EDGE ARTICLE

Check for updates

All publication charges for this article have been paid for by the Royal Society of Chemistry

Mechanochemistry allows carrying out sensitive organometallic reactions in air: glove-box-and-Schlenk-line-free synthesis of oxidative addition complexes from aryl halides and palladium(0)†

Koji Kubota, [iD] *[ab] Rina Takahashi[a] and Hajime Ito [iD] *[ab]

Organic reactions that employ moisture- and/or oxygen-sensitive reagents or intermediates usually involve the use of glove-box or Schlenk-line techniques as well as dry and degassed solvents. Unfortunately, these requirements may greatly reduce the utility of the targeted organic molecules. Herein, we demonstrate that solvent-free mechanochemical synthetic techniques allow using highly oxygen-sensitive palladium(0) species in air for the stoichiometric oxidative addition of aryl halides. The low diffusion efficiency of gaseous oxygen in crystalline or amorphous solid-state reaction mixtures should be the main reason for the low impact of the presence of atmospheric oxygen on the sensitive oxidative addition reactions under the applied conditions. This study thus illustrates the outstanding potential of mechanochemistry to serve as an operationally simple, glove-box-and-Schlenk-line-free synthetic route to organometallic compounds and other valuable synthetic targets, even when sensitive reagents or intermediates are involved.

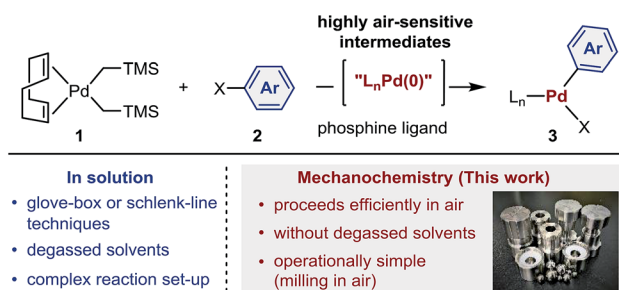## Introduction

Many useful reagents and catalysts employed in the preparation of organic compounds and organometallic complexes are highly reactive and therefore incompatible with exposure to the ambient atmosphere.[1] The techniques required to conduct reactions with these sensitive compounds usually involve gloveboxes and high-vacuum Schlenk lines and are thus costly and demand special training. In addition, dry and degassed organic solvents are required for these reactions. Chemical processes that do not require such precautions are therefore likely to substantially increase the practical utility of the targeted organic molecules.

Palladium complexes obtained from oxidative addition reactions have been widely used in mechanistic studies,[2] as catalyst precursors for several cross-coupling reactions[3] and as stoichiometric aryl-group transfer reagents for the diversification of biomolecules and pharmaceuticals.[4] Dialkylbiaryl phosphine-ligated palladium(ii) complexes developed by Buchwald and co-workers are particularly useful reagents in these

applications due to their high stability and ease of handling.[2a–e,3a,4] One of the most common synthetic routes to these oxidative addition complexes involves reactions between the palladium(0) precursor $(COD)Pd(CH_2TMS)_2$ (COD = 1,5-cyclooctadiene; TMS = trimethylsilyl) (**1**)[5] and aryl halides **2** in the presence of appropriate Buchwald-type ligands (Scheme 1).[2a–e,3a,4] According to the developed protocol reported by Buchwald *et al.*, this procedure generally requires glove-box techniques, given that highly air-sensitive palladium(0) species are involved.[3a,4c] These restrictions may, however, greatly reduce the practical utility of the obtained palladium complexes. The development of scalable, operationally simple and glove-box-and-Schlenk-line-free synthetic methods should therefore be highly beneficial.

[a]Division of Applied Chemistry and Frontier Chemistry Center, Faculty of Engineering, Hokkaido University, Sapporo, Hokkaido, Japan. E-mail: kbt@eng.hokudai.ac.jp; hajito@eng.hokudai.ac.jp

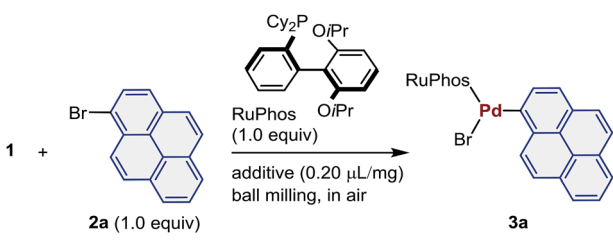*[b]Institute for Chemical Reaction Design and Discovery (WPI-ICReDD), Hokkaido University, Sapporo, Hokkaido, Japan*

† Electronic supplementary information (ESI) available. CCDC 1908179. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c9sc01711a

Scheme 1 Synthesis of palladium-based oxidative addition complexes involving air-sensitive palladium(0) intermediates.

Mechanochemical solvent-free organic reactions using ball milling have emerged as powerful alternatives to synthetic procedures in solution.[6] In particular, Friščić, Bolm, Hernández, James, and Browne have made significant contributions to this research area.[6] However, the benefits of mechanochemistry in the context of organometallic chemistry have not yet been explored systematically,[6m,7–19] and the potential applicability of highly sensitive reagents or intermediates toward mechanochemical organometallic transformations under ambient conditions remains elusive.[14] Herein, we demonstrate that mechanochemistry enables glove-box-and-Schlenk-line-free synthesis of palladium complexes by oxidative additions using readily available starting materials (Scheme 1).[20] This reaction is operationally simple and proceeds efficiently in air to afford a variety of synthetically useful palladium complexes in moderate to high yield. We anticipate that the method presented herein could be readily transferred to the development of glove-box-and-Schlenk-line-free synthetic routes to other valuable organometallic complexes and synthetic targets, even when sensitive reagents or intermediates are involved.

Results and discussion

All mechanochemical reactions were conducted in a Retsch MM 400 mill (stainless-steel milling jar; 30 Hz or 25 Hz; stainless-steel balls). To probe the effectiveness of this mechanochemical approach for the preparation of palladium-based oxidative addition complexes, we initially tested the reaction between 1 and 1-bromopyrene (2a) in the presence of 2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl (RuPhos), which is a commonly used Buchwald-type ligand (Table 1).[21] The corresponding oxidative addition complex (3a) was obtained in moderate yield upon grinding for 30 min in air (40% yield; entry 1). Prolonging the reaction time did not improve the yield (43% yield; entry 2). Subsequently, we attempted milling with a catalytic amount of liquid, the so-called liquid-assisted grinding (LAG), to improve the performance (entries 3–12).[22] Unless otherwise noted, the following reactions with liquid additives are all characterized by the addition of 0.20 μL of liquid per mg of reactant. We found that adding a small amount of tetrahydrofuran (THF) greatly improved the yield of 3a (71% yield; entry 3). Other commonly used organic solvents in palladium-catalyzed cross-coupling reactions such as toluene, acetonitrile (CH$_3$CN), dioxane, dimethyl formamide (DMF), and diethyl ether (Et$_2$O) also improved the efficiency of the reaction (entries 4–8). The use of highly polar solvents such as dimethyl sulfoxide (DMSO) or simple alkanes (pentane and cyclohexane) slightly accelerated the oxidative addition (entries 9–11). Protic solvents such as methanol (MeOH) did not promote the reaction (entry 12). Subsequently, we focused on the identification of the optimal milling parameters for this mechanochemical oxidative addition reaction (entries 13–15). The milling frequency can be reduced to 25 Hz (78% yield; entry 13), while increasing the number of stainless-steel balls did not improve the yield (entries 14 and 15). Notably, the reaction time can be reduced to 10 min without affecting the yield when THF was used as a LAG additive (71% yield; entry 16).

Table 1 Optimization of the reaction conditions[a]

Entry	LAG	Milling frequency (Hz)	Time (min)	NMR yield[b] (%)
1	None	30	30	40
2	None	30	60	43
3	THF	30	30	71
4	Toluene	30	30	61
5	CH$_3$CN	30	30	71
6	Dioxane	30	30	64
7	DMF	30	30	64
8	Et$_2$O	30	30	66
9	DMSO	30	30	55
10	Pentane	30	30	58
11	Cyclohexane	30	30	47
12	MeOH	30	30	48
13	THF	25	30	78[e]
14[c]	THF	25	30	55
15[d]	THF	25	30	67
16	THF	25	10	71

[a] Conditions: 1 (0.05 mmol), 2a (0.05 mmol), RuPhos (0.05 mmol), and the LAG additive (0.2 μL mg^{-1}) in a stainless-steel ball-milling jar (1.5 mL) with a stainless-steel ball (3 mm). [b] Determined by ^{1}H NMR analysis of the crude reaction mixture using an internal standard. [c] Two stainless-steel balls (3 mm) were used. [d] Three stainless-steel balls (3 mm) were used. [e] Isolated yield.

With the optimized conditions in hand, we investigated the effect of different halides and a pseudohalide on the oxidative addition of palladium complexes (Scheme 2). Even though the corresponding aryl chloride (2b) undergoes oxidative addition in solution, the desired oxidative addition complex (3b) was not formed under mechanochemical conditions.[4] When bromide (2c) and the iodide substrates (2d) were used, the products were obtained in 62% and 75% yield, respectively. Although Ondruschka and co-workers reported that aryl bromides were more reactive than aryl iodides in mechanochemical palladium-catalyzed Suzuki–Miyaura coupling reactions,[23] the iodide substrate (2d) provided higher yield in the mechanochemical stoichiometric oxidative addition process. The corresponding aryl triflate (2e) afforded 3e in moderate yield (58%).
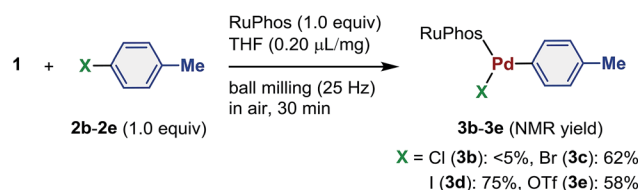
Scheme 2 Mechanochemical synthesis of palladium–based oxidative addition complexes from aryl halides and an aryl pseudohalide.

The aforementioned optimized conditions were used for further evaluation of the substrate scope (Table 2). The reaction of both electron-rich and -poor aryl bromides (**2f–2j**) proceeded smoothly to give the corresponding oxidative addition complexes (**3f–3j**) in good yields (57–76%). 4-Bromophenol (**2k**) also afforded the desired product (**3k**) in moderate yield (35%). The present protocol could also be applied to heteroaryl bromides such as indole (**2l**), thiophene (**2m**), and dibenzofuran (**2n**) derivatives. Palladium(II) complexes containing aromatic hydrocarbon cores (**3a, 3o,** and **3p**) were obtained in 78–92% yield. The reaction of aryl bromides bearing aldehyde **2q** and benzophenone moieties **2r** afforded the desired palladium(II) complexes (**3q** and **3r**),

which are used in bioconjugation applications,[4] in 79% and 61% yield, respectively.

Polymetalated transition-metal complexes have attracted considerable attention due to their unique reactivity and physical properties.[4e,24] The mechanochemical oxidative addition protocol developed herein provides an efficient route for the synthesis of polymetalated palladium complexes (Table 3). The reaction of dibromides **2s** and **2t** in the presence of 2 equiv. of **1** and RuPhos afforded di-palladated **3s** and **3t**, which are useful reagents for macrocyclization of peptides,[4e] in 88% and 85% yield, respectively. The tri-palladated arylamine **3u** and the tetra-palladated pyrene **3v** were synthesized in 91% and 61% yield, respectively under the applied mechanochemical conditions in air. The molecular structure of **3v** in the solid state was unequivocally determined by a single-crystal X-ray diffraction analysis (Fig. 1). The results revealed that two of the four palladium atoms in **3v** adopt a C-bound conformation, while the other two adopt an O-bound conformation in the solid state. The orientation of the phosphine ligands on adjacent palladium atoms is in opposing directions relative to each other, which is probably due to the steric congestion between substituents on the phosphine ligands in the solid state.

Subsequently, we investigated the effect of the phosphine ligand on the mechanochemical palladium-mediated oxidative addition of **2f** (Table 4). The reactions using 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (SPhos) and 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (XPhos) furnished **3w** and **3x** in 44% and 32% yield, respectively.

These palladium-based oxidative addition complexes can also be prepared on the gram-scale in air using mechanochemistry (Scheme 3). For this purpose, the reaction of **2s** (1 mmol) was carried out in a larger stainless-steel ball-milling jar

Table 2 Substrate scope[a]

Table 3 Multiple oxidative additions using mechanochemistry[a]
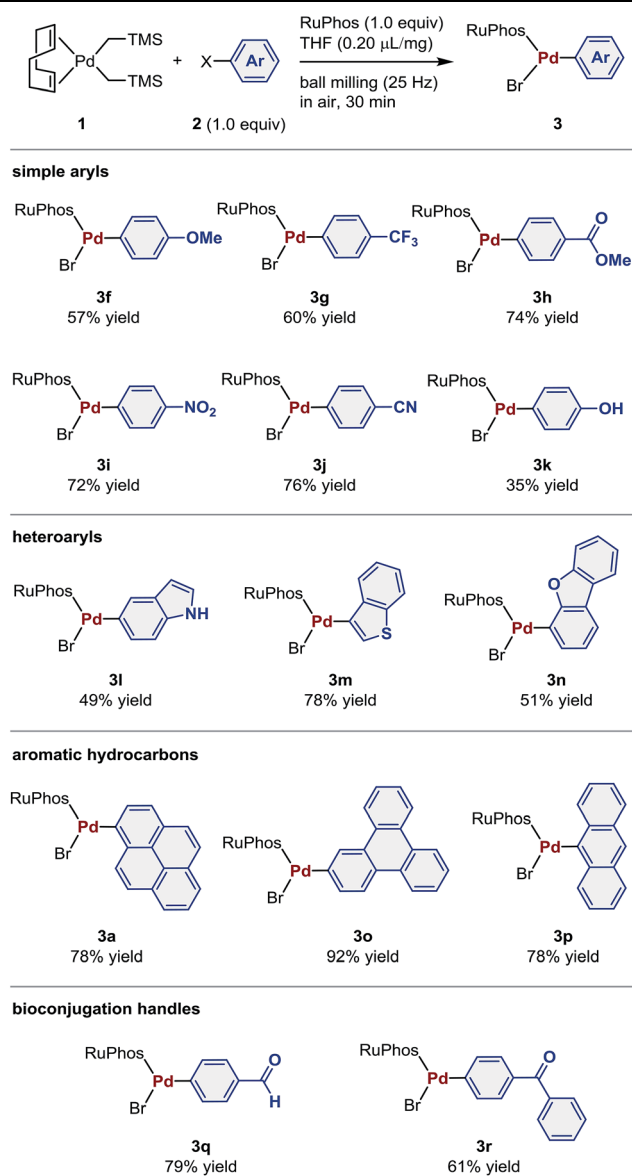
[a] Conditions: **1** (0.12 mmol), **2** (0.12 mmol), RuPhos (0.12 mmol), and THF (0.2 μL mg⁻¹) in a stainless-steel ball-milling jar (1.5 mL) with a stainless-steel ball (3 mm).

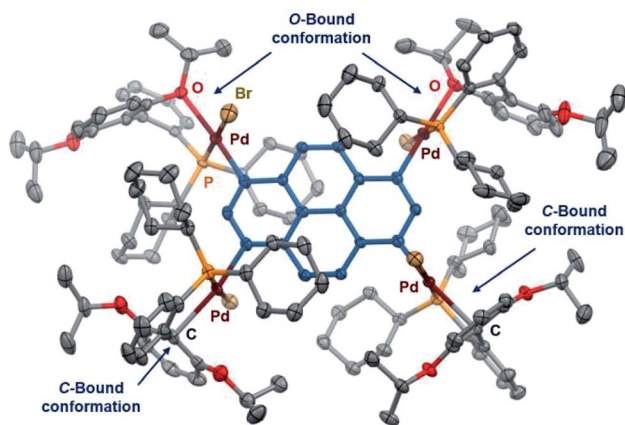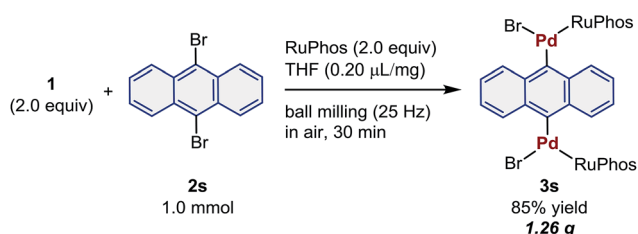[a] See the ESI for the details of the reaction conditions.

Fig. 1 Molecular structure of **3v** in the solid state (thermal ellipsoids at 50% probability; hydrogen atoms and CH_2Cl_2 are omitted for clarity).

Table 4 Ligand effects[a]

[a] Conditions: **1** (0.12 mmol), **2f** (0.12 mmol), ligand (0.12 mmol), and THF (0.2 μL mg^{-1}) in a stainless-steel ball-milling jar (1.5 mL) with a stainless-steel ball (3 mm).

Scheme 3 Gram-scale synthesis of **3s**. Conditions: **1** (2.0 mmol), **2s** (1.0 mmol), RuPhos (2.0 mmol), and THF (0.20 μL mg^{-1}) in a stainless-steel ball-milling jar (25 mL) with two stainless-steel balls (10 mm).

(25 mL) with two stainless-steel balls (10 mm) in air, and the desired oxidative addition complex (**3s**) was obtained in 85% yield (1.26 g). This result clearly demonstrates the potential utility of the present mechanochemical protocol for large-scale preparation of synthetically useful palladium reagents without any special operational skills or precautions.

In order to further explore the practical utility of this protocol, we compared the efficiency of the solution-based and
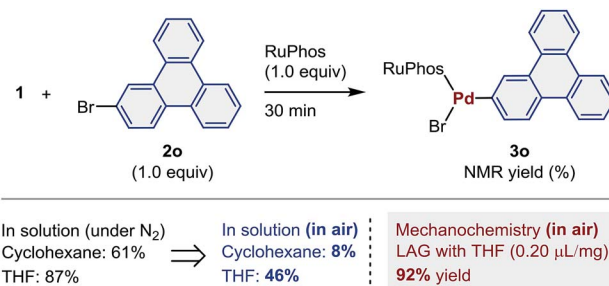
Scheme 4 Comparison of the performance of solution–based and mechanochemical reactions.

the mechanochemical reactions (Scheme 4). The oxidative addition of **2o** under the reported solution-based conditions using cyclohexane or THF as solvents[3a,4] provided **3o** in 61% and 87% yield, respectively. However, when the reactions were conducted in air, significantly lower yields were obtained (8% and 46%, respectively). In contrast, under the aforementioned mechanochemical conditions, the oxidative addition proceeded efficiently, even in air, providing **3o** in 92% yield. These results suggest that gaseous oxygen does not efficiently diffuse through crystalline or amorphous solid-state reaction mixtures,[25,26] which results in little to no impact on the air-sensitive palladium(0)-mediated oxidative addition reactions. Related to this finding, Mack and co-workers have described that the gaseous nature of water and oxygen does not significantly influence moisture-sensitive organic transformations under mechanochemical conditions.[25]

Conclusions

Palladium-based oxidative addition complexes are widely used in mechanistic studies, as catalyst precursors and as stoichiometric aryl-group-transfer reagents. However, the preparation of these complexes generally requires glove-box or Schlenk-line techniques due to the high air-sensitivity of the palladium(0) species involved. We have demonstrated that mechanochemistry allows synthesizing a wide range of Buchwald-type-phosphine-ligated palladium(II)-based oxidative addition complexes in air. The low diffusion efficiency of gaseous oxygen in the solid-state reaction mixture was identified as the most likely reason for the low impact of atmospheric oxygen on these sensitive organometallic reactions. This study illustrates the outstanding potential of mechanochemistry as an operationally simple glove-box-and-Schlenk-line-free synthetic route to valuable organometallic compounds and other attractive synthetic targets, even when highly sensitive reagents or intermediates are involved.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Notes and references

1 *The Manipulations of Air-Sensitive Compounds*, ed. D. F. Shriver and M. A. Drezdon, John Wiley and Sons, New York, 2nd edn, 1986.

2 For selected examples of mechanistic studies using palladium-based oxidative addition complexes, see: (*a*) D. A. Watson, M. Su, G. Teverovskiy, Y. Zhang, J. García-Fortanet, T. Kinzel and S. L. Buchwald, *Science*, 2009, **325**, 1661; (*b*) T. J. Maimone, R. J. Milner, T. Kinzel, Y. Zhang, M. K. Takase and S. L. Buchwald, *J. Am. Chem. Soc.*, 2011, **133**, 18106; (*c*) A. C. Sather, H. G. Lee, V. Y. De La Rosa, Y. Yang, P. Müller and S. L. Buchwald, *J. Am. Chem. Soc.*, 2015, **137**, 13433; (*d*) P. L. Arrechea and S. L. Buchwald, *J. Am. Chem. Soc.*, 2016, **138**, 12486; (*e*) J. M. Dennis, N. A. White, R. Y. Liu and S. L. Buchwald, *J. Am. Chem. Soc.*, 2018, **140**, 4721; (*f*) A. H. Roy and J. F. Hartwig, *J. Am. Chem. Soc.*, 2001, **123**, 1232; (*g*) A. H. Roy and J. F. Hartwig, *J. Am. Chem. Soc.*, 2003, **125**, 13944; (*h*) K. Fujita, M. Yamashita, F. Puschmann, M. M. Alvarez-Falcon, C. D. Incarvito and J. F. Hartwig, *J. Am. Chem. Soc.*, 2006, **128**, 9044; (*i*) M. Yamashita and J. F. Hartwig, *J. Am. Chem. Soc.*, 2004, **126**, 5344; (*j*) D. M. Peacock, Q. Jiang, P. S. Hanley, T. R. Cundari and J. F. Hartwig, *J. Am. Chem. Soc.*, 2018, **140**, 4893; (*k*) A. Maleckis and M. S. Sanford, *Organometallics*, 2014, **33**, 2653; (*l*) A. Maleckis, J. W. Kampf and M. S. Sanford, *J. Am. Chem. Soc.*, 2013, **135**, 6618; (*m*) J. M. Racowski, N. D. Ball and M. S. Sanford, *J. Am. Chem. Soc.*, 2011, **133**, 18022; (*n*) J. F. Hartwig and F. Paul, *J. Am. Chem. Soc.*, 1995, **117**, 5373; (*o*) M. Portnoy and D. Milstein, *Organometallics*, 1993, **12**, 1665; (*p*) C. Amatore and F. Pflüger, *Organometallics*, 1990, **9**, 2276; (*q*) W. R. Moser, A. W. Wang and N. K. Kildahl, *J. Am. Chem. Soc.*, 1988, **110**, 2816; (*r*) T. L. Andersen, S. Kramer, J. Overgaard and T. Skrydstrup, *Organometallics*, 2017, **36**, 2058.

3 For selected examples of the use of palladium-based oxidative addition complexes as catalyst precursors, see: (*a*) B. T. Ingoglia and S. L. Buchwald, *Org. Lett.*, 2017, **19**, 2853; (*b*) J. Vicente, A. Arcas, F. Juliá-Hernández and D. Bautista, *Angew. Chem., Int. Ed.*, 2011, **50**, 6896; (*c*) A. Yokoyama, H. Suzuki, Y. Kubota, K. Ohuchi, H. Higashimura and T. Yokozawa, *J. Am. Chem. Soc.*, 2007, **129**, 7236.

4 For selected examples of the use of palladium-based oxidative addition complexes as stoichiometric aryl-group-transfer reagents for the diversification of biomolecules

and pharmaceuticals, see: (*a*) E. V. Vinogradova, C. Zhang, A. M. Spokoyny and B. L. Pentelute, *Nature*, 2015, **526**, 687; (*b*) W. Zhao, H. G. Lee, S. L. Buchwald and J. M. Hooker, *J. Am. Chem. Soc.*, 2017, **139**, 7152; (*c*) A. J. Rojas, B. L. Pentelute and S. L. Buchwald, *Org. Lett.*, 2017, **19**, 4263; (*d*) H. G. Lee, G. Lautrette, B. L. Pentelute and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2017, **56**, 3177; (*e*) A. J. Rojas, C. Zhang, E. V. Vinogradova, N. Buchwald, J. Reilly, B. L. Pentelute and S. L. Buchwald, *Chem. Sci.*, 2017, **8**, 4257; (*f*) K. Kubota, P. Dai, B. L. Pentelute and S. L. Buchwald, *J. Am. Chem. Soc.*, 2018, **140**, 3128; (*g*) M. R. Uehling, R. P. King, S. W. Krska, T. Cernak and S. L. Buchwald, *Science*, 2019, **363**, 405.

5 (*a*) Y. Pan and G. B. Young, *J. Organomet. Chem.*, 1999, **577**, 257; (*b*) J. R. McAtee, S. E. S. Martin, D. T. Ahneman, K. A. Johnson and D. A. Watson, *Angew. Chem., Int. Ed.*, 2012, **51**, 3663.

6 For recent reviews on organic syntheses 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*) T. Friščić, I. Halasz, V. Štrukil, M. Eckert-Maksić and R. E. Dinnebier, *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.-X. Métro, J. Martinez and F. Lamaty, *ACS Sustainable Chem. Eng.*, 2017, **5**, 9599; (*g*) T. K. Achar, A. Bose and P. Mal, *Beilstein J. Org. Chem.*, 2017, **13**, 1907; (*h*) J.-L. Do and T. Friščić, *Synlett*, 2017, **28**, 2066; (*i*) D. Tan and T. Friščić, *Eur. J. Org. Chem.*, 2018, 18; (*j*) O. Eguaogie, J. S. Vyle, P. F. Conlon, M. A. Gîlea and Y. Liang, *Beilstein J. Org. Chem.*, 2018, **14**, 955; (*k*) J. L. Howard, Q. Cao and D. L. Browne, *Chem. Sci.*, 2018, **9**, 3080; (*l*) J. Andersen and J. Mack, *Green Chem.*, 2018, **20**, 1435; (*m*) N. R. Rightmire and T. P. Hanusa, *Dalton Trans.*, 2016, **45**, 2352; (*n*) M. Leonardi, M. Villacampa and J. C. Menéndez, *Chem. Sci.*, 2018, **9**, 2042.

7 For the mechanochemical synthesis of gold complexes, see: (*a*) A. Zhdanko, M. Ströbele and M. E. Maier, *Chem.–Eur. J.*, 2012, **18**, 14732; (*b*) J. D. Egbert, A. M. Z. Slawin and S. P. Nolan, *Organometallics*, 2013, **32**, 2271.

8 For the mechanochemical synthesis of ferrocene, see: V. D. Makhaev, A. P. Borisov and L. A. Petrova, *J. Organomet. Chem.*, 1999, **590**, 222.

9 For the mechanochemical synthesis of rhenium and manganese complexes, see: J. G. Hernández, I. S. Butler and T. Friščić, *Chem. Sci.*, 2014, **5**, 3576.

10 For the mechanochemical oxidative addition of rhenium complexes, see: J. G. Hernández, N. A. J. Macdonald, C. Mottillo, I. S. Butler and T. Friščić, *Green Chem.*, 2014, **16**, 1087.

11 For the mechanochemical synthesis of nickel and cobalt complexes, see: C. S. B. Gomes, P. T. Gomes and M. T. Duarte, *J. Organomet. Chem.*, 2014, **760**, 101.

12 For the related mechanochemical synthesis of palladium complexes, see: (a) D. Cinčić, M. Juribašić, D. Babić, K. Molčanov, P. Šket and M. Ćurić, *Chem. Commun.*, 2011, **47**, 11543; (b) M. Juribašić, K. Užarević, D. Gracin and M. Ćurić, *Chem. Commun.*, 2014, **50**, 10287.

13 For the mechanochemical synthesis of zinc complexes, see: J. Lewiński, M. Dutkiewicz, M. Lesiuk, W. Śliwiński, K. Zelga, I. Justyniak and J. Lipkowski, *Angew. Chem., Int. Ed.*, 2010, **49**, 8266.

14 Very recently, Browne and co-workers have reported the mechanochemical synthesis of organozinc species in air; see: Q. Cao, J. L. Howard, E. Wheatley and D. L. Browne, *Angew. Chem., Int. Ed.*, 2018, **57**, 11339.

15 For the mechanochemical synthesis of gold–silver honeycomb aggregates, see: M. C. Blanco, J. Cámara, M. C. Gimeno, A. Laguna, S. T. James, M. C. Lagunas and M. D. Villacampa, *Angew. Chem., Int. Ed.*, 2012, **51**, 9777.

16 For the mechanochemical synthesis of aluminium complexes, see: N. R. Rightmire, T. P. Hanusa and A. L. Rheingold, *Organometallics*, 2014, **33**, 5952.

17 For the mechanochemical synthesis of Grignard reagents, see: J. M. Harrowfield, R. J. Hart and C. R. Whitaker, *Aust. J. Chem.*, 2001, **54**, 423.

18 For the mechanochemical synthesis of an iridacycle, see: G. N. Herman, P. Becker and C. Bolm, *Angew. Chem., Int. Ed.*, 2016, **55**, 3781.

19 For the mechanochemical synthesis of a rhodacycle, see: G. N. Herman and C. Bolm, *ACS Catal.*, 2017, **7**, 4592.

20 For selected recent examples of palladium-catalyzed cross-coupling reactions in air using mechanochemistry, see: (a) Q. Cao, W. I. Nicholson, A. C. Jones and D. L. Browne, *Org. Biomol. Chem.*, 2019, **17**, 1722; (b) Q.-L. Shao, Z.-J. Jiang and W.-K. Su, *Tetrahedron Lett.*, 2018, **59**, 2277; (c) K. Kubota, T. Seo, K. Koide, Y. Hasegawa and H. Ito, *Nat. Commun.*, 2019, **10**, 111; (d) V. Declerck, E. Colacino, X. Bantreil, J. Martinez and F. Lamaty, *Chem. Commun.*, 2012, **48**, 11778; (e) G. Cravotto, D. Garella, S. Tagliapietra, A. Stolle, S. Schüßler, S. E. S. Leonhardt and B. Ondruschka, *New J. Chem.*, 2012, **36**, 1304; (f) Z.-J. Jiang, Z.-H. Li, J.-B. Yu and W.-K. Su, *J. Org. Chem.*, 2016, **81**, 10049; (g) H. Cheng, J. G. Hernández and C. Bolm, *Org. Lett.*, 2017, **19**, 6284.

21 (a) D. W. Old, J. P. Wolfe and S. L. Buchwald, *J. Am. Chem. Soc.*, 1998, **120**, 9722; (b) R. Martin and S. L. Buchwald, *Acc. Chem. Res.*, 2008, **41**, 1461.

22 T. Friščić, S. L. Childs, S. A. A. Rizvi and W. Jones, *CrystEngComm*, 2009, **11**, 418.

23 F. Schneider and B. Ondruschka, *ChemSusChem*, 2008, **1**, 622.

24 (a) J. Vicente and M. Lyakhovych, *Organometallics*, 2001, **20**, 4695; (b) J. Vicente, R. V. Shenoy and E. Martínez-Viviente, *Organometallics*, 2009, **28**, 6101; (c) J. Vicente, R. V. Shenoy, E. Martínez-Viviente and P. G. Jones, *Inorg. Chem.*, 2011, **50**, 7189.

25 D. C. Waddell, T. D. Clark and J. Mack, *Tetrahedron Lett.*, 2012, **53**, 4510.

26 C. Bolm and J. D. Hernández, *Angew. Chem., Int. Ed.*, 2019, **58**, 3285.