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Iodinated Aluminum(III) Corroles with Long-Lived Triplet Excited States

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S Supporting Information

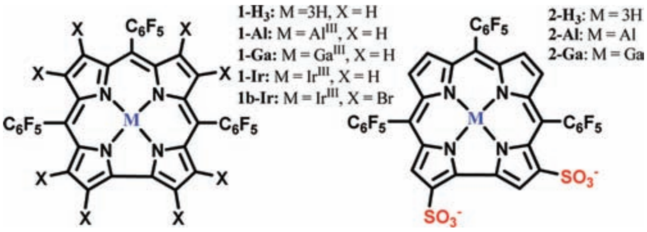
ABSTRACT: The first reported iodination of a corrole leads to selective functionalization of the four C−H bonds on one pole of the macrocycle. An aluminum(III) complex of the tetraiodinated corrole, which exhibits red fluorescence, possesses a long-lived triplet excited state.

Among the most prominent features of porphyrinoids are their photophysical properties: intense visible absorption and (often) emission in the visible or near-IR. Understanding the variables that affect intersystem crossing (ISC) as well as emission wavelengths and lifetimes opens the way for the design of compounds tailored to particular applications. For example, a low ISC yield is important for photodynamic detection (PDD),[1] fluorescence-based imaging,[2] and dye-sensitized solar cell (DSSC) efficiency;[3] hence, free-base porphyrinoids or the corresponding chelates with light post-transition metals are optimal. On the other hand, long-lived triplet excited states are necessary for singlet oxygen production for applications such as photodynamic therapy (PDT).[4] These states are generated through efficient ISC that can be achieved by the inclusion of heavy metals or heavy-atom ring substituents.

The photophysical properties of metallocorroles have not been investigated as extensively as those of metalloporphyrins, although much progress has been made toward understanding the singlet excited states of gallium and aluminum derivatives, among others.[5] The aluminum(III) complex of 5,10,15-tris(pentafluorophenyl)corrole [**1-Al** in Chart 1; an analogue of magnesium(II) in porphyrins and chlorophylls] is brightly fluorescent, with a quantum yield (0.76) exceeding those of all other porphyrinoids.[6] This finding has been attributed to a combination of the electron-withdrawing *meso*-C_6F_5 substituents, a light metal, and the planarity of the macrocycle.

H_3tpfc (**1-H$_3$** in Chart 1) and its metal complexes undergo facile and selective electrophilic substitution,[7] a property that has been exploited for the development of corrole-based fluorescent probes.[8] The gallium(III) complex of an amphiphilic corrole (**2-Ga** in Chart 1) has been used for imaging serum,[9] cells,[8,10] organs, and whole animals (mouse models).[11] One inherent limitation of biological fluorescence imaging is interference from cellular autofluorescence; this problem can be overcome by the use of fluorescence lifetime imaging (FLIM)[12] and/or two photon excitation,[13] but these techniques require very specialized instrumentation. A simpler solution involves the use of chromophores that possess longer luminescence lifetimes at ambient temperatures, although we should note that hitherto long-lived, room-temperature corrole luminescence has been reported only for the six-coordinate iridium(III) complexes **1-Ir** and **1b-Ir** having two trimethylamine or pyridine molecules as axial ligands.[14] Both complexes display phosphorescence at room temperature, with **1b-Ir** exibiting a somewhat longer triplet lifetime than **1-Ir**. Triplet emission from other metallocorroles has been observed only at low temperatures,[15] as for example in the case of partially brominated germanium corroles.[16]

Chart 1. Structures of Corroles and Corresponding Metal Complexes Whose Photophysical Properties Have Been Published Previously[a]



[a] All of the metal complexes have axial ligands, which have been omitted for clarity.

We set out to prepare a new metallocorrole with a long-lived triplet excited state. The compound was designed according to the following criteria: (a) the metal of choice should be aluminum(III), whose corrole complexes have the highest emission quantum yields on record; (b) the heavy-atom substituents required for promoting ISC should be located on the corrole periphery, since the central metal is a relatively light element; (c) the compound should be dipolar and amenable to further chemical modification, in order to broaden the scope of potential applications. The methodology we picked was iodination of **1-Al** because (a) iodine is the heaviest atom that can be readily incorporated in the ring, (b) iodination is likely to be much more selective than bromination,[17] and (c) C−I bonds are good candidates for further chemical manipulation. Our expectations were fulfilled: iodination did not proceed further than four iodides per corrole, all four C−I bonds were formed on one pole of the molecule, and most importantly, a long-lived triplet state was produced upon electronic excitation of the complex.

While molecular iodine reacted with **1-Al**, thin-layer chromatography revealed the formation of multiple products, and full

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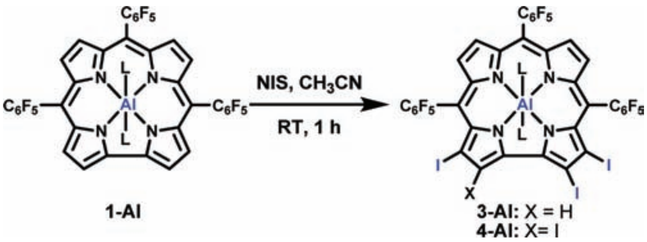
Scheme 1. Selective Iodination of the Aluminum(III) Corrole 1-Al (L = Pyridine)



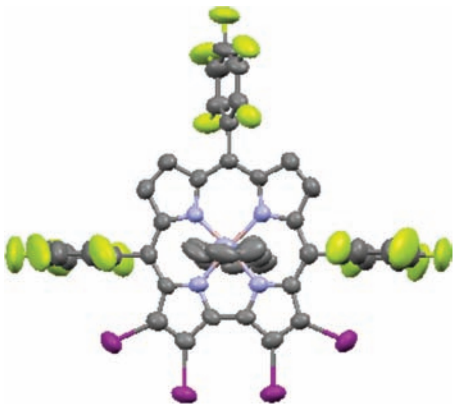


Figure 1. Top view of the molecular structure of **4-Al**. The Al−N bond lengths are 1.8821−1.9123 and 2.1732−2.1787 Å for the equatorial and axial ligands, respectively.

consumption of **1-Al** required many days. With either of the organic reagents *N*-iodosuccinimide (NIS) or 1,3-diiodo-5,5-dimethylhydantoin (DIH),[18] the reaction was complete after 1 h, but NIS provided better results. Only one major product was obtained: **4-Al**, with four new C−I bonds (Scheme 1).[19] Traces of the triiodo species **3-Al** were eliminated by recrystallization. Acetonitrile was the only solvent that gave the desired product in reasonable yield and selectivity, and acidic conditions previously reported for the iodination of aromatic compounds[20] promoted decomposition. We also ran the optimized procedure on the free base **1-H$_3$**, but no pure product could be isolated from the reaction mixture.

The identification of **4-Al** was based on a combination of NMR, UV−vis, and mass spectrometry and was further confirmed by X-ray crystallography. The ^{1}H NMR spectrum (Figure S1a in the Supporting Information) displays two β-pyrrole C−H resonances (2H each), suggesting that the molecule retains a C_2 axis. The large *J* coupling constant (4.5 Hz) indicates that only the directly bound pyrrole subunits were modified, consistent with known reactivity patterns of triarylcorroles.[21] The spectrum also reveals two bound pyridine molecules, which display broad peaks because of the dynamic equilibrium between the five- and six-coordinate species (as reported for **1-Al**).[5] At low temperature, this process is slowed, and the shifted resonances for coordinated pyridines are sharpened (Figure S1b−d). The UV−vis spectrum (Figure S2) of **4-Al** displays maxima that are slightly red-shifted (by 14−22 nm) relative to **1-Al**, as is often observed upon halogenation of corroles or porphyrins that retain planarity.[22] A molar absorptivity of ~10^5 M^{-1} cm^{-1} is maintained upon iodination.[6]

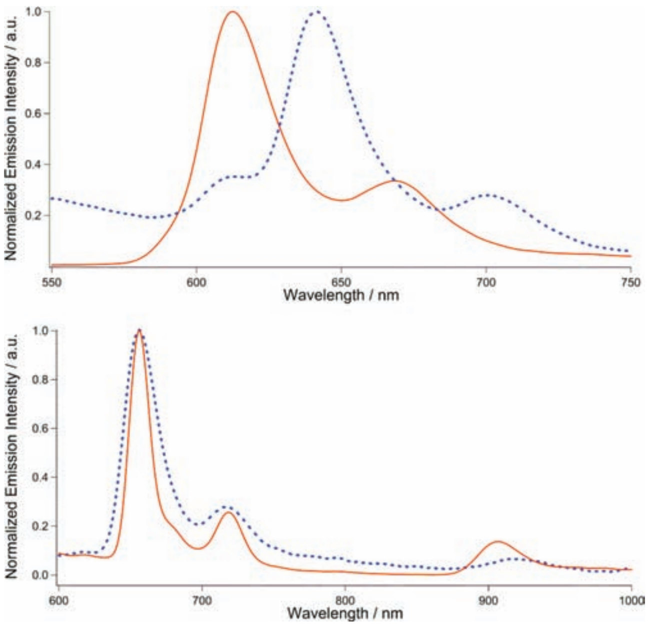


Figure 2. Emission spectra (λ_{ex} = 514 nm) of **4-Al** (top) in pyridine (blue dotted curve) and benzene (red solid curve) at room temperature and (bottom) in toluene in the presence of excess imidazole at room temperature (blue dotted curve) and 77 K (red solid curve).

Analysis of X-ray quality crystals revealed that **4-Al** (Figure 1) retains a planar macrocyclic framework. The deviations of aluminum with respect to the plane defined by the four pyrrole nitrogen atoms are virtually nil (0.003 Å for **1-Al** and 0.007 Å for **4-Al**).[23] As expected, the presence of iodides increases the Al−N$_{pyrrole}$ bond lengths by 0.016−0.022 Å. There are two pyridine(py) ligands in axial coordination sites that are nearly parallel to each other, with a twist angle of 16.75°. This angle is somewhat larger than those reported for other bispyridine metallocorrole complexes (2.3−10.8°).[25] The average Al−N$_{py}$ bond length in **4-Al** is slightly shorter than that in **1-Al** (2.176 vs 2.208 Å, respectively).[23] This bond shortening is consistent with the expected electronic effect of the iodides: the Lewis acidity of the aluminum center is enhanced by removal of electron density from the pyrrole nitrogen atoms, as confirmed by a determination of the affinity of **4-Al** for pyridine in toluene solutions. The equilibrium constant for the equilibrium involving the mono- and bispyridine-coordinated forms of **4-Al** is 508 M^{-1},[24] which is nearly 4 times larger than that of **1-Al** (135 M^{-1}).[5]

Preliminary investigations of the luminescence properties of **4-Al** revealed both short- and long-lived components that are highly sensitive to electronic effects attributable to axial ligation. The primary emission bands are centered at 612 and 669 nm in benzene, where the majority of the complex is five-coordinate, and at 645 and 700 nm in pyridine, where the complex is mostly six-coordinate (Figure 2 top). The quantum yield of 0.1% as well as the independence of the intensities of these bands with respect to both temperature (over the range −20 to +50 °C) and the presence of oxygen is consistent with prompt fluorescence[25] from an excited singlet state that is rapidly quenched by ISC. The triplet state thus obtained is only slightly emissive (phosphorescence at long wavelengths, >850 nm), although it could still be observed at room temperature and even more so at 77 K (Figure 2 bottom).[26] Transient absorption spectroscopy was used to determine the lifetime of this state, which was found to be 92 and 1 μs in degassed and aerobic toluene, respectively.

We have introduced iodination as a new methodology for preparing metallocorroles with unique photophysical properties. The process is facile and leads to selective functionalization of four of the eight peripheral carbon atoms. The tetraiodinated aluminum(III) corrole **4-Al**, which has been fully characterized by NMR spectroscopy and X-ray crystallography, possesses both short- and long-lived excited states. The reaction chemistry of the long-lived triplet state of **4-Al** is currently under investigation in our laboratories, with particular emphasis on work with biologically relevant ligands. Syntheses of derivatives of this unique corrole for in-depth photochemical and photophysical studies also are underway.

ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Crystallographic data for **4-Al** (CIF), materials and methods, and Figures S1−S4. This material is available free of charge via the Internet at http://pubs.acs.org.

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REFERENCES

(1) (a) Lipson, R. L.; Baldes, E. J.; Gray, M. J. *Cancer* **1967**, *20*, 2255. (b) Ackroyd, R.; Kelty, C.; Brown, N.; Reed, M. *Photochem. Photobiol.* **2001**, *74*, 656.

(2) (a) Leinenweber, S. B.; Sheng, H.; Lynch, J. R.; Wang, H.; Batinic-Haberle, I.; Laskowitz, D. T.; Crapo, J. D.; Pearlstein, R. D.; Warner, D. S. *Eur. J. Pharmacol.* **2006**, *531*, 126. (b) Saba, H.; Batinic-Haberle, I.; Munusamy, S.; Mitchell, T.; Lichti, C.; Megyesi, J.; MacMillan-Crow, L. A. *Free Radical Biol. Med.* **2007**, *42*, 1571.

(3) (a) Grätzel, M. *J. Photochem. Photobiol., C* **2003**, *4*, 145. (b) Wang, Q.; Campbell, W. M.; Bonfantani, E. E.; Jolley, K. W.; Officer, D. L.; Walsh, P. J.; Gordon, K.; Humphry-Baker, R.; Nazeeruddin, M. K.; Grätzel, M. *J. Phys. Chem. B* **2005**, *109*, 15397. (c) Walker, D. C. S.; Mahammed, A.; Brunschwig, B. S.; Winkler, J. R.; Gray, H. B.; Zaban, A.; Gross, Z. *J. Porphyrins Phthalocyanines* **2006**, *10*, 1259.

(4) (a) Zenkevich, E.; Sagun, E.; Knyukshto, V.; Shulga, A.; Mironov, A.; Efremova, O.; Bonnett, R.; Songca, S. P.; Kassem, M. *J. Photochem. Photobiol., B* **1996**, *33*, 171. (b) Sessler, J. L.; Miller, R. A. *Biochem. Pharmacol.* **2000**, *59*, 733. (c) Sessler, J. L.; Seidel, D. *Angew. Chem., Int. Ed.* **2003**, *42*, 5134.

(5) Kowalska, D.; Liu, X.; Tripathy, U.; Mahammed, A.; Gross, Z.; Hirayama, S.; Steer, R. P. *Inorg. Chem.* **2009**, *48*, 2670.

(6) Mahammed, A.; Gross, Z. *J. Inorg. Biochem.* **2002**, *88*, 305.

(7) Saltsman, I.; Mahammed, A.; Goldberg, I.; Tkachenko, E.; Botoshansky, M.; Gross, Z. *J. Am. Chem. Soc.* **2002**, *124*, 7411.

(8) Okun, Z.; Kupershmidt, L.; Amit, T.; Mandel, S.; Bar-Am, O.; Youdim, M. B. H.; Gross, Z. *ACS Chem. Biol.* **2009**, *4*, 910.

(9) Haber, A.; Aviram, M.; Gross, Z. *Chem. Sci.* **2011**, *2*, 295.

(10) Agadjanian, H.; Weaver, J. J.; Mahammed, A.; Rentsendorj, A.; Bass, S.; Kim, J.; Dmochowski, I. J.; Margalit, R.; Gray, H. B.; Gross, Z.; Medina-Kauwe, L. K. *Pharm. Res.* **2006**, *23*, 367.

(11) Agadjanian, H.; Ma, J.; Rentsendorj, A.; Valluripalli, V.; Hwang, J. Y.; Mahammed, A.; Farkas, D. L.; Gray, H. B.; Gross, Z.; Medina-Kauwe, L. K. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 6105.

(12) Hwang, J. Y.; Agadjanian, H.; Medina-Kauwe, L. K.; Gross, Z.; Gray, H. B.; Sorasaenee, K.; Farkas, D. L. *Proc. SPIE* **2008**, *6859*, 68590G.

(13) (a) Bestvater, F.; Spiess, E.; Stobrawa, G.; Hacker, M.; Feurer, T.; Porwol, T.; Berchner-Pfannschmidt, U.; Wotzlaw, C.; Acker, H. *J. Microsc.* **2002**, *208*, 108. (b) Durr, N. J.; Larson, T.; Smith, D. K.; Korgel, B. A.; Sokolov, K.; Ben-Yakar, A. *Nano Lett.* **2007**, *7*, 941. (c) Hwang, J. Y.; Wachsmann-Hogiu, S.; Ramanujan, V. K.; Nowatzyk, A. G.; Koronyo, Y.; Medina-Kauwe, L. K.; Gross, Z.; Gray, H. B.; Farkas, D. L. *Biomed. Opt. Express* **2011**, *2*, 356.

(14) Palmer, J. H.; Durrell, A. C.; Gross, Z.; Winkler, J. R.; Gray, H. B. *J. Am. Chem. Soc.* **2010**, *132*, 9230.

(15) Ventura, B.; Degli, E. A.; Koszarna, B.; Gryko, D. T.; Flamigni, L. *New J. Chem.* **2005**, *29*, 1559.

(16) Nardis, S.; Mandoj, F.; Paolesse, R.; Fronczek, F. R.; Smith, K. M.; Prodi, L.; Montalti, M.; Battistini, G. *Eur. J. Inorg. Chem.* **2007**, 2345.

(17) (a) Golubkov, G.; Bendix, J.; Gray, H. B.; Mahammed, A.; Goldberg, I.; DiBilio, A. J.; Gross, Z. *Angew. Chem.* **2001**, *113*, 2190. (b) Aviv-Harel, I.; Gross, Z. *Coord. Chem. Rev.* **2011**, *255*, 717. (c) Du, R. B.; Liu, C.; Shen, D. M.; Chen, Q. Y. *Synlett* **2009**, 2701.

(18) (a) Orazi, O. O.; Corral, R. A.; Bertorello, H. E. *J. Org. Chem.* **1965**, *30*, 1101. (b) Kulbitski, K.; Nisnevich, G.; Gandelman, M. *Adv. Synth. Catal.* **2011**, *353*, 1438.

(19) Synthesis of **4-Al**: A sample of **1-Al** (20 mg, 20 μmol) and excess NIS (45 mg, 200 μmol) were stirred in CH_3CN (5 mL) at room temperature for 1 h. The resulting solution was washed with water, dried over Na_2SO_4, and evaporated. The green-purple product was purified by chromatography (CH_2Cl_2/EtOAc/pyridine = 100:15:1), which afforded pure **4-Al** (20 mg, 67% yield). ^1H NMR (400 MHz, C_6D_6): δ 8.4 (d, J = 4.5 Hz, 2H), 8.6 (d, J = 4.5 Hz, 2H). ^1H NMR (600 MHz, toluene-d_8, 209 K): δ 2.1 (unresolved t, 4H), 4.0 (t, 4H), 4.6 (t, 2H), 8.6 (d, J = 4.0 Hz, 2H), 8.8 (d, J = 4.0 Hz, 2H). ^{19}F NMR (376 MHz, C_6D_6): δ −137.84 (unresolved td, 6F, ortho), −153.19 (t, 3F, para), −162.08 (td, 2F, meta), −162.83 (td, 4F, meta). MS (MALDI−TOF LD$^-$): m/z 1323 ([M]$^-$, 100%). UV−vis (toluene) λ_{max} [ε (M^{-1} cm^{-1})]: 410 [33138], 433 [116392], 596 [30159].

(20) (a) Kraszkiewicz, L.; Sosnowski, M.; Skulski, L. *Tetrahedron* **2004**, *60*, 9113. (b) Chaikovskii, V. K.; Filimonov, V. D.; Funk, A. A.; Skorokhodov, V. I.; Ogorodnikov, V. D. *ChemInform* **2008**, *39*; DOI: 10.1002/chin.200810049.

(21) (a) Mahammed, A.; Goldberg, I.; Gross, Z. *Org. Lett.* **2001**, *3*, 3443. (b) Mahammed, A.; Gross, Z. *J. Porphyrins Phthalocyanines* **2002**, *6*, 553. (c) Balazs, Y. S.; Saltsman, I.; Mahammed, A.; Tkachenko, E.; Golubkov, G.; Levine, J.; Gross, Z. *Magn. Reson. Chem.* **2004**, *42*, 624. (d) Stefanelli, M.; Mastroianni, M.; Nardis, S.; Licoccia, S.; Fronczek, F. R.; Smith, K. M.; Zhu, W.; Ou, Z.; Kadish, K. M.; Paolesse, R. *Inorg. Chem.* **2007**, *46*, 10791. (e) Aviv, I.; Gross, Z. *Chem.—Eur. J.* **2009**, *15*, 8382.

(22) (a) Palmer, J. H.; Day, M. W.; Wilson, A. D.; Henling, L. M.; Gross, Z.; Gray, H. B. *J. Am. Chem. Soc.* **2008**, *130*, 7786. (b) Nguyen, K. A.; Day, P. N.; Pachter, R.; Tretiak, S.; Chernyak, V.; Mukamel, S. *J. Phys. Chem. A* **2002**, *106*, 10285.

(23) Sorasaenee, K.; Taqavi, P.; Henling, L. M.; Gray, H. B.; Tkachenko, E.; Mahammed, A.; Gross, Z. *J. Porphyrins Phthalocyanines* **2007**, *11*, 189.

(24) As determined by a UV−vis titration (see the Supporting Information).

(25) Birks, J. B. *Photophysics of Aromatic Molecules*; Wiley: New York, 1970.

(26) Bonnet, R.; Harriman, A.; Kozyrev, A. N. *J. Chem. Soc., Faraday Trans.* **1992**, *88*, 763.