A Facile and Regioselective Synthesis of Trans-Heterofunctionalized Porphyrazine Derivatives

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New methodology was developed for the selective synthesis of regiochemically defined porphyrazines of the form M[pz(A_2;B_2)] (shown in Chart 1) where A and B represent peripheral functionalization attached to the β-positions of the pyrroles. Specifically, phthalonitriles or derivatives thereof with sterically bulky groups in positions 3 and 6, in particular 4,7-bis(isopropyloxy)-1,3-diiminoisoindoline (**3**) act as a "trans director" when macrocyclized with heteroatom-appended maleonitriles under Linstead conditions, the result being preferential formation of the *trans*-M[pz(A_2;B_2)] pigment where A = SR, NMe_2, OR, as well as R (shown in Chart 2). Linstead crossover macrocyclization of **3** with **4**, **11**, **15**, and **18** gave pigments **10**, **14**, **17**, and **19**, respectively. These pigments were characterized by ^{1}H NMR, ^{13}C NMR, UV−visible spectroscopy, mass spectrometry, microanalysis, and **17** was characterized by single-crystal X-ray analysis.

Introduction

Phthalocyanines and related tetraazamacrocycles have found wide applications in diverse areas such as biomedical agents for diagnosis and therapy,[1,2] chemical sensors,[3] liquid crystals,[4,5] nonlinear optics,[6] Langmuir−Blodgett films,[7] and ladder polymers,[8] and are precursors to new conducting materials. Recently, we reported on the synthesis and novel physical properties of porphyrazines (tetraazaporphyrins) with peripheral heteroatom functionalization, including octathiolates,[9] octa(dialkyl)-amines,[10] and octaol derivatives.[11] Unsymmetrical peripheral functionalization can fine-tune the molecular properties, such as UV−visible absorption bands, and provide precursors to new mutimetallic arrays. However, the statistical comacrocyclization of two maleo- and/or phthalonitriles would produce a mixture of the six M[pz-(A_n;B_{4-n})] from which it would be very difficult to purify the individual components by common chromatographic methods.[12] Three general methods exist for the preparation of M[pz(A_1;B_3)] pigments: the polymer support route,[13−16] subphthalocyanine route,[17−19] and statistical condensation route.[20,21] In contrast, fewer methods exist for the selective preparation of *trans*-M[pz(A_2;B_2)] pigments (Chart 1).[22−26] We recently published a method whereby the "cis" and "trans"[27] isomers with the formula M[pz(A_2;B_2)] can be separated when A and B are chosen to have disparate polarities. In this case, the cis isomer with polar groups on adjacent pyrrole subunits is a more polar molecule than the trans analogue, and the two macrocycles are separable by chromatography.

In this paper, we show that methodology to prepare A_2;B_2 phthalocyanines with a trans configuration[23−26]

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Chart 1. Trans-Functionalized Porphyrazine

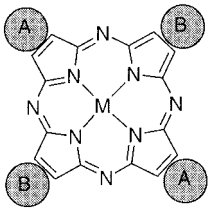
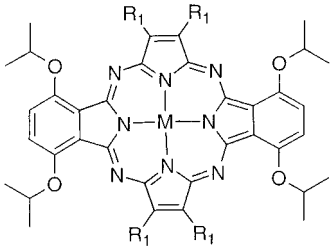
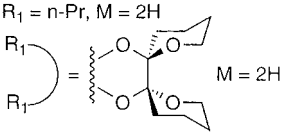


Chart 2. *trans*-M[Pz(A_2;B_2)] Pigments Prepared in This Study



7: R_1 = $N(Me)_2$, M = 2H
10: R_1 = $N(Me)_2$, M = Ni
14: R_1 = SBn, M = 2H
17: R_1 = n-Pr, M = 2H

19:



can be used to preferentially prepare heteroatom-functionalized *trans*-M[pz(A_2;B_2)]. We report that phthalonitriles or derivatives thereof with sterically bulky groups in positions 3 and 6, in particular 4,7-bis(isopropyloxy)-1,3-diiminoisoindoline (**3**), act as a "trans director" when macrocyclized with heteroatom-appended maleonitriles under Linstead conditions, the result being preferential formation of the *trans*-M[pz(A_2;B_2)] pigment where A = SR, NMe_2, OR, as well as R (shown in Chart 2). When A = SR, these pigments have Q-band absorbance red-shifted beyond those given by the intrinsic trans configuration in addition to the red-shift caused by the presence of alkoxy or other electron donating groups α to the point of ring fusion in phthalocyanines,[28−30] and thus have potential biomedical applications.

Results and Discussion

Synthesis. The general synthesis we employ is shown in Scheme 1. The synthesis of the trans-director begins with alkylation of inexpensive, commercially available 2,3-dicyanohydroquinone (**1**) by 2-bromopropane. The resulting hydroquinone diisopropyl ether (**2**) is unreactive under the normal Linstead macrocyclization conditions (a suspension of magnesium butoxide in refluxing butanol), thus necessitating its conversion to the corresponding 1,3-diiminoisoindoline (**3**) by bubbling ammonia through a solution of ethylene glycol at 140−150 °C previously treated with a catalytic amount of Na for 4−5 h. Compound **3** was then macrocyclized with bis(dimethylamino)maleonitrile (**4**), 2,3-bis(benzylthio)maleonitrile (**11**), dipropylmaleonitrile (**15**), and dispiromaleonitrile (**18**). In each case, the product, containing Mg-[pz(A_n;B_{4-n})], was treated with trifluoroacetic acid or acetic acid to form the free base, 2H[pz(A_n;B_{4-n})] and then chromatographed to give the desired *trans*-[pz(A_2;B_2)] systems. The degree to which the formation of this compound was favored was a function of both the ratio of the two cyclization partners and their relative reactivities.

Dimethylamino Porphyrazine Hybrids. Magnesium-templated cyclization of bis(dimethylamino)maleonitrile **4** and a 3-fold excess of diiminoisoindoline **3** produced three pigments; M[pz(A_1;B_3)] (**5**), the *cis*-M[pz(A_2;B_2)] (**6**) and *trans*-M[pz(A_2;B_2)] (**7**) in a 2:1:5 ratio. The metal-free pigments **5**, **6**, and **7** could be isolated directly, but it was simpler to purify the nickel(II) chelates. The ^{1}H NMR spectra of the cis- and trans-macrocycles clearly differentiate between them; in the trans pigment **10**, the protons on the fused aryl rings appeared as a singlet, while in the cis compound **9**, the fused aryl protons gave rise to an AB quartet.

Benzylthio Porphyrazine Hybrids. Magnesium-templated cyclization of 2,3-bis(benzylthio)maleonitrile **11** with **3** in a 1:1 stoichiometric ratio yielded M[pz(A_1;B_3)] (**13**) and *trans*-M[pz(A_2;B_2)] (**14**) in a 2:1 ratio along with trace amounts of octakis(benzylthio)porphyrazine: none of the *cis*-M[pz(A_2;B_2)] pigment was detected. The yield of the trans macrocycle was optimized by the use of only 0.25 equiv of Mg per mole of combined cyclization partners and by heating the reaction mixture for only 6 h at 100 °C. Longer reaction times and higher temperatures produced a complex mixture of pigments with little or no trans-macrocycle. It is possible that the strongly basic conditions resulted in cleavage of the carbon−sulfur bonds via an Eschenmoser-type sulfide contraction.[31] Compound **14** provides a convenient entry into di- and trimetallic arrays since the benzyl groups attached to the sulfur atoms can be removed via reductive cleavage and related tetrathiolates have been shown to bind a variety of metals.[32]

Propyl Porphyrazine Hybrids. Magnesium-templated cyclization of **15** and **3** in a 1:1 stoichiometric ratio yielded the M[pz(A_1;B_3)] (**16**) and *trans*-M[pz(A_2;B_2)] (**17**) in a 1:3 ratio. Interestingly, if between 0.25 and 0.5 equiv of Mg per combined mole of cyclization partners were employed, only a trace amount of porphyrazine was obtained. However, if 1 equiv of Mg per combined mole of cyclization partners was used, the macrocycles could be obtained in a combined yield of 24%. If a 3:1 stoichiometric ratio of **15** to **3** was used, the ratio of pigments **16** to **17** obtained was reversed (30% combined yield).

Spirane Porphyrazine Hybrids. The reaction of dispiromaleonitrile **18** with a 5-fold excess of diiminoisoindoline **3** in the presence of magnesium butoxide allowed the isolation of *trans*-M[pz(A_2;B_2)] (**19**) and of M[pz(A;B_3)] (**20**) in a 3:1 ratio (56% combined yield). The unusually high yield in this reaction reveals an exceptionally good match of the reactivity and stoichiometry between the two reagents **18** and **3**. Maleonitrile **18** has been employed in other high yielding macrocyclization reactions.[11] The trans geometry of **19** is reflected in both

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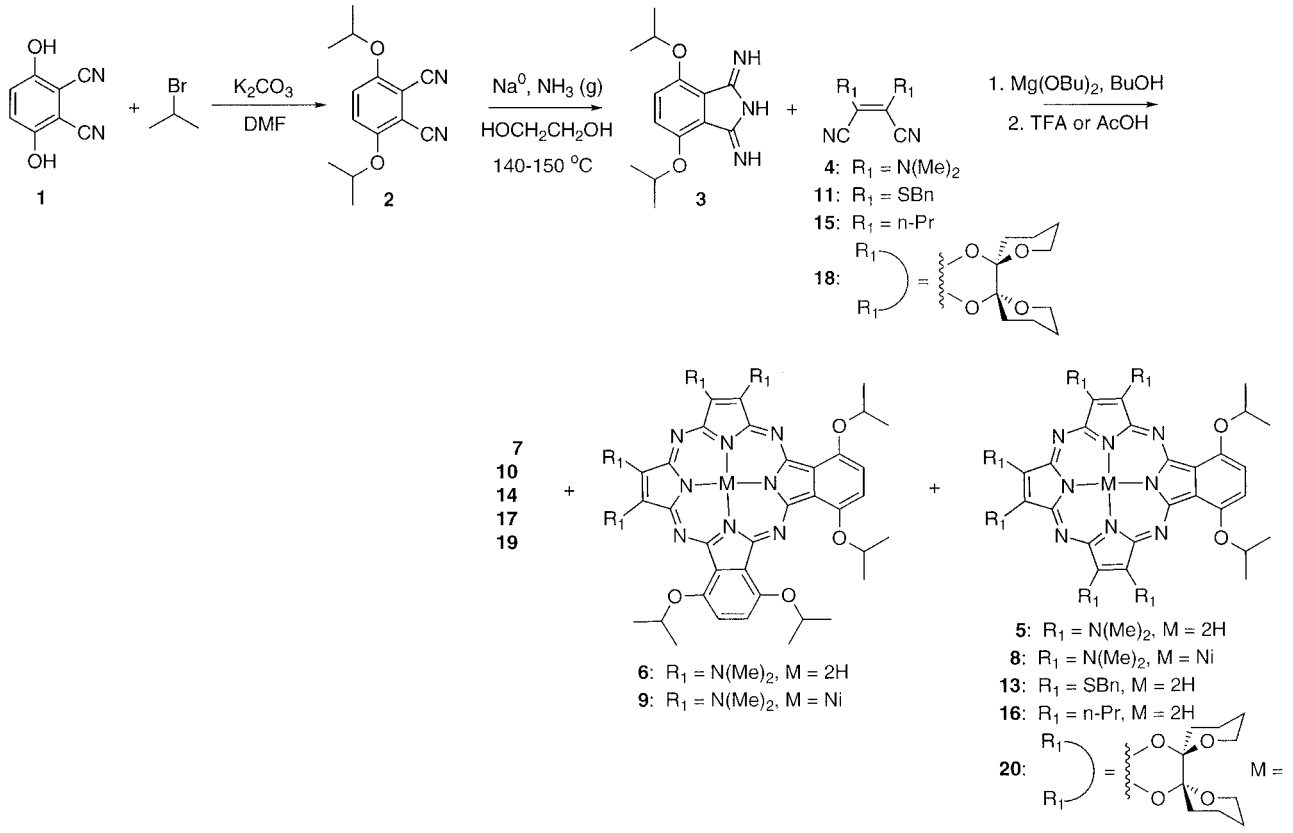
Scheme 1. General Synthesis of Trans-Functionalized Porphyrazines



the ^{1}H and ^{13}C NMR spectra of this compound. Of additional interest is that these spectra highlight the diastereotopicity of the isopropyl groups: the ^{1}H NMR spectrum shows a doublet resonance, and the ^{13}C NMR spectrum reveals an independent resonance, for each methyl group of the isopropyl moiety. A similar situation was observed for the NMR spectra of **20**: while the ^{1}H NMR spectrum provides some indication of the reduced symmetry of the molecule, the ^{13}C NMR spectrum clearly exhibits a more complex resonance pattern.

X-ray Crystallography. The X-ray structural analysis of **17** shows it to be the *trans*-porphyrazine depicted in Figure 1.[33] The macrocyclic 24-atom core of **17** is planar. There is, however, a very slight saddle distortion (ca. 0.15 Å) involving the pyrroles fused to the aryl rings with respect to this plane. The central cavity is symmetrical, with the diagonal nonbonded N···N distances virtually identical at 3.84(2) and 3.87(2) Å. The off-diagonal nonbonded N···N distances are also virtually identical at 2.74(2) and 2.69(2) Å.

It has been shown that peripheral steric congestion causes nonplanarity in porphyrins,[34] while unsymmetrical steric congestion causes elongation of the macrocyclic core along one of its axes.[35] The planar structure of **17** indicates that it does not suffer from steric congestion at the periphery. This result would appear to support the idea that steric congestion in the cis isomer leads to preferential formation of the *trans*-M[pz(A_2;B_2)] isomer. However, the steric energies of the *cis*- and *trans*-M[pz(A_2;B_2)] (A = Pr) pigments, as calculated using the CS Chem3D Pro program, were virtually identical (Table 1). This implies that either a bias toward formation of the trans isomer occurs in an intermediate or a transition state, or instead that the *trans*-M[pz(A_2;B_2)] is preferred because the reactivities of the two cyclization partners

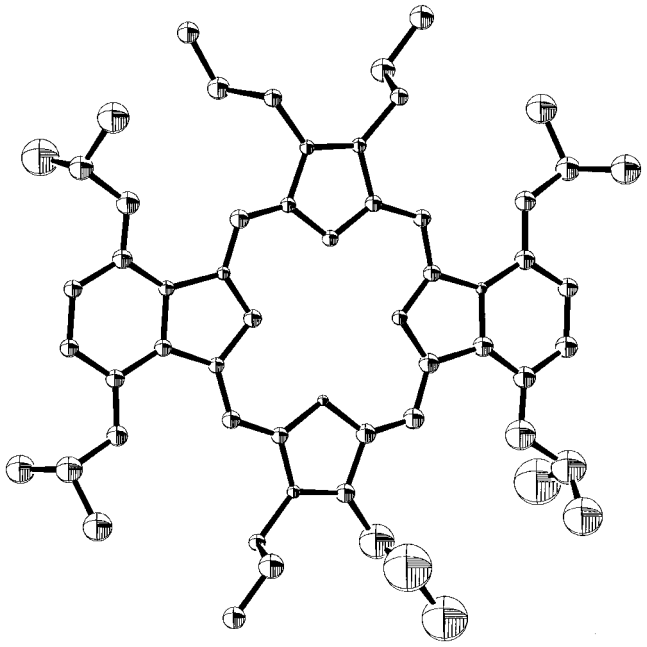


Figure 1. ORTEP diagram of **17** showing the 50% probability thermal ellipsoids. Hydrogen atoms have been omitted for clarity.

(33) The authors have deposited atomic coordinates and a full structure description for **17** with the Cambridge Crystallographic Data Centre. The structure can be obtained upon request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

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Table 1. Minimized Steric Energies of the M[Pz(A_2;B_2)] (A = NMe_2, SBn, OR, and *n*-Pr Isomers Calculated Using the CS Chem3D Pro Program

M[pz(A_2;B_2)]	kcal/mol
cis-2H[pz{$(NMe_2)_4$;B_2}]	118.6
trans-2H[pz{$(NMe_2)_4$;B_2}]	116.4
cis-2H[pz{$(OR)_4$;B_2}]	122.7
trans-2H[pz{$(OR)_4$;B_2}]	115.1
cis-2H[pz{$(SBn)_4$;B_2}]	48.5
trans-2H[pz{$(SBn)_4$;B_2}]	47.9
cis-2H[pz{$(Pr)_4$;B_2}]	61.2
trans-2H[pz{$(Pr)_4$;B_2}]	59.8

are different. Disparate reactivities on different pyrroles and on phthalonitriles and their derivatives has been used successfully to prepare porphyrins[36] and phthalocyanines[22] with D_{2h} symmetry.

Electronic Absorption Spectra. Porphyrazines, like phthalocyanines, show an intense B (Soret) band at $\lambda <$ 400 nm and a Q-band that has its principal absorption at $\lambda >$ 600 nm. The Q-band of a 4-fold symmetric tetraazamacrocycle shows a Q-band with a single origin, whereas compounds with reduced symmetry typically show a split Q-band.[37] Trans-porphyrazines **7** (539, 747 nm), **14** (656, 798 nm), **17** (638, 718 nm), and **19** (632, 705 nm) all have such split Q-bands (Figure 2). The introduction of heteroatoms to the periphery of these *trans*-M[pz(A_2;B_2)] pigments may complicate the spectra by adding n−π* transitions which either broaden the Q-type absorbances or add additional absorbance bands. The propyl-substituted compound **17** has its Q-band split by 1750 cm^{-1} and has a shoulder (ca. 430 nm) on the B band that we assign to the n−π* transition from the meso nitrogens to the macrocycle. The UV−visible spectrum of oxygen-substituted **19** is very similar to that of **17** with the Q-band slightly blue-shifted; it contains an additional band at 451 nm that we assign as the oxygen n−π* transition. The spectrum of sulfur-substituted **14** has a red-shifted Q-band with a large splitting (2710 cm^{-1}). This splitting is comparable to that of a recently reported trans-substituted porphyrazine.[23] The nitrogen-substituted compound **7** has a Q-band that is less red-shifted than that of **14** but with an even larger Q-band splitting (5183 cm^{-1}). The unusual breadth of the individual Q-bands of **7** is due to the n−π* transitions of the dimethylamino nitrogens and possibly to multiple conformations of the dimethylamino nitrogen groups with respect to the plane of the macrocyclic core.

Conclusions

We have developed a simple convenient synthesis of trans-macrocycles **10**, **14**, **17**, and **19** from inexpensive and readily available starting materials. This method is sufficiently mild so that a wide range of functionality and heteroatoms can be tolerated. These trans-porphyrazines all have split Q-bands and it is of particular interest to note that the UV−visible absorption spectrum of **14** includes an intense long-wavelength absorption at ca. 800 nm (log ϵ = 4.72), a wavelength at which mammalian tissue is effectively penetrated by light (potential biomedical agent). These macrocycles will provide a framework upon which metals can be coordinated to the peripheral positions. We are currently investigating the removal of the isopropyl groups from compounds **16** and **17** to generate quinone and bisquinone macrocycles, respectively. Such work will be reported in due course.

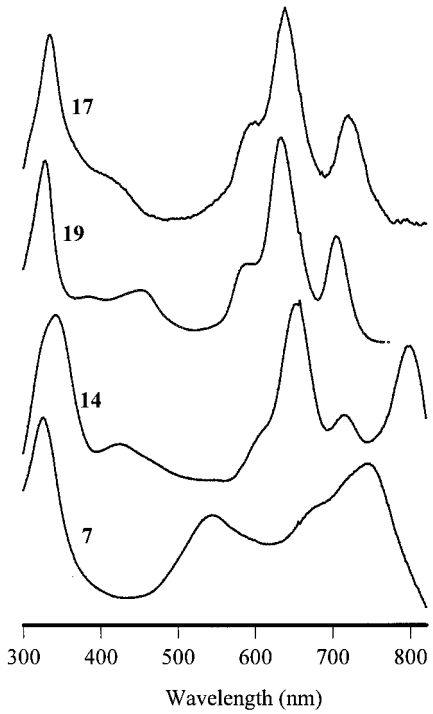

Figure 2. UV−visible absorption spectra (CH_2Cl_2) of the trans-functionalized porphyrazines (from top to bottom) of **17**, **19**, **14**, and **7**.

Experimental Section

General. Bis(dimethylamino)maleonitrile **4**,[38] 2,3-bis(benzylthio)maleonitrile **11**,[39] 4,5-dicyano-4(*Z*)-octene **14**,[40] and dispiromaleonitrile **18**[11] were prepared according to literature procedures.

3,6-Bis(isopropyloxy)-1,2-benzenedinitrile (2). To a well stirred slurry of 3,6-dihydroxy-1,2-benzenedinitrile (**1**) (25 g, 0.156 mol) and K_2CO_3 (48 g, 0.343 mol) in DMF (500 mL) was added 2-bromopropane (40 mL), and the solution was heated at 60 °C for 48 h. At this time an additional portion of 2-bromopropane (10 mL) was added, and the solution was heated at the same temperature for 12 h. The reaction contents were poured into water (2 L), and the solution was vigorously stirred. The resulting white solid was filtered under reduced pressure and then triturated with hot MeOH to yield a white crystalline solid **2** (36 g, 0.147 mol, 94%), mp 191−193 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (d, J = 6.1 Hz, 12H), 4.54 (hp, J = 6.1 Hz, 2H), 7.14 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 73.8, 106.7, 113.2, 120.8, 154.5; IR ν_{max} (CH_2Cl_2) 2232 cm^{-1}; EI MS *m*/*z* 244 (M^+), 202, 160. Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.64, H, 6.66; N, 11.50.

4,7-Bis(isopropyloxy)-1,3-diiminoisoindoline (3). Compound **2** (20 g, 82.0 mmol) was suspended in ethylene glycol (500 mL), freshly cut Na (0.7 g) was added, and the mixture

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was heated to 130 °C under a positive pressure of N_2. At this time NH_3(g) was bubbled through the solution for 5 h while maintaining the temperature between 140 °C and 150 °C. The solution was allowed to cool to room temperature and was poured into water (1 L). The solid obtained was filtered and dried under vacuum to yield a pale brown solid which was recrystallized from MeOH to yield **3**: (18 g, 68.6 mmol, 85%), mp 144−148 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (d, J = 6.1 Hz, 12H), 4.62 (hp, J = 6.1 Hz, 2H), 6.92 (s, 2H), 8.1 (v br s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.0, 71.4, 117.5, 123.6, 147.9, 168.2; EI MS m/z 261 (M^+); IR ν_{max} (CH_2Cl_2) 1641, 1611 cm^{-1}. Anal. Calcd for $C_{14}H_{19}N_3O_2$: C, 64.35; H, 7.33; N, 16.08. Found: C, 63.97; H, 7.53; N, 15.69.

***N,N*-Dimethylamino Porphyrazine Hybrids 7−10.** Magnesium turnings (170 mg, 7.02 mmol) were added to BuOH (100 mL), and the suspension was heated under reflux for 24 h under N_2. At this time **3** (2.3 g, 8.79 mmol) and dinitrile **4** (0.48 g, 2.92 mmol) were added, and the solution was heated under reflux for an additional 24 h. During this time the solution slowly turned from an orange color to brown and finally to blue-black. The BuOH was removed under reduced pressure, and the remaining blue-black residue was dissolved in CH_2Cl_2 (100 mL), cooled to 0 °C with an ice bath and AcOH (20 mL) was added. The solution was stirred at 0 °C for 30 min while being shielded from ambient lighting and poured onto crushed ice containing an excess of NH_4OH. The layers were separated, and the aqueous layer was washed with CH_2Cl_2 until the washings were clear. The organic layers were combined, dried over Na_2SO_4, and concentrated to yield a black residue containing a mixture of **5**, **6**, and **7**. The black residue was not purified but instead converted to the nickel(II) chelates by dissolving the residue in a mixture of 25 mL of chlorobenzene and 25 mL of DMF, adding an excess of Ni(OAc)$_2$·4H$_2$O (1.0 g, 4.0 mmol) and heating the resulting solution at 100 °C for 10 h under N_2. The solvent was removed under reduced pressure to yield a black residue. This was purified by column chromatography (alumina, Brockmann grade III, 70/30 CH_2Cl_2/hexanes eluant) to yield three pigments which eluted in the order **8**, **9**, and **10**. ***trans*-Amino Porphyrazine (7):**[41] mp 190−191 °C dec; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 327 (4.75), 548 (4.68), 747 (4.63) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.86 (s, 2H), 1.72 (d, J = 6.0 Hz, 24H), 3.95 (s, 24H), 5.38 (hp, J = 6.0 Hz, 4H), 5.38 (s, 4H); FABMS m/z 819 (M^+), Calcd for $C_{44}H_{58}N_{12}O_4$: 819. Anal. Calcd for $C_{44}H_{58}N_{12}O_4$: C, 64.53; H, 7.14; N, 20.52. Found: C, 64.97; H, 7.24; N, 20.32. **Ni(II) 3:1 Amino Porphyrazine (8):** (47 mg, 0.058 mmol, 6%); mp 250−253 °C dec; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 315 (4.68), 519 (4.31), 709 (4.50) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.72 (d, J = 6.1 Hz, 12H), 3.66 (s, 12H), 3.69 (s, 12H), 3.88 (s, 12H), 5.16 (hp, J = 6.1 Hz, 2H), 7.40 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.6, 44.8, 44.9, 45.2, 70.9, 113.7, 127.0, 136.8, 139.0, 140.6, 142.9, 143.7, 144.0, 144.3, 148.1; FABMS m/z 796 (M^+), Calcd for $C_{38}H_{52}N_{14}NiO_2$: 796. Anal. Calcd for $C_{38}H_{52}N_{14}NiO_2$: C, 57.37; H, 6.59; N, 24.65. Found: C, 57.71; H, 6.71; N, 24.50. **Ni(II) *cis*-Amino Porphyrazine (9):** (38 mg, 0.044 mmol, 3%); mp 203−205 °C dec; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 318 (4.70), 718 (4.65) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.50 (d, J = 6.2 Hz, 12H), 1.74 (d, J = 6.1 Hz, 12H), 3.68 (s, 12H), 3.87 (s, 12H), 5.02 (hp, J = 6.2 Hz, 2H), 5.19 (hp, J = 6.1 Hz, 2H), 7.44 (dd, J = 8.8 Hz and J = 8.6 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.6, 44.8, 45.1, 70.9, 75.1, 113.1, 122.7, 126.5, 129.5, 137.1, 140.3, 143.4, 144.2, 144.3, 144.9, 148.1, 149.8; FABMS m/z 876 (M^+), Calcd for $C_{44}H_{56}N_{12}NiO_4$: 876. Anal. Calcd for $C_{44}H_{56}N_{12}NiO_4$: C, 60.35; H, 6.45; N, 19.19. Found: C, 60.64; H, 6.51; N, 18.84. **Ni(II) *trans*-Amino Porphyrazine (10):** (190 mg, 0.22 mmol, 15%); mp 215−217 °C; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 321 (4.75), 727 (4.68) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.73 (d, J = 6.0 Hz, 24H), 3.86 (s, 24H), 5.18 (m, 4H), 7.41 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.6, 45.1, 70.9, 113.8, 126.9, 138.6, 143.5, 145.0, 149.2; FABMS m/z 876 (M^+), Calcd for $C_{44}H_{56}N_{12}NiO_4$: 876. Anal. Calcd for $C_{44}H_{56}N_{12}NiO_4$: C, 60.35; H, 6.45; N, 19.19. Found: C, 60.15; H, 6.55; N, 19.03.

Benzylthio Porphyrazine Hybrids 13 and 14. Magnesium turnings (78 mg, 3.2 mmol) were added to PrOH (30 mL), and the suspension was heated under reflux for 16 h under N_2. At this time a mixture of **11** (1.73 g, 5.36 mmol) and diiminoisoindoline **3** (1.42 g, 5.36 mmol) were added, and the solution was heated under reflux for 6 h. The solution immediately turned a dark brown color and after 5 min to green-black. The PrOH was removed under reduced pressure, the green-black residue was dissolved in CH_2Cl_2 (100 mL), and TFA (20 mL) was added. The solution was stirred for 30 min and then poured onto crushed ice containing a large excess of NH_4OH. The mixture was stirred vigorously for 1 h. At this time the organic and aqueous layers were separated, and the aqueous layer was extracted with CH_2Cl_2 until the washings were colorless. The organic layers were then dried over Na_2SO_4, and the solution was concentrated under reduced pressure. The resulting residue was chromatographed (silica gel, 80/20 CH_2Cl_2/hexanes eluant). The pigments eluted in the order **12**, **13**, and **14**. **Octakis(benzylthio)porphyrazine (12):** (50 mg, 0.039 mmol, 3%); mp > 250 °C.[39] **3:1 Benzylthio Porphyrazine (13):** (250 mg, 0.205 mmol, 11%); mp 175−176 °C dec; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 346 (4.66), 488 (4.21), 661 (sh), 703 (4.65), 752 (sh) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.29 (br s, 2H), 1.77 (d, J = 6.0 Hz, 12H), 5.08 (s, 4H), 5.12 (s, 4H), 5.21 (s, 4H), 5.28 (hp, J = 6.0 Hz, 2H), 7.01−7.35 (m, 30H), 7.68 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.6, 39.4, 39.9, 72.5, 119.2, 126.5, 126.9, 127.1, 128.2, 128.3, 128.4, 128.9, 129.1, 137.9, 138.0, 138.3, 139.0, 141.6, 150.2, 151.4, 151.6, 151.8, 154.2, 154.4, 154.7; FABMS m/z 1215 ($M + H^+$), Calcd for $C_{68}H_{61}N_8O_2S_6$: 1215. Anal. Calcd for $C_{68}H_{60}N_8O_2S_6$: C, 67.30; H, 4.98; N, 9.23. Found: C, 67.34; H, 4.95; N, 8.88. ***trans*-Benzylthio Porphyrazine (14):** (120 mg, 0.105 mmol, 5%); mp 201−205 °C dec; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 344 (4.72), 434 (4.23), 656 (4.70), 718 (4.36), 798 (4.72) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ −0.56 (br s, 2H), 1.76 (d, J = 6.0 Hz, 24H), 5.27 (hp, J = 6.0 Hz, 4H), 5.24 (s, 8H), 7.01 (m, 12H), 7.19−7.25 (m, 8H), 7.56 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.7, 36.6, 72.3, 118.3, 126.8, 128.2, 128.4, 129.9, 138.4, 147.1, 147.6, 156.3, 156.8; FABMS m/z 1137 ($M + H^+$), Calcd for $C_{64}H_{63}N_8O_4S_4$: 1137. Anal. Calcd for $C_{64}H_{62}N_8O_4S_4$·H$_2$O: C, 66.64; H, 5.59; N, 9.71. Found: C, 66.58; H, 5.67; N, 9.68.

Propyl Porphyrazine Hybrids 16 and 17. Magnesium turnings (200 mg, 8.22 mmol) were added to BuOH (70 mL), and the solution was heated at reflux for 24 h under N_2. At this time dinitrile **15** (0.67 g, 4.11 mmol) and **3** (1.08 g, 4.11 mmol) were added, and the solution was heated under reflux for an additional 24 h. The solvent was removed under reduced pressure, the remaining blue-green residue was dissolved in CH_2Cl_2 (200 mL), and TFA (25 mL) was added. The resulting mixture was stirred for 1 h and then poured into ice containing an excess of aqueous NH_4OH. The organic layer was separated from the aqueous layer, and the aqueous layer was washed with CH_2Cl_2 until the washings were clear. The combined organic washings were dried over Na_2SO_4, and the solvent was concentrated under reduced pressure. The resulting residue was chromatographed (silica gel, 90/10 CH_2Cl_2/hexanes eluant) to yield two pigments eluting in the order **16** and **17**. **3:1 Propyl Porphyrazine (16):** (60 mg, 0.08 mmol, 6%); mp 168−172 °C dec; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 333 (4.77), 568 (sh), 600 (4.67), 673 (4.55) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ −1.84 (br s, 2H), 1.26 (dt, J = 7.3 Hz and J = 1.2 Hz, 18H), 1.83 (d, J = 6.1 Hz, 6H), 2.39 (m, 12H), 3.80 (t, J = 7.7 Hz, 4H), 4.00 (t, J = 7.7 Hz, 4H), 4.09 (t, J = 7.6 Hz, 4H), 5.37 (m, 2H), 7.55 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 14.6, 14.7, 22.8, 25.2, 25.4, 25.5, 27.9, 28.1, 28.2, 71.7, 118.2, 121.9, 140.8, 141.6, 141.7, 145.1, 145.8, 149.2, 158.9, 161.4; FABMS m/z 733 (M^+), Calcd for $C_{44}H_{60}N_8O_2$: 733. Anal. Calcd for $C_{44}H_{60}N_8O_2$: C, 72.10; H, 8.25; N, 15.29. Found: C, 71.76; H, 8.48; N, 15.17. ***trans*-Propyl Porphyrazine (17):** (300 mg, 0.37 mmol, 18%); mp 260 °C dec; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 333 (4.85), 596 (4.59), 638 (4.88), 718 (4.59) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ −1.60 (br s, 2H), 1.28 (t, J = 7.3 Hz, 12H), 1.81 (d, J = 6.1 Hz, 24H), 2.39 (sextet, J = 7.3 Hz,

(41) Because of the difficulty associated with the purification of compound **7**, no effort was made to quantitate the yield at this stage.

8H), 4.09 (t, J = 7.1 Hz, 8H), 5.36 (hp, J = 6.1 Hz, 4H), 7.51 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6, 22.8, 25.1, 27.9, 71.7, 118.1, 130.0, 141.1, 145.1, 149.1, 158.3; FABMS m/z 815 (M^+), Calcd for $C_{48}H_{62}N_8O_4$: 815. Anal. Calcd for $C_{48}H_{62}N_8O_4$: C, 70.73; H, 7.67; N, 13.75. Found: C, 70.68; H, 7.76; N, 13.63.

Spirane Porphyrazine Hybrids 19 and 20. To Mg turnings (5 mg, 0.21 mmol) in BuOH (4 mL) was added a small crystal of I_2, and the suspension was heated under reflux for 12 h. To the cooled solution were added isoindoline **3** (131 mg, 0.50 mmol) and dinitrile **18** (28 mg, 0.10 mmol), after which the mixture was heated under reflux for 16 h. Removal of the solvent in vacuo, dissolution of the residue in CH_2Cl_2 (15 mL), and filtration through Celite allowed removal of most of the magnesium salts. After solvent removal, AcOH (7 mL) was added to the remaining solid material, and the solution was stirred for 12 h, poured into ice (ca. 50 mL), and neutralized with 1 N NaOH. Suction filtration afforded a dark green solid material which was subjected to column chromatography (silica gel, 70/30 hexanes/ethyl acetate and, subsequently, 95/5 toluene/acetone eluants), eluting the pigments in the order **19** and **20**. When making use of stoichiometric amounts of the starting materials, **19** and **20** were obtained in ca. 1:2 ratio (66% combined yield). ***trans*-Spirane Porphyrazine (19):** (22 mg, 21.1 μmol, 42%); mp 270−272 °C dec; IR ν_{max} (CH_2Cl_2) 1031, 1079, 1104, 1135, 1230, 1299, 1501, 1623, 2856, 2928, 2960, 3601, 3686 cm^{-1}; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 230 (4.50), 327 (4.74), 380 (4.15), 451 (4.20), 586 (4.36), 632 (4.79), 705 (4.51) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ −2.34 (s, 2H), 1.86−1.94 (m, 8H), 1.87 (d, J = 6.0 Hz, 12H), 1.92 (d, J = 6.0 Hz, 12H), 2.09 (d, J = 12.5 Hz, 4H), 2.21 (td, J = 13.2 Hz and J = 4.7 Hz, 4H), 2.62 (d, J = 14.0 Hz, 4H), 2.74 (dd, J = 12.8 Hz and J = 4.0 Hz, 4H), 3.76 (dd, J = 10.3 Hz and J = 2.9 Hz, 4H), 4.31 (td, J = 11.6 Hz and J = 2.6 Hz, 4H), 5.42 (hp, J = 6.1 Hz, 4H) 7.54 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 23.01, 23.05, 24.8, 28.7, 62.5, 74.5, 100.2, 121.8, 131.2, 134.8, 136.2, 150.3, 157.6; FABMS m/z 1043 (M^+); HRFABMS Calcd for $C_{56}H_{67}N_8O_{12}$ ($M + H^+$) 1043.488. Found: 1043.490. **3:1 Spirane Porphyrazine (20):** (5 mg, 4.7 μmol, 14%); mp 231−232 °C dec; IR ν_{max} (CH_2Cl_2) 1079, 1103, 1135, 1230, 1244, 1299, 1502, 1603, 1624, 2938, 2959, 2976, 3362 cm^{-1}; UV−vis (CH_2Cl_2) (log ϵ) λ_{max} 230 (4.25), 331 (4.78), 447 (4.24), 591 (4.58), 667 (4.49) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ −2.79 (s, 2H), 1.75−1.97 (m, 12H), 1.88 (d, J = 6.0 Hz, 6H), 1.93 (d, J = 6.0 Hz, 6H), 2.07−2.24 (m, 12H), 2.54−2.76 (m, 12H), 3.63−3.82 (m, 6H), 4.16−4.38 (m, 6H), 5.44 (hp, J = 6.0 Hz, 2H), 7.58 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 18.4, 22.99, 23.05, 24.8, 25.0, 28.7, 28.9, 29.0, 62.4, 62.5, 62.7, 74.5, 99.8, 100.1, 100.3, 122.3, 131.0, 135.2, 136.0, 136.3, 136.6, 138.1, 150.2, 150.4, 157.9; FABMS m/z 1075 (M^+); HRFABMS Calcd for $C_{56}H_{66}N_8NaO_{14}$ ($M + Na^+$) 1097.460. Found 1097.468.

Crystal Structure Determination of 17. Compound **17** was grown by diffusion of methanol into a solution of **17** in toluene. All measurements were made on an Enraf-Nonius CAD4 diffractometer. Crystal data for $C_{48}H_{62}N_8O_4$ (MW = 815.01) at 153 K (Mo−Kα radiation, λ = 0.710 69 Å, $2\theta_{max}$ = 49.9°, $\omega-\theta$ scan technique), orthorhombic, space group $P2_12_12_1$ (no. 19), a = 9.599(3) Å, b = 20.902(3) Å, c = 22.349(3) Å, V = 4484(1) Å^3, Z = 4, R = 0.095, wR = 0.0730, GOF = 2.39 for 1559 reflections with $I > 3.00\sigma(I)$ and 242 parameters. The structure was solved by direct methods (SIR92),[42] expanded using Fourier techniques, and refined by the full-matrix least-squares technique. Due to the paucity of data, the non-hydrogen atoms were refined isotropically. Hydrogen atoms on the carbon atoms were included in idealized positions but not refined. The Flack parameter supports the proposed model. All calculations were performed using the TEXSAN crystallographic software package of the Molecular structure Corporation (TEXSAN 5.0).

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Supporting Information Available: Copies of the ^{1}H (300 MHz, $CDCl_3$) and ^{13}C (75 MHz, $CDCl_3$) NMR spectra of compounds **19** and **20** and X-ray data of **17** (31 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for information.

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