Supporting Information

Palladium-polymer nanoreactors for the aqueous asymmetric synthesis of therapeutic flavonoids

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Materials

The solvents petroleum ether (40–60 °C), dichloromethane, dichloroethane and acetone, and the reagents, lauroyl peroxide (LPO), 2-cyanopyridine, palladium trifluoroacetate (Pd(TFA)$_2$), chromone, halogenated chromone and aryl boronic acids were purchased from Sigma Aldrich. 1,4-Dioxane, methyl acrylate (MA) and oligo(ethylene glycol) methyl ether methacrylate (OEGMA, $M_n = 300$ g mol$^{-1}$), were purchased from Sigma Aldrich and passed through a column of basic alumina prior to use. 2,2'-Azobisisobutyronitrile (AIBN) was purchased from Sigma Aldrich and recrystallized from
methanol prior to use. The synthesis of 4-cyano-4-(((ethylthio)carbonothioyl)thio) methyl pentanoic acid, the corresponding methyl ester, methyl 4-cyano-4-(((ethylthio)carbonothioyl)thio) pentanoate, and poly(OEGMA) are described in the literature.¹

**Instrumentation**

¹H and ¹³C NMR spectra were recorded at room temperature on Bruker Avance III HD 300 MHz and 400 MHz NMR spectrometers using CDCl₃ as the required solvent. Chemical shifts are reported as δ in parts per million (ppm) relative to the solvent residue. Enantiomeric excess (ee %) was determined by high performance liquid chromatography (HPLC) analysis on a Shimadzu Prominance HPLC with a Chiracel OD-H column 250 mm x 4.6 mm x 5 mm. Size exclusion chromatography (SEC) data was obtained using 2 × PLgel 5 μm mixed-D columns, plus one guard column and dimethyl formamide (DMF) with 5 mM ammonium tetrafluoroborate (NH₄BF₄) as eluent, with a flow rate of 1.0 mL-min⁻¹ at 50 °C. The data was analyzed using Cirrus SEC software and calibrated to poly(methylmethacrylate) (PMMA) standards. IR spectra were collected on a PerkinElmer Spectrum 100 FT-IR spectrometer. UV-Vis spectra were collected on a PerkinElmer Lambda 35 spectrometer using a quartz cell with a 1 cm path length. High resolution mass spectrometry (HR-MS) was conducted on a Bruker UHR-Q-TOF MaXis with electrospray ionization (ESI) using either methanol or acetonitrile as solvent. Transmission electron microscopy (TEM) imaging was performed on a JEOL 2100 TEM operating at 120 kV. Samples for TEM analysis were prepared by drop casting 7 μL of particles suspended in water (0.5 mg·mL⁻¹) onto a carbon/formvar-coated copper grid placed on filter paper. Samples of Pd-nanoreactors were not stained. TEM images were analyzed by ImageJ software, where at least 120 particles were counted for each sample to obtain the average diameter.

**Light scattering analysis**

Data was collected using an ALV/CGS-3 Compact Goniometer System. dn/dc values were determined using a Shodex RI-101 refractometer. The wavelength of the incident beam was 633 nm. 1 mg·mL⁻¹ solutions were filtered through 0.45 μm nylon filters prior to analysis at multiple angles from 80-150° against a toluene standard. The resulting g₁(q, t) autocorrelation functions from DLS analysis for each angle were analyzed by the REPES algorithm¹ to determine a relaxation time, τ. The τ values at each angle were plotted against the square of the scattering wave vector, q to determine the diffusion coefficient D according to equation (1).²

\[ τ^{-1} = q^2 D \]  

(1)

Using SLS analysis at the same angles, partial Zimm plots were obtained and the aggregation number, \( N_{agg} \) for each set of micelles was calculated using equations (2) and (3).³

\[ \frac{Kc}{R_0} \approx \frac{q^2R_g^2}{3M_{w,particle}} + \frac{1}{M_{w,particle}} \]  

(2)

\[ N_{agg} = \frac{M_{w,particle}}{M_{w,polymer}} \]  

(3)

For SLS analysis, the intensity of the scattered light (\( I_{sample} \)) was used to calculate \( Kc/R_0 \) for each angle. It should be noted that since the \( R_0 \) of these micelles were less than 20 nm, the average value of \( Kc/R_0 \) over the angles analyzed was equal to the inverse of the particles’ molecular weight and was used to calculate \( N_{agg} \). In the event of a data point from one observation angle falling outside of 10% error of \( Kc/R_0 \), the point was excluded from the average in the calculation of \( M_{w,particle} \). The core radius (\( R_{core} \)) was calculated from \( N_{agg} \) using equation (4).
Where the core density ($\rho$) was approximated to be the density of methyl acrylate, $N_A$ is Avogadro’s number and $M_{w,\text{core}}$ is the weight average molecular weight of the core-forming block, calculated by the number average molecular weight, $M_n$, determined by $^1$H NMR spectroscopy multiplied by $D$ determined by SEC analysis.

**Synthetic procedures**

\[ \frac{4\pi \rho R_{\text{core}}^3}{3} = \frac{M_{w,\text{core}}}{N_A} \]  \hspace{1cm} (4)

(S,S)-4-Hydroxymethyl-5-phenyl-2-(2′-pyridinyl)-1,2-oxazoline (PyOxA)

**PyOxA alcohol** (Scheme S1) was synthesized according to adapted literature procedures from commercially available 2-cyanopyridine and (S,S)-(−)-2-amino-1-phenyl-1,3-propanediol. A solution of 2-cyanopyridine (5.0 g, 48 mmol), sodium methoxide (1.0 mL of 25 wt% solution in MeOH, 4.8 mmol) and dry MeOH (49 mL) was stirred at room temperature for 48 h. After this time the reaction was quenched by addition of acetic acid (0.27 mL, 4.8 mmol) and the solvent was removed in vacuo. The residue was dissolved in petroleum ether (40-60 °C) and insoluble by-products removed via filtration. Petroleum ether was removed in vacuo and the crude product, methyl picolinimidate, was recovered as an oil and used in the next step without further purification.

Methyl picolinimidate (0.7 g, 5.1 mmol) and (S,S)-(−)-2-amino-1-phenyl-1,3-propanediol (1.1 g, 6.6 mmol) were dissolved in CICH$_2$CH$_2$Cl (4 mL) and stirred under nitrogen at 80 °C for 16 h. After this time the solvent was removed in vacuo, the residue dissolved in CHCl$_3$ (10 mL), washed with deionized water (3 × 10 mL) and the organic layer dried over MgSO$_4$. The solvent was removed in vacuo and **PyOxA alcohol** was obtained as a white solid by suspension of the crude reaction mixture in acetonitrile. The yield was quantitative over the two steps of the reaction, $^5\ [\alpha]^{20}_D +11.8$ (c 5.0 in CHCl$_3$); $\nu_{\text{max}}$ (ATR) 3500–3200, 2951, 2926, 2877, 1587, 1347, 1466, 1118, 968; $\delta_{\text{H}}$ (400 MHz, CDCl$_3$) 3.75 (1H, app d, $J$ 10.1, C(1′′)H$_a$), 4.10 (2H, app d, $J$ 10.1, C(1′′)H$_b$, OH), 4.25–4.27 (1H, m, C(4)H), 5.63 (1H, d, $J$ 7.7, C(3)H), 7.20–7.33 (6H, m, Ph, C(5′)H), 7.62 (1H, app t, $J$ 7.4, C(4′)H), 7.85 (1H, d, $J$ 7.4, C(3′)H), 8.55–8.56 (H, m, C(6′)H); $\delta_{\text{C}}$ (100 MHz, CDCl$_3$) 63.3 (C(1′′)), 76.9 (C(4)), 83.4 (C(5)), 123.8 (C(3′)), 125.7 (C(5′)), 125.9, 125.9, 128.4, 128.7 (Ph), 136.6 (C(4′)), 140.0 (i-Ph), 145.8 (C(2′)), 149.7 (C(6′)), 163.4 (C(2)); HRMS (ESI$^+$) C$_{15}$H$_{16}$N$_2$NaO$_2$ $^+$ ([M+Na$^+$] requires 277.0953; found 277.0947).

(S,S)-4-Methacrylate-5-phenyl-2-(2′-pyridinyl)-1,2-oxazoline (PyOxA)

Acryloyl chloride (353 mg, 3.9 mmol), was added dropwise at 0 °C under a nitrogen atmosphere to a solution of **PyOxA alcohol** (660 mg, 2.6 mmol) and triethylamine (530 mg, 5.2 mmol) in dichloromethane (2 mL) (Scheme S1). After addition, the water/ice bath was removed and the reaction was stirred at room temperature for 12 h. The precipitate was removed by filtration and the filtrate washed with a saturated aqueous solution of NaHCO$_3$ (10 mL) and deionized water (4 × 10 mL).
The organic layer was dried over MgSO₄ and the solvent was removed in vacuo. The monomer PyOxA was recovered as an oil in quantitative yield and was used without further purification; \([\alpha]^{23}_{D} = +28.0\) (c 2 in CH₂Cl₂); \(\nu_{\text{max}}\) (ATR) 3100–2850, 1729, 1260, 1192, 698; \(\delta_{H}\) (300 MHz, CDCl₃) 4.45–4.49 (1H, m, C(1′′)H₈), 4.53–4.59 (2H, m, C(1′′)H₆, C(4)H), 5.53 (1H, d, J 7.1, C(5)H), 5.84 (1H, dd, J 10.4, 1.4, C(5′′)H₈), 6.14 (1H, dd, J 17.1, 10.4, C(4′′)H), 6.42 (1H, dd, J 17.1, 1.4, C(5′′)H₈), 7.34–7.43 (5H, m, Ph), 7.44–7.47 (1H, m, C(5′)H), 7.83 (1H, app td, J 7.8, 1.7, C(4′′)H), 8.10 (1H, d, J 7.8, C(3′′)H), 8.76–8.77 (1H, m, C(6′′)H); \(\delta_c\) (75 MHz, CDCl₃) 65.9 (C(1′′)), 74.1 (C(4)), 83.7 (C(5)), 124.2 (C(3′′)), 125.8, 125.8 (Ph), 126.0 (C(5′)), 127.9 (C(4′′)), 128.6 (Ph), 128.9, 128.9 (Ph), 131.5 (C(5′′)), 136.7 (C(4′′)), 139.8 (i-Ph), 146.2 (C(2′)), 150.1 (C(6′)), 163.8 (C(2)), 165.9 (C(3′′)); HRMS (ESI⁺) C₁₈H₁₆N₂NaO₃⁺ ([M+Na]⁺): 331.1059; found 331.1053.

PyOxA alcohol

Acetyl chloride
Cl₂CH₂, Et₃N
RT, 12 h

PyOxA acetate

Scheme S2 Synthesis of the model compound PyOxA acetate from chiral PyOxA alcohol.

(5,5′)-4-Methylacetate-5-phenyl-2-(2-pyridinyl)-1,2-oxazoline (PyOxA acetate)

Acetyl chloride (310 mg, 3.9 mmol), was added dropwise at 0 °C under a nitrogen atmosphere to a solution of PyOxA alcohol (660 mg, 2.6 mmol) and triethylamine (530 mg, 5.2 mmol) in dichloromethane (2 mL). After addition, the water/ice bath was removed and the reaction was stirred at room temperature for 12 h. The precipitate was removed by filtration and the filtrate washed with a saturated aqueous solution of NaHCO₃ (10 mL) and deionized water (4 x 10 mL). The organic layer was dried over MgSO₄ and the solvent was removed in vacuo. The model compound PyOxA acetate was recovered in quantitative yield and was used without further purification,

\[\frac{[\alpha]^{23}_{D}}{2} = +57.1\] (c 2.25 in CH₂Cl₂); \(\nu_{\text{max}}\) (ATR) 3100–2900, 1741, 1667, 1519, 1235, 1033, 705; \(\delta_{H}\) (300 MHz, CDCl₃) 2.00 (3H, s, C(4′′)H₃), 4.29–4.38 (1H, m, C(1′′)H₈), 4.44–4.46 (2H, m, C(1′′)H₆, C(4)H), 5.42 (1H, d, J 7.3, C(5)H), 7.26–7.35 (5H, m, Ph), 7.36–7.39 (1H, m, C(5′′)H), 7.74 (1H, app td, J 7.7, 1.5, C(4′′)H), 8.03 (1H, d, J 7.8, C(3′′)H), 8.68–8.69 (1H, m, C(6′′)H); \(\delta_c\) (75 MHz, CDCl₃) 20.8 (C(4′′)), 65.3 (C(1′′)), 74.1 (C(4)), 84.3 (C(5)), 124.2 (C(3′′)), 125.8, 125.8 (Ph), 125.9 (C(5′)), 128.6, 128.9, 128.9 (Ph), 136.8 (C(4′)), 139.7 (i-Ph), 146.2 (C(2′)), 150.0 (C(6′)), 164.1 (C(2)), 170.9 (C(3′′)); HRMS (ESI⁺) C₁₈H₁₆N₂NaO₃⁺ ([M+Na]⁺): 319.1059; found 319.1052.

Synthesis of poly(oligo(ethylene glycol) methacrylate) macroCTA

Poly(OEGMA) was synthesized according to a literature procedure.\(^6\) Methyl 4-cyano-4-(((ethylthio)carbonothioyl)thio) pentanoate (86 mg, 0.31 mmol), AIBN (5.1 mg, 0.031 mmol) and OEGMA (\(M_n = 300, 7\) g, 23 mmol) were dissolved in 1,4-dioxiane (14 mL) and added to an ampoule equipped with a magnetic stir bar. The resulting solution was degassed by sparging with argon for 15 min. The RAFT polymerization was carried out at 65 °C for 6 h and after this time the reaction mixture opened to air and cooled on ice to quench polymerization. The polymer was purified by exhaustive dialysis against deionized water (MWCO = 3.5 kDa) and isolated by lyophilization to yield a viscous yellow oil.

\(M_n(\text{NMR}) = 13.8 \text{ kg}\cdot\text{mol}^{-1}\), \(DP(\text{NMR}) = 45\), \(M_n(\text{SEC}) = 13.8 \text{ kg}\cdot\text{mol}^{-1}\), \(D_M = 1.21\).
Synthesis of polymer 1 (poly(OEGMA₄₅-b-(PyOxA₄-co-MA₃₅)))

Scheme S3 Synthesis of polymer 1, poly(OEGMA₄₅-b-(PyOxA₄-co-MA₃₅)), by RAFT polymerization using poly(OEGMA)₄₅ macroCTA and subsequent RAFT end-group removal.

**RAFT polymerization**
Poly(OEGMA)₄₅ (690 mg, 0.05 mmol), methyl acrylate (155 mg, 1.8 mmol), PyOxA (62 mg, 0.2 mmol) and AIBN (1.6 mg, 0.01 mmol) were added to DMF (6 mL) in a 50 mL ampoule equipped with a magnetic stir bar. The resulting solution was degassed by three freeze–pump–thaw cycles and the ampoule was refilled with nitrogen and sealed. The RAFT polymerization was carried out at 75 °C for 7 hours and after this time the reaction mixture was opened to air and cooled on ice to quench polymerization. The polymer was precipitated into cold petroleum ether (40-60 °C) to yield an orange oil. The degree of polymerization and ratio of PyOxA to MA units were determined by ¹H NMR spectroscopy.

Mₙ(NMR) = 18.0 kg·mol⁻¹, DP(NMR) for PyOxA = 4, DP(NMR) for MA = 35, Mₙ(SEC) = 18.6 kg·mol⁻¹, Đₘ = 1.29.

**End-group removal**
The end-group trithiocarbonate functionality of poly(OEGMA₄₅-b-(PyOxA₄-co-MA₃₅)) was removed using an excess of AIBN, according to a procedure reported in literature.⁹ Poly(OEGMA₄₅-b-(PyOxA₄-co-MA₃₅)) (200 mg, 0.01 mmol), AIBN (164 mg, 1 mmol) and LPO (18 mg, 0.05 mmol) were dissolved in dry toluene (50 mL) in an ampoule and the solution degassed by three freeze-pump-thaw cycles and then sealed under nitrogen. The mixture was heated to 80 °C overnight, then allowed to cool to room temperature and the solvent was removed in vacuo. The polymer was dissolved in a minimum volume of THF (2 mL) and precipitated into ice cold petroleum ether (40-60 °C, 15 mL). The product, an off-orange oil, was obtained after decanting the petroleum ether solution. Removal of the trithiocarbonate end-group was confirmed by ¹H NMR spectroscopy, by the disappearance of the proton resonance at ca. δ = 3.23 ppm attributed to the methylene protons adjacent to the trithiocarbonate moiety (Figure S2). Comparison of the SEC chromatograms with UV detection at λ = 309 nm (characteristic absorbance of the trithiocarbonate group) before and after the reaction also confirmed loss of the end-group (Figure S3). Furthermore, ¹H-NMR spectroscopic analysis in CDCl₃ confirmed that the oxazoline functionality remains intact during end-group removal (Figure S2).

Mₙ(SEC) = 18.3 kg·mol⁻¹, Đₘ = 1.29.
Figure S1 Size exclusion chromatograms of poly(OEGMA)$_{45}$ (solid line) and poly(OEGMA$_{45}$-b-(PyOxA$_{4}$-co-MA$_{35}$)) (dashed line) with RI detection using DMF with 5 mM NH$_4$BF$_4$ as the eluent and poly(methylmethacrylate) (PMMA) standards.

Figure S2 $^1$H NMR spectrum (300 MHz, CDCl$_3$) of poly(OEGMA$_{45}$-b-(PyOxA$_{4}$-co-MA$_{35}$)) after end-group removal.
**Synthesis of polymer 2 (poly(OEGMA_{45}-b-MA_{41}))**

**RAFT polymerization**

Poly(OEGMA)_{45} (344 mg, 0.025 mmol), methyl acrylate (86 mg, 1.0 mmol) and AIBN (0.82 mg, 0.005 mmol) were added to 1,4-dioxane (1 mL) in an ampoule equipped with a magnetic stir bar. The resulting solution was degassed by three freeze–pump–thaw cycles and the ampoule was refilled with nitrogen and sealed. The RAFT polymerization was carried out at 65 °C for 6 hours and after this time the reaction mixture was opened to air and cooled on ice to quench polymerization. The polymer was precipitated into ice cold hexane to yield an orange oil. The degree of polymerization of MA was determined by $^1$H NMR spectroscopy. $M_n$(NMR) = 17.3 kg·mol⁻¹, DP(NMR) for MA = 41, $M_n$(SEC) = 16.9 kg·mol⁻¹, $D_M$ = 1.27.

**End-group removal**

The end-group trithiocarbonate functionality of poly(OEGMA_{45}-b-MA_{41}) was removed using an excess of AIBN, according to a procedure reported in literature. Poly(OEGMA_{45}-b-MA_{41}) (200 mg, 0.012 mmol), AIBN (193 mg, 1.2 mmol) and LPO (23 mg, 0.059 mmol) were dissolved in dry toluene (60 mL) in an ampoule and the solution degassed by three freeze-pump-thaw cycles and then sealed.

**Figure S3** Size exclusion chromatogram of poly(OEGMA_{45}-b-(PyOxA_{4}-co-MA_{35})) before (black trace) and after (red dashed trace) end-group removal with AIBN and LPO, with DMF and 5 mM NH$_4$BF$_4$ as the eluent and with UV detection at $\lambda$ = 309 nm.

**Figure S4** Size exclusion chromatogram of poly(OEGMA_{45}-b-(PyOxA_{4}-co-MA_{35})) before (black trace) and after (red dashed trace) end-group removal with AIBN and LPO, with RI detection using DMF with 5 mM NH$_4$BF$_4$ as the eluent and poly(methylmethacrylate) (PMMA) standards.
under nitrogen. The mixture was heated to 80 °C overnight, then allowed to cool to room temperature and the solvent was removed in vacuo. The polymer was dissolved in a minimum volume of THF (2 mL) and precipitated into ice cold petroleum ether (40-60 °C, 15 mL). The product, an off-orange oil, was obtained after decanting the petroleum ether solution. Removal of the trithiocarbonate end-group was confirmed by 1H NMR spectroscopy and SEC analysis with detection at λ = 309 nm. $M_n$(SEC) = 16.4 kg·mol⁻¹, $D_M$ = 1.28.

**Palladium complexation of polymer 1**

Polymer 1 (165 mg, 0.01 mmol that contains 0.04 mmol PyOx), palladium(II) trifluoroacetate Pd(TFA)$_2$ (26.5 mg, 0.08 mmol) and acetone (20 mL) were added to an oven dried ampoule and the resulting solution was degassed via three freeze–pump–thaw cycles and then filled with nitrogen. The solution was stirred at room temperature for two days. After this time, activated charcoal was added to the solution in order to remove excess palladium. The suspension containing the product and charcoal was filtered to afford a light orange clear solution. The solution containing the Pd-polymer 1 complex was concentrated to 10 mg·mL⁻¹.

**Palladium complexation of PyOx acetate**

The model compound PyOx acetate (3 mg, 0.01 mmol), palladium(II) trifluoroacetate Pd(TFA)$_2$ (6.7 mg, 0.02 mmol) and acetone (30 mL) were added to an oven dried ampoule and the resulting solution was degassed via three freeze–pump–thaw cycles and then filled with nitrogen. The solution was stirred at room temperature for two days. After this time, activated charcoal was added to the solution in order to remove excess palladium. The suspension containing the product and charcoal was filtered to afford a light orange clear solution. The solution containing PyOx acetate was analyzed before and after complexation with Pd(TFA)$_2$ by UV-Vis spectroscopy (Figure S3).

![Figure S5](image-url) **Figure S5** Normalized absorption spectrum of PyOx acetate in acetone before (blue) and after complexation with Pd(TFA)$_2$ (red).

**Self-assembly of Pd-polymer 1 in water**

A solution of Pd-polymer 1 in acetone (2 mL, 10 mg·mL⁻¹) was placed in a 20 mL vial equipped with a magnetic stirrer. Using an ice bath, the solution was stirred at 0 °C and 10 mL of deionized water was added dropwise at a rate of 1.5 mL·h⁻¹. The acetone was removed under a gentle flow of nitrogen and the resulting aqueous solution had a concentration of ca. 2 mg·mL⁻¹. For catalysis, this solution of Pd-nanoreactors was concentrated to ca. 10 mg·mL⁻¹.
Self-assembly of polymer 1 in water
A solution of polymer 1 in acetone (1 mL, 10 mg·mL\(^{-1}\)) was placed in a 20 mL vial equipped with a magnetic stirrer. Using an ice bath, the solution was stirred at 0 °C and 10 mL of deionized water was added dropwise at a rate of 1.5 mL·h\(^{-1}\). The acetone was removed under a gentle flow of nitrogen and the resulting aqueous solution had a concentration of ca. 1 mg·mL\(^{-1}\).

Figure S6 TEM images of Pd-nanoreactors without staining.

Figure S7 Static light scattering (SLS) and multi-angle dynamic light scattering (DLS) analysis; and dynamic light scattering distribution (A) and autocorrelation function (B) of polymer 1 micelles in water at 1 mg·mL\(^{-1}\).

Example of catalysis with Pd-PyOx acetate
Pd(OCOCF\(_3\))\(_2\) (4 mg, 5 mol% w.r.t chromone) was mixed with PyOx acetate (5 mg, 6 mol% w.r.t chromone) in dichloroethane (1 mL) in air at room temperature. Afterwards, the aryl boronic acid
(61 mg, 0.5 mmol), NH₄PF₆ (12 mg, 30 mol% w.r.t chromone), chromone (36 mg, 0.25 mmol) and water (25 µL, 5 mol%) were added and the mixture was stirred for 24 h in air at room temperature. After this time, the reaction mixture was washed with deionized water (2 × 1 mL). The organic phase was collected and the solvent removed in vacuo. The product was purified by flash column chromatography (eluent dichloromethane, Rf = 0.4). The enantiomeric excess was determined by HPLC after purification, employing a chiral OD-H column at a flow rate of 1 mL/min and with hexane (0.04% formic acid)/IPA (0.04% formic acid) (90/10 v/v) as eluent.

**Example of catalysis with Pd-nanoreactors**

Chromone (36 mg, 0.25 mmol) and aryl boronic acid (61 mg, 0.5 mmol) were added to 1 mL of an aqueous solution of Pd-nanoreactors ([polymer] = 10 mg·mL⁻¹). The resulting mixture was stirred for 24 h in air at room temperature. After this time, the product was extracted with dichloromethane (2 mL), before the solvent was removed in vacuo. The product was purified by flash column chromatography (eluent dichloromethane, Rf = 0.4). The enantiomeric excess was determined by HPLC after purification, employing a chiral OD-H column at a flow rate of 1 mL/min and with hexane (0.04% formic acid)/IPA (0.04% formic acid) (90/10 v/v) as eluent.

**Characterization data for (R)-2-phenylchroman-4-one**

Following purification by flash column chromatography (R)-1-phenylchroman-3-one was fully characterized: \( [\alpha]_{D}^{25} = +52.5 \) (c 0.36 in CHCl₃); lit.¹¹ for (R)-2-phenylchroman-4-one \( [\alpha]_{D}^{25} = +67.2 \) (c 0.35 in CHCl₃); \( \nu \) max (ATR) 1687, 1604, 1457, 1300, 1066, 988, 763; \( \delta \) n (400 MHz, CDCl₃) 2.81 (1H, dd, \( J = 16.9 \)), 2.8 (C(3)\( n \)), 3.00 (1H, dd, J 16.9, 13.3 (C(3)\( n \))), 5.39 (1H, dd, J 13.3, 2.8, C(2)\( H \)), 6.95–6.98 (2H, m, C(6)\( H \), C(8)\( H \)), 7.28–7.44 (6H, m, C(2′)\( H \), C(3′)\( H \), C(4′)\( H \), C(5′)\( H \), (6′)\( H \), C(7)\( H \)), 7.84–7.86 (1H, m, C(5)\( H \)); \( \delta \) c (100 MHz, CDCl₃) 44.6 (C(3)), 79.5 (C(2)), 118.1 (C(8)), 120.9 (C(4a)), 121.6 (C(6)), 126.1 (C(4′)), 127.0 (C(5)), 128.7, 128.8, 128.8 (C(2′), C(3′), C(5′), C(6′)), 136.2 (C(7)), 138.7 (C(1′)), 161.5 (C(8a)), 191.9 (C(4)); m/z (ESI⁺) 247 ([M+Na⁺]); HRMS (ESI⁺) \( C_{15}H_{13}NaO_{2}^+ \) ([M+Na⁺]) requires 247.0730; found 247.0736.

**Characterization data for (R)-2-(4-chlorophenyl)chroman-4-one**

Following purification by flash column chromatography (R)-2-(4-chlorophenyl)chroman-4-one was fully characterized: \( [\alpha]_{D}^{25} = +54.0 \) (c 2.50 in CHCl₃); lit.¹³ for (S)-2-(4-chlorophenyl)chroman-4-one \( [\alpha]_{D}^{25} = -43.8 \) (c 2.51 in CHCl₃); \( \nu \) max (ATR) 1701, 1602, 1462, 1301, 1225, 907, 765; \( \delta \) n (500 MHz, CDCl₃) 2.81 (1H, dd, J 16.8, 2.9, C(3)\( H \)), 2.97 (1H, dd, J 16.8, 13.2, (C(3)\( H \)), 5.40 (1H, dd, J 13.2, 2.9, C(2)\( H \)), 6.97–7.01 (2H, m, C(6)\( H \), C(8)\( H \)), 7.33–7.37 (4H, m, C(2′)\( H \), C(3′)\( H \), C(5′)\( H \), C(6′)\( H \)), 7.43–7.46 (1H, m, C(7)\( H \)), 7.85–7.87 (1H, m, C(5)\( H \)); \( \delta \) c (125 MHz, CDCl₃) 44.6 (C(3)), 78.8 (C(2)), 118.1 (C(8)), 120.9 (C(4a)), 121.8 (C(6)), 127.1 (C(5)), 127.5, 129.0, 129.0 (C(2′), C(3′), C(5′), C(6′)), 134.6 (C(4′)), 136.3 (C(7)), 137.2 (C(1′)), 161.3 (C(8a)), 191.5 (C(4)); m/z (ESI⁺) 281 ([M+Na⁺]); HRMS (ESI⁺) \( C_{15}H_{13}ClNaO_{2}^+ \) ([M+Na⁺]) requires 281.0340; found 281.0333.
Characterization data for (R)-6-chloro-2-(4-chlorophenyl)chroman-4-one

Following purification by flash column chromatography (R)-1-phenylchroman-3-one was fully characterized\(^{14}\): \([\alpha]_D^{25} = +20.7\) (c 2.49 in CHCl\(_3\)); \(\nu_{\text{max}}\) (ATR) 1685, 1606, 1466, 1272, 1227, 912, 817; \(\delta_H\) (500 MHz, CDCl\(_3\)) 2.89 (1H, dd, J 16.9, 3.0, C(3)H\(_A\)), 3.05 (1H, dd, J 16.9, 13.1, C(3)H\(_B\)), 5.46 (1H, dd, J 13.1, 3.0, C(2)H), 7.02 (1H, d, J 8.9, C(8)H), 7.42 (4H, app s, C(2′)H, C(3′)H, C(5′)H, (6′)H), 7.46 (1H, dd, J 8.9, 2.6, C(7)H), 7.89 (1H, d, J 2.6, C(5)H); \(\delta_C\) (125 MHz, CDCl\(_3\)) 44.2 (C(3)), 79.0 (C(2)), 119.8 (C(8)), 121.6 (C(4a)), 126.4 (C(5)), 127.4 (C(6)), 127.5, 127.5, 129.1, 129.1 (C(2′), C(3′), C(5′), C(6′)), 134.8 (C(4′)), 136.1 (C(7)), 136.7 (C(1′)), 159.7 (C(8a)), 190.3 (C(4)); m/z (ESI\(^{+}\)) 315 ([M+Na]\(^+\); HRMS (ESI\(^{+}\)) \(C_{15}H_{10}Cl_2NaO_2\) ([M+Na]\(^+\)) requires 314.9950; found 314.9948.

Example of catalysis control experiment

Chromone (36 mg, 0.25 mmol) and aryl boronic acid (61 mg, 0.5 mmol) were added to 1 mL of an aqueous solution of polymer 1 ([polymer] = 10 mg·mL\(^{-1}\)). The resulting mixture was stirred for 24 h in air at room temperature. After this time, the product was extracted with dichloromethane (2 mL), before the solvent was removed in vacuo. The crude product was analyzed by \(^1\)H NMR spectroscopic and HPLC analysis in order to assess formation of the product.

Table S1 Control experiments for catalysis with uncomplexed polymer 1, non-PyOx containing polymer 2 and in the absence of PyOx and polymer.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Water (ml)</th>
<th>NH(_4)PF(_6) (mol %)</th>
<th>catalyst</th>
<th>Pd(TFA)(_2) (mol%)</th>
<th>yield (%)</th>
<th>ee(^b) (%)</th>
</tr>
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<tr>
<td>1</td>
<td>1</td>
<td>0.025</td>
<td>Polymer 1</td>
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<td>5</td>
</tr>
<tr>
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<td>30</td>
<td>Polymer 1</td>
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<td>5</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>0.025</td>
<td>Polymer 2</td>
<td>0.5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
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<td>1</td>
<td>30</td>
<td>Polymer 2</td>
<td>0.5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>-</td>
<td>Polymer 2</td>
<td>0.5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>30</td>
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<td>5</td>
<td>5</td>
</tr>
<tr>
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<td>0.025</td>
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<td>-</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>0.025</td>
<td>30</td>
<td>-</td>
<td>5</td>
<td>5</td>
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</tr>
</tbody>
</table>

\(^a\) Reactions of chromone (0.25 mmol) with phenyl boronic acid (0.5 mmol) in air at room temperature for 24 h; 
\(^b\) ee determined by HPLC.
**NMR Spectra**

*Figure S8* $^1$H NMR (400 MHz, top) and $^{13}$C NMR (100 MHz, bottom) spectra of PyOx alcohol in CDCl$_3$. 
Figure S9 $^1$H NMR (300 MHz, top) and $^{13}$C NMR (75 MHz, bottom) spectra of PyOxA in CDCl$_3$. 
Figure S10 $^1$H NMR (300 MHz, top) and $^{13}$C NMR (75 MHz, bottom) spectra of PyOx acetate in CDCl$_3$. 
Figure S11 $^1$H NMR (400 MHz, top) and $^{13}$C NMR (100 MHz, bottom) spectra of (R)-2-phenylchroman-4-one in CDCl$_3$. 
Figure S12 \(^1\)H NMR (400 MHz, top) and \(^{13}\)C NMR (100 MHz, bottom) spectra of \((R)-2-(4\text{-chlorophenyl})\text{chroman-4-one}\) in CDCl\(_3\).
Figure S13 $^1$H NMR (500 MHz, top) and $^{13}$C NMR (125 MHz, bottom) spectra of (R)-6-chloro-2-(4-chlorophenyl)chroman-4-one in CDCl$_3$. 
HPLC Chromatograms

The following conditions were used for the HPLC method: a Chiralcel OD-H column; mobile phase composition at 90:10 v/v hexane (0.04% v/v formic acid)/isopropanol (0.04% v/v formic acid); flow rate at 1.0 mL/min; column temperature held at 30 °C; length of method fixed at 30 min; detection wavelength at 230 nm.

Figure S14 HPLC chromatogram of (R)-2-phenylchroman-4-one obtained by asymmetric catalysis using (top) the Pd-PyOx acetate catalyst (bottom) the Pd-nanoreactor.10
Figure S15 HPLC chromatogram of (R)-2-(4-chlorophenyl)chroman-4-one obtained by asymmetric catalysis using (top) the Pd-PyOx acetate catalyst and (bottom) the Pd-nanoreactor.
Figure S16 HPLC chromatogram of \((R)-6\text{-chloro-2-\{4-chlorophenyl\}}\text{-chroman-4-one}\) obtained by asymmetric catalysis using (top) the \textbf{Pd-PyOx acetate} catalyst and (bottom) the \textbf{Pd-nanoreactor}.
Figure S17 HPLC chromatogram of (RS)-2-phenylchroman-4-one.

References