Remarkable Efficiency Improvement in the Preparation of Insoluble Polymer-Bound (IPB) Enantioselective Catalytic Systems by the Use of Silicone Chemistry.

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Supporting Information

General. All reactions involving sensitive compounds and the catalysis runs were carried out under dry nitrogen, in flame-dried glassware with magnetic stirring. Before use, the solvents were refluxed over the proper drying agent and distilled under nitrogen or at reduced pressure.[1] 1-(tert-butylthio)-1-(trimethylsiloxy)ethene was prepared as described.[2] Divinylbenzene (85%, Aldrich), styrene, α-methylstyrene and methyl pyruvate were distilled under reduced pressure and stored at –20°C. Ethyl glyoxylate was obtained from the commercial solution (50%, Fluka) as described,[3] and contained 30 mol% of toluene (by 1H NMR and GC). The other reagents were generally used as received. 1-Hexadecene used for SiH end-capping was the technical-grade product (Aldrich). Polysiloxanes were purchased from Aldrich (3 containing 26% wt/wt of MeSi(H)O units and 7) or from Gelest (3 containing 15% wt/wt of MeSi(H)O units and 6).

TLC analysis were carried out with Merk 60 F 254 plates (0.2 mm) and chromatography purifications with Macherey-Nagel flash grade silica-gel (230-400 mesh). Melting points (uncorrected) were measured with a Reichert hot stage apparatus. Optical rotation were measured as solutions in 1 dm cells at the sodium D line, using a Jasco DIP360 polarimeter. UV-vis spectra were recorded on a Perkin-Elmer Lambda-9 UV-vis-NIR spectrophotometer. IR spectra were recorded neat or as KBr disks, using a Perkin-Elmer 1600 Series FT-IR; the wavenumber of the principal peaks are reported in cm\(^{-1}\). Where not noted otherwise, 1H and 13C-NMR spectra were recorded as CDCl\(_3\) solutions, on a Varian Gemini 200 or a Varian XL 300, and are reported in ppm relative to TMS (\(\delta^1\)H) or to the solvent (\(\delta^{13}\)C, CDCl\(_3\) at 77.0 ppm). Ion-spray mass spectra (IS-ms) were recorded as methanol solutions on a Perkin-Elmer-Sciex Api III spectrometer. For the GC analysis a BP-1 column (25 m) on a Perkin-Elmer 8420 or a Astec G-TA (50 m) on a Perkin-Elmer Autosystem XL gas chromatograph were used, with nitrogen as the carrier gas; the response factors of the flame ionization detector for relevant compounds were calibrated against standard solutions. HPLC analyses were carried out on a Jasco PU-980 chromatograph, equipped with an UV-975 detector.
Elemental analysis were performed in duplicates by the microanalytical laboratory of the Dipartimento di Scienze e Tecnologie Chimiche dell’Università degli Studi di Udine (Italy).

1. Preparation of the box derivatives 2a and 2b.

For the synthesis of box monomers 2a-b, the general procedure by Evans and co-workers\cite{3} was followed. The use of 2a had been previously described by Corma and co-workers.\cite{4}

**Diethyl 2-methyl-2-(undec-10-enyl)malonate.**

A 500 mL three-necked flask, equipped with a dropping funnel reflux condenser and magnetic stirrer was charged with 50% NaH in mineral oil (6.04 g, 125 mmol) and THF (100 mL). While cooling in an ice bath, diethyl methylmalonate (19.6 mL, 115 mmol) in THF (35 mL) was added dropwise to the rapidly stirred mixture. When the gas evolution had ceased (30 min), the resulting suspension was allowed to warm to room temperature and a solution of undec-10-enyl tosylate\cite{5} (41.0 g, 126 mmol) in THF (60 mL) was added dropwise. The mixture was heated and kept under reflux until disappearance (GC) of the starting malonic ester (5 h). After cooling in an ice bath, the resulting suspension was cautiously treated with saturated NH₄Cl solution (100 mL) and most of the organic solvent removed with a rotary evaporator. The mixture was extracted with Et₂O (2 × 50 mL), the combined organic phases were washed with water until neutral and dried over Na₂SO₄. The solvent was removed under reduced pressure and the residue was purified by distillation under high vacuum, obtaining the product as a pale-yellow liquid (29.5 g, 72% yield).

B.p. 125-127°C (7.5 ×10⁻⁵ mbar). $^1$H-NMR δ: 0.60-2.10 (m, 27H), 4.12 (q, 4H, J=7.1 Hz), 4.85-5.05 (m, 2 H), 5.76 (ddt, 1H, J₁=6.6 Hz, J₂=10.5 Hz, J₃=17.1 Hz). $^{13}$C-NMR δ: 14.9, 19.9, 24.2, 28.9, 29.0, 29.3, 29.4, 29.8, 33.7, 35.6, 53.7, 60.9, 114.3, 138.1, 172.4.

**2-Methyl-2-(undec-10-enyl)malonic acid.**

A 100 mL two-necked flask, equipped with a reflux condenser, was charged with diethyl 2-methyl-2-(undec-10-enyl)malonate (29.5 g, 90.4 mmol) and 18 M KOH (37 mL; CAUTION). The biphasic mixture was heated under reflux until disappearance of the upper organic layer (4 h). After cooling to room temperature the resulting slurry was diluted with water (50 mL) and extracted with Et₂O (2 × 30 mL), discarding the ethereal phases. The aqueous layer was placed in an ice bath and 37% HCl was cautiously added to the rapidly stirred solution, adjusting the pH below 2. The resulting
A white suspension was extracted with Et₂O (2 × 30 mL), washing the combined organic phases with water (2 × 20 mL). After drying (Na₂SO₄), removal of the solvent (35°C, 30 mmHg) afforded the product as a white solid (21.0 g, 86% yield). NMR analysis confirmed that the product was pure enough to be used in the following step without further purification.

M.p. 93-95°C. IS-ms (m/z) -269 (M-H⁺). ¹H-NMR δ: 0.60-2.10 (m, 21H), 4.80-5.06 (m, 2H), 5.80 (ddt, 1H, J₁ = 6.6 Hz, J₂ = 10.5 Hz, J₃ = 17.1 Hz), 10.70 (br s, 2H). ¹³C-NMR δ: 19.8, 24.3, 28.9, 29.0, 29.3, 29.4, 29.5, 29.7, 29.8, 33.7, 35.7, 53.9, 114.3, 138.1, 178.2.

**2-Methyl-2-(undec-10-enyl)malonyl dichloride.**

A two-necked 50 mL flask, equipped with a dropping funnel, was charged with 2-methyl-2-(undec-10-enyl)malonic acid (4.06 g, 15 mmol), CH₂Cl₂ (23 mL) and DMF (100 µl). After cooling in an ice bath, oxalyl chloride (5.80 g, 45 mmol) was added dropwise over 1.5 h and the mixture was allowed to warm at room temperature and stirred overnight. The volatiles were removed under reduced pressure (20 mmHg), affording the product as a dark yellow oil which was directly used in the following step.

¹H-NMR δ: 1.3-1.4 (m, 14H), 1.64 (s, 3H), 1.96-2.14 (m, 4H), 4.86-5.06 (m, 2H), 5.80 (ddt, 1H, J₁ = 6.6 Hz, J₂ = 10.5 Hz, J₃ = 17.1 Hz). ¹³C-NMR δ: 20.2, 23.7, 28.8, 29.9, 29.0, 29.3, 29.5, 33.7, 35.7, 73.0, 114.1, 139.0, 171.3.

**(S,S)-Bis(hydroxyamides). General procedure**

A 50 mL two-necked flask, equipped with a dropping funnel, was charged with (S)-phenylglycinol or (S)-tert-leucinol (8 mmol, 2 eq.), dry CH₂Cl₂ (8.5 mL) and Et₃N (20 mmol, 5 eq.). While cooling at 0°C, a solution of the crude malonyl dichloride (4 mmol) in CH₂Cl₂ (3.5 mL) was added dropwise over 0.5 h to the rapidly stirred solution. After 1 h the resulting suspension was diluted with CH₂Cl₂ (20 mL) and washed sequentially with HCl 1 N (25 mL), sat. NaHCO₃ solution (20 mL) and brine (20 mL), back-extracting each time the aqueous layer with CH₂Cl₂ (10 mL). The combined organic phases were dried over Na₂SO₄ and the removal of the solvent under reduced pressure (35°C, 20 mmHg) afforded the amides as off-white solids, which could be directly used in the following step. For characterization purposes, samples of the products were purified either by flash chromatography (SiO₂, AcOEt : MeOH = 95 : 5, for the Ph-substituted bis-hydroxyamide), or crystallization from n-hexane (for the tBu derivative).
Yield: 93%. R_f (SiO_2, AcOEt: MeOH = 95: 5) = 0.75. M.p. 109-110°C. [α]_D^{23} = + 61.0 (c = 0.50, CH_2Cl_2). IS-MS (m/z): 509(M+H^+), 526(M+NH_4^+), 531(M+Na^+), 547(M+K^+). IR (KBr): 3327, 2926, 2854, 1636, 1522, 1458, 1381, 1260, 910, 754, 699. ^1H-NMR (200 MHz) δ: 1.00-1.45 (m, 14H), 1.46 (s, 3H), 1.81-1.95 (m, 2H), 1.95-2.10 (m, 2H), 3.52 (br s, 2H), 3.70-4.00 (m, 4H), 4.86-5.00 (m, 2H), 5.00-5.24 (m, 2H), 5.81 (ddt, 1H, J_1 = 6.6 Hz, J_2 = 10.4 Hz, J_3 = 17.2 Hz), 7.16-7.36 (m, 11H), 7.43 (d, 1H, J = 7.8 Hz). ^13C-NMR δ: 19.0, 24.5, 28.9, 29.0, 29.4, 33.8, 38.5, 53.8, 55.7, 66.1, 114.1, 126.5, 127.8, 128.8, 128.8, 138.6, 139.2, 173.3, 174.1. Anal. calcd for C_{31}H_{44}N_2O_4: C 73.19, H 8.72, N 5.51; Found: C 73.09, H 8.85, N 5.63.

Yield: 97%. M.p. 104-105°C. [α]_D^{25} = + 18.5 (c = 1.0, CH_2Cl_2). IS-ms (m/z): 469 (M+H^+), 491 (M+Na^+), 486 (M+NH_4^+), 507 (M+K^+). IR (KBr): 3334, 2933, 1644, 1538, 1477, 1398, 1369, 1342, 1263, 1183, 1110, 1050.9, 1022, 1000, 909, 776, 756, 653, 482. ^1H-NMR δ: 0.93 (s, 18H), 1.10-1.45 (m, 14H), 1.45 (s, 3H), 1.70-2.10 (m, 4H), 3.30-3.60 (m, 4H), 3.70-3.78 (m, 4H), 4.86-5.05 (m, 2H), 5.81 (ddt, 1H, J_1 = 6.6 Hz, J_2 = 10.5 Hz, J_3 = 17.1 Hz), 6.41 (d, 1H, J = 9.5 Hz), 6.76 (d, 1H, J = 9.5 Hz). ^13C-NMR δ: 18.9, 24.7, 26.8, 26.9, 28.9, 29.0, 29.4, 33.3, 33.4, 33.7, 38.3, 54.3, 59.5, 59.6, 62.2, 62.3, 114.1, 139.1, 173.7, 174.9. Anal. calcd for C_{27}H_{52}N_2O_4: C 69.19, H 11.18, N 5.98; Found: C 69.28, H 11.01, N 5.88.

**Bis(oxazolines) (S,S)-2a and (S,S)-2b. General procedure**

A 50 mL two-necked flask, equipped with a dropping funnel, was charged with the bis(amide) (4.3 mmol) and dry CH_2Cl_2 (20 mL), followed by DMAP (0.42 mmol) and Et_3N (19 mmol). Tosyl chloride (8.5 mmol) was added at room temperature and the resulting solution was stirred for 24 h. The mixture was diluted with CH_2Cl_2 (30 mL) and washed sequentially with sat. NH_4Cl (30 mL) and 10% NaHCO_3 solution (20 mL), back-extracting each time the aqueous layer with CH_2Cl_2 (10 mL). The combined organic extracts were dried over Na_2SO_4 and the volatiles were removed under vacuum (35°C, 20 mmHg) to give a thick oil that was purified by flash chromatography (CH_2Cl_2 : AcOEt = 9 : 1 as eluent).

**(S,S)-2a.** Yield: 83%. R_f (CHCl_3 : AcOEt = 8 : 2) = 0.57. [α]_D^{25} = -105 (c = 0.50, CH_2Cl_2). IS-MS (m/z): 473(M+H^+), 491(M+NH_4^+), 495(M+Na^+). IR (KBr): 3666,
3033, 2922, 2844, 1655, 1494, 1450, 977, 910, 760, 699. \( ^1 \text{H-NMR (200 MHz)} \) \( \delta \): 1.10-1.48 (m, 14H), 1.65 (s, 3H), 1.93-2.18 (m, 4H), 4.05-4.20 (m, 2H), 4.55-4.74 (m, 2H), 4.86-5.06 (m, 2H), 5.14-5.32 (m, 2H), 5.81 (ddt, 1H, \( J_1 = 6.6 \) Hz, \( J_2 = 10.4 \) Hz, \( J_3 = 17.1 \) Hz), 7.18-7.38 (m, 10H). \( ^{13} \text{C-NMR} \) \( \delta \): 21.5, 24.3, 28.9, 29.1, 29.4, 29.8, 33.7, 36.5, 42.6, 69.4, 69.5, 75.16, 75.23, 114.0, 126.6, 127.4, 128.6, 139.1, 142.38, 142.42, 169.7, 169.8. Anal. calcd for C\textsubscript{31}H\textsubscript{40}N\textsubscript{2}O\textsubscript{2}: C 78.77, H 8.53, N 5.93; Found: C 78.52, H 8.61, N 5.82. 

(S,S)-2b Yield: 83%. \( R_f \) (CH\textsubscript{2}Cl\textsubscript{2} : AcOEt = 9 : 1) = 0.33. \([\alpha]^{23}_{D} = -71.2 \) (c = 2.0, CHCl\textsubscript{3}). IS-ms (\( m/z \)) 433 (M+H\textsuperscript{+}), 451 (M+NH\textsubscript{4}\textsuperscript{+}). IR (KBr): 3076, 2952, 2926, 2855, 1660, 1479, 1466, 1394, 1364, 1234, 1208, 1143, 1094, 1060, 1025, 981, 924, 910, 755. \( ^1 \text{H-NMR} \) \( \delta \): 0.86 (s, 18H), 1.20-1.44 (m, 14H), 1.46 (s, 3H), 1.74-2.10 (m, 4H), 3.64-3.90 (m, 2H), 3.97-4.23 (m, 4H), 4.87-5.03 (m, 2H), 5.80 (ddt, 1H, \( J_1 = 6.6 \) Hz, \( J_2 = 10.5 \) Hz, \( J_3 = 17.1 \) Hz). \( ^{13} \text{C-NMR} \) \( \delta \): 21.3, 24.2, 25.67, 25.74, 28.9, 29.0, 29.4, 33.7, 33.8, 36.4, 42.3, 68.61, 68.63, 75.3, 75.5, 114.0, 139.1, 167.9, 168.3. Anal. calcd for C\textsubscript{27}H\textsubscript{48}N\textsubscript{2}O\textsubscript{2}: C 74.95, H 11.18, N 6.47; Found: C 74.97, H 10.99, N 6.55.

**2. Preparation and characterization of the IPB-box ligands.**

Table 1 summarizes the conditions and the results for the preparation of the materials 8-11 by the procedures detailed in the following paragraphs.

<table>
<thead>
<tr>
<th>Feed mixture composition, SiH/catalyst ratio and isolated amount of purified IPB-box in the preparation of the materials 8-11.(^a)</th>
<th>Catalyst</th>
<th>IPB-box</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feed</td>
<td>catalyst</td>
<td>compound</td>
</tr>
<tr>
<td>SiH/catalyst ratio</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>2a</td>
<td>0.462</td>
<td>0.43</td>
</tr>
<tr>
<td>2b</td>
<td>0.421</td>
<td>0.43</td>
</tr>
<tr>
<td>2b</td>
<td>0.149</td>
<td>0.43</td>
</tr>
<tr>
<td>2b</td>
<td>0.160</td>
<td>0.22</td>
</tr>
</tbody>
</table>

\(^a\) For the definition of \( m_{\text{IPB}} \), \( Y_m \), and \( Y_a \), see the paragraph 2.4.
2.1. Preparation of 4a and 4b by anchoring 2a or 2b to linear poly(methylhydrosiloxane-co-dimethylsiloxane) (PMHS). General procedure.
Under a nitrogen flow, a Schlenk tube was charged with the monomer 2a or 2b (0.2-1 mmol), PMHS 3 (5-6 equivalents SiH, see Table 1) and the Pt catalyst solution (molar ratio SiH/Pt = 4200-5000). After heating for 5 h at 70°C, a sample of the solution was diluted with C₆D₆ and analyzed by NMR.

4a. Selected NMR resonances in C₆D₆-mesitylene: ¹H-NMR (200 MHz) δ: 3.80-3.95, 4.18-4.32 and 4.95-5.10 (m, box ring CH), 5.10 (s, SiH). ¹³C-NMR δ: 17.9 and 23.5 (Si(CH₂CH₂)₆) 69.80, 69.86, 74.92 and 74.94 (box ring sp³ carbons), 169.5 (C=N).

4b. Selected NMR resonances in C₆D₆-mesitylene: ¹H-NMR (200 MHz) δ: 0.88 (tBu), 3.60-3.95 (m, box ring CH), 5.00 (s, SiH). ¹³C-NMR δ: 17.8 and 23.5 (Si(CH₂CH₂)₆) 68.5, 75.7 and 75.9 (box ring sp³ carbons), 167.9 and 168.0 (C=N).

2.2. Preparation of 8 and 9 by cross-linking in bulk. General procedure.
Divinylbenzene (0.5 molar equivalents vs. calculated residual SiH groups, see Table 1) was added to the solution of 4a or 4b and the mixture was heated at 50°C. Under these conditions the formation of an opaque, solid mass was generally observed within 1-2 h. After 18 h at the same temperature, the volatiles were removed under reduced pressure (0.1 mmHg). The resulting solid material was crushed and sequentially extracted in a Soxhlet device with dry CH₂Cl₂ and THF, for 2-3 days. The UV spectra of the final washings were virtually flat in the 240-350 nm region (A < 0.005, 1 cm cell). After drying under vacuum, the polymeric ligands 8 and 9 were obtained as a white powders and characterized by IR, elemental analysis and copper uptake measurements (see below).

8: IR (KBr): 1653 (νC=N). Elemental analysis: 0.57% N. Copper uptake: 0.033 mmol/g.
9: IR (KBr): 1660 (νC=N). Elemental analysis: 0.98% N. Copper uptake: 0.14 mmol/g.
2.2. Preparation of 10 and 11 by cross-linking in film. General procedure.
The solution of 4b was placed under air into a flat PTFE-lined vessel (40 cm^2 bottom area), together with a solution of 6 and 7 (for the exact quantities see Table 1) in toluene (2 mL). The vessel was covered with a glass plate and heated overnight at 50°C to effect the solvent evaporation and polymer cure. The resulting solid film was swollen with a solution of 1-hexadecene (0.56 mL) in toluene (1 mL) and the solvent was evaporated again, by gently heating for 2 h at 50°C. The polymer film was moistened with little n-hexane to facilitate the detachment from the vessel and transferred to a metal-net thimble, which was placed into a Soxhlet device. After continuous extraction over 2-3 days with dry CH₂Cl₂ and THF, the UV spectra of the final washings were flat in the 240-350 nm region (A < 0.005, 1 cm cell). The almost colorless and nearly transparent films 10 and 11 (approx. 0.2-0.4 mm thick) were dried under reduced pressure and characterized by IR, elemental analysis and copper uptake measurements (see below).

10: IR (KBr): 1661 (νC=N). Elemental analysis: 0.61% N. Copper uptake: 0.23 mmol/g.
11: IR (KBr): 1661 (νC=N). Elemental analysis: 0.47% N. Copper uptake: 0.18 mmol/g.

2.3. IPB-box/Cu(OTf)₂ complex preparation and copper uptake determination.[7]
A weighted amount of Cu(OTf)₂ (n_Cu mmol, 2 eq. vs. the theoretical supported box) was placed in a Schlenk tube and dried by briefly heating with a small flame under reduced pressure (0.05 mmHg). The salt was dissolved with dry THF, to afford a concentration ~ 0.02 M, and a weighted sample W of IPB-box 8-11 (about 100 mg) was suspended in the solution. After stirring under nitrogen for 5 h, the clear supernatant was separated from the blue-green insoluble material by filtration (8-9) or siphoning with a canula (10-11). The polymer was washed with dry THF (3 × 5 mL) and dried at 0.05 mmHg to be used in the catalysis runs.
The combined THF phases were gently evaporated to dryness, by warming at 50°C on a hot plate. The pale yellow residue was taken-up in 10 N H₂SO₄ (1.5 mL) and 33% NH₃ solution was added dropwise, to obtain the deep blue tetraminocopper(II) complex. Then, the solution was made acidic with 6 N H₂SO₄ (until fading of blue color) and 85% H₃PO₄ (0.40 mL) [CAUTION: suitable protective gloves and shields should be worn when handling acid and bases; to avoid excessive heating, a slow addition of concentrated ammonia to the acid solution is required]. Solid KI (0.16 g) was added and, as soon as the dissolution of the salt was complete, the resulting dark mixture was quickly titrated with Na₂S₂O₃ standard solution (N_T = 0.02 N). Once most of the iodine had been
consumed starch was added and the titration was continued until fading of the blue color. An end point stable for 30 s could be eventually reached ($V_T$ total volume of Na$_2$S$_2$O$_3$ solution) after addition of 3-4 drops of satd. KSCN. The procedure was validated by repeating the analytical sequence described above with weighted samples of Cu(OTf)$_2$ dissolved in THF; under these conditions, the copper content of the salt resulted 94.6±0.5% of the nominal value (6 experiments).

The metal uptake $U$ of the polymeric ligands **8-11** could be calculated from the measured quantities as:

$$U = \frac{n^0_{\text{Cu}} - N_T \times V_T}{W}$$

**2.4. Yield and ligand availability calculation.**

*Mass yield* in the preparation of **8-11**:

$$Y_m\% = \frac{m_{\text{IPB}}}{M_f} \times 100$$

where $m_{\text{IPB}}$ is the weight of the purified, dry IPB-box and $M_f$ that of the feed mixture (see Table 1).

*Anchoring yield* of the box derivatives:

$$Y_a\% = \frac{L \times m_{\text{IPB}}}{n_{\text{box}}^0} \times 100$$

where $L$ is the box loading of the insoluble material and $n_{\text{box}}^0$ is the initial molar amount of **2a** or **2b**.

The overall yield for the preparation of **8-11** from the starting chiral aminoalcohol could then be calculated from the yield of the soluble derivatives **2a** or **2b** ($Y_{\text{box}}$) as: $Y_{\text{overall}} = Y_{\text{box}} \times Y_a$.

*Availability* of the supported ligand units:

$$A\% = \frac{U}{L} \times 100.$$
3. Heterogeneous enantioselective catalytic runs.

3.1. Glyoxylate-ene reaction.

The complex $8\cdot$Cu(OTf)$_2$ was prepared as described above (par. 2.3) in a Schlenk tube provided with a magnetic stirring bar and a side glass frit ending with a stopcock. To the supported catalyst (135 mg, 0.018 mmol Cu, 10 mol%) in CH$_2$Cl$_2$ (2 mL), $\alpha$-methylstyrene (23 µL, 0.18 mmol) and distilled ethyl glyoxylate (100 µL, ca 0.75 mmol) were added at 0°C and the suspension was stirred overnight, at the same temperature. After 22 h, GC analysis of the supernatant revealed $\geq 90\%$ substrate conversion. The reaction solution was hence removed through the frit, followed by CH$_2$Cl$_2$ washing (3 × 1 mL) of the retained insoluble material. The chromatographic purification of the combined filtrates and the NMR and chiral HPLC characterization of the ene product $12$ were carried out as described by Evans and co-workers. [3]

After briefly drying under vacuum, the recovered insoluble catalyst was directly reused in further reaction runs.

The heterogeneity of the catalytic system was checked by stirring $8\cdot$Cu(OTf)$_2$ with ethyl glyoxylate for 5 h, filtering and adding $\alpha$-methylstyrene to the filtrate: Under these conditions no significant formation of $12$ was observed within 12 h.

3.2. Mukaiyama aldol reaction.

The insoluble Cu(II) complexes were prepared in Schlenk tubes from 10 or 11 and Cu(OTf)$_2$, as described in par. 2.3. To the supported catalyst (0.025 mmol supported Cu, 10 mol%) in THF (1.5 mL), 1-(tet-butylthio)-1-(trimethylsiloxy)ethene (77 µL, 0.30 mmol) and methyl pyruvate (23 µL, 0.25 mmol) were added at -78°C. The Schlenk tube was placed in a cooling bath at the required temperature and the suspension was stirred until complete conversion (GC) of the pyruvate (for the exact conditions, see Table 2 in the text). The solution was removed by siphoning and the insoluble material was washed with THF (2 × 1 mL). After briefly drying, the recovered material was directly used in further catalysis runs.

Concentration of the THF phases afforded a crude product, which was desilylated to give 13,[2] the purification and the determination of the ee of 13 was carried out as described by Evans and co-workers. [2]

To confirm the heterogeneity of the system, one half of the reaction solution from a catalysis run was siphoned under nitrogen into a Schlenk tube placed in an ice bath. More methyl pyruvate (12 µL) and
1-(tert-butylthio)-1-(trimethylsiloxy)ethene (39 µL) were added and the solution was stirred at the same temperature for 18 h. Under these conditions no significant conversion of the pyruvate ester was observed by GC analysis.

3.3. Cyclopropanation reactions. General procedure.

The insoluble Cu(II) complexes were prepared in Schlenk tubes under nitrogen, starting from Cu(OTf)$_2$ and 10 or 11 (par. 2.3). After stirring for 15 min at r.t., the suspension of the polymeric catalyst (0.01 mmol of supported Cu) in n-hexane (2 mL) was treated with a CH$_2$Cl$_2$ solution of phenylhydrazine (5% v/v, 46 µL). The color of the insoluble material changed instantly from blue-green to dark brown. In the case of styrene and 1,1-diphenylethylene the olefin (2 mmol) was added at 25°C and a solution of ethyl diazoacetate (0.21 mL, 1 mmol) in the reaction solvent (3.6 mL) was added over 2.5-21.5 h with a syringe pump. For isobutene, the Schlenk tube was placed into an ice bath and the substrate (ca. 3.9 g, 7 eq.) was directly condensed in the reaction vessel; the slow addition of ethyl diazoacetate (1.05 mL, 5 mmol as a 26% v/v solution in the reaction solvent) was carried out at the same temperature, as described above (for the exact conditions, compare Table 3 in the text).

After the addition of the diazoester had been completed, the mixture was stirred for an additional 0.5 h and nonane and dodecane internal standards (30-100 µL each) were added. Samples of the clear supernatant were analyzed by achiral GC to confirm the complete consumption of the diazoester and to evaluate the selectivity in the formation of the cyclopropanes; for styrene, the trans : cis product ratio was also determined by this technique. The catalyst was then separated from the solution by filtration (9) or siphoning (10 or 11), followed by 2 × 1 mL solvent rinse. The recovered insoluble material was briefly dried under reduced pressure and directly used in further cyclopropanation runs.

The purification of the crude products was carried out by flash chromatography (SiO$_2$, n-hexane : Et$_2$O = 95:5) for 14 (R$^1$ = Ph, R$^2$ = H) and 14 (R$^1$ = R$^2$ = Ph) or bulb-to-bulb distillation for 14 (R$^1$ = R$^2$ = Me), as described by Evans and co-workers.\[8\]

For the determination of the enantiomer composition of the cyclopropane products 14, HPLC or GC with chiral stationary phases was employed; in each case, the configuration of the prevailing stereoisomer was confirmed by measurement of $[\alpha]$$_D$.\[8\]

![Chiralcel OJ, 1 mL/min n-hexane : 2-propanol = 99.6 : 0.4, 225 nm; (1R,2R)-isomer (trans major enantiomer) $t_R$ = 12.0 min, (1S,2R)-isomer (cis minor enantiomer) $t_R$ = 13.6](image-url)
min, (1S,2S)-isomer \((trans\) minor enantiomer) \(t_R = 28.3\) min, (1R,2S)-isomer \((cis\) major enantiomer) \(t_R = 30.2\) min [Note: If the stationary phase is not properly conditioned before use, inversion of the elution order of the two last isomers could occasionally occur; to prevent the misassignment of the stereoisomeric composition, a coupled CD-UV detector was therefore employed in this study. Pure fractions of \(trans\) and \(cis\) diastereoisomers (> 95\% by GC), collected in the chromatographic purification of the crude product, were also analyzed separately, by chiral HPLC, before pooling; for both the \(trans\) and \(cis\) manifold, the enantiomer composition determined under these conditions proved to match that obtained by analysis of the whole diastereomeric mixture].

Chiralcel OD-H, 0.5 mL/min \(n\)-hexane : 2-propanol = 99.5 : 0.5, 225 nm; \((R)\)-enantiomer \(t_R = 22.1\) min, \((S)\)-enantiomer \(t_R = 25.3\) min.

Astec G-TA, 20 psi \(N_2\), 80° C for 11 min, then 10° C/min to 160° C; \((S)\)-enantiomer \(t_R = 9.77\) min, \((R)\)-enantiomer \(t_R = 10.04\) min.

To confirm the heterogeneous nature of the enantioselective catalysis, the solution from a reaction run with isobutene was siphoned under nitrogen into a Schlenk tube and treated with 1,1-diphenylethylene (0.70 mL, 1 mmol) and ethyl diazoacetate (0.21 mL, 2 mmol). Samples of the solution were analyzed (GC) immediately and after 20 h stirring at room temperature: Under these conditions < 5\% conversion of the diazoester was observed. Moreover, after evaporation of the volatile components at 0.05 mmHg, the small amount of \(14\) \((R^1 = R^2 = \text{Ph})\) was isolated and analyzed by chiral HPLC, showing < 2\% \textit{ee} Identical results were obtained by adding isobutene and ethyl diazoacetate to the solutions obtained from the cyclopropanation runs with styrene or 1,1-diphenylethylene.

References.


