Supporting Information

**Light-Driven Enantioselective Organocatalytic β-Benzylaion of Enals**

Luca Dell’Amico, Victor M. Fernández-Alvarez, Feliu Maseras,* and Paolo Melchiorre*

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Supporting Information
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A. General Information

The NMR spectra were recorded at 400 MHz and 500 MHz for $^1$H or at 100 MHz and 125 MHz for $^{13}$C, respectively. The chemical shifts (δ) for $^1$H and $^{13}$C are given in ppm relative to residual signals of the solvents (CHCl$_3$ @ 7.26 ppm $^1$H NMR, 77.16 ppm $^{13}$C NMR). Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal.

High-resolution mass spectra (HRMS) were obtained from the ICIQ High Resolution Mass Spectrometry Unit on Waters GCT gas chromatograph coupled time-of-flight mass spectrometer (GC/MS-TOF) with electron ionization (EI) or MicroTOF II (Bruker Daltonics): HPLC-MS-TOF (ESI). UV-vis measurements were carried out on a Shimadzu UV-2401PC spectrophotometer equipped with photomultiplier detector, double beam optics and D$_2$ and W light sources. X-ray data were obtained from the ICIQ X-Ray Unit using a Bruker-Nonius diffractometer equipped with an APPEX 2 4K CCD area detector. Optical rotations were measured on a Polarimeter Jasco P-1030 and are reported as follows: [α]$_D$, rt (c in g per 100 mL, solvent).

Studies with nanosecond transient absorption spectroscopy (TAS) were performed using an excitation source of Nd:YAG (neodymium-doped yttrium aluminium garnet) tuned with an optical parametric oscillator (OPO) from Opolett as a pump source. This laser produces 6 ns pulses of 1 mJ at a wavelength of 355 nm. The system is completed with two monochromators with double grating at the VIS an IR, and a digital recorder DSP-DAU from RAMDSP. A photodetector amplifiers and a software control complete the TAS system.

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Chromatographic purification of products was accomplished using force-flow chromatography (FC) on silica gel (35-70 mesh). For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF$_{254}$, 0.25 mm) were used, using UV light as the visualising agent and an acidic mixture of ceric ammonium molybdate or basic aqueous potassium permangante (KMnO$_4$), and heat as developing agents. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator.

**Determination of Diastereomeric Ratio.** The diastereomeric ratio for the photoenolization/β-benzylolation sequence (products 5) was determined by $^1$H NMR analysis of the crude reaction mixture through integration of diagnostic signals, and then confirmed by HPLC analysis.

**Determination of Enantiomeric Purity:** HPLC analysis on chiral stationary phase was performed on an Agilent 1200-series instrumentation. Daicel Chiralpak IA, IB, ID, IC and IC-3 columns with hexane/iPrOH or hexane/iPrOH/DCM as the eluents were used. HPLC traces were compared to racemic samples prepared running the reaction in the presence of the racemic catalyst 4b.

**Materials:** Commercial grade reagents and solvents were purchased at the highest commercial quality from Sigma Aldrich, Fluka, Acros Organics, and Alfa Aesar and used as received, unless otherwise stated. The chiral secondary amine catalysts (S)-(−)-a,a-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (4a) and (S)-(−)-a,a-diphenyl-2-pyrrolidinemethanol tert-butyldimethylsilyl ether (4b) are commercially available and were used without further purification.

Aliphatic α,β-unsaturated aldehydes 3 are commercially available and were purchased from Sigma-Aldrich, Alfa Aesar or Acros Organics and used after distillation to avoid any presence of water or other stabilizers, and then stored at 2-4 °C under an argon atmosphere. Enal 3g was prepared according to a previously reported procedure (1). Benzophenones 1a, 1d and 1m were purchased from Sigma-Aldrich and used without further purifications. Benzophenones 1j and 1l were prepared according to (2). The preparation of the other benzophenones is detailed in Section B of the Supporting Information.
B. Substrate Synthesis

**Method A:** The commercially available benzaldehyde derivative S1 (1 equiv.) was dissolved in dry THF (0.25 M) under an argon atmosphere. After cooling to 0 °C, a 0.5 M p-tolylmagnesium bromide solution in THF (1.2 equiv.) was slowly added under vigorous stirring. The mixture was allowed to warm up to ambient temperature (rt). Upon complete consumption of the starting aldehyde S1, as determined by TLC analysis, water was slowly added at 0 °C. The biphasic system was then extracted with Et₂O (x 3). The organic phases were collected and concentrated under vacuum. The crude alcohol intermediate was dissolved in dry DCM (0.2 M solution) without any purification. Then, activated MnO₂ (7 equiv.) was added at once under an argon atmosphere, and the solution was warmed up at reflux for 10 hours. After cooling to ambient temperature, the mixture was filtered through a pad of silica and the residue washed with DCM. The organic solution was concentrated under vacuum and the crude mixture subjected to flash chromatography (FC) purification on silica to afford the benzophenone substrate 1.

**Method B:** The commercially available bromobenzene derivative S2 (1 equiv.) was dissolved in dry THF (0.25 M) under an argon atmosphere. After cooling the mixture to -30 °C, a solution of n-BuLi 1.9 M in hexane (1.5 equiv.) was added dropwise. After the addition, the solution was allowed to warm to ambient temperature and stirring was continued for 1 hour. The commercially available aldehyde derivative S3 (1 equiv., 0.5 M solution in dry THF) was then added dropwise at 0 °C, and stirring was continued over 2 hours. The reaction was then quenched by carefully adding water and extracted with Et₂O (x 3). The organic phases were collected and concentrated under vacuum. The crude alcohol intermediate was then subjected to MnO₂ oxidation as in Method A. FC purification on silica gel afforded the benzophenone substrate 1.
(4-methoxy-2-methylphenyl)(phenyl)methanone (1b). Following the procedure detailed in Method B, 1b was isolated by FC on silica gel (hexane/EtOAc 97:3 v/v) in 77% yield as a colorless oil. TLC (hexane/EtOAc: 95:5 v/v): R_f = 0.32; HRMS calculated for [C_{15}H_{14}O_{2} + Na]^+: 249.0894; found: 249.0894.

^1H NMR (400 MHz, CDCl₃) δ 7.83 – 7.74 (m, 2H), 7.61 – 7.54 (m, 1H), 7.50 – 7.43 (m, 2H), 7.36 (d, J = 8.5 Hz, 1H), 6.85 (dd, J = 2.5, 0.8 Hz, 1H), 6.76 (ddd, J = 8.5, 2.6, 0.6 Hz, 1H), 3.87 (s, 3H, CH₃ OMe), 2.44 (d, J = 0.7 Hz, 3H, CH₃).

^{13}C NMR (100 MHz, CDCl₃) δ 197.7 (C=O), 161.3 (Cq Ar), 140.6 (Cq Ar), 138.8 (Cq Ar), 132.5 (CH Ar), 132.1 (CH Ar), 130.7 (Cq Ar), 130.0 (CH Ar x2), 128.3 (CH Ar x2), 116.8 (CH Ar), 110.1 (CH Ar), 55.3 (CH₃ OMe), 20.8 (CH₃).

1H NMR (400 MHz, CDCl₃) δ 7.85 – 7.78 (m, 2H), 7.62 (ddt, J = 8.7, 6.9, 1.3 Hz, 1H, Ar), 7.55 – 7.42 (m, 4H, Ar), 7.47 – 7.38 (m, 1H, Ar), 7.36 – 7.24 (m, 4H, Ar), 2.27 (s, 3H, CH₃).

^{13}C NMR (100 MHz, CDCl₃) δ 196.9 (C=O), 140.5 (Cq Ar), 137.0 (Cq Ar), 135.5 (Cq Ar), 133.6 (CH Ar), 133.1 (CH Ar), 132.7 (CH Ar), 130.8 (CH Ar), 130.1 (CH Ar x2), 128.7 (CH Ar x2), 118.9 (Cq Ar), 19.5 (CH₃).

(5-bromo-2-methylphenyl)(phenyl)methanone (1c). Following the procedure reported in the literature (2), 1c was isolated by FC on silica (hexane/EtOAc: 98:2 v/v) in 55% yield as a colorless oil. TLC (hexane/EtOAc: 98:2 v/v): R_f = 0.35; HRMS calculated for [C_{14}H_{11}BrO + Na]^+: 296.9895; found: 296.9895.

^1H NMR (400 MHz, CDCl₃) δ 7.85 – 7.78 (m, 2H, Ar), 7.64 – 7.59 (m, 2H, Ar), 7.47 – 7.35 (m, 1H, Ar), 7.36 – 7.21 (m, 4H, Ar), 6.99 – 6.89 (m, 2H, Ar), 3.89 (m, 3H, OMe), 2.33 (s, 3H, CH₃).

^{13}C NMR (100 MHz, CDCl₃) δ 197.4 (C=O), 163.7 (Cq Ar), 139.2 (Cq Ar), 136.2 (Cq Ar), 132.5 (CH Ar x2), 130.8 (CH Ar), 130.5 (Cq Ar), 129.8 (CH Ar), 127.9 (CH Ar), 125.3 (CH Ar), 20.0 (CH₃).

(4-bromophenyl)(o-tolyl)methanone (1g). Following the procedure detailed in Method A, 1g was isolated by FC on silica (hexane/EtOAc: 98:2 v/v) in 76% yield as a colorless oil. TLC (hexane/EtOAc: 98:2 v/v): R_f = 0.34; HRMS calculated for [C_{14}H_{11}BrO + Na]^+: 296.9891; found: 296.9893.

^1H NMR (400 MHz, CDCl₃) δ 7.72 – 7.65 (m, 2H, Ar), 7.64 – 7.59 (m, 2H, Ar), 7.47 – 7.38 (m, 1H, Ar), 7.36 – 7.24 (m, 4H, Ar), 2.35 (s, 3H, CH₃).

^{13}C NMR (100 MHz, CDCl₃) δ 197.5 (C=O), 138.0 (Cq Ar), 136.8 (Cq Ar), 136.5 (Cq Ar), 131.8 (CH Ar x2), 131.6 (CH Ar x2), 131.2 (CH Ar), 130.5 (CH Ar), 128.5 (CH Ar), 128.4 (Cq Ar), 125.3 (CH Ar), 20.0 (CH₃).

(4-methoxyphenyl)(o-tolyl)methanone (1h). Following the procedure detailed in Method A, 1h was isolated by FC on silica (hexane/EtOAc: 98:2 v/v) in 76% yield as a colorless oil. TLC (hexane/EtOAc: 98:2 v/v): R_f = 0.34; HRMS calculated for [C_{15}H_{14}O_{2} + Na]^+: 249.0891; found: 249.0896.

^1H NMR (400 MHz, CDCl₃) δ 7.85 – 7.77 (m, 2H, Ar), 7.43 – 7.35 (m, 1H, Ar), 7.33 – 7.21 (m, 4H, Ar), 6.99 – 6.89 (m, 2H, Ar), 3.89 (s, 3H, CH₃ OMe), 2.33 (s, 3H, CH₃).

^{13}C NMR (100 MHz, CDCl₃) δ 197.4 (C=O), 163.7 (Cq Ar), 139.2 (Cq Ar), 136.2 (Cq Ar), 132.5 (CH Ar x2), 130.8 (CH Ar), 130.5 (Cq Ar), 129.8 (CH Ar), 127.9 (CH Ar), 125.2 (CH Ar), 113.7 (Cq Ar x2), 55.5 (CH₃ OMe), 19.8 (CH₃).
C. General Procedures for the Enantioselective Organocatalytic Photoenolization/β-Benzylation Sequence

General Procedure A (for aliphatic enals)

An oven-dried, 10 mL Schlenk tube was charged with the chiral secondary amine catalyst (S)-(−)-α,α-diphenyl-2-pyrrolidinemethanol tert-butyldimethylsilyl ether 4b (15 mg, 0.04 mmol, 0.2 equiv.), diphenyl phosphoric acid (DPP, 10 mg, 0.04 mmol, 0.2 equiv.) and 5 mL of 1,2-dichlorobenzene (ο-Cl₂C₆H₄). The tube was placed under an argon atmosphere, and then benzophenone 1 (1 equiv.) and a freshly distilled enal 3 (5.5 equiv.) were sequentially added. The mixture was diluted with additional 1 mL of ο-Cl₂C₆H₄. The reaction mixture was degassed via freeze pump thaw: the mixture was cooled to −78 °C and degassed via vacuum evacuation (5 min), backfilled with argon, and then warmed up to ambient temperature (this process was repeated four times). The tube was sealed and positioned approximately 3 cm away from three light sources. A set of household 15 W Black Light Bulbs (BLB) were used for irradiating the reaction mixture (see Figure S1 for the emission spectrum and the reaction set-up). After stirring for 20 hours, the crude mixture was directly charged on a column and subjected to flash chromatography (FC) on silica gel to afford the title compound 5 in the stated yield and optical purity.

Figure S1. Emission spectrum of the 15 W BLB lamp used in this study (left) and the set-up of the reaction (right). The high intensity of emission at 365 nm secured an efficient excitation of the benzophenone substrate 1 and the generation of the reactive photoenol. The use of different light sources, including a compact fluorescence light (CFL) bulb or a white LED strip, resulted in greatly reduced reactivity.
**General Procedure B (for aromatic enals)**

An oven-dried, 10 mL Schlenk tube was charged with the chiral secondary amine catalyst (S)-(−)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether 4a (13 mg, 0.04 mmol, 0.2 equiv.), diphenyl phosphoric acid (DPP, 10 mg, 0.04 mmol, 0.2 equiv.) and 1 mL of toluene. The tube was placed under an argon atmosphere, and then benzophenone 1 (2 equiv.) and a freshly distilled enal 3 (1 equiv.) were sequentially added. The mixture was diluted with additional 1 mL of toluene. The reaction mixture was degassed via freeze pump thaw: the mixture was cooled to −78 °C and degassed via vacuum evacuation (5 min), backfilled with argon, and then warmed up to ambient temperature (this process was repeated four times). The tube was sealed and positioned approximately 3 cm away from three light sources. A set of household 15 W Black Light Bulbs (BLB) were used for irradiating the reaction mixture (see Figure S1 in the previous page for the emission spectrum and the reaction set-up). After stirring for 20 hours, the crude mixture was directly subjected to flash chromatography (FC) to afford the title compound 5 in the stated yield and optical purity.

**Characterization Data**

(S)-3-(2-benzyloxybenzyl)pentanal (5a). Compound 5a was prepared according to the general procedure A, using 2-methylbenzophenone 1a (36 μL, 0.2 mmol, 1 equiv.), trans-2-pentenal (108 μL, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as a colorless oil (34 mg, 61% yield, 90% ee). TLC: (hexane/EtOAc: 90:10 v/v), Rf = 0.32. The ee (90%) was determined by HPLC analysis on a Daicel Chiralpak IC column: 85:15 hexane/iPrOH, flow rate 1.00 mL/min; λ = 254 nm; τmajor = 14.3 min, τminor = 15.6 min. [α]D = +75.6 (c = 0.5 in CHCl3). HRMS calculated for [C17H16O2Na]+: 303.1361; found: 303.1363.

1H NMR (500 MHz, CDCl3) δ 9.58 (s, J = 2.2 Hz, 1H, CHO), 7.86 – 7.76 (m, 2H, Ar), 7.67 – 7.55 (m, 1H, Ar), 7.54 – 7.39 (m, 3H, Ar), 7.38 – 7.25 (m, 3H, Ar), 2.86 (dd, J = 13.7, 6.5 Hz, 1H, H1‘α), 2.57 (dd, J = 13.7, 8.1 Hz, 1H, H1‘β), δ 2.31 (d, J = 2.2 Hz, 1H, H2α), 2.30 (d, J = 2.3 Hz, 1H, H2β) 2.19 (m, 1H, H3), 1.38 – 1.29 (m, 2H, CH2, H4), 0.83 (t, J = 7.4 Hz, 3H, CH3). 13C NMR (125 MHz, CDCl3) δ 202.8 (C=O), 198.4 (CHO), 139.3 (Cq Ar), 138.9 (Cq Ar), 137.8 (Cq Ar), 133.3 (CH Ar) 131.1 (CH Ar), 130.2 (CH Ar), 128.9 (CH Ar x2), 128.5 (CH Ar x2), 125.7 (CH Ar), 47.5 (CH2), 37.5 (CH2), 36.7 (CH), 26.8 (CH2), 10.9 (CH3).

Compound 5a was also obtained through a 1 mmol scale procedure using 2-methylbenzophenone 1a (181 μL, 1 mmol, 1 equiv.), trans-2-pentenal (540 μL, 5.5 mmol, 5.5 equiv.), diphenyl phosphoric acid (25 mg, 0.1 mmol, 0.1 equiv.) and catalyst 4b (75 mg, 0.2 mmol, 0.2 equiv). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 92.8 v/v) to afford the title compound as a colorless oil (157 mg, 56% yield, 93% ee). The ee (93%) was determined by HPLC analysis on a Daicel Chiralpak IC column: 85:15 hexane/iPrOH, flow rate 1.00 mL/min; λ = 254 nm; τmajor = 14.3 min, τminor = 15.6 min.
(S)-4-(2-benzoylphenyl)-3-methylbutanal (5b). Compound 5b was prepared according to the general procedure A using 2-methylbenzophenone 1a (36 µL, 0.2 mmol, 1 equiv), trans-crotonaldehyde (91 µL, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as a colorless oil (34 mg, 64% yield, 79% ee). TLC (hexane/EtOAc: 90/10 v/v): Rf = 0.32. The ee value (79%) was determined by HPLC analysis on a Daicel Chiralpak IC column 85:15 hexane:iPrOH flow rate 1.00 mL/min; λ = 254 nm; τmajor = 11.9 min, τminor = 12.8 min. [α]D = + 17.5 (c = 1.0 in CHCl3). HRMS calculated for [C18H18O2]: 289,1204; found 289,1205.

1H NMR (400 MHz, CDCl3) δ 9.63 (dd, J = 2.6, 1.6 Hz, 1H, CHO), 7.86 – 7.88 (m, 2H, Ar), 7.61 (m, 1H, Ar), 7.52 – 7.42 (m, 3H, Ar), 7.36 – 7.27 (m, 3H, Ar), 2.72 (dd, J = 13.6, 7.1 Hz, 1H, H1'α), 2.66 (dd, J = 13.6, 7.2 Hz, 1H, H1'β), 2.44 – 2.33 (m, 2H, H2), 2.23 (td, J = 8.7, 8.1, 2.6 Hz, 1H, H3), 0.93 (d, J = 6.5 Hz, 3H, CH3).13C NMR (100 MHz, CDCl3) δ 202.5 (C=O), 198.5 (CHO), 139.3 (Cq Ar), 138.8 (Cq Ar), 137.8 (Cq Ar), 133.3 (CH Ar), 131.0 (CH Ar), 130.3 (CH Ar), 130.2 (CH Ar x2), 129.0 (CH Ar), 128.5 (CH Ar x2), 125.7 (CH Ar), 50.3 (CH2), 40.2 (CH2), 30.3 (CH), 20.0 (CH3).

(S)-3-(2-benzoylbenzyl)-4-methylpentanal (5c). Compound 5c was prepared according to the general procedure A using 2-methylbenzophenone 1a (36 µL, 0.2 mmol, 1 equiv), trans-4-methyl-2-pentenal (128 µL, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as a colorless oil (31 mg, 53% yield, 96% ee). TLC (hexane/EtOAc: 90:10 v/v): Rf = 0.35. The ee value (96%) was determined by HPLC analysis on a Daicel Chiralpak IC column 90:10 hexane:iPrOH flow rate 1.00 mL/min; λ = 215 nm; τmajor = 5.4 min, τminor = 4.8 min. [α]D = + 29.8 (c = 1.0 in CHCl3). HRMS calculated for [C20H24O2]: 317,1517; found: 317,1515.

1H NMR (400 MHz, CDCl3) δ 9.51 (t, J = 2.1 Hz, 1H, CHO), 7.85 – 7.80 (m, 2H, Ar), 7.65 – 7.58 (m, 1H, Ar), 7.52 – 7.41 (m, 3H, Ar), 7.36 – 7.27 (m, 3H, Ar), 2.89 (dd, J = 13.8, 5.8 Hz, 1H, H1'α), 2.52 (dd, J = 13.8, 8.6 Hz, 1H, H1'β), 2.29 (dd, J = 6.0, 2.2 Hz, 1H, H2α), 2.26 (dd, J = 6.4, 2.2 Hz, 1H, H2β), 2.23 – 2.20 (m, 1H, H3), 1.68 (m, 1H, H4), 0.83 (dd, J = 2.2 Hz, 3H, CH3), 0.81 (d, J = 2.2 Hz, 3H, CH3).13C NMR (100 MHz, CDCl3) δ 202.9 (C=O), 198.4 (CHO), 139.5 (Cq Ar), 138.9 (Cq Ar), 137.7 (Cq Ar), 133.3 (CH Ar) 131.1 (CH Ar), 130.2 (CH Ar), 130.2 (CH Ar x2), 128.9 (CH Ar x2), 128.5 (CH Ar x2), 125.7 (CH Ar), 44.8 (CH2), 40.86 (CH2), 34.7 (CH), 30.0 (CH), 19.3 (CH3), 18.5 (CH3).

(S)-3-(2-benzoylbenzyl)decanal (5d). Compound 5d was prepared according to the general procedure A, using 2-methylbenzophenone 1a (36 µL, 0.2 mmol, 1 equiv), trans-2-decanal (202 µL, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 95:5 v/v) to afford the title compound as a colorless oil (37 mg, 53% yield, 82% ee). TLC (hexane/EtOAc: 90/10 v/v): Rf = 0.36. The ee value (82%) was determined by HPLC analysis on a Daicel Chiralpak IC column 90:10 hexane:iPrOH flow rate 1.00 mL/min; λ = 254 nm; τmajor = 7.9 min, τminor = 8.5 min. [α]D = + 24.8 (c = 0.4 in CHCl3). HRMS calculated for [C21H30O2]: 345,1830; found: 345,1833.
\[ \text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 9.57 (t, \( J = 2.1 \) Hz, 1H, CHO), 7.81 (m, 2H, CH Ar), 7.66 – 7.56 (m, 1H, Ar), 7.52 – 7.40 (m, 3H, Ar), 7.35 – 7.26 (m, 3H, Ar), 2.87 (dd, \( J = 13.8 \), 6.1 Hz, 1H, H1'\( \alpha \)), 2.56 (dd, \( J = 13.7 \), 7.9 Hz, 1H, H1'\( \beta \)), 2.35 – 2.16 (m, 3H, H2+H3), 1.31 – 1.07 (m, 8H), 0.84 (t, \( J = 6.9 \) Hz, 3H, CH\(_3\)). \( ^{13}\text{C NMR (100 MHz, CDCl}_3 \] \( \delta \) 202.8 (C=O), 198.4 (CHO), 139.4 (Cq Ar), 138.9 (Cq Ar), 137.7 (Cq Ar), 133.3 (CH Ar), 131.1 (CH Ar), 130.2 (CH Ar x2), 128.9 (CH Ar), 128.5 (CH Ar x2), 125.7 (CH Ar), 47.9 (CH\(_2\)), 37.9 (CH\(_2\)), 35.3 (CH\(_2\)), 34.3 (CH\(_2\)), 31.8 (CH), 26.2 (CH\(_2\)), 22.5 (CH\(_2\)), 14.0 (CH\(_3\)).

(S)-3-(2-benzoylbenzyl)-5-phenylpentanal (5e). Compound 5e was prepared according to the general procedure A, using 2-methylbenzophenone 1a (36 \( \mu \)L, 0.2 mmol, 1 equiv.), \textit{trans}-5-phenylpentenal (176 mg, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as a colorless oil (41 mg, 57% yield, 89% ee). TLC (hexane/EtOAc: 90/10 v/v): \( R_f = 0.33 \). The ee value (89%) was determined by HPLC analysis on a Daicel Chiralpak IC column 85:15 hexane:iPrOH flow rate 0.90 mL/min; \( \lambda = 254 \) nm; \( \tau_{major} = 12.6 \) min, \( \tau_{minor} = 13.9 \) min. \( [\alpha]^{25}_D = +98.6 \) (c = 1.0 in CHCl\(_3\)). HRMS calculated for [C\(_{25}\)H\(_{27}\)O\(_2\)+Na\(^+\)]\(^{+}\): 379,1674; found: 379,1677.

\( ^{1}\text{H NMR (400 MHz, CDCl}_3 \] \( \delta \) 9.58 (t, \( J = 2.0 \) Hz, 1H, CHO), 7.81 (m, 2H, Ar), 7.66 – 7.57 (m, 1H, Ar), 7.51 – 7.43 (m, 3H, Ar), 7.38 – 7.29 (m, 3H, Ar), 7.27 – 7.20 (m, 2H, Ar), 7.19 – 7.12 (m, 1H, Ar), 7.09 (m, 2H, Ar), 2.97 (dd, \( J = 13.8 \), 6.0 Hz, 1H, H1'\( \alpha \)), 2.66 (dd, \( J = 13.8 \), 8.0 Hz, 1H, H1'\( \beta \)), 2.60 – 2.49 (m, 1H, H3), 2.37 – 2.35 (m, 1H, H3), 2.31 (m, 2H, H5), 1.64 (m, 2H, H4). \( ^{13}\text{C NMR (100 MHz, CDCl}_3 \] \( \delta \) 202.6 (C=O), 198.4 (CHO), 141.8 (Cq Ar), 139.2 (Cq Ar), 138.9 (Cq Ar), 137.7 (Cq Ar), 133.3 (CH Ar), 131.1 (CH Ar), 130.3 (CH Ar), 130.2 (CH Ar x2), 128.9 (CH Ar), 129.0 (CH Ar), 128.5 (CH Ar x2), 128.3 (CH Ar x2), 128.2 (CH Ar x2), 125.8 (CH Ar), 47.8 (CH\(_2\)), 37.7(CH\(_2\)), 36.1 (CH\(_2\)), 35.1 (CH\(_2\)), 33.0 (CH).
Benzyl (R)-4-(2-benzoylbenzyl)-dihydropyridine-1(2H)-carboxylate (5g). Compound 5g was prepared according to the general procedure A, using 2-methylbenzophenone 1a (36 μL, 0.2 mmol, 1 equiv.), trans-benzyl-(5-oxopentenyl)carbamate (257 mg, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 80:20 v/v) to afford the title compound as a colorless oil (41 mg, 50% yield, 89% ee). TLC (hexane/EtOAc: 85:15 v/v): Rf = 0.35. The ee (89%) was determined by HPLC analysis on a Daicel Chiralpak ID-3 column 87:13 hexane:iPrOH flow rate 0.90 mL/min; λ = 254 nm; τmajor = 15.1 min, τminor = 13.7 min. HRMS calculated for [C23H32NO4+Na]+: 434,1732; found: 434,1733.

\[ \text{H NMR (400 MHz, CDCl}_3) \delta 7.83 - 7.76 (m, 2H, Ar), 7.65 - 7.57 (m, 1H, Ar), 7.50 - 7.43 (m, 3H, Ar), 7.41 - 7.29 (m, 8H, Ar), 7.23 - 7.15 (m, 1H, Ar), 3.56 (p, J = 12.9, 9.1 Hz, 1H, H2'), 2.82 - 2.63 (m, 2H, H4), 2.46 (m, 1H, H3), 1.75 (m, 1H, H1'α), 1.57 - 1.43 (m, 1H, H1'β). \]

\[ \text{13C NMR (100 MHz, CDCl}_3) \delta 198.5 (CHO), 153.4 (Cq Ar), 139.0 (Cq Ar), 138.8 (Cq Ar), 137.8 (Cq Ar), 136.3 (CH Ar), 133.3 (CH Ar), 131.1 (CH Ar), 130.1 (CH Ar x2), 129.0 (CH Ar), 128.5 (CH Ar x2), 128.1 (CH Ar), 128.0 (CH Ar), 124.8 (Cq Ar), 110.1 (CH), 67.5 (CH2 Cbz), 40.6 (CH2), 39.2 (CH2), 33.7 (CH), 27.4 (CH3). \]

The title compound 5g is directly obtained from the corresponding β-benzylated aldehyde (not isolated) spontaneously undergoing a cyclization/condensation sequence involving the amine and the aldehyde moieties (Scheme S2).

\[
\text{Scheme S2. Reaction mechanism for the formation of the cyclic compound 5g.}
\]

(S)-4-(2-benzoylphenyl)-3-phenylbutanal (5h). Compound 5h was prepared according to the general procedure B, using 2-methylbenzophenone 1a (72 μL, 0.4 mmol, 2 equiv.), trans-cinnamaldehyde (25 μL, 0.2 mmol, 1 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4a (13 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 95:5 v/v) to afford the title compound as a colourless oil (37 mg, 57% yield, 94% ee). TLC: (hexane/EtOAc: 90:10 v/v); Rf = 0.31. The ee (94%) was determined by UPC² analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO² to 60:40 CO²:ACN), flow rate 2.00 mL/min; λ = 247 nm; τmajor = 3.17 min, τminor = 3.53 min. [α]²⁰_D = +12.6 (c = 0.5 in CHCl₃). HRMS calculated for [C23H20O₂+Na]⁺: 351,1361; found: 351,1365.

\[ \text{1H NMR (500 MHz, CDCl}_3) \delta 9.56 (t, J = 2.1 Hz, 1H, CHO), 7.75 - 7.68 (m, 2H, Ar), 7.64 - 7.57 (m, 1H, Ar), 7.50 - 7.42 (m, 2H, Ar), 7.37 (m, 2H, Ar), 7.31 - 7.23 (m, 2H, Ar), 7.18 (m, 3H, Ar), 7.15 - 7.10 (m, 1H, Ar), 7.10 - 7.05 (m, 2H, Ar), 3.56 (p, J = 7.6 Hz, 1H, CH H3), 3.15 - 2.99 (m, 2H, CH₃H1'), 2.85 - 2.67 (m, 2H, CH₂ H2). \]

\[ \text{13C NMR (125 MHz, CDCl}_3) \delta 201.6 (C=O), 198.3 (CHO), 142.8 (Cq Ar), 138.8 (Cq Ar), 138.6 (Cq Ar), 137.8 (Cq Ar), 133.2 (CH Ar), 131.2 (CH}
(S)-4-(2-benzoylphenyl)-3-(4-fluorophenyl)butanal (5i). Compound 5i was prepared according to the general procedure B, using 2-methylbenzophenone 1a (72 μL, 0.4 mmol, 2 equiv.), trans-4-fluorocinnamaldehyde (23 μL, 0.2 mmol, 1 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4a (13 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 95:5 v/v) to afford the title compound as a colourless oil (36 mg, 52% yield, 89% ee). TLC: (hexane/EtOAc: 90:10 v/v), Rf = 0.31. The ee (89%) was determined by UPC2 analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO2 to 60:40 CO2:ACN), flow rate 2.00 mL/min; λ = 247 nm; τmajor = 3.96 min. τminor = 3.50 min. [α]D26 = +8.8 (c = 0.5 in CHCl3). HRMS calculated for [C23H15FO+Na]+: 369,1267; found: 369,1269.

1H NMR (400 MHz, Chloroform-d) δ 9.57 (t, J = 1.9 Hz, 1H, CHO), 7.71 – 7.65 (m, 2H, Ar), 7.64 – 7.57 (m, 1H, Ar), 7.45 (m, 2H, Ar), 7.38 (m, 1H, Ar), 7.31 – 7.23 (m, 3H, Ar), 7.17 (m, 1H, Ar), 7.05 – 6.96 (m, 2H, Ar), 6.88 – 6.78 (m, 2H, Ar), 3.56 (p, J = 7.5 Hz, 1H, H3), 3.13 – 2.98 (m, 2H, H1\'), 2.75 (m, 2H, H2). 13C NMR (125 MHz, CDCl3) δ 201.2 (C=O), 198.2 (CHO), 138.7, 138.5, 137.6, 133.2 (CH Ar), 131.2 (CH Ar), 130.3 (CH Ar), 130.2 (CH Ar x2), 129.2 (CH Ar), 129.0 (CH Ar), 129.0 (CH Ar), 128.4 (CH Ar x2), 125.7, 115.4, 115.3, 49.5 (CH), 42.0 (CH2), 40.2 (CH2).

(S)-4-(2-benzoylphenyl)-3-(p-tolyl)butanal (5j). Compound 5j was prepared according to the general procedure B, using 2-methylbenzophenone 1a (72 μL, 0.4 mmol, 2 equiv.), trans-4-methylcinnamaldehyde (29mg, 0.2 mmol, 1 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4a (13 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 95:5 v/v) to afford the title compound as a colourless oil (36 mg, 66% yield, 88% ee). TLC: (hexane/EtOAc: 90:10 v/v), Rf = 0.31. The ee (88%) was determined by UPC2 analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO2 to 60:40 CO2:ACN), flow rate 2.00 mL/min; λ = 247 nm; τmajor = 3.23 min. τminor = 3.71 min. HRMS calculated for [C24H18O2+Na]+: 365,1517; found: 365,1520.

1H NMR (500 MHz, CDCl3) δ 9.55 (t, J = 2.1 Hz, 1H, CHO), 7.73 – 7.65 (m, 2H, Ar), 7.62 – 7.57 (m, 1H, Ar), 7.48 – 7.41 (m, 2H), 7.38 (m, 1H, Ar), 7.29 – 7.18 (m, 3H), 7.03 – 6.89 (m, 4H), 3.50 (dd, J = 15.1, 8.1, 6.9 Hz, 1H, H3), 3.12 (dd, J = 13.7, 8.2 Hz, 1H, H1\', 0.30 (dd, J = 13.6, 7.0 Hz, 1H, H1\'\'), 2.78 – 2.67 (m, 2H, H2), 2.24 (s, 3H, CH3). 13C NMR (125 MHz, CDCl3) δ 201.8 (C=O), 198.3 (CHO), 139.7 (Cq Ar), 139.0 (Cq Ar), 138.6 (Cq Ar), 137.7 (Cq Ar), 136.2 (Cq Ar), 133.1 (CH Ar), 131.2 (CH Ar), 130.3 (CH Ar x2), 130.2 (CH Ar), 129.3 (CH Ar x2), 129.1 (CH Ar), 128.3 (CH Ar x2), 127.4 (CH Ar x2), 125.5 (CH Ar), 49.4 (CH), 41.8 (CH2), 40.1 (CH2), 21.0 (CH3).

(S)-4-(2-benzoylphenyl)-3-(furan-2-yl)butanal (5k). Compound 5k was prepared according to the general procedure B, using 2-methylbenzophenone 1a (72 μL, 0.4 mmol, 2 equiv.), trans-3-(furanyl)acrolein (24.5 mg, 0.2 mmol, 1 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4a (13 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 95:5 v/v) to afford the title compound as a colourless oil (33 mg, 56% yield, 90% ee). TLC:
(hexane/EtOAc: 90:10 v/v), Rf = 0.3. The ee (90%) was determined by UPC^2 analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO\textsubscript{2} to 60:40 CO\textsubscript{2}:ACN), flow rate 2.00 mL/min; λ = 247 nm; τ\textsubscript{major} = 2.86 min, τ\textsubscript{minor} = 2.99 min. [α]\textsuperscript{20}\textsubscript{D} = 17.6 (c = 0.35 in CHCl\textsubscript{3}). HRMS calculated for [C\textsubscript{23}H\textsubscript{25}O\textsubscript{4}Na\textsuperscript{+}]: 341.1154; found: 341.1155.

\textbf{1H NMR (400 MHz, Chloroform-d)} δ 9.63 (t, J = 2.0 Hz, 1H, CHO), 7.84 – 7.74 (m, 2H, Ar), 7.66 – 7.58 (m, 1H, Ar), 7.53 – 7.45 (m, 2H, Ar), 7.43 – 7.24 (m, 5H, Ar), 7.13 (m, 1H, Ar), 6.19 (dd, J = 3.2, 1.8 Hz, 1H, HetAr), 5.90 (dt, J = 3.3, 0.7 Hz, 1H, HetAr), 3.68 (p, J = 7.9 Hz, 1H, H3), 3.16 (dd, J = 13.6, 8.1 Hz, 1H, H1\textquoteright α), 3.01 (dd, J = 13.6, 6.9 Hz, 1H, H1\textquoteright β), 2.75 (ddd, J = 16.8, 8.3, 2.2 Hz, 1H, H2α), 2.67 (ddd, J = 16.8, 6.0, 1.8 Hz, 1H, H2β). \textit{13C NMR (125 MHz, CDCl\textsubscript{3})} δ 204.1 (C=O), 201.2 (CHO), 141.4 (CH Ar), 138.6 (Cq Ar), 138.3 (Cq Ar), 137.7 (Cq Ar), 133.2 (CH Ar), 131.1 (CH Ar), 130.3 (CH Ar x2), 130.3 (CH Ar), 129.2 (CH Ar), 128.4 (CH Ar x2), 125.8 (Cq HetAr), 110.0 (CH HetAr), 106.2 (CH HetAr), 100.0 (CH HetAr), 46.9 (CH), 37.5 (CH\textsubscript{2}), 35.4 (CH\textsubscript{2}).

(S)-3-(2-benzoyl-5-methoxybenzyl)pentanal (5l). Compound 5l was prepared according to the general procedure A, using 2-methyl-4-methoxybenzophenone (45.3 mg, 0.2 mmol, 1 equiv.), \textit{trans}-2-pentenal (108 μL, 1.1 mmol, 5.5 equiv.), diphenyl phorphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 85:15 v/v) to afford the title compound as a colorless oil (32 mg, 52% yield, 90% ee). TLC (hexane/EtOAc: 85/15 v/v): R\textsubscript{f} = 0.34. The ee value (90%) was determined by HPLC analysis on a Daicel Chiralpak IC column 55:42:3 hexane:iPrOH:DCM flow rate 0.90 mL/min; λ = 254 nm; τ\textsubscript{major} = 10.8 min, τ\textsubscript{minor} = 11.8 min. [α]\textsuperscript{20}\textsubscript{D} = +135.7 (c = 1.0 in CHCl\textsubscript{3}). HRMS calculated for [C\textsubscript{22}H\textsubscript{24}O\textsubscript{4}Na\textsuperscript{+}]: 333.1467; found: 333.1466.

\textbf{1H NMR (500 MHz, CDCl\textsubscript{3})} δ 9.63 (t, J = 2.3 Hz, 1H, CHO), 7.81 – 7.75 (m, 2H, Ar), 7.62 – 7.57 (m, 1H), 7.52 – 7.43 (m, 2H, Ar), 7.34 (d, J = 8.5 Hz, 1H, Ar), 6.86 (d, J = 2.6 Hz, 1H, Ar), 6.79 (dd, J = 8.5, 2.6 Hz, 1H, Ar), 3.89 (s, 3H, OMe), 2.97 (dd, J = 13.5, 6.6 Hz, 1H, H1\textquoteright α), 2.68 (dd, J = 13.6, 8.2 Hz, 1H, H1\textquoteright β), 2.35-2.32 (m, 2H, H2), 2.24 (dq, J = 8.2, 6.4 Hz, 1H, H3), 1.46 – 1.30 (m, 2H, H4). 0.87 (t, J = 7.4 Hz, 3H, CH\textsubscript{3}). \textit{13C NMR (125 MHz, CDCl\textsubscript{3})} δ 202.9 (C=O), 197.7 (CHO), 161.2 (Cq Ar), 143.0 (Cq Ar), 138.8 (Cq Ar), 132.7 (CH Ar), 132.4 (CH Ar), 131.0 (Cq Ar), 130.1 (CH Ar), 128.3 (CH Ar), 117.1 (CH Ar), 110.4 (CH Ar), 55.4 (CH\textsubscript{3} OMe), 47.5 (CH\textsubscript{2}), 37.8 (CH\textsubscript{2}), 36.8 (CH\textsubscript{2}), 26.9 (CH\textsubscript{3}), 11.0 (CH\textsubscript{3}).

(S)-3-(2-benzoylbenzyl)pentanal (5m). Compound 5m was prepared according to the general procedure A, using 2-methyl-5-bromobenzophenone (55 mg, 0.2 mmol, 1 equiv.), \textit{trans}-2-pentenal (108 μL, 1.1 mmol, 5.5 equiv.), diphenyl phorphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 85:15 v/v) to afford the title compound as a colorless oil (48 mg, 66% yield, 94% ee). TLC (hexane/EtOAc: 85/15 v/v): R\textsubscript{f} = 0.34. The ee value (94%) was determined by HPLC analysis on a Daicel Chiralpak IA column 96:2:2 hexane:iPrOH:DCM flow rate 0.70 mL/min; λ = 254 nm; τ\textsubscript{major} = 12.0 min, τ\textsubscript{minor} = 12.5 min. [α]\textsuperscript{26}\textsubscript{D} = +168.6 (c = 0.6 in CHCl\textsubscript{3}). HRMS calculated for [C\textsubscript{19}H\textsubscript{25}BrO\textsubscript{2}Na\textsuperscript{+}]: 381.0466; found: 381.0461.

\textbf{1H NMR (400 MHz, CDCl\textsubscript{3})} δ 9.60 (t, J = 2.1 Hz, 1H, CHO), 7.80 (m, 2H, Ar), 7.69 – 7.39 (m, 5H, Ar), 7.30 – 7.18 (m, 1H, Ar), 2.74 (dd, J = 13.8, 6.8 Hz, 1H, H1\textquoteright α), 2.51 (dd, J = 13.8, 6.9 Hz, 1H, H1\textquoteright β), 2.35 – 2.25 (m, 2H, H2α+H2β), 2.14 (dt, J = 13.5, 6.7 Hz, 1H, H3), 1.41 – 1.18 (m, 2H, H4α+H4β), 0.81 (t, J = 7.4 Hz, 3H, CH\textsubscript{3}). \textit{13C NMR (100 MHz, CDCl\textsubscript{3})} δ 202.4 (C=O), 196.7
(S)-3-(2-benzyol-5-methylbenzyl)pentanal (5n). Compound 5n was prepared according to the general procedure A, using 2,4-dimethylbenzophenone (44 mg, 0.2 mmol, 1 equiv.), trans-2-pentenial (108 μL, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as a colorless oil (37 mg, 63% yield, 90% ee). TLC: (hexane/EtOAc: 90:10 v/v), Rf = 0.30. The ee (90%) was determined by HPLC analysis on a Daicel Chiralpak IC column 85:15 hexane:iPrOH flow rate 1.00 mL/min; λ = 254 nm; τmajor = 11.6 min, τminor = 16.7 min. [α]D 26 = +75.6 (c = 0.7 in CHCl3). HRMS calculated for [C20H22O2Na]+: 317,1517; found: 317,1519.

1H NMR (400 MHz, CDCl3) δ 9.60 (t, J = 2.2 Hz, 1H, CHO), 7.83 – 7.76 (m, 2H, Ar), 7.63 – 7.56 (m, 1H, Ar), 7.47 (dd, J = 8.3, 7.1 Hz, 2H, Ar), 7.30 – 7.22 (m, 1H, Ar), 7.16 – 7.05 (m, 2H, Ar), 2.87 (dd, J = 13.6, 6.5 Hz, 1H, H1'α), 2.58 (dd, J = 13.6, 8.2 Hz, 1H, H1'β), 2.42 (s, 3H, Me), 2.31 (m, 2H, H2), 2.20 (dp, J = 8.3, 6.3 Hz, 1H, H3), 1.44 – 1.25 (m, 2H, H4), 0.84 (t, J = 7.4 Hz, 3H, CH3).

13C NMR (100 MHz, CDCl3) δ 203.0 (C=O), 198.4 (CHO), 140.6 (Cq Ar), 139.8 (Cq Ar), 139.4 (Cq Ar), 138.4 (Cq Ar), 138.3 (Cq Ar), 137.0 (Cq Ar), 136.8 (Cq Ar), 133.8 (CH Ar) 133.1 (CH Ar), 132.7 (CH Ar), 131.3 (CH Ar), 131.0 (CH Ar x2), 129.6 (CH Ar), 128.7 (CH Ar x2), 119.6 (CH Ar), 47.3 (CH2), 36.9 (CH2), 36.5 (CH), 26.6 (CH2), 10.9 (CH3).

(S)-4-(2-benzoyl-5-(trifluoromethyl)phenyl)-3-phenylbutanal (5o). Compound 5o was prepared according to the general procedure B using 4-(trifluoromethyl)-2-methylbenzophenone (106mg, 0.4 mmol, 2 equiv.), trans-cinnamaldehyde (25 μL, 0.2 mmol, 1 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4a (13 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 95:5 v/v) to afford the title compound as a colourless oil (46 mg, 58% yield, 97% ee). TLC: (hexane/EtOAc: 90:10 v/v), Rf = 0.33. The ee (97%) was determined by analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO2 to 60:40 CO2:ACN), flow rate 2.00; λ = 247 nm; τmajor = 2.27 min, τminor = 2.51 min. [α]D 26 = 40.3 (c = 0.28 in CHCl3). HRMS calculated for [C25H26F4O2Na]+: 419,1235; found: 419,1237.

1H NMR (500 MHz, CDCl3) δ 9.60 (t, J = 1.9 Hz, 1H, CHO), 7.71 – 7.66 (m, 2H, Ar), 7.66 – 7.61 (m, 1H, Ar), 7.53 – 7.45 (m, 3H, Ar), 7.42 – 7.34 (m, 1H, Ar), 7.32 – 7.30 (m, 1H, Ar), 7.23 – 7.11 (m, 3H, Ar), 7.05 – 7.01 (m, 2H, Ar), 3.53 (tt, J = 8.5, 6.5 Hz, 1H, H3), 3.10 (dd, J = 13.8, 6.4 Hz, 1H, H1’α), 3.05 (dd, J = 13.7, 8.9 Hz, 1H, H1’β), 2.82 (ddd, J = 16.9, 8.1, 2.0 Hz, 1H, H2α), 2.75 (ddd, J = 16.9, 6.7, 1.8 Hz, 1H, H2β).

13C NMR (125 MHz, CDCl3) δ 201.0 (C=O), 197.1 (CHO), 141.9 (Cq Ar), 139.4 (Cq Ar), 136.8 (Cq Ar), 133.8 (CH Ar), 130.2 (CH Ar x2), 129.1 (Cq Ar), 128.9 (Cq Ar), 128.7 (CH Ar x2), 128.6 (CH Ar x2), 127.9, 127.5 (CH Ar x2), 127.0 (CH Ar), 125.6, 122.6, 49.2 (CH), 41.7 (CH2), 36.0 (CH2).

(S)-3-(2-(4-bromobenzyol)benzyl)pentanal (5p). Compound 5p was prepared according to the general procedure A, using (4-bromophenyl)(o-tolyl)methanone (55 mg, 0.2 mmol, 1 equiv.), trans-2-pentenial (108 μL, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture
was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as a colorless oil (44 mg, 61% yield, 91% ee). TLC: (hexane/EtOAc: 90:10 v/v), R$_f$ = 0.32. The ee (91%) was determined by HPLC analysis on a Daicel Chiralpak IC column 97:03 hexane:iPrOH flow rate 0.80 mL/min; $\lambda$ = 254 nm; $\tau_{\text{major}}$ = 14.0 min, $\tau_{\text{minor}}$ = 15.8 min. [$\alpha$]$^{26}_{D}$ = +146.7 (c = 0.5 in CHCl$_3$). HRMS calculated for [C$_{19}$H$_{19}$BrO$_2$+Na]$^+$: 381.0466; found: 381.0466.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.60 (t, $J$ = 2.1 Hz, 1H, CHO), 7.71 – 7.65 (m, 2H, Ar), 7.65 – 7.58 (m, 2H, Ar), 7.46 (m, 1H, Ar), 7.37 – 7.26 (m, 3H, Ar), 2.85 (dd, $J$ = 13.7, 6.6 Hz, 1H, H'1$\alpha$), 2.57 (dd, $J$ = 13.7, 8.2 Hz, 1H, H'1$\beta$), 2.34 – 2.27 (m, 2H, H2), 2.18 (m, 1H, H3), 1.40 – 1.24 (m, 2H, H4), 0.84 (t, $J$ = 7.4 Hz, 3H, CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 202.6 (C=O), 197.3 (CHO), 139.7 (Cq Ar), 139.5 (Cq Ar), 138.5 (Cq Ar), 131.9 (CH Ar x2), 131.6 (CH Ar x2), 131.2 (CH Ar), 130.5 (CH Ar), 128.8 (Cq Ar), 125.8 (CH Ar), 47.5 (CH$_2$), 37.4 (CH$_2$), 36.8 (CH$_2$), 26.8 (CH$_3$), 11.0 (CH$_3$).

Compound 5p was also obtained using a 1 mmol scale procedure using (4-bromophenyl)(o-tolyl)methanone 5p (275 mg, 1 mmol, 1 equiv.), trans-2-pentenal (540 μL, 5.5 mmol, 5.5 equiv.), diphenyl phosphoric acid (25 mg, 0.1 mmol, 0.1 equiv.) and catalyst 4b (75 mg, 0.2 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 92:8 v/v) to afford the title compound as a colorless oil (216 mg, 60% yield, 90% ee). TLC: (hexane/EtOAc: 90:10 v/v). The ee (90%) was determined by HPLC analysis on a Daicel Chiralpak IC column 97:03 hexane:iPrOH flow rate 0.80 mL/min; $\lambda$ = 254 nm; $\tau_{\text{major}}$ = 14.00 min, $\tau_{\text{minor}}$ = 15.79 min.

(S)-3-[2-(4-methoxybenzoyl)benzyl]pentanal (5q). Compound 5q was prepared according to the general procedure A, using (4-methoxyphenyl)(o-tolyl)methanone (45 mg, 0.2 mmol, 1 equiv.), trans-2-pentenal (108 μL, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as a colorless oil (42 mg, 67% yield, 84% ee). TLC: (hexane/EtOAc: 90:10 v/v), R$_f$ = 0.33. The ee (84%) was determined by HPLC analysis on a Daicel Chiralpak IC-3 column 85:15 hexane:iPrOH flow rate 1.00 mL/min; $\lambda$ = 254 nm; $\tau_{\text{major}}$ = 20.3 min, $\tau_{\text{minor}}$ = 22.8 min. [$\alpha$]$^{26}_{D}$ = +150.5 (c = 0.7 in CHCl$_3$). HRMS calculated for [C$_{29}$H$_{22}$O$_4$+Na]$^+$: 333,1467; found: 333,1470.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.58 (t, $J$ = 2.2 Hz, 1H, CHO), 7.88 – 7.75 (m, 2H, Ar), 7.43 (m, 1H, Ar), 7.34 – 7.25 (m, 3H, Ar), 6.98 – 6.89 (m, 2H, Ar), 3.90 (s, 3H, OMe), 2.83 (dd, $J$ = 13.8, 6.5 Hz, 1H, H'1$\alpha$), 2.54 (dd, $J$ = 13.8, 8.2 Hz, 1H, H'1$\beta$), 2.29 (m, 2H, H2), 2.18 (dq, $J$ = 8.2, 6.4 Hz, 1H, H3), 1.37 – 1.28 (m, 2H, H4), 0.83 (t, $J$ = 7.4 Hz, 3H, CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 202.9 (C=O), 197.1 (CHO), 163.8 (Cq Ar), 139.5 (Cq Ar), 138.8 (Cq Ar), 132.5 (CH Ar), 130.9 (CH Ar), 130.6 (Cq Ar), 129.8 (CH Ar), 128.4 (CH Ar), 125.7 (CH Ar), 113.7 (CH Ar), 55.5 (OMe), 47.5 (CH$_2$), 37.4 (CH$_2$), 36.7 (CH$_2$), 26.8 (CH), 11.0 (CH$_3$).

(S)-4-[2-(4-Methoxybenzoyl)phenyl]-3-phenylbutanal (5r). Compound 5r was prepared according to the general procedure B, using (4-methoxyphenyl)(o-tolyl)methanone (90 mg, 0.4 mmol, 2 equiv.), trans-cinnamaldehyde (25 μL, 0.2 mmol, 1 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4a (13 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 95:5 v/v) to afford the title compound as a colourless oil (43 mg, 60% yield, 90% ee). TLC: (hexane/EtOAc: 90:10 v/v), R$_f$ = 0.28. The ee (90%) was determined by UPC$^2$ analysis on a Daicel Chiralpak IC column using a gradient method (from
100% CO$_2$ to 60:40 CO$_2$:ACN), flow rate 2.00 mL/min; λ = 283 nm; $\tau_{\text{major}} = 3.78$ min, $\tau_{\text{minor}} = 4.19$ min. [$\alpha$]$^D_{26} = 63.5$ (c = 0.3 in CHC$_3$). HRMS calculated for [C$_{24}$H$_{12}$O$_3$+Na]$^+$: 381,1467; found: 381,1470.

**1H NMR (500 MHz, CDCl$_3$)** δ 9.60 (t, $J = 1.9$ Hz, 1H, CHO), 7.71–7.66 (m, 2H, Ar), 7.66–7.61 (m, 1H, Ar), 7.53–7.45 (m, 4H, Ar), 7.42–7.34 (m, 2H, Ar), 7.32–7.30 (m, 1H, Ar), 7.23–7.11 (m, 3H, Ar), 7.05–7.01 (m, 2H, Ar), 3.53 (m, 1H, H3), 3.10 (dd, $J = 13.8$, 6.4 Hz, 1H, H1$'$α), 3.05 (dd, $J = 13.7$, 8.9 Hz, 1H, H1$'$β), 2.82 (ddd, $J = 16.9$, 8.1, 2.0 Hz, 1H, H2$α$), 2.75 (ddd, $J = 16.9$, 6.7, 1.8 Hz, 1H, H2$β$). **13C NMR (125 MHz, CDCl$_3$)** δ 201.7 (C=O), 197.0 (CHO), 163.7 (Cq Ar), 142.9 (Cq Ar), 139.2 (Cq Ar), 138.2 (Cq Ar), 132.6 (CH Ar x2), 131.0, 130.6 (Cq Ar), 129.8 (CH Ar), 128.6 (CH Ar), 128.5 (CH Ar x2), 127.5 (CH Ar x2), 126.7 (CH Ar), 125.6 (CH Ar), 113.7 (CH Ar x2), 55.5 (CH$_3$ OMe), 49.1 (CH), 41.9 (CH$_2$), 40.3 (CH$_2$).

(S)-4-[2-(4-fluorobenzoyl)phenyl]-3-phenylbutanal (5s). Compound 5s was prepared according to the general procedure B, using (4-fluorophenyl)(o-tolyl)methanone (86mg, 0.4 mmol, 2 equiv.), trans-cinnamaldehyde (25 μL, 0.2 mmol, 1 equiv.), diphenyl phorphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4a (13 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 95:5 v/v) to afford the title compound as a colourless oil (49 mg, 72% yield, 92% ee). TLC: (hexane/EtOAc: 90:10 v/v), $R_f = 0.30$. The ee (92%) was determined by HPLC analysis on a Daicel Chirapak IC-3 column using an isocratic method (Hexane : i-PrOH, 98:2), flow rate 0.7 mL/min; λ = 254 nm, mL/min; λ = 247 nm; $\tau_{\text{major}} = 14.09$ min, $\tau_{\text{minor}} = 25.20$ min. [$\alpha$]$^D_{26} = +37.6$ (c = 0.5 in CHC$_3$). HRMS calculated for [C$_{25}$H$_{16}$FO$_2$+Na]$^+$: 369,1267; found: 369,1270.

**1H NMR (400 MHz, CDCl$_3$)** δ 9.58 (t, $J = 2.0$ Hz, 1H, CHO), 7.78–7.63 (m, 2H, Ar), 7.38 (m, 1H, Ar), 7.27–7.22 (m, 2H, Ar), 7.22–7.08 (m, 6H, Ar), 7.08–7.02 (m, 2H, Ar), 3.53 (q, $J = 7.5$ Hz, 1H, H3), 3.11 (dd, $J = 13.6$, 8.2 Hz, H1$'$α), 3.04 (dd, $J = 13.6$, 7.0 Hz, 1H, H1$'$β), 2.80–2.72 (m, 2H, 3$H_{2α}$$H_{2β}$). **13C NMR (100 MHz, CDCl$_3$)** δ 201.4 (C=O), 196.7 (CHO), 167.1, 164.5, 142.7 (Cq Ar), 138.8 (Cq Ar), 138.4 (Cq Ar), 134.1 (Cq Ar), 132.9 (CH Ar), 132.8 (CH Ar), 131.3 (CH Ar), 130.3 (CH Ar), 128.9 (CH Ar), 128.6 (CH Ar x2), 127.5 (CH Ar x2), 126.8 (CH Ar), 125.7 (CH Ar), 115.6, 115.4, 49.3 (CH), 42.1 (CH$_2$), 40.0 (CH$_2$).

**(R)-3-[(S)-(2-benzoylphenyl)(phenyl)methyl]pentanal (5t).** Compound 5t was prepared according to the general procedure A, using (2-benzoylphenyl)(phenyl)methanone (54 mg, 0.2 mmol, 1 equiv.), trans-2-pentenal (108 μL, 1.1 mmol, 5.5 equiv.), diphenyl phorphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as colorless oil (32 mg, 45% yield, 98% ee) and as a single diastereoisomer (dr > 20:1, as inferred by $^1$H NMR analysis of the crude mixture). TLC: (hexane/EtOAc: 90:10 v/v), $R_f = 0.33$. The ee (98%) was determined by HPLC analysis on a Daicel Chirapak IC-3 column 85:15 hexane:iPrOH flow rate 0.80 mL/min; λ = 254 nm; $\tau_{\text{major}} = 10.8$ min, $\tau_{\text{minor}} = 11.9$ min. [$\alpha$]$^D_{26} = +13.3$ (c = 0.5 in CHC$_3$). HRMS calculated for [C$_{24}$H$_{22}$O$_2$+Na]$^+$: 379,1674; found: 379,1677.

**1H NMR (400 MHz, CDCl$_3$)** δ 9.54 (t, $J = 1.8$ Hz, 1H, CHO), 7.67–7.60 (m, 2H, Ar), 7.59–7.48 (m, 2H, Ar), 7.40–7.30 (m, 3H, Ar), 7.17–7.01 (m, 7H, Ar), 4.10 (d, $J = 11.6$ Hz, 1H, H1$'$), 2.96 (ddddd, $J = 13.4$, 11.5, 6.0, 3.4 Hz, 1H, H3), 2.40 (d, $J = 1.9$ Hz, 1H, H2$α$), 2.39 (d, $J = 1.9$ Hz, 1H, H2$β$), 1.41–1.28 (m, 1H, H4), 1.16–1.07 (m, 1H, H4), 0.66 (t, $J = 7.4$ Hz, 3H, CH$_3$). **13C NMR (100 MHz, CDCl$_3$)** δ 202.1 (C=O), 198.9 (CHO), 142.8 (Cq Ar), 142.6 (Cq Ar), 139.5 (Cq Ar), 137.9 (Cq Ar), 133.4 (CH Ar), 130.6 (CH Ar), 130.4 (CH Ar x2), 128.5 (CH Ar), 128.5 (CH Ar x2), 128.5 (CH Ar x2), 55.5 (CH$_3$ OMe), 49.1 (CH), 41.9 (CH$_2$), 40.3 (CH$_2$).
(R)-3-[(R)-8-benzoyl-tetrahydrophthalenyl]pentanal (5u). Compound 5u was prepared according to the general procedure A, using phenyl(tetrahydrophthalenyl)methane (47 mg, 0.2 mmol, 1 equiv.), trans-2-pentenal (108 μL, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as an inseparable mixture of two diastereoisomers (colorless oil 30 mg, 47% yield, 97% ee, 7:1 dr, dr inferred by 1H NMR analysis of the crude mixture). TLC: (hexane/EtOAc: 90:10 v/v), Rf = 0.32. The ee (97%) was determined by HPLC analysis on a Daicel Chiralpak IB column 85:15 hexane:iPrOH flow rate 1.00 mL/min; λ = 254 nm; τmajor = 24.0 min, τminor = 30.1 min. [α]26D = - 775.2 (c = 1.00 in CHCl3). HRMS calculated for [C25H25O2Na]+: 343,1674; found: 343,1675.

1H NMR (400 MHz, CDCl3) δ 9.39 (dd, J = 2.9, 2.0 Hz, 1H, CHO), 7.88 – 7.83 (m, 2H, Ar), 7.62 (m, 1H, Ar), 7.49 (m, 2H, Ar), 7.25 – 7.11 (m, 3H), 3.38 (q, J = 6.1 Hz, 1H, H1'), 2.81 (m, 2H, H4), 2.30 – 2.23 (m, 2H, H2), 2.22 – 2.14 (m, 1H, H3), 2.04 – 1.92 (m, 1H, H3α), 1.84 – 1.75 (m, 1H, H3α'), 1.72 – 1.61 (m, 2H, H2'), 1.34 – 1.15 (m, 2H, H4), 0.66 (t, J = 7.4 Hz, CH3). 13C NMR (100 MHz, CDCl3) δ 203.1 (C=O), 198.9 (CHO), 140.3 (Cq Ar), 139.3 (Cq Ar), 138.5 (Cq Ar), 137.7 (Cq Ar), 133.3, 131.1, 130.1 (CH2 Ar x2), 128.5 (CH2 Ar x2), 127.0 (CH Ar), 125.0 (CH Ar), 46.1(CH), 39.8 (CH2), 37.1 (CH2), 30.0 (CH), 23.7 (CH2), 23.1 (CH2), 20.2 (CH2), 11.5 (CH3).

(3R,4R)-4-(2-benzoylphenyl)-3-ethylpentanal (5v). Compound 5v was prepared according to the general procedure A, using 2-ethylbenzophenone (42 mg, 0.2 mmol, 1 equiv.), trans-2-pentenal (108 μL, 1.1 mmol, 5.5 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst 4b (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 90:10 v/v) to afford the title compound as an inseparable mixture of two diastereoisomers (colorless oil, 40 mg, 68% yield, 1:3:1 dr, 87% ee major isomer and 84% ee minor isomer). TLC: (hexane/EtOAc: 90:10 v/v), Rf = 0.29. The ee was determined by HPLC analysis on a Daicel Chiralpak IC-3 column 95:5 hexane:iPrOH flow rate 0.9 mL/min; λ = 254 nm; major diastereoisomer: τmajor = 21.3 min, τminor = 23.7 min (84% ee); minor diastereoisomer: τmajor = 24.4 min, τminor = 26.1 min (87% ee). [α]26D = +5.5 (c = 1.00 in CHCl3). HRMS calculated for [C26H27O2Na]+: 317,1517; found: 317,1520.

Diagnostic signals for the major diastereoisomer: 1H NMR (400 MHz, CDCl3) δ 9.65 (dd, J = 2.5, 1.6 Hz, 1H, CHO), 3.09 (p, J = 7.0 Hz, 1H, H1'), 2.44 (ddd, J = 16.4, 5.0, 1.6 Hz, 1H, H2α), δ 2.30 (dd, J = 7.1, 2.5 Hz, 1H, H2β), δ 1.36 – 1.27 (m, 2H, H4α+H4β), 1.18 (d, J = 7.0 Hz, 3H, CH3), 0.71 (t, J = 7.4 Hz, 3H, CH3).

Diagnostic signals for the minor diastereoisomer: 1H NMR (400 MHz, CDCl3) δ 9.49 (t, J = 2.0 Hz, 1H, CHO), 2.96 – 2.81 (m, 1H, H1'), δ 2.27 – 2.24 (m, 2H, H2), 2.24 – 2.17 (m, 1H, H3), 1.61 – 1.55 (m, 1H, H4α), 1.43 – 1.36 (m, 1H, H4β)1.23 (d, J = 6.8 Hz, 3H, CH3), 0.79 (t, J = 7.5 Hz, 3H, CH3).

Complete overlap of the aromatic signals was observed: 1H NMR (400 MHz, CDCl3) δ 7.86 – 7.79 (m, 4H), 7.65 – 7.57 (m, 2H), 7.52 – 7.41 (m, 9H), 7.31 – 7.25 (m, 5H).

13C NMR (100 MHz, CDCl3) δ 202.8 (C=O), 202.6 (C=O), 198.7 (CHO), 198.7 (CHO), 144.9 (Cq Ar), 144.5 (Cq Ar), 139.1 (Cq Ar x2), 137.8 (Cq Ar), 137.8 (Cq Ar), 133.4 (CH Ar), 133.4 (CH Ar), 130.4 (CH Ar), 130.2 (CH Ar), 130.1 (CH Ar), 128.5 (CH Ar), 128.5 (CH Ar), 128.2 (CH Ar), 128.1 (CH Ar), 127.3 (CH Ar), 127.3 (CH Ar), 125.6 (CH Ar), 125.4 (CH Ar), 46.3 (CH), 45.0
(CH), 40.3 (CH₂), 40.3 (CH₂), 38.2 (CH₂), 37.5 (CH₂), 25.4 (CH), 23.6 (CH), 19.5 (CH₃), 17.6 (CH₃), 11.1 (CH₃), 10.0 (CH₃).

**[(R)-3-[(R)-8-benzoyl-tetrahydronaphthalenyl]-3-(p-tolyl)propanal (5w)]**.

Compound **5w** was prepared according to the general procedure B, using phenyl(tetrahydronaphthalenyl)methanone (96 mg, 0.4 mmol, 2 equiv.), *trans*-cinnamaldehyde (25 μL, 0.2 mmol, 1 equiv.), diphenyl phosphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst **4a** (13 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 93:7 v/v) to afford the title compound as a colourless oil (36.5 mg, 48% yield, 80% ee). TLC: (hexane/EtOAc: 90:10 v/v), Rₓ = 0.33. The ee (80%) was determined by HPLC analysis on a Daicel Chiralpak IC-3 column using a isocratic method (80:20 Hexane:iPrOH), flow rate 0.4 mL/min; λ = 247 nm; τ_major = 24.03 min, τ_minor = 24.92 min. [α]D₂₆ = +18.6 (c = 0.5 in CHCl₃). HRMS calculated for [C₇H₂₆O₂⁺Na⁺]: 405.1830; found: 405.1829.

**¹H NMR (500 MHz, CDCl₃)** δ 9.26 (t, J = 1.9 Hz, 1H, CHO), 7.32 (m, 1H, Ar), 7.22 (m, 3H, Ar), 7.20 – 7.16 (m, 5H, Ar), 7.15 – 7.07 (m, 4H, Ar), 3.66 (ddd, J = 10.0, 4.9, 2.9 Hz, 1H, H₁'), 3.43 (td, J = 9.9, 5.1 Hz, 1H, H₃), 2.84 (m, 2H, H₄'α+H₂α), 2.75 (dd, J = 8.5, 4.7 Hz, 1H, H₂β), 2.58 – 2.49 (ddd, J = 16.8, 5.1, 1.7 Hz, 1H, H₂β), 2.45 (s, 3H, Me), 1.92 (m, 1H, H₃'α), 1.59 (m, 1H, H₃'β), 1.52 – 1.41 (m, 1H, H₂'α), 1.38 – 1.31 (m, 1H, H₂'β). **¹³C NMR (125 MHz, CDCl₃)** δ 202.1 (C=O), 201.3 (CHO), 143.0 (Cq Ar), 140.4 (Cq Ar), 139.6 (Cq Ar), 139.2 (Cq Ar), 139.0 (Cq Ar), 138.4 (Cq Ar), 132.3 (CH Ar), 131.7 (CH Ar), 131.3 (CH Ar), 130.4 (CH Ar), 128.6 (CH Ar x2), 128.5 (CH Ar x2), 128.1 (CH Ar), 126.7 (CH Ar), 125.9 (CH Ar), 125.5 (CH Ar), 125.1 (CH Ar), 48.7 (CH), 42.6 (CH), 40.0 (CH₂), 27.6 (CH₂), 23.7 (CH₂), 21.0 (CH₃ Me), 17.2 (CH₂).
Product Manipulations

The adduct 5 (1 equiv.) was dissolved in dry CHCl₃ (0.03 M solution). Pyrrolidine (20 mol%) and benzoic acid (40 mol%) were sequentially added under an argon atmosphere, and the solution was warmed up to 50 °C. After 48 h stirring, water was added and the biphasic mixture was extracted with DCM (x 3). The organic phases were collected and concentrated under vacuum. The obtained material was then subjected to FC purification to afford the title compound in the stated yield.

(S)-1-(4-bromophenyl)-3-ethylidihydronaphthalene-carbaldehyde (6)
Compound 6 was prepared from (S)-3-(2-(4-bromobenzoyl)benzyl)pentanal 5p (100 mg, 0.27 mmol, 1 equiv.), pyrrolidine (5 μL, 0.05 mmol, 0.2 equiv.) and benzoic acid (13 mg, 0.11 mmol, 0.4 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 97:3 v/v) to afford the title compound as a colorless oil (72 mg, 78% yield, 90% ee). TLC: (hexane/EtOAc: 90:10 v/v), Rₜ = 0.32. The ee (90%) was determined by HPLC analysis on a Daicel Chiralpak IC-3 column 98:2 hexane:iPrOH flow rate 0.80 mL/min; λ = 254 nm; τ_major = 16.51 min, τ_min = 17.37 min. [α]²⁶ D = -4.1 (c = 0.5 g cm⁻³ in CHCl₃). HRMS calculated for [C₁₀H₇BrO⁺Na]⁺: 363,0360; found: 363,0365.

³¹H NMR (500 MHz, Chloroform-d) δ 9.57 (s, 1H, CHO), 7.63 (m, 2H, Ar), 7.32 (td, δ = 7.4, 1.3 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.15 (m, 2H, Ar), 6.83 (dd, δ = 7.8, 1.2 Hz, 1H, Ar), 3.18 – 2.98 (m, 2H, H1α+H3), 2.93 (d, δ = 15.0 Hz, 1H, H1β), 1.49 – 1.38 (m, 1H, H4α), 1.35 – 1.24 (m, 1H, H4β), 0.92 (t, δ = 7.4 Hz, 3H, CH₃). ¹³C NMR (125 MHz, CDCl₃) δ 192.7 (CHO), 152.3 (Cq), 139.0 (Cq Ar), 137.1(Cq Ar), 134.4 (Cq Ar), 134.3 (Cq Ar), 130.5 (CH Ar), 128.9 (CH Ar), 128.1 (CH Ar), 126.6 (CH Ar), 122.8 (Cq), 31.6 (CH₂), 31.3 (CH), 24.1 (CH₂), 11.8 (CH₃).

The absolute configuration of compound 6 was unambiguously inferred by anomalous dispersion X-ray crystallographic analysis (CCDC 1417311), see X-ray Crystallographic Data section.

3-(2-benzoylbenzyl)pentanal (7)
Compound 7 was prepared from 3-((2-benzoylphenyl)(phenyl)methyl)pentanal 5t (17 mg, 0.05 mmol, 1 equiv.), pyrrolidine (0.2 mL of a stock solution in CHCl₃ 0.05 M, 0.2 equiv.) and benzoic acid (0.5 mg, 0.4 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 97:3 v/v) to afford the title compound as a colorless oil (8 mg, 3% yield). TLC: (hexane/EtOAc: 90:10 v/v), Rₜ = 0.32. HRMS calculated for [C₂₅H₂₃O⁺Na]⁺: 361,1576; found: 361,1576.

³¹H NMR (400 MHz, CDCl₃) δ 9.42 (d, δ = 0.6 Hz, 1H, CHO), 7.53 – 7.44 (m, 4H, Ar), 7.37 (m, 1H, Ar), 7.31 – 7.20 (m, 4H, Ar), 7.18 – 7.12 (m, 1H, Ar), 7.09 – 6.97 (m, 3H), 4.25 (s, 1H, H1'), 3.31 (ddd, δ = 7.9, 6.2, 1.5 Hz, 1H, H3), 1.66 – 1.59 (m, 1H, H4α), 1.54 – 1.46 (m, 1H, H4β), 1.07 (t, δ = 7.4 Hz, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 193.2 (CHO), 153.5 (Cq), 143.4 (Cq Ar), 138.4 (Cq Ar), 136.9 (Cq Ar), 136.3 (CH Ar), 135.7 (Cq Ar), 135.3 (CH Ar), 133.1 (CH Ar), 130.8 (CH Ar), 128.6 (CH Ar), 128.5 (CH Ar), 128.3 (CH Ar), 127.5 (CH Ar), 127.3 (CH Ar), 126.3 (Cq), 46.7 (CH), 40.1 (CH), 31.6 (CH₂), 26.1 (CH₂), 12.0 (CH₃).
The stereochemical assignment of compound 7 was based on $^1$H-$^1$H NOESY spectroscopic experiments performed on a 400 MHz instrument. Diagnostic interactions are shown below.

$^1$H-$^1$H NOESY analysis of product 7. Diagnostic nOe interactions.
D. Mechanistic Investigations

1. Transient Absorption Spectroscopy (TAS) Studies

Using the transient spectroscopy system available at the ICIQ (specifications of the equipment can be found in the General Information, page S3), we observed a transient species upon selective irradiation of a $5 \times 10^{-3}$ M solution of 2-methylbenzophenone 1a in cyclohexane, showing an absorption maximum at 450 nm. The half lifetime of the transient was ca. 150 ms (Figure S2). The characteristics of the detected transient are in agreement with literature data obtained upon flash photolysis studies of 1a, which identified the absorption of the ground state ($E$)-photoenol in the region of 400-450 nm (3-5).

![Figure S2](image)

**Figure S2.** Decay of absorption at 450 nm of a transient generated upon 355 nm laser excitation of 2-methylbenzophenone 1a ([1a] = $5 \times 10^{-3}$ M in cyclohexane). ΔOD: optical density variation. $t_{1/2}$ = 150 ms.

We next evaluated the effect of the catalyst 4b on the decay of the absorption of transient ($E$)-photoenol generated from 1a. The results of the flash photolysis studies, conducted in toluene, are shown in Figure S3. We selected a time scale (20 ms) suitable for clearly showing the decay of the transient. It can be appreciated how the formation of the transient is only marginally affected by the presence of increasing amounts of 4b, as indicated by the slight decay of the initial absorption. Repeating the same experiments adding pentenal 3a or cinnamaldehyde did not affect the formation of the transient A to any extent.

![Figure S3](image)

**Figure S3.** Decay of absorption obtained in the presence of the catalyst 4b. Absorption at 450 nm of the transient ($E$)-photoenol A (black line) generated upon 355 nm laser excitation of 2-methylbenzophenone 1a ([1a] = $5 \times 10^{-3}$ M in toluene). Absorption decays (colored lines) observed in the presence of increasing amounts of the amine catalyst 4b. The time scale showed: 20 ms. Studies performed using the transient spectroscopy system specified in the General Information, page S3.
In a typical transient absorption spectroscopy experiment, 2.8 mL of a 5x10^{-3} M toluene solution of 2-methylbenzophenone 1a (0.014 mmol) were added to a screw-top 3.0 mL quartz cuvette. Upon 355 nm laser excitation, the decay of absorption at 450 nm of the transient (E)-photoenol (black line in Figure S3) was collected. The effect of the catalyst 4b was evaluated by sequentially adding, to the original 1a solution, increasing amounts of an equimolar solution of 2-methylbenzophenone 1a and catalyst 4b in toluene (5x10^{-3} M, 1:1 ratio between 1a and 4b). After every addition, the decay of absorption of the transient photoenol was recorded (coloured lines in Figure S3). This procedure allowed us to keep the concentration of 1a constant to 5x10^{-3} M in all the measurements. It is of note that the same experiment, when conducted upon degassing the solutions by bubbling a stream of argon for 10 minutes after every addition, gave a very similar profile for the decay of the transient (E)-photoenol absorption.

Table S1 below shows the volumes of the 1a:4b equimolar solution (5x10^{-3} M in toluene) added to 2.8 mL of a 5x10^{-3} M toluene solution of 2-methylbenzophenone 1a. The corresponding concentration of 4b and the total volume in every measurement is shown, while [1a] is constantly 5x10^{-3} M.

| Volume of 1a:4b equimolar solution (µL) | mmol of 4b (x10^{-5}) | total volume (mL) | [4b] (x10^{-5} M) | Ratio [1a]/[4b] |
|--------------------------------------|------------------------|-------------------|------------------|----------------|
| 0                                    | 0                      | 2.8               | 0                | -              |
| 5                                    | 2.5                    | 2.805             | 0.9              | 560            |
| 10                                   | 5                      | 2.81              | 1.8              | 280            |
| 20                                   | 10                     | 2.82              | 3.5              | 140            |
| 50                                   | 25                     | 2.85              | 8.8              | 56             |

During the last measurement, an equimolar solution of 2-methylbenzophenone 1a and catalyst 4b was used (1a:4b = 1:1).

2. Control Experiments

![Control Experiments Diagram]
When an authentic sample of the cyclic adduct 2b (inseparable mixture of diastereoisomers, synthesized from crotonaldehyde and 2-methylbenzophenone 1a according to: E. Block, R. Stevenson, J. Chem. Soc., Perkin Trans. 1, 1973, 308–313) was subjected to the optimized photo-organocatalytic condition, we did not detect the open product 4b to any extent, but we fully recovered the unreacted adduct 2b. When repeating the experiment at 40 °C, a minor amount (≈ 20%) of the dehydration product of type 6 was recovered. These experiments indicate that the retroaldol-mediated ring-opening of 2 is not a viable pathway for the formation of 4a.

3. Absorption Spectra

![Graph](image1.png)

**Figure S4.** Absorption spectrum of trans-2-pentenal in toluene.

![Graph](image2.png)

**Figure S5.** Absorption spectrum of cinnamaldehyde in toluene.
4. Computational Details

All calculations were carried out using Gaussian09 software. All energies reported in the main text were computed on the full experimental system with the M06-2X functional and the 6-311++G(d,p) basis set, with solvent contributions added using the SMD model. High level QM calculations were carried out on geometries optimized with and ONIOM(QM:MM) approach. The level of theory for the QM part was with the 6-31+G* basis set, with the MM level being UFF. The MM region consisted of the diphenylsiloxy group. The validity of the ONIOM description was confirmed by the similarity of the ONIOM and full QM potential energies in gas phase. Frequency calculations at standard conditions (1 atm, 298 K) were carried out at the ONIOM level to confirm the identity of minima and transition states and compute entropic corrections. Geometry optimizations were carried out without constraints, and IRC calculations were carried out on all transition states to determine connectivity.

Conformational Search

A conformational search was carried out on the iminium ion intermediate C, derived from the condensation of crotonaldehyde with the chiral secondary amine 4a, which corresponds to 120° rotations along the C-C axis that connects with the diarylprolinol-silyl ether unit, and the lowest energy conformation was used in the rest of the calculations. This approach assumes that the most stable conformation in the free substrate will remain unchanged in all stages of the reaction. In fact, the relative energies of the three conformations are 0.0, 6.5, 11.8 kcal·mol⁻¹, so even a low barrier rotation of the diarylprolinol-silyl ether has a higher energy cost than the formation of the product.

Figure S6. Relevant conformations of the iminium ion corresponding to rotations of the diarylprolinol-silyl ether unit. Relative free energies in kcal·mol⁻¹.

Concerning the mechanism in absence of a proton shuttle, TS1 and TS2 differ mainly in the attack conformation, particularly in the orientation of the –OH group in the photoenol. In TS1, the proton points away from the nitrogen which has a deficiency in electron density. As a result, the C-C distance is 2.35 Å. On the other hand, the proton in TS2 points towards the nitrogen which already has amine configuration rather than iminium, and this shift in the electron density is reflected in a larger C-C distance (2.59 Å).

Radical Mechanism

An alternative mechanism could be envisaged where the carbon-carbon bond formation takes place prior to the formation of the ground-state photoenol A, in a competing photoinitiated process. We evaluated this hypothetic mechanism (on a model system where methyl replaces the protecting group) and the results are detailed in Figure S7. After light excitation and intersystem crossing (ISC) to the triplet state (Ks1 and Ks2), 2-methylbenzophenone 1 transfers a hydrogen from the methyl group to the oxygen (Ts1), leading to the triplet alcohol (Ohs1), which can rotate (Ohs2) and undergo a subsequent ISC to form the singlet photoenol A. we evaluated whether there could be bifurcations from both radical
intermediates OHs1 and OHs2, which might be intercepted by the iminium ion affording the final Michael product 4 through the transition states presented in red in Figure S7. However, these steps are not competitive due to the much faster rotation and intersystem crossing to yield the singlet photoenol A. On the basis of these results, a radical mechanism can be ruled out.

Figure S7. Free energy profile for the formation of the photoenol A (black profile) and noncompetitive radical formation of the C-C bond leading to the product (red profile). Energies in kcal·mol⁻¹

Optimized Cartesian Coordinates of Intermediates and Transition States

**Photoenol A**

E(M06-2X/6-311++G(d,p) = -615.796231246

Number of Negative Frequencies = 0

C  -2.455420  -0.922698  0.589928
C  -1.146365  -1.173620  -0.022790
C  -0.278256   0.019314  -0.197928
C  -0.935732  1.324510  -0.212096
C  -2.208237  1.469577   0.213902
C  -2.965745  0.321040  0.685127
H  -3.036580  -1.789057  0.896853
H  -0.349128  2.185333  -0.513048
H  -2.666981  2.453565  0.240954
H  -3.959351  0.475230  1.096602
C  -0.854365  -2.414296  -0.468111
H  0.048643  -2.645085  -1.020819
C  1.074457  -0.034189  -0.330971
O  1.730511  1.108958  -0.701756
H  2.672776  1.016515  -0.497029
C  1.966606  -1.195540  -0.098533
C  2.916686  -1.545906  -1.064494
C  1.931399  -1.895583  1.144402
C  3.801117  -2.599540  -0.834348
H  2.942114  -1.007677  -2.009488
C  2.817850  -2.940666  1.343841
In the table below, the coordinates for selected atoms are listed. The E(M06-2X/6-311++G(d,p)) value is given as \(-1352.98288875\). The number of negative frequencies is 0.

| Element | X     | Y     | Z     |
|---------|-------|-------|-------|
| H       | 1.197028 | -1.615172 | 1.864829 |
| C       | 3.752052 | -3.299009 | 0.368606 |
| H       | 4.524838 | -2.873318 | -1.596657 |
| H       | 2.785633 | -3.476923 | 2.287822 |
| H       | 4.442368 | -4.117331 | 0.551242 |
| H       | -1.547431 | -3.232023 | -0.288504 |

Iminium Ion C (derived from crotonaldehyde and catalyst 4a) - conformation 1

E(M06-2X/6-311++G(d,p)) = -1352.98288875

Number of Negative Frequencies = 0

| C | 0.867029 | -1.895683 | -0.997059 |
| H | 0.307969 | -2.828523 | -1.015704 |
| C | 0.121324 | -0.688568 | -1.202315 |
| H | 0.604237 | 0.280701 | -1.130991 |
| C | -1.206208 | -0.782322 | -1.438639 |
| H | -1.657878 | -1.775081 | -1.483137 |
| C | -2.117742 | 0.370996 | -1.644043 |
| H | -2.920064 | 0.347369 | -0.896954 |
| H | -1.597454 | 1.328459 | -1.582618 |
| H | -2.606219 | 0.287754 | -2.622261 |
| C | 2.867707 | -3.294810 | -0.534467 |
| C | 3.100594 | -0.876634 | -0.912306 |
| C | 3.431007 | -2.945546 | -0.918674 |
| C | 2.475041 | -3.986993 | -1.271109 |
| C | 4.279291 | -1.563507 | -1.586988 |
| H | 3.356122 | -0.499877 | 0.083511 |
| H | 2.661459 | -0.073429 | -1.502337 |
| H | 5.027196 | -2.925088 | -0.076717 |
| H | 4.736026 | -3.678788 | -1.622796 |
| H | 5.205161 | -0.999564 | -1.461662 |
| H | 4.079045 | -1.657259 | -2.658792 |
| N | 2.138833 | -1.992522 | -0.777346 |
| C | 2.611466 | -3.835853 | 0.915472 |
| C | 3.382658 | -5.129336 | 1.275299 |
| C | 3.365274 | -5.583906 | 2.613999 |
| C | 4.079213 | -5.906029 | 0.322753 |
| C | 4.051142 | -6.741095 | 2.990165 |
| H | 2.814218 | -5.038333 | 3.369943 |
| C | 4.759400 | -7.065903 | 0.705337 |
| H | 4.085411 | -5.650025 | -0.723162 |
| C | 4.751257 | -7.479379 | 2.037231 |
| H | 4.032162 | -7.069504 | 4.021192 |
| H | 5.287841 | -7.650825 | -0.036412 |
| H | 5.278058 | -8.378825 | 2.328650 |
| C | 3.026156 | -2.718027 | 1.905863 |
| C | 4.341598 | -2.618690 | 2.421883 |
| C | 2.085376 | -1.743140 | 2.315703 |
| C | 4.694198 | -1.590440 | 3.299748 |
| H | 5.102855 | -3.339959 | 2.156577 |
| C | 2.446856 | -0.717320 | 3.192566 |
| H | 1.068785 | -1.758075 | 1.945523 |
| Element | X   | Y    | Z    |
|---------|-----|------|------|
|       C | 3.749085 | -0.640525 | 3.683597 |
|       H | 5.704406 | -1.531418 | 3.684015 |
|       H | 1.714524 | 0.022664 | 3.488543 |
|       H | 4.025981 | 0.155702 | 4.362341 |
|       O | 1.207473 | -4.033092 | 1.111753 |
|       Si | 0.407685 | -5.463477 | 0.470750 |
|       C | 0.645542 | -6.952329 | 1.576872 |
|       H | 1.624809 | -7.427291 | 1.369926 |
|       H | -0.155048 | -7.691588 | 1.370213 |
|       C | -1.421222 | -5.086868 | 0.499767 |
|       H | -1.634084 | -4.224507 | -0.164330 |
|       H | -1.988491 | -5.972509 | 0.146833 |
|       H | -1.729994 | -4.83917 | 1.535928 |
|       C | 0.803572 | -5.957474 | -1.292503 |
|       H | 1.861872 | -6.263860 | -1.384685 |
|       H | 0.164071 | -6.816892 | -1.571417 |
|       H | 0.581443 | -5.116418 | -1.983177 |

Iminium Ion C (derived from crotonaldehyde and catalyst 4a) - conformation 2

E(M06-2X/6-311++G(d,p) = -1352.97248625

Number of Negative Frequencies = 0

| Element | X   | Y    | Z    |
|---------|-----|------|------|
|       C | 0.866319 | -1.905373 | -1.009493 |
|       H | 0.289113 | -2.816258 | -0.123238 |
|       C | 0.135983 | -0.683376 | -1.186698 |
|       H | 0.610506 | 0.282333 | -1.050559 |
|       C | -1.183481 | -0.762360 | -1.470279 |
|       H | -1.635477 | -1.749942 | -1.577688 |
|       C | -2.087292 | 0.402170 | -1.641936 |
|       H | -2.904024 | 0.346061 | -0.912216 |
|       H | -1.566815 | 1.354315 | -1.525238 |
|       H | -2.557208 | 0.365697 | -2.632008 |
|       C | 2.866371 | -3.342502 | -0.591562 |
|       C | 3.084872 | -0.909379 | -0.832930 |
|       C | 4.337402 | -2.897073 | -0.906003 |
|       H | 2.537928 | -3.978190 | -1.412323 |
|       C | 4.202648 | -1.562122 | -1.628663 |
|       H | 3.435159 | -0.623111 | 0.162490 |
|       H | 2.614112 | -0.085888 | -1.320001 |
|       H | 4.920042 | -2.736498 | 0.006509 |
|       H | 4.851318 | -3.656078 | -1.498866 |
|       H | 5.122022 | -0.974338 | -1.603907 |
|       H | 3.896924 | -1.690540 | -2.672646 |
|       N | 2.120424 | -2.032934 | -0.712149 |
|       C | 2.717097 | -4.056684 | 0.801470 |
|       C | 1.466129 | -4.943023 | 1.015217 |
|       C | 1.301943 | -5.576625 | 2.270061 |
|       C | 0.563683 | -5.293615 | -0.016209 |
|       C | 0.228708 | -6.436885 | 2.511652 |
|       H | 2.012270 | -5.399491 | 3.067076 |
|       C | -0.512711 | -6.150123 | 0.234287 |
Iminium Ion C (derived from crotonaldehyde and catalyst 4a) - conformation 3

E(M06-2X/6-311++G(d,p) = -1352.96410802

Number of Negative Frequencies = 0

C 0.891273  -1.871832  -0.950231
H 0.347156   -2.816448   -0.991035
C 0.138761   -0.675348   -1.184274
H 0.603764   0.300564  -1.089181
C -1.179990  -0.786468  -1.460885
H -1.616293  -1.785025  -1.523124
C -2.101980  0.355144  -1.682564
H -2.920722  0.315826  -0.954053
H -1.597059  1.319485  -1.603740
H -2.567148  0.270249  -2.671914
C 2.873849   -3.278956  -0.473591
C 3.112560   -0.852596  -0.866525
C 4.327423   -2.943862  -0.919134
H 2.420284  -3.889483  -1.261553
C 4.229383  -1.575166  -1.612593
H 3.427214  -0.438279  0.094016
H 2.643409  -0.063899  -1.452942

S27
H  5.070019  -2.881780  -0.132157
H  4.698536  -3.691773  -1.617158
H  5.170062  -1.023180  -1.574300
H  3.941767  -1.683739  -2.663031
N  2.151412  -1.954586  -0.651646
C  2.610266  -4.029965  0.903683
C  3.650392  -3.872591  2.041498
C  3.737189  -4.877693  3.034753
C  4.374744  -2.690379  2.265007
C  4.605768  -4.748658  4.121487
H  3.131016  -5.771962  2.972975
C  5.243142  -2.554571  3.352772
H  4.257264  -1.826797  1.622476
C  5.369704  -3.593538  4.272503
H  4.675818  -5.548144  4.854566
H  5.803529  -1.639257  3.493437
H  6.038367  -3.491835  5.117470
C  1.270634  -3.543339  1.512414
C  1.160917  -2.703209  2.125669
C  0.102410  -4.345064  1.460472
C  -0.051569  -1.827645  2.659870
H  1.999719  -1.594150  2.164787
C  -1.105729  -3.893604  1.998745
H  0.102396  -5.318447  0.989360
C  -1.182651  -2.638318  2.598337
H  -0.115189  -0.847594  3.114847
H  -1.987550  -4.519019  1.944900
H  -2.121431  -2.290808  3.009824
O  2.420941  -5.422212  0.630032
Si  3.718231  -6.386656  -0.052658
C  3.430879  -8.120185  0.578203
H  3.518442  -8.129661  1.684041
H  2.414768  -8.455909  0.286006
H  4.186770  -8.804876  0.141671
C  3.549608  -6.512747  -1.913413
H  3.741813  -5.544553  -2.408826
H  4.275429  -7.260404  -2.293700
H  2.521242  -6.846185  -2.161685
C  5.481301  -5.987459  0.452829
H  5.614840  -6.167285  1.537739
H  6.165718  -6.665740  -0.096335
H  5.761030  -4.950158  0.216082

H_2O
E(M06-2X/6-311++G(d,p)) = -76.4253004768
Number of Negative Frequencies = 0
O  0.98520200  1.06520700  0.00000000
H  1.95160400  1.09942400  0.00000000
H  0.69479800  1.98768100  0.00000000

TS1 (Figure 4 in the main manuscript)
E(M06-2X/6-311++G(d,p)) = -1968.79114978
Number of Negative Frequencies = 1

|   |        |        |        |        |
|---|--------|--------|--------|--------|
| C | -0.072257 | 3.488998 | -0.203340 |    |
| C | 1.078417  | 2.787372 | -0.743494 |    |
| C | 1.496822  | 3.164983 | -2.096547 |    |
| C | 0.680099  | 4.113943 | -2.834322 |    |
| C | -0.411696 | 4.695989 | -2.282736 |    |
| C | -0.792816 | 4.377538 | -0.930191 |    |
| H | -0.362449 | 3.254674 | 0.817691  |    |
| H | 1.005423  | 4.398442 | -3.829160 |    |
| H | -0.979102 | 5.434340 | -2.840458 |    |
| H | -1.656558 | 4.866341 | -0.489885 |    |
| C | 1.546483  | 1.699818 | -0.037952 |    |
| H | -0.362449 | 3.254674 | 0.817691  |    |
| H | 1.005423  | 4.398442 | -3.829160 |    |
| H | -0.979102 | 5.434340 | -2.840458 |    |
| H | -1.656558 | 4.866341 | -0.489885 |    |
| C | 0.762934  | -0.097269 | -2.367157 |    |
| C | 0.284073  | 0.004388 | -1.074507 |    |
| H | 1.162978  | 1.538363 | 0.965609  |    |
| C | 3.805132  | 2.029057 | -2.129987 |    |
| C | 4.443114  | 2.664779 | -1.056020 |    |
| C | 4.369866  | 0.873526 | -2.685009 |    |
| C | 5.616879  | 2.134616 | -0.534520 |    |
| H | 4.012330  | 3.570518 | -0.637793 |    |
| C | 5.542169  | 0.340348 | -2.154268 |    |
| H | 3.875882  | 0.377257 | -3.518674 |    |
| C | 6.164064  | 0.969441 | -1.077190 |    |
| H | 6.112392  | 2.633867 | 0.292078  |    |
| H | 5.967783  | -0.563542 | -2.578734 |    |
| H | 7.080087  | 0.557893 | -0.665008 |    |
| C | 0.275124  | 0.777957 | -3.356288 |    |
| C | -0.379312 | 1.578679 | -3.015638 |    |
| H | 1.498053  | -0.861300 | -2.604762 |    |
| C | 1.345474  | -0.267563 | -5.309449 |    |
| C | -0.015921 | 1.738338 | -5.634778 |    |
| C | 1.940679  | 0.513474 | -6.473895 |    |
| H | 0.732162  | -1.110950 | -5.650082 |    |
| H | 2.091689  | -0.646035 | -4.609656 |    |
| C | 0.794887  | 1.429841 | -6.925979 |    |
| H | 0.336908  | 2.695053 | -5.240600 |    |
| H | 2.790420  | 1.104588 | -6.119672 |    |
| H | 2.290729  | -0.142180 | -7.273686 |    |
| H | 1.176264  | 2.358689 | -7.355741 |    |
| H | 0.222060  | 0.942752 | -7.711015 |    |
| C | -1.579435 | 1.780958 | -5.759556 |    |
| N | 0.479853  | 0.719587 | -4.652271 |    |
| C | 0.562688  | -1.061310 | -0.055770 |    |
| H | 0.420884  | -0.705645 | 0.965924  |    |
| H | -0.139330 | -1.890040 | -0.214417 |    |
| H | 1.576676  | -1.458245 | -0.158520 |    |
| H | -0.584447 | 0.636827 | -0.899277 |    |
Intermediate D (the precursor of the cycloaddition adduct 2b)

E(M06-2X/6-311++G(d,p) = -1968.88215506
Number of Negative Frequencies = 0

C  0.248553  4.471989  -1.035630
C  0.930527  3.278119  -1.273344
C  1.918310  3.243156  -2.270984
C  2.204493  4.388008  -3.012488
C  1.524974  5.579441  -2.756715
C  0.543021  5.620135  -1.770436
H  -0.522231  4.501944  -0.268989
H   2.948197  4.348908  -3.802589
H   1.758512  6.468954  -3.333461
H   0.003893  6.541562  -1.573349
C   0.650697  2.021923  -0.487345
S

C -1.951381 -2.731057 -7.065470  
H -2.131452 -0.845068 -8.039512  
C -1.637676 -2.697055 -4.672539  
H -1.551333 -0.783290 -3.740951  
C -4.598923  3.329627 -4.932982  
C -2.986073  3.154460 -2.429973  
C -1.743667  4.378022 -4.672539  
H -6.045695  0.918831 -8.042935  
H -3.129759  3.647894 -9.601687  
C -1.774444 -3.411401 -5.861662  
H -2.057957 -3.286926 -7.988068  
H -1.495660 -3.225923 -3.738878  
H -4.563071  3.554103 -6.017221  
H -5.243237  2.446179 -4.747100  
H -5.022547  4.208357 -4.405138  
H -2.007604  2.896421 -1.979497  
H -3.257313  4.194969 -2.157511  
H -3.758744  2.456976 -2.046948  
H -1.695190  4.408819 -5.963346  
H -2.154848  5.344018 -4.500327  
H -0.730048  4.251120 -4.428318  
H -5.388257  2.640891 -9.696393  
H -1.742273 -4.493180 -5.850448

TS2

E(M06-2X/6-311++G(d,p)) = -1968.78699666
Number of Negative Frequencies = 1
C   -0.183714  2.250055  0.557814  
C    0.991902  1.793802 -0.173281  
C    1.505666  2.706328 -1.206622  
C    0.825352  3.979596 -1.389895  
C   -0.271700  4.332362 -0.677441  
C   -0.802645  3.428729  0.310921  
H    0.570040  1.585651  1.326631  
H    1.271221  4.726532 -2.045454  
H   -0.719617  5.312771 -0.806606  
H   -1.678334  3.717234  0.883693  
C    1.379210  0.493984  0.030592  
H    2.261829  0.044658 -0.401265  
C    2.538811  2.392733 -2.084827  
O    2.672407  3.048481 -3.256089  
H    1.880144  3.582285 -3.431186  
C    0.523527  0.147329 -3.007493  
C    0.150515 -0.548810 -1.883835  
H    0.873141 -0.079990  0.802222  
C    3.656642  1.458881 -1.877064  
C    4.137223  0.685472 -2.939801  
C    4.315951  1.422040 -0.640648  
C    5.229966 -0.156741 -2.756475  
H    3.654286  0.750421 -3.910817  

S32
| Atm | X    | Y    | Z    |
|-----|------|------|------|
| C   | 5.416179 | 0.593127 | -0.464509 |
| H   | 3.959810 | 2.044514 | 0.176144 |
| C   | 5.867570 | -0.205958 | -1.517777 |
| H   | 5.591053 | -0.763556 | -3.580983 |
| H   | 5.929251 | 0.573403 | 0.491865 |
| H   | 6.725059 | -0.856599 | -1.374977 |
| C   | -0.092163 | 1.388667 | -3.279407 |
| H   | 1.260686 | -0.273194 | -3.685119 |
| C   | 0.814114 | 1.691390 | -5.545027 |
| C   | -0.739014 | 3.374381 | -4.661068 |
| C   | 1.134383 | 3.022091 | -6.214387 |
| H   | 0.230818 | 1.026734 | -6.193882 |
| H   | 1.705266 | 1.165195 | -5.201016 |
| C   | -0.130982 | 3.866574 | -6.006533 |
| H   | -0.406705 | 4.056951 | -3.870458 |
| H   | 2.003630 | 3.476434 | -5.727749 |
| H   | 1.377830 | 2.897969 | -7.271244 |
| H   | 0.108036 | 4.930458 | -5.938261 |
| H   | -0.792565 | 3.764469 | -6.862054 |
| H   | -0.729535 | 1.798769 | -2.496089 |
| N   | -0.016296 | 2.082174 | -4.392203 |
| C   | 0.615271 | -1.946239 | -1.621508 |
| H   | 0.633730 | -2.177990 | -0.554856 |
| H   | -0.083367 | -2.649124 | -2.094262 |
| H   | 1.609121 | -2.120983 | -2.043240 |
| H   | -0.702997 | -0.189176 | -1.312546 |
| C   | -2.301191 | 3.250067 | -4.575013 |
| C   | -2.930157 | 4.507615 | -5.233972 |
| C   | -2.707764 | 1.888448 | -5.207630 |
| O   | -2.538372 | 3.252247 | -3.174342 |
| C   | -3.963339 | 4.447108 | -6.198099 |
| C   | -2.496382 | 5.788150 | -4.818621 |
| C   | -2.657297 | 1.669155 | -6.604981 |
| C   | -2.984214 | 0.767654 | -4.386549 |
| Si  | -4.241999 | 3.449590 | -2.628198 |
| C   | -4.493789 | 5.613220 | -6.756949 |
| H   | -4.409253 | 3.511604 | -6.496324 |
| C   | -3.029147 | 6.949410 | -5.383149 |
| H   | -1.749517 | 5.894712 | -4.043674 |
| C   | -2.931731 | 0.412568 | -7.150970 |
| H   | -2.435382 | 2.467592 | -7.292762 |
| C   | -3.254470 | -0.486538 | -4.938311 |
| H   | -2.966448 | 0.842716 | -3.309898 |
| C   | -4.435191 | 2.408677 | -1.089394 |
| C   | -4.519649 | 5.225536 | -2.120351 |
| C   | -5.615883 | 2.943635 | -3.801951 |
| C   | -4.021595 | 6.862047 | -6.357176 |
| H   | -5.285352 | 5.547326 | -7.492281 |
| H   | -2.677579 | 7.919431 | -5.056224 |
| C   | -3.233631 | -0.663200 | -6.319411 |
| H   | -2.905378 | 0.272869 | -8.224002 |
| X    | Y    | Z    |
|------|------|------|
| -3.466718 | -1.327038 | -4.290154 |
| -4.333362 | 1.335178  | -1.347124 |
| -3.653327 | 2.686625  | -0.354807 |
| -5.436464 | 2.585934  | -0.646181 |
| -4.636468 | 5.861792  | -3.019951 |
| -5.443035 | 5.292826  | -1.509543 |
| -3.653929 | 5.577738  | -1.522676 |
| -5.443035 | 5.292826  | -1.509543 |
| -3.653929 | 5.577738  | -1.522676 |

*Enammonium ion intermediate F*

\[ E(M06-2X/6-311++G(d,p)) = -1968.85589687 \]

Number of Negative Frequencies = 0

C   -1.604808  0.094697  2.952941
C   -0.615200 -0.248963  2.025251
C    0.057319  0.802879  1.370173
C   -0.299705  2.135633  1.610018
C   -1.292392  2.449618  2.533227
C   -1.939056  1.421678  3.215520
H   -2.126885 -0.700935  3.479204
H    0.229625  2.926980  1.085196
H   -1.548361  3.486535  2.726898
H   -2.707172  1.649176  3.948417
C   -0.395566 -1.708552  1.694484
H    0.626174 -1.882553  1.342839
C    1.173076  0.603149  0.385940
O   1.056740  1.047667  -0.759451
H   -0.485260  1.048782 -1.652327
C   -1.162065 -1.562516 -0.686121
C   -1.385418 -2.275844  0.624914
H   -1.091930 -3.321118  0.479718
C    2.845726 -2.263724  1.078040
H   -3.480660 -2.745153  0.328904
H   -2.956015 -2.811179  2.019398
H   -3.222090 -1.251397  1.237163
H   -0.521706 -2.307560  2.603865
C    2.431097  0.051401  0.811568
C    3.366445 -0.415009 -0.167181
C    2.711589 -0.279083  2.166036
C    4.563029 -1.014289  0.203596
H    3.142890 -0.214582 -1.210684
C    3.915961 -0.870305  2.533941
H    1.996861  0.019404  2.928289
C    4.836952 -1.241710  1.554535
H    5.286291 -1.300831 -0.553476
H    4.138585 -1.037934  3.582875
H    5.775080 -1.705655  1.844607
C   -1.650155 -0.352885 -0.940150
| Atom | X         | Y         | Z         |
|------|-----------|-----------|-----------|
| C    | -0.489954 | -2.041883 | -1.393836 |
| C    | -0.468867 | -0.270347 | -3.170129 |
| C    | -2.184907 | 1.466900  | -2.750206 |
| C    | -0.369636 | 0.729298  | -4.323350 |
| H    | -1.015916 | -1.176974 | -3.430252 |
| H    | 0.499981  | -0.547270 | -2.752036 |
| C    | -1.347520 | 1.880973  | -3.993732 |
| H    | -2.200053 | 2.299155  | -2.058369 |
| H    | 0.648055  | 1.112688  | -4.415339 |
| H    | -0.617409 | 0.240124  | -5.266671 |
| H    | -0.773082 | 2.769969  | -5.719300 |
| H    | -1.940932 | 2.164774  | -4.860163 |
| H    | -2.258465 | 0.203186  | -0.234154 |
| N    | -1.228840 | 0.455444  | -2.090364 |
| C    | -3.564529 | -0.352084 | -3.791556 |
| O    | -4.243627 | 0.627739  | -1.708225 |
| C    | -5.828391 | 1.508461  | -4.196154 |
| C    | -4.218792 | 3.302826  | -3.957407 |
| C    | -6.683012 | 2.368972  | -4.889321 |
| C    | -5.159740 | 1.096263  | -5.061877 |
| C    | -3.751610 | 3.354530  | -0.316882 |
| C    | -6.307544 | 3.691655  | -5.119715 |
| H    | -7.641773 | 2.010571  | -5.240951 |
| H    | -4.797986 | 5.190310  | -4.814972 |
| C    | -3.478997 | -2.746541 | -5.289535 |
| H    | -3.184179 | -1.479062 | -6.999552 |
| H    | -3.807961 | -3.750445 | -3.418301 |
| H    | -6.424751 | 3.268470  | -2.013512 |
| H    | -7.156619 | 1.664342  | -1.572822 |
| H    | -7.057352 | 2.995411  | -0.353257 |
| H    | -4.184666 | 0.875367  | 1.482947 |
| H    | -5.728825 | 1.791205  | 1.659386 |
| H    | -5.733498 | 0.156255  | 0.876212 |
| H    | -3.626811 | 3.969595  | -1.228594 |
| H    | -4.215926 | 3.984317  | 0.469193 |
| H    | -2.768052 | 3.000166  | 0.051192 |
| H    | -6.972594 | 4.358376  | -5.653118 |
| H    | -3.429708 | -3.663468 | -5.862407 |
TS3

E(M06-2X/6-311++G(d,p) = -1022.9224926

Number of Negative Frequencies = 1

C  -1.807385  -0.110852  2.842250
C  -0.894686  -0.762621  2.005743
C   0.156882   0.016310  1.471390
C   0.239634  1.397271  1.732919
C  -0.719539  2.023270  2.515019
C  -1.736097  1.257829  3.086864
H  -2.592473  -0.697827  3.311554
H   1.048707  1.977623  1.298088
H  -0.663142  3.091963  2.695382
H  -2.473488  1.726843  3.732006
C  -1.080556  -2.235151  1.729497
H  -0.123196  -2.720237  1.510063
C   1.214082  -0.567477  0.631834
O   0.932875  -1.362448  -0.320505
H   0.245650  -1.519687  -0.808249
C  -2.077922  -2.532355  0.569567
H  -2.040132  -3.619757  0.440900
C   3.519870  -2.178228  0.947753
H  -4.201890  -2.491634  0.150906
H  -3.819555  -2.688515  1.870350
H  -3.663309  -1.103131  1.100236
H  -1.465967  -2.708595  2.639428
C   2.622888  -0.264231  0.841363
C   3.544096  -0.525072  -0.191542
C   3.074315  0.229277  2.078609
C   4.892132  -0.271342  0.006484
H   3.189398  -0.910655  -1.141756
C   4.429185  0.467180  2.271265
H   2.374400  0.393124  2.892194
C   5.333799  0.224420  1.237134
H   5.603085  -0.459511  -0.791512
H   4.781436  0.836208  3.228926
H   6.391999  0.414345  1.392346
C  -1.981268  -0.636519  -1.120025
H  -1.380008  -2.622646  -1.555567
C  -1.136444  -0.710864  -3.433955
C  -2.275330  1.292839  -2.637379
C  -0.676019  0.451876  -4.310413
H  -1.888423  -1.337954  -3.935322
H  -0.312438  -1.357043  -3.114233
C  -1.724818  1.546206  -4.058007
H  -1.886041  2.028600  -1.922942
H   0.319383  0.805020  -3.961651
H  -0.608362  0.169590  -5.363392
H  -1.296083  2.547373  -4.144677
H  -2.540283  1.474003  -4.785871

S36
Iminium ion adduct $E$, the precursor of the Michael product $5b$

$E$(M06-2X/6-311++G(d,p)) = -1968.87401975$

Number of Negative Frequencies = 0
H  -1.056892  -2.794032  -7.682440
C   -2.291059  -0.285468  -10.361948
H  -2.002331  1.244833  -8.921839
C   2.646152  -1.599901  -7.100512
H   1.195669  -0.803399  -8.441357
C   2.009619  -1.767498  -4.778615
H   0.058289  -1.088184  -4.265144
C   -4.289358  -1.922027  -7.043499
C   -4.341733  -0.915279  -4.232677
C   -4.264391  1.064229  -6.463304
C   -2.224882  -1.648258  -10.650773
H   -1.738358  -3.602935  -8.921839
H   -2.657780  0.406008  -11.109599
C   2.953385  -1.952838  -5.787396
H   3.378806  -1.747099  -3.534080
C   2.249829  -2.039130  -3.758747
C   -4.156225  -1.626704  -8.102983
C   -3.774143  -2.884545  -6.844674
C   -5.374058  -2.040604  -6.844674
C   -4.035275  -0.110938  -3.534080
C   -5.448081  -0.929950  -4.311757
C   -3.984853  -1.893358  -3.849991
C   -3.930187  1.301086  -7.491178
H   -5.372634  1.020413  -6.459306
H   -3.942499  1.855684  -5.756448
H   -2.532947  -2.011690  -11.622532
H    3.923474  -2.370872  -5.551550

**TS1-H$_2$O** (Figure 5 in the main text)
E(M06-2X/6-311++G(d,p) = -2045.23493578
Number of Negative Frequencies = 1

C   -0.102487  2.531675  0.758330
C    0.981059  2.095442  -0.107260
C    1.204863  2.891618  -1.317602
C    0.283221  3.974376  -1.613738
C   -0.738941  4.294556  -0.784959
C   -0.932470  3.553007  0.434806
H   -0.250418  1.980776  1.683798
H    0.474970  4.570384  -2.499417
H   -1.387273  5.134797  -1.012568
H   -1.741266  3.829665  1.104427
C    1.561661  0.877939  0.171745
H    2.408828  0.473870  -0.365868
C    2.220161  2.656575  -2.235698
O    2.095816  3.198889  -3.453270
H    2.964775  3.236038  -3.927474
C    0.479509  -0.185536  -2.508180
C    0.162701  -0.506004  -1.204884
H    1.315884  0.394294  1.113037
C    3.497796  1.951760  -1.983950
C    3.978266  1.003009  -2.894585
| Element | X        | Y        | Z       |
|---------|----------|----------|---------|
| C       | -4.354805| 2.921602 | -1.243895|
| C       | -3.566663| 6.043147 | -7.225119|
| H       | -4.970654| 4.698301 | -8.137777|
| H       | -2.106713| 7.154184 | -6.107181|
| C       | -3.365257| -1.443812| -6.060647|
| H       | -3.020139| -0.794215| -8.078536|
| H       | -3.591390| -1.814251| -3.956840|
| H       | -5.451483| 1.104971 | -3.488659|
| H       | -6.512905| 2.549011 | -3.632049|
| H       | -5.404278| 2.124611 | -4.982118|
| H       | -3.755747| 5.642407 | -3.042266|
| H       | -4.831803| 5.194456 | -4.434320|
| H       | -5.507499| 5.282457 | -2.768144|
| H       | -3.703832| 3.636722 | -0.702611|
| H       | -5.407746| 3.073305 | -0.929679|
| H       | -4.042287| 1.883764 | -1.007215|
| H       | -3.897081| 6.900628 | -7.796878|
| H       | -3.629605| -2.453408| -6.347340|

**Intermediate H**

E(M06-2X/6-311++G(d,p) = -2045.30787183

Number of Negative Frequencies = 0

| Element | X        | Y        | Z        |
|---------|----------|----------|----------|
| C       | -2.203643| 3.849615 | 0.108026 |
| H       | -3.214229| 0.738086 | -0.513060|
| H       | -3.037806| 2.024986 | -1.706610|
| H       | -1.190061| 1.535726 | 0.826661 |
| C       | 2.296028 | 3.276577 | -0.476497|
| C       | 3.440646 | 2.661393 | -1.000531|
| C       | 2.140910 | 3.395856 | 0.911104 |
| C       | 4.408725 | 2.148282 | -0.146030|
| H       | 3.564293 | 2.602444 | -2.078043|
| C       | 3.120269 | 2.896126 | 1.763493 |
| H       | 1.263242 | 3.889604 | 1.320316 |
| C       | -0.965606| 3.337184 | -0.298338|
| C       | -0.074781| 4.220794 | -0.939024|
| C       | -0.442676| 5.552358 | -1.177524|
| C       | -1.678931| 6.035690 | -0.764505|
| C       | -2.562104| 5.176560 | -0.113389|
| H       | -2.909091| 3.187174 | 0.616016 |
| H       | 0.272480 | 6.219531 | -1.654377|
| H       | -1.941693| 7.075780 | -0.930890|
| H       | -3.525977| 5.539739 | 0.229735 |
| C       | -0.688147| 1.862720 | -0.091057|
| H       | 0.378735 | 1.674870 | 0.054668 |
| C       | 1.294361 | 3.838501 | -1.414351|
| O       | 1.601248 | 4.055387 | -2.587892|
| H       | -0.760881| 5.371365 | -4.525108|
| C       | -0.400549| 1.223316 | -2.495508|
| C       | -1.192687| 0.950309 | -1.245682|
| H       | -0.935297 | -0.073234| -0.940628|
| C       | -2.703490| 1.017444 | -1.439491|
|   | X         | Y         | Z         |
|---|-----------|-----------|-----------|
| H | -3.025876 | 0.321541  | -2.220188 |
| C | 4.247982  | 2.266425  | 1.236168  |
| H | 5.292575  | 1.666423  | -0.552057 |
| H | 3.006658  | 2.999684  | 2.837983  |
| H | 5.008037  | 1.873037  | 1.904497  |
| O | 0.007018  | 4.799276  | -4.666690 |
| H | 0.547910  | 4.833844  | -3.846021 |
| H | -0.061094 | 3.157810  | 0.061094  |
| C | -0.902401 | 1.769030  | -3.598092 |
| H | 0.657690  | 0.968280  | -2.444690 |
| H | -1.933427 | 2.096008  | -3.682202 |
| C | 1.337729  | 1.681613  | -4.764056 |
| C | -0.669045 | 1.891006  | -6.194666 |
| C | 0.587632  | 0.623696  | -5.504540 |
| H | 1.839490  | 2.265238  | -3.990289 |
| C | 0.587632  | 2.217238  | -7.051136 |
| H | -1.375499 | 2.703425  | -6.313190 |
| H | 2.474811  | 2.867429  | -6.179465 |
| H | 2.444713  | 1.146576  | -6.544702 |
| H | 0.534755  | 3.277543  | -7.311129 |
| H | 0.641514  | 1.675730  | -7.992991 |
| N | -0.104897 | 2.103036  | -4.777914 |
| C | -1.409789 | 0.525025  | -6.428939 |
| C | -1.870832 | 0.291885  | -7.889637 |
| C | -0.442898 | -0.621553 | -6.053644 |
| O | -2.529755 | 0.430912  | -5.541525 |
| C | -2.330910 | -0.990514 | -8.268329 |
| C | -1.896129 | 1.316883  | -8.863742 |
| C | -0.590947 | -1.024486 | -6.931331 |
| C | -0.577546 | -1.322323 | -4.830475 |
| Si| -4.032876 | 1.274212  | -5.902998 |
| C | -2.754936 | -1.246324 | -9.574537 |
| H | -2.366832 | -1.796015 | -7.545580 |
| C | -2.324248 | 1.053813  | -10.168123|
| H | -1.603573 | 2.328878  | -8.630684 |
| C | 1.470661  | -2.052289 | -6.583039 |
| H | 0.712247  | -0.559831 | -7.898667 |
| C | 0.308060  | -2.347451 | -4.488893 |
| H | -1.354204 | -1.074124 | -4.120162 |
| C | -0.547299 | 0.392704  | -7.204719 |
| C | -0.505905 | 1.215212  | -4.345570 |
| C | -3.906706 | 3.088741  | -6.346422 |
| C | -2.747329 | -0.226264 | -10.524796|
| H | -3.097703 | -2.236005 | -9.847246 |
| H | -2.334494 | 1.848396  | -10.903020|
| C | 1.333304  | -2.709016 | -5.361285 |
| H | 2.258094  | -2.343406 | -7.266153 |
| H | 0.198422  | -2.862241 | -3.543082 |
| H | -4.681194 | 0.652021  | -8.217173 |
| H | -4.987211 | -0.703251 | -7.045376 |
| Atom | X     | Y     | Z     |
|------|-------|-------|-------|
| H    | -6.105262 | 0.715339 | -7.122252 |
| H    | -4.604072 | 1.872788 | -3.579302 |
| H    | -6.086662 | 1.572300 | -4.564431 |
| H    | -5.102076 | 0.173039 | -3.968158 |
| H    | -3.413297 | 3.217976 | -7.328821 |
| H    | -4.930536 | 3.510121 | -6.412922 |
| H    | -3.351494 | 3.633725 | -5.555411 |
| H    | -3.080137 | -0.424888 | -11.535302 |
| H    | 2.017010  | -3.504212 | -5.093761 |

**TS3-H₂O** (Figure 5 in the main text)

E(M06-2X/6-31++G(d,p) = -2045.265914

Number of Negative Frequencies = 1

| Atom | X    | Y    | Z    |
|------|------|------|------|
| C    | -1.661763 | 3.431141 | -0.191904 |
| C    | -0.415869 | 2.790134 | -0.261255 |
| C    | 0.724132  | 3.602132 | -0.333093 |
| C    | 0.621739  | 5.002401 | -0.338821 |
| C    | 0.625602  | 5.611993 | -0.269655 |
| C    | -1.773375 | 4.816857 | -0.202247 |
| H    | -2.561913 | 2.823244 | -0.134099 |
| H    | 1.525211  | 5.605948 | -0.396133 |
| H    | -0.702917 | 6.694629 | -0.261773 |
| H    | -2.753724 | 5.280431 | -0.150199 |
| C    | -0.366006 | 1.280787 | -0.327024 |
| H    | 0.666152  | 0.914969 | -0.259213 |
| C    | 2.086274  | 3.039869 | -0.606354 |
| O    | 2.534937  | 3.198987 | -1.762146 |
| H    | 0.189483  | 4.479617 | -2.854776 |
| C    | -0.249507 | 1.062447 | -2.864561 |
| C    | -1.011746 | 0.703895 | -1.604800 |
| H    | -0.892038 | 0.874100 | 0.546510 |
| C    | 2.879354  | 2.372204 | 0.419658 |
| C    | 4.138166  | 1.842636 | 0.086527 |
| C    | 2.383892  | 2.252242 | 1.728369 |
| C    | 4.888743  | 1.196446 | 1.057378 |
| H    | 4.509035  | 1.947316 | -0.928379 |
| C    | 3.140589  | 1.601046 | 2.694225 |
| H    | 1.414082  | 2.670894 | 1.983909 |
| C    | 4.388586  | 1.074438 | 2.357796 |
| H    | 5.862089  | 0.785683 | 0.808762 |
| H    | 2.762598  | 1.504724 | 3.706731 |
| H    | 4.978560  | 0.566217 | 3.114825 |
| O    | 0.713958  | 3.755364 | -3.255672 |
| H    | 1.606533  | 3.587798 | -2.615857 |
| H    | 0.171393  | 2.879359 | -3.131220 |
| C    | -0.937759 | 1.341219 | -4.019730 |
| H    | 0.785835  | 0.720954 | -2.907848 |
| H    | -1.995745 | 1.531779 | -3.880172 |
| C    | 1.001889  | 1.211967 | -5.432299 |
| C    | -1.090126 | 1.827491 | -6.564451 |
| C    | 1.292919  | 1.688612 | -6.845470 |
| Atomo | X      | Y        | Z         |
|-------|--------|----------|-----------|
| C     | 1.238642 | 0.147377 | -5.291635 |
| H     | 1.559829  | 1.781410 | -4.678543 |
| C     | -0.004209 | 1.338974 | -7.565863 |
| H     | -1.110003 | 2.920340 | -6.614679 |
| H     | 1.465556  | 2.770789 | -6.854311 |
| H     | -0.048370 | 1.784641 | -5.269207 |
| C     | -1.136095 | -0.821190| -7.565863 |
| H     | -1.715232 | -1.096808| -0.584426 |
| H     | -1.629921  | -1.245955| -2.351746 |
| H     | 0.145992   | -1.284860| -1.388011 |
| H     | -2.026341  | 1.120255 | -1.688940 |
| C     | 2.546695   | 1.270706 | -6.776441 |
| C     | -3.197478  | 1.644784 | -8.129098 |
| C     | -2.481620  | -0.275486| -6.690879 |
| O     | -3.423808  | 1.692388 | -5.729940 |
| C     | -4.450779  | 1.077296 | -8.453380 |
| C     | -2.626108  | 2.551431 | -9.052189 |
| C     | -2.173837  | -1.065936| -7.824951 |
| C     | -2.762451  | -0.950448| -5.478885 |
| Si    | -3.808325  | 3.395587 | -5.508211 |
| C     | -5.075065  | 1.357246 | -9.671292 |
| H     | -4.941651  | 0.404417 | -7.761170 |
| C     | -3.258399  | 2.830140 | -10.267200|
| H     | -1.733249  | 3.109372 | -8.825328 |
| C     | -2.122841  | -2.459677| -7.739177 |
| H     | -1.965337  | -0.604439| -8.781788 |
| C     | -2.703784  | -2.343885| -5.399779 |
| H     | -3.035820  | -0.411487| -4.583851 |
| C     | -4.185024  | 4.407053 | -7.036634 |
| C     | -5.385196  | 3.409653 | -4.509485 |
| C     | -2.551619  | 4.320388 | -4.468101 |
| C     | -4.475345  | 2.226637 | -10.581100|
| H     | -6.027288  | 0.900629 | -9.908051 |
| C     | -2.811409  | 3.532705 | -10.958887|
| H     | -2.383031  | -3.097662| -6.527255 |
| H     | -1.881127  | -3.046172| -8.616052 |
| H     | -2.913846  | -2.840051| -4.460737 |
| H     | -3.245382  | 4.669081 | -7.560337 |
| H     | -4.876203  | 3.855275 | -7.705058 |
| H     | -6.769265  | 5.350309 | -6.725491 |
| H     | -5.215381  | 5.884160 | -3.547258 |
| H     | -5.692569  | 4.456772 | -4.309986 |
| H     | -6.184702  | 2.890278 | -5.076840 |
| H     | -1.577960  | 4.395516 | -4.988506 |
| H     | -2.930648  | 5.347147 | -4.285309 |
| H     | -2.419529  | 3.816914 | -3.489220 |
| H     | -4.962198  | 2.446962 | -11.522234|
| H     | -2.342234  | -4.177279| -6.462871 |
**E. X-ray Crystallographic Data**

**Single Crystal X-ray Diffraction Data for Compound 6**

X-ray structure determinations: Crystals of compound 6 were obtained by slow diffusion of hexane into a saturated diethyl ether solution. Measurements were made on a Rigaku XtaLab P200 diffractometer equipped with a Pilatus 200K area detector, a Microfocus-HF007 rotating anode with MoKα radiation, Confocal Max Flux optic and a Cryostream Plus low temperature device (T = 100K).

**Table S2. Crystal data and structure refinement for 6 at 100 K: CCDC 1417311**

| Description                                      | Value                                      |
|--------------------------------------------------|--------------------------------------------|
| Identification code                              | LD412                                      |
| Empirical formula                                | C19 H17 Br O                               |
| Formula weight                                   | 341.23                                     |
| Temperature                                      | 100(2) K                                   |
| Wavelength                                       | 0.71073 Å                                  |
| Crystal system                                   | Orthorhombic                               |
| Space group                                       | P2(1)2(1)2(1)                              |
| Unit cell dimensions                             | a = 8.979(3) Å, b = 9.238(3) Å, c = 18.493(7) Å |
| Volume                                           | 1534.0(10) Å³                              |
| Z                                                | 4                                          |
| Density (calculated)                             | 1.478 Mg/m³                                |
| Absorption coefficient                           | 2.680 mm⁻¹                                 |
| F(000)                                           | 696                                        |
| Crystal size                                     | 0.20 x 0.20 x 0.20 mm³                     |
| Theta range for data collection                  | 2.464 to 36.340°.                          |
| Index ranges                                     | -14<=h<=14,-15<=k<=14,-29<=l<=28            |
| Reflections collected                            | 14288                                      |
| Independent reflections                          | 7112[R(int) = 0.0402]                      |
| Completeness to theta =36.340°                   | 98.4%                                      |
| Absorption correction                            | Empirical                                  |
| Max. and min. transmission                       | 0.616 and 0.474                            |
| Refinement method                                | Full-matrix least-squares on F²            |
| Data / restraints / parameters                    | 7112/0/ 192                                |
| Goodness-of-fit on F²                             | 0.832                                      |
| Final R indices [I>2sigma(I)]                    | R1 = 0.0299, wR2 = 0.0542                  |
| R indices (all data)                             | R1 = 0.0476, wR2 = 0.0566                  |
| Flack parameter                                  | x =0.059(7)                                |
| Largest diff. peak and hole                      | 0.846 and -0.458 e.Å⁻³                    |
F. References

1. T. Miura, T. Tanaka, K. Hiraga, S. G. Stewart, M. Murakami, *J. Am. Chem. Soc.* **2013**, *135*, 13652–13655.

2. T. J. Connolly, T. A. Durst, *Tetrahedron* **1997**, *47*, 15969–15982.

3. G. Porter, M. Tchir, *J. Chem. Soc. A*, **1971**, *3772–3777*.

4. K. Uji-Ie, K. Kikuchi, H. Kokubun, *Chem. Lett.* **1977**, *499–502*.

5. K. Uji-Ie, K. Kikuchi, H. Kokobun, *J. Photochem.* **1979**, *10*, 145–157.

6. G. W. T. M. J. Frisch, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, (Ed.: W. CT), **2009**.

7. Y. Zhao, D. G. Truhlar, *Theoretical Chemistry Accounts* **2007**, *120*, 215–241.

8. (a) P. C. Hariharan, J. A. Pople, *Theoretica Chimica Acta* **1973**, *28*, 213–222. (b) P. M. W. Gill, B. G. Johnson, J. A. Pople, M. J. Frisch, *Chem.Phys. Lett.*, **1992**, *197*, 490–505.

9. A. V. Marenich, C. J. Cramer, D. G. Truhlar, *Journal of Physical Chemistry B* **2009**, *113*, 6378–6396.

10. S. Dapprich, I. Komáromi, K. S. Byun, K. Morokuma, M. J. Frisch, *J. Mol. Struct.: THEOCHEM*, **1999**, *461–462*, 1-21.

11. A. K. Rappe, C. J. Casewit, K. S. Colwell, W. A. Goddard, W. M. Skiff, *J. Amer. Chem. Soc.*, **1992**, *114*, 10024–10035.

12. (a) W. J. Hehre, R. Ditchfield, J. A. Pople, *J. Chem. Phys.* **1972**, *56*, 2257–2261. (b) T. Clark, J. Chandrasekhar, G. W. Spitznagel, P. V. R. Schleyer, *J. Comput. Chem.*, **1983**, *4*, 294–301.

13. (a) K. Fukui, *Acc. Chem. Res.*, **1981**, *14*, 363-368. (b) H. P. Hratchian, H. B. Schlegel, *J. Chem. Phys.* **2004**, *120*, 9918–9124.
G. NMR Spectra

![NMR Spectra Image]

![NMR Spectra Image]
H\textsuperscript{1}-H\textsuperscript{1} COSY analysis of compound 5a
$^{1}\text{H-}^{1}\text{H COSY analysis of compound 5f}$
$^1$H-$^1$H COSY analysis of compound 5h
S73
$^1$H-$^1$H COSY analysis of compound 5t
$^1$H-$^1$H COSY analysis for compound 5u
$^1$H-$^1$H COSY analysis for compound 5W
H. HPLC Traces

**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 85:15), flow rate 1.0 mL/min; $\lambda = 254$ nm

**Racemic sample 5a:**

![HPLC trace for racemic sample 5a](image)

| Peak | RetTime | Type | Width | Area   | Height | Area % |
|------|---------|------|-------|--------|--------|--------|
| 1    | 14.139  | BB   | 0.2519| 195.47308 | 12.01039 | 51.4076 |
| 2    | 15.524  | BB   | 0.2792| 184.76846 | 10.30286 | 48.5924 |

**Enantioenriched sample 5a (0.2 mmol reaction scale):**

![HPLC trace for enantioenriched sample 5a](image)

| Peak | RetTime | Type | Width | Area   | Height | Area % |
|------|---------|------|-------|--------|--------|--------|
| 1    | 14.274  | MM   | 0.2757| 1051.20886 | 63.54309 | 94.8604 |
| 2    | 15.633  | MM   | 0.2934| 56.95524  | 3.23578  | 5.1396 |
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 85:15), flow rate 1.0 mL/min; $\lambda = 254$ nm

**Racemic sample 5a (1 mmol reaction scale):**

| Peak RetTime Type Width | Area [mAU*s] | Height [mAU] | Area % |
|------------------------|--------------|--------------|--------|
| 1 14.139 BB 0.2519     | 195.47308    | 12.01039    | 51.4076|
| 2 15.524 BB 0.2792     | 184.76846    | 10.30286    | 48.5924|

**Enantioenriched sample 5a (1 mmol reaction scale):**

| Peak RetTime Type Width | Area [mAU*s] | Height [mAU] | Area % |
|------------------------|--------------|--------------|--------|
| 1 14.609 MM 0.2895     | 927.21368    | 53.37656    | 96.4916|
| 2 16.020 MM 0.3157     | 33.71346     | 1.77991     | 3.5084|
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 85:15), flow rate 1.0 mL/min; λ = 254 nm

Racemic sample 5b:

![Racemic sample 5b chromatogram](image)

| Peak RetTime | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------------|------|-------------|--------------|--------------|--------|
| 1            | BB   | 0.2273      | 997.54041    | 67.15819     | 50.0027|
| 2            | BB   | 0.2453      | 997.43158    | 62.79693     | 49.9973|

Enantioenriched sample 5b:

![Enantioenriched sample 5b chromatogram](image)

| Peak RetTime | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------------|------|-------------|--------------|--------------|--------|
| 1            | MF   | 0.2520      | 5831.54297   | 385.67615    | 89.6108|
| 2            | FM   | 0.2735      | 676.09412    | 41.20249     | 10.3892|
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 90:10), flow rate 1.0 mL/min; $\lambda = 215$ nm

**Racemic sample 5c:**

| Peak RetTime | Type | Width | Area     | Height  | Area % |
|--------------|------|-------|----------|---------|--------|
| #            | [min]| [min]| [mAU*s]  | [mAU]   |        |
| 1            | 4.758 | MM    | 0.1114   | 301.31821| 45.07009 | 50.3551 |
| 2            | 5.385 | MM    | 0.1245   | 297.06821| 39.77979 | 49.6449 |

**Enantioenriched sample 5c:**

| Peak RetTime | Type | Width | Area     | Height  | Area % |
|--------------|------|-------|----------|---------|--------|
| #            | [min]| [min]| [mAU*s]  | [mAU]   |        |
| 1            | 4.770 | MM    | 0.1223   | 12.10833| 1.64966 | 2.1241  |
| 2            | 5.372 | MM    | 0.1718   | 557.92670| 54.11789 | 97.8759 |
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 90:10), flow rate 1.0 mL/min; \( \lambda = 254 \text{ nm} \)

**Racemic sample 5e:**

![Racemic sample 5e](image)

| Peak RetTime | Type | Width | Area     | Height | Area % |
|--------------|------|-------|----------|--------|--------|
| 1            | BB   | 0.1610| 255.80396| 24.67247| 48.0334|
| 2            | BB   | 0.1821| 276.75043| 23.05053| 51.9666|

**Enantioenriched sample 5e:**

![Enantioenriched sample 5e](image)

| Peak RetTime | Type | Width | Area     | Height | Area % |
|--------------|------|-------|----------|--------|--------|
| 1            | MF   | 0.1807| 3335.17310| 307.64209| 90.7485|
| 2            | FM   | 0.2002| 340.00772 | 28.30513 | 9.2515 |
Condition: HPLC analysis on a Daicel Chiralpak IC column using an isocratic method (Hexane : i-PrOH, 85:15), flow rate 0.9 mL/min; λ = 254 nm

Racemic sample 5e:

![Graph of racemic sample 5e with peak details]

| Peak RetTime Type | Width | Area    | Height | Area % |
|-------------------|-------|---------|--------|--------|
| 1                 | 12.196 MM | 0.2750 | 1052.97473 | 63.80602 | 50.2241 |
| 2                 | 13.497 MM | 0.3035 | 1043.57886 | 57.30347 | 49.7759 |

Enantioenriched sample 5e:

![Graph of enantioenriched sample 5e with peak details]

| Peak RetTime Type | Width | Area    | Height | Area % |
|-------------------|-------|---------|--------|--------|
| 1                 | 12.592 MF | 0.3215 | 1.05820e4 | 548.56342 | 89.9866 |
| 2                 | 13.933 FM | 0.3661 | 1177.53223 | 53.60737 | 10.0134 |
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 91:9), flow rate 0.5 mL/min; $\lambda = 254$ nm

**Racemic sample 5f:**

![Racemic sample 5f graph]

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area [%] |
|--------|--------------|------|------------|--------------|--------------|----------|
| 1      | 20.068       | BB   | 0.2926     | 185.21207    | 9.9773      | 49.0140  |
| 2      | 22.322       | BB   | 0.4069     | 192.66386    | 7.23025     | 50.9860  |

**Enantioenriched sample 5f:**

![Enantioenriched sample 5f graph]

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area [%] |
|--------|--------------|------|------------|--------------|--------------|----------|
| 1      | 20.079       | FM   | 0.3323     | 2273.84302   | 114.03586    | 94.2805  |
| 2      | 22.334       | MM   | 0.4458     | 137.94115    | 5.15714     | 5.7195   |
Condition: HPLC analysis on a Daicel Chiralpak ID-3 column using an isocratic method (Hexane : i-PrOH, 87:13), flow rate 0.9 mL/min; $\lambda = 254$ nm

Racemic sample 5g:

Enantioenriched sample 5g:
**Condition:** UPC² analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO² to 60:40 CO²:ACN), flow rate 2.00 mL/min over 5 min; $\lambda = 248$ nm

**Racemic sample 5h:**

![Racemic sample 5h graph]

**Enantiomeriched sample 5h:**

![Enantiomeriched sample 5h graph]
Condition: UPC² analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO² to 60:40 CO²:ACN), flow rate 2.00 mL/min over 5 min; $\lambda = 248$ nm

Racemic sample 5i:

Enantioenriched sample 5i:
**Condition:** UPC² analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO² to 60:40 CO²:ACN), flow rate 2.00 mL/min over 5 min; \( \lambda = 247 \text{ nm} \)

**Racemic sample 5j:**

![Graph of racemic sample 5j]

**Enantioenriched sample 5j:**

![Graph of enantioenriched sample 5j]
**Condition:** UPC² analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO² to 60:40 CO²:ACN), flow rate 2.00 mL/min over 5 min; \( \lambda = 247 \text{ nm} \)

**Racemic sample 5k:**

![Racemic sample 5k graph]

**Enantioenriched sample 5k:**

![Enantioenriched sample 5k graph]
**Condition:** HPLC analysis on a Daicel Chiralpak IC column (55:42:3 hexane:iPrOH:DCM), flow rate 0.90 mL/min; $\lambda = 254$ nm

**Racemic sample 5l:**

![Racemic sample 5l HPLC graph](image)

| Peak RetTime | Type | Width  | Area    | Height  | Area % |
|--------------|------|--------|---------|---------|--------|
| 1            | MF   | 0.2627 | 396.70798 | 25.16487 | 39.2056 |
| 2            | FM   | 0.3300 | 615.15887 | 31.06535 | 60.7944 |

**Enantioenriched sample 5l:**

![Enantioenriched sample 5l HPLC graph](image)

| Peak RetTime | Type | Width  | Area    | Height  | Area % |
|--------------|------|--------|---------|---------|--------|
| 1            | MF   | 0.2668 | 1520.20410 | 94.96627 | 94.8877 |
| 2            | FM   | 0.3703 | 81.90472  | 3.68627  | 5.1123  |
**Condition:** HPLC analysis on a Daicel Chiralpak IA column (96:2:2 hexane:iPrOH:DCM), flow rate 0.70 mL/min; $\lambda = 254$ nm

**Racemic sample 5m:**

![Racemic sample graph](image)

| Peak RetTime Type | Width [min] | Area [mAU*s] | Area [mAU] | %   |
|-------------------|-------------|--------------|------------|-----|
| 1                 | 12.251      | 1040.54736   | 54.16446   | 47.6643 |
| 2                 | 12.811      | 1142.52820   | 57.46648   | 52.3357 |

**Enantioenriched sample 5m:**

![Enantioenriched sample graph](image)

| Peak RetTime Type | Width [min] | Area [mAU*s] | Area [mAU] | %   |
|-------------------|-------------|--------------|------------|-----|
| 1                 | 12.044      | 95.76341     | 6.14630    | 3.1000 |
| 2                 | 12.521      | 2993.40112   | 153.70834  | 96.9000 |
Condition: HPLC analysis on a Daicel Chiralpak IC column (85:15 hexane:iPrOH), flow rate 1.0 mL/min; λ = 254 nm

Racemic sample 5n:

![Graph of racemic sample 5n]

| Peak RetTime | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area [%] |
|--------------|------|-------------|--------------|--------------|---------|
| 1            | MM   | 0.2320      | 252.94456    | 18.17225     | 50.2796 |
| 2            | MM   | 0.2567      | 250.13094    | 14.04841     | 49.7204 |

Enantioenriched sample 5n:

![Graph of enantioenriched sample 5n]

| Peak RetTime | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area [%] |
|--------------|------|-------------|--------------|--------------|---------|
| 1            | MM   | 0.2319      | 296.05478    | 21.27299     | 94.8326 |
| 2            | MM   | 0.2377      | 16.13179     | 9.03017e-1   | 5.1674  |
**Condition:** UPC$^2$ analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO$_2$ to 60:40 CO$_2$:ACN), flow rate 2.00 mL/min over 5 min; $\lambda = 248$ nm

**Racemic sample 5o:**

![Racemic sample 5o](image)

**Enantioenriched sample 5o:**

![Enantioenriched sample 5o](image)
**Condition:** HPLC analysis on a Daicel Chiralpak IC column (97:03 hexane:iPrOH), flow rate 0.8 mL/min; λ = 254 nm

**Racemic sample 5p:**

![Racemic sample 5p HPLC](image)

| Peak RetTime | Type | Width | Area | Height | Area | % |
|--------------|------|-------|------|--------|------|---|
| 1            | 14.109 | 0.2420 | 6801.01104 | 435.69511 | 50.2453 |
| 2            | 15.897  | 0.2758 | 6735.39525  | 378.12573 | 49.7547 |

**Enantioenriched sample 5p:**

![Enantioenriched sample 5p HPLC](image)

| Peak RetTime | Type | Width | Area | Height | Area | % |
|--------------|------|-------|------|--------|------|---|
| 1            | 14.006 | 0.2600 | 2186.09985 | 140.12761 | 95.5526 |
| 2            | 15.794  | 0.2978 | 101.75038 | 5.69487 | 4.4474 |
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column 85:15 hexane:iPrOH flow rate 1.00 mL/min; $\lambda = 254$ nm

**Racemic sample 5q:**

![Racemic sample 5q graph]

| Peak RetTime Type | Width | Area [mAU*s] | Height [mAU] | Area % |
|-------------------|-------|--------------|--------------|-------|
| 1                 | 20.231 min | 0.4230 | 712.05621 | 28.05388 | 50.0497 |
| 2                 | 22.714 min | 0.4810 | 710.64130 | 24.62222 | 49.9503 |

**Enantioenriched sample 5q:**

![Enantioenriched sample 5q graph]

| Peak RetTime Type | Width | Area [mAU*s] | Height [mAU] | Area % |
|-------------------|-------|--------------|--------------|-------|
| 1                 | 20.305 min | 0.4264 | 1672.75500 | 65.38972 | 92.2530 |
| 2                 | 22.824 min | 0.4887 | 140.46997 | 4.79073 | 7.7470 |
**Condition:** UPC² analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO² to 60:40 CO²:ACN), flow rate 2.00 mL/min over 6 min; λ = 283 nm

**Racemic sample 5r:**

![Racemic sample 5r graph]

**Enantioenriched sample 5r:**

![Enantioenriched sample 5r graph]
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 98:2), flow rate 0.7 mL/min; \( \lambda = 254 \) nm

**Racemic sample 5s:**

![Graph](image1)

| Peak | RetTime | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|------|---------|------|-------------|--------------|--------------|--------|
| 1    | 14.090  | BB   | 0.2859      | 6020.34180   | 319.47778    | 50.0292|
| 2    | 25.089  | BB   | 0.5203      | 6013.30566   | 177.03926    | 49.9708|

**Enantioenriched sample 5s:**

![Graph](image2)

| Peak | RetTime | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|------|---------|------|-------------|--------------|--------------|--------|
| 1    | 14.092  | MM   | 0.3268      | 8535.05664   | 435.25729    | 95.6589|
| 2    | 25.192  | MM   | 0.6158      | 397.32693    | 10.48334     | 4.3411 |
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column (85:15 hexane:iPrOH), flow rate 0.8 mL/min; λ = 254 nm

**Racemic sample 5t:**

![Graph of racemic sample 5t](image)

| Peak Ret Time Type | Width  | Area      | Height | Area   |
|-------------------|--------|-----------|--------|--------|
| 1                 | 10.206 | 0.3070    | 534.755 | 29.027 | 46.2820 |
| 2                 | 11.008 | 0.3144    | 620.673 | 32.501 | 53.7160 |

**Enantioenriched sample 5t:**

![Graph of enantioenriched sample 5t](image)

| Peak Ret Time Type | Width  | Area      | Height | Area   |
|-------------------|--------|-----------|--------|--------|
| 1                 | 10.756 | 0.3411    | 1890.73 | 92.380 | 99.0859 |
| 2                 | 11.872 | 0.2888    | 17.443 | 1.0066 | 0.9141 |
**Condition:** HPLC analysis on a Daicel Chiralpak IB column (85:15 hexane:iPrOH), flow rate 1.0 mL/min; \( \lambda = 254 \text{ nm} \)

**Racemic sample 5u:**

![Racemic sample 5u chromatogram](chart)

| Peak | RetTime | Type | Width | Area   | Height | Area  |
|------|---------|------|-------|--------|--------|-------|
| 1    | 24.085  | BB   | 0.4382| 556.50024| 19.70127| 55.0408|
| 2    | 30.691  | MM   | 0.6367| 454.56784| 11.89833| 44.9592|

**Enantioenriched sample 5u:**

![Enantioenriched sample 5u chromatogram](chart)

| Peak | RetTime | Type | Width | Area   | Height | Area  |
|------|---------|------|-------|--------|--------|-------|
| 1    | 24.011  | MM   | 0.4732| 2257.91821| 79.52377| 98.4613|
| 2    | 30.622  | MM   | 0.6882| 35.28564 | 8.80142e-1| 1.5387|
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column (95:5 hexane:iPrOH), flow rate 0.9 mL/min; $\lambda = 254$ nm

**Racemic sample 5v (Major diastereoisomer):**

![HPLC chromatogram for racemic sample 5v]

| Peak RetTime | Type | Width | Area     | Height | Area %  |
|--------------|------|-------|----------|--------|--------|
| 1 25.265     | MF   | 0.4467| 2288.04297| 85.37150| 50.1045|
| 2 26.771     | FM   | 0.4761| 2278.50000| 79.77052| 49.8955|

**Enantioenriched sample 5v:**

![HPLC chromatogram for enantioenriched sample 5v]

| Peak RetTime | Type | Width | Area     | Height | Area %  |
|--------------|------|-------|----------|--------|--------|
| 1 24.438     | FM   | 0.4275| 379.76779| 14.80707| 93.5892|
| 2 26.146     | MM   | 0.4662| 26.01393 | 9.29904e-1| 6.4108|
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column (95:5 hexane:iPrOH), flow rate 0.9 mL/min; $\lambda = 254$ nm

Racemic sample 5v (Minor diastereoisomer):

Enantioenriched sample 5v:
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (80:20 Hexane:iPrOH), flow rate 0.4 mL/min; $\lambda = 247$ nm

**Racemic sample 5w:**

![Graph of racemic sample 5w]

| Peak | RetTime | Type | Width | Area    | Height | Area   | %    |
|------|---------|------|-------|---------|--------|--------|------|
| 1    | 24.041  | BV   | 0.4031| 1.94724e4| 744.71960| 49.1934|      |
| 2    | 24.941  | VB   | 0.4288| 2.01110e4| 722.37164| 50.8066|      |

**Enantioenriched sample 5w:**

![Graph of enantioenriched sample 5w]

| Peak | RetTime | Type | Width | Area    | Height | Area   | %    |
|------|---------|------|-------|---------|--------|--------|------|
| 1    | 24.037  | BV   | 0.4004| 1522.06580| 58.72913| 10.2344|      |
| 2    | 24.918  | VB   | 0.4200| 1.33501e4| 489.78726| 89.7656|      |
**Condition:** HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (98:2 hexane:iPrOH) flow rate 0.80 mL/min; $\lambda = 254$ nm

**Racemic sample 6:**

![Racemic sample 6 Chromatogram](image)

| Peak RetTime Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|------------------|-------------|--------------|--------------|-------|
| 1                | 16.053      | 940.59619    | 54.22182     | 49.4914 |
| 2                | 16.892      | 859.92847    | 52.34462     | 50.5086 |

**Enantioenriched sample 6:**

![Enantioenriched sample 6 Chromatogram](image)

| Peak RetTime Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|------------------|-------------|--------------|--------------|-------|
| 1                | 16.509      | 254.46493    | 1.46060      | 4.8113 |
| 2                | 17.370      | 582.94232    | 28.99752     | 95.1887 |