

**Solid-state cross-coupling reactions of insoluble aryl halides
under polymer-assisted grinding conditions**

Journal:	<i>Faraday Discussions</i>
Manuscript ID	FD-ART-05-2022-000121.R1
Article Type:	Paper
Date Submitted by the Author:	06-Jul-2022
Complete List of Authors:	Kubota, Koji; Hokkaido University, Department of Applied Chemistry, Faculty of Engineering Seo, Tamae; Hokkaido University Ito, Hajime; Hokkaido University, Department of Applied Chemistry, Faculty of Engineering

ARTICLE

Solid-state cross-coupling reactions of insoluble aryl halides under polymer-assisted grinding conditions

Received 00th January 20xx,
Accepted 00th January 20xx

Koji Kubota,^{*a,b} Tamae Seo,^a and Hajime Ito^{*a,b}

DOI: 10.1039/x0xx00000x

In this study, polymer-assisted grinding (POLAG), a ball milling technique based on the use of polymer additives, was applied to mechanochemical solid-state Suzuki–Miyaura cross-coupling reactions of insoluble aryl halides. We found that the efficiency of this challenging solid-state cross-coupling was improved by the addition of polytetrafluoroethylene (PTFE) as a POLAG additive under high-temperature ball-milling conditions. Our results suggest that POLAG is a promising approach for controlling the reactivity of insoluble substrates that are barely reactive under conventional solution-based conditions.

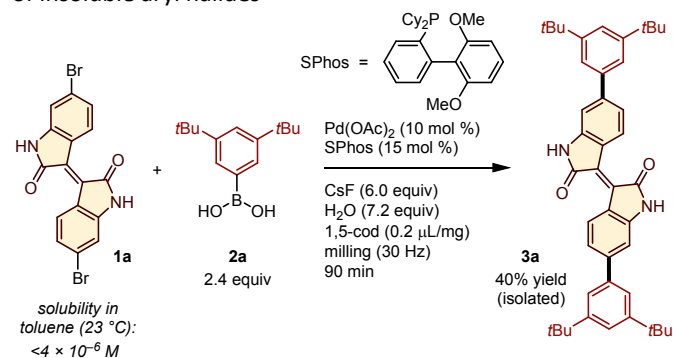
Introduction

Mechanochemical organic synthesis has been attracting attention as a new, environmentally friendly synthetic technology for the preparation of valuable molecules in pharmaceuticals and material sciences as it eliminates the use of substantial amounts of potentially harmful organic solvents.^{1,2} In addition, ball-milling enables solid-state organic reactions, thereby providing exciting opportunities to explore novel synthetic strategies in a solid-state reaction environment.^{1–3} Importantly, solid-state conditions can enable various transformations of poorly soluble or insoluble organic compounds that are barely reactive in solution. However, the applicability of mechanochemical synthesis to such insoluble substrates remains poorly explored.^{3a,3d,3g,4}

Recently, we reported the solid-state Suzuki–Miyaura cross-coupling of a wide variety of extremely unreactive and poorly soluble aryl halides, such as 6,6-dibromoisoindigo (**1a**), in the presence of a Pd(OAc)₂/SPhos/1,5-cod catalytic system under high-temperature ball-milling conditions (Scheme 1).^{3d,3h,5} We used 1,5-cyclooctadiene (1,5-cod) as an additive for liquid-assisted grinding (LAG)^{6,7}, which acts as both a dispersant for palladium-based catalysts to suppress undesired aggregation of nanoparticles and a stabilizer for the monomeric Pd(0) active species.^{3b–3d} That study illustrated the potential of solid-state mechanochemistry for accessing an uncharted area of chemical space through cross-coupling of insoluble organic compounds. However, as the yields of coupling products were low to moderate, the efficiency of the solid-state cross-coupling requires significant improvement.^{3d} Attempts at solid-state cross-coupling under various LAG conditions did not result in improved efficiency.^{3d}

Previously, ball-milling with polymers as additives, i.e., polymer-assisted grinding (POLAG), facilitated organic reactions and co-crystallization by improving the mixing efficiency of solid substrates.^{8,9} For example, Lamaty et al. reported that POLAG in the presence of polyethylene glycols (PEGs) improved the efficiency of mechanochemical Mizoroki–Heck reactions.⁹ Furthermore, flexible polymers can form nanocarbon-based composites through polymer impregnation in the microstructures.¹⁰ Based on these studies, in this study, we investigated the Suzuki–Miyaura cross-coupling reactions of insoluble aryl halides using POLAG, through which the polymers could weaken the intermolecular interactions among the insoluble solid substrates, thereby enabling efficient cross-coupling.^{3h}

Scheme 1. Previous work: solid-state cross-coupling reactions of insoluble aryl halides



Experimental section

Solid-state cross-coupling of insoluble aryl halides using polymer-assisted-grinding

Reactions were conducted in a Retch MM400 ball mill in a stainless steel milling jar (1.5 mL) at 30 Hz using a stainless steel ball (diameter: 5 mm) for 90 min. We used a commercially available temperature-controllable heat gun, which was placed directly above the ball-milling jar to control the reaction

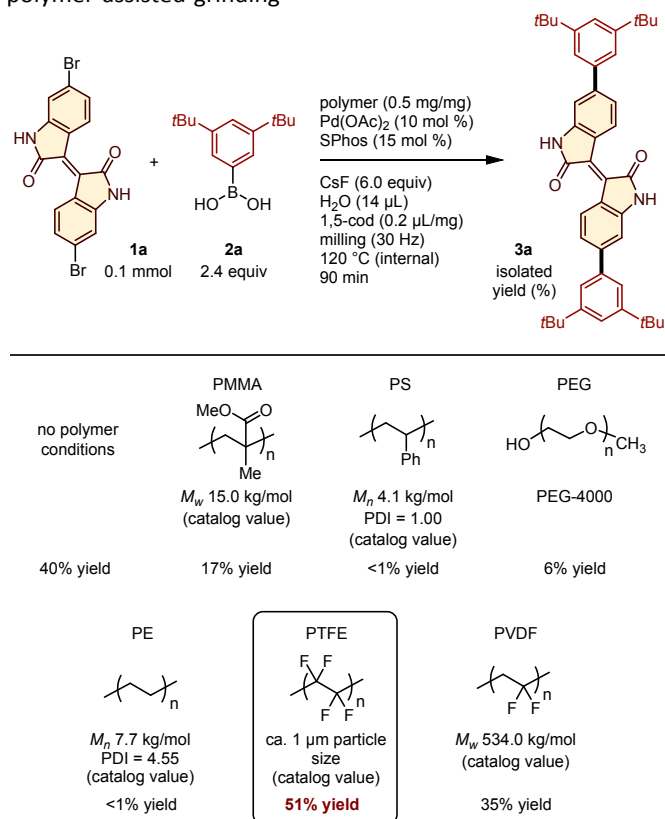
^a Division of Applied Chemistry, Graduate School of Engineering, Hokkaido University, Sapporo, Hokkaido, Japan.

^b Institute for Chemical Reaction Design and Discovery (WPI-ICReDD), Hokkaido University, Sapporo, Hokkaido, Japan.

Electronic Supplementary Information (ESI) available: See DOI: 10.1039/x0xx00000x

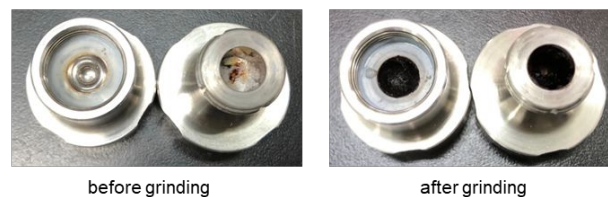
temperature (details in Supporting Information).^{3d} Reactions were performed using a heat gun preset to 250 °C, and the internal temperature of the reaction mixture (120 °C) was assessed by thermography immediately after opening the milling jar (details in Supporting Information). First, we conducted polymer screening for the solid-state cross-coupling of 6,6-dibromoisoindigo (**1a**), which has a solubility of $<4 \times 10^{-6}$ M in toluene at 23 °C^{3d,11}, in the presence of Pd(OAc)₂/SPhos/1,5-cod^{3d,3h} and 3,5-di-*tert*-butylphenyl boronic acid (**2a**) under high-temperature ball-milling conditions (Scheme 2). We added various commercially available polymers (0.5 mg/mg; 100 mg under the current conditions) to the reaction mixture to determine whether POLAG can improve reaction efficiency (Scheme 2). Reactions with poly(methyl methacrylate) (PMMA) or polystyrene (PS) afforded a lower yield of **3a** than reactions without polymers (17% and <1% yield, respectively). The addition of PEG, which was previously used in the mechanochemical Mizoroki–Heck coupling,⁹ did not improve the yield (6%). Reaction with polyethylene (PE) produced only trace amounts of **3a** (<1% yield). However, polytetrafluoroethylene (PTFE) with a particle size of ~1 μm improved the efficiency, affording a better yield of **3a** than that previously reported (51% yield).^{3d} The reaction with polyvinylidene fluoride (PVDF) furnished **3a** in a moderate yield (35%). Notably, the reaction mixture obtained after ball milling without polymer additives appeared as a black solid (Figure 1a), whereas that obtained after POLAG with PTFE appeared as a dark pink paste-like solid (Figure 1b).

Scheme 2. Screening of polymeric materials as additives for polymer-assisted-grinding^a



^aConditions: **1a** (0.10 mmol), **2a** (0.24 mmol), Pd(OAc)₂ (0.01 mmol), SPhos (0.015 mmol), CsF (0.6 mmol), polymer (0.5 mg/mg), H₂O (14 μL), and 1,5-cod (0.20 μL) in a stainless steel ball-milling jar (1.5 mL).

(a) reaction without polymer additives



(b) reaction with PTFE

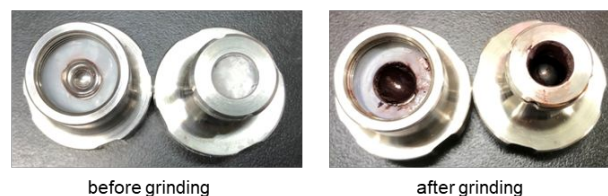


Figure 1. Reaction mixture after the cross-coupling of **1a** (a) without polymer additives and (b) with PTFE.

Next, we tested other mechanochemical conditions in the presence of the POLAG additive, PTFE (Table 1). Decreasing the amount of PTFE led to a lower yield of **3a** (entries 1 and 2). The reaction with 50 μL of water slightly improved the yield of **3a** (56%, entry 3). However, the use of 20 mol% Pd(OAc)₂ and 40 mol% SPhos significantly decreased the reaction efficiency (5%, entry 4). We then used PTFE with different particle sizes (entries 5 and 6). Interestingly, using larger PTFE particles (particle size: <12 μm and >40 μm) resulted in poor yields (16% and 3%, respectively).

Table 1. Optimization study for POLAG^a

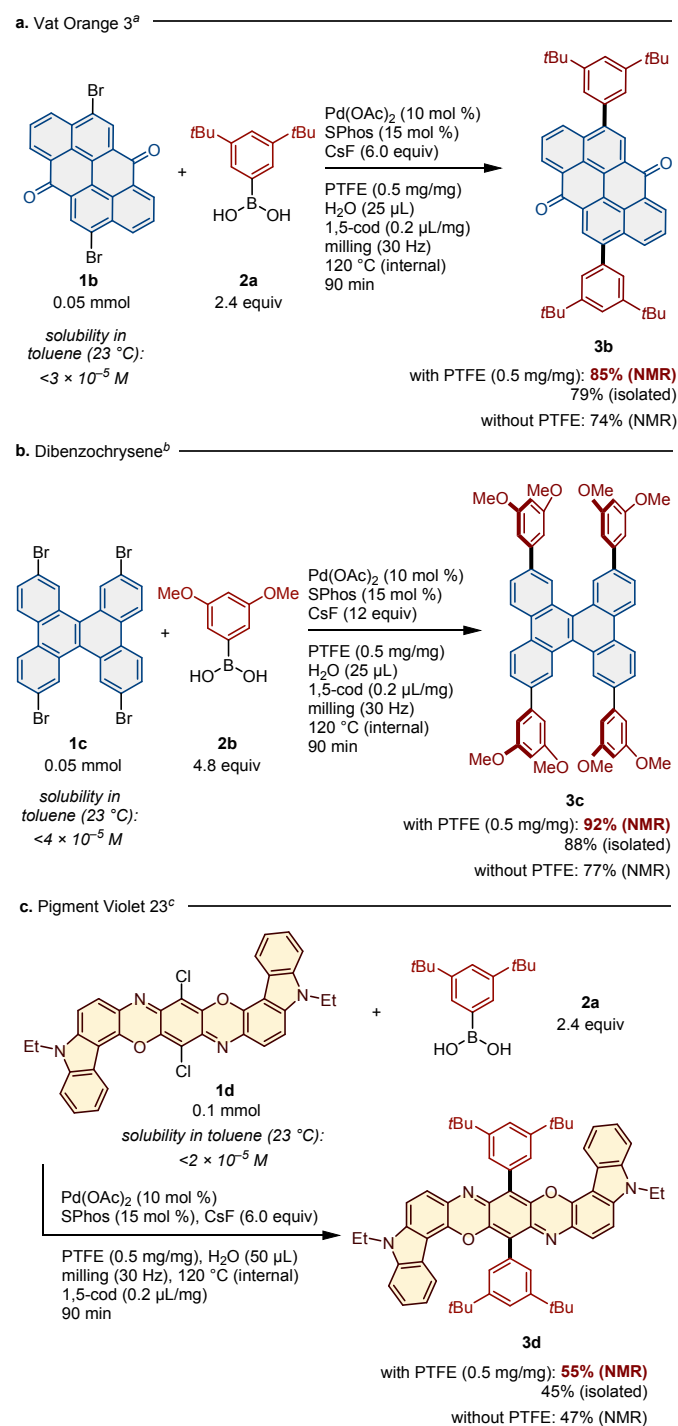
entry	PTFE (mg/mg)	PTFE (size, μm)	H ₂ O (μL)	yield (%)
1	0.5	ca. 1	14	51
2	0.25	ca. 1	14	41
3	0.5	ca. 1	50	56
4 ^b	0.5	ca. 1	50	5
5	0.5	<12	50	16
6	0.5	>40	50	3

^aConditions: **1a** (0.10 mmol), **2a** (0.24 mmol), Pd(OAc)₂ (0.01 mmol), SPhos (0.015 mmol), CsF (0.6 mmol), PTFE, H₂O, and 1,5-cod (0.20 μL/mg) in a stainless steel ball-milling jar (1.5 mL). ^bPd(OAc)₂ (20 mol%) and SPhos (40 mol%).

Moreover, we investigated solid-state cross-coupling reactions of other insoluble aryl halides using the optimized POLAG conditions (Scheme 3). First, we selected Vat Orange 3 (**1b**), which is a pigment with an extremely low solubility in common organic solvents (e.g., solubility in toluene = $<3 \times 10^{-5}$ M at 23 °C).^{3d,11} Such poorly soluble aryl halides react with significantly low efficiencies in conventional solution-based cross-coupling reactions.^{12,13} Although our previously developed solid-state Pd(OAc)₂/SPhos/1,5-cod catalytic system allowed efficient Suzuki–Miyaura cross-coupling of **1b** to form the coupling product **3b** in 74% yield (Scheme 3a),^{3d} the newly developed POLAG conditions afforded **3b** in a higher yield (85% yield, Scheme 3a).¹⁴ Furthermore, the reaction of 3,6,11,14-tetrabromodibenzo[*g,p*]chrysene (**1c**), another insoluble substrate (solubility in toluene = $<4 \times 10^{-5}$ M at 23 °C)^{11,15}, proceeded smoothly to produce **3c** in excellent yield (92%) under POLAG conditions (Scheme 3b). Without PTFE, **3c** was obtained in a lower yield (77%), thus demonstrating the effectiveness of the POLAG approach (Scheme 3b). Finally, we performed the reaction of Pigment Violet 23 (**1d**), which has an extremely low solubility (solubility in toluene = $<2 \times 10^{-5}$ M at 23 °C)^{3d,11}; moreover, the intrinsic inertness of the carbon-chlorine bond in **1d** is a significant barrier to cross-coupling and notably, there are no reported cross-coupling reactions of **1d** under conventional solution-based conditions. However, our previously developed ball-milling conditions allowed efficient coupling of **1d** to afford **3d** in 47% yield.^{3d} Moreover, our POLAG-PTFE approach further improved the reaction efficiency and the yield of **3d** (55%, Scheme 3c).

Powder X-ray diffraction (PXRD) analysis was used to determine whether the phase and crystallinity of the aryl halides changed during the reaction under POLAG conditions (Figure 2). The results of the PXRD analysis of **1b**, PTFE, and their ball-milled mixture showed that the diffraction patterns did not change in the mixture, confirming that the crystallites of **1b** remain the same under the ball-milling conditions. Furthermore, we used scanning electron microscopy (SEM) to confirm the changes in the microstructures of the solid-state reaction mixtures under POLAG conditions (Figure 3). The SEM image of the reaction mixture of **1a** and **2a** without PTFE shows the formation of powders, in which the particle sizes are in the order of several hundred micrometers (Figure 3a). Interestingly, the SEM image of the reaction mixture with PTFE clearly shows a uniformity in the larger microstructures compared to that in the reaction mixture without PTFE (Figure 3b). This result suggests that PTFE and solid substrates were inextricably mixed at the micrometer scale under the ball-milling conditions. Although further mechanistic studies are required, we speculate that PTFE could weaken the intermolecular interactions among the solid substrates to afford a partially amorphous-like phase at the interface of the polymeric domain and crystalline substrates, thereby facilitating efficient cross-coupling reactions.^{3h}

Scheme 3. Solid-state cross-coupling reactions of aryl halides insoluble in organic solvents under polymer-assisted-grinding conditions using PTFE at high temperature



^aConditions: **1b** (0.05 mmol), **2a** (0.12 mmol), Pd(OAc)₂ (0.005 mmol), SPhos (0.0075 mmol), CsF (0.3 mmol), PTFE (0.5 mg/mg), H₂O (50 µL), and 1,5-cod (0.20 µL/mg) in a stainless steel ball-milling jar (1.5 mL).

^bConditions: **1c** (0.05 mmol), **2b** (0.24 mmol), Pd(OAc)₂ (0.005 mmol), SPhos (0.0075 mmol), CsF (0.6 mmol), PTFE (0.5 mg/mg), H₂O (25 µL), and 1,5-cod (0.20 µL) in a stainless steel ball-milling jar (1.5 mL).

^cConditions: **1d** (0.10 mmol), **2a** (0.24 mmol), Pd(OAc)₂ (0.01 mmol),

SPhos (0.015 mmol), CsF (0.6 mmol), PTFE (0.5 mg/mg), H₂O (50 μ L), and 1,5-cod (0.20 μ L/mg) in a stainless steel ball-milling jar (1.5 mL).

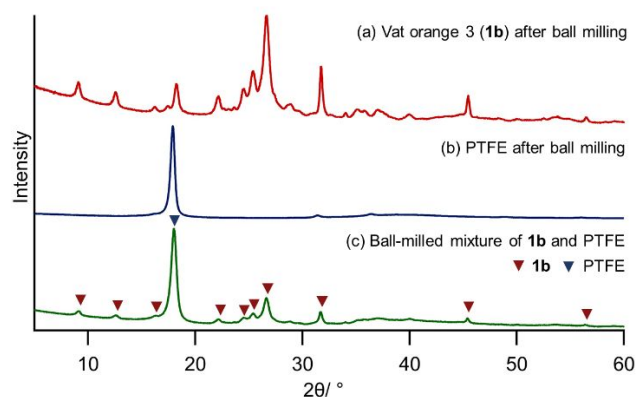
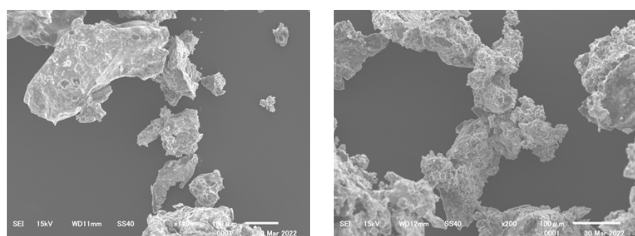


Figure 2. PXRD analysis of the ball-milled mixture of **1b** and PTFE.

(a) reaction mixture without polymer additives



(b) reaction mixture with PTFE

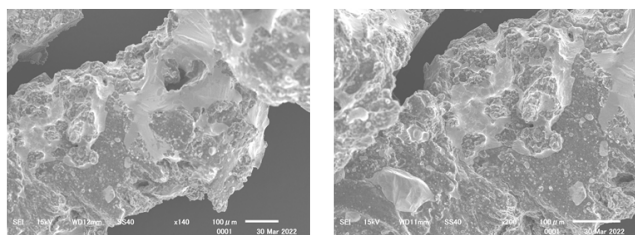
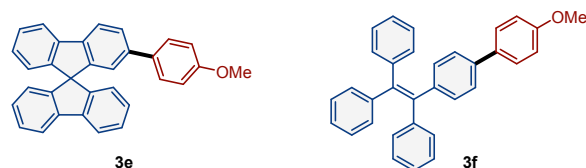
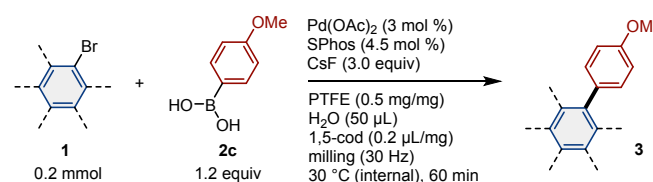


Figure 3. SEM analysis of the crude reaction mixture of **1a** and **2a** obtained under ball-milling conditions (a) without PTFE and (b) with PTFE.

Furthermore, we investigated the solid-state cross-coupling of solid aryl bromides soluble in organic solvents at room temperature (Scheme 4). Considering that these substrates (**1e–g**) were rapidly converted into the corresponding coupling products (**3e–g**) under high-temperature ball-milling conditions with or without PTFE,^{3h} we conducted the same solid-state coupling reactions under POLAG conditions at room temperature to determine its effectiveness for this class of substrates. The cross-coupling of 2-bromo-9,9'-spirobi[9H-fluorene] (**1e**) was greatly accelerated by the addition of PTFE to form **3e** in quantitative yield. However, the reactions of the other solid substrates **1f** and **1g** did not demonstrate such acceleration in the presence of PTFE. These results suggest that the acceleration effect of PTFE addition could be attributed to higher temperatures. We then investigated reactions of 6,6-dibromoisindigo (**1a**) under POLAG conditions using PTFE at temperatures higher (135 $^{\circ}$ C) or lower (80 $^{\circ}$ C) than 120 $^{\circ}$ C

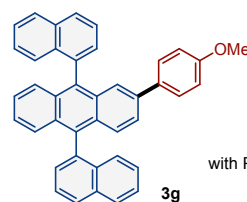
(details in Supporting Information). Both conditions were found to reduce the yields (20% and 8% yields, respectively), suggesting that the acceleration effect is very sensitive to reaction temperature and seems to be more pronounced at temperatures of 120 $^{\circ}$ C.

Scheme 4. Solid-state cross-coupling reactions of aryl bromides soluble in organic solvents under polymer-assisted-grinding conditions using PTFE at room temperature^a



with PTFE (0.5 mg/mg): >99% (NMR)
without PTFE: 45% (NMR)

with PTFE (0.5 mg/mg): 20% (NMR)
without PTFE: 39% (NMR)



with PTFE (0.5 mg/mg): 3% (NMR)
without PTFE: 12% (NMR)

^aConditions: **1** (0.20 mmol), **2c** (0.24 mmol), Pd(OAc)₂ (0.006 mmol), SPhos (0.009 mmol), CsF (0.6 mmol), PTFE (0.5 mg/mg), H₂O (50 μ L), and 1,5-cod (0.20 μ L/mg) in a stainless steel ball-milling jar (1.5 mL).

Conclusions

We discovered that POLAG conditions using PTFE improved the solid-state Suzuki–Miyaura cross-coupling reaction efficiency of aryl halides that are insoluble in organic solvents and barely reactive under conventional solution-based conditions. Although the improvement by POLAG is not so significant in the present study, this is an important advance in solid-state coupling chemistry considering the tremendous difficulty of reactions with poorly soluble compounds. We expect that the POLAG approach will inspire the development of powerful mechanochemical cross-coupling strategies to expand the chemistry of insoluble starting materials.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was financially supported by the Japan Society for the Promotion of Science (JSPS) via KAKENHI grants 22H00318, 21H01926 and 22H05328, the JST via the CREST grant

JPMJCR19R1, FOREST grant PJ2521A02I, and the Institute for Chemical Reaction Design and Discovery (ICReDD) established by the World Premier International Research Initiative (WPI), MEXT, Japan. We thank Dr. Yunpeng Gao for his help in cross-checking the experiments.

Notes and references

- For recent reviews on organic synthesis using mechanochemistry, see: (a) S. L. James, C. J. Adams, C. Bolm, D. Braga, P. Collier, T. Friščić, F. Grepioni, K. D. M. Harris, G. Hyett, W. Jones, A. Krebs, J. Mack, L. Maini, A. G. Orpen, I. P. Parkin, W. C. Shearouse, J. W. Steed, and D. C. Waddell, *Chem. Soc. Rev.*, 2012, **41**, 413; (b) G.-W. Wang, *Chem. Soc. Rev.*, 2013, **42**, 7668; (c) J.-L. Do and T. Friščić, *ACS Cent. Sci.*, 2017, **3**, 13; (d) J. G. Hernández and C. Bolm, *J. Org. Chem.*, 2017, **82**, 4007; (e) J. G. Hernández, *Chem.–Eur. J.*, 2017, **23**, 17157; (f) T. K. Achar, A. Bose, P. Mal, *Beilstein J. Org. Chem.*, 2017, **13**, 1907; (g) J.-L. Do and T. Friščić, *Synlett*, 2017, **28**, 2066; (h) D. Tan and T. Friščić, *Eur. J. Org. Chem.*, 2018, **18**; (i) J. L. Howard, Q. Cao, and D. L. Browne, *Chem. Sci.*, 2018, **9**, 3080; (j) J. Andersen and J. Mack, *Green Chem.*, 2018, **20**, 1435; (k) N. R. Rightmire and T. P. Hanusa, *Dalton Trans.*, 2016, **45**, 2352; (l) M. Leonardi, M. Villacampa, and J. C. Menéndez, *Chem. Sci.*, 2018, **9**, 2042; (m) D. Tan, L. Loots, and T. Friščić, *Chem. Commun.*, 2016, **52**, 7760; (n) D. Tan and F. García, *Chem. Soc. Rev.*, 2019, **48**, 2274; (o) C. Bolm and J. G. Hernández, *Angew. Chem., Int. Ed.*, 2019, **58**, 3285; (p) T. Friščić, C. Mottillo, and H. M. Titi, *Angew. Chem. Int. Ed.*, 2020, **59**, 1018; (q) K. Kubota and H. Ito, *Trends Chem.*, 2020, **2**, 1066; (r) I. N. Egorov, S. Santra, D. S. Kopchuk, I. S. Kovalev, G. V. Zyryanov, A. Majee, B. C. Ranu, V. L. Rusinov, and O. N. Chupakhin, *Green Chem.*, 2020, **22**, 302; (s) A. Porcheddu, E. Colacino, L. De Luca, and F. Delogu, *ACS Catal.*, 2020, **10**, 8344; (t) P. Ying, J. Yu and W. Su, *Adv. Synth. Catal.*, 2021, **363**, 1246; (u) K. J. Ardila-Fierro and J. G. Hernández, *ChemSusChem*, 2021, **14**, 2145.
- (a) K. Tanaka, *Solvent-Free Organic Synthesis*, 2nd revised edn, Wiley-VCH, Weinheim, 2009; (b) F. Toda, *Organic Solid-State Reactions*, Springer, Berlin Heidelberg, 2004; (c) F. Toda, *Acc. Chem. Res.*, 1995, **28**, 480; (d) K. Tanaka and F. Toda, *Chem. Rev.*, 2000, **100**, 1025.
- For selected examples of solid-state organic transformations using ball milling from our group, see: (a) K. Kubota, Y. Pang, A. Miura, and H. Ito, *Science*, 2019, **366**, 1500; (b) K. Kubota, R. Takahashi, and H. Ito, *Chem. Sci.*, 2019, **10**, 5837–5842; (c) K. Kubota, T. Seo, K. Koide, S. Hasegawa, and H. Ito, *Nat. Commun.*, 2019, **10**, 111; (d) T. Seo, T. Toyoshima, K. Kubota, and H. Ito, *J. Am. Chem. Soc.*, 2021, **143**, 6165–6175; (e) Y. Pang, J. W. Lee, K. Kubota, and H. Ito, *Angew. Chem. Int. Ed.*, 2020, **59**, 22570–22576; (f) K. Kubota, N. Toyoshima, D. Miura, J. Jiang, S. Maeda, M. Jin, and H. Ito, *Angew. Chem. Int. Ed.*, 2021, **60**, 16003–16008; (g) R. Takahashi, A. Hu, P. Gao, Y. Gao, Y. Pang, T. Seo, S. Maeda, J. Jiang, H. Takaya, K. Kubota, and H. Ito, *Nat. Commun.*, 2021, **12**, 6691; (h) K. Kubota, K. Kondo, T. Seo, and H. Ito, *Synlett*, 2022, **33**, 898–902.
- G. Bárti, D. Csókás, T. Yong, S. M. Tam, R. R. S. Shi, R. D. Webster, I. Pápai, F. Garcia, and M. C. Stuparu, *Angew. Chem. Int. Ed.*, 2020, **59**, 21620.
- Pioneering studies on mechanochemical Suzuki-Miyaura cross-coupling reactions, see: (a) S. F. Nielsen, D. Peters, and O. Axelsson, *Synth. Commun.*, 2000, **30**, 3501; (b) L. M. Klingensmith and N. E. Leadbeater, *Tetrahedron Lett.*, 2003, **44**, 765; (c) F. Bernhardt, R. Trozki, T. Szuppa, A. Stolle, and B. Ondruschka, *Beilstein J. Org. Chem.*, 2010, **6**, 30; (d) F. Schneider, T. Szuppa, A. Stolle, B. Ondruschka, and H. Hopf, *Green Chem.*, 2009, **11**, 1894; (e) F. Schneider, A. Stolle, B. Ondruschka, and H. Hopf, *Org. Process Res. Dev.*, 2009, **13**, 44.
- For selected early examples and reviews of liquid-assisted grinding, see: (a) T. Friščić, S. L. Childs, S. A. Rizvi, and W. Jones, *CrystEngComm.*, 2009, **11**, 418; (b) T. Friščić, D. G. Reid, I. Halasz, R. S. Stein, R. E. Dinnebier, and M. J. Duer, *Angew. Chem. Int. Ed.*, 2010, **49**, 712; (c) P. Ying, J. Yu, and W. Su, *Adv. Synth. Catal.*, 2021, **363**, 1246.
- For the first application of liquid-assisted grinding to mechanochemical Suzuki-Miyaura coupling, see: Z. J. Jiang, Z. H. Li, J. B. Yu, and W. K. Su, *J. Org. Chem.*, 2016, **81**, 10049.
- For selected examples of polymer-assisted grinding in organic chemistry, see: (a) A. Mascitti, M. Lupacchini, R. Guerra, I. Taydakov, L. Tonucci, N. Alessandro, F. Lamaty, J. Martinez, and E. Colacino, *Beilstein J. Org. Chem.*, 2017, **13**, 19; (b) D. Hasa, G. S. Rauber, D. Voinovich, and W. Jones, *Angew. Chem. Int. Ed.*, 2015, **127**, 7974; (c) D. Hasa, E. Carlino, and W. Jones, *Cryst. Growth. Des.*, 2016, **16**, 1772; (d) D. Scaramuzza, G. S. Rauber, D. Voinovich, and D. Hasa, *Cryst. Growth. Des.*, 2018, **18**, 5245.
- For the first application of polymer-assisted grinding in a palladium-catalyzed cross-coupling reaction, see: V. Declerck, E. Colacino, X. Bantreil, J. Martinez, and F. Lamaty, *Chem. Commun.*, 2012, **48**, 11778.
- For selected examples of the formation of polymer/nanocarbon composite materials, see: (a) Y. Li, Y. Li, X. Huang, H. Zheng, G. Lu, Z. Xi, and G. Wang, *Compos. Sci. Technol.*, 2020, **195**, 108197; (b) A. Sari, A. Bicer, F. A. Al-Sulaiman, A. Karaipekli, and V. V. Tyagi, *Energy Build.*, 2018, **164**, 166; (c) Y. Zhang, J. Wang, J. Qiu, X. Lin, M. M. Umair, R. Lu, S. Zhang, and B. Tang, *Appl. Energy*, 2019, **237**, 83.
- This temperature represents the temperature of the room where the experiment was conducted to determine the concentration.
- (a) J. B. Giguère, Q. Verolet, and J. F. Morin, *Chem. Eur. J.*, 2013, **19**, 372; (b) J. B. Giguère, J. Boismenu-Lavoie, and J. F. Morin, *J. Org. Chem.*, 2014, **79**, 2404.
- For selected reviews on palladium-catalyzed cross-coupling chemistry, see: (a) C. C. C. Johansson Seehurn, M. O. Kitching, T. J. Colacot, and V. Snieckus, *Angew. Chem. Int. Ed.*, 2012, **51**, 5062; (b) A. Molnár, *Palladium-Catalyzed Coupling Reactions: Practical Aspects and Future Developments*; Wiley-VCH: Weinheim, 2013; (c) A. Meijere and F. Diederich, *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed; Wiley-VCH: Weinheim, 2008; (d) N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457; (e) A. J. J. Lennox and G. C. Lloyd-Jones, *Chem. Soc. Rev.*, 2014, **43**, 412; (f) R. Martin and S. L. Buchwald, *Acc. Chem. Res.*, 2008, **41**, 1461; (g) P. Ruiz-Castillo and S. L. Buchwald, *Chem. Rev.*, 2016, **116**, 12564; (h) A. C. Sather and S. L. Buchwald, *Acc. Chem. Res.*, 2016, **49**, 2146; (i) B. T. Ingoglia, C. C. Wagen, and S. L. Buchwald, *Tetrahedron*, 2019, **75**, 4199.
- The reaction of **1b** was performed several times, and **3b** was obtained in between 79% and 99% yield. This is presumably due to impurities in **1b** or to the low reproducibility of the mixing efficiency of the polymer and the substrate under the present ball-milling conditions.
- (a) U. Koldemir, J. S. Tinkham, R. Johnson, B. Lim, H. A. Yemam, K. J. Gagnon, S. Parkin, and A. Sellinger, *J. Mater. Chem. C*, 2017, **5**, 8723; (b) X.-Y. Liu, X. Tang, Y. Zhao, D. Zhao, J. Fan, and L.-S. Liao, *Dyes Pigment.*, 2017, **146**, 234; (c) S. Wang, P. Yang, K. Chang, W. Lv, B. Mi, J. Song, X. Zhao, and Z. Gao, *Org. Electron.*, 2019, **74**, 269.