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## PAPER



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# Eco-friendly Suzuki–Miyaura coupling of arylboronic acids to aromatic ketones catalyzed by the oxime-palladacycle in biosolvent 2-MeTHF<sup>†</sup>

Oxime-palladacycle catalyzed Suzuki-Miyaura cross-coupling reaction of acid chlorides and arylboronic

acids to yield aryl ketones was developed. The remarkable benefit of this method is the use of water

immiscible (practically) 2-MeTHF as solvent, which provides easy isolation of the crude reaction mixture just by separation of 2-MeTHF-water layers, and then evaporation of 2-MeTHF. Moreover, the use of

relatively equal proportion of substrates and less generation of side products make the method highly

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#### Introduction

Ketones are ubiquitous structural motifs found across various natural products, pharmaceuticals and agrochemicals.<sup>1</sup> They also represent a wide range of ideal starting materials for the synthesis of cyanohydrins, oximes, carbazones, acetals, pinacols, *etc.* Conventional routes to synthesize ketone are the Friedel–Crafts acylation<sup>2</sup> and Suzuki–Miyaura cross-coupling of aryl halides with organometallic reagents under a carbon monoxide atmosphere.<sup>3</sup> However, the formation of tertiary alcohols and isomeric mixtures due to limited regioselectivity,<sup>4</sup> and the use of corrosive AlCl<sub>3</sub> and toxic carbon monoxide<sup>5</sup> are certain difficulties associated with these methods.

atom economic.

The palladium catalyzed Suzuki–Miyaura cross-coupling of acid derivatives with organoborons represents another powerful tool to access ketones (Scheme 1).<sup>6</sup> This methodology has gained immense attention as it relies on the use of easily accessible, widely functionalized, relatively low-toxic,<sup>7</sup> heat and moisture stable organoborons. Moreover, the use of active and commercially available acid derivatives presents wide scope to various ketone derivatives. In recent years, numerous significant outcomes have been achieved using diverse palladium catalysts *viz*. PdCl<sub>2</sub>,<sup>8</sup> Pd(OAc)<sub>2</sub>,<sup>9</sup> Pd/C,<sup>6b</sup> Pd(dba)<sub>2</sub>,<sup>10</sup> Pd(PPh<sub>3</sub>)<sub>4</sub>,<sup>11</sup> PdCl<sub>2</sub>(dppf),<sup>12</sup> POPd,<sup>13</sup> Pd<sub>2</sub>dba<sub>3</sub>,<sup>14</sup> imidazolium chloride tagged Pd(II) complex<sup>15</sup> and (BeDABCO)<sub>2</sub>Pd<sub>2</sub>Cl<sub>6</sub>,<sup>16</sup> under reaction systems, like toluene, THF, water, water–acetone, ionic liquid or hydrated base, *etc.* In fact, synthetic methods based on the use of these solvents present the following disadvantages: (i) the possibility of generation of

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less reactive acid anhydride or carboxylic acid in an aqueous system needing high substrate loading;<sup>6b</sup> (ii) formation of emulsions, rag layers at the phase interface and poor extraction yields; and (iii) the long and troublesome synthetic procedures for ionic liquids.<sup>17</sup> Overall, it is estimated that around 80% of the chemical waste produced from drug synthesis corresponds to the organic solvent.<sup>18</sup> Thus, while designing the acid halide-based reactions particular care should be taken in the choice of the solvent.

Recently, Pace and co-workers reported the excellent preparation of Weinreb amides starting from acid halides in a biphasic system water-2-methyltetrahydrofuran (2-MeTHF).<sup>19</sup> Importantly, they obtained a range of pure products by simple removal of 2-MeTHF in good yields and purity, and did not use extra solvent during the work-up process. Interestingly, 2-MeTHF resembles toluene or THF in terms of physical properties, and when used in organometallic reactions it offers both economical and environmentally friendly advantages over common aprotic solvents.<sup>20,21</sup> In reactions including Grignard reagent,<sup>22</sup> organopalladium, organozinc and LiAlH<sub>4</sub> reductions,<sup>23</sup> 2-MeTHF has found widespread application. 2-MeTHF has been reported to work like THF in nickel<sup>24</sup> and copper<sup>25</sup> catalyzed couplings. Pharmaceutical process development researchers have found that the use of 2-MeTHF provides superior diastereoselectivity when compared with other solvents.26

The growing interest towards 2-MeTHF is also due to its adherence with several Green Chemistry principles.<sup>27</sup> Among

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Table 1 Effects of catalyst loading, temperature and time<sup>a</sup>



 $^a$  Reaction conditions: 2a (0.5 mmol), 3a (0.55 mmol), 2-MeTHF (4 mL), K<sub>2</sub>CO<sub>3</sub> (1 mmol).  $^b$  Isolated yield.

them, the 3rd (less hazardous chemical synthesis – permitted daily exposure of 2-MeTHF in human is upto 6.2 mg day<sup>-1</sup>),<sup>28</sup> 5th (safer solvents and auxiliaries), 7th (use of renewable feedstocks – it can be obtained from biomass feedstock like furfural or levulinic acid derived from corncobs and sugarcane)<sup>20a</sup> and the 10th (design for degradation – it degrades by factors like air and sunlight, probably *via* oxidation and ring-opening)<sup>29</sup> principles refer it as a suitable green solvent for both academia and industries.

In recent years, many workers have focused their research interests on the application of oxime-palladacycles, which have exhibited high catalytic activity in various cross-coupling reactions.<sup>30</sup> They are stable to heat, air and moisture, and easily accessible from low-cost starting materials. However, to the best of our knowledge, oxime-palladacycles have never been studied for the coupling of acid chlorides and arylboronic acids. As part of our ongoing efforts to develop transition-metal-catalyzed reactions,<sup>6b,31</sup> we herein report the use of a combination of oxime-palladacycle **1** and 2-MeTHF in the coupling of acid chlorides (Table 1). The present method provides easy isolation of the reaction mixture without the use of additional organic solvent, which would enhance the application scope of the acylation coupling to a more acceptable level.

#### Results and discussion

The investigation was initiated by using a model reaction between benzoyl chloride **2a** and phenylboronic acid **3a** in the presence of palladacycle **1** (1 mol% Pd) and  $K_2CO_3$  (2 equiv.) under open air conditions in 2-MeTHF at reflux. The results are summarized in Table 1. The desired benzophenone **4aa** was formed in 98% isolated yield within 4 h (Table 1, entry 1). Upon optimizing the reaction conditions with different catalyst loading, best results have been obtained by using catalyst **1** (0.4 mol% Pd) in 2-MeTHF at reflux (Table 1, entry 5). Cross-coupling using commonly employed palladium source like Pd(OAc)<sub>2</sub>, PdCl<sub>2</sub> and Pd/C gave

Table 2 Screening solvents and bases<sup>a</sup>

$\begin{array}{c c} O & OH & O\\ \hline C & HO & \\ 2a & 3a \end{array} \xrightarrow{I (0.4 \text{ mol}\%\text{Pd}), \text{ Base}} & O\\ \hline Solvent, \text{ reflux} & 4aa \end{array}$							
Entry	Solvent	Base	Time (h)	Yield <sup><math>b</math></sup> (%)			
1	2-MeTHF	K <sub>2</sub> CO <sub>3</sub>	4	97			
2	Acetone	$K_2CO_3$	12	84			
3	Toluene	$K_2CO_3$	5.5	95			
4	DMF	$K_2CO_3$	8	77 <sup>c</sup>			
5	THF	$K_2CO_3$	6.5	88			
6	i-PrOH	$K_2CO_3$	4	$28^d$			
7	Acetonitrile	$K_2CO_3$	6	83			
8	DCM	$K_2CO_3$	6	73			
9	PEG-400	$K_2CO_3$	5.5	$87^e$			
10	2-MeTHF-H <sub>2</sub> O	$K_2CO_3$	6	$65^f$			
11	2-MeTHF	$K_2CO_3$	6	$74^g$			
12	2-MeTHF	$Na_2CO_3$	7.5	87			
13	2-MeTHF	$Cs_2CO_3$	5	91			
14	2-MeTHF	Na <sub>3</sub> PO <sub>4</sub> ·12H <sub>2</sub> O	5	89			
15	2-MeTHF	КОН	6	58			
16	2-MeTHF	NaOH	6	49			
17	2-MeTHF	Et <sub>3</sub> N	6	43			
18	2-MeTHF	_	6	Trace			

<sup>*a*</sup> Reaction conditions: **2a** (0.5 mmol), **3a** (0.55 mmol), **1** (0.4 mol% Pd), solvent (4 mL), base (1 mmol). <sup>*b*</sup> Isolated yield. <sup>*c*</sup> Treated at 120 °C. <sup>*d*</sup> Isopropyl benzoate was formed 36% (GC yield). <sup>*e*</sup> Treated at 80 °C. <sup>*f*</sup> (3:1) ratio. <sup>*g*</sup> N<sub>2</sub> (1 atm).

comparably lower yield under present reaction conditions (Table 1, entries 8–10).

Encouraged by the highest yield in the presence of 0.4 mol% Pd catalyst **1**, we further optimized the effect of different solvents and bases (Table 2). It has been shown that the reaction proceeded with 84% isolated yield within 12 hours in acetone (Table 2, entry 2). Screening of other solvents indicated that toluene (Table 2, entry 3) was optimal; whereas DMF, acetonitrile, dichloromethane and PEG-400 gave yields lower than 87% (Table 2, entries 4, 7, 8 and 9, respectively). The use of isopropanol produces isopropyl benzoate in high amounts (Table 2, entry 6). The use of co-solvent 2-MeTHF-H<sub>2</sub>O (3:1) afforded **4aa** in 65% yield (Table 2, entry 10). This may be due to the hydrolysis of benzoyl chloride or the formation of the aryloxy anion intermediate from arylboronic acid.

From these results it seems that various organic solvents could be employed for the acylation reaction with oxime-palladacycle; however, we decided to examine 2-MeTHF as the solvent for further studies. The reason for our decision was that 2-MeTHF is non-carcinogenic and is practically not miscible with water (4 g/100 mL),<sup>32</sup> which provides easy isolation during work-up step without needing to add any noxious volatile solvent [see Experimental procedure]. Reaction under a N<sub>2</sub> atmosphere provides slightly lower yield of the coupling product (Table 2, entry 11). This suggests that the presence of dissolved air in 2-MeTHF accelerates the catalytic cycle by enhancing the rate of activation of arylboronic acid to aryl ion species, vital for catalytictransmetalation step.

We next examined the effect of different bases, and found that the inorganic bases like  $Na_2CO_3$ ,  $Cs_2CO_3$  and  $Na_3PO_4$ ·12H<sub>2</sub>O have considerable effect on the reaction efficiency (Table 2, entries 12–14). Alkali metal hydroxides afforded the desired

R <sup>1</sup> -	COCI + R <sup>2</sup> -B(O) 2 3	H) <sub>2</sub>	, K <sub>2</sub> CO <sub>3</sub> ► 60 °C ► F	0 II R <sup>1<sup>-C</sup> R<sup>2</sup> <b>4</b></sup>
Entry	R <sup>1</sup> , 2	R <sup>2</sup> , 3	4	Yield <sup><math>b</math></sup> (%)
1	C <sub>6</sub> H <sub>5</sub> , 2a	C <sub>6</sub> H <sub>5</sub> , 3a	4aa	97
2	$C_6H_5$ , 2a	4-MeC <sub>6</sub> H <sub>4</sub> , 3b	4ab	96
3	C <sub>6</sub> H <sub>5</sub> , 2a	4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub> , 3c	4ac	93
4	$C_6H_5$ , 2a	4-ClC <sub>6</sub> H <sub>4</sub> , 3d	4ad	91
5	$C_6H_5$ , 2a	4-FC <sub>6</sub> H <sub>4</sub> , 3e	4ae	90
6	$C_6H_5$ , 2a	4-CNC <sub>6</sub> H <sub>4</sub> , 3f	4af	94
7	$4 - NO_2C_6H_4$ , 2b	$C_6H_5$ , 3a	4ba	87
8	$4\text{-ClC}_6\text{H}_4, 2c$	$C_6H_5$ , 3a	4ca	91
9	4-MeOC <sub>6</sub> H <sub>4</sub> , 2c	$I C_6H_5$ , 3a	4da	95
10	4-MeOC <sub>6</sub> H <sub>4</sub> , 2c	$4 - ClC_6H_4$ , 3d	4dd	89
11	4-ClC <sub>6</sub> H <sub>4</sub> , 2c	4-MeOC <sub>6</sub> H <sub>4</sub> , 39	g 4cg	91
12	4-MeOC <sub>6</sub> H <sub>4</sub> , 2c	4-MeOC <sub>6</sub> H <sub>4</sub> , 39	g 4dg	94
13	CH <sub>3</sub> , 2e	C <sub>6</sub> H <sub>5</sub> , 3a	4ea	$0^{c}$
14	C <sub>3</sub> H <sub>7</sub> , 2f	C <sub>6</sub> H <sub>5</sub> , 3a	4fa	0 <sup>c</sup>

<sup>*a*</sup> Reaction conditions: **2a–g** (0.5 mmol), **3a–g** (0.55 mmol), **1** (0.4 mol% Pd),  $K_2CO_3$  (1 mmol), 2-MeTHF (4 mL) at 80 °C under air for 6 h. <sup>*b*</sup> Isolated yield. <sup>*c*</sup> Treated for 12 h.

product within 49–58% yield (Table 2, entries 15 and 16). Organic base ( $Et_3N$ ) gave much lower yield of the product (Table 2, entry 17). However, in the absence of any base no traceable amount of product was observed (Table 2, entry 18).

With the standard reaction conditions, we next explored the substrate scope and limitations of the reaction by employing a variety of acid chlorides **2a–d** and arylboronic acids **3a–g** (Table 3). The standard reaction conditions were found to be compatible with a wide range of electronically diverse substrates. Though, slight electronic interventions due to the substituent were also observed in certain cases. It is found that both neutral and electron rich acid chloride reacts more efficiently with both electron-rich and -poor arylboronic acids (Table 3, entries 1–6 and 10–12). It is also noteworthy that the reaction conditions tolerate the halogen substituent in both substrates, which are usually used in various cross-coupling reactions, and thus exhibits further synthetic utility. Unfortunately, the aliphatic acid chlorides did not respond to the present reaction conditions, even after 12 h (Table 3, entries 13 and 14).

It is well established from the literature that the oxime-derived palladacycles are catalytically inactive species which supplies active Pd(0) to the reaction mixture.<sup>30</sup> Thus, they act as a reservoir of highly active Pd(0) species, which are generated by the reaction of palladacycle with one or more components of the reaction mixture and are usually released into the catalytic cycle at a slower rate than that of the catalytic reaction. This slow releasing property prevents unwanted inactivation processes such as nucleation and growth of large inactive palladium particles within the reaction system.

Catalyst poisons that could selectively stop the catalytic activity of Pd-catalysts can be used to determine the involved active catalytically species. To date, the Hg(0) poisoning test has been recognized as the most powerful in metal-catalyzed reactions.<sup>33</sup> Hg(0) amalgamates strongly with Pd(0), Rh(0) and Ni(0)-based complexes,<sup>34</sup> thereby blocking the access of the active site to the

substrate. Thus, a Pd(0) species can possibly be poisoned by adding excess Hg(0) (molar ratio to [Pd] ~ 400) to the reaction mixture during the reaction. This suppression of the reaction is generally considered as evidence for the presence of Pd(0) as the active species. For the Hg-poisoning test, we have performed a coupling reaction between benzoyl chloride **2a** and phenylboronic acid **3a** using catalyst **1** (0.4 mol% Pd). After 1 h of reaction (41% conversions *vide* GC-MS) excess Hg(0) was added to the reaction mixture and stirred for next 6 h. It should be noted that the catalytic activity apparently gets hindered even after 6 h of constant stirring (indicated by GC-MS). This finding suggests that the true active catalyst during the reaction is Pd(0) species. The formation of palladium nanoparticles during the reaction is also demonstrated by TEM analysis (see Fig. S1, ESI†).

On the basis of the literature reports,<sup>10,35</sup> the reaction mechanism of this acylation reaction was hypothesized as shown in Scheme 2. Initially, Pd(0) is formed by the reduction of the Pd–C bond of complex 1, and then the oxidative addition of acid chloride 2 to Pd(0) produces the acylpalladium( $\pi$ ) chloride intermediate **A**. Under alkaline conditions, subsequent transmetallation of ArB(OH)<sub>2</sub> **3** to acylpalladium intermediate **A** takes place at the Pd–Cl bond to generate (acyl)(aryl)palladium( $\pi$ ) species **B**. Finally, the reductive elimination of species **B** delivers the oxidative coupling product **4**, regenerating the active Pd(0) species and resuming the catalytic cycle.

The cross-coupling reactions are implemented on a regular basis in large scale chemical industries due to the wide accessibility and functionality of organometallic derivatives, and mild reaction conditions. Thus, we were keen to explore the scope for scale-up to prepare grams instead of milligrams of biaryl ketones. With the optimized reaction conditions and easy work-up procedure on a small scale, we next investigated their performance upon scale-up. Thus, the reaction of excess benzoyl chloride **2a** (5 mmol), phenylboronic acid **3a** (5.5 mmol),  $K_2CO_3$  (10 mmol), complex **1** (4 mol% Pd) and 2-MeTHF (20 mL) was performed at 80 °C for 4 h. We were able to isolate 0.8987 grams (98.7%) of benzophenone **4aa**.

Although most aqueous protocols described in the literature do use some amount of water as solvent, they often require excessive amounts of toxic organic solvents during product extraction from the water medium. Thus, making the total



Scheme 2 Probable reaction pathways.

 Table 4
 Comparison of palladium catalysts for the Suzuki–Miyuara coupling reaction

$\begin{array}{c} O \\ C \\ C \\ 2a \\ 2a \\ 3a \\ 3a \\ C \\ $							
Entry	Conditions	Catalyst (mol%)	Yield, 4aa	Ref.			
1	<b>2a</b> (1.0 mmol), <b>3a</b> (1.2 mmol), Pd/C, K <sub>2</sub> CO <sub>3</sub> , acetone–H <sub>2</sub> O, 60 °C	3	93	6 <i>b</i>			
2	2a (1.0 mmol), 3a (1.2 mmol), Pd(PPh <sub>3</sub> ) <sub>4</sub> , Cs <sub>2</sub> CO <sub>3</sub> , toluene, N <sub>2</sub> , 100 °C, 16 h	5	80	11 <i>a</i>			
3	2a (0.75 mmol), 3a (0.5 mmol), (BeDABCO) <sub>2</sub> Pd <sub>2</sub> Cl <sub>6</sub> , K <sub>2</sub> CO <sub>3</sub> , toluene, rt, 1 h	0.4	96	16			
4	2a (1.5 mmol), 3a (1 mmol), PdCl <sub>2</sub> , Na <sub>2</sub> CO <sub>3</sub> , grinding, 25-30 °C, 5 min	3.3	90	8 <i>b</i>			
5	2a (1 mmol), 3a (0.5 mmol), Pd(PPh <sub>3</sub> ) <sub>4</sub> , Cs <sub>2</sub> CO <sub>3</sub> , toluene, MW, 10 min	5	68	14			
6	2a (0.5 mmol), 3a (0.55 mmol), catalyst 1, K <sub>2</sub> CO <sub>3</sub> , 2-MeTHF, 80 °C, 4 h	0.4	97	Present work			

relative amount of noxious solvent in the entire process much higher, negating the main objective of green chemistry. Importantly, by using 2-MeTHF the crude mixture of cross-coupling products was simply extracted by quenching with water followed by the separation of the resulting 2-MeTHF-water phases and drying, without the need to use additional organic solvent during the entire workup procedure. Thus, the present method is an excellent example of real green chemistry. Moreover, upon comparing with the previously reported catalyst system, our approach shows significant advantages (Table 4).

#### Conclusion

In conclusion, the oxime-palladacycle catalyzed Suzuki-type carbonylation reaction *via* the cleavage of the C–Cl bond of acid chlorides to yield aryl ketones has been described for the first time. Overall, this protocol offers a mild and efficient alternative to the existing methods, as (i) the oxime-palladacycle pre-catalysts are easily accessible and highly efficient, (ii) the solvent is biologically obtainable, and (iii) is immiscible in water, and this property minimizes the dissolution of moisture in the solvent surface, and avoids the need to maintain inert conditions, (iv) the crude reaction mixture was isolated just by separation of 2-MeTHF-water layers and then evaporation of 2-MeTHF, without the use of additional organic solvent, and (v) high atom economy (64.2%) and *E*-factor (39.3) due to the relatively equal proportion of substrates (2nd Green Chemistry principle).

### Experimental

## Typical experimental procedure for Suzuki-Miyaura cross-coupling of arylboronic acids

A 50 mL branched test tube was charged with a mixture of  $K_2CO_3$  (138 mg, 1.0 mmol), complex 1 (0.4 mol% Pd), 2-MeTHF (4 mL) under open air. The solution was heated to 80 °C on a Process Station Personal Synthesizer with continuous stirring, and added with phenylboronic acid **3a** (0.55 mmol) and benzoyl chloride **2a** (0.5 mmol). The mixture was stirred at 80 °C for 4 h and progress of the reaction was monitored using TLC. After completion of the reaction, the resulting mixture was added to a saturated solution of brine (4 mL). The resulting water-organic phases were separated and the organic phase (in 2-MeTHF) was

dried over anhydrous Na $_2$ SO $_4$ , filtered and evaporated under reduced pressure. The resultant residue was subjected to silica gel column chromatography (eluent, 10–15%: ethyl acetate/hexane) to afford the desired product.

Benzophenone (**4aa**):<sup>36</sup> white solid, yield: 97%, 88.2 mg; m.p. 48–49 °C (literature,<sup>37</sup> 47–48.5 °C), <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, ppm)  $\delta$ : 7.81–7.79 (m, 4H), 7.57 (t, *J* = 7.7 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 4H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz, ppm)  $\delta$ : 196.9, 137.6, 132.5, 130.1, 128.3; FT-IR (KBr, cm<sup>-1</sup>): 1659 ( $\nu_{C=O}$ ); GC-MS *m/z*: 182.1 (M<sup>+</sup>, 100).

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#### Notes and references

- (a) N. D. Kimpe, M. Keppens and G. Froncg, Chem. Commun., 1996, 635; (b) B. M. Baughman, E. Stennett, R. E. Lipner, A. C. Rudawsky and S. J. Schidtke, J. Phys. Chem. A, 2009, 113, 8011; (c) A. L. Ong, A. H. Kamaruddin and S. Bhatia, Process Biochem., 2005, 40, 3526; (d) A. Wen, Z. Wang, T. Hang, Y. Jia, T. Zhang, Y. Wu, X. Gao and Z. Yang, J. Chromatogr. B: Anal. Technol. Biomed. Life Sci., 2007, 856, 348; (e) M. Furusawa, Y. Ido, T. Tanaka, T. Ito, K. Nakaya, I. Ibrahim, M. Ohyama, M. Iinuma, Y. Shirataka and Y. Takahashi, Helv. Chim. Acta, 2005, 88, 1048.
- 2 (a) A. Furstner, D. Voigtlander, W. Schrader, D. Giebel and M. T. Reetz, Org. Lett., 2001, 3, 417; (b) J. Ross and J. Xiao, Green Chem., 2002, 4, 129; (c) S. Gmouh, H. Yang and M. Vaultier, Org. Lett., 2003, 5, 2219; (d) M. Rueping and B. J. Nachtsheim, Beilstein J. Org. Chem., 2010, 6, 1.
- 3 (*a*) T. Ishiyama, H. Kizaki, N. Miyaura and A. Suzuki, *Tetrahedron Lett.*, 1993, 34, 7595; (*b*) T. Ishiyama, H. Kizaki, T. Hayashi, A. Suzuki and N. Miyaura, *J. Org. Chem.*, 1998, 63, 4726; (*c*) H. Neumann, A. Brennfhrer and M. Beller, *Adv. Synth. Catal.*, 2008, 350, 2437; (*d*) M. Cai, G. Zheng, L. Zha and J. Peng, *Eur. J. Org. Chem.*, 2009, 1585; (*e*) M. V. Khedkar, P. J. Tambade, Z. S. Qureshi and B. M. Bhanage, *Eur. J. Org. Chem.*, 2010, 6981 and references cited therein; (*f*) M. V. Khedkar, T. Sasaki and B. M. Bhanage, *RSC Adv.*, 2013, 3, 7791.

- 4 (a) P. H. Gore, *Chem. Rev.*, 1955, 55, 229; (b) E. Fillion,
  D. Fishlock, A. Wilsily and J. M. Goll, *J. Org. Chem.*, 2005,
  70, 1316.
- 5 (*a*) T. Choshi, S. Yamada, E. Sugino, T. Kuwada and S. Hibino, *J. Org. Chem.*, 1995, **60**, 5899; (*b*) X. F. Wu, H. Neumann, A. Spannenberg, T. Schulz, H. J. Jiao and M. Beller, *J. Am. Chem. Soc.*, 2010, **132**, 14596.
- 6 (*a*) M. Blangetti, H. Rosso, C. Prandi, A. Deagostino and P. Venturello, *Molecules*, 2013, **18**, 1188; (*b*) M. Mondal and U. Bora, *Appl. Organomet. Chem.*, 2014, **28**, 354 and reference cited therein.
- 7 In general boronic acids are non-toxic; however, 50% of aryl boronic acids are mutagenic.
- 8 (a) N. A. Bumagin and D. N. Korolev, *Tetrahedron Lett.*, 1999,
  40, 3057; (b) B. P. Bandgar and A. V. Patil, *Tetrahedron Lett.*, 2005, 46, 7627.
- 9 B. Xin, Y. Zhang and K. Cheng, J. Org. Chem., 2006, 71, 5725.
- D. Ogawa, K. Hyodo, M. Suetsugu, J. Li, Y. Inoue, M. Fujisawa, M. Iwasaki, K. Takagi and Y. Nishihara, *Tetrahedron*, 2013, 69, 2565.
- (a) M. Haddach and J. R. McCarthy, *Tetrahedron Lett.*, 1999, 40, 3109; (b) H. Chen and M.-Z. Deng, *Org. Lett.*, 2000, 2, 1649; (c) Y. Urawa and K. Ogura, *Tetrahedron Lett.*, 2003, 44, 271; (d) S. Eddarir, N. Cotelle, Y. Bakkour and C. Rolando, *Tetrahedron Lett.*, 2003, 44, 5359.
- 12 Y. Nishihara, Y. Inoue, M. Fujisawa and K. Takagi, *Synlett*, 2005, 2309.
- 13 K. Ekoue-Kovi, H. Xu and C. Wolf, *Tetrahedron Lett.*, 2008, **49**, 5773.
- 14 V. Polackova, S. Toma and I. Augustinova, *Tetrahedron*, 2006, **62**, 11675.
- 15 L. Zhang, J. Wu, L. Shi, C. Xia and F. Li, *Tetrahedron Lett.*, 2011, 52, 3897.
- 16 F. Rafiee and A. R. Hajipour, *Appl. Organomet. Chem.*, 2015, 29, 181.
- 17 (*a*) P. G. Jessop, *Green Chem.*, 2011, **13**, 1391; (*b*) Y. Zhang, B. R. Bakshi and E. S. Demessie, *Environ. Sci. Technol.*, 2008, **42**, 1724.
- 18 J. M. Fortunak, Future Med. Chem., 2009, 1, 571.
- 19 V. Pace, L. Castoldi, A. R. Alcántara and W. Holzera, *RSC Adv.*, 2013, 3, 10158.
- 20 (a) D. F. Aycock, Org. Process Res. Dev., 2007, 11, 156;
  (b) Y. Gu and F. Jérôme, Chem. Soc. Rev., 2013, 42, 9550.
- 21 Other advantages of 2-MeTHF includes: (i) easy aqueous phase separation due to immiscibility with water; (ii) reuse and recycling due to azeotrope with water; (iii) better stability to acids and bases; and (iv) low volatility and higher flash point; (v) the lowest carbon footprint amongst industrial solvents, see: ref. 20.
- 22 A. Kadam, M. Nguyen, M. Kopach, P. Richardson, F. Gallou, Z.-K. Wane and W. Zhang, *Green Chem.*, 2013, **15**, 1880.

- 23 B. Comanita and D. Aycock, *Industrie Pharma Magazine*, 2005, 7, 54.
- 24 S. D. Ramgren, L. Hie, Y. Ye and N. K. Garg, Org. Lett., 2013, 15, 3950.
- 25 D. R. Spring, S. Krishnan and S. L. Schreiber, J. Am. Chem. Soc., 2000, **122**, 5656.
- 26 (a) L. Delhaye, A. Merschaert, P. Delbeke and W. Brione, Org. Process Res. Dev., 2007, 11, 689; (b) M. Guillaume, J. Cuypers and J. Dingenen, Org. Process Res. Dev., 2007, 11, 1079.
- 27 P. Anastas and N. Eghbali, Chem. Soc. Rev., 2010, 39, 301.
- 28 V. Antonucci, J. Coleman, J. B. Ferry, N. Johnson, M. Mathe, J. P. Scott and J. Xu, Org. Process Res. Dev., 2011, 15, 939.
- 29 V. Pace, P. Hoyos, L. Castoldi, P. D. de María and A. R. Alcántara, *ChemSusChem*, 2012, 5, 1369.
- 30 (a) E. Alacid, D. A. Alonso, L. Botella, C. Nájera and M. C. Pacheco, *Chem. Rec.*, 2006, 6, 117; (b) D. A. Alonso and C. Nájera, *Chem. Soc. Rev.*, 2010, 39, 2891.
- 31 (a) M. Mondal and U. Bora, Green Chem., 2012, 14, 1873;
  (b) M. Mondal, G. Sarmah, K. Gogoi and U. Bora, Tetrahedron Lett., 2012, 53, 6219; (c) M. Mondal and U. Bora, Tetrahedron Lett., 2014, 55, 3038; (d) T. Begum, M. Mondal, P. K. Gogoi and U. Bora, RSC Adv., 2015, 5, 38085; (e) A. Gogoi, A. Dewan, G. Borah and U. Bora, New J. Chem., 2015, 5, 39, 3341; (f) A. Gogoi, A. Dewan and U. Bora, RSC Adv., 2015, 5, 16; (g) T. Begum, A. Gogoi, P. K. Gogoi and U. Bora, Tetrahedron Lett., 2015, 56, 95.
- 32 V. Pace, Aust. J. Chem., 2012, 65, 301.
- 33 (a) G. M. Whitesides, M. Hackett, R. L. Brainard, J. P. P. M. Lavalleye, A. F. Sowinski, A. N. Izumi, S. S. Moore, D. W. Brown and E. M. Staudt, *Organometallics*, 1985, 4, 819; (b) C. Paal and W. Hartmann, *Chem. Ber.*, 1918, 51, 711.
- 34 (a) D. R. Anton and R. H. Crabtree, Organometallics, 1983,
  2, 855; (b) L. N. Lewis and N. Lewis, J. Am. Chem. Soc., 1986,
  108, 7228; (c) Y. Lin and R. G. Finke, Inorg. Chem., 1994,
  33, 4891; (d) K. S. Weddle, J. D. Aiken III and R. G. Finke,
  J. Am. Chem. Soc., 1998, 120, 5653; (e) R. van Asselt and
  C. J. Elsevier, J. Mol. Catal., 1991, 65, L13; (f) P. Foley,
  R. DiCosimo and G. M. Whitesides, J. Am. Chem. Soc., 1980,
  102, 6713; (g) G. Süss-Fink, M. Faure and T. R. Ward, Angew.
  Chem., Int. Ed., 2002, 41, 99; (h) L. N. Lewis, J. Am. Chem.
  Soc., 1986, 108, 743.
- 35 (a) J. Chen, Y. Peng, M. Liu, J. Ding, W. Su and H. Wua, Adv. Synth. Catal., 2012, 2117; (b) Y. B. Kwon, B. R. Choi, S. H. Lee, J. Seo and C. M. Yoon, Bull. Korean Chem. Soc., 2010, 31, 2672; (c) K. Tatsumi, T. Fujihara, J. Terao and Y. Tsuji, Chem. Commun., 2014, 50, 8476; (d) L. J. Goossen and K. Ghosh, Eur. J. Org. Chem., 2002, 3254; (e) H. Tatamidani, F. Kakiuchi and N. Chatani, Org. Lett., 2004, 6, 3597.
- 36 A. Yu, L. Shen, X. Cui, D. Peng and Y. Wu, *Tetrahedron*, 2012, 68, 2283.
- 37 S. S. Kulp and M. J. McGee, J. Org. Chem., 1983, 48, 4097.