Porphyrinoid Chemistry

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Metal-Mediated C–H Bond Activation in a Carbon-Substituted Hemiporphyrazine**

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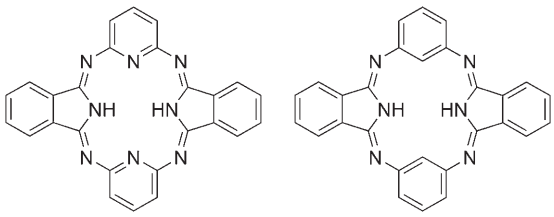
Unlike many C–H bond activations,[1] nucleophilic substitution reactions on aromatic rings with hydride as the leaving group can be difficult to achieve. Nucleophilic substitution of arenes by halide loss has been known for many decades. However, C–H aromatic substitutions have been known only since the late 1970s and proceed only under certain reaction conditions.[2] Electron-withdrawing substituents are required on the aromatic ring, and frequently only strong nucleophiles such as NH_2^- can readily attack. Alternative methods can be used to assist replacement of an aromatic hydride. Vicarious nucleophilic aromatic substitution can be used in the activation of arene C–H bonds, which is promoted by loss of HX.[3] In addition, oxidants can also be employed to effect loss of hydride in a process known as oxidative nucleophilic substitution of hydrogen (ONSH).[4] Herein, we present an unusual nucleophilic aromatic substitution with the relatively weak nucleophile pyridine in the dicarbahemiporphyrazine macrocycle, which may occur through an ONSH mechanism. Upon metalation with copper, nucleophilic attack of the internal carbon atom with pyridine is promoted by the reduction of the metal from Cu^{II} to Cu^{I}. This reaction proceeds under very mild conditions in air and represents a potential new means to activate C–H bonds with transition metals.

The metalation of porphyrin analogues and isomers with interior carbon positions has become an area of significant activity.[5] The chemistry of the N-confused porphyrins,[6] benziporphyrins,[7] and azuliporphyrins[8] all involve macrocycles in which an aromatic C–H bond is in close proximity to the metal binding site. The interior C–H bond can remain intact upon metal binding, as observed in the Mn,[9] Fe,[10] and Zn[11] complexes of N-confused porphyrins.[6] The exact nature of this C–H metal "agostic" interaction is still under investigation, but the proximity of a metal center to this carbon atom activates it toward nucleophilic and electrophilic attack. Indirect evidence of such metal-mediated chemistry has been seen in the copper-mediated oxidative degradation of an N-confused porphyrin[12] and silver-catalyzed C–N bond formation in *m*-benziporphyrin.[13]

In the early 1950s, Elvidge and Linstead reported the synthesis of the hemiporphyrazine macrocycle (Scheme 1).[14]



Scheme 1. The structures of hemiporphyrazine (left) and the N-deficient analogue dicarbaporphyrazine (right).

The hemiporphyrazines bear a superficial resemblance to phthalocyanine, but the phthalocyanines are aromatic systems of 18 π electrons while the hemiporphyrazines are systems of 20 π electrons.[15] Linstead et al. later prepared a series of porphyrazine derivatives in which one or two of the central metal-binding nitrogen atoms were replaced with CH groups. In one case, 2,6-diaminopyridine was replaced by 1,3-diaminobenzene, and the macrocycle **1** is thus doubly N-deficient.[16] This molecule can be considered as a dicarbahemiporphyrazine (dchp).

Although there are only two nitrogen atoms within the core of the ring, macrocycle **1** does bind metal ions (Scheme 2,

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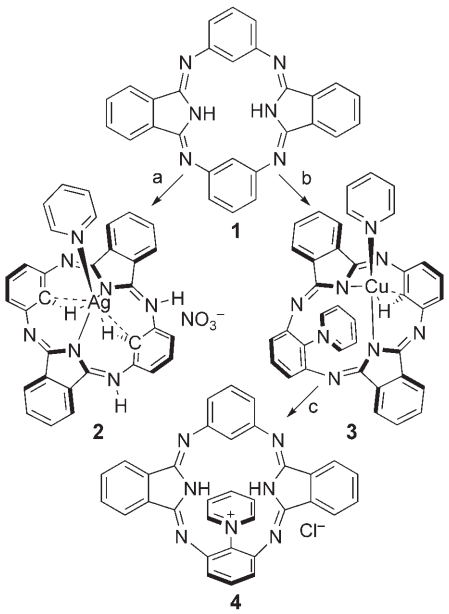

Scheme 2. Synthesis of compounds **2**, **3**, and **4**, starting from **1**. Reagents: a) $AgNO_3$, pyridine, MeOH, air; b) Cu^{I} or Cu^{II} salt, pyridine, MeOH, air; c) CH_2Cl_2, air.

Figure 1).[17] The reaction of **1** with $AgNO_3$ afforded [Ag(dchp)py]NO_3 (**2**; py = pyridine), a pseudo-three-coordinate Ag^{I} species. The presence of an NO_3^- counterion in the unit

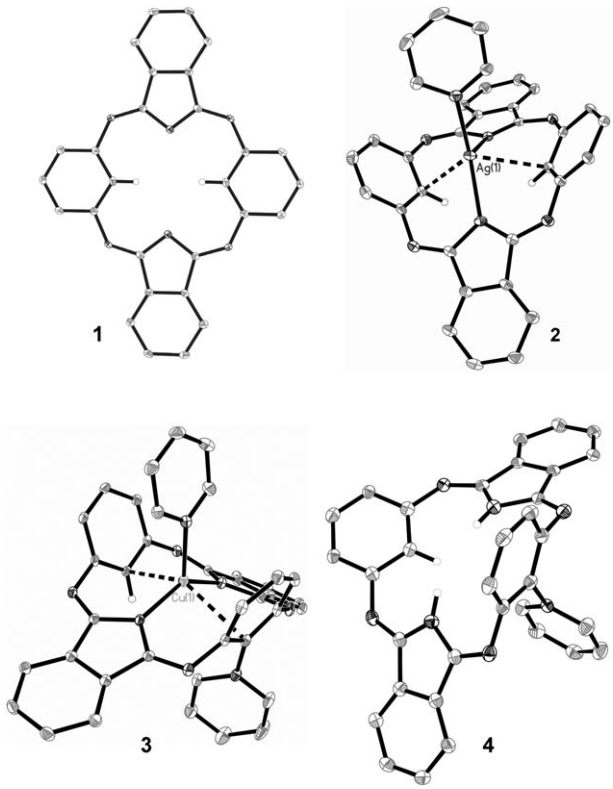

Figure 1. Thermal-ellipsoid diagrams (35% probability level) of all reactants and products from Scheme 2 (C light gray, N dark gray). Hydrogen atoms have been omitted for clarity, with the exception of the internal CH groups and NH groups.

cell of **2** indicates that the ligand binds to the Ag^{I} cation in a neutral tautomeric form.[17] We believe that two of the external nitrogen atoms are protonated in this complex to achieve charge balance. This situation is in contrast to that of **3** (see below), in which the positive charges of the pyridinium moiety and the Cu^{I} ion are balanced by the negative charges of the two deprotonated core nitrogen atoms. The metal–macrocycle Ag–N bond lengths in **2** are relatively large (ca. 2.36 Å), in part owing to the steric interaction of the benzene rings. The Ag–C distances are 2.62 and 2.71 Å, which are too large for a strong silver–arene interaction,[18] but the carbon atoms are within close proximity of the metal ion. The metal center is located out of the plane of the macrocycle (from the plane of the four *meso* nitrogen atoms) by 1.35 Å, which represents a larger distance than seen in the metallo-N-confused porphyrins.[6] Compound **2** is diamagnetic, and the ^{109}Ag NMR spectroscopic signal of this compound is observed at $\delta = 377$ ppm.

The reactions of **1** with a variety of Cu salts such as $Cu(CH_3COO)_2{\cdot}2H_2O$ and $[Cu(CH_3CN)_4]BF_4$ in the presence of air and pyridine did not produce stable Cu^{II} compounds. Instead, the macrocycle reacted with pyridine after metalation to form the species [Cu(dchp-py)(py)] (**3**).[17] Species **3** is a Cu^{I} compound in which a pyridine molecule has formed a C–N bond at one of the two internal CH positions. We isolated two crystal forms of this complex from different solvents. As in the Ag compound, the Cu^{I} center is pseudo-three-coordinate and bound to both of the internal nitrogen atoms from the ring and one axial pyridine ligand, with Cu–N bond lengths ranging between 2.03 and 2.08 Å.

Both the remaining interior C–H bond and the new C–N bond are in close proximity to the metal center in this new complex, with average Cu–C(H) and Cu–C(N) bond lengths of about 2.41 Å and 2.74 Å, respectively. As in species **2**, the metal center in **3** is located out of the plane of the macrocycle by 0.77 Å, which is just over half of the corresponding distance observed in compound **2**. The ^1H NMR chemical shift of the proton in the interior C–H bond changes slightly from that of the unmetalated ligand **1**, moving from $\delta = 6.77$ to 7.31 ppm. We believe that this reaction proceeds through Cu^{II}-assisted elimination of hydride, and the hydride reduces the metal center to Cu^{I}, which is more stable in the low-coordinate environment of the ligand.[19] An alternate mechanism to ONSH might involve the initial formation of a highly oxidized Cu^{III} center with a metal–carbon bond (by activation of one of the internal CH groups). Chelation of pyridine and reductive elimination would then produce the pyridine adduct **3**.

Recrystallization of **3** in dichloromethane in air resulted in the loss of pyridine and demetalation to yield the free ligand. The free-base species H_2dchp-py (**4**) retains the pendant pyridine moiety at the interior carbon position.[17] The C–N bond length in this species is 1.46 Å, which is identical to that seen in both crystal forms of the copper complex. We believe that dioxygen reacts with **3** and the solvent (dichloromethane) to produce $CuCl_2$ and the protonated free base **4**.

In conclusion, metalation of the dicarbahemiporphyrazine **1** with the redox-active metal copper activates an interior C–H bond toward nucleophilic substitution. This reaction

proceeds through an ONSH mechanism in which the Cu^{II} center accepts a hydride and is reduced to Cu^{I}. We are continuing our investigations into the metal complexes of both singly and doubly N-deficient hemiporphyrazines.

Experimental Section

Dicarbahemiporphyrazine (dchp, **1**) was synthesized as described in the literature.[14,16] Crystals of the planar dicationic form of **1** were grown from a mixture of formic acid and diethyl ether (1:1).

2: $AgNO_3$ (102 mg, 0.6 mmol) was added to a solution of **1** (132 mg, 0.3 mmol) in pyridine (10 mL), and the mixture was stirred for 30 minutes at room temperature. The resulting solution was filtered, and the filtrate was layered with diethyl ether. Orange-red crystals of **2** were collected after four days. Yield: 0.082 g (40%). ^{1}H NMR (300 MHz, [D$_5$]pyridine): $\delta = 8.32$ (q, $J = 3.0$ Hz, 4H), 8.11 (d, $J = 7.2$ Hz, 1H), 7.98 (t, $J = 3.6$ Hz, 1H), 7.91 (m, 2H) 7.36 (s, 5H), 7.12 (dd, $J = 2.4$, 5.1 Hz, 0.5H), 6.91 (s, 0.5H), 6.80 (d, $J = 6.6$ Hz, 0.5H), 6.70 (d, $J = 7.5$ Hz, 0.5H), 6.62 (m, 0.5H), 6.45 ppm (dd, $J =$ 2.1, 7.8 Hz, 0.5H); ^{109}Ag NMR (14.0 MHz, [D$_5$]pyridine): $\delta =$ 377.1 ppm; high-res. ESI-MS (positive ion): m/z: 547.0 [Ag(dchp)]$^+$. The material loses the axially coordinated solvent rapidly, with only 0.5 equivalents of pyridine remaining after standing. Elemental analysis (%) calcd for $C_{30.5}H_{24.5}N_{7.5}O_5Ag$: C 53.58, H 3.58, N 15.36; found: C 53.60, H 3.07, N 15.37.

3: Compound **3** was synthesized by three different routes. All reactions were carried out aerobically. Route 1: Compound **1** (439 mg, 1 mmol) was dissolved in hot *n*-butanol (30 mL), and a solution of $Cu(CH_3CO_2)_2{\cdot}2H_2O$ (399 mg, 2 mmol) in methanol (5 mL) was added. The resulting mixture was heated at reflux for 12 h. The resulting brown precipitate was collected by filtration and washed with methanol and diethyl ether. The product was then dissolved in pyridine (10 mL), and diethyl ether was allowed to diffuse into the solution. Deep red crystals of **3** were collected after several days and were suitable for X-ray diffraction (crystal **3a**). Route 2: Compound **1** (132 mg, 0.3 mmol) was dissolved in pyridine (10 mL), and $Cu(CH_3CO_2)_2{\cdot}2H_2O$ (120 mg, 0.6 mmol) was added to the solution with stirring. The mixture turned to deep red almost immediately and was heated at reflux for 24 h. After the mixture had been filtered, the resulting solution was layered with diethyl ether. Deep red single crystals were collected after several days. Single crystals for X-ray diffraction were grown from toluene/methanol (1:1, crystal **3b**). Route 3: Compound **1** (132 mg, 0.3 mmol) and $[Cu(CH_3CN)_4]BF_4$ (124 mg, 0.4 mmol) were mixed in pyridine (10 mL). The mixture was stirred at room temperature for 30 minutes. Diethyl ether was allowed to diffuse into the resulting solution, and the crystals that formed after several days were identical to those from Route 1. Yield (from Route 1): 0.312 g, 48%. ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 8.34$ (s, 4H), 8.18 (t, $J = 7.8$ Hz, 1H), 7.92 (d, $J =$ 7.3 Hz, 2H), 7.74 (t, $J = 7.4$ Hz, 2H), 7.64 (m, 4H), 7.46 (m, 4H), 7.31 (s, 1H), 7.21 (m, 4H), 6.98 (t, $J = 7.8$ Hz, 1H), 6.87 (t, $J = 7.8$ hz, 1H), 6.57 (d, $J = 7.8$ Hz) 2H), 6.42 ppm (d, $J = 7.8$ Hz, 2H); ^{13}C NMR (75.4 MHz, [D$_6$]DMSO): $\delta = 170.2$, 164.8, 150.1, 149.9, 147.8, 147.4, 144.8, 140.1, 138.3, 136.1, 133.7, 130.6, 130.2, 126.3, 123.7, 121.5, 120.7, 118.4, 117.2 ppm; high-res. ESI-MS (positive ion): m/z: 516.2 [H$_2$dchp-py]$^+$. Elemental analysis (%) calcd for $C_{83}H_{67}N_{16}O_5Cu_2$: C 66.65, H 4.51, N 14.98; found: C 66.20, H 4.31, N 15.96.

4: Compound **1** (132 mg, 0.3 mmol) and $Cu(CH_3CO_2)_2{\cdot}2H_2O$ (120 mg, 0.6 mmol) were mixed in pyridine (10 mL). The solution turned to deep red immediately and was heated at reflux for 24 h. The resulting solution was slowly layered with CH_2Cl_2. The resultant solution turned from red to blue upon oxidation with air. Yellow-orange crystals of **4** were collected after several days. Yield: 0.016 g (10%). ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta = 11.17$ (s, 2H), 10.09 (s, 0.5H), 9.62 (d, $J = 6.0$ Hz, 1H), 9.19 (d, $J = 6.0$ Hz, 1H), 8.93 (s, 1H), 8.50 (m, 2H), 8.36 (d, $J = 7.3$ Hz, 2H), 8.14 (t, $J = 6.0$ Hz, 1H), 8.05 (t, $J = 6.0$ Hz, 1H), 7.62 (m, 8H), 7.44 (m, 2H), 7.34 (d, $J = 8.1$ Hz, 2H), 7.07 (d, $J = 6.9$ Hz, 1H), 6.87 (m, 1H), 6.78 ppm (d, $J = 7.9$ Hz, 2H); ^{13}C NMR (75.4 MHz, [D$_6$]DMSO): $\delta = 169.5$, 166.8, 148.7, 147.9, 138.8, 137.0, 136.5, 132.9, 131.6, 131.3, 129.2, 128.6, 125.4, 122.1, 122.0, 118.8, 117.2, 116.9 ppm; high-res. ESI-MS (positive ion): m/z: 516.2 [Hdchp-py]$^+$. Elemental analysis (%) calcd for $C_{33}H_{32}N_7OCl_3$: C 61.64, H 4.08, N 15.25; found: C 61.44, H 4.10, N 14.48.

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[1] B. A. Arndtsen, R. G. Bergman, T. A. Mobley, T. H. Peterson, *Acc. Chem. Res.* **1995**, *28*, 154; C. G. Jia, T. Kitamura, Y. Fujiwara, *Acc. Chem. Res.* **2001**, *34*, 633; W. D. Jones, *Acc. Chem. Res.* **2003**, *36*, 140.
[2] M. Mąkosza, J. Winiarski, *Acc. Chem. Res.* **1987**, *20*, 282.
[3] M. Mąkosza, A. Kwast, *Eur. J. Org. Chem.* **2004**, *10*, 2125; S. Florio, P. Lorusso, R. Luisi, C. Granito, L. Ronzini, L. Troisi, *Eur. J. Org. Chem.* **2004**, *10*, 2118; M. D. Drew, D. A. Jackson, N. J. Lawrence, J. Liddle, R. G. Pritchard, *Chem. Commun.* **1997**, 189.
[4] M. Mąkosza, K. Wojciechowski, *Chem. Rev.* **2004**, *104*, 2631.
[5] *The Porphyrin Handbook, Vol. II* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Academic Press, New York, **2000**.
[6] J. D. Harvey, C. J. Ziegler, *Coord. Chem. Rev.* **2003**, *247*, 1; P. J. Chimielewski, L. Latos-Grażyński, *Coord. Chem. Rev.* **2005**, *249*, 2510.
[7] M. Stępień, L. Latos-Grażyński, *Acc. Chem. Res.* **2005**, *38*, 88.
[8] T. D. Lash, *Synlett* **2000**, *3*, 279; T. D. Lash, D. A. Colby, G. M. E. Ferrence, *J. Org. Chem.* **2003**, *68*, 4533.
[9] J. D. Harvey, C. J. Ziegler, *Chem. Commun.* **2003**, *23*, 2890.
[10] W.-C. Chen, C.-H. Hung, *Inorg. Chem.* **2001**, *40*, 5070.
[11] H. Furuta, T. Ishizuka, A. Osuka, *J. Am. Chem. Soc.* **2002**, *124*, 5622.
[12] H. Furuta, H. Maeda, A. Osuka, *Org. Lett.* **2002**, *4*, 181.
[13] M. Stepien, L. Latos-Grażyński, *J. Am. Chem. Soc.* **2002**, *124*, 3838.
[14] J. A. Elvidge, J. P. Linstead, *J. Chem. Soc.* **1952**, 5008.
[15] F. Fernández-Lázaro, T. Torres, B. Hauschel, M. Hanack, *Chem. Rev.* **1998**, *98*, 563.
[16] P. F. Clark, J. A. Elvidge, R. P. Linstead, *J. Chem. Soc.* **1954**, 2490; J. A. Elvidge, J. H. Golden, *J. Chem. Soc.* **1957**, 700; R. P. Smirnov, *Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.* **1967**, *10*, 1169.
[17] Crystal data for **1**: triclinic, space group $P\bar{1}$, $a = 5.0864(12)$, $b =$ 11.867(3), $c = 12.441(3)$ Å, $\alpha = 71.651(4)$, $\beta = 89.775(4)$, $\gamma =$ 78.614(4)°, $V = 697.4(3)$ Å^3, $Z = 1$, $\rho = 1.482$ g cm^{-3}, $R_1 = 0.0665$, $wR_2 = 0.1298$ (for 3200 reflections, $I_o > 2\sigma(I_o)$). Crystal data for **2**: triclinic, space group $P\bar{1}$, $a = 8.7694(13)$, $b = 13.3129(19)$, $c =$ 14.937(2) Å, $\alpha = 73.503(2)$, $\beta = 81.501(2)$, $\gamma = 73.782(2)$°, $V =$ 1601.1(4) Å^3, $Z = 2$, $\rho = 1.463$ g cm^{-3}, $R_1 = 0.0472$, $wR_2 = 0.1029$ (for 7400 reflections, $I_o > 2\sigma(I_o)$). Crystal data for **3a**: monoclinic, space group $P2_1/c$, $a = 14.2673(11)$, $b = 13.1552(10)$, $c =$ 24.0192(13) Å, $\beta = 126.441(3)$, $V = 3626.7(4)$ Å^3, $Z = 4$, $\rho =$ 1.349 g cm^{-3}, $R_1 = 0.0438$, $wR_2 = 0.1013$ (for 8715 reflections, $I_o > 2\sigma(I_o)$). Crystal data for **3b**: monoclinic, space group $P2_1/n$ $a = 10.2762(11)$, $b = 43.463(5)$, $c = 16.4235(17)$ Å, $\beta =$ 101.059(2)°, $V = 7199.1(13)$ Å^3, $Z = 4$, $\rho = 1.394$ g cm^{-3}, $R_1 =$ 0.0568, $wR_2 = 0.1208$ (for 17298 reflections, $I_o > 2\sigma(I_o)$). Crystal data for **4**: $P\bar{1}$, $a = 8.5234(11)$, $b = 13.7264(17)$, $c =$ 14.0816(18) Å, $\alpha = 91.287(2)$, $\beta = 97.805(2)$, $\gamma = 96.667(2)$°, $V =$ 1620.0(4) Å^3, $Z = 2$, $\rho = 1.413$ g cm^{-3}, $R_1 = 0.0814$, $wR_2 = 0.2100$ (for 6313 reflections, $I_o > 2\sigma(I_o)$). Data were collected at 100 K (Bruker-AXS SMART CCD diffractometer with $Mo_{K\alpha}$ radia-

tion, $\lambda = 0.71073$ Å) and corrected for absorption (empirical SADABS). The structures were solved by direct methods and refined by full-matrix least-squares procedures (SHELX97). CCDC-603061–603065 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[18] K. Shelly, D. C. Finster, Y. J. Lee, W. R. Scheidt, C. A. Reed, *J. Am. Chem. Soc.* **1985**, *107*, 5955; I. F. , Jr., Taylor, E. A. Hall, E. L. Amma, *J. Am. Chem. Soc.* **1969**, *91*, 5745.

[19] K. M. Kadish, C. Araullo, G. B. Maiya, D. Sazou, J.-M. Barbe, R. Guilard, *Inorg. Chem.* **1989**, *28*, 2528.

