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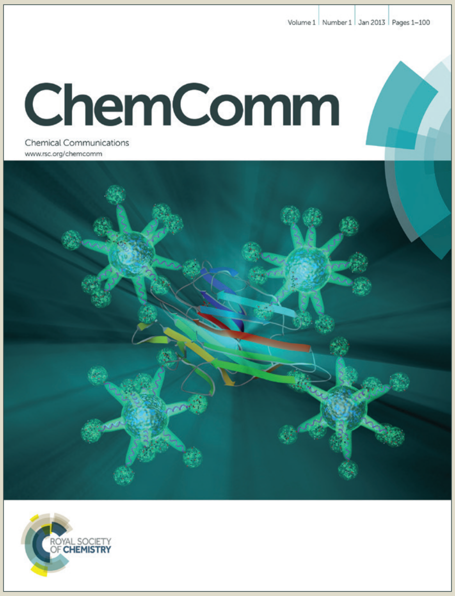

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ARTICLE TYPE

# Versatile palladium-catalyzed C–H olefination of (hetero)arenes at room temperature

**Zhijie She, Yang Shi, Yumin Huang, Yangyang Cheng, Feijie Song* and Jingsong You***

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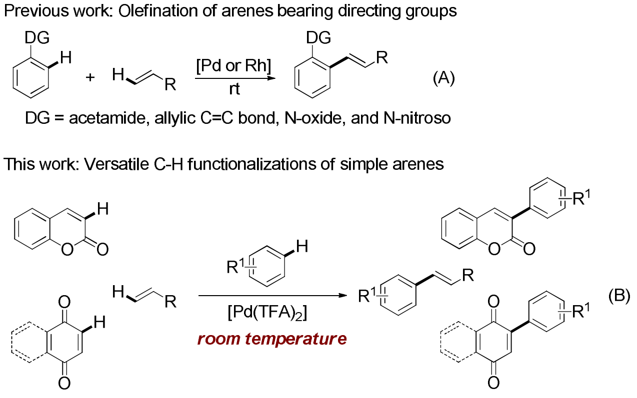
**The room-temperature oxidative C–H/C–H cross-couplings between (hetero)arenes and alkenes, coumarins or quinones have been reported by using a highly electrophilic palladium species [Pd(TFA)$_2$] generated in situ from Pd(OAc)$_2$ and TFA as the catalyst and cheap (NH$_4$)$_2$S$_2$O$_8$ as the oxidant under air.**

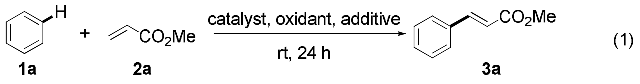
The oxidative C–H/C–H cross-coupling of arenes with alkenes, known as the Fujiwara-Moritani reaction,[1] has been recognized as a powerful strategy for the synthesis of vinyl arene derivatives.[2] The olefination of various aromatic compounds including arenes bearing directing groups have been achieved by using Pd,[3] Rh,[4] and Ru[5] complexes as the catalysts. Compared with the Mizoroki-Heck reaction that employs aryl halides as the coupling partner, the Fujiwara-Moritani reaction avoids the prefunctionalization of the aryl counterparts and obviates the production of salt wastes generating from aryl halides and bases. However, such transformations usually necessitate elevated temperatures to facilitate the cleavage of C–H bonds. Very recently, a few examples of the chelation-assisted olefination of arenes have been realized at room temperature by using acetamide,[6] allylic C–C double bond,[7] N-oxide,[8] and N-nitroso[9] as the directing groups (Scheme 1A). In contrast, the room-temperature C–H olefination of non-chelation-assisted arenes remains unsolved (usually, the reaction temperature range between 90 °C and 180 °C).[3a-g,4e,5a] From both academic and industrial point of view, it is desirable to realize the direct C–H bond olefination of simple arenes under mild reaction conditions.

Pd(TFA)$_2$ has demonstrated to be a highly efficient catalyst for the direct C–H functionalization of arenes. By employing this highly electrophilic palladium species (sometimes generated in situ from Pd(OAc)$_2$ and TFA) as the catalyst, a large number of transformations such as addition,[10] acetoxylation,[11] arylation,[11,12] carboxylation,[13] and decarboxylative acylation reaction[14] have been realized at ambient temperature. Following our continuous interest in the direct C–H olefination reactions,[3k,8,15] we envisioned that it was possible to realize the C–H olefination of simple arenes under mild reaction conditions by using Pd(TFA)$_2$ as the catalyst. The high electrophilicity of Pd(TFA)$_2$ may favor the C–H metalation of arenes and thus facilitate the occurrence of the subsequent olefination reaction. In this paper, we would like to report the room-temperature oxidative C–H/C–H cross-coupling of simple arenes with alkenes by using [Pd(TFA)$_2$] generated in situ from Pd(OAc)$_2$ and TFA as the catalyst and cheap (NH$_4$)$_2$S$_2$O$_8$ as the oxidant (Scheme 1B). Notably, this protocol is also applicable to the alkene-related structures such as quinones and coumarins.



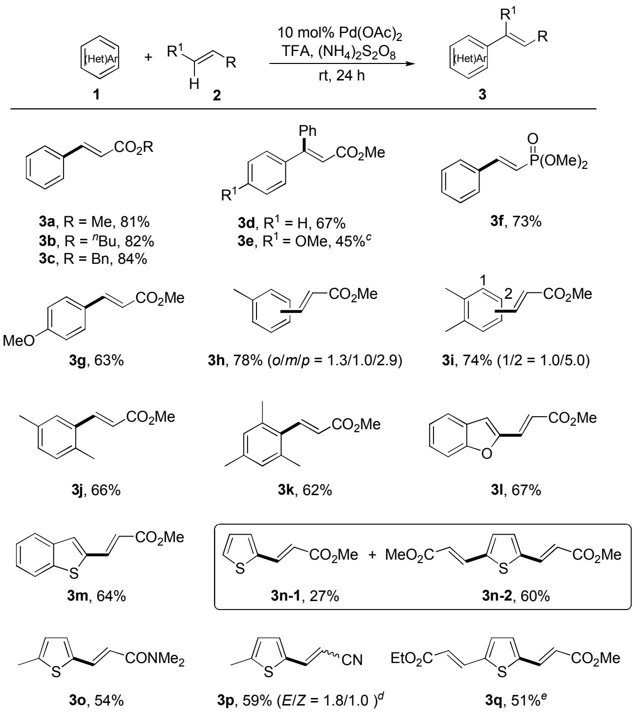
**Scheme 1** The room-temperature C–H olefination of arenes.

Initially, the reaction of benzene **1a** with methyl acrylate **2a** was optimized at room temperature (eqn (1) and Table S1). No reaction occurred when 10 mol% Pd(OAc)$_2$ or Pd(TFA)$_2$ was used as the catalyst in the presence of 2.0 equiv of (NH$_4$)$_2$S$_2$O$_8$ (Table S1, entries 1 and 2). However, addition of 5.0 equiv of trifluoroacetic acid (TFA) to the Pd(OAc)$_2$ or Pd(TFA)$_2$ system delivered the desired product **3a** in 81% and 72% yields, respectively (Table S1, entries 3 and 4). These results indicated that the in situ generated [Pd(TFA)$_2$] was crucial for the smooth happening of the reaction. The use of K$_2$S$_2$O$_8$, Na$_2$S$_2$O$_8$, and NFSI as oxidants all afforded **3a** in 57%-71% yields (Table S1, entries 6-8). Notably, 1.0 atm of O$_2$ could also promote the formation of **3a**, albeit with a lower yield of 44% (Table S1, entry 9). We also screened the amounts of Pd(OAc)$_2$, TFA, and benzene (Table S1, entries 11-15) and found that 75.0 equiv of benzene in combination with 10 mol% of Pd(OAc)$_2$, 5.0 equiv of TFA, and 2.0 equiv of (NH$_4$)$_2$S$_2$O$_8$ was the optimal reaction condition to afford **3a** in 81% yield (Table S1, entry 3). Decreasing the amounts of benzene led to the lower yields of **3a** and 3.0 equiv of benzene could not even afford any **3a** (Table S1, entries 14-15).



With the optimized reaction conditions in hand, we then explored the substrate scope with respect to arenes and alkenes (Table 1). Electron-deficient alkenes such as acrylates, βsubstituted acrylate, and vinylphosphonate efficiently underwent the coupling reaction with benzene **1a** to give the olefinated products in good yields (Table 1, **3a**-**3f**). Notably, the reaction of benzene with (*E*)-methyl 3-(4-methoxyphenyl)acrylate **2e** delivered (*E*)-**3e** as a single product, demonstrating a high *E*/*Z* selectivity of the coupling reaction with 1,2-disubstituted alkenes. Mono, di, and tri-substituted arenes were amenable to this reaction (Table 1, **3g**-**3k**). The substituents on arenes could be electeron-rich groups such as methyl and methoxyl goups. However, the electeron-deficient groups such as bromo and chloro were not tolerated. It was worth to note that the *para*-olefinated product **3g** was obtained as a single isomer when anisloe was subjected to the standard condition.

**Table 1** Pd(II)-catalyzed oxidative C–H/C–H cross-coupling of (hetero)arenes with alkenes under air at room temperature[a,b]

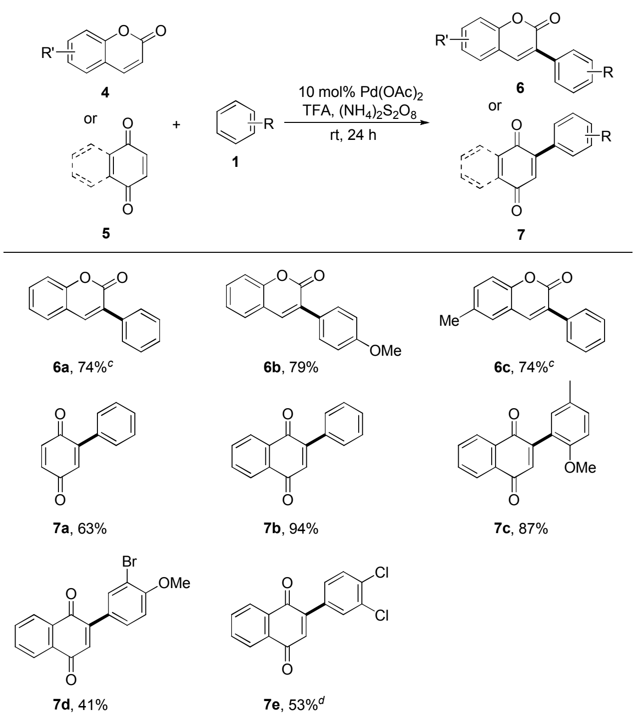


[a] Reaction conditions for arenes: alkene (0.3 mmol), arene **1** (22.5 mmol), $Pd(OAc)_2$ (0.03 mmol, 10 mol%), $(NH_4)_2S_2O_8$ (0.6 mmol) and TFA (1.5 mmol) at rt under air for 24 h; reaction conditions for heteroarenes: alkene (0.6 mmol), heteroarene **1** (0.3 mmol), $Pd(OAc)_2$ (0.03 mmol, 10 mol%), $(NH_4)_2S_2O_8$ (0.6 mmol) and TFA (1.5 mmol) in $CH_2Cl_2$ (2.0 mL) under air at rt for 48 h. [b] Isolated yield. [c] The starting alkene was recovered in 45% yield. [d] Acrylonitrile (1.5 mmol) with Selectfluor (0.6 mmol) as the oxidant. [e] 24 h.

Subsequently, we investigated the feasibility of this protocol to the C–H cleavage/olefination of electon-rich heteroarenes. Thiophenes, benzothiophenes and benzofurans coupled with methyl acrylate **2a** to afford the desired **3l**-**3q** in 51%-87% yields. Remarkably, the amounts of heteroarenes were allowed to be decreased to 0.5 equiv in these cases, demonstrating the higher reactivity of heteroarenes than arenes in the catalytic system. When thiophene was employed as the substrate, both the mono- and di-olefinated products **3n-1** and **3n-2** were obtained with **3n-2** as the major product. Unfortunately, the reaction of indoles with acrylate afforded complex mixtures probably due to the easy oxidation and decomposition of indoles under the strong oxidative conditions.

Next, we continued to expand the substrate scope of this protocol. The synthesis of arylated coumarins has drawn the interest of many chemists[16] because such molecules exhibit a broad range of biological activities.[17] Very recently, Jafarpour and co-workers reported the regioselective C3-arylation of coumarins by using 10 mol% $Pd(OAc)_2$ as the catalyst and TFAA as the additive at a high temperature of 120 $^{o}$C.[16d] As coumarins could be regarded as the ester-substituted cyclic alkenes, we then attempted the oxidative C–H/C–H cross-coupling of coumarins with arenes at room temperature. Pleasantly, the reaction occurred in a highly regioselective manner and the 3-arylated coumarins were obtained in 74%-79% yields (Table 2, **6a**-**6c**).

**Table 2** Scope of the arylation of coumarins and quinones at room temperature[a,b]



[a] Reaction conditions: coumarin **4** or quinone **5** (0.3 mmol), arene **1** (22.5 mmol), $Pd(OAc)_2$ (0.03 mmol, 10 mol%), $(NH_4)_2S_2O_8$ (0.6 mmol) and TFA (1.5 mmol) at rt under air for 24 h. [b] Isolated yield. [c] 48 h. [d] TFA (3.0 mmol) for 48 h.

Arylated quinones have been found wide applications in the dye industry in virtue of their significant coloring properties.[18] Consequently, a variety of methods have been established for the synthesis of such molecules.[19] Our group recently reported a highly efficient approach to arylquinones through the oxidation of hydroquinones and subsequent palladium-catalyzed oxidative C–H/C–H cross-coupling of the resulting quinones with arenes.[20] However, this reaction suffered from the employment of stoichiometric amounts of $Ag_2CO_3$ as the oxidant and a high reaction temperature (140 $^{o}$C). Pleasantly, by using the $[Pd(TFA)_2]/(NH_4)_2S_2O_8$ catalytic system described herein, the coupling of quinones with arenes worked smoothly at room temperature to afford the desired arylquinones **7** in modest to excellent yields (Table 2, **7a**-**7e**). Besides electron-donating groups, electron-deficient arenes such as 1,2-dichlorobenzene were also tolerated (Table 2, **7e**). A controlled experiment of 1,4-naphthoquinone with benzene indicated that no reaction occurred in the absence of $Pd(OAc)_2$.[21]

In conclusion, by employing a highly electrophilic $[Pd(TFA)_2]$ as the catalyst and the inexpensive and environmentally friendly $(NH_4)_2S_2O_8$ as the oxidant, we have successfully realized the oxidative C–H/C–H cross-coupling of (hetero)arenes with alkenes under air at room temperature. More importantly, the current methodology can also be applied to the couplings between simple arenes and other important alkene-related functional molecules such as coumarins and quinones. These transformations are operationally simple and do not require the exclusion of air or moisture.

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## Notes and references

[a] *Key Laboratory of Green Chemistry and Technology of Ministry of Education, College of Chemistry, and State Key Laboratory of Biotherapy, West China Medical School, Sichuan University, 29 Wangjiang Road, Chengdu 610064, PR China. Fax: (+86) 28-85412203; E-mail: jsyou@scu.edu.cn; fsong@scu.edu.cn*

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1 I. Moritani and Y. Fujiwara, *Tetrahedron Lett.*, 1967, **8**, 1119.

2 (*a*) J. L. Bras and J. Muzart, *Chem. Rev.*, 2011, **111**, 1170; (*b*) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215; (*c*) C. Liu, H. Zhang, W. Shi and A. Lei, *Chem. Rev.*, 2011, **111**, 1780; (*d*) S. I. Kozhushkov and L. Ackermann, *Chem. Sci.*, 2013, **4**, 886; (*e*) Y. Wu, J. Wang, F. Mao and F. Y. Kwong, *Chem. Asian J.*, 2014, **9**, 26.

3 For selected examples of Pd-catalyzed olefination of simple arenes, see: (*a*) C. Jia, W. Lu, T. Kitamura and Y. Fujiwara, *Org. Lett.*, 1999, **1**, 2097; (*b*) T. Matsumoto and H. Yoshida, *Chem. Lett.*, 2000, 1064; (*c*) M. Dams, D. E. De. Vos, S. Celen and P. A. Jacobs, *Angew. Chem. Int. Ed.*, 2003, **42**, 3512; (*d*) T. Yokota, M. Tani, S. Sakaguchi and Y. Ishii, *J. Am. Chem. Soc.*, 2003, **125**, 1476; (*e*) Y.-H. Zhang, B.-F. Shi and J.-Q. Yu, *J. Am. Chem. Soc.*, 2009, **131**, 5072; (*f*) A. Kubota, M. H. Emmert and M. S. Sanford, *Org. Lett.*, 2012, **14**, 1760; (*g*) B. P. Babu, X. Meng and J.-E. Bäckvall, *Chem.–Eur. J.*, 2013, **19**, 4140; for selected recent examples of Pd-catalyzed olefination of arenes with directing groups, see: (*h*) A. García-Rubia, B. Urones, R. G. Arrayás and J. C. Carretero, *Angew. Chem. Int. Ed.*, 2011, **50**, 10927; (*i*) C. Huang, B. Chattopadhyay and V. Gevorgyan, *J. Am. Chem. Soc.*, 2011, **133**, 12406; (*j*) R. D. Baxter, D. Sale, K. M. Engle, J.-Q. Yu and D. G. Blackmond, *J. Am. Chem. Soc.*, 2012, **134**, 4600; (*k*) X. Cong, J. You, G. Gao and J. Lan, *Chem. Commun.*, 2013, **49**, 662; (*l*) H.-L. Wang, R.-B. Hu, H. Zhang, A.-X. Zhou and S.-D. Yang, *Org. Lett.*, 2013, **15**, 5302.

4 For selected recent examples of Rh-catalyzed olefination of arenes, see: (*a*) F. W. Patureau, T. Besset and F. Glorius, *Angew. Chem. Int. Ed.*, 2011, **50**, 1064; (*b*) S. Rakshit, C. Grohmann, T. Besset and F. Glorius, *J. Am. Chem. Soc.*, 2011, **133**, 2350; (*c*) C. Wang, H. Chen, Z. Wang, J. Chen and Y. Huang, *Angew. Chem. Int. Ed.*, 2012, **51**, 7242; (*d*) P. Zhao, R. Niu, F. Wang, K. Han and X. Li, *Org. Lett.*, 2012, **14**, 4166; (*e*) L. Zheng and J. Wang, *Chem.–Eur. J.*, 2012, **18**, 9699; (*f*) Y. Wang, C. Li, Y. Li, F. Yin and X.-S. Wang, *Adv. Synth. Catal.*, 2013, **355**, 1724; (*g*) D. Zhao, C. Nimphius, M. Lindale and F. Glorius, *Org. Lett.*, 2013, **15**, 4504; (*h*) T. Zhang, L. Wu and X. Li, *Org. Lett.*, 2013, **15**, 6294; (*i*)Y. Dong and G. Liu, *Chem. Commun.*, 2013, **49**, 8066; (*j*) C. Suzuki, K. Morimoto, K. Hirano, T. Satoh and M. Miura, *Adv. Synth. Catal.*, 2014, **356**, 1521; (*k*) K. Nobushige, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2014, **16**, 1188; (*l*) N.-J. Wang, S.-T. Mei, L. Shuai, Y. Yuan and Y. Wei, *Org. Lett.*, 2014, **16**, 3040; (*m*) K. Parthasarathy and C. Bolm, *Chem.–Eur. J.*, **2014**, 20, 4896.

5 For selected examples of Ru-catalyzed olefination of arenes, see: (*a*) H. Weissman, X. Song and D. Milstein, *J. Am. Chem. Soc.*, 2001, **123**, 337; (*b*) L. Ackermann, L. Wang, R. Wolfram and A. V. Lygin, *Org. Lett.*, 2012, **14**, 728; (*c*) B. Li, J. Ma, N. Wang, H. Feng, S. Xu and B. Wang, *Org. Lett.*, 2012, **14**, 736; (*d*) K. Padala and M. Jeganmohan, *Org. Lett.*, 2012, **14**, 1134; (*e*) K. Graczyk, W. Ma and L. Ackermann, *Org. Lett.*, 2012, **14**, 4110; (*f*) K. Padala, S. Pimparkar, P. Madasamy and M. Jeganmohan, *Chem. Commun.*, 2012, **48**, 7140; (*g*) J. Li, C. Kornhaaβ and L. Ackermann, *Chem. Commun.*, 2012, **48**, 11343; (*h*) W. Ma and L. Ackermann, *Chem.–Eur. J.*, 2013, **19**, 13925; (*i*) H. Li, X. Xie and L. Wang, *Chem. Commun.*, 2014, **50**, 4218.

6 (*a*) M. D. K. Boele, G. P. F. van Strijdonck, A. H. M. de Vries, P. C. J. Kamer, J. G. de Vries and P. W. N. M. van Leeuwen, *J. Am. Chem. Soc.*, 2002, **124**, 1586; (*b*) T. Nishikata and B. H. Lipshutz, *Org. Lett.*, 2010, **12**, 1972; (*c*) B. S. Kim, C. Jang, D. J. Lee and S. W. Youn, *Chem. Asian J.*, 2010, **5**, 2336; (*d*) X. Liu and K. K. Hii, *J. Org. Chem*, 2011, **76**, 8022; (*e*) B. Schmidt and N. Elizarov, *Chem. Commun.*, 2012, **48**, 4350.

7 P. Gandeepan and C.-H. Cheng, *J. Am. Chem. Soc.*, 2012, **134**, 5738.

8 X. Huang, J. Huang, C. Du, X. Zhang, F. Song and J. You, *Angew. Chem. Int. Ed.*, 2013, **52**, 12970.

9 B. Liu, Y. Fan, Y. Gao, C. Sun, C. Xu and J. Zhu, *J. Am. Chem. Soc.*, 2013, **135**, 468.

10 (*a*) C. Jia, D. Piao, J. Oyamada, W. Lu, T. Kitamura and Y. Fujiwara, *Science*, 2000, **287**, 1992; (*b*) C. Jia, W. Lu, J. Oyamada, T. Kitamura, K. Matsuda, M. Irie and Y. Fujiwara, *J. Am. Chem. Soc.*, 2000, **122**, 7252.

11 F. Yang, F. Song, W. Li, J. Lan and J. You, *RSC Adv.*, 2013, **3**, 9649.

12 R. Li, L. Jiang and W. Lu, *Organometallics*, 2006, **25**, 5973.

13 Y. Taniguchi, Y. Yamaoka, K. Nakata, K. Takaki and Y. Fujiwara, *Chem. Lett.*, 1995, 345.

14 P. Fang, M. Li and H. Ge, *J. Am. Chem. Soc.*, 2010, **132**, 11898.

15 (*a*) Y. Huang, F. Song, Z. Wang, P. Xi, N. Wu, Z. Wang, J. Lan and J. You, *Chem. Commun.*, 2012, **48**, 2864; (*b*) L.-Q. Zhang, S. Yang, X. Huang, J. You and F. Song, *Chem. Commun.*, 2013, **49**, 8830.

16 For selected examples, see: (*a*) M. Khoobi, M. Alipour, S. Zarei, F. Jafarpour and A. Shafiee, *Chem. Commun.*, 2012, **48**, 2985; (*b*) Y. Li, Z. Qi, H. Wang, X. Fu and C. Duan, *J. Org. Chem.*, 2012, **77**, 2053; (*c*) M. Min and S. Hong, *Chem. Commun.*, 2012, **48**, 9613; (*d*) F. Jafarpour, H. Hazrati, N. Mohasselyazdi, M. Khoobi and A. Shafiee, *Chem. Commun.*, 2013, **49**, 10935.

17 (*a*) L. M. Kabeya, A. A. de Marchi, A. Kanashiro, N. P. Lopes, C. H. T. P. da Silva, M. T. Pupo and Y. M. Lucisano-Valima, *Bioorg. Med. Chem.*, 2007, **15**, 1516; (*b*) L. You, R. An, X. Wang and Y. Li, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 7426; (*c*) P. Anand, B. Singh and N. Singh, *Bioorg. Med. Chem. Lett.*, 2012, **20**, 1175; (*d*) D. Olmedo, R. Sancho, L. M. Bedoya, J. L. López-Pérez, E. del Olmo, E. Muñoz, J. Alcamí, M. P. Gupta and A. S. Feliciano, *Molecules*, 2012, **17**, 9245; (*e*) M. J. Matos, S. Vazquez-Rodriguez, L. Santana, E. Uriarte, C. Fuentes-Edfuf , Y. Santos and A. Muñoz-Crego, *Molecules*, 2013, **18**, 1394.

18 T. Bechtold, in *Handbook of Natural Colorants*, ed. T. Bechtold and R. Mussak, Wiley, New York, 2009, 151.

19 For selected examples, see: (*a*) H.-B. Zhang, L. Liu, Y.-J. Chen, D. Wang and C.-J. Li, *Adv. Synth. Catal.*, 2006, **348**, 229; (*b*) M. R. Heinrich, *Chem.–Eur. J.*, 2009, **15**, 820; (*c*) X. Gan, W. Jiang, W. Wang and L. Hu, *Org. Lett.*, 2009, **11**, 589; (*d*) M. T. Molina, C. Navarro, A. Moreno and A. G. Csákÿ, *Org. Lett.*, 2009, **11**, 4938; (*e*) O. M. Demchuk and K. M. Pietrusiewicz, *Synlett*, 2009, 1149; (*f*) Y. Fujiwara, V. Domingo, I. B. Seiple, R. Gianatassio, M. D. Bel and P. S. Baran, *J. Am. Chem. Soc.*, 2011, **133**, 3292; (*g*) J. Wang, S. Wang, G. Wang, J. Zhang and X.-Q. Yu, *Chem. Commun.,* 2012, **48**, 11769.

20 S. Zhang, F. Song, D. Zhao and J. You, *Chem. Commun.*, 2013, **49**, 4558;

21 K. Kapłon, O. M. Demchuk, M. Wieczorek and K. M. Pietrusiewicz, *Curr. Chem. Lett.*, 2014, **3**, 23.