JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

Communication

pubs.acs.org/JACS

Single-Handed Helical Poly(quinoxaline-2,3-diyl)s Bearing Achiral 4-Aminopyrid-3-yl Pendants as Highly Enantioselective, Reusable Chiral Nucleophilic Organocatalysts in the Steglich Reaction

Takeshi Yamamoto, Ryo Murakami, and Michinori Suginome*

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Katsura, Nishikyo-ku, Kyoto 615-8510, Japan

Supporting Information

ABSTRACT: Helically chiral poly(quinoxaline-2,3-diyl)s bearing 4-aminopyrid-3-yl pendants were synthesized as new helical-polymer-based chiral nucleophilic organocatalysts. The obtained chiral nucleophilic polymer catalysts exhibited high catalytic activity, enantioselectivity, and reusability in asymmetric Steglich rearrangement of oxazolyl carbonate to *C*-carboxyazlactone. The polyquinoxaline-based, helically chiral DMAP catalyst mediated intramolecular acyl transfer selectively, by contrast with known small-molecule-based chiral organocatalysts, which also mediate intermolecular acyl transfers.

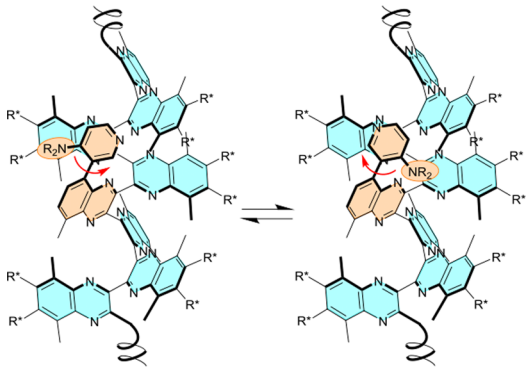
Polymer-based immobilized chiral catalysts, in which conventional small-molecule-based chiral catalysts are embedded in common polymers, attract much interest from the viewpoint of practical asymmetric synthesis because they are easily separable from the reaction mixtures and reusable by virtue of the insoluble nature of the polymer backbones.[1] By contrast, increasing attention is being focused on utilization of the helical macromolecular scaffold[2] as a source of chirality in catalytic asymmetric reactions.[3] In addition to the separability/reusability issues, the macromolecular chiral scaffold is highly expected to serve as huge chiral steric shielding, which could be superior to small-molecule-based chiral structures. However, there has been only limited success in the use of helical macromolecules as the scaffolds of chiral catalysts. There are some successes in the use of helically chiral poly(arylacetylene)s bearing chiral organocatalytic pendants such as cinchona alkaloids,[4] proline-based groups,[5] and oligopeptides.[6] In these cases, the enantioselectivities mainly arise from the chiral pendants with relatively minor contribution of macromolecular chirality. There is another class of polymer-based chiral catalysts whose enantio-discrimination relies solely on the main-chain chirality of helical macromolecules with attachment of achiral ligand/organocatalytic pendants.[7] This approach is extremely attractive because it only requires the introduction of simple, achiral ligand/organocatalytic pendants, although there has been no highly enantioselective macromolecular catalyst within this class.

In 2009, we established poly(quinoixaline-2,3-diyl)s (hereafter PQX) as the first chiral macromolecular scaffolds that achieve high enantioselectivities (up to 98% ee) without the assistance of additional chiralities in the pendants.[8] In this system, attachment of achiral *o*-(diarylphosphino)phenyl pendants allows high enantioselectivity in palladium-catalyzed hydrosilylation of styrenes. Subsequently, we could successfully apply the catalysts to several palladium-catalyzed reactions with high enantioselectivity.[9] Moreover, we have shown that the induction of helical chirality largely depends upon the nature of solvents:[10] the helicity can be inverted between two solvents such as chloroform/1,1,2-trichloroethane,[10a,b] cyclopentyl methyl ether/*t*-butyl methyl ether,[10c] and even *n*-octane/cyclooctane.[10d] Our current interest is to verify the extensibility of PQX as a general chiral platform onto which various achiral pendants are attached to gain high enantioselectivities in various asymmetric reactions.

Incorporation of pyridyl pendants is highly attractive, because they serve not only as a ligand in transition-metal catalysts[11] but also as chiral bases or nucleophilic organocatalysts.[12,13] In this paper, we report the synthesis of a series of PQXs bearing 4-aminopyrid-3-yl pendants and their use in asymmetric Steglich rearrangement.[13−15] We found high catalytic activity of one of the derivatives, which allows us to attain high enantioselectivity with remarkably low catalyst loading and to reuse the catalyst at least 11 times without any drop of selectivity or catalytic activity.

Our molecular design is shown in Scheme 1. 4-Amino-substituted pyrid-3-yl groups are introduced at the 5-position of the quinoxaline rings in the helical backbone of PQX, of which right-handed (*P*-) helicity is induced by the (*R*)-chiral side chains. The axial chirality between the pyridyl and the quinoxaline rings is not fixed and induced thermodynamically by the *P*-helical structure of PQX. Their synthesis was performed by postpolyme-

Scheme 1. (*P*)-PQX-Based Nucleophilic Organocatalyst



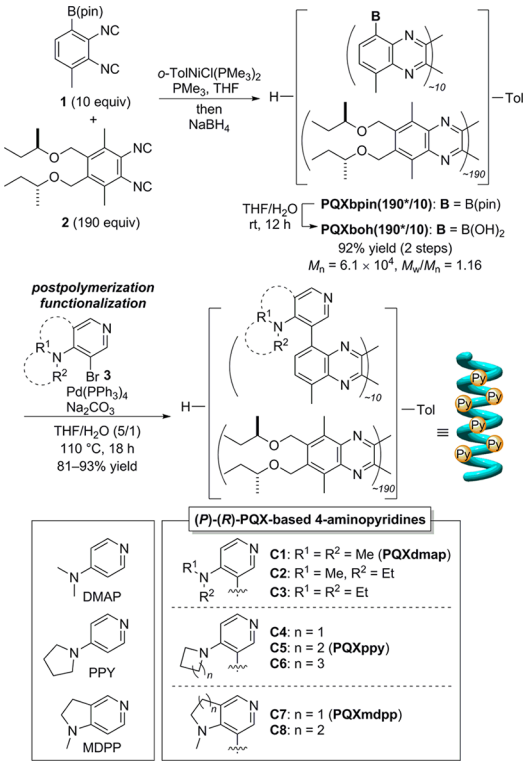
Received: November 30, 2016
Published: February 5, 2017

ACS Publications © 2017 American Chemical Society

DOI: 10.1021/jacs.6b12349
J. Am. Chem. Soc. 2017, 139, 2557−2560

rization functionalization of **PQXboh** bearing a boronyl pendant at the 5-position of the quinoxaline ring (Scheme 2). Synthesis of

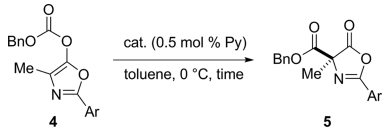
Scheme 2. Synthesis of Polyquinoxaline-Based Helically Chiral Nucleophilic Catalysts



the corresponding *ortho*-diisocyanobenzene monomer **1** bearing a B(pin) pendant is shown in the Supporting Information (SI). In the presence of an organonickel initiator, living random copolymerization of **1** and chiral monomer **2**, which has (*R*)-2-butoxymethyl side chains, gave (*P*)-(*R*)-**PQXbpin** bearing 10 boronyl units along with 190 chiral units on average. Hydrolysis of the B(pin) group on the quinoxaline ring proceeded smoothly in a mixture of THF/H_2O, giving (*P*)-(*R*)-**PQXboh**. (*P*)-(*R*)-**PQXdmap** (**C1**) bearing the DMAP pendant was obtained in high yield through Suzuki–Miyaura cross-coupling of (*P*)-(*R*)-**PQXboh** with 3-bromo-4-dimethylaminopyridine, which is readily available by bromination of the corresponding 4-(dimethylamino)pyridine. Conversion of the boronyl group on **PQXboh** was confirmed by ^{1}H NMR spectroscopy. PQX derivatives bearing a 4-dialkyl amino group (**C2** and **C3**), cyclic amino group (**C4**, **PQXppy** (**C5**), and **C6**), and fused cyclic amino group (**PQXmdpp** (**C7**) and **C8**)) were also prepared under similar reactiotn conditions.

The obtained (*P*)-(*R*)-PQX derivatives were used in asymmetric Steglich rearrangement,[13,15] in which oxazolyl carbonates isomerize to *C*-carboxyazlactones forming a quaternary stereocenter (Table 1). In the presence of (*P*)-(*R*)-**PQXdmap** (**C1**) (0.5 mol % pyridyl pendants), rearrangement of oxazolyl carbonate **4Aa** proceeded at 0 °C. In the screening of reaction solvent, toluene showed the higher enantioselectivity than chloroform and THF, giving **5Aa** in 92% yield with 62% ee (entry 1, see SI). Replacement of the methyl group(s) on the amino group of catalyst **C1** with ethyl group(s) (**C2** and **C3**) decreased both catalytic activity and enantioselectivity (entries 2 and 3). PQXs bearing azetidino (**C4**) or pyrrolidino group **PQXppy** (**C5**)

Table 1. Asymmetric Steglich Rearrangement Using (*P*)-(*R*)-PQXdmap Derivatives[a]



entry	cat.	Ar	time (h)	% yield[b]	% ee[c]
1	**C1**	4-MeOC$_6$H$_4$ (**4Aa**)	35	92 (**5Aa**)	62
2	**C2**	**4Aa**	96	84 (**5Aa**)	60
3	**C3**	**4Aa**	120	90 (**5Aa**)	52
4	**C4**	**4Aa**	12	89 (**5Aa**)	62
5	**C5**	**4Aa**	12	96 (**5Aa**)	60
6	**C6**	**4Aa**	300	77[d] (**5Aa**)	42
7	**C7**	**4Aa**	3	99 (**5Aa**)	69
8	**C8**	**4Aa**	11	83 (**5Aa**)	50
9	**C7**	4-ClC$_6$H$_4$ (**4Ba**)	1	91 (**5Ba**)	72
10	**C7**	4-CF$_3$C$_6$H$_4$ (**4Ca**)	1	88 (**5Ca**)	75
11[e]	**C7**	4-CF$_3$C$_6$H$_4$ (**4Ca**)	1	78 (**5Ca**)	−45

[a] **4Aa** (0.3 mmol), and (*P*)-(*R*)-**PQXdmap** derivatives (0.5 mol % pyridyl pendants) were stirred in solvent (6.0 mL) at 0 °C. [b] Isolated yield. [c] Determined by chiral SFC analysis. [d] 88% conversion. NMR yield. [e] The reaction was carried out using (*M*)-(*R*)-**C7** in a 1:1 mixture of toluene and 1,1,2-trichloroethane.

showed high catalytic activities with moderate enantioselectivities (entries 4 and 5), whereas **C6** bearing piperidino group exhibited low catalytic activity and enantioselectivity (entry 6). PQXs bearing a fused cyclic amino group also served as efficient catalysts (entries 7 and 8). In these series, **PQXmdpp** (**C7**) bearing *N*-methyldihydropyrrolopyridine (MDPP) pendants afforded the highest catalytic activity and enantioselectivity. These results clearly suggest that higher coplanarity of the dialkylamino moiety and the pyridine ring enhances both the catalytic activity and enantioselectivity. The effect of the substituents in 2-methyloxazolyl carbonates **4** on the reactivity and enantioselectivity was also evaluated using (*P*)-(*R*)-**C7**. The presence of an electron-withdrawing group on the benzene ring significantly enhanced the reactivity of the substrate (entries 9 and 10). The ee of the product at 0 °C was improved to 75% ee by using **4Ca** bearing a 4-trifluoromethyl group.

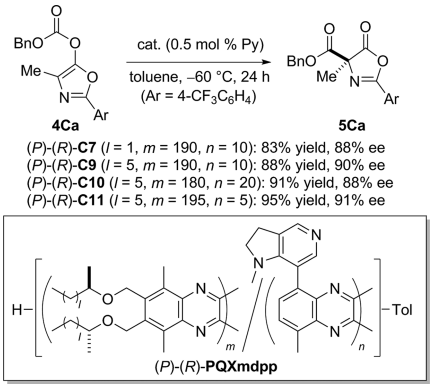
According to our previous works,[9,10] we also conducted solvent-dependent helix inversion of **C7** to reverse the enantioselectivity.[13i] We found that the helical chirality of (*P*)-(*R*)-**C7** could be completely changed to (*M*)-helix in a 1:1 mixture of toluene and 1,1,2-trichloroethane (see SI). Thus obtained (*M*)-(*R*)-**C7** afforded enantiomeric product **5Ca** in 78% yield but with lower enantiomeric excess (45% ee), probably because of negative solvent effect of 1,1,2-trichloroethane used as a cosolvent in the reaction (entry 11).

The catalytic activities of **PQXdmap** (**C1**) and **PQXmdpp** (**C7**) were compared by NMR experiments at 24 °C in benzene-d_6 (see SI). In terms of the half-life of **4Aa** ($t_{1/2}$), **C7** showed 9-fold higher catalyst activity ($t_{1/2}$ = 27 min) than **C1** ($t_{1/2}$ = 247 min). It should be noted that $t_{1/2}$ of **C7** was identical to that of MDPP in spite of the presence of the highly sterically demanding helical polymer backbone.

Based on these results, further optimization of catalyst structure was performed at −60 °C, keeping the polymerization degree of the catalysts ($m + n$ = 200, Scheme 3). With (*P*)-(*R*)-**C7**, ee of the product was improved to 88% by lowering the reaction temperature to −60 °C. Under the same reaction conditions, (*P*)-(*R*)-**C9** (n = 10) bearing (*R*)-2-octyloxymethyl side chains,

DOI: 10.1021/jacs.6b12349
J. Am. Chem. Soc. 2017, 139, 2557–2560

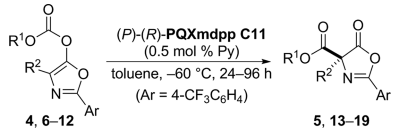
Scheme 3. Optimization of the Polymer Structure



which induces the right-handed structure more efficiently,[10b] showed higher enantioselectivity, giving **5Ca** with 90% ee. Increase of the ratio of the pyridyl units ((*P*)-(*R*)-**C10**, $n = 20$) resulted in a little decrease in enantioselectivity (88% ee). We finally obtained 91% ee by using (*P*)-(*R*)-**C11**, in which less pyridyl units ($n = 5$) are contained.

Under the optimized conditions using (*P*)-(*R*)-**C11**, substrate structure was varied at −60 °C by using oxazolyl carbonates bearing a 4-trifluoromethylphenyl group (Table 2). As for the

Table 2. Scope of the Substrate[a]



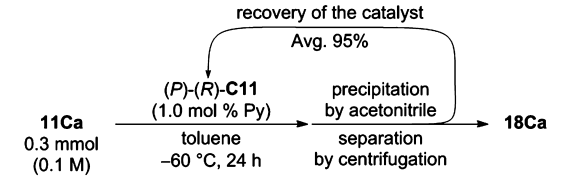
entry	substrate	R^1	R^2	% yield[b]	% ee[c]
1	**4Ca**	Bn	Me	91 (**5Ca**)	92
2	**4Cb**	4-$MeC_6H_4CH_2$	Me	88 (**5Cb**)[d]	90
3	**4Cc**	4-$CF_3C_6H_4CH_2$	Me	72 (**5Cc**)	92
4	**4Cd**	1-naphthylmethyl	Me	98 (**5Cd**)	94
5	**4Ce**	Me	Me	57 (**5Ce**)[d]	71
6	**4Cf**	$MeOCH_2CH_2$	Me	71 (**5Cf**)	90
7	**6Ca**	Bn	Et	96 (**13Ca**)	94
8	**7Ca**	Bn	Pr	86 (**14Ca**)	92
9	**8Ca**	Bn	$^iPrCH_2$	79 (**15Ca**)	86
10	**9Ca**	Bn	Bn	93 (**16Ca**)	91
11	**10Ca**	Bn	$MeSCH_2CH_2$	85 (**17Ca**)	87
12	**11Ca**	Bn	allyl	82 (**18Ca**)	93
13[e]	**11Ca**	Bn	allyl	88 (**18Ca**)	92
14[f]	**12Ca**	Bn	Ph	79 (**19Ca**)	18

[a]Oxazolyl carbonate (0.1 mmol), and **PQXmdpp** (0.5 mol % pyridyl pendants) were stirred in solvent (2.0 mL) at −60 °C. [b]Isolated yield. [c]Determined by chiral SFC analysis. [d]NMR yield. [e]**11Ca** (3.0 mmol), and **PQXmdpp** (0.1 mol % pyridyl pendants) were stirred in solvent (3.0 mL) at −60 °C. [f]Reaction at 0 °C for 48 h.

effect of the acyl groups, benzyl, *p*-substituted benzyl, and 1-naphthyl groups afforded high enantioselectivities (entries 1−4). Although methylcarbonate **4Ce** showed lower ee (entry 5), 2-methoxyethyl carbonate **4Cf** gave high ee (entry 6). Substituents on the oxazole core were varied using benzyl carbonates. Oxazolyl carbonates bearing alkyl groups such as ethyl, propyl, and isobutyl groups afforded the corresponding products with 94%, 92%, and 86% ee, respectively (entries 7−9). Benzyl, methylthioethyl, and allyl substituted carbonates also afforded the corresponding products in high yields with high enantioselectivities (entries 10−12). It is noteworthy that gram-scale synthesis of allyl substituted **18Ca** needed catalyst loading of 0.1 mol % of (*P*)-(*R*)-**C11**, giving 1.07 g of **18Ca** in 88% yield with 92% ee (entry 13). To our knowledge, there has been no single example of the use of less than 0.5 mol % of chiral nucleophilic catalyst in the asymmetric Steglich rearrangement.[13h] Phenyl substituted **12Ca**, which resulted in low conversion at −60 °C, was converted to **19Ca** in 79% yield at 0 °C with low enantioselectivity (entry 14).

Taking advantage of using a polymer scaffold, we demonstrated reuse of **PQXmdpp C11** (Scheme 4). After the initial reaction of

Scheme 4. Reuse of the Polymer Catalyst



run	% yield	% ee	run	% yield	% ee	run	% yield	% ee
initial	99	91	4	98	92	8	99	92
1	99	92	5	97	93	9	97	93
2	99	92	6	99	92	10	96	93
3	99	92	7	99	93	11	99	93

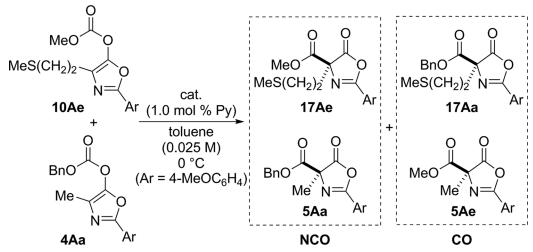
11Ca with 1.0 mol % (*P*)-(*R*)-**C11**, acetonitrile was added to the reaction mixture to precipitate (*P*)-(*R*)-**C11**. Centrifugation of the resulting suspension under air allowed recovery of (*P*)-(*R*)-**C11** along with separation of the product in the solution. After drying under vacuum, the recovered (*P*)-(*R*)-**C11** could be reused 11 times without any fall in the catalytic activity and enantioselectivity. On average, 95% (*P*)-(*R*)-**C11** was recovered in each cycle.

To elucidate the reaction mechanism of the Steglich rearrangement in the presence of **PQXmdpp**, crossover experiments were conducted using an equimolar amount of **4Aa** and **10Ae** in the presence of several nucleophilic catalysts at 0 °C (Table 3).[13a] The use of DMAP or MDPP resulted in the formation of crossover products (**CO**) along with noncrossover products (**NCO**) in ratios of 2.4:1 and 1:1, respectively (entries 1 and 2). Similar formation of crossover products was generally observed in asymmetric Steglich reactions in which crossover experiments were conducted.[13a,h,15a,f,g] This scrambling has been well explained by the involvement of intermolecular acyl transfer from acylpyridinium intermediate to the enolate generated from the substrate. A DMAP-type catalyst **20** bearing a quinoxalinyl group at 3-position also afforded a significant amount of the crossover products (entry 3). Moreover, PS-DMAP, i.e., DMAP immobilized on polystyrene, afforded crossover products with the same ratio as DMAP (entry 4). By contrast, no crossover products were observed when **PQXdmap C1** and **PQXmdpp C7** and **C9** were employed as catalysts (entries 5−7). These results strongly suggest that the highly sterically demanding polymer scaffold of PQX protects the acylpyridinium intermediate from attack by the enolates generated on the other **PQXmdpp** molecules or promotes the intramolecular acyl transfer significantly.

In conclusion, we established the synthesis of helically chiral polyquinoxaline-based DMAP-type nucleophilic catalysts via postpolymerization functionalization of polyquinoxalines bearing boronyl pendants. The obtained (*P*)-(*R*)-**PQXmdpp** showed high catalyst activity and enantioselectivity in an asymmetric Steglich rearrangement, giving *C*-carboxyazlactones in high yields up to 94% ee. The observed macromolecular effect on the selective intramolecular reaction pathway opens up a new synthetic

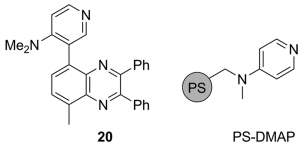
DOI: 10.1021/jacs.6b12349
J. Am. Chem. Soc. 2017, 139, 2557−2560

Table 3. Crossover Experiment[a]



entry	catalyst	NCO:CO[b]
1	DMAP	2.4:1
2	MDPP	1:1
3	**20**	1.7:1
4[c]	PS-DMAP	2.4:1
5	(*P*)-(*R*)-**C1**	>50:1
6	(*P*)-(*R*)-**C7**	>50:1
7	(*P*)-(*R*)-**C9**	>50:1

[a]**10Ae** (0.15 mmol), **4Aa** (0.15 mmol), and catalyst (1.0 mol % pyridyl pendants) were stirred in toluene (6.0 mL) at 0 °C. [b]Determined by ^{1}H NMR analysis. [c]8.8 mol % pyridyl pendants.



strategy using the polymer catalyst. Application of the helical-polymer-based chiral nucleophilic catalysts in other catalytic asymmetric reactions is now being undertaken in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b12349.

Experimental details and product characterization (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*suginome@sbchem.kyoto-u.ac.jp

ORCID

Michinori Suginome: 0000-0003-3023-2219

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by JSPS KAKENHI Grant Number JP15H05811 in Precisely Designed Catalysts with Customized Scaffolding.

■ REFERENCES

(1) (a) Ding, K.; Uozumi, Y. *Handbook of Asymmetric Heterogeneous Catalysis*; Wiley-VHC: Weinheim, 2008. (b) Lu, J.; Toy, P. H. *Chem. Rev.* **2009**, *109*, 815. (c) Itsuno, S. *Polymeric Chiral Catalyst Design and Chiral Polymer Synthesis*; John Wiley and Sons: Hoboken, 2011. (d) Itsuno, S.; Hassan, M. M. *RSC Adv.* **2014**, *4*, 52023.

(2) (a) Nakano, T.; Okamoto, Y. *Chem. Rev.* **2001**, *101*, 4013. (b) Yashima, E.; Maeda, K.; Iida, H.; Furusho, Y.; Nagai, K. *Chem. Rev.* **2009**, *109*, 6102. (c) Yashima, E.; Ousaka, N.; Taura, D.; Shimomura, K.; Ikai, T.; Maeda, K. *Chem. Rev.* **2016**, *116*, 13752.

(3) Megens, R. P.; Roelfes, G. *Chem. - Eur. J.* **2011**, *17*, 8514.

(4) Tang, Z.; Iida, H.; Hu, H.-Y.; Yashima, E. *ACS Macro Lett.* **2012**, *1*, 261.

(5) Ikeda, A.; Terada, K.; Shiotsuki, M.; Sanda, F. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 3783.

(6) Maeda, K.; Tanaka, K.; Morino, K.; Yashima, E. *Macromolecules* **2007**, *40*, 6783.

(7) (a) Reggelin, M.; Schultz, M.; Holbach, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 1614. (b) Reggelin, M.; Doerr, S.; Klussmann, M.; Schultz, M.; Holbach, M. *Proc. Natl. Acad. Sci. U. S. A.* **2004**, *101*, 5461. (c) Roelfes, G.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 3230. (d) Coquière, D.; Feringa, B. L.; Roelfes, G. *Angew. Chem., Int. Ed.* **2007**, *46*, 9308. (e) Boersma, A. J.; Feringa, B. L.; Roelfes, G. *Angew. Chem., Int. Ed.* **2009**, *48*, 3346. (f) Boersma, A. J.; Coquière, D.; Geerdink, D.; Rosati, F.; Feringa, B. L.; Roelfes, G. *Nat. Chem.* **2010**, *2*, 991. (g) Boersma, A. J.; Megens, R. P.; Feringa, B. L.; Roelfes, G. *Chem. Soc. Rev.* **2010**, *39*, 2083. (h) Takata, L. M. S.; Iida, H.; Shimomura, K.; Hayashi, K.; dos Santos, A. A.; Yashima, E. *Macromol. Rapid Commun.* **2015**, *36*, 2047.

(8) (a) Yamamoto, T.; Suginome, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 539. (b) Yamamoto, T.; Yamada, T.; Nagata, Y.; Suginome, M. *J. Am. Chem. Soc.* **2010**, *132*, 7899.

(9) (a) Yamamoto, T.; Akai, Y.; Nagata, Y.; Suginome, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 8844. (b) Akai, Y.; Yamamoto, T.; Nagata, Y.; Ohmura, T.; Suginome, M. *J. Am. Chem. Soc.* **2012**, *134*, 11092. (c) Suginome, M.; Yamamoto, T.; Nagata, Y.; Yamada, T.; Akai, Y. *Pure Appl. Chem.* **2012**, *84*, 1759. (d) Akai, Y.; Konnert, L.; Yamamoto, T.; Suginome, M. *Chem. Commun.* **2015**, *51*, 7211. (e) Yamamoto, T.; Akai, Y.; Suginome, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 12785.

(10) (a) Yamada, T.; Nagata, Y.; Suginome, M. *Chem. Commun.* **2010**, *46*, 4914. (b) Nagata, Y.; Yamada, T.; Adachi, T.; Akai, Y.; Yamamoto, T.; Suginome, M. *J. Am. Chem. Soc.* **2013**, *135*, 10104. (c) Nagata, Y.; Kuroda, T.; Takagi, K.; Suginome, M. *Chem. Sci.* **2014**, *5*, 4953. (d) Nagata, Y.; Nishikawa, T.; Suginome, M. *J. Am. Chem. Soc.* **2014**, *136*, 15901.

(11) Kwong, H.-L.; Yeung, H.-L.; Yeung, C.-T.; Lee, W.-S.; Lee, C.-S.; Wong, W.-L. *Coord. Chem. Rev.* **2007**, *251*, 2188.

(12) (a) Vedejs, E.; Chen, X. H. *J. Am. Chem. Soc.* **1996**, *118*, 1809. (b) Ruble, J. C.; Fu, G. C. *J. Org. Chem.* **1996**, *61*, 7230. (c) Kawabata, T.; Nagato, M.; Takasu, K.; Fuji, K. *J. Am. Chem. Soc.* **1997**, *119*, 3169. (d) Fu, G. C. *Acc. Chem. Res.* **2000**, *33*, 412. (e) Spivey, A. C.; Fekner, T.; Spey, S. E. *J. Org. Chem.* **2000**, *65*, 3154. (f) Pelotier, B.; Priem, G.; Campbell, I. B.; Macdonald, S. J. F.; Anson, M. S. *Synlett* **2003**, 679. (g) Fu, G. C. *Acc. Chem. Res.* **2004**, *37*, 542. (h) Wurz, R. P. *Chem. Rev.* **2007**, *107*, 5570. (i) Crittall, M. R.; Rzepa, H. S.; Carbery, D. R. *Org. Lett.* **2011**, *13*, 1250. (j) Larionov, E.; Mahesh, M.; Spivey, A. C.; Wei, Y.; Zipse, H. *J. Am. Chem. Soc.* **2012**, *134*, 9390. (k) Ma, G. Y.; Deng, J.; Sibi, M. P. *Angew. Chem., Int. Ed.* **2014**, *53*, 11818. (l) Fujii, K.; Mitsudo, K.; Mandai, H.; Suga, S. *Bull. Chem. Soc. Jpn.* **2016**, *89*, 1081.

(13) (a) Ruble, J. C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 11532. (b) Hills, I. D.; Fu, G. C. *Angew. Chem., Int. Ed.* **2003**, *42*, 3921. (c) Shaw, S. A.; Aleman, P.; Vedejs, E. *J. Am. Chem. Soc.* **2003**, *125*, 13368. (d) Shaw, S. A.; Aleman, P.; Christy, J.; Kampf, J. W.; Va, P.; Vedejs, E. *J. Am. Chem. Soc.* **2006**, *128*, 925. (e) Nguyen, H. V.; Butler, D. C. D.; Richards, C. J. *Org. Lett.* **2006**, *8*, 769. (f) Duffey, T. A.; Shaw, S. A.; Vedejs, E. *J. Am. Chem. Soc.* **2009**, *131*, 14. (g) Mandai, H.; Fujiwara, T.; Noda, K.; Fujii, K.; Mitsudo, K.; Korenaga, T.; Suga, S. *Org. Lett.* **2015**, *17*, 4436. (h) Mandai, H.; Fujii, K.; Yasuhara, H.; Abe, K.; Mitsudo, K.; Korenaga, T.; Suga, S. *Nat. Commun.* **2016**, *7*, 11297. (i) Chen, C.-T.; Tsai, C.-C.; Tsou, P.-K.; Huang, G.-T.; Yu, C.-H. *Chem. Sci.* **2017**, *8*, 524.

(14) Steglich, W.; Höfle, G. *Tetrahedron Lett.* **1970**, *11*, 4727.

(15) (a) Thomson, J. E.; Rix, K.; Smith, A. D. *Org. Lett.* **2006**, *8*, 3785. (b) Joannesse, C.; Johnston, C. P.; Concellón, C.; Simal, C.; Philp, D.; Smith, A. D. *Angew. Chem., Int. Ed.* **2009**, *48*, 8914. (c) Uraguchi, D.; Koshimoto, K.; Miyake, S.; Ooi, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 5567. (d) Zhang, Z.; Xie, F.; Jia, J.; Zhang, W. *J. Am. Chem. Soc.* **2010**, *132*, 15939. (e) De, C. K.; Mittal, N.; Seidel, D. *J. Am. Chem. Soc.* **2011**, *133*, 16802. (f) Campbell, C. D.; Concellón, C.; Smith, A. D. *Tetrahedron: Asymmetry* **2011**, *22*, 797. (g) Joannesse, C.; Johnston, C. P.; Morrill, L. C.; Woods, P. A.; Kieffer, M.; Nigst, T. A.; Mayr, H.; Lebl, T.; Philp, D.; Bragg, R. A.; Smith, A. D. *Chem. - Eur. J.* **2012**, *18*, 2398.

DOI: 10.1021/jacs.6b12349
J. Am. Chem. Soc. 2017, 139, 2557−2560