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Copper-catalyzed one-pot reactions of acetyl chloride, *o*-halobenzoic acids and Wittig reagents toward 3-methyl isocoumarin synthesis†

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The one-pot reactions of acetyl chloride, *o*-halobenzoic acids and Wittig reagents providing 3-methyl isocoumarins have been furnished *via* tandem Wittig reaction, oxa-Michael addition and C–C cross coupling. Three new chemical bonds including one C–O, one C=C and one C–C bond are generated *via* the catalysis of a simple copper salt for the heterocycle construction.

Introduction

The copper-catalyzed Ullmann-type C–C cross coupling reaction between aryl/vinyl halides and active carbon coupling partners is an important tool in the generation of new carbon–carbon bonds.[1] While significant contribution of such transformation has been furnished in the synthesis of divergent organic products *via* both direct coupling process or tandem reactions initiated by this coupling transformation, one of the major restrictions in the Ullmann C–C cross coupling reaction is that the scope of the carbon coupling partners is rather narrow. In most of the related known literature, active methylenes such as 1,3-dicarbonyl or analogous compounds are predominantly used as the reaction partners of aryl/vinyl halides,[2] and alternative reactants in such reactions are rarely known.[3] Accordingly, the limited substrate scope has also hampered the application of this C–C cross coupling in the synthesis of more structurally diversified organic products. Therefore, in order to promote the application of the Ullmann C–C coupling as broad as those equivalent C-heteroatom coupling versions, discovering practical reaction partners constitutes the main present challenge. Our group has previously reported the copper-catalyzed C–C coupling initiated tandem reactions toward the synthesis of benzofurans[4] and indoles[5] wherein the *in situ* generated allenes are utilized as the carbon coupling partners of the Ar–halogen bond to enable the product construction. In despite of these successful examples, it should be noted that examples on the C–C coupling reactions employing allenes as coupling partners are still rather scarce.

Isocoumarins are a class of typical heterocycles with broad spectrum biological activity, and this backbone also constitutes the central fragment of many natural products.[6] Based on known literature, isocoumarins can be synthesized with different strategies,[7] such as the tandem annulations initiated by Ar–H bond addition to alkynes,[8] diazo functionalized ketones[9] or cyclic alkenyl carbonates,[10] the intramolecular cross coupling of Ar–halogen and vinyl C–H bond,[11] the addition of Ar–halogen bond to alkynes,[12] ring expansion reactions,[13] the oxidative coupling of benzoic acids and vinylarene,[14] among others.[15] Regardless the enriched availability on synthetic methods, it is notable that most of the reported methods on isocoumarin synthesis require the presence of noble metal reagent such as Pd, Ru, Rh, Ag or Au as catalyst with few exception. To our knowledge, a synthetic route *via* tandem reaction initiated by copper-catalyzed allene-based Ullmann-type C–C coupling has not yet been known. Considering the power of multicomponent reactions[16] as well as related cascade reactions[17] in providing efficient organic synthesis, and in continuous to our research efforts in developing copper-catalyzed cross coupling and their application in designing tandem reactions,[18] we report herein a new tandem assembly consists of the *in situ* allene generation, the oxa-Michael addition and intramolecular C–C coupling for the synthesis of 3-methyl isocoumarins. The *in situ* generation and utilization of the unstable allene substrates as well as the low cost copper-catalyst of the present work feature as advantageous over similar known work employing noble metal Ag catalyst and two-step synthesis.[11]

Results and discussion

The investigation started from the reaction of Wittig reagent **1a**, acetyl chloride **2a** and *o*-iodobenzoic acid **3a** in the presence of CuI and Cs_2CO_3. By heating at 100 °C in DMSO, the target product **4a** was acquired with 27% yield (entry 1, Table 1). Subsequently, entries employing different copper catalysts such as CuBr, CuO and $Cu(OAc)_2$ were examined, and $Cu(OAc)_2$ displayed much better catalytic efficiency than other candidates

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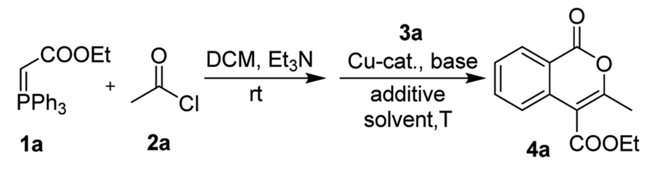
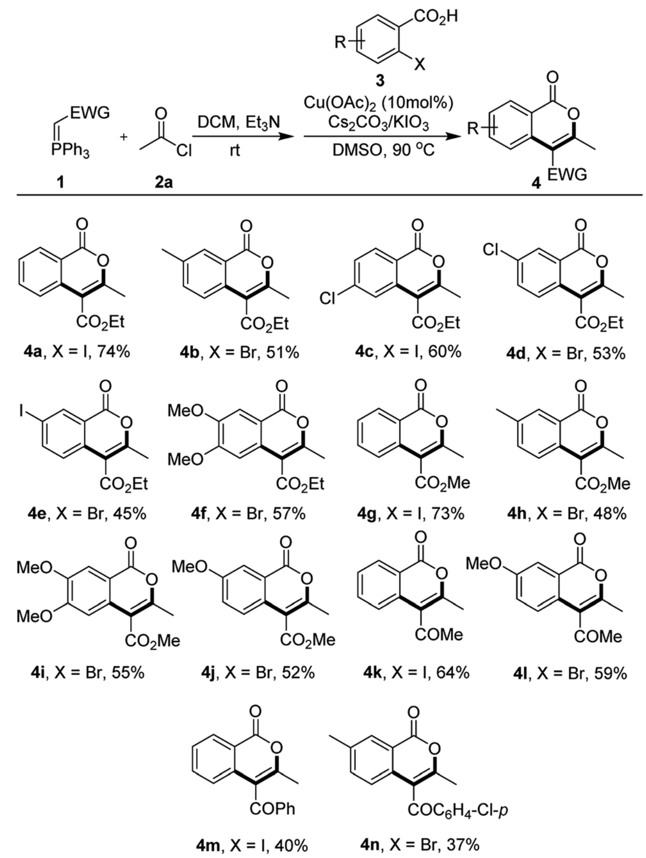
Table 1 Optimization on reaction conditions[a]



Entry	Catalyst	Base	Additive	Solvent	Yield[b] (%)
1	CuI	Cs_2CO_3	—	DMSO	27
2	CuBr	Cs_2CO_3	—	DMSO	28
3	CuO	Cs_2CO_3	—	DMSO	21
4	$Cu(OAc)_2$	Cs_2CO_3	—	DMSO	45
5	$Cu(OAc)_2$	K_2CO_3	—	DMSO	27
6	$Cu(OAc)_2$	K_3PO_4		DMSO	Trace
7	$Cu(OAc)_2$	$NaHCO_3$	—	DMSO	Trace
8	$Cu(OAc)_2$	EtONa	—	DMSO	Trace
9	$Cu(OAc)_2$	Et_3N	—	DMSO	Trace
10	$Cu(OAc)_2$	Cs_2CO_3	—	DMF	26
11	$Cu(OAc)_2$	Cs_2CO_3	—	1,4-Dioxane	39
12	$Cu(OAc)_2$	Cs_2CO_3	—	*p*-Xylene	NR
13	$Cu(OAc)_2$	Cs_2CO_3	—	H_2O	NR
14	$Cu(OAc)_2$	Cs_2CO_3	KBr	DMSO	49
15	$Cu(OAc)_2$	Cs_2CO_3	KI	DMSO	52
16	$Cu(OAc)_2$	Cs_2CO_3	KIO_3	DMSO	56
17	$Cu(OAc)_2$	Cs_2CO_3	MnO_2	DMSO	54
18[c]	$Cu(OAc)_2$	Cs_2CO_3	KIO_3	DMSO	74
19[d]	$Cu(OAc)_2$	Cs_2CO_3	KIO_3	DMSO	53

[a] The reactions were generally carried out with stepwise one-pot operation (see Experimental sections for details) **1a** (0.6 mmol), **2a** (0.9 mmol), **3a** (*o*-iodobenzoic acid, 0.3 mmol), catalyst (0.03 mmol), base (0.75 mmol), additive (0.6 mmol, if applicable) and *n*-hexane (3 mL) in solvent (2 mL), stirred at 100 °C for 12 h (TLC); commercial $Cu(OAc)_2 \cdot H_2O$ was used in all entries. [b] Yield of isolated product based on **1a**. [c] The temperature was 90 °C. [d] The temperature was 110 °C.

Table 2 Scope in the three-component isocoumarin synthesis[a,b]

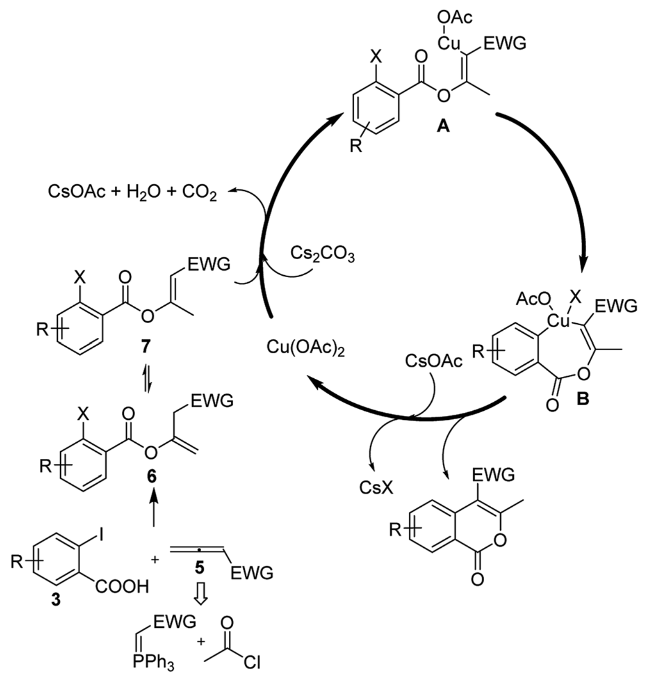


[a] The reactions were generally carried out with one-pot stepwise operation (see Experimental sections for details): **1** (0.6 mmol), **2a** (0.9 mmol), **3** (0.3 mmol), $Cu(OAc)_2$ (0.03 mmol), Cs_2CO_3 (0.75 mmol), KIO_3 (0.6 mmol) and *n*-hexane (3 mL)/DMSO (2 mL), stirred at 90 °C for 12 h. [b] Yield of isolated product.

(entries 2–4, Table 1). The reactions conducted in the presence of different base additives, including K_2CO_3, K_3PO_4, $NaHCO_3$, EtONa and Et_3N, however, was not able to give better result (entries 5–9, Table 1). The employment of reaction medium of different polarity such as DMF, toluene and water *etc.* failed to improve the expect product generation, either (entries 10–13, Table 1). However, attempt in employing oxidative potassium iodate was found to be useful in enhancing the yield of **4a** (entries 14–17, Table 2). Finally, the variation on the reaction temperature proved that 90 °C was proper for the reaction (entries 18–19, Table 1).

In subsequent work, the scope of this three-component tandem reaction on the synthesis of isocoumarins **4** was explored. As showing in Table 2, both *o*-iodo- and *o*-bromobenzoic acids could be used as building blocks in this kind of synthesis. The general tendency was that iodinated benzoic acids provided corresponding products with higher yield than those equivalent entries employing *o*-bromobenzoic acids, suggesting that the reactivity of the Ar–X bond evidently influenced the efficiency of the target product synthesis (comparing **4a**, **4c**, **4g** with **4b**, **4d**, **4e**, **4f**, **4h**, **4i** and **4j** in Table 2). On the other hand, the entries employing aryl ketone-based Wittig reagents gave much lower yield of corresponding isocoumarins than those ones constructed by alkyl ketone-based Wittig reagents (comparing **4k**, **4l** with **4m**, **4n** in Table 2), which indicated that the electron withdrawing effect resulting from the aryl ring was negative to expect reaction by reducing the nucleophilicity of the α-carbon in the *in situ* generated allene intermediate. In addition, the attempts in employing other linear acyl chlorides such as propionyl chloride and butyryl chloride for the reaction failed to give the expected isocoumarins. The consequence might be attributed to the additional steric effect resulting from the alkyl substitution with corresponding allene intermediate **5** which hampled the addition of the carboxylic acid ion of weak nucleophilicity.

To illustrate the possible process forming the isocoumarin products *via* the copper-catalyzed C–C coupling, a plausible mechanism for the present tandem reactions is proposed in Scheme 1. The reaction is supposed to start from the oxa-Michael addition of the carboxylic acid to the *in situ* generated allene intermediate **5** which provides vinyl ether **6.** The tautomerization of **6** leads to the occurrence of the intermediate



Scheme 1 The plausible reaction mechanism.

7. Under the promotion of the Cs_2CO_3, the nucleophilic carbon site in intermediate **7** attacks $Cu(OAc)_2$ *via* a formal nucleophilic substitution to afford Cu(II) complex **A**. Subsequently, the oxidative addition of the copper site to the Ar–X bond takes place and generates the seven-membered Cu(IV) complex **B**. Finally, the reductive elimination on **B** allowed the production of target product **4** and the regeneration of the Cu(II) catalyst. The role of KIO_3 in the reaction is not yet clear, a possibility is that the KIO_3 can oxidise the halid (X^-) produced during the product formation and promote the reaction to run toward the positive direction.

Conclusions

In summary, we have established a tandem reaction tactic wherein the Wittig reaction, oxa-Michael addition and a copper-catalyzed Ullmann-type C–C coupling have been involved for the facile synthesis of 3-methyl isocoumarins. This synthetic method starts from simple materials and require no noble metal catalyst, which can be a useful complementary approach in the synthesis of valuable isocoumarin scaffolds.

Experimental section

General procedure for the synthesis of isocoumarins 4

In a 25 mL round-bottom flask was charged with phosphorus ylide **1** (0.6 mmol), CH_2Cl_2 (1 mL), and Et_3N (0.66 mmol). A solution of acetyl chloride **2a** (0.9 mmol) in CH_2Cl_2 (1 mL) was added dropwise with stirring. After an additional 4 h stirring, the CH_2Cl_2 was completely evaporated under reduced pressure. *n*-Hexane (3 mL), *o*-halobenzoic acid **3** (0.3 mmol), $Cu(OAc)_2$ (0.03 mmol), Cs_2CO_3 (0.75 mmol), KIO_3 (0.6 mmol) and DMSO (2 mL) were then consequently added. The resulting mixture was heated at 90 °C for 12 h (TLC). The reaction mixture was allowed to cool to rt, and H_2O (10 mL) was added. The resulting suspension was extracted with ethyl acetate (3 × 10 mL). The organic phases were combined and dried over Na_2SO_4. After filtration and removing the solvent at reduced pressure, the residue was subjected to silica gel column chromatography to give the pure product by using mixed petroleum ether/ethyl acetate (v/v = 20 : 1) as the eluent.

Ethyl 3-methyl-1-oxo-1*H*-isochromene-4-carboxylate (4a).[11] Yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.0 Hz, 1H), 7.78–7.72 (m, 2H), 7.52 (t, J = 7.2 Hz, 1H), 4.49–4.43 (m, 2H), 2.46 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 165.8, 161.2, 157.7, 135.1, 134.6, 129.7, 128.2, 124.1, 119.5, 110.3, 61.7, 19.3, 14.3.

Ethyl 3,7-dimethyl-1-oxo-1*H*-isochromene-4-carboxylate (4b). White soild; mp 76–78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 4.48–4.42 (m, 2H), 2.45 (s, 6H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 165.9, 161.4, 156.9, 138.4, 136.3, 132.1, 129.3, 124.1, 119.4, 110.1, 61.6, 21.2, 19.2, 14.3; ESI-HRMS calcd for $C_{14}H_{15}O_4$ $[M + H]^+$ 247.0965, found 247.0966.

Ethyl 7-chloro-3-methyl-1-oxo-1*H*-isochromene-4-carboxylate (4d).[11] White soild; mp 97–99 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 2.0 Hz, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.67 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 4.48–4.42 (m, 2H), 2.48 (s, 3H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 165.4, 160.1, 158.5, 135.4, 134.1, 133.1, 129.0, 126.0, 120.9, 109.6, 61.9, 19.5, 14.2.

Methyl 3-methyl-1-oxo-1*H*-isochromene-4-carboxylate (4g). Colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, J = 7.6 Hz, 1H), 7.75–7.73 (m, 2H), 7.53–7.49 (m, 1H), 3.98 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.2, 161.1, 135.1, 134.5, 129.6, 128.2, 124.2, 119.4, 110.0, 52.4, 19.4; ESI-HRMS calcd for $C_{12}H_{11}O_4$ $[M + H]^+$ 219.0652, found 219.0655.

Methyl 6,7-dimethoxy-3-methyl-1-oxo-1*H*-isochromene-4-carboxylate (4i). White solid; mp 154–156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (s, 1H), 7.33 (s, 1H), 3.99 (s, 3H), 3.98 (s, 3H), 3.97 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.53, 166.52, 158.0, 155.3, 149.6, 130.3, 112.7, 109.5, 109.2, 105.5, 56.3, 56.2, 52.3, 19.8; ESI-HRMS calcd for $C_{14}H_{15}O_6$ $[M + H]^+$ 279.0863, found 279.0862.

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Notes and references

1 For selected reviews, see: (*a*) F. Monnier and M. Taillefer, *Angew. Chem., Int. Ed.*, 2008, **47**, 3096; (*b*) F. Monnier and M. Taillefer, *Angew. Chem., Int. Ed.*, 2009, **48**, 6954; (*c*) J. Hassan, M. Sévignon, C. Gozzi, E. Schulz and M. Lemaire, *Chem. Rev.*, 2002, **102**, 1359; (*d*) C. Sambiagio, S. P. Marsden, A. J. Blacker and P. C. McGowan, *Chem. Soc. Rev.*, 2014, **43**, 3525; (*e*) Y. Liu and J.-P. Wan, *Chem.–Asian*

J., 2012, **7**, 1488; (*f*) Y. Liu and J.-P. Wan, *Org. Biomol. Chem.*, 2011, **9**, 6873.

2 (*a*) C. He, G. Zhang, J. Ke, H. Zhang, J. T. Miller, A. J. Kropf and A. Lei, *J. Am. Chem. Soc.*, 2013, **135**, 488; (*b*) E. J. Hennessy and S. L. Buchwald, *Org. Lett.*, 2002, **4**, 269; (*c*) H.-J. Cristau, P. P. Cellier, J.-F. Spindler and M. Taillefer, *Chem.–Eur. J.*, 2004, **10**, 5607; (*d*) Q. Niu, H. Mao, G. Yuan, J. Gao, H. Liu, Y. Tu, X. Wang and X. Lv, *Adv. Synth. Catal.*, 2013, **355**, 1185; (*e*) S. F. Yip, H. Y. Cheung, Z. Zhou and F. Y. Kwong, *Org. Lett.*, 2007, **9**, 3469; (*f*) D. Yang, H. Yang and H. Fu, *Chem. Commun.*, 2011, **47**, 2348; (*g*) Y. Fang and C. Li, *J. Org. Chem.*, 2006, **71**, 6427; (*h*) B. Lu and D. Ma, *Org. Lett.*, 2006, **8**, 6115; (*i*) J. Lu, X. Gong, H. Yang and H. Fu, *Chem. Commun.*, 2010, **46**, 4172; (*j*) C. C. Malakar, D. Schmidt, J. Conrad and U. Beifuss, *Org. Lett.*, 2011, **13**, 1972; (*k*) M. Jiang, J. Li, F. Wang, Y. Zhao, F. Zhao, X. Dong and W. Zhao, *Org. Lett.*, 2012, **14**, 1420; (*l*) Z. Lou, S. Zhang, C. Chen, X. Pan, M. Li and L. Wen, *Adv. Synth. Catal.*, 2014, **356**, 153.

3 (*a*) B. Li, S. Guo, J. Zhang, X. Zhang and X. Fan, *J. Org. Chem.*, 2015, **80**, 5444; (*b*) X. Wang, J. Liu, H. Guo, C. Ma, X. Gao, K. Zhou and G. Huang, *Synthesis*, 2012, **44**, 1037; (*c*) Q. Cai, J. Yan and K. Ding, *Org. Lett.*, 2012, **41**, 3332.

4 (*a*) Y. Liu, H. Wang and J.-P. Wan, *J. Org. Chem.*, 2014, **79**, 10599; (*b*) J.-P. Wan, H. Wang, Y. Liu and H. Ding, *Org. Lett.*, 2014, **16**, 5160.

5 B. Huang, D. Hu, J. Wang, J.-P. Wan and Y. Liu, *Tetrahedron Lett.*, 2015, **56**, 2551.

6 (*a*) S. Pal, V. Chatare and M. Pal, *Curr. Org. Chem.*, 2011, **15**, 782; (*b*) G. Qadeer, N. H. Rama and S. J. H. Shah, *Arkivoc*, 2007, **XIV**, 12; (*c*) A. Saeed, *Eur. J. Med. Chem.*, 2016, **116**, 290; (*d*) K. Tianpanich, S. Prachya, S. Wiyakrutta, C. Mahidol, S. Ruchirawat and P. Kittakoop, *J. Nat. Prod.*, 2011, **74**, 79; (*e*) K. Nozawa, M. Yamada, Y. Tsuda, K. Kawai and S. Nakajima, *Chem. Pharm. Bull.*, 1981, **29**, 2689; (*f*) J. M. Dickinson, *Nat. Prod. Rep.*, 1993, **10**, 71; (*g*) J. E. Kerrigan, J. Oleksyszyn, C.-M. Kam, J. Selzler and J. C. Powers, *J. Med. Chem.*, 1995, **38**, 544.

7 For reviews, see: (*a*) Z. Ashraf, *Chem. Heterocycl. Compd.*, 2016, **52**, 149; (*b*) A. Saeed, M. Haroon, F. Muhammad, F. A. Larik, E.-S. Hesham and P. A. Channar, *J. Organomet. Chem.*, 2017, **834**, 88.

8 (*a*) J. Mo, L. Wang and X. Cui, *Org. Lett.*, 2015, **17**, 4960; (*b*) X. G. Li, K. Liu, G. Zou and P. N. Liu, *Adv. Synth. Catal.*, 2014, **356**, 1496; (*c*) L. Song, J. Xiao, W. Dong, Z. Peng and D. An, *Eur. J. Org. Chem.*, 2017, 341; (*d*) P. B. Dalvi, K.-L. Lin, M. V. Kulkarni and C.-M. Sun, *Org. Lett.*, 2016, **18**, 3706; (*e*) K. S. Singh, S. G. Sawant and P. H. Dixneuf, *ChemCatChem*, 2016, **8**, 1046; (*f*) Y. Unoh, K. Hirano, T. Satoh and M. Miura, *Tetrahedron*, 2013, **69**, 4454; (*g*) L. Ackermann, J. Pospech, K. Graczyk and K. Rauch, *Org. Lett.*, 2012, **14**, 930; (*h*) R. K. Chinnagolla and M. Jeganmohan, *Chem. Commun.*, 2012, **48**, 2030.

9 (*a*) X. G. Li, M. Sun, K. Liu, Q. Jin and P. N. Liu, *Chem. Commun.*, 2015, **51**, 2380; (*b*) C. Yang, X. He, L. Zhang, G. Han, Y. Zuo and Y. Shang, *J. Org. Chem.*, 2017, **82**, 2081.

10 Y. Hara, S. Onodera, T. Kochi and F. Kakiuchi, *Org. Lett.*, 2015, **17**, 4850.

11 N. Panda, P. Mishra and I. Mattan, *J. Org. Chem.*, 2016, **81**, 1047.

12 (*a*) H. Liu, Y. Yang, J. Wu, X.-N. Wang and J. Chang, *Chem. Commun.*, 2016, **52**, 6801; (*b*) X. Guo, *J. Org. Chem.*, 2013, **78**, 1660; (*c*) R. C. Larock, M. J. Doty and X. Han, *J. Org. Chem.*, 1999, **64**, 8770; (*d*) M. A. Waseem, Shireen, A. A. Abumahdi, A. Srivastava, A. Srivastava, Rahila and I. R. Siddiqui, *Catal. Commun.*, 2014, **55**, 70; (*e*) M. R. Kumar, F. M. Irudayanathan, J. H. Moon and S. Lee, *Adv. Synth. Catal.*, 2013, **355**, 3221.

13 (*a*) F.-J. Zhang, M.-Y. Sun, Y.-J. Dang, X.-Y. Meng, B. Jiang, W.-J. Hao and S.-J. Tu, *Tetrahedron*, 2014, **70**, 9628; (*b*) S. Pathak, D. Das, A. Kundu, S. Maity, N. Guchhait and A. Pramanik, *RSC Adv.*, 2015, **5**, 17308; (*c*) P. M. Shpuntov, V. A. Shcherbinin, V. T. Abaev and A. V. Butin, *Tetrahedron Lett.*, 2016, **57**, 1483; (*d*) P. P. Kaishap, B. Sarma and S. Gogoi, *Chem. Commun.*, 2016, **52**, 9809; (*e*) R. Prakash, K. Shekarrao, S. Gogoi and R. C. Boruah, *Chem. Commun.*, 2015, **51**, 9972.

14 D. Nandi, D. Ghosh, S.-J. Chen, B.-C. Kuo, N. M. Wang and H. M. Lee, *J. Org. Chem.*, 2013, **78**, 3445.

15 (*a*) Y. He, X. Zhang, N. Shen and X. Fan, *J. Org. Chem.*, 2013, **78**, 10178; (*b*) Q. Yuan, Z.-B. Chen, F.-L. Zhang and Y.-M. Zhu, *Org. Biomol. Chem.*, 2017, **15**, 1628; (*c*) K. Sudarshan, M. K. Manna and I. S. Aidhen, *Eur. J. Org. Chem.*, 2015, 1797; (*d*) N. A. Mallampudi, G. S. Reddy, S. Maity and D. K. Mohapatra, *Org. Lett.*, 2017, **19**, 2074; (*e*) S.-L. Zhang and Z.-L. Yu, *Org. Biomol. Chem.*, 2016, **14**, 10511; (*f*) M. Toure, S. Jaime-Figureroa, G. M. Burslem and C. M. Crews, *Eur. J. Org. Chem.*, 2016, 4171; (*g*) M. Zhang, H.-J. Zhang, T. Han, W. Ruan and T.-B. Wen, *J. Org. Chem.*, 2015, **80**, 620; (*h*) B. Chen and S. Ma, *Org. Lett.*, 2013, **15**, 3884; (*i*) X.-D. Fei, Z.-Y. Ge, T. Tang, Y.-M. Zhu and S.-J. Ji, *J. Org. Chem.*, 2012, **77**, 10321; (*j*) P.-Y. Chen, K.-S. Huang, C.-C. Tsai, T.-P. Wang and E.-C. Wang, *Org. Lett.*, 2012, **14**, 4930; (*k*) S. Cai, F. Wang and C. Xi, *J. Org. Chem.*, 2012, **77**, 2331.

16 For selected references on multicomponent reactions, see: (*a*) B. B. Toure and D. G. Hall, *Chem. Rev.*, 2009, **109**, 4439; (*b*) A. Dömling, W. Wang and K. Wang, *Chem. Rev.*, 2012, **112**, 3083; (*c*) Y. Liu, H. Wang and J.-P. Wan, *Asian J. Org. Chem.*, 2013, **2**, 374; (*d*) F. Shi, Z.-L. Tao, S.-W. Luo, S.-J. Tu and L.-Z. Gong, *Chem.–Eur. J.*, 2012, **18**, 6885; (*e*) F. Shi, G.-J. Xing, R.-Y. Zhu, W. Tan and S. Tu, *Org. Lett.*, 2013, **15**, 128; (*f*) W. Dai, X.-L. Jiang, J.-Y. Tao and F. Shi, *J. Org. Chem.*, 2016, **81**, 185; (*g*) J.-P. Wan, Y. Lin, Q. Huang and Y. Liu, *J. Org. Chem.*, 2014, **79**, 7232.

17 For selected references on cascade reactions, see: (*a*) K. C. Nicolaou and J. S. Chen, *Chem. Soc. Rev.*, 2009, **38**, 2993; (*b*) C. Grondal, M. Jeanty and D. Enders, *Nat. Chem.*, 2010, **2**, 167; (*c*) J.-P. Wan and Y. Gao, *Chem. Rec.*, 2016, **16**, 1164; (*d*) Y.-C. Zhang, J.-J. Zhao, F. Jiang, S.-B. Sun and F. Shi, *Angew. Chem., Int. Ed.*, 2014, **53**, 13912; (*e*) F. Shi, H.-H. Zhang, X.-X. Sun, J. Liang, T. Fan and S.-J. Tu, *Chem.–Eur. J.*, 2015, **21**, 3465; (*f*) F. Jiang, Y.-C. Zhang,

X. Yang, Q.-N. Zhu and F. Shi, *Synlett*, 2016, **27**, 575; (*g*) J.-P. Wan, Y. Jing, C. Hu and S. Sheng, *J. Org. Chem.*, 2016, **81**, 6826; (*h*) Y. Li, J.-P. Wan and C. Wen, *Tetrahedron*, 2017, **73**, 2323.

18 (*a*) X. Chen, W. Hao and Y. Liu, *Org. Biomol. Chem.*, 2017, **15**, 3423; (*b*) Y. Liu, M. Huang and L. Wei, *Asian J. Org. Chem.*, 2017, **6**, 41; (*c*) Y. Liu, H. Wang, J. Zhang, J.-P. Wan and C. Wen, *RSC Adv.*, 2014, **4**, 19472; (*d*) Y. Liu, B. Huang, X. Cao, D. Wu and J.-P. Wan, *RSC Adv.*, 2014, **4**, 37733; (*e*) Y. Liu, H. Wang, X. Cao, Z. Fang and J.-P. Wan, *Synthesis*, 2013, **45**, 2977.