Organic LETTERS

Letter

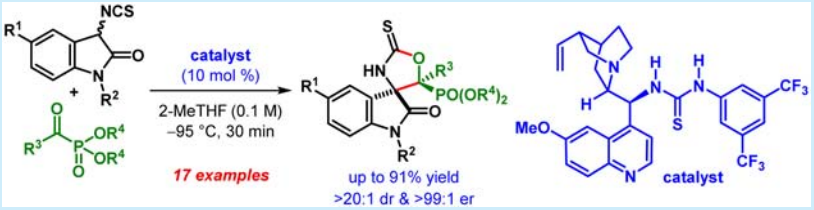
pubs.acs.org/OrgLett

Catalytic Aldol–Cyclization Cascade of 3-Isothiocyanato Oxindoles with α-Ketophosphonates for the Enantioselective Synthesis of β-Amino-α-hydroxyphosphonates

Satavisha Kayal and Santanu Mukherjee*

Department of Organic Chemistry, Indian Institute of Science, Bangalore - 560012, India

Supporting Information



ABSTRACT: A cascade aldol–cyclization reaction between 3-isothiocyanato oxindoles and α-ketophosphonates has been developed for the synthesis of β-amino-α-hydroxyphosphonate derivatives. Catalyzed by a quinine-based tertiary amino-thiourea derivative, this reaction delivers 2-thioxooxazolidinyl phosphonates based on a spirooxindole scaffold bearing two contiguous quaternary stereogenic centers in high yields with excellent diastereo- (up to >20:1 dr) and enantioselectivities (up to >99:1 er).

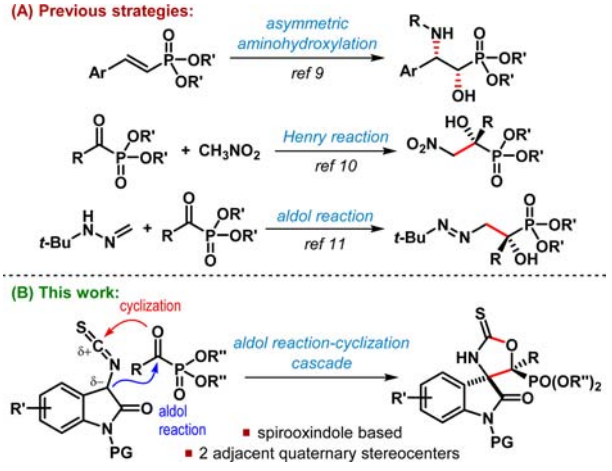
Phosphonic acids are generally regarded as the structural and functional analogues of carboxylic acids. As a result, amino and/or hydroxy-functionalized phosphonic acids and their derivatives are found to display inhibitory activities toward a wide range of enzymes such as renin, HIV protease, thrombin, and various classes of protein tyrosine kinases and phosphatases.[1] Quite predictably, the biological activities of amino- or hydroxy-phosphonic acids and their derivatives are almost always dictated by their absolute configuration.[2] Therefore, enantioselective synthesis of such functionalized phosphonic acids and their derivatives is of general interest.[3]

Similarly, the oxindole scaffold containing a quaternary stereocenter at the C3 position is a privileged structural motif present in many biologically active molecules and natural products.[4] In this respect, spirooxindoles have received special attention during the past few years.[5]

Considering the importance of both the above-mentioned structural features, we were intrigued by the possibility of combining them in a conformationally rigid chiral scaffold. We reasoned that highly functionalized phosphonic acid derivatives based on a spirooxindole framework could be of potential biological significance, if synthesized in enantiopure form. As part of our research program on the catalytic enantioselective synthesis of highly functionalized aminophosphonic acids,[6] we were particularly interested in β-amino-α-hydroxyphosphonic acids due to their rich biological activities.[1,7]

Compared to other aminophosphonic acids,[3] the catalytic asymmetric synthesis of β-amino-α-hydroxyphosphonate derivatives remained relatively underdeveloped.[8] Palmisano, Sisti and co-workers developed the first enantioselective synthesis of β-amino-α-hydroxyphosphonates through catalytic asymmetric aminohydroxylation of α,β-unsaturated phosphonates (Scheme 1A).[9] Enantioselective Henry reaction of α-ketophosphonates emerged as an alternative strategy due to the work of Zhao et al.[10]

Scheme 1. Catalytic Enantioselective Synthesis of β-Amino-α-hydroxyphosphonate Derivatives



Very recently, Lassaletta reported a catalytic 1,2-addition of a methylenehydrazine derivative to α-ketophosphonates for the enantioselective synthesis of β-amino-α-hydroxyphosphonates.[11]

However, to the best of our knowledge, the enantioselective synthesis of β-amino-α-hydroxyphosphonates containing two adjacent quaternary stereocenters has never been reported. In fact, β-amino-α-hydroxyphosphonates based on a oxindole

Received: October 9, 2015
Published: October 29, 2015

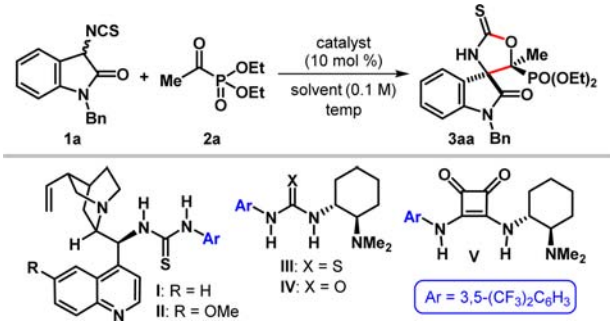
DOI: 10.1021/acs.orglett.5b02929
Org. Lett. 2015, 17, 5508–5511

framework remained unknown, even today.[12] Herein we disclose the first catalytic diastereo- and enantioselective synthesis of β-amino-α-hydroxyphosphonate derivatives based on a spirooxindole framework (Scheme 1B). This is also the first enantioselective synthesis of β-amino-α-hydroxyphosphonates containing two contiguous quaternary stereocenters.

We envisioned the use of 3-isothiocyanato oxindoles considering their recent insurgence as a highly reactive ambiphilic synthon to spirooxindoles.[13,14] We surmised that the alkoxide generated during the diastereo- and enantioselectivity-determining aldol reaction between 3-isothiocyanato oxindoles and α-ketophosphonates should be intercepted by the isothiocyanate moiety to furnish the desired spirooxindoles containing the β-amino-α-hydroxyphosphonate functionality (Scheme 1B). Bifunctional tertiary amino-(thio)urea derivatives[15] were selected as the catalyst candidates, considering their precedence in similar transformations.[13,14]

Accordingly, we began our investigation by designing a model reaction between *N*-benzyl-3-isothiocyanato oxindole **1a** and diethyl acetylphosphonate **2a** (Table 1). The near spontaneous

Table 1. Catalyst Screening and Reaction Optimization[a]



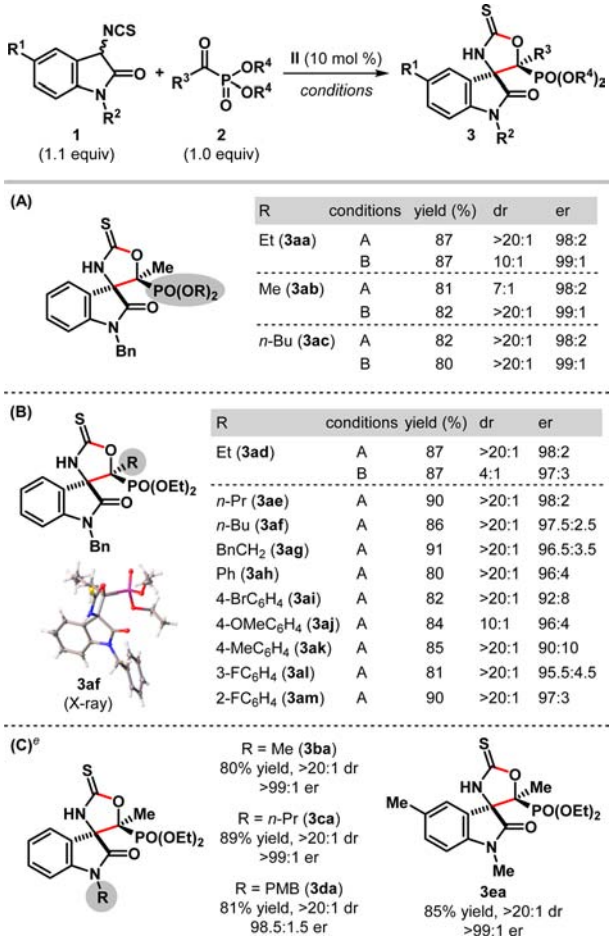
entry	cat.	solvent	temp, °C	*t*, min[b]	dr[c]	er[d]
1	–	CH_2Cl_2	25	5	n.d.	–
2	**I**	CH_2Cl_2	25	5	8:1	92:8
3	**I**	CH_2Cl_2	−20	5	3:1	95:5
4	**I**	CH_2Cl_2	−40	5	9:1	95.5:4.5
5	**I**	CH_2Cl_2	−78	5	10:1	97:3
6	**I**	CH_2Cl_2	−82	5	15:1	98:2
7	**II**	CH_2Cl_2	−78	5	15:1	99:1
8	**III**	CH_2Cl_2	−78	5	>20:1	6.5:93.5
9	**IV**	CH_2Cl_2	−78	5	5:1	3.5:96.5
10	**V**	CH_2Cl_2	−78	5	7:1	4:96
11	**II**	toluene	−78	5	10:1	99:1
12	**II**	2-MeTHF	−78	5	10:1	98:2
13	**II**	2-MeTHF	−95	30[e]	>20:1	98:2

[a]Reactions were performed using 1.1 equiv of **1a** and 1.0 equiv of **2a**. [b]Time required for complete consumption of **2a**. [c]Diastereomeric ratio (dr) as determined by ^{1}H NMR analysis of the crude reaction mixture; n.d. = not determined. [d]Enantiomeric ratio (er) as determined by HPLC analysis using a column with a chiral stationary phase. [e]The reaction was conducted with slow addition of **1a** over 30 min.

reaction at 25 °C in CH_2Cl_2 in the absence of any catalyst clearly confirms the reactive nature of both **1a** and **2a** (entry 1). The same reaction, when conducted in the presence of cinchonidine-derived bifunctional thiourea **I**, led to the formation of β-amino-α-hydroxyphosphonic acid derivative **3aa**, rather surprisingly, with good diastereoselectivity and promising enantioselectivity (entry 2). Lowering the reaction temperature offered beneficial influence on both dr and er without compromising the reaction rate (entries 3−6). Quinine-derived thiourea **II** turned out to be a better catalyst, and at −78 °C, **3aa** could be obtained with 15:1 dr and 99:1 er (entry 7). Bifunctional (thio)ureas and squaramide derived from *trans*-1,2-diaminocyclohexane (**III**−**V**) are equally active, even though somewhat less enantioselective (entries 8−10). Halogenated solvents could be avoided as a similar level of selectivity was obtained when the reaction was conducted in toluene or 2-MeTHF (entries 11−12). In fact, **3aa** was obtained practically as a single diastereomer in excellent er when the reaction was carried out in 2-MeTHF at −95 °C with slow addition of **1a** over 30 min (entry 13).

Having optimized the catalyst, the generality of this cascade reaction was evaluated. As shown in Table 2, we selected two sets of conditions using 10 mol % of quinine-derived thiourea **II**: Under *conditions A*, the reaction was carried out in 2-MeTHF at −95 °C with slow addition of **1** over 30 min, while *conditions B* include the reaction in toluene at −78 °C with slow addition of **1** over 5 min. The reactions were found to be practically diffusion controlled under both of these conditions, and complete

Table 2. Substrate Scope[a,b,c,d]



R	conditions	yield (%)	dr	er
Et (**3aa**)	A	87	>20:1	98:2
	B	87	10:1	99:1
Me (**3ab**)	A	81	7:1	98:2
	B	82	>20:1	99:1
n-Bu (**3ac**)	A	82	>20:1	98:2
	B	80	>20:1	99:1

R	conditions	yield (%)	dr	er
Et (**3ad**)	A	87	>20:1	98:2
	B	87	4:1	97:3
n-Pr (**3ae**)	A	90	>20:1	98:2
n-Bu (**3af**)	A	86	>20:1	97.5:2.5
$BnCH_2$ (**3ag**)	A	91	>20:1	96.5:3.5
Ph (**3ah**)	A	80	>20:1	96:4
4-BrC_6H_4 (**3ai**)	A	82	>20:1	92:8
4-$OMeC_6H_4$ (**3aj**)	A	84	10:1	96:4
4-MeC_6H_4 (**3ak**)	A	85	>20:1	90:10
3-FC_6H_4 (**3al**)	A	81	>20:1	95.5:4.5
2-FC_6H_4 (**3am**)	A	90	>20:1	97:3

[a]Reactions were performed on a 0.05 mmol scale. *Conditions A*: reaction in 2-MeTHF (0.1 M) at −95 °C with slow addition of **1** over 30 min. *Conditions B*: reaction in toluene (0.1 M) at −78 °C with slow addition of **1** over 5 min. [b]Yields correspond to the isolated yield. [c]Diastereomeric ratio (dr) was determined by ^{1}H NMR analysis of the crude reaction mixture. [d]Enantiomeric ratio (er) was determined by HPLC analysis using a chiral stationary phase. [e]Reactions under conditions A.

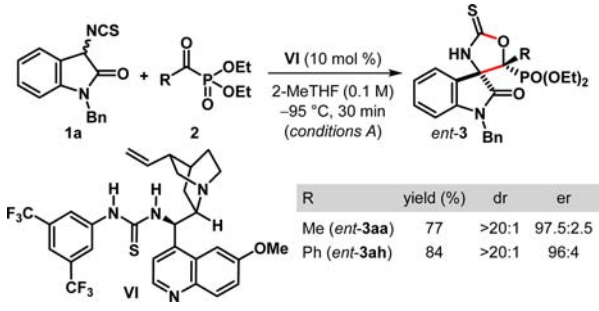
DOI: 10.1021/acs.orglett.5b02929
Org. Lett. 2015, 17, 5508−5511

consumption of **2** was observed immediately upon addition of **1**. The optimum catalyst and reaction conditions were found to be applicable for a broad range of α-ketophosphonates (**2**), and in all the cases the products were obtained in high yields (Table 2A–B). Even though comparable enantioselectivities were observed under both conditions for aliphatic α-ketophosphonates, *conditions A* were found to be more suitable for aromatic α-ketophosphonates. However, in almost all cases β-amino-α-hydroxyphosphonate derivatives (**3**) were obtained as a single diastereomer with good to excellent er. Similarly, 3-isothiocyanato oxindoles (**1**) with different N-substituents as well as 1,5-dimethyl derivative were also tolerated and the products were obtained in high yields as a single diastereomer with outstanding enantioselectivities (Table 2C). Further scope with respect to differently substituted 3-isothiocyanato oxindoles could not be demonstrated because of limited access to such compounds and their precursors.

X-ray diffraction analysis of the single crystals obtained for **3af** established its relative and absolute configuration (Table 2B).[16] The stereochemistry of the remaining products was assigned by analogy as the same.

A prominent drawback of the use of cinchona alkaloids or their derivatives as a catalyst is the nonavailability of their respective enantiomers. As a result, the accessibility of both product antipodes with equally high enantioselectivities cannot be guaranteed.[17] We were pleased to note that the enantiomeric products (*ent*-**3**) of this cascade reaction could be obtained using quinidine-derived thiourea (**VI**) as a single diastereomer in high yields with equally high enantioselectivities, as exemplified by *ent*-**3aa** and *ent*-**3ah** (Scheme 2).

Scheme 2. Synthesis of Enantiomeric Products



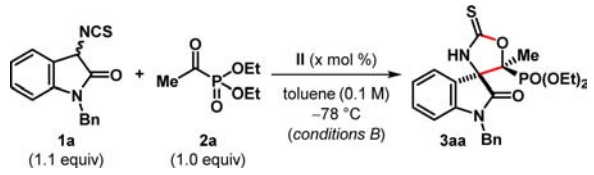
R	yield (%)	dr	er
Me (*ent*-**3aa**)	77	>20:1	97.5:2.5
Ph (*ent*-**3ah**)	84	>20:1	96:4

Intrigued by the high reactivity of the substrates and fast reactions, we decided to test the viability of this protocol at lower catalyst loading. As detailed in Table 3, the catalyst loading could be reduced down to 2 mol % without affecting the reaction rate or dr, and the product could still be isolated with high er (entry 3). Further lowering of the catalyst loading led to considerable loss in reaction rate and stereoselectivities (entry 4).

The expediency of our protocol was then tested by carrying out the cascade aldol–cyclization reaction on a 0.5 mmol scale using only 2 mol % of the catalyst **II** (Schme 3A). Notwithstanding the longer reaction time, **3aa** was isolated in 80% yield with the same level of diastereo- and enantioselectivity as observed for small scale experimentation (Table 3, entry 3).

The products of this reaction can be modified to allow easy access to differently functionalized spirooxindoles (Scheme 3B). Thus, methylation of **3aa** under mild conditions furnished spirocyclic 2-methylthio-oxazoline derivative **4** in 93% yield. Spirooxindole **4** bears structural resemblances to spirobrassinins, a family of natural products with a broad spectrum of biological

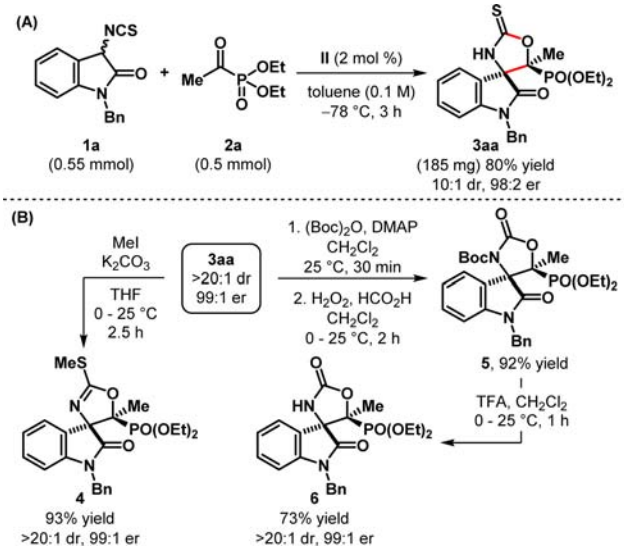
Table 3. Reaction with a Lower Catalyst Loading[a]



entry	*x*	*t*, min[b]	dr[c]	er[d]
1	10	5	10:1	99:1
2	5	5	10:1	98.5:1.5
3	2	5	10:1	98:2
4	1	20	5:1	77:23

[a]Reactions were performed on a 0.05 mmol scale. [b]Time required for complete consumption of **2a**. [c]Diastereomeric ratio (dr) as determined by ^{1}H NMR analysis of the crude reaction mixture. [d]Enantiomeric ratio (er) as determined by HPLC analysis using a column with a chiral stationary phase.

Scheme 3. (A) Large-Scale Experiment and (B) Functionalization of the Product



activities.[18] Regardless of the popularity of 3-isothiocyanato oxindoles as an ambiphilic synthon, the corresponding isocyanates, to our knowledge, have never been used in enantioselective synthesis. Fortunately, the products can be oxidized to the corresponding oxo-analogs by treatment with aqueous hydrogen peroxide under acidic conditions. For example, oxazolidinyl spirooxindole **6** could be obtained in good yield from **3aa** following a three-step sequence. No loss of enantiopurity was observed during any of these synthetic transformations.

In summary, we have developed a cascade aldol–cyclization reaction between 3-isothiocyanato oxindoles and α-ketophosphonates for the synthesis of spirooxindole-based β-amino-α-hydroxyphosphonate derivatives. Catalyzed by cinchona alkaloids-based bifunctional thiourea derivatives, this protocol delivers 2-thioxooxazolidinyl phosphonates bearing two adjacent quaternary stereogenic centers, generally in high yields with excellent diastereo- and enantioselectivities.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02929.

DOI: 10.1021/acs.orglett.5b02929
Org. Lett. 2015, 17, 5508–5511

Experimental details (PDF)
Characterization data (PDF)
Crystallographic data for **3af** (CIF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: sm@orgchem.iisc.ernet.in.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work is funded by the DAE-BRNS [Grant No. 2013/37C/56/BRNS/2440] and CSIR [Grant No. 02(0207)/14/EMR-II]. S.K. thanks the Council of Scientific and Industrial Research (CSIR), New Delhi for a doctoral fellowship. We wish to thank Mr. Prodip Howlader (Department of Inorganic and Physical Chemistry, IISc, Bangalore) for his help with the X-ray structure analysis.

REFERENCES

(1) (a) Mucha, A.; Kafarski, P.; Berlicki, Ł. *J. Med. Chem.* **2011**, *54*, 5955. (b) Tao, M.; Bihovsky, R.; Wells, G. J.; Mallamo, J. P. *J. Med. Chem.* **1998**, *41*, 3912. (c) Patel, D. V.; Rielly-Gauvin, K.; Ryono, D. E.; Free, C. A.; Rogers, W. L.; Smith, S. A.; DeForrest, J. M.; Oehl, R. S.; Petrillo, E. W., Jr. *J. Med. Chem.* **1995**, *38*, 4557. (d) Wester, R. T.; Chambers, R. J.; Green, M. D.; Murphy, W. R. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 2005. (e) Stowasser, B.; Budt, K.-H.; Jian-Qi, L.; Peyman, A.; Ruppert, D. *Tetrahedron Lett.* **1992**, *33*, 6625. (f) Patel, D. V.; Rielly-Gauvin, K.; Ryono, D. E. *Tetrahedron Lett.* **1990**, *31*, 5587. (g) Dellaria, J. F., Jr.; Maki, R. G.; Stein, H. H.; Cohen, J.; Whittern, D.; Marsh, K.; Hoffman, D. J.; Plattner, J. J.; Perun, T. J. *J. Med. Chem.* **1990**, *33*, 534.

(2) (a) Coeffard, V.; Beaudet, I.; Evain, M.; Le Grognec, E. L.; Quintard, J.-P. *Eur. J. Org. Chem.* **2008**, *2008*, 3344. (b) Drag, M.; Pawelczak, M.; Kafarski, P. *Chirality* **2003**, *15*, S104. (c) Smith, A. B., III; Yager, K. M.; Taylor, C. M. *J. Am. Chem. Soc.* **1995**, *117*, 10879. (d) Allen, J. G.; Atherton, F. R.; Hall, M. J.; Hassall, C. H.; Holmes, S. W.; Lambert, R. W.; Nisbet, L. J.; Ringrose, P. S. *Nature* **1978**, *272*, 56.

(3) For selected reviews, see: (a) Dzięgielewski, M.; Pięta, J.; Kamińska, E.; Albrecht, Ł. *Eur. J. Org. Chem.* **2015**, 677. (b) Zhao, D.; Wang, R. *Chem. Soc. Rev.* **2012**, *41*, 2095. (c) Bhadury, P. S.; Li, H. *Synlett* **2012**, *23*, 1108. (d) Albrecht, Ł.; Albrecht, A.; Krawczyk, H.; Jørgensen, K. A. *Chem. - Eur. J.* **2010**, *16*, 28. (e) Ma, J.-A. *Chem. Soc. Rev.* **2006**, *35*, 630. (f) Palacios, F.; Alonso, C.; de los Santos, J. M. *Chem. Rev.* **2005**, *105*, 899.

(4) (a) Zhou, F.; Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381. (b) Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8748. (c) Marti, C.; Carreira, E. M. *Eur. J. Org. Chem.* **2003**, 2209. (d) Lin, H.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 36.

(5) For selected reviews, see: (a) Cheng, D.; Ishihara, Y.; Tan, B.; Barbas, C. F., III *ACS Catal.* **2014**, *4*, 743. (b) Hong, L.; Wang, R. *Adv. Synth. Catal.* **2013**, *355*, 1023. (c) Singh, G. S.; Desta, Z. Y. *Chem. Rev.* **2012**, *112*, 6104. (d) Ball-Jones, N. R.; Badillo, J. J.; Franz, A. K. *Org. Biomol. Chem.* **2012**, *10*, 5165. (e) Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, 3003.

(6) Tripathi, C. B.; Kayal, S.; Mukherjee, S. *Org. Lett.* **2012**, *14*, 3296.

(7) (a) Mastalerz, P.; Kafarski, P. In *Aminophosphonic and Aminophosphinic Acids-Chemistry and Biological Activity*; Kukhar, V. P., Hudson, H. R., Eds.; John Wiley: Chichester, 2000; pp 1−31. (b) Wróblewski, A. E.; Piotrowska, D. G. *Tetrahedron: Asymmetry* **2000**, *11*, 2615. (c) Ojima, I.; Lin, S.; Wang, T. *Curr. Med. Chem.* **1999**, *6*, 927. (d) Patel, D. V.; Rielly-Gauvin, K.; Ryono, D. E. *Tetrahedron Lett.* **1990**, *31*, 5591.

(8) (a) Seo, Y. J.; Kim, J.; Lee, H.-K. *J. Org. Chem.* **2015**, *80*, 8887. (b) Zhang, H.; Wen, X.; Gan, L.; Peng, Y. *Org. Lett.* **2012**, *14*, 2126. For catalytic enantioselective synthesis of α-amino-β-hydroxyphosphonates, see: (c) Cao, Y.-M.; Shen, F.-F.; Zhang, F.-T.; Zhang, J.-L.; Wang, R. *Angew. Chem., Int. Ed.* **2014**, *53*, 1862. (d) Han, W.-Y.; Zhao, J.-Q.; Wu, Z.-J.; Zhang, X.-M.; Yuan, W.-C. *J. Org. Chem.* **2013**, *78*, 10541. (e) Togni, A.; Pastor, S. D. *Tetrahedron Lett.* **1989**, *30*, 1071.

(9) (a) Cravotto, G.; Giovenzana, G. B.; Pagliarin, R.; Palmisano, G.; Sisti, M. *Tetrahedron: Asymmetry* **1998**, *9*, 745. Also see: (b) Thomas, A. A.; Sharpless, K. B. *J. Org. Chem.* **1999**, *64*, 8379.

(10) (a) Mandal, T.; Samanta, S.; Zhao, C.-G. *Org. Lett.* **2007**, *9*, 943. Also see: (b) Chen, X.; Wang, J.; Zhu, Y.; Shang, D.; Gao, B.; Liu, X.; Feng, X.; Su, Z.; Hu, C. *Chem. - Eur. J.* **2008**, *14*, 10896.

(11) Serrano, I.; Monge, D.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *Chem. Commun.* **2015**, *51*, 4077.

(12) For enantioselective synthesis of oxindole-based α-aminophosphonic acids, see: (a) Kumar, A.; Sharma, V.; Kaur, J.; Kumar, V.; Mahajan, S.; Kumar, N.; Chimni, S. S. *Tetrahedron* **2014**, *70*, 7044. (b) George, J.; Sridhar, B.; Reddy, B. V. S. *Org. Biomol. Chem.* **2014**, *12*, 1595.

(13) For selected examples, see: (a) Zhao, J.-Q.; Zhou, M.-Q.; Wu, Z.-J.; Wang, Z.-H.; Yue, D.-F.; Xu, X.-Y.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2015**, *17*, 2238. (b) Cai, H.; Zhou, Y.; Zhang, D.; Xu, J.; Liu, H. *Chem. Commun.* **2014**, *50*, 14771. (c) Kayal, S.; Mukherjee, S. *Eur. J. Org. Chem.* **2014**, 6696. (d) Tan, F.; Lu, L.-Q.; Yang, Q.-Q.; Guo, W.; Bian, Q.; Chen, J.-R.; Xiao, W.-J. *Chem. - Eur. J.* **2014**, *20*, 3415. (e) Liu, X.-L.; Han, W.-Y.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2013**, *15*, 1246. (f) Chen, Q.; Liang, J.; Wang, S.; Wang, D.; Wang, R. *Chem. Commun.* **2013**, *49*, 1657. (g) Jiang, Y.; Pei, C.-K.; Du, D.; Li, X.-G.; He, Y.-N.; Xu, Q.; Shi, M. *Eur. J. Org. Chem.* **2013**, 7895. (h) Han, W.-Y.; Li, S.-W.; Wu, Z.-J.; Zhang, X.-M.; Yuan, W.-C. *Chem. - Eur. J.* **2013**, *19*, 5551. (i) Tan, F.; Cheng, H.-G.; Feng, B.; Zou, Y.-Q.; Duan, S.-W.; Chen, J.-R.; Xiao, W.-J. *Eur. J. Org. Chem.* **2013**, *2013*, 2071. (j) Kato, S.; Kanai, M.; Matsunaga, S. *Chem. - Asian J.* **2013**, *8*, 1768. (k) Wu, H.; Zhang, L.-L.; Tian, Z.-Q.; Huang, Y.-D.; Wang, Y.-M. *Chem. - Eur. J.* **2013**, *19*, 1747. (l) Cao, Y.-M.; Shen, F.-F.; Zhang, F.-T.; Wang, R. *Chem. - Eur. J.* **2013**, *19*, 1184. (m) Kato, S.; Yoshino, T.; Shibasaki, M.; Kanai, M.; Matsunaga, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 7007. (n) Chen, W.-B.; Wu, Z.-J.; Hu, J.; Cun, L.-F.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2011**, *13*, 2472.

(14) For a review, see: Han, W.-Y.; Zhao, J.-Q.; Zuo, J.; Xu, X.-Y.; Zhang, X.-M.; Yuan, W.-C. *Adv. Synth. Catal.* **2015**, *357*, 3007.

(15) For pioneering contributions, see: (a) Bernardi, L.; Fini, F.; Herrera, R. P.; Ricci, A.; Sgarzani, V. *Tetrahedron* **2006**, *62*, 375. (b) McCooey, S. H.; Connon, S. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 6367. (c) Ye, J.; Dixon, D. J.; Hynes, P. S. *Chem. Commun.* **2005**, 4481. (d) Vakulya, B.; Varga, S.; Csámpai, A.; Soós, T. *Org. Lett.* **2005**, *7*, 1967. (e) Li, B.-J.; Jiang, L.; Liu, M.; Chen, Y.-C.; Ding, L.-S.; Wu, Y. *Synlett* **2005**, 603. (f) Okino, T.; Hoashi, Y.; Takemoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 12672. For selected reviews, see: (g) Siau, W.-Y.; Wang, J. *Catal. Sci. Technol.* **2011**, *1*, 1298. (h) Connon, S. J. *Chem. Commun.* **2008**, 2499.

(16) CCDC 1429374 contains the crystallographic data for **3af**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(17) For representative examples, see: (a) Choudhury, A. R.; Mukherjee, S. *Org. Biomol. Chem.* **2012**, *10*, 7313. (b) Wynberg, H.; Staring, E. G. J. *J. Am. Chem. Soc.* **1982**, *104*, 166.

(18) For selected examples, see: (a) Kang, T.-H.; Matsumoto, K.; Tohda, M.; Murakami, Y.; Takayama, H.; Kitajima, M.; Aimi, N.; Watanabe, H. *Eur. J. Pharmacol.* **2002**, *444*, 39. (b) Pedras, M. S. C.; Okanga, F. I.; Zaharia, I. L.; Khan, A. Q. *Phytochemistry* **2000**, *53*, 161. (c) Baur, E.; Stãdler, K.; Monde, K.; Takasugi, M. *Chemoecology* **1998**, *8*, 163.

DOI: 10.1021/acs.orglett.5b02929
Org. Lett. 2015, 17, 5508−5511