Electronic Supplementary Information

Chiral Metal-Macrocyle Frameworks:
Supramolecular Chirality Induction and Helicity Inversion
of the Helical Macrocyclic Structures

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1. Materials and methods

Solvents and reagents were purchased from TCI Co., Ltd., Sigma-Aldrich Co., Kanto chemical Co., Inc. and WAKO Pure Chemical Industries Ltd. All chemicals were used without further purification. All $^1$H NMR spectra were recorded on a Bruker AVANCEIII 500 and a Bruker DRX 500 (500 MHz) spectrometers. The residual solvents are used as the internal standard for $^1$H NMR (DMSO-$d_6$: 2.50 ppm for DMSO-$d_5$, 1:9 (v/v) DMSO-$d_6$/CD$_2$Cl$_2$: 5.31 ppm for CDHCl$_2$). Infrared (IR) spectra were obtained with a JASCO FT/IR 4200 spectrometer using a ZnSe ATR method. UV-vis absorption spectra were recorded on a HITACHI U-3500 spectrophotometer. Thermogravimetric (TG) analyses were conducted with a Rigaku Thermo plus TG8120. Elemental analyses were performed on a YANAKO MT-6. Solution-phase and diffuse reflectance CD measurements were carried out with a JASCO J-820 spectropolarimeter. Powder X-ray analyses were conducted using a Rigaku Miniflex diffractometer with CuK$\alpha$ radiation. Microwave irradiation experiments were performed using an Anton Paar GmbH Monowave 300 single-mode microwave reactor. Single-crystal X-ray crystallographic analyses were performed using a Rigaku RAXIS-RAPID imaging plate diffractometer with MoK$\alpha$ radiation, and obtained data were calculated using the CrystalStructure crystallographic software package except for refinement, which was performed using SHELXL-97. Some of solvent and guest molecules in all the crystal structures were
highly disordered. The volume of the solvent-accessible void was calculated with the program PLATON\textsuperscript{2} using crystal structures omitting all solvent molecules. Several restraints (bond distances, angles and thermal parameters) were applied to solvent and guest molecules in all the crystal structures. All of the non-hydrogen atoms of Pd\textsubscript{3}LCl\textsubscript{6} and one CHCl\textsubscript{3} molecule in MMF-3 were refined anisotropically, while those of other solvent and guest molecules were refined isotropically. Hydrogen atoms were placed at the calculated positions and refined using a riding model. In the crystallographic analyses of MMF-2, we took account of two types of twinning by merohedry, twinning by inversion and rotation with twin laws (010, 100, 00–1), (0–10, –100, 00–1) or (–100, 00–1, 0–10), simultaneously. The X-ray structures were displayed using Mercury and CrystalExplorer.\textsuperscript{3} The X-ray crystallographic coordinates for structures reported in this paper have been deposited at the Cambridge Crystallographic Data Centre under deposition numbers CCDC 989061 (\textit{rac}-MMF-2), 989062 ((\textit{P})-enriched MMF-2), 989063 ((\textit{M})-enriched MMF-2), 989064 ((\textit{P})-enriched MMF-2 formed in the presence of D-riboono-1,4-lactone), 989065 ((\textit{M})-enriched MMF-2 formed in the presence of L-gulonic acid \gamma-lactone), 989066 (MMF-3), 989067 ((\textit{M})-enriched MMF-2 as a seed crystal for a crystal growth experiment), 989068 ((\textit{M})-enriched MMF-2 after crystal growth), 989069 (\textit{rac}-MMF-2 as a seed crystal for a crystal growth experiment) and 989070 (\textit{rac}-MMF-2 after crystal growth). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre (\url{http://www.ccdc.cam.ac.uk/data_request/cif}).

\textbf{2. Structural analyses of Pd\textsubscript{3}LCl\textsubscript{6} in solution}

\textit{Preparation of Pd\textsubscript{3}LCl\textsubscript{6} in 1:9 (v/v) DMSO-d\textsubscript{6}/CD\textsubscript{2}Cl\textsubscript{2}}

To a CD\textsubscript{2}Cl\textsubscript{2} solution of ligand L (10.0 mM, 55 \textmu L, 0.55 \textmu mol) were added a DMSO-d\textsubscript{6} solution of PdCl\textsubscript{2}(CH\textsubscript{3}CN)\textsubscript{2} (50.0 mM, 31 \textmu L, 1.55 \textmu mol, 2.8 equiv.), DMSO-d\textsubscript{6} (22 \textmu L), and CD\textsubscript{2}Cl\textsubscript{2} (425 \textmu L), and the mixture was allowed to stand for 5 min at room temperature ([L] = 1.03 mM). Its \textsuperscript{1}H NMR spectrum showed a formation of Pd\textsubscript{3}LCl\textsubscript{6}.

\textsuperscript{1}H NMR (500 MHz, 1:9 (v/v) DMSO-d\textsubscript{6}/CD\textsubscript{2}Cl\textsubscript{2}, 293 K): \(\delta\) 8.13 (br, 3H), 7.45-7.44 (d, \(J = 7.0\) Hz 1H), 7.23-7.15 (m, 6H), 6.76-6.73 (dd, \(J = 7.0, 7.0\) Hz 3H), 5.56 (d, \(J = 7.4\) Hz, 3H), 4.59 (br, 3H), 4.01 (d, \(J = 12.5\) Hz, 3H), 3.70 (d, \(J = 12.5\) Hz, 3H), 1.48 (br, 3H).


$^1$H EXSY NMR measurements

$^1$H EXSY NMR measurements were conducted using a Bruker DRX500 (500 MHz) spectrometer at 292 K using the standard pulse sequence for phase-sensitive NOESY experiments programmed in XWinNMR Bruker software. A relaxation decay (D1) was set to 2 s, and various mixing times ($\tau_m$: 5~400 ms) were chosen.

From EXSY measurements, if populations of both exchangeable species are equal, rate constants of exchange processes between two spectroscopically-distinct states ($k$) are derived according to the equation:

$$
k = \frac{1}{\tau_m} \ln \frac{r + 1}{r - 1}
$$

$$
r = \frac{I_{AA} + I_{BB}}{I_{AB} + I_{BA}}
$$

where $\tau_m$ is mixing time of measurement, and $I_{AA}$ and $I_{BB}$ are the intensities of diagonal peaks, and $I_{AB}$ and $I_{BA}$ are those of cross peaks. The intensities of diagonal and cross peaks were calculated by using Topspin 3.0 after phase and baseline corrections in both dimensions. Using the calculated intensities, the rate constant ($k$) was estimated from the slope of the plots of $\ln[r + 1]/[r - 1]$ versus mixing time at short mixing time values.

Titration experiments of D-glucurono-6,3-lactone or D-glucono-1,5-lactone into Pd$_3$LCl$_6$

in a 1:9 (v/v) mixture of DMSO-$d_6$/CD$_2$Cl$_2$

To a CD$_2$Cl$_2$ solution of ligand L (10 mM, 60 µL, 0.60 µmol) were added a DMSO-$d_6$ solution of PdCl$_2$(CH$_3$CN)$_2$ (50.7 mM, 38 µL, 1.93 µmol, 3.2 equiv.), DMSO-$d_6$ (20 µL), and CD$_2$Cl$_2$ (462 µL). To the resulting solution was added an appropriate amount of a DMSO-$d_6$ solution of D-glucurono-6,3-lactone (1.81 M) and CD$_2$Cl$_2$ to keep the solvent ratio (DMSO-$d_6$/CD$_2$Cl$_2$ = 1:9) constant.
Figure S1. $^1$H NMR spectra of ligand \( L \) with different amounts of \( \text{PdCl}_2(\text{CH}_3\text{CN})_2 \) (500 MHz, 1:9 (v/v) DMSO-$d_6$/CD$_2$Cl$_2$, 293 K). (a) \([L] = 1.21 \text{ mM}\); (b) \([L] = 0.97 \text{ mM}, \text{PdCl}_2(\text{CH}_3\text{CN})_2 = 1.0 \text{ equiv.}\); (c) \([L] = 0.81 \text{ mM}, \text{PdCl}_2(\text{CH}_3\text{CN})_2 = 2.0 \text{ equiv.}\); (d) \([L] = 0.70 \text{ mM}, \text{PdCl}_2(\text{CH}_3\text{CN})_2 = 3.0 \text{ equiv.}\). The intensity of spectrum (a) is decreased to one-tenth.

Figure S2. Variable temperature $^1$H NMR spectra of a mixture of ligand \( L \) and 3 equiv. of \( \text{PdCl}_2(\text{CH}_3\text{CN})_2 \) (500 MHz, 1:9 (v/v) DMSO-$d_6$/CD$_2$Cl$_2$, \([L] = 0.70 \text{ mM}\)). (a) 293; (b) 273; (c) 253; (d) 243 K. The signals derived from \( p \)-phenylene moieties were highly...
broadened at 293 K due to the rotational motion, whereas the four $ph$ signals newly observed at lower temperature can be assigned to signals of the phenylene moiety, $k-n$. 
Figure S3. $^1$H-$^1$H COSY spectrum of a mixture of ligand L and 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$ (500 MHz, 1:9 (v/v) DMSO-$d_6$/CD$_2$Cl$_2$, 292 K, [L] = 1.1 mM).
Figure S4. $^1$H-$^1$H ROESY spectrum of a mixture of ligand L and 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$ (500 MHz, 1:9 (v/v) DMSO-$d_6$/CD$_2$Cl$_2$, 292 K, [L] = 1.1 mM). ex: chemical exchange peaks.
Figure S5. $^1$H-$^1$H EXSY spectra of a mixture of ligand L and 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$ (500 MHz, 1:9 (v/v) DMSO-$d_6$/CD$_2$Cl$_2$, 292 K, [L] = 1.1 mM, mixing time $\tau_m = 10$ ms). (a) An enlarged spectrum around methylene signals, (b) the overall spectrum. Red circles represent peaks used for the calculation of an exchange rate constant.

Figure S6. Plot of $\ln\left[(r + 1)/(r - 1)\right]$ vs mixing time $\tau_m$ for a mixture of ligand L and 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$ from $^1$H-$^1$H EXSY spectra (500 MHz, 1:9 (v/v) DMSO-$d_6$/CD$_2$Cl$_2$, 292 K) recorded with different mixing times.
Figure S7. $^1$H NMR spectra of a mixture of ligand L and 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$ in the (a,c) absence or presence of (b) D-glucurono-6,3-lactone (70 equiv.) or (d) D-glucono-1,5-lactone (30 equiv.) (500 MHz, 1:9 (v/v) DMSO-$d_6$/CD$_2$Cl$_2$, 292 K, [L] = 1.1 mM). No signal shifts due to diastereomeric aggregation were observed in the $^1$H NMR spectra except a slight upfield shift of the amine proton signals. This result indicates that the interactions between the chirality induction reagents and the $syn$-Pd$_3$LCl$_6$ are too weak to change the balance of the equilibrium.

**Solution-phase CD measurements of a mixture of Pd$_3$LCl$_6$ and D-glucurono-6,3-lactone or D-glucono-1,5-lactone in 1:9 (v/v) DMSO/CH$_2$Cl$_2$**

A DMSO solution of Pd$_3$LCl$_6$ was prepared by dissolving ligand L (1.15 mg, 1.82 µmol) into a DMSO solution of PdCl$_2$(CH$_3$CN)$_2$ (49.8 mM, 110 µL, 5.48 µmol, 3.01 equiv.). To this DMSO solution of Pd$_3$LCl$_6$ (16.6 mM, 48 µL, 0.79 µmol) was added a DMSO solution of D-glucurono-6,3-lactone (1.81 M, 30.5 µL, 55.2 µmol, 70 equiv.), DMSO (20.5 µL) and CH$_2$Cl$_2$ (895 µL). The resulting solution was analyzed by solution-phase CD spectroscopy.
Figure S8. Solution-phase CD and UV-vis absorption spectra of a solution containing ligand L, 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$ and 70 equiv. of D-glucurono-6,3-lactone ([L] = 0.8 mM, 25 ºC, 1:9 (v/v) DMSO/CH$_2$Cl$_2$, l = 0.1 cm). (a) Time course measurements, (b) comparison between a solution of ligand L, 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$ and 70 equiv. of D-glucurono-6,3-lactone and that of D-glucurono-6,3-lactone only ([D-glucurono-6,3-lactone] = 56 mM, 25 ºC, 1:9 (v/v) DMSO/CH$_2$Cl$_2$, l = 0.1 cm). No chirality induction effects were confirmed by solution-phase CD spectroscopy. No Cotton effects were observed in the region from 270 nm to 450 nm due to the absorption of Pd$_3$LCl$_6$ in the presence of D-glucurono-6,3-lactone or D-glucono-1,5-lactone.
**Figure S9.** Solution-phase CD and UV-vis absorption spectra of a solution containing ligand L, 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$, and 30 equiv. of D-glucono-1,5-lactone ([L] = 0.8 mM, 25 °C, 1:9 (v/v) DMSO/CH$_2$Cl$_2$, l = 0.1 cm). (a) Time course measurements, (b) comparison between the solution of ligand L, 3 equiv. of PdCl$_2$(CH$_3$CN)$_2$ and 30 equiv. of D-glucono-1,5-lactone and that of D-glucono-1,5-lactone only ([D-glucono-1,5-lactone] = 24 mM, 25 °C, 1:9 (v/v) DMSO/CH$_2$Cl$_2$, l = 0.1 cm).

Digestion experiments of as-synthesized (P)- or (M)-enriched MMF-2 into DMSO-$d_6$

Single-crystals of as-synthesized (P)- or (M)-enriched MMF-2 were collected and air-dried for 30 sec. The resulting crystals were dissolved in DMSO-$d_6$ (500 µL), followed by $^1$H NMR measurement.
Figure S10. $^1$H NMR spectra (500 MHz, DMSO-$d_6$, 300 K) of (a) D-glucurono-6,3-lactone and (b) a digested sample of as-synthesized ($M$)-enriched MMF-2.

Figure S11. $^1$H NMR spectra (500 MHz, DMSO-$d_6$, 300 K) of (a) D-glucono-1,5-lactone and (b) a digested sample of as-synthesized ($P$)-enriched MMF-2.


Synthesis of rac-MMF-2

Ligand L (3.18 mg, 5.04 µmol) was dissolved in a mixed solvent of CH$_2$Cl$_2$ (400 µL) and DMSO (203 µL). To this solution was added a DMSO solution of PdCl$_2$(CH$_3$CN)$_2$ (50.0 mM, 301 µL, 15.1 µmol, 3.00 equiv.) and H$_2$O (5.0 µL). The solution was divided into six equal parts (150 µL each), to which was added CH$_2$Cl$_2$ (680 µL). The resulting mixture was then kept standing at 25 °C for a week to obtain yellow block single-crystals (as-synthesized crystals). The yellow crystals were washed with a 1:1 (v/v) mixed solvent of CH$_2$Cl$_2$/CH$_3$CN and soaked in a 1:1 (v/v) mixed solvent of CH$_2$Cl$_2$/CH$_3$CN. After 1 day, the crystals were washed with CH$_2$Cl$_2$ and soaked in CH$_2$Cl$_2$ for 1 day. The resulting crystals were collected and air-dried quickly on a filter paper to obtain rac-MMF-2 single-crystals, Pd$_3$LCl$_6$·(CH$_2$Cl)$_2$·7·(H$_2$O)$_{1.5}$, (3.96 mg, 2.37 µmol, 47%). The washed rac-MMF-2 crystals were characterized by elemental analysis, IR spectroscopy, thermogravimetric analysis, powder and single-crystal X-ray diffraction (XRD).
amount of CH₂Cl₂ contained in the single-crystals was determined by ¹H NMR spectrum of a digested sample, and the amount of H₂O was calculated by the least square refinement using elemental analysis data shown below.

**Elemental analysis**: calcd for C₄₂H₄₂Cl₆N₆Pd₃(CH₂Cl₂)₅.7(H₂O)₁.5: C 34.23, H 3.40, N 5.02; found: C 34.40, H 3.78, N 4.83.

IR (ATR): ν 3503, 3092, 2845, 1732, 1716, 1698, 1610, 1558, 1541, 1497, 1456, 1422, 1340, 1267, 1219, 1162, 1113, 1038, 1023, 988, 950, 854 cm⁻¹.

Crystal data for (Pd₃LCl₆)₂(CH₂Cl₂)₆.9(H₂O)₁.5: C₹₀.₀₉H₁₀₈.₅₅Cl₂₄.₁₉N₁₂O₁₆.₁₈Pd₆, F_w = 2954.44, crystal dimensions 0.33 × 0.30 × 0.30 mm³, cubic, space group I2₁3, a = 31.4049(6) Å, V = 30973.7(10) Å³, Z = 8, ρ_calcd = 1.257 g cm⁻³, µ = 1.1495 cm⁻¹, T = 93 K, λ (MoKα) = 0.71075 Å, 2θ_max = 55.0°, 149996/11849 reflections collected/unique, R₁ = 0.0595 (I > 2σ(I)), wR₂ = 0.1548 (for all data), GOF = 1.089, Flack parameter = 0.50(5) (Friedel Pairs = 5604), largest diff. peak and hole 1.11/−0.64 eÅ⁻³. CCDC deposit number 989061. See below for the details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

**Restraints for dichloromethane molecules**
Geometrical restraints; DFIX (d = 1.7800, s = 0.0200): Cl₁S–Cl₁S, C₁S–Cl₂S, C₁₁T–C₁₁T, C₁T–C₁₂T, C₁₃S–C₂S, C₁₄S–C₂S, C₃S–C₁₅S, C₃S–Cl₆S, C₄S–Cl₇S. DANG (d = 2.8519 s = 0.0400): Cl₁₁S–Cl₁₂S. DANG (d = 2.7850, s = 0.0400): C₁₁T–Cl₁₂T. DANG (d = 2.8756 s = 0.0400): Cl₁₃S–Cl₁₄S. DANG (d = 2.8837, s = 0.0400): Cl₁₆S–Cl₁₅S.

**PLAT602.ALERT_2_A** Structure contains solvent accessible VOIDS
Response: Several solvents were severely disordered.

**Composition analyses of rac-MMF-2 by digestion experiments**

The washed rac-MMF-2 crystals were collected and air-dried quickly on a filter paper. The crystals were dissolved in DMSO-d₆ (ca. 500 µL). The resulting DMSO-d₆ solution
was analyzed by $^1$H NMR spectroscopy in the presence of DCl/D$_2$O ([DCl] = ca. 140 mM).

**Figure S12.** Partial $^1$H NMR spectra (500 MHz, DMSO-$d_6$, 293 K) after dissolving crystals in DMSO-$d_6$ in the presence of excess DCl/D$_2$O. (a) 1st, (b) 2nd and (c) 3rd trials.

**Table S1.** Molar ratios of ligand L to CH$_2$Cl$_2$ determined by $^1$H NMR spectroscopy

<table>
<thead>
<tr>
<th>Molar ratio of ligand to CH$_2$Cl$_2^a$</th>
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<tbody>
<tr>
<td>1st trial</td>
</tr>
<tr>
<td>1 : 5.86</td>
</tr>
<tr>
<td>2nd trial</td>
</tr>
<tr>
<td>1 : 6.03</td>
</tr>
<tr>
<td>3rd trial</td>
</tr>
<tr>
<td>1 : 5.42</td>
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<tr>
<td>Average</td>
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<td>1 : 5.7(3)</td>
</tr>
</tbody>
</table>

$a$: The molar ratio was calculated by the integral ratio of signal $d$ to CH$_2$Cl$_2$.

**Table S2.** The number of CH$_2$Cl$_2$ molecules encapsulated in a unit cell determined by $^1$H NMR spectroscopy

<table>
<thead>
<tr>
<th>CH$_2$Cl$_2$ in the unit cell</th>
<th>CH$_2$Cl$_2$-occupied void space (Å$^3$, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>91.2</td>
<td>5563, 34</td>
</tr>
</tbody>
</table>

The unit cell is composed of 16 Pd$_3$-complexes. The volume of CH$_2$Cl$_2$ was calculated on Spartan 06 (61 Å$^3$) and the equilibrium geometry was determined by DFT calculation.
(B3LYP 6-31G*). The total volume of the void space of a unit cell is 16173 Å³ calculated by PLATON.

**Thermogravimetric analysis of rac-MMF-2**

The washed rac-MMF-2 crystals preserved in CH₂Cl₂ were collected on a filter paper and air-dried quickly. The resulting crystals were analyzed by thermogravimetric analysis.

![Thermogravimetric analysis of rac-MMF-2](image)

**Figure S13.** Thermogravimetric analysis of rac-MMF-2. Measurement condition: 22 ~ 300 °C, 5 K/min, N₂ flow 150 mL/min. The 25% weight loss was approximately equal to the amount of solvents included in the crystals (31%).

**4. Synthesis and characterization of (M)-enriched MMF-2**

**Synthesis of (M)-enriched MMF-2**

Ligand L (2.87 mg, 4.55 µmol) was dissolved in a mixed solvent of CH₂Cl₂ (360 µL) and DMSO (8 µL). To this solution was added a DMSO solution of D-glucurono-6,3-lactone (1.82 M, 175 µL, 319 µmol, 70 equiv.), a DMSO solution of PdCl₂(CH₃CN)₂ (50.1 mM, 272 µL, 13.6 µmol, 3.0 equiv.) and H₂O (4.5 µL). The resulting solution was divided into six equally parts (130 µL each), to which was added CH₂Cl₂ (590 µL). The resulting mixture was then kept standing at 25 °C for a week to obtain yellow block single-crystals (as-synthesized crystals). The yellow crystals were washed with a 1:1 (v/v) mixed solvent of CH₂Cl₂ and CH₃CN and soaked in a 1:1 (v/v)
mixed solvent of CH₂Cl₂ and CH₃CN. After 1 day, the crystals were washed with CH₂Cl₂ and soaked in CH₂Cl₂ for 1 day. The resulting crystals were collected and air-dried quickly on a filter paper to obtain (M)-enriched MMF-2 single-crystals, Pd₃LCl₆·(CH₂Cl₂)₆.9, (4.70 mg, 2.69 µmol, 59%). The washed (M)-enriched MMF-2 crystals were characterized by elemental analysis and multiple single-crystal XRD. The amount of CH₂Cl₂ contained in a single-crystal was determined by ¹H NMR spectroscopy using a digested sample, and the amount of H₂O was calculated by the least square refinement using elemental analysis data shown below.

**Elemental analysis:** calcd for C₄₂H₄₂Cl₆N₆Pd₃·(CH₂Cl₂)₆.9: C 33.58, H 3.22, N 4.81; found: C 33.97, H 3.57, N 4.90.

**Crystal data for (Pd₃LCl₆)₂·(CH₂Cl₂)₄.₈¹·(H₂O)₅.₅₄:** C₈₈₈₁H₁₀₄.₇₀Cl₁₂.₆₁N₁₂O₅.₅₄Pd₆, F w = 2833.48, crystal dimensions 0.32 × 0.26 × 0.25 mm³, cubic, space group I₄₁3, a = 31.3834(10) Å, V = 30909.9(17) Å³, Z = 8, ρ calc = 1.218 g cm⁻³, µ = 10.951 cm⁻¹, T = 95 K, λ (MoKα) = 0.71075 Å, 2θ max = 55.0°, 142621/11829 reflections collected/unique, R₁ = 0.0840 (I > 2σ(I)), wR₂ = 0.2381 (for all data), GOF = 1.037, Flack parameter = 0.06(7) (Friedel Pairs = 5594), largest diff. peak and hole 2.02/–0.88 eÅ⁻³. CCDC deposit number 989063. See below for details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

**Restraints for dichloromethane molecules**

Geometrical restraints; DFIX (d = 1.7800, s = 0.0200): Cl1S–Cl1S, Cl1T–Cl1S, Cl2S–C2S, C2S–Cl2T, Cl3S–C3S, C3S–Cl3T. DANG (d = 2.8900, s = 0.0400): Cl1S–C11T. DANG (d = 2.9173, s = 0.0400): Cl2S–Cl2T. DANG (d = 2.9100 s = 0.0400): Cl3S–Cl3T.

**PLAT602_ALERT_2_A Structure contains solvent accessible VOIDS**

Response: Several solvents were severely disordered.

**Composition analyses of (M)-enriched MMF-2 by digestion experiments**
The washed (M)-enriched MMF-2 crystals were collected and air-dried quickly on a filter paper. The crystals were dissolved in DMSO-d₆ (ca. 500 µL). The resulting DMSO-d₆ solution was analyzed by ¹H NMR spectroscopy in the presence of DCl/D₂O ([DCl] = ca. 140 mM).

**Figure S14.** Partial ¹H NMR spectra (500 MHz, DMSO-d₆, 293 K) after dissolving crystals in DMSO-d₆ in the presence of excess DCl/D₂O. (a) 1st, (b) 2nd and (c) 3rd trials.

**Table S3.** Molar ratio of ligand L to CH₂Cl₂ determined by ¹H NMR spectroscopy

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<th>Molar ratio of ligand to CH₂Cl₂&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
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<tbody>
<tr>
<td>1st trial</td>
<td>1 : 6.97</td>
</tr>
<tr>
<td>2nd trial</td>
<td>1 : 6.97</td>
</tr>
<tr>
<td>3rd trial</td>
<td>1 : 6.90</td>
</tr>
<tr>
<td>Average</td>
<td>1 : 6.95(4)</td>
</tr>
</tbody>
</table>

<sup>a</sup>: The molar ratio was calculated by the integral ratio of signal d to CH₂Cl₂.
Table S4. The number of CH$_2$Cl$_2$ molecules encapsulated in a unit cell determined by $^1$H NMR spectroscopy

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<th>CH$_2$Cl$_2$-occupied void space (Å$^3$, %)</th>
</tr>
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<tbody>
<tr>
<td>111</td>
<td>6783, 42</td>
</tr>
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A unit cell is composed of 16 Pd$_3$-complexes. The volume of CH$_2$Cl$_2$ was calculated on Spartan 06 (61 Å$^3$) and the equilibrium geometry was determined by DFT calculation (B3LYP 6-31G*). The total volume of the void space of a unit cell is 16173 Å$^3$ calculated by PLATON.

Table S5. Summary of crystal data of seven randomly selected and washed MMF-2 crystals synthesized under an optimized condition

![Diagram](image)

Optimization of asymmetric crystallization conditions for (M)-enriched MMF-2

Optimization of the amount of water

Ligand L (1.63 mg, 2.58 µmol) was dissolved in a mixed solvent of CH$_2$Cl$_2$ (200 µL) and DMSO (56 µL). To this solution were added a DMSO solution of D-glucurono-6,3-lactone (1.34 M, 48 µL, 64.3 µmol, 25 equiv.) and PdCl$_2$(CH$_3$CN)$_2$ (50.3 mM, 154 µL, 7.75 µmol, 3.0 equiv.). The resulting solution was divided into 6
portions (70 µL). The appropriate amount of water (0.4 ~ 4 µL) and CH₂Cl₂ (32 µL) were added to each sample, and the resulting solutions were kept standing for a week to afford single-crystals of MMF-2. The single-crystals were washed with and soaked in a 1:1 (v/v) mixed solvent of CH₂Cl₂ and CH₃CN for 1 day, and then washed with and soaked in pure CH₂Cl₂ for 1 day. The resulting washed crystals were analyzed by single-crystal X-ray diffraction.

Optimization of the amount of D-glucurono-6,3-lactone

Ligand L (1.26 mg, 2.00 µmol) was dissolved in CH₂Cl₂ (160 µL). To a CH₂Cl₂ solution of ligand L were added a DMSO solution of D-glucurono-6,3-lactone (1.80 M, 79 µL, 142 µmol, 71 equiv.), PdCl₂(CH₃CN)₂ (49.9 mM, 120 µL, 5.99 µmol, 3.0 equiv.) and water (2.0 µL). This solution was divided into 3 portions (110 µL). CH₂Cl₂ (500 µL) were added to each sample, and the resulting solutions were kept standing for a week to afford single-crystals of MMF-2. The single-crystals were washed with and soaked in a 1:1 (v/v) mixed solvent of CH₂Cl₂ and CH₃CN for 1 day, and then washed with and soaked in pure CH₂Cl₂ for 1 day. The resulting washed crystals were analyzed by single-crystal X-ray diffraction.

Table S6. Optimization of the amount of water for asymmetric crystallization of MMF-2

<table>
<thead>
<tr>
<th>Entry</th>
<th>Equiv. of water</th>
<th>Crystal size (mm)</th>
<th>a (Å)</th>
<th>R₁</th>
<th>wR₂</th>
<th>Flack parameter</th>
<th>P : M</th>
<th>BASF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0.23 x 0.20 x 0.17</td>
<td>31.3518(8)</td>
<td>0.0823</td>
<td>0.2181</td>
<td>0.10(7)</td>
<td>10.90</td>
<td>19.53</td>
</tr>
<tr>
<td>2</td>
<td>0.1</td>
<td>0.32 x 0.29 x 0.19</td>
<td>31.488(2)</td>
<td>0.0794</td>
<td>0.2065</td>
<td>0.27(8)</td>
<td>27.73</td>
<td>30.92</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>0.47 x 0.37 x 0.32</td>
<td>31.343(2)</td>
<td>0.0812</td>
<td>0.2171</td>
<td>0.37(8)</td>
<td>37.63</td>
<td>40.47</td>
</tr>
<tr>
<td>4</td>
<td>1.0</td>
<td>0.47 x 0.40 x 0.32</td>
<td>31.397(1)</td>
<td>0.0728</td>
<td>0.1892</td>
<td>0.28(7)</td>
<td>28.72</td>
<td>35.81</td>
</tr>
</tbody>
</table>

BASF (batch scale factor): ratio (%) of the minor component generated by the rotational twin
Table S7. Optimization of the amount of D-glucurono-6,3-lactone for asymmetric crystallization of MMF-2

<table>
<thead>
<tr>
<th>Entry</th>
<th>Equiv. of lactone</th>
<th>Crystal size (mm)</th>
<th>a</th>
<th>R₁</th>
<th>wR₂</th>
<th>Flack parameter</th>
<th>P : M</th>
<th>BASF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>0.32 x 0.29 x 0.19</td>
<td>31.488(2)</td>
<td>0.0794</td>
<td>0.2065</td>
<td>0.27(8)</td>
<td>27.73</td>
<td>30.92</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>0.22 x 0.21 x 0.20</td>
<td>31.389(2)</td>
<td>0.0877</td>
<td>0.2267</td>
<td>0.22(9)</td>
<td>22.78</td>
<td>28.92</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>0.31 x 0.29 x 0.27</td>
<td>31.4133(8)</td>
<td>0.0672</td>
<td>0.1852</td>
<td>0.09(6)</td>
<td>9.91</td>
<td>15.35</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>0.30 x 0.28 x 0.26</td>
<td>31.3995(8)</td>
<td>0.0862</td>
<td>0.2414</td>
<td>0.09(7)</td>
<td>9.91</td>
<td>10.10</td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>0.32 x 0.26 x 0.25</td>
<td>31.383(1)</td>
<td>0.0840</td>
<td>0.2381</td>
<td>0.06(7)</td>
<td>6.94</td>
<td>6.40</td>
</tr>
</tbody>
</table>

BASF (batch scale factor): ratio (%) of the minor component generated by the rotational twin

5. Synthesis and characterization of (P)-enriched MMF-2

Synthesis of (P)-enriched MMF-2

Ligand L (3.26 mg, 5.17 µmol) was dissolved in a mixed solvent of CH₂Cl₂ (410 µL) and DMSO (122 µL). To this solution were added a DMSO solution of D-glucurono-1,5-lactone (1.80 M, 86 µL, 155 µmol, 30.0 equiv.), a DMSO solution of PdCl₂(CH₃CN)₂ (50.2 mM, 309 µL, 15.5 µmol, 3.0 equiv.) and H₂O (5.2 µL). The resulting solution was divided into six equal parts (155 µL each), to which was added CH₂Cl₂ (860 µL). The resulting mixture was then kept standing at 25 °C for a week to obtain yellow block single-crystals (as-synthesized crystals). The yellow crystals were washed with a 1:1 (v/v) mixed solvent of CH₂Cl₂ and CH₃CN and soaked in a 1:1 (v/v) mixed solvent of CH₂Cl₂ and CH₃CN. After 1 day, the crystals were washed with CH₂Cl₂ and soaked in CH₂Cl₂ for 1 day. The resulting crystals were collected and air-dried quickly on a filter paper to obtain single-crystals of (P)-enriched MMF-2, Pd₃LCl₆·(CH₂Cl₂)₆·(H₂O), (3.12 mg, 1.85 µmol, 36%). The washed (P)-enriched MMF-2 crystals were characterized by elemental analysis and multiple single-crystal XRD. The amount of CH₂Cl₂ contained in a single-crystal was determined by ¹H NMR spectroscopy.
using a digested sample, and the amount of H₂O was calculated by the least square refinement using elemental analysis data shown below.

**Elemental analysis:** calcd for C₄₂H₄₂Cl₆N₆Pd₃·(CH₂Cl₂)₆·0·(H₂O): C 34.11, H 3.34, N 4.97; found: C 34.54, H 3.57, N 4.41.

**Crystal data for (Pd₃L₃Cl₆)₂·(CH₂Cl₂)₄.77·(H₂O)₄.92:** C₈₈.₇₇H₁₀₃.₃₈Cl₂₁.₅₄N₁₂O₄.₉₂Pd₆, F_w = 2819.27, crystal dimensions 0.25 × 0.23 × 0.21 mm³, cubic, space group I2₁3, a = 31.4950(7) Å, V = 31240.9(12) Å³, Z = 8, ρ_calcd = 1.199 g cm⁻³, μ = 10.817 cm⁻¹, T = 97 K, λ (MoKα) = 0.71075 Å, 2θ_max = 55.0°, 136000/11931 reflections collected/unique, R₁ = 0.0917 (I > 2σ(I)), wR₂ = 0.2429 (for all data), GOF = 1.045, Flack parameter = 0.07(8) (Friedel Pairs = 5643), largest diff. peak and hole 1.66 /−0.64 eÅ⁻³. CCDC deposit number 989062. See below for the details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

**Restraints for dichloromethane molecules**

Geometrical restraints; DFIX (d = 1.7800, s = 0.0100): Cl1S–C1S, C1S–Cl1T, Cl2S–C2S, C2S–Cl2T, Cl3S–C3S, C3S–Cl3T. DANG (d = 2.9028, s = 0.0200): Cl1S–Cl1T, DANG (d = 2.8996, s = 0.0200): Cl2S–Cl2T, DANG (d = 2.9025, s = 0.0400): Cl3S–Cl3T.

**PLAT602_ALERT_2_A Structure contains solvent accessible VOIDS**

Response: Several solvents were severely disordered.
Table S8. Summary of crystal data of six randomly selected MMF-2 crystals synthesized under an optimized condition

<table>
<thead>
<tr>
<th>Entry</th>
<th>Crystal size (mm)</th>
<th>a (Å)</th>
<th>R₁</th>
<th>wR₂</th>
<th>Flack parameter</th>
<th>P : M</th>
<th>BASF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.41 × 0.37 × 0.26</td>
<td>31.3632(7)</td>
<td>0.0984</td>
<td>0.2726</td>
<td>0.07(9)</td>
<td>93.7</td>
<td>19.13</td>
</tr>
<tr>
<td>2</td>
<td>0.35 × 0.31 × 0.29</td>
<td>31.3420(6)</td>
<td>0.1528</td>
<td>0.3705</td>
<td>0.09(13)</td>
<td>91.9</td>
<td>23.03</td>
</tr>
<tr>
<td>3</td>
<td>0.25 × 0.23 × 0.21</td>
<td>31.4950(7)</td>
<td>0.0917</td>
<td>0.2429</td>
<td>0.07(8)</td>
<td>93.7</td>
<td>17.50</td>
</tr>
<tr>
<td>4</td>
<td>0.21 × 0.19 × 0.18</td>
<td>31.4509(6)</td>
<td>0.0850</td>
<td>0.2273</td>
<td>0.16(8)</td>
<td>84.16</td>
<td>21.88</td>
</tr>
<tr>
<td>5</td>
<td>0.23 × 0.21 × 0.20</td>
<td>31.5257(9)</td>
<td>0.0999</td>
<td>0.2627</td>
<td>0.04(9)</td>
<td>96.4</td>
<td>18.19</td>
</tr>
<tr>
<td>6</td>
<td>0.21 × 0.18 × 0.16</td>
<td>31.5590(6)</td>
<td>0.0895</td>
<td>0.2339</td>
<td>0.15(8)</td>
<td>85.15</td>
<td>23.12</td>
</tr>
</tbody>
</table>

BASF (batch scale factor): ratio (%) of the minor component generated by the rotational twin

Optimization of asymmetric crystallization condition for (P)-enriched MMF-2

Optimization of the amount of d-glucono-1,5-lactone

Ligand L (1.10 mg, 1.74 µmol) was dissolved in a mixed solvent of CH₂Cl₂ (140 µL) and DMSO (42 µL). To a DMSO-CH₂Cl₂ solution of ligand L were added a DMSO solution of d-glucono-1,5-lactone (1.83 M, 28.6 µL, 52.3 µmol, 30 equiv.), PdCl₂(CH₃CN)₂ (50.2 mM, 104 µL, 5.22 µmol, 3.0 equiv.) and H₂O (1.7 µL). This solution was divided into 3 portions (90 µL). CH₂Cl₂ (410 µL) was added to each sample, and the resulting solutions were kept for a week to afford single-crystals of MMF-2. The single-crystals were washed with and soaked in a 1:1 (v/v) mixed solvent of CH₂Cl₂ and CH₃CN for 1 day, and then washed with and soaked in pure CH₂Cl₂ for 1 day. The resulting washed crystals were analyzed by single-crystal X-ray diffraction.
Table S9. Optimization of the amount of D-glucono-1,5-lactone for asymmetric crystallization of MMF-2

<table>
<thead>
<tr>
<th>Entry</th>
<th>Equiv. of lactone</th>
<th>Crystal size (mm)</th>
<th>a</th>
<th>( R_1 )</th>
<th>( wR_2 )</th>
<th>Flack parameter</th>
<th>P : M</th>
<th>BASF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>20</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>0.41 × 0.37 × 0.26</td>
<td>31.3632(7)</td>
<td>0.0984</td>
<td>0.2726</td>
<td>0.07(9)</td>
<td>7:93</td>
<td>19.13</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>0.24 × 0.23 × 0.19</td>
<td>31.4212(6)</td>
<td>0.0785</td>
<td>0.2125</td>
<td>0.14(7)</td>
<td>14.86</td>
<td>20.80</td>
</tr>
</tbody>
</table>

a: Only powder product was obtained.
BASF (batch scale factor): ratio (%) of the minor component generated by the rotational twin

**Solid-phase CD measurement of (M)-enriched MMF-2**

![Solid-phase CD measurement of (M)-enriched MMF-2](image)

**Figure S15.** Diffuse reflectance CD (upper) and UV (bottom) spectra of (M)-enriched MMF-2 crystals grinded on an agate mortar with KCl.
6. Asymmetric crystallization of MMF-2 using other enantiopure compounds

Asymmetric crystallization using D-ribo-no-1,4-lactone as a chirality induction reagent

Ligand L (1.02 mg, 1.62 μmol) was dissolved in a mixed solvent of CH₂Cl₂ (127 μL) and DMSO (29 μL). To this solution were added a DMSO solution of D-ribo-no-1,4-lactone (1.83 M, 35.5 μL, 65.0 μmol, 40 equiv.), a DMSO solution of PdCl₂(CH₃CN)₂ (50.1 mM, 97 μL, 4.86 μmol, 3.0 equiv.) and H₂O (1.6 μL). The resulting solution was divided into three equal parts (90 μL each). CH₂Cl₂ (410 μL) was added to each sample, and the resulting solutions were kept standing for a week at 25 °C to obtain yellow block single-crystals. The yellow crystals were washed with and soaked in a 1:1 (v/v) mixed solvent of CH₂Cl₂ and CH₃CN for 1 day, then washed with CH₂Cl₂ and soaked in CH₂Cl₂ for 1 day. The washed crystals were analyzed by single-crystal X-ray diffraction.

Crystal data for (Pd₃LCl₉)_2·(CH₂Cl₂)₄·(H₂O)₄·0.89·(H₂O)₄·89 Pd₆, F_w = 2777.11, crystal dimensions 0.26 × 0.24 × 0.22 mm³, cubic, space group I2₁3, a = 31.4527(16) Å, V = 31115(3) Å³, Z = 8, ρ_calcd = 1.186 g cm⁻³, μ = 10.689 cm⁻¹, T = 100 K, λ (MoKα) = 0.71075 Å, 2θ_max = 55.0°, 137623/11870 reflections collected/unique, R₁ = 0.0940 (I > 2σ(I)), wR₂ = 0.2416 (for all data), GOF = 1.030, Flack parameter = 0.25(9) (Friedel Pairs = 5610), largest diff. peak and hole 3.43 /–1.01 eÅ⁻³. CCDC deposit number 989064. See below for the details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

Restraints for dichloromethane molecules

Geometrical restraints; DFIX (d = 1.7800, s = 0.0100): Cl₁S–C₁S, Cl₁T–C₁S, Cl₂S–C₂T, Cl₂T–C₂T, Cl₃S–C₃S, Cl₃T–C₃S. DANG (d = 2.8842, s = 0.0200): Cl₁S–Cl₁T. DANG (d = 2.8924, s = 0.0200) Cl₂S–Cl₂T. DANG (d = 2.9132, s = 0.0400) Cl₃S–Cl₃T.

PLAT602_ALERT_2_A Structure contains solvent accessible VOIDS

Response: Several solvents were severely disordered.

Asymmetric crystallization using L-gulonic acid γ-lactone as a chirality induction reagent
Ligand L (0.62 mg, 0.98 μmol) was dissolved in a mixed solvent of CH₂Cl₂ (85 μL) and DMSO (19 μL). To this solution were added a DMSO solution of L-gulonic acid γ-lactone (1.04 M, 17 μL, 17.7 μmol, 18 equiv.) and a DMSO solution of PdCl₂(CH₃CN)₂ (47.9 mM, 62 μL, 2.97 μmol, 3.0 equiv.). To this solution was added CH₂Cl₂ (800 μL), and the resulting solution was kept standing for a week at 25 °C to obtain yellow block single-crystals. The yellow crystals were washed with a 1:1 (v/v) mixed solvent of CH₂Cl₂ and CH₃CN and soaked in a 1:1 (v/v) mixed solvent of CH₂Cl₂ and CH₃CN for 1 day, then washed with and soaked in CH₂Cl₂ for 1 day. The washed crystals were analyzed by single-crystal X-ray diffraction.

Crystal data for (Pd₃LCl₆)₂(CH₂Cl₂)₄·(H₂O)₆: C₈₈H₁₀₆Cl₂₁₆N₁₂O₆₂Pd₆, Fₜₙ = 2851.97, crystal dimensions 0.25 × 0.20 × 0.15 mm³, cubic, space group I₂₁₃, a = 31.493(3) Å, V = 31236(4) Å³, Z = 8, ρcalcd = 1.213 g cm⁻³, μ = 10.849 cm⁻¹, T = 93 K, λ (MoKα) = 0.71075 Å, 2θmax = 55.0°, 154203/11897 reflections collected/unique, R₁ = 0.0829 (I > 2σ(I)), wR₂ = 0.2137 (for all data), GOF = 1.047, Flack parameter = 0.17(8) (Friedel Pairs = 5623), largest diff. peak and hole 1.41/–0.67 eÅ⁻³. CCDC deposit number 989065. See below for the details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

Restraints for dichloromethane molecules
Geometrical restraints; DFIX (d = 1.7800, s = 0.0100): C1S–Cl1S, C1S–Cl1T, C2S–Cl2T, Cl2S–C2S, C3S–Cl3S, Cl3T–C3S. DANG (d = 2.8931, s = 0.0200): Cl1T–Cl1S. DANG (d = 2.8846, s = 0.0200): Cl2T–Cl2S. DANG (d = 2.8753, s = 0.0400): Cl3T–Cl3S

PLAT602_ALERT_2_A Structure contains solvent accessible VOIDS
Response: Several solvents were severely disordered.

PLAT430_ALERT_2_A Short Inter D...A Contact O4W .. O4W .. 2.51 Ang.
Response: A water molecule was disordered along a three rotational axis.

General procedure of trials of asymmetric crystallization using various kinds of optically-pure compounds
Ligand L (0.36 mg, 0.57 µmol) was dissolved in CH$_2$Cl$_2$ (71 µL). To this solution were added a saturated DMSO solution of L-phenylalanine (21 µL) and a DMSO solution of PdCl$_2$(CH$_3$CN)$_2$ (47.9 mM, 36 µL, 1.72 µmol, 3.0 equiv.). CH$_2$Cl$_2$ (500 µL) was added to the solution, and the resulting mixture was kept standing for a week at 25 °C to obtain yellow block single-crystals. The yellow crystals were washed with a 1:1 (v/v) mixed solvent of CH$_2$Cl$_2$ and CH$_3$CN and soaked in a 1:1 (v/v) mixed solvent of CH$_2$Cl$_2$ and CH$_3$CN for 1 day, then washed with and soaked in CH$_2$Cl$_2$ for 1 day. The washed crystals were analyzed by single-crystal X-ray diffraction.
Table S10. Summary for asymmetric crystallization in the presence of chiral additives

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Chiral additive</th>
<th>Equiv.</th>
<th>Results</th>
<th>Flack parameter</th>
<th>$P : M$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>D-Glucose</td>
<td>12.5</td>
<td>Amorphous</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>D-Mannose</td>
<td>12.6</td>
<td>Amorphous</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>Sucrose</td>
<td>3.1</td>
<td>Single crystals</td>
<td>0.31(10)</td>
<td>69:31</td>
</tr>
<tr>
<td>4</td>
<td>L-Tartaric acid</td>
<td>9.4</td>
<td>No solid</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>(--)-Menthol</td>
<td>100</td>
<td>Single crystals</td>
<td>0.34(17)</td>
<td>34:66</td>
</tr>
<tr>
<td>6</td>
<td>Cinchonidine</td>
<td>10</td>
<td>No solid</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>Camphor</td>
<td>1000</td>
<td>Single crystals</td>
<td>0.45(8)</td>
<td>55:45</td>
</tr>
<tr>
<td>8</td>
<td>(R)-Propylene carbonate</td>
<td>1000</td>
<td>Yellow powder</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>9</td>
<td>(--) 2,3-O-Isopropylidene-o-threitol</td>
<td>1000</td>
<td>Yellow powder</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>10</td>
<td>L-Phenylalanine</td>
<td>–a</td>
<td>Single crystals</td>
<td>0.22(7)</td>
<td>22:78</td>
</tr>
<tr>
<td>11</td>
<td>Phe-OMe-HCl salt</td>
<td>–a</td>
<td>No solid</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>12</td>
<td>L-Tyrosine</td>
<td>–a</td>
<td>No solid</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>13</td>
<td>L-Histidine</td>
<td>–a</td>
<td>Single crystals</td>
<td>0.44(11)</td>
<td>44:56</td>
</tr>
<tr>
<td>14</td>
<td>L-Tryptophane</td>
<td>–a</td>
<td>No solid</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>15</td>
<td>L-Arginine</td>
<td>–a</td>
<td>Yellow powder</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>16</td>
<td>L-Proline</td>
<td>–a</td>
<td>Single crystals</td>
<td>0.43(10)</td>
<td>43:57</td>
</tr>
<tr>
<td>17</td>
<td>Stirring$^b$</td>
<td>–</td>
<td>Yellow powder</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*a*: Saturated DMSO solutions of chiral additives were used.  
*b*: The solution was stirred during crystallization.
Crystal growth experiments

Crystal growth experiment of (M)-enriched MMF-2 as a seed crystal

A washed (M)-enriched MMF-2 crystal was analyzed by single-crystal X-ray diffraction. The analyzed crystal was used as a seed crystal. A supersaturated solution of \( \text{Pd}_3\text{LCl}_6 \) in 1:9 (v/v) DMSO/\( \text{CH}_2\text{Cl}_2 \) was prepared as follows. Ligand \( \text{L} \) (0.58 mg, 0.92 \( \mu \)mol) was dissolved in a mixed solvent of \( \text{CH}_2\text{Cl}_2 \) (67 \( \mu \)L) and DMSO (37 \( \mu \)L). To this solution were added a DMSO solution of \( \text{PdCl}_2(\text{CH}_3\text{CN})_2 \) (50.0 mM, 55 \( \mu \)L, 2.75 \( \mu \)mol, 3.0 equiv.) and \( \text{CH}_2\text{Cl}_2 \) (760 \( \mu \)L). To this supersaturated solution of \( \text{Pd}_3\text{LCl}_6 \), a seed crystal was added. After a week, the grown crystal was washed with and soaked in a 1:1 (v/v) mixed solvent of \( \text{CH}_2\text{Cl}_2 \) and \( \text{CH}_3\text{CN} \) for 1 day. The crystal was washed with pure \( \text{CH}_2\text{Cl}_2 \) (0.5 mL \( \times \) 3) and soaked in \( \text{CH}_2\text{Cl}_2 \) for 1 day. The resulting crystal was analyzed by single-crystal X-ray diffraction.

Crystal data of the seed crystal

Crystal data for \( (\text{Pd}_3\text{LCl}_6)_2(\text{CH}_2\text{Cl}_2)_{4.53}(\text{H}_2\text{O})_{6.96} \): \( \text{C}_{88.53}\text{H}_{106.99}\text{Cl}_{21.07}\text{N}_{12}\text{O}_{6.96}\text{Pd}_6 \), \( F_w = 2836.00 \), crystal dimensions 0.19 \( \times \) 0.17 \( \times \) 0.15 mm\(^3\), cubic, space group \( I2_13 \), \( a = 31.3922(6) \) Å, \( V = 30936.0(10) \) Å\(^3\), \( Z = 8 \), \( \rho_{\text{calcd}} = 1.218 \) g cm\(^{-3}\), \( \mu = 10.859 \) cm\(^{-1}\), \( T = 93 \) K, \( \lambda (\text{MoK}\alpha) = 0.71075 \) Å, \( 2\theta_{\text{max}} = 55.0^\circ \), 146665/11810 reflections collected/unique, \( R_1 = 0.0961 \) (\( I > 2\sigma(I) \)), \( wR_2 = 0.2535 \) (for all data), \( \text{GOF} = 1.024 \), Flack parameter = 0.20(9) (Friedel Pairs = 5580), largest diff. peak and hole 2.99/\( -0.83 \) eÅ\(^{-3}\). CCDC deposit number 989067. See below for the details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

Restraints for dichloromethane molecules

Geometrical restraints; DFIX \( (d = 1.7800, s = 0.0100) \): \( \text{C1S} - \text{Cl1S}, \text{C1S} - \text{Cl1T}, \text{C2S} - \text{Cl2S}, \text{Cl2T} - \text{C2S}, \text{C3S} - \text{Cl3S}, \text{Cl3T} - \text{C3S} \). DANG \( (d = 2.8961, s = 0.0200) \): \( \text{Cl1T} - \text{Cl1S} \). DANG \( (d = 2.8874, s = 0.0400) \): \( \text{Cl3T} - \text{Cl3S} \).

PLAT602_ALERT_2_A Structure contains solvent accessible VOIDS

Response: Several solvents were severely disordered.

PLAT430_ALERT_2_A Short Inter D...A Contact O3W..O3W..2.30 Ang.
Response: A water molecule was disordered along a three rotational axis.

Crystal data of the grown crystal

Crystal data for (Pd$_3$LCl)$_2$·(CH$_2$Cl)$_2$·(H$_2$O)$_{5.43}$: C$_{88.34}$H$_{103.54}$Cl$_{20.68}$N$_{12}$O$_{5.43}$Pd$_6$, $F_w$ = 2791.93, crystal dimensions 0.31 × 0.27 × 0.20 mm$^3$, cubic, space group I2$_1$3, $a$ = 31.3469(8) Å, $V$ = 30802.2(13) Å$^3$, $Z$ = 8, $\rho_{\text{calc}}$ = 1.204 g cm$^{-3}$, $\mu$ = 10.823 cm$^{-1}$, $T$ = 93 K, $\lambda$ (MoK$\alpha$) = 0.71075 Å, $2\theta_{\text{max}}$ = 54.9°, 142347/11787 reflections collected/unique, $R_1$ = 0.0799 ($I > 2\sigma(I)$), $wR_2$ = 0.2120 (for all data), GOF = 1.073, Flack parameter = 0.46(8) (Friedel Pairs = 5574), largest diff. peak and hole 1.78/–0.80 eÅ$^{-3}$. CCDC deposit number 989068. See below for the details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

Restraints for dichloromethane molecules

Geometrical restraints; DFIX ($d$ = 1.7800, $s$ = 0.0100): C1S–Cl1S, C1S–Cl1T, Cl2S–C2S, C2S–Cl2T, C3S–Cl3S, Cl3T–C3S. DANG ($d$ = 2.8990, $s$ = 0.0200): Cl1T–Cl1S. DANG ($d$ = 2.8985, $s$ = 0.0200): C3S–Cl3T.

PLAT602_ALERT_2_A Structure contains solvent accessible VOIDS

Response: Several solvents were severely disordered.

PLAT430_ALERT_2_A Short Inter D...A Contact O3W..O3W..2.27 Ang.

Response: A water molecule was disordered along a three rotational axis.

Crystal growth experiment of rac-MMF-2 as a seed crystal

A washed rac-MMF-2 crystal was analyzed by single-crystal X-ray diffraction. The analyzed crystal was used as a seed crystal. A supersaturated solution of Pd$_3$LCl$_6$ in 1:9 (v/v) DMSO/CH$_2$Cl$_2$ was prepared as follows. Ligand L (2.95 mg, 4.68 µmol) was dissolved in a mixed solvent of CH$_2$Cl$_2$ (400 µL) and DMSO (100 µL). To this solution were added a DMSO solution of D-glucurono-6,3-lactone (1.33 M, 88 µL, 117 µmol, 25.0 equiv.) and a DMSO solution of PdCl$_2$(CH$_3$CN)$_2$ (50.1 mM, 280 µL, 14.0 µmol, 3.0 equiv.) (Final concentration: 5.39 mM, 868 µL). The resulting solution (140 µL) and CH$_2$Cl$_2$ (760 µL) were mixed to obtain a supersaturated solution of Pd$_3$LCl$_6$. To this
supersaturated solution of Pd$_3$LCl$_6$ a seed crystal was added. After a week, the grown crystals were washed with a 1:1 (v/v) mixed solvent of CH$_2$Cl$_2$ and CH$_3$CN and soaked in a 1:1 (v/v) mixed solvent of CH$_2$Cl$_2$ and CH$_3$CN for 1 day. The crystal was washed with pure CH$_2$Cl$_2$ (0.5 mL \times 3) and soaked in CH$_2$Cl$_2$ for 1 day. The resulting crystal was analyzed by single-crystal X-ray diffraction.

Crystal data of the seed crystal

Crystal data for (Pd$_3$LCl$_6$)$_2$·(CH$_2$Cl$_2$)$_{4.52}$(H$_2$O)$_{5.14}$: C$_{88.49}$H$_{103.18}$Cl$_{20.98}$N$_{12}$O$_{5.10}$Pd$_6$, $F_w = 2798.73$, crystal dimensions 0.23 \times 0.21 \times 0.17 \text{ mm}^3$, cubic, space group $I2_13$, $a = 31.4043(6)$ Å, $V = 30971.8(10)$ Å$^3$, $Z = 8$, $\rho_{\text{calcld}} = 1.200 \text{ g cm}^{-3}$, $\mu = 10.809 \text{ cm}^{-1}$, $T = 93$ K, $\lambda$ (MoK$_\alpha$) = 0.71075 Å, $2\theta_{\text{max}} = 54.9^\circ$, 129995/11841 reflections collected/unique, $R_1 = 0.0835$ ($I > 2\sigma(I)$), $wR_2 = 0.2102$ (for all data), GOF = 1.016, Flack parameter = 0.41(8) (Friedel Pairs = 5598), largest diff. peak and hole 1.22/–0.82 eÅ$^{-3}$. CCDC deposit number 989069. See below for the details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

Restraints for dichloromethane molecules

Geometrical restraints; DFIX ($d = 1.7800$, $s = 0.0100$): C1S–Cl1S, Cl1T–C1S, Cl2S–C2S, Cl2T–C2S, C3S–Cl3S, Cl3T–C3S. DANG ($d = 2.8933$, $s = 0.0200$): Cl1T–Cl1S. DANG ($d = 2.8928$, $s = 0.0200$): Cl2S–Cl2T. DANG ($d = 2.8878$, $s = 0.0400$): Cl3S–Cl3T.

Restrains on anisotropic displacement parameters; SIMU ($s = 0.02$ $st = 0.04$): C1S–Cl1S–Cl1T.

PLAT602_ALERT_2_A Structure contains solvent accessible VOIDS

Response: Several solvents were severely disordered.

PLAT430_ALERT_2_A Short Inter D...A Contact O3W..O3W..2.43 Ang.

Response: A water molecule was disordered along a three rotational axis.

Crystal data of the grown crystal

Crystal data for (Pd$_3$LCl$_6$)$_2$·(CH$_2$Cl$_2$)$_{4.52}$(H$_2$O)$_{5.14}$: C$_{88.52}$H$_{103.31}$Cl$_{21.04}$N$_{12}$O$_{5.14}$Pd$_6$, $F_w = 2801.99$, crystal dimensions 0.31 \times 0.24 \times 0.22 \text{ mm}^3$, cubic, space group $I2_13$, $a =$
31.4477(6) Å, \( V = 31100.4(10) \) Å\(^3\), \( Z = 8 \), \( \rho_{\text{calc}} = 1.197 \) g cm\(^{-3}\), \( \mu = 10.780 \) cm\(^{-1}\), \( T = 93 \) K, \( \lambda (\text{MoK}\alpha) = 0.71075 \) Å, \( 2\theta_{\text{max}} = 55.0^\circ \), 135501/11895 reflections collected/unique, \( R_1 = 0.0758 \) (\( I > 2\sigma(I) \)), \( wR_2 = 0.1999 \) (for all data), GOF = 1.070, Flack parameter = 0.19(7) (Friedel Pairs = 5625), largest diff. peak and hole 1.48/–0.80 eÅ\(^{-3}\). CCDC deposit number 989070. See below for the details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

**Restraints for dichloromethane molecules**

Geometrical restraints; DFIX (\( d = 1.7800, \ s = 0.0100 \)): Cl1S–C1S, C1S–Cl1T, Cl2S–C2S, C2S–Cl2T, Cl3S–C3S, C3S–Cl3T, Cl1S–Cl1T. DANG (\( d = 2.9005, \ s = 0.0200 \)): Cl2T–Cl2S. DANG (\( d = 2.8872, \ s = 0.0200 \)): Cl3T–Cl3S.

**PLAT602_ALERT_2_A Structure contains solvent accessible VOIDS**

Response: Several solvents were severely disordered.

**Table S11. Summary of crystal data before and after further crystal growth**

<table>
<thead>
<tr>
<th></th>
<th>Crystal size (mm)</th>
<th>( R_1 )</th>
<th>( wR_2 )</th>
<th>Flack parameter</th>
<th>( P: M )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before growth</td>
<td>0.19 × 0.17 × 0.15</td>
<td>0.0987</td>
<td>0.2619</td>
<td>0.20(10)</td>
<td>20:80</td>
</tr>
<tr>
<td>After growth</td>
<td>0.32 × 0.27 × 0.20</td>
<td>0.0833</td>
<td>0.2242</td>
<td>0.46(9)</td>
<td>46:54</td>
</tr>
</tbody>
</table>

**Table S12. Summary of crystal data before and after further crystal growth**
Comment: To evaluate the possibility of chirality induction in the crystal growth process, we conducted crystal growth experiments using a seed crystal of \((M)\)-enriched MMF-2 or \(rac\)-MMF-2 in the absence or presence of an optically-pure lactone, respectively. The size and Flack parameter of the seed crystal of moderately \((M)\)-enriched MMF-2 were determined by single-crystal XRD before the crystal growth experiment (crystal size: \(0.19 \times 0.17 \times 0.15 \text{ mm}^3\), Flack parameter: 0.20(9)). The seed crystal was then soaked into a 1:9 (v/v) mixed solvent of DMSO and CH\(_2\)Cl\(_2\) solution containing Pd\(_3\)LCl\(_6\) only at 25 °C for a week. The result of single-crystal XRD analysis was that the crystal was significantly grown (0.31 \(\times\) 0.27 \(\times\) 0.20 mm\(^3\)), and its Flack parameter approached almost 0.50 (0.46(8)). This result suggests that \((M)\)-selective crystal growth did not occur in the outer shell of the resulting single-crystal. In contrast, the crystal growth of a seed crystal of \(rac\)-MMF-2 (crystal size: \(0.23 \times 0.21 \times 0.17 \text{ mm}^3\), Flack parameter: 0.41(8)) in the presence of d-glucurono-6,3-lactone gave rise to chirality induction. After the crystal growth under the same condition, the crystal was significantly grown (0.31 \(\times\) 0.24 \(\times\) 0.22 mm\(^3\)) to an \((M)\)-enriched single-crystal (Flack parameter: 0.19(7)). This enantio preference of the crystal growth was the same as expected from that of single-crystals obtained from a solution containing a mixture of \((M)\)- and \((P)\)-isomers of syn-Pd\(_3\)LCl\(_6\) in the presence of d-glucurono-6,3-lactone. This observation suggests that the crystal was grown in an enantioselective manner with the aid of the lactones. Another point of importance is that the chirality induction occurs independently of the crystal surface.
features of MMF-2. The involvement of the nucleation process in the chirality induction remains unclear.

8. Synthesis and characterization of MMF-3

Synthesis of MMF-3 through single-crystal to single-crystal transformation

The washed MMF-2 crystals were soaked into CHCl₃ at 50 °C for a week. The resulting crystal transformed into MMF-3 through helicity inversion of Pd₃-macrocycles.

Crystal data for (Pd₃LCl₆)(CHCl₃)₂·9(H₂O): C₄₇.₄₁H₄₉.₄₁Cl₂₂.₂₃N₆OPd₃, F_w = 1826.60, crystal dimensions 0.28 × 0.25 × 0.21 mm³, cubic, space group I-43d, a = 31.3274(6) Å, V = 30745.0(10) Å³, Z = 16, ρ_calcd = 1.578 g cm⁻³, μ = 1.502 cm⁻¹, T = 97 K, λ (MoKα) = 0.71075 Å, 2θ_max = 54.9°, 143862/5866 reflections collected/unique, R₁ = 0.0629 (I > 2σ(I)), wR₂ = 0.1823 (for all data), GOF = 1.058, Flack parameter (Friedel Pairs = 2771) = 0.01(6), largest diff. peak and hole 1.40/-1.05 eÅ⁻³. CCDC deposit number 989066. See below for the details of applied restraints and response to alert A pointed out in the IUCR’s checkCIF routine.

Restraints for chloroform molecules
Geometrical restraints; DFIX (d = 1.7800, s = 0.0200): C3S–Cl7S, C3S–Cl5S, C3S–Cl6S, C2S–Cl4S, C2T–Cl4S, Cl7S–Cl6S. DANG (d = 2.8405, s = 0.0400): Cl6S–Cl5S. DANG (d = 2.8560, s = 0.0400): Cl5S–Cl7S.
Figure S16. Intermolecular interactions of Pd$_3$LCl$_6$ in MMF-2 (left) and MMF-3 (right).
Composition analyses of MMF-3 by digestion experiments

Figure S17. Partial $^1$H NMR spectra (500 MHz, DMSO-$d_6$, 293 K) after dissolving crystals in DMSO-$d_6$ in the presence of excess DCl-D$_2$O. (a) 1st, (b) 2nd and (c) 3rd trials.

Table S13. Molar ratios of ligand L to CHCl$_3$ determined by $^1$H NMR spectroscopy

<table>
<thead>
<tr>
<th>Trial</th>
<th>Molar ratio of ligand to CHCl$_3$ $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st trial</td>
<td>1 : 4.26</td>
</tr>
<tr>
<td>2nd trial</td>
<td>1 : 4.28</td>
</tr>
<tr>
<td>3rd trial</td>
<td>1 : 4.51</td>
</tr>
<tr>
<td>Average</td>
<td>1 : 4.35(14)</td>
</tr>
</tbody>
</table>

$^a$: The molar ratio was calculated by the integral ratio of signal $d$ to CHCl$_3$

Table S14. The number of CHCl$_3$ molecules encapsulated in a unit cell determined by $^1$H NMR spectroscopy

<table>
<thead>
<tr>
<th>CHCl$_3$ in a unit cell</th>
<th>CHCl$_3$-occupied void space ($\text{Å}^3$, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>5250, 32</td>
</tr>
</tbody>
</table>

A unit cell is composed of 16 Pd$_3$-complexes. The volume of CHCl$_3$ was calculated on Spartan 06 (75 Å$^3$) and the equilibrium geometry was determined by DFT calculation (B3LYP 6-31G*). The total volume of the void space of a unit cell is 16173 Å$^3$ calculated by PLATON.

S36
Thermogravimetric analysis of MMF-3

Figure S18. Thermogravimetric analysis of MMF-3. Measurement condition: 22 ~ 300 °C, 5 K/min, N\textsubscript{2} flow 150 mL/min. The 34% weight loss was approximately equal to the amount of solvents included in the crystals (31%).

Powder X-ray diffractions of rac-MMF-2 after soaked in CHCl\textsubscript{3}

Conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temp. (°C)</th>
<th>Time</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50</td>
<td>3 days</td>
<td>MMF-2 + MMF-3</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>7 days</td>
<td>MMF-3</td>
</tr>
<tr>
<td>3\textsuperscript{a}</td>
<td>120</td>
<td>1 h</td>
<td>MMF-3</td>
</tr>
<tr>
<td>4\textsuperscript{a}</td>
<td>120</td>
<td>2 h</td>
<td>MMF-3</td>
</tr>
</tbody>
</table>

\textsuperscript{a}: Under microwave irradiation
Figure S19. Powder X-ray diffractions of rac-MMF-2 after soaked in CHCl₃ under different conditions.

9. References for electronic supplementary information

1. Sheldrick, G. M. *SHELXL-97, Program for refinement of crystal structure* (University of Göttingen, Göttingen, Germany, 1997).