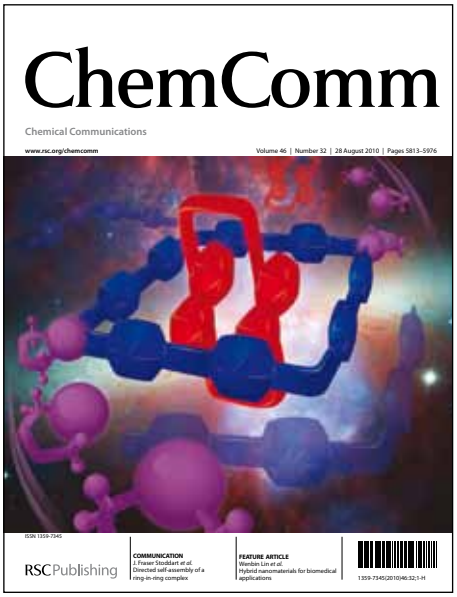
ChemComm

# Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: C. Wang, Q. Li, T. Liu, L. Wei, X. Zhou and H. Tao, *Chem. Commun.*, 2013, DOI: 10.1039/C3CC45493B.




This is an *Accepted Manuscript*, which has been through the RSC Publishing peer review process and has been accepted for publication.

*Accepted Manuscripts* are published online shortly after acceptance, which is prior to technical editing, formatting and proof reading. This free service from RSC Publishing allows authors to make their results available to the community, in citable form, before publication of the edited article. This *Accepted Manuscript* will be replaced by the edited and formatted *Advance Article* as soon as this is available.

To cite this manuscript please use its permanent Digital Object Identifier (DOI®), which is identical for all formats of publication.

More information about *Accepted Manuscripts* can be found in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics contained in the manuscript submitted by the author(s) which may alter content, and that the standard **Terms & Conditions** and the **ethical guidelines** that apply to the journal are still applicable. In no event shall the RSC be held responsible for any errors or omissions in these *Accepted Manuscript* manuscripts or any consequences arising from the use of any information contained in them.

Dynamic Article Links ▶
View Article Online
DOI: 10.1039/C3CC45493B

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/chemcomm

Communication

# *exo*-Selective Construction of Spiro-[butyrolactone-pyrrolidine] *via* 1,3-Dipolar Cycloaddition of Azomethine Ylides with α-Methylene-γ-butyrolactone Catalyzed by Cu(I)/DTBM-BIPHEP†

**Qing-Hua Li,[a] Tang-Lin Liu,[a] Liang Wei,[a] Xiang Zhou,[a] Hai-Yan Tao,[a] and Chun-Jiang Wang*[a,b]**

***Received (in XXX, XXX) Xth XXXXXXXXX 200X, Accepted Xth XXXXXXXXX 200X***
**DOI: 10.1039/b000000x**

**An expedient access to optically active spiro-[butyrolactone-pyrrolidine] was successfully developed *via* an unprecedented Cu(I)-catalyzed *exo*-selective 1,3-DC of azomethine ylides with α-methylene-γ-butyrolactone, which exhibited high diastereoselectivity (>98:2), excellent enantioselectivity (96–>99% ee) and broad substrate scope under mild conditions.**

The privileged spirocyclic [butyrolactone-pyrrolidine] skeletons with multiple contiguous stereogenic centers are the core structural elements prevalent in a large number of natural alkaloids and unnatural compounds exhibiting important biological activities and building blocks in organic synthesis,[1] typical examples are shown in Figure 1. Spirocycle **A** and **B** are the key intermediates for the synthesis of complex marine alkaloid (-)-sarain A[2a] and *Cephalotaxus* alkaloid cephalotaxine,[2b] and spirocyclic **C** exhibits anticancer activity.[3] Inspired by the varied and significant biological activities, different synthetic approaches have been developed in pursuit of the structurally diversified and stereocontrolled [butyrolactone-pyrrolidine] skeletons in the past decades. The catalytic asymmetric 1,3-dipolar cycloaddition[4,5] of azomethine ylides to electron-deficient alkenes provides a powerful and atom-economical route to synthesize a variety of structurally and stereochemically rich spirocyclic pyrrolidines bearing spiro quaternary stereogenic center.[6,7] The first catalytic asymmetric synthesis of spiro pyrrolidine-oxindole derivatives was realized by Gong *via* an elegant organocatalyzed asymmetric 1,3-dipolar cycloaddition reaction between *N*-Ac 2-oxoindolin-3-ylidenes and *in situ* formed azomethine ylides.[6a] Subsequently, Cu(I)-catalyzed asymmetric 1,3-dipolar cycloaddition for constructing such structures was reported by Waldmann and us, respectively.[6b,6c] Recently, asymmetric approach to spiro pyrrolidine-oxindoles was also fulfilled by Arai and co-workers[6d] employing Ni(II)-complex and Wang[6e] employing amine-thiourea as the organocatalyst. Despite excellent results achieved for asymmetric synthesis of spirocyclic pyrrolidines, most of dipolarophiles applied in these reactions are 2-oxoindolin-3-ylidene,[6a-e] cyclopropyliden acetates,[7a] and 2-alkylidene cycloketones.[7b] In contrast, α-methylene-γ-butyrolactone have been seldom studied in the catalytic asymmetric 1,3-dipolar cycloaddition although the lactone moiety possesses highly biological activity profile.[8] To the best of our knowledge, only limited racemic examples have been reported involving α-methylene-γ-butyrolactone as the dipolarophile so far.[9] and we believe this represents a major challenge.

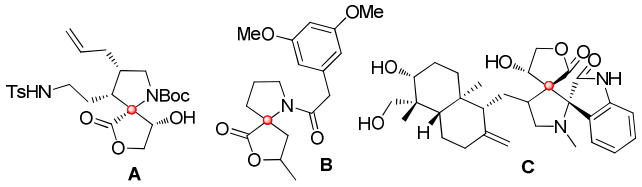
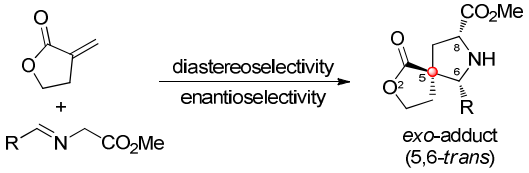



**Figure 1.** Key intermediates containing spiro-[butylactone-pyrrolidine] motifs.

Herein, we reported an unprecedented Cu(I)-catalyzed asymmetric 1,3-dipolar cycloaddition of various azomethine ylides with α-methylene-γ-butyrolactone, providing the efficient and facile access to the bioactive *exo*-selective[10] spiro-[butyrolactone-pyrrolidine] with excellent levels of diastereo-selectivity and enantioselectivity.




**Scheme 1.** *exo*-Selective construction of spiro-[butyrolactone-pyrrolidine] via 1,3-DC of azomethine ylide with α-methylene-γ-butyrolactone.

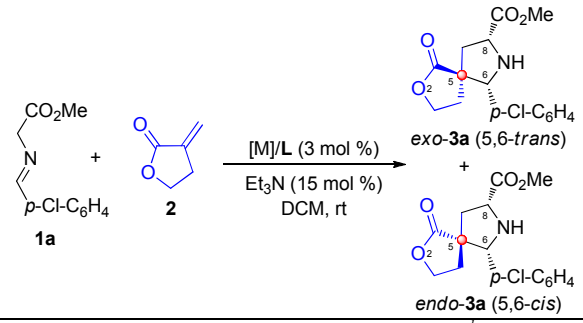
Initially, we began our investigation by using α-methylene-γ-butyrolactone **2** and *N*-(4-chloro-benzylidene)-glycine methyl ester **1a** as the dipolar in the presence of AgOAc/(*S*)-BINAP **L1** (3 mol%) and $Et_3N$ (15 mol%) in DCM at room temperature. Gratifyingly, the 1,3-dipolar addition reaction proceeded smoothly affording *exo*-adduct **3a** as the major diastereomer (*exo*/*endo* = 66:34) with moderate enantioselectivity (Table 1, entry 1). Encouraged by this result, different metal salts and chiral bisphosphine ligands were subsequently examined to establish optimal reaction conditions, and the representative

[a]*College of Chemistry and Molecular Sciences, Wuhan University, Wuhan 430072, China. E-mail: cjwang@whu.edu.cn Fax: 86-27-68754067*
[b]*State Key Laboratory of Elemento-organic Chemistry, Nankai University Tianjin, 300071, China*
†Electronic supplementary information (ESI) available: Experimental section. CCDC 935824. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0cc00000x.

View Article Online
DOI: 10.1039/C3CC45493B

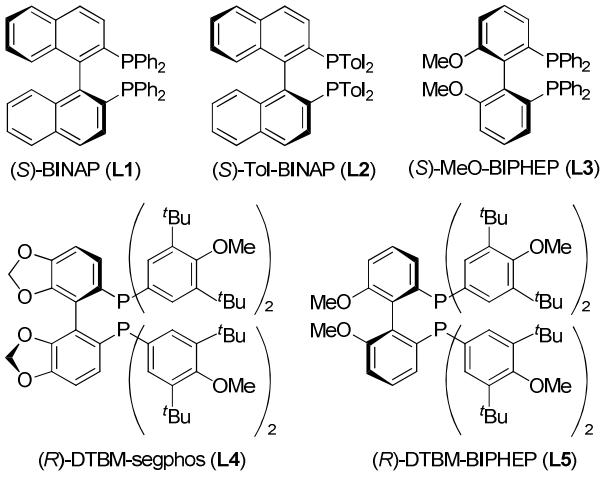


**Table 1.** Screening studies of the catalytic asymmetric 1,3-DC of imino ester **1a** with α-methylene-γ-butyrolactone **2**[a]




| Entry | [M] | L | *exo*/*endo* | Yield (%)[b] | Ee (%)[c] |
|---|---|---|---|---|---|
| 1 | AgOAc | **L1** | 66:34 | 75 | 55 |
| 2 | $Cu(CH_3CN)_4BF_4$ | **L1** | 60:40 | 80 | 74 |
| 3 | $Cu(CH_3CN)_4BF_4$ | **L2** | 83:17 | 79 | 50 |
| 4 | $Cu(CH_3CN)_4BF_4$ | **L3** | 83:17 | 72 | 83 |
| 5 | $Cu(CH_3CN)_4BF_4$ | **L4** | >98:2 | 85 | >99 |
| 6 | $Cu(CH_3CN)_4BF_4$ | **L5** | >98:2 | 88 | >99 |

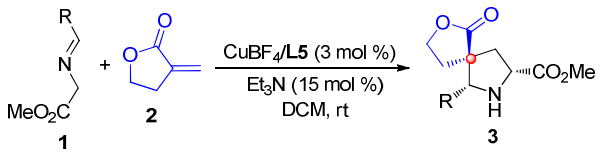
[a] All reactions were carried out with 0.35 mmol of **1a** and 0.23 mmol of **2** in 2 mL solvent for 1-2 h. [b] Isolated yields of both *exo*-**3a** and *endo*-**3a**. [c] Ee of *exo*-**3a** was determined by HPLC analysis.




results were summarized in Table 1. Both AgOAc/(*S*)-BINAP and $Cu(MeCN)_4BF_4$/(*S*)-BINAP complexes exhibited high *exo*-selectivity, but copper complex gave better asymmetric induction and higher catalytic activity, which was chosen as the metal precursor in the further ligand survey (Table 1, entries 1 and 2). The *exo*-selectivity was improved to 83:17 when another two commercially-available chiral axially bisphosphine ligand (*S*)-Tol-BINAP (**L2**) or (*S*)-MeO-BIPHEP (**L3**) was employed in this transformation, but the latter exhibited better enantioselective control (entries 3 and 4). Further ligand screening chiral axially biphenyl bisphosphine skeleton revealed that the bulky and electron-donating biphenyl ligands (*R*)-DTBM-segphos and (*R*)-DTBM-BIPHEP ((2,2'-bis[di(3,5-di-*t*-butyl-4-methoxyphenyl) phosphino]-6,6'-dimeth-oxy-1,1'-biphenyl)) not only remarkably improved the diastereoselectivity (>98:2) but also gave almost perfect enantioselectivity (Table 1, entries 5 and 6).

To explore the scope of the reaction, the Cu(I)/(*R*)-DTBM-BIPHEP catalyzed 1,3-dipolar cycloaddition of various imino esters derived from glycinate with α-methylene butyrolactone were carried out under the optimized reaction conditions. The results are summarized in Table 2, all reactions proceeded smoothly regardless of the substitution pattern on the aromatic

**Table 2.** Substrate scope of Cu(I)-catalyzed *exo*-selective 1,3-DC of various imino esters **1** with α-methylene-γ-butyrolactone **2**[a]




| Entry | R | 3 | Yield (%)[b] | Ee (%)[c] |
|---|---|---|---|---|
| 1 | *p*-Cl-$C_6H_4$ (**1a**) | **3a** | 88 | >99 |
| 2 | *o*-Cl-$C_6H_4$ (**1b**) | **3b** | 80 | 98 |
| 3 | *m*-Cl-$C_6H_4$ (**1c**) | **3c** | 72 | 99 |
| 4 | *p*-Br-$C_6H_4$ (**1d**) | **3d** | 85 | 99 |
| 5 | Ph (**1e**) | **3e** | 83 | 99 |
| 6 | *p*-Me-$C_6H_4$ (**1f**) | **3f** | 78 | 99 |
| 7 | *o*-Me-$C_6H_4$ (**1g**) | **3g** | 70 | 99 |
| 8 | *m*-Me-$C_6H_4$ (**1h**) | **3h** | 75 | 97 |
| 9 | *p*-MeO-$C_6H_4$ (**1i**) | **3i** | 80 | 99 |
| 10 | 2-furyl (**1j**) | **3j** | 74 | 98 |
| 11 | 2-thienyl (**1k**) | **3k** | 84 | 96 |
| 12 | 1-Napthyl (**1l**) | **3l** | 83 | 97 |
| 13 | 2-Napthyl (**1m**) | **3m** | 85 | 98 |
| 14[d] | $PhCH_2CH_2$ (**1n**) | **3n** | 62 | 99 |
| 15[d] | Cy (**1o**) | **3o** | 65 | 96 |

[a] All reactions were carried out with 0.35 mmol of **1** and 0.23 mmol of **2** in 2 mL DCM for 1-2 h. [b] Isolated yield. [c] Determined by HPLC analysis. [d] Inorganic base $CsCO_3$ was used, 10 h.

ring to give the corresponding *exo*-selective spiro-[butyrolactone-pyrrolidines] **3** in good yields and with excellent enantioselectivities (96->99% ee) as single diastereomers (entries 1-9). It is noteworthy that comparable results were still achieved for the sterically hindered *ortho*-chloro and *ortho*-methyl-substituted imino esters **1b** and **1g** in terms of diastereo-/enantioselectivity (entries 2 and 7). Additionally, the heteroaryl substituted imino esters **1j** and **1k** were also tolerated in this transformation leading to 98% and 96% ee, respectively (entries 10 and 11). Similarly, high enantioselectivity was obtained in the reaction of imine **1l** and **1m**, derived from 1-naphthylaldehyde, 2-naphthylaldehyde with **2** to afford the adducts **3l** and **3m** with 97% and 98% ee, respectively (entries 12 and 13). Remarkably, less reactive alkyl substituted imino esters worked well in this transformation affording the similarly high level of diastereo-/enantioselectivity (entries 14 and 15).

Having successfully achieved the excellent stereoselectivity in the 1,3-dipolar cycloaddition of α-methylene-γ-butyrolactone with glycine derived imino esters, we next turned our attention to the more challenging homoserine lactone derived cyclic imines, from which tricyclic skeleton bearing two quaternery stereogenic centers and two butylactones would be generated simultaneously in this transformation. A wide range of cyclic imino esters **4a**-**4m**, derived from various aromatic or aliphatic aldehydes, reacted smoothly with α-methylene-γ-butyrolactone **2** to afford the corresponding tricyclic adducts **5a**-**5m** in good yields and excellent stereoselectivities (Table 3). Both electron-donating and electron-withdrawing substituents at different positions on the aromatic ring were tolerated (entries 1-9). Interestingly, *ortho*-chloro and *ortho*-methyl-substituted imino esters **4b** and **4g** gave ee values up to 99% without losing both yields and stereoselectivities (entries 2 and 7). Cyclic imino esters **4k** derived from 2-naphthylaldehyde also worked well in this transformation to provide **5k** with satisfactory result (entry 11). It is noteworthy that better result was achieved for heteroaromatic aldehyde derived imino ester **4j** (entry 10). Comparable outcomes were

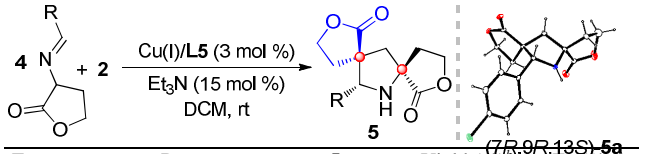
View Article Online
DOI: 10.1039/C3CC45493B





also achieved for the less reactive imino ester derived from aliphatic cyclohexanecarbaldehyde and 3-phenylpropanaldehyde, respectively (entries 12 and 13). No cycloaddition reaction occurred when trisubstituted (*E*)-3-benzylidenedihydrofuran-2(3*H*)-one was tested as the dipolarophile probably due to the unfavored steric hindrance and the less reactivity.

**Table 3.** Substrate scope of Cu(I)-catalyzed *exo*-selective 1,3-DC of various cyclic imino esters **4** with α-methylene-γ-butyrolactone **2**[a]




| Entry | R | 5 | Yield (%)[b] | Ee (%)[c] |
|---|---|---|---|---|
| 1[d] | *p*-Cl-$C_6H_4$ (**4a**) | **5a** | 82 | >99 |
| 2 | *o*-Cl-$C_6H_4$ (**4b**) | **5b** | 80 | >99 |
| 3 | *m*-Cl-$C_6H_4$ (**4c**) | **5c** | 81 | 99 |
| 4 | *p*-Br-$C_6H_4$ (**4d**) | **5d** | 84 | 99 |
| 5 | Ph (**4e**) | **5e** | 83 | >99 |
| 6 | *p*-Me-$C_6H_4$ (**4f**) | **5f** | 75 | >99 |
| 7 | *o*-Me-$C_6H_4$ (**4g**) | **5g** | 68 | >99 |
| 8 | *m*-Me-$C_6H_4$ (**4h**) | **5h** | 75 | >99 |
| 9 | *p*-MeO-$C_6H_4$ (**4i**) | **5i** | 80 | >99 |
| 10 | 2-thienyl (**4j**) | **5j** | 84 | >99 |
| 11 | 2-Napthyl (**4k**) | **5k** | 82 | >99 |
| 12[e] | $PhCH_2CH_2$ (**4l**) | **5l** | 60 | 99 |
| 13[e] | Cy (**4m**) | **5m** | 67 | 97 |

[a] All reactions were carried out with 0.35 mmol of **4** and 0.23 mmol of **2** in 2 mL solvent for 1-2 h. [b] Isolated yield. [c] Ee was determined by HPLC analysis. [d] The absolute configuration of **5a** was determined as (7*R*,9*R*,13*S*) by X-ray diffraction analysis. [e] Inorganic base $CsCO_3$ was used, 10 h.

In summary, we have successfully developed a Cu(I)-catalyzed *exo*-selective 1,3-dipolar cycloaddition reaction of azomethine ylides with α-methylene-γ-butyrolactone to provide a series of spirocyclic-[butyrolactone-pyrrolidine] bearing one to two quaternary stereogenic centers for the first time (See ESI for the proposed transition states for the *exo*-selectivity). The readily available precursors were emlpoyed under mild conditions for the straightforward construction of highly functionalized bicyclic or tricyclic skeletons with excellent levels of stereocontrol, and the great importance of the enantiomerically enriched spiro-[butyrolactone-pyrrolidine] make the current methodology particularly interesting in synthetic chemistry. Efforts are currently underway to elucidate the mechanistic details and the scope and limitations of this reaction, and the results will be reported in due course.

This work is supported by the 973 program (2011CB808600), NSFC (20972117, 21172176), NCET-10-0649, IRT1030, and the Fundamental Research Funds for the Central Universities.

## Notes and references

‡ Crystal data for (7*R*,9*R*,13*S*)-**5a**: $C_{16}H_{16}ClNO_4$, $M_r$ = 321.75, $T$ = 293 K, Orthorhombic, space group $P2_12_12_1$, $a$ = 6.4177(9), $b$ = 12.2541(18), $c$ = 19.540(3) Å, $V$ = 1536.7(4) Å$^3$, $Z$ = 4, 2619 unique reflections, final $R_1$ = 0.0805 and $wR_2$ = 0.2547 for 3006 observed [$I>2\sigma(I)$] reflections, Flack $\chi$ = 0.2(2). CCDC 935824.


1 For very recent review, see: (*a*) L. Hong and R. Wang, *Adv. Synth. Catal.*, 2013, **355**, 1023; (*b*) *The Alkaloids*, Vol. *14*; J. S. Bindra, R. H. F. Manske, Eds.; Academic Press: New York, 1973; (c) C. V. Galliford and K. A. Scheidt, *Angew. Chem., Int. Ed.*, 2007, **46**, 8748; (*d*) T. H. Kang, K. Matsumoto, Y. Murakami, H. Takayama, M. Kitajima, N. Aimi and H. Watanabe, *Eur. J. Pharmacol.*, 2002, **444**, 39; (*e*) K. K. Lee, B.-N. Zhou, D. G. I. Kingston, A. J. Vaisberg and G. B. Hammond, *Planta Med.*, 1999, **65**, 759; (*f*) A. A. Raj, R. Raghunathan, M. R. SrideviKumari and N. Raman, *Bioorg. Med. Chem.*, 2003, **11**, 407.

2 (*a*) M. H. Becker, P. Chua, R. Downham, C. J. Douglas, N. K. Garg, S. Hiebert, S. Jaroch, R. T. Matsuoka, J. A. Middleton, F. W. Ng and L. E. Overman, *J. Am. Chem. Soc.*, 2007, **129**, 11987. (*b*) M. R. Sun, H. T. Lu, Y. Z. Wang, H. Yang and H. M. Liu, *J. Org. Chem.*, 2009, **74**, 2213.

3 A. Hazra, Y. P. Bharitkar, D. Chakraborty, S. K. Mondal, N. Singal, S. Mondal, A. Maity, R. Paira, S. Banerjee and N. B. Mondal, *ACS Comb. Sci.,* 2013, **15**, 41.

4 For recent reviews about 1,3-dipolar cycloaddition reactions of azomethine ylides, see: (*a*) J. Yu, F. Shi and L.-Z. Gong, *Acc. Chem. Res.*, 2011, **44**, 1156; (*b*) J. Adrio and J. C. Carretero, *Chem. Commun.*, 2011, **47**, 6784; (*c*) B. Engels and M. Christl, *Angew. Chem., Int. Ed.*, 2009, **48**, 7968; (*d*) L. M. Stanley and M. P. Sibi, *Chem. Rev.*, 2008, **108**, 2887; (*e*) M. Alvarez-Corral, M. Munoz-Dorado and I. Rodrıguez-Garcıa, *Chem. Rev.*, 2008, **108**, 3174; (*f*) M. Bonin, A. Chauveau and L. Micouin, *Synlett*, 2006, 2349; (*g*) C. Nájera and J. M. Sansano, *Angew. Chem., Int. Ed.,* 2005, **44**, 6272.

5 For first catalytic asymmetric 1,3-dipolar cycloaddition reactions of azomethine ylides, see: (*a*) J. M. Longmire, B. Wang and X. Zhang, *J. Am. Chem. Soc.*, 2002, **124**, 13400; (*b*) A. S. Gothelf, K. V. Gothelf, R. G. Hazell and K. A. Jørgensen, *Angew. Chem., Int. Ed.*, 2002, **41**, 4236; For recent examples, see: (*c*) L. He, X.-H. Chen, D.-N. Wang, S.-W. Luo, W.-Q. Zhang, J. Yu, L. Ren and L.-Z. Gong, *J. Am. Chem. Soc.*, 2011, **133**, 13504; (*d*) X.-H. Chen, W.-Q. Zhang and L.-Z. Gong, *J. Am. Chem. Soc.*, 2008, **130**, 5652; (*e*) W. Zeng, G.-Y. Chen, Y.-G. Zhou and Y.-X. Li, *J. Am. Chem. Soc.*, 2007, **129**, 750; (*f*) W. Zeng and Y.-G. Zhou, *Org. Lett.*, 2005, **7**, 5055; (*g*) J.-W. Shi, M.-X. Zhao, Z.-Y. Lei and M. Shi, *J. Org. Chem.*, 2008, **73**, 305; (*h*) T. Arai, A. Mishiro, N. Yokoyama, K. Suzuli and H. Sato, *J. Am. Chem. Soc.*, 2010, **132**, 5338; (*i*) C. Nájera, M. D. G. Retamosa and J. Sansano, *Angew. Chem., Int. Ed.*, 2008, **47**, 6055; (*j*) C. Chen, X. Li and S. L. Schreiber, *J. Am. Chem. Soc.*, 2003, **125**, 10174; (*k*) X.-X. Yan, Q. Peng, Y. Zhang, K. Zhang, W. Hong, X.-L. Hou and Y.-D. Wu, *Angew. Chem., Int. Ed.*, 2006, **45**, 1979. (*l*) S. Cabrera, R. Gómez Arrayás and J. C. Carretero, *J. Am. Chem. Soc.*, 2005, **127**, 16394; (*m*) S. Saito, T. Tsubogo and S. Kobayashi, *J. Am. Chem. Soc.*, 2007, **129**, 5364; (*n*) Y. Yamashita, T. Imaizumi and S. Kobayashi, *Angew. Chem., Int. Ed.*, 2011, **50**, 4893; (*o*) H. Y. Kim, J.-Y. Li, S. Kim and K. Oh, *J. Am. Chem. Soc.*, 2011, **133**, 20750; (*p*) J. Hernández-Toribio, S. Padilla, J. Adrio and J. C. Carretero, *Angew. Chem., Int. Ed.*, 2012, **51**, 8854.

6 (*a*) X.-H. Chen, Q. Wei, S.-W. Luo, H. Xiao and L.-Z. Gong, *J. Am. Chem. Soc.*, 2009, **131**, 13819; (*b*) A. P. Antonchick, C. Gerding-Reimers, M. Catarinella, M. Schürmann, H. Preut, S. Ziegler, D. Rauh and H. Waldmann, *Nature Chem.*, 2010, **2**, 735; (*c*) T.-L. Liu, Z.-Y. Xue, H.-Y. Tao and C.-J. Wang, *Org. Biomol. Chem.*, 2011, **9**, 1980; (*d*) A. Awata and T. Arai, *Chem. Eur. J.*, 2012, **18**, 8278; (*e*) L. Wang, X.-M. Shi, W.-P. Dong, L.-P. Zhu, R. Wang, *Chem. Commun.*, 2013, **49**, 3458; (*f*) T.-L. Liu, Z.-L. He, H.-Y. Tao and C.-J. Wang, *Chem. Eur. J.*, 2012, **18**, 8042; (*g*) K. Liu, H.-L. Teng, L. Yao, H.-Y. Tao and C.-J. Wang, *Org. Lett.* 2013, **15**, 2250.

7 (*a*) T.-L. Liu, Z.-L. He, H.-Y. Tao, Y.-P. Cai and C.-J. Wang, *Chem. Commun.*, 2011, **47**, 2616; (*b*) T.-L. Liu, Z.-L. He, Q.-H. Li, H.-Y. Tao and C.-J. Wang, *Adv. Synth. Catal.,* 2011, **353**, 1713.

8 (*a*) S. M. Kupchan, M. A. Eakin and A. M. Thomas, *J. Med. Chem.*, 1971, **14**, 1147; (*b*) J. R. Carney, A. T. Pham, W. Y. Yoshida and P. J. Scheuer, *Tetrahedron Lett.*, 1992, **33**, 7115; (*c*) K. Koike, Y. Suzuki, and T. Ohmoto, *Phytochemistry*, 1994, **35**, 701; (*d*) J.-Y. Su, Y.-L. Zhong and L.-M. Zeng, *J. Nat. Prod.*, 1993, **56**, 288; (*e*) T. Murakami, Y. Morikawa, M. Hashimoto, T. Okuno and Y. Harada, *Org. Lett.*, 2004, **6**, 157.

9 (*a*) J. Castulik, J. Marek and C. Mazal, *Tetrahedron*, 2001, **57**, 8339; (*b*) S. M. Jenkins, H. J. Wadsworth and S. Bromidge, *J. Med. Chem.*, 1992, **35**, 2392; (*c*) N. D. Yates, D. A. Peters, P. A. Allway, R. L. Beddoes, *Heterocycles*, 1995, **40**, 331.

10 For the early examples on the catalytic asymmetric *exo*-selective 1,3-dioplar cycloaddition of azomethine ylides, see: (*a*) Y. Oderaotoshi, W. Cheng, S. Fujitomi, Y. Kasano, S. Minakata and M. Komatsu, *Org. Lett.*, 2003, **5**, 5043. (*b*) W. Gao, X. Zhang, and M. Raghunath, *Org. Lett.,* 2005, **7**, 4241.