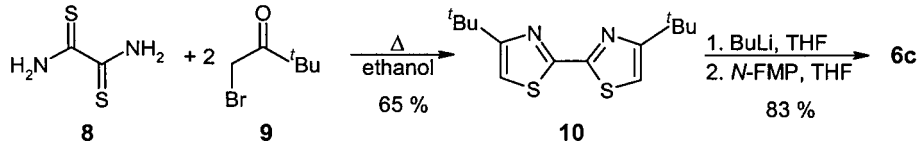
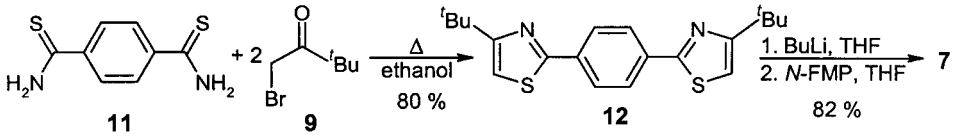
Indeed, compounds **6c** and **7** were readily available by a two-step reaction sequence from the related thiocarbamides **8** or **11** as starting material[2]) [10]. As shown in *Scheme 1*, the thiazole-containing subunit **10** or **12** could be obtained in good yields by cyclocondensation of **8** or **11** with the α-halo ketone **9** in EtOH. After treatment of **10**

Scheme 1





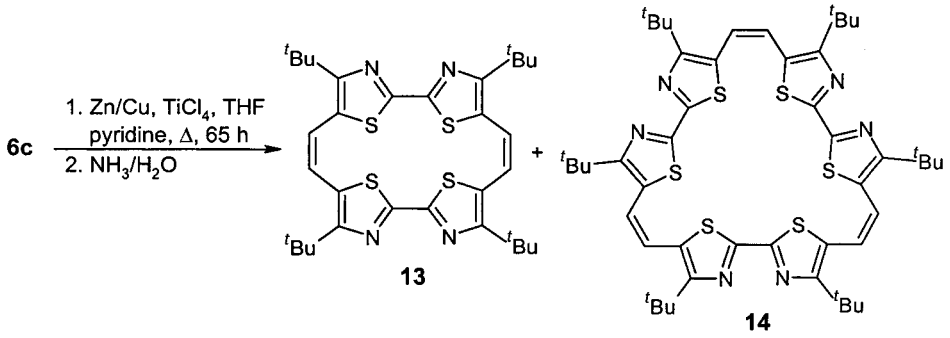
[1]) A MM2 force-field calculation of **5** performed on Chem3D Pro (Version 4.0) indicated, in contrast to **4**, that the formation of a nearly planar ring system by oxidation of **5** should be possible.

[2]) We have previously reported the syntheses of **6a–c** [9].

or **12** with 2 equiv. of BuLi in dry THF at $-78°$ and quenching of the resulting dilithiated intermediates with *N*-formylmorpholine (= morpholine-4-carboxaldehyde; *N*-FMP), the desired dicarboxaldehydes **6c** and **7** were readily formed [11]. To complete deprotonation of **10** or **12**, the reaction mixture had to be warmed to $-30°$ for 60 min after addition of BuLi.

According to our optimized procedures [5], the reductive *McMurry*-type dimerization of the bis-formylated subunit **6c** with low-valent titanium prepared by treatment of $TiCl_4$ with the Zn/Cu couple in THF gave, after workup and chromatographic purification on silica gel, a yellow product containing a mixture of the desired 1,4,11,14-tetraaza[20]annulene **13** and the related hexaaza[30]annulene **14**. This mixture could only be separated by gel permeation chromatography (GPC), giving **13** and **14** as yellow, air- and light-stable crystals in a yield of 6.4 and 9.8%, respectively (*Scheme 2*). However, by application of this methodology to the dimerization of the corresponding dicarbaldehydes **6a**,**b** [9], the intermolecular *McMurry* coupling did not afford a desired [20]annulene like **4**. Only polymeric material could be obtained, in contrast to the results observed for the reaction of **6c**. A possible reason for the success of the dimerization of **6c** could be the preorientation of the CHO groups induced by the bulky vicinal substituents [12].

Scheme 2

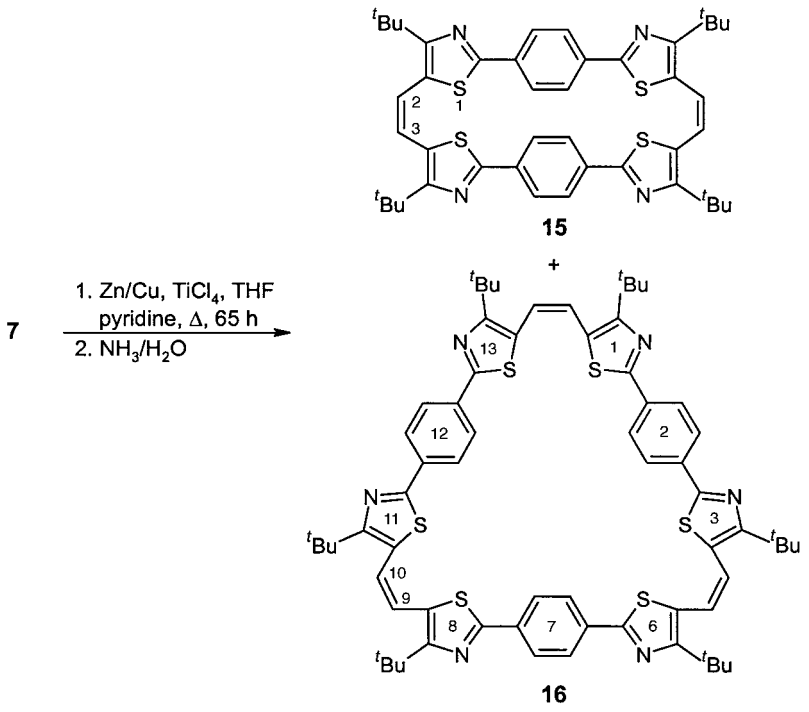


The spectroscopic properties of the thiazole-derived annulenes **13** and **14** are similar to those of the related compounds **1**–**3** and do not reflect the typical paratropic behavior of the planar annulene structures of the porphycenes [4] [5] [13]. The ^{1}H-NMR spectrum of **13**, *e.g.*, shows 1*s* at 6.92 ppm for the olefinic protons and 1*s* at 1.39 ppm for the ^{t}Bu groups, indicative of a symmetrical structure without an obvious ring current. The UV/VIS spectrum of **13**, which shows no absorption maximum over 400 nm, exhibits only modest conjugation between the bithiazole units, as expected for a non-planar conformer [5] [14]. The spectroscopic properties of the aza[30]annulene **14** are very similar to those of **13**.

The reductive *McMurry*-type dimerization can also be applied to the synthesis of the phenylene-expanded cyclophane **15** by dimerization of the dicarbaldehyde **7** (*Scheme 3*). After chromatographic purification on silica gel followed by gel-permeation chromatography, pure **15** was obtained in 9.8% yield. However, the cyclophane **16** could be obtained as the main product in a yield of 21.8%. The yellow

crystalline products **15** and **16** show spectroscopic properties similar to those of the macroheterocycles **13** and **14** described above. The ^{1}H-NMR spectrum of **15**, *e.g.*, shows 3 *s* at 7.58 (arom. H), 6.96 (olefinic H), and 1.43 (^{t}-Bu) ppm, indicating that there is no obvious ring current in the molecule besides that of the heterocyclic moieties. Thus, it can be assumed that the molecules are non-planar [5] [14].

Scheme 3



Although an aromatization of the cyclophane **15** seemed to be possible[1]), all attempts to convert **15** by oxidation with several oxidation reagents into the corresponding expanded dicationic aromatic porphycene analogue failed. In all cases, unchanged **15** was recovered.

In conclusion, we have shown that bithiazole-dicarbaldehydes can be used as building blocks for the synthesis of thiazole-containing macrocycles related to porphycene as well as for the synthesis of expanded porphyrinoids by *McMurry* coupling. The success of these dimerizations strongly depends on the presence of a bulky substituent in the position vicinal to the CHO group of **6** and **7**. The property of the 2,2′-bithiazole moiety in **13** and **14** with respect to the complexation of transition-metal atoms could provide a series of metallic complexes with interesting properties [6]. Continuous work in this direction is in progress.

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Experimental Part

General. All reactions requiring anh. and anaerobic conditions were carried out under Ar in flame-dried glassware. Solvents were purified and dried according to standard procedures [14]. THF was distilled from potassium benzophenone prior to use. Column chromatography (CC): silica gel (60–200 mesh) from *E. Merck KGaA*, Darmstadt. Gel permeation chromatography (GPC): *Bio-Beads-S-X1* gel permeation gel (200–400 mesh) from *Bio-Rad*, München, swelled in THF. M.p.: *Reichert* melting-point microscope; uncorrected. UV/Vis Spectra: *Hewlett-Packard-HP-8452A* diode array spectrophotometer; λ_{max} in nm ($\lg \varepsilon$). IR Spectra: *Perkin-Elmer-PE-1600-FT-IR* spectrophotometer; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Bruker-WM-250* spectrometer (at 250.13 and 62.9 MHz, resp.) or *Bruker-AM-360* spectrometer (at 360.12 and 90.6 MHz, resp.); chemical shifts δ in ppm rel. to internal $SiMe_4$; *J* values in Hz. EI-MS: *Varian-MAT-311-A* mass spectrometer or *JOEL-JEI-MS-700* sector-field mass spectrometer at 70 eV; *m/z* (rel.%). Elemental analyses: *Foss-Heraeus Vario EL*.

*4,4′-Di(*tert-*butyl)-2,2′-bithiazole* (**10**). To a suspension of dithiooxamide (**8**; 2.40 g, 20.0 mmol) in dry EtOH (50 ml), 1-bromo-3,3-dimethylbutan-2-one (**9**; 5.9 ml, 44.0 mmol) was added in one portion. The mixture was stirred under reflux for 6 h (→ yellow precipitate). After cooling to 0°, the resulting black mixture was filtered and the yellow precipitate dissolved in Et_2O (300 ml). The org. layer was neutralized with sat. aq. $NaHCO_3$ soln. (100 ml), washed with H_2O (2 × 50 ml), dried ($MgSO_4$) and evaporated. Recrystallization of the crude product from hexane yielded pure **10** (3.65 g, 65%). Colorless needles. M.p. 169°. UV/VIS (CH_2Cl_2): 230 (3.89), 238 (sh, 3.79), 330 (4.16), 346 (sh, 3.99). IR (KBr): 3121*m*, 2960*s*, 2923*m*, 2900*m*, 1504*m*, 1492*s*, 1451*m*, 1396*s*, 1357*s*, 1233*m*, 1103*m*, 961*s*, 886*s*, 880*s*, 750*s*. ^1H-NMR ($CDCl_3$, 250 MHz): 6.94 (*s*, H–C(5), H–C(5′)); 1.37 (*s*, 2 ^{t}Bu). ^{13}C-NMR ($CDCl_3$, 63 MHz): 167.8; 160.9; 112.0; 34.9; 30.1. EI-MS: 280 (93, M^+), 265 (100, $[M - Me]^+$), 250 (10, $[M - 2\ Me]^+$), 249 (28), 125 (20), 111 (20), 97 (13), 65 (14). HR-MS: 280.1068 ($C_{14}H_{20}N_2S_2^+$; calc. 280.1068). Anal. calc. for $C_{14}H_{20}N_2S_2$: C 59.96, H 7.18, N 9.98, S 22.86; found: C 59.90, H 7.11, N 10.09, S 23.12.

*2,2′-(1,4-Phenylene)bis[4-(*tert-*butyl)thiazole]* (**12**). To a suspension of dithioterephthalamide (**11**; 1.97 g, 10.0 mmol) in dry EtOH (60 ml), 1-bromo-3,3-dimethyl-butan-2-on (**9**; 2.8 ml, 21.0 mmol) was added in one portion. The mixture was stirred under reflux for 3 h. After cooling to r.t., the yellow soln. was diluted with $CHCl_3$ (300 ml), neutralized with sat. aq. $NaHCO_3$ soln. (100 ml), and washed with H_2O (3 × 100 ml). The org. layer was dried ($MgSO_4$), filtered, and evaporated, the residue purified by CC (hexane/AcOEt, 10:3), and the crude product recrystallized from EtOH: **12** (2.85 g, 80%). Colorless prisms. M.p. 112°. UV/VIS (CH_2Cl_2): 239 (3.94), 341 (4.49), 359 (sh, 4.29). IR (KBr): 3122*w*, 2959*s*, 2865*m*, 1503*s*, 1456*m*, 1366*m*, 1281*w*, 1251*m*, 1101*m*, 987*s*, 917*m*, 840*s*, 747*s*, 705*m*, 602*s*. ^1H-NMR ($CDCl_3$, 250 MHz): 7.99 (*s*, C_6H_4); 6.90 (*s*, 2 H, H–C(5)); 1.49 (*s*, 2 ^{t}Bu). ^{13}C-NMR ($CDCl_3$, 63 MHz): 168.1; 166.1; 135.2; 126.8; 110.6; 35.0; 30.1. EI-MS: 356 (100, M^+), 341 (81, $[M - Me]^+$), 325 (20), 227 (12), 163 (29), 65 (20), 45 (17). HR-MS: 356.1380 ($C_{20}H_{24}N_2S_2^+$; calc. 356.1381). Anal. calc. for $C_{20}H_{24}N_2S_2$: C 67.37, H 6.78, N 7.85, S 17.99; found: C 67.49, H 6.73, N 7.83, S 17.92.

Dicarbaldehydes **6c** *and* **7**: *General Procedure.* To a soln. of 5.0 mmol of **10** or **12** in dry THF (100 ml), 1.6M BuLi in hexane (6.9 ml, 11.0 mmol) was added slowly within 15 min at −78°. To complete deprotonation, the mixture was warmed to −30° for 60 min. Then the suspension was cooled to −78° and a soln. of *N*-formylmorpholine (1.38 g, 12.0 mmol) in dry THF (5 ml) was added slowly. After stirring for an additional 2 h at −78°, the mixture was allowed to warm to r.t. within 6 h and then added to a soln. of 2N HCl (100 ml) with ice cooling. The aq. phase was neutralized with solid $NaHCO_3$ and extracted with CH_2Cl_2 (4 × 50 ml). The combined org. phases were washed with H_2O (50 ml), dried ($MgSO_4$), and evaporated. The crude product was purified by recrystallization.

*4,4′-Di(*tert-*butyl)-2,2′-bithiazole-5,5′-dicarbaldehyde* (**6c**): Recrystallization from hexane yielded pure **6c** (1.40 g, 83%). Yellow needles. M.p. 272°. UV/VIS (CH_2Cl_2): 236 (4.02), 268 (3.68), 368 (4.41), 390 (sh, 4.23). IR (KBr): 2970*m*, 2901*w*, 2869*w*, 1653*s*, 1480*m*, 1437*w*, 1385*m*, 1314*m*, 1220*m*, 1196*m*, 1180*m*, 989*m*, 727*w*, 675*w*. ^1H-NMR ($CDCl_3$, 250 MHz): 10.46 (*s*, 2 CHO); 1.57 (*s*, 2 ^{t}Bu). ^{13}C-NMR ($CDCl_3$, 91 MHz): 183.6; 172.9; 163.5; 136.8; 37.7; 31.9. EI-MS: 336 (100, M^+), 321 (77, $[M - CH_3]^+$), 307 (36, $[M - CHO]^+$), 293 (30), 266 (77), 195

(20), 99 (32), 83 (19), 65 (22), 55 (15), 45 (23). HR-MS: 336.0966 ($C_{16}H_{20}N_2O_2S_2^+$; calc. 336.0966). Anal. calc. for $C_{16}H_{20}N_2O_2S_2$: C 57.12, H 5.99, N 8.32, S 19.06; found: C 57.24, H 5.95, N 8.42, S 18.86.

*2,2′-(1,4-Phenylene)bis[4-(*tert*-butyl)thiazole-5-carbaldehyde]* (**7**). Recrystallization from toluene/hexane 1:1 yielded pure **7** (1.70 g, 82%). Yellow crystals. M.p. 285–287°. UV/VIS (CH_2Cl_2): 246 (4.14), 391 (4.47). IR (KBr): 3045*w*, 2962*s*, 2925*m*, 2865*m*, 1651*s*, 1435*m*, 1392*m*, 1361*w*, 1286*m*, 1199*s*, 1001*s*, 839*m*, 687*m*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 10.45 (*s*, 2 CHO); 8.10 (*s*, C_6H_4); 1.60 (*s*, 2 ^{t}Bu). ^{13}C-NMR ($CDCl_3$, 63 MHz): 183.4; 173.1; 170.0; 135.3; 134.7; 127.6; 37.8; 32.0. EI-MS: 412 (100, M^+), 397 (61, $[M-CH_3]^+$), 383 (33, $[M-CHO]^+$), 369 (24), 342 (88), 99 (14). HR-MS: 412.1278 ($C_{22}H_{24}N_2O_2S_2^+$, calc. 412.1279). Anal. calc. for $C_{22}H_{24}N_2O_2S_2$ (412.56): C 64.05, H 5.86, N 6.78, S 15.54; found: C 64.09, H 5.71, N 6.90, S 15.70.

McMurry-*Cyclization of Dicarbaldehydes* **6c** *and* **7**: *General Procedure.* To a suspension of the Zn/Cu couple (4.0 g, 60.0 mmol) in dry THF (200 ml), $TiCl_4$ (3.3 ml, 30.0 mmol) was added by syringe at 0° within 15 min. After addition of dry pyridine (1.5 ml), the suspension was refluxed for 2 h. To this freshly prepared and gently refluxing *McMurry* suspension, a soln. of 3.0 mmol of **6c** or **7** in dry THF (500 ml) was added dropwise within 60 h. After stirring an additional 5 h under reflux, the dark yellow mixture was allowed to cool to r.t. and filtered through *Celite*. The filtrate was hydrolyzed with 13% aq. NH_3 soln. (400 ml) and extracted with CH_2Cl_2 (3 × 200 ml). The org. layer was washed with H_2O (2 × 200 ml), dried ($MgSO_4$), and evaporated. CC (hexane/ACOEt, 10:1) yielded one yellow fraction containing a mixture of dimer and trimer, which were separated by GPC (THF).

5,10,15,20-Tetra-(tert-*butyl)-2,19:3,6:9,12:13,16-tetraepithio-1,4,11,14-tetraaza[20]annulene* (=*4,9,14,19-Tetra(*tert-*butyl)-21,22,23,24-tetrathia-3,10,13,20-tetraazapentacyclo[16.2.1.1.*^{2,5}*.1*^{8,11}*.1*^{12,15}*]tetracosa-1(20),2,4,6,8,10,12,14,16,18-decaene*; **13**) *and 5,10,15,20,25,30-Hexa(*tert-*butyl)-2,29:3,6:9,12:13,16:19,22:23,26-hexaepithio-1,4,11,14,21,24-hexaaza[30]annulene* (=*4,9,14,19,24,29-Hexa(*tert-*butyl)-31,32,33,34,35,36-hexathia-3,10,13,20,23,30-hexaazaheptacyclo[26.2.1.1*^{2,5}*.1*^{8,11}*.1*^{12,15}*.1*^{18,21}*.1*^{22,25}*]hexatriaconta-1(30),2,4,6,8,10,12,14,16,18,20, 22,24,26,28-pentadecane:* **14**): On GPC (THF), trimer **14** was eluted first, followed by the dimer **13**.

Data of **13**: Recrystallization from hexane yielded **13** (58.3 mg, 6.4%). Yellow prisms. M.p. 285–287°. UV/VIS (CH_2Cl_2): 335 (4.36), 380 (sh, 3.78). IR (KBr): 3028*w*, 2959*s*, 2924*m*, 2900*m*, 2864*m*, 1497*s*, 1483*m*, 1404*m*, 1389*m*, 1180*m*, 963*s*, 948*w*, 879*m*, 803*m*, 609*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 6.92 (*s*, H–C(7), H–C(8), H–C(17), H–C(18)); 1.39 (*s*, 4 ^{t}Bu). ^{13}C-NMR ($CDCl_3$, 91 MHz): 163.6; 159.2; 130.9; 127.2; 36.5; 30.5. EI-MS: 608 (100, M^+), 593 (41, $[M-Me]^+$), 304 (8, M^{2+}), 83 (10), 69 (20), 57 (46, ^{t}Bu$^+$). HR-MS: 608.2138 ($C_{32}H_{40}N_4S_4^+$, calc. 608.2136). Anal. calc. for $C_{32}H_{40}N_4S_4$ (608.95): C 63.12, H 6.62, N 9.19, S 21.06; found: C 63.25, H 6.51, N 9.13, S 21.18.

Data of **14**: Recrystallization from hexane yielded **14** (89.1 mg, 9.8%). Yellow prisms. M.p. >350°. UV/VIS (CH_2Cl_2): 230 (4.12), 266 (3.98), 342 (4.57), 370 (sh, 4.17). IR (KBr): 2962*s*, 2928*m*, 2866*m*, 1506*m*, 1480*m*, 1410*m*, 1364*m*, 1220*w*, 966*s*, 882*m*, 806*w*, 686*w*. ^{1}H-NMR ($CDCl_3$, 250 MHz): 6.87 (*s*, H–C(7), H–C(8), H–C(17), H–C(18), H–C(27), H–C(28)); 1.42 (*s*, 6 ^{t}Bu). ^{13}C-NMR ($CDCl_3$, 63 MHz): 162.9; 158.1; 127.1; 124.8; 36.1; 30.4. EI-MS: 912 (100, M^+), 897 (15, $[M-Me]^+$), 456 (21, M^{2+}), 441 (5), 57 (20, ^{t}Bu$^+$). HR-MS: 912.3208 ($C_{48}H_{60}N_6S_6^+$; calc. 912.3204). Anal. calc. for $C_{48}H_{60}N_6S_6$ (913.39): C 63.12, H 6.62, N 9.19, S 21.06; found: C 63.07, H 6.63, N 9.23, S 21.11.

1^4*,3*^{4}*,6*^{4}*,8*^{4}*-Tetra(*tert-*butyl)-1,3,8(2,5),6(5,2)-tetrathiazola-2,7(1,4)-dibenzenacyclodecaphan-4,9-dien-* (=*4,9,18,23-Tetra(*tert-*butyl)-31,32,35,36-tetrathia-3,10,17,24-tetraazaheptacyclo[24.2.2.2.*^{12,15}*.1*^{2,5}*.1*^{8,11}*.1*^{16,19}*.1*^{22,25}*]-hexatriaconta-1(28),2,4,6,8,10,12,14,16,18,20,22,24,26,29,33-hexadecaene;* **15**) *and 1*^{4}*,3*^{4}*,6*^{4}*,8*^{4}*,11*^{4}*,13*^{4}*-Hexa(*tert-*butyl)-1,3,8,13(2,5),6,11(5,2)-hexathiazola-2,7,12(1, 4)-tribenzenacyclopentadecaphan-4,9,14-triene* (=*4,9,18,23,32,37-Hexa(*tert-*butyl)-45,46,49,50,53,54-Hexathia-3,10,17,24,31,38-hexaazadecacyclo[38.2.2.2*^{12,15}*.2*^{26,29}*.1*^{2,5}*.1*^{8,11}*.1*^{16,19}*.1*^{22,25}*.1*^{30,33}*.1*^{36,39}*]tetrapentaconta-1(42),2,4,6,8,10,12,14,16,18,20,22,24,26,28,30,32,34,36,38,40,43,47,51-tetracosaene;* **16**)[3]. On GPC (THF), trimer **16** was eluted first, followed by dimer **15**.

Data of **15**: Recrystallization from hexane/$CHCl_3$ 1:1 yielded **15** (112.2 mg, 9.8%). Yellow prisms. M.p. 353–354°. UV/VIS (CH_2Cl_2): 255 (4.82), 262 (4.89), 270 (4.84), 352 (4.80). IR (KBr): 3047*w*, 2956*s*, 2899*m*, 2864*m*, 1499*m*, 1457*s*, 1391*m*, 1305*w*, 1246*m*, 1111*w*, 987*s*, 921*w*, 852*m*, 730*m*, 684*w*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 7.58 (*s*, H–C(2^2), H–C(2^3), H–C(2^5), H–C(2^6), H–C(7^2), H–C(7^3), H–C(7^5), H–C(6^6)); 6.97 (*s*, H–C(4), H–C(5), H–C(9), H–C(10)); 1.47 (*s*, 4 ^{t}Bu). ^{13}C-NMR ($CDCl_3$, 91 MHz): 165.1; 163.9; 134.5; 126.9; 126.7; 124.5; 36.4; 30.8. EI-MS: 760 (100, M^+), 745 (16, $[M-Me]^+$), 380 (11, M^{2+}), 71 (14), 57 (14, ^{t}Bu$^+$). HR-MS: 760.2761 ($C_{44}H_{48}N_4S_4^+$, calc. 760.2762). Anal. calc. for $C_{44}H_{48}N_4S_4$ (761.13): C 69.43, H 6.36, N 7.36, S 16.85; found: C 69.35, H 6.43, N 7.45, S 16.82.

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[3] For phane nomenclature, see [15].

Data of **16**: Recrystallization from toluene yielded **16** (250.2 mg, 21.8%). Yellow prisms. M.p. $>350°$. UV/VIS (CH_2Cl_2): 365 (5.04). IR (KBr): 3032*w*, 2955*s*, 2899*m*, 2863*m*, 1507*m*, 1481*m*, 1452*m*, 1390*w*, 1362*m*, 1252*m*, 1187*m*, 1109*m*, 989*s*, 850*m*, 836*m*, 758*m*. ^{1}H-NMR ($CDCl_3$, 360 MHz): 7.79 (*s*, H–C(2^2), H–C(2^3), H–C(2^5), H–C(2^6), H–C(7^2), H–C(7^3), H–C(7^5), H–C(7^6), H–C(12^2), H–C(12^3), H–C(12^5), H–C(12^6)); 6.89 (*s*, H–C(4), H–C(5), H–C(9), H–C(10), H–C(14), H–C(15)); 1.49 (*s*, 6 ^{t}Bu). ^{13}C-NMR ($CDCl_3$, 91 MHz): 164.1; 163.6; 134.6; 126.5; 125.7; 122.9; 36.4; 30.8. EI-MS: 1140 (36, M^+), 1125 (35, $[M-Me]^+$), 764 (31), 750 (41), 570 (7, M^{2+}), 274 (70), 234 (20), 135 (100), 57 (30, $^tBu^+$). Anal. calc. for $C_{66}H_{72}N_6S_6$ (1141.69): C 69.43, H 6.36, N 7.36, S 16.85; found: C 69.34, H 6.36, N 7.33, S 17.10.

REFERENCES

[1] 'Porphyrin Photosensitization', Ed. D. Kessel and J. Dougherty, Plenum Press, New York 1983; C. J. Gomer, 'Photodynamic Therapy', Pergamon Press, Oxford 1987; T. J. Dougherty, *Pharm. News* **1994**, *1*, 15; D. Dolphin, *Can. J. Chem.* **1994**, *72*, 10005; R. Bonnett, *Chem. Soc. Rev.* **1995**, 19; E. D. Sternberger, D. Dolphin, C. Brückner, *Tetrahedron* **1998**, *54*, 4151; D. Wöhrle, A. Hirth, T. Bogdahn-Rai, G. Schnurpfeil, M. Shopova, *Russ. Chem. Bull.* **1998**, *47*, 807; A. Hirth, U. Michelsen, D. Wöhrle, *Chem. in unserer Zeit* **1999**, *33*, 84.

[2] P. J. Garratt, 'Aromaticity', J. Wiley & Sons, New York, 1986; H. Hosoya, *Top. Curr. Chem.* **1990**, *153*, 255; E. Vogel, *Pure Appl. Chem.* **1993**, *65*, 143; E. Vogel, *J. Heterocycl. Chem.* **1996**, *33*, 1461.

[3] J. K. Sessler, A. K. Burell, *Top. Curr. Chem.* **1991**, *161*, 177; B. Franck, A. Nonn, *Angew. Chem.* **1995**, *107*, 1941; *Angew. Chem., Int. Ed.* **1995**, *34*, 1795; J. K. Sessler, S. J. Weghorn, 'Expanded, Contracted and Isomeric Porphyrins', Pergamon Press, Oxford 1997; A. Jasat, D. Dolphin, *Chem. Rev.* **1997**, *97*, 2267; F.-P. Montforts, M. Glasenapp-Breiling, D. Kusch, 'Methods of Organic Chemistry (Houben-Weyl)' 4th edn. Thieme, Stuttgart 1998, vol. IV/E 9d, p. 577.

[4] G. DeMunno, F. Lucchesini, R. Neidlein, *Tetrahedron* **1993**, *49*, 6863; F. Ellinger, A. Gieren, T. Hübner, J. Lex, F. Lucchesini, A. Merz, R. Neidlein, J. Salbeck, *Monatsh. Chem.* **1993**, *124*, 931; U. Dahlmann, C. Krieger, R. Neidlein, *Eur. J. Org. Chem.* **1998**, 525.

[5] T. Nussbaumer, C. Krieger, R. Neidlein, *Eur. J. Org. Chem.* **2000**, submitted.

[6] N. Seko, K. Yoshino, K. Yokota, G. Tsukamoto, *Chem. Pharm. Bull.* **1991**, *39*, 651; H. Sasaki, S. Takanori, K. Yamamoto, Y. Nakamoto, *Chem. Pharm. Bull.* **1996**, *44*, 1761; H. Sasaki, A. Suehiro, Y. Nakamoto, *Chem. Pharm. Bull.* **1997**, *45*, 189; J-M. Lehn, J-B. Regnouf de Vains, *Helv. Chim. Acta* **1992**, *75*, 1221; V-M. Mukkala, P. Liitti, I. Hemmilae, H. Takalo, C. Matachescu, K. Jouko, *Helv. Chim. Acta* **1996**, *79*, 295; J-B. Regnouf de Vains, S. Pellet-Rostaing, R. Lamartine, P. Meallier, S. Guittonneau, B. Fenet, *Helv. Chim. Acta* **1997**, *80*, 1229; H. Sasaki, S. A. Kane, S. M. Hecht, *J. Am. Chem. Soc.* **1995**, *117*, 9107; J-B. Regnouf de Vains, S. Pellet-Rostaing, R. Lamartine, *Tetrahedron Lett.* **1996**, *37*, 5889; J-B. Regnouf de Vains, S. Pellet-Rostaing, R. Lamartine, B. Fenet, *Inorg. Chem. Commun.* **1999**, *2*, 44.

[7] J. E. McMurry, *Chem. Rev.* **1989**, *89*, 1513; D. Lenoir, *Synthesis* **1989**, 883; A. Fürstner, B. Bogdanovic, *Angew. Chem.* **1996**, *108*, 2582; *Angew. Chem., Int. Ed.* **1996**, *35*, 2442.

[8] E. Vogel, M. Köcher, H. Schmickler, J. Lex, *Angew. Chem.* **1986**, *98*, 262; *Angew. Chem., Int. Ed.* **1986**, *25*, 257.

[9] T. Nussbaumer, R. Neidlein, *Heterocycles* **2000**, *52*, 349.

[10] J. V. Metzger, 'Comprehensive Heterocyclic Chemistry', Pergamon Press, Oxford 1984, Vol. 6, p. 235.

[11] A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, *Synthesis* **1987**, 998.

[12] E. Vogel, M. Balci, K. Pramod, P. Koch, J. Lex, O. Ermer, *Angew. Chem.* **1987**, *99*, 909; *ibid. Int. Ed. Engl.* **1987**, *26*, 928; R. Guilard, M. A. Aukauloo, C. Tardieux, E. Vogel, *Synthesis* **1995**, 1480; S. Nonell, N. Bou, J. I. Borrell, J. Teixido, A. Villanueva, A. Juarranz, M. Canete, *Tetrahedron Lett.* **1995**, *36*, 3405.

[13] A. Strand, B. Thulin, O. Wennerström, *Acta Chem. Scand. B* **1977**, *32*, 521; K. Ankner, B. Lamm, B. Thulin, O. Wennerström, *J. Chem. Soc., Perkin Trans. 2* **1980**, 1301; Z. Hu, J. L. Atwood, M. P. Cava, *J. Org. Chem.* **1994**, *59*, 8071.

[14] D. D. Perrin, W. L. F. Armarego, 'Purification of Laboratory Chemicals', 3rd edn., Pergamon Press, Oxford 1988.

[15] W. H. Powell, *Pure Appl. Chem.* **1998**, *70*, 1513.

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