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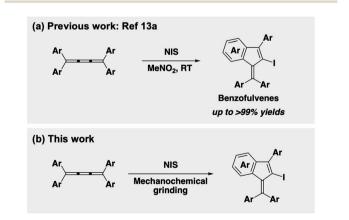
Mechanochemical transformation of tetraaryl[3] cumulenes to benzofulvenes *via* electrophilic iodocyclization[†]

Fumitoshi Yagishita, ២ *^{ab} Shoma Mukai,^a Sota Abe,^a Shoko Ueta,^a Yasushi Yoshida, 咆 ^c Yukihiro Arakawa, 🔎 ^a Keiji Minagawa^a and Yasushi Imada D ^a

We demonstrate solvent-free mechanochemical iodocyclization of tetraaryl[3] cumulenes using N-iodosuccinimides as the first example of the molecular transformation of cumulenes based on mechanochemistry. This mechanochemical reaction provides the corresponding benzofulvenes in good yields, overcoming the limitation of conventional methods using organic solvents.

Molecular transformation based on mechanochemistry has drawn considerable attention in organic synthesis owing to some advantages such as shorter reaction time and reduction or elimination of solvent use.¹ Therefore, many efforts have been devoted to developing mechanochemical synthesis including oxidation,² reduction,³ condensation,⁴ metalation,⁵ and transition metal-catalysed cross-coupling reactions.⁶ In addition, the mechanochemistry-based synthetic methods overcome the solubility issues in organic synthesis and enable the molecular transformation of insoluble organic compounds under milling conditions.⁷

Cumulenes, which have cumulative C–C double bonds, are recognized as an important class of sp-hybridized carbons that have unique structural properties and reactivities leading to a wide variety of hydrocarbon structures through dimerization,⁸ trimerization,⁹ intermolecular cycloaddition,¹⁰ and related cyclization reactions.¹¹ Although the mechanochemical synthesis of odd-numbered tetraaryl[*n*]cumulenes has been reported,¹² the molecular transformation of cumulenes based on mechanochemistry remains unexplored. Initially, we aimed to optimize the reaction conditions for the iodocyclization reaction of tetraaryl[3]cumulenes 1 using tetraphenyl[3]cumulene (1a) as a model substrate. The results are summarized in Table 1.



"Department of Applied Chemistry, Tokushima University, 2-1 Minamijosanjima, Tokushima 770-8506, Japan. E-mail: yagishitaf@tokushima-u.ac.jp

Scheme 1 Construction of a benzofulvene scaffold by the iodocyclization reactions of tetraaryl[3]cumulenes.

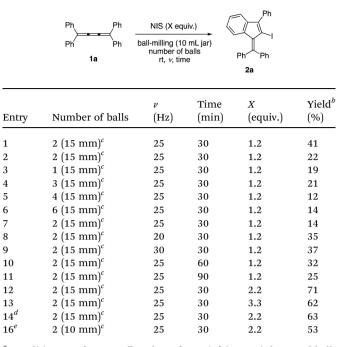
Recently, we reported the iodocyclization reactions of tetraaryl[3]cumulenes affording benzofulvene and tetraaryl[5] cumulene affording fulvene scaffolds in solution, respectively.¹³ For example, the electrophilic iodocyclization reaction of tetraaryl[3]cumulenes **1** using *N*-iodosuccinimide (NIS) proceeded smoothly *via* an iodonium intermediate in nitromethane at ambient temperature and gave the corresponding benzofulvenes **2** in good-to-high yields (Scheme 1a).^{13a} We also reported that the other common organic solvents were found to be ineffective for this reaction. Due to the potential applications of benzofulvene as a versatile building block for functional materials,¹⁴ it is important to develop environmentally friendly synthetic methods. Here we demonstrate the solvent-free iodocyclization reaction of tetraaryl[3]cumulenes **1** leading to benzofulvenes **2** under milling conditions (Scheme 1b).

^bInstitute of Post-LED Photonics, Tokushima University, 2-1 Minamijosanjima, Tokushima 770-8506, Japan

^cDepartment of Applied Chemistry and Biotechnology, Graduate School of Engineering, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan

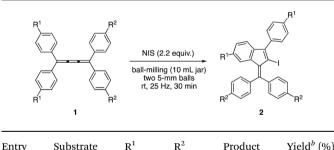
[†] Electronic supplementary information (ESI) available: Additional figures and NMR spectra. CCDC 2340176. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d4mr00022f

 Table 1
 Optimization of reaction conditions^a



^{*a*} Conditions: **1a** (0.3 mmol) and NIS (X equiv.) in a stainless-steel ballmilling jar (10 mL). ^{*b*} The yields were determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. ^{*c*} The values in parentheses are the diameters of balls. ^{*d*} ZrO₂ jar and balls were used instead of stainless-steel jar and balls. ^{*e*} 5 mL stainless-steel jar was used instead of 10 mL stainless-steel jar.

Table 2Scope and limitation of mechanochemical iodocyclization oftetraaryl[3]cumulenes 1 a



Enery	Substrate	ĸ	ĸ	Tiouuee	field (70)
1	1a	н	н	2a	69
2	1b	Ме	Ме	2b	91
3	1c	ОМе	ОМе	2c	14
4	1d	F	F	2d	0
5	1e	Cl	Cl	2e	Trace
6	1f	OMe	Н	2 f	61
7	1g	OMe	Me	2g	90
8	1h	OMe	Cl	2h	82

 a Conditions: 1 (0.3 mmol) and NIS (0.66 mmol) in a stainless-steel ballmilling jar (10 mL) equipped with two stainless-steel balls of 15 mm diameter. b Isolated yields.

When 0.3 mmol of **1a** and 1.2 equiv. of NIS were placed in a 10 mL stainless-steel jar equipped with two stainless-steel balls of 15 mm diameter and agitated at 25 Hz in a vibratory

ball-mill for 30 minutes, the objective benzofulvene 2a was obtained in 41% yield (entry 1). The use of iodine instead of NIS as the iodonium cation source decreased the yield of 2a (entry 2). The other combinations of the number of balls and their diameter also resulted in lower yields (entry 1 vs. entries 3-7). The reactions at the milling frequencies of 20 or 30 Hz led to low yields (entries 8 and 9). The longer reaction time slightly decreased the yields of 2a (entries 10 and 11). Notably, increasing the amount of NIS improved the reaction and the benzofulvene 2a was obtained in up to 71% yields (entries 12 and 13). The use of a ZrO₂ jar and balls resulted in lower yield than the use of a stainless-steel jar and balls (entry 14). We also conducted the reaction in a 5 mL jar equipped with two stainless-steel balls of 10 mm diameter. However, the use of a 5 mL jar was ineffective for this reaction (entry 15). Because the use of 2.2 equiv. of NIS led to the highest yield, we found that the reaction using 2.2 equiv. of NIS in a 10 mL stainlesssteel jar equipped with two stainless-steel balls of 15 mm diameter at a milling frequency of 25 Hz for 30 minutes provides the optimum conditions for this reaction (entry 12).

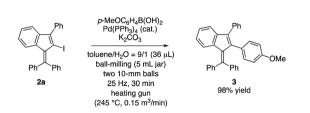
Next, we investigated the substrate scope using various tetraaryl[3]cumulenes **1** under the optimized reaction conditions (Table 2).

The reaction using tetrakis(*p*-methylphenyl)[3]cumulene (1b) proceeded smoothly under milling conditions; the corresponding benzofulvene 2b was obtained in 91% yield. On the other hand, mechanochemical iodocyclization of 1c gave the benzofulvene 2c in low yield owing to the formation of unidentified oligomer products under milling conditions. Similar unidentified oligomer formation was observed in the absence of NIS under milling conditions. Because the formation of oligomer products was observed after the mechanochemical reaction of 1c even in the absence of NIS, we consider that the oligomerization of 1c preferentially occurs rather than intermolecular reaction under milling conditions. Halogen substituents such as F (1d) and Cl (1e) at aryl rings were ineffective for electrophilic iodocyclization owing to the unfavorable nucleophilic attack of the electron-deficient aryl ring on iodonium intermediates. It was found that the regioselective iodocyclization of unsymmetrical tetraaryl[3]cumulenes 1f-h occurred from the electron-rich aromatic ring to the iodonium cation, affording the corresponding benzofulvenes 2f-h as the sole product in good yield, respectively. The structures of 2f and 2g were determined by ¹H NMR according to our previous report.^{13a} The structure of 2h was determined by NMR spectroscopy, HRMS, and single-crystal crystallographic analysis. Xray analysis of 2h unequivocally revealed that the iodocyclization occurred at the *p*-methoxyphenyl ring, resulting in the formation of a methoxy-substituted benzofulvene scaffold (Fig. S1[†]).

Recently, Ito and co-workers have developed a hightemperature ball-milling technique for the palladiumcatalysed Suzuki–Miyaura cross-coupling reaction of insoluble aryl halides with aryl boronic acids.^{7b} Their accomplishments encouraged us to demonstrate the iodocyclization reaction of tetraaryl[3]cumulenes under high-temperature milling conditions. In this study, we demonstrated the iodocyclization



Scheme 2 Mechanochemical iodocyclization reaction of 1a at high temperature.



Scheme 3 Mechanochemical Suzuki–Miyaura cross-coupling reaction of benzofulvene 2a with *p*-methoxyphenylboronic acid at high temperature.

reactions of **1a** and **1e** using a temperature-controllable heating gun with a preset temperature of 245 °C under milling conditions. After heating for 30 minutes, the internal temperature reached 144 °C, which was confirmed with an infrared radiation thermometer. Notably, the reaction of **1a** proceeded smoothly even in the presence of **1.2** equiv. of NIS and provided the benzofulvene **2a** in 90% yield (Scheme 2). Unfortunately, the high-temperature ball-milling technique did not improve the iodocyclization of tetrakis(*p*-chlorophenyl)[3]cumulene (**1e**) and the reaction afforded a trace amount of complex mixture.

We previously reported the utility of 1-(diphenylmethylene)-3-phenyl-2-iodo-1*H*-indene (2a) as a coupling partner in the common transition metal-catalysed cross-coupling reactions in solution, leading to tetrafunctionalized benzofulvenes.^{13a} From the viewpoint of green chemistry, we conducted the mechanochemical Suzuki–Miyaura cross-coupling reaction of 2a with *p*methoxyphenylboronic acid under liquid-assisted griding (LAG) conditions. The reaction proceeded smoothly at high temperature conditions and provided the corresponding tetraarylated benzofulvene 3 in 98% yield (Scheme 3).

Conclusions

In conclusion, we have demonstrated the solvent-free mechanochemical iodocyclization of seven tetraaryl[3]cumulenes. Although the reactions of **1d** and **1e** having four electron deficient aryl rings did not proceed owing to their low nucleophilicities, the reactions of other tetraaryl[3]cumulenes gave the corresponding benzofulvenes **2** in up to 91% yield even under milling conditions. This environmentally friendly approach enabled the molecular transformation of tetraaryl[3]cumulenes to benzofulvenes without using nitromethane, which has explosive properties. The high-temperature ball-milling technique was also found to promote the iodocyclization reaction of **1a**, providing benzofulvene **2a** in 90% yield even in the presence of **1**.2 equiv. of NIS. In addition, the LAG mechanochemical Suzuki–Miyaura cross-coupling reaction of **2a** provided the highly functionalized benzofulvene scaffold in 98% yield.

Author contributions

Fumitoshi Yagishita: conceptualization, methodology, writing – original draft; Shoma Mukai: investigation; Sota Abe: investigation; Shoko Ueta: investigation; Yasushi Yoshida: investigation; Yukihiro Arakawa: investigation; Keiji Minagawa: writing – review & editing; Yasushi Imada: supervision, writing – review & editing.

Conflicts of interest

There are no conflicts to declare.

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