Research Note

Studies on the Mechanochemically Induced Chromene-annulation of meso-Tetrakis(pentafluorophenyl)-2,3-dihydroxychlorin: Non-Innocence of the Grinding Aids

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ABSTRACT: The modification of chlorins to fine-tune their optical properties is important for their application in medical and technical fields. The solution phase, base-induced formation of a chromene-annulated chlorin from the corresponding *meso*-tetrakis(pentafluorophenyl)-2,3-dihydroxychlorin by intramolecular S_NAr displacement of an *o*-F atom of a *meso*-aryl group by an adjacent hydroxy group is well-known. Organic transformations performed by grinding the dry reagents together promise to be a much greener and possibly simpler method compared to traditional solution-based reactions. However, the use of such mechanochemical approaches to accomplish porphyrinoid chromophore modifications are virtually unexplored. We report here the translation of the solution-based base-induced formation of a chromene-annulated chlorin to a solid state mechanochemical reaction in a planetary powder mill. The factors determining the success (and failure) of the reaction are delineated. While this report shows that porphyrinoid framework modifications can principally be induced mechanochemically, the mechanochemical reaction is not (yet) competitive with the solution state reaction. The outcome of the reaction is very sensitive to the particular milling conditions, specifically the grinding aids used. What we previously believed to be inert or merely basic aids affected the significant degradation of the porphyrin/chlorin under the milling conditions, a finding that might limit mechanochemical approaches in porphyrinoid chemistry.

KEYWORDS: mechanochemical syntheses, *meso*-arylporphyrins, chlorin modifications, annulated chlorins

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INTRODUCTION

Hydroporphyrins – primarily chlorins and bacteriochlorins, are nature's photosynthetic pigments [1-3]. The ability of the hydroporphyrins to harvest light energy to ultimately drive the reduction of CO_2 to carbohydrates makes hydroporphyrins very attractive pigments to study in artificial light harvesting systems [4-7]. Their capacity to photosensitize oxygen with red or NIR light makes them also attractive as photochemotherapeutics [8-12]. Moreover, their bright fluorescence emissions suggest their use as imaging agents, optical labels, or in chemosensing systems [13].

The conversion of *meso*-tetraarylporphyrins to hydroporphyrins has been amply studied [3,14,15], including the regio- and stereo-chemistry underlying a number of conversions [16-18]. Examples include the diimide reduction of *meso*-tetraarylporphyrin to produce chlorin **1** [19-22], a number of 1,3-dipolar addition reactions to generate chlorins **2**, **3**, or the corresponding bacterio- and isobacterio-chlorin-type bis-adducts, such as bacteriochlorin **4** [17,23-28] (Figure 1). Once established, options to further modulate the hydroporphyrin chromophore in subsequent reactions exist [29,30].

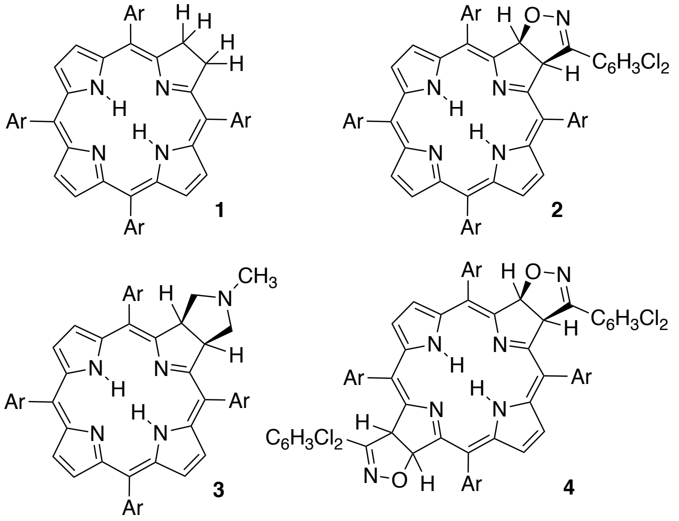
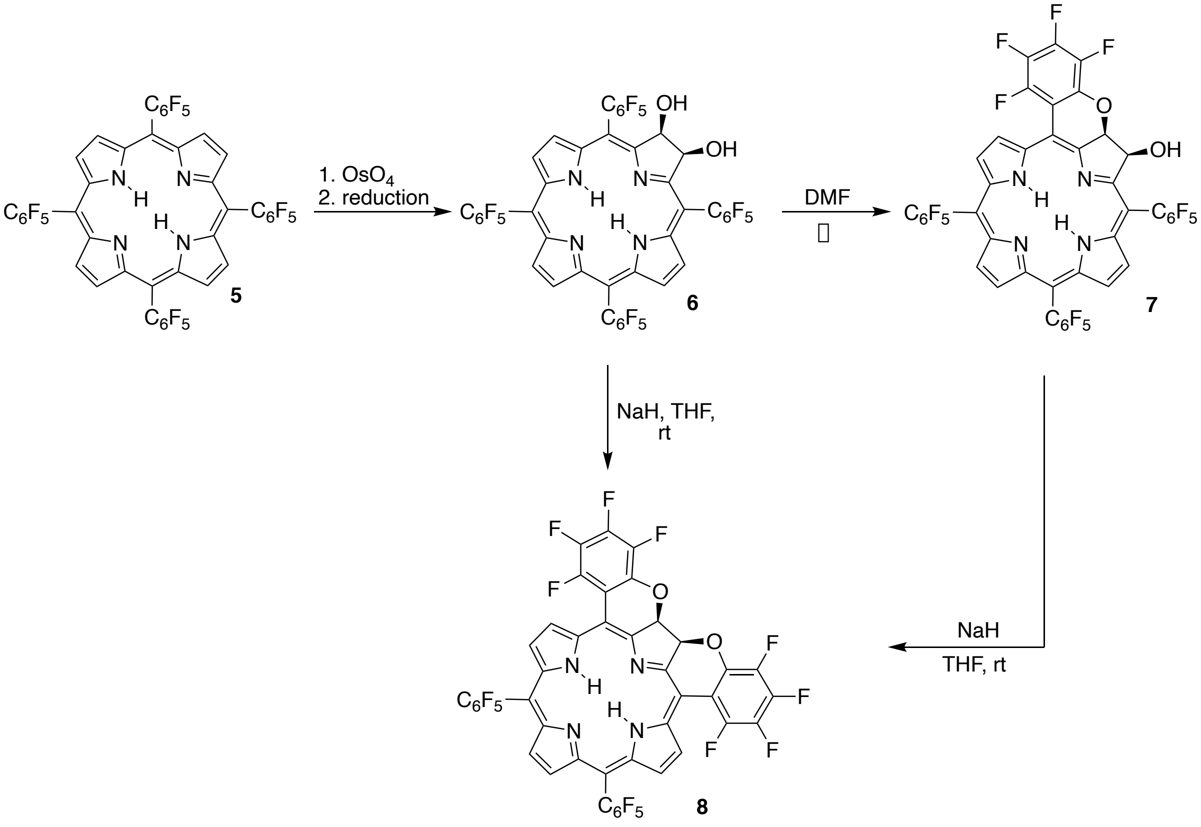


Figure 1. Examples of literature-known synthetic chlorins.

We [31,32], and others [33,34], described the OsO_4-mediated dihydroxylation of *meso*-arylporphyrins, such as *meso*-tetrakis(pentafluorophenyl)porphyrin **5** [35], to generate the corresponding 2,3-*vic*-dihydroxychlorin **6** (Scheme 1) and tetrahydroxybacteriochlorins (not shown). We further presented a number of functional group conversions of the dihydroxypyrroline moieties to, e.g., oxazole, imidazolone, or morpholine building blocks, thus generating hydroporphyrin analogues [36,37]. We also reported a way to tune the optical properties of 2,3-dihydroxychlorin **6** by treatment in hot DMF [35]. This induced an intramolecular S_NAr reaction between one of the diol hydroxy groups and the *o*-F-atoms of the flanking *meso*-C_6F_5 group, forming chromene-annulated chlorin **7** (Scheme 1) [35]. Using a strong base, bis-annulation could be affected also, forming bis-annulated chlorin **8** [35]. A similar intramolecular formation of an annulated chromene was also observed in other chlorins [29] and a hexaphyrin [38]. The products resulting from the mono- and bis-annulation of the two stereoisomers of the tetrahydroxybacteriochlorins were also studied [39]. Further (oxidative) modifications of **7** were reported [30].



Scheme 1. Syntheses of chlorin diol **6** by OsO_4-mediated dihydroxylation of a *meso*-tetraarylporphyrin **5** [32], and generation of chromene-annulated chlorins **7** and **8** [35].

Like other chromophores containing β-to-*o*-phenyl linkages [40], the longest wavelength absorbance band of the mono-annulated chlorin **7** is red-shifted compared to the spectrum of the parent chlorin **6** (by 16 nm); for the bis-annulated chlorin **8**, a shift of 24 nm was recorded [35]. These modestly shifted bathochromic optical spectra were rationalized by a combination of the modulation of the chromophore conformation, induced by the annulation reaction, and the increased π-overlap between the phenyl group and chlorin chromophore resulting from the smaller dihedral angle between them [41,42].

Mechanochemistry broadly refers to chemical syntheses where reactant activation is induced by mechanical force [43-47]. One mechanochemical approach employs a powder mill in which the dry reagents are intensely ground together to affect their reaction. Possible advantages of such solid-state reactions over conventional solution-based reactions are the avoidance of a reaction solvent, decreased reaction times, access to different reaction pathways, or the absence of added heat [43-48]. The lack of a reaction solvent circumvents the health or environmental hazards and energy costs associated with the handling, heating, cooling, and removal of solvents, respectively. Albeit some mechanochemical reactions may be able to avoid solvents altogether, it must be noted that many reactions run in the mill will still use solvents in subsequent product isolation and purification steps [49]. Nonetheless, the mechanochemical approach may still represent a greener alternative to corresponding solution-based reactions.

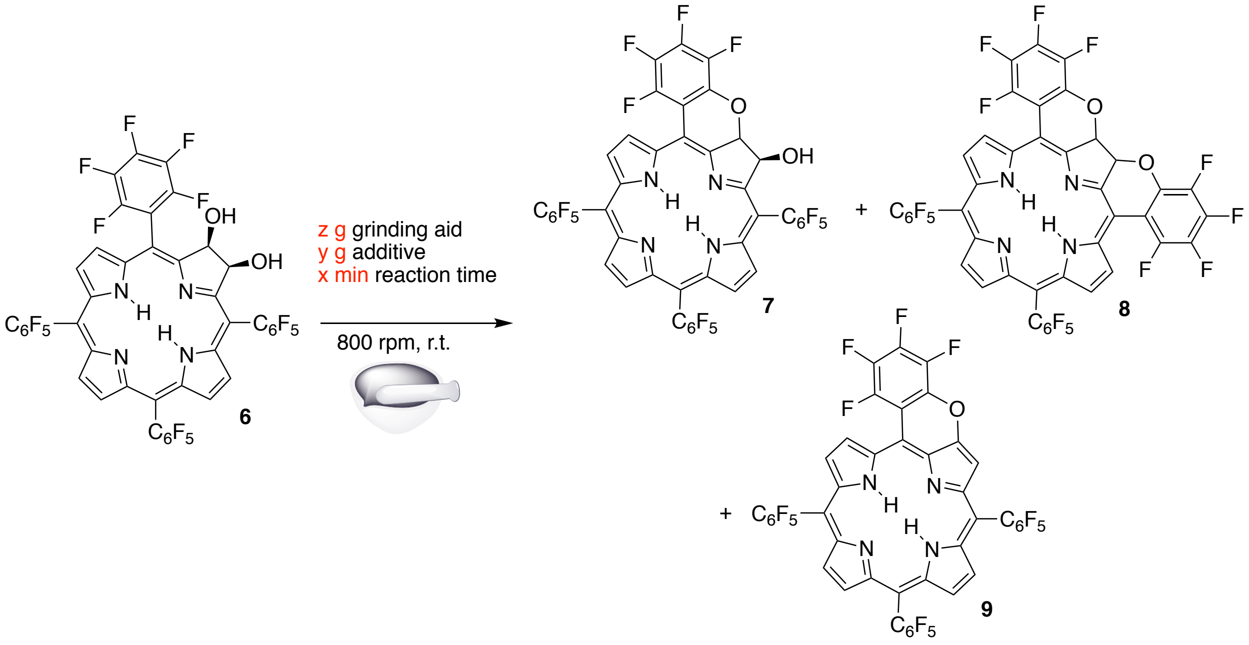
As a consequence of their potential advantages, syntheses under mechanochemical conditions in ball mills have found broad applications in organic and inorganic syntheses [43-46,48-54]. Yet, mechanochemical approaches in porphyrin chemistry are rare: The principle applicability of a ball mill to synthesize *meso*-tetraphenylporphyrin [55] and to insert a range of transition metals into *meso*-tetraphenylporphyrin was shown [49]. Later, we studied the experimental parameters for the use of a planetary ball mill in the mechanochemical insertion of primarily zinc(II), copper(II), and magnesium(II) using the corresponding M(II) salts into a range of free base porphyrins in detail [52], as well as reported on the use of $Co_2(CO)_8$ for the mechanochemical insertion of cobalt(II) [54].

An important parameter in ball mill reactions is the use of (inert) grinding aids. They help to create homogeneity and to bring about critical energy transfer from the mill/balls to the reagents. Frequently, their use is also employed when at least one of the reaction components is a liquid or if the reaction generates a by-product that results the mixture to become sticky. These grinding aids are usually intended to be chemically inert [45]. However, in all cases studied by us, it became quickly clear that the influences of the experimental parameters, including the grinding aids used, were complex; most critically, our findings suggested the grinding aids to be not as innocent as initially believed [49,52,54]. In fact, this non-innocence of the ‘grinding aid’ can also be exploited to either drive reductions (by the substrate) and formation of metal nanoparticles from precursor compounds [47] or affect piezo-electrical electron transfer catalysis [56].

We report here on our investigation on the suitability of a planetary ball mill to induce the annulation of chlorin **6** to form the chromene-annulated products **7** or **8** as a prototype mechanochemically driven organic porphyrin framework transformation. We will report the outcome of varying the mechanochemical conditions, grinding aids, and additives. While we will show that the reaction can indeed be induced mechanochemically and that the optimization of the reaction follows somewhat chemical intuition, we ultimately failed to identify mechanochemical reaction conditions that are in terms of yields superior or even equal to the corresponding solution state reactions. Thus, we will not be able to offer a practical mechanochemical alternative to the corresponding solution state reaction. Instead, the study expands on our earlier observations about the non-inert nature of a number of grinding aids – an aspect generally not much elaborated on in the current mechanochemical literature. Thereby, this report highlights the limitations of translating seemingly straight-forward solution state reactions in porphyrin chemistry to mechanochemical conditions.

RESULTS AND DISCUSSION

We set out a series of experiments in which we milled chlorin **6** in the presence of different (basic) grinding aids, additional bases, and various milling times (Scheme 2). We kept the milling conditions (i.e., milling speed, 50 mL agate milling vessel and number and size of agate balls, and the ambient reaction temperature constant). We screened the progress of the reaction using TLC of a extract from an aliquot of the reaction mixture taken in intervals and estimated from this the conversion of the starting material and/or the formation of the desired chromene-annulated products **7** and **8**. In select cases, we quantitatively extracted all porphyrins and, following their chromatographic purification, determined their yields gravimetrically. The key findings of our investigation are tabulated below (Table 1).



Scheme 2. Syntheses of chromene-annulated chlorins under mechanochemical conditions; the experimental variables are indicated in red.

To avoid the gummy masses that formed during milling experiments of porphyrins as pure compounds, solid grinding aids were added. The ideal solid grinding aid is inert and forms free-flowing powders with the reactants/products. This assure proper mixing and the minimization of dead reaction space issues: the standard ‘small-scale’ commercial planetary mills use reaction vessels that are too large (minimum in our system, 25 mL) for the small scale (10 to 100 mg) porphyrin reactions which are typically performed in our laboratory. In the absence of the added grinding aids, the bulk of the porphyrins (and reagents) get trapped in the dead space of the vessels as the balls do not reach into the corners of the cylindrically shaped reaction vessels. However, our experience has shown (see below) that because of the ‘stickiness’ of very finely ground powders, dead space issues are not entirely eliminated, even when dry or in the presence of a grinding aid.

Importantly, the acid-base properties of the grinding aids have been shown to have a significant effect on metal insertion reactions into porphyrins [52,54], demonstrating that they are much more than mere mechanical aids. This may be important in the conversion of diol **6** to the chromene-annulated chlorins **7** or **8**. For one, the reaction generates one or two equivalents of HF, respectively. The solution-state reaction is also base-induced, presumably because the base deprotonates the alcohol moiety to render it more nucleophilic toward replacement of the *o*-F atom along an $\mathrm{S_NAr}$ reaction trajectory; the base then also captures the HF. Next to the use of intrinsically basic grinding aids, we also tested the addition of solid organic and inorganic bases to ‘neutral’ grinding aids.

Entry No.	**Grinding Aid**[a]	**Base Additive**	**Reaction Time [min]**	**Product(s)**	**% Conversion of Starting Diol 6**[b] **(Isolated Yield of product)**
1	silica gel	with or without LiOH (10 mg)	75	insoluble degradation product	> 95%[c]
2	CaO (activated,[d] or not)	none	50	**7** + traces of **8** and **9**	80% (27% **7** + 34% **6** recovered)[e]
3	CaO	LiOH (10 mg)	40	**7**	60%
4	CaO	KOH (10 mg)	60	**7**	50%
5	CaO[d]	DABCO (10 mg)	60	**7**	70%
6	MgO	none	40	**7** + polar side products	50%
7	MgO[d]	none	40	**7** + traces[g] of **8** and **9** + polar side products	70% (13.6% **7**)[f]
8	neutral Al_2O_3	none	60	**7** + non-polar and polar side products	25%
9	basic Al_2O_3 (activated,[d] or not)	with or without DABCO (10 mg)	60	**7** + insoluble product	< 5%
10	Li_2CO_3	none	20	**7** + traces[g] of **8** and **9** + polar side products	70%
11	Li_2CO_3	LiOH (10 mg)	40	**7** + polar side products	40%
12	Na_2CO_3	none	60	**7** + non-polar side products	40%
13	K_2CO_3	none	60	**7**	60%
14	Cs_2CO_3	none	60	**7** + side products	40%

[a] 0.5 g grinding aid at 10-30 mg scales of diol **6**

[b] Based on assessment of remaining starting material using TLC; estimated accuracy ±20%.

[c] Starting material not fully recoverable as early as 20 min into the reaction.

[d] Activated at 120 °C at high vacuum, 10 min.

[e] At 30 mg scale of **6**.

[f] At 25 mg scale of **6**.

[g] Visible using preparative plate chromatography of the entire quantitiy of the run.

The use of silica gel as a grinding aid alone failed to produce the target product, even after long milling time (75 min) (Entry 1). In fact, the starting diol degraded appreciably over time, forming an intractable, greyish product firmly adhering to the silica gelClearly, any colors associated with a porphyrinic chromophore were gone, indicating the possibility of chromophore carbonization [57]. We also observed this detrimental property of silica gel under powder mill conditions in our previous studies; we suspected that, perhaps, piezoelectric effects would play a role in this effective removal of the chromophore [52]. While the mechanistic origins remain to be fully understood, mechanochemical degradations of organic molecules on solid phases using mechanochemistry is well-known. For instance, the dehalogenation or complete destruction of, for example, environmental contaminants on clays or hydrocarbon to carbon conversions on silica gel in a mill are well-known; radicals have been implied in these reactions [58-60]. The addition of the solid, inorganic strong base LiOH (Entry 1) – chosen because it is less hygroscopic compared to KOH or NaOH – to silica gel did not change the outcome of the reaction.

Calcium(II) ions have a very high affinity for fluoride, forming CaF_2 [61]. CaO (quicklime) is a readily available solid base that can bind HF very effectively, albeit it is a relatively soft grinding aid (Mohs hardness of ~3.6) [62]. Indeed, CaO proved to be an effective grinding aid, affecting the conversion of diol **6** primarily to chromene-annulated product **7** and trace (< 3%) amounts of the bis-annulated chromene product **8** (Entry 2). After extraction of all CH_2Cl_2-soluble fractions and a preparative plate chromatographic separation of the product mixture, we observed the formation of a number of other products in small (< 5%) amounts, only one of which we were able to identify; it proved to be the dehydration product of target chlorin **7**, chromene annulated porphyrin **9**. This novel product was identified based on its diagnostic ^{1}H NMR, UV-vis spectroscopic properties, and composition, as tested by HR-MS (APCI+) (for details, see ESI). We previously observed the dehydration of the β,β'-dihydroxylated pyrroline moiety in hydroporphyrins to form a β-hydroxy-pyrrole moiety under thermal conditions [32,63].

However, while the solution state annulation reactions are resonably high-yielding (65% yield for **6** to **7**; 80-85% yield for the reaction using the Pd(II) and Pt(II) complexes of **6**) [35,39], the isolated yields of mono-annulated chlorin **7** remained disappointingly low in the mechanochemical reactions (Table 1). Furthermore, attempts to improve the yield of bis-chromene annulated product **8** by either increasing the reaction time or the relative ratio of CaO to chlorin **6** were not successful. The thermal activation of CaO prior to usage in the reaction also had little to no effect on the reaction yield or time to completion (Entry 2). The addition of solid mineral (LiOH, KOH) or organic base (1,4-diazabicyclo[2.2.2]octane (DABCO)) additives did not fundamentally improve the yield or accelerate the reaction either (Entries 3-5). From a practical point of view, the hygroscopic bases also made the handling and retrieving of the reaction mixtures from the reaction vessel difficult.

The time course of the reaction is shown in Figure 2. The percent conversion of diol **6** increases for about 80 min at the chosen grinding speed until it plateaus at about 80%. We we attribute this to the dead volume effect rather than the reaction reaching an equilibrium state or exhaustion of the base present. A relatively large fraction (estimated to be up to 20%) of the overall small amount of the very finely ground reaction mixture (510–530 mg) cakes up and gets immobilized in the dead space corners of the reaction vessels, not partaking in the grinding action. Thus, the analysis of a small sample from the bulk material suggested full consumption of the starting materials; this signaled the endpoint of the reactions and the quantitative removal and extraction of the reaction mixtures was undertaken. However, the subsequent chromatographic isolation showed the presence of a significant residual amount of the starting material.

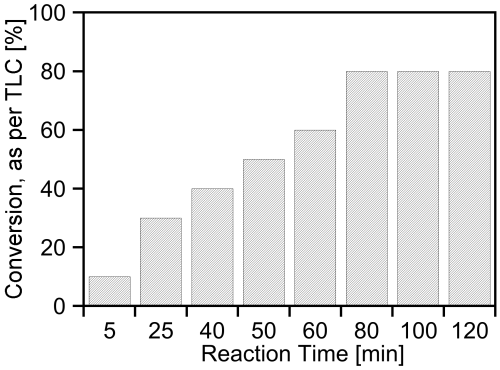


Figure 2. Time dependence of % conversion of diol chlorin **6**. *Conditions*: 0.5 g CaO, activated at 120 °C and high vacuum for 10 min, acting both as a base and grinding aid, no additive.

The dead space problem, however, is not the primary reason for the low yield. Upon completion of the reaction, the colorless CaO became a finely ground green powder. Even after extraction with CH_2Cl_2 or CH_2Cl_2/MeOH, the CaO remained colored, indicating that some product was still strongly adhering to it. We then digested the CaO with 1.0 M aq HCl and extracted the solution with CH_2Cl_2. Only little more product **7** could be obtained but a TLC analysis of the extract revealed the presence of relatively large amounts of a swath of intractable green, porphyrinic (as per UV-vis spectra analysis) products of very high polarity. We suspect that multiple dehalogenation/oxygen replacement reactions within the *meso*-C_6F_5 groups took place. We believe the formation of those products to be the factor for the lower-than-expected isolated yields of product **7**.

Grinding of pure *meso*-tetraphenylporphyrin, *meso*-tetrakis(pentafluorophenyl)porphyrin (**5**), or β-octaethylporphyrin with CaO or K_2CO_3 (under the standard milling conditions of Table 1, 80 min) did not result in the chromophore degradation as observed when grinding these porphyrins with silica gel. Thus, unreacted porphyrins could be retrieved with an average 70–75% recovery. Nonetheless, both CaO and K_2CO_3 remained coloured after extraction with CH_2Cl_2 or more polar solvents, such as 20% MeOH in CH_2Cl_2.

Compared to CaO, MgO is a less basic but harder oxide (Mohs hardness of 5.8) [62], yet we find it nearly equally well suited as grinding aid/base for the mechanochemical chromene-annulated porphyrin formation (Entries 6-7). A small increase in the activity of MgO through thermal activation prior to its use as grinding aid/base can be achieved (cf. Entries 6 and 7). The use of MgO did not mitigate the challenges of product isolation/formation of intractable products encountered with the use of CaO. Like with the use of CaO, the use of MgO as grinding aid gave, in addition to main product **7**, a trace amount of bis-chromene product **8** and chromene-annulated porphyrin **9**. The latter product was not observed in the solution state annulation reactions [35,39]. The observation of alternative reaction pathway using milling conditions compared to standard solution conditions is well documented in the literature [43-46,48].

Entries 8 and 9 evaluated the efficacy of alumina, a much harder oxide (hardness is widely varying with the degree of calcination of the alumina prepared for chromatography, though none will reach the Mohs hardness of 9 seen in corundum) [62]. Neutral and basic alumina were tested. Surprisingly, the neutral alumina proved to be more effective than the basic alumina (with or without the addition of DABCO, a solid organic base), but with an estimated 25% conversion of **6**, even neutral alumina is not competitive to the solution state reaction. However, concomitant with the diminished reactivity, the formation of side products or the degradation of the starting material was also much less pronounced.

The use of the carbonates of group I elements as grinding aid was also tested (Entries 10–14). They were successful in effecting the desired transformation and produced similar product distributions as with the use of CaO or MgO, including the formation of significant quantities of very polar porphyrinic side products, especially in the case of Li_2CO_3 (Entries 10 and 11). Among all the carbonates tested, the use of K_2CO_3 appears to be the best to cleanly affect the transformation of the diol to the annulated product.

CONCLUSIONS

Although ball milling was used in organic synthesis for a range of organic and inorganic transformations [43-47,50,51,53], we found that that the translation of a seemingly straight-forward solution reaction to mechanochemical conditions posed limitations. While the principle feasibility of inducing the chromene-annulation of diol chlorin **6** to form annulated chlorin **7** with good conversion rates in a planetary ball mill could be shown, the mechanochemical reaction was not without its problems and cannot yet compete with the corresponding solution-based reaction. The biggest issues were presented by the low isolated yields of the reaction. The formation of side products not observed in solution (like the dehydrated chromene-annulated porphyrin **9**) played only a minor complicating role.

The low yields of the desired product **7** could be traced to the extensive degradation of the porphyrinic macrocycles on several grinding aids. However, the presence of the grindings aids was needed beyond their utilization as, for instance, Brønsted bases, to bulk up the otherwise small-scale reactions (tens of milligrams) in the relatively large-scale milling vessels (25 mL). This aspect appears to be setting the mechanochemical method applied here to porphyrin chemistry apart from most other mechanochemical syntheses reported to date that involve the use of ‘bulk quantities’ of pure solid starting materials and reagent [43-47,50,51,53]. These reactions therefore could forego the use of a grinding aid, or the bulk of the reactants effectively acted also as grindings aids and/or substrates for the desirable products formed [47]. However, we found that a range of ostensibly ‘inert’ grinding aids (whether also used as Brønsted bases in the reaction, or not) were indeed not at all inert, rather led to significant and yet to be fully understood porphyrin degradations. These fell into two categories: Either the chromophores were permanently heterogenized on the grinding aids, presumably because of reactions of the nucleophilic oxides and carbonates with the pentafluorophenyl groups or the chromophores were carbonized. The latter pathway is similar to earlier findings of the (desirable) degradation of organic pollutants (like halogenated hydrocarbons) on, for example, silica gel [57-60].

We cannot be sure about unpublished negative experiences made by others with failed mechanochemical reactions in the presence of grinding aids. However, we are also not aware of systematic studies that investigate the influence of various (inert) grinding aids on a given specific transformation (as opposed to general degradation reactions [58-60]), though the influence of even subtle reaction condition changes are well-known. For instance, one study tested the influence of the grinding jar/balls material on the outcome of Suzuki coupling reactions and found significant effects [64]. Inversely, multiple reactions performed under high-energy conditions (i.e., high milling speed on the planetary or rotary mill, long reaction times without grinding aid) did not impact the yields negatively [64-66].

The drive to greener and better synthetic methodologies in porphyrin chemistry will continue, including the search for suitable mechanochemical approaches. However, unless truly inert grinding aids can be identified, the observation of extensive porphyrin degradation limits the applicability of the planetary ball mills in synthetic porphyrin chemistry, at least for the reaction tested which require grinding aids, high-energy settings, and longer than 10-20 min reaction times [52,54].

On the other hand, this finding also suggests further studies on the molecular origins of the sensitivity of otherwise robust porphyrins to being ground with many 'inert' solids.

EXPERIMENTAL

Materials. All reagents and solvents were from commercial sources and were used, unless otherwise noted, without prior treatment or purification. Activated CaO and MgO were prepared by heating to at least 120 °C internal temperature (measured with the use of a digital infrared thermometer gun) under high vacuum for 10 min. After cooling under nitrogen, the activated grinding aids were used immediately. Diol **6** [32] and its chromene-annulated derivatives **7** [35] and **8** [35] were prepared as described in the literature (Scheme 1). Aluminum-backed, silica gel 60, 250 µm thickness analytical plates were used for analytical TLC; 20 × 20 cm, glass-backed, silica gel 60, 500 μm thickness preparative TLC plates, and standard grade, 60 Å, 32 × 63 μm flash column silica gel were used for preparative chromatography.

Instruments. All UV-vis spectra were recorded on a Cary 50 UV-vis spectrometer (Varian). A Fritsch GmbH, Germany, planetary micro mill (Pulverisette 7 classic line) equipped with 2 grinding vessels was used in the milling experiments, with the main disc speeds ranging between 100 and 800 rpm. All reactions were carried out in an agate vessel (inner dimensions were 45 mm diameter, 37 mm height, volume ~50 mL) equipped with 5 agate balls (12 mm) with a total weight of ~13.6 g (for additional information, see ESI [51]).

General Procedure for Preparing Chromene-Annulated Chlorin. *meso*-Tetrakis(pentafluorophenyl)-2,3-dihydroxychlorin synthesized according to established literature procedure [35], was added to a 50 mL agate vessel equipped with a five 12 mm agate balls. Subsequently, 0.5 g of grinding aid (activated or non-activated) and 10 mg of base additive (where applicable) were added to the reaction vessel and the reaction mixture was milled at 800 rpm for the total time indicated. The reaction progress was monitored intermittently via TLC and UV-vis spectroscopy and the conversion yields were estimated visually (see also ESI). Isolated yields were determined gravimetrically after extraction of the reaction products using CH_2Cl_2 and purification using column or preparative TLC.

β-dehydroxy-*meso*-tetrakis(pentafluorophenyl)-chromene-annulated porphyrin **9** formed in trace (< 5%) amounts in the reactions for Entries 2 and 7 of Table 1. It was pooled and purified using preparative plate chromatography (silica-CH_2Cl_2). R_f (silica-hexanes/75% CH_2Cl_2) = 0.76; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.59 (dd, ^3J = 11.6 Hz, ^4J = 4.8 Hz, 1H), 9.02 (dd, ^3J = 12.4 Hz, ^4J = 4.8 Hz, 2H), 8.89 (d, ^3J = 5.2 Hz, 1H), 8.80 (dd, ^3J = 10.4 Hz, ^4J = 4.8 Hz, 2H), 8.53 (s, 1H), –2.41 (s, 2H, exchangeable with D_2O) ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ -136.5 (td, ^3J = 22.9 Hz, ^5J = 7.5 Hz, 4F), -136.8 and -136.8 to -136.9 (overlapping dd and m, ^3J = 22.9 Hz, ^5J = 7.5 Hz, 3F), -151.2 to -151.4 (m, 3F), -152.9 (t, ^3J = 21.1 Hz, 1F), -159.1 (dd, ^3J = 20.7 Hz, ^5J = 8.3 Hz, 1F), -161.0 (td, ^3J = 22.6 Hz, ^5J = 7.5 Hz, 2F), -161.3 to -161.4 (m, 5F) ppm; UV-vis (CH_2Cl_2) λ_{max} (log ε) 414 (5.28), 515 (4.03), 551 (3.86), 584 (3.69), 637 (3.18) nm; HRMS (APCI+) *m/z*: Calc'd for $C_{44}H_{10}F_{19}N_4O$ $[M + H]^+$ 971.0551; Found 971.0546.

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Supporting information

A reproduction of the experimental data, including of the novel compound **9** is given in the supplementary material. This material is available free of charge via the Internet at http://www.worldscinet.com/jpp/jpp.shtml.

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