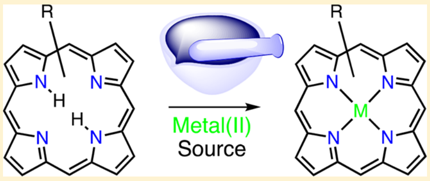
Inorganic Chemistry
Article
Cite This: Inorg. Chem. XXXX, XXX, XXX−XXX
pubs.acs.org/IC

Observations on the Mechanochemical Insertion of Zinc(II), Copper(II), Magnesium(II), and Select Other Metal(II) Ions into Porphyrins

Adewole O. Atoyebi and Christian Brückner*

Department of Chemistry, University of Connecticut, Unit 3060, Storrs, Connecticut 06269-3060, United States

Supporting Information



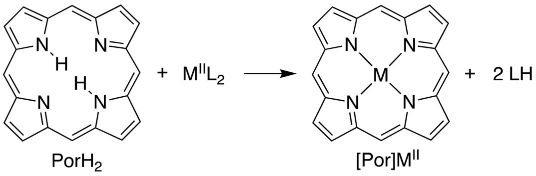
ABSTRACT: Building on a proof of concept study that showed the possibility of the mechanochemical insertion of some M(II) metals into *meso*-tetraphenylporphyrin using a ball mill as an alternative to traditional solution-based methods, we present here a detailed study of the influence of the many experimental variables on the reaction outcome performed in a planetary mill. Using primarily the mechanochemical zinc, copper, and magnesium insertion reactions, the scope and limits of the type of porphyrins (electron-rich or electron-poor *meso*-tetraarylporphyrins, synthetic or naturally occurring octaalkylporphyrins, and *meso*-triphenylcorrole) and metal ion sources suitable for this metal insertion modality were determined. We demonstrate the influence of the experimental metal insertion parameters, such as ball mill speed and reaction time, and investigated the often surprising roles of a variety of grinding agents. Also, the mechanochemical reaction conditions that remove zinc from a zinc porphyrin complex or exchange it for copper were studied. Using some standardized conditions, we also screened the feasibility of a number of other metal(II) insertion reactions (VO, Ni, Fe, Co, Ag, Cd, Pd, Pt, Pb). The underlying factors determining the rates of the insertion reactions were found to be complex and not always readily predictable. Some findings of fundamental significance for the mechanistic understanding of the mechanochemical insertion of metal ions into porphyrins are highlighted. Particularly the mechanochemical insertion of Mg(II) is a mild alternative to established solution methods. The work provides a baseline from which the practitioner may start to evaluate the mechanochemical metal insertion into porphyrins using a planetary ball mill.

INTRODUCTION

Mechanochemistry is a broad term that defines chemical syntheses where activation is induced by mechanical force, such as through grinding or the use of ultrasonic waves.[1,2] The use of ball mills in which the dry, solid reagents are intensely ground together to induce a reaction is particularly attractive. Possible advantages of solid state reactions over conventional solution-based reactions, in general,[3] and mechanochemical methods employing mills, in particular, are the avoidance of a reaction solvent, frequently decreased reaction times, increased reaction selectivity, or access to different reaction pathways, although it is rare to have a single mechanochemical reaction encompass all advantages.[1,2] There is a growing concern toward the use of many of the common solvents in chemical synthesis because of their associated health or environmental hazards.[1,2a] Mechanochemical processes avoiding a reaction solvent altogether offer a greener alternative, particularly also when factoring in the energetic cost savings and hazards avoided that are associated with solvent heating, cooling, and removal. Syntheses under mechanochemical conditions in ball mills have found broad application in organic synthesis (C−C and C-heteroatom formations) and the synthesis of metal coordination complexes, including the formation of inorganic materials such as MOFs.[1,2,4]

The formation of metalloporphyrinoids is key for the broad utilization of porphyrinoids in, for example, catalysis,[5] biomedicine,[6,7] molecular electronics,[8] or artificial light-harvesting.[9] The formation of metalloporphyrins from their free bases is a classic metathesis reaction.[10] In its simplest form, the reaction of a divalent metal salt (ML_2) with a dibasic porphyrin ($PorH_2$) forms the neutral metalloporphyrin [Por]M and corresponding acid of the metal salt anion (LH; Scheme 1):[11]

Scheme 1. Generalized Metal Insertion Reaction into Porphyrins



Many variations of this reaction are known, such as involving metals of lower oxidation states, the participation of redox reactions during the metal insertion step, axial ligands to the metalloporphyrin, the formation of double-decker complexes, etc.[10,12] Generally, the rate-limiting steps are determined by the considerable kinetic barrier of the metal insertion step into the planar and relatively rigid porphyrin.[11] The planar

Received: January 7, 2019

DOI: 10.1021/acs.inorgchem.9b00052

porphyrin points its (protonated) donor atoms of low basicity toward the center of its (small) central cavity. Nature overcomes these barriers in the metal (iron) insertion enzymes (ferrochelatases) by inducing a deformation of the porphyrin (protoporphyrin IX) from planarity upon binding to the enzyme, thereby exposing the inner NH/N atoms; this deformation enzyme therefore catalyzes the formation of the hemes.[13] There are also the intrinsic kinetic barriers inherent to any specific metal ion that need to be overcome. Therefore, traditional approaches toward the formation of metalloporphyrins generally employ the reaction of the porphyrin and a metal salt (in a low oxidation state) in a high-boiling donor solvent (pyridine, bp 115 °C; DMF, bp 153 °C; PhCN, bp 191 °C) under reflux conditions over extended periods of time, although some metals insert also under milder conditions (in hot or warm $CHCl_3$/MeOH mixtures, for example).[10,14] The stable oxidation state of the metal in the metalloporphyrin is then frequently reached by a subsequent (air) oxidation reaction.[10,12] As a consequence of the often relatively harsh conditions, metal insertion reactions into more sensitive porphyrinoids can be accompanied by considerable macrocycle degradation or other unwanted side reactions, driving the search for alternative methodologies.[15]

Surprisingly, therefore, the first—and to date lone—proof of concept study on the mechanochemical preparation of metalloporphyrins was presented by James and co-workers only most recently.[15b] Their report described the variously successful mechanochemical insertion of Zn(II), Ni(II), Cu(II), and Fe(II) salts into a single porphyrin, *meso*-tetraphenylporphyrin (**TPP**), using a shaker mill. The insertions of Li, Mg, Mn, Co, Au, and Pt were described as unsuccessful. Some variations of the variables of the mechanochemical reaction conditions were reported for a number of failed reactions only.

Herein, we investigate in more depth the use of a planetary ball mill in the formation of zinc and copper porphyrins with respect to the type of porphyrins susceptible to this metal insertion modality (electron-rich or electron-poor *meso*-tetraarylporphyrins, octaalkylporphyrins, as well as *meso*-triarylcorrole and, peripherally, *meso*-tetraarylchlorins), the suitability of various metal ion sources with respect to yield and reaction times for the formation of the metalloporphyrin, as well as variation of the insertion conditions (the grinding energy applied–i.e., ball mill speeds and vessel volumes, reaction times, addition of grinding agents). We also studied mechanochemical reaction conditions that remove the zinc ion or exchange it with a copper ion. We expand on an unexpected observation, namely, the insertion of Mg(II) mediated by Florisil, a magnesium silicate. We also report on the (in)ability to insert of a number of other (transition) metal ions (VO, Ni, Fe, Co, Ag, Cd, Pd, Pt, Pb) using a broader screening, with some notable differences or qualifications of the findings by James and co-workers.[15b] We will reveal findings that are important for the mechanistic understanding of the mechanochemical metal insertion pathway as well as demonstrate that mechanochemical metal insertion conditions are sometimes advantageous over solution state conditions. In any case, we will report that mechanochemical metal insertion reactions into porphyrins are fraught with their own sets of difficulties, surprises, and shortcomings.

■ RESULTS AND DISCUSSION

Mechanochemical Insertion of Zinc into TPP. The grinding together of free base **TPP** with 1.1 equiv of zinc acetate ($Zn(OAc)_2 \cdot 2H_2O$) in a planetary ball micromill (Fritsch GmbH, Germany, Pulverisette 7 classic line) equipped with two 12.5 or 50 mL volume agate grinding vessels containing with five agate balls (for additional information, see Experimental Section and Supporting Information) at ambient conditions (air conditioned to 22 °C, ∼40−50% rel. humidity) resulted in its quantitative conversion to the corresponding zinc complex, [**TPP**]**Zn**, within 10 to 15 min (entry 1−1). The time needed for the completion of the reaction was estimated by retrieval of small aliquots from the vessel at certain time intervals and their analyses by TLC and UV−vis spectroscopy (see Supporting Information). The precision of the reaction times quoted is therefore also determined by the sampling frequency, typically ±5 min in runs shorter than 30 min, and ±15 min for longer runs. Because of the retrieval of the aliquots, the grinding was intermittently stopped, but the run times listed are the actual run times without inclusion of any pauses. The interruptions also assured that the vessels did not warm to any appreciable extent (we note exceptions below), minimizing temperature effects. We also explicitly monitored the temperature in some runs, assuring us that the bulk temperatures in these runs did not exceed a few degrees Celsius above ambient temperature. Using representative larger scale reactions, we confirmed the quantitative conversion of the starting porphyrin by column chromatographic isolation and gravimetric analysis of the products.

The mechanical energy applied, i.e., increasing rotational speed or use of a larger grinding vessel that exposes its contents to larger impact and shear forces,[2b] had a direct effect on the reaction times: The faster the rotational speed or the larger the vessel, the faster the zinc insertion reaction (Figure 1). This clearly demonstrated that the metal insertion is the result of mechanochemical action.

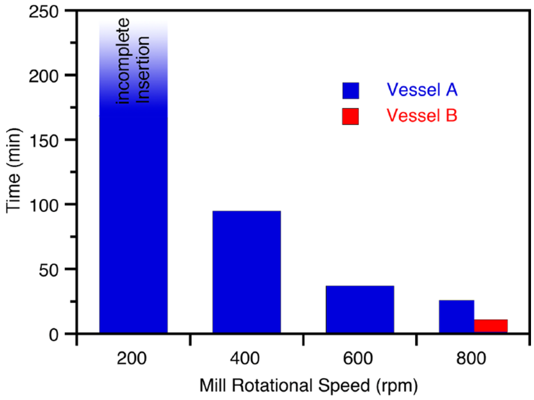
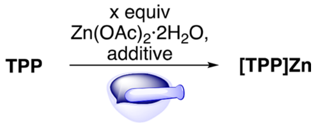


Figure 1. Rotation speed (mechanical energy) dependence of the time needed for the quantitative insertion of zinc into **TPP**. Conditions: 12.0 mg **TPP** and 85.7 mg (20 equiv) $Zn(OAc)_2 \cdot 2H_2O$.

The stoichiometric ratio of zinc source to free base porphyrin had comparably little impact on the speed of formation of the complex (entries 1−1, 1−3, 1−5, and 1−7). In a series of runs in which the porphyrin:metal source was varied from 1:1.1 to 1:20, the time of the reaction to completion was shortened only by a maximum factor of 2.

The series of experiments leading to Table 1 identified standard reaction conditions (800 rpm, 50 mL agate vessel, discontinuous runs) that were then used in the bulk of the subsequent experiments to map the scopes and limits of the mechanochemical metal insertion reactions. The conditions used should not suggest that, for instance, lower stoichiometric amounts of metal source would not lead to reaction completion. In fact, James and co-workers successfully used 1:1 metal source to **TPP** ratios.[15b]

Table 1. Effect of the Stoichiometric Ratio of the Zinc Source and Free Base TPP on the Time to Completion of the Zinc Insertion Reaction[a]



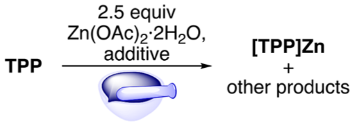
entry	*x* equiv $Zn(OAc)_2 \cdot 2H_2O$	additive	time to completion
1–1	1.1		10–15 min
1–2	1.1	0.5 g silica	30 min
1–3	2.5		10–15 min
1–4	2.5	0.5 g silica	15 min
1–5	5		10 min
1–6	5	0.5 g silica	15 min
1–7	20		10 min
1–8	20	0.5 g silica	15 min

[a]Reaction conditions: Rotational speed of 800 rpm, 50 mL agate vessel, milled in ∼5 min intervals with ∼2 min breaks.

Mechanochemical Grinding Aids. The addition of grinding aids has been shown to be advantageous in mechanochemical reactions.[16] We tested the effects of the addition of silica gel (ratio **TPP**/silica ∼ 1:42 by weight) to reactions with varying porphyrin/metal ratios (Table 1). The addition of the silica gel effectively diluted the reactants by a factor of ∼50, but this slowed the reaction down by only a factor of ∼2 (cf., e.g., entries 1–1 and 1–2). However, the presence of the silica gel helped much in forming a homogeneous mixture of the reagents, minimized the amount of unreacted porphyrin left in the inevitable "dead space" of the milling vessel, and assisted in the retrieval of the very fine and sticky product mixture from the vessel walls and grinding balls, possibly also by absorbing the (acetic) acid formed during the reactions. Silica gel was therefore routinely added in subsequent experiments. Extraction/filtration of the reaction mixture using, e.g., CH_2Cl_2 readily separated the product **[TPP]Zn** from the silica gel. The isolated yields of crystallized **[TPP]Zn** were identical to comparison solution reactions. Some advantages of the solvent-less mechanochemical insertion step were therefore mitigated during workup. However, since the focus of this study was to broadly screen the multiple factors that influence the mechanochemical metal insertion reactions, we chose convenience and comparability of the various reactions over largest overall practical benefits. James and co-workers have shown that the use of 1.0 equiv of a zinc salt of a volatile acid (zinc acetate) avoids this solvent-based workup—a simple drying step was sufficient to remove the only byproduct (acetic acid) in the quantitative conversions they reported.[15b]

The additive is not innocent in the mechanochemical zinc insertion reaction, however. Different additives had starkly varying effects on the rates of the metal insertion reaction (Table 2). In this comparison, we ignore grain size effects; even if initial grain size differences existed, the grains break down in the mill within the first seconds of any run, i.e., at a much faster rate than the metal insertion reaction. We found indications that mechanical as well as chemical factors play a role in the outcome of the reactions. Some additives seem to have had no effect beyond being a mechanical aid, like rock salt (Mohs hardness 2.0–2.5; entry 2–8) or sea sand (Mohs hardness, depending on purity, ∼6; 7 for pure quartz; entry 2–2). Softer aids, like montmorillonite (Mohs hardness of 1–2; entry 2–7) and particularly cellulose (entry 2–9) result in slower reaction rates. Overall, silica gel (of unspecified hardness; the hardness of fused silica gels varies and is much lower than that of crystalline or glassy SiO_2)[17] caused the largest rate acceleration, explaining why the reactions "diluted" with silica gel were still fast compared to the rate of the "undiluted" reactions (Table 1).

Table 2. Effect of Various Additives on the Time to Completion of the Zinc Insertion into TPP[a]



entry	0.5 g additives	product(s)	time to completion or % conversion
2–1	silica	**[TPP]Zn**	15 min
2–2	quartz sand (sea sand, washed)	**[TPP]Zn**	20 min
2–3	silica-NH_2	**[TPP]Zn**	≤65% conversion after 60 min
2–4	neutral alumina, Brock activity I	**[TPP]Zn**	40 min
2–5	basic alumina,[b] Brock activity I	NR[d] after 60 min	
2–6	acidic alumina, Brock activity I	**[TPP]Zn**	>95% conversion after 35 min
2–7	montmorillonite	**[TPP]Zn**	30 min
2–8	sodium chloride	**[TPP]Zn**	35–40 min
2–9	cellulose powder MN 300	**[TPP]Zn**	≤70% conversion after 50 min
2–10[c]	florisil ($MgO{:}xSiO_2 \cdot H_2O$)	**[TPP]Zn** and **[TPP]Mg** in a ∼80:20 ratio	>70% conversion after 60 min

[a]Reaction conditions: Rotational speed of 800 rpm, 50 mL agate vessel, 2.5 equiv $Zn(OAc)_2 \cdot 2H_2O$, milled at ∼5 min intervals with ∼2 min breaks. [b]Notable heating of the reaction vessel took place when using this additive. [c]The reaction was optimized for Mg-insertion, see Table 8. [d]NR: no reaction observed

The three different (neutral, basic, and acidic) aluminas tested (entries 2–4, 2–5, and 2–6) had the same Brock activity level I. Assuming all also had the same mechanical effects because of similar hardness, the starkly different ways in which they affect the metal insertion reaction rate allow only the conclusion that their different (surface) chemistries are responsible for their different effects: Acidic alumina is the fastest (entry 2–6), neutral alumina much slower (entry 2–4, rate comparable to that with the hard "neutral" additive sodium chloride (entry 2–8), or the softer montmorillonite, entry 2–7), and no reaction was observed in the presence of the basic alumina (entry 2–5). [Hardness of the aluminas used was not determined but is drastically lower for the noncrystalline aluminas than for their very hard crystalline counterparts (corundum) of Mohs hardness of up to 9. We observed a significant warming of the reaction vessel when using basic alumina, perhaps an indicator of its greater hardness; we also like to point out the potential hardness incompatibility of the agate vessel/balls and the aluminas should they contain crystalline phases. This will lead to mechanical damage of the vessel. Pitting of the agate vessels/balls over time was indeed observed, but could not be attributed solely to the runs using alumina.] Tellingly, the reaction in the presence of basic silica gel modified with amine groups (entry 2–3) is also very slow. Inversely, the rates of zinc insertion in the presence of regular silica (that tends to be slightly acidic) is faster compared to that of the more neutral sand of approximate identical bulk composition (entry 2–2).

This suggests that porphyrin protonation and the concomitant conformational distortion[18] might be an important aspect for the mechanochemical insertion of zinc into a porphyrin. In fact, some correlation between the pK_3 of porphyrins and copper insertions rates were drawn.[19] Inversely, assistance in porphyrin deprotonation by the basicity of particular grinding agents may not be needed. Alas, too acidic insertion conditions are detrimental (at least for the zinc insertion reaction), as we show below that visible (bulk) diprotonation of **TPP** by strong acids effectively blocks any zinc insertion. The base conditions could theoretically also convert the zinc ion to a basic salt, but we will show below that ZnO and the zinc carbonates/hydroxides/oxides formed on the surface of zinc powder are still competent sources of zinc for the formation of zinc porphyrins.

Unexpected was the outcome of the experiment using Florisil, a magnesium silicate ($MgO{:}x SiO_2{\cdot}H_2O$): The zinc as well as the magnesium complexes of **TPP** were formed (entry 2–10). We did not pursue the use of Florisil as a grinding aid any further, but for more details on this surprising pathway of formation of [**TPP**]**Mg** and other magnesium porphyrins, see below.

Overall, we found silica gel to be the most generally suitable and convenient grinding aid for the insertion of zinc into porphyrins. We have therefore used silica gel as the grinding aid in the standardized conditions chosen for the bulk of the subsequent experiments described. The overall conclusion from the screening of the grinding aids is that the practitioner must select a possible grinding aid with great care as it is far from innocent with respect to the metal insertion reaction. The following studies will highlight this in a drastic manner.

Mechanochemical Porphyrin Degradation. When using grinding aids—and particularly silica gel—in metal insertion reactions requiring milling times exceeding 30 min, we observed severe degradations of the porphyrins. When milling porphyrins, the metal source, and silica gel over extended periods of time, we noticed also that the color of the reaction mixtures invariably started to lose the deep color of the porphyrin; the mixtures turned over time into a dull gray. We therefore milled **TPP**, **T^{F}PP**, and **OEP** with silica gel (in the absence of metal sources) for up to 120 min. After a given time, we extracted the mixtures with a standardized amount of solvent and analyzed the extracts by HPLC (Figure 2A).

All porphyrin peaks gradually decreased over time, with less than 10% residual **TPP** after 2 h of milling time, and with no new product becoming apparent by HPLC (see Supporting Information) or TLC. In fact, we could not extract the gray product from the silica gel with any solvent tested. **T^{F}PP** degraded ~30% faster than **TPP**, and **OEP** yet another ~30% faster. Again, no products could be identified, although a number of direct oxidation products of **TPP**,[20] **T^{F}PP**,[21] and **OEP**[22] are known. The rates of degradation vary in the presence of the metal salts (not shown), likely reflecting the stability of the metalloporphyrins toward (oxidative) degradation.[20−22] On the upside, except for the reactions involving the chlorins (see below, Table 4, entries 4–11 and 4–12), the degradation products that formed did not interfere with the isolation or purity of the target products.

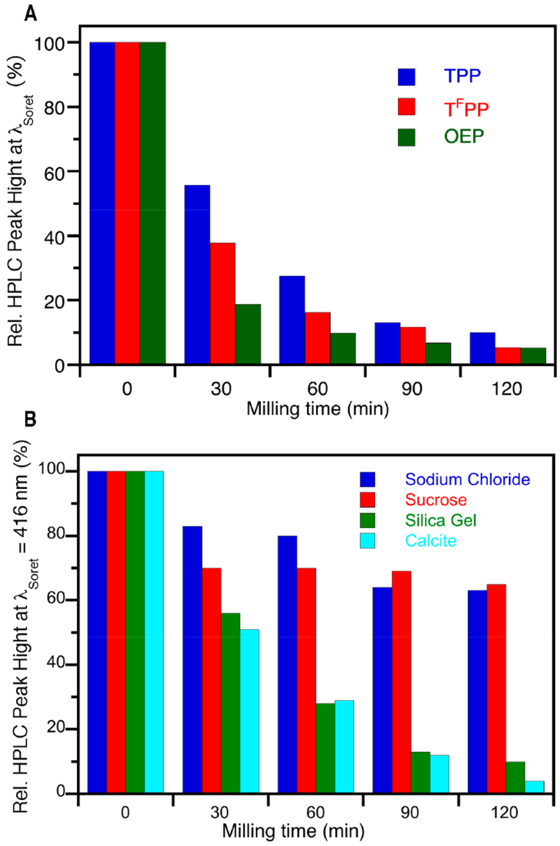


Figure 2. (A) Time course of the degradation of different porphyrins indicated using the additive silica gel. (B) Time course of the degradation of **TPP** on the additives indicated. Conditions: 5.0 mg of porphyrin milled with 0.5 g of additive at a rotational speed of 800 rpm in a 50 mL agate vessel.

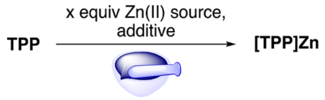
The nature of the grinding agent had a profound effect on the rate of **TPP** degradation (Figure 2B). Sodium chloride and sucrose led to a much less severe degradation of the porphyrin (and some of this "degradation" may be an artifact attributable to the difficulty of extracting the porphyrin from the ground sugar that turns over time into a sticky paste). On the other hand, calcite ($CaCO_3$ in the form of Iceland spar) degraded **TPP** even faster than silica gel.

The milling-based mechanochemical degradation of polymers is under active investigation.[23] As well, the mechanochemical dehalogenation of, for example, environmental pollutants milled with a number of reactive ingredients (such as CaO or Fe powder) has been under investigation for some time.[24] However, we are not aware of reports of the mechanochemical degradation of the otherwise very robust porphyrins under milling conditions with supposedly "inert" grinding agents. We speculate that piezoelectric effects might play a role. Sodium chloride, for example, is not a piezoelectric material, and while the others are, including crystalline sucrose (albeit its noncrystalline, malleable form it quickly forms in the mill is not piezoelectric), the degradation mechanism operative here clearly requires further study.

We must conclude that the mechanochemical reaction conditions in the planetary mill in the presence of some grinding aids cannot be considered mild, and the reaction times should be minimized. Furthermore, the grinding aids are in more than one way noninnocent, again highlighting that the practitioner must select a grinding aid with great care and be aware of possible degradation reactions.

Zinc Sources for the Mechanochemical Preparation of [TPP]Zn. Next to zinc acetate, various other zinc sources proved to be competent in the delivery of zinc ions to free base **TPP** (Table 3). Zinc perchlorate ($Zn(ClO_4)_2 \cdot 6H_2O$) was suitable, but much slower (>50 min, entry 3−1) than zinc acetate (15 min, entry 1−4) under otherwise identical conditions. The addition of base to the zinc perchlorate reaction accelerated the reaction (entry 3−2). Surprisingly, zinc chloride ($ZnCl_2$) failed to insert zinc without the addition of a solid base (DABCO; entries 3−3 and 3−4, respectively). In the absence of this base, the mixture turned green over time, the color of the diprotonated porphyrin.

Table 3. Effect of Various Zinc Sources on the Time to Completion of the Zinc Insertion into TPP[a]



entry	x equiv Zn(II) source	additives	time to completion or % conversion
3−1	2.5 equiv $Zn(ClO_4)_2 \cdot 6H_2O$	0.5 g silica	>90% conversion after 50 min
3−2	5 equiv $Zn(ClO_4)_2 \cdot 6H_2O$ + 5 equiv DABCO	0.5 g silica	40 min
3−3	5 equiv $ZnCl_2$	0.5 g silica	NR[c] after 115 min (protonation of TPP visible)
3−4	5 equiv $ZnCl_2$ + 5 equiv DABCO	0.5 g silica	>96% conversion after 30 min
3−5	5 equiv zinc powder, < 44 μm grain size		30−40 min
3−6	5 equiv zinc powder, < 44 μm grain size	0.5 g silica	>60% conversion after 80 min
3−7	5 equiv ZnO		55 min
3−8	5 equiv ZnO	0.5 g silica	>60% conversion after 80 min
3−9	5 + 10 equiv ZnS[b]		~50% after 40 min and 5 equiv ZnS, > 90% after 70 min and additional 10 equiv ZnS

[a]Reaction conditions: rotational speed of 800 rpm, 50 mL agate vessel, milled at ~5 min intervals with ~2 min breaks; silica gel (40−75 μm particle size). [b]Unspecified polymorph. [c]NR: no reaction observed.

Zinc oxide and zinc powder were also suitable for the insertion of zinc into **TPP**; moreover, the addition of silica gel to these reactions proved detrimental (entries 3−5 to 3−8). In the case of zinc powder, we assume that the surface zinc oxides/hydroxides/carbonates are the source of the zinc ions. Because of their insolubility in organic solvents, neither source is suitable for solution state zinc insertion reactions. Powdered ZnS can also be used as a zinc source (entry 3−9), but the reaction is significantly slower than the reaction with ZnO (entry 3−7).

Overall, these experiments suggest that zinc sources containing more basic counteranions are advantageous over comparable sources with less basic counteranions (AcO^- over ClO_4^- and O^{2-} over S^{2-}, respectively). This trend is in contrast to the effects of the additives where the more acidic additives led to faster rates, possibly pointing at their different roles in the mechanism of the mechanochemical zinc insertion reaction.

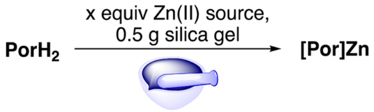
However, as we will show below (Table 7), this interpretation is not fully holding true for the insertion of Cu(II) that is much less sensitive to the acidity of the environment at which metal insertion is still observed. Our results vary significantly from those by James and co-workers who reported the inability to insert zinc into **TPP** using ZnO or $[Zn_5(CO_3)_2(OH)_6]$, even upon the addition of small amounts of solvent (DMF, MeOH, or H_2O).[15b] Our utilization of a more aggressive planetary mill instead of the shaker mill used by James and co-workers might be source of the observed differences.[2d]

Mechanochemical Zinc Insertion into Other Porphyrins. Other porphyrins were also susceptible toward the mechanochemical insertion of Zn(II) using a number of zinc sources, each with their own insertion rates (Table 4). The *β*-octaalkylporphyrin **OEP** reacted (entries 4−1 to 4−3) at rates comparable to that of **TPP** with zinc acetate (cf. entries 1−2 and 4−1) but comparably faster with zinc powder (cf. entries 3−6 and 4−2) and zinc oxide (cf. entries 3−8 and 4−3). Protoporphyrin IX, as its dimethyl ester (**PPIX-DME**, entry 4−4), and etioporphyrin I (**ETIO-I**, entry 4−5) were chosen as derivatives closely related to the naturally occurring *β*-alkylporphyrins.[25] Both are faster than **TPP** and more in line with the structurally related **OEP**. The electron-poor *meso*-tetrakis(pentafluorophenyl)porphyrin **T^{F}PP** is slower overall (entry 4−6 to 4−8), with 5 equiv of zinc oxide accomplishing within 60 min only a conversion of about 50%. The metal complexes of electron-rich *meso*-tetrakis(thien-2- and 3-yl)-porphyrins **T(^{2}Thiop)P** and **T(^{3}Thiop)P** have found utility in a number of electrocatalytic and sensing applications.[26] **T(^{2}Thiop)P** and **T(^{3}Thiop)P** react somewhat slower than **TPP** (entries 4−9 and 4−10, respectively) but nonetheless form smoothly the expected zinc chelates in under 60 min.

The *meso*-tetraaryl-2,3-dihydroxychlorins **$(OH)_2$TPC** and **$(OH)_2$T^{F}PC** are representatives of a class of relatively robust chlorins[27] but are nonetheless prone to acid- or thermally induced dehydration and HF-elimination reactions; metal insertion reactions into these chlorins are therefore not always unproblematic.[15c,27b] Indeed, the mechanochemical insertion of zinc, even under the most optimal conditions (entries 4−11 and 4−12), was possible but were accompanied by extensive (20−40% decomposition), complex, and ill-defined degradation reactions. We found that the corresponding solution state insertion of zinc using zinc acetate in a $CHCl_3$/MeOH mixture takes place readily upon slight warming.[27] We thus abandoned experiments using these chlorin diols and focused on the principal factors controlling the metal insertions into porphyrins.

Mechanochemical Demetalation of [TPP]Zn. The acid-induced demetalation of zinc porphyrins is a well-known and a frequently practiced reaction, traditionally requiring the washing of a solution of **[TPP]Zn** dissolved in organic solvents with a ~3 M aqueous solution of a strong mineral acid

Table 4. Effect of Various Free Base Porphyrins and Varying Zn(II) Sources on the Time of Completion of the Zinc Insertion Reaction[a]

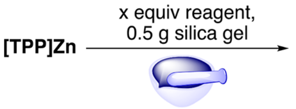


entry	substrate	*x* equiv Zn(II) source	product(s)	time to completion or % conversion
4−1	**OEP**	1.1 equiv $Zn(OAc)_2 \cdot 2H_2O$	[**OEP**]**Zn**	20 min
4−2	**OEP**	5 equiv zinc powder	[**OEP**]**Zn**	20 min
4−3	**OEP**	5 equiv ZnO	[**OEP**]**Zn**	20 min
4−4	**PPIX-DME**	2.5 equiv $Zn(OAc)_2 \cdot 2H_2O$	[**PPIX-DME**]**Zn**	<15 min
4−5	**ETIO-I**	2.5 equiv $Zn(OAc)_2 \cdot 2H_2O$	[**ETIO I**]**Zn**	10 min
4−6	**T^{F}PP**	1.1 equiv $Zn(OAc)_2 \cdot 2H_2O$	[**T^{F}PP**]**Zn**	25 min
4−7	**T^{F}PP**	5 equiv zinc powder	[**T^{F}PP**]**Zn**	30 min
4−8	**T^{F}PP**	5 equiv ZnO	[**T^{F}PP**]**Zn**	>50% conversion after 60 min
4−9	**T(^{2}Thiop)P**	3.0 equiv $Zn(OAc)_2 \cdot 2H_2O$	[**T(^{2}Thiop)P**]**Zn**	60 min[b]
4−10	**T(^{3}Thiop)P**	2.5 equiv $Zn(OAc)_2 \cdot 2H_2O$	[**T(^{3}Thiop)P**]**Zn**	40 min
4−11	**(OH)$_2$TPC**	2.5 equiv $Zn(OAc)_2 \cdot 2H_2O$	[**(OH)$_2$TPC**]**Zn**	60 min (40% decomposition)
4−12	**(OH)$_2$T^{F}PC**	2.5 equiv $Zn(OAc)_2 \cdot 2H_2O$	[**(OH)$_2$T^{F}PC**]**Zn**	60 min (20% decomposition)

[a] Reaction conditions: rotational speed of 800 rpm, 50 mL agate vessel, milled at ∼5 min intervals with ∼2 min breaks; silica gel (40−75 μm particle size). [b] Reaction was run initially with 1.5 equiv $Zn(OAc)_2 \cdot 2H_2O$ and an additional 1.5 equiv of $Zn(OAc)_2 \cdot 2H_2O$ were introduced 40 min into the reaction.

(HCl is typically used) or the addition of *p*-TSA monohydrate or TFA to an organic solution of the zinc porphyrin.[10] We find now that the demetalation of [**TPP**]**Zn** can also be achieved mechanochemically using a variety of solid acids (Table 5).

Table 5. Reaction Conditions and Times for the Removal of Zinc(II) from [TPP]Zn[a]



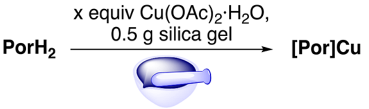
entry	reagent	product	time to completion
5−1	10 equiv $pTsOH \cdot H_2O$	TPP	30 min
5−2	10 equiv $ClCH_2CO_2H$	TPP	20 min
5−3	0.5 g Dowex HCR-W2, H^+-form, 16−40 mesh size	TPP	<25 min
5−4	5 equiv EDTA	NR[b] after 60 min	
5−5	5 equiv $Na_2EDTA \cdot 2H_2O$	NR[b] after 60 min	

[a] Reaction conditions: Rotational speed of 800 rpm, 50 mL agate vessel, milled at ∼5 min intervals with ∼2 min breaks; 0.5 g silica gel (40−75 μm particle size). [b] NR: no reaction observed.

Thus, milling [**TPP**]**Zn** with *p*-TSA monohydrate (entry 5−1), monochloroacetic acid (entry 5−2), or Dowex, a sulfonated polystyrol-based ion-exchange resin in the acidic form (entry 5−3), resulted in the conversion of the purple color of the metalloporphyrin to bright green, the color of the diprotonated porphyrin,[18] indicating that an irreversible demetalation had taken place. In contrast, strong chelating agents like EDTA or its disodium salt $Na_2EDTA \cdot 2H_2O$ did not elicit a mechanochemical demetalation of [**TPP**]**Zn** (entries 5−4 and 5−5).

Mechanochemical Copper Insertion into Porphyrins. The insertion of copper into porphyrins generally requires higher boiling solvents or longer reaction times than the insertion of zinc; in turn, the resulting copper complexes are much more resistant to acid-induced demetalation (requiring concentrated H_2SO_4 for their demetalation).[10] In general, the mechanochemical copper insertion reactions proceeded smoothly with the electron-rich or -poor tetraarylporphyrins **TPP**, **T^{F}PP**, **T(^{2}Thiop)P**, and **T(^{3}Thiop)P** and the octaalkylporphyrin **OEP** (Table 6). This confirms the results by James and co-workers for **TPP**.[15b] Since all these copper insertions proceeded satisfactorily under the standard conditions tested, we did not test a variation of the metal source or the effects of other additives than silica gel. However, it is known from solution experiments that the anion of the metal source plays a role in the metal insertion rate (cf. also the zinc insertion experiments).[28] A mechanochemical demetalation of [**TPP**]**Cu** could not be achieved under any of the reaction conditions tested.

Table 6. Various Free Base Porphyrins and Their Time of Completion of the Mechanochemical Copper Insertion Reaction[a]

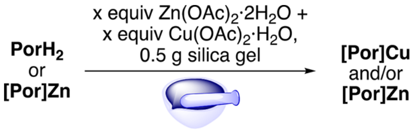


entry	substrate	$Cu(OAc)_2 \cdot H_2O$	product(s)	time to completion
6−1	**TPP**	1.5 equiv	[**TPP**]**Cu**	15 min
6−2	**OEP**	1.5 equiv	[**OEP**]**Cu**	15 min
6−3	**T^{F}PP**	1.5 equiv	[**T^{F}PP**]**Cu**	15 min
6−4	**T(^{2}Thiop)P**	2.5 equiv	[**T(^{2}Thiop)P**]**Cu**	30 min
6−5	**T(^{3}Thiop)P**	2.5 equiv	[**T(^{3}Thiop)P**]**Cu**	30 min
6−6	**TPCorrole**	2.5 equiv	[**TPCorrole**]**Cu**	30 min

[a] Reaction conditions: Rotational speed of 800 rpm, 50 mL agate vessel, milled at ∼5 min intervals with ∼2 min breaks; 0.5 g silica gel (40−75 μm particle size).

meso-Triarylcorroles form stable copper(III) complexes that are produced by spontaneous air oxidation of the initially formed copper(II) complex.[29] We found now that mechanochemical conditions are also suited for the formation of the [*meso*-triphenylcorrolato]copper(III) complex [**TPCorrole**]-

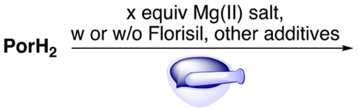
Table 7. Outcomes of Zinc/Copper Insertion Competition and Metal Replacement Reactions[a]



	substrate	x equiv Zn(OAc)$_2$·2H$_2$O	x equiv Cu(OAc)$_2$·H$_2$O	product(s)	time to completion or % conversion
7−1	**TPP**	2.5 equiv	2.5 equiv	**[TPP]Cu**: **[TPP]Zn**	90:10 after 10 min 100:0 after 40 min
7−2	**T^{F}PP**	2.5 equiv	2.5 equiv	**[T^{F}PP]Cu**: **[T^{F}PP]Zn**	98:2 after 10 min
7−3	**OEP**	2.5 equiv	2.5 equiv	**[OEP]Cu**: **[OEP]Zn**	98:2 after 10 min
7−4	**[TPP]Zn**		2.5 equiv	**[TPP]Cu**	40 min
7−5	**[OEP]Zn**		2.5 equiv	**[OEP]Cu**	40 min
7−6	**[T^{F}PP]Zn**		2.5 equiv	**[T^{F}PP]Cu**	<50% conversion after 60 min
7−7	**[T^{F}PP]Zn**		2.5 equiv +7.0 equiv of p-TSA	**[T^{F}PP]Cu**	60 min

[a] Reaction conditions: rotational speed of 800 rpm, 50 mL agate vessel, milled at ∼5 min intervals with ∼2 min breaks; 0.5 g silica gel (40−75 μm particle size).

Table 8. Outcomes of the Mechanochemical Metal Insertion Reactions of TPP, T^{F}PP, and OEP Using Florisil and Mg(II) Sources[a]



entry	substrate	x equiv Mg(II) source	additives	product	time to completion or % conversion
8−1	**TPP** or **OEP**		0.5 g Florisil	**[TPP]Mg** or **[OEP]Mg**	<10% conversion after 120 min
8−2	**TPP**	10 equiv MgCl$_2$	0.5 g Florisil	**[TPP]Mg**	90 min
8−3	**TPP**	10 equiv MgCl$_2$	0.5 g Florisil, 10 equiv DABCO	**[TPP]Mg**	90 min
8−4	**TPP**	2.5 equiv MgBr$_2$ or MgI$_2$	0.5 g Florisil, 2.5 equiv DABCO	**[TPP]Mg**	<60 min
8−5	**TPP**	2.5 equiv MgBr$_2$	0.5 g talc	**[TPP]Mg**	<20% conversion after 60 min
8−6	**TPP**	5 equiv MgBr$_2$ or MgI$_2$	with or without 5 equiv DABCO	NR[b]	after 120 min
8−7	**OEP**	5 equiv MgBr$_2$ or MgI$_2$	0.5 g Florisil, with or without 5 equiv DABCO	**[OEP]Mg**	<60 min
8−8	**OEP**	5 equiv MgBr$_2$	0.5 g talc	**[OEP]Mg**	<20% conversion after 60 min
8−9	**OEP**	5 equiv MgBr$_2$ or MgI$_2$	5 equiv DABCO	NR[b]	after 120 min
8−10	**T^{F}PP**	5 equiv MgBr$_2$ or MgI$_2$	0.5 g Florisil, 5 equiv DABCO	**[T^{F}PP]Mg**	<20% conversion after 120 min
8−11	**T^{F}PP**	5 equiv MgBr$_2$ or MgI$_2$	5 equiv DABCO	NR[b]	120 min

[a] Reaction conditions: Rotational speed of 800 rpm, 50 mL agate vessel, milled at ∼ 5−20 min intervals with ∼2 min breaks; with or without additives (silica gel 40−75 μm particle size, Florisil 100−200 mesh). [b] NR: no reaction observed.

Cu.[29a] This suggests that metal insertion reactions requiring a more complex insertion mechanism are also accessible using mechanochemical approaches (cf. also to the silver(II) and silver(III) insertions using a Ag(I) source into porphyrins and corrole, respectively, Table 10).

Mechanochemical Competition Metal Insertions. The rapid insertion of copper prompted the question of what the outcome of zinc and copper competition insertion experiments would reveal (Table 7). Starting with 2.5 equiv of each of the zinc and copper acetates, the copper insertion product **[TPP]Cu** rapidly becomes the dominating species and, in fact, replaces over time all of zinc in the **[TPP]Zn** initially formed (entry 7−1). These dynamics are also observed for **T^{F}PP** (entry 7−2) and **OEP** (entry 7−3). In fact, grinding the pure preformed zinc complexes **[TPP]Zn** (entry 7−4), **[OEP]Zn** (entry 7−5), or **[T^{F}PP]Zn** (entry 7−6) with copper acetate converts them over time to the corresponding copper complexes, although the latter less basic ligand reacted slower and required the addition of acid for completion (entry 7−7).

While **[TPP]Cu** is also the predominant product in corresponding solution state competition experiments and is the sole product at higher metal/porphyrin ratios (Table S1), the zinc-to-copper replacement reactions are not observed under neutral solution conditions (Table S2) but require the addition of acid to enable rapid metal exchange. The acid added needs to be strong enough to push out the zinc without being too strong to prevent copper insertion. In transference, the transmetalation experiments indicated that using silica gel as an additive in the mechanochemical reactions rendered a significant acidic character to the reaction conditions.

Mechanochemical Insertion of Magnesium into Porphyrins. Building on the unexpected observation that the use of magnesium silicate, Florisil, as grinding agent proved to be a source of Mg(II) for the formation of **[TPP]Mg** (entry 2−10), we investigated this reaction in more depth (Table 8). The classic Mg(II) insertion methods involve Grignard reagents or hindered phenoxy magnesium iodide complexes at elevated temperatures[10] or MgCl$_2$ in refluxing DMF or pyridine,[14,15] whereby more recent methods using organic amines and inorganic magnesium salts (particularly MgBr$_2$ or MgI$_2$) have allowed milder conditions.[15a]

To bring the mechanochemical magnesium insertion reaction to completion in **TPP** and **OEP**, we found that

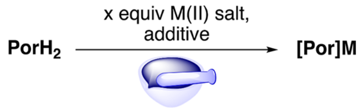
Florisil alone was not sufficient (entry 8−1), but the addition of 10 equiv of $MgCl_2$ with (entry 8−2) or without (entry 8−3) the addition of a solid base (DABCO) was needed. $Mg(OAc)_2 \cdot 4H_2O$, in the presence or absence of a base and/or Florisil, proved unsuitable for the metal insertion reaction (see Supporting Information). However, the use of $MgBr_2$ or MgI_2 in the presence of base is rapid (entry 8−4), even when using a smaller stoichiometric excess of metal salt. Most crucially, however, the use of Florisil is essential. Thus, the reaction of **TPP** with $MgBr_2$ or MgI_2 in the presence or absence of base fails when Florisil is absent (entry 8−6). Silica gel as an additive also had no effect on the magnesium insertion reactions (see Supporting Information). Correspondingly, the insertion of Mg into **TPP** was reported to be unsuccessful by James and co-workers.[15b] This key finding is also replicated with **OEP** (entries 8−7 versus 8−8) and **T^{F}PP** (entries 8−10 versus 8−11) that otherwise insert magnesium more rapidly or more slowly than **TPP**, respectively, mirroring the trends seen also for other metals. In comparison to reactions that use the crystalline magnesium silicate talc ($Mg_3Si_4O_{10}(OH)_2$) as a grinding aid (entries 8−4 versus 8−5 and entries 8−8 versus 8−9), we find talc to be much inferior to Florisil, though still better than the organic base DABCO (entry 8−11). We cannot offer an explanation for these observations, except to say that we do not believe it is the basicity of the silicate that enables this reaction.

In summary, the amorphous, synthetic magnesium silicate Florisil, in combination with the magnesium salts of the heavier halogens, mediates the insertion of magnesium into porphyrins cleanly under astoundingly mild methods, introducing mechanochemical methods as an alternative to traditional solution-based methods to accomplish magnesium insertions. Once again, the “grinding aid” Florisil plays a much more complex role in the mechanochemical metal insertion reaction than we anticipated.

Mechanochemical Insertion of Select Other Period 3 and 4 Metals into Porphyrins. In an extension to the copper, zinc, and magnesium insertion experiments, we screened a range of other two-valent metals for the suitability of their mechanochemical insertion into a number of synthetic porphyrins. The mechanochemical reaction of VO acetyl acetonate with **TPP** in the presence of silica gel is slow (Table 9, entry 9−1), with a [**TPP**]**VO**/**TPP** ratio exceeding 1:1 only after 100 min of reaction time. The high insertion barrier of VO into **TPP** can also be gleaned from the high-temperature conditions needed for solution state VO insertions.[10] The porphyrin degradation reaction described above becomes prominent during such longer reaction times in the ball mill, severely reducing the overall isolated yield of product. This makes long mill runs in the presence of silica gel unattractive, even though the (unknown) porphyrin degradation products are not hindering the clean elution of the product [**TPP**]**VO** via column chromatography.

The solution state insertion of iron(II) and cobalt(II) into porphyrins requires reflux conditions of high temperature solvents.[10,14] The mechanochemical reaction of $FeCl_2$with **TPP**, **T^{F}PP**, or **OEP** yielded even after 80 min reaction time less than 5% conversion to a product of the expected UV spectra for the corresponding [**porphyrin**]**FeCl** complexes (entry 9−2). The use of $Fe(OAc)_2$ only marginally improved the outcome for **TPP** (entry 9−3). These results are in concord with the 7% yield James and co-workers reported for the formation of [**TPP**]**Fe** using $Fe(OAc)_2$ (in the absence of silica gel) after 3 h in the shaker mill (i.e., a 6-fold longer time than for a comparable zinc insertion at a 50% slower oscillation frequency).[15b]

Table 9. Outcomes of the Mechanochemical Metal Insertion Reactions of TPP, T^{F}PP, and OEP Using select other Period 3 and 4 M(II) Sources[a]



entry	substrate	*x* equiv reagent(s), additive	product	time to completion/ degree of conversion
9−1	**TPP**	2.5 equiv $VO(acac)_2$, 0.5 g silica gel	[**TPP**]**VO**	>50% conversion after 100 min
9−2	**TPP**, **T^{F}PP**, **OEP**	5−10 equiv $FeCl_2 \cdot 4H_2O$, 0.5 g silica gel	[**TPP**]**FeCl**	<5% conversion after 80 min
9−3	**TPP**	1.5 equiv $Fe(OAc)_2$	[**TPP**]**FeOAc**	<15% conversion after 180 min
9−4	**TPP**	2.5 equiv $CoCl_2 \cdot 6H_2O$ or $Co(OAc)_2 \cdot 4H_2O$, 0.5 g silica gel	NR[b] after 80 min	
9−5	**OEP**	2.5 equiv $Co(OAc)_2 \cdot 4H_2O$, 0.5 g silica gel	[**OEP**]**Co**	>50% conversion after 60 min
9−6	**TPP**	5 equiv $NiCl_2 \cdot 6H_2O$, 0.5 g silica gel	[**TPP**]**Ni**	40 min
9−7	**TPP**	1.5 equiv $Ni(OAc)_2 \cdot 4H_2O$	[**TPP**]**Ni**	40 min
9−8	**TPP**	2.5 equiv $Ni(OAc)_2 \cdot 4H_2O$, 0.5 g silica gel	[**TPP**]**Ni**	40 min
9−9	**T^{F}PP**	5 equiv $NiCl_2 \cdot 6H_2O$, 0.5 g silica gel	[**T^{F}PP**]**Ni**	∼ 65% conversion after 100 min
9−10	**T^{F}PP**	1.5 equiv $Ni(OAc)_2 \cdot 4H_2O$, 0.5 g silica gel	NR[b] after 90 min	
9−11	**OEP**	1.5 equiv $Ni(OAc)_2 \cdot 4H_2O$	[**OEP**]**Ni**	40 min

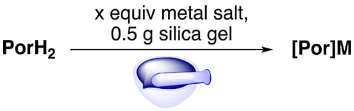
[a] Reaction conditions: rotational speed of 800 rpm, 50 mL agate vessel, milled at ∼5−20 min intervals with ∼2 min breaks; with or without additives (silica gel 40−75 μm particle size, Florisil 100−200 mesh). [b] NR: no reaction observed.

Neither we nor James and co-workers succeeded in the insertion of cobalt (using $Co(OAc)_2$ or $CoCl_2$) into **TPP** (entry 9−4).[15b] However, we found **OEP** to convert to ∼50% forming [**OEP**]**Co** after milling with $Co(OAc)_2$ and silica gel for 60 min (entry 9−5).

The insertion of nickel into porphyrins is traditionally performed in refluxing DMF[14] but also takes place in hot pyridine (bp = 115 °C)[10] or even in refluxing $CHCl_3$/MeOH (∼60 °C) over the course of 5 days.[30] The mechanochemical insertion of nickel into porphyrins is possible, with notable differences between varying nickel sources. The general trends observed for the different porphyrins are preserved: Inserting nickel into **TPP** and **OEP** using $NiCl_2$ (with silica gel) or $Ni(OAc)_2 \cdot 4H_2O$ (with or without silica gel) is facile (entries 9−6 through 9−8, and 9−11, respectively) and much slower for **T^{F}PP** (entry 9−9), whereby the use of $Ni(OAc)_2 \cdot 4H_2O$ with silica gel is inadequate to effect any reaction (entry 9−10). In comparison to the corresponding zinc insertion reactions (Tables 1 and 3), therefore, the suitability of the respective acetate and chloride salts is inverted. Our results for **TPP** are commensurate with those reported by James and co-workers.[15b]

Mechanochemical Insertion of Select Other Period 5 and 6 Metals into Porphyrins. Some period 5 and 6 metals proved also susceptible to mechanochemical insertion into a

Table 10. Outcomes of the Mechanochemical Metal Insertion Reactions of TPP, T^FPP, and OEP Using a Period 5 and 6 Metal Source[a]



entry	substrate	x equiv reagent(s)	product	time to completion/degree of conversion
10−1	**TPP**	20 equiv AgOAc	[**TPP**]Ag	<70% conversion after 120 min
10−2	**T^FPP**	20 equiv AgOAc	[**T^FPP**]Ag	20 min
10−3	**OEP**	20 equiv AgOAc	[**OEP**]Ag	<30% conversion after 60 min
10−4	**TPCorrole**	5 eq AgOAc	[**TPCorrole**]**Ag(III)**	30 min
10−5	**TPP**	5 equiv $Pd(OAc)_2$	[**TPP**]**Pd**	85% conversion after 60 min
10−6	**TPP**	2.5 equiv $PdCl_2$	[**TPP**]**Pd**	40 min
10−7	**T^FPP**	5 equiv $Pd(OAc)_2$	[**T^FPP**]**Pd**	<45% conversion after 30 min[b]
10−8	**T^FPP**	5 equiv $PdCl_2$ with/without 5 equiv DABCO	[**T^FPP**]**Pd**	<30% conversion after 50 min
10−9	**OEP**	5 equiv $PdCl_2$	[**OEP**]**Pd**	∼ 75% conversion after 60 min
10−10	**OEP**	5 equiv $Pd(OAc)_2$	[**OEP**]**Pd**	<30 min
10−11	**TPP** or **T^FPP** or **OEP**	10 equiv $CdCl_2 \cdot 2.5H_2O$, with/without silica gel	NR[c] after 90 min	
10−12	**TPP** or **T^FPP** or **OEP**	5 equiv $Pb(OAc)_2 \cdot 3H_2O$	NR[c] after 90 min	
10−13	**TPP**	5 equiv $Pb(OAc)_2 \cdot 3H_2O$, no silica gel	[**TPP**]**Pb**	<15% conversion after 180 min
10−14	**TPP**	2.5 equiv $PtCl_2$ with/without 2.5 equiv DABCO	[**TPP**]**Pt**	<40% conversion after 60 min

[a] Reaction conditions: rotational speed of 800 rpm, 50 mL agate vessel, milled at ∼5 min intervals with ∼2 min breaks; 0.5 g silica gel (40−75 μm particle size). [b] Reaction did not proceed significantly with time (we tested up to 85 min), even after the addition of additional $Pd(OAc)_2$. [c] NR: no reaction observed

porphyrin (Table 10). The stable oxidation state of silver in porphyrins is Ag(II), in corroles Ag(III).[31] The standard conditions to insert silver into porphyrins is the use of Ag(OAc) in warm pyridine.[10] Thus, the insertion reaction is characterized by a disproportionation reaction: 2 equiv of Ag(OAc) reacts with one porphyrin to form the silver(II) porphyrin and elemental silver and acetic acid;[14] for the tribasic corroles, three Ag(OAc)'s react with one macrocycle to form the silver(III) corrole and 2 equiv of elemental silver.[32] We found that the mechanochemical insertion of silver into porphyrins is possible, but it requires a larger stoichiometric excesses of Ag(OAc) than in solution. Like for other metals, the insertion rates are much porphyrin-dependent: The electron-rich porphyrins **TPP** and **OEP** insert silver only partially after 1 or 2 h reaction times (entries 10−1 and 10−3), while the corresponding reaction involving the electron-poor porphyrin **T^FPP** is completed after 20 min (entry 10−2). Triphenylcorrole **TPCorrole** forms quantitatively the Ag(III) complex after 30 min (entry 10−4), another indication for the unusually facile oxidation of the silver to its unusually high oxidation state imposed upon it by the ligand.[32] We attribute the negative result James and co-workers reported for their attempt to insert silver into **TPP** primarily to their using an insufficient amount (1 equiv) of Ag(OAc).[15b]

Palladium(II) and platinum(II) (hydro)porphyrins have found multiple uses as photosensitizers,[33] optical oxygen sensors,[34] or photocatalysts.[35] Their preparation involves the use of Pd(II) and Pt(II) salts under high temperature conditions.[10,12b] Surprisingly, therefore, the mechanochemical insertion of Pd(II) into **TPP**, **T^FPP**, and **OEP** is relatively effortless (entries 10−5 through 10−10), but completion of the reaction cannot always be achieved within 60 min under the standard conditions tested. The influences of the reactivity of the porphyrin observed for other metals (not involving a redox reaction as part of the metal insertion) are preserved: **OEP** inserts faster than **TPP** that is much faster than **T^FPP**. A conclusion of whether $PdCl_2$ or $Pd(OAc)_2$ is a generally better (faster) metal source cannot be derived.

Both Cd(II) and Pb(II) can be inserted into porphyrins (heating of the porphyrin and the corresponding salts in pyridine or DMF), albeit the resulting metalloporphyrins are, by virtue of the large metal ions, not sitting in the plane of the porphyrin,[36] rather sensitive to acid-induced demetalations.[10,14] None of the porphyrins tested showed any sign that Cd(II) or Pb(II) could be inserted mechanochemically (entries 10−11 to 10−14).

Particularly the solution state insertion of the kinetically rather inert Pt(II) into porphyrins requires extended periods of high heat or forcing microwave conditions.[10,12b,15c] In light of this, the 40% insertion of Pt(II) into **TPP** after 60 min grinding using 2.5 equiv of $PtCl_2$ with or without the addition of a solid base is remarkable. However, we did not attempt to optimize this mechanochemical insertion reaction, but nonetheless like to point out its promise.

■ SUMMARY AND CONCLUSIONS

This work began to lay out for the practitioner the scope and limits of using a planetary ball mill for the mechanochemical insertion of a range of metal ions into porphyrins as an alternative to traditional solution-based methods. We tested a wide range of porphyrins, metals, and metal sources and detailed the influences of porphyrins, metal salts, time, grinding additives, and, in some cases, bases, on the outcome of the reactions. We thereby much extended precedent work.[15b] A solid acid-induced mechanochemical removal of zinc from zinc porphyrins could also be accomplished.

Given the ostensibly simple mechanochemical reactions under investigation, their details proved to be surprisingly complex. Some findings have significance for the fundamental mechanisms underlying mechanochemical metal insertion reactions, but some findings must remain unexplained. Perhaps the easiest to understand are the influences of the porphyrin: the more basic, the easier (i.e., faster) is the metal insertion.

The influence of the metal ion source (anion influence) is often straightforward for a given metal but not readily explained, or therefore predictable, across different metals. In some cases, the more basic anion acetate is more advantageous to use than the less basic chloride, but in other cases the reverse is true.

A number of metal ions are suitable to be inserted mechanochemically, whereby their ease of insertion roughly correlates with the severity of the classic solution state insertion reaction conditions. Nonetheless, distinct differences in the corresponding solution state reactions are notable. For instance, in the solution state, copper ions at neutral conditions do not compete the zinc out of zinc porphyrins, but in the solid state reactions this is readily accomplished. Also, Mg(II) porphyrins can be formed under unusually mild conditions by grinding a porphyrin together with common magnesium sources but needing a specific insertion mediator—the magnesium silicate Florisil. The group 10 metals Pd(II) and Pt(II) are also notoriously hard to insert into porphyrins, but they inserted under comparably mild mechanochemical reaction conditions, albeit an optimization of these reactions was not attempted.

Perhaps the most enigmatic factors involve the influence of the grinding reagents. While they provide some practical advantages with respect to product retrieval and mixing efficiencies, particularly when running small scale reactions, many are not at all inert. While some, depending on their nature, stunt or accelerate the metal insertion reactions, some lead over time also to an extensive mechanochemical degradation of the porphyrin. Others, like Florisil, are obligatory for the insertion of magnesium. This suggests that a judicious choice of grinding reagent needs to be made to balance all their inherent advantages and disadvantages. At this point, their positive or negative influences cannot be predicted and would need to be determined experimentally. This clearly highlights that much still remains to be understood regarding mechanochemical syntheses.[1,2] However, the study also demonstrates that mechanochemical methods clearly possess potential for the insertion of metals into porphyrins.

EXPERIMENTAL SECTION

Materials. All solvents and reagents (Aldrich, Acros) were used as received. **TPP**,[37] **T^{F}PP**,[38] **OEP**,[39] **ETIO-I**,[40] **PPIX-DME**,[41] ***meso*-TPCorrole**,[42] **T(^{2}Thiop)P**,[43] **T(^{3}Thiop)P**,[43b] **(OH)$_2$TPC**,[27a] and **(OH)$_2$T^{F}PC**[27b] were prepared as described in the literature, were sourced from commercial suppliers, or were gifted to us. The known metalloporphyrins that were used as comparison materials were prepared by metal insertions into the corresponding free base chromophores using traditional methods.[10]

Analytical (aluminum backed, silica gel 60, 250 μm thickness) and preparative (20 × 20 cm, glass backed, silica gel 60, 500 μm thickness) TLC plates and standard grade, 60 Å, 32−63 μm flash column silica gel were used. Additives: silica gel (Sorbent Technologies, USA; particle size, 40−75 μm; surface area, 450−550 m^2/g; pH, 6.0−7.0), quartz sand (sea sand, washed, Aldrich, particle size 0.1−0.315 mm, pH of 400 g/L slurry 5−8; slurry), silica-NH_2 (Si-WAX from Silicycle, Canada; propylamine-functionalized silica gel, $pK_a = 9.8$, particle size: 40−63 μm), neutral alumina, Brock activity I (Sorbent Technologies, USA; particle size: 50−200 μm), basic alumina, Brock activity I (Sorbent Technologies, USA; particle size: 50−200 μm), acidic alumina, Brock activity I (M. Woelm, Germany), montmorillonite (Aldrich, USA; 250 m^2/g, pH 3−4), sodium chloride (Aldrich, USA), cellulose powder (Macherey, Nagel & Co., Germany; MN 300), Florisil (Aldrich, USA; 100−200 mesh), talc (Aldrich, 10 μm powder), calcite (Educational Innovations; Iceland spar, crystals of multicm dimensions), and Dowex HCR-W2, H^+-form (J.T. Baker, USA; spherical beads, 16−40 mesh).

All metal salts were sourced from commercial suppliers and were reagent grade, or better.

Instruments. A Fritsch GmbH, Germany, Pulverise planetary micro mill (Pulverisette 7 classic line) equipped with two agate grinding vessels was used in the milling experiment, with main disc speeds ranging from 100 to 800 rpm. Small vessel A: volume 12.5 mL, equipped with five agate balls (10 mm), total weight ~7.0 g. Large vessel B: Inner dimensions were 45 mm diameter, 37 mm height, volume 50 mL, equipped with eight agate balls (10 mm) with a total weight of ~13.6 g (for additional information, see Supporting Information).

HPLC (Agilent 1100 Series) equipped with a Grace analytical normal-phase Apollo silica column (4.6 × 250 mm, 5 μm). Samples were dissolved in ethyl acetate prior to injection. Detection wavelength was set to 400 nm.

UV−vis spectra were recorded on a Varian Cary 50 spectrophotometer in the solvents indicted.

Typical Procedure. In a typical experiment, a 50 mL agate grinding jar equipped with eight 10 mm agate balls was charged with 12.0 mg of free base porphyrin, the appropriate equivalents of divalent metal ion source, and a solid additive (500 mg; 1:42 (w/w) ratio of with respect to the free base porphyrin). This mixture was milled in a planetary ball mill at the disc speeds indicated (typically 800 rpm) for the time indicated. During this time, aliquots were retrieved at different time intervals to monitor the progress of the reaction. These aliquots were placed into a small pipet with a cotton plug and extracted with CH_2Cl_2, and the eluent was analyzed by TLC (silica gel), UV−vis spectrophotometry, or HPLC, as appropriate.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.inorgchem.9b00052.

> Details to the ball mill used, experimental details, and a reproduction of a number of representative TLCs, UV−vis spectra, and HPLC traces used in the compilation of the data tables (PDF)

AUTHOR INFORMATION

Corresponding Author

*Tel.: +01 (860) 486-2743. E-mail: c.bruckner@uconn.edu.

ORCID

Adewole O. Atoyebi: 0000-0002-9495-5072
Christian Brückner: 0000-0002-1560-7345

Author Contributions

The manuscript was written through contributions of both authors; both have also given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

Funding for this work was provided by the U.S. National Science Foundation (NSF) through grants CHE-1465133 and CHE-1800631. We thank David Dolphin, University of British Columbia, and Chi-Kwong (Chris) Chang, Michigan State University, for a donation of the octaalkylporphyrins used in this study.

■ REFERENCES

(1) James, S. L.; Adams, C. J.; Bolm, C.; Braga, D.; Collier, P.; Friščić, T.; Grepioni, F.; Harris, K. D. M.; Hyett, G.; Jones, W.; Krebs, A.; Mack, J.; Maini, L.; Orpen, A. G.; Parkin, I. P.; Shearouse, W. C.; Steed, J. W.; Waddell, D. C. Mechanochemistry: Opportunities for New and Cleaner Synthesis. *Chem. Soc. Rev.* **2012**, *41*, 413−447.

(2) (a) Walsh, P. J.; Li, H.; de Parrodi, C. A. A Green Chemistry Approach to Asymmetric Catalysis: Solvent-Free and Highly Concentrated Reactions. *Chem. Rev.* **2007**, *107*, 2503−2545. (b) Howard, J. L.; Cao, Q.; Browne, D. L. Mechanochemistry as an Emerging Tool for Molecular Synthesis: What Can It Offer? *Chem. Sci.* **2018**, *9*, 3080−3094. (c) Takacs, L. The Historical Development of Mechanochemistry. *Chem. Soc. Rev.* **2013**, *42*, 7649−7659. (d) Baláž, P. *Mechanochemistry in Nanoscience and Minerals Engineering*; Springer-Verlag: Berlin, 2008.

(3) Toda, F. Solid State Organic Chemistry: Efficient Reactions, Remarkable Yields, and Stereoselectivity. *Acc. Chem. Res.* **1995**, *28*, 480−486.

(4) (a) Mottillo, C.; Friščić, T. Advances in Solid-State Transformations of Coordination Bonds: From the Ball Mill to the Aging Chamber. *Molecules* **2017**, *22*, 144. (b) Garay, A. L.; Pichon, A.; James, S. L. Solvent-Free Synthesis of Metal Complexes. *Chem. Soc. Rev.* **2007**, *36*, 846−855.

(5) Barona-Castaño, C. J.; Carmona-Vargas, C. C.; Brocksom, J. T.; de Oliveira, T. K. Porphyrins as Catalysts in Scalable Organic Reactions. *Molecules* **2016**, *21*, 310.

(6) Chandra, R.; Tiwari, M.; Kaur, P.; Sharma, M.; Jain, R.; Dass, S. Metalloporphyrins—Applications and Clinical Significance. *Indian J. Clin. Biochem.* **2000**, *15*, 183−199.

(7) Huang, H.; Song, W.; Rieffel, J.; Lovell, J. F. Emerging Applications of Porphyrins in Photomedicine. *Front. Phys.* **2015**, *3*, 23.

(8) Jurow, M.; Schuckman, A. E.; Batteas, J. D.; Drain, C. M. Porphyrins as Molecular Electronic Components of Functional Devices. *Coord. Chem. Rev.* **2010**, *254*, 2297−2310.

(9) Hedley, G. J.; Ruseckas, A.; Samuel, I. D. W. Light Harvesting for Organic Photovoltaics. *Chem. Rev.* **2017**, *117*, 796−837.

(10) (a) Buchler, J. W. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. *1*, pp 389−483. (b) Sanders, J. K. M.; Bampos, N.; Clyde-Watson, Z.; Darling, S. L.; Hawley, J. C.; Kim, H.-J.; Mak, C. C.; Webb, S. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000; Vol. 3, pp 1−48.

(11) Longo, F. R.; Brown, E. M.; Rau, W. G.; Adler, A. D. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. *5*, pp 459−481.

(12) (a) Buchler, J. W.; Ng, D. K. P. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Elsevier, 2000; Vol. 3, pp 245−294. (b) Buchler, J. W.; Dreher, C.; Künzel, F. M. Synthesis and Coordination Chemistry of Noble Metal Porphyrins. *Struct. Bonding (Berlin)* **1995**, *84*, 1−69. (c) Buchler, J. W. In *Porphyrins and Metalloporphyrins* Elsevier Scientific Pub. Co., 1975; pp 157−231.

(13) (a) Dailey, H. A.; Dailey, T. A. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2003; Vol. *12*, pp 93−121. (b) Sigfridsson, E.; Ryde, U. The Importance of Porphyrin Distortions for the Ferrochelatase Reaction. *JBIC, J. Biol. Inorg. Chem.* **2003**, *8*, 273−282.

(14) Adler, A. D.; Longo, F. R.; Kampas, F.; Kim, J. On the Preparation of Metalloporphyrins. *J. Inorg. Nucl. Chem.* **1970**, *32*, 2443−2445.

(15) (a) Lindsey, J. S.; Woodford, J. N. A Simple Method for Preparing Magnesium Porphyrins. *Inorg. Chem.* **1995**, *34*, 1063−1069. (b) Ralphs, K.; Zhang, C.; James, S. L. Solventless Mechanochemical Metallation of Porphyrins. *Green Chem.* **2017**, *19*, 102−105. (c) Dean, M. L.; Schmink, J. R.; Leadbeater, N. E.; Brückner, C. Microwave-Promoted Insertion of Group 10 Metals into Free Base Porphyrins and Chlorins: Scope and Limitations. *Dalton Trans* **2008**, 1341−1345. (d) Peters, M. K.; Herges, R. Insertion of Ni(I) into Porphyrins at Room Temperature: Preparation of Ni(II)Porphyrins, and Ni(II)-Chlorins and Observation of Hydroporphyrin Intermediates. *Inorg. Chem.* **2018**, *57*, 3177−3182.

(16) Do, J.-L.; Mottillo, C.; Tan, D.; Štrukil, V.; Friščić, T. Mechanochemical Ruthenium-Catalyzed Olefin Metathesis. *J. Am. Chem. Soc.* **2015**, *137*, 2476−2479.

(17) Abramoff, B.; Klein, L. C. Mechanical Properties of Silica Xerogels. *J. Am. Ceram. Soc.* **1991**, *74*, 1469−1471.

(18) Stone, A.; Fleischer, E. B. The Molecular and Crystal Structure of Porphyrin Diacids. *J. Am. Chem. Soc.* **1968**, *90*, 2735−2748.

(19) Datta-Gupta, N.; Malakar, D.; Jones, V. O.; Wright, T. A Simple Methods for the Determination of pK_3 Values of Porphyrins. *Chem. Lett.* **1986**, *15*, 1659−1662.

(20) Yu, Y.; Lv, H.; Ke, X.; Yang, B.; Zhang, J.-L. Ruthenium-Catalyzed Oxidation of the Porphyrin *β*,*β*′-Pyrrolic Ring: A General and Efficient Approach to Porpholactones. *Adv. Synth. Catal.* **2012**, *354*, 3509−3516.

(21) (a) Gouterman, M.; Hall, R. J.; Khalil, G. E.; Martin, P. C.; Shankland, E. G.; Cerny, R. L. Tetrakis(Pentafluorophenyl)-Porpholactone. *J. Am. Chem. Soc.* **1989**, *111*, 3702−3707. (b) Ke, X.-S.; Chang, Y.; Chen, J.-Z.; Tian, J.; Mack, J.; Cheng, X.; Shen, Z.; Zhang, J.-L. Porphodilactones as Synthetic Chlorophylls: Relative Orientation of *β*-Substituents on a Pyrrolic Ring Tunes NIR Absorption. *J. Am. Chem. Soc.* **2014**, *136*, 9598−9607. (c) Hewage, N.; Daddario, P.; Lau, K. S. F.; Guberman-Pfeffer, M. J.; Gascón, J. A.; Zeller, M.; Lee, C. O.; Khalil, G. E.; Gouterman, M.; Brückner, C. Bacterio- and Isobacterio-Dilactones by Stepwise or Direct Oxidations of *meso*-Tetrakis(pentafluorophenyl)porphyrin. *J. Org. Chem.* **2019**, *84*, 239−256.

(22) (a) Inhoffen, H. H.; Nolte, W. Oxidative Umlagerungen am Octaäthylporphyrin zu Geminiporphin-Polyketonen. *Liebigs Ann. Chem.* **1969**, *725*, 167−176. (b) Sharma, M.; Meehan, E.; Mercado, B. Q.; Brückner, C. *β*-Alkyloxazolochlorins: Revisiting the Ozonation of Octaalkylporphyrins, and Beyond. *Chem. - Eur. J.* **2016**, *22*, 11706−11718.

(23) Kleine, T.; Buendia, J.; Bolm, C. Mechanochemical Degradation of Lignin and Wood by Solvent-Free Grinding in a Reactive Medium. *Green Chem.* **2013**, *15*, 160−166.

(24) Zhang, K.; Huang, J.; Zhang, W.; Yu, Y.; Deng, S.; Yu, G. Mechanochemical Degradation of Tetrabromobisphenol A: Performance, Products and Pathway. *J. Hazard. Mater.* **2012**, *243*, 278−285.

(25) Smith, K. M. Protoporphyrin IX: Some Recent Research. *Acc. Chem. Res.* **1979**, *12*, 374−381.

(26) (a) Chen, W.; Wang, Y.; Brückner, C.; Li, C. M.; Lei, Y. Poly[*meso*-Tetrakis(2-thienyl)porphyrin] for the Sensitive Electrochemical Detection of Explosives. *Sens. Actuators, B* **2010**, *B147*, 191−197. (b) Chen, W.; Ding, Y.; Akhigbe, J.; Brückner, C.; Li, C. M.; Lei, Y. Enhanced Electrochemical Oxygen Reduction-Based Glucose Sensing Using Glucose Oxidase on Nanodendritic Poly[*meso*-tetrakis(2-thienyl)porphyrinato]cobalt(II)-SWNT Composite Electrodes. *Biosens. Bioelectron.* **2010**, *26*, 504−510. (c) Chen, W.; Akhigbe, J.; Brückner, C.; Li, C. M.; Lei, Y. Electrocatalytic Four-Electron Reduction of Dioxygen by Electrochemically Deposited Poly{[*meso*-tetrakis(2-thienyl)porphyrinato]cobalt(II)}. *J. Phys. Chem. C* **2010**, *114*, 8633−8638.

(27) (a) Brückner, C.; Rettig, S. J.; Dolphin, D. Formation of a *meso*-Tetraphenylsecochlorin and a Homoporphyrin with a Twist. *J. Org. Chem.* **1998**, *63*, 2094−2098. (b) Hyland, M. A.; Morton, M. D.; Brückner, C. *meso*-Tetra(pentafluorophenyl)porphyrin-Derived Chromene-Annulated Chlorins. *J. Org. Chem.* **2012**, *77*, 3038−3048.

(28) Datta-Gupta, N.; Malakar, D.; Datta-Gupta, S.; Gibson, R. Kinetics of Copper(II) Incorporation in a Porphyrin Using Four Copper Salts. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2339−2340.

(29) (a) Brückner, C.; Briñas, R. P.; Krause Bauer, J. A. X-Ray Structure and Variable Temperature NMR Spectra of [*meso*-Triarylcorrolato]copper(III). *Inorg. Chem.* **2003**, *42*, 4495−4497. (b) Will, S.; Lex, J.; Vogel, E.; Schmickler, H.; Gisselbrecht, J.-P.; Haubtmann, C.; Bernard, M.; Gorss, M. Nickel and Copper Corroles: Well-Known Complexes in a New Light. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 357−361. (c) Lu, G.; Lin, W.; Fang, Y.; Zhu, W.; Ji, X.; Ou,

DOI: 10.1021/acs.inorgchem.9b00052

Z. Synthesis and Electrochemical Properties of *meso*-Phenyl Substituted Copper Corroles: Solvent Effect on Copper Oxidation State. *J. Porphyrins Phthalocyanines* **2011**, *15*, 1265−1274. (d) Bröring, M.; Brégier, F.; Cónsul Tejero, E.; Hell, C.; Holthausen, M. C. Revisiting the Electronic Ground State of Copper Corroles. *Angew. Chem., Int. Ed.* **2007**, *46*, 445−448.

(30) Strohmeier, M.; Orendt, A. M.; Facelli, J. C.; Solum, M. S.; Pugmire, R. J.; Parry, R. W.; Grant, D. M. Solid State ^{15}N and ^{13}C NMR Study of Several Metal 5,10,15,20-Tetraphenylporphyrin Complexes. *J. Am. Chem. Soc.* **1997**, *119*, 7114−7120.

(31) Brückner, C. The Silver Complexes of Porphyrins, Corroles and Carbaporphyrins: Silver in the Oxidation States + II and + III. *J. Chem. Educ.* **2004**, *81*, 1665−1670.

(32) Brückner, C.; Barta, C. A.; Briñas, R. P.; Krause Bauer, J. A. Synthesis and Structure of [*meso*-Triarylcorrolato]Silver(III). *Inorg. Chem.* **2003**, *42*, 1673−1680.

(33) Brandis, A. S.; Salomon, Y.; Scherz, A. In *Chlorophylls and Bacteriochlorophylls*; Grimm, B., Porra, R. J., Rüdinger, W., Scheer, H., Eds.; Springer: Dordrecht, NL, 2006; pp 485−494.

(34) (a) Papkovsky, D. B.; Ponomarev, G. V.; Wolfbeis, O. S. Longwave Luminescent Porphyrin Probes. *Spectrochim. Acta, Part A* **1996**, *52A*, 1629−1638. (b) Briñas, R. P.; Troxler, T.; Hochstrasser, R. M.; Vinogradov, S. A. Phosphorescent Oxygen Sensor with Dendritic Protection and Two-Photon Absorbing Antenna. *J. Am. Chem. Soc.* **2005**, *127*, 11851−11862.

(35) To, W.-P.; Liu, Y.; Lau, T.-C.; Che, C.-M. A Robust Palladium(II)−Porphyrin Complex as Catalyst for Visible Light Induced Oxidative C−H Functionalization. *Chem. - Eur. J.* **2013**, *19*, 5654−5664.

(36) Barkigia, K. M.; Fajer, J.; Adler, A. D.; Williams, G. J. B. Crystal and Molecular Structure of (5,10,15,20-Tetra-*N*-propylporphinato)-lead(II): A "Roof" Porphyrin. *Inorg. Chem.* **1980**, *19*, 2057−2061.

(37) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. A Simplified Synthesis for TPP. *J. Org. Chem.* **1967**, *32*, 476.

(38) Spellane, P. J.; Gouterman, M.; Antipas, A.; Kim, S.; Liu, Y. C. Electronic Spectra and Four-Orbital Energies of Free-Base, Zinc, Copper, and Palladium Tetrakis(perfluorophenyl)porphyrins. *Inorg. Chem.* **1980**, *19*, 386−391.

(39) (a) Sessler, J. L.; Mozaffari, A.; Johnson, M. R. 3,4-Diethylpyrrole and 2,3,7,8,12,13,17,18-Octaethylporphyrin. *Org. Synth.* **1992**, *70*, 68−78. (b) Paine, J. B., III; Kirshner, W. B.; Moskowitz, D. W.; Dolphin, D. An Improved Synthesis of Octaethylporphyrin. *J. Org. Chem.* **1976**, *41*, 3857−3860.

(40) Smith, K. M.; Eivazi, F. Synthesis of Etioporphyrin by Monopyrrole Tetramerization. *J. Org. Chem.* **1979**, *44*, 2591−2592.

(41) Linn, J. A.; Schreiner, A. F. A Convenient Small Scale Synthesis of Protoporphyrin IX Dimethyl Ester from Hemin. *Inorg. Chim. Acta* **1979**, *35*, L339−L340.

(42) Briñas, R. P.; Brückner, C. Triarylcorroles by Oxidative Coupling of Triaryltetrapyrranes. *Synlett* **2001**, *2001*, 442−444.

(43) (a) Ono, N.; Miyagawa, H.; Ueta, T.; Ogawa, T.; Tani, H. Synthesis of 3,4-Diarylpyrroles and Conversion into Dodecaarylporphyrins; a New Approach to Porphyrins with Altered Redox Potentials. *J. Chem. Soc., Perkin Trans. 1* **1998**, *1*, 1595−1601. (b) Bhyrappa, P.; Bhavana, P. *meso*-Tetrathienylporphyrins: Electrochemical and Axial Ligand Properties. *Chem. Phys. Lett.* **2001**, *349*, 399−404.