



Mechanochemical McMurry reaction†

Cite this: *RSC Mechanochem.*, 2025, 2, 636Sayan K. Jana,‡ Sakshi Ajay Shirsath,‡ Debjyoti Bhattacharjee,‡ Pramod Kumar  ‡ and Biplab Maji  *Received 9th May 2025
Accepted 11th June 2025

DOI: 10.1039/d5mr00065c

rsc.li/RSCMechanochem

In this study, a mechanochemical adaptation of the McMurry coupling reaction was developed to synthesize ethylenes using Zn/TiCl₄/Et₃N as reagents. Leveraging solvent-free ball-milling conditions, the method achieved up to 97% yield across >23 substrates. The reaction was performed without inert gas protection in a Teflon milling jar and was found to be scalable and to accommodate various functional groups.

With the increase in methodological implications and promising growth in photochemistry,¹ electrochemistry,² flow chemistry,³ and mechanochemistry,⁴ chemists are becoming more inclined to pursue sustainable chemical syntheses. Though each methodology has its unique approach toward this goal, mechanochemistry is quite effective at mediating the reaction in the solid phase within a reduced reaction time.⁵ Traditional methods have emphasized solvents as a major component in facilitating the collisions of the reagents. However, at the same time, the use of solvents consistently has adverse effects on atom economy, reaction time, and energy requirements.⁶

The formation of olefins is a crucial step in organic synthesis, enabling the creation of a wide range of natural and synthetic compounds used in healthcare, industry, and functional materials. Various strategies have been developed to achieve olefination reactions with precise control over stereoselectivity, regioselectivity, and chemoselectivity. Key methods include the Wittig reaction, Horner–Wadsworth–Emmons reaction, Julia–Kocienski olefination, and Tebbe olefination.^{7a,b} Additionally, catalytic-scale olefination reactions such as olefin metathesis (*e.g.*, Grubbs metathesis) and cross-coupling reactions (*e.g.*, the Heck reaction) remain extensively studied and widely applied in modern synthesis.^{8a,b}

In the 1980s, the emergence of the McMurry coupling reaction,^{9a-c} involving the reductive coupling of two carbonyl compounds, established a pathway to synthesize alkenes, including tetra-aryl ethylenes (TAEs),^{10a-d} which are of broad interest in material science,¹¹ supramolecular chemistry,^{12a-c} the pharmaceutical industry,^{10c,13} and biomedical applications (Fig. 1A). This thermal reaction is a two-step process and is mediated by low-valent-titanium-based reagents, which, due to their extreme sensitivity, are generated *in situ* using stable Ti(III) and Ti(IV) precursors and metal reductants (Zn, Zn–Cu, K, Li, *etc.*) in an inert solvent under rigorous exclusion of air and moisture (Fig. 1B).¹⁴ The success of the reaction depends on the first step, the generation of the low-valent Ti species. Additionally, sparingly soluble carbonyl compounds hardly proceed to quantitative yields.¹⁵

In this regard, the mechanochemical McMurry coupling appears promising for the synthesis of TSEs. Deploying mechanical stress and shear could enable milder reaction conditions. Moreover, decreased reaction time and inert-gas-protection-free product formation without solvent could bring additional advantages. Ito and co-workers have recently unveiled the potential of mechanochemistry for various organic transformations.^{16a-c} Metallic-zinc-mediated mechanochemical Simmons–Smith cyclopropanation *via* ball milling has also been reported by Browne.¹⁷ We reported the mechanochemical Clemmensen reduction reaction.¹⁸ In the current work, we developed a McMurry coupling reaction performed under ball-milling conditions and requiring neither inert gas nor solvent (Fig. 1C). The method enabled the coupling of a diverse range of carbonyls, including sparingly soluble substrates, allowing the synthesis of tetrasubstituted ethylenes (TSEs) in high yields.

Proceeding with our proposition, we chose benzophenone **1a** as a model substrate for generating tetra-phenyl ethylene (TPE, **2a**) using TiCl₄ and zinc powder as the reducing reagent and trimethylamine base without solvent (Table 1). A one-pot, two-step ball-milling strategy was adopted for the reaction. The first step generated the low-valent Ti species (Ti_{4–n}Cl_{4–n}) for the de-oxygenative reductive olefination of carbonyls.

Department of Chemical Sciences, Indian Institute of Science Education and Research Kolkata, Mohanpur 741246, WB, India. E-mail: bm@iiserkol.ac.in

† Electronic supplementary information (ESI) available: Synthesis and characterization details (PDF). See DOI: <https://doi.org/10.1039/d5mr00065c>

‡ These authors contributed equally.



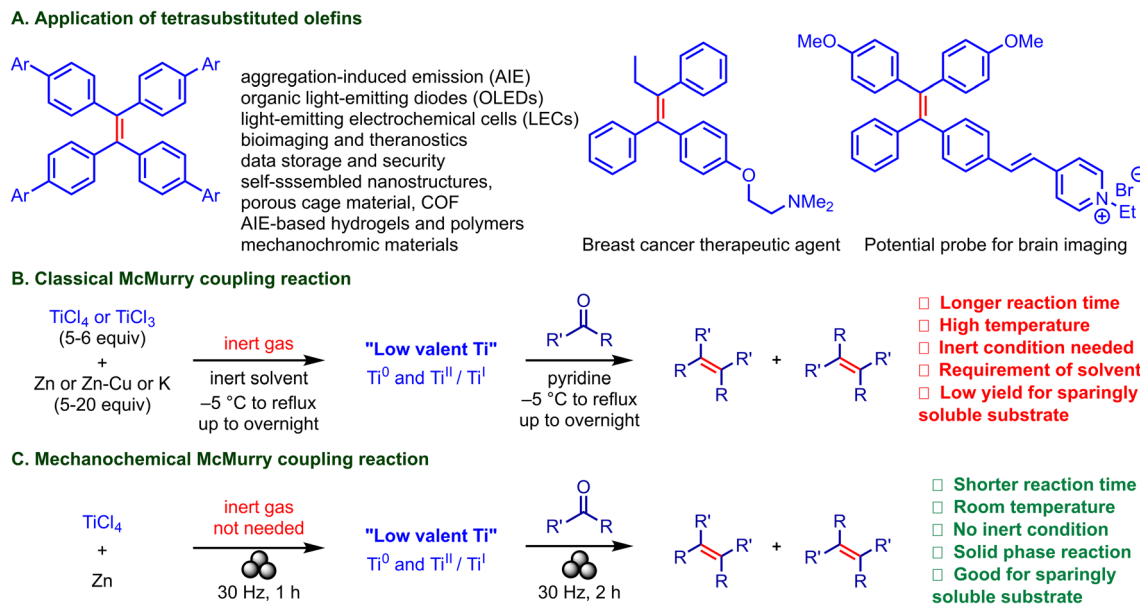
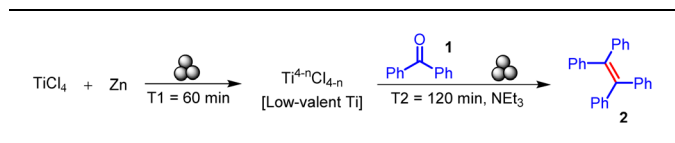


Fig. 1 Applications of tetrasubstituted olefins (A); classical McMurry coupling reaction under thermal conditions (B); and mechanochemical synthesis of tetrasubstituted olefins using the McMurry coupling reaction under ball-milling conditions (C).

Table 1 Optimization of the reaction conditions^a



Entry	Variations from the above condition	2a (% yield)
1	None	99
2	T2 = 90 min	64
3	T1 (90 min) and T2 (90 min)	83
4	T1 (60 min) and T2 (90 min)	64
5	TiCl_4 (0.6 mmol), Zn (1.0 mmol)	47
6	TiCl_4 (0.4 mmol), Zn (1.0 mmol)	45
7	Pyridine instead of NEt_3 (T2 = 90 min)	12
8	K_2CO_3 instead of NEt_3 (T2 = 90 min)	13
9	Without NEt_3	Trace
10	One 10 mm-diameter SS ball	63
11	Four 5 mm-diameter SS balls	60
12	20 Hz oscillation frequency	75
13	Two 10 mm-diameter Zr balls	94
14	Two 10 mm-diameter Teflon balls	70
15 ^b	Two 10 mm-diameter Teflon balls	97

^a Reaction conditions: TiCl_4 (0.6 mmol) and Zn (1.2 mmol), two 10 mm-diameter SS balls in a 5-mL SS jar, T1 = 60 min, at 30 Hz. Then **1** (0.1 mmol), and Et_3N (0.7 mmol), T2 = 120 min at 30 Hz. Yield was calculated using GC-FID, taking mesitylene as an internal standard.

^b 5-mL Teflon jar was used.

All the reagents were weighed and mixed in air under ambient conditions. A mixture of TiCl_4 (6 equiv.) and Zn (12 equiv.) was placed in a stainless steel (SS) jar with 10 mm-diameter SS balls and oscillated at 30 Hz for T1 (=60 min). Subsequently, Et_3N (7 equiv.) and carbonyl compound were

added to the resulting mixture, which was then milled again for T2 (=120 min). As a result, an excellent yield of 99% for **2** was achieved to our delight (Table 1, entry 1).

While screening the reaction conditions, we found that the milling times T1 and T2 played a crucial role in achieving a higher yield of product **2**. Shortening T2 from 120 to 90 min decreased the yield to 64% (entry 2). With T2 at 90 min, changing T1 to 90 min increased the yield to 83% (entry 3), while reducing T1 to 60 further reduced the yield to 64% (entry 4). A similar effect was observed for the amounts of TiCl_4 and Zn used, as decreasing them reduced the yield to 45–47% (entries 5 and 6) at T1 = 60 min and T2 = 90 min. The pivotal role of the base was also noticed, as changing it from triethylamine to pyridine drastically reduced the yield to 12% (entry 7). In addition, when using K_2CO_3 or not including base, no **2a** formed (entries 8 and 9).

Next, we optimized key milling parameters, including the ball-to-reagent mass ratio, oscillation frequency, and milling medium, as they in general significantly influence reaction kinetics. Reducing the number of stainless steel (SS) balls negatively impacted the yield (entry 10). Increasing the ball number while decreasing its size and keeping the mass ratio constant also resulted in a lower yield (entry 11). Similarly, lowering the oscillation frequency diminished the reaction efficiency (entry 12).

To address corrosion observed during milling, we tested alternative solutions. Replacing SS balls with zirconium (Zr) balls gave a comparable yield but did not resolve the corrosion issue (entry 13). Using Teflon balls reduced corrosion but delivered a lower 70% yield (entry 14). We then designed a custom-made Teflon tube, which can be inserted into the SS milling jar (see ESI†). The tube, combined with Teflon balls, provided an excellent 97% yield of **2a** with no corrosion (entry 15).



These optimized conditions encouraged us to further investigate the substrate scope for TAE synthesis (Fig. 2). Benzophenones containing various alkyl groups (3–5) and halogens (6–8) reacted smoothly under these conditions, delivering TAEs in excellent 91–98% yields. Fluorenone also reacted smoothly under these conditions, delivering **9** in an excellent 96% yield. However, a benzophenone derivative having a reducible cyano functional group failed to produce **10** under these conditions.

Furthermore, when acetophenones were treated under these ball-milling reaction conditions, tetrasubstituted olefins were produced in high yields, albeit in moderate to low *E/Z* ratios. Electron-neutral, electron-rich, and electron-deficient acetophenones reacted similarly well, producing olefins **11–18** in 81–96% yields with 1:1 to 5:1 *E/Z* ratios. The highest regioselectivity (5:1) was seen for bromo-substituted acetophenone **17**. The reaction also accommodated the free phenolic OH group to produce **18** in 76% yield. However, an indenone-based substrate

failed to produce **19** under this condition, possibly due to the higher crowding in the product.

Various benzaldehydes were also tested as substrates. The reaction proceeded smoothly, and stilbenes **21–28** were isolated in high 70–93% yields. Importantly, exclusively *E*-selectivity was observed. In these cases, functional groups including Me (**21**), Ph (**22**), OMe (**23**), SMe (**24**), halogens (**25–27**), and CF₃ (**28**) were tolerated. However, when cyanobenzaldehyde was used as a substrate, the reaction failed to produce the desired product in an appreciable yield.

To demonstrate the practical utility of this protocol, we investigated a 10-fold scale up of the synthesis of **7** (Fig. 3a). The mechanochemical McMurry reaction was carried out on a scale of 1 mmol in a 10 mL stainless steel ball-milling jar with four 10 mm-diameter SS balls. It produced **7** in 67% yield. Compound **7** was reacted with boronic acid **29** to obtain the C4 symmetric compound **30**, an important building block for synthesizing covalent organic frameworks (COFs, Fig. 3b).

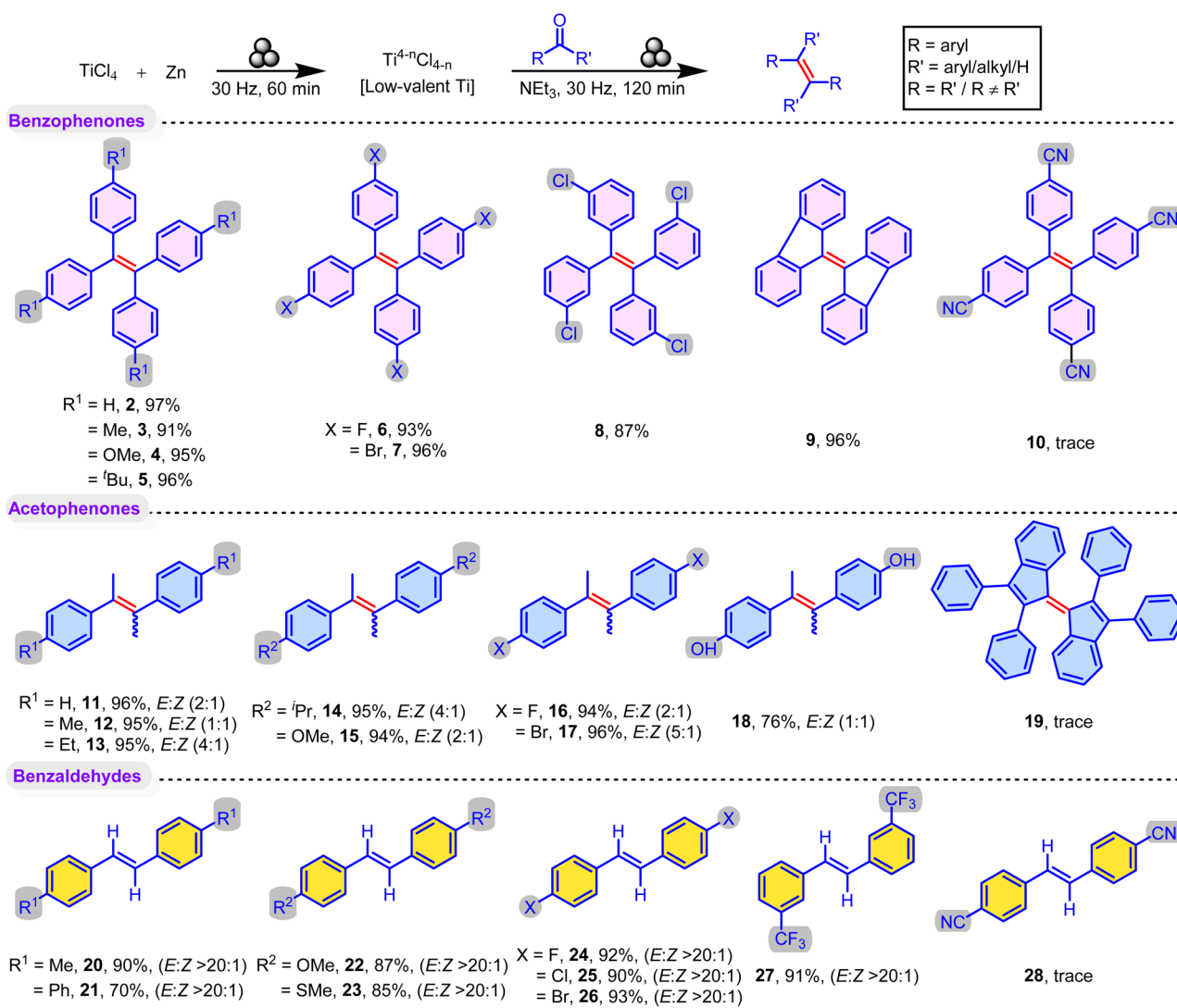


Fig. 2 ^aReaction conditions: Table 1, entry 15. Isolated yield. *E* : *Z* ratios were determined from ¹H-NMR analysis of the crude reaction mixture.



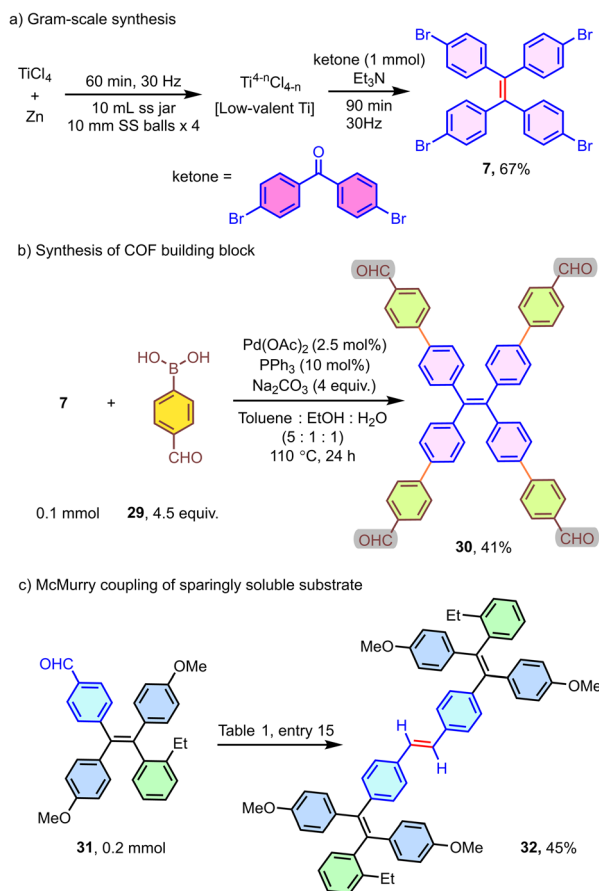


Fig. 3 (a) Scaled-up mechanochemical synthesis. (b) Synthesis of COF building blocks. (c) McMurry coupling of a sparingly soluble substrate.

Because of their importance in applications including organic light-emitting diodes, organic photovoltaics, organic semiconductors, and organic thin-film transistors, the functionalization of TAEs and the synthesis of conjugated alkenes have attracted considerable attention. We were therefore inspired to investigate the possibility of using our mechanorod approach to promote deoxygenative dimerization of TAEs. In this regard, carbaldehyde **31** was chosen as the model. The mechanochemical reaction under these conditions produced the desired olefin **32** with a 45% yield (Fig. 3c). Notably, the low solubility of compound **31** demonstrates the utility of mechanochemical reactions for modulating challenging reactions in the solid state.

Conclusions

The potential of mechanochemistry as a sustainable method for organic synthesis has been demonstrated in this work. We established the synthesis of TAEs and TSEs in an environmentally friendly and cost-effective manner with excellent yields and broad functional group tolerance under solvent-free ball-milling conditions. By eliminating the need for solvents, costly catalysts, and sensitive reaction conditions, this technique allows for the synthesis of clean reaction products in less

time than do conventional methods. These results demonstrated mechanochemistry as an environmentally benign and scalable route to green chemistry advancement.

Data availability

The ESI† includes all experimental details, including optimization of the synthetic method, synthesis and characterization of all starting materials and products reported in this study, and NMR spectra of all products.

Author contributions

S. K. J., D. B., and B. M. conceived and designed the project. S. K. J., S. A. S., D. B., and P. K. performed the experiments and contributed equally to this work. S. K. J., P. K., and B. M. wrote the manuscript. B. M. acquired the funding and directed the research.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

S. K. J. and P. K. acknowledge, respectively, PMRF and CSIR for PhD fellowships. The authors thank DST-ANRF (erstwhile SERB) (Grant No. SCP/2022/000352) for financial support.

Notes and references

- N. Hoffmann, *Chem. Rev.*, 2008, **108**, 1052–1103.
- M. Yan, Y. Kawamata and P. S. Baran, *Chem. Rev.*, 2017, **117**, 13230–13319.
- H. L. D. Hayes and C. J. Mallia, *Org. Process Res. Dev.*, 2024, **28**, 1327–1354.
- J. L. Howard, Q. Cao and D. L. Browne, *Chem. Sci.*, 2018, **9**, 3080–3094.
- S. Pagola, *Crystals*, 2023, **13**, 124.
- X. Liu, Y. Li, L. Zeng, X. Li, N. Chen, S. Bai, H. He, Q. Wang and C. Zhang, *Adv. Mater.*, 2022, **34**, 2108327.
- (a) B. Huang, Y. Shen, Z. Mao, Y. Liu and S. Cui, *Org. Lett.*, 2016, **18**, 4888–4891; (b) K. Esfandiartard, J. Mai and S. Ott, *J. Am. Chem. Soc.*, 2017, **139**, 2940–2943.
- (a) O. M. Ogba, N. C. Warner, D. J. O'Leary and R. H. Grubbs, *Chem. Soc. Rev.*, 2018, **47**, 4510–4544; (b) I. P. Beletskaya and A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009–3066.
- (a) M. Ephritikhine and C. Villiers, in *Modern Carbonyl Olefination*, 2003, pp. 223–285, DOI: [10.1002/3527601880.ch6](https://doi.org/10.1002/3527601880.ch6); (b) J. E. McMurry and M. P. Fleming, *J. Am. Chem. Soc.*, 1974, **96**, 4708–4709; (c) T. Takeda and A. Tsubouchi, *J. Am. Chem. Soc.*, 1974, **96**, 4708–4709.
- (a) P. Kumar and B. Maji, *J. Mater. Chem. A*, 2023, **11**, 20752–20760; (b) R. P. Tanpure, A. R. Harkrider, T. E. Strecker, E. Hamel, M. L. Trawick and K. G. Pinney, *Bioorg. Med. Chem.*, 2009, **17**, 6993–7001; (c) M. Banerjee, S. J. Emond, S. V. Lindeman and R. Rathore, *J. Org. Chem.*, 2007, **72**,



- 8054–8061; (d) M. Zhang, Y. Yao, P. J. Stang and W. Zhao, *Angew. Chem., Int. Ed.*, 2020, **59**, 20090–20098.
- 11 B. C. Patra and S. Bhattacharya, *Chem. Mater.*, 2021, **33**, 8512–8523.
- 12 (a) Y. Hong, J. W. Y. Lam and B. Z. Tang, *Chem. Soc. Rev.*, 2011, **40**, 5361–5388; (b) M. L. Saha, X. Yan and P. J. Stang, *Acc. Chem. Res.*, 2016, **49**, 2527–2539; (c) X. Yan, T. R. Cook, P. Wang, F. Huang and P. J. Stang, *Nat. Chem.*, 2015, **7**, 342–348.
- 13 K. Ohta, A. Kaise, F. Taguchi, S. Aoto, T. Ogawa and Y. Endo, *Molecules*, 2019, **24**, 3966.
- 14 X.-F. Duan, J. Zeng, J.-W. Lü and Z.-B. Zhang, *J. Org. Chem.*, 2006, **71**, 9873–9876.
- 15 T. Seo, in *Palladium-Catalyzed Mechanochemical Cross-Coupling Reactions*, ed. T. Seo, Springer Nature Singapore, Singapore, 2024, pp. 93–142, DOI: [10.1007/978-981-97-1991-4_4](https://doi.org/10.1007/978-981-97-1991-4_4).
- 16 (a) K. Kondo, K. Kubota and H. Ito, *Chem. Sci.*, 2024, **15**, 4452–4457; (b) K. Kubota, T. Endo, M. Uesugi, Y. Hayashi and H. Ito, *ChemSusChem*, 2022, **15**, e202102132; (c) R. Takahashi, A. Hu, P. Gao, Y. Gao, Y. Pang, T. Seo, J. Jiang, S. Maeda, H. Takaya, K. Kubota and H. Ito, *Nat. Commun.*, 2021, **12**, 6691.
- 17 L. Pontini, J. A. Leitch and D. L. Browne, *Green Chem.*, 2023, **25**, 4319–4325.
- 18 D. Bhattacharjee, S. K. Jana and B. Maji, *Synthesis*, 2024, **57**, 84–90.

