Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: M. Dabiri, N. Farajinia Lehi, S. Kazemi Movahed and H. R. Khavasi, *Org. Biomol. Chem.*, 2017, DOI: 10.1039/C7OB01534H.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/C7OB01534H

Journal Name

ARTICLE

Pd-catalyzed regioselective C-H halogenation of quinazolinones and benzoxazianones

Minoo Dabiri,* Noushin Farajinia Lehi, Siyavash Kazemi Movahed and Hamid Reza Khavasi

aReceived 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

A Pd-catalyzed ortho-selective halogenation of benzoxazinone and quinazolinone scaffolds have been described employing *N*-halosuccinimide as both halogen source and oxidant reagent via C–H bond activation. This transformation shows high chemo- and rigoselectivitiy and demonstrates a broad range of benzoxazinone and quinazolinone substrates with different functional groups and has been scaled up to gram level.

Introduction

Recently, the development in Pd-catalyzed selective functionalization of C–H bonds has witnessed tremendous progress as an efficient, straightforward, valuable, and atom-economical process to form carbon-carbon and carbon-heteroatom bonds.[1] Synthetic endeavours have concentrated on several C–H functionalization, such as amination,[2] arylation,[3] cyanation,[4] halogenations,[5] oxygenation,[6] and sulfonylation[7] by activation of both sp^2 and sp^3 C–H bonds. Among them, Pd-catalyzed selective *ortho*-halogenation of sp^2 C–H bonds[5] have attracted much interest because aromatic halides are highly valuable starting materials for synthetic elaboration due to their role as precursors in the benzyne generation,[8] nucleophilic aromatic substitution,[9] synthesis of organometallic reagents,[10] as well as transition-metal catalyzed cross-coupling reactions.[11] Considerable endeavours have been made for the selective *ortho*-halogenation of sp^2 C–H bonds by using directing groups (DGs), including azoxybenzenes,[5d] carbamates,[5c-5e] cyano,[5j] oxime ethers,[5i] pyridines,[5f] and various *N*-heterocycles.[5a,5b] Although in some cases, the DG needs to be pre-built-in and so removed afterward.[5g,5f,5i] Several halogen sources have been used such as CaX_2,[12a] CuX_2,[12b] 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ),[12c] and *N*-halosuccinimides (NXSs).[5a,5b,5d,5e,5f,5g] Commonly, this reaction needs using an external oxidant such as $Cu(OTFA)_2$[12a] and $Cu(OAc)_2$.[12b] Among halogen sources, NXSs act as both halogen source and oxidant reagent.

Benzoxazinone and quinazolinone scaffolds are ubiquitous building block in many natural products and bioactive molecules such as bouchardatin, cetilistat, dictyoquinazol A, luotonin A, AX-9657, and TEI-6344, and are as well defined as an excellent class of pharmacologically active compounds exhibiting anti-cancer, anti-inflammatory, antihypertensive, anti-diabetic, antimicrobial, antimalarial, chymotrypsin inhibitor, HSV-1 and serine protease inhibitors, and inhibitors of leucocyte elastase and analgesic activities (Figure 1).[13] Consequently, the structure of benzoxazinone and quinazolinone have been an intensive research focus in synthetic chemistry.

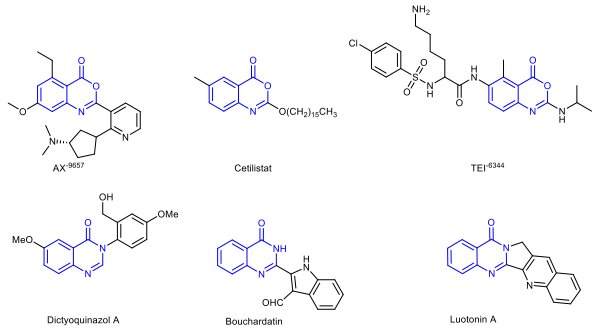


Figure 1. Representative examples of biologically active benzoxazinone and quinazolinone

To the best of our knowledge, transition-metal catalyzed ortho-C-H halogenations have not been reported for benzoxazinone and quinazolinone scaffolds. Herein, we report that a simple, efficient, and general, methodology for the *ortho*-selective halogenations of benzoxazinone and quinazolinone scaffolds to give the *ortho*-halogenated products in good yields.

Results and discussion

In order to optimize the reaction conditions series of experiments with different parameters were performed for a typical reaction of 2-phenylquinazolin-4(3*H*)-one and *N*-bromosuccinimide (NBS). These parameters were an additive, catalyst, solvent, oxidant, and temperature. In $Pd(OAc)_2$ (5 mol%), NBS (1.2 eq.) as oxidant and bromine source at 100°C in 1,2-dichloroethane (DCE), failed to provide any product (Table 1, entry 1). Inspired by the work of Nicholas,[5e] the effect *p*-toluenesulfonic acid (*p*-TsOH) as an acidic additive, was tested

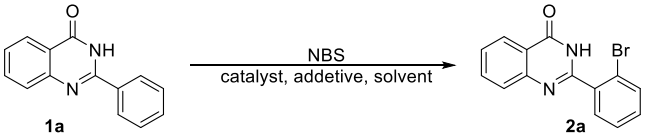
Faculty of Chemistry; Shahid Beheshti University; Tehran 1983969411 Islamic Republic of Iran E-mail: m-dabiri@sbu.ac.ir

†Electronic Supplementary Information (ESI) available: [copy of ^{1}H NMR, ^{13}C NMR and Mass spectra]. See DOI: 10.1039/x0xx00000x

that the *in situ* generated of an electron-deficient Pd complex.[5g] The yield was enhanced by the addition 0.5 eq. of *p*-TsOH in the reaction medium (Table 1, entry 2). Thus, the acidic additives, including trifluoromethanesulfonic acid (TfOH), trifluoroacetic acid (TFA), AcOH were tested in DCE (Table 1, entries 2–5). The best result was obtained by using *p*-TsOH as an acidic additive in the model reaction (Table 1, entry 2). The loading of the acidic additive was optimized (Table 1, entries 6 and 7). The addition of 1 eq. of the additive did not change in yield; however, the yield decreased when the amount of *p*-TsOH was reduced to 0.25 eq. Under these conditions, the effect of solvent was investigated on the halogenation of quinazolinone (Table 1, entries 8–10). It was found that the choice of solvent had a significant influence on this transformation. A higher yield was obtained when DCE was used as a solvent (Table 1, entry 2). The desired product was slightly obtained in *p*-TsOH with commonly metal salts, including $PdCl_2$, $Cu(OAc)_2$ and AgOAc (Table 1, entries 11–13). Additionally, the different types of co-oxidants such as $Na_2S_2O_8$, $K_2S_2O_8$, and $Cu(OAc)_2$ were tested and showed less efficient and afford in low yields (Table 1, entries 14–16). The reactions were carried out at different amounts of $Pd(OAc)_2$ ranging from 2.5 to 15 mol% (Table 1, entries 2, 17 -19). It was found 10 mol% of $Pd(OAc)_2$ is sufficient to push forward this reaction. The increasing of the loading $Pd(OAc)_2$ to 15 mol % did not show any effect on the yield. Also, no significant improvement in the product yield was observed even when the reaction temperature was increased from 100 °C to 120 °C (Table 1, entry 20).

Having obtained the optimal reaction conditions, we set out to explore the scope of the reaction of different 2-arylquinazolin-4(3*H*)-ones. The *N*-chlorosuccinimide (NCS) and *N*-iodosuccinimide (NIS) was used as halogen sources for the halogenation of 2-phenylquinazolin-4(3*H*)-one (Table 2, entries 2 and 3). The order of reactivity of NXSs under optimal conditions is NBS > NIS > NCS (Table 2, entries 1-3). The bromination with 2-arylquinazolin-4(3*H*)-ones bearing electron-donating and electron-withdrawing groups on the aryl ring was done. The results demonstrated that the electronic characteristics of substituents on the aryl ring have the significant influence on the reaction yields (Table 2, entries 4–6). The electron-donating group (*p*-Me) was more reactive compared with the electron-withdrawing group (*p*-NO_2) (Table 2, entries 4 and 6), which could be an attributed to the electrophilic halogenation C–H activation to form a C–Pd bond.[14] Additionally, the reaction was chemoselective in the case of Me-substituted quinazolinone (**1b**). The halogenations of benzylic positions by NXSs were reported.[5f] However, here 2-(2-halo-4-methylphenyl)quinazolin-4(3*H*)-ones were obtained in a chemospecificity manner (Table 2, entries 4 and 5). Interestingly, in meta-substituted quinazolinone (**1e**), the I, Br and Cl did not displace between quinazolinone ring and the substituent (Cl) (Table 2, entries 8-10). These results shown the steric hindrance in halogantation.

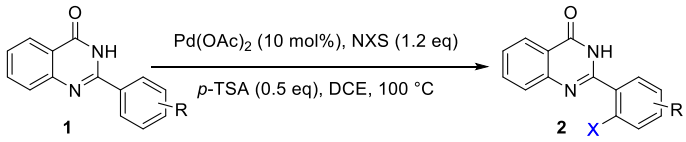
Table 1. Optimization of the reaction conditions[a].

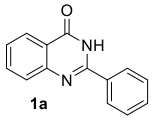
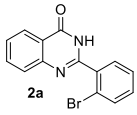
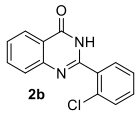
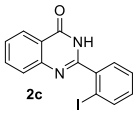
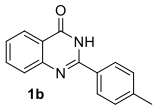
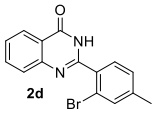
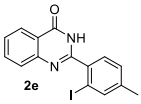
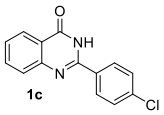
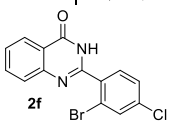
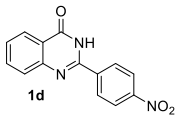
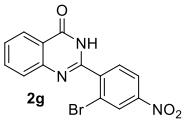
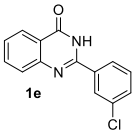
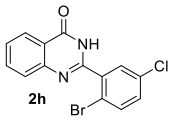
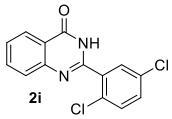
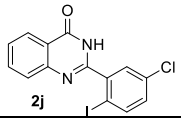


Entry	Catalyst (mol%)	Solvent	Additive (equiv.)	Yield (%)[b]
1	$Pd(OAc)_2$ (5)	DCE	-	Trace
2	$Pd(OAc)_2$ (5)	DCE	*p*-TsOH (0.5)	55
3	$Pd(OAc)_2$ (5)	DCE	TFA (0.5)	24
4	$Pd(OAc)_2$ (5)	DCE	AcOH (0.5)	15
5	$Pd(OAc)_2$ (5)	DCE	TfOH (0.5)	43
6	$Pd(OAc)_2$ (5)	DCE	*p*-TsOH (0.25)	31
7	$Pd(OAc)_2$ (5)	DCE	*p*-TsOH (1)	56
8	$Pd(OAc)_2$ (5)	1,4-dioxane	*p*-TsOH (0.5)	36
9	$Pd(OAc)_2$ (5)	CH_3CN	*p*-TsOH (0.5)	44
10	$Pd(OAc)_2$ (5)	$PhCH_3$	*p*-TsOH (0.5)	Trace
11	$PdCl_2$ (5)	DCE	*p*-TsOH (0.5)	38
12	$Cu(OAc)_2$ (5)	DCE	*p*-TsOH (0.5)	19
13	AgOAc (5)	DCE	*p*-TsOH (0.5)	Trace
14	$Pd(OAc)_2$ (5)	DCE	$Na_2S_2O_8$ (2), *p*-TsOH (0.5)	10
15	$Pd(OAc)_2$ (5)	DCE	$K_2S_2O_8$ (2), *p*-TsOH (0.5)	Trace
16	$Pd(OAc)_2$ (5)	DCE	$Cu(OAc)_2$ (1) *p*-TsOH (0.5)	31
17	$Pd(OAc)_2$ (2.5)	DCE	*p*-TsOH (0.5)	23
18	$Pd(OAc)_2$ (10)	DCE	*p*-TsOH (0.5)	76
19	$Pd(OAc)_2$ (15)	DCE	*p*-TsOH (0.5)	76
20[c]	$Pd(OAc)_2$ (10)	DCE	*p*-TsOH (0.5)	76

[a]2-phenylquinazolin-4(3*H*)-one (0.5 mmol), NBS (0.6 mol), catalyst (X mol %), additive (X mmol), solvent (3 mL) Temp. = 100 °C, Time = 4 h; [b] Isolated yield; [c]Temp. = 120 °C

Table 2. Ortho halogenation of quinazolinones[a]



Entry	Quinazolinone	NXS	Product	Yield[b]
1		NBS		76%
2	1a	NCS		63%
3	1a	NIS		79%
4		NBS		83%
5	1b	NIS		76%
6		NBS		75%
7		NBS		51%
8		NBS		64%
9	1e	NCS		50%
10	1e	NIS		55%

[a] quinazolinone (1 mmol), NXS (1.2 mol), $Pd(OAc)_2$ (10 mol %), *p*-TsOH (0.5 mmol), DCE (3 mL) Temp. = 100 °C, and Time = 4 h; [b] Isolated yield.

The structure of the product **2d** was confirmed unambiguously by single crystal X-ray analysis (Figure 2).

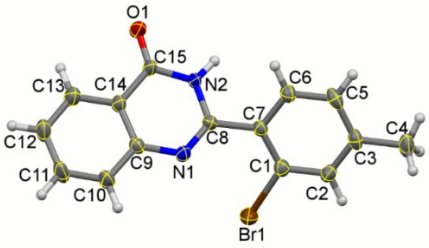
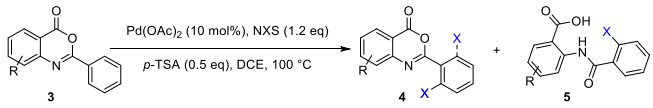
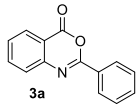
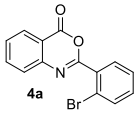
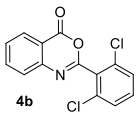
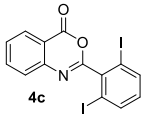
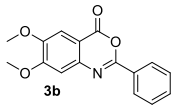
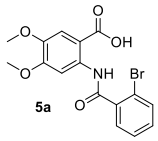
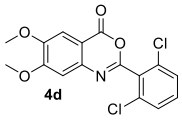
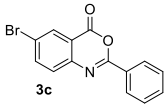
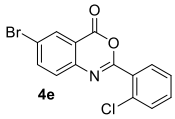
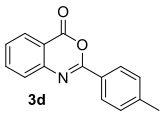
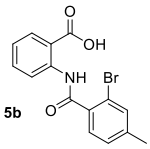
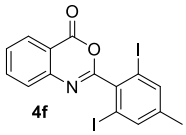
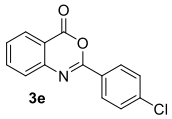
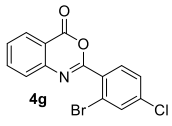
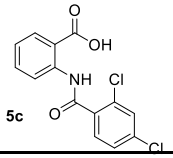


Figure 2. X-ray crystal structure of **2d.**

To further explore the potential of this protocol for the halogenation, the benzoxazinones (**3**) were selected as an activated C-H compound in the halogenation (Table 3). The desired halogenated benzoxazinones were obtained in moderate yields. Interestingly, in chlorination and iodination of benzoxazinones, the dihalogenated product was the major product (Table 3, entries 2, 3, 5, and 9). The increasing amount NCS and NIS to 3 eq. increased the yield of dihalogenated products. Additionally, the hydrolysis of the halogenated benzoxazinones (**5a-c**) were observed, which could be a reflection on the instability of benzoxazinones in acidic medium (Table 3, entries 4, 7, and 10).[15] We studied the reaction conditions by the varying of the solvent, temperature and time to increase the product 4 stability (Table S1). Unfortunately, these efforts don't effect in elimination this by-product (**5**). Also, the reaction was chemoselective in the case of Me-substituted benzoxazinone (**3d**) (Table 3, entries 7 and 8).

Table 3. Ortho halogenation of benzoxazinones[a]



Entry	benzoxazinone	NXS	Product	Yield[b]
1		NBS		61%
2	3a	NCS		45%, 87%[c]
3	3a	NIS		49%, 88%[c]
4		NBS		41%
5	3b	NCS		43%, 81%[c]
6		NCS		54%
7		NBS		46%
8	3d	NIS		68
9		NBS		72
10	3e	NCS		45

[a] benzoxazinone(1 mmol), NXS (1.2 mol), $Pd(OAc)_2$ (10 mol %), *p*-TsOH (0.5 mmol), DCE (3 mL) Temp. = 100 °C, and Time = 4 h; [b] Isolated yield; [c] NXS (3 mol)

Finally, the structure of the product **4d** was confirmed unambiguously by single crystal X-ray analysis (Figure 3).

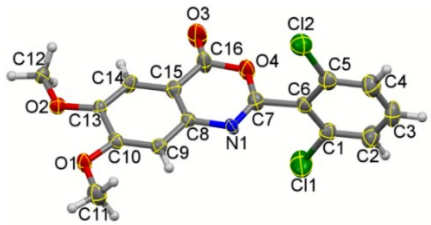
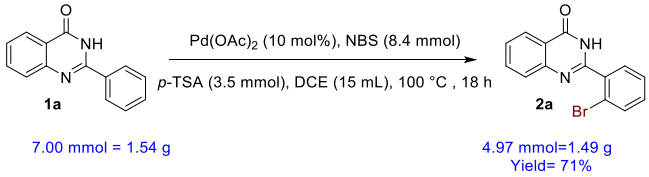


Figure 3. X-ray crystal structure of **4d**.

To demonstrate the efficiency and practicality of this catalytic process, a 7 mmol scale bromination reaction was conducted using **1a** as a substrate, and the reaction proceeded smoothly to afford the halogenated product **2a** in 71% isolated yield (Scheme 1).



Scheme 1. Examining scalability of the bromination of 2-phenylquinazolin-4(3*H*)-one

A plausible mechanism for the transformation, based on previous literature,[5g,5d] is described in (Figure 4). Initially, a five-membered cyclopalladium (II) intermediate **I** is generated with the assistance of the nitrogen by chelation directed C–H activation, which is generally considered to be a better coordinating atom than oxygen. *p*-TsOH as an acidic additive might be included in the *in situ* generation of an electron-deficient Pd complex, Pd(*p*-TsO)$_2$, which can promote more challenging C–H activation through weak coordination.[5g] Oxidative addition of NXS to the cyclopalladium leads to the formation of Pd(IV) complex **II**. The final step involved carbon–halogrn bond-forming reductive elimination to give the halogenated product and regenerate active Pd(II) species to continue the catalytic cycle. Alternatively, the reaction may also proceed via a bimetallic Pd(III)–Pd(III) intermediate pathway for carbon-halogen bond-forming reactions as identified by Ritter *et al.*[16]

View Article Online
DOI: 10.1039/C7OB01574H

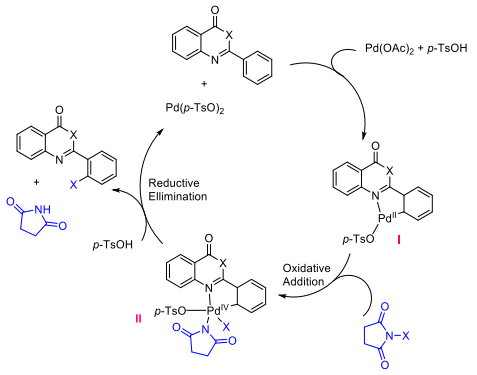


Figure 4. Plausible mechanism for *ortho*-halogenation of benzoxazinone and quinazolinone scaffolds

Experimental

Experimental section

General

All starting materials were obtained from Merck Millipore or Sigma-Aldrich, and were used without further purification. Melting points were measured on an Elecrtothermal 9100 apparatus and are uncorrected. Mass spectra were recorded on an Agilent Technology (HP) 5973 NetworkMass Selective Detector operating at an ionization potential of 70 eV. IR spectra were recorded on a Bomem MB-Series FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKERDRX-300AVANCEspectrometer at 300 and 75 MHz and 500AVANCEspectrometer at 500 and 126 MHz, respectively. ^{1}H and ^{13}CNMR spectra were obtained in DMSO-d_6 using TMS as internal standard. Elemental analyses were performed using a Heraeus CHN-O Rapid analyzer.

General procedure for the halogenation of quinazolinones and benzoxazinones

To a 10 mL single-neck round-bottom flask equipped with a magnetic stir bar were added the quinazolinones or benzoxazinones (1 mmol), NXS (1.2 mmol), p-TsOH.H_2O (0.5 mmol) and $Pd(OAc)_2$ (0.1 mmol,) in turn. Subsequently, the solvent (DCE, 3 mL) was added. The reaction mixture was stirred at 100 °C, and the completion of the reaction was monitored using TLC. After the reaction had been completed, the solvent was evaporated under vacuum. The residue diluted with ethyl acetate (2 × 10 mL) and the organic layer was further washed with brine solution. The organic layers were dried over Na_2SO_4, filtered, and concentrated. Finally, the halogenated product was purified by thin layer chromatography to afford the desired pure coupling product.

Procedure for Gram-Scale Reaction

2-Phenylquinazolin-4(3*H*)-one (7 mmol, 1.54 g), NBS (8.4 mmol, 1.49 g), *p*-TsOH.H_2O (3.5 mmol, 0.67 g), and $Pd(OAc)_2$ (0.7 mmol, 0.16 g) were added to a balloon equipped with a magnetic stirring bar followed by the addition of DCE (15 mL). The reaction mixture was stirred at 100 °C and the completion of the reaction was monitored using TLC (n-hexane). After the reaction was completed, the solvent was evaporated by vacuum. The residue diluted with ethyl acetate (2 × 20 mL) and the organic layer was further washed with brine solution. Afterward, the organic layer was separated and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure using a rotary evaporator. Purification was accomplished using column chromatography using silica gel as the stationary phase (n-hexane).

Conclusions

In summary, a practical, Pd(II) catalyzed *ortho*-selective direct halogenation has been developed for the synthesis of the *ortho*-halogenated benzoxazinone and quinazolinone scaffolds by *N*-halosuccinimide as an oxidant and halogen source. The different NXS can be employed as useful halogenating reagents in this transformation. Additionally, this transformation can also be scaled up to gram level.

Acknowledgements

We gratefully acknowledge financial support from the Research Council of Shahid Beheshti University and financial support provided by the Iran National Science Foundation (INSF).

References

1 a) T. W. Lyons and M. S. Sanford, *Chem. Rev.*, 2010, **110**, 1147-1169; b) X. Chen, K. M. Engle, D.-H. Wang and J.-Q. Yu, *Angew. Chem., Int. Ed.,* 2009, **48**, 5094-5115; c) V. B. Purohit, S. C. Karad, K. H. Patel and D. K. Raval, *Catal. Sci. Technol.,* 2015, **5**, 3113-3118; d) K. M. Engle, T.-S. Mei, M. Wasa and J.-Q. Yu, *Acc. Chem. Res.,* 2011, **45**, 788-802.

2 a) J. Jiao, K. Murakami and K. Itami, *ACS Catal.,* 2016, **6**, 610–633; b) J. Pan, M. Su and S. L. Buchwald, *Angew. Chem. Int. Ed.,* 2011, **50**, 8647–8651; c) D. Zhu, G. Yang, J. He, L. Chu, G. Chen, W. Gong, K. Chen, M. D. Eastgate and J.-Q. Yu, *Angew. Chem. Int. Ed.,* 2015, **54**, 2497-2500; d) J. A. Jordan-Hore, C. C. C. Johansson, M. Gulias, E. M. Beck and M. J. Gaunt, *J. Am. Chem. Soc.,* 2008, **130**, 16184–16186

3 a) J. K. Laha, R. A. Bhimpuria, D. V. Prajapati, N. Dayal and S. Sharma, *Chem. Commun.,* 2016, **52**, 4329-4332; b) D. Wang, W. Liu, F. Yi, Y. Zhao and J. Chen, *Org. Biomol. Chem.,* 2016, **14**, 1921-1924; c) M. Murai, M. Yanagawa, M. Nakamura and K. Takai, *Asian J. Org. Chem.,* 2016, **5**, 629-635; d) Y. Xu, M. C. Young, C. Wang, D. M. Magness and G. Dong, *Angew. Chem. Int. Ed.*, 2016, **55**, 9084-9087.

4 a) A. Mishra, T. Kumari Vats and I. Deb, *J. Org. Chem.,* 2016, **81**, 6525–6534; b) J. Peng, J. Zhao, Z. Hu, D. Liang, J. Huang and Q. Zhu, *Org. Lett.,* 2012, **14**, 4966–4969.

5 a) S. K. Santra, A. Banerjee, N. Khatun, A. Samanta and B. K. Patel, *RSC Adv.,* 2015, **5**, 11960–11965; b) P. Sadhu, S. K. Alla and T. Punniyamurthy, *J. Org. Chem.,* 2013, **78**, 6104−6111; c) X. Sun, X. Yao, C. Zhang and Y. Rao, *Chem. Commun.,* 2015, **51**, 10014-10017; d) M. Sun, X. Chen, L. Zhang, W. Sun, Z. Wang, P. Guo, Y.-M. Li and X.-J. Yang, *Org. Biomol. Chem.*, 2016, **14**, 323–329; e) A. John and K. M. Nicholas, *J. Org. Chem.*, 2012, **77**, 5600−5605; f) F. M. Moghaddam, G. Tavakoli, B. Saeednia, P. Langer and B. Jafari, *J. Org. Chem.,* 2016, **81**, 3868−3876; g) X. Sun, Y. Sun, C. Zhang and Y. Rao, *Chem. Commun.,* 2014, **50**, 1262-1264; h) S. L. Whitfield and M. S. Sanford, *J. Am. Chem. Soc.*, 2007, **129**, 15142-15143; i) E. Dubost, C. Fossey, T. Cailly,

View Article Online
DOI: 10.1039/C7OB01534H

S. Rault and F. Fabis, *J. Org. Chem.*, 2011, **76**, 6414-6420; j) B. Du, X. Jiang and P. Sun, *J. Org. Chem.,* 2013, **78**, 2786-2791.

6 a) A. Irastorza, J. M. Aizpurua and A. Correa, *Org. Lett.*, 2016, **18**, 1080–1083; b) S. K. Guchhait, V. Chaudhary, V. A. Rana, G. Priyadarshani, S. Kandekar and M. Kashyap, *Org. Lett.*, 2016, **18**, 1534–1537; c) D. Kalyani and M. S. Sanford, *Org. Lett.,* 2005, **7**, 4149–4152.

7 a) W.-H. Rao, B.-B. Zhan, K. Chen, P.-X. Ling, Z.-Z. Zhang and B.-F. Shi, *Org. Lett.,* 2015, **17**, 3552–3555; b) Y. Xu, P. Liu, S.-L. Li and P. Sun, *J. Org. Chem.,* 2015, **80**, 1269–1274.

8 R. H. Levin,. in *Reactive Intermediates*; (Eds Jones, M. and Moss, R. A.) Wiley-Interscience, New York, 1985 Vol. 3, pp 1–18.

9 *Organic Reaction Mechanism*, (Eds M. R. Crampton, A. J. Knipe) Wiley, New York, 2007.

10 a) N. Sotomayor and E. Lete, *Curr. Org. Chem.,* 2003, **7**, 275-300; b) *Handbook of Grignard Reagents*, (Eds. G. S. Silverman, P. E. Rakita) Dekker, New York, 1996

11 a) *Metal Catalyzed Cross Coupling Reactions*, (Eds. F. Diederich and P. J. Stang) Wiley-VCH, Weinheim, 1998; b) A. deMeijere, F. Diederich in *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2004.

12 a) B. Song, X. Zheng, J. Mo and B. Xu, *Adv. Synth. Catal.,* 2010, **352**, 329–335; b) X. Wan, Z. Ma, B. Li, K. Zhang, S. Cao, S. Zhang and Z. Shi, *J. Am. Chem. Soc*., 2006, **128**, 7416-7417; c) Q. Zhang, F. Yang and Y. Wu, *Org. Chem. Front.,* 2014, **1**, 694–697.

13 a) P. K. Gupta, N. Yadav, S. Jaiswal, M. Asad, R. Kant and K. Hajela, *Chem. Eur. J.,* 2015, **21**, 13210–13215; b) B. Majhi, D. Kundu, T. Ghosh and B. C. Ranua, *Adv. Synth. Catal.,* 2016, **358**, 283–295.

14 L. G. Voskressensky, N. E. Golantsov and A. M. Maharramov, *Synthesis,* 2016, **48**, 615-643.

15 a) T. Cohen and J. Lipowitz, *J. Am. Chem. Soc.,* 1964, **86**, 5611–5616; b) M. C. Etter, Z. U. Lipkowska, C. Decoret, J. Royer, F. Bayard and J. Vicens, *Mol. Cryst. Liq. Cryst. Inc.,* 1988, **161**, 43-53.

16 a) D. C. Powers, M. A. L. Geibel, J. E. M. N. Klein and T. Ritter, *J. Am. Chem. Soc*., 2009, **131**, 17050-17051; b) D. C. Powers and T. Ritter, *Nat. Chem.,* 2009, **1**, 302-309; c) D. C. Powers and T. Ritter, *Acc. Chem. Res.,* 2012, **45**, 840-850.