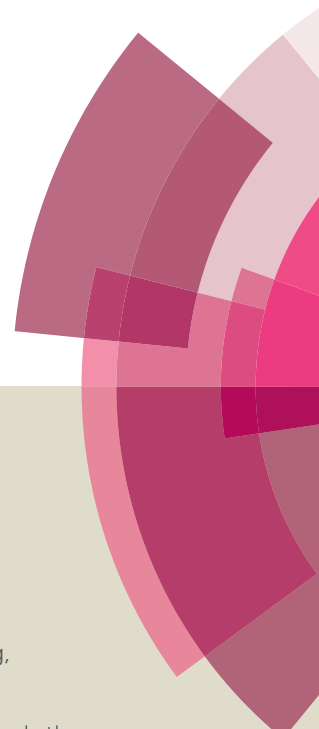


Organic & Biomolecular Chemistry

Accepted Manuscript



This article can be cited before page numbers have been issued, to do this please use: A. Xia, C. Zhang, Y. Zhang, Y. Guo, X. Zhang, Z. Li and D. Xu, *Org. Biomol. Chem.*, 2015, DOI: 10.1039/C5OB01442E.



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.

ARTICLE

Jørgensen – Hayashi Catalyst Supported on Poly(ethylene glycol)s as Highly Efficient and Reusable Organocatalysts for Enamine-Catalyzed Asymmetric Michael Reaction

Cite this: DOI:
10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Ai-Bao Xia, Can Zhang, Yan-Peng Zhang, Yan-Jun Guo, Xiao-Long Zhang, Zhao-Bo Li and Dan-Qian Xu^{*,a}

A new kind of recyclable and reusable PEG-supported Jørgensen – Hayashi catalyst is synthesized for the first time and proven to be efficient for the enamine-catalyzed asymmetric Michael reaction with generally moderate to good diastereoselectivity and high to excellent enantioselectivity (up to 6 : 1 dr, 99% ee). The prepared PEG-supported catalyst can be recovered eight times and found to provide similar diastereoselectivity and enantioselectivity to unsupported functional catalyst.

Introduction

The use of organocatalysis as a new powerful tool for the asymmetric synthesis of pharmaceutical intermediates, biologically active compounds, and natural products has grown in recent years.¹ Various efficient organocatalysts, such as the S-proline and its derivatives, imidazolidine, and other chiral organocatalysts, have been used in organocatalytic methods.² However, high organocatalyst loadings (10 mol% to 30 mol%) are generally required in those transformations to afford ideal catalytic performance. Furthermore, homogeneous organocatalysts cannot be easily separated from reaction systems to further reuse them. Therefore, the development of catalyst immobilization may aid us in overcoming these problems, and it also holds great significance in both economic and environmental concerns.³

(S) - α , α - diarylprolinol silyl ethers, also known as Jørgensen–Hayashi catalysts, were proven to be promising organocatalysts,⁴ and various different approaches for the immobilization of Jørgensen–Hayashi catalyst have been reported. Whereas the use of insoluble heterogeneous supports has gained widespread attention,⁵ immobilization on soluble homogeneous polymers has scarcely been reported.⁶ For example, Zeitler and co-workers have reported on a type of MeOPEG-supported Jørgensen–Hayashi catalyst through a stable 1,2,3-triazole linkage, and the immobilized catalyst provides unchanged reactivity and selectivity as compared with the homogeneous catalyst^{6g}. In this article, we report the synthesis of unsupported functional Jørgensen–Hayashi catalyst **1** and its

polyethylene glycol(PEG)-supported derivatives **2** through thiol–ene coupling for the first time (Figure 1)^{5f, 5g, 7}, as well as their application in enamine-catalyzed asymmetric Michael reaction⁸.

Results and discussion

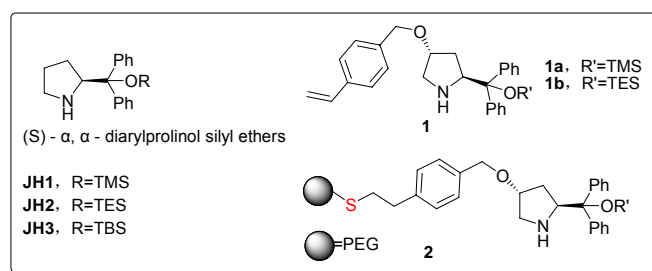
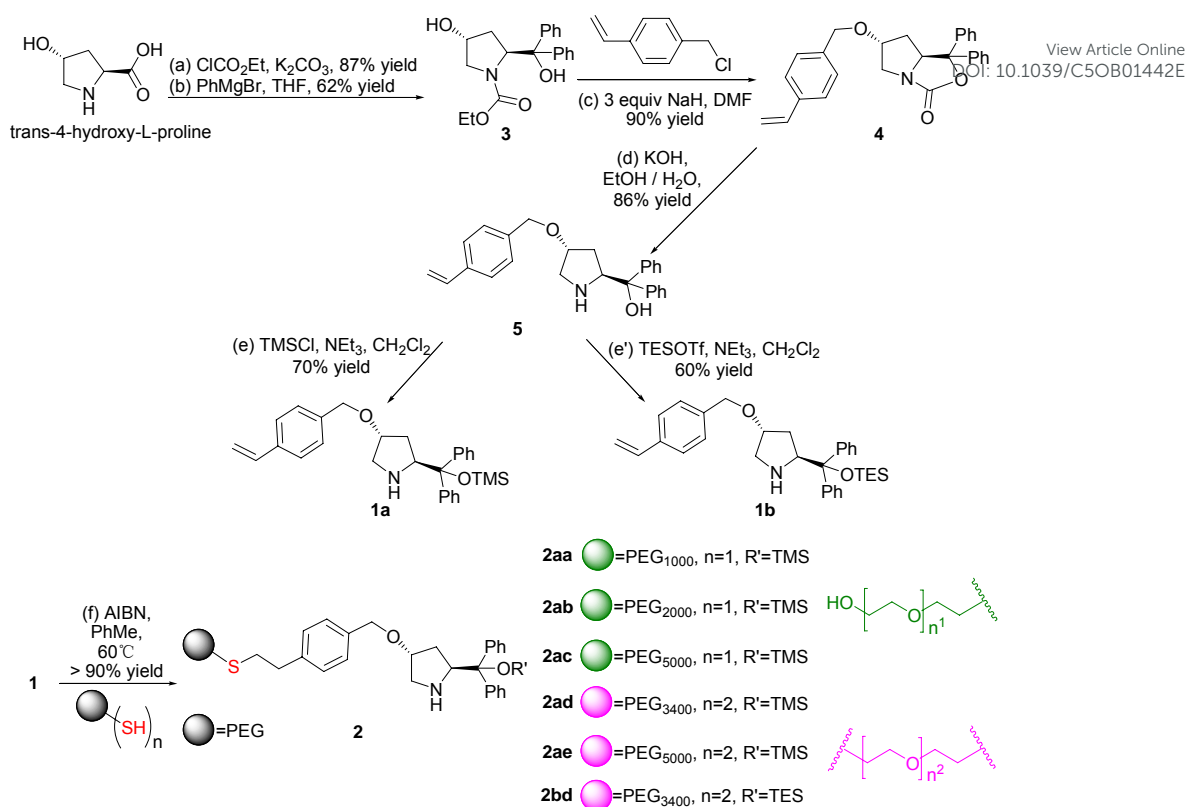


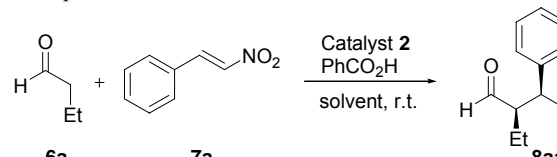
Figure 1. Catalysts used in this study

As described in Scheme 1, the unsupported functional Jørgensen–Hayashi catalyst **1** was accordingly synthesized and immobilized onto the thiol PEG. The PEG-supported Jørgensen–Hayashi catalysts **2** could be obtained in a very good overall yield (> 41% from **3**).^{6g} According to the elemental analysis of nitrogen, the loading of functional Jørgensen–Hayashi catalyst **1a** on PEG-supported **2aa**, **2ab**, **2ac**, **2ad** and **2ae** was 0.65 mmol/g, 0.39 mmol/g, 0.17 mmol/g, 0.3 mmol/g and 0.19 mmol/g, respectively. And the loading of functional Jørgensen–Hayashi catalyst **1b** on PEG-supported **2bd** was 0.29 mmol/g.



Scheme 1. Synthesis of the Unsupported Functional Jørgensen–Hayashi Catalyst **1** and the PEG-Immobilized **2** from trans-4-Hydroxy-L-Proline

Table 1. Catalyst Screening and Reaction Optimization^a

							
Entry	Cat	solvent	time (day)	C ^b (%)	Y ^c (%)	dr ^d	ee ^e (%)
1	1a	none	1	> 99	90	1.8:1	94
2	1b	none	1	95	88	1.9:1	92
3	JH1	none	1	95	89	2.6:1	94
4	JH2	none	1	92	89	2.6:1	89
5	JH3	none	1	88	85	2.6:1	88
6	2aa	none	7	< 5			
7	2ab	none	7	< 5			
8	2ac	none	7	15	10	1.1:1	99
9	2ad	none	7	64	60	3:1	98
10	2ae	none	7	41	37	2:1	99
11	2ad	PhMe	4	41	35	5:1	87
12	2ad	(CH ₂ Cl) ₂	4	86	73	10:1	90
13	2ad	EtOH	4	> 99	87	2:1	86
14	2ad	MeOH	2	> 99	86	2.7:1	90
15	2ad	H ₂ O	2	> 99	85	1.5:1	87
16	2ad	(CH ₂ Cl) ₂ : H ₂ O (1:1)	2	> 99	55	1.5:1	90
17	2ad	(CH ₂ Cl) ₂ : H ₂ O (3:1)	2	> 99	87	5:1	97
18	2ad	(CH ₂ Cl) ₂ : H ₂ O (5:1)	2	67	31	4.6:1	92

^a Unless otherwise stated, the reaction was conducted by stirring in solvent (0.25 mL) using **6a** (0.5 mmol) and **7a** (0.1 mmol) with 5 mol% catalyst and 10 mol% PhCO_2H at room temperature. ^b The conversion, determined by GC-MS. ^c Isolated yield of **8aa**. ^d The dr value of *syn:anti*, determined through HPLC analysis on a Chiralcel OD-H. ^e The ee value of the *syn* isomer, determined through HPLC analysis on a Chiralcel OD-H.

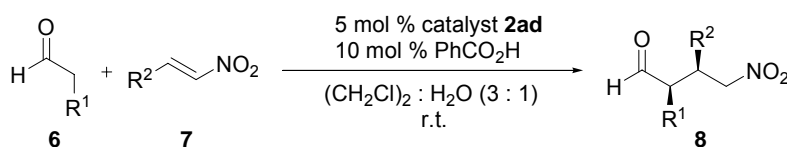
The unsupported functional Jørgensen–Hayashi catalysts **1**, regular Jørgensen–Hayashi catalysts **JH** and the PEG-supported Jørgensen–Hayashi catalysts **2** were then evaluated for the enamine-catalyzed asymmetric Michael reaction of butyraldehyde **6a** and *trans*- β -nitrostyrene **7a** without solvent at room temperature (Table 1, entries 1–10). Pleasingly, using catalysts **1a**, **1b**, **JH1**, **JH2** and **JH3**, Michael product **8aa** was obtained as the major product with significant similar diastereo- and enantiocontrol (Table 1, entries 1–5). Furthermore, among the tested PEG-supported Jørgensen–Hayashi catalysts (entries 6–10), **2ad** (entry 9), which exhibited slightly better diastereoselectivity and enantioselectivity than the unsupported functional catalyst **1** (entry 1), was found to be the best catalyst among the supported catalysts for the reaction, providing **8aa** in 64% conversion, 3:1 dr with corresponding 98%, and 67% ee. Subsequent evaluation of solvent effects improved the yield to 87% when (CH₂Cl)₂:H₂O (3:1) was used as the solvent (entries 11–18).

After obtaining the optimized reaction conditions, a series of experiments were performed to investigate the substrate scope for the enamine-catalyzed asymmetric Michael reaction of aldehydes **6** and *trans*- β -nitrostyrenes **7**. As summarized in Table 2, different combinations of **6** and **7** were allowed to react smoothly in the presence of 5 mol% of the supported catalyst **2ad** to afford the expected adducts **8** in moderate to excellent yields (40% to 95%), moderate to good diastereoselectivities (1:1 to 6:1 dr) and high to excellent enantioselectivities (*syn* isomer, 85% to 99% ee). Variations in the aldehydes **6** (Table 2, entries 1–6) as well as in the nitroolefins **7a–7g** (Table 2, entries 7–13) are well tolerated. Aldehyde **6f** with more sterically demanding moiety in the β -

position also yielded the addition product **8fa** with high enantioselectivity (85% ee) (Table 2, entry 6). In addition, also the nitrodiene **7h** with aldehyde **6a** was also successfully converted to the conjugate addition product in good yield and excellent enantioselectivity (Table 2, entry 14). These results demonstrate that the PEG-supported Jørgensen–Hayashi catalyst **2ad** is a highly efficient catalyst.

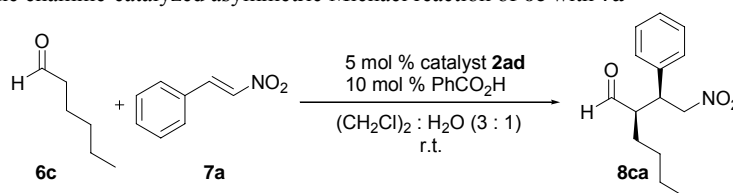
Next, the recyclability and stability of the PEG-supported catalyst **2ad** was examined. The recycling experiment was performed at the premise of recovering the PEG-supported catalyst by using acid-based extraction method. After the Michael reaction, the recovered PEG-supported catalyst was extracted from the aqueous phase, dried, and then directly subjected to the next run. As shown in Table 3, the PEG-supported catalyst **2ad** can be reused for at least eight times without losing the enantioselectivity (94 to 99% ee) and diastereoselectivity (dr 4:1 to 5:1). After the seventh run, due to the hydrolysis of the silyl ether, we could observe a significant decrease in catalytic activity, although diastereoselectivity and enantioselectivity maintained. But after simply treating the deactivated PEG-supported catalyst **2ad** with ClSi(CH₃)₃ in CH₂Cl₂, the catalytic activity of the **2ad** can be recovered effectively (Table 3, entry 9).^{5d, 5i} The **JH1** was also tested in the recycling experiment, in the fourth run with the recovered catalyst, quite low yield (only 14%) with constant level of diastereo- and enantioselectivity was observed (Table 3, entry 4). And when the PEG-supported catalyst **2bd** with more robust TES was used, it can be reused for eight times without losing the enantioselectivity (99% ee) and diastereoselectivity (dr 9:1 to 10:1).

Table 2. Scope of the enamine-catalyzed asymmetric Michael reaction^a



Entry	R ¹ / 6	R ² / 7	8 / yield ^b (%)	dr ^c (<i>syn:anti</i>)	ee ^d (%)
1	Et / 6a	C ₆ H ₅ / 7a	8aa / 87	5:1	97
2	Pr / 6b	C ₆ H ₅ / 7a	8ba / 90	5:1	87
3	Butyl / 6c	C ₆ H ₅ / 7a	8ca / 93	4:1	91
4	Pentyl / 6d	C ₆ H ₅ / 7a	8da / 70	4:1	99
5 ^e	Hexyl / 6e	C ₆ H ₅ / 7a	8ea / 92	5:1	96
6	<i>i</i> -Pr / 6f	C ₆ H ₅ / 7a	8fa / 40	1:1	85
7 ^e	Et / 6a	4-CH ₃ -C ₆ H ₄ / 7b	8ab / 85	6:1	98
8	Et / 6a	4-Br-C ₆ H ₄ / 7c	8ac / 91	1:1	92
9 ^e	Et / 6a	3-Br-C ₆ H ₄ / 7d	8ad / 86	3:1	99
10 ^e	Et / 6a	2-Br-C ₆ H ₄ / 7e	8ae / 88	3:1	99
11	Et / 6a	2-Thienyl / 7f	8af / 75	2:1	98
12	Butyl / 6c	4-Br-C ₆ H ₄ / 7c	8cc / 95	5:1	99
13	Butyl / 6c	4-Cl-C ₆ H ₄ / 7g	8cg / 57	3:1	99
14	Et / 6a	4-Br-C ₆ H ₄ CH=CH / 7h	8ah / 68	2:1	89

^a Unless otherwise stated, the reaction was conducted by stirring in 0.25 mL solvent using **6** (0.5 mmol) and **7** (0.1 mmol) with 5 mol% catalyst **2ad** and 10 mol% PhCO₂H at room temperature for 2 days. In the case of racemic samples, 50 mol% DL-proline were used in DMF. ^b Isolated yield. ^c Determined by chiral-phase HPLC. ^d The ee value of the *syn* isomer, determined by chiral-phase HPLC. ^e The ee value of the *syn* isomer was determined by chiral HPLC analysis after conversion of the aldehyde into the corresponding alcohol by reduction with NaBH₄.

Table 3. Recycling of **2ad** for the enamine-catalyzed asymmetric Michael reaction of **6c** with **7a**^aView Article Online
DOI: 10.1039/C5OB01442E

recycle	method	yield of 8ca ^b (%)	dr ^c (syn:anti)	ee ^c (%) (syn)
	A	79	5:1	96
	B	60	4:1	99
	C	82	9:1	99
1	A	79	5:1	96
	B	58	4:1	99
	C	80	9:1	99
2	A	78	4:1	99
	B	58	4:1	99
	C	79	9:1	99
3	A	67	5:1	99
	B	59	5:1	99
	C	78	9:1	99
4	A	71	5:1	98
	B	14	5:1	99
	C	76	9:1	99
5	A	69	4:1	94
	C	76	10:1	99
6	A	65	5:1	95
	C	76	10:1	99
7	A	55(71) ^d	5:1 (5:1) ^d	97 (97) ^d
	C	75	10:1	99
8	A	46(71) ^e	5:1 (5:1) ^e	97 (97) ^e
	C	75	9:1	99
9 ^f	A	69	5:1	95

^a Method A: unless otherwise stated, the reaction was conducted by stirring in 5 mL solvent using **6c** (2.4 mmol) and **7a** (2 mmol) with 5 mol% catalyst **2ad** and 10 mol% PhCO₂H at room temperature in 2 days. Method B: **JH1** was used as the catalyst. Method C: **2bd** was used as the catalyst. ^b Isolated yield of **8ca**. ^c Determined through HPLC analysis on a Chiralcel OD-H. ^d Reaction time = 3 days. ^e Reaction time = 5 days. ^f Using the reactivated catalyst **2ad**.

Conclusions

In summary, a novel recyclable, and reusable PEG-supported Jørgensen–Hayashi catalyst is synthesized for the first time. The catalyst is proven to be efficient catalyst for the enamine-catalyzed asymmetric Michael reaction of a wide range of aldehydes with both nitroolefins and nitrodiene. Moderate to excellent yield (40% to 95%), moderate to good diastereoselectivities (1:1 to 6:1 dr), and high to excellent enantioselectivities (87% to 99% ee) are achieved using only 5 mol% PEG-supported catalyst loading. The prepared PEG-supported catalyst can be recovered eight times and found to provide similar diastereoselectivity and enantioselectivity to unsupported functional catalyst. Further study on the wide application of this efficient strategy for the synthesis of potentially valuable chiral molecules is under investigation in our laboratory.

Experimental

General information

The ¹H NMR and ¹³C NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane. GC–MS experiments were performed on a GC system with a mass selective detector. HRMS data were measured on a LC/TOF-MS with ESI source or GC/TOF-MS with EI source. Elemental analyses of N, C, and H, and IR spectra were performed for catalysts **2aa**, **2ab**, **2ac**, **2ad**, **2ae** and **2bd**. Column chromatography and flash chromatography experiments were performed on silica gel (200–300 mesh) eluting with ethyl ether and petroleum ether. TLC experiments were carried out on glass-backed silica plates. In each case, enantiomeric ratio was determined on a chiral column in comparison with authentic racemates by chiral HPLC. Compound **3** was synthesized according to the reference 6g.

Conventional procedure for the synthesis of PEG-supported Jørgensen–Hayashi catalysts **2**

Synthesis of compound **4**

Sodium hydride (1.69 g, 0.044 mmol, 4.4 equiv., 60 (w%)) was

added in a N₂-filled round-bottom flask containing 30 mL dried DMF at room temperature with stirring for 10 min. Then, the solution of **3** (3.41 g, 0.01 mmol, 1 equiv.) in 9 mL of dried DMF was added in 30 min at 0 °C. After an hour, 1-(chloromethyl)-4-vinylbenzene (1.67 g, 0.011 mmol, 1.1 equiv.) was added slowly using a septum. The resulting reaction mixture was allowed to react with stirring at ambient temperature. Subsequently, the reaction was quenched with diethyl ether (10 mL) and water (10 mL). The layers were separated and the aqueous phase was extracted with diethyl ether several times. The combined organic layers were washed with water, dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 8/1 to 5/1) to afford the product **4**, yield: 18.5 g, 90 %; yellow oil; ¹H NMR (500 MHz, CDCl₃): δ = 7.58–7.56 (m, 2H), 7.45–7.42 (m, 2H), 7.41–7.37 (m, 6H), 7.35–7.27 (m, 4H), 6.76–6.72 (q, *J* = 11.0, 17.5 Hz, 1H), 5.81–5.78 (m, 1H), 5.31–5.28 (m, 1H), 4.90–4.93 (q, *J* = 5.0, 11.5 Hz, 1H), 4.48 (s, 2H), 4.18 (t, *J* = 5.5 Hz, 1H), 4.08–4.05 (q, *J* = 5.5, 12.5 Hz, 1H), 3.38–3.35 (m, 1H), 1.96–1.92 (q, *J* = 5.0, 13.5 Hz, 1H), 1.25–1.19 (m, 1H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ = 160.4, 143.0, 140.2, 137.4, 137.2, 136.4 (×2), 128.7 (×2), 128.5 (×2), 128.0 (×2), 127.8, 126.4 (×2), 126.1 (×2), 125.5 (×2), 114.2, 85.8, 78.4, 71.1, 67.5, 53.8, 36.2 ppm; GC-MS: *m/z* 411.2 (100), 165.1, 91.1. HRMS (ESI-TOF) *m/z*: [M + H]⁺ Calcd for C₂₇H₂₆NO₃ 412.1913; Found 412.1922.

Synthesis of compound 5

A N₂-filled three-necked round-bottom flask was charged with **4** (4.11 g, 0.01 mmol) in 25 mL ethanol. Potassium hydroxide (1.12 g, 0.02 mmol, 2 equiv.) in water (4.6 mL) was added in a drop-wise manner. After being stirred for 30 h at 45 °C, the reaction was diluted with ethyl acetate. The layers were separated and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate 8/1 to 4/1) to afford the product **5**, yield: 16.6 g, 86 %; white solid, mp: 70.4 °C; ¹H NMR (500 MHz, CDCl₃): δ = 7.62 (*d*, *J* = 7.0 Hz, 2H), 7.53 (*t*, *J* = 1.0 Hz, 2H), 7.43 (*d*, *J* = 8.5 Hz, 2H), 7.36–7.30 (m, 6H), 7.24–7.19 (m, 2H), 6.79–6.73 (q, *J* = 10.5, 17.5 Hz, 1H), 5.78 (*d*, *J* = 17.5 Hz, 1H), 5.28 (*d*, *J* = 11.0 Hz, 1H), 4.63–4.60 (q, *J* = 6.5, 9.5 Hz, 1H), 4.49–4.44 (m, 2H), 4.09–4.07 (m, 1H), 3.20–3.16 (m, 2H), 1.86–1.80 (m, 1H), 1.74–1.70 (m, 1H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ = 147.8, 145.0, 138.0, 137.1, 136.6, 128.3 (×2), 128.0 (×2), 127.8 (×2), 126.6, 126.4, 126.3 (×2), 126.0 (×2), 125.5 (×2), 113.9, 79.5, 76.9, 70.6, 63.5, 52.6, 33.0 ppm; (ESI+) *m/z* 386.28; HRMS (ESI-TOF) *m/z*: [M + H]⁺ Calcd for C₂₆H₂₈NO₂ 386.2115; Found 386.2119.

Synthesis of compound 1

Fresh triethylamine (1.31 g, 0.013 mmol, 1.3 equiv.) was added slowly to a solution of **5** (3.85 g, 0.01 mmol, 1 equiv.) in anhydrous dichloromethane (30 mL) under N₂-atmosphere. After being stirred for 10 min, fresh chlorotrimethylsilane (1.19 g, 0.011 mmol, 1.1 equiv.) or TESOTf (2.91 g, 0.011 mmol, 1.1 equiv.) was added in a drop-wise manner at 0 °C. The reaction was allowed proceed with stirring at ambient temperature for a further 3 days. Subsequently, the mixture was poured into ice water followed by extraction with dichloromethane. The

combined organic layer was washed with brine and dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/ethyl ether 5/1 to 3/1) to afford the product **1. 1a**, yield: 3.2 g, 70 %; colorless liquid; ¹H NMR (500 MHz, CDCl₃): δ = 7.52–7.50 (m, 2H), 7.41–7.38 (m, 4H), 7.32–7.24 (m, 8H), 6.77–6.71 (q, *J* = 11.0, 18.0 Hz, 1H), 5.77 (*d*, *J* = 18.0 Hz, 1H), 5.26 (*d*, *J* = 10.5 Hz, 1H), 4.42 (*t*, *J* = 5.5 Hz, 3H), 3.84–3.83 (m, 1H), 3.05–3.03 (m, 1H), 2.88–2.85 (m, 1H), 1.78–1.75 (m, 2H), 0.06 (s, 9H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ = 146.5, 145.3, 138.1, 137.0, 136.6, 128.5 (×2), 127.9 (×2), 127.7 (×2), 127.6 (×2), 127.5 (×2), 127.0, 126.9, 126.3 (×2), 113.8, 82.8, 79.0, 70.6, 63.8, 52.8, 34.3, 2.2 (×3) ppm; (ESI+) *m/z* 458.21; HRMS (ESI-TOF) *m/z*: [M + H]⁺ Calcd for C₂₉H₃₆NO₂Si 458.2516; Found 458.2515. **1b**, yield: 3.0 g, 60 %; colorless liquid; ¹H NMR (500 MHz, CDCl₃): δ = 7.64–7.63 (m, 2H), 7.51–7.47 (m, 4H), 7.41–7.36 (m, 8H), 6.87–6.81 (q, *J* = 11.0, 17.5 Hz, 1H), 5.87 (*d*, *J* = 18.0 Hz, 1H), 5.36 (*d*, *J* = 11 Hz, 1H), 4.54–4.46 (m, 3H), 3.85 (m, 1H), 3.15–2.98 (m, 1H), 2.85–2.82 (m, 1H), 1.95–1.78 (m, 2H), 1.10–0.94 (m, 9H), 0.70–0.63 (m, 2H), 0.51–0.46 (m, 4H) ppm; ¹³C NMR (125 MHz, CDCl₃): δ = 145.5, 145.2, 138.2, 136.9, 136.6, 128.8 (×2), 128.0 (×2), 127.8 (×2), 127.6 (×2), 127.2 (×2), 127.0, 126.9, 126.2 (×2), 113.7, 82.6, 79.3, 70.6, 63.9, 52.9, 34.5, 7.2 (×3), 6.5 (×3) ppm; (ESI+) *m/z* 500.27; HRMS (ESI-TOF) *m/z*: [M + H]⁺ Calcd for C₃₂H₄₂NO₂Si 500.2985; Found 500.2983.

Synthesis of PEG-supported Jørgensen – Hayashi catalysts 2

A mixture of **1** (0.038 g, 0.082 mmol, 1.1 equiv.), PEG-SH (0.075 mmol, 1 equiv.), AIBN (0.012 g, 0.075 mmol, 1 equiv.) in toluene (1.5 mL) was stirred at 60 °C for 1d, then the reaction mixture was precipitated with diethyl ether, filtered, and dried under vacuum. In the case of SH-PEG-SH, **1** (0.072 g, 0.157 mmol, 2.1 equiv.) and AIBN (0.024 g, 0.15 mmol, 2 equiv.) were used. Anal. Calcd. for **2aa** Found: C, 58.40; H, 8.41; N, 0.91. IR (KBr): γ_{max}/cm⁻¹ 3731, 2924, 1105, 951, 757. Anal. Calcd. for **2ab** Found: C, 56.80; H, 8.51; N, 0.55. IR (KBr): γ_{max}/cm⁻¹ 3731, 2869, 1108, 950, 707. Anal. Calcd. for **2ac** Found: C, 54.80; H, 9.10; N, 0.24. IR (KBr): γ_{max}/cm⁻¹ 3731, 3504, 1110, 955, 759. Anal. Calcd. for **2ad** Found: C, 54.80; H, 8.32; N, 0.42. IR (KBr): γ_{max}/cm⁻¹ 3429, 2885, 1112, 956, 760. Anal. Calcd. for **2ae** Found: C, 54.70; H, 8.40; N, 0.27. IR (KBr): γ_{max}/cm⁻¹ 3430, 2876, 1109, 953, 732. Anal. Calcd. for **2bd** Found: C, 54.81; H, 8.33; N, 0.41. IR (KBr): γ_{max}/cm⁻¹ 3443, 2874, 1112, 951, 706.

Conventional procedure for the asymmetric Michael reaction catalyzed by 2d

Solvent (0.25 mL) was added to a mixture of aldehydes **6** (0.5 mmol) with nitroolefins or nitrodiene **7** (0.1 mmol) in the presence of 5 mol% catalyst **2ad** and 10 mol% PhCO₂H at room temperature with vigorous stirring. After 2 days, the reaction mixture was extracted with DCM, washed with water, dried, and concentrated. The residue was purified by flash chromatography on silica gel (ethyl ether/petroleum ether = 1:3 as eluent) to yield the faintly yellow liquid products **8**. Enantiomeric ratio was determined by HPLC analysis on a chiral column.

(2R,3R)-2-ethyl-4-nitro-3-phenylbutanal (8aa).^{5a} yield: 19.2 mg, 87 %; 97 % ee; 5:1 dr; yellow liquid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/i-PrOH (95:5) as the eluent, Flow: 1.0 mL/min;

UV = 224 nm; $t_{\text{syn}}^{\text{minor}} = 37.573$ min, $t_{\text{syn}}^{\text{major}} = 32.482$ min; $t_{\text{anti}}^{\text{minor}} = 58.752$ min, $t_{\text{anti}}^{\text{major}} = 34.854$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.72$ (d, $J = 2.5$ Hz, 1H), 7.36–7.34 (m, 2H), 7.31–7.28 (m, 1H), 7.19–7.17 (m, 2H), 4.74–4.61 (m, 2H), 3.84–3.77 (m, 1H), 2.71–2.66 (m, 1H), 1.55–1.46 (m, 2H), 0.82 (t, $J = 7.5$ Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3): $\delta = 203.1$, 136.8, 129.1 ($\times 2$), 128.1, 128.0 ($\times 2$), 78.5, 53.4, 42.8, 20.4, 10.7 ppm; GC–MS: m/z 145.1, 117.1, 104.1, 91.1 (100), 77.1.

(R)-2-((R)-2-nitro-1-phenylethyl)pentanal (8ba).^{5a} yield: 21.2 mg, 90 %; 87 % ee; 5:1 dr; yellow liquid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/*i*-PrOH (90:10) as the eluent, Flow: 1.0 mL/min; UV = 228 nm; $t_{\text{syn}}^{\text{minor}} = 22.518$ min, $t_{\text{syn}}^{\text{major}} = 24.932$ min; $t_{\text{anti}}^{\text{minor}} = 20.212$ min, $t_{\text{anti}}^{\text{major}} = 34.877$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.72$ (d, $J = 3.0$ Hz, 1H), 7.38–7.34 (m, 2H), 7.33–7.30 (m, 1H), 7.20–7.18 (m, 2H), 4.74–4.64 (m, 2H), 3.81–3.77 (m, 1H), 2.74–2.70 (m, 1H), 1.51–1.47 (m, 1H), 1.39–1.32 (m, 2H), 1.22–1.18 (m, 1H), 0.82 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 203.2$, 136.9, 129.1 ($\times 2$), 128.2, 128.0 ($\times 2$), 78.4, 53.9, 43.3, 29.5, 19.8, 13.9 ppm; GC–MS: m/z 145.2 (100), 117.2, 104.2, 91.2, 77.2.

(R)-2-((R)-2-nitro-1-phenylethyl)hexanal (8ca).^{5a} yield: 21.16 mg, 93 %; 91 % ee; 4:1 dr; yellow liquid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/*i*-PrOH (90:10) as the eluent, Flow: 1.0 mL/min; UV = 228 nm; $t_{\text{syn}}^{\text{minor}} = 17.039$ min, $t_{\text{syn}}^{\text{major}} = 20.918$ min; $t_{\text{anti}}^{\text{minor}} = 18.612$ min, $t_{\text{anti}}^{\text{major}} = 29.811$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.71$ (d, $J = 3.0$ Hz, 1H), 7.37–7.34 (m, 2H), 7.32–7.29 (m, 1H), 7.20–7.18 (m, 2H), 4.74–4.63 (m, 2H), 3.81–3.77 (m, 1H), 2.73–2.69 (m, 1H), 1.51–1.47 (m, 1H), 1.43–1.40 (m, 1H), 1.28–1.19 (m, 2H), 1.18–1.13 (m, 2H), 0.79 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 203.3$, 136.9, 129.1 ($\times 2$), 128.1, 128.0 ($\times 2$), 78.4, 53.9, 43.2, 28.5, 27.0, 22.5, 13.6 ppm; GC–MS: m/z 145.2 (100), 117.2, 105.2, 104.2, 91.2.

(R)-2-((R)-2-nitro-1-phenylethyl)heptanal (8da).^{5a} yield: 18.41 mg, 70 %; 99 % ee; 4:1 dr; yellow liquid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/*i*-PrOH (90:10) as the eluent, Flow: 1.0 mL/min; UV = 228 nm; $t_{\text{syn}}^{\text{major}} = 19.745$ min; $t_{\text{anti}}^{\text{minor}} = 26.491$ min, $t_{\text{anti}}^{\text{major}} = 17.652$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.69$ (d, $J = 2.5$ Hz, 1H), 7.36–7.33 (m, 2H), 7.31–7.28 (m, 1H), 7.19–7.18 (m, 2H), 4.74–4.63 (m, 2H), 3.82–3.77 (m, 1H), 2.72–2.70 (m, 1H), 1.49–1.47 (m, 1H), 1.39–1.38 (m, 1H), 1.28–1.11 (m, 6H), 0.81 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 203.2$, 136.8, 129.0 ($\times 2$), 128.0 ($\times 3$), 78.4, 53.8, 43.1, 31.5, 27.2, 26.0, 22.1, 13.7 ppm; GC–MS: m/z 117.1 (100), 115.1, 104.1, 77.1, 91.1.

(R)-2-((R)-2-nitro-1-phenylethyl)octanal (8ea).^{8f} yield: 25.48 mg, 96 %; 11% ee; 5:1 dr; yellow liquid; The product was converted to the corresponding alcohol with NaBH_4 and enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/*i*-PrOH (95:5) as the eluent, Flow: 1.0 mL/min; UV = 208 nm; $t_{\text{syn}}^{\text{minor}} = 12.866$ min, $t_{\text{syn}}^{\text{major}} = 11.493$ min; $t_{\text{anti}}^{\text{minor}} = 16.479$ min, $t_{\text{anti}}^{\text{major}} = 14.199$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.67$ (d, $J = 2.5$ Hz, 1H), 7.34–7.31 (m, 2H), 7.28–7.25 (m, 1H), 7.18–7.17 (m, 2H), 4.72–4.61 (m, 2H), 3.81–3.76 (m, 1H), 2.72–2.67 (m, 1H), 1.48–1.10 (m, 10H), 0.81 (t, $J = 6.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 203.3$, 136.9, 129.1 ($\times 2$), 128.0 ($\times 3$), 78.4, 53.9, 43.2, 31.4, 28.5, 27.3, 26.4, 22.4, 14.0 ppm; GC–MS: m/z 145.1 (100), 105.1, 104.1, 91.1, 78.1.

(2R,3R)-2-isopropyl-4-nitro-3-phenylbutanal (8fa).^{5a} yield: 9.40 mg, 40 %; 85 %; 47 % ee; 1:1 dr; white solid, mp: 114.4 °C; The enantiomeric excess was determined by HPLC on Daicel Chiralpak IC-H with hexane/*i*-PrOH (95:5) as the eluent, Flow: 1.0 mL/min; UV = 212 nm; $t_{\text{syn}}^{\text{minor}} = 29.745$ min, $t_{\text{syn}}^{\text{major}} = 33.878$ min; $t_{\text{anti}}^{\text{minor}} = 14.439$ min, $t_{\text{anti}}^{\text{major}} = 19.159$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.91$ (d, $J = 2.0$ Hz, 1H), 7.36–7.33 (m, 2H), 7.30–7.27 (m, 1H), 7.21–7.20 (m, 2H), 4.70–4.55 (m, 1H), 3.94–3.89 (m, 1H), 2.80–2.77 (m, 1H), 1.73–1.69 (m, 1H), 1.09 (d, $J = 7.0$ Hz, 3H), 0.87 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 204.4$, 137.2, 129.1 ($\times 2$), 128.0 ($\times 3$), 79.0, 58.7, 42.0, 27.9, 21.6, 16.9 ppm; GC–MS: m/z 145.2 (100), 104.2, 117.2, 131.2, 91.2.

(2R,3R)-2-ethyl-4-nitro-3-p-tolylbutanal (8ab).^{8h} yield: 19.98 mg, 98 %; 43 % ee; 6:1 dr; yellow liquid; The product was converted to the corresponding alcohol with NaBH_4 and enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/*i*-PrOH (97:3) as the eluent, Flow: 1.0 mL/min; UV = 212 nm; $t_{\text{syn}}^{\text{minor}} = 59.725$ min, $t_{\text{syn}}^{\text{major}} = 63.937$ min; $t_{\text{anti}}^{\text{minor}} = 47.476$ min, $t_{\text{anti}}^{\text{major}} = 51.595$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.72$ (d, $J = 3.0$ Hz, 1H), 7.16–7.13 (m, 2H), 7.08–7.06 (m, 2H), 4.72–4.59 (m, 2H), 3.77–3.76 (m, 1H), 2.67–2.65 (m, 1H), 2.33 (s, 3H), 1.53–1.50 (m, 2H), 0.84 (t, $J = 7.0$ Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3): $\delta = 203.3$, 137.9, 133.7, 129.8 ($\times 2$), 127.9 ($\times 2$), 78.7, 55.1, 42.4, 21.0, 20.4, 10.7 ppm; GC–MS: m/z 159.2, 143.2, 118.2 (100), 117.2, 91.2.

(2R,3R)-3-(4-bromophenyl)-2-ethyl-4-nitrobutanal (8ac).^{8e} yield: 27.21 mg, 92 %; 75 % ee; 1:1 dr; yellow liquid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak IC-H with hexane/*i*-PrOH (95:5) as the eluent, Flow: 1.0 mL/min; UV = 228 nm; $t_{\text{syn}}^{\text{minor}} = 41.210$ min, $t_{\text{syn}}^{\text{major}} = 44.663$ min; $t_{\text{anti}}^{\text{minor}} = 36.397$ min, $t_{\text{anti}}^{\text{major}} = 26.531$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.71$ (d, $J = 2.5$ Hz, 1H), 7.49–7.47 (m, 2H), 7.08–7.07 (m, 2H), 4.74–4.57 (m, 2H), 3.80–3.75 (m, 1H), 2.69–2.64 (m, 1H), 1.57–1.45 (m, 2H), 0.83 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 204.8$, 136.0, 132.4 ($\times 2$), 129.8 ($\times 2$), 122.2, 78.3, 54.7, 42.2, 20.4, 10.6 ppm; GC–MS: m/z 223.0, 115.1 (100), 103.1, 91.1, 77.1.

(2R,3R)-3-(3-bromophenyl)-2-ethyl-4-nitrobutanal (8ad). yield: 25.71 mg, 86 %; 99 % ee; 99:1 dr; yellow liquid; The product was converted to the corresponding alcohol with NaBH_4 and enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/*i*-PrOH (97:3) as the eluent, Flow: 0.6 mL/min; UV = 228 nm; $t_{\text{syn}}^{\text{major}} = 80.238$ min; $t_{\text{anti}}^{\text{minor}} = 58.952$ min, $t_{\text{anti}}^{\text{major}} = 62.618$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.70$ (d, $J = 2.5$ Hz, 1H), 7.44–7.41 (m, 1H), 7.36–7.35 (m, 1H), 7.24–7.18 (m, 1H), 7.14–7.13 (m, 1H), 4.74–4.59 (m, 2H), 3.82–3.75 (m, 1H), 2.70–2.65 (m, 1H), 1.57–1.46 (m, 2H), 0.84 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 202.7$, 139.4, 131.4, 131.1, 130.7, 126.7, 123.1, 78.1, 54.7, 42.2, 20.4, 10.6 ppm; GC–MS: m/z 169.0, 115.1 (100), 103.1, 91.1, 77.1. HRMS (EI-TOF) m/z : [M]⁺ Calcd for $\text{C}_{12}\text{H}_{14}\text{BrNO}_3$ 299.0157; Found 299.0163.

(2R,3R)-3-(2-bromophenyl)-2-ethyl-4-nitrobutanal (8ae).^{8e} yield: 26.31 mg, 88 %; 99 % ee; 3:1 dr; yellow liquid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/*i*-PrOH (90:10) as the eluent, Flow: 1.0 mL/min; UV = 232 nm; $t_{\text{syn}}^{\text{major}} = 29.997$ min; $t_{\text{anti}}^{\text{minor}} = 41.356$ min, $t_{\text{anti}}^{\text{major}} = 28.786$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.73$ (d, $J = 2.0$ Hz, 1H), 7.61–7.60 (m, 1H), 7.33–7.30 (m, 1H), 7.22–7.18 (m, 1H), 7.17–7.13 (m, 1H), 4.87–4.67 (m, 2H), 4.38–4.37 (m, 1H), 2.93 (s, 1H), 1.66–1.57

(m, 1H), 1.56–1.47 (m, 1H), 0.67 (t, $J = 15.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 202.9, 136.3, 133.9, 129.5$ ($\times 2$), 128.1 ($\times 2$), 77.4, 54.4, 41.3, 19.6, 11.6 ppm; GC–MS: m/z 184.1 (100), 169.1, 115.1, 104.2, 77.2.

(2R,3S)-2-ethyl-4-nitro-3-(thiophen-2-yl)butanal (8af).^{8g} yield: 17.03 mg, 98 %; 70 % ee; 2:1 dr; yellow liquid; The product was converted to the corresponding alcohol with NaBH_4 and enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/*i*-PrOH (98:2) as the eluent, Flow: 0.5 mL/min; UV = 228 nm; $t^{\text{syn}}_{\text{minor}} = 123.112$ min, $t^{\text{syn}}_{\text{major}} = 129.573$ min; $t^{\text{anti}}_{\text{minor}} = 113.667$ min, $t^{\text{anti}}_{\text{major}} = 105.861$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.717$ (d, $J = 2.0$ Hz, 1H), 7.25–7.23 (m, 1H), 6.96–6.94 (m, 1H), 6.91–6.90 (m, 1H), 4.75–4.62 (m, 2H), 4.20–4.14 (m, 1H), 2.72–2.67 (m, 1H), 1.69–1.61 (m, 2H), 0.87 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 202.5, 139.5, 127.2, 127.1, 125.3, 78.9, 55.8, 38.4, 20.3, 10.9$ ppm; GC–MS: m/z 180.1, 151.1, 110.1 (100), 137.1, 97.1.

(R)-2-((R)-1-(4-bromophenyl)-2-nitroethyl)hexanal (8cc). yield: 31.07 mg, 95 %; 99 % ee; 5:1 dr; yellow liquid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak AD-H with hexane/*i*-PrOH (95:5) as the eluent, Flow: 1.0 mL/min; UV = 228 nm; $t^{\text{syn}}_{\text{minor}} = 16.159$ min, $t^{\text{syn}}_{\text{major}} = 13.972$ min; $t^{\text{anti}}_{\text{major}} = 19.652$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.68$ (d, $J = 7.0$ Hz, 1H), 7.49–7.47 (m, 2H), 7.08–7.07 (m, 2H), 4.72–4.59 (m, 2H), 3.79–3.74 (m, 1H), 2.71–2.66 (m, 1H), 1.48–1.37 (m, 2H), 1.26–1.14 (m, 4H), 0.79 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 202.8, 136.0, 132.2$ ($\times 2$), 129.7 ($\times 2$), 122.1, 78.1, 53.6, 42.5, 28.4, 27.0, 22.5, 13.6 ppm; GC–MS: m/z 184.0, 115.1 (100), 103.1, 91.1, 77.1. HRMS (EI-TOF) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{14}\text{H}_{17}\text{BrO}$ 280.0463 $[\text{M} - \text{HNO}_2]^+$; Found 280.0473.

(R)-2-((R)-1-(4-chlorophenyl)-2-nitroethyl)hexanal (8cg). yield: 16.13 mg, 57 %; 99 % ee; 3:1 dr; yellow liquid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak OD-H with hexane/*i*-PrOH (97:3) as the eluent, Flow: 1.0 mL/min; UV = 228 nm; $t^{\text{syn}}_{\text{minor}} = 30.762$ min, $t^{\text{anti}}_{\text{major}} = 32.548$ min; $t^{\text{anti}}_{\text{major}} = 37.866$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.70$ (d, $J = 5.0$ Hz, 1H), 7.35–7.32 (m, 2H), 7.15–7.12 (m, 2H), 4.73–4.60 (m, 2H), 3.80–3.75 (m, 1H), 2.71–2.67 (m, 1H), 1.49–1.40 (m, 2H), 1.25–1.16 (m, 4H), 0.81 (t, $J = 5.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 202.8, 135.4, 131.1, 129.4$ ($\times 2$), 129.4 ($\times 2$), 78.2, 53.7, 42.5, 28.4, 27.1, 22.5, 13.6 ppm; GC–MS: m/z 179.0, 138.0 (100), 115.1, 103.1, 77.1. HRMS (EI-TOF) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{14}\text{H}_{17}\text{ClO}$ 236.0968 $[\text{M} - \text{HNO}_2]^+$; Found 236.0979.

(2R,3S,E)-5-(4-bromophenyl)-2-ethyl-3-(nitromethyl)pent-4-enal (8ah). yield: 22.10 mg, 68 %; 90 % ee; 2:1 dr; yellow liquid; The enantiomeric excess was determined by HPLC on Daicel Chiralpak IC-H with hexane/*i*-PrOH (95:5) as the eluent, Flow: 1.0 mL/min; UV = 228 nm; $t^{\text{syn}}_{\text{minor}} = 37.184$ min, $t^{\text{syn}}_{\text{major}} = 41.757$ min; $t^{\text{anti}}_{\text{minor}} = 31.478$ min, $t^{\text{anti}}_{\text{major}} = 25.638$ min; ^1H NMR (500 MHz, CDCl_3): $\delta = 9.69$ (d, $J = 2.0$ Hz, 1H), 7.43–7.41 (m, 2H), 7.20–7.18 (m, 2H), 6.48–6.45 (m, 1H), 6.00–5.59 (q, $J = 9.5, 16.0$ Hz, 1H), 4.58–4.46 (m, 2H), 3.56–3.31 (m, 1H), 2.51–2.47 (m, 1H), 1.79–1.66 (m, 2H), 0.97 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): $\delta = 202.6, 134.8, 133.8, 131.7$ ($\times 2$), 128.0 ($\times 2$), 124.6, 122.0, 77.6, 54.2, 40.9, 20.0, 11.1 ppm; GC–MS: m/z 171.1, 129.1 (100), 141.1, 115.1, 77.1. HRMS (EI-TOF) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{14}\text{H}_{16}\text{BrNO}_3$ 325.0314; Found 325.0302.

Recycling of catalyst 2ad or 2bd

After 2 days, 50 mL ethyl ether and 20 mL (0.1 (w %)) aqueous NaOH solution were added in the reaction solution. Then the layers were separated and the aqueous phase was extracted by CH_2Cl_2 (25 mL $\times 3$), simply dried over anhydrous Na_2SO_4 and then subjected to the next run directly. And the PEG supported catalysts can be easily recovered in quantitative yields for each run.

Reactivating of the deactivation catalyst 2ad

Fresh triethylamine (1.3 eq) was added slowly to a solution of the recovered deactivation PEG-supported catalyst **2ad** (1 equiv.) in anhydrous DCM (10 mL) under N_2 -atmosphere. After being stirred for 10 min, fresh chlorotrimethylsilane (2 equiv.) was added in a drop-wise manner at 0 °C. The reaction was allowed proceed with stirring at ambient temperature for a further 3 days. Subsequently, the mixture was poured into ice water followed by extraction with DCM. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 , concentrated, and dissolved in toluene. The mixture was further precipitated with diethyl ether, filtered, and dried under vacuum to obtain the reactivated catalyst **2ad**.

Acknowledgements

Financially supported by the NSFC (21202149), the Foundation of Public Projects of Zhejiang Province (2014C31144), Zhejiang Key Course of Chemical Engineering and Technology, and Zhejiang Key Laboratory of Green Pesticides and Cleaner Production Technology.

Notes and references

^a Catalytic Hydrogenation Research Centre, State Key Laboratory Breeding Base of Green Chemistry-Synthesis Technology, Zhejiang University of Technology, Hangzhou, 310014, China; E-mail: chrc@zjut.edu.cn.

Electronic Supplementary Information (ESI) available: experimental procedures, characterizations, NMR spectra and HPLC spectra are available. See DOI: 10.1039/b000000x/

- (a) B. List and J. W. Yang, *Science* **2006**, *313*, 1584; (b) M. J. Gaunt, C. C. C. Johansson, A. McNally and N. C. Vo, *Drug Discovery Today* **2007**, *12*, 8; (c) D. W. C. MacMillan, *Nature* **2008**, *455*, 304; (d) S. Bertelsen and K. A. Jørgensen, *Chem. Soc. Rev.* **2009**, *38*, 2178; (e) E. Marqués-López, R. P. Herrera and M. Christmann, *Nat. Prod. Rep.* **2010**, *27*, 1138; (f) J. Alemán and S. Cabrera, *Chem. Soc. Rev.* **2013**, *42*, 774.
- (a) Special Issue on Organocatalysis: *Chem. Rev.* **2007**, *107*, issue 17; For selected book, see: (b) A. Berkessel and H. Gröger, *Asymmetric Organocatalysis*; Wiley-VCH: Weinheim, Germany, **2004**; For selected reviews, see: (c) A. Moyano and R. Ríos, *Chem. Rev.* **2011**, *111*, 4703; (d) L. Albrecht, H. Jiang and K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2011**, *50*, 8492; (e) C. Bhanja, S. Jena, S. Nayak and S. Mohapatra, *Beilstein J. Org. Chem.* **2012**, *8*, 1668; (f) J. Duan and P. Li, *Catal. Sci. Technol.* **2014**, *4*, 311.
- For selected reviews, see: (a) Special Issue on Recoverable Catalysts and Reagents: *Chem. Rev.* **2002**, *102*, issue 10; (b) Special Issue on Multiphase Catalysis, Green Solvents and Immobilization: *Adv. Synth. Catal.* **2006**, *348*, issue 12–13; (c) Special Issue on Facilitated Synthesis: *Chem. Rev.* **2009**, *109*, issue 2; (d) T. E. Kristensen and T. Hansen, *Eur. J. Org. Chem.* **2010**, 3179.
- (a) C. Palomo and A. Mielgo, *Angew. Chem. Int. Ed.* **2006**, *45*, 7876; (b) A. Mielgo and C. Palomo, *Chem. Asian J.* **2008**, *3*, 922; (c) K. L.

View Article Online

DOI: 10.1039/C5OB01442E

- Jensen, G. Dickmeiss, H. Jiang, L. Albrecht and K. A. Jørgensen, *Acc. Chem. Res.* **2012**, *45*, 248.
- 5 (a) Y. Li, X. -Y. Liu and G. Zhao, *Tetrahedron: Asymmetry* **2006**, *17*, 2034; (b) C. Röeben, M. Stasiak, B. Janza, A. Greiner, J. H. Wendorff and A. Studer, *Synthesis* **2008**, 2163; (c) M. C. Varela, S. M. Dixon, K. S. Lam and N. E. Schore, *Tetrahedron* **2008**, *64*, 10087; (d) E. Alza and M. A. Pericàs, *Adv. Synth. Catal.* **2009**, *351*, 3051; (e) T. E. Kristensen, K. Vestli, M. G. Jakobsen, F. K. Hansen and T. Hansen, *J. Org. Chem.* **2010**, *75*, 1620; (f) B. G. Wang, B. C. Ma, Q. Wang and W. Wang, *Adv. Synth. Catal.* **2010**, *352*, 2923; (g) G. Francesco, G. Michelangelo, A. Paola, C. Vincenzo and N. Renato, *Catal. Commun.* **2011**, *16*, 75; (h) P. Riente, C. Mendoza and M. A. Pericàs, *J. Mater. Chem.* **2011**, *21*, 7350; (i) E. Alza, S. Sayalero, P. Kasaplar, D. Almasi and M. A. Pericàs, *Chem. Eur. J.* **2011**, *17*, 11585; (j) C. A. Wang, Z. K. Zhang, T. Yue, Y. L. Sun, L. Wang, W. D. Wang, Y. Zhang, C. Liu and W. Wang, *Chem. Eur. J.* **2012**, *18*, 6718; (k) M. Keller, A. Perrier, R. Linhardt, L. Travers, S. Wittmann, A. -M. Caminade, J. -P. Majoral, O. Reiser and A. Ouali, *Adv. Synth. Catal.* **2013**, *355*, 1748.
- 6 For selected reviews, see: (a) M. Benaglia, *New J. Chem.* **2006**, *30*, 1525; (b) M. Gruttadauria, F. Giacalone and R. Noto, *Chem. Soc. Rev.* **2008**, *37*, 1666. for selected examples, see: (c) L. Zu, H. Li, J. Wang, X. Yu and W. Wang, *Tetrahedron Lett.* **2006**, *47*, 5131; (d) M. Gruttadauria, F. Giacalone, A. M. Marculescu, P. L. Meo, S. Riel and R. Noto, *Eur. J. Org. Chem.* **2007**, 4688; (e) O. V. Maltsev, A. S. Kucherenko and S. G. Zlotin, *Eur. J. Org. Chem.* **2009**, 5134; (f) Z. Zheng, B. L. Perkins and B. Ni, *J. Am. Chem. Soc.* **2010**, *132*, 50; (g) I. Mager and K. Zeitler, *Org. Lett.* **2010**, *12*, 1480.
- 7 For selected reviews, see: (a) C. E. Hoyle and C. N. Bowman, *Angew. Chem. Int. Ed.* **2010**, *49*, 1540. for selected examples, see: (b) F. Giacalone, M. Gruttadauria, A. M. Marculescu and R. Noto, *Tetrahedron Lett.* **2007**, *48*, 255; (c) M. Gruttadauria, F. Giacalone, A. M. Marculescu and R. Noto, *Adv. Synth. Catal.* **2008**, *350*, 1397; (d) P. Yu, J. He and C. Guo, *Chem. Commun.* **2008**, 2355.
- 8 For selected reviews, see: (a) R. Ballini, G. Bosica, D. Fiorini, A. Palmieri and M. Petrini, *Chem. Rev.* **2005**, *105*, 933; (b) D. Almasi, D. A. Alonso and C. Najera, *Tetrahedron: Asymmetry* **2007**, *18*, 299; (c) S. B. Tsogoeva, *Eur. J. Org. Chem.* **2007**, 1701; (d) J. Wang, P. Li, P. Y. Choy, A. S. C. Chan and F. Y. Kwong, *ChemCatChem* **2012**, *4*, 917. For selected examples, see: (e) M. Lombardo, M. Chiarucci, A. Quintavalla and C. Trombinia, *Adv. Synth. Catal.* **2009**, *351*, 2801; (f) Y. Chuan, G. Chen and Y. Peng, *Tetrahedron Lett.* **2009**, *50*, 3054; (g) Y. Arakawa, M. Wiesner and H. Wennemers, *Adv. Synth. Catal.* **2011**, *353*, 1201; (h) K. Xu, S. Zhang, Y. Hu, Z. Zha and Z. Wang, *Chem. Eur. J.* **2013**, *19*, 3573.