

Mechanochemistry

International Edition: DOI: 10.1002/anie.201905670
German Edition: DOI: 10.1002/ange.201905670Mechanosynthesis of Odd-Numbered Tetraaryl[*n*]cumulenes

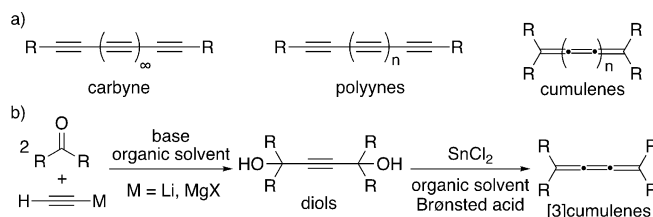
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In memory of Professor Dieter Enders

Abstract: A mechanochemical synthesis of one-dimensional carbon allotrope carbyne model compounds, namely tetraaryl[*n*]cumulenes (*n* = 3, 5) was realized. Central for the mechanochemical synthesis of the cumulenic carbon nanostructures were the development of a mechanochemical Favorskii alkynylation-type reaction and the implementation of a solvent-free, acid-free reductive elimination with tin(II) chloride by ball milling.

The use of mechanical energy to facilitate chemical reactions and physical transformations has been rapidly gaining terrain in various fields of the chemical sciences.^[1] One of the most distinct benefits of mechanochemical syntheses by ball milling is the possibility to generate unique product compositions compared to solution-based protocols.^[2] This alteration in chemical reactivity has been identified to be, at least partially, a consequence of the exertion of mechanical forces under solvent-free conditions, or the use of only catalytic amounts of organic solvents.^[3,4] Thus, new avenues to react chemicals that differ in their solubility profiles were opened,^[5] for which finding a common reaction medium would be otherwise problematic. Such advantages by mechanochemistry have proven particularly valuable in areas of research focused on the synthesis and functionalization of poorly soluble two- and three-dimensional carbon-based materials. Examples include the iconic mechanochemical dimerization of C₆₀,^[6] the development of mechanically based procedures for the delamination of graphite,^[7] the mechanochemical functionalization of graphene nanosheets,^[8] and the recent mechanochemical synthesis of nanographenes,^[9] to name just a few.^[6b] Conversely, mechanochemical synthesis or functionalization of one-dimensional carbon nanostructures, such as carbyne model compounds have remained unexplored.

For practical reasons such as accessibility, stability, and simplicity, polyynes and cumulenes have become ideal model compounds to predict and to study the expected physicochemical properties of carbyne (Scheme 1 a).^[10] In the case of cumulenes, various synthetic methods have been established



Scheme 1. a) Carbyne, polyynes, and cumulenes. b) The most common solution-based approach towards the synthesis of [3]cumulenes.

to produce or to connect sp-hybridized carbons into cumulenic structures of various lengths, [3]cumulenes being the simplest examples and therefore the most investigated ones.^[10b,11] Commonly, [3]cumulenes are synthesized by a two-step route involving the addition of a Li- or Mg-acetylide to ketones in solution, followed by reductive elimination of the corresponding 1,4-butyndiols using KI/H₂SO₄, SnCl₂/AcOH, or SnCl₂/HCl in organic solvents (Scheme 1 b).^[10b,11] Although widely applied, these strategies are not universal and become impractical if the cumulene precursors exhibit poor solubility in organic solvents or when acid-labile substituents decorate the structure of the starting materials and products.

With these precedents in mind, we wondered if the stability of [*n*]cumulenes would allow the establishment of a mechanochemical route to access such unique carbon structures. Herein, we report a proof-of-principle study demonstrating the realization of this concept.

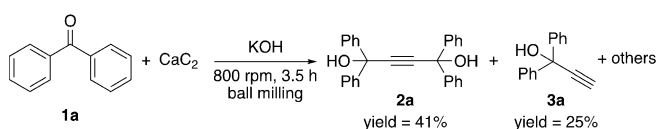
As starting point, we envisioned that a mechanochemical activation of benzophenone (**1a**) and solid calcium carbide (CaC₂)^[12] in the ball mill would enable the mechanochemical synthesis of propargylic diol **2a** through a double alkynylation reaction. Previous attempts to use CaC₂ as a surrogate of acetylene in solution-based alkynylation reactions have afforded mostly propargyl alcohols such as **3a** after the ethynylation of carbonylic compounds.^[13,14] However, our recent findings on the mechanochemical copper(I)-catalyzed A³ coupling with calcium carbide revealed that activation of CaC₂ under solvent-free and water-free conditions by mechanochemistry principally harnessed the reactivity of the acetylide ion (C₂⁻²) from CaC₂,^[3] rather than following the common approach of producing gaseous acetylene from CaC₂ and water.^[12] Initial experiments, milling **1a** and CaC₂ (1:2 ratio) for 3 h at 800 rpm in a planetary ball mill did not promote any chemical transformation, and only **1a** was recovered after the workup of the reaction mixture. Then, a series of additives were tested with aim of facilitating the activation of CaC₂, for example, through a mechanochemical salt metathesis reaction.^[15]

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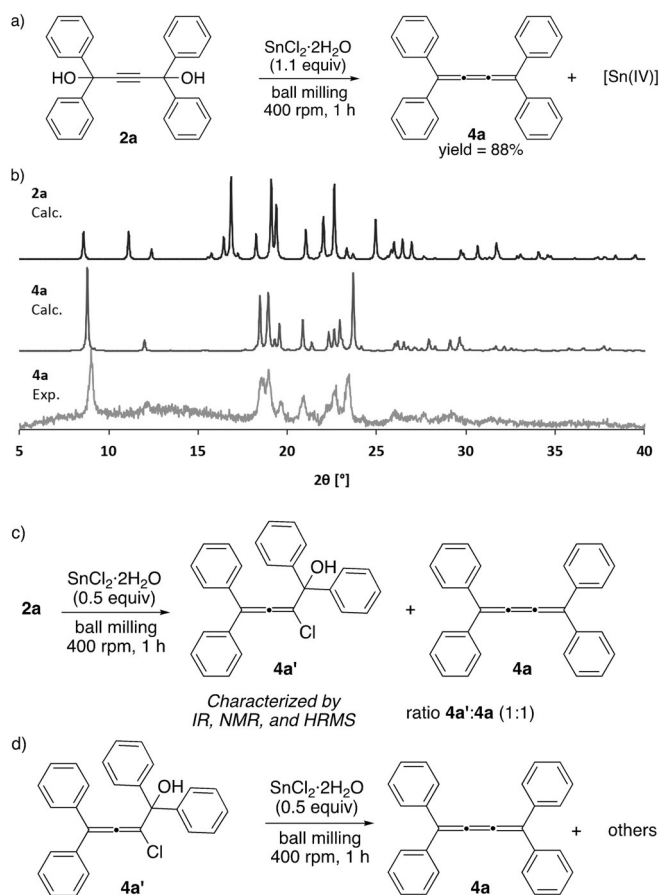
Experimentally, CaC_2 and the corresponding additives (KX; X = F, Cl, Br, I or K_2CO_3), were milled for 30 min prior the addition of **1a**, followed by a second milling period of 3 h. Analysis of the reaction mixture revealed that only KI and K_2CO_3 had led to formation of the expected products **2a** and **3a**, albeit in trace amounts (for details, see the Supporting Information). Next, KOH was used as an additive to favor a Favorskii alkynylation-type reaction.^[16] Pleasingly, this time, the solvent-free mechanochemical reaction afforded propargylic diol **2a** and propargyl alcohol **3a** in 41 % yield and 25 % yield, respectively (Scheme 2).^[17]



Scheme 2. Mechanochemical alkylation reaction between **1a** and CaC_2 .

The use of NaOH, LiOH, or $\text{Ca}(\text{OH})_2$ instead of KOH led to a drop in reactivity (for details, see the Supporting Information), ruling out the basicity of the additive as the main contributor for the chemical reactivity observed by ball milling. Instead, this indicates that the driving force of the reaction might rather be associated with the relative free energies of formation and lattice energies of the additives.^[18]

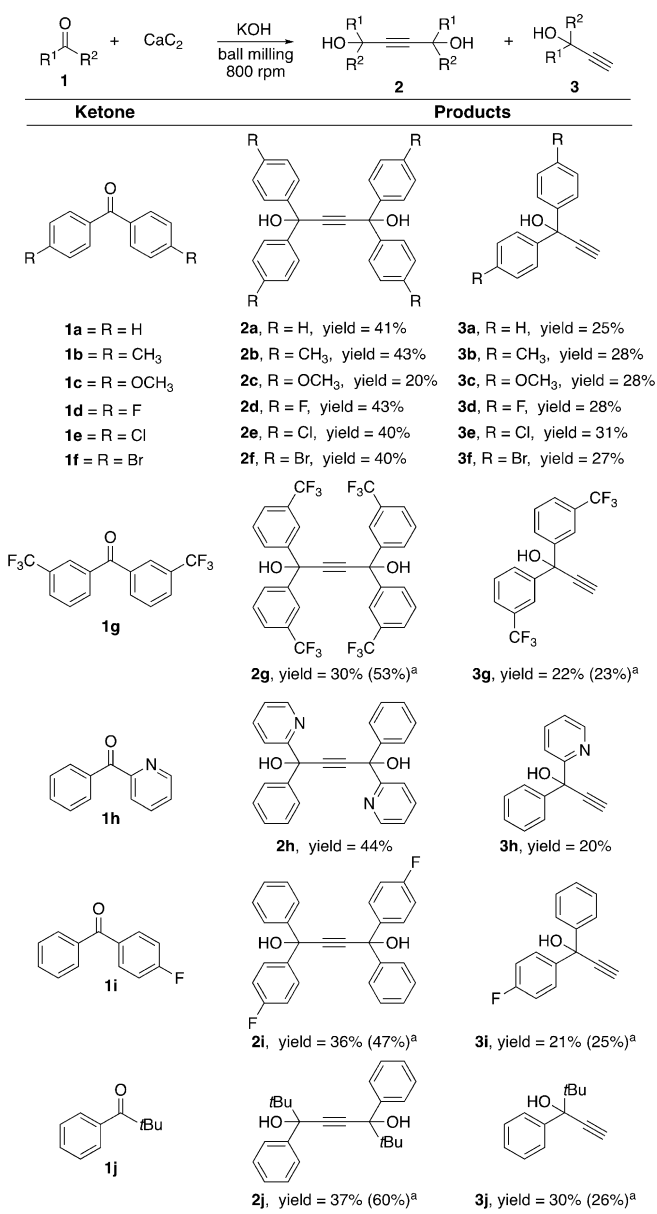
Having established a mechanochemical route to access propargylic diol **2a**, we then focused on the synthesis of [3]cumulene **4a**.^[19] As mentioned above, typically, reductive elimination of propargylic diols is carried out using tin(II) chloride (SnCl_2 or $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$) in organic solvents such as diethyl ether or THF, commonly in the presence of Brønsted acids.^[20] Along these lines, in a recent work, Yamago and co-workers reported that the mixture of SnCl_2 and HCl generated the ate complex H_2SnCl_4 , which has been credited to serve as a more active reducing agent formed in situ during the reaction.^[21] However, Brønsted acid-free Sn-mediated reductive eliminations are also known.^[20] Collectively, these observations made us curious to see whether a solvent-free, acid-free mechanochemical Sn^{II}-mediated reduction of diol **2a** in the ball mill would lead to the formation of [3]cumulene **4a** (Scheme 3a). To test this idea, **2a** and $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (1:1.1 ratio) were reacted for 1 h in a planetary ball mill. At the end of the milling, a bright yellow solid reaction mixture was observed. Analysis of this solid by powder X-ray diffraction (PXRD) techniques revealed the disappearance of Bragg reflections corresponding to **2a** and the presence of a new set of reflections that resembled the expected PXRD pattern of [3]cumulene **4a** (Scheme 3b). Isolation of **4a** from the inorganic residue was carried out by dissolving **4a** in a minimal amount of organic solvent, and by passing such solution through a pad of Celite (a similar yield was obtained after purification of **4a** by column chromatography or extraction). Repeating the reaction using anhydrous SnCl_2 under inert atmosphere gave similar results, thereby ruling out a potential formation of catalytic amounts of HCl from water present in $\text{SnCl}_2 \cdot x\text{H}_2\text{O}$. Interestingly, carrying out the mechanochemical reaction using a ratio **2a**/ $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (1:0.5) led to the



Scheme 3. a) Mechanochemical reductive elimination of **2a**. b) PXRD patterns for: **2a** (top),^[24a] **4a** (middle),^[24b] solid recovered after the reaction of **2a** and $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ (1.1 equiv) (bottom). c) Reductive elimination of **2a** using 0.5 equiv of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$. d) Use of **4a'** in the synthesis of **4a**.

formation of [3]cumulene **4a** together with 1,1,4,4-tetra-phenyl-2-chlorobuta-2,3-dien-1-ol (**4a'**) (Scheme 3c) (**4a**:**4a'** ca. 1:1 ratio indicated by ^1H NMR spectroscopy at RT). The identity of **4a'** was confirmed by various analytic techniques and by independent synthesis.^[22a] Moreover, milling independently synthesized **4a'** and $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ led to the formation of [3]cumulene **4a**, together with the concomitant formation of unidentified byproducts (Scheme 3d); thereby indicating that compounds like chloroallene **4a'** could correspond to some of the long sought-after intermediates in reductive elimination of diols with stannous chloride (for a plausible mechanism, see the Supporting Information).^[20,21,23]

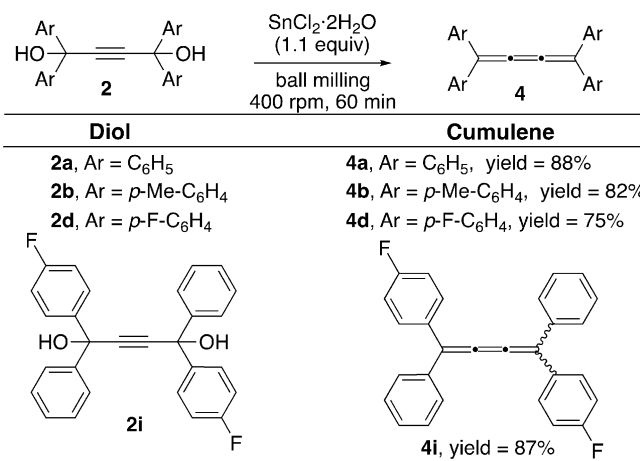
Next, using the established ball milling conditions for the mechanochemical Favorskii alkynylation-type reaction, a series of ketones **1a–j**, calcium carbide, and KOH were reacted (Scheme 4). Gratifyingly, benzophenone derivatives bearing electron-donating (**1b–c**) and electron-withdrawing groups (**1d–g**) tolerated the mechanochemical protocol (Scheme 4). Similarly, unsymmetrical ketones such as phenyl 2-pyridyl ketone (**1h**), 4-fluorobenzophenone (**1i**), and *tert*-butyl phenyl ketone (**1j**) also underwent the mechanochemical alkynylation reactions affording the correspond-



Scheme 4. Mechanochemical synthesis of propargylic diols **2a–j** and propargyl alcohols **3a–j** using calcium carbide.^[a] Yields in parenthesis correspond to five-fold scale-up experiments using a 45 mL ZrO₂ milling vessel.

ing 2-butyne-1,4-diols **2h–j** and propargyl alcohols **3h–j** (Scheme 4).

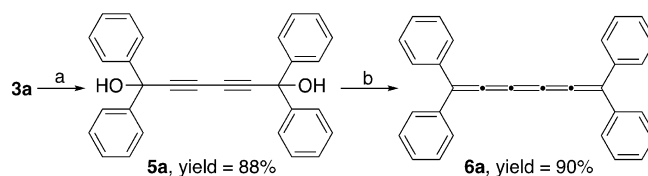
With a library of mechanochemically synthesized 2-butyne-1,4-diols **2** at our disposal, we selected a few additional representative examples to test the mechanochemical SnCl₂-mediated reductive elimination. Pleasingly, the application of the ball milling protocol to **2b** afforded the expected [3]cumulene **4b** in 82% yield (Scheme 5). The use of halogen substituted aryl alkynediol **2d** led to the formation of [3]cumulene **4d** in 75% yield (Scheme 5). Additionally, unsymmetrical alkynediol **2i** reacted smoothly to provide the *Z* and *E* isomers **4i** (ratio 1:1 indicated by ¹⁹F NMR spectroscopy at RT) in 87% yield (Scheme 5).^[19c] On the contrary, milling 2-pyridyl substituted alkynediol **2h** with



Scheme 5. Synthesis of [3]cumulenes **4**.

SnCl₂·2H₂O afforded a complex mixture of unidentified products.^[25] Similarly, less reactive alkyl- and aryl-substituted diol **2j**, failed to undergo the reductive elimination using SnCl₂·2H₂O by ball milling. Although this time, ketone **2j** remained unreactive. In general, synthesis of alkyl substituted [*n*]cumulenes is more difficult compared to aryl- [*n*]cumulenes.^[10b] Moreover, stability of cumulenes increases with the use of steric bulk end groups.^[11]

Having demonstrated not only the usefulness of the mechanochemically synthesized 2-butyne-1,4-diols **2** but also the relative stability of [3]cumulenes in the ball mill, we decided to use propargyl alcohol **3a** as a building block for the mechanochemical synthesis of the much more interesting [5]cumulenic unit.^[10b] Thus, **3a** was reacted in the presence of CuCl and tetramethylethylenediamine (TMEDA) through a mechanochemical copper-mediated oxidative coupling to afford hexa-2,4-diyne-1,6-diol (**5a**) in 88% yield (Scheme 6).^[26]



Scheme 6. Mechanochemical synthesis of [5]cumulene **6a**. a) CuCl (1.0 equiv), TMEDA (1.0 equiv), 800 rpm, 120 min. b) SnCl₂·2H₂O (1.0 equiv), 400 rpm, 60 min.

Then, solid **5a** was milled in the presence of SnCl₂·2H₂O for 60 min at 400 rpm in a planetary ball mill to give a dark red solid. Immediate analysis of the crude reaction mixture by solution NMR spectroscopy confirmed the formation of [5]cumulene **6a** upon milling. Isolation of **6a** was accomplished after dissolving **6a** in a minimal amount of organic solvent, and by passing such solution through a pad of Celite to give **6a** in 90% yield (Scheme 6).

In summary, we have developed a mechanochemical route to access tetraaryl[*n*]cumulenes (*n* = 3, 5) by implementation of ball milling techniques. The synthetic approach towards tetraaryl[3]cumulenes **4** encompasses the mechanochemical

activation of ketones, calcium carbide, and potassium hydroxide through a Favorskii alkynylation-type reaction in a ball mill, followed by the establishment of a solventless and acid-free SnCl_2 -mediated reductive elimination of propargylic diols **2**. Particularly interesting was the observation that mechanochemical reductive elimination of **2a** with substoichiometric amounts of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ enabled the isolation of one intermediate of the reaction, thereby gaining insight into the mechanism of the transformation. Additionally, the mechanochemical approach was successfully extended to the synthesis of the illustrative tetraphenyl[5]cumulene (**6a**) after a mechanochemical copper-mediated oxidative coupling of propargylic alcohol **3a** followed by reductive elimination of diyne diol **5a** with $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$. From a more general perspective, we foresee the protocols reported in this work to be applicable in areas such as material sciences for the mechanosyntheses of carbon-based materials from CaC_2 ,^[27] and in supramolecular chemistry for the mechanosynthesis of, for example, conjugated polycyclic hydrocarbons and cumulenes derived from poorly soluble starting materials or from acid-labile precursors.

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Conflict of interest

The authors declare no conflict of interest.

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