Syntheses of Octa(2-heteroaryl) Azaphthalocyanines

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Abstract. Magnesium, copper(II) and nickel(II) complexes of octasubstituted azaphthalocyanines **3** – **5** have been prepared from di-fur-2-yl, di-thien-2-yl and di-pyrid-2-yl pyrazine-2,3-dicarbonitriles **2**. Compounds **2** were prepared in good yields from condensations of diaminomaleonitrile and the diketones 2,2'-furil, 2,2'-thenil and 2,2'-pyridil. AzaPcs **3**–**5** give green pyridine solutions with Q-bands at 650–670 nm and ε-values of 60 000–190 000.

AzaPcs, the aza-analogues of phthalocyanines, are presently receiving considerable attention, and have been explored for applications, *e.g*. as traditional industrial dyes and pigments [1], as advanced materials in high technology applications [2], and in photodynamic cancer therapy [3]. An important quality of the AzaPcs, compared to the Pcs, is the enhanced solublility caused by the additional nitrogen atoms in the macrocycle. Substituents in the periphery of the AzaPcs may further enhance their solubility, and also influence the electronic excitation energies of these compounds.

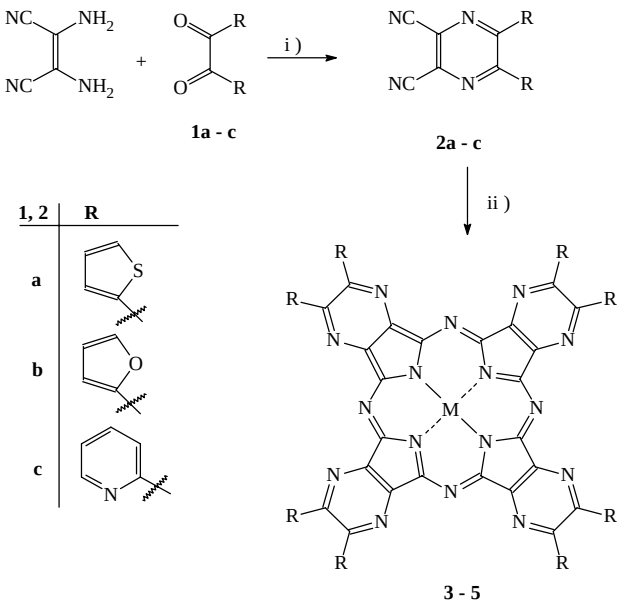
Previously, we have reported [4–6] octasubstituted AzaPcs where heteroatoms, *i.e.* sulfur, oxygen or nitrogen link the substituents to the macrocycle. Some of the sulfur-, and all of the oxygen-bound substituents were exchangeable during the cyclotetramerization reactions, due to the electron-withdrawing pyrazine-dicarbonitrile system.

Octasubstituted AzaPcs with carbon linked substituents are better known, and in addition to those mentioned in a recent review [7], there are other examples, *e.g*. [8–11]. Condensation reactions of diaminomaleonitrile and α-diketones give pyrazine-dicarbonitriles, which are cyclized to this type of substituted AzaPcs.

Presently our aim was to synthesize octasubstituted AzaPcs with heteroaromatic side chains bound to the macrocycle through carbon–carbon bonds, thus providing stable substituents. The heteroaromatic substituents are expected to influence both polarity and the electronic spectra of the macrocycles.

Results and Discussion

Diaminomaleonitrile (DAMN) and the α-diketones 2,2'-thenil (**1a**), 2,2'-furil (**1b**) and 2,2'-pyridil (**1c**) gave the corresponding pyrazines **2a**–**c**. Compounds **2a** and **2b** were obtained in good yields from reactions in acetic acid solutions, whereas no reaction was observed between **1a** or **1b** with DAMN in refluxing acetonitrile. However, **2c** was obtained



i) HOAc or MeCN, reflux
ii) Mg, PrOH, reflux , or, $CuCl_2$, $HCONH_2$, or, $NiCl_2$, $HCONH_2$

3-5	M	R
3a	Mg	
4a	Mg	
4b	Cu	
4c	Ni	
5a	Mg	
5b	Cu	

Scheme 1 Syntheses of octa(2-heteroaryl)azaphthalocyanines

  1436-9966/99/3410X-83 $ 17.50 + .50/0

in 79% yield upon heating **1c** and DAMN in acetonitrile. The electron withdrawing pyridine rings of **1c** apparently facilitate the condensation with DAMN. In one experiment, where less solvent was used for the preparation of **2c**, a high melting product was obtained as a precipitate from the acetonitrile solution after a reaction time of about one hour. This product was identified as a dihydrate of compound **2c**, 5,6-dihydro-5,6-di-pyrid-2-yl-5,6-di-hydroxypyrazine-2,3-di-carbonitrile.

Reactions of **2** with magnesium propoxide in propanol gave MgAzaPcs **3a** and **4a** in good yields, and **5a** in 31% yield. Attempts to use magnesium methoxide in methanol for these preparations gave mixtures of decomposition products and the target compounds which could not be purified. The magnesium complexes **3a, 4a** and **5a** are easily soluble in pyridine and give green solutions.

Cu(II) AzaPc **4b** was obtained from a hot formamide solution of **2b** and anhydrous cupric chloride. A similar reaction between **2c** and cupric chloride gave **5b** in admixture with **5b** complexed with additional copper. The element analyses showed higher than the calculated value of copper, even after stirring the product with aqueous ammonium hydroxide for 24 hours. The TOF-SIMS MS analysis of this product clearly identified **5b** as $(M + H)^+$ at 1 200 u, and also $(M + Cu)^+$ at 1 262 u. Fragmentation patterns indicate that the additional copper atoms are complexed to, or between, the pyridine substituents. Nickel(II) AzaPc **4c** was prepared from nickel(II) chloride and **2b** in hot formamide and was identified as a quasimolecular ion peak pattern in a negative TOF-SIMS spectrum. However, thiophene substituted pyrazine **2a** gave only decomposition products from reactions with nickel(II) or copper(II) chloride.

These examples indicate that exploration of analogous AzaPcs would be of interest.

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Experimental

Mass spectra were obtained on an AEI MS-902 spectrometer at 70 eV electron energy. IR spectra were obtained on a Nicolet 20-SXC FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX 400 NMR spectrometer at 399.65 MHz and at 100.40 MHz, respectively, and with tetramethylsilane (TMS) as internal standard. UV/VIS spectra were obtained on a Perkin Elmer 522 UV-VIS spectrophotometer. Microanalyses were performed by *Analytische Laboratorien*, D-51789 Lindlar, Germany. The TOF-SIMS (Ar^+) mass spectra of **4c** and **5b** were obtained by *Institut Fresenius Angewandte Festkörperanalytik GmbH*, 65220 Taunusstein,Germany. Melting points were obtained on a Büchi 530 melting point apparatus and are uncorrected. Merck Kieselgel 60F 254 was used for TLC and Merck silica 63–200 µm was used for column chromatography. Diaminomaleonitrile was obtained from Janssen, 1-propanol was dried over potassium carbonate, distilled and stored over molecular sieves, 3 Å. 2,2'-Furil (**1b**), and 2,2'-pyridil (**1c**), were obtained from Aldrich. *2,2'-Thenil* (**1a**), was prepared in two steps from thiophene-2-carbaldehyde (Janssen). A reaction of thiophene-2-carbaldehyde with 3-benzyl-5-(2-hydroxyethyl)-4-methyl-1,3-thiazolium bromide [12] as a catalyst [13] gave predominantly 2,2'-thenoin, which was oxidised to **1a** by leaving a solution of 2,2'-thenoin in methanol and triethylamine in an open crystallisation disc for 24 hours. Compound **1a** was purified by chromatography on silica with dichloromethane (DCM), *m.p.* 80–81 °C, [14] *m.p.* 81–82 °C. Total yield of **1a** from thiophene-2-carbaldehyde was about 65%. Cupric chloride dihydrate and nickel(II) chloride hexahydrate were heated at 180 °C until dry.

Pyrazines 2a,b

A solution of compound **1** (4 mmol) and diaminomaleonitrile (5 mmol, 0.54 g) in glacial acetic acid (20 ml) was heated under reflux for 16 hours (**1a**) and 3 hours (**1b**). The solvent was removed under reduced pressure, and the solid residue was extracted with DCM. The solution was chromatographed on silica with DCM, and the solid residue was filtered with *n*-hexane and a small amount of diethyl ether.

5,6-Di-thien-2-ylpyrazine-2,3-dicarbonitrile (**2a**)

Yield 0.76g (65%), *m.p.* 179–80 °C. – MS *m/z* (% rel. int.): 296 (16.05), 295 (28.18), 294 (100, M), 293 (78.36), 292 (11.27). – ^{1}H NMR ($CDCl_3$): δ/ppm = 7.08 (1H, m), 7.62 (2H, m). – ^{13}C NMR ($CDCl_3$): δ/ppm = 112.96 (CN), 128.23, 128.41, 131.44, 133.07, 138.03, 147.91. – IR (KBr): ν/cm^{-1} = 3 100, 2 229 (CN), 1 504, 1 420, 1 388, 850, 726. Found 294.0031, calcd. for $C_{14}H_6N_4S_2$ 294.0034.

5,6-Di-fur-2-ylpyrazine-2,3-dicarbonitrile (**2b**)

Yield 0.91 g (87%), *m.p.* 153–154 °C. – MS *m/z* (% rel. int.): 264 (2.02), 263 (18.99), 262 (100, M), 245 (27.36). – IR(KBr): ν/cm^{-1} = 3 245, 3 205, 2 239 (CN), 1 566, 1 510, 1 484, 1 362, 1 234, 1 092, 1 024, 883, 755. – ^{1}H NMR ($CDCl_3$): δ/ppm = 6.66 (1H, s), 7.20 (1H, s), 7.66 (1H, s). – ^{13}C NMR ($CDCl_3$): δ/ppm = 113.03, 113.17, 118.01, 125.91, 128.49, 141.95, 146.70, 148.41. ound 262.0488, calcd. for $C_{14}H_6N_4O_2$ 262.0419.

5,6-Di-pyrid-2-ylpyrazine-2,3-dicarbonitrile (**2c**)

A solution of **1c** (10 mmol, 2.12 g) and diaminomaleonitrile (10 mmol, 1.08 g) in acetonitrile (40 ml) was heated under reflux for 3 hours. The solvent was removed under reduced pressure, the solid residue was extracted with DCM (2 × 50 ml), and undissolved material (0.30 g) was discarded. The combined DCM extracts were concentrated and chromatographed on silica with acetone. The solvent was removed from the eluates, and the remaining solids were filtered with diethyl ether to yield 2.25 g (79%) of **2c**, *m.p.* 174–176 °C. – MS *m/z* (% rel. int.): 285 (11.40), 284 (63.36, M), 283 (100). – IR(KBr): ν/cm^{-1} = 3 065 (w), 2 237 (w), 2 209 (CN), 1 692, 1 586, 1 384, 1 094, 995, 792, 740. – ^{1}H NMR ($CDCl_3$): δ/ppm = 7.45 (1H, s), 8.00 (2H, s), 8.34 (1H, s). – ^{13}C NMR ($CDCl_3$): δ/ppm = 114.01 (CN), 124.32, 124.69, 130.79, 137.36, 148.62, 153.42, 153.76. Found 284.0808, calcd. for $C_{16}H_8N_6$ 284.0810.

In another experiment, the same reaction conditions were used, except that 25 ml of acetonitrile was used instead of 40 ml. A solid precipitate appeared after about one hour, and was removed by filtration at the end of the reaction. Yield 0.81 g (25 %), *m.p.* 282–284 °C dec. of 5,6-dihydro-5,6-di-pyrid-2-yl-5,6-bis(hydroxy)-pyrazine-2,3-dicarbonitrile. – MS

m/z (% rel. int.): 320 (0.8), 319, (5.1), 318 (33.1, M), 106 (88.8), 78 (100). – IR(KBr): ν/cm^{-1} = 3 285, 3 090–2 920 (broad), 2 212 (CN), 1 707, 1 585, 1 471 (s), 1 332, 1 232, 1 167, 1 089, 1 011, 749. – ^{1}H NMR (DMSO-d$_6$): δ/ppm = 7.77 (1H, m), 8.14 (2H, m), 8.77 (1H, m), 11.54 (2H, broad s). – ^{13}C NMR (DMSO-d$_6$):δ/ppm = 112.79, 113.05, 123.26, 128.08, 138.31, 147.43, 148.80, 162.69. The acetonitrile filtrate was treated as described above and yielded 1.44 g (51%), *m.p.* 174–176 °C of **2c**.

Magnesium Complexes 3a, 4a and 5a

Magnesium propoxide was prepared by heating a nitrogen flushed mixture of magnesium (7 mmol, 0.18 g), iodine (one crystal) and propanol (10 ml) for 8 hours under reflux. Compounds **2a** and **2b** (2.0 mmol) were added and dissolved in the magnesium propoxide slurry within a few minutes. Compound **2c** (2.0 mmol) was dissolved in dry dioxane (10 ml) and was added to the magnesium propoxide slurry. The reaction mixtures turned dark in about 30 minutes and were heated under reflux for 8 hours. The solvent was removed under reduced pressure, water (60 ml) and glacial acetic acid (15 ml) were added, and the mixture was stirred at ambient temperature for 2 hours. The dark solid was filtered off, washed on the filter with large amounts of water, several portions of methanol, diethyl ether or acetone, depending on the product solubility.

{29H,31H-[2,3,9,10,16,17,23,24-Octakis(thien-2-yl)-1,4,8,11,15,18,22,25-(octaza)phthalocyaninato](2-)-N^{29}, N^{30},N^{31},N^{32}}magnesium (**3a**)

Yield 0.51 g (85%) of a dark blue powder. – UV (abs. pyridine): λ/nm, (ε) = 390 (102 000), 610 (15 000), 675 (182 000) IR(KBr): ν/cm^{-1} = 1517, 1421, 1363, 1311, 1231, 1174, 1092, 884, 777, 702.

$C_{56}H_{24}N_{16}S_8Mg \cdot 2H_2O$ (1237.8)

Calcd.:	C 54.34	H 2.28	N 18.11	S 20.72	Mg 1.96
Found:	C 54.11	H 2.66	N 17.71	S 20.10	Mg 1.80.

{29H,31H-[2,3,9,10,16,17,23,24-Octakis(fur-2-yl)-1,4,8,11,15,18,22,25-(octaza)phthalocyaninato](2-)-N^{29},N^{30},N^{31},N^{32}}magnesium (**4a**)

Yield 0.40 g (75%) of a dark blue powder. – UV (abs. pyridine): λ/nm, (ε) = 392 (63 000), 614 (13 000), 678 (120 000). IR(KBr): ν/cm^{-1} = 1640 (w), 1480, 1336, 1255, 1113, 1015, 888, 778.

$C_{56}H_{24}N_{16}O_8Mg \cdot 2H_2O$ (1109.3)

Calcd.:	C 60.64	H 2.54	N 20.20	Mg 2.19
Found:	C 60.37	H 2.70	N 20.03	Mg 2.10.

{29H,31H-[2,3,9,10,16,17,23,24-Octakis(pyrid-2-yl)-1,4,8,11,15,18,22,25-(octaza)phthalocyaninato](2-)-N^{29}, N^{30}, N^{31}, N^{32}}magnesium (**5a**)

Yield 0.18 g (31%) of a dark blue powder. – UV (abs. pyridine): λ/nm, (ε) = 305 (127 900), 370 (97 200), 595 (23 900), 660 (160 350). – IR(KBr): ν/cm^{-1} = 1586, 1473, 1244, 1192, 1115, 955, 790, 748, 711.

Copper Complexes 4b and 5b

Compound **2b** or **2c** (1 mmol) was dissolved in formamide (5 ml) at 165 °C. Dry cupric chloride (1 mmol, 0.13 g) was added to the stirred solution, and the reaction mixture was heated with stirring at 165 °C for 15 minutes. The dark suspension was cooled to ambient temperature, water (100 ml) was added. The dark solid was filtered off after 2–5 hours, washed thoroughly with water, and then with acetone.

{29H,31H-[2,3,9,10,16,17,23,24-Octakis(fur-2-yl)-1,4,8,11,15,18,22,25-(octaza)phthalocyaninato](2-)-N^{29},N^{30},N^{31},N^{32}}copper(II) (**4b**)

Yield 0.23 g (83%) of a dark powder. – UV (abs. pyridine): λ/nm, (ε) = 390 (48 000), 605 (13 000), 674 (67 000). – IR(KBr): ν/cm^{-1} = 1572, 1542, 1477 (s), 1334, 1257, 1121, 1015, 890, 779, 748.

{29H,31H-[2,3,9,10,16,17,23,24-Octakis(pyrid-2-yl)-1,4,8,11,15,18,22,25-(octaza)phthalocyaninato](2-)-N^{29}, N^{30}, N^{31},N^{32}}copper(II) (**5b**)

Yield 0.14 g (47%) of a dark blue powder. – UV (abs. pyridine): λ/nm, (ε) = 375 (77 000), 588 (28 000), 650 (170 000). IR(KBr): ν/cm^{-1} = 1586, 1552, 1357, 1247, 1124, 767, 749, 712.

$C_{64}H_{32}N_{24}Cu \cdot 2CuCl_2$ (1469.6)

Calcd.:	C 52.31	H 2.19	N 22.88	Cu 12.97
Found:	C 50.31	H 2.69	N 22.10	Cu 14.35.

The product was stirred at ambient temperature with saturated aqueous ammonium hydroxide (20 ml) for 24 hours, filtered, washed thoroughly with water and gave 0.11 g of a dark powder. – UV (abs. pyridine): λ/nm, (ε) = 305 (225 600), 375 (112 800), 587 (36 000), 650 (199 200). – MS TOF-SIMS (Ar$^+$): a molecular ion cluster centered at 1200 amu, corresponding to $C_{64}H_{33}N_{24}Cu$, $[M + H]^+$ and a molecular ion cluster centered at 1262 amu, corresponding to $C_{64}H_{32}N_{24}Cu_2$, $[M + Cu]^+$ *i.e.* with excess copper atoms.

$C_{64}H_{32}N_{24}Cu$ (1200.7)

Calcd.:	C 64.02	H 2.69	N 28.00	Cu 5.30
Found:	C 58.77	H 3.14	N 25.66	Cu 6.04.

Nickel Complex 4c

{29H,31H-[2,3,9,10,16,17,23,24-Octakis(fur-2-yl)-1,4,8,11,15,18,22,25-(octaza)phthalocyaninato](2-)-N^{29},N^{30},N^{31},N^{32}}nickel(II) (**4c**)

Compound **4c** was prepared by the same method as for **4b** and **5b**, except that nickel(II) chloride was used instead of cupric chloride. Yield 0.27 g (97%) of a dark powder. – UV (abs. pyridine): λ/nm, (ε) = 394 (90 000), 662 (55 000), 690 (sh, 30 000). – MS TOF-SIMS (Ar$^+$): the quasi molecular ion peak pattern at 1106 amu, corresponding to $C_{56}H_{24}N_{16}O_8Ni$ $[M]^-$ was observed in the negative TOF-SIMS spectrum.

$C_{56}H_{24}N_{16}O_8Ni \cdot 2H_2O$ (1143,7)

Calcd.:	C 58.81	H 2.47	N 19.60	Ni 5.13
Found:	C 58.04	H 2.72	N 21.61	Ni 5.23.

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