GENERAL MATERIALS AND METHODS

All non-aqueous reactions were carried out in flame- and/or oven-dried glasswares using standard syringe-septum operations under argon atmosphere and magnetically stirred unless otherwise noted. All reactions were monitored by analytical thin-layer chromatography using pre-coated silica gel plates with F254 indicator from Merck or Whatman. Visualization was accomplished by UV light (254 nm) or phosphomolybdic acid. Flash column chromatography was performed according to the method of Still, using silica gel (mesh 230-400) supplied by Silicycle. Room temperature means 20±1 ºC. All reactions were carried out with anhydrous solvents unless otherwise noted. Anhydrous tetrahydrofuran, dichloromethane, diethyl ether, acetonitrile and toluene were dried with an M BRAUN solvent purification system (A2 Alumina). Anhydrous grade benzene, DMSO, chloroform and methanol were purchased from Aldrich and used without further purification. Dess-Martin periodinane was prepared according to the literature procedures (Frigerio, M.; Santagostino, M.; Sputore, S. J. Org. Chem. 1999, 64, 4537-4538 and Meyer, S. D.; Schreiber, S. L. J. Org. Chem. 1994, 59, 7549). All other reagents, unless otherwise noted, were purchased from commercial vendors and used without further purification. Analytical high-performance liquid chromatography (HPLC) was performed on Varian ProStar series equipped with a variable wavelength detector using Chiralcel OJ-H column (0.46 cm × 25 cm) from Daicel. 1H NMR and 13C NMR spectra were recorded on a Bruker Avance 500 (500 MHz 1H, 125 MHz 13C). Chemical shift values (δ) are reported in ppm (tetramethylsilane δ = 0 ppm for 1H; residual chloroform δ = 77.0 ppm for 13C). The proton spectra are reported as follows δ (multiplicity, coupling constant J, number of protons). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), pent (pentet), m (multiplet) and br (broad),
etc. Low resolution mass spectra (LRMS) were obtained on a QSTAR (Applied SCIEX Biochemistry/MDS) spectrometer.

**Synthetic procedures and characterization of products**

**General procedure for the preparation of amino acid salt catalysts**

(S)-3-(2-naphthyl)-L-alanine (69.9 mg, 0.325 mmol, 1 eq) and tetrabutylammonium hydroxide 30-hydrate (reagent from Fluka, 259.6 mg, 0.325 mmol, 1 eq) are dissolved in 2 mL Et₂O and 2 mL MeOH by sonication at room temperature for 5 minutes to give a slightly yellow color solution. It is then concentrated under vacuum and azeotropically dried with 3×10 mL benzene and finally high vacuum for 30 minutes. The residue is dissolved in 12 mL CHCl₃ (or MeOH in the case of alkali metal salt, when solubility in chloroform is poor) and added 391.1 mg silica gel. After concentration under vacuum and drying under high vacuum, 531.5 mg yellow color fine powder of silica gel absorbed tetrabutylammonium salt of (S)-3-(2-naphthyl)-L-alanine is obtained and used as such.

For calculating the amount of catalyst, we assume quantitative conversion of this acid-base reaction, so that the formal “molecular weight” is 531.5 mg/0.325 mmol = 1635 mg/mmol.

**Preparation of 1 and 2**

\[
\text{trans-1,4-cyclohexanediolmethanol (S1) (57.68 g, 400 mmol, 2 eq)} \]

is dissolved in 320 mL DMF at room temperature, then TBSCl (30.15 g, 200 mmol, 1 eq) and imidazole (16.34 g, 240 mmol, 1.2 eq) are added. After stirring at room temperature for 29 hours, the reaction is quenched by 300 mL brine, partitioned with 300 mL Et₂O. The aqueous phase is
extracted by 3×150 mL Et₂O, the combined organic phase was washed by 3×100 mL brine, and dried over MgSO₄. Filtration, concentration and chromatography (silica gel, hexanes: EtOAc 10:1) affords the monoprotected TBS ether S₂ (42.3 g, 82% yield) \([R_f = 0.50\) (silica gel, hexanes: EtOAc 1:1)]. S₂ (6.75 g, 26.1 mmol, 1 eq) is dissolved in 20 mL CHCl₃ at room temperature, then p-TsCl (6.45 g, 33.9 mmol, 1.3 eq) in 70 mL CHCl₃ and pyridine (6.3 mL, 78.3 mmol, 3 eq) are added in this sequence. After stirring at room temperature for 16 hours, the reaction mixture is concentrated under vacuum to give a white semi-solid; 100 mL Et₂O is then added and the solution filtrated to remove most pyridinium hydrochloride salts. After concentration and chromatography (silica gel, hexanes: EtOAc 10:1), tosylate S₃ (10.44 g, 97% yield) is obtained as colorless oil. S₃: \(R_f = 0.50\) (silica gel, hexanes: EtOAc 3:1); \(^1\)H NMR (500 MHz, CDCl₃): \(\delta = 7.78\) (d, \(J = 8.0\) Hz, 2H), 7.34 (d, \(J = 7.9\) Hz, 2H), 3.82 (d, \(J = 6.4\) Hz, 2H), 3.38 (d, \(J = 6.2\) Hz, 2H), 2.45 (s, 3H), 1.78-1.76 (m, 4H), 1.76-1.75 (m, 1H), 1.40-1.30 (m, 1H), 1.00-0.80 (m, 4H), 0.88 (s, 9H), 0.01 (s, 6H); \(^1^3\)C NMR (125 MHz, CDCl₃): \(\delta = 144.6, 133.1, 129.8, 127.8, 75.3, 68.4, 40.1, 37.4, 28.5, 28.5, 25.9, 21.6, 18.3, -5.4\).

S₃ (10.44 g, 25.3 mmol, 1 eq) and NaCN (1.86 g, 37.9 mmol, 1.5 eq) are dissolved in 90 mL DMSO, and then heated at 100 °C for 2.5 hours. After cooling down, it is diluted with 90 mL Et₂O, washed by 50 mL water and 40 mL brine, dried over MgSO₄. Filtration and concentration afford the crude cyanide S₄ (6.10 g, 90% yield) \([R_f = 0.31\) (silica gel, hexanes: EtOAc 10:1)] as slightly yellow oil, which is used in the next step without further purifications. S₄ (6.10 g, 22.8 mmol, 1 eq) is dissolved in 80 mL ether and then cooled down to -78 °C. DIBAL-H (27.4 mL, 27.4 mmol, 1.2 eq) is added and the reaction mixture is gradually warmed up to 10 °C over 5 hours. Quenching at -78 °C by 4 mL MeOH is followed by stirring with 70 mL saturated aqueous sodium potassium tartrate solution for 2 hours until the two layers are well separated. The aqueous phase is extracted by 2×100 mL Et₂O, the combined organic phase was washed by 2×50 mL brine, and dried over MgSO₄. Filtration and concentration affords the crude aldehyde S₅ (6.04 g,
98% yield) as colorless oil, which is used in the next step without further purifications. 

\[ \text{S5: } R_f = 0.34 \text{ (silica gel, hexanes: EtOAc 10:1); } ^1\text{H NMR (500 MHz, CDCl}_3\text{): } \delta = 9.76 \text{ (t, } J = 2.3 \text{ Hz, 1H), 3.40 \text{ (d, } J = 6.3 \text{ Hz, 2H), 2.35-2.28 \text{ (m, 2H), 1.85-1.72 \text{ (m, 5H), 1.48-1.36 \text{ (m, 1H), 1.05-0.92 \text{ (m, 4H), 0.89 \text{ (s, 9H), 0.02 \text{ (s, 6H).}}}}\]

\[ \text{OTBS} \quad \overset{2 \text{ eq NaH}}{\longrightarrow} \quad \overset{0^\circ \text{C}}{\longrightarrow} \quad \overset{70\% \text{ yield}}{\longrightarrow} \quad \text{OTBS} \]

\( \text{S5} (6.04 \text{ g, 22.3 mmol, 1 eq}) \) in 27 mL THF is added via cannula to a premixed solution of NaH (60% in mineral oil, 1.78 g, 44.6 mmol, 2 eq) and diethyl (2-oxopropyl)-phosphonate (8.66 g, 44.6 mmol, 2 eq) in 50 mL THF (room temperature 15 min until gas generation ceased) at 0 \( ^\circ \text{C} \). The reaction mixture is stirred and gradually warmed up to room temperature over 12 hours and then quenched by 100 mL half saturated aqueous NH\(_4\)Cl solution. Extraction by 3×100 mL Et\(_2\)O is followed by washing the combined organic phase by 50 mL brine. Drying over MgSO\(_4\), filtration, concentration and chromatography (silica gel, hexanes: EtOAc 20:1), afforded unsaturated ketone \( \text{S6} (4.85 \text{ g, 70\% yield}) \) as colorless oil. 

\[ \text{S6: } R_f = 0.22 \text{ (silica gel, hexanes: EtOAc 10:1); } ^1\text{H NMR (500 MHz, CDCl}_3\text{): } \delta = 6.78 \text{ (dt, } J = 15.9, 7.4 \text{ Hz, 1H), 6.05 \text{ (d, } J = 15.9 \text{ Hz, 1H), 3.39 \text{ (m, 2H), 2.24 \text{ (s, 3H), 2.14-2.12 \text{ (m, 2H), 1.79-1.74 \text{ (m, 4H), 1.42-1.36 \text{ (m, 2H), 1.00-0.88 \text{ (m, 4H), 0.89 \text{ (s, 9H), 0.03 \text{ (s, 6H).}}}}\]

To a solution of \( \text{S6} (3.48 \text{ g, 11.2 mmol, 1 eq}) \) in 130 mL EtOH is added 34 mL 5%(v/v) conc. HCl(aq) in EtOH at room temperature. After stirring at room temperature for 30 minutes, ethanol is evaporated under vacuum. Partition with 425 mL EtOAc and 250 mL half saturated aqueous NaHCO\(_3\) solution is followed by extraction of aqueous phase with 2×100 mL EtOAc. The combined organic phase is washed by 100 mL brine, dried over Na\(_2\)SO\(_4\). Filtration, concentration and chromatography (silica gel, hexanes: EtOAc 1:1), afforded alcohol \( \text{S7} (2.00 \text{ g, 91\% yield}) \) as colorless oil. 

\[ \text{S7: } R_f = 0.36 \text{ (silica gel, hexanes: EtOAc 1:1); } ^1\text{H NMR (500 MHz, CDCl}_3\text{): } \delta = 6.78 \text{ (dt, } J = 15.8, 7.5 \text{ Hz, 1H), 6.06 \text{ (d, } J = 15.8 \text{ Hz, 1H), 3.45 \text{ (m, 2H), 2.24 \text{ (s, 3H), 2.23-2.08 \text{ (m, 2H), 1.83-1.76 \text{ (m, 4H), 1.43-1.38 \text{ (m,}}\]
2H), 1.00-0.89 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 198.7, 147.1, 132.3, 68.5, 40.3, 40.2, 37.4, 32.4, 29.2, 26.9.

S7 (83.0 mg, 0.423 mmol, 1 eq) is dissolved in 5 mL CH$_2$Cl$_2$ at room temperature and then added NaHCO$_3$ (71.1 mg, 0.846 mmol, 2 eq) and Dess-Martin periodinane (215.2 mg, 1.2 eq). After stirring at room temperature for 1 hour, the reaction mixture is directly loaded to column chromatography (silica gel, hexanes: EtOAc 10:1) to afforded aldehyde 1 (72.3 mg, 88% yield) as colorless oil. 1: $R_f$ = 0.48 (silica gel, hexanes: EtOAc 1:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 9.62 (s, 1H), 6.77 (dt, $J$ = 15.8, 7.4 Hz, 1H), 6.08 (d, $J$ = 15.8 Hz, 1H), 2.25 (s, 3H), 2.25-2.13 (m, 3H), 2.05-1.97 (m, 2H), 1.90-1.84 (m, 2H), 1.49-1.39 (m, 1H), 1.33-1.22 (m, 2H), 1.09-0.97 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 204.4, 198.5, 146.3, 132.5, 50.1, 39.9, 36.7, 31.6, 27.0, 25.7. Aldehyde 1 (15.2 mg, 0.0777 mmol, 1 eq) and silica gel absorbed tetrabutylammonium salt of (S)-3-(2-naphthyl)-D-alanine (formal “molecular weight” = 1684 mg/mmol, 65.4 mg, 50 mol%) are suspended in 0.8 mL cyclopentyl methyl ether and stirred at room temperature for 120 hours. The reaction mixture is then diluted with Et$_2$O and filtered with Et$_2$O washing. After drying under vacuum, the recovered catalyst (64.8 mg, 99% recovery) is used repeatedly in the 2nd run and 3rd runs for the same reactions. The filtrate is concentrated and purified by column chromatography (silica gel, hexanes: EtOAc 10:1) to afforded the tricyclic product 2 (11.5 mg, 84% yield) as colorless oil, no intermediate Michael adduct is observed in the crude NMR. The enantiomeric excess of 2 was determined to be 97% by chiral HPLC analysis (Chiralcel OJ-H, hexanes/isopropanol= 99.4:0.6, flow rate= 0.5 mL/min, $t_{major}$ = 20.8 min, $t_{minor}$ = 19.8 min). 2: $R_f$ = 0.48 (silica gel, hexanes: EtOAc 3:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 6.50 (d, $J$ = 10.0 Hz, 1H), 5.83 (d, $J$ = 10.0, 1H), 2.45-2.38 (m, 1H), 2.34-2.26 (m, 1H), 2.20-2.11 (m, 1H), 1.98-1.90 (m, 1H), 1.74-1.56 (m, 7H), 1.49-1.38 (m, 2H), 1.12-1.06 (m, 1H); $^{13}$C NMR
(125 MHz, CDCl₃): δ = 200.6, 158.1, 127.3, 41.8, 35.4, 33.9, 33.1, 31.8, 25.9, 24.8, 24.8, 24.4.
$^1$H NMR spectrum
(500 MHz, CDCl$_3$)

$^{13}$C NMR spectrum
(125 MHz, CDCl$_3$)
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$^1$H NMR spectrum
(500 MHz, CDCl$_3$)

$^{13}$C NMR spectrum
(125 MHz, CDCl$_3$)

and HPLC trace
(97% ee)