

Cite this: *RSC Adv.*, 2017, 7, 29515

Received 15th April 2017

Accepted 31st May 2017

DOI: 10.1039/c7ra04264g

rsc.li/rsc-advances

Lewis base-catalyzed diastereoselective [3 + 2] cycloaddition reaction of nitrones with electron-deficient alkenes: an access to isoxazolidine derivatives†

Honglei Liu,^a Yan Zhao,^a Zhen Li,^a Hao Jia,^a Cheng Zhang,^a Yumei Xiao^a and Hongchao Guo^{ab*}

A Lewis base-catalyzed [3 + 2] cycloaddition reaction of nitrones with electron-deficient alkenes has been achieved under mild reaction conditions, affording various functionalized isoxazolidine derivatives as single diastereomers in moderate to excellent yields.

Nucleophilic phosphine-catalyzed cycloaddition reactions provide important access to various synthetically useful or biologically important carbo- and heterocyclic compounds¹ and serve as the key step for the total synthesis of some natural products.² During the past several decades a wide range of cycloaddition reactions have been developed.^{3–11} A variety of phosphine acceptors such as activated allenes, alkynes and alkenes and electrophilic coupling partners such as aldehydes, alkenes, imines, and aziridines have been exploited for these reactions.¹ In the past five years, 1,3-dipoles such as *N,N'* or *C,N*-cyclic azomethine imines and azomethine ylides have been used as versatile electrophilic coupling partners for phosphine-catalyzed [3 + 2],¹² [3 + 3],^{12,13} [4 + 3]^{12,14} and [3 + 2 + 3]¹² cycloadditions with activated allenes, alkynes, alkenes and MBH carbonates, producing biologically important nitrogen-containing heterocycles, such as tetrahydropyrazolopyrazolone, tetrahydropyranzolo-pyridazinone, tetrahydropyrazolodiazepinone, tetrahydropyrazolo-diazocinone, tricyclic dihydroisoquinoline and tetrahydro-isoquinoline derivatives.^{12–14} Although these dipoles have displayed diverse reactivities in the phosphine-catalyzed cycloadditions, the scope of 1,3-dipoles is still limited to azomethine imines and azomethine ylides. Other kinds of 1,3-dipoles have received little attention and have not been explored in phosphine-catalyzed cycloadditions. In this context, we tried to develop novel cycloaddition reactions based on other 1,3-dipoles, such as nitrones.¹⁵ Nitrones are readily accessible and stable compounds and

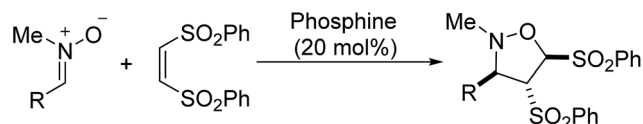
worked as efficient 1,3-dipoles in various cycloadditions to provide diverse cyclic compounds,¹⁵ which are important precursors for synthesis of bioactive compounds, natural products and other useful compounds.¹⁶ Herein, we present the first phosphine-catalyzed [3 + 2] cycloaddition reaction of various nitrones with electron-deficient alkenes for synthesis of functionalized isoxazolidines, which are potential scaffolds for the synthesis of pharmacologically active molecules (Scheme 1).

In our initial investigation, the reaction of *N*-methyl-1-phenylmethanimine oxide **1a** with (*Z*)-1,2-bis(phenylsulfonyl)ethylene **2** was chosen as the model reaction (Table 1). The reaction of **1a** and **2** was carried out in dichloromethane at room temperature in the absence of catalyst for 48 h, no new spots was observed by TLC monitoring (Table 1, entry 1). In the presence of 20 mol% PPh₃, the nitrone **1a** was treated with the alkene **2** in dichloromethane at room temperature for 48 h, leading to a desired [3 + 2] cycloaddition product isoxazolidine derivative **3a** as a single diastereomer in 99% yield (entry 2). The relative configuration of the product isoxazolidine derivative **3a** was unequivocally determined through the related X-ray crystallographic data of the homologous compound **3b** in Table 2.¹⁷ Several nucleophilic phosphines such as PBu₃, Me₂PPh, MePPh₂, EtPPh₂, *n*-PrPPh₂, *i*-PrPPh₂, *t*-BuPPh₂ and CyPPh₂ were next screened. Among these phosphines, both Me₂PPh and MePPh₂ were identified as the most effective catalysts for this reaction (entries 4 and 5). Other phosphines including PBu₃, EtPPh₂, *n*-PrPPh₂, *i*-PrPPh₂ and CyPPh₂ could also promote the reaction, but

^aDepartment of Applied Chemistry, China Agricultural University, Beijing 100193, China. E-mail: hchgao@cau.edu.cn

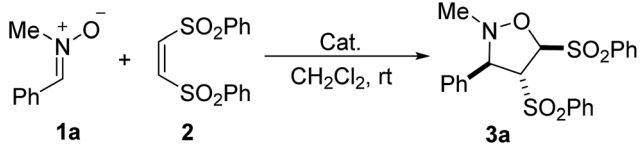
^bKey Laboratory of Green Pesticide and Agricultural Bioengineering, Ministry of Education, Guizhou University, Guiyang 550025, China

† Electronic supplementary information (ESI) available: Experimental procedures, spectral data and crystallographic data. CCDC 1532199. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7ra04264g



Scheme 1 Lewis base-catalyzed [3 + 2] cycloaddition of nitrones with electron-deficient alkene.



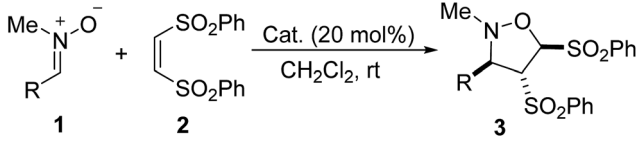
Table 1 Screening of the reaction conditions^a


Entry	Catalyst	Yield ^b (%)
1 ^b	—	0
2	PPh ₃	99
3	PBu ₃	60
4	Me ₂ PPh	95
5	MePPh ₂	97
6	EtPPh ₂	77
7	<i>n</i> -PrPPh ₂	89
8	<i>i</i> -PrPPh ₂	68
9	<i>t</i> -BuPPh ₂	Trace
10	CyPPh ₂	37
11	Et ₃ N	66
12	DABCO	36
13	DBU	99
14	DMAP	99
15 ^c	PPh ₃	50
16 ^d	PPh ₃	32

^a Reactions of **1** (0.1 mmol), **2** (0.12 mmol) and catalyst (0.02 mmol) were carried out in 2.5 mL of CH₂Cl₂ at room temperature for 48 h. ^b Without catalyst. ^c 10 mol% catalyst was used. ^d 5 mol% catalyst was used.

giving the corresponding product in lower 37–89% yields (entries 3, 6–8, and 10). With the use of *t*-BuPPh₂ as the catalyst, only trace of [3 + 2] cycloaddition product was obtained. Some tertiary amines, such as trimethylamine (Et₃N), 1,4-diazobicyclo[2.2.2]octane (DABCO), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and 4-dimethylamino-pyridine (DMAP), have also been examined and displayed moderate to excellent catalytic activity (entries 11–14). The DBU and DMAP led to 99% yield of the product **3a** (entries 13 and 14). In the presence of Ph₃P, the catalyst loading was attempted to be decreased to 10 mol% and 5 mol%, but the yield was reduced to 50% yield and 32% yield, respectively (entries 15 and 16).

With the optimal reaction conditions in hand, we next investigated the scope of the Lewis base-catalyzed [3 + 2] cycloaddition of nitrones with alkenes. With 20 mol% of PPh₃ or DMAP as the catalyst, various nitrones **1** underwent [3 + 2] cycloaddition reaction with (*Z*)-1,2-bis(phenylsulfonyl)ethylene **2** in dichloromethane at rt for 48–120 h, providing a variety of 4,5-bis(phenylsulfonyl)isoxazolidine derivatives (**3a–3v**) in moderate to excellent yields (Table 2, entries 1–22). Nitrones bearing whether electron-donating or withdrawing groups on the benzene ring worked smoothly to afford the corresponding products in satisfactory yields (entries 2–21). The methoxy-substituted nitrones were not very active, requiring longer reaction time (entries 7–12). Those nitrones having di and trisubstituted aryl groups were also tolerated, leading to good yields of the [3 + 2] cycloadducts (entries 5–6, 10–12). Particularly, the cycloaddition of 2-naphthyl-

Table 2 Scope of nitronium 1^a


Entry	Cat.	R	t/h	3	Yield (%)
1	Ph ₃ P	C ₆ H ₅ (1a)	48	3a	99
2	DMAP	2-MeC ₆ H ₄ (1b)	48	3b	81
3	DMAP	3-MeC ₆ H ₄ (1c)	48	3c	74
4	DMAP	4-MeC ₆ H ₄ (1d)	48	3d	69
5	Ph ₃ P	2,4-Me ₂ C ₆ H ₃ (1e)	48	3e	90
6	Ph ₃ P	3,4-Me ₂ C ₆ H ₃ (1f)	48	3f	87
7	Ph ₃ P	2-MeOC ₆ H ₄ (1g)	120	3g	76
8	Ph ₃ P	3-MeOC ₆ H ₄ (1h)	120	3h	80
9	Ph ₃ P	4-MeOC ₆ H ₄ (1i)	120	3i	63
10	DMAP	2,3-(OMe) ₂ C ₆ H ₃ (1j)	120	3j	77
11	Ph ₃ P	2,4-(OMe) ₂ C ₆ H ₃ (1k)	120	3k	75
12	Ph ₃ P	2,3,4-(OMe) ₃ C ₆ H ₂ (1l)	120	3l	78
13	Ph ₃ P	4-NMe ₂ C ₆ H ₄ (1m)	48	3m	65
14	Ph ₃ P	2-FC ₆ H ₄ (1n)	48	3n	51
15	Ph ₃ P	2-ClC ₆ H ₄ (1o)	48	3o	91
16	DMAP	3-ClC ₆ H ₄ (1p)	48	3p	62
17	DMAP	4-ClC ₆ H ₄ (1q)	48	3q	61
18	Ph ₃ P	2-BrC ₆ H ₄ (1r)	48	3r	83
19	DMAP	3-BrC ₆ H ₄ (1s)	48	3s	41
20	Ph ₃ P	4-BrC ₆ H ₄ (1t)	48	3t	62
21	DMAP	4-PhC ₆ H ₄ (1u)	48	3u	75
22	Ph ₃ P	2-Naphthyl (1v)	48	3v	99

^a Reactions of **1** (0.2 mmol), **2** (0.24 mmol) and the catalyst (0.04 mmol) were carried out in 5 mL of CH₂Cl₂ at room temperature.

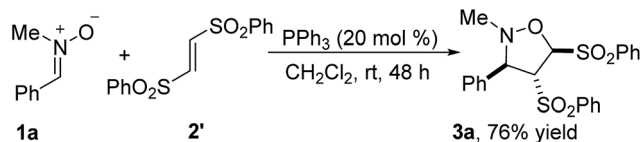
substituted nitronium (**1v**) proceeded efficiently to give the product **3v** in 99% yield (entry 22).

The reaction of nitronium **1a** with (*E*)-1,2-bis(phenylsulfonyl)ethylene **2'** has also been performed, producing 76% yield of the identical product **3a** with the reaction of (*Z*)-1,2-bis(phenylsulfonyl)ethylene **2** (Scheme 2). It indicated that the stereoselectivity of the reaction was not influenced by the configuration of carbon-carbon double bond in the alkene **2** and **2'**.

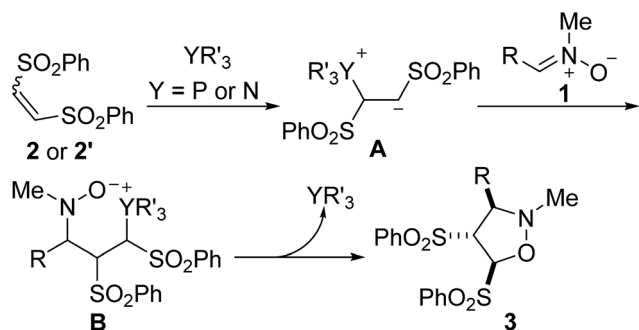
The proposed mechanism for [3 + 2] cycloaddition of the nitronium **1** with 1,2-bis(phenylsulfonyl)ethylene **2** is presented in Scheme 3. Conjugate addition of the phosphine or tertiary amine to the alkene **2** or **2'** gives the zwitterion intermediate **A**, which then attacks nitronium **1** to give the intermediate **B**. It undergoes an intramolecular nucleophilic attack to accomplish the [3 + 2] cyclization to give the product **3** with simultaneous regeneration of the catalyst. Since whether (*Z*)-alkene **2** or (*E*)-alkene **2'** produced the identical intermediate **A**, the stereochemistry of the reaction cannot be influenced by the configuration of the alkene.

The present reaction is quite robust. The reaction of 0.81 g of nitronium **1e** with alkene **2** still worked efficiently to produce the desired product **3e** in 78% yield (Scheme 4). To further demonstrate the reaction could be a practical tool for the synthesis of other valuable compounds, some synthetic transformations of

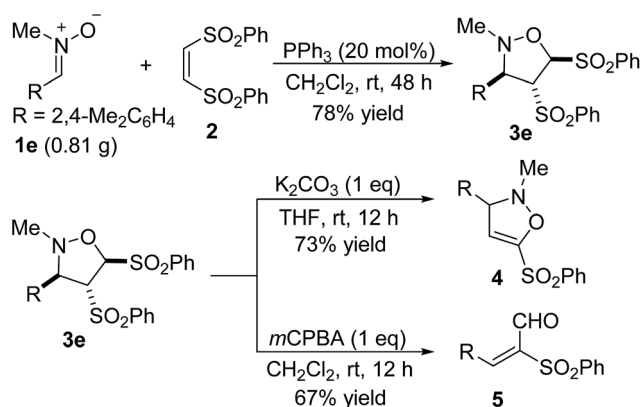




Scheme 2 PPh₃-catalyzed [3 + 2] cycloaddition of nitron **1a** with (E)-1,2-bis(phenylsulfonyl)ethylene **2'**.



Scheme 3 Proposed mechanism for the [3 + 2] cycloaddition.



Scheme 4 Gram-scale synthesis and further transformations of the cycloadduct.

cycloadduct **3e** were tried (Scheme 4). Treatment of the product **3e** with 1 equiv. K₂CO₃ in THF resulted in elimination of one of two phenylsulfonyl groups, affording the derivative **4** in 73% yield. The oxidation of **3e** with 1 equiv. of mCPBA in dichloromethane gave an α,β-unsaturated aldehyde **5** in 67% yield.

Conclusions

We have developed a Lewis base-catalyzed [3 + 2] cycloaddition reaction of nitrones with electron-deficient alkene, giving various functionalized isoxazolidine derivatives in moderate to excellent yields. A variety of nitrones underwent the reaction smoothly under the mild reaction conditions. The scaled-up reaction and further transformation of the cycloadducts demonstrated that the reaction could be a practical tool for organic synthesis.

Acknowledgements

This work is supported by the NSFC (No. 21172253, 21372256 and 21572264).

Notes and references

- For recent reviews, see: (a) X. Lu, C. Zhang and Z. Xu, *Acc. Chem. Res.*, 2001, **34**, 535; (b) J. L. Methot and W. R. Roush, *Adv. Synth. Catal.*, 2004, **346**, 1035; (c) L.-W. Ye, J. Zhou and Y. Tang, *Chem. Soc. Rev.*, 2008, **37**, 1140; (d) C. E. Aroyan, A. Dermenci and S. J. Miller, *Tetrahedron*, 2009, **65**, 4069; (e) B. J. Cowen and S. J. Miller, *Chem. Soc. Rev.*, 2009, **38**, 3102; (f) A. Marinetti and A. Voituriez, *Synlett*, 2010, 174; (g) S.-X. Wang, X. Y. Han, F. R. Zhong, Y. Q. Wang and Y. X. Lu, *Synlett*, 2011, 2766; (h) Q.-Y. Zhao, Z. Lian, Y. Wei and M. Shi, *Chem. Commun.*, 2012, **48**, 1724; (i) Y. C. Fan and O. Kwon, *Chem. Commun.*, 2013, **49**, 11588; (j) Z. Wang, X. Xu and O. Kwon, *Chem. Soc. Rev.*, 2014, **43**, 2927; (k) Y. Xiao, Z. Sun, H. Guo and O. Kwon, *Beilstein J. Org. Chem.*, 2014, **10**, 2089; (l) P. Xie and Y. Huang, *Org. Biomol. Chem.*, 2015, **13**, 8578; (m) Y. Xiao, H. Guo and O. Kwon, *Aldrichimica Acta*, 2016, **49**, 3; (n) T. Wang, X. Han, F. Zhong, W. Yao and Y. Lu, *Acc. Chem. Res.*, 2016, **49**, 1369.
- For application in synthesis of natural products, see: (a) J. C. Wang and M. J. Krische, *Angew. Chem., Int. Ed.*, 2003, **42**, 5855; (b) K. Agapiou and M. J. Krische, *Org. Lett.*, 2003, **5**, 1737; (c) Y. S. Tran and O. Kwon, *Org. Lett.*, 2005, **7**, 4289; (d) R. A. Jones and M. J. Krische, *Org. Lett.*, 2009, **11**, 1849; (e) M. Sampath, P.-Y. B. Lee and T. P. Loh, *Chem. Sci.*, 2011, **2**, 1988; (f) I. P. Andrews and O. Kwon, *Chem. Sci.*, 2012, **3**, 2510; (g) R. A. Villa, Q. H. Xu and O. Kwon, *Org. Lett.*, 2012, **14**, 4634; (h) G. A. Barcan, A. Patel, K. N. Houk and O. Kwon, *Org. Lett.*, 2012, **14**, 5388; (i) L. Cai, K. Zhang and O. Kwon, *J. Am. Chem. Soc.*, 2016, **138**, 3298.
- For [2 + 1] annulation, see: (a) S. Xu, L. Zhou, R. Ma, H. Song and Z. He, *Org. Lett.*, 2010, **12**, 544; (b) A. A. Ibrahim, P. H. Wei, G. D. Harzmann and N. J. Kerrigan, *J. Org. Chem.*, 2010, **75**, 7901; (c) S. Chen, E. C. Salo, K. A. Wheele and N. J. Kerrigan, *Org. Lett.*, 2012, **14**, 1784. For [2 + 2] annulation, see: (d) Z. Yang, H. Yu, L. Zhang, H. Wei, Y. Xiao, L. Chen and H. Guo, *Chem.-Asian J.*, 2014, **9**, 313.
- For representative examples on [3 + 2] annulation, see: (a) C. Zhang and X. Lu, *J. Org. Chem.*, 1995, **60**, 2906; (b) G. Zhu, Z. Chen, Q. Jiang, D. Xiao, P. Cao and X. Zhang, *J. Am. Chem. Soc.*, 1997, **119**, 3836; (c) J.-C. Wang, S.-S. Ng and M. J. Krische, *J. Am. Chem. Soc.*, 2003, **125**, 3682; (d) J. E. Wilson and G. C. Fu, *Angew. Chem., Int. Ed.*, 2006, **45**, 1426; (e) Y. Xia, Y. Liang, Y. Chen, M. Wang, L. Jiao, F. Huang, S. Liu, Y. Li and Z.-X. Yu, *J. Am. Chem. Soc.*, 2007, **129**, 3470; (f) B. J. Cowen and S. J. Miller, *J. Am. Chem. Soc.*, 2007, **129**, 10988; (g) A. Voituriez, A. Panossian, N. Fleury-Bregeot, P. Retailleau and A. Marinetti, *J. Am. Chem. Soc.*, 2008, **130**, 14030; (h) Y. Q. Fang and E. N. Jacobsen, *J. Am. Chem. Soc.*, 2008, **130**, 5660; (i)



- M. Sampath and T.-P. Loh, *Chem. Sci.*, 2010, **1**, 739; (j) H. Xiao, Z. Chai, C. W. Zheng, Y. Q. Yang, W. Liu, J. K. Zhang and G. Zhao, *Angew. Chem., Int. Ed.*, 2010, **49**, 4467; (k) Y. Fujiwara and G. C. Fu, *J. Am. Chem. Soc.*, 2011, **133**, 12293; (l) X. Han, Y. Wang, F. Zhong and Y. Lu, *J. Am. Chem. Soc.*, 2011, **133**, 1726; (m) F. Zhong, X. Han, Y. Wang and Y. Lu, *Angew. Chem., Int. Ed.*, 2011, **50**, 7837; (n) D. Duvvuru, N. Pinto, C. Gomez, J.-F. Betzer, P. Retailleau, A. Voituriez and A. Marinetti, *Adv. Synth. Catal.*, 2012, **354**, 408; (o) Q. Zhao, X. Han, Y. Wei, M. Shi and Y. Lu, *Chem. Commun.*, 2012, **48**, 970; (p) X. Han, F. Zhong, Y. Wang and Y. Lu, *Angew. Chem., Int. Ed.*, 2012, **51**, 767; (q) D. Wang, Y. Wei and M. Shi, *Chem. Commun.*, 2012, **48**, 2764; (r) F. Zhong, G. Chen, X. Han, W. Yao and Y. Lu, *Org. Lett.*, 2012, **14**, 3764; (s) H.-P. Deng, Y. Wei and M. Shi, *Adv. Synth. Catal.*, 2012, **354**, 783; (t) J. Marco-Martinez, V. Marcos, S. Reboredo, S. Filippone and N. Martin, *Angew. Chem., Int. Ed.*, 2013, **52**, 5115; (u) H. Yu, L. Zhang, Z. Yang, Z. Li, Y. Zhao, Y. Xiao and H. Guo, *J. Org. Chem.*, 2013, **78**, 8427; (v) X.-N. Zhang and M. Shi, *ACS Catal.*, 2013, **3**, 507; (w) D. Wang, Y. Lei, Y. Wei and M. Shi, *Chem.-Eur. J.*, 2014, **20**, 15325; (x) C. E. Henry, Q. H. Xu, Y. C. Fan, T. J. Martin, L. Belding, T. Dudding and O. Kwon, *J. Am. Chem. Soc.*, 2014, **136**, 11890; (y) Z. Gao, C. Wang, C. Yuan, L. Zhou, Z. Sun, Y. Xiao and H. Guo, *RSC Adv.*, 2015, **5**, 105359; (z) X. Han, W.-L. Chan, W. Yao, Y. Wang and Y. Lu, *Angew. Chem., Int. Ed.*, 2016, **55**, 6492.
- 5 For [4 + 1] annulation, see: (a) X. Meng, Y. Huang and R. Chen, *Org. Lett.*, 2009, **11**, 137; (b) Q. Zhang, L. Yang and X. Tong, *J. Am. Chem. Soc.*, 2010, **132**, 2550; (c) X. N. Zhang, H. P. Deng, L. Huang, Y. Wei and M. Shi, *Chem. Commun.*, 2012, **48**, 8664; (d) D. T. Ziegler, L. Riesgo, T. Ikeda, Y. Fujiwara and G. C. Fu, *Angew. Chem., Int. Ed.*, 2014, **53**, 13183; (e) X. Han, W. Yao, T. Wang, Y. R. Tan, Z. Yan, J. Kwiatkowski and Y. Lu, *Angew. Chem., Int. Ed.*, 2014, **53**, 5643; (f) S. Kramer and G. C. Fu, *J. Am. Chem. Soc.*, 2015, **137**, 3803; (g) Z. Gao, C. Wang, C. Yuan, L. Zhou, Y. Xiao and H. Guo, *Chem. Commun.*, 2015, **51**, 12653.
- 6 For [4 + 2] annulation, see: (a) M. P. S. Ishar, K. Kumar, S. Kaur, S. Kumar, N. K. Girdhar, S. Sachar, A. Marwaha and A. Kapoor, *Org. Lett.*, 2001, **3**, 2133; (b) X.-F. Zhu, J. Lan and O. Kwon, *J. Am. Chem. Soc.*, 2003, **125**, 4716; (c) R. P. Wurz and G. C. Fu, *J. Am. Chem. Soc.*, 2005, **127**, 12234; (d) X.-F. Zhu, A.-P. Schaffner, R. C. Li and O. Kwon, *Org. Lett.*, 2005, **7**, 2977; (e) Y. S. Tran and O. Kwon, *J. Am. Chem. Soc.*, 2007, **129**, 12632; (f) S. Castellano, H. D. G. Fiji, S. S. Kinderman, M. Watanabe, P. de Leon, F. Tamanoi and O. Kwon, *J. Am. Chem. Soc.*, 2007, **129**, 5843; (g) X. Meng, Y. Huang, H. Zhao, P. Xie, J. Ma and R. Chen, *Org. Lett.*, 2009, **11**, 991; (h) H. Xiao, Z. Chai, H. F. Wang, X. W. Wang, D. D. Cao, W. Liu, Y. P. Lu, Y. Q. Yang and G. Zhao, *Chem.-Eur. J.*, 2011, **17**, 10562; (i) F. Zhong, X. Han, Y. Wang and Y. Lu, *Chem. Sci.*, 2012, **3**, 1231; (j) H. Xiao, Z. Chai, D. Cao, H. Wang, J. Chen and G. Zhao, *Org. Biomol. Chem.*, 2012, **10**, 3195; (k) S. Takizawa, F. A. Arteaga, Y. Yoshida, M. Suzuki and H. Sasai, *Asian J. Org. Chem.*, 2014, **3**, 412; (l) H. Yu, L. Zhang, Z. Li, H. Liu, B. Wang, Y. Xiao and H. Guo, *Tetrahedron*, 2014, **70**, 340; (m) W. J. Yao, X. W. Dou and Y. Lu, *J. Am. Chem. Soc.*, 2015, **137**, 54; (n) W. Yang, Y. Zhang, S. Qiu, C. Zhao, L. Zhang, H. Liu, L. Zhou, Y. Xiao and H. Guo, *RSC Adv.*, 2015, **5**, 62343; (o) H. Liu, Y. Liu, C. Yuan, G.-P. Wang, S.-F. Zhu, Y. Wu, B. Wang, Z. Sun, Y. Xiao, Q.-L. Zhou and H. Guo, *Org. Lett.*, 2016, **18**, 1302; (p) C. Wang, Z. Gao, L. Zhou, C. Yuan, Z. Xun, Y. Xiao and H. Guo, *Org. Lett.*, 2016, **18**, 3418; (q) C. Wang, H. Jia, C. Zhang, Z. Gao, L. Zhou, C. Yuan, Y. Xiao and H. Guo, *J. Org. Chem.*, 2017, **82**, 633.
- 7 For an example of [3 + 3] cycloaddition, see: H. Guo, Q. Xu and O. Kwon, *J. Am. Chem. Soc.*, 2009, **131**, 6318.
- 8 For [4 + 3] annulation, see: (a) K. Kumar, R. Kapoor, A. Kapur and M. P. S. Ishar, *Org. Lett.*, 2000, **2**, 2023; (b) S. Zheng and X. Lu, *Org. Lett.*, 2009, **11**, 3978; (c) R. Zhou, J. Wang, C. Duan and Z. He, *Org. Lett.*, 2012, **14**, 6134.
- 9 For [2 + 2 + 2] annulation, see: X. Zhu, C. E. Henry, J. Wang, T. Dudding and O. Kwon, *Org. Lett.*, 2005, **7**, 1387.
- 10 For an example of [8 + 2] cycloaddition, see: K. Kumar, A. Kapur and M. P. S. Ishar, *Org. Lett.*, 2000, **2**, 787.
- 11 For selected examples on other annulations, see: (a) B. M. Trost and C.-J. Li, *J. Am. Chem. Soc.*, 1994, **116**, 10819; (b) C. Lu and X. Lu, *Org. Lett.*, 2002, **4**, 4677; (c) B. Liu, R. Davis, B. Joshi and D. W. Reynolds, *J. Org. Chem.*, 2002, **67**, 4595; (d) H. Kuroda, I. Tomita and T. Endo, *Org. Lett.*, 2003, **5**, 129; (e) Y. Du, X. Lu and C. Zhang, *Angew. Chem., Int. Ed.*, 2003, **42**, 1035; (f) R. K. Thalji and W. R. Roush, *J. Am. Chem. Soc.*, 2005, **127**, 16778; (g) F. Silva, M. Sawaki and V. Gouverneur, *Org. Lett.*, 2006, **8**, 5417; (h) S. Gabillet, D. Lecercle, O. Loreau, M. Carboni, S. Dezard, J.-M. Gomis and F. Taran, *Org. Lett.*, 2007, **9**, 3925; (i) V. Nair, S. C. Mathew, A. T. Biju and E. Suresh, *Angew. Chem., Int. Ed.*, 2007, **46**, 2070; (j) L.-W. Ye, X.-L. Sun, Q.-G. Wang and Y. Tang, *Angew. Chem., Int. Ed.*, 2007, **46**, 5951; (k) V. Sriramurthy, G. A. Barcan and O. Kwon, *J. Am. Chem. Soc.*, 2007, **129**, 12928; (l) Y. K. Chung and G. C. Fu, *Angew. Chem., Int. Ed.*, 2009, **48**, 2225; (m) L. W. Ye, S. B. Wang, Q. G. Wang, X. L. Sun, Y. Tang and Y. G. Zhou, *Chem. Commun.*, 2009, **45**, 3092; (n) S. Takizawa, N. Inoue, S. Hirata and H. Sasai, *Angew. Chem., Int. Ed.*, 2010, **49**, 9725; (o) Z. Shi, P. Yu, T. P. Loh and G. Zhong, *Angew. Chem., Int. Ed.*, 2012, **51**, 7825; (p) F. Zhong, X. Dou, X. Han, W. Yao, Q. Zhu, Y. Meng and Y. Lu, *Angew. Chem., Int. Ed.*, 2013, **52**, 943; (q) R. J. Lundgren, A. Wilsily, N. Marion, C. Ma, Y. K. Chung and G. C. Fu, *Angew. Chem., Int. Ed.*, 2013, **52**, 2525.
- 12 (a) R. Na, C. Jing, Q. Xu, H. Jiang, X. Wu, Y. Shi, J. Zhong, M. Wang, D. Benitez, E. Tkatchouk, W. A. Goddard III, H. Guo and O. Kwon, *J. Am. Chem. Soc.*, 2011, **133**, 13337; (b) Z. Li, H. Yu, H. Liu, L. Zhang, H. Jiang, B. Wang and H. Guo, *Chem.-Eur. J.*, 2014, **20**, 1731; (c) D. Wang, Y. Lei, Y. Wei and M. Shi, *Chem.-Eur. J.*, 2014, **20**, 15325; (d) C. Yuan, L. Zhou, Z. Sun and H. Guo, *RSC Adv.*, 2016, **6**, 77931.
- 13 (a) J. Liu, H. Liu, R. Na, G. Wang, Z. Li, H. Yu, M. Wang, J. Zhong and H. Guo, *Chem. Lett.*, 2012, **41**, 218; (b) L. Zhang, H. Liu, G. Qiao, Z. Hou, Y. Liu, Y. Xiao and



- H. Guo, *J. Am. Chem. Soc.*, 2015, **137**, 4316; (c) L. Liang and Y. Huang, *Org. Lett.*, 2016, **18**, 2604; (d) Z. Li, H. Yu, Y. Liu, L. Zhou, Z. Sun and H. Guo, *Adv. Synth. Catal.*, 2016, **358**, 1880.
- 14 (a) C. Jing, R. Na, B. Wang, H. Liu, L. Zhang, J. Liu, M. Wang, J. Zhong, O. Kwon and H. Guo, *Adv. Synth. Catal.*, 2012, **354**, 1023; (b) Z. Li, H. Yu, Y. Feng, Z. Hou, L. Zhang, W. Yang, Y. Wu, Y. Xiao and H. Guo, *RSC Adv.*, 2015, **5**, 34481; (c) C. Yuan, L. Zhou, M. Xia, Z. Sun, D. Wang and H. Guo, *Org. Lett.*, 2016, **18**, 5644.
- 15 For some reviews on 1,3-dipolar cycloadditions of nitrones, see: (a) M. Frederikson, *Tetrahedron*, 1997, **53**, 403; (b) K. V. Gothelf and K. A. Jørgensen, *Chem. Commun.*, 2000, 1449; (c) R. C. F. Jones and J. N. Martin, *The Chemistry of Heterocyclic Compounds*, in *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*, ed. A. Padwa and W. H. Pearson, Wiley, New York, 2002, vol. 59, pp. 1–81; (d) K. V. Gothelf, in *Cycloaddition Reactions in Organic Synthesis*, ed. S. Kobayashi and K. A. Jørgensen, Wiley-VCH, Weinheim, Germany, 2002, pp. 211–245; (e) *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry—Toward Heterocycles and Natural Products*, ed. A. Padwa and W. H. Pearson, John Wiley and Sons, Hoboken, NJ, 2003; (f) P. N. Confalone and E. M. Huie, The [3 + 2] Nitron-Olefin Cycloaddition Reaction, in *Organic Reactions*, John Wiley & Sons, 2004, vol. 36, p. 1; (g) H. Feuer, *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis*, 2nd edn, John Wiley & Sons, Hoboken, NJ, 2008; (h) T. Hashimoto and K. Maruoka, in *Handbook of Cyclization Reactions*, ed. S. Ma, Wiley-VCH, Weinheim, Germany, 2009, ch. 3, pp. 87–168; (i) L. L. Anderson, M. A. Kroc, T. W. Reidl and J. Son, *J. Org. Chem.*, 2016, **81**, 9521. For two examples on cycloaddition of nitrones with phenylsulfonyl alkenes, see: (j) M. Burdisso, R. Gandolfi and P. Grünanger, *J. Org. Chem.*, 1990, **55**, 3427; (k) Y. Dürüst and C. Altuğ, *J. Heterocycl. Chem.*, 2006, **43**, 1267.
- 16 (a) A. R. Minter, B. B. Brennan and A. K. Mapp, *J. Am. Chem. Soc.*, 2004, **126**, 10504; (b) I. A. O'Neil, V. E. Ramos, G. L. Ellis, E. Cleator, A. P. Chorlton and S. B. Kalindjian, *Tetrahedron Lett.*, 2004, **45**, 3659; (c) A. T. Saito, T. Yamada, S. Miyazaki and T. Otani, *Tetrahedron Lett.*, 2004, **45**, 9581; (d) A. T. Saito, T. Yamada, S. Miyazaki and T. Otani, *Tetrahedron Lett.*, 2004, **45**, 9585; (e) N. R. Iralapati, J. E. Baldwin, R. M. Adlington, G. J. Pritchard and A. R. Cowley, *Tetrahedron*, 2005, **61**, 1773; (f) J. K. Gallos, C. I. Stathakis, S. S. Kotoulas and A. E. Koumbis, *J. Org. Chem.*, 2005, **70**, 6884; (g) S. Akai, K. Tanimoto, Y. Kanao, S. Omura and Y. Kita, *Chem. Commun.*, 2005, 2369; (h) S. M. Lait, D. A. Rankic and B. A. Keay, *Chem. Rev.*, 2007, **107**, 767; (i) M. S. Wilson and A. Padwa, *J. Org. Chem.*, 2008, **73**, 9601; (j) K. Clinch, G. B. Evans, R. F. Fröhlich, R. H. Furneaux, P. M. Kelly, L. Legentil, A. S. Murkin, L. Li, V. L. Schramm, P. C. Tyler and A. D. Woolhouse, *J. Med. Chem.*, 2009, **52**, 1126; (k) D. G. Piotrowska, J. Balzarini and I. E. Glowacka, *Eur. J. Med. Chem.*, 2012, **47**, 501; (l) C.-Z. Yao, Z.-F. Xiao, X.-S. Ning, J. Liu, X.-W. Zhang and Y.-B. Kang, *Org. Lett.*, 2014, **16**, 5824; (m) J. Hoogenboom, H. Zuilhof and T. Wennekes, *Org. Lett.*, 2015, **17**, 5550.
- 17 The crystallographic data for **3b** has been deposited with the Cambridge Crystallographic Data Centre as supplementary number CCDC 1532199 (see ESI).

