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FULL PAPER

Direct Exploitation of the Ethynyl Moiety in Calcium Carbide Through Sealed Ball Milling

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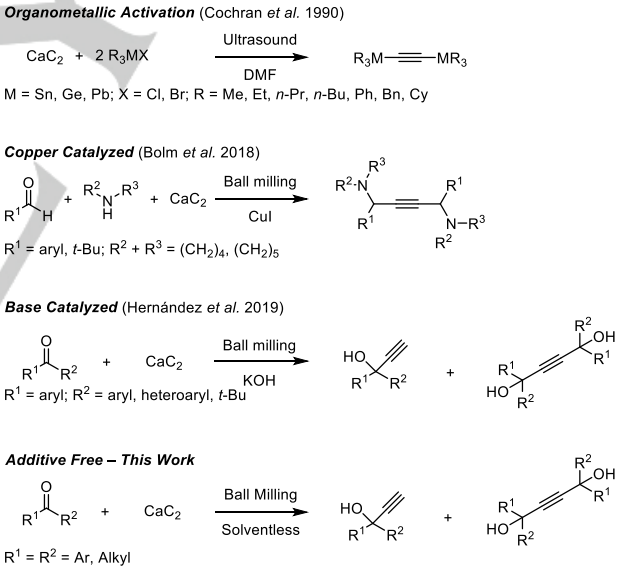
Abstract: Ball milling of calcium carbide (CaC_2) enables the reaction of its ethynyl moiety with organic electrophiles. This was realized simply by co-milling CaC_2 with organic substrates in a sealed jar without the need for an additive or a catalyst. Various ketones including those bearing α-hydrogens were ethynylated in good yields at short reaction times. Aryl halides are also amenable substrates for this protocol as they furnish aryl ethynes through a benzyne intermediate. This method offers a practical and cheap alternative to the established procedures for introducing of ethynyl functionalities.

Introduction

"*Calcium carbide has no value for the synthetical processes of organic chemistry*" is an infamous quote of Harry C. Jones dating back more than 120 years.[1] Even though this is not entirely true, today we are still challenged by the problems associated with exploring and exploiting the full potential of CaC_2 as a valuable starting material for organic synthesis.[2] Beginning with the commercial production of calcium carbide (CaC_2) in 1892,[3] the idea lingered on how to transfer the ethynyl moiety from a crystalline, insoluble inorganic carbide into organic molecules.[4] The ability to construct C–C bonds in a highly efficient manner from such a cheap, readily available, and stable starting material has obvious synthetic utility and value.[5] Therefore, many attempts have been devoted to utilizing CaC_2 in organic synthesis during the early decades of the 20th century.[6] Oroshnik and Mebane showed that calcium diacetylide (HC≡C–Ca–C≡CH) readily reacts with ketones to furnish the desired propargyl alcohols,[7] but the low solubility of polymeric calcium acetylide (i.e., CaC_2) prevents the direct addition to carbonyl compounds. Increasing the solubility of calcium carbide with additives has become a renewed subject of investigation and various organic transformations utilizing such a strategy were reported recently.[2b, 2c, 8] The inherently nearly impenetrable and mechanically hard structure of solid CaC_2 evoked the idea of using ultrasound or mechanical force ball milling techniques.[9]

Shearing and friction of solid materials induced by mechanical energy fractures the solid into fine particles, thus enabling materials to react. Bearing this idea in mind, Li *et al.* reported the direct alkynylation of polyhalogenated hydrocarbons with CaC_2 using a planetary ball mill.[9b, 10] Despite this impressive achievement, it has yet to be demonstrated that the suggested polyalkynylated product can be isolated using this protocol. Later on, Borchardt and co-workers described a one-pot mechanochemical synthesis of *N*-doped porous carbons using a planetary ball mill.[11] The authors carefully monitored the reaction progress and used various techniques for their product characterization but ruled out the presence of sp-hybridized carbon in the final product as evident from Raman spectroscopy.



Scheme 1. Progress in the mechanochemical activation of calcium carbide.

The most promising result for mechano-activation of CaC_2 was reported by Bolm and Hernández et al. who successfully exploited CaC_2 in a one-pot three component synthesis of 1,4-diamino-2-butynes (Scheme 1).[12] Contrary to a previous report for the same reaction under conventional conditions, the disubstituted product (1,4-diamino-2-butyne) was preferentially obtained under milling conditions. The same authors also described a mechanochemical Favorskii-type alkynylation reaction under solvent-free conditions using calcium carbide and a fourfold stoichiometric ratio of KOH.[13] The method offers

advantages over the previous procedure where benzene and a reaction time of several days were required.[14] Despite such notable advances, a relatively limited substrate scope arose from base promoted aldol condensation of ketones bearing α-hydrogens, which limits the broad application of this method.[15]

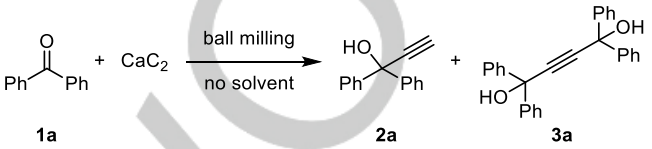
The additive-free reactions reported by Li et al.[8h, 9b, 10b, 10c] are indeed different from that of Bolm and Hernández who utilized a catalyst or an additive; no reaction occurred in the absence of an additive.[13] Therefore, the question remains whether it is possible to transfer the ethynyl moiety directly from CaC_2 without the need for an additive or a catalyst. A way to activate neat CaC_2 and understand the fundamental issues could greatly facilitate the use of CaC_2 in organic synthesis. Here we report the ethynylation of ketones using CaC_2 directly without additive. So far, various reagents including alkali metal acetylides or ethynyl Grignard reagents have been utilized for ethynylation reactions, however, the preparation of these reagents requires strong bases, dry solvents, and acetylene gas, which makes them expensive and inconvenient to handle.[16] Therefore, replacing traditional acetylide reagents with CaC_2 would be highly desirable. In theory, the activation of CaC_2 through mechanical milling seems plausible as small particles with high surface areas are expected to be much more reactive and even pyrophoric when exposed to air.[17] The essential challenge is the determination of the factors of the milling process that affect the reactivity of the formed small reactive particles.

Results and Discussion

We began with the ball milling reaction of benzophenone with CaC_2 in a tungsten carbide (WC) jar at a frequency of 30 Hz for 40 min. However, only black insoluble carbon ensued (Table 1, entry 1); the starting materials could not be recovered from the reaction mixture. Only a stainless steel (SS) jar provided some evidence for product formation upon TLC analysis (Table 1, entry 3). To avoid heating the sample through the milling process the reaction was performed at low temperatures (Table 1, footnote *d*). To our delight, the reaction progressed well with a total product yield of 53% and a 1:2 *mono:di* ratio (Table 1, entry 4). This kind of transformation has not been reported using CaC_2 without the need for an additive or a catalyst. Almost the same yield was obtained when the amounts of starting materials were doubled (Table 1, entry 5), implying scalability. Even though we obtained a reasonable yield, the low mass balance (~70%) remained unsatisfactory. This may be rationalized by the so-called "hot spot theory" that assumes that local temperatures at tips of propagating cracks may reach several hundreds or thousands of degrees Celsius in a fraction of a second.[18] In fact, the high frequency vibration allows some air flow into the jar, thereby burning the organic matter in the milling process; depending on oxygen supply, this delivers carbon monoxide or carbon black.

The mass loss was confirmed when the reaction time for entry 4 of Table 1 was extended to 80 min giving only 17% yield. The airflow could be readily prevented by applying grease to seal the circumference of the jar screw cap, and we were delighted to isolate the desired products in 75% yield with a 1:2 *mono:di* ratio (Table 1, entry 6). We also tested the reactivity of pre-milled CaC_2, however, these fine powder or nanoparticle forms are highly sensitive to air and moisture. For instance, the yield was almost cut in half when benzophenone was added to pre-milled calcium carbide, indicating that active CaC_2 readily decomposes upon exposure to air (Table 1, entry 6). With this result, we further optimized the molar ratio of benzophenone to CaC_2 (the average purity was taken into account); a molar ratio of 0.28:6 was by far the best (Table 1, entries 7–9). The reaction at low impact milling afforded high yields and better mass balance than entry 6, albeit at longer reaction times (Table 1, entry 11).

Table 1. Optimization of the Conditions of the Reaction of Calcium Carbide (CaC_2) with Benzophenone (**1a**) under Ball Milling Conditions in Different Stainless Steel (SS) or Tungsten Carbide (WC) Jars.[a]



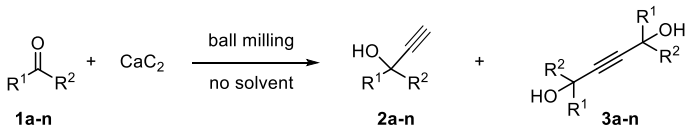
1a **2a** **3a**

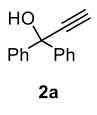
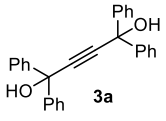
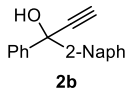
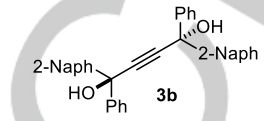
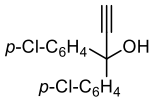
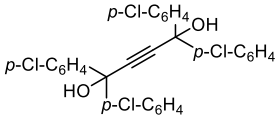
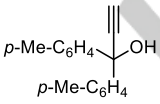
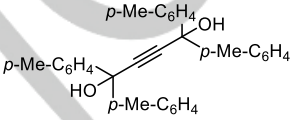
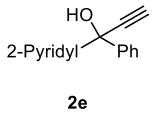
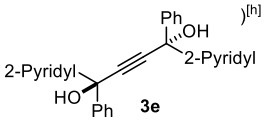
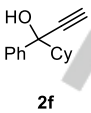
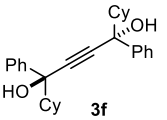
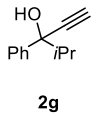
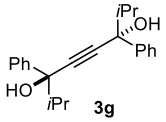
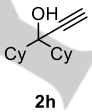
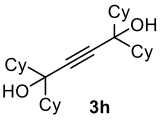
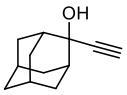
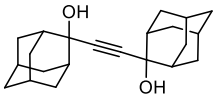
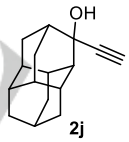
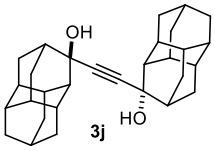
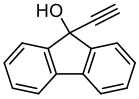
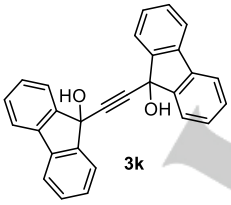
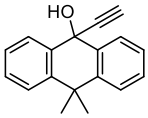
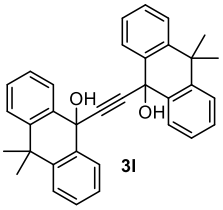
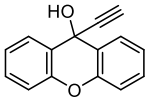
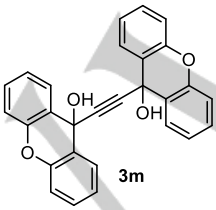
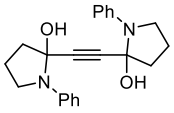
Entry	**1a** (mmol)	CaC_2 (mmol)	*t* (min)	Jar	Yield (%)[b]	
					2a	**3a**
1	0.14	3	40	WC	–	–
2[c]	0.14	3	40	WC	–	–
3	0.14	3	40	SS	trace	trace
4[d,e,f]	0.14	3	40	SS	17	36
5[d]	0.28	6	40	SS	19	39
6[g]	0.28	6	40	WC	**25**[h]	**50**[h,i]
7	0.28	3	40	WC	9	15
8	0.28	9	40	WC	23	40
9	0.28	12	40	WC	27	39
10	0.28	6	60	SS	15	37
11[j]	0.28	6	80	WC	15	47[k]

[a] *Reaction conditions:* Crushed CaC_2 and **1a** placed in a 20 mL SS or WC jar and milled for the indicated time at 30 Hz. [b] Yields determined by ^{1}H NMR using 1,4-dinitrobenzene as internal standard. [c] Jar sealed under Ar atmosphere. [d] Jar cooled every 10 min by immersion into a liquid nitrogen bath for ca. 1 min. [e] 16% of **1a** remained unreacted according NMR analysis. [f] 17% yield of products obtained when milling continued for 80 min. [g] Addition of benzophenone to milled calcium carbide at room temperature reduced the yield to half. [h] Yield of isolated product. [i] 6% of **1a** recovered. [j] Reaction performed at 25 Hz. [k] 22% of **1a** remained.

Note that the mass ratio of the starting materials is critical and a free flow powder is needed to drive the reaction. As a result, increasing the ratio of benzophenone decreases the yield due to the formation of a wet cohesive mixture (Table 1, entry 7). With the optimized conditions in hand, other ketones were investigated for the direct ethynylation with calcium carbide (Table 2). Bulky 2-naphthyl phenyl ketone gave moderate yields of isolated products under both 30 and 25 Hz milling conditions, with decreased selectivity for di-substituted product. Improved yields were achieved when 0.22 mmol (0.05 g, the optimized mass ratio according to Table 1) of **1b** was employed.

Table 2. Ball Milling Alkynylation of Ketones using Calcium Carbide.[a]



Products	*t* (min), *f* (Hz), yield (%)[b], *mono*:*di*[c]	Products	*t* (min), *f* (Hz), yield (%)[b], *mono*:*di*[c]
 **2a**  **3a**	40, 30, **75**[d], 1:2	 **2b**  **3b**	40, 30, 43[d], 1:1.7 80, 25, 44[d], 1:1.3 40, 30, **55**[e], 1:1.7
 **2c**  **3c**	40, 30, 31[f], 1:2.2 50, 25, 35, 1:2 80, 25, **48**[g], 1:1.8	 **2d**  **3d**	40, 30, 36, 1:2 55, 30, **50**, 1:1.5
 **2e**  **3e**	60, 25, **42**, 1:2 40, 30, 20, 1:1.5 40, 30, 25[i], 1:1.7	 **2f**  **3f**	40, 30, **62**, 1:1.4[j] 80, 25, 50, 1:1.3[j]
 **2g**  **3g**	40, 30, **47**[d,k], 1:1.6	 **2h**  **3h**	40, 30, **45**[d], 1:2
 **2i**  **3i**	40, 30, 54, 1:2.2 80, 25, **71**[l], 1:4.5	 **2j**  **3j**	40, 30, **56**[d,k], 1:2
 **2k**  **3k**	40, 30, 29[d], 1.3:1 80, 25, **38**, 1:2	 **2l**  **3l**	40, 30, 21[m], 1:1 60, 30, 15, 1.5:1 80, 25, 21[n], 1:1.4 150, 25, **25**[n], 1:1.5
 **2m**  **3m**	40, 30,–,–	 **2n**  **3n**	40, 30,–,–

[a] *Reaction conditions:* Ketone (0.28 mmol), CaC_2 (6 mmol) milled for specified time in a grease sealed 25 mL tungsten carbide jar. [b] Yields determined by ^1H NMR using 1,4-dinitrobenzene as internal standard. [c] Ratio determined by NMR. [d] Yield of isolated product. [e] 0.22 mmol of ketone used. [f] 12% of **1c** remained (NMR). [g] 7% of 4,4′-dichlorobenzophenone remained (NMR). [h] 3,4,5-Trimethoxybenzaldehyde used as internal standard. [i] Jar cooled every 10 min by immersion into a liquid nitrogen bath for ca. 1 min. [j] **3f** obtained as mixture of diastereomers. [k] 6.8 mmol of CaC_2 used. [l] 8% of adamantanone remained (NMR). [m] 44% of **1j** remained (NMR). [n] More than 50% of substrate remained (NMR).

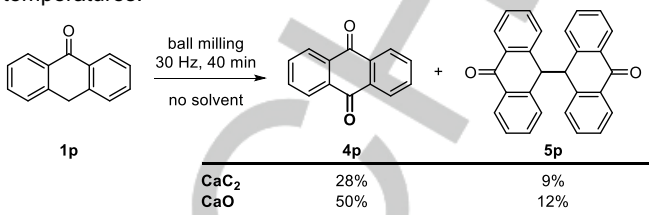
4,4′-Dichlorobenzophenone (**1c**) afforded low yield under optimized reaction conditions with small amounts of unreacted starting material (12% by NMR). The chlorine in **1c** possibly provides an opportunity for halogen replacement (*vide infra*), leading to low yield. The side reactions could be diminished by conducting the reaction at low impact milling, giving the

ethynylated products in 48% after 80 min. Similar results were obtained with 4,4'-dimethylbenzophenone (**1d**) providing the corresponding products in total 50% yields and a 1:1.5 mono:di ratio. Ketone bearing heterocyclic moieties also react with CaC_2 to give the corresponding products in similar yields at low impact conditions. In contrast, high impact milling provided only low yields with somewhat lower selectivity even at low temperature.

Notably, enolizable ketones **1f** and **1g** were also tolerated and furnished the corresponding products in good yields; aliphatic ketones were also ethynylated (Table 2, entries **1h**–**1j**). Non-enolizable adamantanone **1i** afforded the products in 54% yield and a 1:2.2 mono:di ratio, and the yield could be increased to 71% under low impact conditions. A similar result was obtained in case of bulky diamantanone **1j** (Table 2). In general, benzo-fused cyclic ketones were less reactive than the benzophenone derivatives. The reaction of fluorenone **1k** with calcium carbide provided **2k** and **3k** in 38% yield and a 1:2 mono:di ratio at 25 Hz whereas high impact milling gave lower yield with inversed selectivity. 10,10-Dimethylanthrone **1l** gave similar results and no significant improvement was observed even after prolonged reaction time. Xanthone **1m** and 1-phenyl-2-pyrrolidinone **1n** were unreactive under our reaction conditions.

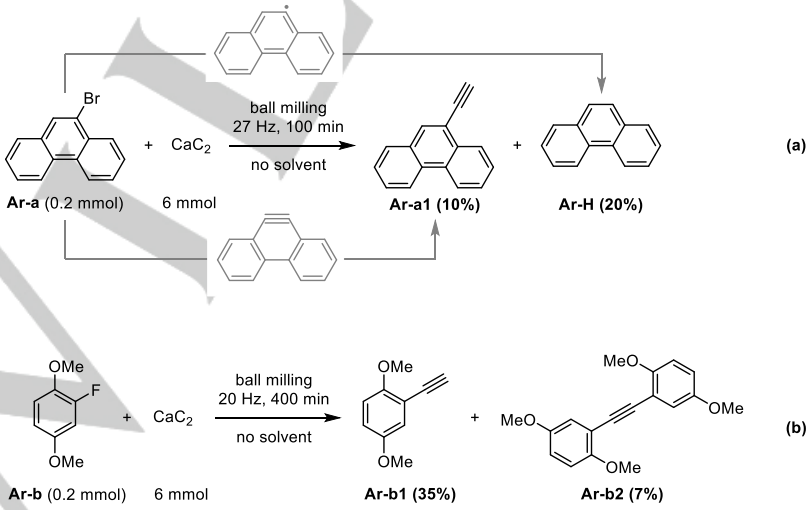
Our efforts to extend our protocol to aldehydes was met with mixed success. 3,4,5-trimethoxybenzaldehyde (**1o**) was exploited as a solid aldehyde in a similar manner (see Supplementary Information for details) but only low product yields along with Cannizzaro side products and an ester were obtained after 80 min milling at 25 Hz (Scheme S1). Shortening the milling process to 60 min at 25 Hz and utilizing low temperatures improved the yields (Scheme S1).

In the course of our studies, an unexpected result observed with anthrone **1p** piqued our curiosity about the mechanism and also lends support to the need of excluding air entering the system. Instead of the desired alkynylated product, the reaction was accompanied with the formation of anthraquinone **4p** and dianthrone **5p** in 28% and 9%, respectively. This result apparently conflicts with the intrinsic reducing property of CaC_2.[19] Since CaO is the main impurity of CaC_2, we reasoned that the contribution from the CaO might facilitate benzylic oxidation.[20] To probe this hypothesis, a control experiment was performed in the presence of CaO. Surprisingly, 50% of anthraquinone **4p** and 12% of dianthrone **5p** were obtained, proving that calcium oxide could act as a reasonably effective oxidizing agent under these conditions (Scheme 2). This result is consistent with the previous findings that CaC_2 promotes formation of radicals at high temperatures.[19]



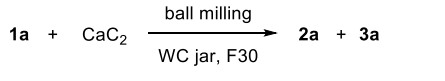
Scheme 2. Ball Milling Reaction of Anthrone with CaC_2 and CaO.

Stimulated by the indication of radical reactivity, we then became interested in the chemical reactivity of CaC_2 toward aryl halides under ball milling conditions. Aryl ethynes are the building blocks often encountered within a wide range of natural and synthetic organic materials. The Sonogashira coupling of acetylenes with aryl halides, provides a useful tool for accessing of mono and diaryl-substituted acetylenes.[21] However, even with considerable effort, the high cost and environmental issues associated with the use of palladium catalysts, expensive ligands as well as the use of protected acetylenes restrict the industrial application of the Sonogashira method. Having established alternative reaction conditions, we probed the feasibility of a catalyst and ligand-free alkynylation of aryl halides under ball milling, conditions.[22] A test reaction using 9-bromophenanthrene (**Ar-a**) as a substrate showed that the reaction did produce the desired product, 9-ethynylphenanthrene (**Ar-a1**), albeit in low yield. The competitive formation of phenanthrene (**Ar-H**) implicate that both radical[19] and dehydrohalogenation (benzyne formation)[22] pathways are probably involved (Scheme 3a).



Scheme 3. Additive-Free Reaction of Calcium Carbide with Aryl Halides under Ball Milling Conditions.

Aryl fluorides have less tendency to radical formation and are more prone to generate benzyne intermediates when exposed to base catalysts.[23] Hence, 2-fluoro-1,4-dimethoxybenzene (**Ar-b**) was subjected to ethynylation under milling conditions. In a series of test reactions, we found that performing the reaction using low frequency with an elongated time improves the yield to 42% of mono- and di-substituted (Scheme 3b). Clearly, this reaction is also assisted by the formation of highly stable CaF_2.



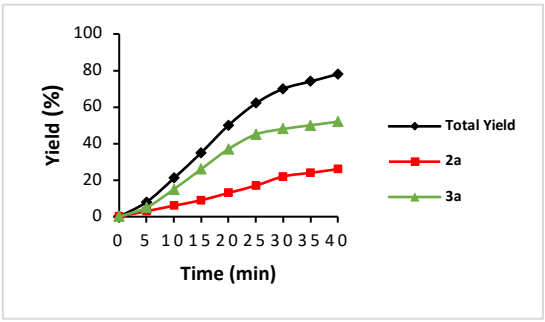


Figure 1. Time/yield Profile of **1a** with CaC_2 under Ball Milling Conditions.

To gain preliminary insight into what happens in the ball milling for the ketone alkynylation, we monitored the overall reaction rate using benzophenone **1a** as the test substrate in a tungsten carbide (WC) jar at a frequency of 30 Hz. The time/yield profile of this reaction suggests that di-substituted product **3a** may form from a doubly deprotonated (and complexed with Ca^{2+}) **2a** adduct (Figure 1). Consequently, a reduction in the concentration of **1a** led to a decrease in the rate of the formation of **3a** at around 25 min.

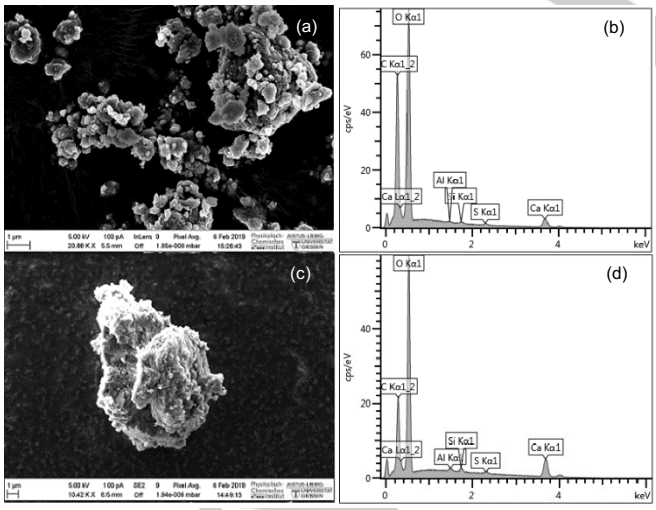


Figure 2. Scanning electron micrographs image and EDX spectrum of: (a,b) CaC_2 particles milled in a grease-sealed jar; (c,d) CaC_2 particles milled in a non-grease-sealed jar. The samples were prepared by milling at 30 Hz for 40 min in a tungsten carbide jar and were measured under argon atmosphere.

The surface morphologies of the milled CaC_2 particles were analyzed by scanning electron microscopy (SEM). The milled CaC_2 particles in grease-sealed jar are discrete and flaky in shape with a diameter range of nm to μm (Figure 2a) whereas the CaC_2 particles in an ungreased jar show amorphous morphology with micrometer dimensions (Figure 2c). A key difference was observed in the corresponding EDX spectra: The carbon content of the former (15.5%) was significantly higher than the later (5.0%). This implies that carbon content was reduced due to the diffusion of moisture and oxygen through the jar's screw cap during the milling process (Figures 2b and 2d). This finding also confirms our results above (Table 1) that tight sealing of the ball milling jar is essential to utilize the starting materials more effectively. We suggest that milling of CaC_2 generates crystal defects on the surface of CaC_2 nanoparticles leading to formation of highly reactive acetylide species. If unprotected from oxygen and moisture, these activated acetylides rapidly react to give carbon monoxide/carbon or acetylene gas that is rapidly lost. In sealed containers, the activated acetylides react with electrophiles instead.

Conclusion

We demonstrate that CaC_2 can be mechanochemically activated through mechanical milling. Unlike all previous approaches for the activation of CaC_2, which usually require base and/or catalysts, our method delivers the product without the need for a catalyst or an additive. This allowed us to alkynate various ketones including those are bearing α-hydrogens in good yields with a preference for disubstitued products. Some selected aryl halides were alkynylated with good selectivities as well. This method represents a practical approach for the activation of CaC_2 and opens new opportunities for its use in synthesis. A key finding is that the ball milling jars have to be as air tight as possible to avoid the loss of material through the escape of acetylene gas or "burning" with oxygen. As an outlook, we suggest that modifications of the jars to have much tighter sealing and better temperature control would greatly improve the efficiency of this approach in general.

Experimental Section

General Information

Caution: Milling of calcium carbide under high frequency in an air protected WC jar produces CaC_2 nanoparticles that can spontaneously ignite in air.

All chemicals were purchased from Aldrich, Alfa Aesar and Acros Organics in reagent grade or better quality and used without further purification. All of the ball milling reactions were performed in a Retsch MM 400 mixer mill with 20 mL grinding vessels. Analytical thin-layer chromatography (TLC) was performed on plastic-backed silica gel 60 coated with a fluorescence indicator. Visualization of TLC plate was performed by UV (254 nm) or phosphomolybdic/permanganate stains. Flash column chromatography was conducted using Merck silica gel 60 (0.040–0.063 mm). ^1H and ^{13}C spectra were measured with Bruker spectrometer Avance II 400 MHz (AV 400) and Avance III 600 MHz (AV 600), using TMS as the internal standard. Chemical shifts are reported in parts per million (ppm). The progress of

reactions was monitored by GC-MS analyses with a Quadrupol-MS HP MSD 5971(EI) and HP 5890A GC equipped with a J & W Scientific fused silica GC column (30 m × 0.250 mm, 0.25 micron DB–5MS stationary phase: 5% phenyl and 95% methyl silicone) using He (4.6 grade) as carrier gas; T-program standard 60–250 °C (15 °C/min heating rate), injector and transfer line 250 °C. Calcium carbide (72–82%) was purchased from Acros Organics.

General procedure for reactions of ketones with calcium carbide under ball milling conditions

Silicone grease was applied to completely fill the interstitial spaces of the inner screw thread of a 20 mL WC jar. Crushed CaC_2 (x mmol) and ketone (y mmol) were placed into the jar as indicated in Table 2. The jar was tightly closed and milled at specified frequency and indicated time. The jar was then allowed to reach room temperature and then carefully opened under fume hood. Ethyl acetate was added to almost fill the jar and then the rest of calcium carbide was quenched followed by slow addition of water (the mixture must be gently stirred by means of a spatula during the addition of water). The reaction mixture was filtered through a pad of celite and washed with ethyl acetate. The filtrate was washed with brine and the organic layers was dried over Na_2SO_4, filtered and concentrated to give the crude products. Pure propargyl alcohols were obtained by column chromatography on silica gel.

1,1-Diphenyl-prop-2-yn-1-ol (2a).[13] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.54 – 7.52 (m, 4H), 7.33 – 7.29 (m, 4H), 7.24 – 7.20 (m, 2H), 6.81 (s, 1H), 3.81 (s, 1H) ppm; ^{13}C NMR (101 MHz, DMSO-d_6) δ = 146.0, 127.9, 127.1, 125.6, 87.4, 76.9, 72.6. HRMS Calcd for $C_{15}H_{12}O$ [M + Na]$^+$ 231.0780; Found 231.0778.

1,1,4,4-Tetraphenylbut-2-yne-1,4-diol (3a).[13] ^{1}H NMR (400 MHz, DMSO-d6) δ = 7.59 (d, *J* = 7.4 Hz, 8H), 7.31 (t, *J* = 7.5 Hz, 8H), 7.22 (t, *J* = 7.3 Hz, 4H), 6.88 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 146.9, 128.42, 127.5, 126.2, 89.8, 73.5. HRMS Calcd for $C_{28}H_{22}O_2$ [M + Na]$^+$ 413.1512; Found 413.1522.

1-(Naphthalen-2-yl)-1-phenylprop-2-yn-1-ol (2b).[24] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.15 (s, 1H), 7.97 – 7.92 (m, 1H), 7.88 – 7.81 (m, 2H), 7.61 – 7.45 (m, 5H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 6.98 (s, 1H), 3.89 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 145.7, 143.3, 132.4, 132.1, 128.1, 128.0, 127.7, 127.3, 127.2, 126.3, 126.1, 125.7, 124.5, 123.4, 87.2, 77.3, 72.8. HRMS Calcd for $C_{19}H_{14}O$ [M + Na]$^+$ 281.0937; Found 281.0935.

1,4-Di(naphthalen-2-yl)-1,4-diphenylbut-2-yne-1,4-diol (3b). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.25 – 8.22 (m, 2H), 7.89 – 7.79 (m, 6H), 7.73 – 7.67 (m, 4H), 7.64 (dt, *J* = 8.7, 2.1 Hz, 2H), 7.53 – 7.46 (m, 4H), 7.34 (td, *J* = 7.6, 1.9 Hz, 4H), 7.27 – 7.22 (m, 2H), 7.10 (d, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 146.1, 146.1, 143.8, 143.8, 132.4, 132.1, 128.0, 127.7, 127.4, 127.2, 126.3, 126.1, 125.9, 124.7, 123.7, 89.6, 73.1. HRMS Calcd for $C_{19}H_{14}O$ [M + Na]$^+$ 513.1825; Found 513.1827.

1,1-Bis(4-chlorophenyl)prop-2-yn-1-ol (2c).[13] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.50 (d, *J* = 8.6 Hz, 5H), 7.39 (d, *J* = 8.6 Hz, 5H), 7.07 (s, 1H), 3.92 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 144.5, 132.0, 128.1, 127.5, 86.3, 77.7, 71.8. HRMS Calcd for $C_{15}H_{10}Cl_2O$ [M – H]$^+$ 275.0036; Found 275.0033.

1,1,4,4-Tetrakis(4-chlorophenyl)but-2-yne-1,4-diol (3c).[13] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.54 (d, *J* = 8.7 Hz, 8H), 7.40 (d, *J* = 8.7 Hz, 8H), 7.17 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 144.7, 132.1, 128.1, 127.5, 88.8, 72.1. HRMS Calcd for $C_{28}H_{18}Cl_4O_2$ [M + Cl]$^-$ 562.9725; Found 562.966.

1,1-Bis(4-methylphenyl)prop-2-yn-1-ol (2d).[13] ^{1}H NMR (400 MHz, DMSO-d_6) δ = ^{1}H NMR (400 MHz, DMSO) δ = 7.37 (d, *J* = 8.3 Hz, 4H), 7.11 (d, *J* = 8.0 Hz, 4H), 6.65 (s, 1H), 3.75 (s, 1H), 2.26 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 143.3, 136.1, 128.4, 125.5, 87.7, 76.5, 72.3, 20.5. HRMS Calcd for $C_{17}H_{16}O$ [M + Na]$^+$ 259.1093; Found 259.1095.

1,1,4,4-Tetrakis(4-methylphenyl)but-2-yne-1,4-diol (3d).[13] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.42 (d, *J* = 7.9 Hz, 8H), 7.09 (d, *J* = 7.9 Hz, 8H), 6.67 (s, 2H), 2.25 (s, 12H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 143.8, 136.0, 128.4, 125.7, 89.2, 72.7, 20.5. HRMS Calcd for $C_{32}H_{30}O_2$ [M + Na]$^+$ 469.2138; Found 469.2136.

1-Phenyl-1-(pyridin-2-yl)prop-2-yn-1-ol (2e).[13] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.47 – 8.45 (m, 1H), 7.83 – 7.76 (m, 1H), 7.74 – 7.69 (m, 1H), 7.59 – 7.55 (m, 2H), 7.33 – 7.21 (m, 4H), 6.95 (s, 1H), 3.67 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 163.0, 148.3, 144.9, 137.0, 127.7, 127.2, 126.0, 122.4, 119.3, 87.1, 76.3, 73.8. HRMS Calcd for $C_{14}H_{11}NO$ [M + Na]$^+$ 232.0733; Found 232.0736.

1,4-Diphenyl-1,4-di(pyridin-2-yl)but-2-yne-1,4-diol (3e).[13] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.50 (dt, *J* = 4.7, 1.2 Hz, 2H), 7.86 – 7.79 (m, 4H), 7.70 – 7.62 (m, 4H), 7.33 – 7.18 (m, 8H), 6.91 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 163.2, 148.3, 145.30, 137.0, 127.7, 127.2, 126.3, 122.4, 119.6, 88.5, 74.1. HRMS Calcd for $C_{26}H_{20}N_2O_2$ [M + H]$^+$ 393.1598; Found 393.1596.

1-Cyclohexyl-1-phenylprop-2-yn-1-ol (2f).[25] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.52 – 7.47 (m, 2H), 7.36 – 7.30 (m, 2H), 7.28 – 7.20 (m, 1H), 5.88 (s, 1H), 3.51 (s, 1H), 1.85 – 1.81 (m, 1H), 1.70 – 1.50 (m, 4H), 1.44 (m, 1H), 1.12 – 0.93 (m, 5H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 144.4, 127.4, 126.9, 126.0, 86.6, 75.9, 74.4, 49.6, 27.2, 26.9, 25.9, 25.7. HRMS Calcd for $C_{15}H_{18}O$ [M + Na]$^+$ 237.1250; Found 237.1248.

1,4-Di(cyclohexyl)-1,4-diphenylbut-2-yne-1,4-diol (3f). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.62 – 7.56 (m, 4H), 7.36 – 7.30 (m, 4H), 7.28 – 7.22 (m, 2H), 5.83 (s, 1H), 5.81 (s, 1H), 2.04 – 1.95 (m, 2H), 1.74 – 1.69 (m, 2H), 1.64 – 1.55 (m, 6H), 1.45 – 1.36 (m, 2H), 1.26 – 0.99 (m, 10H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 145.0, 145.0, 127.4, 126.9, 126.4, 126.3, 87.5, 87.5, 75.0, 74.9, 50.2, 50.2, 27.4, 27.4, 27.3, 27.2, 26.1, 26.1, 25.8. HRMS Calcd for $C_{28}H_{34}O_2$ [M + Na]$^+$ 425.2451; Found 425.2448.

4-Methyl-3-phenylpent-1-yn-3-ol (2g).[24] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65 – 7.59 (m, 2H), 7.38 – 7.28 (m, 3H), 2.69 (s, 1H), 2.38 (s, 1H), 2.11 (sept, *J* = 6.7 Hz, 1H), 1.08 (d, *J* = 6.6 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 143.4, 127.9, 127.7, 126.1, 85.0, 74.9, 40.2, 17.9, 17.3. HRMS Calcd for $C_{12}H_{14}O$ [M + Na]$^+$ 197.0937; Found 197.0939.

2,7-Dimethyl-3,6-diphenyloct-4-yne-3,6-diol (3g). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.64 – 7.57 (m, 4H), 7.38 – 7.22 (m, 6H), 5.86 (d, 2H), 2.03 – 1.93 (m, 2H), 1.04 – 0.99 (dd, *J* = 6.6, 4.1 Hz, 6H), 0.78 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 145.1, 145.0, 127.4, 127.4, 126.9, 126.3, 126.2, 87.3, 87.2, 75.4, 75.3, 40.4, 40.3, 17.9, 17.8, 17.6, 17.6. HRMS Calcd for $C_{22}H_{26}O_2$ [M + Na]$^+$ 345.1825; Found 345.1822.

1,1-Dicyclohexyl-prop-2-yn-1-ol (2h).[26] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.40 (s, 1H), 1.88 – 1.16 (m, 22H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 86.0, 76.8, 73.6, 43.6, 27.8, 26.7, 26.6, 26.5, 26.2. HRMS Calcd for $C_{15}H_{24}O$ [M + Na]$^+$ 243.1719; Found 243.1716.

1,1,4,4-Tetracyclohexylbut-2-yne-1,4-diol (3h). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.86 – 0.99 (m, 44H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 87.4, 77.0, 43.9, 28.1, 26.8, 26.7, 26.6, 26.4. HRMS Calcd for $C_{28}H_{46}O_2$ [M + Na]$^+$ 437.3390; Found 437.3389.

2-Ethynyl adamantan-2-ol (2i).[27] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 5.35 (s, 1H), 3.30 (s, 1H), 2.14 – 2.02 (m, 4H), 1.82 – 1.62 (m, 8H), 1.46 – 1.41 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ =89.6, 74.2, 70.2, 37.8, 37.2, 34.6, 31.1, 26.3, 26.3. HRMS Calcd for $C_{12}H_{16}O$ [M + Na]$^+$ 199.1093; Found 199.1090.

2,2'-(Ethyne-1,2-diyl)bis(adamantan-2-ol) (3i).[28] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 5.15 (s, 2H), 2.14 – 2.08 (m, 8H), 1.82 – 1.62 (m, 16H), 1.46 – 1.41 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 88.9, 70.3, 38.2, 37.4, 34.8, 31.3, 26.5, 26.4. HRMS Calcd for $C_{22}H_{30}O_2$ [M + Na]$^+$ 349.2138; Found 349.2136.

3-Ethynyl-3-diamantanol (2j). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 5.26 (s, 1H), 3.27 (s, 1H), 2.12 – 1.96 (m, 4H), 1.76 – 1.53 (m, 13H), 1.38 (dt, *J* =

12.3, 2.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 89.3, 74.3, 71.0, 46.6, 37.2, 36.9, 36.9, 36.5, 35.6, 35.6, 35.6, 34.8, 34.4, 31.7, 30.7, 25.5. HRMS Calcd for $C_{16}H_{20}O$ [M + Na]$^+$ 251.1406; Found 251.1403.

3,3'-(Ethyne-1,2-diyl)bis(3-diamantanol) (3j). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.32 (s, 2H), 2.13 – 1.56 (m, 34H), 1.51 – 1.42 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 89.4, 73.3, 47.8, 37.9, 37.7, 37.5, 37.3, 36.9, 36.4, 36.3, 36.00, 35.6, 32.4, 31.7, 26.3. HRMS Calcd for $C_{30}H_{38}O_2$ [M + Na]$^+$ 453.2764; Found 453.2763.

9-Ethynyl-9*H*-fluoren-9-ol (2k).[29] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.77 (d, *J* = 7.1 Hz, 2H), 7.63 (d, *J* = 7.1 Hz, 2H), 7.43 – 7.33 (m, 4H), 6.57 (s, 1H), 3.36 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 147.8, 138.4, 129.2, 128.2, 124.3, 120.2, 85.7, 73.3, 72.7. HRMS Calcd for $C_{16}H_{13}O$ [M – OH + MeOH]$^+$ 221.0961; Found 221.0990.

9,9'-(Ethyne-1,2-diyl)bis(9*H*-fluoren-9-ol) (3k).[29] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.74 (d, *J* = 7.1 Hz, 4H), 7.55 (d, *J* = 7.0 Hz, 4H), 7.42 – 7.30 (m, 8H), 6.44 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 147.9, 138.4, 129.1, 128.3, 124.3, 120.2, 83.0, 73.5. HRMS Calcd for $C_{28}H_{18}O_2$ [M + Na]$^+$ 409.1199; Found 409.1198.

9-Ethynyl-10,10-dimethyl-9,10-dihydroanthracen-9-ol (2l). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.91 (dd, *J* = 7.5, 1.8 Hz, 2H), 7.64 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.40 – 7.30 (m, 4H), 6.59 (s, 1H), 3.56 (s, 1H), 1.70 (s, 3H), 1.55 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 141.9, 137.9, 128.1, 127.5, 126.2, 125.5, 89.4, 75.7, 65.2, 37.5, 33.2, 31.3. HRMS Calcd for $C_{18}H_{16}O$ [M + Na]$^+$ 271.1093; Found 271.1110.

9,9'-(Ethyne-1,2-diyl)bis(10,10-dimethyl-9,10-dihydroanthracen-9-ol) (3l). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.79 (dd, *J* = 7.8, 1.4 Hz, 4H), 7.57 (dd, *J* = 7.9, 0.9 Hz, 4H), 7.34 – 7.29 (m, 4H), 7.24 (m, 4H), 6.32 (s, 2H), 1.61 (s, 6H), 1.35 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 142.6, 138.6, 128.4, 128.1, 126.5, 125.8, 90.4, 66.4, 38.1, 32.9, 32.1. HRMS Calcd for $C_{34}H_{29}O$ [M – OH]$^+$ 453.2213; Found 453.2191.

1-(3,4,5-Trimethoxyphenyl)prop-2-yn-1-ol (2o).[30] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 6.76 (s, 2H), 6.01 (d, *J* = 6.0 Hz, 1H), 5.27 (dd, *J* = 6.0, 2.3 Hz, 1H), 3.77 (s, 6H), 3.64 (s, 3H), 3.48 (d, *J* = 2.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 152.6, 137.6, 136.8, 103.6, 85.5, 75.7, 62.4, 60.0, 55.8. HRMS Calcd for $C_{12}H_{14}O_4$ [M + Na]$^+$ 245.0784; Found 245.0787.

1,4-Bis-(3,4,5-trimethoxyphenyl)but-2-in-1,4-diol (3o).[30] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 6.76 (s, 4H), 5.98 (d, 2H), 5.35 (q, 2H), 3.73 (d, 12H), 3.64 (s, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 152.6, 138.0, 136.8, 103.7, 86.3, 86.2, 62.6, 59.9, 55.7, 55.7. HRMS Calcd for $C_{22}H_{26}O_8$ [M + Na]$^+$ 441.1520; Found 441.1522.

(3,4,5-Trimethoxyphenyl)methanol (5o).[31] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 6.62 (s, 2H), 5.15 (t, *J* = 5.8 Hz, 1H), 4.42 (d, *J* = 5.7 Hz, 2H), 3.75 (s, 6H), 3.62 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 152.7, 138.3, 136.1, 103.4, 63.0, 60.0, 55.7. HRMS Calcd for $C_{10}H_{14}O_4$ [M + Na]$^+$ 221.0784; Found 221.0783.

3,4,5-Trimethoxybenzyl 3,4,5-trimethoxybenzoate (6o).[32] ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.28 (s, 2H), 6.80 (s, 2H), 5.27 (s, 2H), 3.83 (s, 6H), 3.78 (s, 6H), 3.74 (s, 3H), 3.66 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ = 165.2, 152.9, 152.8, 141.9, 137.2, 131.7, 124.7, 106.5, 105.3, 66.4, 60.1, 60.0, 56.00, 55.9. HRMS Calcd for $C_{20}H_{24}O_8$ [M + Na]$^+$ 415.1363; Found 415.1361.

Anthraquinone (4p).[33] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.35 – 8.29 (m, 4H), 7.83 – 7.78 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 183.2, 134.1, 133.6, 127.3. HRMS Calcd for $C_{14}H_9O_2$ [M + H]$^+$ 209.0597; Found 209.063.

Bianthrone (5p).[34] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.03 – 7.84 (m, 4H), 7.47 – 7.36 (m, 8H), 6.89 – 6.84 (m, 4H), 4.78 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 183.2, 140.1, 134.0, 132.4, 128.7, 128.1, 126.9, 54.6. HRMS Calcd for $C_{28}H_{18}O_2$ [M + Na]$^+$ 409.1199; Found 409.1199.

9-Ethynylphenanthrene (Ar-a1).[35] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.72 – 8.65 (m, 2H), 8.50 – 8.44 (m, 1H), 8.07 (s, 1H), 7.86 (d, *J* = 7.3 Hz, 1H), 7.73 – 7.66 (m, 3H), 7.64 – 7.58 (m, 1H), 3.48 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 133.1, 131.3, 131.1, 130.6, 130.2, 128.8, 127.9, 127.3, 127.1, 127.0, 122.9, 122.8, 118.7, 82.1, 81.7. HRMS Calcd for $C_{16}H_{10}$ [M + H]$^+$ 203.0946; Found 203.0948.

Phenanthrene (Ar-H).[36] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.71 (d, *J* = 8.1 Hz, 2H), 7.90 (dd, *J* = 7.8, 1.2 Hz, 2H), 7.75 (s, 2H), 7.70 – 7.58 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 132.3, 130.5, 128.8, 127.1, 126.8, 122.9. HRMS Calcd for $C_{14}H_{10}$ [M + H]$^+$ 179.0855; Found 179.0853.

1-Ethynyl-2,5-dimethoxybenzene (Ar-b1).[37] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.01 (d, *J* = 3.0 Hz, 1H), 6.88 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.82 (d, *J* = 9.0 Hz, 1H), 3.86 (s, 3H), 3.76 (s, 3H), 3.30 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 155.3, 153.3, 118.9, 116.4, 112.1, 111.8, 81.2, 80.2, 56.6, 55.9. HRMS Calcd for $C_{10}H_{10}O_2$ [M + Na]$^+$ 185.0573; Found 185.0575.

Bis(2,5-dimethoxyphenyl)acetylene (Ar-b2).[38] ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.08 (d, *J* = 2.7 Hz, 2H), 6.87 – 6.81 (m, 4H), 3.89 (s, 6H), 3.79 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 154.7, 153.4, 118.2, 116.0, 113.4, 112.4, 89.9, 56.8, 56.0. HRMS Calcd for $C_{18}H_{18}O_4$ [M + Na]$^+$ 321.1097; Found 321.1095.

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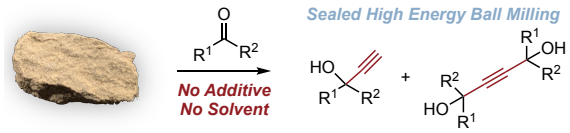

Sealed ball milling provides a novel way of activation of calcium carbide where no additive is required to transfer the acetylide moiety to organic molecules. Various ketones and even aryl halides can thereby be ethynylated.

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