



Cite this: *Chem. Commun.*, 2019, 55, 4047

Received 5th February 2019,
Accepted 6th March 2019

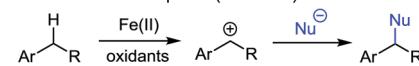
DOI: 10.1039/c9cc01060b

rsc.li/chemcomm

We report herein an alkenylation of benzylic $C(sp^3)$ -H bonds with diazo compounds *via* carbon cation intermediates with DDQ as the oxidant in the presence of a catalytic amount of Fe(II). Diphenylmethane, toluene, benzyl methyl sulfide and their derivatives could be applied as substrates to afford the tetra-substituted olefin products, which may serve as useful building blocks in organic synthesis.

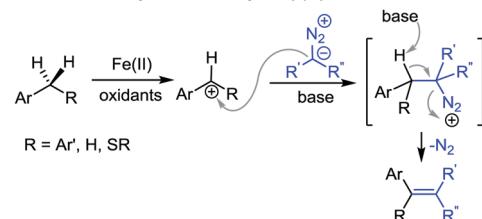
Transition-metal-catalyzed oxidative transformation of $C(sp^3)$ -H bonds has emerged as one of the important tools in synthetic organic chemistry.^{1–4} In particular, Fe(II)-catalyzed oxidative coupling of benzylic $C(sp^3)$ -H bonds has attracted considerable attention.^{5,6} The general pathway of this type of transformation is shown in Scheme 1a. In the presence of an oxidant and Fe(II) catalyst, a benzylic cation is generated through hydrogen abstraction followed by single electron oxidation of the generated benzylic radical species. The benzylic cation is then trapped by a nucleophile to deliver the product. With the Fe(II)/2,3-dichloro-5,6-dicyanoquinone (DDQ) reaction system, various nucleophiles have been explored in the benzylic $C(sp^3)$ -H bond functionalization.^{5–11} For example, Shi *et al.* reported an oxidative coupling of $C(sp^3)$ -H bonds with arenes and vinyl acetates with Fe(II) catalyst and DDQ as the oxidant.^{8,9} Jiao *et al.* explored azides as the nucleophiles in the amidation reaction of diphenylmethane through benzylic $C(sp^3)$ -H bond cleavage and Schmidt rearrangement.¹⁰ In 2015, Song *et al.* used 1,3-dicarbonyl compounds as the nucleophiles in a similar reaction system with arylmethanes.¹¹ While significant progress has been made in this arena, the scope of this type of transformation is still limited. Thus, further exploration of other nucleophiles is highly desirable.

a. Fe(II)-catalyzed benzylic $C(sp^3)$ -H bond functionalization with various nucleophiles (refs. 5–11)



R = NR₂, OR, SR, aryl, alkyl; Nu = arenes, alkenes, acetylenes, azides, 1, 3-dicarbonyl compounds.

b. oxidative alkenylation of benzylic $C(sp^3)$ -H bonds with diazo compounds



Scheme 1 Fe(II)-Catalyzed oxidative coupling of benzylic $C(sp^3)$ -H bonds.

On the other hand, diazo compounds have found wide applications as carbene precursors in transition-metal-catalyzed reactions.¹² The diazo compounds have also been used as nucleophiles in various transformations.¹³ In particular, the reaction of diazo compounds with carbon cations is well-known in the literature.¹⁴ We thus conceived that for the above-mentioned Fe(II)-catalyzed oxidative cleavage of benzylic $C(sp^3)$ -H bonds, it might be possible to apply diazo compounds as the nucleophiles to trap the benzylic carbon cation. The reaction is expected to generate diazonium intermediates followed by dinitrogen extrusion to afford olefin products (Scheme 1b). We report herein the study along this line, namely the $FeCl_2$ -catalyzed alkenylation of benzylic $C(sp^3)$ -H bonds with diazoesters in the presence of DDQ as the oxidant.

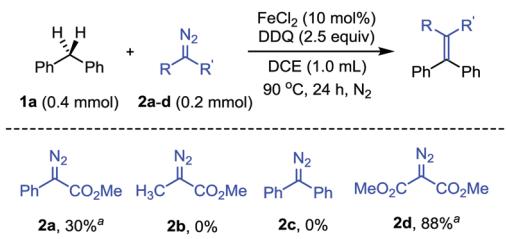
To begin with, we have evaluated the compatibility of the diazo compounds under the reaction conditions with $FeCl_2$ catalyst and DDQ oxidant (Scheme 2). Diphenylmethane **1a** was chosen as the substrate to investigate the benzylic $C(sp^3)$ -H bond transformation with diazo compounds. We first tested the reaction between **1a** (0.4 mmol) and phenyldiazoacetate **2a**

^a Beijing National Laboratory of Molecular Sciences (BNLMS), Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China.

E-mail: wangjb@pku.edu.cn

^b Department of Chemistry, Fudan University, Shanghai 200433, China

† Electronic supplementary information (ESI) available: Experimental details, characterization data. See DOI: 10.1039/c9cc01060b

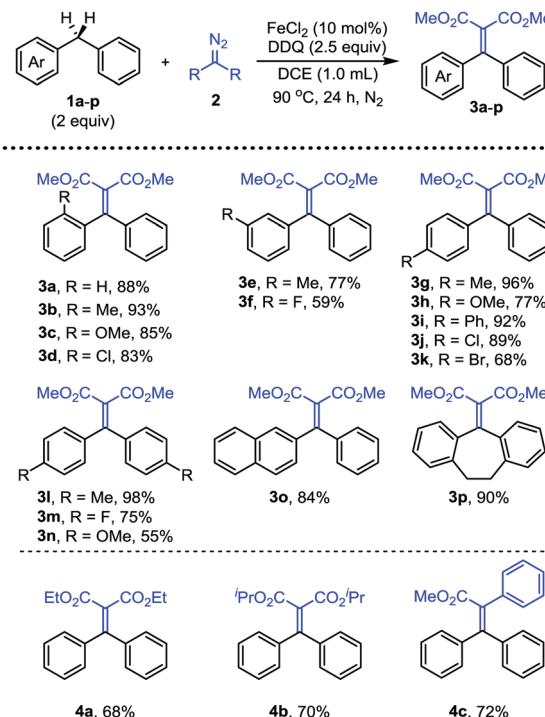


Scheme 2 Evaluation of the compatibility of diazo compounds.

(0.2 mmol) with 10 mol% FeCl_2 and DDQ (0.5 mmol) in 1,2-dichloroethane (DCE, 1.0 mL) at 90 °C for 24 h. Gratifyingly, the expected methyl 2,3,3-triphenylacrylate product was obtained, albeit in a low yield. However, with methyl 2-diazopropanoate **2b** as the nucleophile, the reaction failed to afford the expected olefin product. Similarly, the reaction with (diazomethylene)dibenzene **2c** also gave no olefin product. The low yields or no product formation with the diazo substrates **2a–c** were attributed to the side reactions of the diazo substrates under the reaction conditions, mainly the dimerization and oxidation of the diazo compounds. We then turned our attention to dimethyl 2-diazomalonate **2d**, which was known to be the diazo compound with relatively high stability. As expected, the dimethyl 2-diazomalonate **2d** was compatible with the reaction conditions and afforded the olefin product in 88% yield. Furthermore, control experiments showed that no C–H bond insertion product could be detected in the absence of DDQ. However, in the absence of FeCl_2 catalyst, the olefin product could be obtained in 30% yield.

With dimethyl 2-diazomalonate **2d** as the nucleophile, we then investigated the scope of a series of substituted diphenylmethanes **1a–p** (Scheme 3). The substrates with electron-withdrawing and electron-donating groups at the *ortho* position of the phenyl ring both afforded the corresponding products **3a–d** in good yields. The results indicated that a steric effect did not affect the reaction efficiency. The substrates with electron-rich or weakly electron deficient substituents at the *meta* position of the phenyl ring could also smoothly participate in the reaction (**3e**, **3h**). In addition, the substituted groups with various electronic properties on the *para* phenyl ring were also tolerated (**3g–k**). The reaction with other diphenylmethane derivatives, such as symmetrical and unsymmetrical disubstituted derivatives, also afforded the corresponding products **3l–p** in moderate to good yields under the standard conditions.

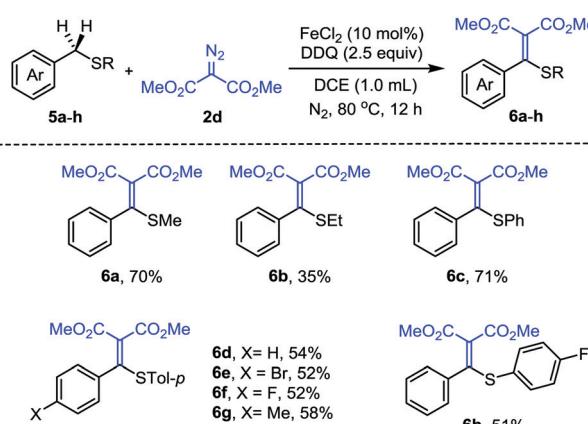
Next, we have examined the substrate scope of the diazo compounds (Scheme 3). The reactions with diethyl 2-diazomalonate **2e** and diisopropyl 2-diazomalonate **2f** afforded the products in similar yields (**4a**, **4b**). Notably, for the reaction with methyl phenyldiazoacetate **2a**, when the diazo substrate was added using a syringe pump over a period of 30 min, the corresponding product **4c** could be obtained in 72% yield. Slow addition of the diazo substrate is necessary in this case for avoiding the oxidation of the diazo substrate. Other aryl-diazoacetates were also subjected to the reaction under the



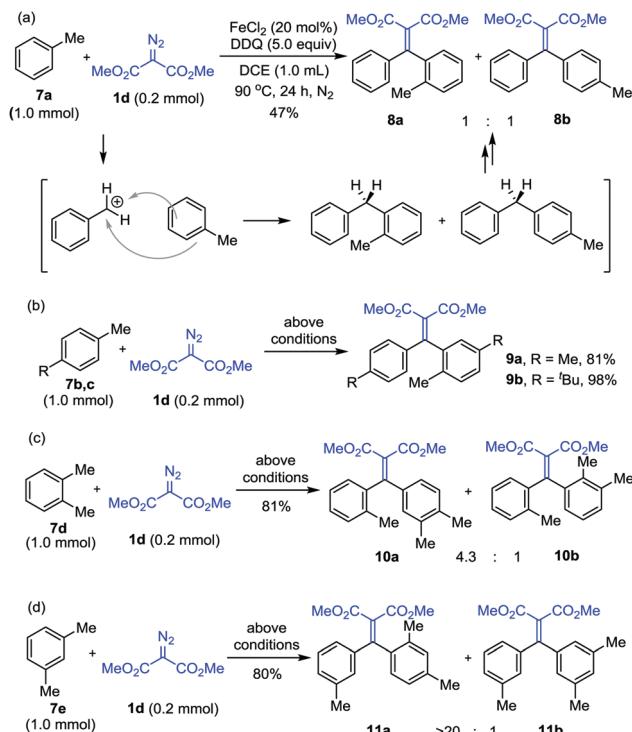
Scheme 3 Evaluation of substrate scope of diphenylmethanes.

same conditions, however, the reactions only offered complicated mixtures.

Furthermore, we have explored the reactivity of other benzylic $\text{C}(\text{sp}^3)\text{–H}$ bonds under the same conditions. We have found that the reaction with benzyl methyl sulfide **5a** could also afford the alkenylation product **6a** in 70% yield. We then evaluated the scope of a series of benzyl sulfide derivatives **5a–h** (Scheme 4). The substrates with different substituents on sulfur, such as ethyl, phenyl, *p*-tolyl and *p*-FC₆H₄[–], could afford the corresponding alkenylation products in moderate yields (**6b–d**, **6h**). The substituents on the benzyl aromatic ring also tolerated the reaction conditions (**6e–g**). Benzyl methyl sulfoxide failed to afford the alkenylation products, presumably due to its oxidation to sulfone. It is worth mentioning that alkenyl sulfides



Scheme 4 Reaction with benzyl sulfide derivatives.



Scheme 5 Reaction with toluene and its derivatives.

are valuable building blocks widely used as enolate surrogates, Michael acceptors, or intermediates in organic synthesis.¹⁵

Interestingly, when toluene **7a** was submitted to the reaction under slightly modified conditions (20 mol% FeCl_2 and 1.0 mmol DDQ in 1.0 mL DCE at 90 °C for 24 h), the benzylic cation intermediate first underwent Friedel–Crafts reaction with the substrate to give diphenylmethane, which was further followed by alkenylation with diazo substrate **1d** to deliver the products **8a** and **8b** in a 1:1 ratio. The toluene substrates bearing substituents **7b–e** were also examined. The reactions with these substrates all proceeded similarly, affording products **9a,b**, **10a,b** and **11a,b**, respectively. The regioselectivity was

found relevant to the position and steric bulk of the substituents (Scheme 5).

Based on the previous reports, we have proposed a plausible reaction mechanism, as shown in Scheme 6.^{5–11} First, radical **A** is generated through hydrogen abstraction from the substrate **1a** by FeCl_2 and DDQ. In this process, hydrogen is reduced to a proton through single electron transfer to $\text{Fe}(\text{II})/\text{DDQ}$, generating $\text{Fe}(\text{III})$ intermediate **B**. Subsequently, single electron transfer (SET) from **A** to **B** leads to the formation of carbon cation **C**, which reacts with nucleophilic diazo substrate **2d** to form **D**. From **D** deprotonation and elimination of N_2 occur to deliver the product **3a**, with the regeneration of $\text{Fe}(\text{II})$ and 2,3-dichloro-5,6-dicyanohydroquinone **E** (Scheme 6).

In summary, we have developed the first alkenylation of benzylic $\text{C}(\text{sp}^3)$ –H bonds with diazo compounds under the FeCl_2/DDQ reaction system. The oxidative reaction conditions are compatible with a wide range of diazo substrates. The reaction provides an efficient and unique method for the synthesis of substituted olefins.

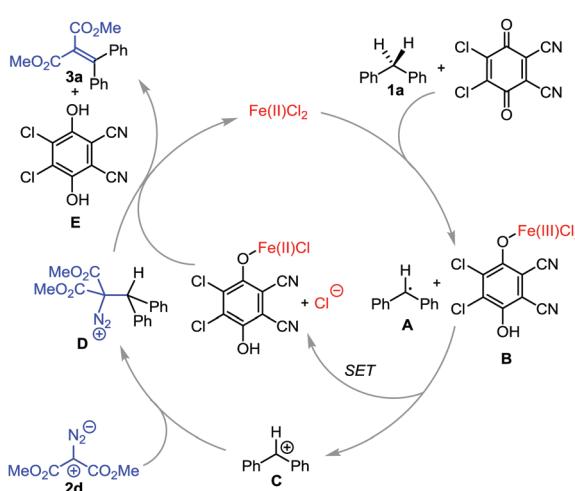
The project is supported by 973 Program (No. 2015CB856600) and NSFC (Grant 21871010).

Conflicts of interest

There are no conflicts to declare.

Notes and references

- (a) C. J. Li, *Acc. Chem. Res.*, 2009, **42**, 335–344; (b) S. A. Girard, T. Knauber and C. J. Li, *Angew. Chem., Int. Ed.*, 2014, **53**, 74–100.
- P. Xie, Y. J. Xie, B. Qian, H. Zhou, C. G. Xia and H. M. Huang, *J. Am. Chem. Soc.*, 2012, **134**, 9902–9905.
- R.-Y. Zhu, T. G. Saint-Denis, Y. Shao, J. He, J. D. Sieber, C. H. Senanayake and J. Q. Yu, *J. Am. Chem. Soc.*, 2017, **139**, 5724–5727.
- T. Stopka, L. Marzo, M. Zurro, S. Janich, E. U. Wurthwein, C. G. Daniliuc, J. Aleman and O. G. Mancheno, *Angew. Chem., Int. Ed.*, 2015, **54**, 5049–5053.
- (a) Z. P. Li, L. Cao and C.-J. Li, *Angew. Chem., Int. Ed.*, 2007, **46**, 6505–6507; (b) Y. H. Zhang and C.-J. Li, *J. Am. Chem. Soc.*, 2006, **128**, 4242–4243.
- (a) Z. P. Li, R. Yu and H. J. Li, *Angew. Chem., Int. Ed.*, 2008, **47**, 7497–7500; (b) S. G. Pan, J. H. Liu, H. R. Li, Z. Y. Wang, X. W. Guo and Z. P. Li, *Org. Lett.*, 2010, **12**, 1932–1935; (c) F. Jia and Z. P. Li, *Org. Chem. Front.*, 2014, **1**, 194–214.
- (a) F. Kakiuchi, K. Tsuchiya, M. Matsumoto, E. Mizushima and N. Chatani, *J. Am. Chem. Soc.*, 2004, **126**, 12792–12793; (b) Y. Aihara, M. Tobisu, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.*, 2014, **136**, 15509–15512; (c) J. Liu, H. Zhang, H. Yi, C. Liu and A. W. Lei, *Sci. China: Chem.*, 2015, **58**, 1323–1328; (d) S. B. Guo, Y. X. Li, Y. Wang, X. Guo, X. Meng and B. H. Chen, *Adv. Synth. Catal.*, 2015, **357**, 950–954.
- Y. Z. Li, B. J. Li, X. Y. Lu, S. Lin and Z. J. Shi, *Angew. Chem., Int. Ed.*, 2009, **48**, 3817–3820.
- C. X. Song, G. X. Cai, T. R. Farrell, Z. P. Jiang, H. Li, L. B. Gan and Z. J. Shi, *Chem. Commun.*, 2009, 6002–6004.
- C. Qin, W. Zhou, F. Chen, Y. Ou and N. Jiao, *Angew. Chem., Int. Ed.*, 2011, **50**, 12595.
- K. Yang and Q. L. Song, *Org. Lett.*, 2015, **17**, 548–551.
- For reviews on diazo compounds, see: (a) T. Ye and M. A. McKervey, *Chem. Rev.*, 1994, **94**, 1091–1160; (b) M. P. Doyle, M. A. McKervey and T. Ye, in *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, Wiley, New York, 1998; (c) Z. Zhang and J. Wang, *Tetrahedron*, 2008, **64**, 6577–6605; (d) A. Ford, H. Miel, A. Ring, C. N. Slattery, A. R. Maguire and M. A. McKervey, *Chem. Rev.*, 2015, **115**, 9981–10080.



Scheme 6 The proposed reaction mechanism.

13 (a) Y. Zhao and J. Wang, *Synlett*, 2005, 2886–2892; (b) Y. Zhang and J. Wang, *Chem. Commun.*, 2009, 5350–5361.

14 (a) T. Stopka, L. Marzo, M. Zurro, S. Janich, E.-U. Würthwein, C. G. Daniliuc, J. Alemán and O. G. Mancheño, *Angew. Chem., Int. Ed.*, 2015, **54**, 5049–5053; (b) T. Bug, M. Hartnagel, C. Schlierf and H. Mayr, *Chem. – Eur. J.*, 2003, **9**, 4068–4076; (c) H. Jangra, Q. Chen, E. Fuks, I. Zenz, P. Mayer, A. R. Ofial, H. Zipse and H. Mayr, *J. Am. Chem. Soc.*, 2018, **140**, 16758–16772.

15 (a) Y. Dong, M. Wang, J. Liu, W. Ma and Q. Liu, *Chem. Commun.*, 2011, **47**, 7380–7382; (b) N. Velasco, C. Virumbrales, R. Sanz, S. Suárez-Pantiga and M. A. Fernández-Rodríguez, *Org. Lett.*, 2018, **20**, 2848–2852.