



KJE-3900

Master's Thesis in CHEMISTRY

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DEMETALATION OF METALCORROLES

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October 2008

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# DEMETALATION OF METALLOCORROLES

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**Keywords:** Corrole, copper, demetalation, synthesis, high valent, ligand non-innocence.

**Abstract:** Although the chemistry of corroles has grown spectacularly in recent years, the field has been marred by the lack of convenient protocols for demetalation of metallocorroles. In this thesis, I have developed a superior procedure for demetalating copper corroles with concentrated  $\text{H}_2\text{SO}_4$  and 5-200 equiv  $\text{FeCl}_2$  or  $\text{SnCl}_2$ . The yields obtained with this reductive procedure are generally substantially better than with  $\text{CHCl}_3/\text{H}_2\text{SO}_4$ ,  $\text{CH}_2\text{Cl}_2/\text{H}_2\text{SO}_4$ , or  $\text{H}_2\text{SO}_4$  alone. With an oxidation-prone metallocorrole such as  $\text{Cu}[\text{T}(p\text{-OMeP})\text{C}]$ , the reductive protocol was essential for obtaining any measurable yield of the free base at all. Free-base  $\beta$ -octabromo-*meso*-triarylcorroles were also obtained in pure form, in good yields, and with relative ease via this procedure.

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Tromsø, June 2008

*Can Capar*

## ABBREVIATIONS

Cu[TPC]: Copper 5,10,15-triphenylcorrole

Cu[T(p-OCH<sub>3</sub>-P)C]: Copper 5,10,15-tris(4-methoxyphenyl)corrole

Cu[T(p-CF<sub>3</sub>P)C]: Copper 5,10,15-tris(4-trifluoromethylphenyl)corrole

Cu[Br<sub>8</sub>TPC]: Copper  $\beta$ -Octabromo-meso-triphenylcorrole

Cu[Br<sub>8</sub>T(p-CF<sub>3</sub>-P)C]: Copper  $\beta$ -octabromo-meso-tris(4-trifluoromethylphenyl)corrole

Cu[Br<sub>8</sub>T(p-OCH<sub>3</sub>-P)C]: Copper  $\beta$ -octabromo-*meso*-tris(4-methoxyphenyl)corrole

NaBH<sub>4</sub>: Sodium borohydride

Ph: Phenyl

OMe: Methoxy

Ar: Aryl

OH: Hydroxyl

TFA: Trifluoroacetic acid

HCl : Hydrochloric acid

HBr: Hydrobromic acid

H<sub>2</sub>SO<sub>4</sub>: Sulfuric acid

CH<sub>2</sub>Cl<sub>2</sub>: Dichloromethane

CHCl<sub>3</sub>: Chloroform

HCHO: Formaldehyde (Methanal)

MeOH: Methanol

DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone

P-Chloranil: Tetrachloro-1, 4-Benzoquinone

HOMO: Highest occupied molecular orbital

LUMO: Lowest unoccupied molecular orbital

NaHCO<sub>3</sub>: Sodium hydrogen carbonate

Na<sub>2</sub>SO<sub>4</sub>: Sodium sulfate

TLC: Thin layer chromatography

FeCl<sub>2</sub>: Iron(II) Chloride

SnCl<sub>2</sub>: Tin(II) chloride

CH<sub>3</sub>COOH: Acetic acid

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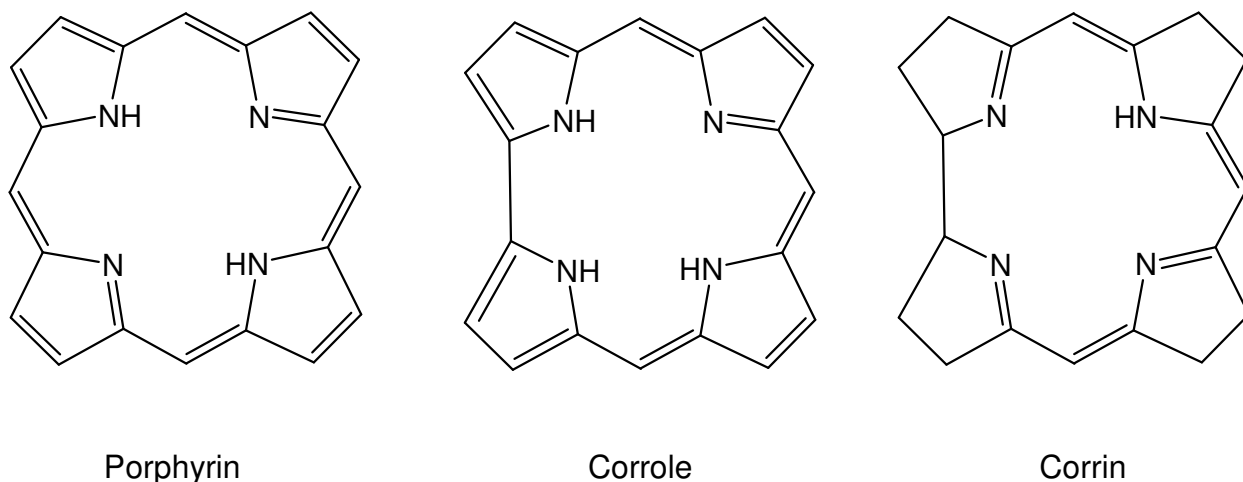
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# 1 INTRODUCTION

## 1.1 Corroles

Corroles are tetrapyrrolic macrocycles, containing the skeletal structure of corrin, with its direct pyrrole-pyrrole link, and retain 18  $\pi$ -electron aromatic core of a porphyrin. Corroles can be considered as intermediates between porphyrins and corrins.



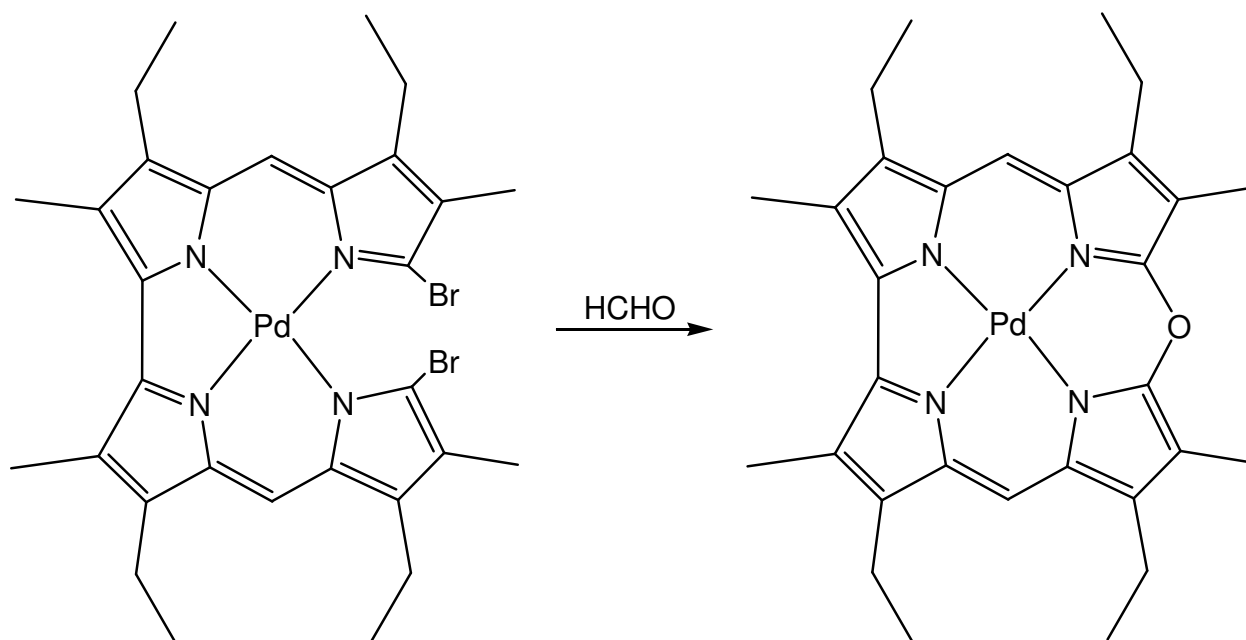
**Figure 1.1** Skeletal structures of porphyrin, corrole, corrin.

Corroles were first synthesized by Johnson and Kay in 1965<sup>1</sup>. But the name corrole was first appeared in 1960<sup>2</sup> as “pentadehydrocorrin”. In the same 1960 paper, Johnson and Price exchanged the name “pentadehydrocorrin” with corrole adding a footnote: “We are indebted to the Editor for this suggestion”. Three years later Johnson and coworkers reported the error of “pentadehydrocorrin” which was actually a palladium complex of the cyclic ether<sup>3</sup>, Pd 10-oxacorrole shown in figure 1.2. The first corrole was believed to be a palladium complex with a hydroxyl axial ligand (Figure 1.3).

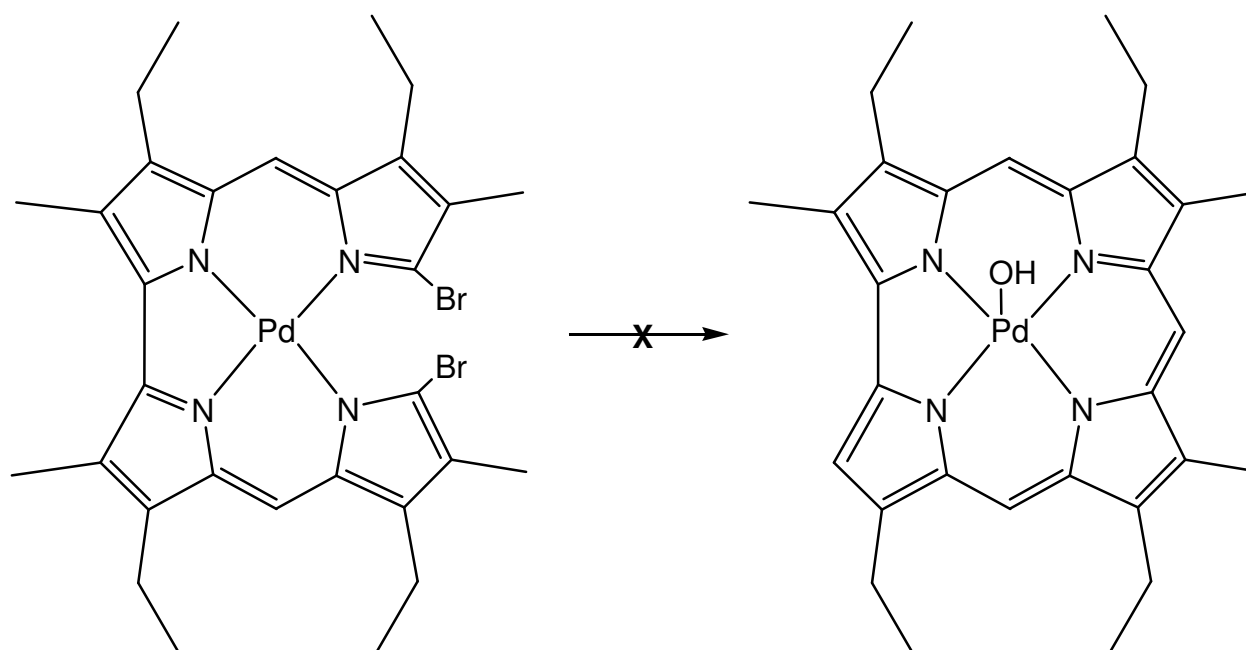
<sup>1</sup> Johnson, A.W.; Kay, I.T. *J. Chem. Soc.* **1965**, 1620.

<sup>2</sup> Johnson, A.W.; Price R. *J. Chem. Soc.* **1960**, 1649.

<sup>3</sup> Johnson, A.W.; Kay, I.T.; Rodrigo R. *J. Chem. Soc.* **1963**, 2336.



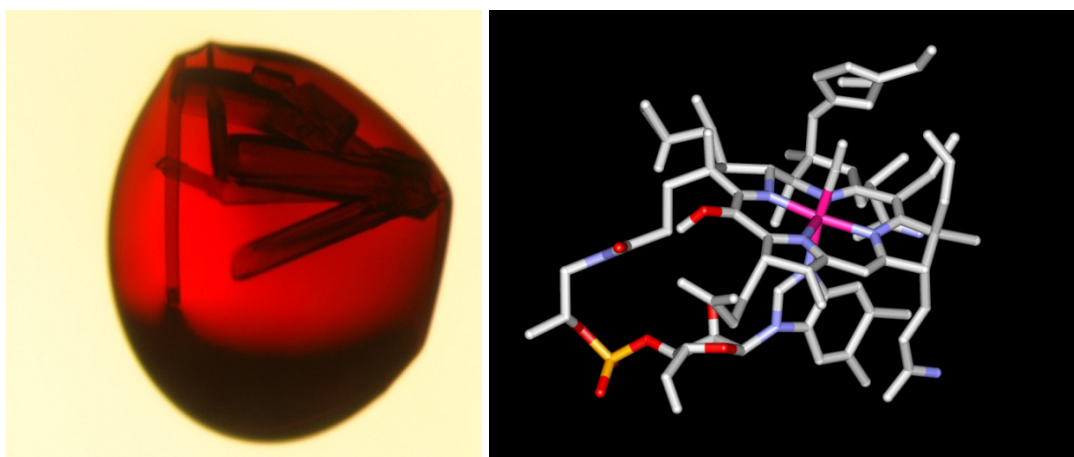
**Figure 1.2** Pd 10-oxacorrole was incorrectly believed to be the first corrole.



**Figure 1.3** The first corrole was believed to be Pd complex with a hydroxyl axial ligand.

Perhaps this error was for the reason of predicted corrole structure had two hydrogens and therefore dianionic instead of the actual trianionic feature. Finally, Johnson and Kay synthesized the true corrole in 1965<sup>1</sup> and they also prepared the first metallocorroles with nickel, copper and

cobalt. They renamed them “tetrahydrocorrin” and stated the term corrole should only be used for “tetrahydrocorrin”. Johnson’s idea was to use a corrole as the precursor of the corrin ring for the preparation of vitamin B<sub>12</sub> (shown in figure 1.4). Unfortunately this approach was unsuccessful, and for a long time this macrocycle remained in the shadow of porphyrin chemistry, with its peculiar characteristic being that it was only the first example of a synthetic tetrapyrrolic macrocycle with a direct pyrrole-pyrrole link. The first synthesis of corroles from readily available starting materials was multi-step, with poor yields in many of the reactions. Thus, while corroles have been known for over 40 years, research in the field remained undeveloped. The total synthesis of vitamin B<sub>12</sub> is also multistep (almost a hundred steps) and remains the only total synthesis of B<sub>12</sub> published by Woodward<sup>4</sup>. Industrial production of B<sub>12</sub> is through fermentation of selected microorganisms<sup>5</sup>.



**Figure 1.4** The structure determination of Vitamin B<sub>12</sub> (cyanocobalamin). B<sub>12</sub> was crystallized in our laboratory as red crystals (left). The crystal structure of B<sub>12</sub> (right). The corrin ring forms the core of the structure.

It wasn’t until the discovery of new synthetic methods for corroles developed in 1999 by different groups working independently that research in this area really started to expand<sup>6,7</sup>. A

<sup>4</sup> Khan, A.G.; Easwaran, S.V. *Science* **1976** 196: 1410.

<sup>5</sup> Martens, J.H.; Barg, H.; Warren, M.J.; Jahn, D. *Appl. Microbiol. Biotechnol.* **2002** 58: 275.

<sup>6</sup> Paolesse, R.; Jaquinod, L.; Nurco, D.J.; Mini, S.; Sagone, F.; Boschi, T.; Smith, K. M. *Chem. Commun.* **1999**, 1307.

<sup>7</sup> Gross, Z.; Galili, N.; Saltsman, I. *Angew. Chem., Int. Ed. Engl.* **1999**, 38, 1427.

major finding in terms of the coordination chemistry of corroles prior to the discovery of the one-pot syntheses was the discovery by Vogel and co-workers that trianionic corrole ligands stabilize high-valent transition-metal ions such as Cu(III)<sup>8</sup>, Fe(IV)<sup>9</sup> and Co(IV,V)<sup>10,11</sup>. In fact one particular corrole available through a method developed by Zeev Gross, 5,10,15 tris(pentafluorophenyl)corrole, has been shown to stabilize four formal oxidation states of chromium, Cr(III, IV, V, IV)<sup>12</sup>.

What makes corroles so interesting? Many high valent transition metal complexes occur as the critical reactive intermediates of a variety of oxidative processes such as C-H activation in both nature (i.e. as metalloenzymes) and industrial processes. One of the structures present in many enzymes is the corrinoid structure and some of the corroles form very tight conjugates with proteins, opening up possibilities for use in biological systems<sup>13,14</sup>. Also among the interesting attributes of corroles are their photophysical properties. Corroles generally show porphyrin type spectra, with strong absorptions in the visible range associated with very highly colored compounds. As well, the direct pyrrole-pyrrole linkage seems to give corroles stronger fluorescence properties than their porphyrin counterparts<sup>15</sup>. Much of the driving force behind contemporary porphyrin chemistry is the search for long wavelength absorbing and fluorescing chromophores suitable for use as imaging agents or photosensitizers in photomedicine. These properties open up potential for using corroles in many other applications, including such diverse areas as cancer diagnosis and treatment, and solar cell research.

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<sup>8</sup> Will, S.; Lex, J.; Vogel, E.; Schmickler, H.; Gisselbrecht, J.-P.; Hauptmann, C.; Bernard, M.; Gorss, M. *Angew. Chem.* **1997**, 109, 367; *Angew. Chem. Int. Ed. Engl.* **1997**, 36, 357.

<sup>9</sup> Vogel, E.; Will, S.; Tilling, A.S.; Neumann, L.; Lex, J.; Bill, E.; Trautwein, A.X.; Wieghardt, K. *Angew. Chem.* **1994**, 106, 771; *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 731.

<sup>10</sup> Van Caemelbecke, E.; Will, S.; Autret, M.; Adamian, V.A.; Lex, J.; Gisselbrecht, J.P.; Gross, M.; Vogel, E.; Kadish, K. M., *Inorg. Chem.* **1996**, 35, 184.

<sup>11</sup> Will, S.; Lex, J.; Vogel, E.; Adamian, V.A.; Van Caemelbecke, E.; Kadish, K. M. *Inorg. Chem.* **1996**, 35, 5577.

<sup>12</sup> Meier-Callahan, A. E.; Di Bilio, A.J.; Simkhovich, L.; Mahammed, A.; Goldberg, I.; Gray, H.B.; Gross, Z. *Inorg. Chem.* **2001**, 40, 6788.

<sup>13</sup> Aviezer, D.; Cotton, S.; David, M.; Segev, A.; Khaselev, N.; Galili, N.; Gross, Z.; Yayon, A. *Cancer Research* **2000**, 60, 2973.

<sup>14</sup> Mahammed, A.; Gray, H.B.; Weaver, J.J.; Sorasaene, K.; Gross, Z. *Bioconj. Chem.* **2004**, 15, 738.

<sup>15</sup> Bendix, J.; Dmochowski, I.J.; Gray, H.B.; Mahammed, A.; Simkhovich, L.; Gross, Z. *Angew. Chem. Int. Ed.* **2000**, 39, 4048.

## 1.2 One pot synthesis of corroles

As early as 1996, Rose et al.<sup>16</sup> reported the isolation of meso-tris(4-tert-butyl-2,6-dinitrophenyl)corrole as a minor by-product of a classical porphyrin synthesis, but the significance of this finding went almost unnoticed. In 1999 Paolesse et al.<sup>6</sup> and Gross et al.<sup>7</sup> independently developed one pot synthesis of corroles. The research group of Paolesse prepared a wide variety of free-base triaryl corroles under Adler–Longo-type protic-acid-catalyzed reaction conditions with glacial acetic acid as the solvent but with a pyrrole/aldehyde molar ratio of 3:1 (Figure 1.5). The research group of Gross reported an essentially solvent-free and catalyst-free pyrrole-aldehyde condensation in an open vessel followed by oxidation with DDQ to yield free base corroles (Figure 1.5). In fact, at the beginning, Gross group's research goal was to develop a simple synthetic methodology for the preparation of porphyrins. The solvent-free method could only synthesize relatively electron-deficient corroles. Ghosh et al.<sup>17</sup> modified the Gross method to synthesize corroles from more electron donating aldehydes and made the solvent-free corrole synthesis more general. Optimization of corrole synthesis by several research groups<sup>18,19,20</sup> improved the corrole yields to 15-20%. In 2003, Gryko and coworkers<sup>21</sup> introduced practical (a fifteen minutes) meso-aryl substituted A<sub>3</sub> corrole synthesis (Figure 1.6). Gryko and coworkers<sup>22</sup> developed more general and efficient synthesis of meso-substituted A<sub>3</sub> and A<sub>2</sub>B corroles in 2006, bringing the highest yields for A<sub>3</sub> corroles 14-27% (Figure 1.6) and for A<sub>2</sub>B corroles 45-56% (Figure 1.7).

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<sup>16</sup> Rose, E.; Kossanyi, A.; Quelquejeu, M.; Soleilhavoup, M.; Duwavran, F.; Bernard, N.; Lecas, A. *J. Am. Chem. Soc.* **1996**, 118, 1567.

<sup>17</sup> Wasbotten, I.H.; Wondimagegn, T.; Ghosh, A. *J. Am. Chem. Soc.* **2002**, 124, 8104.

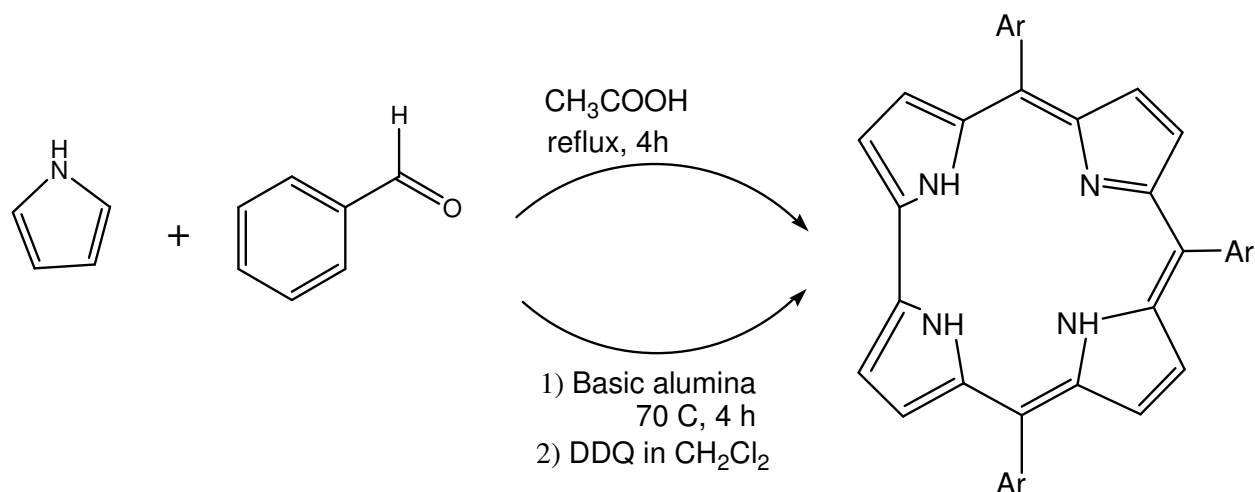
<sup>18</sup> Ka, J.-W.; Cho, W.-S.; Lee, C.-H. *Tetrahedron Lett.* **2000**, 41, 8121.

<sup>19</sup> Paolesse, R.; Marini, A.; Nardis, S.; Froiio, A.; Mandoj, F.; Nurco, D. J.; Prodi, L.; Montalti, M.; Smith, K. M. *J. Porphyrins Phthalocyanines* **2003**, 7, 25.

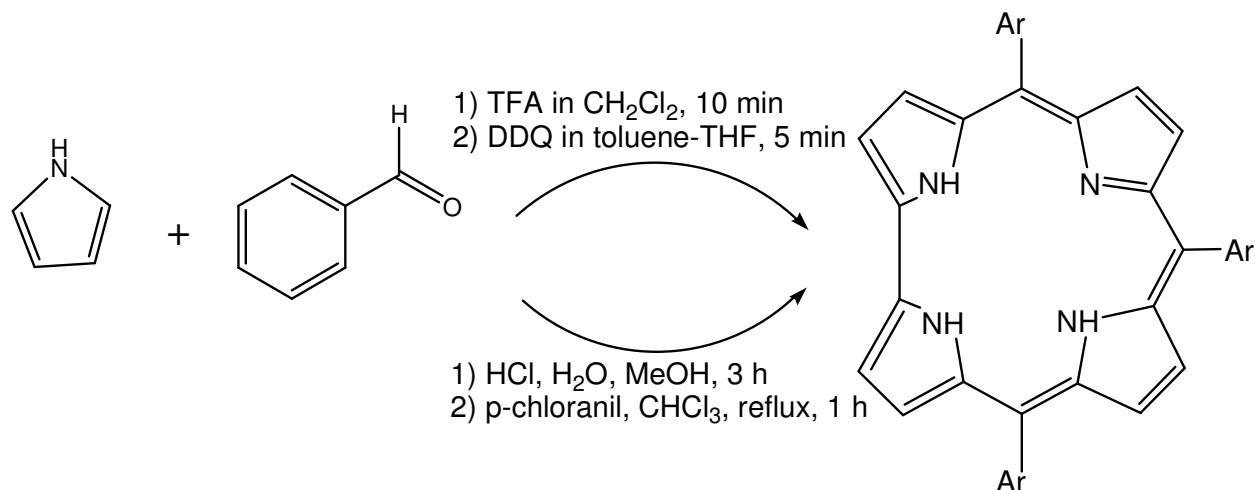
<sup>20</sup> Collman, J. P.; Decreau, R. A. *Tetrahedron Lett.* **2003**, 44, 1207.

<sup>21</sup> Gryko, D.T.; Koszarna, B. *Org. Biomol. Chem.* **1** **2003**, 350.

<sup>22</sup> Koszarna, B.; Gryko, D.T. *J. Org. Chem.* **2006**, 71, 3707.



**Figure 1.5** The first one-pot synthesis of corroles by Paolesse et al. (top, Ar=Ph) with 3:1 molar ratio of pyrrole and aldehyde and Gross et al. (bottom, Ar=PhF<sub>5</sub>) with 1:1 molar ratio of pyrrole and aldehyde.



**Figure 1.6** One-pot synthesis of meso A<sub>3</sub>-corrole by Gryko and coworkers (Ar=Ph).

Gryko et al.<sup>23</sup> synthesized the A<sub>2</sub>B-corroles bearing in mind Lindsey's acid catalyzed reaction of dipyrromethanes (DPMs) with aldehydes to give the corresponding *trans*-A<sub>2</sub>B<sub>2</sub>-porphyrins<sup>24,25</sup>. Two other analogous, short reports appeared at about the same time. Brückner et al.<sup>26</sup> found that when aldehydes react with sterically unhindered DPMs (present in sixfold molar excess) under

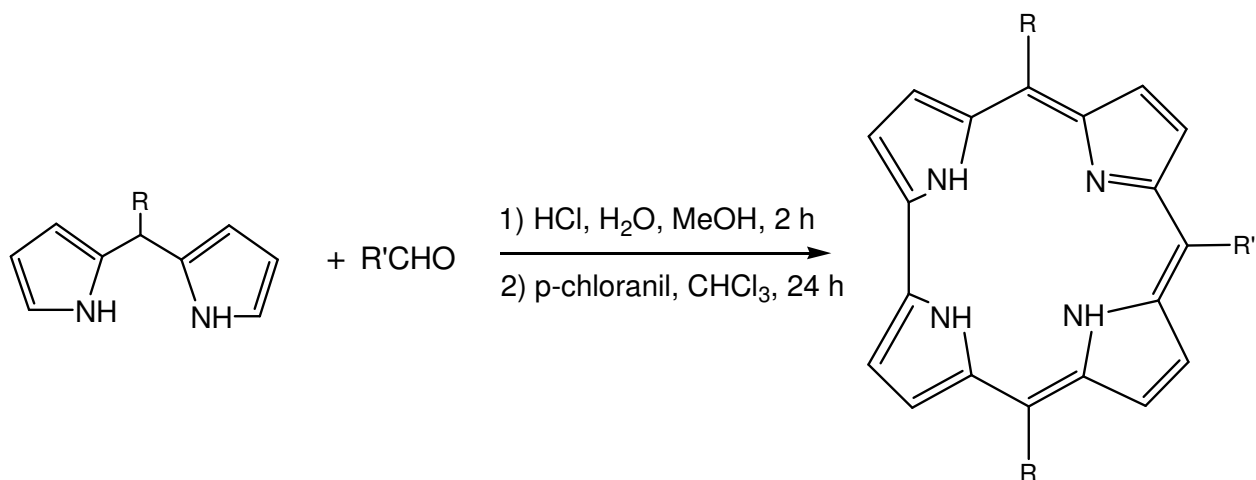
<sup>23</sup> Gryko, D.T. *Eur. J. Org. Chem.* **2002**, 1735.

<sup>24</sup> Lee, C.-H.; Lindsey, J. S. *Tetrahedron* **1994**, *50*, 11427.

<sup>25</sup> Littler, B.J.; Ciringh, Y.; Lindsey, J.S. *J. Org. Chem.* **1999**, *64*, 2864.

<sup>26</sup> Brinas, R.P.; Brückner, C. *Synlett* **2001**, 442.

TFA catalysis, *trans*-A<sub>2</sub>B-corroles are formed in 20-40% yield. Dehaen and coworkers<sup>27</sup> used BF<sub>3</sub>·OEt<sub>2</sub> as a catalyst for the reaction of 5-(2,6-dichlorophenyl)dipyrromethane with reactive aldehydes. Often they separated the bilanes prior to conversion into corroles. Taking advantage of the earlier findings of the Lee group<sup>18</sup>; purified bilanes were oxidized to corroles. Finally Gryko et al.<sup>22</sup> optimized the yields of *trans*-A<sub>2</sub>B-corroles to 45-56% in 2006 (Figure 1.7).



**Figure 1.7** Synthesis of meso-substituted *trans* A<sub>2</sub>B corrole from dipyrromethane by Gryko et al.<sup>22</sup>

Corroles with substituents in both meso- and  $\beta$ - positions have also been synthesized using dipyrromethanes and aldehydes as precursors as reported by Guilard, Kadish and coworkers<sup>28</sup>. The same strategy was subsequently used by the same authors to prepare “face-to-face” bis(corroles) linked by an anthracenyl or a biphenyl bridge.<sup>29</sup> Halogenation of corroles at  $\beta$ -positions have been done both from dipyrromethanes<sup>30</sup> and pyrroles<sup>17,31</sup>.

<sup>27</sup> Asokan, C.V.; Smeets, S.; Dehaen, W. *Tetrahedron Lett.* **2001**, *42*, 4483.

<sup>28</sup> Guilard, R.; Gros, C.P.; Bolze, F.; Jerome F.; Ou Z.; Shao, J.; Fischer J.; Weiss R.; Kadish K. M. *Inorg. Chem.* **2001**, *40*, 4845.

<sup>29</sup> Guilard, R.; Jerome F.; Gros, C. P.; Barbe, J.-M.; Ou, Z.; Shao, J.; Fischer, J.; Weiss, R.; Kadish, K. M. *Inorg. Chem.* **2001**, *40*, 4856.

<sup>30</sup> Steene, E.; Dey, A.; Ghosh, A. *J. Am. Chem. Soc.*, **2003**, *125*, 16300.

<sup>31</sup> Paolesse, R.; Nardis, S.; Sagone, F.; Khoury, R.G. *J. Org. Chem.*, **2001**, *66*, 2, 550.

## 2 GENERAL PROPERTIES

### 2.1 General Properties of Corroles

Like typical aromatic compounds unsubstituted corroles are mostly planar, but with a distortion caused by the short N-N contact, brought about by the direct pyrrole-pyrrole linkage. The steric strain forces the molecule slightly out of the plane of the four nitrogens. The lack of one *meso* carbon is the reason causes the macrocycle to be trivalent.

One of the significant characteristics of corroles is the three protons in the inner core; for this reason, the corrole acts as a trianionic ligand different from corrins and porphyrins that are, respectively, monoanionic and dianionic ligands. In the corrole structure the imino nitrogen atom is located at position 22, according to the calculations performed by Dyke et al.<sup>32</sup>; in 1997. Ghosh and Jynge<sup>33</sup> reported a detailed theoretical study that suggested the presence of fast NH tautomerism in the corrole free base, with no significant energy difference between the possible tautomers. An X-ray structure of the free base corrole is also in agreement with the suggestion of an equal arrangement of hydrogen on each inner core nitrogen atom. Thus, it is necessary to take into account the fact that the inner core hydrogen atoms are subject to shifts to give rapidly interconverting tautomers.

Spectral properties of corroles confirm their aromaticity; their UV-visible spectra show an intense absorption around 400 nm and weaker bands in the 500-600 nm region. These bands can be related to the Soret and Q bands of the porphyrins and indicate the presence of an aromatic system. The corroles show an intense luminescence band around 600 nm, with a lifetime in the nanosecond region and a very short Stokes-shift. Furthermore, a diamagnetic ring current effect is also present in the NMR spectra of corroles, and all resonances show significant shifts similar to those observed in the porphyrin analogues.

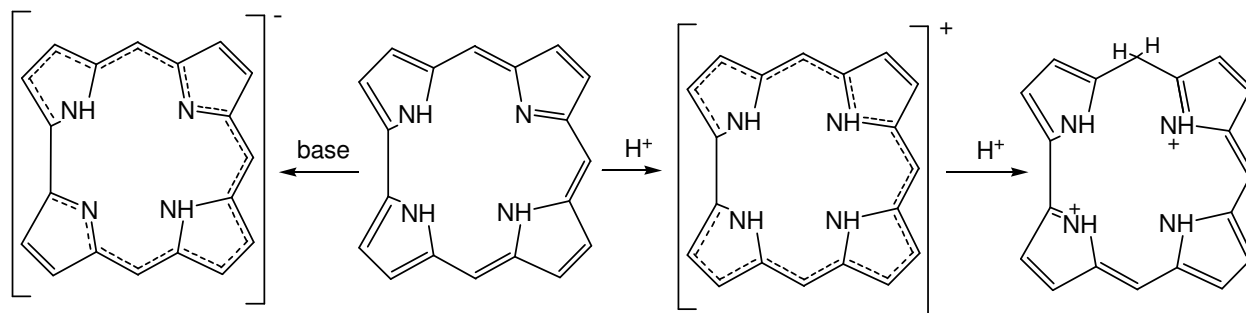
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<sup>32</sup> Dyke, J. M.; Hush, N.S.; Williams, M.L.; Woolsey, I. S. *Mol. Phys.* **1971**, 20, 1149.

<sup>33</sup> Ghosh, A.; Jynge, K. *Chem. Eur. J.* **1997**, 3, 823.



Corroles are more acidic than porphyrins, and the free-base derivatives readily form monoanionic species in dilute basic solutions (Figure 2.1); the monoanionic free-base corroles are still aromatic, and they retain the Soret band in their electronic absorption spectra. Corroles react with dilute acids to generate monoprotonated derivatives; these monocationic species are aromatic, indicating that the addition of a proton occurs at the inner core nitrogen atom (Figure 2.1). Stronger acidic conditions cause significant changes in the corrole absorption spectra, with the disappearance of the Soret band. The site of protonation appears to be at the 5 (or 15)-position, based on spectroscopic analysis<sup>34</sup>, with resulting interruption of the  $\pi$ -conjugated system (Figure 2.1).



**Figure 2.1** Structural changes in basic and acidic conditions.

## 2.2 Metallocorroles

Porphyrinoids are of perfect size to bind nearly all metal ions. Metalloporphyrins are known for all transition metals, the lanthanides, and many of the actinides and main group elements. Although the coordination chemistry of corroles is far from being as developed as that of porphyrins, it is not unreasonable to believe that the number of metals coordinated to corroles can be greatly expanded in the future.

The most distinct difference between porphyrins and corroles is the direct carbon-carbon bond between two pyrrole rings in corroles. The lack of a *meso* carbon leads to a smaller cavity than in

<sup>34</sup> Broadhurst, M.J.; Grigg, R.; Johnson, A.W.; Shelton G. *J. Chem. Soc., Perkin Trans. 1*, **1972**, 143.

the case of porphyrins and also reduces the symmetry from  $D_{4h}$  to the lower  $C_{2v}$ . Being a trianionic macrocycle with a comparably small cavity gives to corroles excellent chelating properties. The most stable oxidation numbers in metallocorroles are often one positive charge higher than in the case of the analogous metalloporphyrins. The smaller trianionic corrolato ligand has a greater ability to stabilize higher central metal oxidation states than the larger dianionic porphyrinato ligand. The ability of corroles to stabilize higher oxidation states of the metal makes its coordination chemistry particularly interesting.

### ***2.3 Preparation of metallocorroles***

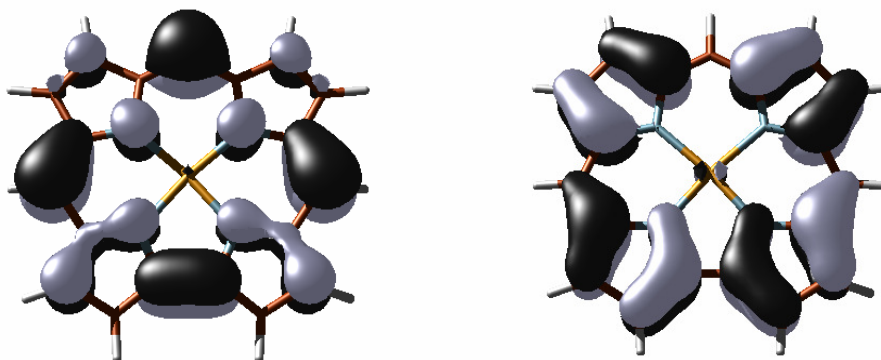
For the preparation of metallocorroles; the cyclization of a,c-biladiene in the presence of a metal salt is the most direct approach, but it cannot be generalized because some metal ions are able to catalyze the cyclization of the open-chain tetrapyrrole without being coordinated, and the product of the reaction is then the corresponding corrole free-base. In this case it is necessary to react the pre-formed macrocycle with the appropriate metal carrier (such as acetates, halides and carbonyls) in an organic solvent, such as toluene, pyridine, N,N-dimethylformamide (DMF); furthermore, this method generally affords higher yields of the corresponding metallocorrole.

### ***2.4 Metal-ligand orbital interactions***

Like porphyrins, corroles obey Gouterman's four-orbital model<sup>35</sup>. The two nearly degenerate HOMOs ( $a_2$  and  $b_1$ ) well separated from the rest of the occupied orbitals and the two nearly degenerate LUMOs well separated from the other unoccupied orbitals. Like the porphyrin  $a_{1u}$  HOMO, the corrole  $a_2$  HOMO has no or relatively small amplitudes at the *meso* positions and like the porphyrin  $a_{2u}$  HOMO, the corrole  $b_1$  HOMO has large amplitudes at the *meso* positions (Figure 2.2).

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<sup>35</sup> Ghosh, A.; Wondimagegn, T.; Parusel, A. B. J. *J. Am. Chem. Soc.* **2000**, 122, 5100.



**Figure 2.2** The  $b_1$  (left) and the  $a_2$  (right) HOMOs of  $(\text{Corrole})\text{Cu}^{\text{III}}$ , chosen as a representative closed-shell metallocorrole.

Due to different amplitudes at the meso positions, electron donating or electron withdrawing peripheral substituents affect the  $a_2$  and the  $b_1$  HOMOs differently. With large amplitudes on the *meso* carbons, the  $b_1$  HOMO will be stabilized by electron withdrawing *meso* substituents and destabilized by electron donating meso substituents. The  $a_2$  HOMO has small amplitude at the *meso* positions and is not expected to be strongly affected by meso substituents. On the other hand, substituents in  $\beta$  position should primarily affect the  $a_2$  HOMO.

In corroles the metal-nitrogen bond distances are generally shorter than analogous porphyrinates. This result has been attributed both the smaller core of the corrole ligand and to the higher oxidation state of the metal ion.

The square planar coordination is surprisingly common with metallocorroles. The octahedral coordination is frequently seen in porphyrins but is rather rare in corroles. The square pyramidal coordination occurs when neutral (pyridine) or charged ( $\text{Cl}^-$ ,  $\text{OH}^-$ ) ligands occupy the axial position. Although the others are not common, in total twelve different types of coordination schemes are known for the metallocorroles.

## 2.5 Electrochemistry

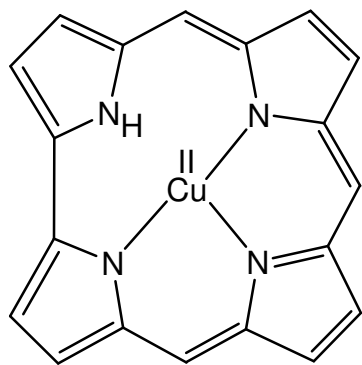
Corroles are generally easier to oxidize than analogous porphyrin ligands. For example octaethylcorrole (OEC)H<sub>3</sub> is oxidized at 0.38 V, whereas no reductions can be detected up to -1.6 V. This compares with octaethylporphyrin (OEP)H<sub>3</sub>, which is oxidized at 0.81 V and reduced at -1.46 V. Similarly the first oxidation potentials of Sn(OEC)Cl and Sn(OEP)Cl<sub>2</sub> are 0.67 V and 1.36 V respectively. The facile oxidation of the corroles allows a transfer of electrons from the  $\pi$ -electron system of the corrole ligand to the metal, making high-valent metal ions possible and thus leading to complexes that can be described as  $\pi$ -cation radicals in their neutral form. It has been accepted that, the corrole ligand in many high-valent metallocorroles behaves non-innocent. The oxidation potential of metallocorroles varies considerably depending upon the nature of the macrocycle and/or the axial ligands. By substituting carbons in  $\beta$  or *meso* positions with more electron withdrawing atoms (Br, N) the ring is expected to be less electron rich and therefore less likely to be partly oxidized. Similarly, the oxidation potentials of the Sn<sup>IV</sup>Ph and Fe<sup>IV</sup>Ph complexes are significantly lower than those of the Sn<sup>IV</sup>Cl, and Fe<sup>IV</sup>Cl complexes<sup>36</sup>. This may indicate that highly electron-deficient corrole complexes, has relatively little radical character, i.e. is relatively innocent, and, correspondingly, the metal is more “truly” high-valent than in complexes with more electron-rich corrole ligands<sup>17</sup>.

## 2.6 Copper Corroles

Copper corrole was the first reported metallocorrole together with nickel and cobalt<sup>1</sup>. Due to the existence of Soret band, neutral behavior and the paramagnetic nature copper corroles were assigned an M(II) complex with “extra” hydrogen placed on N-21 position (Figure 2.3).

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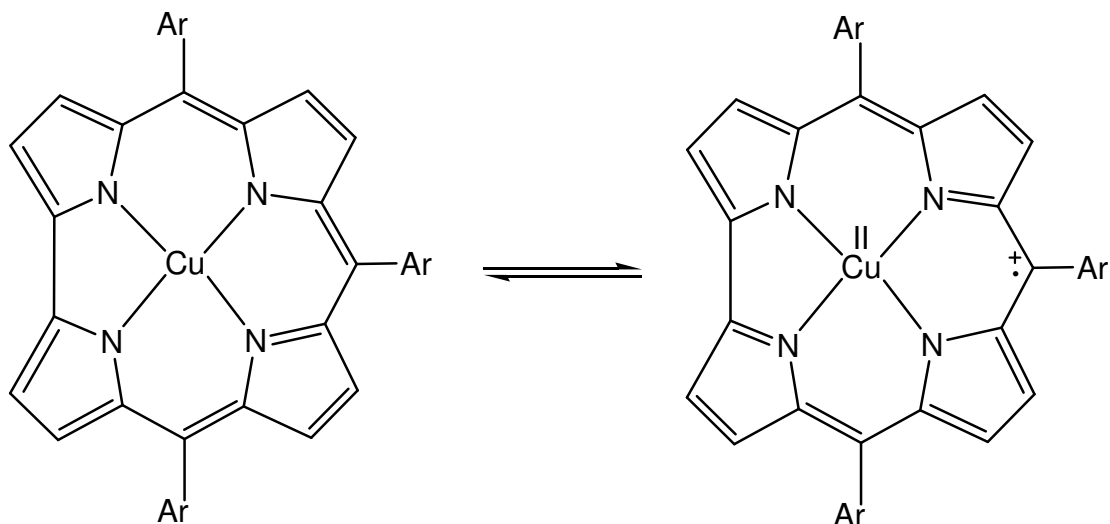
<sup>36</sup> Erben, C.; Will S.; Kadish, K. M. In the Porphyrin Handbook; Kadish, K. M.; Smith, K. M.; Guillard, R. eds.; Academic: New York, **2000**; Vol. 2, Chapter 12, p 233.



**Figure 2.3** The first predicted structure of copper corrole.

In 1997 Vogel and coworkers hypothesized that copper corroles can be considered as metal (III) neutral complexes. X-ray structural analysis confirmed this hypothesis and demonstrated that the complex is almost planar with no evidence of the presence of the residual hydrogen atom<sup>8</sup>.

Copper corroles are effectively diamagnetic in the solid state, as are other square planar  $d^8$  Cu(III) compounds. In contrast, the NMR spectra show strong temperature dependence. Sharp signals were obtained at room temperature, whereas a significant amount of line broadening appears with increase in temperature. This temperature dependent magnetic behavior was explained in terms of an equilibrium between the Cu(III) corrole and the Cu(II) complex of the corrole  $\pi$ -cation radical (Figure 2.4).



**Figure 2.4** The equilibrium between Cu(III) corrole and Cu(II) radical complexes.

Speculation that the corrole ligand has a non-innocent character stimulated renewed interest in this field. In all cases the ground state is corrole-copper(III) complex, but is only slightly lower in energy than that of the corrole-copper(II) radical. The latest studies including molecular structures show evidence of the contributions from both states<sup>37,38</sup>. The oxidation state of the metal centers in corrole complexes is currently a topic of lively debate.

Another unusual property of copper corroles was discovered by Ghosh et al.<sup>17</sup>. They showed that Cu(III) and other high valent transition metal corroles exhibit intense, exquisitely substituent-sensitive absorptions in the Soret region. This feature is specific for high-valent complexes and is not shared by free base and non-high-valent transition metal tetrapyrroles. They attributed the reason of the substitute effect to the ligand-to-metal charge transfer (LMCT).

The most detailed electrochemistry of copper corroles was reported for (OEC)Cu, which undergoes three reversible oxidations and one reversible reduction in dichloromethane (OEC=octaethylcorrole). (OEC)Cu reduced at -0.34 which leads to the formation of [(OEC)Cu]<sup>-</sup>. The first, second and third oxidation potentials of (OEC)Cu are 0.43 V, 0.57 V and 1.14 V respectively. After reduction and oxidation the EPR spectra are characteristic of corrole copper(II) and-copper(III) radicals, respectively. Taken together all the experimental data of copper corroles, indicate that while their reduction is metal-centered, the oxidation is corrole-centered.

There are in total five copper corrole X-ray structures determined up to date<sup>8,37,38,39,40</sup>. In view of the crystallographic evidence, copper corroles are non-planar and saddled distortion is general feature of all copper corroles. All interpretations and most calculations however have been based on the assumption that copper corroles are essentially planar species. The saddling distortion of

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<sup>37</sup> Luobeznova, I.; Simkhovich, L.; Goldberg, I.; Gross, Z. *Eur. J. Inorg. Chem.* **2004**, 1724.

<sup>38</sup> Bröring, M.; Brégier, F.; Tejero, E. C.; Hell, C.; Holthausen, M. C. *Angew. Chem. Int. Ed.* **2007**, 46, 445.

<sup>39</sup> Brückner, C.; Brinas, R.P.; Krause-Bauer, J.A. *Inorg. Chem.* **2003**, 42, 4495.

<sup>40</sup> Guillard, R.; Gros, C.P.; Barbe, J.-M.; Espinosa, E.; Jérôme, F.; Tabard, A. *Inorg. Chem.* **2004**, 43, 7441.

the corrole ligand in the singlet states allows attractive  $\sigma$ - $\pi$  interactions between the copper  $3dx^2-y^2$   $\sigma$  orbital and a corrole  $b_1 \pi$  orbital, as discussed earlier by Ghosh and coworkers<sup>17</sup>. According to Bröring et al<sup>38</sup> in the limiting cases, these interaction can be described as either an additional dative two-electron bond to a Lewis acidic  $\text{Cu}^{\text{III}}$  ion, or as a strong antiferromagnetic exchange coupling of an electron in a singly occupied  $\pi$  orbital with the unpaired d electron of a  $\text{Cu}^{\text{II}}$  ion. Their calculations suggest that continues transition between these two descriptions occurs, depending on the degree of molecular distortion.

The Cu-N bonds range 1.868 to 1.896 Å and are significantly shorter than  $\text{Cu}^{\text{II}}$  complexes (typical values are 1.95-2.15 Å with N-donor ligands), but they are in the range of values for  $\text{Cu}^{\text{III}}$  compounds with N-donor ligands (1.804-1.907 Å). Moreover, in many tetracoordinate  $\text{Cu}^{\text{II}}$  complexes of tetraarylporphyrins the Cu-N bond lengths are within a similar general range of 1.97-2.00 Å, irrespective of the intermolecular organization<sup>41,42</sup> whereas even in non-cyclic  $\text{Cu}^{\text{III}}$ - $\text{N}_4$  square planar complexes the Cu-N bond distances are essentially in the same range<sup>43,44</sup> (1.804-1.907 Å). This observation was used for showing an extra evidence for corrole-copper<sup>III</sup> electronic state. Surprising contradiction was developed by Bröring et al<sup>38</sup> in 2007. Bröring's group found it unfair to compare the Cu-N bond lengths between porphyrin and corrole complexes since they have different cavities. It wasn't satisfying for them to attribute the shorter Cu-N bond lengths to the Cu(III) high-valency. A better refence ligand would be an aromatic porphyrinoid with the contracted  $\text{N}_4$  core of corrole and the double negative charge of porphyrin. They prepared copper 10-oxacorrole and corresponding copper corrole (Figure 2.5).

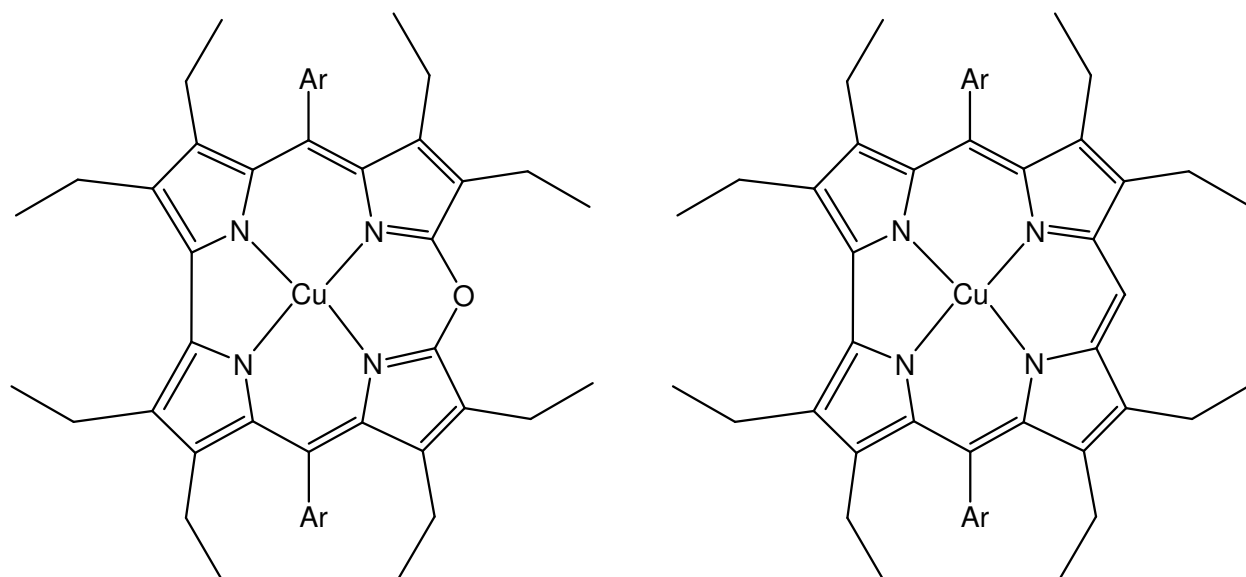
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<sup>41</sup> Kumar, R.K.; Balasubramanian, S.; Goldberg, I. *Inorg. Chem.* **1998**, *37*, 541.

<sup>42</sup> Posner, Y.D.; Dahal, S.; Goldberg I. *Angew. Chem. Int. Ed.* **2000**, *39*, 1288.

<sup>43</sup> Ruiz, R.; Surville-Barland, C.; Aukauloo, A. ; Anxolabehere-Mallart, E.; Journaux, Y. ; Cano, J.; Munoz, M.C. *J. Chem. Soc., Dalton Trans.* **1997**, 745.

<sup>44</sup> Melnik, M.; Kabesova, M. *J. Coord. Chem.* **2000**, *50*, 323.



Ar= Phenyl

**Figure 2.5** Copper 10-oxacorrole (left) and corresponding copper corrole (right) prepared by Bröring et al<sup>38</sup>.

Copper 10-oxacorrole is aromatic, neutral and according to EPR spectrum a copper(II) complex. What was surprising was that the Cu-N bond distances were in average slightly shorter than the corresponding Cu<sup>III</sup> corrole. In the crystallographic structure of both complexes the Cu-N bond distances are 1.884-1.896 Å for (Cu<sup>II</sup>)10-oxacorrole and for the corresponding Cu<sup>III</sup> corrole 1.883-1.907 Å. Their final conclusion was that although copper corroles can only be described as copper<sup>III</sup> species taking together all the experimental evidences, a better description would be Cu<sup>II</sup> according to their DFT/XRD study and Cu-N distances do not necessarily reflect the oxidation state of the central ion. In my opinion, as copper corroles are such substituent-sensitive species, this comparison still is not fair enough to conclude such a strong contradictory statement. My study on demetalation provides experimental data on substituent-sensitivity of Cu-N bond strengths of the copper corroles.



## 3 DEMETALATION

### 3.1 Demetalation of Porphyrins

Demetalation reaction is as old as the beginning of the porphyrin chemistry. Porphyrin chemistry began in 1864 when Stokes<sup>45</sup> isolated the mixture of chlorophylls *a* and *b* from green leaves by using partition methods. Afterwards, Nencki<sup>46</sup> isolated the first pure porphyrin directly from isolated heme. The chemists tried to explore the content of these molecules by chemical manipulation, such as burning, oxidization, reduction, and pyrolysis. In 1906 Willstätter's group<sup>47</sup> separated the two chlorophylls (*a* and *b*) from each other, they also introduced the column chromatography for the separation. After separation, from combustion experiments, Willstätter realized that these chlorophylls contained the metal magnesium. One year later, he confirmed that magnesium was part of the chlorophyll molecule from his experiments and he reported that chlorophylls were organomagnesium complexes. After that, experiments were performed to remove the magnesium and to generate a metal-free product, named "pheophytin". Thereby the demetalation experiment was first introduced. Then, in 1925, Keilin<sup>48</sup> discovered that heme was an organic complex of iron. His discovery was soon confirmed by Fischer and Kämmerer. Also, iron was removed from heme, and protoporphyrin IX was generated. Since the beginning of synthetic porphyrin chemistry metalation/demetalation protocols were widely performed for synthesis by metal induced cyclization and for functionalization of metalloporphyrin followed by demetalation in both cases. Metal coordination not only protects the inner nitrogens from electrophilic reagents, strong bases or protonation, but also has activating, directing, stabilizing effects on macrocycle.

Some metal ions serve as activating groups. For instance the nitration, chlorination and formylation of the  $\beta$ -positions of meso-tetraarylporphyrins proceed smoothly only in the form of

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<sup>45</sup> Stokes, G.G. *J. Chem. Soc.*, **1864**, 17, 304.

<sup>46</sup> Nencki, M., *Arch. Exptl. Path. Parmakol.* **1888**, 24, 430.

<sup>47</sup> Willstätter, R.; Stoll, A., *Investigations on Chlorophyll*, Science Press, Lancaster, Ohio, **1928**.

<sup>48</sup> Keilin, D., *Proc. R. Soc. London, B*, **1925**, 98, 312.

their Cu<sup>II</sup>, Ni<sup>II</sup>, or Pd<sup>II</sup> derivatives<sup>49</sup>. Some metal ions act as directing groups. For example, the OsO<sub>4</sub> mediated dihydroxylation of free base chlorins results specifically in the formation of bacteriochlorin chromophores, while dihydroxylation of the corresponding [chlorinato]Zn<sup>II</sup> complexes results exclusively in the formation of iso-bacteriochlorins<sup>50</sup>. This directing effect is general. Metal ions have a stabilizing effect. In some cases while metal complexes can be chromatographed, isolated and crystallized, the corresponding free base decomposes rapidly. Central metals can also act as templates. For instance, Ni<sup>II</sup> is known to induce non-planar conformations in inherently planar free base porphyrinic macrocycles and it increases the degree of distortion of non-planar free base porphyrins<sup>51</sup>. Additionally, metal coordination is necessary with proton sensitive reagents, such as, for example, lithium alkyls, to prevent their reaction with the inner core hydrogens. Zinc(II), cadmium(II) and magnesium(II) are easily and readily demetalated, sometimes under the reaction conditions. Therefore the nickel(II), copper(II) and iron(III) complexes are most often used. After the synthesis of metalloporphyrin or further functionalization the porphyrin free bases are successfully obtained by demetalation sometimes with 98-99% yields. Demetalation is performed under acidic conditions, the strength of the acid required depending upon the stability of the metal complex. Although not common, reductive demetalation for example with NaBH<sub>4</sub><sup>52</sup> is also known in porphyrin chemistry.

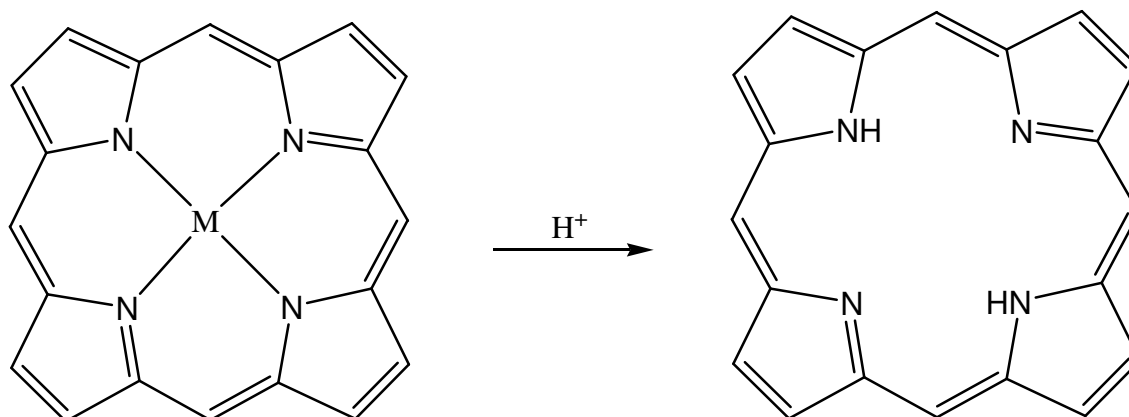
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<sup>49</sup> (a) Nitration: Catalano, M. M.; Crossley, M. J.; Harding, M. M.; King, L.G. *J. Chem. Soc. Chem. Commun.* **1984**, 1535. (b) Chlorination: Wijesekera, T.; Dupre, D.; Cader, M.S.R.; Dolphin, D. *Bull. Soc. Chim. Fr.* **1996**, 133, 765. (c) Formylation: Buchler, J.W.; Dreher, C.; Herget, G. *Liebigs Ann. Chem.* **1988**, 43.

<sup>50</sup> Brückner, C.; Dolphin, D. *Tetrahedron Lett.* **1995**, 36, 9425.

<sup>51</sup> Wondimagegn, T.; Ghosh, A. *J. Phys. Chem. B* **2000**, 104, 10858.

<sup>52</sup> Cowan, J.A.; Sanders, J.R.M. *Tetrahedron Letters*, **1986**, 27, 10, 1201.



**Figure 3.1** Demetalation of porphyrin under acidic conditions.

### ***3.2 Demetalation of corroles***

In the case of corroles demetalation procedure has been marred from the beginning of the first synthesis. The difficulty of demetalation constrained the development of the corrole synthetic chemistry in order to reach the versatility achieved in the case of porphyrins. In some cases corrole chemists have circumvented this problem by carrying out the reaction directly on the corrole free base, taking advantage of its higher reactivity, compared with porphyrin.

The difficulty of demetalation of corroles can be attributed to;

- a) The smaller core, shorter metal-nitrogen bonds.
- b) Lower stability than porphyrin; easy decomposition.
- c) High valency of the metal ion.
- d) Easier oxidized than porphyrin.
- e) Better donor properties; higher acidity than porphyrin.

As a consequence, for demetalation of corroles more acidic conditions are necessary. Sometimes even in harsh acidic conditions the removal of the metal ion is not possible. Most often increased rigorous acidic conditions results in undesired corrole modification or even in the decomposition of the macrocycle. In almost a half century of corrole chemistry, only three corrole demetalation

procedures have been reported. In 2001 Bröring et al.<sup>53</sup> synthesized Mn<sup>III</sup>(OEC) from manganese induced cyclization and obtained the free base by demetalation of the complex with HBr in acetic acid (OEC=octaethylcorrole). In 2003 Brückner et al.<sup>54</sup> have observed the demetalation of silver(III) triarylcorroles in CHCl<sub>3</sub> or CH<sub>2</sub>Cl<sub>2</sub> solutions, by using concentrated aqueous HCl in a biphasic system. However, experimental details and yields of these reactions are not available and, furthermore, the scope of the demetalation procedure for different corroles is still not available. These metal complexes were not useful for further functionalization. Manganese derivatives require the use of high boiling solvents for their preparation and their paramagnetism prevents the exploitation of NMR spectroscopy for easy reaction monitoring or product characterization. Silver corroles have not yet been reported in the case of β-alkyl corroles and, in addition, they seem to be too unstable in several reaction conditions. In March 2008 Paloesse et al.<sup>55</sup> reported the first detailed corrole demetalation procedure using copper corroles. Paloesse has added an annotation to the title “an old dream turning into reality”. At the same time I have completed the work on demetalation. Paloesse’s group and I independently developed two different demetalation procedures with different types of corrole macrocycles but with copper complexes. Zn, Ni and Cu complexes are most often used for further functionalization of the porphyrin macrocycles. Zn is not useful in the case of corrole, since the corresponding metal complex is not stable; Ni complexes are paramagnetic and more difficult to prepare. Copper corroles are easily prepared, versatile, stable and diamagnetic, thus quite suitable for further functionalization. Paloesse et al. reported that the best results were obtained by adding neat H<sub>2</sub>SO<sub>4</sub> drop-wise, to a CHCl<sub>3</sub> solution of copper corrole.

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<sup>53</sup> Bröring M.; Hell, C. *Chem. Commun.* **2001**, 2336.

<sup>54</sup> Brückner, C.; Barta, C.A.; Brinas, R.P.; Bauer A.K. *Inorg. Chem.* **2003**, 42, 1673.

<sup>55</sup> Mandoj, F.; Nardis, S.; Pomarico, G.; Paolesse, R. *J. Porphyrins Phthalocyanines*, **2008**, 12, 19.

## 4 EXPERIMENTAL SECTION

### 4.1 General Synthesis

**Materials.** All reagents and solvents were used as purchased, except pyrrole, which was predried and distilled from CaH<sub>2</sub> at low pressure. Silica gel 60 (0.040-0.063 mm particle size; 230-400 mesh; Merck) was used for flash chromatography.

**Instrumentation.** Ultraviolet-visible spectra were recorded on an HP 8453 spectrophotometer using dichloromethane as solvent. Proton NMR spectra were recorded on a Mercury Plus Varian spectrometer (400 MHz for <sup>1</sup>H) at room temperature in chloroform-*d*. Proton chemical shifts ( $\delta$ ) in *ppm* were referenced to residual chloroform ( $\delta = 7.2$  ppm). MALDI-TOF mass spectra were recorded on a Waters Micromass MALDI micro MX Mass Spectrometer using  $\alpha$ -cyano-4-hydroxycinnamic acid (CHCA) as the matrix. Satisfactory elemental analyses were obtained in each case from Atlantic Microlabs, Inc.

**Synthesis of corrole starting materials.** Free-base corroles were synthesized according to Gryko and coworkers<sup>22</sup>. Copper triarylcorroles and their  $\beta$ -octabromo derivatives were synthesized, as described by Ghosh and coworkers<sup>17</sup>.

**General procedure for the demetalation of the copper corroles.** Into a 25-mL or 50-mL round-bottomed flask equipped with a magnetic stirrer, 10 mg of copper corrole and 5-200 equiv of anhydrous FeCl<sub>2</sub> (Sigma-Aldrich) or SnCl<sub>2</sub> (Alfa-Aesar) were introduced. Concentrated H<sub>2</sub>SO<sub>4</sub> (95-97%, Merck, 0.8-2.0 mL) was added dropwise and the reaction mixture was alternately stirred/swirled and sonicated for 2 min to 1 h, depending on the particular copper corrole. The progress of the reaction, as measured by the disappearance of the copper corrole, was monitored by UV-vis spectroscopy and by TLC. After apparent consumption of the copper corrole, the reaction mixture was quenched with distilled H<sub>2</sub>O and then extracted with CHCl<sub>3</sub>. The green organic phase was repeatedly washed with distilled water and then twice with saturated aqueous NaHCO<sub>3</sub>. The organic phase was then dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered, mixed with about 0.5 g silica and evaporated under vacuum. The residue thus obtained was

chromatographed on a silica gel column with n-hexane/CH<sub>2</sub>Cl<sub>2</sub> as eluent to give the free-base corrole as the second or third band (small quantities of unreacted copper corrole was usually the first band). Spectroscopic data for free-base and copper triphenylcorrole, *meso*-tris(4-methoxyphenyl)corrole, *meso*-tris(4-trifluoromethylphenyl)corrole,  $\beta$ -octabromo *meso*-triphenylcorrole were in agreement with those reported previously<sup>17</sup>. Additional details for each demetalation experiment are provided below.

#### ***4.2 Demetalation of copper 5,10,15-triphenylcorrole***

##### **Cu[TPC]:**

Into a 25-mL round-bottomed flask containing 10 mg of the corrole and 200 equiv of FeCl<sub>2</sub>, 0.8 mL of concentrated H<sub>2</sub>SO<sub>4</sub> was added dropwise, with stirring. The resulting suspension was stirred for 3 min. After work-up of the reaction mixture, the green residue obtained was chromatographed on a silica gel column, first with 7:3 n-hexane/CH<sub>2</sub>Cl<sub>2</sub> to elute unreacted Cu[TPC] (1.4 mg) as the first band and then with 2:3 n-hexane/CH<sub>2</sub>Cl<sub>2</sub> to elute free-base *meso*-triphenylcorrole (6.1 mg). Yield: 68%. For the SnCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub> demetalation, 10 mg of the corrole, 100 equiv of SnCl<sub>2</sub> and 1 mL H<sub>2</sub>SO<sub>4</sub> were stirred and sonicated alternately for 5 min. After work-up and purification, Cu[TPC] (1.2 mg) and TPC (6.9 mg) were obtained. Yield of TPC: 77%. UV-Vis (CH<sub>2</sub>Cl<sub>2</sub>):  $\lambda_{\max}$  (nm), [(log  $\epsilon$  (M<sup>-1</sup>cm<sup>-1</sup>)): 417 (5.13), 578 (4.20), 620 (4.11), 651 (4.08). MS (MALDI-TOF, major isotopomer): M<sup>+</sup> = 526.13 (expt), 526.21 (calcd).

#### ***4.3 Demetalation of copper 5,10,15-tris(4-methoxyphenyl)corrole***

##### **Cu[T(p-OCH<sub>3</sub>-P)C]:**

Into a 25-mL round-bottomed flask containing 10 mg of the corrole and 200 equiv of FeCl<sub>2</sub>, 0.8 mL of concentrated H<sub>2</sub>SO<sub>4</sub> was added dropwise, with stirring. The resulting suspension was stirred for 2 min. The green residue obtained at the end of the work-up phase was chromatographed on silica gel with 2:3 n-hexane/CH<sub>2</sub>Cl<sub>2</sub> to afford *meso*-tris(4-methoxyphenyl)corrole. Yield: 75%. The SnCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub> demetalation was performed exactly as

with FeCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub>. After work-up and purification yield of the free-base was 77%. UV-Vis (CH<sub>2</sub>Cl<sub>2</sub>): λ<sub>max</sub> (nm), [(log ε (M<sup>-1</sup>cm<sup>-1</sup>)): 419 (4.52), 577 (3.63), 624 (3.61), 655 (3.58). MS (MALDI-TOF, major isotopomer): M<sup>+</sup> = 615.32 (expt), 616.25 (calcd).

#### **4.4 Demetalation of copper 5,10,15-tris(4-trifluoromethylphenyl)corrole Cu[T(*p*-CF<sub>3</sub>P)C]:**

To the copper corrole (10 mg) and 5 equiv of FeCl<sub>2</sub> in 50-mL round-bottomed flask was added 2.0 mL of concentrated H<sub>2</sub>SO<sub>4</sub> and the suspension was stirred for 1 h. After work-up of the reaction mixture, the green residue obtained was chromatographed on silica gel with 2:1 n-hexane/CH<sub>2</sub>Cl<sub>2</sub> to afford *meso*-tris(4-trifluoromethylphenyl)corrole. Yield: 69%. The SnCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub> demetalation was performed exactly as with FeCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub>. After work-up and purification, an inseparable mixture of the copper complex and the free-base was obtained. The reaction was also conducted on a larger scale: 60 mg of the copper complex, 5 equiv FeCl<sub>2</sub> and 3mL concentrated H<sub>2</sub>SO<sub>4</sub> were introduced in that order into a 50-mL round-bottomed flask. The mixture was stirred for 1 hour. Work-up and purification as described above gave 41 mg (74%) of H<sub>3</sub>[T(*p*-CF<sub>3</sub>P)C]. UV-Vis (CH<sub>2</sub>Cl<sub>2</sub>): λ<sub>max</sub> (nm), [(log ε (M<sup>-1</sup>cm<sup>-1</sup>)): 418 (4.63), 580 (3.84), 617 (3.71), 647 (3.61). MS (MALDI-TOF, major isotopomer): M<sup>+</sup> = 730.30 (expt), 730.18 (calcd).

#### **4.5 Demetalation of copper β-Octabromo-meso-triphenylcorrole Cu[Br<sub>8</sub>TPC]:**

To the copper corrole (10 mg) and 5 equiv of FeCl<sub>2</sub> in 50-mL round-bottomed flask was added in a dropwise manner 1.0 mL of concentrated H<sub>2</sub>SO<sub>4</sub> and the suspension sonicated and stirred alternately for 50 min. After work-up, the green residue obtained was chromatographed on silica gel with 1:1 n-hexane/CH<sub>2</sub>Cl<sub>2</sub>. Unreacted copper corrole was obtained as the first band. The eluent was then changed to neat CH<sub>2</sub>Cl<sub>2</sub> or CHCl<sub>3</sub> to yield free-base β-octabromo-*meso*-triphenylcorrole as the last band. After solvent removal, the green product was crystallized from 1:1 CHCl<sub>3</sub>/n-hexane to afford 5.3 mg of the pure free base. Yield: 55%. The SnCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub> demetalation was performed exactly as with FeCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub>. After work-up and purification, an inseparable mixture of the copper complex and the free-base was obtained. The reaction was

also conducted on a larger scale: 64 mg of the copper complex, 5 equiv FeCl<sub>2</sub> and 2 mL concentrated H<sub>2</sub>SO<sub>4</sub> were introduced in that order into a 50-mL round-bottomed flask. The mixture was stirred and sonicated alternately for 2 hours. Work-up and purification as described above gave 48 mg (79%) of H<sub>3</sub>[Br<sub>8</sub>TPC]. UV-Vis (CH<sub>2</sub>Cl<sub>2</sub>): λ<sub>max</sub> (nm), [(log ε (M<sup>-1</sup>cm<sup>-1</sup>))]: 444 (4.84), 553 (3.80), 593 (3.85), 703 (3.88). MS (MALDI-TOF, major isotopomer): M<sup>+</sup> = 1158.76 (expt), 1157.49 (calcd).

#### ***4.6 Demetalation of copper β-octabromo-meso-tris(4-trifluoromethylphenyl)corrole***

##### **Cu[Br<sub>8</sub>T(p-CF<sub>3</sub>-P)C]:**

To the copper corrole (10 mg) and 5 equiv of FeCl<sub>2</sub> in 50-mL round-bottomed flask was added in a dropwise manner 2.0 mL of concentrated H<sub>2</sub>SO<sub>4</sub> and the suspension sonicated and stirred alternately for 1 h. After work-up of the reaction mixture, the green residue obtained was chromatographed on silica gel with 3:2 n-hexane/CH<sub>2</sub>Cl<sub>2</sub> to give green free-base β-octabromo-meso-tris(4-trifluoromethyl-phenyl)corrole. Yield: 82%.

The SnCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub> demetalation was performed exactly as with FeCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub>. After work-up and purification, yield of the free-base was 85%. UV-Vis (CH<sub>2</sub>Cl<sub>2</sub>): λ<sub>max</sub> (nm), [(log ε (M<sup>-1</sup>cm<sup>-1</sup>))]: 447 (4.86), 597(5.04), 697 (3.97). <sup>1</sup>H NMR: δ 8.08-8.00 (4H, 5,15- *o* or *m* and 2H, 10-*o* or *m*, Ph); 7.96-7.86 (4H, 5,15- *m* or *o* and 2H, 10- *m* or *o*, Ph). MS (MALDI-TOF, major isotopomer): M<sup>+</sup> = 1361.63 (expt), 1361.45 (calcd).

#### ***4.7 Demetalation of copper β -octabromo-meso-tris(4-methoxyphenyl)corrole***

##### **Cu[Br<sub>8</sub>T(p-OCH<sub>3</sub>-P)C]:**

To the copper corrole (10 mg) and 100 equiv of FeCl<sub>2</sub> in 50-mL round-bottomed flask was added in a dropwise manner 1.0 mL of concentrated H<sub>2</sub>SO<sub>4</sub> and the suspension sonicated and stirred alternately for 20 min. After work-up of the reaction mixture, the green residue obtained was

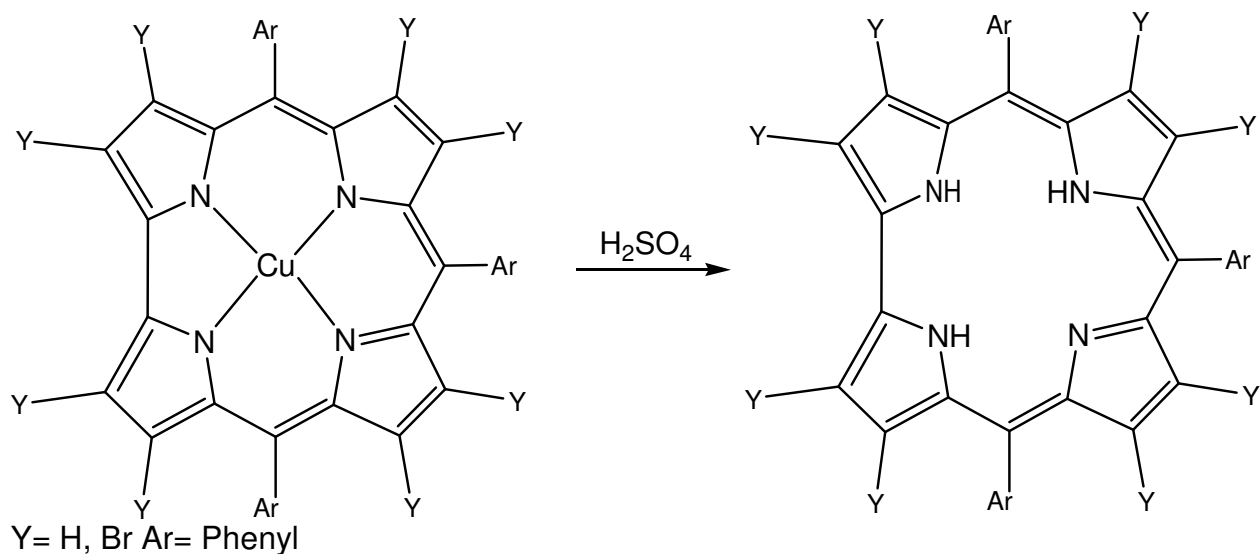


chromatographed on silica gel with 2:3 n-hexane/CH<sub>2</sub>Cl<sub>2</sub>, yielding the green free-base  $\beta$ -octabromo-*meso*-tris(4-methoxyphenyl)corrole (7.7 mg). Yield: 81%. UV-Vis (CH<sub>2</sub>Cl<sub>2</sub>):  $\lambda_{\text{max}}$  (nm), [(log  $\epsilon$  (M<sup>-1</sup>cm<sup>-1</sup>)]: 450 (4.41), 601(3.55), 715 (3.72). <sup>1</sup>H NMR:  $\delta$  7.85-7.75 (4H, 5,15- *o* or *m* and 2H, 10-*o* or *m*, Ph; overlapping doublets); 7.25-7.10 (4H, 5,15- *m* or *o* and 2H, 10- *m* or *o*, Ph); 3.99 (s, 6H, 5,15-*p*-OCH<sub>3</sub>, Ph); 3.98 (s, 3H, 10- *p*-OCH<sub>3</sub>, Ph). MS (MALDI-TOF, major isotopomer): M<sup>+</sup> = 1248.76 (expt), 1247.52 (calcd). Elemental analysis: 38.50% C (38.30% calcd), 1.94% H (calcd 1.88%), 4.49% N (calcd 4.43%). For the SnCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub> demetalation, 10 mg of the corrole, 100 equiv of SnCl<sub>2</sub> and 1mL H<sub>2</sub>SO<sub>4</sub> were stirred and sonicated alternately for 20 min. After work-up and purification, 8.2 mg of the free base was obtained. Yield: 85%.

## 5 RESULTS AND DISCUSSIONS

### 5.1 Demetalating Agent:

The demetalation reactions were carried out with acid. Reductive demetalation was also tried with a strong reducing agent ( $\text{NaBH}_4$ ) in the absence of an acid but wasn't effective. In the reaction with acid, the acid hydrogenates the central nitrogens and pushes the metal out. Central nitrogen's lone pair electrons leave the metal's d-orbitals and coordinate with protons. The corrole is oxidized to its neutral state.



**Figure 5.1** Demetalation of copper corrole with sulfuric acid.

### 5.2 Acid:

For all the cases concentrated sulfuric acid was the only acid capable of demetalating the complexes. TFA, HCl, HBr and oxalic acid were tried. HCl was not strong enough to cause any demetalation. Even the excess of concentrated HCl in a long reaction time did not remove the copper metal from the corrole.  $\text{Cu}[\text{T}(p\text{-OCH}_3\text{-P})\text{C}]$  was the easiest to demetalate among all the

studied corroles. The excess of concentrated HBr demetalated Cu[T(*p*-OCH<sub>3</sub>-P)C] but simultaneously converted the corrole to other unidentified compounds. A mixture of TFA in HCl or HBr was tried but didn't cause demetalation. Dilute H<sub>2</sub>SO<sub>4</sub> with different molarities did not demetalate. Oxalic acid besides being moderate acid is known as a reducing agent. However oxalic acid was too weak to cause any demetalation even for Cu[T(*p*-OCH<sub>3</sub>-P)C] which demetalates easily. A mixture of sulfuric acid and oxalic acid was applied to benefit oxalic acid's reducing character; it further prevented the demetalation compare to sulfuric acid alone. Concentrated H<sub>2</sub>SO<sub>4</sub> was the best and the only agent to cause demetalation in all studied copper corroles.

### ***5.3 Solvent:***

Sulfuric acid being very polar liquid is itself an excellent solvent. It efficiently dissolves the corroles. Although using organic solvents is common in porphyrin demetalation reactions, using organic solvents had negative effect in my demetalation reactions. Dichloromethane and chloroform have been tried for investigation of solvent effect. Using organic solvents either totally inhibited the isolation of any product or considerably decreased the yields (see Table 5.1). Using dichloromethane as a solvent gave relatively better results than chloroform but still had the negative effect (Table 5.1). The main reason of the negative effect is believed to be due to two phases formed by acid and organic solvent. Sulfuric acid ( $d=1.84\text{ g/cm}^3$ ) is heavier than CH<sub>2</sub>Cl<sub>2</sub> ( $d=1.3255\text{ g/cm}^3$ ) and forms the lower layer. The corrole is mixed in two layers. But the demetalation always happens in the acid layer. The samples were checked in both layers. The organic layer contains only undemetalated corroles while acid layer contains mainly demetalated corroles. Moreover solvent usage increases the byproduct percentage at the end of the reaction. Although the densities of CH<sub>2</sub>Cl<sub>2</sub> and CHCl<sub>3</sub> ( $d=1.48\text{ g/cm}^3$ ) are close to each other the effects on demetalation are different. The reason is believed to be; CHCl<sub>3</sub> dissolves the corrole better than CH<sub>2</sub>Cl<sub>2</sub>. In the two layers between CHCl<sub>3</sub> and acid, CHCl<sub>3</sub> contains the larger amount of the copper corroles leaving little amount for demetalation in the acid layer. Using organic solvent and creating biphasic system has also positive effect. It has protective effect on sensitive corroles against the acid. For example before the procedure of using reducing agent was found (chapter

5.4), it was only possible to isolate the demetalated Cu[TPC] by using biphasic system with chloroform or dichloromethane (Table 5.1). Otherwise sulfuric acid alone, besides demetalating the metallocorrole simultaneously converts the macrocycle to byproducts.

Complex	H <sub>2</sub> SO <sub>4</sub> , CHCl <sub>3</sub>	H <sub>2</sub> SO <sub>4</sub> , CH <sub>2</sub> Cl <sub>2</sub>	H <sub>2</sub> SO <sub>4</sub> only	H <sub>2</sub> SO <sub>4</sub> + FeCl <sub>2</sub>	H <sub>2</sub> SO <sub>4</sub> + SnCl <sub>2</sub>
Cu[TPC]	18	18	-	68	77
Cu[T( <i>p</i> -OMeP)C]	-	-	-	75	77
Cu[T( <i>p</i> -CF <sub>3</sub> P)C]	Not attempted	26	37	74	Inseparable mixture
Cu[Br <sub>8</sub> TPC]	Inseparable impurities	Inseparable impurities	Inseparable impurities	79	Inseparable mixture
Cu[Br <sub>8</sub> T( <i>p</i> -CF <sub>3</sub> P)C]	10	22	33	82	85
Cu[Br <sub>8</sub> T( <i>p</i> -OCH <sub>3</sub> P)C]	35	79	-	81	85

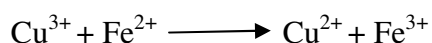
**Table 5.1** Comparison of demetalation yields (%) under different reaction conditions.

#### 5.4 Additives:

Adding Iron(II) chloride (FeCl<sub>2</sub>) considerably increased the yields in all cases. I may say 100% in Cu[T(*p*-OCH<sub>3</sub>-P)C] which couldn't be isolated without using FeCl<sub>2</sub> (Table 5.1). Perhaps the most interesting part of this project was the finding of FeCl<sub>2</sub> effect on demetalation which has not been reported yet. The ferrous compounds are known as reducing agent especially for metal containing compounds. The main goal of adding FeCl<sub>2</sub> was to use the ferrous ion's reducing ability. Perhaps other compound of a ferrous ion would show similar effect. Anhydrous FeCl<sub>2</sub>

was the only ferrous compound available in our laboratory. Demetalation of the copper corrole had the question of “what happens to  $\text{Cu}^{3+}$  ion after being separated from corrole?” This problem is not present in copper porphyrins where the copper ion is in its most stable divalent state.  $\text{Cu}^{3+}$  is quite unstable and would probably be converted to its 2+ oxidation state immediately after disassociating from the corrole. I have suspected that while  $\text{Cu}^{3+}$  reduces to its divalent state it would cause unpleasant byproduct formation. Attempts to purify the byproducts of the demetalation reaction of  $\text{Cu}[\text{T}(p\text{-CF}_3\text{-P})\text{C}]$  have been partially successful. MALDI-TOF analysis gave information about oxidized demetalated corrole rings. I have decided to add mild reducing agent with the hope of protecting the corrole macrocycle from oxidative breakdown. I thought the proper reducing agent would be non-organic, metallic and ionic. Hopefully it would undergo to a redox reaction with  $\text{Cu}^{3+}$  ion. Adding  $\text{FeCl}_2$  as a reducing agent to a reaction immediately showed increased yields.

Iron is more stable in its trivalent state and one electron oxidation of divalent iron is in favor according to half reaction energy potential. Since reduction of trivalent copper ion to its stable divalent form is in favor, a redox reaction between iron and copper ions would be favored.

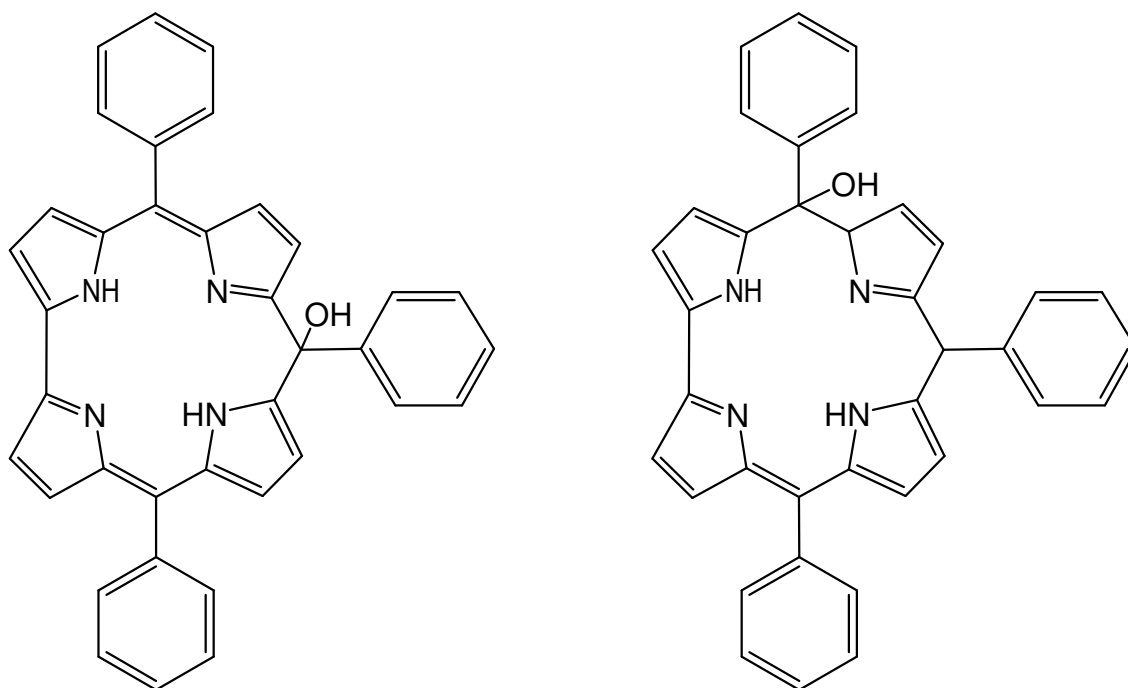


This can prevent the oxidation of the ring by  $\text{Cu}^{3+}$  ion and increase the yield dramatically. When small  $\text{Cu}^{3+}$  ion is reduced to the larger, much more easily displaced  $\text{Cu}^{2+}$  ion considerable decrease on reaction time seems to be reasonable.

Ferrous ion can also prevent unpleasant reactions between corrole ring and sulfuric acid by undergoing redox reaction with sulfuric acid. For example the isolation of demetalated  $\text{H}_3[\text{T}(p\text{-OCH}_3\text{-P})\text{C}]$  and  $\text{H}_3[\text{Br}_8\text{TPC}]$  could only be possible using approximately 200 equiv  $\text{FeCl}_2$ . Otherwise  $\text{H}_2\text{SO}_4$  converted the corroles to other demetalated green byproducts (Table 5.1).

Later on Tin(II) chloride ( $\text{SnCl}_2$ ) was tried as another reducing agent.  $\text{SnCl}_2$  is known for its wide use as a reducing agent in acid solution.  $\text{SnCl}_2$  showed the same effects like  $\text{FeCl}_2$  and even with higher yields in some cases. Demetalation of  $\text{Cu}[\text{T}(p\text{-CF}_3\text{P})\text{C}]$  and  $\text{Cu}[\text{Br}_8\text{TPC}]$  with  $\text{SnCl}_2$  did not work well and resulted to inseparable mixtures of the free bases and their copper complexes (Table 5.1).

Paolesse et al.<sup>55</sup> identified the main byproduct of demetalated Cu[TPC] as H<sub>2</sub>(10-OH)TPisoC and H<sub>2</sub>(5-OH)TPisoC as shown in figure 5.2. The plausible pathway for the isocorrole formation during the demetalation reaction is probably due to the easy oxidation of the corrole ring to give a  $\pi$ -radical cation, which can be then attacked by a molecule of water at both *meso*-positions, to give the isocorrole species H<sub>2</sub>(10-OH)TPisoC and H<sub>2</sub>(5-OH)TPisoC<sup>55</sup>. By using MALDI-TOF spectroscopy I have analyzed additional two OH attached instead of one OH group on H<sub>3</sub>[T(*p*-CF<sub>3</sub>-P)C].



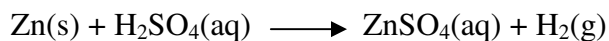
**Figure 5.2** Molecular structure of H<sub>2</sub>(10-OH)TPisoC (right) and H<sub>2</sub>(5-OH)TPisoC (left).

The most probable assumption is Cu<sup>3+</sup> ion reduces to Cu<sup>2+</sup> before it leaves the corrole, thus causing the oxidation of the corrole ring. The oxidation is not necessarily due to from acidic conditions; Paolesse's group<sup>56</sup> recently reported the formation of isocorroles by reaction of corrole with DDQ. Paolesse et al.<sup>55</sup> reported that carrying out the reaction under an inert atmosphere doesn't give significant variations in the isocorrole formation.

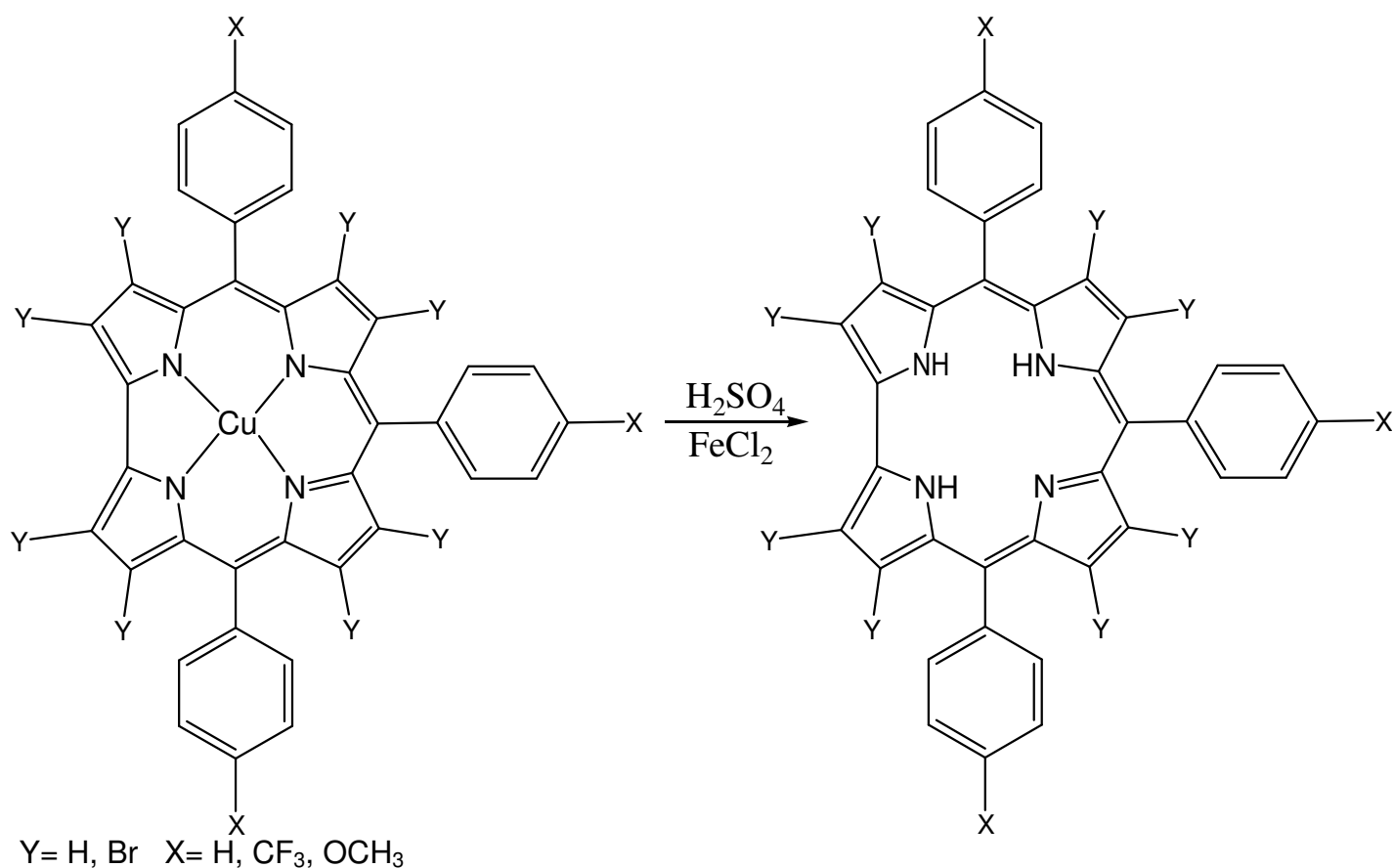
As mentioned in chapter 2.6; all experimental evidences for the reduction of copper corroles is metal-centered while the oxidation is corrole-centered. I have exploited this feature of copper corroles by reducing the metal center with FeCl<sub>2</sub> or SnCl<sub>2</sub>.

<sup>56</sup> Nardis, S.; Pomarico, G.; Fronczek, F.R.; Vicente, M.G.V.; Paolesse, R. *Tetrahedron Lett.* **2007**, 48, 8643.

Zinc powder was also tried as another additive. Zn powder is a strong reducing agent and reacts violently with oxidants. Zinc reacts with sulfuric acid to produce zinc sulfate and hydrogen gases and Cu(II) ion is known to catalyze this reaction.



However, using Zn powder as reducing agent did not work well. Although it seemed to show protective effect by preventing the conversion of the corrole to unidentified green substances in easily demetalating Cu[T(*p*-OCH<sub>3</sub>-P)C], zinc powder did not help in the isolation of the free base H<sub>3</sub>[T(*p*-OCH<sub>3</sub>-P)C]. In the case of Cu[T(*p*-CF<sub>3</sub>P)C] a poor yield (20%) was obtained.



**Figure 5.3** The demetalation reaction of the studied copper corroles.

## 5.5 Amounts of reactants:

As may be seen from a perusal of the experimental section (chapter 4), relatively electron-rich copper corroles required large quantities (100-200 equiv) of  $\text{FeCl}_2$  or  $\text{SnCl}_2$ , whereas the more electron-deficient copper corroles needed only 5 equiv of  $\text{FeCl}_2$ . A plausible explanation for this difference is that the excess  $\text{FeCl}_2$  or  $\text{SnCl}_2$  protects the more easily oxidized free-base corroles from oxidative breakdown under the demetalation procedure. The amount of reducing agents ( $\text{FeCl}_2$ ,  $\text{SnCl}_2$ ) especially with electron-rich copper corroles may seem fairly large at first glimpse. As seen in experimental section, for 10 mg of copper corrole 0.8 to 2.0 ml concentrated  $\text{H}_2\text{SO}_4$  were used depending upon the macrocycle. For example 10 mg of  $\text{Cu}[\text{T}(p\text{-OCH}_3\text{-P})\text{C}]$  is 0.0148 mmol whereas 0.8 ml of 96% of  $\text{H}_2\text{SO}_4$  is 14.41 mmol. There is a 973.65 fold mmol excess of acid which reacts with the copper corrole. However it should be considered that there are four nitrogens versus two protons of the sulfuric acid. Stoichiometrically approx. 500 mmol equiv of acid are present. This number may be seen too big. In all cases the amounts of acids were the minimum amounts capable to dissolve the reactants properly. The excess amount of acid was necessary to push the metal out. Additionally the excess acid was necessary to speed up the reaction. For example using less  $\text{H}_2\text{SO}_4$  with  $\text{Cu}[\text{T}(p\text{-CF}_3\text{P})\text{C}]$  and  $\text{Cu}[\text{Br}_8\text{T}(p\text{-CF}_3\text{P})\text{C}]$  gave lower yields and longer reaction times under the same conditions. Since there is an excess amount of acid it was essential to add large amounts of  $\text{FeCl}_2$  or  $\text{SnCl}_2$  to protect the unpleasant reactions between  $\text{H}_2\text{SO}_4$  and the corrole ring. For example for  $\text{Cu}[\text{T}(p\text{-OCH}_3\text{-P})\text{C}]$ , 100 equiv of  $\text{SnCl}_2$  was tried in 2 min of reaction time. The yield was 45%.  $\text{SnCl}_2$  of 200 equiv in 4 min was performed for the same amount of copper corrole and acid. The yield was 50%.  $\text{SnCl}_2$  of 200 equiv in 2 min was performed for the same amount of copper corrole and acid. The yield was 77%. It is important to bear in mind the use of minimum amount of acid when the reactions are carried out in larger scales. For example for 10 mg of  $\text{Cu}[\text{T}(p\text{-CF}_3\text{P})\text{C}]$  best result was obtained with 2 mL of acid. When the reaction was conducted using 60 mg of  $\text{Cu}[\text{T}(p\text{-CF}_3\text{P})\text{C}]$  best results was obtained with only 3 mL of acid. More than 3 mL of acids increased the by product formations and hence decreased the yields. In other words; when the amount of copper corrole is increased, the amount of acid is required does not increases in the same ratio and should always be kept at minimum range.



### ***5.6 Reaction time:***

Reaction time is highly dependent upon the corrole macrocycle as well. Corroles with electron withdrawing substituent groups take longer time to demetalate. Corroles with electron donating substituent groups immediately demetalate when they are in contact with acid. This follows the complete conversion of the free base corrole to the oxidized byproducts after 3 minutes. Therefore the reaction time should not go beyond 3 minutes with electron donating substituent groups. In all cases at least 10% of copper corrole remained undemetalated though large amount of sulfuric acid and long reaction time were used. Using organic solvents considerably prolonged the reaction time. Using  $\text{FeCl}_2$  or  $\text{SnCl}_2$  decreases the reaction time by 50%.

### ***5.7 Sonication:***

Applying sonication during the reaction period speeded up the demetalation in octa-brominated copper corroles. The sonication is commonly used to speed the dissolution, by breaking intermolecular interactions. It might also provide energy for the chemical reaction of the out-pushed copper ion to stabilize it in a new molecule. Indeed the reaction flask was becoming warm during the sonication. This warmth wasn't observed, only with stirring under the same conditions. A study by J.A. Cowan and J.R.M. Sanders on reductive demetalation of copper porphyrin<sup>52</sup> demonstrates that reductive demetalation of Cu porphyrins requires attack of the reducing agent on one face of the porphyrin, the central metal ion then leaves from the opposite side of the molecule. I believe that sonication might provide proper condition for such a mechanism.

### ***5.8 Substituent Effect:***

The other contribution of this study is providing experimental data on metal-ligand coordination strength with electron-donating and withdrawing substituent groups. One can think that the corrole with electron-donating substituent groups would be more difficult to demetalate because their central nitrogens would strongly provide electron pairs to the metal. But according to my results; the more electron-withdrawing substituent groups are more difficult to demetalate. The

copper corroles with strong electron-donating groups immediately demetalate, followed by conversion to oxidized byproducts sometimes making me unable to isolate the desired free base. A plausible explanation would be the effect of “the extent of the high-valency” of the metal ion. In copper corroles there is an equilibrium between Cu(III) corrole and Cu(II) radical complexes as mentioned in chapter 2.6. These interactions can be described as a continuous transition between an additional dative two-electron bond to a Lewis acidic Cu(III) ion and as a strong antiferromagnetic exchange coupling of an electron in a singly occupied  $\pi$  orbital with the unpaired d electron of a Cu(II) ion. Since the more electron-deficient corrole coordinate more high-valent metal ion; the former case has stronger effect on the strength of the metal-ligand coordination.

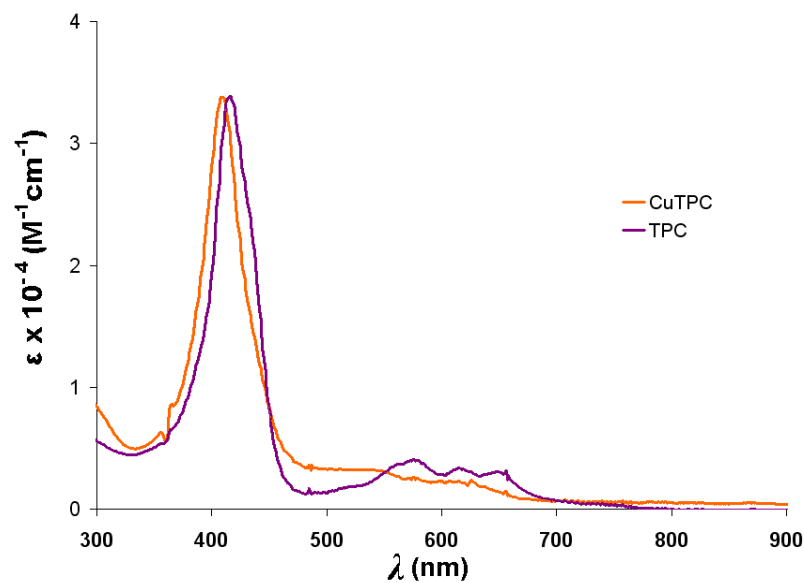
## 6 CONCLUSIONS

I like to conclude with the following statements:

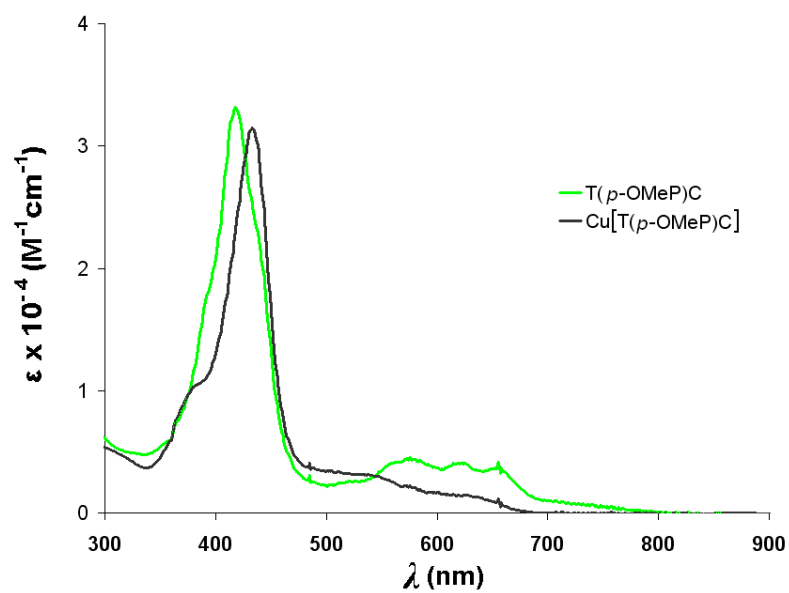
- i) The difficulty of demetalation constricted the development of the corrole synthetic chemistry in order to reach the versatility achieved in the case of porphyrins. In this thesis a general demetalation procedure was developed by choosing different types of copper corroles as template. Copper corroles are the best suited metallocorroles for further functionalization. Demetalation reactions are short and vary between 2 min-2 h. The yields are high and vary between 74%-85%.
- ii) While experimental work of the thesis was completed. Paolesse and coworkers<sup>55</sup> reported the first general corrole demetalation procedure in March 2008. However, I have developed a completely different demetalation procedure. Paolesse and coworkers's demetalation procedure involves ( $\text{CHCl}_3/\text{H}_2\text{SO}_4$ , 10:1 v/v), whereas my method involves solvent free ( $\text{FeCl}_2$  or  $\text{SnCl}_2/\text{H}_2\text{SO}_4$ ) procedure. Using organic solvents had negative effect in my reactions.
- iii) The exact comparison between two methods is not possible since studied complexes are not the same except  $\text{Cu}[\text{TPC}]$  and  $\text{Cu}[\text{Br}_8\text{TPC}]$ . For  $\text{Cu}[\text{TPC}]$ , Paolesse and coworker's  $\text{CHCl}_3/\text{H}_2\text{SO}_4$  method results in 83% yield, whereas the best yield I've obtained was with  $\text{SnCl}_2/\text{H}_2\text{SO}_4$  method (77%). For  $\text{Cu}[\text{Br}_8\text{TPC}]$  Paolesse and coworkers do not report a yield, whereas  $\text{FeCl}_2/\text{H}_2\text{SO}_4$  method results in 79% yield.
- iv) This method may be superior than the method described by Paolesse et al. because the byproduct formation and sometimes complete decomposition to the byproducts are similar to the ones I've observed. Although the corroles are not the same, the byproducts are identical oxidized species. This problem was easily circumvented by adding mild reducing agent ( $\text{FeCl}_2$ ,  $\text{SnCl}_2$ ) and substantially improved the yields in all cases in 50% shorter reaction times.

- v) For the first time fully  $\beta$ -brominated free base corroles were synthesized. Paolesse's<sup>55</sup> earlier report on  $H_3[Br_8TPC]$  synthesis from the direct bromination of free base  $H_3[TPC]$  was incorrect. Thus  $H_3[Br_8TPC]$  was for the first time synthesized by these two different demetalation procedures and within this study  $\beta$ -octa-brominated free base  $[Br_8T(p-OCH_3P)C]$  was for the first time synthesized in 85% yield.
- vi) I believe that the method described in this thesis is quite general. Both electron-rich and electron-deficient corroles can be reliably demetalated by fine adjustment of the amount of acid, reducing agent and the reaction time. It can even be extended to porphyrin demetalation especially when the metal is coordinated in its higher oxidation state than its stable state. With this method while the acid protonates the nitrogens and pushes the coordinated metal out, the metal ion can safely be reduced by the proper reducing agent to its stable state.
- vii) In summary, the first general corrole demetalation procedures were developed. Highly promising synthetic paths were finally opened. This was a dream in almost half century of corrole chemistry. As Paolesse expressed "an old dream turning into reality".

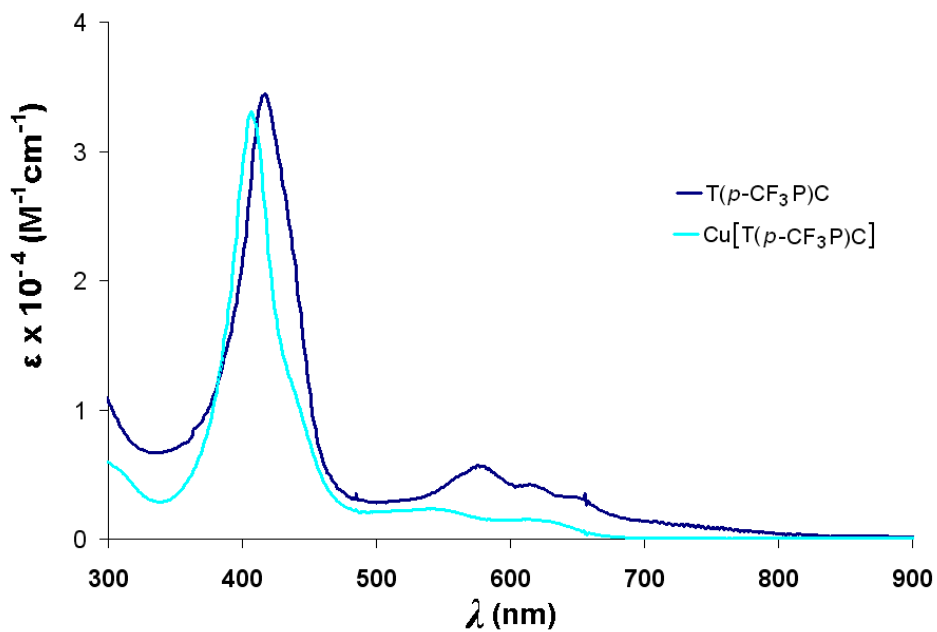
## APPENDIX



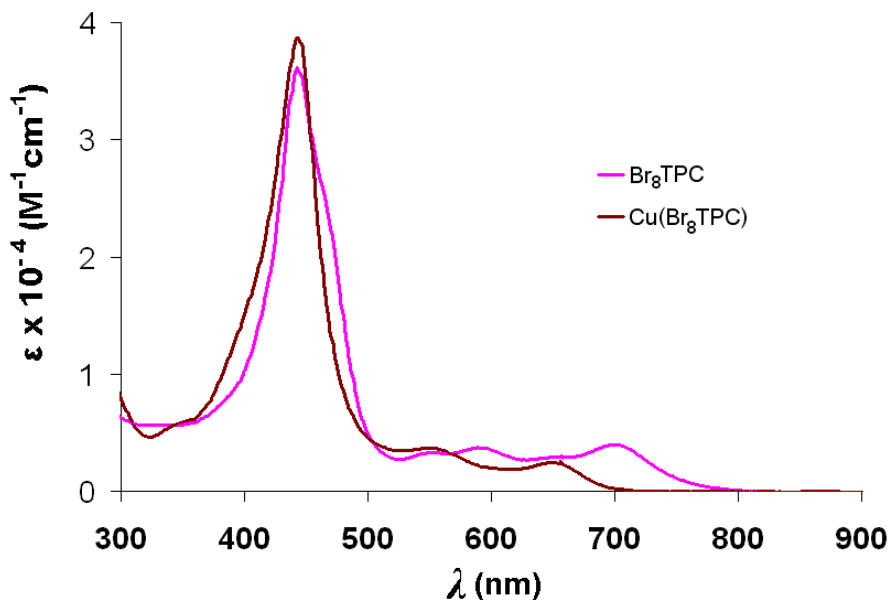
UV-visible spectra of Cu[TPC] and its demetalated free base corrole.



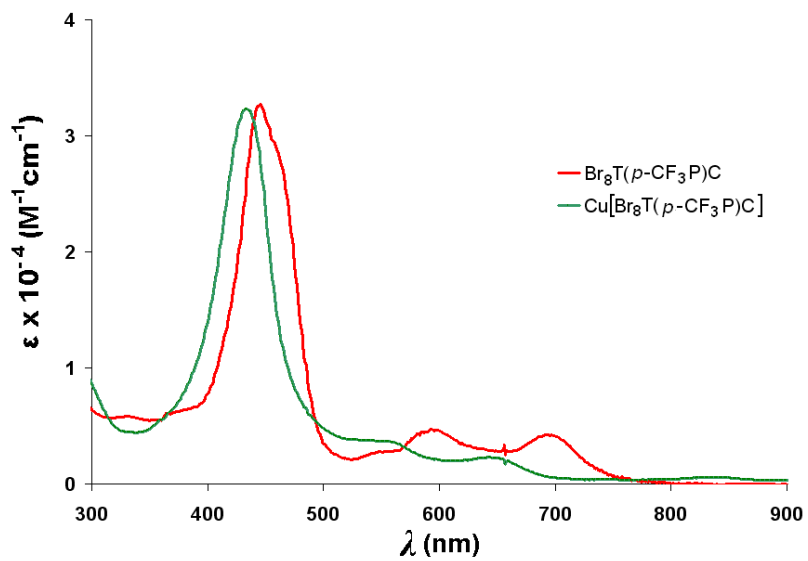
UV-visible spectra of Cu[T(*p*-OMeP)C] and its demetalated free base corrole.



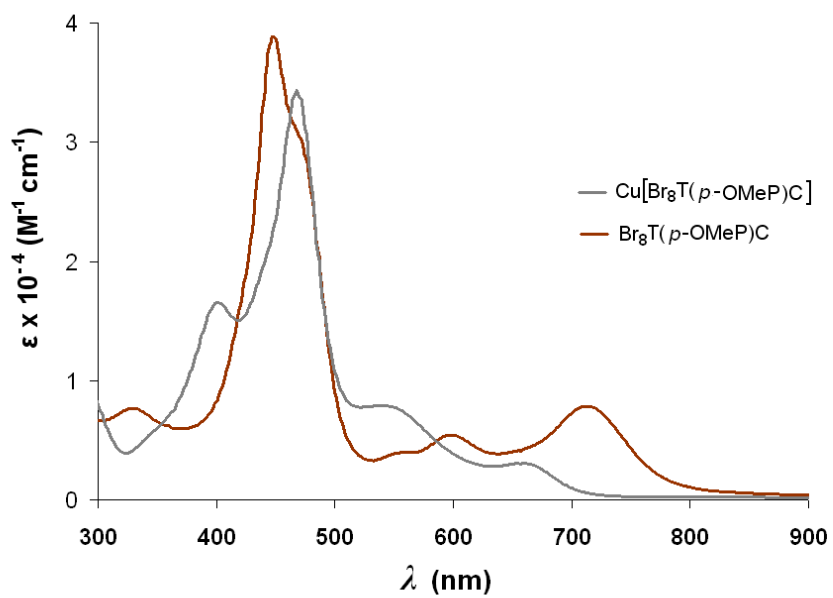
UV-visible spectra of  $\text{Cu}[T(p\text{-CF}_3\text{P})\text{C}]$  and its demetalated free base corrole.



UV-visible spectra of  $\text{Cu}[\text{Br}_8\text{TPC}]$  and its demetalated free base corrole.

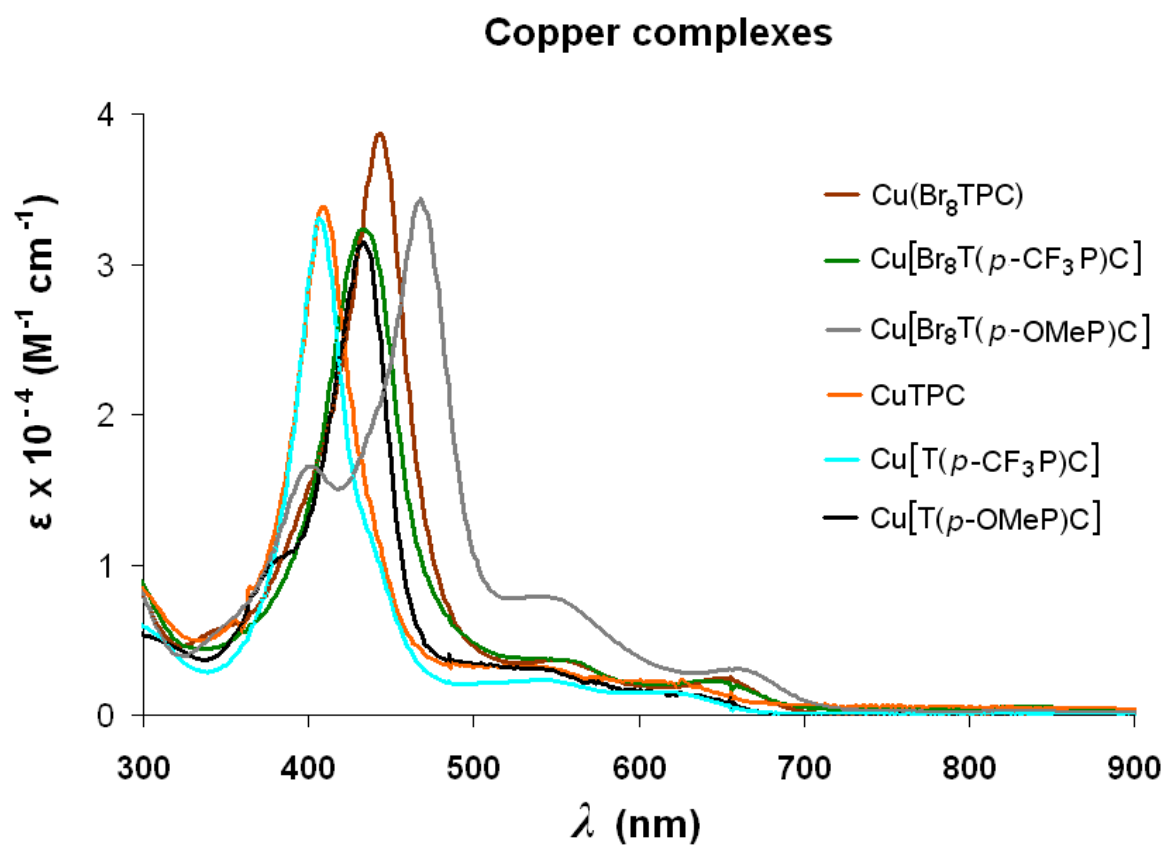


UV-visible spectra of Cu[Br<sub>8</sub>T(p-CF<sub>3</sub>P)C] and it's demetalated free base corrole.



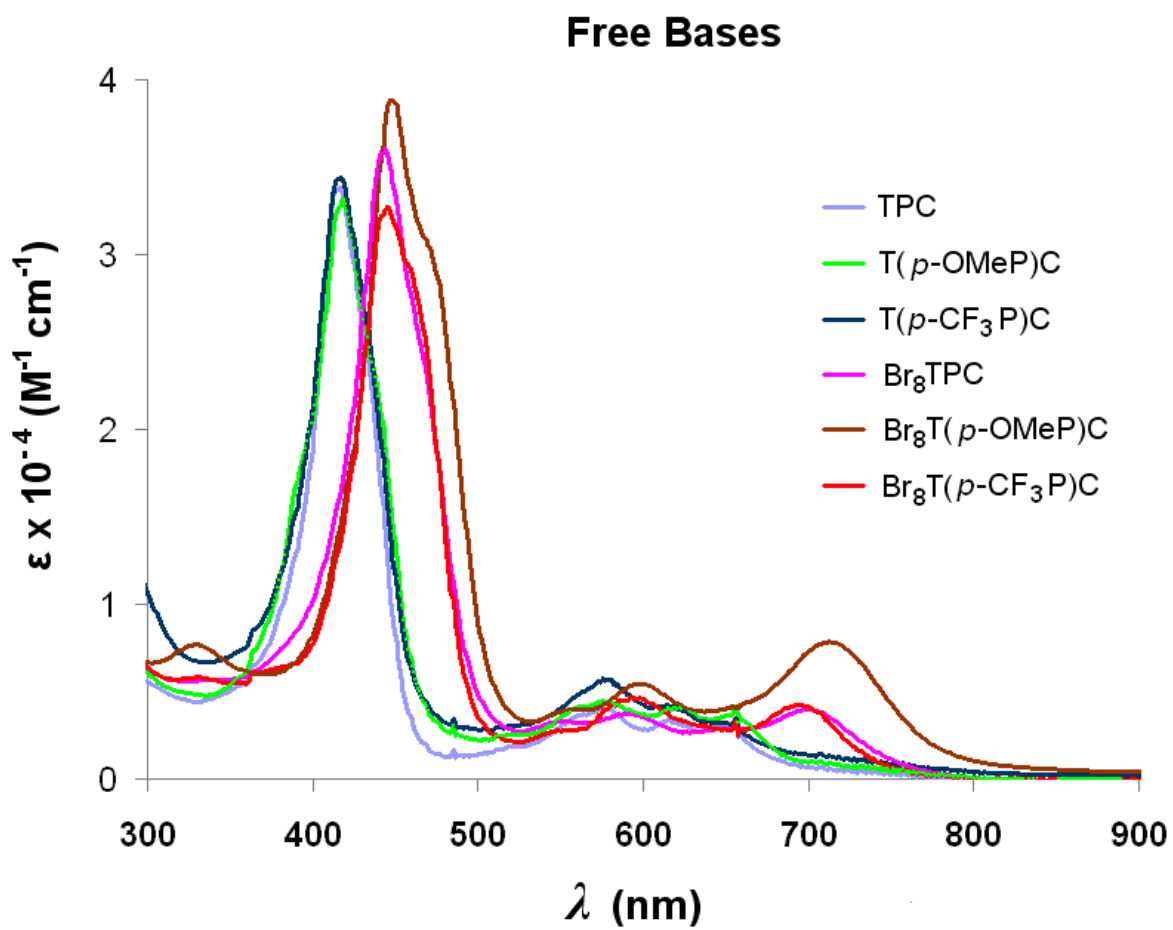
UV-visible spectra of Cu[Br<sub>8</sub>T(p-OCH<sub>3</sub>P)C] and it's demetalated free base corrole.

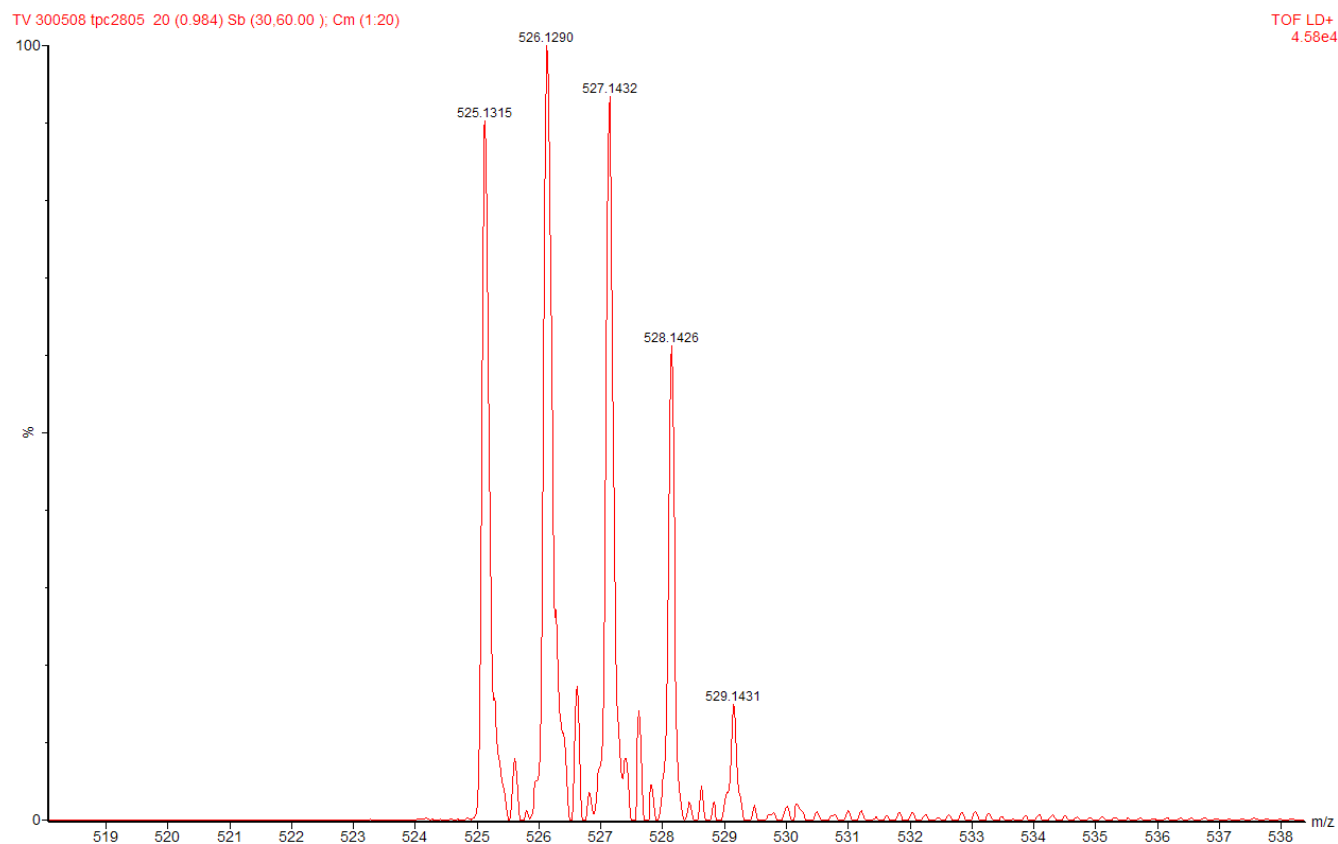
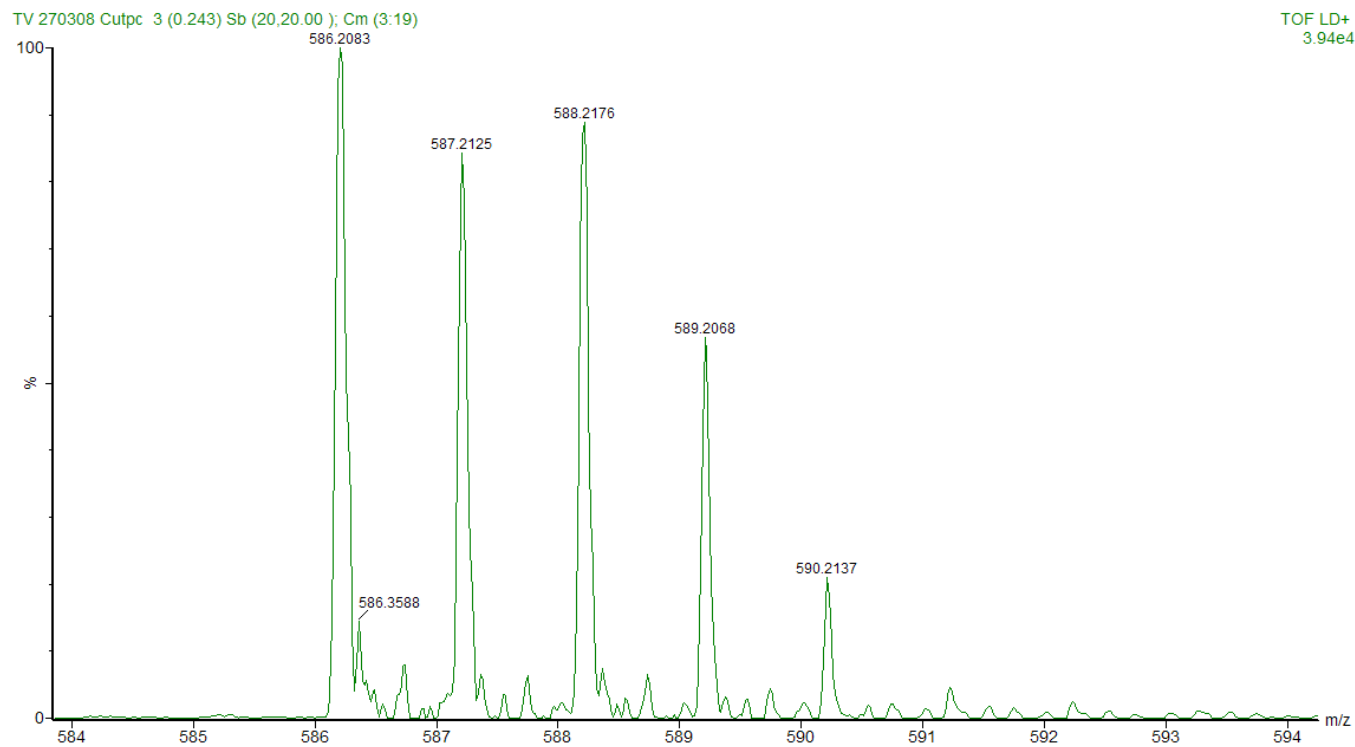
UV-visible spectra of studied copper corroles.



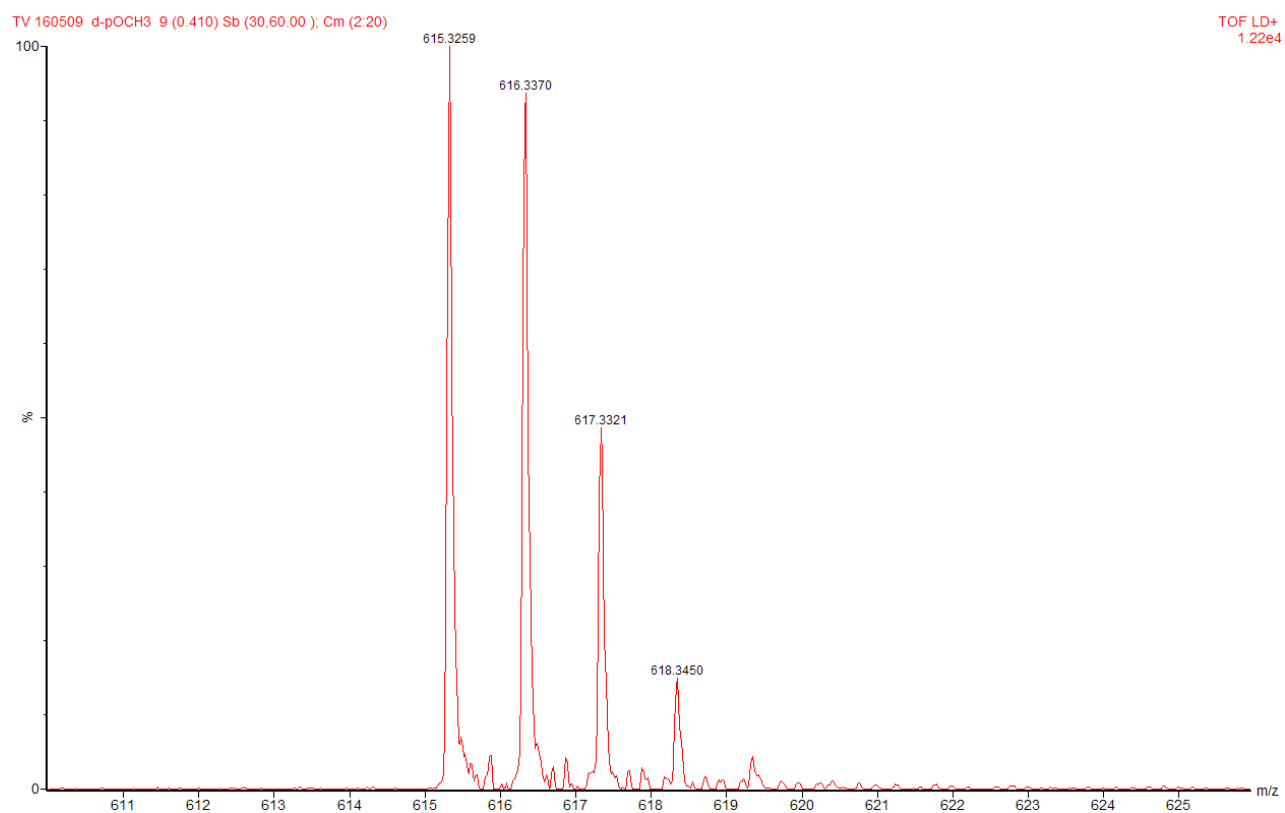
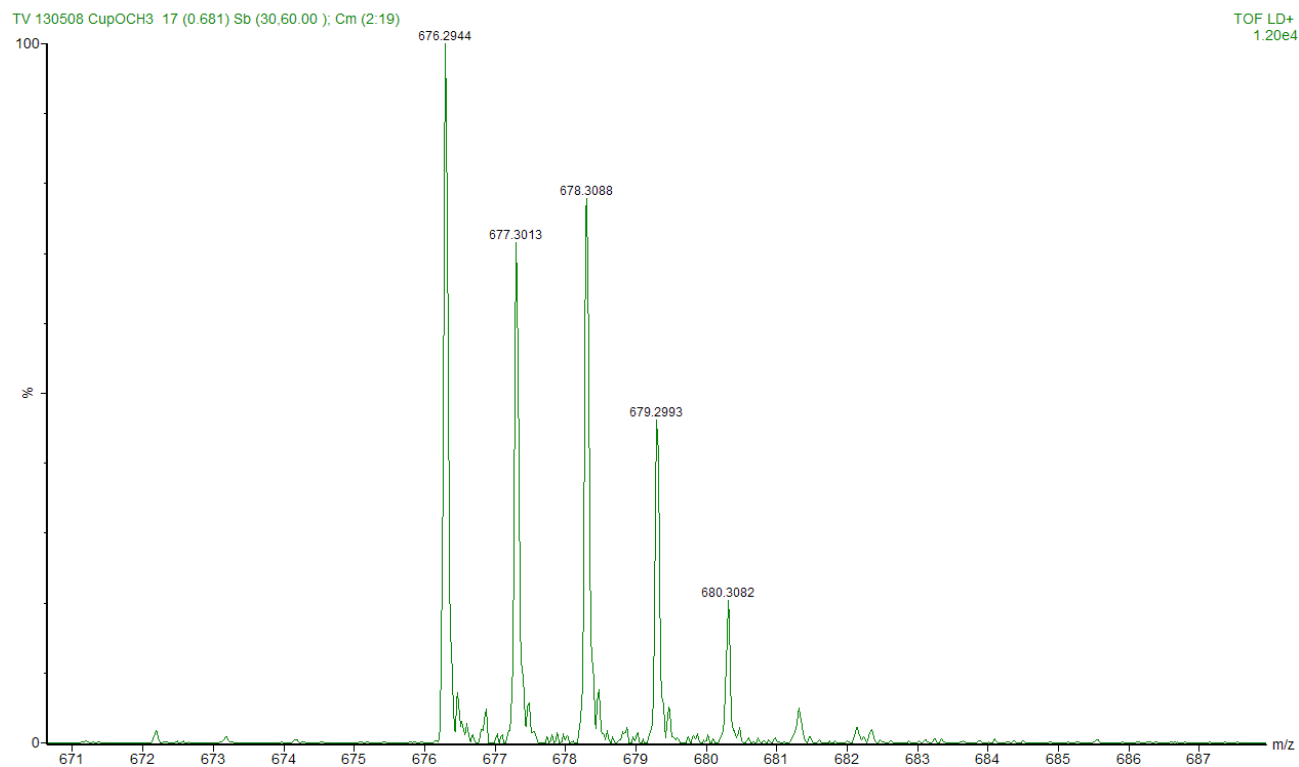


UV-visible spectra of demetalated free base corroles.

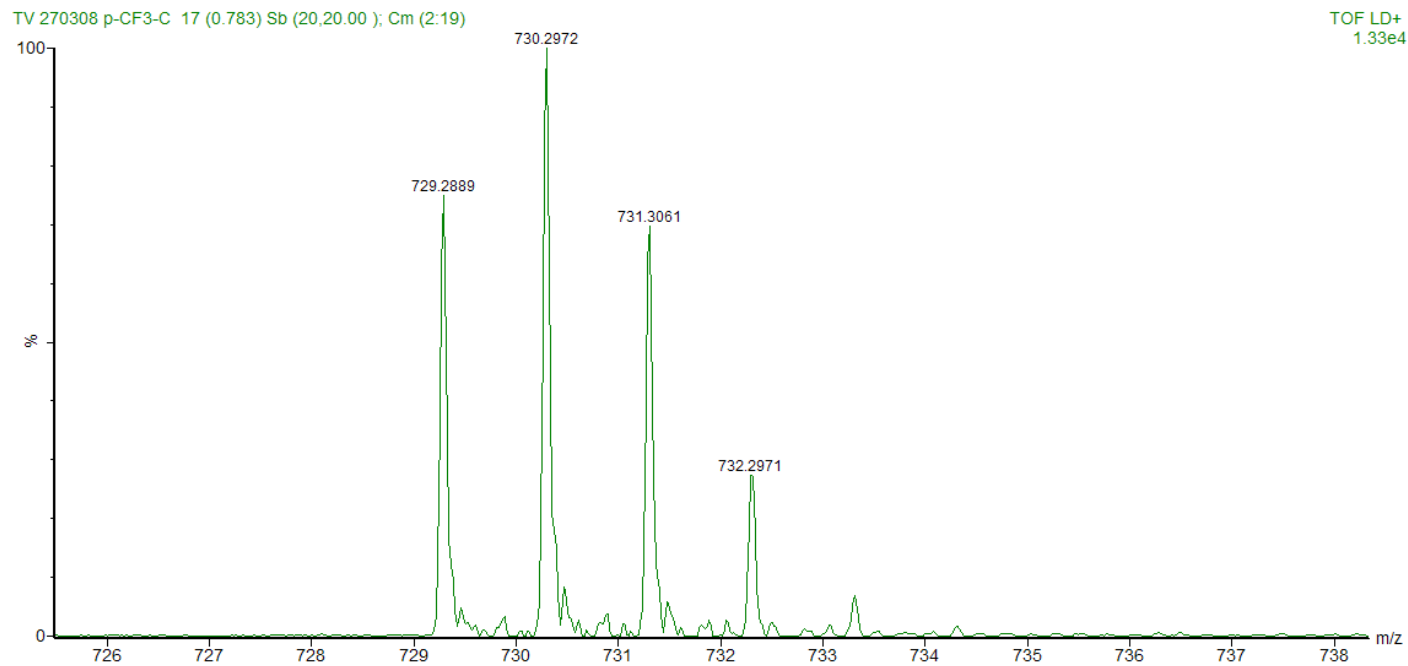
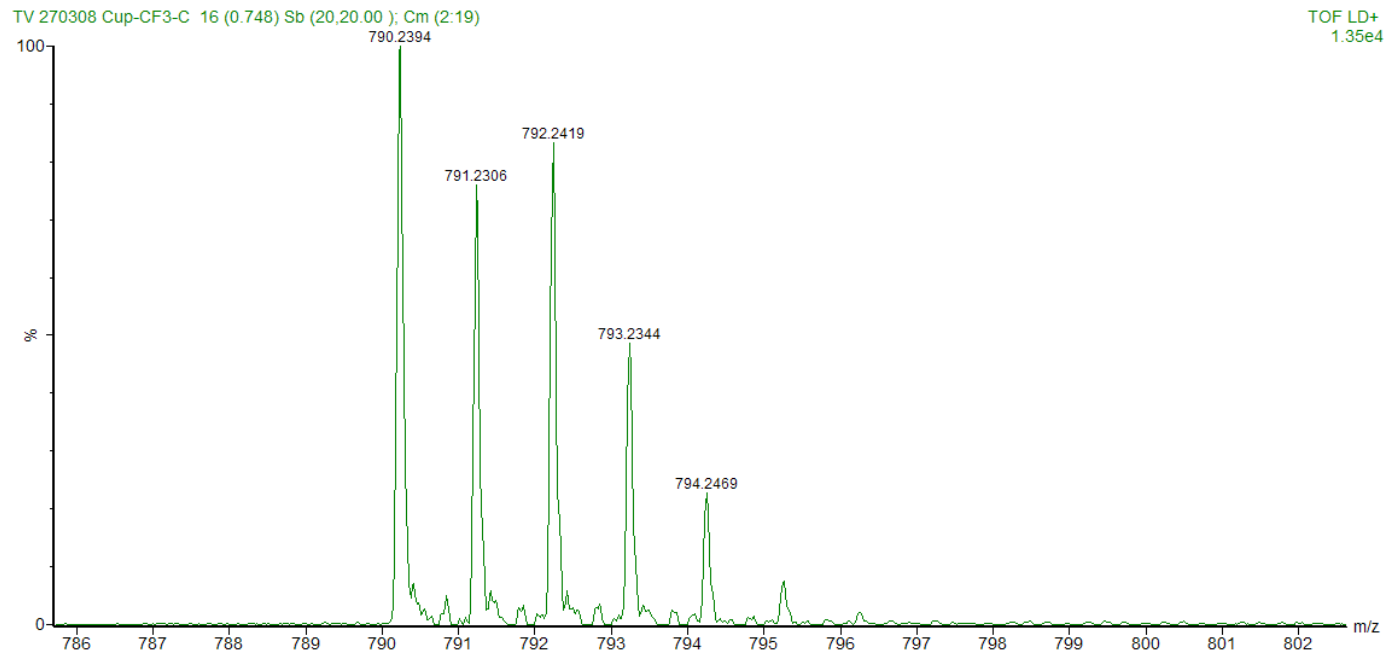




MALDI-TOF mass spectra of Cu[TPC] and it's demetalated free base corrole.



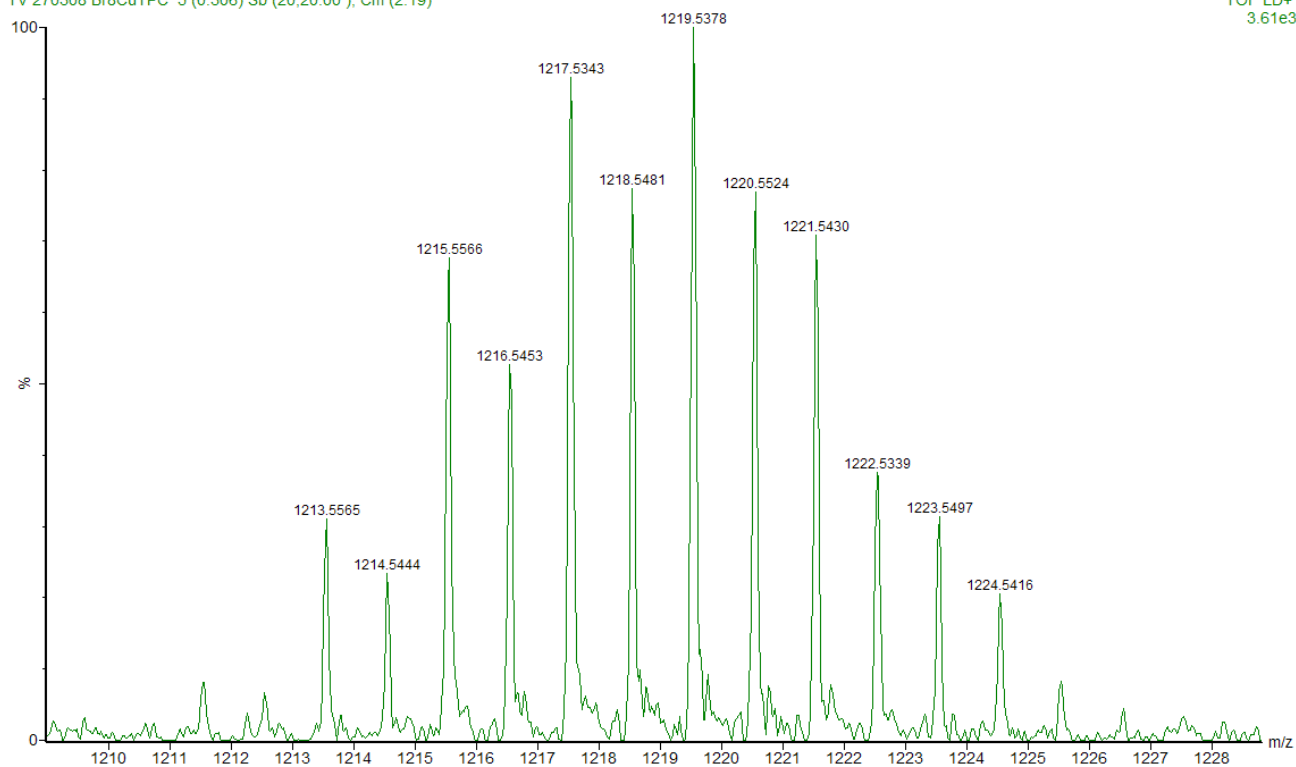
MALDI-TOF mass spectra of Cu[T(*p*-OMeP)C] and its demetalated free base corrole.



MALDI-TOF mass spectra of Cu[T(*p*-CF<sub>3</sub>P)C] and it's demetallated free base corrole.

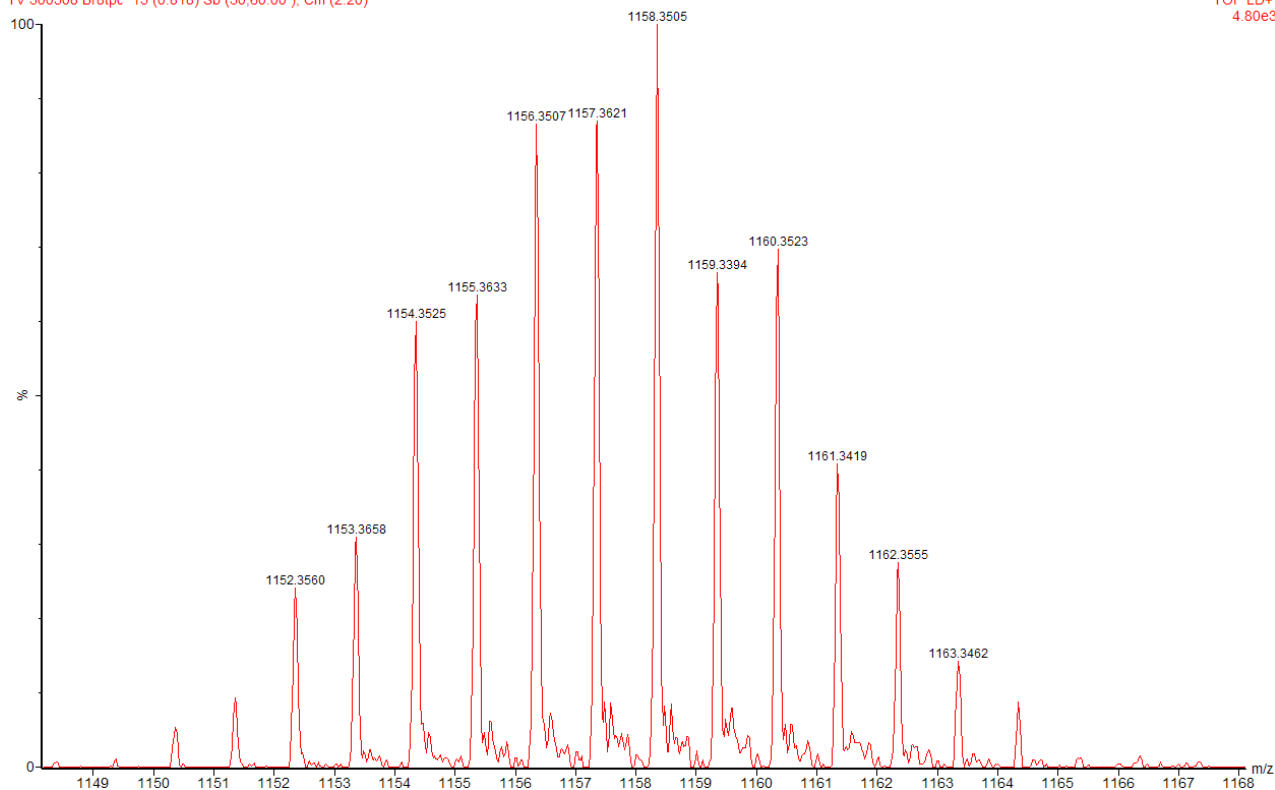
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TOF LD+  
3.61e3



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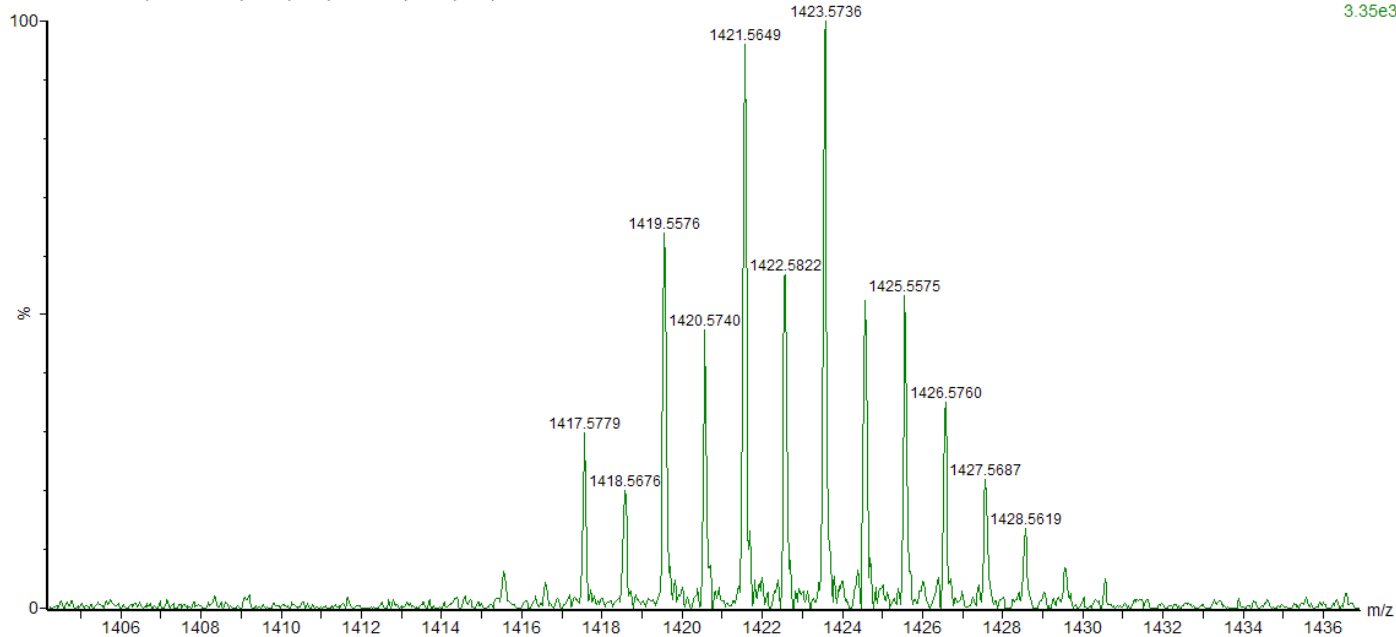
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4.80e3



MALDI-TOF mass spectra of Cu[Br<sub>8</sub>TPC] and it's demetallated free base corrole.

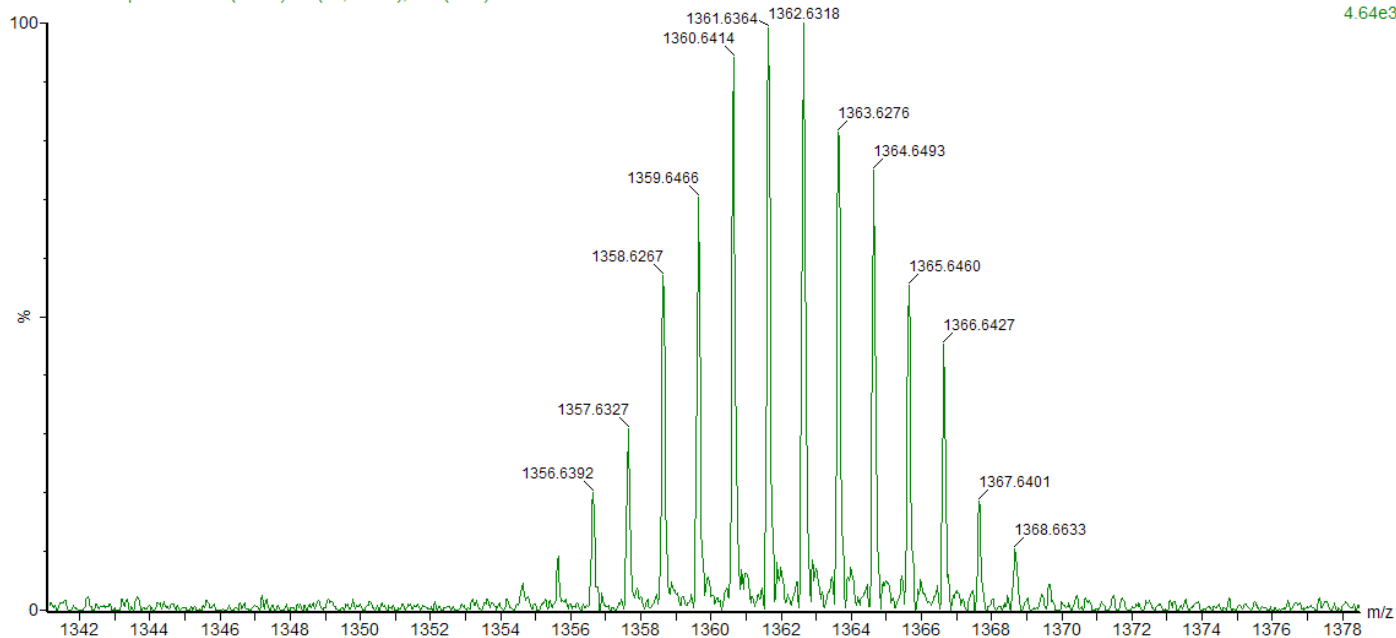
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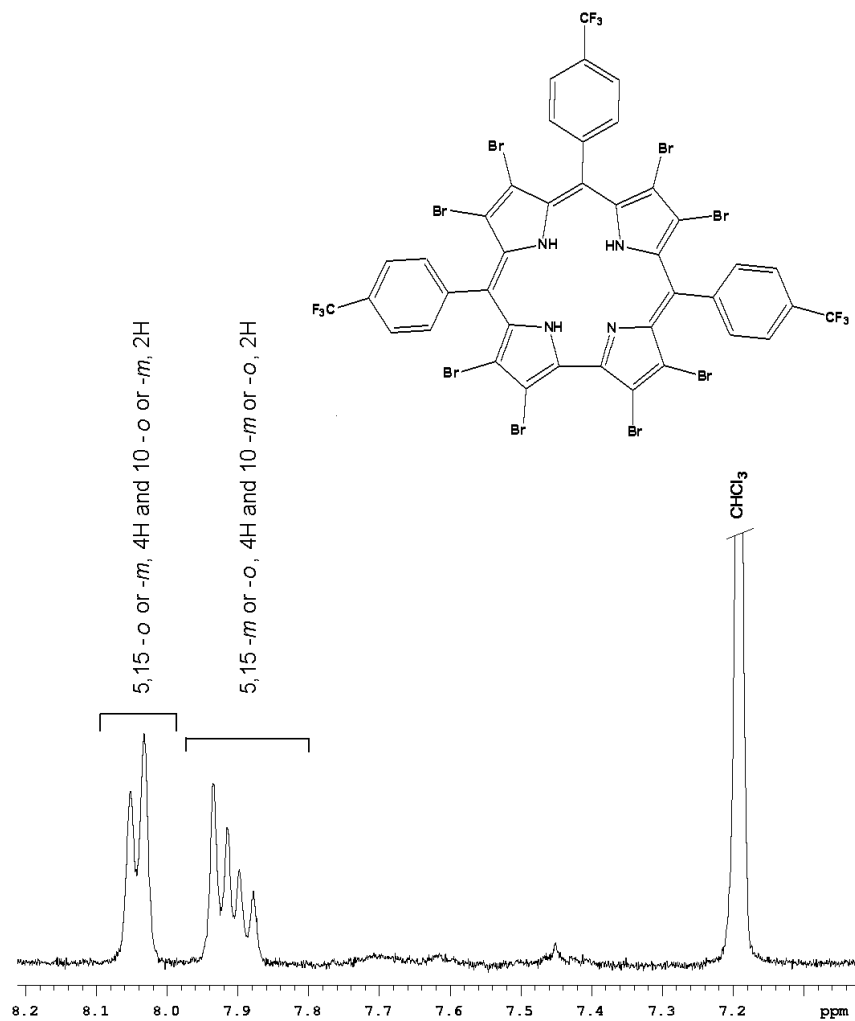


TV 270308 Br8p-CF3-C 15 (0.852) Sb (20,20.00) ; Cm (1:19)

TOF LD+  
4.64e3



MALDI-TOF mass spectra of  $\text{Cu}[\text{Br}_8\text{T}(p\text{-CF}_3\text{P})\text{C}]$  and its demetallated free base corrole.



$^1\text{H-NMR}$  spectra of  $\text{Cu}[\text{Br}_8\text{T}(p\text{-CF}_3\text{P})\text{C}]$

## REFERENCES

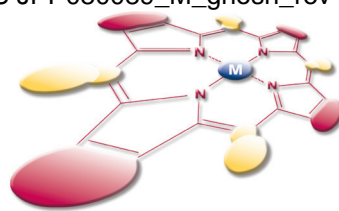
- <sup>1</sup> Johnson, A.W.; Kay, I.T. *J. Chem. Soc.* **1965**, 1620.
- <sup>2</sup> Johnson, A.W.; Price R. *J. Chem. Soc.* **1960**, 1649.
- <sup>3</sup> Johnson, A.W.; Kay, I.T.; Rodrigo R. *J. Chem. Soc.* **1963**, 2336.
- <sup>4</sup> Khan, A.G.; Easwaran, S.V. *Science* **1976** 196: 1410.
- <sup>5</sup> Martens, J.H.; Barg, H.; Warren, M.J.; Jahn, D. *Appl. Microbiol. Biotechnol.* **2002** 58: 275.
- <sup>6</sup> Paolesse, R.; Jaquinod, L.; Nurco, D.J.; Mini, S.; Sagone, F.; Boschi, T.; Smith, K. M. *Chem. Commun.* **1999**, 1307.
- <sup>7</sup> Gross, Z.; Galili, N.; Saltsman, I. *Angew. Chem., Int. Ed. Engl.* **1999**, 38, 1427.
- <sup>8</sup> Will, S.; Lex, J.; Vogel, E.; Schmickler, H.; Gisselbrecht, J.-P.; Hauptmann, C.; Bernard, M.; Gorss, M. *Angew. Chem.* **1997**, 109, 367; *Angew. Chem. Int. Ed. Engl.* **1997**, 36, 357.
- <sup>9</sup> Vogel, E.; Will, S.; Tilling, A.S.; Neumann, L.; Lex, J.; Bill, E.; Trautwein, A.X.; Wieghardt, K. *Angew. Chem.* **1994**, 106, 771; *Angew. Chem. Int. Ed. Engl.* **1994**, 33, 731.
- <sup>10</sup> Van Caemelbecke, E.; Will, S.; Autret, M.; Adamian, V.A.; Lex, J.; Gisselbrecht, J.P.; Gross, M.; Vogel, E.; Kadish, K. M., *Inorg. Chem.* **1996**, 35, 184.
- <sup>11</sup> Will, S.; Lex, J.; Vogel, E.; Adamian, V.A.; Van Caemelbecke, E.; Kadish, K. M. *Inorg. Chem.* **1996**, 35, 5577.
- <sup>12</sup> Meier-Callahan, A. E.; Di Bilio, A.J.; Simkhovich, L.; Mahammed, A.; Goldberg, I.; Gray, H.B.; Gross, Z. *Inorg. Chem.* **2001**, 40, 6788.
- <sup>13</sup> Aviezer, D.; Cotton, S.; David, M.; Segev, A.; Khaselev, N.; Galili, N.; Gross, Z.; Yayon, A. *Cancer Research* **2000**, 60, 2973.
- <sup>14</sup> Mahammed, A.; Gray, H.B.; Weaver, J.J.; Sorasaene, K.; Gross, Z. *Bioconj. Chem.* **2004**, 15, 738.
- <sup>15</sup> Bendix, J.; Dmochowski, I.J.; Gray, H.B.; Mahammed, A.; Simkhovich, L.; Gross, Z. *Angew. Chem. Int. Ed.* **2000**, 39, 4048.
- <sup>16</sup> Rose, E.; Kossanyi, A.; Quelquejeu, M.; Soleilhavoup, M.; Duwavran, F.; Bernard, N.; Lecas, A. *J. Am. Chem. Soc.* **1996**, 118, 1567.
- <sup>17</sup> Wasbotten, I.H.; Wondimagegn, T.; Ghosh, A. *J. Am. Chem. Soc.* **2002**, 124, 8104.
- <sup>18</sup> Ka, J.-W.; Cho, W.-S.; Lee, C.-H. *Tetrahedron Lett.* **2000**, 41, 8121.



- <sup>19</sup> Paollesse, R.; Marini, A.; Nardis, S.; Froiio, A.; Mandoj, F.; Nurco, D. J.; Prodi, L.; Montalti, M.; Smith, K. M. *J. Porphyrins Phthalocyanines* **2003**, *7*, 25.
- <sup>20</sup> Collman, J. P.; Decreau, R. A. *Tetrahedron Lett.* **2003**, *44*, 1207.
- <sup>21</sup> Gryko, D.T.; Koszarna, B. *Org. Biomol. Chem.* **1** **2003**, 350.
- <sup>22</sup> Koszarna, B.; Gryko, D.T. *J. Org. Chem.* **2006**, *71*, 3707.
- <sup>23</sup> Gryko, D.T. *Eur. J. Org. Chem.* **2002**, 1735.
- <sup>24</sup> Lee, C.-H.; Lindsey, J. S. *Tetrahedron* **1994**, *50*, 11427.
- <sup>25</sup> Littler, B.J.; Ciringh, Y.; Lindsey, J.S. *J. Org. Chem.* **1999**, *64*, 2864.
- <sup>26</sup> Brinas, R.P.; Brückner, C. *Synlett* **2001**, 442.
- <sup>27</sup> Asokan, C.V.; Smeets, S.; Dehaen, W. *Tetrahedron Lett.* **2001**, *42*, 4483.
- <sup>28</sup> Guillard, R.; Gros, C.P.; Bolze, F.; Jerome F.; Ou Z.; Shao, J.; Fischer J.; Weiss R.; Kadish K. M. *Inorg. Chem.* **2001**, *40*, 4845.
- <sup>29</sup> Guillard, R.; Jerome F.; Gros, C. P.; Barbe, J.-M.; Ou, Z.; Shao, J.; Fischer, J.; Weiss, R.; Kadish, K. M. *Inorg. Chem.* **2001**, *40*, 4856.
- <sup>30</sup> Steene, E.; Dey, A.; Ghosh, A. *J. Am. Chem. Soc.*, **2003**, *125*, 16300.
- <sup>31</sup> Paollesse, R.; Nardis, S.; Sagone, F.; Khoury, R.G. *J. Org. Chem.*, **2001**, *66*, 2, 550.
- <sup>32</sup> Dyke, J. M.; Hush, N.S.; Williams, M.L.; Woolsey, I. S. *Mol. Phys.* **1971**, *20*, 1149.
- <sup>33</sup> Ghosh, A.; Jynge, K. *Chem. Eur. J.* **1997**, *3*, 823.
- <sup>34</sup> Broadhurst, M.J.; Grigg, R.; Johnson, A.W.; Shelton G. *J. Chem. Soc., Perkin Trans. 1*, **1972**, 143.
- <sup>35</sup> Ghosh, A.; Wondimagegn, T.; Parusel, A. B. J. *J. Am. Chem. Soc.* **2000**, *122*, 5100.
- <sup>36</sup> Erben, C.; Will S.; Kadish, K. M. In the Porphyrin Handbook; Kadish, K. M.; Smith, K. M.; Guillard, R. eds.; Academic: New York, **2000**; Vol. 2, Chapter 12, p 233.
- <sup>37</sup> Luobeznova, I.; Simkhovich, L.; Goldberg, I.; Gross, Z. *Eur. J. Inorg. Chem.* **2004**, 1724.
- <sup>38</sup> Bröring, M.; Brégier, F.; Tejero, E. C.; Hell, C.; Holthausen, M. C. *Angew. Chem. Int. Ed.* **2007**, *46*, 445.
- <sup>39</sup> Brückner, C.; Brinas, R.P.; Krause-Bauer, J.A. *Inorg. Chem.* **2003**, *42*, 4495.
- <sup>40</sup> Guillard, R.; Gros, C.P.; Barbe, J.-M.; Espinosa, E.; Jérôme, F.; Tabard, A. *Inorg. Chem.* **2004**, *43*, 7441.
- <sup>41</sup> Kumar, R.K.; Balasubramanian, S.; Goldberg, I. *Inorg. Chem.* **1998**, *37*, 541.
- <sup>42</sup> Posner, Y.D.; Dahal, S.; Goldberg I. *Angew. Chem. Int. Ed.* **2000**, *39*, 1288.

- <sup>43</sup> Ruiz, R.; Surville-Barland, C.; Aukauloo, A. ; Anxolabehere-Mallart, E.; Journaux, Y. ; Cano, J.; Munoz, M.C. *J. Chem. Soc., Dalton Trans.* **1997**, 745.
- <sup>44</sup> Melnik, M.; Kabesova, M. *J. Coord. Chem.* **2000**, 50, 323.
- <sup>45</sup> Stokes, G.G. *J. Chem. Soc.*, **1864**, 17, 304.
- <sup>46</sup> Nencki, M., *Arch. Exptl. Path. Parmakol.* **1888**, 24, 430.
- <sup>47</sup> Willstätter, R.; Stoll, A., *Investigations on Chlorophyll*, Science Press, Lancaster, Ohio, **1928**.
- <sup>48</sup> Keilin, D., *Proc. R. Soc. London, B*, **1925**, 98, 312.
- <sup>49</sup> (a) Nitration: Catalano, M. M.; Crossley, M. J.; Harding, M. M.; King, L.G. *J. Chem. Soc. Chem. Commun.* **1984**, 1535. (b) Chlorination: Wijesekera, T.; Dupre, D.; Cader, M.S.R.; Dolphin, D. *Bull. Soc. Chim. Fr.* **1996**, 133, 765. (c) Formylation: Buchler, J.W.; Dreher, C.; Herget, G. *Liebigs Ann. Chem.* **1988**, 43.
- <sup>50</sup> Brückner, C.; Dolphin, D. *Tetrahedron Lett.* **1995**, 36, 9425.
- <sup>51</sup> Wondimagegn, T.; Ghosh, A. *J. Phys. Chem. B* **2000**, 104, 10858.
- <sup>52</sup> Cowan, J.A.; Sanders, J.R.M. *Tetrahedron Letters*, **1986**, 27, 10, 1201.
- <sup>53</sup> Bröring M.; Hell, C. *Chem. Commun.* **2001**, 2336.
- <sup>54</sup> Brückner, C.; Barta, C.A.; Brinas, R.P.; Bauer A.K. *Inorg. Chem.* **2003**, 42, 1673.
- <sup>55</sup> Mandoj, F.; Nardis, S.; Pomarico, G.; Paolesse, R. *J Porphyrins Phthalocyanines*, **2008**, 12, 19.
- <sup>56</sup> Nardis, S.; Pomarico, G.; Fronczek, F.R.; Vicente, M.G.V.; Paolesse, R. *Tetrahedron Lett.* **2007**, 48, 8643.

# CONTENTS

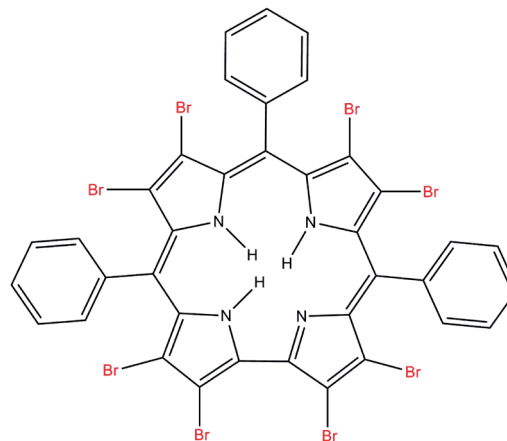


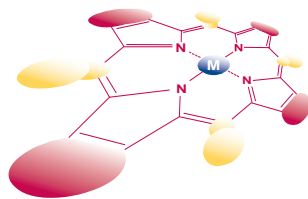
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## Reductive demetalation of copper corroles: first simple route to free-base $\beta$ -octabromocorroles

Can Capar, Kolle Ekane Thomas and Abhik Ghosh\*

Reductive demetalation with  $\text{H}_2\text{SO}_4$  and  $\text{FeCl}_2/\text{SnCl}_2$  provides a superior method of demetalating copper corroles, relative to  $\text{H}_2\text{SO}_4$  alone. The reductive method affords convenient access to free-base  $\beta$ -octabromo-*meso*-triarylcorroles, which have otherwise proved relatively inaccessible.





# Reductive demetalation of copper corroles: first simple route to free-base $\beta$ -octabromocorroles

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**ABSTRACT:** Although the chemistry of corroles has grown spectacularly in recent years, the field has been marred by the lack of convenient protocols for demetalation of metallocorroles. Reported herein is a superior procedure for demetalating copper corroles with concentrated  $\text{H}_2\text{SO}_4$  and 5-200 equiv  $\text{FeCl}_2$  or  $\text{SnCl}_2$ . The yields obtained with this reductive procedure are generally substantially better than with  $\text{CHCl}_3/\text{H}_2\text{SO}_4$ ,  $\text{CH}_2\text{Cl}_2/\text{H}_2\text{SO}_4$ , or  $\text{H}_2\text{SO}_4$  alone. With an oxidation-prone metallocorrole such as  $\text{Cu}[\text{T}(p\text{-OMeP})\text{C}]$ , the reductive protocol was essential for obtaining any measurable yield of the free base at all. Free-base  $\beta$ -octabromo-*meso*-triarylcorroles were also obtained in pure form, in good yields, and with relative ease *via* this procedure. Copyright © 2008 Society of Porphyrins & Phthalocyanines.

**KEYWORDS:** demetalation, corrole, octabromocorrole.

## INTRODUCTION

Ever since the development of convenient one-pot syntheses of corroles a few years ago [1, 2], their chemistry has blossomed in the most extraordinary manner [3, 4]. Indeed, both the coordination chemistry and range of applications of corroles promise to be just as diverse as those of porphyrins. Unfortunately, the field has been marred by a crucial irritant: unlike metalloporphyrins, for which a host of demetalation procedures are available [5], no such broadly applicable procedure has been available for corroles. Thus, until most recently, just two isolated instances of demetalation of a corrole were documented, one of  $\text{Mn}[\text{OEC}]$  [ $\text{Mn}(\text{III})$  octaethylcorrole] with  $\text{HBr}/\text{HOAc}$  [6] and the other of  $\text{Ag}(\text{III})$  triarylcorroles with aqueous  $\text{HCl}$  in a biphasic medium [7]. Earlier this year, while this paper was in preparation, Paolesse and coworkers reported a considerably more general method for corrole demetalation, involving  $\text{CHCl}_3/\text{H}_2\text{SO}_4$  [8]. In our own studies, we also found concen-

trated  $\text{H}_2\text{SO}_4$  to be the acid of choice, with, however, a crucial twist: concentrated  $\text{H}_2\text{SO}_4$  with several equivalents of  $\text{FeCl}_2$  or  $\text{SnCl}_2$  (relative to the metallocorrole) resulted in dramatically better yields of free-base corrole, fewer impurities and somewhat shorter reaction times, compared to  $\text{H}_2\text{SO}_4$  alone.

## RESULTS AND DISCUSSION

Just as  $\text{Ni}(\text{II})$ ,  $\text{Cu}(\text{II})$ , and  $\text{Zn}(\text{II})$  porphyrins are most often used for porphyrin functionalization,  $\text{Cu}(\text{III})$  corroles play a similar role in corrole chemistry. As stable, diamagnetic species that are readily characterized (although a number of them exhibit thermally accessible, paramagnetic  $\text{Cu}(\text{II})$  corrole $^{*2}$ -excited states) [9],  $\text{Cu}$  corroles are ideally suited for peripheral functionalization and subsequent elaboration of the corrole macrocycle [10]. We therefore chose to focus our efforts on copper corroles in this study.

Table 1 presents our experimental results for six copper corroles, including three  $\text{Cu}$  triarylcorroles as well as their  $\beta$ -octabromo derivatives [10]. As shown, neat concentrated  $\text{H}_2\text{SO}_4$  gave useful,

$\diamond$ SPP full member in good standing

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if rather low, yields for only a couple of the most electron-deficient copper corroles. Adding a solvent such as  $\text{CHCl}_3$  or  $\text{CH}_2\text{Cl}_2$  (the best conditions being about 20:1 v/v solvent: $\text{H}_2\text{SO}_4$ ) improved matters in certain cases, resulting in useful yields for the corroles in question. With two exceptions,  $\text{Cu}[\text{TPC}]$  (copper triphenylcorrole) and  $\text{Cu}[\text{Br}_8\text{TPC}]$ , the complexes studied by us and Paolesse and coworkers are not the same, so an exact comparison is not possible. However, for  $\text{Cu}[\text{TPC}]$ , we failed to reproduce the high yield of free-base corrole (83%), reported by Paolesse and coworkers [8]. The  $\text{H}_2\text{SO}_4$ /solvent procedure also led to a rather intractable, impure product for  $\text{Cu}[\text{Br}_8\text{TPC}]$ .

Addition of several equivalents of  $\text{FeCl}_2$  or  $\text{SnCl}_2$  resulted in dramatic improvement in the demetalation yield for all the complexes studied. Thus, a yield of about 70% could be reliably obtained in nearly all cases. The importance of this finding for the entire corrole field can hardly be exaggerated. A wide variety of functionalized corroles that until now could only be obtained in metal-complexed form should now be available as free bases for re-complexation and further synthetic elaboration. Indeed, the present  $\text{H}_2\text{SO}_4/\text{FeCl}_2$  or  $\text{H}_2\text{SO}_4/\text{SnCl}_2$  method already provides the first simple, reasonably general route to free-base  $\beta$ -octabromo-*meso*-triarylcorroles.

The exact conditions that proved most effective for the different copper corroles studied suggests that the  $\text{FeCl}_2$  plays multiple roles in the demetalation process. Almost certainly, the first role of the  $\text{FeCl}_2$  is as a reductant; it reduces the small  $\text{Cu}(\text{III})$  ion to the larger, much more easily displaced  $\text{Cu}(\text{II})$  ion. However, the fact that vastly different amounts of  $\text{FeCl}_2$  or  $\text{SnCl}_2$  – from 5 to 200 equiv – are needed for different copper corroles suggests that a second factor must be involved. As may be seen from a perusal of the Experimental section, relatively electron-rich copper corroles required large quantities (100-200 equiv) of  $\text{FeCl}_2$  or  $\text{SnCl}_2$ , whereas the more electron-deficient copper corroles needed only a few equivalents of  $\text{FeCl}_2$ . A plausible explanation for this difference is that the excess  $\text{FeCl}_2$  or  $\text{SnCl}_2$  protects

the more easily oxidized free-base corroles from oxidative breakdown under the demetalation procedure.

## EXPERIMENTAL

### Materials

All reagents and solvents were used as purchased, except pyrrole, which was predried and distilled from  $\text{CaH}_2$  at low pressure. Silica gel 60 (0.040-0.063 mm particle size; 230-400 mesh; Merck) was used for flash chromatography.

### Instrumentation

Ultraviolet-visible spectra were recorded on an HP 8453 spectrophotometer using dichloromethane as solvent. Proton NMR spectra were recorded on a Mercury Plus Varian spectrometer (400 MHz for  $^1\text{H}$ ) at room temperature in chloroform-*d*. Proton chemical shifts ( $\delta$ ) in ppm were referenced to residual chloroform ( $\delta = 7.2$  ppm). MALDI-TOF mass spectra were recorded on a Waters Micromass MALDI micro MX Mass Spectrometer using  $\alpha$ -cyano-4-hydroxycinnamic acid (CHCA) as the matrix. Satisfactory elemental analyses were obtained in each case from Atlantic Microlabs, Inc.

### Synthesis of corrole starting materials

Free-base corroles were synthesized according to Gryko and coworkers [1c]. Copper triarylcorroles and their  $\beta$ -octabromo derivatives were synthesized, as described by Ghosh and coworkers [10].

### General procedure for the demetalation of copper corroles

Into a 25 mL or 50 mL round-bottomed flask equipped with a magnetic stirrer, copper corrole (10 mg) and anhydrous  $\text{FeCl}_2$  (Sigma-Aldrich) or  $\text{SnCl}_2$  (Alfa-Aesar) (5-200 equiv) were introduced. Con-

**Table 1.** Comparison of demetalation yields (%) under different reaction conditions

Complex	$\text{H}_2\text{SO}_4, \text{CHCl}_3$	$\text{H}_2\text{SO}_4, \text{CH}_2\text{Cl}_2$	$\text{H}_2\text{SO}_4$ only	$\text{H}_2\text{SO}_4 + \text{FeCl}_2$	$\text{H}_2\text{SO}_4 + \text{SnCl}_2$
$\text{Cu}[\text{TPC}]$	18	18	-	68	77
$\text{Cu}[\text{T}(p\text{-OMeP})\text{C}]$	-	-	-	75	77
$\text{Cu}[\text{T}(p\text{-CF}_3\text{P})\text{C}]$	not attempted	26	37	74	inseparable mixture
$\text{Cu}[\text{Br}_8\text{TPC}]$	inseparable impurities	inseparable impurities	inseparable impurities	79	inseparable mixture
$\text{Cu}[\text{Br}_8\text{T}(p\text{-OMeP})\text{C}]$	35	79	-	81	85
$\text{Cu}[\text{Br}_8\text{T}(p\text{-CF}_3\text{P})\text{C}]$	10	22	33	82	85

centrated  $\text{H}_2\text{SO}_4$  (95-97%, Merck, 0.8-2.0 mL) was added dropwise and the reaction mixture was alternately stirred/swirled and sonicated for 2 min to 1 h, depending on the particular copper corrole. The progress of the reaction, as measured by the disappearance of the copper corrole, was monitored by UV-vis spectroscopy and by TLC. After apparent consumption of the copper corrole, the reaction mixture was quenched with distilled  $\text{H}_2\text{O}$  and then extracted with  $\text{CHCl}_3$ . The green organic phase was repeatedly washed with distilled water and then twice with saturated aqueous  $\text{NaHCO}_3$ . The organic phase was then dried with anhydrous  $\text{Na}_2\text{SO}_4$ , filtered, mixed with about 0.5 g silica and evaporated under vacuum. The residue thus obtained was chromatographed on a silica gel column with *n*-hexane/ $\text{CH}_2\text{Cl}_2$  as eluent to give the free-base corrole as the second or third band (small quantities of unreacted copper corrole was usually the first band). Spectroscopic data for free-base and copper triphenylcorrole, *meso*-tris(4-methoxyphenyl)corrole, *meso*-tris(4-trifluoromethylphenyl)corrole,  $\beta$ -octabromo-*meso*-triphenylcorrole were in agreement with those reported previously [10]. Additional details for each demetalation experiment are provided below.

**Demetalation of copper 5,10,15-triphenylcorrole.** Into a 25 mL round-bottomed flask containing the corrole (10 mg) and  $\text{FeCl}_2$  (200 equiv), concentrated  $\text{H}_2\text{SO}_4$  (0.8 mL) was added dropwise, with stirring. The resulting suspension was stirred for 3 min. After work-up of the reaction mixture (as described above), the green residue obtained was chromatographed on a silica gel column, first with 7:3 *n*-hexane/ $\text{CH}_2\text{Cl}_2$  to elute unreacted  $\text{Cu}[\text{TPC}]$  (1.4 mg) as the first band and then with 2:3 *n*-hexane/ $\text{CH}_2\text{Cl}_2$  to elute free-base *meso*-triphenylcorrole (6.1 mg). Yield: 68%. UV-vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$ , nm (log  $\epsilon$ ,  $\text{M}^{-1}\cdot\text{cm}^{-1}$ ) 417 (5.13), 578 (4.20), 620 (4.11), 651 (4.08). MS (MALDI-TOF, major isotopomer):  $m/z$   $[\text{M}]^+$  526.13 (expt.), 526.21 (calcd.). For the  $\text{SnCl}_2/\text{H}_2\text{SO}_4$  demetalation, the corrole (10 mg),  $\text{SnCl}_2$  (100 equiv) and  $\text{H}_2\text{SO}_4$  (1 mL) were stirred and sonicated, alternately, for 5 min. After work-up and purification,  $\text{Cu}[\text{TPC}]$  (1.2 mg) and  $\text{H}_3[\text{TPC}]$  (6.9 mg) were obtained. Yield of  $\text{H}_3[\text{TPC}]$ : 77%.

**Demetalation of copper 5,10,15-tris(4-methoxyphenyl)corrole.** The reaction conditions and reaction time were exactly as in the above case. The green residue obtained at the end of the work-up phase was chromatographed on silica gel with 2:3 *n*-hexane/ $\text{CH}_2\text{Cl}_2$  to afford the free-base *meso*-tris(4-methoxyphenyl)corrole. Yield: 75%. UV-vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$ , nm (log  $\epsilon$ ,  $\text{M}^{-1}\cdot\text{cm}^{-1}$ ) 419 (4.52), 577 (3.63), 624 (3.61), 655 (3.58). MS (MALDI-TOF, major isotopomer):  $m/z$   $[\text{M}]^+$  616.33 (expt.), 616.24 (calcd.). The  $\text{SnCl}_2/\text{H}_2\text{SO}_4$  demetalation was performed exactly as with  $\text{FeCl}_2/\text{H}_2\text{SO}_4$ . After work-up and purification,

the yield of the free-base was 77%.

**Demetalation of copper 5,10,15-tris(4-trifluoromethylphenyl)corrole.** To the copper corrole (10 mg) and  $\text{FeCl}_2$  (5 equiv) in a 50 mL round-bottomed flask, concentrated  $\text{H}_2\text{SO}_4$  (2.0 mL) was added. The suspension was stirred for 1 h. After work-up of the reaction mixture, the green residue obtained was chromatographed on silica gel with 2:1 *n*-hexane/ $\text{CH}_2\text{Cl}_2$  to afford free-base *meso*-tris(4-trifluoromethylphenyl)corrole. Yield: 69%. UV-vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$ , nm (log  $\epsilon$ ,  $\text{M}^{-1}\cdot\text{cm}^{-1}$ ) 418 (4.63), 580 (3.84), 617 (3.71), 647 (3.61). MS (MALDI-TOF, major isotopomer):  $m/z$   $[\text{M}]^+$  730.30 (expt.), 730.18 (calcd.). On a larger scale, the copper complex (60 mg),  $\text{FeCl}_2$  (5 equiv) and concentrated  $\text{H}_2\text{SO}_4$  (3 mL) were introduced in that order into a 50 mL round-bottomed flask. The mixture was stirred and sonicated alternately for 1 h. Work-up and purification as described above gave 41 mg (74%) of the free-base. The  $\text{SnCl}_2/\text{H}_2\text{SO}_4$  demetalation was performed exactly as with  $\text{FeCl}_2/\text{H}_2\text{SO}_4$ . After work-up and purification, however, an inseparable mixture of compounds was obtained.

**Demetalation of copper  $\beta$ -octabromo-*meso*-triphenylcorrole.** To the copper corrole (10 mg) and  $\text{FeCl}_2$  (5 equiv) in a 50 mL round-bottomed flask, concentrated  $\text{H}_2\text{SO}_4$  (1.0 mL) was added in a dropwise manner. The suspension was sonicated and stirred alternately for 50 min. After work-up, the green residue obtained was chromatographed on silica gel with 1:1 *n*-hexane/ $\text{CH}_2\text{Cl}_2$ . Unreacted copper corrole was obtained as the first band. The eluent was then changed to neat  $\text{CH}_2\text{Cl}_2$  or  $\text{CHCl}_3$  to yield free-base  $\beta$ -octabromo-*meso*-triphenylcorrole as the last band. After solvent removal, the green product was crystallized from 1:1  $\text{CHCl}_3/n$ -hexane to afford 5.3 mg of the pure free base. Yield: 55%. UV-vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$ , nm (log  $\epsilon$ ,  $\text{M}^{-1}\cdot\text{cm}^{-1}$ ) 444 (4.84), 553 (3.80), 593 (3.85), 703 (3.88). MS (MALDI-TOF, major isotopomer):  $m/z$   $[\text{M} + \text{H}]^+$  1158.76 (expt.), 1158.49 (calcd.). On a larger scale, the copper complex (64 mg),  $\text{FeCl}_2$  (5 equiv) and concentrated  $\text{H}_2\text{SO}_4$  (2 mL) were introduced in that order into a 50 mL round-bottomed flask. The mixture was stirred and sonicated alternately for 2 h. Work-up and purification as described above gave 48 mg (79%) of the free base. The  $\text{SnCl}_2/\text{H}_2\text{SO}_4$  demetalation was performed exactly as with  $\text{FeCl}_2/\text{H}_2\text{SO}_4$ . However, work-up and attempted purification led only to an inseparable mixture of compounds.

**Demetalation of copper  $\beta$ -octabromo-*meso*-tris(4-methoxyphenyl)corrole.** To the copper corrole (10 mg) and  $\text{FeCl}_2$  (100 equiv) in a 50 mL round-bottomed flask, concentrated  $\text{H}_2\text{SO}_4$  (1.0 mL) was added in a dropwise manner. The suspension was sonicated and stirred alternately for 20 min. After work-up of the reaction mixture, the green residue obtained was

chromatographed on silica gel with 2:3 *n*-hexane/CH<sub>2</sub>Cl<sub>2</sub>, yielding the green free-base  $\beta$ -octabromo-*meso*-tris(4-methoxyphenyl)corrole (7.7 mg). Yield: 81%. UV-vis (CH<sub>2</sub>Cl<sub>2</sub>):  $\lambda_{\max}$ , nm (log  $\epsilon$ , M<sup>-1</sup>.cm<sup>-1</sup>) 450 (4.41), 601(3.55), 715 (3.72). <sup>1</sup>H NMR:  $\delta$ , ppm 7.85-7.75 (4H, 5,15- *o* or *m* and 2H, 10-*o* or *m*, Ph; overlapping doublets); 7.25-7.10 (4H, 5,15- *m* or *o* and 2H, 10- *m* or *o*, Ph); 3.99 (s, 6H, 5,15-*p*-OCH<sub>3</sub>, Ph); 3.98 (s, 3H, 10- *p*-OCH<sub>3</sub>, Ph). MS (MALDI-TOF, major isotopomer): *m/z* [M + H]<sup>+</sup> 1248.76 (expt.), 1248.53 (calcd.). Elemental analysis: 38.50% C (38.30% calcd.), 1.94% H (calcd. 1.88%), 4.49% N (calcd. 4.43%). For the SnCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub> demetalation, the corrole (10mg), SnCl<sub>2</sub> (100 equiv) and H<sub>2</sub>SO<sub>4</sub> (1 mL) were stirred and sonicated alternately for 20 min. After work-up and purification, 8.2 mg of the free base was obtained. Yield: 85%.

**Demetalation of copper  $\beta$ -octabromo-*meso*-tris(4-trifluoromethylphenyl)corrole.** To the copper corrole (10 mg) and FeCl<sub>2</sub> (5 equiv) in a 50 mL round-bottomed flask, concentrated H<sub>2</sub>SO<sub>4</sub> (2.0 mL) was added dropwise. The mixture was stirred and sonicated alternately for 1 h. After work-up of the reaction mixture, the green residue obtained was chromatographed on silica gel with 3:2 *n*-hexane/CH<sub>2</sub>Cl<sub>2</sub> to give green free-base  $\beta$ -octabromo-*meso*-tris(4-trifluoromethylphenyl)corrole. Yield: 82%. UV-vis (CH<sub>2</sub>Cl<sub>2</sub>):  $\lambda_{\max}$ , nm (log  $\epsilon$ , M<sup>-1</sup>.cm<sup>-1</sup>) 447 (4.86), 597(5.04), 697 (3.97). <sup>1</sup>H NMR:  $\delta$  8.08-8.00 (4H, 5,15- *o* or *m* and 2H, 10-*o* or *m*, Ph); 7.96-7.86 (4H, 5,15- *m* or *o* and 2H, 10- *m* or *o*, Ph). MS (MALDI-TOF, major isotopomer): *m/z* [M]<sup>+</sup> 1361.63 (expt.), 1361.45 (calcd.). Demetalation with SnCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub> was performed exactly as with FeCl<sub>2</sub>/H<sub>2</sub>SO<sub>4</sub>. After work-up and purification, the yield of the free base was 85%.

## CONCLUSION

In summary, reducing conditions, as afforded by an excess of FeCl<sub>2</sub>, in concert with concentrated H<sub>2</sub>SO<sub>4</sub>, provide a reasonably general and convenient method for the demetalation of copper corroles. The added FeCl<sub>2</sub> results in sharp increases in the yield of the free base corrole as well as in fewer impurities, relative to H<sub>2</sub>SO<sub>4</sub> alone. Thanks to the new method, free-base  $\beta$ -octabromo-*meso*-triarylcorroles, otherwise rather inaccessible, are now obtainable with comparative ease.

## Supporting information

Details of analytical data (10 pages) are given in the supplementary material. This material is available at <http://www.u-bourgogne.fr/jpp/>.

## REFERENCES

1. a) Gross Z, Galili N and Saltsman I. *Angew. Chem. Int. Ed.* 1999; **38**: 1427-1429. b) Paolesse R, Jaquinod L, Nurco DJ, Mini S, Sagone F, Boschi T and Smith K. M. *Chem. Comm.* 1999; 1307-1308. c) Koszarna B and Gryko DT. *J. Org. Chem.* 2006; **71**: 3707-3717.
2. Reviews: a) Ghosh A. *Angew. Chem., Int. Ed.* 2004; **43**: 1918-1931. b) Gryko DT. *Eur. J. Inorg. Chem.* 2002; 1735-1743.
3. Gross Z and Gray HB. *Comments Inorg. Chem.* 2006; **27**: 61-72.
4. Aviv I and Gross Z. *Chem. Comm.* 2007; 1987-1999.
5. Fuhrhop J-H and Smith KM. In *Porphyrins and Metalloporphyrins* Smith KM. (Ed.) Elsevier: Amsterdam, 1975; pp 757-910.
6. Bröring M and Hell C. *Chem. Comm.* 2001; 2336-2337.
7. Brückner C, Barta CA, Brinas RP and Bauer AK. *Inorg. Chem.* 2003; **42**: 1673-1680.
8. Mandoj F, Nardis S, Pomarico G and Paolesse R. *J. Porphyrins Phthalocyanines* 2008; **12**: 19-26.
9. Selected references on copper corroles: a) Steene E, Dey A and Ghosh A. *J. Am. Chem. Soc.* 2003; **125**: 16300-16309. b) Ou Z, Shao J, Zhao H, Ohkubo K and Wasbotten IH, Fukuzumi S, Ghosh A and Kadish KM. *J. Porphyrins Phthalocyanines* 2004, **8**: 1236-1247. c) Brückner C, Brinas RP and Bauer JAK. *Inorg. Chem.* 2003, **42**: 4495-4497. d) Luobeznova I, Simkhovich L, Goldberg I and Gross Z. *Eur. J. Inorg. Chem.* 2004, **8**: 1724-1732.
10. Wasbotten IH, Wondimagegn T and Ghosh A. *J. Am. Chem. Soc.* 2002; **124**: 8104-8116.