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Selective Substitution of Corroles: Nitration, Hydroformylation, and Chlorosulfonation

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Abstract: This work demonstrates the feasibility and powerfulness of electrophilic substitution on the peripheral carbon atoms of triarylcorroles as a synthetic tool to new derivatives. The large difference in the reactivity of the various carbon atoms on the macrocycle was shown to be of electronic rather than steric origin. A careful choice of reagents and a delicate control of reaction conditions allowed the selective syntheses of novel derivatives, in all of which substitution took place selectively in only the directly joined pyrrole rings of the macrocycle. This was proven by a combination of X-ray crystallography of the various products and detailed analysis of their NMR spectra.

Introduction

For decades, the chemistry of corroles was almost entirely limited to derivatives with fully alkylated β-pyrrole positions,[1] with only three examples of meso-only substituted corroles.[2] This situation changed dramatically in 1999 with the disclosure of the first facile methodologies for the synthesis of 5,10,15-triarylcorroles from simple aldehydes and pyrrole;[3] about 80 new corroles that are substituted only at the three *meso*-carbon atoms were reported by now.[4] This development finally opened the gate for extensive investigations of corroles in the many applications that tetraarylporphyrins are constantly utilized.[5] Particularly, the metal complexes of 5,10,15-tris(pentafluorophenyl)corrole (**1** in Scheme 1) were shown to be very efficient catalysts for atom (oxygen) and group (carbene, nitrene) transfer to organic substrates.[6] In fact, for the latter reactions, the corrole metal complexes are significantly more efficient than analogous porphyrins.[6c,e] In addition, a water-soluble derivative of **1** (obtained by replacing its para-F atoms by pyridylium cations) was shown to be more efficient in inhibiting growth factors in tumor cells than analogous porphyrins, and novel photophysical properties of nontransition metal corroles were recently disclosed.[7,8]

The two major structural peculiarities of corroles relative to porphyrins are the presence of three rather than two NH protons in the coordination core and the lower symmetry. Large emphasis was given to the first feature, particularly for stabilization of metal ions in high oxidation states,[9] while the other one was ignored. For example, although N-substituted corroles were reported as early as 1965,[10] the fact that these molecules are chiral was not appreciated until most recently.[11] A different aspect is the possibility of selective substitution of the macrocycle's protons, which could not be explored for the traditional corroles because they were fully alkylated at the β-pyrrole carbon atoms.[12] On the other hand, electrophilic substitution of

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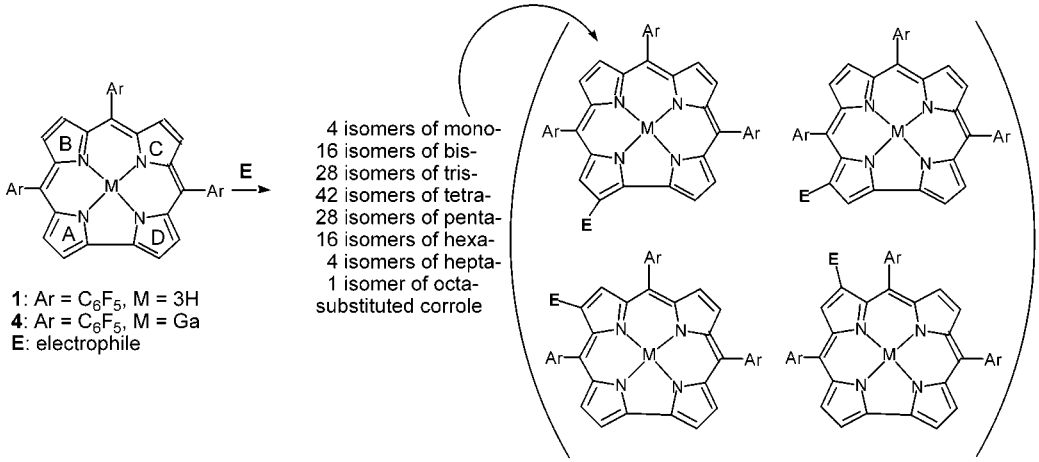
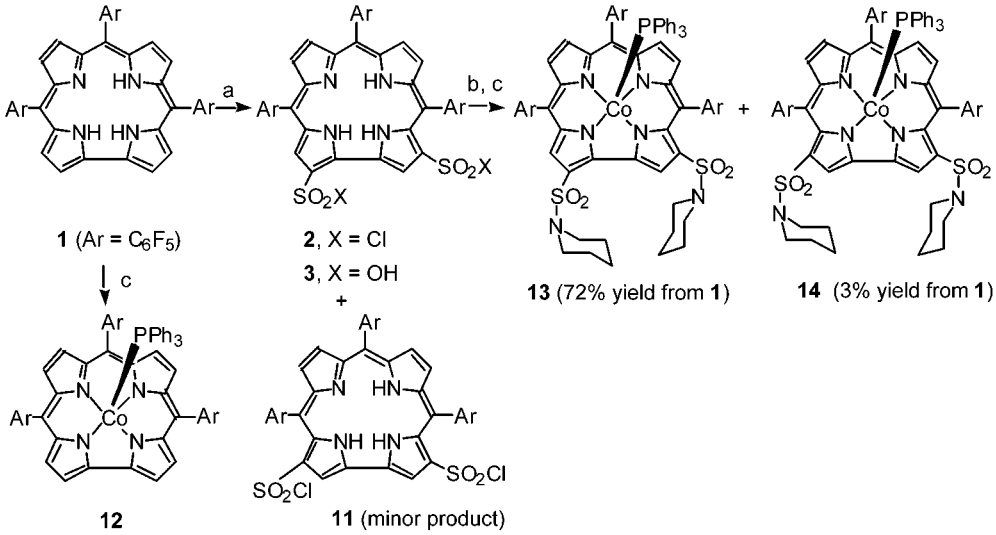
Scheme 1. Structures of **1** and **4** and the 139 Possible Products in Their Nonselective Electrophilic Substitution



Scheme 2. Selective Chlorosulfonation of Corrole **1**



porphyrins and phthalocyanines either proceeds to completion or provides an almost intractable mixture of products and isomers.[13] For example, even a bis-sulfonated phthalocyanine that was separated from mono- and multisulfonated products was shown to be a mixture of at least eight isomers.[14] In principle, the situation for meso-only substituted corroles could be better if the four different β-pyrrole carbon atoms display highly significant different reactivities. Otherwise, the number of possible products will be exceedingly large, up to 140 (Scheme 1).

In a recent preliminary publication, we have shown that chlorosulfonation of **1** proceeds with excellent selectivity as to produce the bis-functionalized corrole **2** in high yield (Scheme 2).[15] Hydrolysis of **2** provided the bis-sulfonic acid derivative **3**, in which the clear separation of the hydrophilic residues from the lipophilic parts provides amphiphilicity, a highly desirable feature in many applications. We now demonstrate that the selective functionalization of corroles is not limited to chlorosulfonic acid and also present several metal complexes of **3**.

Experimental Section

Physical Methods. The NMR spectra were recorded on a Bruker AM200 spectrometer, operating at 200 MHz for ^{1}H and 188 MHz for ^{19}F. Chemical shifts in the ^{1}H NMR spectra are reported in ppm relative to residual hydrogens in the deuterated solvents: $\delta = 7.20$ and 7.24 for benzene and chloroform, respectively, and to $CFCl_3$ ($\delta = 0.00$) in the ^{19}F NMR spectra. Coupling constants J are reported in Hz. A HP 8452A diode array spectrophotometer was used to record the electronic spectra. Mass spectroscopy was performed on a Finnigan TSQ 70 instrument with isobutane as carrier gas. The diffraction measurements were carried out on a Nonius Kappa CCD diffractometer, using graphite monochromated Mo Kα radiation ($\lambda = 0.7107$ Å).

Materials. All reagents were purchased from commercial sources and used as received unless otherwise noted. Acetonitrile was dried over P_2O_5 and distilled.

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Synthetic Methods. The synthetic details for the preparation of 5,10,15-tris(pentafluorophenyl)corrole (H_3(tpfc), **1**) and 5,10,15-tris-(pentafluorophenyl)corrolato gallium(III)(pyridine) (Ga(tpfc)(pyr), **4**) are provided in previous publications.[3,8]

Nitration of 4, the Gallium Complex of 1. (a) Conditions for Mononitration. **4** (40 mg, 0.043 mmol), sodium nitrite (290 mg, 4 mmol), and dry acetonitrile (5 mL) were placed in a two-necked flask, and the suspension was stirred for 10 min under Ar. Tris(4-bromophenyl)aminium hexachloroantimonate (**5**, 24 mg, 0.03 mmol, 75 mol %) was added, and stirring was continued for 1 h at room temperature, after which the solvent was evaporated to dryness. The crude material was separated and purified on a silica gel column eluted with 20% ethyl acetate in hexane, as to provide two fractions ($R_f = 0.43$ (major) and $R_f = 0.26$ (minor) on silica with hexane:ethyl acetate/3:2). Recrystallization from dichloromethane/hexane of the two fractions afforded 38 mg (84% yield) of 3-nitro-5,10,15-tris(pentafluorophenyl)corrolato gallium(III)(bis-pyridine) (**6**) and 4 mg (8.9% yield) of 3,17-dinitro-5,10,15-tris(pentafluorophenyl)corrolato gallium(III)(bis-pyridine) (**7**).

6. ^{1}H NMR ($CDCl_3$): $\delta = 9.69$ (s, 1H), 8.71 (d, ^3J(H,H) = 4.1 Hz, 1H), 8.61 (t, ^3J(H,H) = 5.1 Hz, 2H), 8.45 (d, ^3J(H,H) = 4.1 Hz, 1H), 8.32 (d, ^3J(H,H) = 4.6 Hz, 2H), 6.01 (t, ^3J(H,H) = 7.7 Hz, 2H), 5.89 (m, 4H), 5.55 (t, ^3J(H,H) = 6.2 Hz, 4H). ^{19}F NMR ($CDCl_3$): $\delta = -139.07$ (t, ^3J(F,F) = 12.6 Hz, 4F), −140.38 (dd, ^3J(F,F) = 24.6 Hz, ^4J(F,F) = 6.7 Hz, 2F), −152.15 (td, ^3J(F,F) = 21.9 Hz, ^4J(F,F) = 5.2 Hz, 2F), −153.59 (t, ^3J(F,F) = 21.4 Hz, 1F), −161.95 (m, 4F), −163.5 (td, ^3J(F,F) = 23.1 Hz, ^4J(F,F) = 6.9 Hz, 2F). UV/vis (EtOAc): λ_{max} 442 nm (ϵ 101 000), 612 (30 000). MS (DCI$^-$): *m/z* 906.9 [M − 2 pyridine]$^-$.

7. ^{1}H NMR ($CDCl_3$): $\delta = 9.54$ (s, 2H), 8.61 (d, ^3J(H,H) = 4.57 Hz, 2H), 8.35 (d, ^3J(H,H) = 4.6 Hz, 2H), 7.35 (t, ^3J(H,H) = 7.62 Hz, 2H), 6.60 (t, ^3J(H,H) = 6.06 Hz, 4H), 6.3 (br s, 4H). ^{19}F NMR ($CDCl_3$): $\delta = -139.04$ (dd, ^3J(F,F) = 19.9 Hz, ^4J(F,F) = 6.7 Hz, 2F), −140.53 (dd, ^3J(F,F) = 18.0 Hz, ^4J(F,F) = 6.7 Hz, 4F), −150.86 (t, ^3J(F,F) = 21.4 Hz, 1F), −152.06 (t, ^3J(F,F) = 21.2 Hz, 2F), −161.37 (td, ^3J(F,F) = 22.1 Hz, ^4J(F,F) = 6.2 Hz, 2F), −162.58 (td, ^3J(F,F) = 22.1 Hz, ^4J(F,F) = 6.5 Hz, 4F). UV/vis (EtOAc): λ_{max} 324 nm (ϵ 26 500), 380 (17 000), 460 (46 200), 644 (31 000). MS (DCI$^-$): *m/z* 951 [M − 2 pyridine]$^-$.

(b) Conditions for Bis-nitration. The same reaction conditions as above were utilized, but with more tris(4-bromophenyl)aminium hexachloroantimonate (68.8 mg, 0.08 mmol, 200 mol %). The crude material was separated and purified on a silica gel column eluted with 20% ethyl acetate in hexane, as to provide three fractions: **6** (2%), **7** (94%), and traces of 3,17,18-trinitro-5,10,15-tris(pentafluorophenyl)-corrolato gallium(III)(bis-pyridine) **8** ($R_f = 0.12$ on silica with hexane: ethyl acetate/3:2).

(c) Conditions for Tris-nitration. Using identical reaction conditions as above, but with 300 mol % tris(4-bromophenyl)aminium hexachloroantimonate (103 mg, 0.12 mmol), we separated the crude material and purified it on a silica gel column eluted with 20% ethyl acetate in hexane, as to provide three fractions: traces of **6**, **7** (58%), and **8** (27%).

8. ^{1}H NMR ($CDCl_3$): $\delta = 9.84$ (s, 1H), 8.44 & 8.39 (overlapping doublets, 2H), 8.18 & 8.14 (overlapping doublets, 2H), 7.36 (t, ^3J(H,H) = 7.6 Hz, 2H), 6.81 (br s, 4H), 6.08 (br s, 4H). ^{19}F NMR ($CDCl_3$): $\delta = -138.23$ (m, 4F), −139.95 (d, ^3J(F,F) = 16.1 Hz, 2F), −149.24 (t, ^3J(F,F) = 20.4 Hz, 1F), −150.93 (t, ^3J(F,F) = 20.8 Hz, 1F), −152.04 (t, ^3J(F,F) = 20.7 Hz, 1F), −160.65 (t, ^3J(F,F) = 20.4 Hz, 4F), −161.98 (t, ^3J(F,F) = 20.6 Hz, 2F). UV/vis (EtOAc): λ_{max} 326 nm (ϵ 25 000), 416 (42 000), 456 (31 000), 616 (29 000), 668 (28 000). MS (DCI$^-$): *m/z* 997 [M − 2 pyridine]$^-$.

The X-ray quality crystals of complexes **6**, **7**, and **8** were obtained via slow crystallization from mixtures of benzene/heptane, $CHCl_3$/heptane, and CH_2Cl_2/hexane, respectively, with small amounts of pyridine present in all cases.

Hydroformylation of 4, the Gallium Complex of 1. (a) Conditions for Monosubstitution. DMF (0.16 mL) was cooled to 5−10 °C, $POCl_3$ (0.12 mL, 1.16 mmol) was added under N_2, and the mixture was stirred for 15 min. The ice bath was removed, and the solution was stirred for another 15 min. Dry dichloromethane (4 mL) was then added, and the reagent was cooled to 0−5 °C. A limited amount of the reagent (0.428 mL) was added dropwise to a solution of **4** (100 mg, 0.106 mmol) in 8 mL of CH_2Cl_2. During addition, the solution turned from red to deep green, and after 3−5 min, TLC (silica, CH_2Cl_2:hexane, 2:1, and some drops of pyridine) showed no starting material. A saturated solution of Na_2CO_3 (50 mL) was added, and the mixture was stirred overnight, after which the organic phase was separated. The water phase was extracted by CH_2Cl_2 three times, the organic phases were combined, washed by brine, dried by Na_2SO_4, and the solvents were evaporated. Column chromatography on silica (eluent, CH_2Cl_2:hexane:pyridine, which was gradually changed from 100:20:0.2 to 60:100:0.4) afforded 3-formyl-5,10,15-tris(pentafluorophenyl)corrolato gallium(III)(pyridine) (**9**) as green-blue crystals (yield 0.091 g, 87% after recrystallization from CH_2Cl_2, hexane, and some drops of pyridine). ^{1}H NMR ($CDCl_3$): δ 10.52 (s, 1H, CHO), 9.65 (s, 1H, α-CHO), 9.11 (d, ^3J(H,H) = 4.1 Hz, 1H), 8.76 (d, ^3J(H,H) = 4.7 Hz, 1H), 8.73 (d, ^3J(H,H) = 4.1 Hz, 1H), 8.67 (d, ^3J(H,H) = 4.8 Hz, 1H), 8.52 (d, ^3J(H,H) = 4.8 Hz, 1H), 8.48 (d, ^3J(H,H) = 4.7 Hz, 1H), 6.77 (tt, ^3J(H,H) = 7.7 Hz, ^4J(H,H) = 1.5 Hz, 1H), 6.00 (td, ^3J(H,H) = 6.6 Hz, ^4J(H,H) = 1.24 Hz, 2H), 3.29 (d, ^3J(H,H) = 5.0 Hz, 2H). ^{19}F NMR ($CDCl_3$): δ −138.1 (m (overlapping doublet), 4F), −138.96 (dd, ^3J(F,F) = 24.16 Hz, ^4J(F,F) = 8.27 Hz, 2F), −153.02 (t, ^3J(F,F) = 20.34 Hz, 1F), −153.05 (t, ^3J(F,F) = 20.68 Hz, 1F), −153.38 (t, ^3J(F,F) = 21.24 Hz, 1F), −162.4 (m, 6F). UV/vis (CH_2Cl_2): λ_{max} (ϵ (M^{-1} cm^{-1})) = 410 nm (41 300), 432 (171 500), 602 (24 600), 620 (28 600). IR ($CHCl_3$, cm^{-1}): 1653 (CO). MS (DCI$^+$): *m/z* (%) 891 ([MH$^+$], 100). MS (DCI$^-$): *m/z* (%) 890 ([M$^-$], 100), 862 ([M −CO], 20). $R_f = 0.18$ (CH_2Cl_2:hexane, 2:1, and some drops of pyridine). Further elution by CH_2Cl_2:pyridine (100: 0.5) gives 2,17-bis-formyl-5,10,15-tris(pentafluorophenyl)corrolato gallium(III)(bis-pyridine) (**10**) (yield 0.004 g, 3.5% after recrystallization from CH_2Cl_2, hexane, and some drops of pyridine). ^{1}H NMR ($CDCl_3$): δ 11.13 (s, 1H, CHO), 10.57 (s, 1H, CHO), 10.03 (s, 1H, α-CHO), 9.01 (s, 1H, α-CHO), 8.67 (d, ^3J(H,H) = 4.76 Hz, 1H), 8.60 (d, ^3J(H,H)- = 4.78 Hz, 1H), 8.38 & 8.37 (overlapping doublets, 2H), 7.04 (td, ^3J(H,H) = 7.68, ^4J(H,H) = 1.6 Hz, 2H), 6.33 (t, ^3J(H,H) = 7.06, 4H), 4.33 (br s, 4H). ^{19}F NMR ($CDCl_3$): δ −138.08 (m, 4F), −139.57 (dd, ^3J(F,F) = 23.97, ^4J(F,F) = 8.08 Hz, 2F), −152.15 (t, ^3J(F,F) = 42.49 Hz, 1F), −152.74 (t, ^3J(F,F) = 42.11 Hz), −153.05 (t, ^3J(F,F) = 42.11 Hz, 1F), −161.48 (dt, ^3J(F,F) = 43.43 Hz, ^4J(F,F) = 7.33 Hz, 2F), −161.87 (dt, ^3J(F,F) = 44.46 Hz, ^4J(F,F) = 7.52 Hz, 2F), −162.71 (dt, ^3J(F,F) = 44.84 Hz, ^4J(F,F) = 7.33 Hz, 2F). UV/vis (CH_2Cl_2): λ_{max} (ϵ (M^{-1} cm^{-1})) = 416 nm (20 700), 436 (57 100), 612 (16 400), 636 (12 600). IR ($CHCl_3$, cm^{-1}): 1674 (CO). MS (DCI$^+$): *m/z* (%) 919 ([MH$^+$], 100). MS (DCI$^-$): *m/z* (%) 918 ([M$^-$], 100), 890 ([M$^-$ − CO], 40). $R_f = 0.11$ (CH_2Cl_2:hexane, 2:1, and some drops of pyridine).

(b) Conditions for Bis-substitution. DMF (1.6 mL) was cooled to 5−10 °C, $POCl_3$ (1.22 mL, 11.6 mmol) was added under N_2, and the mixture was stirred for 15 min. The ice bath was removed, and the solution was stirred for another 15 min. Dry dichloromethane (2 mL) was then added, and the reagent was cooled to 0−5 °C. This solution was added dropwise to a solution of **4** (100 mg, 0.106 mmol) in 2 mL of CH_2Cl_2. During addition, the solution turned from red to deep green, and after 3−5 min, TLC (silica, CH_2Cl_2:hexane, 2:1, and some drops of pyridine) showed no starting material. A saturated solution of Na_2CO_3 was added, and the mixture was stirred overnight, after which the organic phase was separated. The aqueous phase was extracted by CH_2Cl_2, the organic phases were collected and washed by brine, dried by Na_2SO_4, and solvents were evaporated. Column chromatography on silica (eluent:CH_2Cl_2:hexane:pyridine, which was gradually changed from 100:20:0.2 to 60:100:0.4) afforded **9** as green-blue crystals (yield

0.015 g, 15% after recrystallization from CH_2Cl_2, hexane, and some drops of pyridine). Further elution by CH_2Cl_2:pyridine (100:0.5) provides **10** (yield 0.075 g, 64% after recrystallization from CH_2Cl_2, hexane, and some drops of pyridine).

Chlorosulfonation of 1 (Preparation of 2 and 3). Eighty milligrams of **1** (100 μmol) and 2 mL of chlorosulfonic acid (30 mmol) were stirred at 25 °C for 5 min, after which the reaction mixture was cooled by an ice bath and treated with small ice chips (5−10 g, caution!). The product was obtained via the addition of 20 mL of distilled water and CH_2Cl_2 (the CH_2Cl_2 solution was washed three times with distilled water) and evaporation. On the basis of NMR spectroscopy, **2** was obtained in quantitative yield. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.44 (s, 1H), 8.95 (s, 1H), 8.60 (d, J = 5.0 Hz, 1H), 8.50 (d, J = 5.0 Hz, 1H), 8.41 (d, J = 5.0 Hz, 1H), 8.18 (d, J = 5.0 Hz, 1H). ^{19}F NMR (188 MHz, $CDCl_3$): δ = −137.5 (d, J = 21.1 Hz, 4F), −138.3 (d, J = 18.1 Hz, 2F), −149.6 (t, J = 21.31, 1F), −150.1 (t, J = 21.21, 2F), −160.0 (m, 4F), −161.6 (m, 2F). MS (DCI$^-$): m/z (%) 991.8 (5) [M$^-$], 892 (20) [M$^-$ − SO_2Cl].

A suspension of **2** in 20 mL of water was refluxed for 12 h. The solution was filtered and evaporated to dryness as to provide **3** in 71% yield based on **1** (68 mg, 71 μmol). ^{1}H NMR (CD_3OD): δ = 9.68 (br s, 1H), 9.14 (d, J = 4.8 Hz, 1H), 8.98 (d, J = 4.8 Hz, 1H), 8.90 (br s, 1H), 8.86 (d, J = 4.8 Hz, 1H), 8.84 (d, J = 4.8 Hz, 1H). ^{19}F NMR (188 MHz, CD_3OD): δ = −137.5 (d, J = 20.3 Hz, 2F), −137.8 (d, J = 19.6 Hz, 4F), −149.8 (t, J = 20.3, 1F), −150.8 (t, J = 20.1, 1F), −152.1 (t, J = 19.4, 1F), −160.3 (m, 2F), −160.8 (m, 2F), −163.1 (m, 2F). UV/vis (buffer solution, pH 7.00): λ_{max} (ϵ (M^{-1} cm^{-1})) = 414 (71 000), 430 (62 000), 588 (15 000), 620 (27 000). MS (MALDI-TOF): m/z 956.6 [M$^+$].

Chlorosulfonation of 1, Followed by Amidation and Insertion of Cobalt (Preparation of 13 and 14). As described in our previous publication,[15] the successive treatment of complex **2**, obtained as described above, with piperidine, cobalt(II) acetate, and triphenylphosphine allows the isolation of 2,17-substituted complex **13** in 72% yield via recrystallization from benzene/heptane, while the 3,17-substituted isomer **14** is obtained in 3% yield from chromatographic treatment of the mother liquor. X-ray quality crystals of complex **14** were obtained from benzene/heptane.

Metalation of 3. Insertion of Gallium(III). A solution of **3** (20 mg, 21 μmol) in pyridine (10 mL) was added to a flask that contains a large excess (about 0.2 g) of flame-dried $GaCl_3$, and the reaction mixture was heated to reflux for 30 min under argon, followed by evaporation of the solvent. The inorganic salts were separated by column chromatography on silica (eluent, MeOH:pyridine = 20:1), affording 21 mg (19 μmol, 90% yield) of the (pyridine)gallium(III) complex of **3**.

^{1}H NMR (CD_3OD): δ = 9.77 (s, 1H), 8.77 (s, 1H), 8.70 (d, ^3J(H,H) = 4.8 Hz, 1H), 8.57 (d, ^3J(H,H) = 4.8 Hz, 1H), 8.48 (t, ^3J(H,H) = 4.3 Hz, 2H), 8.27 (br s, 2H), 7.71 (t, 1H), 7.30 (br s, 2H). ^{19}F NMR (CD_3OD): δ = −135.2 (d, ^3J(F,F) = 23.0 Hz, 2F), −136.8 (d, ^3J(F,F) = 23.5 Hz, 4F), −153.5 (t, ^3J(F,F) = 20.1 Hz, 1F), −154.1 (t, ^3J(F,F) = 20.5 Hz, 1F), −156.2 (t, ^3J(F,F) = 20.3 Hz, 1FF), −162.2 (m, 4F), −165.1 (m, 2F). UV/vis (buffer solution, pH 7.30): λ_{max} 424 nm (ϵ 75 000), 588 (13 600), 610 (17 300). MS (MALDI-TOF): m/z 1022.2 [M$^+$ − pyridine, 100%] and a characteristic isotopic pattern of 1023.2 (55%), 1024.2 (92%), 1025.2 (58%).

Insertion of Manganese(III). A flask loaded with a 10 mL of DMF solution of **3** (15 mg, 16 μmol) and $Mn(OAc)_2 \cdot 4H_2O$ (15 mg, 61 μmol) was heated to reflux for 15 min, followed by evaporation of the solvent. The inorganic salts were separated by column chromatography on silica (eluent: EtOH), affording 15 mg (15 μmol, 94% yield) of the manganese(III) complex of **3**.

UV/vis (buffer solution, pH 7.30): λ_{max} 392 nm (ϵ 19 000), 422 (21 000), 480 (17 000), 644 (11 500), 610 (9500), 576 (9000). MS (MALDI-TOF): m/z 1007.9 [M$^+$, 100%], 108.9 [MH$^+$, 85%].

Insertion of Cobalt(III). A 10 mL EtOH solution of **3** (10 mg, 10 μmol) and NaOAc (30 mg, 0.37 mmol) was mixed for 5 min at 25 °C, after which PPh_3 (20 mg, 76 μmol) and $Co(OAc)_2 \cdot 4H_2O$ (20 mg, 80 μmol) were added, and the solution was mixed for another 30 min. Following solvent evaporation, column chromatography on silica with CH_2Cl_2 as eluent was used to remove the excess of PPh_3 and EtOH to free the product from inorganic salts, as to afford 12 mg (9 μmol, 90% yield) of the (triphenylphosphine)cobalt(III) complex of **3**.

^{1}H NMR (CD_3OD): δ = 9.40 (s, 1H), 8.40 (m, 5H), 7.05 (t, ^3J(H,H) = 8.0 Hz, 3H), 6.70 (t, ^3J(H,H) = 7.7 Hz, 6H), 4.60 (dd, ^3J(H,H) = 7.8 Hz, ^3J(P,H) = 11.3 Hz, 6H). ^{19}F NMR (CD_3OD): δ = −134.9 (dd, ^3J(F,F) = 24.0 Hz, ^4J(F,F) = 7.0 Hz, 1F), −135.2 (dd, ^3J(F,F) = 24.0 Hz, ^4J(F,F) = 7.0 Hz, 1F), −135.7 (dd, ^3J(F,F) = 24.0 Hz, ^4J(F,F) = 7.0 Hz, 1F), −136.7 (dd, ^3J(F,F) = 24.0 Hz, ^4J(F,F) = 7.0 Hz, 1F), −137.0 (m, 2F), −152.7 (t, ^3J(F,F) = 20.0 Hz, 1F), −153.0 (t, ^3J(F,F) = 20.0 Hz, 1F), −155.5 (t, ^3J(F,F) = 20.0 Hz, 1F), −161.4 (m, 4F), −164.7 (m, 2F). UV/vis (MeOH): λ_{max} (ϵ) 378 nm (32 000), 410 (33 000), 558 (8600), 594 (9000).

Insertion of Tin(IV). A 10 mL DMF solution of **3** (12 mg, 13 μmol) and $SnCl_2 \cdot 2H_2O$ (12 mg, 53 μmol) was heated to reflux for 30 min, followed by evaporation of the solvent. Addition of CH_2Cl_2 to the residue, filtration, and solvent evaporation afforded 13 mg (12 μmol, 92% yield) of the (chloro)tin(IV) complex of **3** after evaporation.

^{1}H NMR (CD_3OD): δ = 10.04 (s, 1H), 9.04 (d, ^3J(H,H) = 4.8 Hz, 1H), 8.96 (s, 1H), 8.94 (d, ^3J(H,H) = 5.2 Hz, 1H), 8.84 (d, ^3J(H,H) = 4.3 Hz, 2H). ^{19}F NMR (CD_3OD): δ = −135.1 (m, 2F), −136.8 (m, 4F), −151.8 (t, ^3J(F,F) = 20.2 Hz, 1F), −152.4 (t, ^3J(F,F) = 20.0 Hz, 1F), −154.7 (t, ^3J(F,F) = 20.0 Hz, 1F), −161.2 (m, 4F), −164.3 (m, 2F). UV/vis (MeOH): λ_{max} (ϵ) 424 nm (140 000), 582 (16 000), 602 (18 000). MS (FAB$^-$): m/z 1107.38 [M$^-$].

Insertion of Chromium(III). One portion of $CrCl_2$ (40 mg, 0.33 mmol) was added at once to a 10 mL pyridine solution of **3** (14 mg, 15 μmol), and the mixture was heated immediately to reflux for 30 min. The solvent was evaporated, and inorganic salts were removed via column chromatography on silica (eluent, MeOH:pyridine = 20:1). Dissolving the dried product in CH_2Cl_2, filtration, and solvent evaporation afforded 16 mg (14 μmol, 93% yield) of the (bis-pyridine)-chromium(III) complex of **3**.

UV/vis (MeOH/pyridine 5%): λ_{max} (ϵ) 320 nm (11 000), 420 (19 000), 434 (22 000), 476 (6300), 542 (3700), 586 (5100), 614 (6300), 648 (7300).

Crystallography. The crystalline samples of **6** and **8** were covered with a thin layer of light oil and cooled to 110−115 K to minimize the escape of volatile crystallization solvents and minimize thermal motion/structural disorder effects. Crystal structures of **7** and **14** were analyzed at room temperature. The intensity data were corrected for absorption. The structures were solved by direct methods (SHELXS-86 and SIR-92),[16] and refined by full-matrix least-squares on F^2 (SHELXL-97).[17] All non-hydrogen atoms of the corroles were refined anisotropically. The hydrogens were located in idealized positions, and were refined using a riding model with fixed thermal parameters [$U_{ij} = 1.2U_{ij}$ (equiv) for the atom to which they are bonded]. The four corrole compounds cocrystallized with additional guest/solvent components trapped, and severely disordered, in the lattice. In addition, partial rotational disorder characterizes some of the pentafluorophenyl rings of the corroles (as it is demonstrated, in particular, by excessively large thermal displacement parameters of the corresponding atoms), affecting to some extent (particularly in **7** and **8**) the precision of the crystallographic determination. Yet, in all cases the crystallographic analysis provided an unequivocal description of the respective molecular structures, adding confidence to the conclusions based on the spectroscopic analyses.

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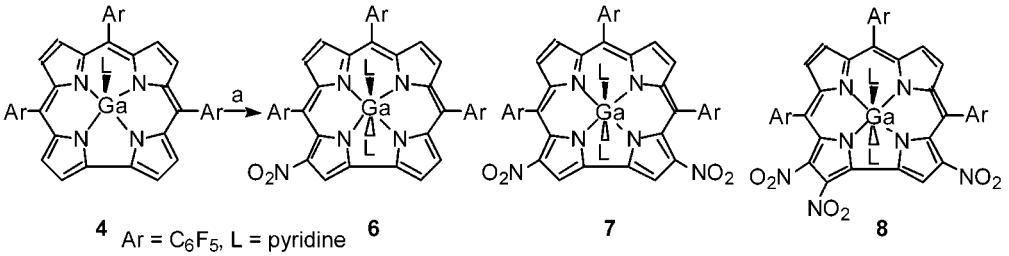
Scheme 3. Selective Nitration of **4**



a. 40 mmol **4**, 4 μmol $NaNO_2$, 5 mL CH_3CN, Ar, + $(Ar_3N^{+\cdot})(SbCl_6^-)$ (**5**, Ar = 4-bromophenyl)
30 μmol **5**: 84% **6**, 9% **7**
80 μmol **5**: 2% **6**, 94% **7**, <1% **8**
120 μmol **5**: <1% **6**, 58% **7**, 27% **8**

Crystal Data. 6. $C_{42}H_{12}F_{15}GaN_6O_2\cdot(C_6H_6)$, $M = 1065.4$, orthorhombic, space group $P2_12_12_1$, $a = 12.0410(2)$, $b = 18.2040(3)$, $c = 18.5900(3)$ Å, $V = 4074.8(1)$ Å^3, $Z = 4$, $T = 110(2)$ K, $D_c = 1.737$ g cm^{-3}, μ(Mo Kα) = 0.80 mm^{-1}, 5283 unique reflections to $2\theta_{max} = 55.7°$, 662 refined parameters, $R_1 = 0.046$ for 4374 observations with $I > 2\sigma(I)$, $R_1 = 0.064$ (w$R_2 = 0.113$) for all unique data. Molecules of the benzene solvent exhibit an in-plane rotational disorder, which was modeled by two possible orientations with occupancy factors of 0.71(3) for the major site and 0.29 for the minor one. This compound crystallized as a racemic twin.

7. $C_{47}H_{16}F_{15}GaN_8O_4\cdot NaNO_3$, $M = 1196.4$, monoclinic, space group $P2_1/c$, $a = 17.9080(4)$, $b = 12.5160(2)$, $c = 25.1330(5)$ Å, $\beta = 122.650(2)°$, $V = 4743.1(2)$ Å^3, $Z = 4$, $T = 293(2)$ K, $D_c = 1.675$ g cm^{-3}, μ(Mo Kα) = 0.71 mm^{-1}, 8117 unique reflections to $2\theta_{max} = 50.0°$, 738 refined parameters, $R_1 = 0.069$ for 2987 observations with $I > 2\sigma(I)$, $R_1 = 0.158$ (w$R_2 = 0.181$) for all unique data. The experimental measurements were carried out in this case at room temperature, at which the analyzed crystal exhibited somewhat poor diffraction because of the considerable disordered guest species. Thus, the structure of the sodium nitrate could not be precisely modeled.

8. $C_{42}H_{10}F_{15}GaN_8O_6\cdot CH_2Cl_2\cdot C_6H_{12}$, $M = 1246.4$, monoclinic, space group $P2_1/c$, $a = 11.3990(3)$, $b = 19.0230(4)$, $c = 22.7610(6)$ Å, $\beta = 104.564(1)°$, $V = 4777.0(2)$ Å^3, $Z = 4$, $T = 110(2)$ K, $D_c = 1.733$ g cm^{-3}, μ(Mo Kα) = 0.81 mm^{-1}, 10 262 unique reflections to $2\theta_{max} = 55.7°$, 799 refined parameters, $R_1 = 0.101$ for 6276 observations with $I > 2\sigma(I)$, $R_1 = 0.160$ (w$R_2 = 0.312$) for all unique data. The crystals turned out to be partly twinned. Moreover, the dichloromethane and hexane solvent species are severely disordered in the crystal lattice even at the low temperature and could not be reliably modeled and refined. The pentafluorophenyl rings also exhibit large-amplitude thermal motion about axes connecting them to the main corrole ring, hence, the relatively high R factors.

14. $C_{65}H_{41}CoF_{15}N_6O_4PS_2\cdot C_6H_6$, $M = 1487.2$, triclinic, space group P-1, $a = 13.827(3)$, $b = 13.815(3)$, $c = 18.209(4)$ Å, $\alpha = 76.76(2)$, $\beta = 79.18$, $\gamma = 70.13(2)°$, $V = 3161.2(12)$ Å^3, $Z = 2$, $T = 293(2)$ K, $D_c = 1.562$ g cm^{-3}, μ(Mo Kα) = 0.46 mm^{-1}, 8592 unique reflections to $2\theta_{max} = 46.0°$, 799 refined parameters, $R_1 = 0.105$ for 5128 observations with $I > 2\sigma(I)$, $R_1 = 0.167$ (w$R_2 = 0.270$) for all unique data. The crystals of this compound were diffracting poorly because of wide-amplitude thermal motion of the included solvent and the various substituents on the corrole ring.

Results

Initially, all three reactions were attempted on the metal-free corrole **1**. Chlorosulfonation proceeded very well, but poor results were obtained for hydroformylation and nitration. Accordingly, the two latter reactions were performed on the gallium(III) complex of **1** (**4**), similar to the well-documented approach of using zinc(II) and other metals in porphyrins. Complex **4** was previously shown to be a pentacoordinated complex both in solution and in the solid phase.[8] The NMR examinations show that the same holds for complex **9**, while **6**, **7**, **8**, and **10** were obtained as hexacoordinated (bis-pyridine) complexes. This factor was taken into consideration for calculation of the chemical yield. The lability of the sixth ligand[8b] is responsible for the fact that the X-ray quality crystals of complexes **6** and **8** contain only a single pyridine ligand.

Nitration. The nitration of **4** was performed by its mixing with a suspension of $NaNO_2$ in CH_3CN (no reaction) and at-once addition of a limited amount of the one-electron oxidant tris(4-bromophenyl)aminium hexachloroantimonate (**5**). With 75 mol % oxidant, the major product was the mononitro corrole **6** (isolated yield: 84%), with 200 mol % oxidant, the bis-nitro complex **7** was isolated in 94% yield, and with 300 mol % of **5**, the trinitrocorrole **8** and **7** were isolated in 27 and 58% yield, respectively (Scheme 3). Most important, all three products were obtained as single isomers, that is, only one out of four possible mono-, one out of 16 bis-, and one out of 28 tris-nitro corroles. This was elucidated by NMR spectroscopy and further substantiated by X-ray crystallography of all three nitro-substituted corroles.

Hydroformylation. For the synthesis of the monosubstituted corrole, a limited amount of the Vielsmeier reagent was used, and the desired product (**9**) was obtained in 87% yield as a single isomer, accompanied by a small amount of the bis-substituted product (**10**). On the other hand, the reaction does not proceed further than bis-substitution even with a 100-fold excess of reagent, and **10** can be isolated in 64% yield without any indication for other isomers. On the basis of a spectral comparison (^{1}H and ^{19}F NMR) with the nitro-substituted products, the substitution patterns are identical for the mononitro and the monoformyl corroles, but different for the bis-substituted products.

Chlorosulfonation. This reaction was only performed with excess reagent, which served as solvent as well. Only bis-substituted products were obtained, in a ratio of 96:4 in favor of the 2,17- relative to the 3,17-substituted isomer. Upon hydrolysis, the bis-sulfonate corrole **3** was obtained in 71% relative to **1**. Interestingly, applying the same reaction conditions for either the gallium complex **4** or the metal-free 5,10,15-tris-(2,6-difluorophenyl)corrole resulted in much lower selectivities (no attempts were made to separate the products or to find alternative reaction conditions).

Metalation of 3. Gallium(III), chromium(III), manganese(III), cobalt(III), and tin(IV) were inserted in the inner core of

3, using the methods that were developed for metal insertion into **1**.[6,8,18] In all of the cases, the reactions proceeded quantitatively, and the products were identified via comparison to the corresponding metal complexes of **1**.

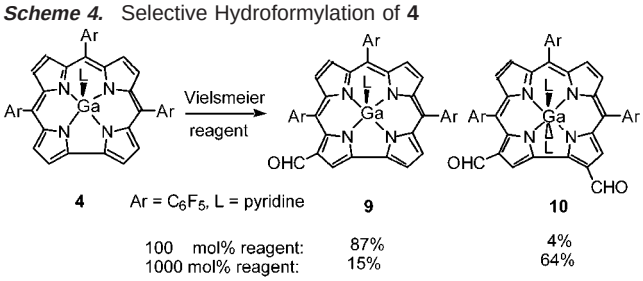
Discussion

The most remarkable result of these studies is the high selectivity that is displayed by corrole **1** and its gallium(III) complex **4** in their reactions with all three systems. However, a prerequisite for elucidating possible reasons for this phenomenon is to discuss the synthetic and possibly mechanistic aspects and the way that the structures were determined.

Syntheses. (a) Nitration. The nitration of **4** was first attempted with a variety of reagents that were previously used with zinc(II) and other metal porphyrins: HNO_3/H_2SO_4, HNO_3/AcOH, N_2O_4, cerium(IV) ammonium nitrate (CAN), and $AgNO_2/I_2$.[19] Yet, all of these conditions led to significant decomposition of the corrole ring and to mixtures of products resulting from polynitration. During these attempts, we noted the reports that in many cases (particularly with the $AgNO_2/I_2$ system) the porphyrin is first oxidized to its π-cation radical which subsequently reacts with NO_2^-.[20] Accordingly, we have prepared the already reported π-cation radical of **4**, obtained via oxidation with tris(4-bromophenyl)aminium hexachloroantimonate (**5**),[8a] and reacted it with NO_2^-. To our surprise, while addition of **5** prior to the nucleophile gave negative results, the opposite order of addition was very successful. In addition, it was easy to control the extent of substitution by adjusting the amount of **5** (Scheme 3). Importantly, even with only 75 mol % of **5**, the starting material was fully consumed, and the mono- and dinitro corroles **6** and **7** were isolated in 84 and 9% yield, respectively, clearly indicative of a chain reaction. Accordingly, we suggest that under these reaction conditions (very large excess of $NaNO_2$ relative to **4**), **5** oxidizes NO_2^- to NO_2, rather than **4** to its π-cation radical. Supporting evidence for this hypothesis is provided by the following observations: the best results with all previous mentioned methods were obtained with N_2O_4, selective nitration (to the C3-position) by the **5**/$NaNO_2$ system was obtained even with a corrole metal complex that is not oxidizable by **5** (the tin complex (tpfc)SnCl),[6c] and the regioisomer of the bis-substituted product in the **5**/$NaNO_2$ system is different from that obtained with the clearly electrophilic reagents (the Vielsmeier reagent and chlorosulfonic acid).

(b) Hydroformylation. The obvious choice for this reaction was the Vielsmeier reagent, which was previously used for the substitution of both the *meso*- and the β-pyrrole carbon atoms of porphyrins and the *meso*-carbon atoms of octa-alkyl corroles.[12,21] These literature reports reveal several important

Scheme 4. Selective Hydroformylation of **4**



findings: the reaction conditions employed for corroles are milder, the meso positions are more reactive than the β-pyrroles in both macrocycles, and there is no selectivity in the very few cases that proceed beyond monosubstitution. In contrast, in the reaction of **4** with 110 mol % of reagent at room temperature, only one out of the four possible monosubstituted products was obtained (**9**, Scheme 4), together with small amounts of the 2,17 bis-substituted corrole (**10**). The latter was the main product (64% yield) when up to 1000 mol % of reagent was used, and there were no indications for any of the other 15 different bis-formyl corroles that could have been formed in principle. Although both **9** and **10** were stable compounds, we were not able to grow X-ray quality crystals. Fortunately, the presence of the formyl groups allowed for quite straightforward identification of the products' structures.

(c) Chlorosulfonation. The two major advantages of chlorosulfonation relative to direct sulfonation are the much milder reaction conditions (0−25 °C vs >100 °C) and the larger synthetic utility of the product (RSO_2Cl vs RSO_3H). On the other hand, the large reactivity of chlorosulfonic acid (CSA) presents a problem in reactants with multiple reactive sites; the preferred sites for substitution reactions of tetraarylporphyrins with CSA are the aryls, and the various available positions in phthalocyanines are substituted with very low selectivity.[22] In sharp contrast, the reaction of **1** with excess CSA displays very high selectivity for the 2,17-bis-substituted corrole **2**. The only other product (**11**, =3%) was the 3,17-isomer, which was isolated after amidation of **2** by piperidine and subsequent metalation by cobalt (Scheme 2). Both the 2,17- and the 3,17-regioisomers were fully characterized by NMR spectroscopy and X-ray crystallography of their (triphenylphosphine)cobalt(III) complexes, **13** and **14**, respectively.

(d) Metalation. The most variable compounds obtained in this study are **2** and **3**, because of the easy substitution of the chloride in the $-SO_2Cl$ functions of **2** and the large variety of metal ions that can be inserted into either **2** or **3**. As the first option was already demonstrated in our previous publication,[15] we turned our attention to the metalation of **3**. Generally, the same methods that were developed for corrole **1** worked for **3**

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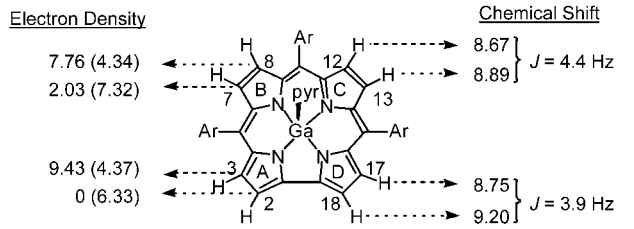

Figure 1. Drawing and numbering system of **4**, the ^{1}H NMR chemical shifts of its β-pyrrole protons (in C_6D_6), and the calculated HOMO electron density on the β-pyrrole carbon atoms (numbers in parentheses are for the close-in-energy HOMO-1).

as well: $Co(OAc)_2/PPh_3$/EtOH for obtaining the (triphenylphosphine)cobalt(III) complex of **3**, $CrCl_2$/pyridine for the (bis-pyridine)chromium(III) complex, $Mn(OAc)_2$/DMF for the manganese(III) complex, $SnCl_2{\cdot}2H_2O$/DMF for the (chloro)tin(IV) complex, and $GaCl_3$/pyridine for the gallium(III) complex. Both **3** and its metal complexes were soluble in water, and at the low concentrations that are relevant for UV−vis measurements (10^{-4}−10^{-6} M), the linear plots obtained for elucidating the ϵ values indicate the absence of aggregation.

Structural Elucidation. (a) NMR Spectroscopy. A prerequisite for determining the structures of the reaction products of **1** and **4** with the various reagents via NMR spectroscopy is the assignment of the CH protons in the starting materials. However, a rigorous spectral analysis was never performed for any corrole, including the long-known alkyl-substituted derivatives such as octaethylcorrole. Accordingly, we have addressed this issue by examining **1** and a large range of its diamagnetic metal complexes (Co^{III}, Rh^{III}, Fe(NO), Al^{III}, Ga^{III}, Ge^{IV}, Sn^{IV}, and P^{V}) by a combination of advanced NMR techniques and isotopic labeling.[23] The main findings of these studies were that in all cases the four expected doublets ($C_2H{=}C_{18}H$, $C_3H{=}C_{17}H$, $C_7H{=}C_{13}H$, $C_8H{=}C_{12}H$, see Figure 1 for **4**) are divided into two groups that differ significantly in their *J*-coupling constants. The $J = 5.1$−4.4 Hz and $J = 3.9$−4.3 Hz were assigned as reflecting $C_7H{-}C_8H$ ($={C_{12}H{-}C_{13}H}$) and $C_2H{-}C_3H$ ($={C_{17}H{-}C_{18}H}$) coupling, respectively. In addition, we noted that the $C_2{-}C_3$ and $C_{17}{-}C_{18}$ bonds (1.376, 1.383 Å for **4**) are significantly longer than $C_7{-}C_8$ and $C_{12}{-}C_{13}$ (1.358, 1.358 Å for **4**). These two trends corroborate each other, as an inverse correlation between C=C bond lengths and CH=CH coupling constants has been observed in other five-membered rings.[24] The differentiation between C_2H ($={C_{18}H}$) and C_3H ($={C_{17}H}$) was less obvious, but we found that the former protons always appear at lower field. This outcome is reasonable, considering the chemical shifts of the relevant protons in directly joined α-α'-bypyrroles.[25] We have also observed that the signal of C_2H is sharper than that of C_3H, probably because of the absence of remote coupling by fluorine atoms from *meso*-C_6F_5 in the former. The most difficult task is the differentiation between C_7H and C_8H, but this is not required for the present purposes (vide infra). To conclude, the chemical shifts and coupling constants of **4** are shown in Figure 1. Thus, assuming that the trend of the coupling constants of C_2H, C_3H, $C_{17}H$, $C_{18}H$ being smaller than those of C_7H, C_8H, $C_{12}H$, $C_{13}H$ remains conserved in the substituted corroles allows for a straightforward structural assignment of the products, especially when aided by symmetry considerations.

The products from the nitration reactions were assigned as follows. First, there are four CH protons with large *J*-coupling constants (>4.5 Hz) in the mono- and bis-nitro products (**6**, **7**, Table 1), indicating that C_7H, C_8H, $C_{12}H$, $C_{13}H$ are not substituted therein. Second, the observation of only one singlet for two CH protons in the bis-nitro complex **7** enforces the conservation of C_{2v}-symmetry. Third, the sole singlet in the tris-nitro complex **8** can only be explained by double substitution of one of the double bonds. This reduces the number of possible isomers for each product to only two: 2- or 3-nitro for **6**, 2,18- or 3,17-dinitro for **7**, and 2,3,17- or 2,3,18-trinitro for **8**. The differentiation between the remaining possibilities requires arguments based on chemical shifts, which although being less reliable, were found to be applicable in the present cases. Thus, the singlet at 9.69 ppm for **6** is more consistent with the effect of a single β-nitro group on the chemical shift of C_2H (9.15 ppm in **4**) than of C_3H (8.70 ppm in **4**), suggesting the location of the nitro group on C_3. This conclusion, together with the C_{2v}-symmetry indicated by the observation of only one singlet for **7** (at 9.54 ppm), leads to its assignment as a 3,17- rather than a 2,18-bis-nitro corrole. Finally, the observation of only one singlet (at 9.84 pmm) for **8** can only be explained if two of its three nitro groups are located on the same carbon−carbon bond, leaving no doubts for its assignment as the 2,3,17-trinitrocorrole.

The spectroscopic analysis of **6**−**8** is confirmed via the X-ray structures of the complexes (Figures 2−4). This adds confidence to the assignment of **9** and **10**, which failed to provide X-ray quality crystals. For **9**, the presence of only one doublet with a small *J*-coupling constant (4.1 Hz) is consistent with substitution at either C_2 or C_3. Support for the latter option is provided by the chemical shift of the singlet (9.65 ppm) and its comparison to that of the C_2H in the nonsubstituted **4** (9.15 ppm) and the 3-nitrocorrole **6** (9.69 ppm). In addition, NOE experiments show that the C_2H is in proximity with both $C_{18}H$ (at 9.11 ppm) and the formyl proton, while the sole interaction of the latter proton is with C_2H. This rules out substitution at C2, because in such a case the formyl proton should experience NOE interactions with both C_3H and $C_{18}H$. As for **10**, the observation of two singlets (10.03 and 9.01 ppm) enforces asymmetric substitution, and the absence of small *J*-coupling constants for the remaining doublets leads to the conclusion that the formyl groups are located on C3 and C18 (=C2 and C17).

The ^{1}H NMR inspection of the crude reaction product from the chlorosulfonation of **1** revealed that it contains, in addition to the previously described 3,18-bis-chlorosulfonato corrole **2**,[15] a minor product (=3%, **11**) that displaced only one singlet at 9.06 ppm. This limited information was inadequate for a reliable assignment of the substitution pattern in **11**, especially because the resonances of its other protons were hidden by the major isomer. Yet, the sequence of amidation, cobalt insertion, and chromatography allowed the separation of the main and minor (triphenylphosphine)cobalt(III) complexes (**13** and **14**, respectively, in Scheme 2) and the comparison of chemical shifts therein with the corresponding complex of **1** (**12**, Table 1). The observation of only one singlet served to confirm the C_{2v}

(23) Saltsman, I.; Balazs, Y.; Mahammed, A.; Tkachenko, E.; Golubkov, G.; Gross, Z., manuscript in preparation.
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Table 1. Chemical Shifts (in $CDCl_3$ for Compounds **1**−**11** and in C_6D_6 for **12**−**14**) and *J*-Coupling Constants (Hz, in Parentheses) of the Protons in All Compounds Described in This Work

	substituted carbon atom(s)	C2H	C3H	C17H	C18H	C7H, C13H	C8H, C12H
1	none	9.10 (4.4)	8.57 (4.4)	8.57 (4.4)	9.10 (4.4)	8.75 (4.4)	8.57 (4.4)
11	3,17-$(SO_2Cl)_2$	9.06 (s)			9.06 (s)	*a*	*a*
2[b]	3,18-$(SO_2Cl)_2$	9.44 (s)		8.95 (s)		8.60 (5.0)	8.41 (5.0)
						8.50 (5.0)	8.18 (5.0)
12	none	8.66 (4.6)	8.08 (4.6)	8.08 (4.6)	8.66 (4.6)	8.42 (5.0)	8.28 (5.0)
14	3,17-$(SO_2pip)_2$	9.05 (s)			9.05 (s)	8.34 (4.9)	8.20 (4.9)
13[b]	3,18-$(SO_2pip)_2$	9.64 (s)		8.68 (s)		8.37 (5.0)	8.24 (5.0)
						8.15 (4.7)	8.13 (4.7)
4	none	9.15 (4.0)	8.70 (4.0)	8.70 (4.0)	9.15 (4.0)	8.83 (4.5)	8.61 (4.5)
6	3-NO_2	9.69 (s)		8.71 (4.1)	8.45 (4.1)	8.32 (4.6)	8.61 (5.1)
7	3,17-$(NO_2)_2$	9.54 (s)			9.54 (s)	8.61 (4.6)	8.35 (4.6)
8[c]	2,3,17-$(NO_2)_3$				9.84 (s)	8.14, 8.18	8.39, 8.44
9	3-CHO	9.65 (s)		8.73 (4.1)	9.11 (4.1)	8.76 (4.7)	8.48 (4.7)
						8.67 (4.8)	8.52 (4.8)
10[b,c]	3,18-$(CHO)_2$	10.03 (s)		9.01 (s)		8.67 (4.8)	8.60 (4.8)
						8.38	8.37

[a] Could not be determined because they are hidden by the main isomer **2**. [b] For easier comparison, the isomers are named 3,18- in the table, rather than the correct nomenclature of 2,17- that is used in the text. [c] Some of the coupling constants were not determined because of too closely spaced chemical shifts.

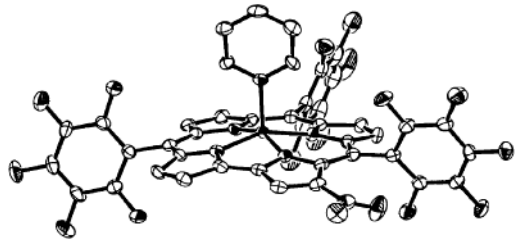

Figure 2. Molecular structure of **6**. The observed Ga−N coordination distances to the four pyrrole and the pyridyl nitrogens are 1.972, 1.926, 1.942, 1.938, and 2.039(4) Å, respectively.

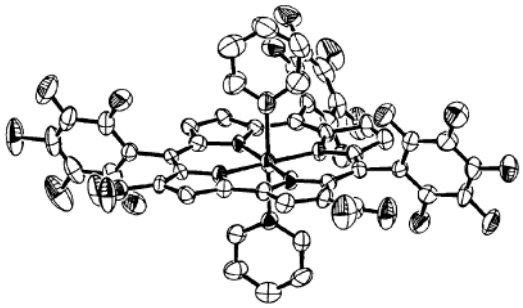

Figure 3. Molecular structure of **7**. The observed Ga−N coordination distances to the four pyrrole and the two pyridyl nitrogens are 1.924, 1.909, 1.913, 1.940, 2.234, and 2.284(6) Å, respectively.

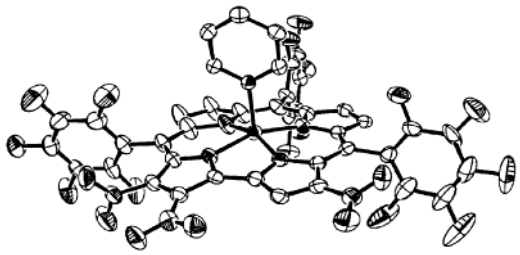

Figure 4. Molecular structure of **8**. The observed Ga−N coordination distances to the four pyrrole and the pyridyl nitrogens are 1.954, 1.918, 1.909, 1.958, and 2.055(5) Å, respectively.

symmetry in **14** (also holds for its precursor, **11**), and the large *J*-coupling constant (4.9 Hz) ruled out substitution at either C7 and C13 or C8 and C12. In addition, the chemical shift of the singlet in **14** (9.05 ppm) is consistent with substitution at C3 and C17 (a shift of 0.39 ppm of C2H relative to **12**) rather than on C2 and C18 (a shift of 0.97 ppm of C3H relative to **12**). This conclusion is further strengthened by the data of **13**, which show that it requires two proximate sulfamido groups for affecting a shift of 0.98 ppm for its C2H relative to **12**.

(b) X-ray Crystallography. X-ray quality crystals were obtained for all three nitration products (**6**, **7**, and **8**, Figures 2−4) and the (triphenylphosphine)cobalt(III) complexes of the amidated chlorosulfonation products (**13** (previously reported) and **14**, Figure 5). The comparison between the molecular structures of **13** and **14** suggests that steric factors do not play a major role in the large selectivity obtained by chlosulfonation reaction of **1** in favor of the 3,18- (=2,17) relative to the 3,17-isomer (96:4). In fact, Figure 5 shows a marked similarity between **13** and **14** (apart from the different disposition of the sulfonate substituents). In both structures, the corrole macrocycle is roughly planar, and the cobalt ion deviates about 0.3 Å from the mean corrole plane toward the axial triphenylphosphine ligand. The 1-piperidinesulfonate groups reside in sterically unhindered areas away from the triphenylphosphine ligand, and can adapt different orientations with respect to the corrole framework even at the supposedly more crowded positions at C_3/C_{17}, as is evident in Figure 5.

The mononitro- and trinitro-substituted complexes **6** (Figure 2) and **8** (Figure 4) are five coordinate with a single pyridine species as an axial ligand. In these two corroles, the Ga ion deviates by 0.376 Å (in **6**) and 0.301 Å (in **8**) from the plane of the four pyrrole nitrogens, assuming a square-pyramidal coordination environment and imparting to the complexes a domed conformation. This involves also a slight upward rotation of the pyrrole rings with respect to the mean plane of the corrole macrocycle toward the metal. Thus, in the resulting domed structures, the inner N-atoms lie 0.3−0.4 Å above the plane of the eight peripheral carbon atoms (i.e., the four outer C−C bonds of the pyrrole rings) that compose the outer rim of the corrole framework. On the other hand, the dinitro-substituted complex **7** (Figure 3) is six-coordinate with two pyridyl axial ligands bound to the Ga ion from opposite sides (at a slightly longer coordination distance than in the five-coordinate complexes). This coordination number is apparently unique to the trianionic corroles; that is, we are not aware of hexacoordinated gallium-

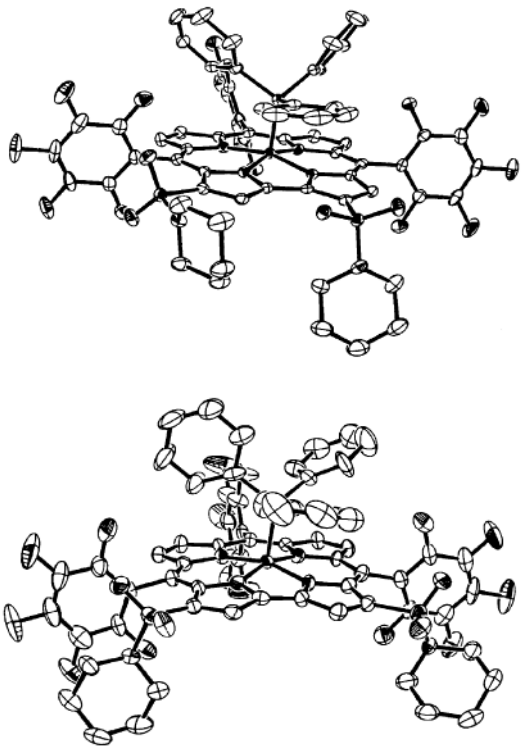

Figure 5. Comparison of the molecular structures of (top) **13** (shown with 50% probability ellipsoids at 110 K)[15] and (bottom) **14** (35% ellipsoids at 273 K). The observed Co−N and Co−P coordination distances are 1.867−1.874(3) and 2.225(1) Å in **13**, and 1.852−1.867(7) and 2.217(3) Å in **14**. The C−S bond lengths of the sulfonate substituents to the corrole ring are C_3−S 1.760(3) and C_{18}−S 1.737(3) Å in **13**, and C_3−S 1.738(10) and C_{17}−S 1.724(10) Å in **14**.

(III) complexes with dianionic porphyrin or phthalocyanine ligands.

Correspondingly, in this structure, the corrole ring is essentially planar with an octahedral coordination environment around the metal. The two pyridyls are roughly parallel to each other, with a twist angle between their planes of approximately 14°. It is interesting to note that, whenever possible, the nitro substituents are nearly coplanar with the adjacent pyrrole rings to enhance electron delocalization. The dihedral angles between the plane of the nitro groups and the pyrrole rings they are attached to are within 9−25° in **6**, **7**, and for two out of the three substituents in **8**. Only the third NO_2 group on the doubly substituted pyrrole in **8** (bound to C_{17}) is aligned in a perpendicular manner (the corresponding dihedral angle is 84°) to minimize steric hindrance as well as electrostatic repulsion with the neighboring nitro and pentafluorophenyl fragments. In all three complexes, the pentafluorophenyl rings are oriented in an almost perpendicular manner with respect to corrole ring, all the corresponding dihedral angles being within 71−86°. Moreover, in perfect agreement with the NMR data for **6**−**8** and earlier structural observations in **4**, these three structures show systematically that the peripheral C−C bond lengths in pyrrole rings A and D are longer than those in rings B and C. These findings are consistent with the higher reactivity of the former sites toward chemical substitution, as well with the analysis of the *J*-coupling constants. The corresponding C_2−C_3 and C_{17}−C_{18} bond distances are 1.389 and 1.381 Å in **6**, 1.396 and 1.399 Å in **7**, and 1.396 and 1.376 in **8**; the C_7−C_8 and C_{12}−C_{13} ones are 1.341 and 1.358 Å in **6**, 1.329 and 1.337 Å in **7**, and 1.337 and 1.327 Å in **8**.

Source of Selectivity. The results show that the first substitution on both **1** and **4** is invariably directed to C3 and that the second substitution occurs at C17 for nitration and on C18 for hydroformylation and chlorosulfonation (together with a small amount on C17). In addition, the third nitration takes place at C18 rather than in any of the other positions that are much more remote from the first two nitro groups. This clearly demonstrates the vast difference between the carbon atoms located on the directly joined A and D pyrrole rings (C2, C3, C17, C18) and the *meso*-carbon bridged B and C rings (C7, C8, C12, C13). The crystallographic and spectroscopic data show that the relevant C=C bonds in rings A and D are relatively long, thus suggesting that their larger reactivity is because of the less aromatic character therein. As for the C3 versus C2 selectivity, the crystallographic results suggest that it is not because of steric forces. Accordingly, it almost enforces the conclusion that this position is much more electron-rich than all others. A verification of this hypothesis is provided in Figure 1, which shows the π-electron density at all β-pyrrole carbon atoms obtained from the recently published DFT calculations on **4**.[8a] Apparently, the differences are large enough for complete direction of electrophilic reagents to C3. In addition, the deactivating effect of the first substituent in each case ($-SO_2Cl$, $-[CH{=}NMe_2]$, NO_2) is expected to be more significant at C2 and C17 than on C18 because of alternation. This explains the selective formation of 3,18-bis-substituted products in the reactions with CSA and the Vielsmeier reagent.

In the synthetic part, we have already provided indications that suggest that nitration of **4** by the **5**/$NaNO_2$ system proceeds via NO_2, that is, a radical rather than an electrophilic reagent. This hypothesis is further supported by the following observations. The selectivity for nitration (3,17-bis-nitro in **7**) is different, only this reaction proceeds behind bis-substitution (2,3,17-tris-nitro in **8**), and the third nitration occurs on an already nitrated pyrrole ring (D) rather than on the yet non-reacted B or C rings. All together, these results provide strong evidence for a radical rather than electrophilic reaction pathway.

Summary and Conclusions

We have demonstrated in this work the feasibility and powerfulness of electrophilic substitution on triarylcorroles as a synthetic tool to new derivatives. The large difference in the reactivity of the various carbon atoms on the macrocycle was shown to be of electronic rather than steric origin. A careful choice of reagents and a delicate control of reaction conditions allowed the selective syntheses of novel derivatives, in all of which substitution took place selectively in only one-half of the macrocycle. This was proven by a combination of X-ray crystallography of the various products and detailed analysis of their NMR spectra, the latter of which also paves the way for future studies of different corroles and different reagents. All the substituents that were introduced into the corrole's skeleton (chlorosulfonyl, formyl, nitro) can, in principle, be transformed into water-solubilizing groups by routine methods (hydrolysis, oxidation, reduction), resulting in amphiphilic corroles. This was demonstrated for the chlorosulfonation product, which was also shown to chelate a variety of metal ions. The utilization of these corroles and their metal complexes

in several applications is the subject of ongoing research in our laboratories.

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Supporting Information Available: Details of the X-ray crystallographic data collection and structure refinement, tables of atomic coordinates, bond distances and angles, anisotropic thermal parameters, and hydrogen atom positions for **6**, **7**, **8**, and **14** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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