HAL
open science

Enantioselective hydrophosphonylation of N -Boc imines using chiral guanidine–thiourea catalysts

Louis Chassillan, Yasuhiro Yamashita, Woo-Jin Yoo, Martial Toffano, Régis Guillot, Shū Kobayashi, Giang Vo-Thanh

To cite this version:

Louis Chassillan, Yasuhiro Yamashita, Woo-Jin Yoo, Martial Toffano, Régis Guillot, et al.. Enantioselective hydrophosphonylation of N -Boc imines using chiral guanidine–thiourea catalysts. Organic & Biomolecular Chemistry, 2021, 19 (48), pp.10560-10564. 10.1039/D1OB01953H . hal-03815260

HAL Id: hal-03815260

https://hal.science/hal-03815260

Submitted on 14 Oct 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

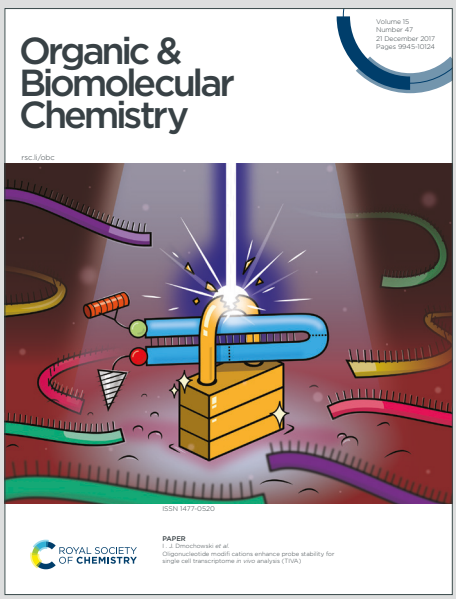
Check for updates

View Article Online
View Journal

Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: L. Chassillan, Y. Yamashita, W. Yoo, M. TOFFANO, R. Guillot, S. Kobayashi and G. Vo-Thanh, *Org. Biomol. Chem.*, 2021, DOI: 10.1039/D1OB01953H.



This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.

ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/D1OB01953H

COMMUNICATION

Enantioselective Hydrophosphonylation of *N*-Boc Imines using Chiral Guanidine–Thiourea Catalysts

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

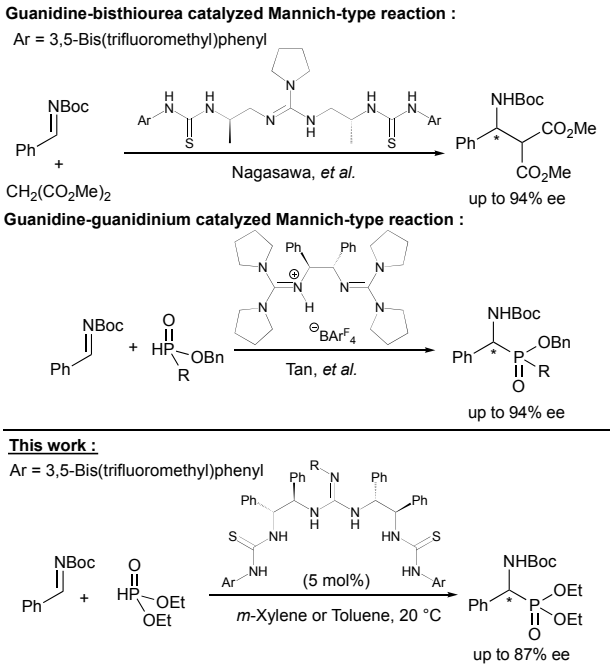
Louis Chassillan,[a,b] Yasuhiro Yamashita,[b] Woo-Jin Yoo,[b] Martial Toffano,[a] Régis Guillot,[a] Shū Kobayashi,[b]* Giang Vo-Thanh[a]*

Published on 23 November 2021. Downloaded by UNIVERSITE PARIS-SACLAY on 11/23/2021 12:22:09 PM.

The enantioselective hydrophosphonylation of *N*-Boc imines was investigated using a new family of pseudo-symmetric guanidine–thiourea catalysts, providing α-amino phosphonates in moderate to high yields with good enantioselectivity. The catalyst was heterogenized by polymerization with styrene and the resulting catalyst was applied to reactions under continuous-flow conditions.

Guanidines are well-known common organic functions that have interesting chemical and biological properties. They can be found in natural products[1] and have become increasingly attractive in the field of organocatalysis.[2] The guanidine functional group can be used as a superbase to deprotonate high pK_a pronucleophiles,[3] and synergic catalysis can be obtained by combining guanidine with H-bond donors. Indeed, combining strong Brønsted base and H-bond donor allows bifunctional catalysis to be performed by activating both nucleophile and electrophile at the same time. In the past few years, several guanidine–H-bond donor catalysts have been developed and were found to be very efficient for several reactions.[4]

Nagasawa *et al.* reported the synthesis and use of linear and conformationally flexible guanidine–bis-thiourea/urea catalysts in multiple reactions, providing good yields and good enantioselectivity.[5] It was shown by Eyring analysis that enantioinduction by Nagasawa's guanidine–thioureas was entropy-driven because of the flexibility of the methylene or ethylene linker (Scheme 1). Although it was shown that the control of catalyst flexibility can have a beneficial impact on the catalysis,[6] rigidification of catalyst scaffolds remains a common strategy to achieve highly enantioselective reactions, as it can allow for stabilization of transition states and induce better definition of chiral binding pockets by steric repulsion.



Scheme 1 Guanidine-catalyzed asymmetric Mannich-type reactions

Especially in the field of hydrogen bond catalysis, rigidity plays an important role, and many researchers have reported rigid thiourea catalysts bearing constrained diamine ligands such as chiral cyclohexane diamine or diphenylethylene diamine.[7] Therefore, by using such kind of diamine structure instead of methylene or ethylene chiral spacer we could access new constrained guanidine–bis-thiourea catalysts. This new kind of structure could allow for efficient reactions such as Michael and Mannich-type reactions. For instance, Nagasawa *et al.* achieved a highly enantioselective entropy-driven addition of malonates to *N*-Boc imines using a guanidine–thiourea catalyst.[8] Additionally, Tan *et al.* reported an efficient enantioselective phospha-Mannich reaction of benzyl phosphinates with *N*-Ts imines catalyzed by a guanidinium–guanidine catalyst.[9]

With this information in hand, we decided to develop new rigid guanidine–thiourea catalysts to perform asymmetric

[a] Université Paris-Saclay, Institut de Chimie Moléculaire et des Matériaux d'Orsay 91405 Orsay, France
[b] Department of Chemistry, School of Science, The University of Tokyo, Bunkyo-ku, Tokyo, 113-0033, Japan
† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

Organic & Biomolecular Chemistry Accepted Manuscript

View Article Online
DOI: 10.1039/D1OB01953H

Published on 23 November 2021. Downloaded by UNIVERSITE PARIS-SACLAY on 11/23/2021 12:22:09 PM.

reactions. The catalyst design was carried out first to have a small library of guanidine-thiourea catalysts bearing rigid catalyst backbones, and those were applied for the catalytic asymmetric hydrophosphonylation of imines which appeared to be an important reaction to access α-amino phosphonates. α-Amino phosphonates are very versatile compounds that are nowadays used in numerous fields because of their remarkable biological properties[10] and because they can be used as amino-acid analogues and/or useful synthetic intermediates.[11] Even though three-components reaction involving carbonyl amine and phosphite was developed (Kabachnik-Fields reaction),[12] the direct nucleophilic addition of phosphonates to imines (Pudovik reaction) remains a straightforward way to synthesize α-amino phosphonates.[13] The catalytic addition of nucleophiles to imines has been studied widely and several catalytic systems have been developed.[14] However, only few examples of asymmetric phospha-Mannich reaction on ketimine/aldimine using chiral superbase catalysts were reported.[9,15] Although the reaction can be performed using common bases, the use of organic superbases could drastically increase the efficiency of the reaction. Here, we report the synthesis of spatially constrained guanidine–thiourea catalysts and their use in the asymmetric hydrophosphonylation of *N*-Boc imines.

As a starting point, *N*-Boc imine **1a** and diethyl phosphonate (**2a**) were selected as model substrates for screening to optimize the reaction conditions. Several chiral guanidine–thiourea catalysts were synthesized using three different diamines: (*R,R*)-1,2-diaminocyclohexane, (*R,R*)-1,2-diphenylethylene diamine and *N*-Boc-(*S*)-2-(aminoethyl) pyrrolidine, which was directly synthesized from *N*-Boc-L-proline in four steps. All five guanidine–thiourea catalysts were synthesized by using adapted procedures (Chart 1).[16]

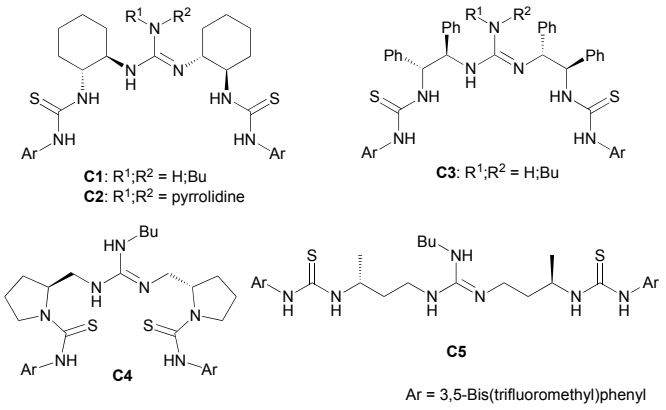
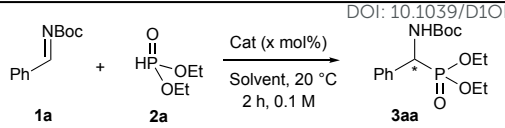


Chart 1 Catalyst structures

Compounds **C1** and **C2** were synthesized first and tested for the asymmetric hydrophosphonylation reaction, giving the desired product **3aa** in 76% and 68% yield, respectively. We hypothesized that using a secondary amine on the guanidine moiety would lead to a better definition of the chiral environment by making the upper part of the catalyst more hindered; however, the use of **C2** gave 28% ee compared with49% ee for **C1** (Table 1, entries 1-2). Compound **C3** was then synthesized using a bulkier diamine and provided better

Table 1 Catalyst and solvent screening[a]



Entry	***Cat***	x (mol%)	*Solvent*	*Yield (%)*	*ee (%)*
1	**C1**	20	Toluene	76	49
2	**C2**	20	Toluene	68	28
3	**C3**	20	Toluene	83	86
4	**C3**	10	Toluene	76	86
5	**C3**	5	Toluene	76	86
6	**C4**	5	Toluene	24	16
7	**C5**	5	Toluene	70	51
8	**C3**	5	*m*-Xylene	74	87
9	**C3**	5	*n*-Hexane	65	85
10	**C3**	5	Petroleum ether	65	78
11	**C3**	5	Mesitylene	63	86
12	**C3**	5	Acetonitrile	trace	44
13	**C3**	5	THF	65	63
14	**C3**	5	EtOAc	38	59
15	**C3**	5	DIPE	15	35
16[b]	**C3**	2	*m*-Xylene	61	84

[a] Reaction conditions: **1a** (0.10 mmol), **2a** (0.12 mmol), and **Cat.** (x mol%) in solvent (1.0 mL) at 20 °C for 2 h. Yields determined by isolation. [b] The reaction was conducted under the following conditions: **1a** (0.30 mmol), **2a** (0.36 mmol), and **C3** (2 mol%) in *m*-Xylene (1.0 mL) at 20 °C for 12 h.

results, affording product **3aa** in 83% yield with 86% ee. At this point, the efficiency of the catalyst was investigated, and catalyst loading was modified (entries 3–5). The guanidine–thiourea catalysts were found to be very efficient for this reaction; with 5 mol% of **C3** catalyst, full conversion was reached after only 2 hours. The same reaction using cinchona derivatives such as quinine usually require much longer reaction times (typically 2–3 days).[17] Another proline-basedcatalyst, **C4**, was also synthesized and used in the hydrophosphonylation reaction, providing 24% yield with 16% ee (entry 6). We assume that the specific structure of this catalyst might be responsible for loss of efficiency because the secondary thioureas can only form one hydrogen bond. Finally, one example of a flexible guanidine–thiourea catalyst was synthesized by following Nagasawa's procedure.[16] In this case, similar results to those obtained with **C1** were obtained and product **3aa** was obtained in 70% yield with 51% ee (entry 7).

Having identified the best catalyst to perform the asymmetric hydrophosphonylation of phosphonate **1a** and imine **2a** (Table 1), conditions were optimized starting with the solvents. As a general tendency, the reaction provided higher ees and yields in hydrocarbon solvents (entries 5 and 8–11). The use of polar solvents, such as THF or EtOAc (entries 13 and 14), led to lower yields and enantioselectivities. In the case of an ether, only 15% yield was obtained (entry 15), and only a trace amount of product was isolated when acetonitrile was used (entry 12). Finally, *m*-xylene was selected as the best solvent, and reducing the catalyst loading was investigated. When 2 mol% of **C3** was employed, good ee was obtained but the yield dropped even in longer reaction time (entry 16). Next, the scope of the reaction and the influence of a range of parameters were investigated with *m*-xylene (Scheme 2).

Organic & Biomolecular Chemistry Accepted Manuscript

This journal is © The Royal Society of Chemistry 20xx

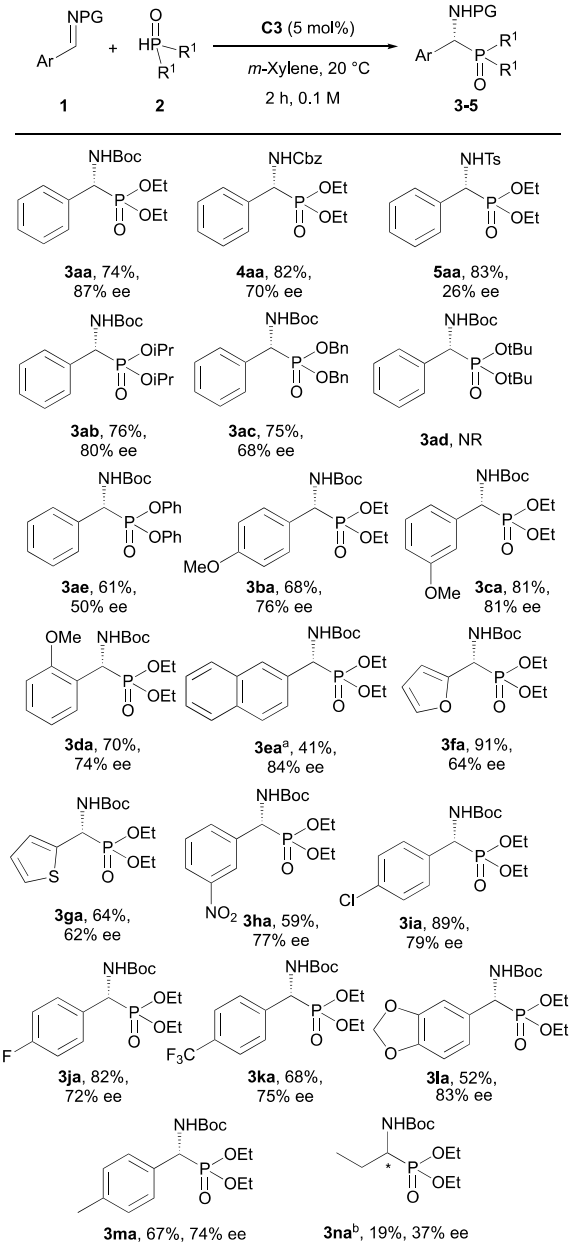
Please do not adjust margins

View Article Online
DOI: 10.1039/D1OB01953H

Published on 23 November 2021. Downloaded by UNIVERSITE PARIS-SACLAY on 11/23/2021 12:22:09 PM.

Organic & Biomolecular Chemistry Accepted Manuscript

The effect of the N-protecting groups was briefly investigated and it was found that substrates with carbamate-type protecting groups, such as Boc and Cbz, gave higher enantioselectivities than those with a Ts group (Scheme 2, **3aa**, **4aa**, **5aa**). Indeed, carbamate groups can provide a better interaction with the thiourea moiety of the catalyst by forming hydrogen bonds with the oxygen of the carbonyl bond and the nitrogen of the carbamate moiety. A range of phosphonate nucleophiles were then used and although similar yields were obtained, bulkier phosphonates such as diisopropyl or dibenzyl phosphonates (Scheme 2, **3ab**, **3ac**) led to a moderate drop of ee compared with **3aa**. However, no reaction occurred when *tert*-butyl phosphonate was used. Diphenyphosphonate was also tested, but both yield and ee were lower (**3ae**).



Scheme 2 Substrates scope for the enantioselective hydrophosphonylation of *N*-Boc imines. Reaction conditions: **1** (0.10 mmol), **2** (0.12 mmol), and **C3** (5 mol%) in *m*-xylene (1.0 mL) at 20 °C for 2 h. Yields determined by isolation. [a] Reaction was carried out for 48 h due to poor solubility of 2-naphthyl imine. [b] *N*-Boc-α-(phenylsulfonyl) propylamine (0.30 mmol), **2** (0.36 mmol), **C3** (20 mol%), Cs_2CO_3 (0.36 mmol) in *m*-xylene (3.0 mL) at 0 °C for 20 h. Yields determined by isolation.

The scope of imine substrates was finally investigated (Scheme 2, **3ba–ma**). From imines bearing electron-withdrawing groups (Scheme 2, **3ha–ka**) and electron-donating groups (Scheme 2, **3ba–da**; **3la–ma**) to imines bearing heteroaromatic moieties (Scheme 2, **3fa–ga)**, a wide range of imines were tolerated. In the case of **3ea**, because of the poor solubility of the substrate in *m*-xylene, a lower yield (41%) was obtained, even when the reaction was run for 48h. Otherwise, yields generally varied from 52% for product **3la** to 91% for product **3fa.** The *R*-absolute configuration of product **3aa** was determined by X-ray diffraction analysis (see Supporting Information). An aliphatic imine was also investigated. Due to instability of the imines, the imine precursor was treated with Cs_2CO_3 in situ to form the imine, however the desired product was obtained in low yield with only 37% enantioselectivity.

The 3D structure of **C3**·HCl salt was also obtained by X-ray diffraction (see Figure 1). The **C3**·HCl salt crystallized as a dimer in the P1 space group cell. Interestingly, the thiourea moieties played an important role in the crystal structure, with both sulfur atoms being linked to the central guanidine by hydrogen bonds. Notably, the chloride anion formed a bridge between two molecules of the catalyst by forming hydrogen bonds between the guanidinium proton and the acidic protons of the thioureas moieties of the second **C3**·HCl molecule, resulting in the formation of layers.

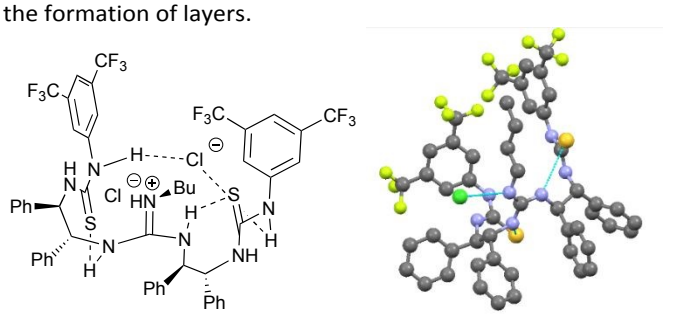


Figure 1 **C3**·HCl salt crystal structure

Based on previous studies investigating the mechanism of several guanidine–thiourea catalyzed reactions[18], we assume that the reaction proceeds in three major steps (Figure 2). First, the guanidine acts as a strong Brønsted base to deprotonate the phosphonate and form the guanidinium phosphonate salt **I** (Figure 2). After activation of the phosphorus nucleophile by deprotonation, the second thiourea of the catalyst interacts with the electrophile through hydrogen-bond formation with the carbamate moiety of the *N*-Boc imine to provide intermediate **II** (Figure 2). Owing to the synergic activation of the phosphonate and imine by the catalyst, an optimum chiral environment is obtained because of the strong interactions of the guanidinium and thiourea moieties with the substrates. Finally, after the reaction of the phosphonate and the imine in the chiral pocket provided by the catalyst through hydrogen bonds, the chiral α-amino phosphonate product is obtained and the free base guanidine **C3** is regenerated.

Please do not adjust margins

View Article Online
DOI: 10.1039/D1OB01957H

Published on 23 November 2021. Downloaded by UNIVERSITE PARIS-SACLAY on 11/23/2021 12:22:09 PM.

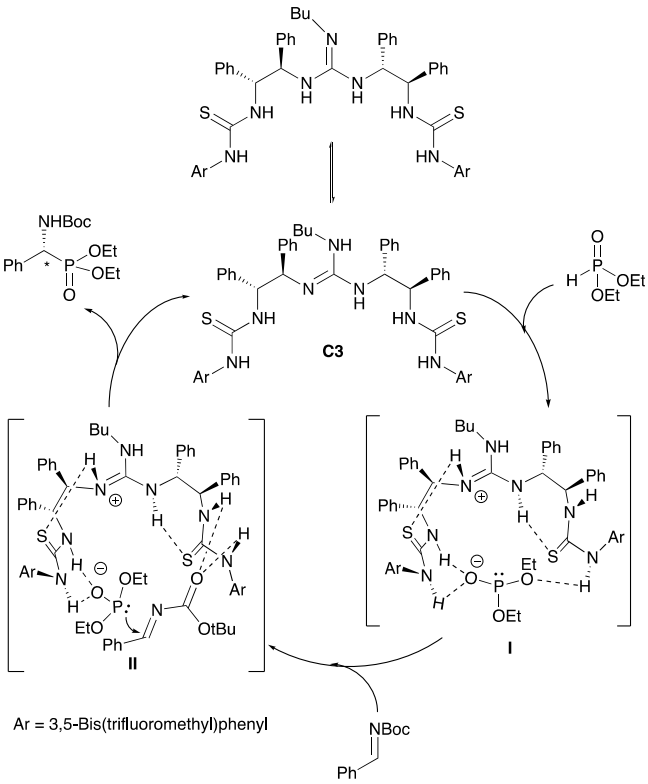
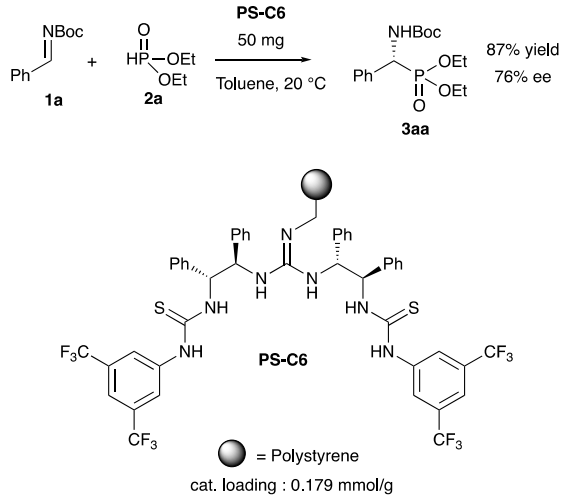


Figure 2 Plausible mechanism

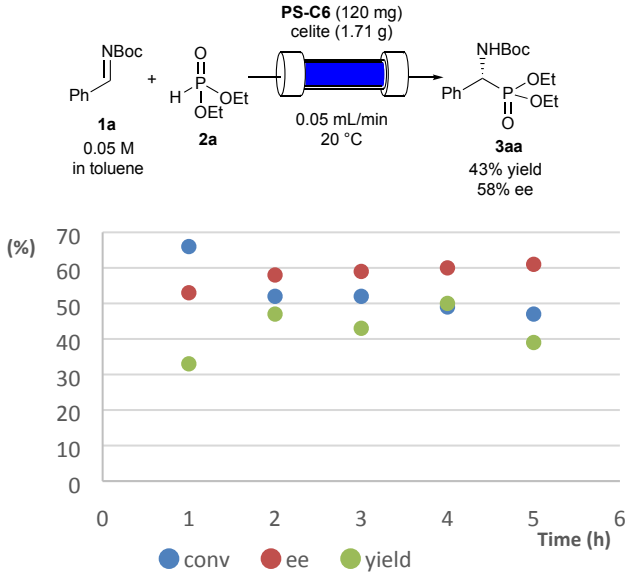
With the results obtained in the homogeneous system, we decided to immobilize our catalyst on a polymeric matrix in order to perform the synthesis of α-amino phosphonates under continuous-flow conditions. Regarding the similar results obtained previously when performing the reaction in toluene or *m*-Xylene (Table 1), we decided to perform the continuous-flow experiment in toluene which appears to be a more common and practical alternative. First, a polymerizable monomer bearing a vinyl styrene group on the guanidine moiety was synthesized by using a procedure similar to those used for other catalysts. Then, polymerization of **C6** was performed under suspension polymerization conditions by mixing **C6**·HCl salt, styrene and divinyl benzene. The free-base polymer was obtained by stirring the polymer in a mixture of DCM and aq. K_2CO_3. After washing and drying, the ability of the resulting polymer **PS-C6** to catalyze the asymmetric hydrophosphonylation was assessed using **1a** and **2a** under batch heterogeneous conditions (Scheme 3) in Toluene. Product **3aa** was obtained in 79% yield with 83% ee, which appeared to be slightly lower than those obtained under homogeneous conditions.

Scheme 3 Hydrophosphonylation of *N*-Boc imine **1a** catalyzed by **PS-C6** under batch conditions [a]



[a] Reaction conditions: **1a** (0.10 mmol), **2a** (0.12 mmol), and **PS-C6** (50 mg, 9 mol%) in solvent (1.0 mL) at 20 °C for 16 h. The conversion was determined by ¹H NMR and the yield was determined by isolation.

The polymer was then mixed with Celite and packed in a reactor (5 × 1 cm) for testing under continuous-flow conditions. The reaction between **1a** and **2a** under continuous-flow conditions was run for 5 hours and data were collected after stabilization of the system (Scheme 4). Under these conditions, the flow reaction appeared to be less efficient than homogeneous and heterogeneous batch conditions. During the first hour, 70% conversion was observed, but conversion progressively decreased over time because of deactivation of the catalyst; however, the ee seemed to be stable. Relative to the conversion, the isolated yield also seemed to be reasonable.



Scheme 4 Fifth-run flow experiment

In conclusion, we have developed a new series of guanidine–thiourea catalysts, synthesized from constrained diamine ligands, which were found to be highly effective for the asymmetric hydrophosphonylation of *N*-Boc imines, providing α-amino phosphonates with yields up to 91% and ee up to 87%. Moreover, the catalyst was successfully heterogenized by polymerization with styrene, and the α-amino phosphonate was also synthesized under continuous-flow conditions.

Organic & Biomolecular Chemistry Accepted Manuscript

This journal is © The Royal Society of Chemistry 20xx

Please do not adjust margins

View Article Online
DOI: 10.1039/D1OB01953H

Published on 23 November 2021. Downloaded by UNIVERSITE PARIS-SACLAY on 11/23/2021 12:22:09 PM.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgement

We thank Rigaku Co. for X-ray single-crystal structure analysis of **C3**·HCl. This work was partially supported by the Agency for Medical Research and Development (S.K.), and by the Japan Society for the Promotion of Science KAKENHI Grant Number JP 17H06448 (Y.Y.). We are grateful to the University Paris-Saclay for a doctoral fellowship to L.C., and the CNRS (UMR 8182) for financial support.

Notes and references

1 R. G. S. Berlinck, A. F. Bertonha, M. Takaki, J. P. G. Rodriguez, *Nat. Prod. Rep.,* 2017, **34**, 1264-1301.

2 (a) D. Leow, C. H. Tan, *Chem. Asian. J.,* 2009, **4**, 488-507; (b) H. Chou, D. Leow, C. Tan, *Chem. Asian. J.,* 2019, **14**, 3803-3822; (c) T. Ishikawa, T. Isobe, *Chem. Eur. J.,* 2002, **8**, 552-557; (d) S. Dong, X. Feng, X. Liu, *Chem. Soc. Rev.,* 2018, **47**, 8525-8540.

3 (a) T. Ishikawa, in *Superbases for Organic Synthesis: Guanidines, Amidines, Phosphazenes and Related Organocatalysts*, *John Wiley & Sons,* 2009, pp. 93-143; (b) Y. W. Wang, Z. Y. Cao, Q. H. Li, Prof. G. Q. Lin, J. Zhou, P. Tian, *Angew. Chem. Int. Ed.,* 2020, **59**, 8004-8014.

4 (a) B. Fang, X. Liu, J. Zhao, Y. Tang, L. Lin, X. Feng, *J. Org. Chem.,* 2015, **80**, 3332-3338; (b) K. Hosoya, M. Odagi, K. Nagasawa, K. *Tetrahedron Lett.,* 2018, **59**, 687-696; (c) M. Kato, K. Yasui, M. Yamanaka, K. Nagasawa, *Asian. J. Org. Chem.,* 2016, **5**, 380-388; (d) M. Odagi, Y. Yamamoto, K. Nagasawa, *Angew. Chem.,* 2018, **130**, 2251-2254; (e) M. Odagi, K. Takayama, M. Sato, M. Yamanaka, K. Nagasawa, *Molecules*, 2015, **20**, 12590-12598; (f) Y. Sohtome, N. Horitsugi, R. Takagi, K. Nagasawa, *Adv. Synth. Catal.,* 2011, **353**, 2631-2636; (g) Y. Sohtome, K. Nagasawa, *Synlett*, 2010, 1-22; (h) X. Fu, W-T. Loh, Y. Zhang, T. Chen, T. Ma, H. Liu, J. Wang, C-H. Tan, *Angew. Chem. Int. Ed.,* 2009, **48**, 7387-7390.

5 (a) Y. Sohtome, B. Shin, N. Horitsugi, K. Noguchi, K. Nagasawa, *Chem. Asian. J.,* 2011, **6**, 2463-2470; (b) K. Takada, N. Takemura, K. Cho, Y. Sohtome, K. Nagasawa, *Tetrahedron Lett.,* 2008, **49**, 1623-1626; (c) N. Horitsugi, K. Kojima, K. Yasui, Y. Sohtome, K. Nagasawa, *Asian J. Org. Chem.,* 2014, **3**, 445-448.

6 J. M. Crawford, M. S. Sigman, *Synthesis,* 2019, **5**, 1021-1036.

7 (a) M. S. Sigman and E. N. Jacobsen, *J. Am. Chem. Soc.,* 1998, **120**, 4901-4902; (b) T. Okino, Y. Hoashi, Y. Takemoto, *J. Am. Chem. Soc*., 2003, **125**, 12672-12673; (c) A. Berkessel, K. Roland, J. M. Neudörfl, *Org. Lett*., 2006, **8**, 4195-4198; (d) S. B. Tsogoeva, S. Wei, *Chem. Commun.,* 2006, 1451-1453; (e) Y. Sohtome, A. Tanatani, Y. Hashimoto, K. Nagasawa *Tetrahedron Lett.*, 2004, **45**, 5589-5592.

8 (a) Y. Sohtome, S. Tanaka, K. Takada, T. Yamaguchi, K. Nagasawa, *Angew. Chem. Int. Ed.,* 2010, **49**, 9254-9257; (b) Y. Sohtome, T. Yamaguchi, S. Tanaka and K. Nagasawa, *Org. Biomol. Chem.,* 2013, **11**, 2780-2786.

9 X. Fu, W. T. Loh, Y. Zhang, T. Chen, T. Ma, H. Liu, J. Wang, C. H. Tan, *Angew. Chem. Int. Ed*., 2009, **48**, 7387-7390.

10 P. Kafarski, B. Lejczak, *Phosphorus. Sulfur. Silicon. Relat. Elem.,* 1991, **63**, 193-215.

11 (a) M. Mikołajczyk, *Pure Appl. Chem.,* 2019, **91**, 811-838. Reviews of α-aminophosphonate synthesis: (b) A. Maestro, E. M. de Marigorta, F. Palacios, J. Vicario, *Asian J. Org. Chem.* 2020, **9**, 538-548; (c) R. A. Shastri, *Chem. Sci. Trans.* 2019, **8**, 359-367; (d) W. M. Abdou, R. F. Barghash, M. S. Bekheit, *Synth. Commun.* 2015, **45**, 1929-1963; (e) K. Bera, I. N. N. Namboothiri, *Asian J. Org. Chem.* 2014, **3**, 1234-1260; (f) K. Bera, D. Nadkarni, I. N. N. Namboothiri, *J. Chem. Sci.*, 2013, **125**, 443-465.

12 For a recent review on Kabachnick-Fields reaction: G. Sravya, A. Balakrishna, G. V. Zyryanov, G. Mohan, C. S. Reddy, N. B. Reddy, *Phosphorus, Sulfur and Silicon and the Rel Elem*, 2021, **196**, 353.

13 A.N Pudovik, I.V Konovalova, *Synthesis,* 1979, **2**, 81-96. For recent reviews on Pudovik reaction: (a) R. P. Herrera, *Chem. Rec.*, 2017, **17**, 833; (b) P. S. Bhadury, H. Li, *Synlett*, 2012, **23**, 1108-1131; (c) P. Merino, E. Marqués-Lopez, R. P. Herrera, *Adv. Synth. Cat.*, 2008, **350**, 1195-1208.

14 (a) S. Kobayashi, Y. Mori, J. S. Fossy, M. M. Salter, *Chem. Rev.*, 2011, **111**, 2626-2704; (b) J. Vesely, R. Rios, *Chem. Soc. Rev.,* 2014, **43**, 611-630; (c) S. Kobayashi, H. Ishitani, *Chem. Rev.*, 1999, **99**, 1069-1094.

15 G. P. Robertson, A. J. M. Farley, D. J. Dixon, *Synlett,* **2016**, *27*, 21-24.

16 Y. Sohtome, B. Shin, N. Horitsugi, R. Takagi, K. Noguchi, K. Nagasawa*, Angew. Chem. Int. Ed.*, 2010, **49**, 7299-7303.

17 (a) D. Pettersen, M. Marcolini, L. Bernardi, F. Fini, R. P. Herrera, V. Sgarzani, A. Ricci, *J. Org. Chem.,* 2006, **71**, 6269-6272. (b) W. Li, Y. Wang, D. Xu, *Eur. J. Org. Chem*., 2018, **39**, 5422–5426.

18 (a) M. Kato, S. Hirao, K. Nakano, M. Sato, M. Yamanaka, Y. Sohtome, K. Nagasawa, *Chem. Eur. J.,* 2015, **21**, 18606-18612; (b) K. Nakano, T. Orihara, M. Kawaguchi K. Hosoya, S.Hirao, R. Tsutsumi, M. Yamanaka, M. Odagi, K. Nagasawa, *Tetrahedron.,* 2021, **92**, 132281.

Organic & Biomolecular Chemistry Accepted Manuscript

Please do not adjust margins