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Chiral Calcium Organophosphate-Catalyzed Enantioselective Electrophilic Amination of Enamides

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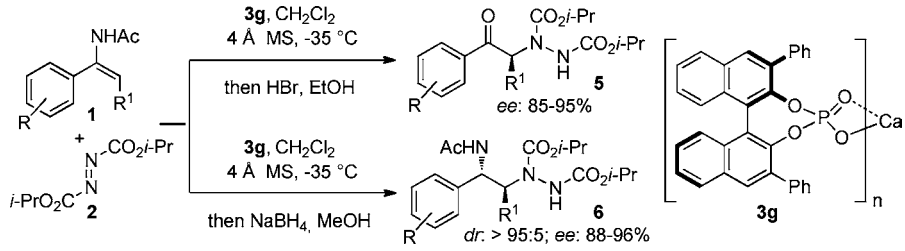
ABSTRACT



Highly enantioselective direct amination of enamides catalyzed by chiral nonracemic calcium bis(phosphate) complex 3g afforded optically active 1,2-hydrazinoimines 4. Following a subsequent in situ hydrolysis or reduction, 2-hydrazinoketones 5 or *syn*-1,2-disubstituted 1,2-diamines 6 were obtained in high yields and excellent enantiomeric excess.

The importance of enamides (enecarbamates)[1,2] as useful nucleophiles in enantioselective addition reactions has been growing enormously ever since Kobayashi's seminal report in 2004.[2b] The Lewis acid and Brønsted acid catalyzed enantioselective C−C bond forming processes involving enamides and carbon-centered electrophiles[2−6] are now well established. However, reports on nucleophilic addition of enamides to electrophilic nitrogen atom remained scarce, in sharp contrast to the enamine chemistry.[7−11] Kobayashi et al. reported the first examples of enantioselective amination of (*E*)-enecarbamates using chiral diamines-Cu(OTf)$_2$ complexes as catalysts.[4d,12] Very recently, Feng et al. detailed a chiral *N*,*N*-dioxide-Cu(OTf)$_2$ complex-catalyzed asymmetric α-amination of (*Z*)-enamides.[13] To the best of our knowledge, no example of Brønsted acid catalyzed asymmetric α-aminations of enamides (enecarbamates) with azodicarboxylates has been described.[14] In connection with our studies on small organic molecule-catalyzed transformation

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(1) For review see: (a) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054. (b) Nugenta, T. C.; El-Shazlya, M. *Adv. Synth. Catal.* **2010**, *352*, 753.

(2) (a) Carbery, D. R. *Org. Biomol. Chem.* **2008**, *6*, 3455. (b) Matsubara, R.; Kobayashi, S. *Acc. Chem. Res.* **2008**, *41*, 292.

(3) For selected examples with imines as electrophiles, see: (a) Matsubara, R.; Nakamura, Y.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 1679. (b) Kiyohara, H.; Matsubara, R.; Kobayashi, S. *Org. Lett.* **2006**, *8*, 5333. (c) Terada, M.; Machioka, K.; Sorimachi, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2254. (d) Matsubara, R.; Doko, T.; Uetake, R.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 3047. (e) Terada, K.; Machioka, K.; Sorimachi, K. *J. Am. Chem. Soc.* **2007**, *129*, 10336. (f) Baudequin, C.; Zamfir, A.; Tsogoeva, S. B. *Chem. Commun.* **2008**, 4637. (g) Terada, M.; Machioka, K.; Sorimachi, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 2553. (h) Liu, H.; Dagousset, G.; Masson, G.; Retailleau, P.; Zhu, J. *J. Am. Chem. Soc.* **2009**, *131*, 4598. (i) Dagousset, G.; Drouet, F.; Masson, G.; Zhu, J. *Org. Lett.* **2009**, *11*, 5546.

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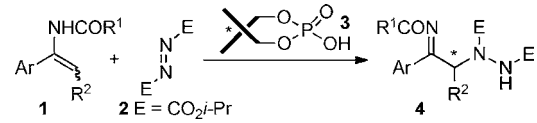
of enecarbamates[3g,h] and our ongoing project on catalytic asymmetric synthesis,[15] we were interested in examining a chiral phosphoric acid-catalyzed amination of enamides using azodicarboxylate as an electrophilic partner.

Chiral BINOL-derived phosphoric acids, pioneered by Akiyama et al. and Terada et al., are now well-established bifunctional organocatalysts that are particularly effective in catalyzing the addition of nucleophiles to imines.[16,17] Therefore, we reasoned that chiral phosphoric acids might be able to activate both enamides **1** and azodicarboxylates **2** to provide an asymmetric environment for the desired enantioselective amination process (Scheme 1).

Scheme 1. Catalytic Enantioselective α-Amination of Enamides



To validate our hypothesis, we initially examined the reaction of (*E*)-*N*-(1-phenylprop-1-en-1-yl)acetamide (**1a**) with diisopropyl azodicarboxylate (**2a**) in the presence of 10 mol % of chiral phosphoric acid **3a** in DCM at −35 °C. This resulted in the formation of the desired 1,2-hydrazinoimine **4a**, accompanied by the 1,2-hydrazinoketone **5a**. Although addition of molecular sieves in the reaction prevented the hydrolysis of the unstable *N*-acylimine **4a**, the enantioselectivities and yields were determined for compound **5a**, obtained by in situ hydrolysis of **4a** under acidic conditions (EtOH and 33% HBr in AcOH, v/v = 1/10). Phosphoric acids with different steric environment (**3a**−**f**, Figure 1) were next examined. It was found that the less

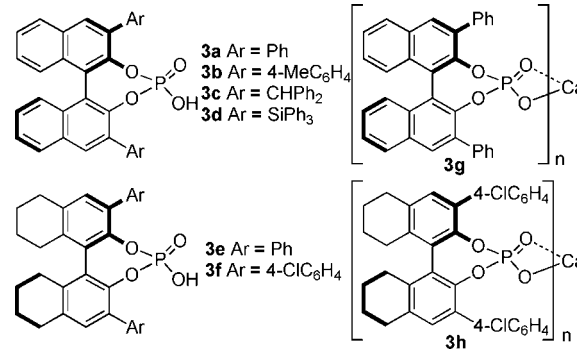


Figure 1. List of phosphoric acids examined.

hindered phosphoric acid **3a** was the most effective in terms of both yield and ee of the product (entries 2−7, Table 1).

During this study we noticed that enantioselectivities (from 78% to 89%) and yields (from 45% to quantitative) under the optimal conditions varied considerably depending on the batch of **3a** used. Following Ding's observation,[18] **3a** washed with HCl was used as catalyst that led indeed to the

(4) For selected examples with aldehydes and ketones as electrophiles, see: (a) Matsubara, R.; Nakamura, Y.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3258. (b) Fossey, J. S.; Matsubara, R.; Vital, P.; Kobayashi, S. *Org. Biomol. Chem.* **2005**, *3*, 2910. (c) Matsubara, R.; Kawai, N.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 3814. (d) Terada, M.; Soga, K.; Momiyama, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 4122. (e) Yang, L.; Wang, D.-X.; Huang, Z.-T.; Wang, M. X. *J. Am. Chem. Soc.* **2009**, *131*, 10390.

(5) For selected examples with Michael acceptors as electrophiles, see: (a) Berthiol, F.; Matsubara, R.; Kawai, N.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 7803. (b) Hayashi, Y.; Gotoh, H.; Masui, R.; Ishikawa, H. *Angew. Chem., Int. Ed.* **2010**, *47*, 4012. (c) Zu, L.; Xie, H.; Li, H.; Wang, J.; Yu, X.; Wang, W. *Chem.—Eur. J.* **2008**, *14*, 6333.

(6) Guo, Q.-X.; Peng, Y.-G.; Zhang, J.-W.; Song, L.; Feng, Z.; Gong, L.-Z. *Org. Lett.* **2009**, *11*, 4620.

(7) For selected pioneering work on asymetric α-amination using azodicarboxylate as electrophilic nitrogen, see: Evans, D. A.; Nelson, S. G. *J. Am. Chem. Soc.* **1997**, *119*, 6452.

(8) For general reviews of α-amination, see: (a) Bøgevig, A.; Juhl, K.; Kumaragurubaran, N.; Zhuang, W.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1790. (b) Erdik, E. *Tetrahedron* **2004**, *60*, 8747. (c) Greck, C.; Drouillat, B.; Thomassigny, C. *Eur. J. Org. Chem.* **2004**, 1377. (d) Marigo, M.; Jørgensen, K. A. *Chem. Commun.* **2006**, 2001. (e) Nájera, C.; Sansano, J. M. *Chem. Rev.* **2007**, *107*, 4584. (f) Vilaivan, T.; Bhanthmnavin, W. *Molecules* **2010**, *15*, 917.

(9) For selected reviews on enamine catalysis, see: (a) Dalko, P. I. *Enantioselective Organocatalysis*; Wiley-VCH: Weinheim, 2007. (b) Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471. (c) MacMillan, D. W. C. *Nature* **2008**, *455*, 304. (d) Melchiorre, P.; Marigo, M.; Carlone, A.; Bartoli, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 6138. (e) Bertelsen, S.; Jørgensen, K. A. *Chem. Soc. Rev.* **2009**, *38*, 2178.

(10) For selected examples of proline-catalyzed α-amination of aldehydes and ketones with dialkylazodicarboxylate, see: (a) List, B. *J. Am. Chem. Soc.* **2002**, *124*, 5656. (b) Kumaragurubaran, N.; Juhl, K.; Zhuang, W.; Bøgevig, A.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 6254. (c) Vogt, H.; Vanderheriden, S.; Bröse, S. *Chem. Commun.* **2003**, 2448. (d) Chowdari, N. S.; Ramachary, D. B.; Barbas, C. F., III *Org. Lett.* **2003**, *5*, 1685. (e) Dahlin, N.; Bøgevig, A.; Adolfsson, H. *Adv. Synth. Catal.* **2004**, *346*, 1101. (f) Suri, J. T.; Steiner, D.; Barbas, C. F., III *Org. Lett.* **2005**, *7*, 3885. (g) Franzén, J.; Marigo, M.; Fielenbach, D.; Wabnitz, T.; Kjærsgaard, A.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 18296. (h) Baumann, T.; Vogt, H.; Bräse, S. *Eur. J. Org. Chem.* **2007**, 266. (i) Kotkar, S. P.; Chavan, V. B.; Sudalai, A. *Org. Lett.* **2007**, *9*, 1001. (j) Dinér, P.; Kjærsgaard, A.; Lie, M. A.; Jørgensen, K. A. *Chem.—Eur. J.* **2008**, *14*, 122. (k) Hayashi, Y.; Aratake, S.; Imai, Y.; Hibino, K.; Chen, Q.-Y.; Yamaguchi, J.; Uchimaru, T. *Chem. Asian J.* **2008**, *3*, 225. (l) Baumann, T.; Bächle, M.; Hartmann, C.; Bräse, S. *Eur. J. Org. Chem.* **2008**, 2207. (m) Liu, P.-M.; Magar, D. R.; Chen, K. *Eur. J. Org. Chem.* **2010**, 5705.

(11) For selected examples of Cinchona-catalyzed α-amination of ketones with dialkylazodicarboxylate, see: Liu, T.-Y.; Cui, H.-L.; Zhang, Y.; Jiang, K.; Du, W.; He, Z.-Q.; Chen, Y. C. *Org. Lett.* **2007**, *9*, 3671.

(12) Matsubara, R.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 7993.

(13) Chang, L.; Kuang, Y.; Qin, B.; Zhou, X.; Liu, X.; Lin, L.; Feng, X. *Org. Lett.* **2010**, *12*, 2214.

(14) During preparation of this manuscript, Zhong reported a chiral phosphoric acid-catalyzed asymmetric α-aminoxylation of enecarbamates; see: Lu, M.; Lu, Y.; Zhu, D.; Zeng, X.; Li, X.; Zhong, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 8588.

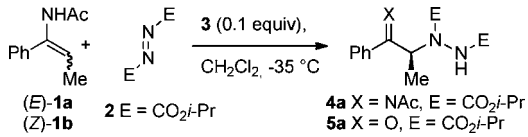
(15) (a) Wang, S.-X.; Wang, M.-X.; Wang, D.-X.; Zhu, J. *Org. Lett.* **2007**, *9*, 3615. (b) Wang, S.-X.; Wang, M.-X.; Wang, D.-X.; Zhu, J. *Eur. J. Org. Chem.* **2007**, 4076. (c) Wang, S.-X.; Wang, M.-X.; Wang, D.-X.; Zhu, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 388. (d) Yue, T.; Wang, M.-X.; Wang, D.-X.; Zhu, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 9554. (e) Yue, T.; Wang, M.-X.; Wang, D.-X.; Masson, G.; Zhu, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6717.

(16) For recent reviews on chiral phosphoric acid catalysis, see: (a) Akiyama, T.; Itoh, J.; Fuchibe, K. *Adv. Synth. Catal.* **2006**, *348*, 999. (b) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744. (c) Terada, M. *Chem. Commun.* **2008**, 4097. (d) Terada, M. *Synthesis* **2010**, 1929.

(17) For recent reviews on Brønsted acid catalysis, see: (a) Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713. (b) Yu, X.; Wang, W. *Chem. Asian J.* **2008**, *3*, 516. (c) Kampen, D.; Reisinger, C. M.; List, B. *Top. Curr. Chem.* **2010**, *291*, 395.

(18) Xu, S.; Wang, Z.; Zhang, X.; Zhang, X.; Ding, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 2840.

Table 1. Synthesis of 1,2-Hydrazinoketones: A Survey of Reaction Conditions



entry	1	additive	3	yield of **4a** (%)[e]	yield of **5a** (%)[e]	ee (%)[f,g]
1[a]	*E*-**1a**	no	**3a**[c]	35	29 (**5a**)	80
2[b]	*E*-**1a**	MS4Å	**3a**[c]		99 (**5a**)	89
3[b]	*E*-**1a**	MS4Å	**3b**[c]		56 (**5a**)	71
4[b]	*E*-**1a**	MS4Å	**3c**[c]		66 (**5a**)	18
5[b]	*E*-**1a**	MS4Å	**3d**[c]		57 (**5a**)	8
6[b]	*E*-**1a**	MS4Å	**3e**[c]		44 (**5a**)	88
7[b]	*E*-**1a**	MS4Å	**3f**[c]		59 (**5a**)	78
8[b]	*E*-**1a**	MS4Å	**3a**[d]		92 (**5a**)	85[h]
9[b]	*E*-**1a**	MS4Å	**3g**		75 (**5a**)	95
10[b]	*E*-**1a**	MS4Å	**3h**		91 (**5a**)	89
11[b]	*Z*-**1a**	MS4Å	**3g**		23 (**5a**)	0

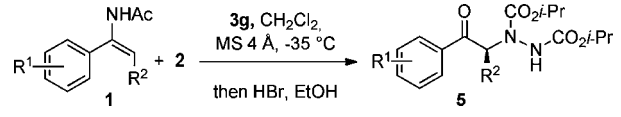
[a] Experimental conditions: **1a**/**2a**/**3** = 1.0/5.0/0.1 in CH_2Cl_2 (c = 0.1) at −35 °C. [b] General conditions: **1a**/**2a**/**3** = 1.0/5.0/0.1 in CH_2Cl_2 (c = 0.1) at −35 °C followed by acid hydrolysis with EtOH and 33% HBr in AcOH (v:v = 1/10). [c] Purified on silica gel. [d] Washed with HCl after purification on silica gel. [e] Yields refer to chromatographically pure products. [f] Enantiomeric excess was determined by chiral HPLC analysis. [g] For the determination of the absolute configuration, see the Supporting Information. [h] An additional experiment was performed with 20 mol % of phosphoric acid **3a** leading to **5a** in similar yield and ee.

reproducible ee values and yields. However, a slightly lower enantioselectivity was obtained with this acid-washed catalyst (entry 8). Inspired by the work of Ishihara,[19,20] the catalytic efficiency of chiral calcium phosphates **3g** and **3h** derived from **3a** and **3f**, respectively, were tested (entries 9 and 10, Table 1). Gratefully, with catalyst **3g**, compound **5a** was produced in 75% yield with 95% ee and the result was perfectly reproducible.[21−24] The same enantiomer of **5a** was produced whether **3a** or **3g** was used as a catalyst and the absolute configuration of **5a** was determined to be (*S*) by comparison of the sign of its optical rotation with that of the literature data.[13]

We have also examined the effect of the alkene geometry of enamides on the reaction outcome. It was observed that the (*Z*)-isomer **1b** (entry 11, Table 1) was much less reactive and no reaction took place at −35 °C. Performing the reaction at room temperature afforded the desired product **5a** in low yield with no enantioselectivity. These results are therefore complementary to Feng's catalytic system wherein the (*Z*)-enamides were the preferred substrates for the similar amination reaction.[13]

Having identified the optimum conditions, we explored the reaction scope using different (*E*)-*N*-(1-arylprop-1-en-1-yl)acetamides **1**. Results are summarized in Table 2.

Table 2. Scope of the Enantioselective Ca-Phosphate-Catalyzed Synthesis of 1,2-Hydrazinoketones.[a]



entry	R^1	R^2	5	yield (%)[b]	ee (%)[c]
1	3-Cl	Me	**5b**	80	90
2	4-Cl	Me	**5c**	97	85
3	3-F	Me	**5d**	77	90
4	4-Br	Me	**5e**	76	93
5	4-Me	Me	**5f**	83	88
6	4-OMe	Me	**5g**	73	91
7	4-CF_3	Me	**5h**	75	93
8	H	Et	**5i**	91	89[d]
9	H	*n*-Pr	**5j**	94	94

[a] General conditions: **1a**/**2a**/**3** = 1.1/5.0/0.1 in CH_2Cl_2 (c = 0.1) at −35 °C followed by acid hydrolysis with EtOH and 33% HBr in AcOH (v/v = 1/10). [b] Yields refer to chromatographically pure products. [c] Enantiomeric excess was determined by chiral HPLC analysis. [d] With 10 mol % of **3a**.

Enamides bearing electron-neutral, -rich, and -poor aromatic substituents at α-position react smoothly with **2** to give, after in situ hydrolysis, 2-hydrazinoketones **5** in good yields (75−97%) and excellent enantioselectivities (85−97% ee). In addition, enamide having a longer alkyl chain at the β-position, which gave low enantioselectivity in a previous report,[13] are suitable substrates (entries 8 and 9). With (*E*)-*N*-(1-phenylpent-1-en-1-yl)acetamides (**1j**, R^1 = H, R^2 = *n*-Pr), the corresponding hydrazinoketone **5j** was obtained in 94% yield with 97% ee.

With this transformation in hand, we next turned our attention to the in situ reduction of hydrazinoimines to 1,2-diamines which are very useful chiral ligands, auxiliaries, and building blocks in the synthesis of natural and bioactive products.[25] Reduction of **4a** with $NaBH_4$ (−78 to −45 °C, MeOH) according to Kobayashi et al. provided the *syn*-1,2-

(19) (a) Hatano, M.; Moriyama, K.; Maki, T.; Ishihara, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 3823. (b) Klussmann, M.; Ratjen, L.; Hoffmann, S.; Wakchaure, V.; Goddard, R.; List, B. *Synlett* **2010**, 2189. (c) For an example of phosphoramide/calcium complex, see: Rueping, M.; Theissmann, T.; Kuenkel, A.; Koenigs, R. M. *Angew. Chem., Int. Ed.* **2008**, *47*, 6798.

(20) (a) Hatano, M.; Ikeno, T.; Matsumura, T.; Torii, S.; Ishihara, K. *Adv. Synth. Catal.* **2008**, *350*, 1776. For a full account, see: (b) Hatano, M.; Ishihara, K. *Synthesis* **2010**, 3785.

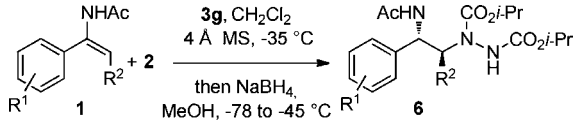
(21) For selected examples of phosphate ligands, see: (a) Suzuki, S.; Furono, H.; Yokoyama, Y.; Inanaga, J. *Tetrahedron: Asymmetry* **2006**, *17*, 504. (b) Yue, T.; Wang, M.-X.; Wang, D.-X.; Masson, G.; Zhu, J. *J. Org. Chem.* **2009**, *74*, 8396. (c) Yang, L.; Zhu, Q.; Guo, S.; Qian, B.; Xia, C.; Huang, H. *Chem.—Eur. J.* **2010**, *16*, 1638.

(22) For selected examples using combined chiral Brønsted acids and transition metals, see: (a) Komanduri, V.; Krische, M. J. *J. Am. Chem. Soc.* **2006**, *128*, 16448. (b) Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496. (c) Mukherjee, S.; List, B. *J. Am. Chem. Soc.* **2007**, *129*, 11336. (d) Hu, W.; Xu, X.; Zhou, J.; Liu, W.-J.; Huang, H.; Hu, J.; Yang, L.; Gong, L.-Z. *J. Am. Chem. Soc.* **2008**, *130*, 7782. (e) Li, C.; Wang, C.; Villa-Marcos, B.; Xiao, J. *J. Am. Chem. Soc.* **2008**, *130*, 14450. (f) Xu, X.; Zhou, J.; Yang, L.; Hu, W. *Chem. Commun.* **2008**, 6564. (g) Guo, Z.; Shi, T.; Jiang, J.; Yang, L.; Hu, W. *Org. Biomol. Chem.* **2009**, 5028. (h) Li, C.; Villa-Marcos, B.; Xiao, J. *J. Am. Chem. Soc.* **2009**, *131*, 6967. (i) Tetrade, M.; Toda, Y. *J. Am. Chem. Soc.* **2009**, *131*, 6354. (j) Lu, Y.; Johnstone, T. C.; Arndtsen, B. A. *J. Am. Chem. Soc.* **2009**, *131*, 11284. (k) Klussmann, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 7124. (l) Liu, X.-Y.; Che, C.-M. *Org. Lett.* **2009**, *11*, 4204. (m) Garcia-Garcia, P.; Lay, F.; Garcia-Garcia, P.; Rabalakos, C.; List, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 4363. (n) Shen, K.; Liu, X.; Cai, Y.; Lin, L.; Feng, X. *Chem.—Eur. J.* **2009**, *15*, 6008. (o) Yazaki, R.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 10275.

(23) The combination of chiral Brønsted acid and MgF_2: Lv, J.; Li, X.; Zhong, L.; Luo, S.; Cheng, J.-P. *Org. Lett.* **2010**, *12*, 1096.

diamine[26] **6a** in high diastereoselectivity (>95:5 dr).[27] This reduction step was found to be compatible with the amination process. Indeed, a one-pot amination/reduction process furnished *syn*-1,2-diamine **6a** in 84% yield with 92% ee (entry 1, Table 3). Other representative chiral 1,2-diamines

Table 3. Scope of the Enantioselective Ca-Phosphate-Catalyzed One-Step Synthesis of 1,2-Hydrazinoamines[a]



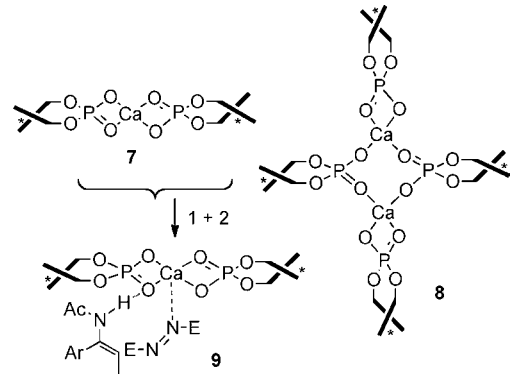
entry	R^1	R^2	**6**	yield (%)[b]	ee (%)[c]
1	H	Me	**6a**	84	92
2	3-F	Me	**6b**	88	88
3	4-CF_3	Me	**6c**	84	93
4	H	*n*-Pr	**6d**	99	96

[a] General conditions: **1a**/**2a**/**3** = 1.0/5.0/0.1 in CH_2Cl_2 (c = 0.1) at −35 °C followed by addition of $NaBH_4$ in MeOH. [b] Yields refer to chromatographically pure products. [c] Enantiomeric excess was determined by chiral HPLC analysis.

prepared were enlisted in Table 3. In general, diamines **6** were isolated in slightly higher yields than hydrazinoketones **5**. As expected, the ee of products **5** and **6** obtained by these two different one-pot processes were almost identical, reflecting directly the enantioselectivity of the amination step.

The precise structure of the catalyst **3g** is actually not known; however, we believe that divalent-Ca is able to react with Brønsted acids to form an oligomeric calcium complex as predicted by Ishihara et al.[18,28−30] The observed ^{31}P NMR chemical shift of **3g** agreed well with the chemical shifts observed for the oligomeric form reported previously (see the Supporting Information).[19a] Moreover, the catalyst **3a** gave a MALDI-TOF spectrum that exhibits [M + H] peaks at *m*/*z* 1039 and 2077, corresponding to monometallic and dimetallic species **7** and **8**, respectively (Scheme 2). In light of Ishihara's recent observation, we assumed that addition

Scheme 2. Ternary Complex, a Hypothetic Intermediate



of enamide **1** and azodicarboxylate **2** to **3g** could generate a monometallic complex with concurrent formation of an intermediate of type **9**.[19a,28] A pseudointramolecular *Si*-face attack of enamide **1** onto azodicarboxylate **2** would then take place to afford the observed (*S*)-hydrazinoimines **4** (Scheme 2).

In summary, we demonstrated that a chiral nonracemic calcium bis(phosphate) complex **3g** is capable of catalyzing an enantioselective nucleophilic addition of enamides to azodicarboxylate providing chiral enantio-enriched 1,2-hydrazinoimines. Subsequent in situ hydrolysis or diastereoselective reduction of imine function led to 2-hydrazinoketones and 1,2 diamines, respectively, in excellent yields and enantioselectivities. Further investigation to understand the reaction mechanism is underway.

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Supporting Information Available: Catalysis optimization, spectroscopic data, and ee measurement. This material is available free of charge via the Internet at http://pubs.acs.org.

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(24) For recent reviews combining metal and Brønsted acid, see: (a) Rueping, M.; Koenigs, R. M.; Atodiresei, I. *Chem.—Eur. J.* **2010**, *16*, 9350. (b) Shao, Z. H.; Zhang, H. B. *Chem. Soc. Rev.* **2009**, *38*, 2745. (c) Lacour, J.; Moraleda, D. *Chem. Commun.* **2009**, 7073.

(25) For a review on vicinal diamines, see: Lucet, D.; Le Gall, T.; Mioskowski, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 2580.

(26) The *syn* 1,2-diamine was incorrectly named *anti*.

(27) Partial transacylation of **6** was observed when the reduction was carried out at −45 °C.

(28) For a review, see: Harder, S. *Chem. Rev.* **2010**, *110*, 3852.

(29) Example of monomeric structure of Ca-complex: Mashima, K.; Sugiyama, J. H.; Kanehisa, N.; Kai, Y.; Yasuda, H.; Nakamura, A. *J. Am. Chem. Soc.* **1994**, *116*, 6977.

(30) For selected examples of chiral Ca^{II}-salt catalyses, see: (a) Suzuki, T.; Yamagiwa, N.; Matsuo, Y.; Sakamoto, S.; Yamaguchi, K.; Shibasaki, M.; Noyori, R. *Tetrahedron Lett.* **2001**, *42*, 4669. (b) Kumaraswamy, G.; Sastry, M. N. V.; Jena, N. *Tetrahedron Lett.* **2001**, *42*, 8515. (c) Kumaraswamy, G.; Sastry, M. N. V.; Jena, N.; Kumar, K. R.; Vairamani, M. *Tetrahedron: Asymmetry* **2003**, *14*, 3797. (d) Kumaraswamy, G.; Jena, N.; Sastry, M. N. V.; Padmaja, M.; Markondaiah, B. *Adv. Synth. Catal.* **2005**, *347*, 867. (e) Saito, S.; Tsubogo, T.; Kobayashi, S. *J. Am. Chem. Soc.* **2007**, *129*, 5364. (f) Tsubogo, T.; Saito, S.; Seki, K.; Yamashita, Y.; Kobayashi, S. *J. Am. Chem. Soc.* **2008**, *130*, 13321. (g) Kobayashi, S.; Tsubogo, T.; Saito, S.; Yamashita, Y. *Org. Lett.* **2008**, *10*, 807. (h) Poisson, T.; Tsubogo, T.; Yamashita, Y.; Kobayashi, S. *J. Org. Chem.* **2010**, *75*, 963.