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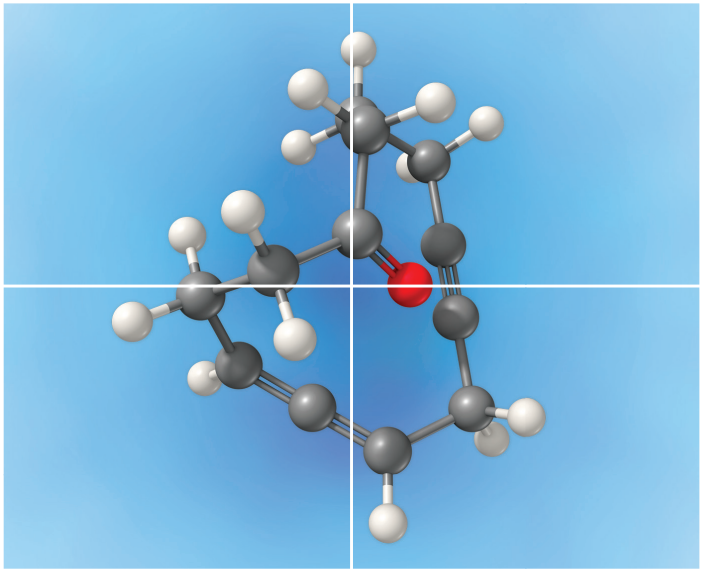

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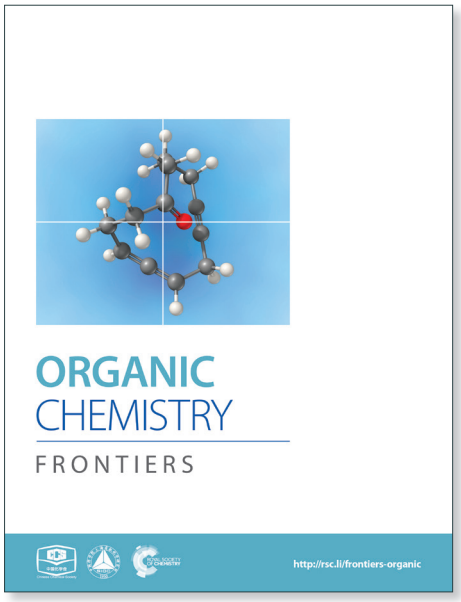

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A Sidearm-Assisted Phosphine for Catalytic Ylide Intramolecular Cyclopropanation

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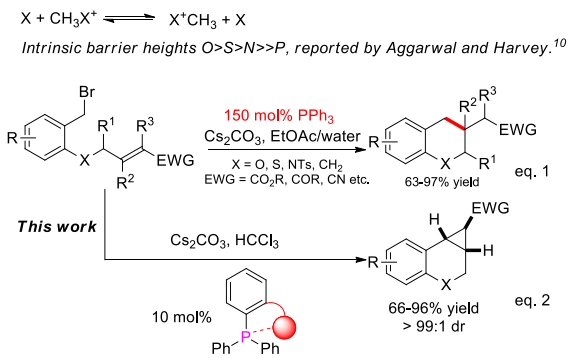
The first phosphine-catalyzed cyclopropanation reaction via covalent ylide catalysis has been realized with high efficiency in the presence of sidearm-assisted phosphine catalysts. An ether sidearm group is found critical to turn on the catalytic activity. Crystal structures of the catalyst-derived phosphonium salts indicated a significant O…P+ interaction between the pendant ether oxygen and the phosphonium center, which is believed to favor the catalyst regeneration. DFT calculations rationalize the insight of the sidearm effects.

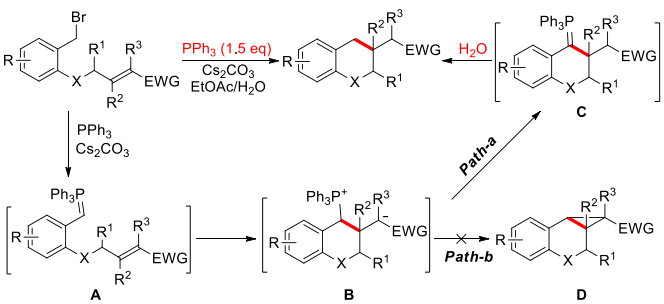
Ylide cyclopropanation provides a convenient and attractive method for the synthesis of cyclopropanes, important motif frequently occurred in natural products as well as synthetically useful intermediates.[1,2] Although both phosphorus ylide reactions and phosphine-catalyzed reactions have been intensively studied in the past decades,[3,4] phosphine-catalyzed cyclopropanation remains elusive.[5-9] Rational theoretical studies by Aggarwal and Harvey on the leaving group ability of onium ylides shows that compared with other ylides, such as ammonium, oxonium, sulfonium ylides, the phosphonium ylide need to overcome much higher energy barrier to act as a leaving group in a S_N2 substitution reaction (Scheme 1).[10] Accordingly, the key step is to regenerate phosphine in the ylide cyclopropanation to complete the catalytic cycle.[5] As the leaving group ability depends on the nature of phosphine, it could be envisioned that a rational design of phosphine would provide a solution for the catalyst turnover in such a reaction. Based on this idea, recently, we found that the introduction of a sidearm, an ether group at the *ortho*-position of triphenylphosphine (Ph_3P), could substantially alter the phosphine reactivity to enable its regeneration via a S_N2 substitution, allowing the realization of the first phosphine-catalyzed cyclopropanation reaction (eq. 2 in Scheme 1). In this communication, we wish to report our efforts on this subject.

Recently, we reported an intramolecular conjugation for the synthesis of chromans and relevant analogues in the presence of 150 mol% PPh_3.[11] The mechanism of this reaction is proposed as shown in Scheme 2. According to this mechanism, two factors are crucial to change the pathway to the cyclopropane: reducing the hydrolysis rate and/or improving the leaving ability of phosphine. We envisioned that tuning the steric hindrance around the phosphorus in the phosphine might balance the nucleophilicity and leaving group ability, switching ylide hydrolysis into S_N2 substitution and giving cyclopropanes as the desired products.

Scheme 1. Leaving group ability of phosphine and phosphine-mediated annulation reactions.

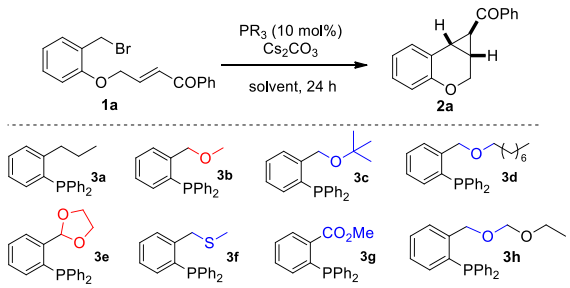


Scheme 2. Reaction pathway to conjugation product.



As PPh_3 is inert to this reaction (entry 1), initially, we synthesized bulky phosphines **3a** and **3b** with an *ortho*-propyl group and an *ortho*-methoxymethyl group. With 10 mol% of **3a**, no cyclopropanation product was obtained at room temperature, however, with 10 mol% of **3b** as a catalyst, we found that the desired cyclopropane was afforded with 33% yield (entries 2 & 3). In contrast, several other common phosphines with varied electronic nature were also tested in this reaction, but no product could be isolated in all these cases (entries 4-6). Then we employed **3b** as the catalyst for further study. In the presence of 10 mol% **3b**, optimization of the reaction parameters (temperature, solvent, and base) increased the yield to 64% (entry 7-13). As the activity was improved by replacement of *ortho*-propyl group in **3a** with the *ortho* ether group in **3b** (sidearm effect), it intrigued us to prepare several phosphine catalysts that also have this ether functional group for enhancing the efficiency. Though decreased yields were obtained with **3c** and **3d** (entry 14 & 15), possibly caused by the steric hindrance of the ether group, to our delight, less hindered acetal phosphine **3e** was found very effective for this cyclopropanation, improving the yield to 90% (entry 20 & 21). In contrast, thioether **3f** gave lower yield, and ester **3g** was even inactive (entry 17 & 18). With **3h** as catalyst, 53% yield was obtained. Noticeably, neither sulfide nor amine catalyst afforded the desired cyclopropanation product even under the optimal literature condition although tetrahydrothiophene is very efficient for the phenol derived α,β-unsaturated ester.[6c,7a]

Table 1. Reaction optimization.[a]

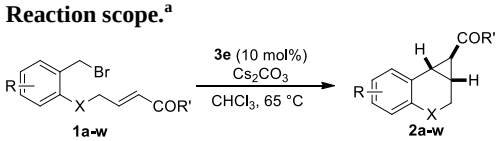


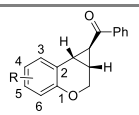
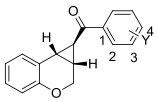
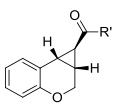
Entry	PR_3	Solvent	*t* (°C)	t (h)	Yield (%)[b]
1	PPh_3	DCE	rt	21	-
2	**3a**	DCE	rt	21	-
3	**3b**	DCE	rt	21	33
4	PCy_3	DCE	rt	21	-
5	$(4\text{-}ClC_6H_4)_3P$	DCE	rt	21	-
6	$(4\text{-}MeOC_6H_4)_3P$	DCE	rt	21	-
7	**3b**	DCE	80	20	52
8	**3b**	DME	80	16	15
9	**3b**	$PhCH_3$	80	16	7
10	**3b**	CH_3CN	80	14	24
11	**3b**	$CHCl_3$	65	24	64
12	**3b**/Na_2CO_3	$CHCl_3$	65	24	-
13	**3b**/K_2CO_3	$CHCl_3$	65	24	54
14	**3c**	$CHCl_3$	65	24	46
15	**3d**	$CHCl_3$	65	24	41
16	**3e**	$CHCl_3$	65	24	77
17	**3f**	$CHCl_3$	65	24	25
18	**3g**	$CHCl_3$	65	24	-
19	**3h**	$CHCl_3$	65	24	53
20	**3e**	$CHCl_3$	65	48	80
21[c]	**3e**	$CHCl_3$	65	48	90
22	tetrahydrothiophene	DCE	80	34	-
23	DIBACO/ Na_2CO_3	CH_3CN	80	24	-

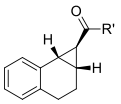
[a] Reaction conditions: **1a** (0.3 mmol), catalyst (10 mol%), base (0.6 mmol), solvent (4 mL). DABCO=1,4-diazobicyclo[2.2.2]octane. [b] Isolated yield. [c] With 20 mol% catalyst.

The scope of this cyclopropanation reaction was investigated under the optimized reaction condition, and the results are tabulated in Table 2. Various α,β-unsaturated carbonyl compounds with different structures worked well, giving the desired [n.1.0] bicycloalkanes **2a-w** in good to high yields. Notably, in all examples, only a single diastereoisomers were observed. Electron nature of the substituent on the phenol ring slightly influences the yields (83-93%, entries 1–6). The substituent effect is more obvious on the benzoyl part, in which the electron-donating groups gave in general higher yields (entries 8-14), probably because the electron-donating group would increase the nucleophilicity of the enolate in the key intramolecular S_N2-substitution step to regenerate the catalyst. Remarkably, aliphatic enone is also suitable for this reaction (94%, entry 17). And the all carbon [n.1.0] bicycles can also be obtained in even higher yields (91-95%, entries 18-21). It is worth mentioning that enal substrate **1v** was also compatible with the current reaction conditions; and the product **2v** is a key intermediate for the synthesis of a potential antidepressant.[12] The α,β-unsaturated ester **1w** was also examined as substrate, by using 20 mol% of **3e**, after 45 hours, 71% yield was obtained in toluene at 110 °C(entry 23).

Table 2. Reaction scope.[a]



Entry	Product		t (h)	Yield (%)[b]
				
1[c]	R = H	**2a**	25	90
2	4-Me	**2b**	46	92
3	4-OMe	**2c**	37	84
4[c]	4-Br	**2d**	26	83
5	6-Me	**2e**	37	93 [14]
6	6-F	**2f**	40	86
7	5,6-Benzo	**2g**	40	91
				
8[c]	Y = 2-OMe	**2h**	40	96
9[c]	3-OMe	**2i**	21	94
10[c]	4-OMe	**2j**	26	91
11[c]	4-F	**2k**	26	80
12[c]	4-Br	**2l**	25	66
13[c]	4-Ph	**2m**	40	84
14[c]	2,3-Benzo	**2n**	63	80
				
15[c]	R' = 2-furyl	**2o**	18	72
16[c]	2-thienyl	**2p**	18	84
17[c]	Cy	**2q**	24	94



18	R' = 2-furyl	**2r**	45	92
19[c]	2-thienyl	**2s**	45	91
20	Ph	**2t**	68	95
21[c]	4-BrC_6H_4	**2u**	63	93
22[c]	H	**2v**	18	81
23[d]	OCH_2CF_3	**2w**	45	71

[a] Reaction conditions: **1a** (0.3 mmol), **3e** (10 mol%), base (0.6 mmol), $CHCl_3$ (4 mL). [b] Isolated yield. [c] With 20 mol% **3e.** [d] With 20 mol% **3e**, in toluene, at 110 °C.

To further understand the role of the sidearm effect, we developed the single crystals of phosphonium salt **4a**, **4b** and **4e**, which are derived from phosphine **3a**, **3b** and **3e**.[13] Interestingly, the approaching of the oxygen atom to the phosphonium was observed, with an O…P distance of 3.22 Å and 3.38 Å respectively, which are quite near the sum of the van der Waals radii (3.32 Å) (Figure 1). In a stark contrast, the C atom is apart from the P atom in the *ortho*-propyl group substituted phosphine. This interesting phenomenon indicated that interactions between the O atom and P atom might account for the positive effect of ether sidearm. A similar interaction of Te^{+}…O was also observed in the crystal structure of a telluronium salt containing an ether group.[15]

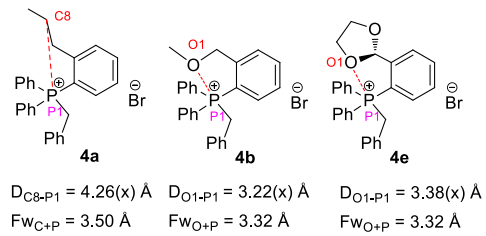


Figure 1. X-ray crystal structures data of the phosphonium salts.

To rationalize the sidearm effect, density functional theory (DFT)[16] studies have been performed with GAUSSIAN09 program[17] using the M06[18] method. For Cs atom the SDD basis set with Effective Core Potential (ECP)[19] was used; for the rest atoms, the 6-31+G** basis set was used. Geometry optimization was performed in chloroform (ε=4.711) using the SMD [20] method. Harmonic vibration frequency calculations were carried out at 338.15K, the optimized structures are all shown to be either minima (with no imaginary frequency) or transition states (with one imaginary frequency).

Both the poor and the optimal phosphines, PPh_3 and **3e**, were used to explore the reaction pathways ***Path-a*** and ***Path-b*** starting from intermediate **B**. As shown in Figure 2, for PPh_3, the hydrogen shift pathway (10.5 kcal/mol) is more favorable than the cyclopropanation pathway (11.6 kcal/mol), which is consistent well with the experimental observations that only a trace amount of cyclopropanation product was obtained. For theoptimal phosphine **3e**, the barrier of cyclopropanation (11.8 kcal/mol) is almost the same as that of PPh_3. However, the barriers of the hydrogen shift pathways increase to 12.9 kcal/mol (**3e-TS-H-*Shift***) and 11.7 kcal/mol (**3e-TS-H-*Shift2***), respectively. Thus, the cyclopropanation pathway becomes favorable for **3e**.

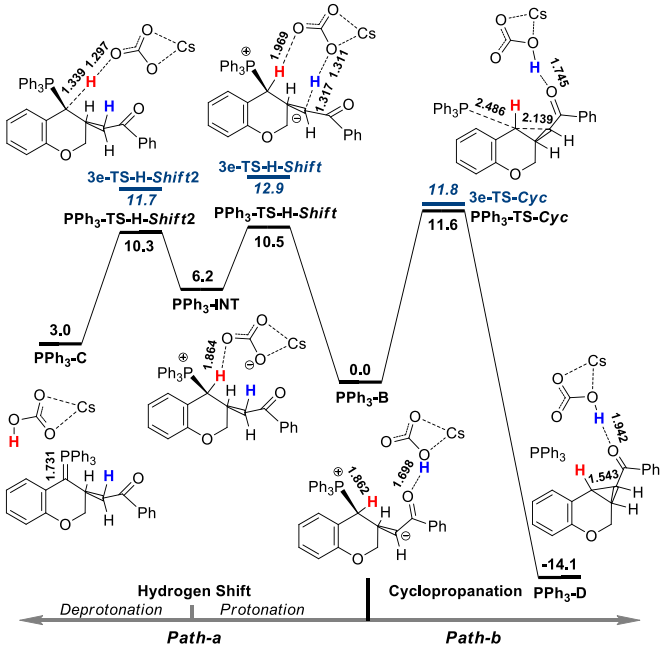


Figure 2. **The calculated reaction pathways for phosphine PPh_3. The energy barriers for phosphine 3e were also given (in italic). The selected bond lengths are in angstroms, and the relative free energies in chloroform (Gsol) are in kcal/mol. Calculated at the M06/6-31+G**/SDD level.**

These results indicate that the sidearm on the phosphine changes the selectivity of the reaction mainly by suppressing the hydrogen shift process. A detailed structural analysis[21] shows that in **3e-B**, the acetal group increases the repulsion among the three phenyl rings on the P atom, leading to a more flat "umbrella", which is more sensitive to steric effect. Compared with **PPh_3-TS-H-*Shift***, the attacking of $CsHCO_3$ on the phosphonium group in **3e-TS-H-*Shift*** causes larger repulsion, resulting in a more rigid structure with entropy loss of 4.759 cal•mol^{-1}•K^{-1}, which equivalent to a barrier increase of 1.6 kcal/mol. Based on these understandings, it is natural that the phosphonium group has much less effect on the "backside-attack" cyclopropanation transition state than the "side-attack" protonation transition state. For phosphine **3a**, **3b** and **3f**, the rate determining steps of ***Path-a*** and ***Path-b*** were also calculated, and the results are in good agreement with the experiments.[21]

Conclusions

In summary, a phosphine-catalyzed cyclopropanation reaction has successfully realized for the first time with an ether sidearm-assisted phosphine catalyst. X-ray crystal analysis indicated an interaction between the ether oxygen and the phosphonium atom, which was believed to be crucial for switching the phosphine reactivity from a typical ylide route to an unprecedented catalytic cyclopropanation path. DFT calculations rationalize the insight of the sidearm effects. This beneficial effect of a sidearm group would provide a brightening idea for the design and modification of phosphines and other sulfide and amine catalysts. Further investigation on the mechanism and the development of an asymmetric version are in progress in our laboratory.

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Notes and references

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Electronic Supplementary Information (ESI) available: Experimental procedures and the characterization data of new compounds. See DOI: 10.1039/c000000x/

1 (a) A. H. Li, L. X. Dai and V. K. Aggarwal, *Chem. Rev.* 1997, **97**, 2341; (b) L. X. Dai, X. L. Hou and Y. G. Zhou, *Pure Appl. Chem.* 1999, **71**, 369; (c) H. Lebel, J. F. Marcoux, C. Molinaro and A. B. Charette, *Chem. Rev.* 2003, **103**, 977; (d) Y. Tang, S. Ye and X. L. Sun, *Synlett* 2005, 2720; (e) H. Pellissier, *Tetrahedron* 2008, **64**, 7041.

2 For recent examples of cyclopropanation with ylide reagents, see: (a) J. Wang, X. H. Liu, S. X. Dong, L. L. Lin and X. M. Feng, *J. Org. Chem.* 2013, **78**, 6322; (b) C. Q. Wang, *Tetrahedron Lett.* 2012, **53**, 7003; (c) L. Q. Lu, Z. H. Ming, J. An, C. Li, J. R. Chen and W. J. Xiao, *J. Org. Chem.* 2012, ***77***, 1072; (d) A. Biswas, S. De Sarkar, L. Tebben and A. Studer, *Chem. Commun.* 2012, **48**, 5190; (e) R. Zhou, X. M. Deng, J. C. Zheng, Q. Shen, X. L. Sun and Y. Tang, *Chinese J. Chem.* 2011, **29**, 995; (f) Y. Cheng, J. An, L. Q. Lu, L. Luo, Z. Y. Wang, J. R. Chen and W. J. Xiao, *J. Org. Chem.* 2011, **76**, 281; (g) B. H. Zhu, R. Zhou, J. C. Zheng, X. M. Deng, X. L. Sun, Q. Shen and Y. Tang, *J. Org. Chem.* 2010, **75**, 3454; (h) S. L. Riches, C. Saha, N. F. Filgueira, E. Grange, E. M. McGarrigle and V. K. Aggarwal, *J. Am. Chem. Soc.* 2010, **132**, 7626; (i) R. Appel, N. Hartmann and H. Mayr, *J. Am. Chem. Soc.* 2010, **132**, 17894; (j) C. Y. Zhu, X. Y. Cao, B. H. Zhu, C. Deng, X. L. Sun, B. Q. Wang, Q. Shen and Y. Tang, *Chem.—Eur. J.* 2009, **15**, 11465; (k) Y. H. Zhao, G. Zhao and W. G. Cao, *Tetrahedron: Asymmetry* 2007, **18**, 2462; (l) R. K. Kunz and D. W. C. MacMillan, *J. Am. Chem. Soc.* 2005, **127**, 3240.

3 For reviews on phosphine catalysis, see: (a) O. I. Kolodiazhnyi, *Phosphorus Ylides: Chemistry and Application in Organic Synthesis*, Wiley-VCH, New York, 1999; (b) X. Y. Lu, C. M. Zhang and Z. R. Xu, *Acc. Chem. Res.* 2001, **34**, 535; (c) J. L. Methot and W. R. Roush, *Adv. Synth. Catal.* 2004, **346**, 1035; (d) S. E. Denmark and G. L. Beutner, *Angew. Chem. Int. Ed.* 2008, **47**, 1560; (e) A. Marinetti, and A. Voituriez, *Synlett* 2010, 174; (f) Y. Wei and M. Shi, *Acc. Chem. Res.* 2010, **43,** 1005; (g) X. L. Sun and Y. Tang, *Acc. Chem. Res.* 2008, **41**, 937; (h) L. W. Ye, J. Zhou and Y. Tang, *Chem. Soc. Rev.* 2008, **37**, 1140.

4 Recent examples on phosphine catalysis: (a) F. R. Zhong, X. W. Dou, X. Y. Han, W. J. Yao, Q. Zhu, Y. Z. Meng and Y. X. Lu, *Angew. Chem. Int. Ed.* 2013, **52**, 943; (b) R. J. Lundgren, A. Wilsily, N. Marion, C. Ma, Y. K. Chung and G. C. Fu, *Angew. Chem. Int. Ed.* 2013, **52**, 2525; (c) X. Y. Han, F. R. Zhong, Y. Q. Wang and Y. X. Lu, *Angew. Chem. Int. Ed.* 2012, **51**, 767; (d) F. R. Zhong, X. Y. Han, Y. Q. Wang and Y. X. Lu, *Angew. Chem. Int. Ed.* 2011, **50**, 7837; (e) B. Tan, N. R. Candeias and C. F. Barbas, *J. Am. Chem. Soc.* 2011, **133**, 4672; (f) 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; (g) J. E. Wilson, J. W. Sun and G. C. Fu, *Angew. Chem. Int. Ed.* 2010, **49**, 161; (h) S. Takizawa, N. Inoue, S. Hirata and H. Sasai, *Angew. Chem. Int. Ed.* 2010, **49**, 9725; (i) Y. Q. Jiang, Y. L. Shi and M. Shi, *J. Am. Chem. Soc.* 2008, **130**, 7202; (j) L. W. Ye, X. L. Sun, Q. G. Wang and Y. Tang, *Angew. Chem. Int. Ed.* 2007, **46**, 5951.

5 For reviews on catalytic ylide cyclopropanation, see: (a) E. M. McGarrigle, E. L. Myers, O. Illa, M. A. Shaw, S. L. Riches and V. K. Aggarwal, *Chem. Rev.* 2007, **107**, 5841; (b) S.-H. Liao, P. Wang, Y. Tang, *Covalent Activations: Ylides* In *Comprehensive Enantioselective Organocatalysis: Catalysts, Reactions, and Applications* (P. Dalko, Ed.), Wiley-VCH & Sons, Weinheim, Germany, **2013**.

6 For examples of sulfide-catalyzed cyclopropanation, see: (a) V. K. Aggarwal, H. W. Smith, G. Hynd, R. V. H. Jones, R. Fieldhouse and S. E. Spey, *J. Chem. Soc., Perkin Trans. 1* 2000, 3267; (b) X. M. Deng, P. Cai, S. Ye, X. L. Sun, W. W. Liao, K. Li, Y. Tang, Y. D. Wu and L. X. Dai, *J. Am. Chem. Soc.* 2006, **128**, 9730; (c) L. W. Ye, X. L. Sun, C. Y. Li and Y. Tang, *J. Org. Chem.* 2007, **72**, 1335.

7 For examples of amine-catalyzed ylide cyclopropanation, see: (a) C. D. Papageorgiou, S. V. Ley and M. J. Gaunt, *Angew. Chem. Int. Ed.* 2003, **42**, 828; (b) N. Bremeyer, S. C. Smith, S. V. Ley and M. J. Gaunt, *Angew. Chem. Int. Ed.* 2004, **43**, 2681; (c) C. D. Papageorgiou, M. A. C. de Dios, S. V. Ley and M. J. Gaunt, *Angew. Chem. Int. Ed.* 2004, **43**, 4641; (d) C. C. C. Johansson, N. Bremeyer, S. V. Ley, D. R. Owen, S. C. Smith and M. J. Gaunt, *Angew. Chem. Int. Ed.* 2006, **45**, 6024; (e) I. S. del Villar, A. Gradillas, G. Dominguez and J. Perez-Castells, *Tetrahedron Lett.* 2010, **51**, 3095.

8 For Te, As-catalyzed cyclopropanation, see: (a) Y. Z. Huang, Y. Tang, Z. L. Zhou, W. Xia and L. P. Shi, *J. Chem. Soc. Perkin Ttrans. 1* 1994, 893; (b) W. W. Liao, K. Li and Y. Tang, *J. Am. Chem. Soc.* 2003, **125**, 13030; (c) H. Jiang, X. L. Sun, C. Y. Zhu, L. X. Dai and Y. Tang, *Tetrahedron* 2008, **64**, 5032.

9 For examples of cyclopropantion using stoicheomethric phosphonium ylides, see: (a) S. Redon, S. Leleu, X. Pannecoucke, X. Franck and F. Outurquin, *Tetrahedron* 2008, **64,** 9293; (b) E. Bunuel, S. D. Bull, S. G. Davies, A. C. Garner, E. D. Savory, A. D. Smith, R. J. Vickers and D. J. Watkin, *Org. Biomol. Chem.* 2003, **1**, 2531; (c) S. Ahmad, L. M. Doweyko, S. Dugar, N. Grazier, K. Ngu, S. C. Wu, K. J. Yost, B. C. Chen, J. Z. Gougoutas, J. D. DiMarco, S. J. Lan, B. J. Gavin, A. Y. Chen, C. R. Dorso, R. Serafino, M. Kirby and K. S. Atwal, *J. Med. Chem.* 2001, **44**, 3302; (d) A. Krief, L. Provins and A. Froidbise, *Tetrahedron Lett.* 1998, **39**, 1437. Aslo see ref 3a.

10 V. K. Aggarwal, J. N. Harvey and R. Robiette, *Angew. Chem. Int. Ed.* 2005, **44**, 5468.

11 J. B. Zhu, P. Wang, S. H. Liao and Y. Tang, *Chem. Commun.* 2013, **49**, 4570.

12 A. A. Cordi, I. Berque-Bestel, T. Persigand, J. M. Lacoste, A. Newman-Tancredi, V. Audinot and M. J. Millan, *J. Med. Chem.* 2001, **44,** 787.

13 CCDC 992105 (**4a**), CCDC 962019 (**4b**), CCDC 962015 (**4e**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data

Centre via www.ccdc.cam.ac.uk/data_request/cif. For crystal stuctures of **4a**, **4b** and **4e**, see Supporting information.

14 When the Z-isomer of **1e** was employed as substrate in the catalytic ylide intramolecular cyclopropanation, the desired product **2e** was produced in 21% yield with the same diastereoselectivity of the E-configuration substrate **1e**, and 51% of the Z-isomer was recovered.

15 Z. Z. Huang, S. Ye, W. Xia, Y. H. Yu and Y. Tang, *J. Org. Chem.* 2002, **67**, 3096.

16 (a) P. Hohenberg and W. Kohn, *Phys. Rev.* 1964, **136**, B864. (b) W. Kohn and L. Sham, *J. Phys. Rev.* 1965, **140**, A1133.

17 Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G.. A. Petersson, H. Nakatsuji, M. Caricato, X. Li,H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng,. J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven,. A. Jr. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand,K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels,O. Farkas, J. B. Foresman, J. V. Ortiz,J. Cioslowski, D. J. Fox, Gaussian, Inc., Wallingford CT, **2009**.

18 Y. Zhao and D. G. Truhlar, *Theor. Chem. Acc.* 2008, **120**, 215.

19 P. Fuentealba, H. Preuss, H. Stoll and L. Von Szentpály, *Chem. Phys. Lett.* 1982, **89**, 418.

20 A. V. Marenich, C. J. Cramer and D. G. Truhlar, *J. Phys. Chem.* 2009, **113**, 6378.

21 For details, see Supporting Information.

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