JOC Note

pubs.acs.org/joc

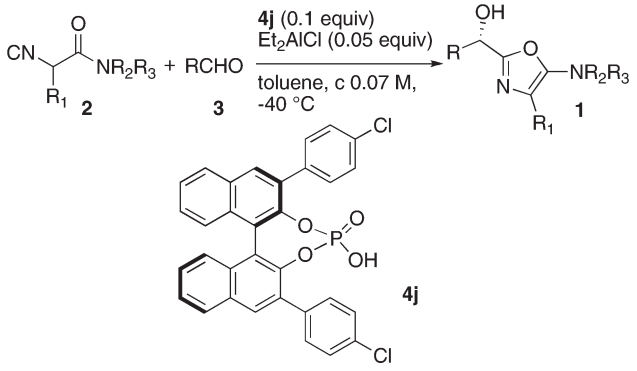
Catalytic Asymmetric Passerini-Type Reaction: Chiral Aluminum−Organophosphate-Catalyzed Enantioselective α-Addition of Isocyanides to Aldehydes

Tao Yue,[†,‡] Mei-Xiang Wang,*[,†,‡] De-Xian Wang,[†,‡] Géraldine Masson,[§] and Jieping Zhu*[,§]

[†]*Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China,* [‡]*Key Laboratory of Bioorganic Phosphrous Chemistry & Chemical Biology (Ministry of Education), Department of Chemistry, Tsinghua University, Beijing 100084, China, and* [§]*Institut de Chimie des Substances Naturelles, CNRS, 91198 Gif-sur-Yvette Cedex, France*

mxwang@iccas.ac.cn; zhu@icsn.cnrs-gif.fr

Received August 17, 2009



A chiral Lewis acid catalyst was prepared by mixing 2 equiv of chiral binol-derived organophosphoric acid and 1 equiv of Et_2AlCl. In the presence of a catalytic amount of $[\mathbf{4j}]_2$Al(III)Cl complex (0.05 equiv), reaction between α-isocyanoacetamides (**2**) and aldehydes (**3**) afforded the corresponding 5-aminooxazoles (**1**) in good yields and enantioselectivities. Complex $[\mathbf{4j}]_2$Al(III)Cl isolated as a white solid displayed similar reactivity as that prepared in situ.

In view of the extraordinary molecular diversity and complexity that one can create by taking advantage of the carbene-like reactivity of isocyanides,[1] the development of catalysts for enantioselective nucleophilic addition of divalent isonitrile carbon to polarized double bonds (carbonyl group, imine, etc.) could have significant impact in synthetic organic chemistry and medicinal chemistry.[2] In spite of the great efforts dedicated to this field, only limited success has been recorded highlighting the difficulties associated with the development of such a catalyst.[3] In this context, Denmark developed a Lewis base-catalyzed enantioselective two-component Passerini-like reaction.[4] Dömling performed a massive parallel screening of a large number of metal−ligand combinations and found that a stoichiometric amount of Ti-Taddol complex was capable of promoting the Passerini three-component (P-3CR) reaction to afford the α-acyloxyamides in moderate enantioselectivity.[5] Schreiber demonstrated that an indan (PyBox)−Cu(II) complex was able to catalyze the P-3CR; however, enantio-enriched Passerini adducts were obtained only when the chelating aldehydes were used as a reaction partner.[6] We have reported that chiral (salen)Al(III)Cl[7] was able to catalyze efficiently the reaction of nonchelating aldehydes, isocyanides, and carboxylic acids or hydrazoic acid leading to the P-3CR adducts in good to excellent enantioselectivities.[8]

The difficulty encounted in developing enantioselective catalysts for the α-addition of isocyanides to aldehydes is intriguing since a variety of chiral Lewis acids and Brønsted acids are known to catalyze the enantioselective addition of nucleophiles to the carbonyl group. We have previously shown that (salen)Al(III)Cl is able to catalyze the reaction of aldehydes (**3**) and α-isocyanoacetamides (**2**) to afford the

(1) (a) Dömling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168–3210. (b) Banfi, L.; Riva, R. In *Organic Reactions*; Overman, L. E., Ed.; Wiley: Hoboken, NJ, 2005; Vol. 65, pp 1−140. (c) Marcaccini, S.; Torroba, T. *Nat. Protoc.* **2007**, *2*, 632–639.

(2) (a) Hulme, C.; Gore, V. *Curr. Med. Chem.* **2003**, *10*, 51–80. (b) Orru, R. V. A.; De Greef, M. *Synthesis* **2003**, 1471–1499. (c) Nair, V.; Rajesh, C.; Vinod, A. U.; Bindu, S.; Sreekanth, A. R.; Mathen, J. S.; Balagopal, L. *Acc. Chem. Res.* **2003**, *36*, 899–907. (d) Zhu, J. *Eur. J. Org. Chem.* **2003**, 1133–1144. (e) Dömling, A. *Chem. Rev.* **2006**, *106*, 17–89. (f) Tempest, P. *Curr. Opin. Drug Discovery Dev.* **2005**, *8*, 776–788. (g) Akritopoulou-Zanze, I.; Djuric, S. W. *Heterocycles* **2007**, *73*, 125–147. (h) Isambert, N.; Lavilla, R. *Chem.—Eur. J.* **2008**, *14*, 8444–8454. (i) Wessjohann, L. A.; Rivera, D. G.; Vercillo, O. E. *Chem. Rev.* **2009**, *109*, 796–814. (j) El Kaim, L.; Grimaud, L. *Tetrahedron* **2009**, *65*, 2153–2171.

(3) Reviews on enantioselective MCRs: (a) Seayad, J.; List, B. Catalytic Asymmetric Multicomponent Reactions. In *Multicomponent reaction*; Zhu, J., Bienaymé, H., Eds.; Wiley-VCH: Weinheim, Germany, 2005; pp 277−299. (b) D. Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570–1581. (c) Guillena, G.; Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2007**, *18*, 693–700. (d) Gong, L.-Z.; Chen, X.-H.; Xu, X.-Y. *Chem.—Eur. J.* **2007**, *13*, 8920–8926.

(4) (a) Denmark, S.; Fan, Y. *J. Am. Chem. Soc.* **2003**, *125*, 7825–7827. (b) Denmark, S.; Fan, Y. *J. Org. Chem.* **2005**, *70*, 9667–9676.

(5) Kusebauch, U.; Beck, B.; Messer, K.; Herdtweck, E.; Dömling, A. *Org. Lett.* **2003**, *5*, 4021–4024.

(6) Andreana, P. R.; Liu, C. C.; Schreiber, S. L. *Org. Lett.* **2004**, *6*, 4231–4233.

(7) Reviews: (a) Larrow, J. F.; Jacobsen, E. N. *Top. Organomet. Chem.* **2004**, *6*, 123–152. (b) Katsuki, T. *Chem. Soc. Rev.* **2004**, *33*, 437–444. (c) Structure of group 13 compounds incorporating salen ligands: Atwood, D. A.; Harvey, M. *J. Chem. Rev.* **2001**, *101*, 37–52.

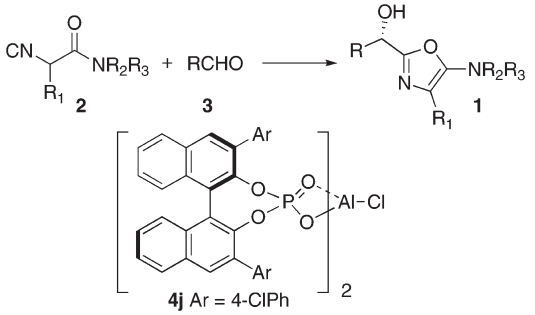
(8) (a) Wang, S. -X.; Wang, M.-X.; Wang, D.-X.; Zhu, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 388–391. (b) Yue, T.; Wang, M.-X.; Wang, D.-X.; Zhu, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 9554–9457.

(9) Synthesis of oxazoles from α-isocyanoacetamides: (a) Janvier, P.; Sun, X.; Bienaymé, H.; Zhu, J. *J. Am. Chem. Soc.* **2002**, *124*, 2560–2567. (b) Janvier, P.; Bois-Choussy, M.; Bienaymé, H.; Zhu, J. *Angew. Chem., Int. Ed.* **2003**, *42*, 811–814. (c) Cuny, G.; Gamez-Montano, R.; Zhu, J. *Tetrahedron* **2004**, *60*, 4879–4885. (d) Pirali, T.; Tron, G. C.; Zhu, J. *Org. Lett.* **2006**, *8*, 4145–4148. (e) Pirali, T.; Tron, G.; Masson, G.; Zhu, J. *Org. Lett.* **2007**, *9*, 5275–5278. (f) Elders, N.; Ruijter, R.; de Kanter, F. J. J.; Groen, M. B.; Orru, R. V. A. *Chem.—Eur. J.* **2008**, *14*, 4961–4973. (h) Scheffelaar, R.; Paravidino, M.; Muilwijk, D.; Spek, A. L.; de Kanter, F. J. J.; Orru, R. V. A.; Ruijter, R. *Org. Lett.* **2009**, *11*, 125–128.

(10) (a) Wang, S.-X.; Wang, M.-X.; Wang, D.-X.; Zhu, J. *Org. Lett.* **2007**, *9*, 3615–3618. (b) Wang, S.-X.; Wang, M.-X.; Wang, D.-X.; Zhu, J. *Eur. J. Org. Chem.* **2007**, 4076–4080.

Published on Web 09/29/2009 DOI: 10.1021/jo9017765

SCHEME 1. A Chiral Al−Organophosphate-Catalyzed Enantioselective α-Addition of α-Isocyanoacetamides to Aldehydes

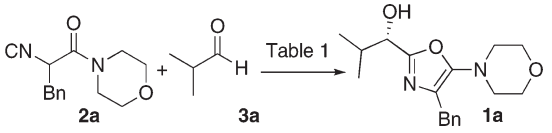


enantiomerically enriched 2-(1-hydroxyalkyl)-5-aminooxazoles (**1**).[9,10] Very recently, Matsunaga, Shibasaki, and coworkers elegantly demonstrated that a heterobimetallic Ga/Yb-Schiff base complex was highly efficient in catalyzing the same reaction providing 5-aminooxazoles (**1**) in excellent yields and enantioselectivities.[11] As a continuation of our interests in this reaction, we report herein the development of a chiral aluminum organophosphate catalyst and its application in the synthesis of enantio-enriched 2-(1-hydroxyalkyl)-5-aminooxazoles (**1**) by reaction of α-isocyanoacetamides (**2**) and aldehydes (**3**, Scheme 1).

Chiral phosphoric acids are now well established as bifunctional organocatalysts, particularly in catalyzing the addition of nucleophiles to imines/acylimines[12,13] However, examples on the enantioselective activation of aldehydes using this family of Brønsted acids were rare.[14] We initially examined the reaction of α-benzyl-α-isocyanoacetamide (**2a**) and 2-methylpropanal (**3a**)[15] in the presence of chiral phosphoric acids. Although the reaction did proceed, the enantioselectivity was low (entry 1, Table 1).[16] Stimulated by the work of Furono and Inanaga on the activation of carbonyl compounds by chiral rare earth organophosphates,[17] in conjunction with the established catalytic power of Al-based chiral Lewis acid on the above transformation,[8,10] the reaction between **2a** and **3a** was performed in the presence of phosphoric acid **4** and Et_2AlCl. As shown in Table 1, the ratio of **4a** to Et_2AlCl influenced the reaction outcome and the best ee was obtained when they were mixed in a 2/1 ratio (entry 2). Interestingly, when **4a** and Et_2AlCl were used in a 1/1 ratio, the sense of asymmetric induction was reversed (entry 3). This intriguing result provided indirect evidence that the Al−organophosphate complex was indeed an active catalytic species and that the chiral environment varied depending on the number of phosphate ligands associated with the metal center. Similar ee was observed when the loading of Et_2AlCl and phosphoric acid was reduced to 5 and 10 mol %, respectively (entry 6).

Different phosphoric acids (Figure 1) were next screened under the following conditions: **4** (0.1 equiv), Et_2AlCl (0.05

TABLE 1. Reaction of 2a and 3a in the Presence of Phosphoric Acid 4a and Et_2AlCl[a]



entry	**4** (equiv)	Et_2AlCl (equiv)	T (° C)	yield[b]	ee[c]
1	**4a** (0.2)		−20	71	22
2	**4a** (0.2)	0.1	−20	68	49
3	**4a** (0.1)	0.1	−20	89	−16
4	**4a** (0.24)	0.1	−20	78	40
5	**4a** (0.3)	0.1	−20	71	39
6	**4a** (0.1)	0.05	−20	68	47
7	**4b** (0.1)	0.05	−20	62	12
8	**4c** (0.1)	0.05	−20	22	5
9	**4d** (0.1)	0.05	−20	23	22
10	**4e** (0.1)	0.05	−20	89	7
11	**4f** (0.1)	0.05	−20	80	33
12	**4g** (0.1)	0.05	−20	91	48
13	**4h** (0.1)	0.05	−20	65	22
14	**4i** (0.1)	0.05	−20	84	62
15	**4j** (0.1)	0.05	−20	82	51
16	**4k** (0.1)	0.05	−20	57	0
17	**4l** (0.1)	0.05	−20	87	51
18	**4j** (0.1)	0.05	−40	81	59
19	**4j** (0.1)[d]	0.05	−40	81	71
20	**4j** (0.1)[e]	0.05	−40	71	71

[a]General reaction conditions: **2a/3a** = 1/1, in toluene c = 0.1 M. [b]Yield of chromatographically pure material. [c]Determined by chiral HPLC analysis. [d]Reaction performed at c = 0.07 M. [e]Reaction performed at c = 0.05 M.

(11) Mihara, H.; Xu, Y.; Shepherd, N. E.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2009**, *131*, 8384–8385.

(12) Selected examples: (a) Akiyama, T.; Itoh, J.; Yokota, K.; Fuchibe, K. *Angew. Chem., Int. Ed.* **2004**, *43*, 1566–1568. (b) Uraguchi, D.; Terada, M. *J. Am. Chem. Soc.* **2004**, *126*, 11804–11805. (c) Rowland, G. B.; Zhang, H.; Rowland, E. B.; Chennamadhavuni, S.; Wang, Y.; Antilla, J. C. *J. Am. Chem. Soc.* **2005**, *127*, 15696–15697. (d) Hofmann, S.; Seayad, A. M.; List, B. *Angew. Chem., Int. Ed.* **2005**, *44*, 7424–7427. (e) Rueping, M.; Sugiono, E.; Azap, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 2617–2619. (f) Storer, R. I.; Carrera, D. E.; Ni, D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 84–86. (g) Chen, X.-H.; Xu, X.-Y.; Liu, H.; Cun, L.-F.; Gong, L.-Z. *J. Am. Chem. Soc.* **2006**, *128*, 14802–14803. (h) Kang, Q.; Zhao, Z.-A.; You, S.-L. *J. Am. Chem. Soc.* **2007**, *129*, 1484–1485. (i) Jia, Y.-X.; Zhong, J.; Zhu, S.-F.; Zhang, C.-M.; Zhou, Q. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 5565–5567. (j) Wanner, M. J.; van der Haas, R. N. S.; de Cuba, K. R.; van Maarseveen, J. H.; Hiemstra, H. *Angew. Chem., Int. Ed.* **2007**, *46*, 7485–7487. (k) Sickert, M.; Schneider, C. *Angew. Chem., Int. Ed.* **2008**, *47*, 3631–3634. (l) Baudequin, C.; Zamfir, A.; Tsogoeva, S. B. *Chem. Commun.* **2008**, 4637–4639. (m) Enders, D.; Narine, A. A.; Toulgoat, F.; Bisschops, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 5661–5665. (n) Xu, S.; Wang, Z; Zhang, X.; Zhang, X.; Ding, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 2840–2843. (o) Jiang, J.; Yu, J.; Sun, X.-X.; Rao, Q.-Q.; Gong, L.-Z. *Angew. Chem., Int. Ed.* **2008**, *47*, 2458–2462. (p) Cheng, X.; Goddard, R.; Buth, G.; List, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 5079–5081. (q) Guo, Q.-S.; Du, D.-M.; Xu, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 759. (r) Rueping, M.; Antonchick, A. P.; Sugiono, E.; Grenader, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 908–910. (s) Liu, H.; Dagousset, G.; Masson, G.; Zhu, J. *J. Am. Chem. Soc.* **2009**, *131*, 4598–4599. (t) Terada, M.; Machioka, K.; Sorimachi, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 2553–2556. (u) Akiyama, T.; Suzuki, T.; Mori, K. *Org. Lett.* **2009**, *11*, 2445–2447.

(13) (a) Akiyama, T. *Chem. Rev.* **2007**, *107*, 5744–5758. (b) Terada, M. *Chem. Commun.* **2008**, 4097–4112. (c) Doyle, A. G.; Jacobsen, E. N. *Chem. Rev.* **2007**, *107*, 5713–5743.

(14) (a) Nakashima, D.; Yamamoto, H. *J. Am. Chem. Soc.* **2006**, *128*, 9626–9627. (b) Rueping, M.; Ieawsuwan, W.; Antonchick, A. P.; Nachtsheim, B. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 2097–2100. (c) Rueping, M.; Nachtsheim, B. J.; Moreth, S. A.; Bolte, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 593–596. (d) Terada, M.; Soga, K.; Momiyama, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 4122–4125. (e) Garcia-Garcia, P.; Lay, F.; Garcia-Garcia, P.; Rabalakos, C.; List, B. *Angew. Chem., Int. Ed.* **2009**, *48*, 4363–4366.

(15) The α-isocyanoacetamides are easily available, see: (a) Fayol, A.; Housseman, C.; Sun, X.; Janvier, P.; Bienaymé, H.; Zhu, J. *Synthesis* **2005**, 161–165. (b) Housseman, C.; Zhu, J. *Synlett* **2006**, 1777–1779. (c) Dömling, A.; Beck, B.; Fuchs, T.; Yazbak, A. *J. Comb. Chem.* **2006**, *8*, 872–880.

(16) For phosphoric acids- and phosphinic acids-catalyzed Ugi-type reactions, see: (a) Pan, S. C.; List, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 3622–3625. (b) Yue, T.; Wang, M.-X.; Wang, D.-X.; Masson, G.; Zhu, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6717–6721.

(17) (a) Jin, X. L.; Sugihara, H.; Daikai, K.; Tateishi, H.; Jin, Y. Z.; Furono, H.; Inanaga, J. *Tetrahedron* **2002**, *58*, 8321–8329. (b) Furono, H.; Hayano, T.; Kambara, T.; Sugimoto, Y.; Hanamoto, T.; Tanaka, Y.; Jin, Y. Z.; Kagawa, T.; Inanaga, J. *Tetrahedron* **2003**, *59*, 10509–10523. (c) Suzuki, S.; Furono, H.; Yokoyama, Y.; Inanaga, J. *Tetrahedron: Asymmetry* **2006**, *17*, 504–507.

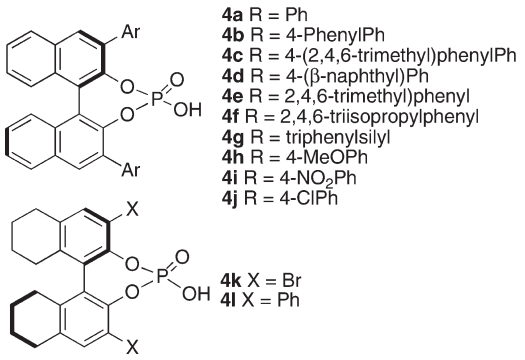


FIGURE 1. List of phosphoric acids examined.

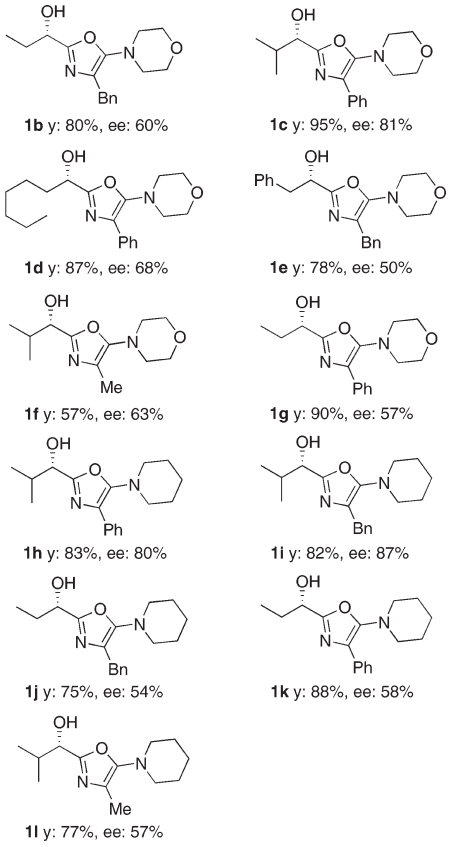
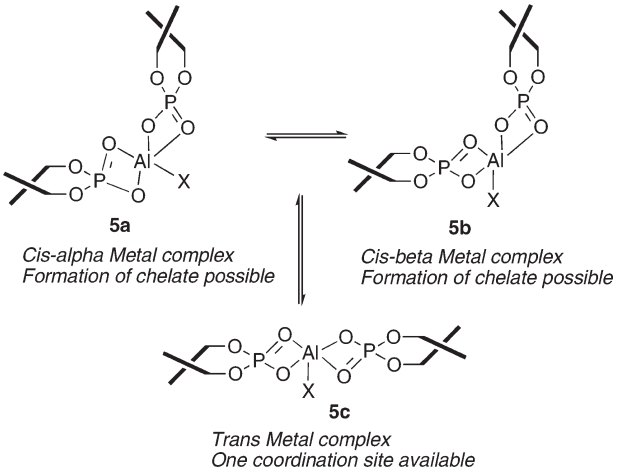


FIGURE 2. Al-organophosphate-catalyzed synthesis of 2-(1-hydroxyalkyl)-5-aminooxazoles (**1**). General reaction conditions: **2**/**3** = 1/1, toluene (c = 0.05 M), **4j**/Et_2AlCl (0.05 equiv), −40 °C, 48 h. y: Yield of chromatographically pure material. Determined by chiral HPLC analysis.

equiv), toluene, c = 0.1 M, −20 °C. Increasing the size of the Ar group reduced the ee of the oxazole **1a** (entries 7−11). Introduction of an electron-donating group at the 4-position of the Ar group exerted also a negative effect on the reaction (entry 13), whereas the presence of an electron-withdrawing group (**4i**, **4j**) in the Ar group increased the ee of **1a** (entries 14 and 15), probably due to the slightly increased Lewis acidity of the catalyst in the latter cases. Using phosphoric acid ***4l***, an octahydro-analogue of **4a**, afforded ee similar to that obtained with **4a** (entry 17). Finally, it was found that the reaction concentration influenced the ee of the product. Reducing the concentration from c = 0.1 to 0.07 M, the

SCHEME 2. Possible Conformations of Complex $[4]_2Al(III)Cl$



5-aminooxazole **1a** was produced in 81% yield with 71% ee (entry 19). Further decreasing the concentration (c = 0.05 M) led to a reduced yield of **1a** without significant impact on the ee.

The scope of the reaction was explored by using the optimized conditions (0.1 equiv of **4j**,[18] 0.05 equiv of Et_2AlCl, toluene, −40 °C, c = 0.07 M) with representative aldehydes and α-isocyanoacetamides (Figure 2). Aliphatic aldehydes, including propionaldehyde, hexanal, isobutyraldehyde, and 3-phenylpropanal, gave the corresponding oxazoles in good yields and good enantioselectivities. The α-branched aldehyde gave in general higher ee than the linear ones (**1i**, ee 87%). The α-phenyl-, α-benzyl-, and α-methyl-substituted α-isocyanoacetamides participated well in this reaction to afford the expected adducts. The absolute configuration of these oxazoles was determined to be (*S*) by comparing the optical rotation value with that of the known compounds.[10a]

The phosphoric acid **4j** is insoluble in toluene. However, by adding 0.5 equiv of Et_2AlCl into the suspension, a clear solution was formed. Evaporation of solvent allowed us to isolate a presumed catalyst $(\mathbf{4j})_2AlCl$ in the form of white solid.[19] Reaction of **2a** and **3a** in the presence of 5 mol % of this presynthesized catalyst afforded **1a** in 82% yield with 71% ee. These results indicated that the isolated catalyst has the same catalytic properties as that generated in situ. However, attempts to obtain a single crystal failed and ^{1}HNMR data did not allow us to propose a structure for this Al complex. In principle, the 2 to 1 complex formed between phosphoric acid and Et_2AlCl could exist in three different conformers **5a**, **5b**, and **5c** and they could have different catalytic properties (Scheme 2).[7b] The moderate ee obtained in this work may in part due to the conformational mobility of this complex. We are currently attempting to synthesize ligands that could potentially favor the trans-metal complex of type **5c**. We assumed that access to this conformer would be essential for achieving the high ee of compoud **1**.[8,10]

(18) Using phosphoric acid **4i** as ligand gave non-reproducible results, presumably due to the interaction between the nitro group and aluminium. The reaction was preferably performed at 0.05 M instead of 0.07 M for the solubility issue.

(19) For the synthesis of $(TFA)_2AlMe$, see: (a) Itoh, A.; Oshima, K.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2050–2054. (b) Hashimoto, S.; Itoh, A.; Kitagawa, Y.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 4192–4194.

In summary, we have reported an efficient phosphoric acid−Al complex-catalyzed α-addition of α-isocyanoacetamides to aldehydes for the synthesis of enantio-enriched 2-(1-hydroxyalkyl)-5-aminooxazoles. In view of the frequent occurrence of oxazole in natural products and medicinally relevant compounds, its unique reactivity for generating the molecular complexity, and diversity,[20,21] we believe that the present protocol could be of synthetic value. We also expected applications of these Al−phosphate complexes in other catalytic asymmetric transformations.[22]

Experiment Section

General Procedure. In a flame-dried round-bottomed flask equipped with a stir bar were added binol-derived phosphoric acid (**4j**, 0.025 mmol) and dry toluene (1 mL). The mixture was stirred at room temperature for several minutes, to which a solution of Et_2AlCl (0.0125 mmol) in toluene was added. The mixture was then stirred at room temperature until a clear solution was formed. The aldehyde (0.25 mmol, in 0.5 mL of toluene) was then introduced and the resulting mixture was stirred at room temperature for 30 min. The reaction mixture was cooled to −40 °C and a solution of α-isocyanoacetamide (0.25 mmol) in toluene (2.0 mL) was added slowly via a syringe pump (addition time 1.5 h). After being stirred at −40 °C for 48 h, the reaction mixture was purified by flash column chromatography (SiO_2, petroleum ether then petroleum ether/EtOAc = 1/1) to give the corresponding oxazole. 2-Methyl-1-(5-morpholino-4-phenyloxazol-2-yl)propan-1-ol (**1c**): white solid, mp 117−118 °C; $[\alpha]^{20}_D$ +5.5 (*c* 0.85, $CHCl_3$); yield 95%, ee 81% (ADH, hexane/^{i}PrOH = 9/1, 25 °C, 0.5 mL/min); IR (KBr) ν 3237, 2966, 2849, 1636, 1381, 1114, cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz) δ 7.95 (d, J = 8.5 Hz, 2H), 7.42−7.37 (m, 2H), 7.29−7.24 (m, 1H), 4.49 (t, J = 5.9 Hz, 1H), 3.87−3.84 (m, 4H), 3.11−3.08 (m, 4H), 2.96 (d, J = 5.9 Hz, 1H), 2.21−2.15 (m, 1H), 1.00 (d, J = 7.1 Hz, 3H), 0.98 (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.7, 151.1, 131.6, 128.5, 127.1, 125.9, 123.7, 73.0, 66.9, 50.4, 33.5, 18.4, 17.3 ; MS (ESI) m/z 303 (M + H), 325 (M + Na). Anal. Calcd for $C_{17}H_{22}N_2O_3$: C, 67.53; H, 7.33; N, 9.26. Found: C, 67.24; H, 7.33; N, 9.26.

Acknowledgment. We gratefully acknowledge the National Science Foundation of China (NSFC) and CNRS (France) for financial support.

Supporting Information Available: Experimental procedures, product characterization, as well as copies of ^{1}H NMR of of **1a**−**1*l*** and chiral HPLC analysis of **1a**−**1*l***. This material is available free of charge via the Internet at http://pubs.acs.org.

(20) Selected examples: (a) Fayol, A.; Zhu, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 3633–3635. (b) Janvier, P.; Bienaymé, H.; Zhu, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 4291–4294. (c) Gámez-Montaño, R.; González-Zamora, E.; Potier, P.; Zhu, J. *Tetrahedron* **2002**, *58*, 6351–6358. (d) Fayol, A.; Zhu, J. *Org. Lett.* **2005**, *7*, 239–242. (e) Bughin, C.; Masson, G.; Zhu, J. *J. Org. Chem.* **2007**, *72*, 1826–1829. (f) Bonne, D.; Dekhane, M.; Zhu, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 2485–2488.

(21) For reviews on the chemistry of oxazole see: (a) Karpeiskii, M. Y.; Florent'ev, V. L. *Russ. Chem. Rev.* **1969**, *38*, 540–546. (b) Jacobi, P. A. *Adv. Heterocycl. Nat. Prod. Synth.* **1992**, *2*, 251−298. (c) Yeh, V. S. C. *Tetrahedron* **2004**, *60*, 11995–12042.

(22) For reviews on Al-Binol complex catalyzed asymmetric reactions, see: (a) Wulff, W. D. Chiral aluminium Lewis acids in organic synthesis. In *Lewis acids in organic synthesis*; Yamamoto, H., Ed.; Wiley-VCH: Weinheim, Germany, 2000; pp 283−354. (b) Gröger, H. *Chem.—Eur. J.* **2001**, *7*, 5247–5251.