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Preparation of Magnesium Azaphthalocyanines by Cyclotetramerisation of *S*-Substituted 4,5-Disulfanylpyrazine-2,3-dicarbonitriles

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Four novel *S*-substituted 4,5-disulfanylpyrazine-2,3-dicarbonitriles have been obtained in a multistep synthesis from diaminomaleonitrile. Two of these dicarbonitriles, with ethyl or benzyl *S*-substituents, give pure magnesium azaphthalocyanines in good yields when reacted with magnesium propoxide in propanol and dioxane. Aromatic *S*-substituents are less stable during the reaction conditions used for cyclisations, and product mixtures are obtained.

Aza analogs of phthalocyanines (AzaPc) are formed by cyclotetramerisation of pyrazine-2,3-dicarbonitrile, or its substituted derivatives. Applications of the parent phthalocyanines are often restricted owing to their extremely low solubility in most organic solvents. The introduction of eight additional nitrogen atoms into the macrocycle is expected to alter some of the phthalocyanine characteristics, including their solubility. The AzaPc are presently receiving considerable attention. For instance, some water soluble AzaPc have been prepared for use in photodynamic therapy,[1] and some new azatriphenylene macrocycles have been reported[2] as potential mesomorphic materials. AzaPc are expected to find use in most of the areas where phthalocyanines are applied, e.g., traditionally as industrial dyes and pigments,[3] as advanced materials in high technology applications,[4] and in photodynamic cancer therapy.[5]

Recently we have reported exploratory studies of porphyrazines and phthalocyanines with 1,2,5-thiadiazoles or -selenadiazoles in the periphery of the macrocycles.[6,7] The peripheral heteroatoms, and particularly the chalcogen atoms, are expected to promote electronic interactions between adjacent molecular stacks. By introducing various peripheral substituents, one might be able to study their effects on intra- and inter-stack structures, and their influence on electron mobilities.

This paper presents the preparation of some novel *S*-substituted 5,6-disulfanylpyrazine-2,3-dicarbonitriles, and the cyclotetramerisation of two dinitriles to the corresponding magnesium azaphthalocyanines.

Results and discussion

The inexpensive, commercially available diaminomaleonitrile is a well known source for various vicinal, unsaturated dinitriles. For instance, 1,2,5-thiadiazole-3,4-dicarbonitrile is prepared in almost quantitative yield by reaction with thionyl chloride,[8] and some metal porphyrazines have been prepared from this dinitrile.[6] A recent study by Hoffman[9] describes tetraalkylations of diaminomaleonitrile, and subsequent cyclotetramerisations of these dinitriles.

In relation to our present studies, both the parent pyrazine-2,3-dicarbonitrile and its 5,6-dimethyl derivative have been known for many years,[10–12] and Linstead,[11] Brach[13] and Wöhrle[14] have reported azaphthalocyanines derived from these dinitriles.

Our strategy for introducing substituents into the pyrazine ring, and with sulfur directly bound to the pyrazine 5- and 6-positions, was to prepare 5,6-dichloropyrazine-2,3-dicarbonitrile **2** from the corresponding cyclic diamide **1** by a procedure previously reported.[15] Our efforts to repeat the reported preparation of **1**, gave some unexpected results (Scheme 1). During some initial experiments, caution was not taken to add the suspension of diaminomaleonitrile at a very slow rate to the solution of oxalyl chloride in dioxane. As a consequence, large amounts of a solid precipitate formed during the first part of the reaction. This precipitate was found to be *N,N'*-bis[(*Z*)-3-amino(dinitrilo)but-2-

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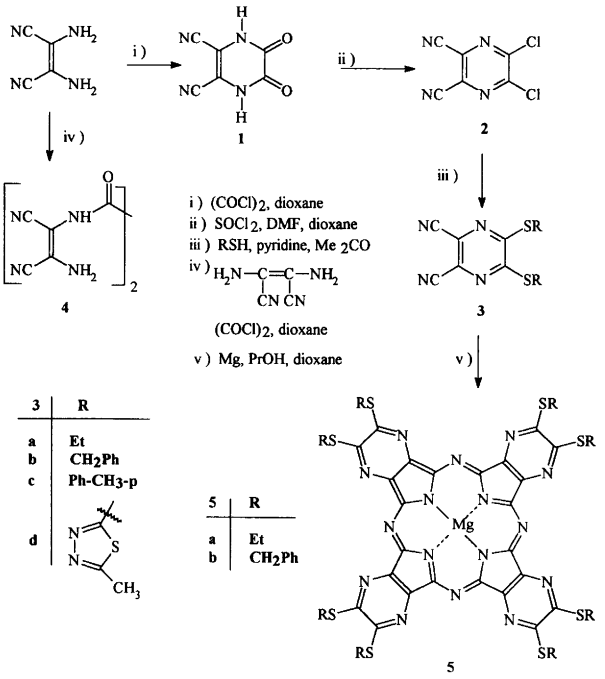

Scheme 1. Preparations of dicarbonitriles **3** and azaphthalocyanines **5**.

en-2-yl]oxamide, compound **4**, which could not be reacted further with oxalyl chloride to form pyrazine **2**. Compound **2** was obtained from **1** by using a lower reaction temperature and time than reported[15] since extensive decomposition was observed on attempted reproduction of the original method. Chromatography on silica was required to obtain **2** as a pure compound.

The chlorines of compound **2** were easily replaced by thiolate anions, prepared as pyridinium salts from the corresponding thiols. Compounds **3** were obtained in excellent yields from these reactions.

The cyclisations of compounds **3** were attempted by the method first described by Linstead,[16] using magnesium propoxide in propanol. The dinitriles were, however, practically insoluble in propanol, and those reactions gave mainly brown, tarry products. We obtained the magnesium azaphthalocyanines **5a** and **5b** in 72% and 61% yields, respectively, by refluxing magnesium in propanol for at least 7 h, before adding a solution (or in part suspension) of the dinitrile **3** in dioxane. The reaction mixtures turned dark blue–green in less than 1 h. Thus, an inert solvent such as dioxane, which can dissolve the dinitriles, is essential for the formation of the macrocycles **5**. Compounds **5a** and **5b** are soluble in pyridine and tetrahydrofuran.

The electronic spectra of compounds **5a** and **5b** were as expected for phthalocyanines, with Q-bands at about 650 nm, and very high values of ε (240 000–220 000). Microanalyses confirmed the structures of compounds **5**, and it is noteworthy that analogous to magnesium phthalocyanines,[17] each of these compounds has added two molecules of water. No molecular ions could be obtained of compounds **5** when flash evaporation, using DEI (desorption electron ionisation), was attempted. Fragments due to decomposition of the side chains were, however, observed. The fragility of the bonds between pyrazine and the sulfur side chains was further confirmed by the attempts to cyclise the dinitriles **3c** and **3d**. These reactions, using the same method as for the preparations of **5a** and **5b**, gave product mixtures, as evidenced by electronic spectra with lower values of ε (150–190 000 at 640 nm) and microanalyses showing a lower sulfur content and higher nitrogen content than calculated.

Conclusions

In the present paper we have explored a reaction sequence from diaminomaleonitrile to some novel *S*-substituted disulfanylpyrazine dicarbonitriles. The transformation of these pyrazine dicarbonitriles to the magnesium azaphthalocyanines **5**, appears to be dependent on the substituents attached to the pyrazine ring. Thus, benzylsulfanyl and ethylsulfanyl substituents favor clean cyclisation reactions, whereas arylsulfanyl substituents seem more prone to solvolysis and give product mixtures. These, and arylsulfanyl analogously substituted azaphthalocyanines, warrant further studies. Work is in progress in which a variety of substituents and complexing metals is being explored.

Experimental

General. Mass spectra of compounds **1–4** were obtained on an AEI MS-902 spectrometer at 70 eV electron energy, and of compounds **5** on a VG ProSpec-3000-Q mass spectrometer from Fisons Instruments, England. Samples of compounds **5** were flash evaporated using the DCI/DEI probe, and ionised by electron ionisation (EI). 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 an 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. 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 gel 63–200 μm was used for column chromatography. Diaminomaleonitrile and 2-sulfanyl-5-methyl-1,3,4-thiadiazole were obtained from Janssen. Dioxane was purified by passage through a short column of activated basic alumina S, and then stored over molecular sieves, 3 Å, and 1-propanol was dried over potassium carbonate, distilled and stored over molecular sieves, 3 Å.

2,3-Dioxo-1,2,3,4-tetrahydropyrazine-5,6-dicarbonitrile, **1**. A solution of diaminomaleonitrile (9.6 g, 89 mmol) in dioxane (500 ml) was added dropwise to a vigorously stirred solution of oxalyl chloride (28.8 g, 227 mmol) in

dioxane (250 ml) over 3 h, and with slow heating of the reaction mixture to 50 °C. Stirring was continued at this temperature for another 3 h. The solution was concentrated, and the crystals that formed were filtered off and yielded 12.7 g (88%), m.p. 240–280 °C (slow decomp.), lit.[18] 270 °C. IR (KBr): 3427, 3111, 2930, 2735, 2236, 1717 (s), 1367, 1304, 1110, 864 cm^{-1}. ^{13}C NMR [$(CD_3)_2SO$]: δ 106.15, 111.38, 155.25.

5,6-Dichloropyrazine-2,3-dicarbonitrile, **2**. A mixture of **1** (10.0 g, 62 mmol), thionyl chloride (22 ml, 303 mmol) and dioxane (400 ml) was stirred at 60 °C for 1 h. DMF (10 ml, 130 mmol) was added, and the dark reaction mixture was stirred and heated for another 1.5 h. The solvent was removed under reduced pressure, and the residue was extracted with hot toluene (400 ml, and 200 ml). After removal of the toluene, a tan solid was obtained, 8.4 g (68%), m.p. 155–158 °C. The crude product was chromatographed on silica with acetone, and 6.7 g (55%) of **2** was obtained, m.p. 188–190 °C, lit.[15] m.p. 179–180 °C. IR (KBr): 2250 (w), 1504, 1363, 1342, 1320, 1264, 1171, 1133, 987, 731 cm^{-1}. ^{13}C NMR [$(CD_3)_2SO$]: δ 110.70 (CN), 125.52 (C-2, C-3), 153.89 (C-5, C-6).

General procedure for the preparation of compounds **3**. Compound **2** (0.59 g, 3 mmol) was dissolved in acetone (30 ml). The thiol (6 mmol) was added, and pyridine (0.55 g, 7 mmol) was then added. The reaction mixture was stirred at ambient temperature, 18 h for **3a**, and 2 h for **3b–3d**. The solvent was removed under reduced pressure at 40 °C, the solid residue was extracted with dichloromethane (20 ml), and the extract was chromatographed on a short silica column with dichloromethane. Pure compound **3d** was obtained by another work-up procedure, namely acetone was removed from the crude reaction mixture, water was added to the solid residue, and the water-insoluble material was filtered off.

5,6-Bis(ethylsulfanyl)pyrazine-2,3-dicarbonitrile, **3a**. 0.56 g (75%), m.p. 128–129 °C. MS [*m/z* (%rel. int.)]: 252 (4.6), 251 (5.4), 250 (39.6, *M*), 223 (11.0), 222 (15.6), 221 (100), 193 (12.3), 190 (7.2), 189 (17.5), 188 (11.7). Found 250.0344, calc. for $C_{10}H_{10}N_4S_2$ 250.0347. IR (KBr) : 2932, 2236, 1479 (s), 1306, 1285, 1264, 1155 (s), 1138, 983 cm.$^{-1}$ ^1H NMR ($CDCl_3$): δ 1.42 (3 H, t, J= 6.5 Hz), 3.28 (2 H, q, J=6.5 Hz). ^{13}C NMR ($CDCl_3$): 13.59 (CH_3), 25.85 (CH_2), 113.78 (CN), 126.21 (C-2, C-3), 160.35 (C-5, C-6).

5,6-Bis(benzylsulfanyl)pyrazine-2,3-dicarbonitrile, **3b**. 0.96 g (85%), m.p. 160–161 °C. MS [*m/z* (%rel. int.)]: 375 (1.5), 374 (6.1, *M*), 285 (2.9), 284 (5.2), 283 (27.6), 91 (100). Found 374.0657, calc. for $C_{20}H_{14}N_4S_2$ 374.0660. IR (KBr) : 3057, 3030 (w), 2557 (w), 2230, 1483 (s), 1454, 1282, 1151, 988, 713 cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.45 (s, CH_2), 7.33 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ 35.65 (CH_2), 113.54 (CN), 126.35, 128.11, 128.81, 129.37, 134.71, 159.38 (C-5, C-6).

5,6-Bis(p-tolylsulfanyl)pyrazine-2,3-dicarbonitrile, **3c**. 0.91 g (81%), m.p. 223–224 °C. MS [*m/z* (%rel. int.)]: 377 (3.3), 376 (12.1), 375 (27.7), 374 (100, *M*), 373 (52.7), 251 (15.0), 124 (10.0), 123 (13.2). Found 374.0657, calc. for $C_{20}H_{14}N_4S_2$ 374.0660. IR (KBr): 2921, 2235, 1595 (w), 1480 (s), 1305, 1281, 1144, 975, 806, 505 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.44 (3 H, s), 7.30 (2 H, d, J=8 Hz), 7.41 (2 H, d, J= 8 Hz). ^{13}C NMR ($CDCl_3$): δ 21.48 (CH_3), 113.41 (CN), 121.21, 127.37, 130.76, 135.32, 141.33, 159.58 (C-5, C-6).

5,6-Bis[(5-methyl-1,3,4-thiadiazol-2-yl)sulfanyl]pyrazine-2,3-dicarbonitrile, **3d**. 1.05 g (89%), m.p. 215–216 °C decomp. MS [*m/z* (% rel. int.)]: 392 (0.4), 391 (0.4), 390 (1.9, *M*), 261 (10.0), 260 (13.9), 259 (100), 154 (42.5), 132 (15.3). Found 389.9594, calc. for $C_{12}H_6N_8S_4$ 389.9598. IR (KBr): 2236 (w), 1500, 1369 (w), 1311, 1282, 1202, 1148, 1058, 974 cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.94 (3 H, s). ^{13}C NMR [$(CD_3)_2SO$]: δ 15.57 (CH_3), 113.37 (CN), 128.86, 153.54, 154.58, 171.47.

N,N′-*Bis[(Z)-3-amino(dinitrilo)but-2-en-2-yl]oxamide,* **4**. A solution of diaminomaleonitrile (9.6 g, 89 mmol) in dry dioxane (320 ml) was added at ambient temperature over 30 min to a stirred solution of oxalyl chloride (24.0 g, 189 mmol) in dry dioxane (200 ml). A yellow paste was formed, and the suspension was stirred at ambient temperature for 1 h, then at 50 °C for 4 h. The precipitate was filtered, washed with heptane (40 ml) and dried to yield 8.0 g (68%), m.p. 267–280 °C (slow decomp.). MS [*m/z* (%rel. int.)]: 272 (0.3, *M*+2), 271 (2, *M*+1), 270 (16, *M*), 252 (3), 242 (3), 108 (100). Found: 270.0616, calc. for $C_{10}H_6N_8O_2$ 270.0614. IR (KBr): 3382, 3323, 3256, 3194, 2986, 2956, 2917, 2895, 2861, 2250, 2241, 2203, 1709 (s), 1685, 1673, 1640 (s), 1615, 1486, 1455, 1390, 1290, 1257, 1115, 1080, 892, 867, 828, 681 cm^{-1}. ^1H NMR [$(CD_3)_2SO$]: δ 7.55 (4 H, s), 10.14 (2 H, s). No change of the spectrum was observed upon addition of D_2O. ^{13}C NMR [$(CD_3)_2SO$]: δ 87.3 (C–NH), 113.7 (CN), 116.8 (CN), 128.1 (C–NH_2), 157.7 (CO).

General procedure for the preparation of compounds **5**. A mixture of magnesium turnings (0.2 g, 8 mmol), one crystal of iodine, and 1-propanol (10 ml) was flushed with nitrogen for about 10 min, then heated under reflux for 7 h. A solution of **3** (1.6 mmol) in dry dioxane (25 ml) was added, and heating under reflux was continued for 18 h. The dark blue–green reaction mixture was evaporated to dryness, and water (40 ml) and acetic acid (30 ml) were added to the solid residue. The mixture was stirred for 2 h at ambient temperature, filtered, and the dark solid was washed on the filter with copious amounts of water and diethyl ether. The solid was stirred with acetone (25 ml), filtered and finally washed with diethyl ether.

Mass spectra of compounds **5a** *and* **5b**. The magnesium complexes **5** are thermally unstable and decompose even when flash evaporated in the mass spectrometer ion source. Minor peaks due to the starting material **3** were present in the spectra. The base peak at *m/z* 76 in the spectrum of **5a** is probably due to dicyanoacetylene. This

peak is smaller in the spectrum of **5b**, where the base peaks were at *m/z* 91/92 (toluene).

{29H,31H-[2,3,9,10,16,17,23,24-Octakis(ethylsulfanyl)-1,4,8,11,15,18,22,25-(octaza)phthalocyaninato](2−)-N^{29},N^{30},N^{31},N^{32}*}magnesium,* **5a**, 0.295 g (72%), m.p. >300 °C. IR (KBr): 3424 (s, br), 2966, 2928, 2870, 1637 (w), 1510 (w), 1450 (w), 1395 (w), 1334 (w), 1256 (s), 1229 (s), 1166 (s), 1095, 976, 782 cm^{-1}. UV [abs. pyridine (ε)]: 380 (125 200), 590 (33 100), 652 (217 400) nm. Anal. Found: C 45.17; H 4.13; Mg 2.19; N 20.88; S 21.05. Calc. for $C_{40}H_{40}MgN_{16}S_8+2H_2O$: C 45.25; H 4.18; Mg 2.29; N 21.11; S 24.16.

{29H,31H-[2,3,9,10,16,17,23,24-Octakis(benzylsulfanyl)-1,4,8,11,15,18,22,25-(octaza)phthalocyaninato]-(2−)-N^{29},N^{30},N^{31},N^{32}*}magnesium,* **5b**, 0.37 g (61%), m.p. >300 °C. IR (KBr): 1636 (w), 1508 (w), 1494 (w), 1451 (w), 1257, 1229, 1158 (s), 1093, 976, 781, 696 cm^{-1}. UV [abs. pyridine (ε)]: 380 (142 000), 593 (36 000), 626 (36 000), 654 (240 000) nm. Anal. Found: C 61.43; H 3.94; Mg 1.51; N 14.41; S 16.22. Calc. for $C_{80}H_{56}MgN_{16}S_8+2H_2O$: C 61.66; H 3.88; Mg 1.56; N 14.38; S 16.46.

Reaction of **3c** *with magnesium propoxide in propanol and dioxane.* Dark blue powder, 0.15 g (26%). IR (KBr): 2966, 2874, 1520, 1491, 1438, 1333, 1241, 1151, 1033, 808 cm^{-1}. UV [abs. pyridine (ε)]: 380 (135 800), 586 37 500), 642 (194 600) nm. Anal. Found: C 59.66; H 4.85; Mg 1.47; N 17.19; S 10.02. Calc. for $C_{80}H_{56}MgN_{16}S_8+2H_2O$: C 61.66; H 3.88; Mg 1.56; N 14.38; S 16.46.

Reaction of **3d** *with magnesium propoxide in propanol and dioxane.* Purplish/black powder, 0.22 g (35%). IR (KBr): 3425 (s, br), 2968, 2937, 2878, 1637, 1525, 1438, 1380, 1298, 1247, 1057, 975, 750 cm^{-1}. UV [abs. pyridine (ε)]: 366 (148 500), 576 (35 600), 631 (147 500) nm. Anal. Found: C 47.88; H 4.42; Mg 1.26; N 21.80; S 9.10. Calc. for $C_{48}H_{24}MgN_{32}S_{16}$: C 36.34; H 1.53; Mg 1.53; N 28.26; S 32.34.

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