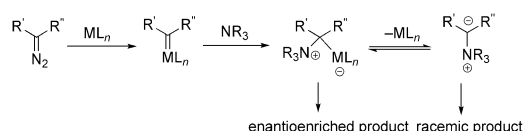


Dirhodium Carboxylates Catalyzed Enantioselective Coupling Reactions of α -Diazophosphonates, Anilines, and Electron-Deficient Aldehydes**

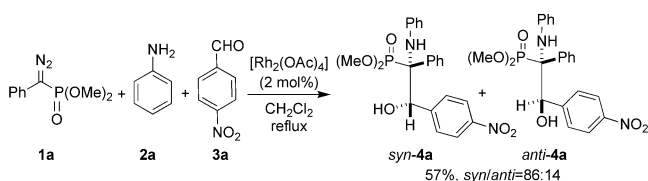
Cong-Ying Zhou, Jing-Cui Wang, Jinhu Wei, Zhen-Jiang Xu, Zhen Guo, Kam-Hung Low, and Chi-Ming Che*

Ammonium ylides are versatile intermediates that are frequently used in the synthesis of complex and diverse nitrogen-containing compounds.^[1,2] Transition-metal complexes, including dirhodium(II,II) carboxylates, copper(II) acetylacetonate, and ruthenium(II) porphyrins, are effective catalysts for the generation of ammonium ylides through decomposition of diazo compounds in the presence of amines.^[2] While highly enantioselective alkene cyclopropanation,^[2,3] carbene X–H (X = C, Si, N, O) insertion,^[4–8] and transformation reactions of oxygen ylides^[9,10] and sulfur ylides^[11] have been achieved by decomposition of diazo compounds in the presence of chiral transition-metal complexes, transition-metal-catalyzed asymmetric reactions of ammonium ylides are rare. The major challenge in developing highly enantioselective metal-catalyzed ammonium ylide reactions is the equilibrium between the metal-bound/stabilized ylide (referred to as metal-bound ylide) and the free ylide; the latter leads to the formation of racemic product (Scheme 1).

In this study, we examined the three-component coupling reaction of α -diazophosphonates, anilines, and electron-deficient aldehydes to give α -amino- β -hydroxyphosphonate compounds (Scheme 2).^[12] α -Amino phosphonic acid compounds are key substrates used in the synthesis of phosphonopeptides and could act as enzyme inhibitors, antibiotics, plant growth regulators, and haptens of catalytic antibodies.^[13]



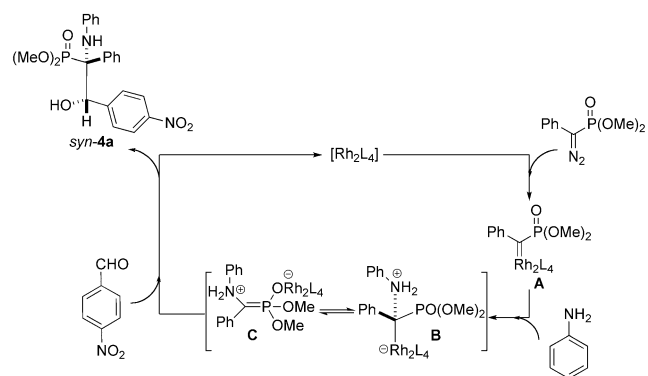
Scheme 1. Ammonium ylide formation by the reaction of metal carbeneoid with amine. L = ligand, M = metal.



Scheme 2. Three-component coupling reaction to *syn*-**4a** and *anti*-**4a**.

At the outset, the reaction of dimethyl α -diazo(benzyl)phosphonate **1a**, aniline **2a**, 4-nitrobenzaldehyde **3a**, and $[\text{Rh}_2(\text{OAc})_4]$ catalyst (2 mol %) in CH_2Cl_2 at 40°C for 15 hours afforded the two diastereomers *syn*-**4a** and *anti*-**4a** in 57% overall yield and with a *syn/anti* ratio of 86:14 (Scheme 2). The structure of the major isomer *syn*-**4a** was determined by X-ray crystallography (see the Supporting Information).

A proposed mechanism for this Rh-catalyzed three-component reaction is shown in Scheme 3. With reference to previous work on Brønsted acid/ $[\text{Rh}_2(\text{OAc})_4]$ -catalyzed coupling reaction of diazoester, carbamate, and imine,^[14c] the rhodium catalyst decomposes α -diazophosphonate to generate Rh–carbene species **A**, which is trapped by aniline to give



Scheme 3. Proposed mechanism for the three-component coupling reaction.

[*] J.-C. Wang^[*,†], Z.-J. Xu, Prof. Dr. C.-M. Che
Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis,
Shanghai Institute of Organic Chemistry
354 Feng Lin Road, Shanghai (China)

C.-Y. Zhou^[*,†], J. Wei, Z. Guo, K.-H. Low
Department of Chemistry, State Key Laboratory of Synthetic
Chemistry and Open Laboratory of Chemical Biology of the Institute
of Molecular Technology for Drug Discovery and Synthesis
University of Hong Kong, Pokfulam Road (Hong Kong, China)

[†] These authors contributed equally to this work.

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metal-bound ammonium ylide intermediate **B/C**. Subsequent nucleophilic addition of the intermediate to the aldehyde gives the α -amino- β -hydroxyphosphonate.

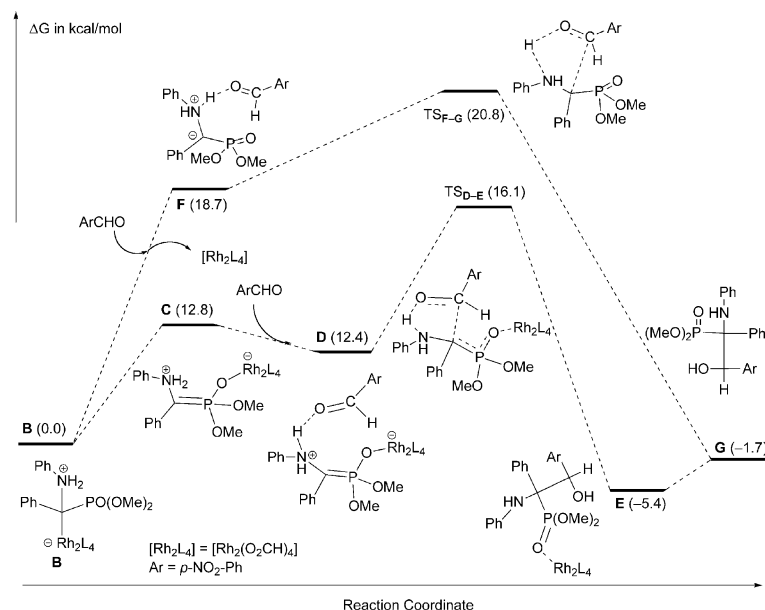
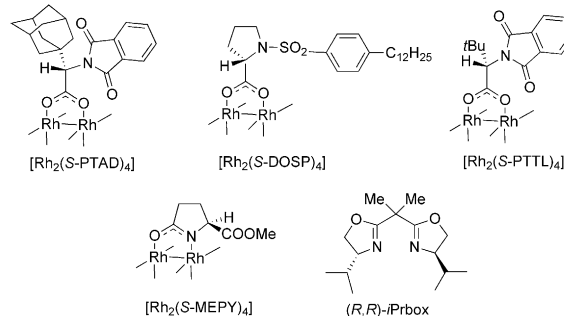
To examine the significance of metal-bound ylide intermediate **B/C** in the reaction, we performed DFT calculations using B3LYP functionals to examine the addition of ylide intermediate **B/C** to the aldehyde in the three-component reaction of **1a**, **2a**, and **3a** catalyzed by $[\text{Rh}_2(\text{O}_2\text{CH})_4]$. The computed free-energy surface is shown in Scheme 4. The formation of **C** from **B** is endergonic by $12.8 \text{ kcal mol}^{-1}$, but the subsequent nucleophilic addition of **C** to the aldehyde via **D** is relatively facile, requiring an activation free energy of $3.7 \text{ kcal mol}^{-1}$. In contrast, the pathway via the free ylide has an overall activation free energy of $20.8 \text{ kcal mol}^{-1}$ via $\text{TS}_{\text{F-G}}$, which is $4.7 \text{ kcal mol}^{-1}$ higher than that for the pathway via **C** ($16.1 \text{ kcal mol}^{-1}$). Our effort to locate the transition state of the direct addition of **B** to the aldehyde was unsuccessful. These results show that addition of metal-bound intermediate **C** to the aldehyde is the reaction pathway with the lowest energy. We anticipated that chirality transfer would occur in this pathway via the metal-bound ylide if a chiral dirhodium-(II,II) catalyst was used.

To validate our hypothesis, a series of chiral dirhodium-(II,II) carboxylates and the Cu^{I} complex of (*R,R*)-iPrbox, which have been reported to give excellent enantioselectivity in alkene cyclopropanation and carbene C–H insertion reactions, were examined for the three-component coupling reaction of **1a**, **2a**, and **3a** (Table 1). With $[\text{Rh}_2(\text{S-PTAD})_4]$ ^[15] as catalyst, **4a** was obtained in 73 % yield with a *syn/anti* ratio of 80:20 and an *ee* value of 77 % (Table 1, entry 1). $[\text{Rh}_2(\text{S-DOSP})_4]$ ^[16] and $[\text{Rh}_2(\text{S-PTTL})_4]$ ^[17] gave *syn-4a* with 22 % and 68 % *ee*, respectively (Table 1, entries 2 and 3). $[\text{Rh}_2(\text{S-MEPY})_4]$ ^[18] failed to catalyze this reaction (Table 1, entry 4). When $\text{CuOTf}/(\text{R,R})$ -iPrbox was used, both product yield and enantioselectivity were low (Table 1, entry 5). With $[\text{Rh}_2(\text{S-PTAD})_4]$ as catalyst, CH_2Cl_2 was the best solvent

Table 1: Catalyst screening and optimization of the coupling reaction of **1a**, **2a**, and **3a**.^[a]

Entry	Catalyst	Solvent	T [°C]	Yield ^[b] [%]	<i>syn/anti</i> ^[c]	<i>ee</i> (<i>syn</i>) [%] ^[d]
1	$[\text{Rh}_2(\text{S-PTAD})_4]$	CH_2Cl_2	40	73	80:20	77
2	$[\text{Rh}_2(\text{S-DOSP})_4]$	CH_2Cl_2	40	54	84:16	22
3	$[\text{Rh}_2(\text{S-PTTL})_4]$	CH_2Cl_2	40	65	81:19	68
4	$[\text{Rh}_2(\text{S-MEPY})_4]$	CH_2Cl_2	40	n.r.	–	–
5	$\text{CuOTf}/(\text{R,R})$ -iPrbox	CH_2Cl_2	40	32	90:10	9
6	$[\text{Rh}_2(\text{S-PTAD})_4]$	toluene	40	35	62:38	27
7	$[\text{Rh}_2(\text{S-PTAD})_4]$	DMB	40	n.r.	–	–
8 ^[e]	$[\text{Rh}_2(\text{S-PTAD})_4]$	CH_2Cl_2	25	54	85:15	64
9	$[\text{Rh}_2(\text{S-PTAD})_4]$	$(\text{CH}_2\text{Cl})_2$	85	30	66:34	42

[a] **1a**:**2a**:**3a**:catalyst = 1:1.5:3:0.02, reaction time = 12–15 h. [b] Yields of isolated products. [c] Ratio of *syn/anti* determined by ^1H NMR spectroscopy. [d] Determined by HPLC on a chiral stationary phase. [e] Reaction time was 40 h. DMB = 2,2-dimethylbutane; n.r. = no reaction; OTf = trifluoromethanesulfonate.



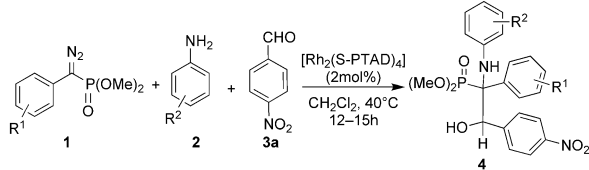
Scheme 4. Computed free-energy surface for the coupling reaction.

(Table 1, entries 1, 6, and 7). Lowering the reaction temperature to room temperature resulted in a long reaction time (40 h) and lower product yield and enantioselectivity (Table 1, entry 8). Increasing the reaction temperature to 85°C led to reduction of both the product yield and enantioselectivity (Table 1, entry 9).

The scope of $[\text{Rh}_2(\text{S-PTAD})_4]$ -catalyzed three-component coupling reactions of derivatives **1** of dimethyl α -diazo(benzyl)phosphonate, anilines **2**, and 4-nitrobenzaldehyde **3a** was examined with the optimized conditions (Table 2). Bulky *ortho* substituent(s) on aniline significantly improved the enantioselectivity up to 98 % and diastereoselectivity up to 90:10 (Table 2, entries 1–5). Substitution at the *meta* position has a slight impact on both the enantioselectivity and diastereoselectivity (Table 2, entries 6–7). When 4-chloroaniline **2i** was used, product **4i** was obtained in 91 % *ee* (Table 2, entry 8).

The effect of substitution on the benzyl group of diazo compound **1** was examined by using 2-

Table 2: Scope of enantioselective three-component coupling reaction of derivatives **1** of dimethyl α -diazo(benzyl)phosphonate, anilines **2**, and 4-nitrobenzaldehyde **3a**.^[a]



Entry	1	R ¹	2	R ²	4, Yield [%] ^[b]	syn/anti ^[c]	ee (syn) [%] ^[d]
1	1a	H	2b	2-Me	4b, 80	89:11	96
2	1a	H	2c	2-Br	4c, 85	90:10	98
3	1a	H	2d	2-Cl	4d, 81	83:17	89
4	1a	H	2e:		4e, 82	89:11	94
5	1a	H	2f	2-Br, 4-Cl	4f, 86	86:14	95
6	1a	H	2g:		4g, 69	78:22	74
7	1a	H	2h	3-Cl	4h, 75	81:19	73
8	1a	H	2i	4-Cl	4i, 78	90:10	91
9	1a	H	2j	3-OMe	4j, 56	76:24	60
10	1b	4-Cl	2b	2-Me	4k, 78	84:16	89
11	1c	4-Me	2b	2-Me	4l, 78	88:12	97
12	1d	4-OMe	2b	2-Me	4m, 56	87:13	71
13	1b	4-Cl	2e:		4n, 80	87:13	94
14	1c	4-Me	2k	2-F	4o, 83	82:18	79
15	1c	4-Me	2l	2-Br, 4-F	4p, 82	80:20	93

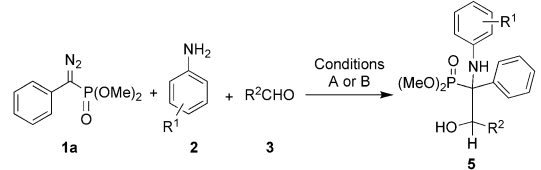
[a] **1**:**2**:**3a**:catalyst = 1:1.5:3:0.02. [b] Yields of isolated products.

[c] Determined by ¹H NMR spectroscopy. [d] Determined by HPLC on a chiral stationary phase.

methylaniline **2b** or 4-aminoindane **2e** as substrate. Both Cl and Me substituents led to high *ee* values (89–97%, entries 10, 11, and 13). However, with the OMe substituent, the enantioselectivity decreased to 71% *ee* (Table 2, entry 12). The reaction of **1c**, **3a**, and 2-fluoroaniline **2k** (Table 2, entry 14) gave comparable enantioselectivity (79% *ee*) to that obtained for the reaction of **1a**, **3a**, and **2a** (Table 1, entry 1). Presumably, the steric effect of an 2-F substituent of aniline is not large. This suggestion is supported by the reaction of **1c**, **3a**, and 4-fluoro-2-bromoaniline **2l**, affording the corresponding product **4p** in 93% *ee* (Table 2, entry 15). Changing **1a** to diethyl α -diazo(benzyl)phosphonate led to corresponding product in 74% yield with 79:21 d.r. and 57% *ee*. The absolute configuration of *syn*-**4l** was determined to be 2*S*,3*S* by X-ray crystallography using anomalous dispersion effects in diffraction measurements on the crystal (see Figure S2 in the Supporting Information).

We next extended the scope of aldehydes for this three-component reaction (Table 3, entries 1–8). Various electron-deficient aldehydes underwent the three-component reaction with [Rh₂(S-PTAD)₄] or [Rh₂(S-PTTL)₄] as catalyst to give the corresponding products in 64–83% yield with 85:15–94:6 d.r. and 66–86% *ee*. With [Rh₂(S-PTAD)₄] as catalyst, 4-carbomethoxybenzaldehyde **3b** was less reactive than **3a**,

Table 3: Scope of enantioselective three-component coupling reaction of dimethyl α -diazo(benzyl)phosphonate **1a**, anilines **2**, and electron-deficient aldehydes **3**.^[a]



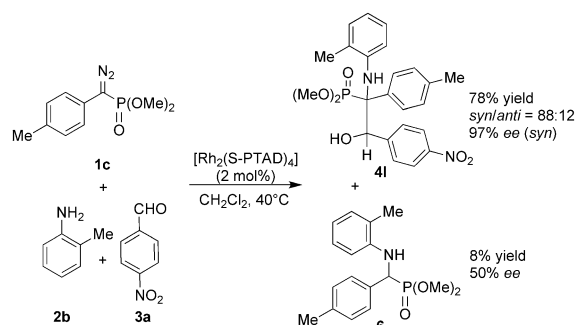
Entry	2	3	R ²	5, Yield [%] ^[b]	syn/anti ^[c]	ee (syn) [%] ^[d]
1 ^[e]	2c	3b	4-CO ₂ Me	5a, 77	91:9	66
2 ^[f]	2c	3b	4-CO ₂ Me	5a, 79	87:13	79
3 ^[e]	2c	3c	4-NO ₂	5b, 69 ^[h]	89:11	67
4 ^[f]	2c	3c	4-NO ₂	5b, 77	88:12	86
5 ^[g]	2c	3d:		5c, 64	87:13	77
6 ^[f]	2c	3d:		5c, 65	85:15	75
7 ^[e]	2c	3e:		5d, 0		
8 ^[f]	2c	3e:		5d, 83 ^[i]	94:6	80
9 ^[e]	2b	3b	4-CO ₂ Me	5e, 69	90:10	61
10 ^[f]	2b	3b	4-CO ₂ Me	5e, 75	88:12	79
11 ^[e]	2b	3c	4-NO ₂	5f, 71 ^[j]	85:15	75
12 ^[f]	2b	3c	4-NO ₂	5f, 74	83:17	79

Conditions A: [Rh₂(S-PTAD)₄] (2 mol%), CH₂Cl₂, 40°C, 24 h. Conditions B: [Rh₂(S-PTTL)₄] (2 mol%), CH₂Cl₂, 40°C, 12–15 h. [a] **1a**:**2**:**3**:catalyst = 1:1.5:3:0.02. [b] Yields of isolated products. [c] Determined by ¹H NMR spectroscopy. [d] Determined by HPLC on a chiral stationary phase. [e] Conditions A. [f] Conditions B. [g] Conditions A with reaction time of 15 h. [h] Yield of isolated product based on substrate conversion of 90%. [i] Yield of isolated product based on substrate conversion of 75%. [j] Yield of isolated product based on substrate conversion of 85%.

requiring a reaction time of 24 hours and giving the corresponding product in 77% yield and 66% *ee* (Table 3, entry 1). When the less sterically encumbered [Rh₂(S-PTTL)₄] was used as catalyst, the reaction was completed in 15 hours and led to slightly higher product yield and enantioselectivity (79% *ee*, Table 3, entry 2). Similar results were obtained for the reaction of **1a**, **2c**, and 3-nitrobenzaldehyde **3c** (Table 3, entries 3 and 4). When heteroaromatic aldehyde **3d** was used, catalysis with [Rh₂(S-PTAD)₄] and [Rh₂(S-PTTL)₄] led to **5c** in 64% and 65% yields and with 77% *ee* and 75% *ee*, respectively (Table 3, entries 5 and 6). The vinyl aldehyde **3e** was reactive and gave **5d** in 83% yield and with 80% *ee* when [Rh₂(S-PTTL)₄] was used as catalyst, but failed to give **5d** when [Rh₂(S-PTAD)₄] was used instead (Table 3, entries 7 and 8). Similarly, the reactions of 2-methylaniline **2b**, **1a**, and aldehyde **3b** or **3c** gave comparable results to that obtained for the similar reaction with 2-bromoaniline **2c** (Table 3, entries 9–12).

In all of the entries depicted in Tables 2 and 3, the products of carbene N–H insertion of anilines were detected

in 2–10% yields. The N–H insertion product **6** formed in the reaction of **1c**, **2b**, and **3a** (Scheme 5, Table 2, entry 11) was isolated in 8% yield and in 50% ee in contrast to 97% ee of



Scheme 5. Formation of three-component coupling product **4l** versus N–H insertion product **6**.

the corresponding three-component coupling product *syn*-**4l**. This result suggests that the metal-bound ylide intermediate **B/C** may not be the sole species responsible for the carbene N–H insertion of anilines. Recent studies showed that transition-metal-catalyzed carbene insertion into the N–H bond of amines could be a stepwise process that involves initial ammonium ylide formation followed by [1,2]-proton shift.^[6d,8,14]

In summary, we have developed a highly enantioselective metal-catalyzed three-component coupling reaction of α -diazophosphonates, anilines, and electron-deficient aldehydes. By using the chiral rhodium catalysts $[\text{Rh}_2(\text{S-PTAD})_4]$ or $[\text{Rh}_2(\text{S-PTTL})_4]$, a series of α -amino- β -hydroxyphosphonates were obtained in good to high yields and with good to high enantioselectivities. The high level of enantiocontrol provides evidence for the intermediacy of a metal-bound ammonium ylide in the nucleophilic addition step.

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- Reviews: a) E. Vedejs, F. G. West, *Chem. Rev.* **1986**, 86, 941; b) A.-H. Li, L.-X. Dai, V. K. Aggarwal, *Chem. Rev.* **1997**, 97, 2341; c) *Nitrogen, Oxygen and Sulfur Ylides Chemistry. A Practical Approach in Chemistry* (Ed.: J. S. Clark), Oxford University Press, Oxford, **2002**; d) J. B. Sweeney, *Chem. Soc. Rev.* **2009**, 38, 1027.
- Reviews: a) M. P. Doyle, *Chem. Rev.* **1986**, 86, 919; b) A. Padwa, S. F. Hornbuckle, *Chem. Rev.* **1991**, 91, 263; c) T. Ye, M. A. McKerver, *Chem. Rev.* **1994**, 94, 1091; d) A. Padwa, M. D. Weingarten, *Chem. Rev.* **1996**, 96, 223; e) M. P. Doyle, M. A. McKerver, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*, Wiley, New York, **1998**; f) M. P. Doyle, D. C. Forbes, *Chem. Rev.* **1998**, 98, 911; g) J. A. Vanecko, H. Wan, F. G. West, *Tetrahedron* **2006**, 62, 1043; h) Z. Zhang, J. Wang, *Tetrahedron* **2008**, 64, 6577; i) A. Padwa, *Chem. Soc. Rev.* **2009**, 38, 3072; j) C.-Y. Zhou, J.-S. Huang, C.-M. Che, *Synlett* **2010**, 2681.

- For enantioselective cyclopropanation, see: H. Lebel, J.-F. Marcoux, C. Molinaro, A. B. Charette, *Chem. Rev.* **2003**, 103, 977.
- For enantioselective carbene C–H insertion, see: a) H. M. L. Davies, R. E. J. Beckwith, *Chem. Rev.* **2003**, 103, 2861; b) M. P. Doyle, R. Duffy, M. Ratnikov, L. Zhou, *Chem. Rev.* **2010**, 110, 704; c) H. M. L. Davies, D. Morton, *Chem. Soc. Rev.* **2011**, 40, 1857.
- For enantioselective carbene Si–H insertion, see: a) H. M. L. Davies, T. Hansen, J. Rutberg, P. R. Bruzinski, *Tetrahedron Lett.* **1997**, 38, 1741; b) Y.-Z. Zhang, S.-F. Zhu, L.-X. Wang, Q.-L. Zhou, *Angew. Chem.* **2008**, 120, 8624; *Angew. Chem. Int. Ed.* **2008**, 47, 8496; c) Y. Yasutomi, H. Suematsu, T. Katsuki, *J. Am. Chem. Soc.* **2010**, 132, 4510.
- For enantioselective carbene N–H insertion, see: a) B. Liu, S.-F. Zhu, W. Zhang, C. Chen, Q.-L. Zhou, *J. Am. Chem. Soc.* **2007**, 129, 5834; b) E. C. Lee, G. C. Fu, *J. Am. Chem. Soc.* **2007**, 129, 12066; c) Z. Hou, J. Wang, P. He, J. Wang, B. Qin, X. Liu, L. Lin, X. Feng, *Angew. Chem.* **2010**, 122, 4873; *Angew. Chem. Int. Ed.* **2010**, 49, 4763; d) B. Xu, S.-F. Zhu, X.-L. Xie, J.-J. Shen, Q.-L. Zhou, *Angew. Chem.* **2011**, 123, 11685; *Angew. Chem. Int. Ed.* **2011**, 50, 11483; e) S.-F. Zhu, B. Xu, G.-P. Wang, Q.-L. Zhou, *J. Am. Chem. Soc.* **2012**, 134, 436.
- For enantioselective carbene O–H insertion, see: a) T. C. Maier, G. C. Fu, *J. Am. Chem. Soc.* **2006**, 128, 4594; b) C. Chen, S.-F. Zhu, B. Liu, L.-X. Wang, Q.-L. Zhou, *J. Am. Chem. Soc.* **2007**, 129, 12616; c) S.-F. Zhu, C. Chen, Y. Cai, Q.-L. Zhou, *Angew. Chem.* **2008**, 120, 946; *Angew. Chem. Int. Ed.* **2008**, 47, 932; d) S.-F. Zhu, Y. Cai, H.-X. Mao, J.-H. Xie, Q.-L. Zhou, *Nat. Chem.* **2010**, 2, 546; e) S.-F. Zhu, W.-Q. Chen, Q.-Q. Zhang, H.-X. Mao, Q.-L. Zhou, *Synlett* **2011**, 919.
- Detailed DFT calculations on Cu^{I} - and Rh^{II} -catalyzed O–H insertion of water with diazo compounds has been reported: Y. Liang, H. Zhou, Z.-X. Yu, *J. Am. Chem. Soc.* **2009**, 131, 17783.
- For enantioselective [2,3]-sigmatropic rearrangement of oxonium ylide, see: a) M. P. Doyle, D. C. Forbes, M. M. Vasbinder, C. S. Peterson, *J. Am. Chem. Soc.* **1998**, 120, 7653; b) Z. Li, H. M. L. Davies, *J. Am. Chem. Soc.* **2010**, 132, 396; c) B. T. Parr, Z. Li, H. M. L. Davies, *Chem. Sci.* **2011**, 2, 2378; d) Z. Li, B. T. Parr, H. M. L. Davies, *J. Am. Chem. Soc.* **2012**, 134, 10942.
- For enantioselective 1,3-dipolar cycloaddition of carbonyl ylide, see: a) S. Kitagaki, M. Anada, O. Kataoka, K. Matsuno, C. Umeda, N. Watanabe, S.-I. Hashimoto, *J. Am. Chem. Soc.* **1999**, 121, 1417; b) D. M. Hodgson, P. A. Stuppel, F. Y. T. M. Pierard, A. H. Labande, C. Johnstone, *Chem. Eur. J.* **2001**, 7, 4465; c) D. M. Hodgson, T. Brückl, R. Glen, A. H. Labande, D. A. Selden, A. G. Dossetter, A. J. Redgrave, *Proc. Natl. Acad. Sci. USA* **2004**, 101, 5450.
- For enantioselective [2,3]-sigmatropic rearrangement of sulfonium ylide, see: M. Ma, L. Peng, C. Li, X. Zhang, J. Wang, *J. Am. Chem. Soc.* **2005**, 127, 15016.
- α -Amino- β -hydroxyphosphonate moieties are found in bioactive molecules. See: a) A. Schweifer, F. Hammerschmidt, *Bioorg. Med. Chem. Lett.* **2008**, 18, 3056; b) M. Staake, J. Chauhan, D. Zhou, A. Shanker, A. De Chatterjee, S. Das, S. E. Patterson, *Org. Lett.* **2010**, 12, 4596.
- Reviews: a) P. Kafarski, B. Lejczak, *Phosphorus Sulfur Silicon Relat. Elem.* **1991**, 63, 193; b) *Aminophosphonic and Amino-phosphinic Acids* (Eds.: V. P. Kukhar, H. R. Hudson), Wiley, New York, **2000**.
- Hu and co-workers reported a related, three-component reaction in which an ammonium ylide, generated in situ through decomposition of a diazo compound by $[\text{Rh}_2(\text{OAc})_4]$ in the presence of aniline or carbamate, was trapped by aldehyde or imine to give α -amino- β -hydroxy esters or α,β -diamino esters. In reference [14c], highly asymmetric induction was achieved by chiral phosphoric acid; a) Y. Wang, Y. Zhu, Z. Chen, A. Mi, W.

- Hu, M. P. Doyle, *Org. Lett.* **2003**, 5, 3923; b) Y. Wang, Z. Chen, A. Mi, W. Hu, *Chem. Commun.* **2004**, 2486; c) J. Jiang, H.-D. Xu, J.-B. Xi, B.-Y. Ren, F.-P. Lv, X. Guo, L.-Q. Jiang, Z.-Y. Zhang, W.-H. Hu, *J. Am. Chem. Soc.* **2011**, 133, 8428.
- [15] R. P. Reddy, G. H. Lee, H. M. L. Davies, *Org. Lett.* **2006**, 8, 3437.
- [16] H. M. L. Davies, P. R. Bruzinski, D. H. Lake, N. Kong, M. J. Fall, *J. Am. Chem. Soc.* **1996**, 118, 6897.
- [17] S. Hashimoto, N. Watanabe, T. Sato, M. Shiro, S. Ikegami, *Tetrahedron Lett.* **1993**, 34, 5109.
- [18] M. P. Doyle, A. van Oeveren, L. J. Westrum, M. N. Protopopova, T. W. Clayton, Jr., *J. Am. Chem. Soc.* **1991**, 113, 8982.
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