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Supporting Information

Light-Driven Enantioselective Organocatalytic β-Benzylation of Enals

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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: $[\alpha]_D$ 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 Opolette 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.

The authors are indebted to the team of the Research Support Area at ICIQ, in particular to: Dr. Eduardo Escudero-Adan (X-ray Unit), Dr. Marta Giménez (Chemical Reaction Technologies Unit), and Dr. Javier Pérez (Photophysics Unit). Grace Fox is thanked for proofreading the manuscript.

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.

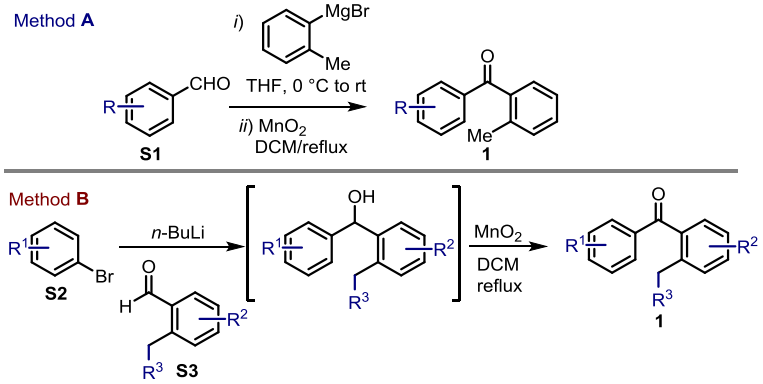
Determination of Diastereomeric Ratio. The diastereomeric ratio for the photoenolization/β-benzylation sequence (products **5**) was determined by ^{1}H NMR analysis of the crude reaction mixture through integration of diagnostic signals, and then confirmed by HPLC analysis.

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)-(–)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether (**4a**) and (*S*)-(−)-α,α-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.

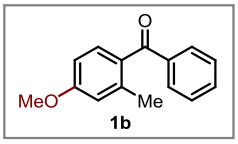
B. Substrate Synthesis



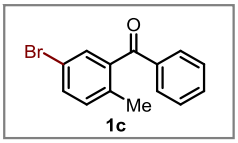
Scheme S1. Synthetic pathways for preparing the benzophenone substrates **1**

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 ºC, 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 ºC. The biphasic system was then extracted with Et_2O (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 MnO_2 (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**.

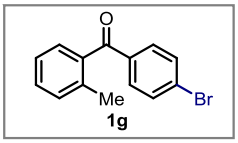
Method B: The commercially available bromobenzene derivative **S2** (1 equiv.) was dissolved in dry THF (0.25 M) under an argon atmosphere. After cooling the mixture to -30 ºC, a solution of *n*-BuLi 1.9 M in hexane (1.5 equiv.) was added dropwise. After the addition, the solution was allowed to warm 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 ºC, and stirring was continued over 2 hours. The reaction was then quenched by carefully adding water and extracted with Et_2O (x 3). The organic phases were collected and concentrated under vacuum. The crude alcohol intermediate was then subjected to MnO_2 oxidation as in Method A. FC purification on silica gel afforded the benzophenone substrate **1**.



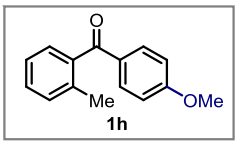
(4-methoxy-2-methylphenyl)(phenyl)methanone (1b). Following the procedure detailed in Method B, **1b** was isolated by FC on silica gel (hexane/EtOAc 97:3 v/v) in 77% yield as a colorless oil. TLC (hexane/EtOAc: 95:5 v/v): R_f = 0.32; HRMS calculated for $[C_{15}H_{14}O_2+Na]^+$: 249.0891; found: 249.0894.
^{1}H NMR (400 MHz, $CDCl_3$) 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, CH_3 OMe), 2.44 (d, *J* = 0.7 Hz, 3H, CH_3). **^{13}C NMR (100 MHz, $CDCl_3$)** 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 (CH_3 OMe), 20.8 (CH_3).



(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 $[C_{14}H_{11}BrO+Na]^+$: 296.9891; found: 296.9895.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.78 (m, 2H, Ar), 7.62 (ddt, *J* = 8.7, 6.9, 1.3 Hz, 1H, Ar), 7.55 – 7.42 (m, 4H, Ar), 7.19 (dd, *J* = 8.2, 0.8 Hz, 1H, Ar), 2.27 (s, 3H, CH_3). **^{13}C NMR (100 MHz, $CDCl_3$)** 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 (CH_3).



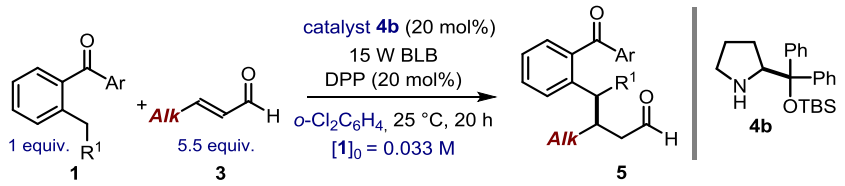
(4-bromophenyl)(o-tolyl)methanone (1g). Following the procedure detailed in Method A, **1e** was isolated by FC on silica (hexane/EtOAc: 98:2 v/v) in 76% yield as a colorless oil. TLC (hexane/EtOAc: 98:2 v/v): R_f = 0.34; HRMS calculated for $[C_{14}H_{11}BrO+Na]^+$: 296.9891; found: 296.9893.
^{1}H NMR (400 MHz, $CDCl_3$) 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, 1H, CH_3). **^{13}C NMR (100 MHz, $CDCl_3$)** 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 (CH_3).



(4-methoxyphenyl)(o-tolyl)methanone (1h). Following the procedure detailed in Method A, **1e** 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.
^{1}H NMR (400 MHz, $CDCl_3$) 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, CH_3 OMe), 2.33 (s, 3H, CH_3). **^{13}C NMR (100 MHz, $CDCl_3$)** 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 (CH_3 OMe), 19.8 (CH_3).

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 (*o*-$Cl_2C_6H_4$). 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 *o*-$Cl_2C_6H_4$. 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.

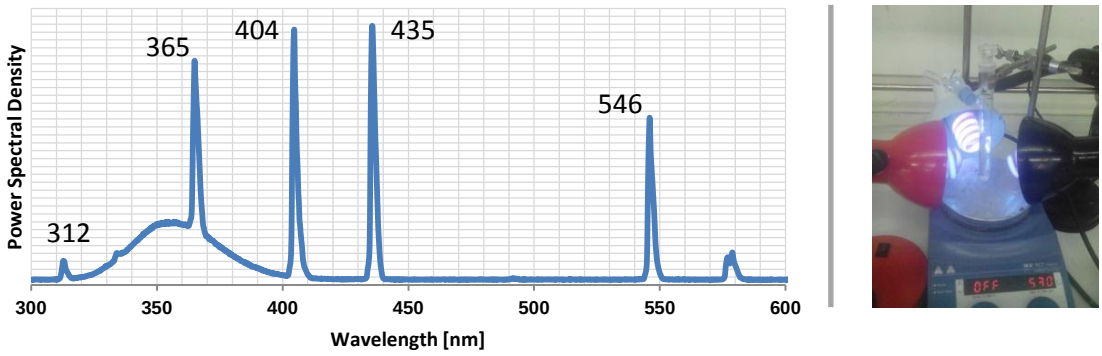
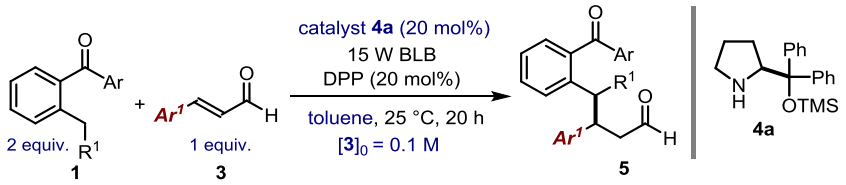


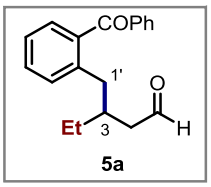
Figure S1. Emission spectrum of the 15 W BLB lamp used in this study (left) and the set-up of the reaction (right). The high intensity of emission at 365 nm secured an efficient excitation of the benzophenone substrate **1** and the generation of the reactive photoenol. The use of different light sources, 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.

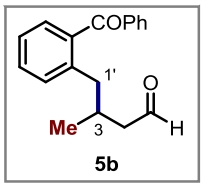
Characterization Data



(*S*)-3-(2-benzoylbenzyl)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 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 a colorless oil (34 mg, 61% yield, 90% ee). TLC: (hexane/EtOAc: 90:10 v/v), R_f = 0.32. The ee (90%) was determined by HPLC analysis on a Daicel Chiralpak IC column: 85:15 hexane/*i*PrOH, flow rate 1.00 mL/min; λ = 254 nm; τ_{major} = 14.3 min, τ_{minor} = 15.6 min. $[\alpha]^{26}_D$ = +75.6 (c = 0.5 in $CHCl_3$). HRMS calculated for $[C_{19}H_{20}O_2+Na]^+$: 303,1361; found: 303,1363.

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.58 (t, *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, CH_2, H4), 0.83 (t, *J* = 7.4 Hz, 3H, CH_3). **^{13}C NMR (125 MHz, $CDCl_3$)** 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 x2), 130.2 (CH Ar), 128.9 (CH Ar x2), 128.5 (CH Ar x2), 125.7 (CH Ar), 47.5 (CH_2), 37.5 (CH_2), 36.7 (CH), 26.8 (CH_2), 10.9 (CH_3).

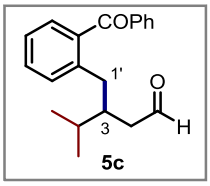
Compound **5a** was also obtained through a 1 mmol scale procedure using 2-methylbenzophenone **1a** (181 µL, 1 mmol, 1 equiv.), *trans*-2-pentenal (540 µL, 5.5 mmol, 5.5 equiv.), diphenyl phorphoric acid (25 mg, 0.1 mmol, 0.1 equiv.) and catalyst **4b** (75 mg, 0.2 mmol, 0.2 equiv). The crude mixture 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/*i*PrOH, flow rate 1.00 mL/min; λ = 254 nm; τ_{major} = 14.3 min, τ_{minor} = 15.6 min.



5b

(*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 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 a colorless oil (34 mg, 64% yield, 79% ee). TLC (hexane/EtOAc: 90/10 v/v): R_f = 0.32. The *ee* value (79%) was determined by HPLC analysis on a Daicel Chiralpak IC column 85:15 hexane:*i*PrOH flow rate 1.00 mL/min; λ = 254 nm; τ_{major} = 11.9 min, τ_{minor} = 12.8 min. $[\alpha]^{26}_D$ = + 17.5 (c = 1.0 in $CHCl_3$). HRMS calculated for $[C_{18}H_{18}O_2+Na]^+$: 289,1204; found 289,1205.

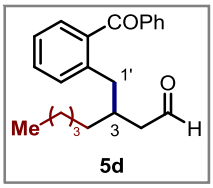
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (dd, *J* = 2.6, 1.6 Hz, 1H, CHO), 7.86 – 7.78 (m, 2H, Ar), 7.61 (m, 1H, Ar), 7.52 – 7.42 (m, 3H, Ar), 7.36 – 7.27 (m, 3H, Ar), 2.72 (dd, *J* = 13.6, 7.1 Hz, 1H, H1'α), 2.66 (dd, *J* = 13.7, 7.2 Hz, 1H, H1' β), 2.44 – 2.33 (m, 2H, H2), 2.23 (td, *J* = 8.7, 8.1, 2.6 Hz, 1H, H3), 0.93 (d, *J* = 6.5 Hz, 3H, CH_3).**^{13}C NMR (100 MHz, $CDCl_3$)** 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 (CH_2), 40.2 (CH_2), 30.3 (CH), 20.0 (CH_3).



5c

(*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 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 a colorless oil (31 mg, 53% yield, 96% ee). TLC (hexane/EtOAc: 90/10 v/v): R_f = 0.35. The *ee* value (96%) was determined by HPLC analysis on a Daicel Chiralpak IC column 90:10 hexane:*i*PrOH flow rate 1.00 mL/min; λ = 215 nm; τ_{major} = 5.4 min, τ_{minor} = 4.8 min. $[\alpha]^{26}_D$ = + 29.8 (c = 1.0 in $CHCl_3$). HRMS calculated for $[C_{20}H_{22}O_2+Na]^+$: 317,1517; found: 317,1515.

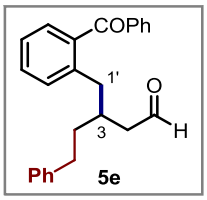
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (t, *J* = 2.1 Hz, 1H, CHO), 7.85 – 7.80 (m, 2H, Ar), 7.65 – 7.58 (m, 1H, Ar), 7.52 – 7.41 (m, 3H, Ar), 7.36 – 7.27 (m, 3H, Ar), 2.89 (dd, *J* = 13.8, 5.8 Hz, 1H, H1'α), 2.52 (dd, *J* = 13.8, 8.6 Hz, 1H, H1' β), 2.29 (dd, *J* = 6.0, 2.2 Hz, 1H, H2α), 2.26 (dd, *J* = 6.4, 2.2 Hz, 1H, H2β), 2.23 – 2.20 (m, 1H, H3), 1.68 (m, 1H, H4), 0.83 (d, *J* = 2.2 Hz, 3H, CH_3), 0.81 (d, *J* = 2.2 Hz, 3H, CH3). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 202.9 (C=O), 198.4 (CHO), 139.5 (Cq Ar), 1389.0 (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 (CH_2), 40.86 (CH_2), 34.7 (CH), 30.0 (CH), 19.3 (CH_3), 18.5 (CH_3).



5d

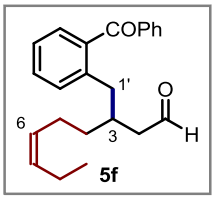
(*S*)-3-(2-benzoylbenzyl)decanal (5d). Compound **5d** was prepared according to the general procedure A, using 2-methylbenzophenone **1a** (36 µL, 0.2 mmol, 1 equiv.), *trans*-2-decenal (202 µL, 1.1 mmol, 5.5 equiv.), diphenyl phorphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst **4b** (15 mg, 0.04 mmol, 0.2 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 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): R_f = 0.36. The *ee* value (82%) was determined by HPLC analysis on a Daicel Chiralpak IC column 90:10 hexane:*i*PrOH flow rate 1.00 mL/min; λ = 254 nm; τ_{major} = 7.9 min, τ_{minor} = 8.5 min. $[\alpha]^{26}_D$ = + 24.8 (c = 0.4 in $CHCl_3$). HRMS calculated for $[C_{24}H_{30}O_2+Na]^+$: 345,1830; found: 345,1833.

^{1}H NMR (400 MHz, $CDCl_3$) δ 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'α), 2.56 (dd, *J* = 13.7, 7.9 Hz, 1H, H1'β), 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}C NMR (100 MHz, $CDCl_3$)** δ 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).



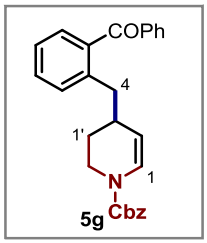
(*S*)-3-(2-benzoylbenzyl)-5-phenylpentanal (5e). Compound **5e** was prepared according to the general procedure A, using 2-methylbenzophenone **1a** (36 µL, 0.2 mmol, 1 equiv.), *trans*-5-phenylpentenal (176 mg, 1.1 mmol, 5.5 equiv.), diphenyl phorphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst **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 a colorless oil (41 mg, 57% yield, 80% ee). TLC (hexane/EtOAc: 90/10 v/v): R_f = 0.33. The *ee* value (80%) was determined by HPLC analysis on a Daicel Chiralpak IC column 85:15 hexane:*i*PrOH flow rate 0.90 mL/min; λ = 254 nm; τ_{major} = 12.6 min, τ_{minor} = 13.9 min. $[\alpha]^{26}_D$ = +98.6 (c = 1.0 in $CHCl_3$). HRMS calculated for $[C_{25}H_{24}O_2+Na]^+$: 379,1674; found: 379,1677.

^{1}H NMR (400 MHz, $CDCl_3$) δ 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'α), 2.66 (dd, *J* = 13.8, 8.0 Hz, 1H, H1'β), 2.60 – 2.49 (m, 2H, H2), 2.39 – 2.35 (m, 1H, H3), 2.31 (m, 2H, H5), 1.64 (m, 2H, H4).**^{13}C NMR (100 MHz, $CDCl_3$)** [1] δ 202.4(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), 130.1 (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).



(*S*,*Z*)-3-(2-benzoylbenzyl)non-6-enal (5f). Compound **5f** was prepared according to the general procedure A, using 2-methylbenzophenone **1a** (36 µL, 0.2 mmol, 1 equiv.), *trans*-2,*cis*-6-nonadienal (177 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: 95:5 v/v) to afford the title compound as a colorless oil (37 mg, 55% 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 91:9 hexane:*i*PrOH flow rate 0.50 mL/min; λ = 254 nm; τ_{major} = 20.1 min, τ_{minor} = 22.3 min. $[\alpha]^{26}_D$ = + 100.2 (c = 1.0 in $CHCl_3$). HRMS calculated for $[C_{23}H_{26}O_2+Na]^+$: 357,1830; found: 357,1832.

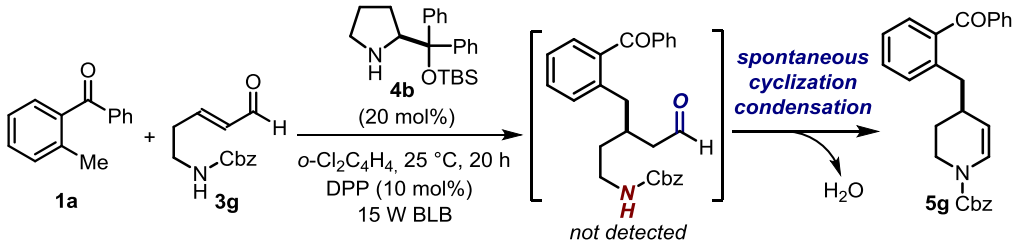
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (t, *J* = 2.1 Hz, 1H, CHO), 7.86 – 7.77 (m, 2H, Ar), 7.65 – 7.56 (m, 1H, Ar), 7.53 – 7.39 (m, 3H, Ar), 7.36 – 7.26 (m, 3H, Ar), 5.38 – 5.26 (m, 1H, H6), 5.24 – 5.11 (m, 1H, H7), 2.86 (dd, *J* = 13.8, 6.0 Hz, 1H, H1'α), 2.62 (dd, *J* = 13.7, 7.7 Hz, 1H H1'β), 2.37 – 2.20 (m, 3H, H2+H3), 2.05 – 1.88 (m, 4H, H5+H8), 1.40 – 1.29 (m, 2H, H4), 0.92 (t, *J* = 7.5 Hz, 3H, CH_3).**^{13}C NMR (100 MHz, $CDCl_3$)** ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6 (C=O), 198.4 (CHO), 139.2 (Cq Ar), 138.9 Cq Ar), 137.7 (Cq Ar), 133.3 (CH Ar), 132.1 (CH C=C), 131.0 (CH Ar), 130.3 (CH Ar), 130.2 (CH Ar x2), 128.9 (CH Ar), 128.5 (CH Ar x2), 128.2 (CH C=C), 125.8 (CH Ar), 47.8 (CH_2), 37.8 (CH_2), 35.0 (CH_2), 34.3 (CH), 24.3 (CH_2), 20.5 (CH_2), 14.3 (CH_3).



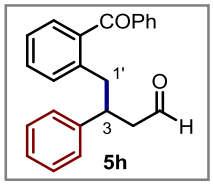
Benzyl (*R*)-4-(2-benzoylbenzyl)-dihydropyridine-1(2H)-carboxylate (5g). Compound **5g** was prepared according to the general procedure A, using 2-methylbenzophenone **1a** (36 µL, 0.2 mmol, 1 equiv.), *trans*-benzyl-(5-oxopenten1yl)carbamate (257 mg, 1.1 mmol, 5.5 equiv.), diphenyl phorphoric acid (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: 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): R_f = 0.35. The *ee* (89%) was determine by HPLC analysis on a Daicel Chiralpak ID-3 column 87:13 hexane:*i*PrOH flow rate 0.90 mL/min; λ = 254 nm; τ_{major} = 15.1 min, τ_{minor} = 13.7 min. HRMS calculated for $[C_{27}H_{25}NO_3+Na]^+$: 434,1732; found: 434,1733.

^{1}H NMR (400 MHz, $CDCl_3$) δ 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), 6.79 (dd, *J* = 36.4, 8.4 Hz, 1H, H1)., 5.18 (s, 2H, CH_2 Cbz), 4.74 (m, H2), 3.79 – 3.66 (m, 1H, H2'α), 3.39 (ddd, *J* = 12.9, 9.1, 3.6 Hz, 1H, H2'β), 2.82 – 2.63 (m, 2H, H4), 2.46 (m, 1H, H3), 1.78 (m, 1H, H1'α), 1.57 – 1.43 (m, 1H, H1'α).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 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), 128.5 (CH Ar x2), 128.1 (CH Ar), 128.0 (CH Ar), 125.6 (CH Ar), 124.4 (CH), 110.1 (CH), 67.5 (CH_2 Cbz), 40.6 (CH_2), 39.2 (CH_2), 33.7 (CH), 27.4 (CH_2).

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).



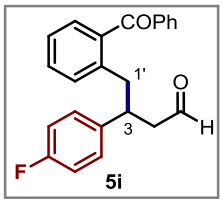
Scheme S2. Reaction mechanism for the formation of the cyclic compound **5g**.



(*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 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 (37 mg, 57% yield, 94% ee). TLC: (hexane/EtOAc: 90:10 v/v), R_f = 0.31. The ee (94%) 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 = 247 nm; τ_{major} = 3.17 min, τ_{minor} = 3.53 min. $[\alpha]^{26}_D$ = +12.6 (c = 0.5 in $CHCl_3$). HRMS calculated for $[C_{23}H_{20}O_2+Na]^+$: 351,1361; found: 351,1365.

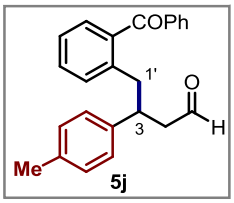
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (t, *J* = 2.1 Hz, 1H, CHO), 7.75 – 7.68 (m, 2H, Ar), 7.64 – 7.57 (m, 1H, Ar), 7.50 – 7.42 (m, 2H, Ar), 7.37 (m, 2H, Ar), 7.31 – 7.23 (m, 2H, Ar), 7.18 (m, 3H, Ar), 7.15 – 7.10 (m, 1H, Ar), 7.10 – 7.05 (m, 2H, Ar), 3.56 (p, *J* = 7.6 Hz, 1H, CH H3), 3.15 – 2.99 (m, 2H, CH_2 H1'), 2.85 – 2.67 (m, 2H, CH_2 H2). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 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

Ar), 130.3 (CH Ar x2), 130.2 (CH Ar), 129.2 (CH Ar), 128.6 (CH Ar x2), 128.4 (CH Ar x2), 127.5 (CH Ar x2), 126.7 (CH Ar), 125.6 (CH Ar), 49.2 (CH), 42.0 (CH_2), 40.2 (CH_2).



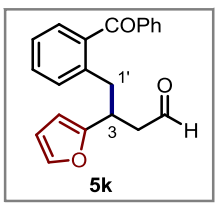
(*S*)-4-(2-benzoylphenyl)-3-(4-fluorophenyl)butanal (**5i**). Compound **5i** was prepared according to the general procedure B, using 2-methylbenzophenone **1a** (72 µL, 0.4 mmol, 2 equiv.), *trans*-4-fluorocinnamaldehyde (23 µL, 0.2 mmol, 1 equiv.), diphenyl phorphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) 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 (36 mg, 52% yield, 89% ee). TLC: (hexane/EtOAc: 90:10 v/v), R_f = 0.31. The ee (89%) 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 = 247 nm nm; τ_{major} = 3.96 min, τ_{minor} = 3.50 min. $[\alpha]^{26}_D$ = +8.8 (c = 0.5 in $CHCl_3$). HRMS calculated for $[C_{23}H_{19}FO_2+Na]^+$: 369,1267; found: 369,1269.

^{1}H 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). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 201.2 (C=O), 198.2 8CHO), 138.7, 138.5, 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), 41.4 (CH_2), 40.2 (CH_2).



(*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 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 (45 mg, 66% yield, 88% ee). TLC: (hexane/EtOAc: 90:10 v/v), R_f = 0.31. The ee (88%) 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 = 247 nm; τ_{major} = 3.23 min, τ_{minor} = 3.71 min. HRMS calculated for $[C_{24}H_{22}O_2+Na]^+$: 365,1517; found: 365,1520.

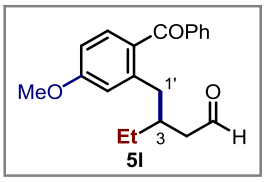
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (t, *J* = 2.1 Hz, 1H, CHO), 7.73 – 7.65 (m, 2H, Ar), 7.62 – 7.57 (m, 1H, Ar), 7.48 – 7.41 (m, 2H), 7.38 (m, 1H, Ar), 7.29 – 7.18 (m, 3H), 7.03 – 6.89 (m, 4H), 3.50 (ddd, *J* = 15.1, 8.1, 6.9 Hz, 1H, H3), 3.12 (dd, *J* = 13.7, 8.2 Hz, 1H, H1'α), 3.03 (dd, *J* = 13.6, 7.0 Hz, 1H, H1'β), 2.78 – 2.67 (m, 2H, H2), 2.24 (s, 3H, CH_3). **^{13}C NMR (125 MHz, $CDCl_3$)** 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 (CH_2), 40.1 (CH_2), 21.0 (CH_3).



(*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 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 (33 mg, 56% yield, 90% ee). TLC:

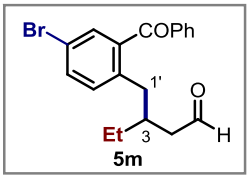
(hexane/EtOAc: 90:10 v/v), R_f = 0.3. The ee (90%) was determined by UPC^2 analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO^2 to 60:40 CO^2:ACN), flow rate 2.00 mL/min; λ = 247 nm; τ_{major} = 2.86 min, τ_{minor} = 2.99 min. $[\alpha]^{26}_D$ = 17.6 (c = 0.35 in $CHCl_3$). HRMS calculated for $[C_{21}H_{18}O_3+Na]^+$: 341,1154; found: 341,1155.

^{1}H 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'α), 3.01 (dd, *J* = 13.6, 6.9 Hz, 1H, H1'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). **^{13}C NMR (125 MHz, $CDCl_3$)** 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_2), 35.4 (CH_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.), *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_f = 0.34. The *ee* value (90%) was determined by HPLC analysis on a Daicel Chiralpak IC column 55:42:3 hexane:*i*PrOH:DCM flow rate 0.90 mL/min; λ = 254 nm; τ_{major} = 10.8 min, τ_{minor} = 11.8 min. $[\alpha]^{26}_D$ = + 135.7 (c = 1.0 in $CHCl_3$). HRMS calculated for $[C_{22}H_{22}O_3+Na]^+$: 333,1467; found: 333,1466.

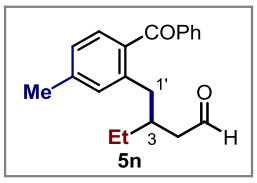
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.63 (t, *J* = 2.3 Hz, 1H, CHO), 7.81 – 7.75 (m, 2H, Ar), 7.62 – 7.57 (m, 1H), 7.52 – 7.43 (m, 2H, Ar), 7.34 (d, *J* = 8.5 Hz, 1H, Ar), 6.86 (d, *J* = 2.6 Hz, 1H, Ar), 6.79 (dd, *J* = 8.5, 2.6 Hz, 1H, Ar), 3.89 (s, 3H, OMe), 2.97 (dd, *J* = 13.5, 6.6 Hz, 1H, H1'α), 2.68 (dd, *J* = 13.6, 8.2 Hz, 1H, H1'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_3). **^{13}C NMR (125 MHz, $CDCl_3$)** 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_3 OMe), 47.5 (CH_2), 37.8 (CH_2), 36.8 (CH_2), 26.9 (CH), 11.0 (CH_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.), *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_f = 0.34. The *ee* value (94%) was determined by HPLC analysis on a Daicel Chiralpak IA column 96:2:2 hexane:*i*PrOH:DCM flow rate 0.70 mL/min; λ = 254 nm; τ_{major} = 12.0 min, τ_{minor} = 12.5 min. $[\alpha]^{26}_D$ = +168.6 (c = 0.6 in $CHCl_3$). HRMS calculated for $[C_{19}H_{29}BrO_2+Na]^+$: 381,0466; found: 381,0461.

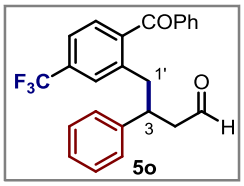
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (t, *J* = 2.1 Hz, 1H, CHO), 7.80 (m, 2H, Ar), 7.69 – 7.39 (m, 5H, Ar), 7.30 – 7.18 (m, 1H, Ar), 2.74 (dd, *J* = 13.8, 6.8 Hz, 1H, H1'α), 2.51 (dd, *J* = 13.8, 6.9 Hz, 1H, H1'β), 2.35 – 2.25 (m, 2H, H2α+H2β), 2.14 (dt, *J* = 13.5, 6.7 Hz, 1H, H3), 1.41 – 1.18 (m, 2H, H4α+H4β), 0.81 (t, *J* = 7.4 Hz, 3H, CH_3). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 202.4 (C=O), 196.7

(CHO), 140.82 (Cq Ar), 138.2 (Cq Ar), 137.0 (Cq Ar), 133.8 (CH Ar) 133.1 (CH Ar), 132.7 (CH Ar x2), 131.3 (CH Ar), 130.1 (CH Ar x2), 128.7 (CH Ar x2), 119.6 (CH Ar), 47.3 (CH_2), 36.9 (CH_2), 36.5 (CH), 26.6 (CH_2), 10.9 (CH_3).



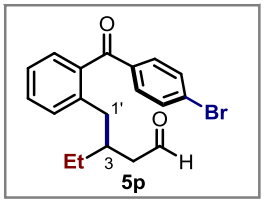
(*S*)-3-(2-benzoyl-5-methylbenzyl)pentanal (5n). Compound **5n** was prepared according to the general procedure A, using 2,4-dimethylbenzophenone (44 mg, 0.2 mmol, 1 equiv.), *trans*-2-pentenal (108 µL, 1.1 mmol, 5.5 equiv.), diphenyl phorphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst **4b** (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 a colorless oil (37 mg, 63% yield, 90% ee). TLC: (hexane/EtOAc: 90:10 v/v), R_f = 0.30. The ee (90%) was determined by HPLC analysis on a Daicel Chiralpak IC column 85:15 hexane:*i*PrOH flow rate 1.00 mL/min; λ = 254 nm; τ_{major} = 11.6 min, τ_{minor} = 16.7 min. $[\alpha]^{26}_D$ = +75.6 (c = 0.7 in $CHCl_3$). HRMS calculated for $[C_{20}H_{22}O_2+Na]^+$: 317,1517; found: 317,1519.

^{1}H NMR (400 MHz, $CDCl_3$) 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, CH_3).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 203.0 (C=O), 198.4 (CHO), 140.6 (Cq Ar), 139.8 (Cq Ar), 138.2 (Cq Ar), 135.9 (Cq Ar), 133.0 (CH Ar), 131.9 (CH Ar), 130.1 (CH Ar x2), 129.6 (CH Ar), 128.4 (CH Ar x2), 126.3 (CH Ar), 47.5 (CH_2), 37.5 (CH_2), 36.8 (CH), 26.9 (CH_3), 21.5 (CH_2), 11.0. (CH_3).



(*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 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 (46 mg, 58% yield, 97% ee). TLC: (hexane/EtOAc: 90:10 v/v), R_f = 0.33. The ee (97%) was determined by 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; λ = 247 nm; τ_{major} = 2.27 min, τ_{minor} = 2.51 min. $[\alpha]^{26}_D$ = 40.3 (c = 0.28 in $CHCl_3$). HRMS calculated for $[C_{24}H_{19}F_3O_2+Na]^+$: 419,1235; found: 419,1237.

^{1}H 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, 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).**^{13}C NMR (125 MHz, $CDCl_3$)** 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 (CH_2), 40.0 (CH_2).

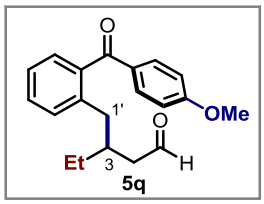


(*S*)-3-(2-(4-bromobenzoyl)benzyl)pentanal (5p). Compound **5p** was prepared according to the general procedure A, using (4-bromophenyl)(o-tolyl)methanone (55 mg , 0.2 mmol, 1 equiv.), *trans*-2-pentenal (108 µL, 1.1 mmol, 5.5 equiv.), diphenyl phorphoric acid (10 mg, 0.04 mmol, 0.2 equiv.) and catalyst **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 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:*i*PrOH flow rate 0.80 mL/min; λ = 254 nm; τ_{major} = 14.0 min, τ_{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.

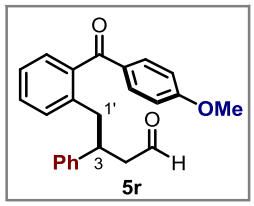
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (t, *J* = 2.1 Hz, 1H, CHO), 7.71 – 7.65 (m, 2H, Ar), 7.65 – 7.58 (m, 2H, Ar), 7.46 (m, 1H, Ar), 7.37 – 7.26 (m, 3H, Ar), 2.85 (dd, *J* = 13.7, 6.6 Hz, 1H, H1'α), 2.57 (dd, *J* = 13.7, 8.2 Hz, 1H, H1'β), 2.34 – 2.27 (m, 2H, H2), 2.18 (m, 1H, H3), 1.40 – 1.24 (m, 2H, H4), 0.84 (t, *J* = 7.4 Hz, 3H, CH_3). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 202.6 (C=O), 197.3 (CHO), 139.5 (Cq Ar), 138.3 (Cq Ar), 136.5 (Cq Ar), 131.9 (CH Ar x2), 131.6 (CH Ar x2), 131.2 (CH Ar), 130.5 (CH Ar), 128.8 (CH Ar), 128.6 (Cq Ar), 125.8 (CH Ar), 47.5 (CH_2), 37.4 (CH_2), 36.8 (CH_2), 26.8 (CH), 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 phorphoric 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:*i*PrOH flow rate 0.80 mL/min; λ = 254 nm; τ_{major} = 14.00 min, τ_{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 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 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:*i*PrOH flow rate 1.00 mL/min; λ = 254 nm; τ_{major} = 20.3 min, τ_{minor} = 22.8 min. $[\alpha]^{26}_D$ = +150.5 (c = 0.7 in $CHCl_3$). HRMS calculated for $[C_{20}H_{22}O_3+Na]^+$: 333,1467; found: 333,1470.

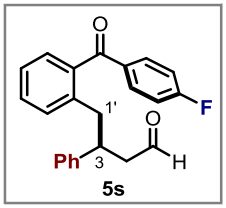
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (t, *J* = 2.2 Hz, 1H, CHO), 7.88 – 7.75 (m, 2H, Ar), 7.43 (m, 1H, Ar), 7.34 – 7.25 (m, 3H, Ar), 6.98 – 6.89 (m, 2H, Ar), 3.90 (s, 3H, OMe), 2.83 (dd, *J* = 13.8, 6.5 Hz, 1H, H1'α), 2.54 (dd, *J* = 13.8, 8.2 Hz, 1H, H1'β), 2.29 (m, 2H, H2), 2.18 (dq, *J* = 8.2, 6.4 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, $CDCl_3$)** δ 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 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 (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; τ_{major} = 3.78 min, τ_{minor} = 4.19 min. $[\alpha]^{26}_D$ = 63.5 (c = 0.3 in $CHCl_3$). HRMS calculated for $[C_{24}H_{22}O_3+Na]^+$: 381,1467; found: 381,1470.

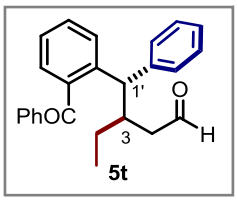
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (t, *J* = 1.9 Hz, 1H, CHO), 7.71 – 7.66 (m, 2H, Ar), 7.66 – 7.61 (m, 1H, Ar), 7.53 – 7.45 (m, 4H, Ar), 7.42 – 7.34 (m, 2H, Ar), 7.32 – 7.30 (m, 1H, Ar), 7.23 – 7.11 (m, 3H, Ar), 7.05 – 7.01 (m, 2H, Ar), 3.53 (m, 1H, H3), 3.10 (dd, J = 13.8, 6.4 Hz, 1H, H1'α), 3.05 (dd, J = 13.7, 8.9 Hz, 1H, H1'β), 2.82 (ddd, J = 16.9, 8.1, 2.0 Hz, 1H, H2α), 2.75 (ddd, J = 16.9, 6.7, 1.8 Hz, 1H, H2β). **^{13}C 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).



5s

(*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 Chiralpak 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; τ_{major} = 14.09 min, τ_{minor} = 25.20 min. $[\alpha]^{26}_D$ = +37.6 (c = 0.5 in $CHCl_3$). HRMS calculated for $[C_{23}H_{19}FO_2+Na]^+$: 369,1267; found: 369,1270.

^{1}H 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, H2α+H2β). **^{13}C 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), 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).

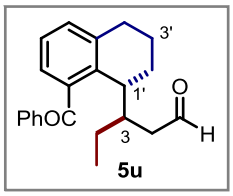


5t

(*R*)-3-[(*S*)-(2-benzoylphenyl)(phenyl)methyl]pentanal (5t). Compound **5t** was prepared according to the general procedure A, using (2-benzylphenyl)(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 a 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: 87:13 v/v), R_f = 0.33. The ee (98%) was determined by HPLC analysis on a Daicel Chiralpak IC-3 column 85:15 hexane:*i*PrOH flow rate 0.80 mL/min; λ = 254 nm; τ_{major} = 10.8 min, τ_{minor} = 11.9 min. $[\alpha]^{26}_D$ = + 13.3 (c = 0.5 in $CHCl_3$). HRMS calculated for $[C_{25}H_{24}O_2+Na]^+$: 379,1674; found: 379,1677.

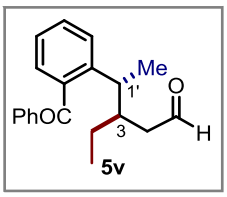
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.54 (t, *J* = 1.8 Hz, 1H, CHO), 7.67 – 7.60 (m, 2H, Ar), 7.59 – 7.48 (m, 2H, Ar), 7.40 – 7.30 (m, 3H, Ar), 7.17 – 7.01 (m, 7H, Ar), 4.10 (d, *J* = 11.6 Hz, 1H, H1'), 2.96 (dddd, *J* = 13.4, 11.5, 6.0, 3.4 Hz, 1H, H3), 2.40 (d, *J* = 1.9 Hz, 1H, H2α), 2.39 (d, *J* = 1.9 Hz, 1H, H2α), 1.41 – 1.28 (m, 1H, H4), 1.16-1.07 (m, 1H, H4), 0.66 (t, *J* = 7.4 Hz, 3H, CH_3).**^{13}C 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),

128.4 (CH Ar x2), 128.2 (CH Ar x2), 127.9 (CH Ar), 126.3 (CH Ar), 125.6 (CH Ar), 50.2 (CH C1'), 46.3 (CH_2), 37.8 (CH_2), 25.0 (CH), 10.0 (CH_3).



(*R*)-3-[(*R*)-8-benzoyl-tetrahydronaphthalenyl]pentanal (5u). Compound **5u** was prepared according to the general procedure A, using phenyl(tetrahydronaphthalenyl)methanone (47 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 an inseparable mixture of two diastereoisomers (colorless oil 30 mg, 47% yield, 97% ee, 7:1 dr, dr inferred by ^{1}H NMR analysis of the crude mixture). TLC: (hexane/EtOAc: 90:10 v/v), R_f = 0.32. The ee (97%) was determined by HPLC analysis on a Daicel Chiralpak IB column 85:15 hexane:*i*PrOH flow rate 1.00 mL/min; λ = 254 nm; τ_{major} = 24.0 min, τ_{minor} = 30.1 min. $[\alpha]^{26}_D$ = - 775.2 (c = 1.00 in $CHCl_3$). HRMS calculated for $[C_{22}H_{24}O_2+Na]^+$: 343,1674; found: 343,1675.

^{1}H NMR (400 MHz, $CDCl_3$) 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, H3'α), 1.84 – 1.75 (m, 1H, H3'a), 1.72 – 1.61 (m, 2H, H2'), 1.34 – 1.15 (m, 2H, H4), 0.66 (t, *J* = 7.4 Hz, CH_3).**^{13}C NMR (100 MHz, $CDCl_3$)** 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 (CH_2 Ar x2), 128.5 (CH_2 Ar x2), 127.0 (CH Ar), 125.0 (CH Ar), 46.1(CH) , 39.8 (CH_2), 37.1 (CH_2), 30.0 (CH), 23.7 (CH_2), 23.1 (CH_2), 20.2 (CH_2), 11.5 (CH_3).



(3*R*,4*R*)-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 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 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), R_f = 0.29. The *ee* was determined by HPLC analysis on a Daicel Chiralpak IC-3 column 95:5 hexane:*i*PrOH flow rate 0.9 mL/min; λ = 254 nm; major diastereoisomer: τ_{major} = 21.3 min, τ_{minor} = 23.7 min (84% *ee*); minor diastereoisomer: τ_{major} = 24.4 min, τ_{minor} = 26.1 min (87% *ee*). $[\alpha]^{26}_D$ = +5.5 (c = 1.00 in $CHCl_3$). HRMS calculated for $[C_{20}H_{22}O_2+Na]^+$: 317,1517; found: 317,1520.

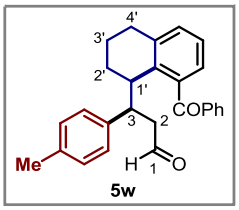
***Diagnostic signals for the major diastereoisomer:* ^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.65 (dd, *J* = 2.5, 1.6 Hz, 1H, CHO), 3.09 (p, *J* = 7.0 Hz, 1H, H1'), 2.44 (ddd, *J* = 16.4, 5.0, 1.6 Hz, 1H, H2α), δ 2.30 (dd, *J* = 7.1, 2.5 Hz, 1H, H2β), δ 1.36 – 1.27 (m, 2H, H4α+H4β), 1.18 (d, *J* = 7.0 Hz, 3H, CH_3), 0.71 (t, *J* = 7.4 Hz, 3H, CH_3).

***Diagnostic signals for the minor diastereoisomer:* ^{1}H NMR (400 MHz, $CDCl_3$)** 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, CH_3), 0.79 (t, *J* = 7.5 Hz, 3H, CH_3).

***Complete overlap of the aromatic signals was observed:* ^{1}H NMR (400 MHz, $CDCl_3$)** 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).

^{13}C NMR (100 MHz, $CDCl_3$) 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), 127.2 (CH Ar), 125.6 (CH Ar), 125.4 (CH Ar), 46.3 (CH), 45.0

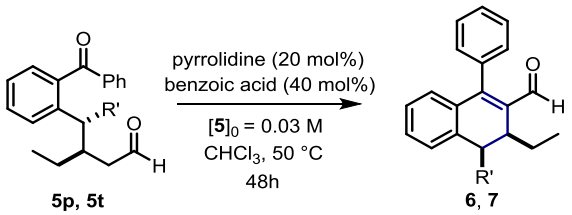
(CH), 40.3 (CH_2), 40.3 (CH_2), 38.2 (CH_2), 37.5 (CH_2), 25.4 (CH), 23.6 (CH), 19.5 (CH_3), 17.6 (CH_3), 11.1 (CH_3), 10.0 (CH_3).



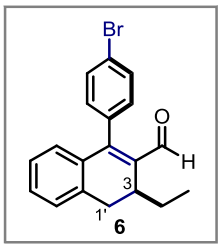
(*R*)-3-[(*R*)-8-benzoyl-tetrahydronaphthalenyl]-3-(*p*-tolyl)propanal (**5w**). Compound **5w** was prepared according to the general procedure B, using phenyl(tetrahydronaphthalenyl)methanone (96 mg, 0.4 mmol, 2 equiv.), *trans*-cinnamaldehyde (25 µL, 0.2 mmol, 1 equiv.), diphenyl phorphoric acid (10 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: 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), R_f = 0.33. The ee (80%) was determined by HPLC analysis on a Daicel Chiralpak IC-3 column using a isocratic method (80:20 Hexane:*i*PrOH), flow rate 0.4 mL/min; λ = 247 nm; τ_{major} = 24.03 min, τ_{minor} = 24.92 min. $[\alpha]^{26}_D$ = +18.6 (c = 0.5 in $CHCl_3$). HRMS calculated for $[C_{27}H_{26}O_2+Na]^+$: 405,1830; found: 405,1829.

^{1}H NMR (500 MHz, $CDCl_3$) 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, H4β), 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).**^{13}C NMR (125 MHz, $CDCl_3$)** 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), 48.7 (CH), 42.6 (CH), 40.0 (CH_2), 27.6 (CH_2), 23.7 (CH_2), 21.0 (CH_3 Me), 17.2 (CH_2).

Product Manipulations

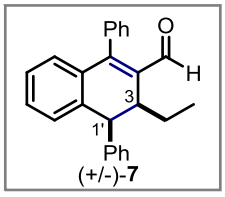


The adduct **5** (1 equiv.) was dissolved in dry $CHCl_3$ (0.03 M solution). Pyrrolidine (20 mol%) and benzoic acid (40 mol%) were sequentially added under an argon atmosphere, and the solution was warmed up to 50 ºC. After 48 h stirring, water was added and the biphasic mixture was extracted with DCM (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-ethyldihydronaphthalenecarbaldehyde (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), R_f = 0.32. The ee (90%) was determined by HPLC analysis on a Daicel Chiralpak IC-3 column 98:2 hexane:*i*PrOH flow rate 0.80 mL/min; λ = 254 nm; τ_{major} = 16.51 min, τ_{minor} = 17.37 min. $[\alpha]^{26}_D$ = -4.1 (*c* = 0.5 g cm^{-3} in $CHCl_3$). HRMS calculated for $[C_{19}H_{17}BrO+Na]^+$: 363,0360; found: 363,0365.

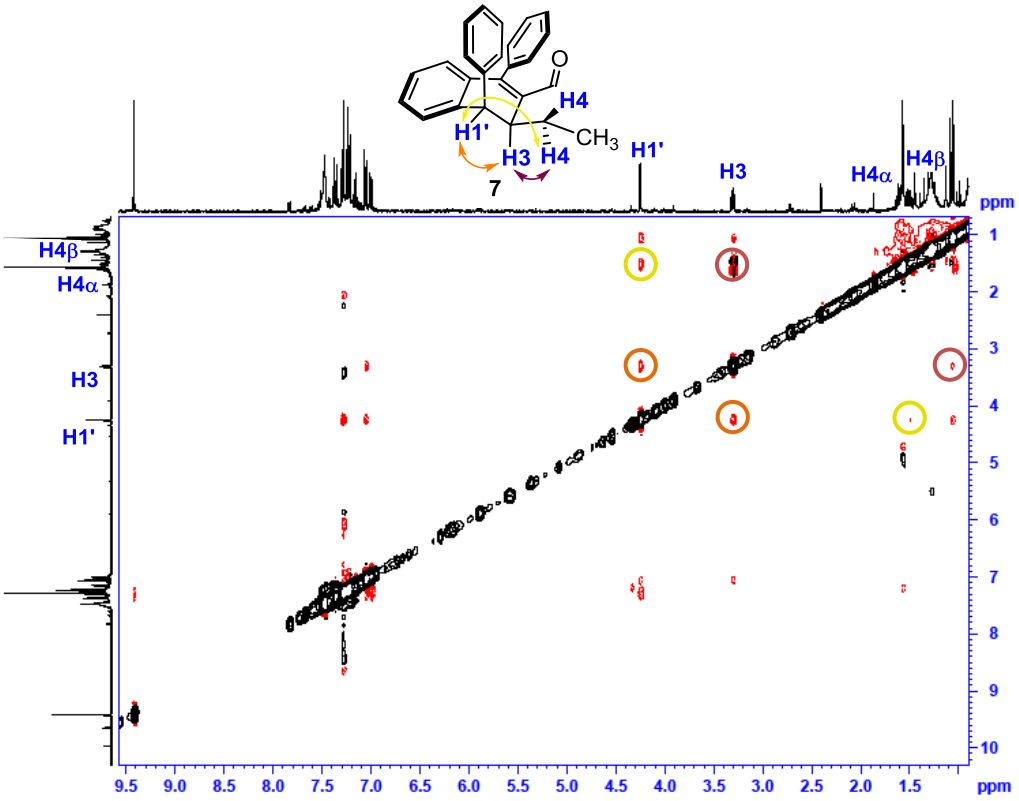
^{1}H NMR (500 MHz, Chloroform-*d*) δ 9.57 (s, 1H, CHO), 7.63 (m, 2H, Ar), 7.32 (td, *J* = 7.4, 1.3 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.15 (m, 2H, Ar), 6.83 (dd, *J* = 7.8, 1.2 Hz, 1H, Ar), 3.18 – 2.98 (m, 2H, H1'α+H3), 2.93 (d, *J* = 15.0 Hz, 1H, H1'β), 1.49 – 1.38 (m, 1H, H4α), 1.35 – 1.24 (m, 1H, H4β), 0.92 (t, *J* = 7.4 Hz, 3H, CH_3).**^{13}C NMR (125 MHz, $CDCl_3$)** 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 (CH_2), 31.3 (CH), 24.1 (CH_2), 11.8 (CH_3).
The absolute configuration of compound **6** was unambiguously inferred by anomalous dispersion X-ray crystallographic analysis (CCDC 1417311), see X-ray Crystallographic Data section.

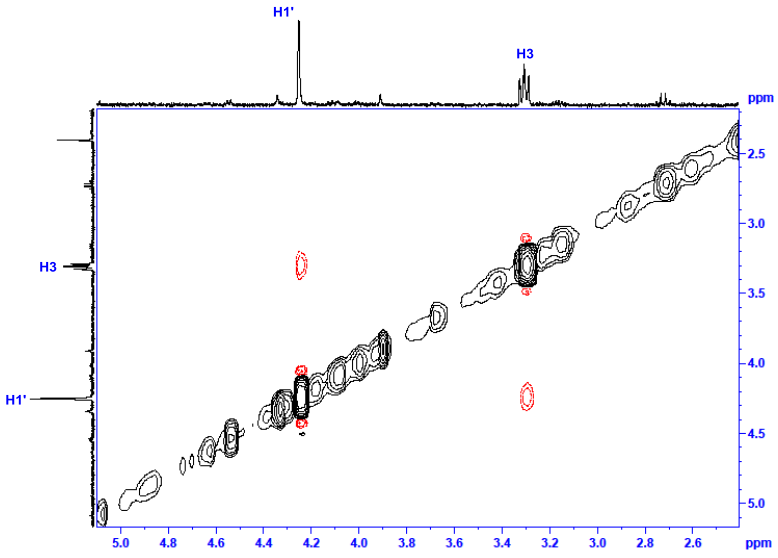


3-(2-benzoylbenzyl)pentanal (7). Compound **7** was prepared from 3-[(2-benzoylphenyl)(phenyl)methyl]pentanal **5t** (17 mg , 0.05 mmol, 1 equiv.), pyrrolidine (0.2 mL of a stock solution in $CHCl_3$ 0.05 M, 0.2 equiv.) and benzoic acid (2.5 mg, 0.4 equiv.). The crude mixture was purified by flash column chromatography (hexane/EtOAc: 97:3 v/v) to afford the title compound as a colorless oil (8 mg, 48% yield). TLC: (hexane/EtOAc: 90:10 v/v), R_f = 0.32. HRMS calculated for $[C_{25}H_{22}O+Na]^+$: 361,1568; found: 361,1576.
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.42 (d, *J* = 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, 4H), 7.18 – 7.12 (m, 1H), 7.09 – 6.97 (m, 3H), 4.25 (s, 1H, H1'), 3.31 (ddd, *J* = 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, *J* = 7.4 Hz, 3H, CH_3).**^{13}C NMR (100 MHz, $CDCl_3$)** δ 193.2 (CHO), 153.5 (Cq), 143.4 (Cq Ar), 138.4.0 (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 (CH_2), 26.1 (CH_2), 12.0 (CH_3).

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 $5x10^{-3}$ 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*).

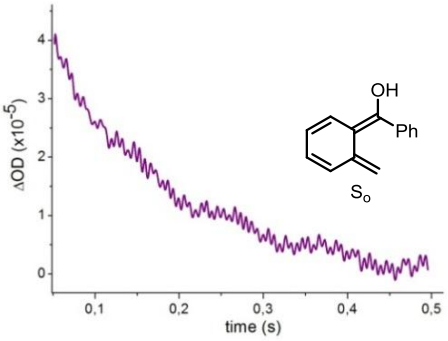


Figure S2. Decay of absorption at 450 nm of a transient generated upon 355 nm laser excitation of 2-methylbenzophenone **1a** ([**1a**] = $5x10^{-3}$ M in cyclohexane). ΔOD: optical density variation. $\tau_{1/2}$ = 150 ms.

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.

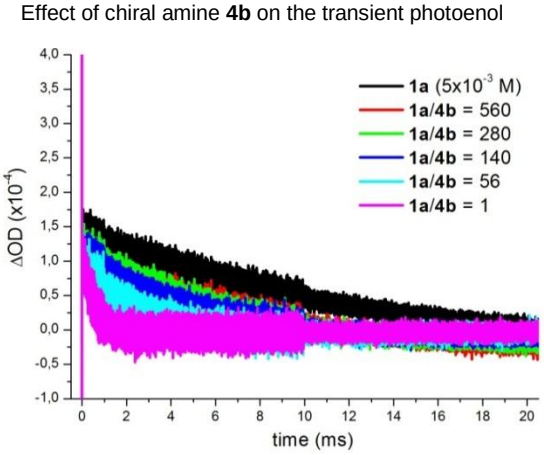


Figure S3. Decay of absorption obtained in the presence of the catalyst 4b. Absorption at 450 nm of the transient (*E*)-photoenol **A** (black line) generated upon 355 nm laser excitation of 2-methylbenzophenone **1a** ([**1a**] = $5x10^{-3}$ M in toluene). Absorption decays (colored lines) observed 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.

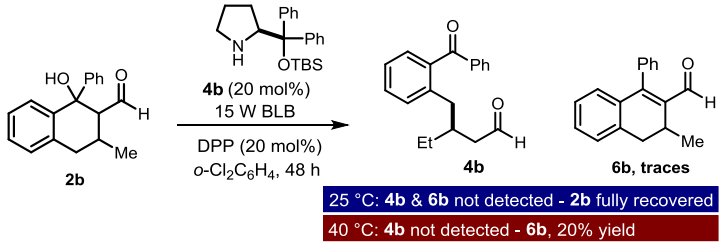
Table S1 below shows the volumes of the **1a**:**4b** equimolar solution ($5x10^{-3}$ M in toluene) added to 2.8 mL of a $5x10^{-3}$ M toluene solution of 2-methylbenzophenone **1a**. The corresponding concentration of **4b** and the total volume in every measurement is shown, while [**1a**] is constantly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

Table S1. Volumes of a **1a**:**4b** equimolar solution ($5x10^{-3}$ M in toluene) added to the initial solution of **1a** (2.8 mL of a $5x10^{-3}$ M toluene solution, 0.014 mmol) and the corresponding concentrations of **4b** in every measurement.

Volume of 1a:4b equimolar solution (µL)	**mmol of 4b** ($x10^{-5}$)	**total volume (mL)**	**[4b]** ($x10^{-5}$ M)	**Ratio** $\frac{[1a]}{[4b]}$
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



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 ºC, a minor amount (≈ 20%) of the dehydration product of type **6** was recovered. These experiments indicate that the retro-aldol-mediated ring-opening of **2** is not a viable pathway for the formation of **4a**.

3. Absorption Spectra

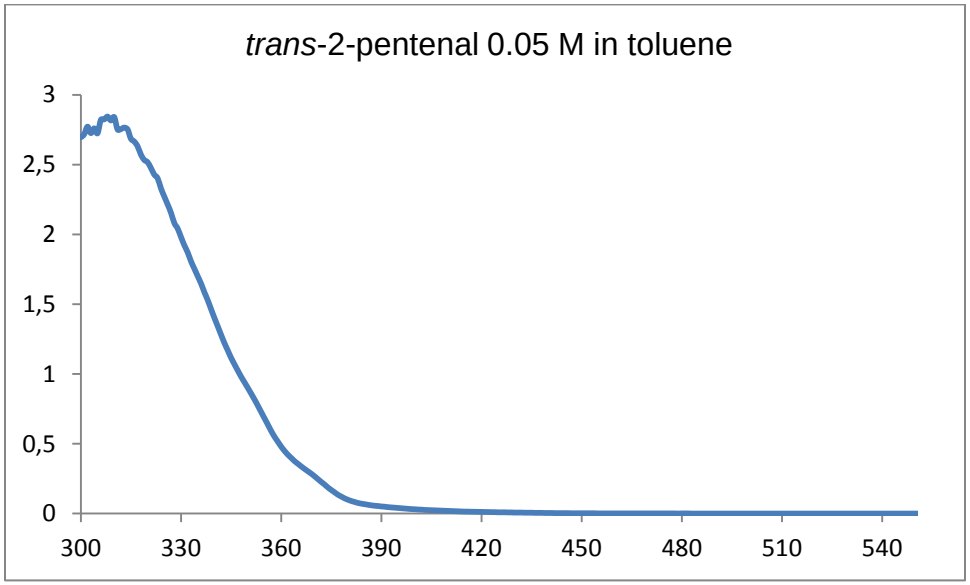


Figure S4. Absportion spectrum of trans-2-pentenal in toluene.

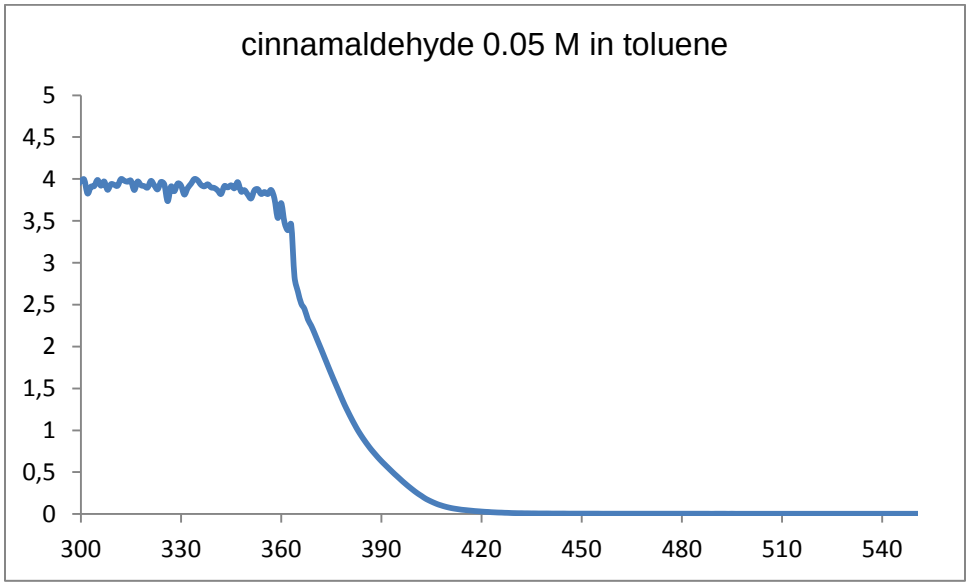


Figure S5. Absorption spectrum of cinnamaldehyde in toluene.

4. Computational Details

All calculations were carried out using Gaussian09 software (*6*).[1] All energies reported in the main text were computed on the full experimental system with the M06-2X functional (*7*) and the 6-311++G(d,p) basis set (*8*), with solvent contributions added using the SMD model (*9*). High level QM calculations were carried out on geometries optimized with and ONIOM(QM:MM) approach (*10*). The level of theory for the QM part was with the 6-31+G* basis set, with the MM level being UFF (*11*). 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 (*12*, *13*).

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 (Figure S6). 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.

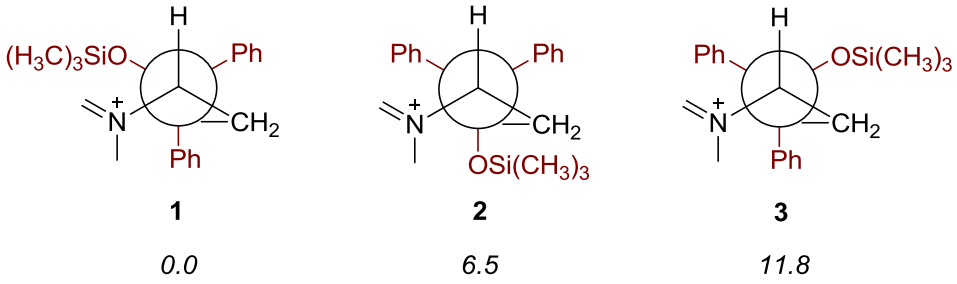


Figure S6. Relevant conformations of the iminium ion corresponding to rotations of the diarylprolinol-silyl ether unit. Relative free energies in kcal·mol^{-1}.

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 (**Kes1** and **Kes2**), 2-methylbenzophenone **1** transfers a hydrogen from the methyl group to the oxygen (**TSs1**) 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.

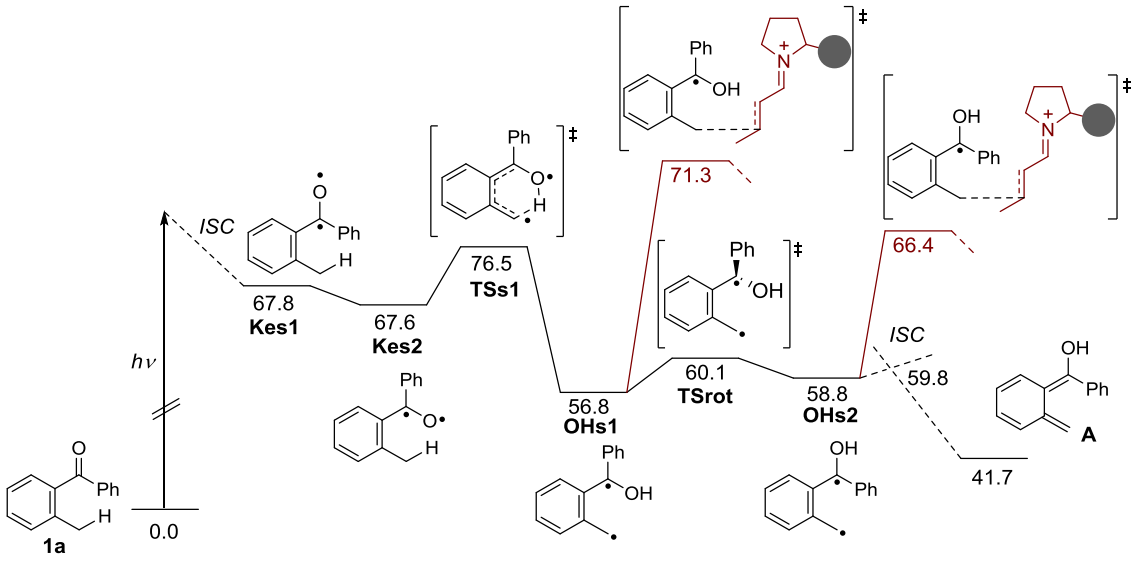


Figure S7. Free energy profile for the formation of the photoenol **A** (black profile) and noncompetitive radical formation of the C-C bond leading to the product (red profile). Energies in kcal·mol^{-1}

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	-0.466811
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	1.114402
C	3.801117	-2.599540	-0.834348
H	2.942114	-1.007677	-2.009488
C	2.817850	-2.940666	1.343841

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	4.341007	-2.945546	-0.918674
H	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	2.138835	-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

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	0.589503	-6.640098	2.639627
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	-4.838917	1.535928
C	0.803572	-5.954747	-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

C	0.866319	-1.905373	-1.009493
H	0.289113	-2.816258	-1.123238
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	-0.058588	-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

H	0.685331	-4.956109	-1.029259
C	-0.686844	-6.711797	1.498164
H	0.111170	-6.894503	3.485373
H	-1.202578	-6.396321	-0.562720
H	-1.517841	-7.379555	1.684866
C	3.881556	-5.064805	0.911042
C	3.997779	-6.115680	-0.027442
C	4.844997	-4.984985	1.943386
C	5.041129	-7.040588	0.057824
H	3.276882	-6.219443	-0.828007
C	5.885622	-5.915078	2.021327
H	4.802337	-4.210089	2.696690
C	5.984565	-6.939906	1.080054
H	5.116806	-7.837980	-0.670096
H	6.616914	-5.841324	2.815957
H	6.791643	-7.658174	1.144485
O	2.900598	-3.071775	1.826087
Si	1.548343	-2.255084	2.609119
C	1.731369	-2.559045	4.443366
H	1.565001	-3.631794	4.666703
H	2.752775	-2.269365	4.764664
H	0.984783	-1.951710	4.995027
C	1.725167	-0.407951	2.392952
H	1.395345	-0.109562	1.379802
H	1.088578	0.109874	3.139274
H	2.783388	-0.114970	2.549322
C	-0.227678	-2.701717	2.183576
H	-0.376479	-2.835679	1.100943
H	-0.529951	-3.624007	2.716619
H	-0.888848	-1.880212	2.527085

*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

H	5.070019	-2.881780	-0.132157
H	4.698536	-3.691773	-1.617158
H	5.170062	-1.023180	-1.574300
H	3.941767	-1.687389	-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	-2.680379	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	-5.541844	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	-2.270320	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	2.437267	1.147965	-0.304367
C	2.604212	2.635098	-2.737699
O	2.660371	2.774650	-4.083256
H	3.578473	2.665820	-4.383758
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
H	-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

C	-1.952587	2.579236	-7.039041
C	-2.921211	2.142630	-7.974215
C	-1.362320	3.847380	-7.253988
C	-3.229584	2.909913	-9.101124
H	-3.469803	1.225137	-7.842509
C	-1.674905	4.608159	-8.382996
H	-0.665447	4.262900	-6.539289
C	-2.601591	4.136291	-9.310113
H	-3.968535	2.556449	-9.808706
H	-1.204961	5.571644	-8.532219
H	-2.846527	4.729259	-10.181749
C	-2.090656	0.314379	-5.711956
C	-1.961848	-0.558916	-6.818069
C	-2.533614	-0.247850	-4.490392
C	-2.330497	-1.903466	-6.724256
H	-1.598160	-0.210543	-7.770994
C	-2.898011	-1.593208	-4.402067
H	-2.584497	0.344474	-3.587279
C	-2.802839	-2.419131	-5.519440
H	-2.242351	-2.548916	-7.588662
H	-3.242706	-1.998337	-3.459421
H	-3.082843	-3.462160	-5.448358
O	-2.016838	2.502582	-4.605072
Si	-3.697477	3.008712	-4.502354
C	-4.980722	1.731992	-4.989127
H	-5.002423	0.913161	-4.242582
H	-5.977775	2.217526	-5.003783
H	-4.774858	1.317517	-5.991087
C	-4.002939	4.590874	-5.451526
H	-3.150765	5.284568	-5.299649
H	-4.126642	4.373434	-6.530378
H	-4.932882	5.065950	-5.077755
C	-4.020102	3.405132	-2.707664
H	-3.402365	4.273986	-2.405156
H	-5.092593	3.652098	-2.569107
H	-3.757097	2.527054	-2.082678

*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

H	1.450217	1.878810	0.251850
C	2.576597	1.904386	-2.574757
O	3.138666	1.892375	-3.890447
H	4.058305	2.197010	-3.839002
C	1.423166	0.848488	-2.656358
C	0.568292	0.745389	-1.357889
H	-0.277514	2.128912	0.082469
C	3.642563	1.472109	-1.571517
C	3.999394	2.253874	-0.471498
C	4.319597	0.266179	-1.797231
C	5.001638	1.825642	0.400271
H	3.499996	3.202404	-0.291479
C	5.319626	-0.160152	-0.930322
H	4.071905	-0.341572	-2.665231
C	5.658967	0.619015	0.176873
H	5.269926	2.442013	1.252678
H	5.834798	-1.097340	-1.117376
H	6.437636	0.287870	0.857003
C	0.544145	1.304391	-3.769019
H	-0.136423	2.118435	-3.530951
H	1.860306	-0.126162	-2.887326
C	1.484950	-0.083544	-5.563971
C	-0.383800	1.441963	-6.049554
C	1.750044	0.577181	-6.907355
H	1.003666	-1.060827	-5.673245
H	2.363111	-0.152821	-4.927363
C	0.361649	1.049927	-7.363279
H	-0.311580	2.516143	-5.923319
H	2.424478	1.425587	-6.753770
H	2.210339	-0.111147	-7.618312
H	0.455836	1.911154	-8.025747
H	-0.126305	0.265928	-7.936553
N	0.509379	0.862297	-4.970765
C	0.954317	-0.491261	-0.545280
H	0.338330	-0.552353	0.357174
H	0.804247	-1.412124	-1.118641
H	2.004121	-0.441503	-0.236243
H	-0.479009	0.622735	-1.667523
C	-1.866970	0.964294	-5.884955
C	-2.834815	1.463008	-6.984848
C	-1.852957	-0.584914	-5.891433
O	-2.357372	1.345142	-4.595509
C	-4.142934	0.929277	-7.037057
C	-2.491958	2.465031	-7.920043
C	-1.990356	-1.334540	-7.085071
C	-1.677627	-1.300680	-4.682875
Si	-2.875629	2.998348	-4.286830
C	-5.051295	1.344973	-8.013436
H	-4.460547	0.187572	-6.314754
C	-3.407434	2.879320	-8.891916
H	-1.535977	2.960138	-7.896609

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	-4.857922
C	-4.682080	2.315682	-8.943472
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

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	-2.583872	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

H	-3.466718	-1.327038	-4.290154
H	-4.333362	1.335178	-1.347124
H	-3.653327	2.686625	-0.354807
H	-5.436464	2.585934	-0.646181
H	-4.636468	5.861792	-3.019951
H	-5.443035	5.292826	-1.509543
H	-3.653929	5.577738	-1.522676
H	-5.346373	2.045619	-4.387627
H	-6.521720	2.713226	-3.204992
H	-5.865670	3.782198	-4.479361
H	-4.437602	7.762805	-6.789551
H	-3.440677	-1.636541	-6.744982

*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

H	-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	-3.719300
H	-1.940932	2.164774	-4.860163
H	-2.258465	0.203186	-0.234154
N	-1.228840	0.455444	-2.090364
C	-3.654757	0.956866	-2.971220
C	-4.566906	1.950295	-3.734457
C	-3.594529	-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	-3.399659	-0.330307	-5.192619
C	-3.758488	-1.613446	-3.169559
Si	-4.869840	1.891843	-0.653896
C	-6.683012	2.368972	-4.889321
H	-6.154243	0.492153	-4.013301
C	-5.080549	4.158667	-4.649391
H	-3.292887	3.718420	-3.591209
C	-3.337535	-1.515973	-5.928780
H	-3.311786	0.604035	-5.727538
C	-3.693060	-2.794579	-3.912977
H	-3.920668	-1.700194	-2.104062
C	-6.543699	2.514872	-1.210815
C	-5.159740	1.096263	1.008577
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	-1.650795	-1.926133	-0.762394
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

H	-2.427547	0.026967	-0.375426
N	-1.722474	-0.033379	-2.283234
C	-3.870010	1.397003	-2.532563
C	-4.342978	2.673657	-3.289179
C	-4.499526	0.065851	-3.047340
O	-4.121817	1.560388	-1.133043
C	-5.447124	2.686810	-4.175563
C	-3.691025	3.905961	-3.043047
C	-4.565568	-0.268015	-4.424023
C	-4.938305	-0.914496	-2.130230
Si	-5.714499	2.060813	-0.579289
C	-5.834465	3.861610	-4.826174
H	-6.039992	1.807542	-4.363633
C	-4.082700	5.075600	-3.698835
H	-2.884123	3.976022	-2.328039
C	-5.058667	-1.504900	-4.848272
H	-4.290105	0.429339	-5.195498
C	-5.432569	-2.148646	-2.558896
H	-4.902065	-0.730275	-1.070159
C	-7.181145	1.191331	-1.358469
C	-5.773597	1.651675	1.241245
C	-5.950933	3.911487	-0.709800
C	-5.148466	5.052102	-4.595352
H	-6.677915	3.849685	-5.504498
H	-3.564764	6.005143	-3.500951
C	-5.489717	-2.445389	-3.917144
H	-5.112262	-1.730929	-5.905520
H	-5.768787	-2.878263	-1.833739
H	-7.124638	1.218433	-2.460225
H	-7.226316	0.139203	-1.012921
H	-8.110624	1.703902	-1.036925
H	-4.935229	2.159392	1.761139
H	-6.738103	1.994397	1.668720
H	-5.678839	0.554635	1.375269
H	-6.232616	4.188973	-1.744451
H	-6.767081	4.223398	-0.026559
H	-5.013219	4.427833	-0.419415
H	-5.453953	5.960354	-5.098462
H	-5.872015	-3.402187	-4.248432

*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

C	-1.857411	4.173067	0.164988
C	-0.677779	3.512177	-0.193646
C	0.433441	4.288752	-0.561469
C	0.350361	5.684115	-0.575193
C	-0.830477	6.322765	-0.207898
C	-1.937841	5.562901	0.166168
H	-2.724177	3.583212	0.457343
H	1.221086	6.266680	-0.865173

H	-0.883857	7.406944	-0.208553
H	-2.861005	6.051933	0.462096
C	-0.667732	2.000219	-0.255547
H	0.352285	1.607470	-0.145830
C	1.741462	3.662685	-0.980730
O	2.025593	3.599208	-2.169880
C	-0.450999	1.982331	-2.747360
C	-1.268661	1.451162	-1.566872
H	-1.247047	1.595622	0.582454
C	2.659958	3.150588	0.069558
C	3.850920	2.523118	-0.321195
C	2.357183	3.288718	1.429879
C	4.726410	2.035067	0.639995
H	4.074914	2.435610	-1.380140
C	3.237988	2.798922	2.390769
H	1.441294	3.786858	1.736487
C	4.419111	2.172404	1.996261
H	5.650403	1.551198	0.338672
H	3.006310	2.910901	3.445268
H	5.106644	1.792743	2.746267
H	-0.390732	3.082557	-2.709378
C	-0.998223	1.624134	-4.076151
H	0.586028	1.630649	-2.675405
H	-2.038695	1.312168	-4.159133
C	1.046638	2.261635	-5.244157
C	-0.829188	1.319653	-6.539863
C	0.973566	3.002608	-6.570282
H	1.774625	1.443320	-5.270880
H	1.243801	2.892415	-4.375367
C	0.167411	2.065574	-7.483252
H	-1.798697	1.798072	-6.618551
H	0.452997	3.954672	-6.426559
H	1.966788	3.216942	-6.968311
H	-0.374786	2.647502	-8.229616
H	0.838675	1.409039	-8.029927
N	-0.316073	1.675268	-5.161800
C	-1.288999	-0.077519	-1.554337
H	-1.878296	-0.453143	-0.713067
H	-1.725622	-0.496552	-2.468854
H	-0.271973	-0.475584	-1.456459
H	-2.297238	1.831663	-1.654854
C	-0.965539	-0.233065	-6.711524
C	-1.416272	-0.696459	-8.117880
C	0.420355	-0.855189	-6.402513
O	-1.857423	-0.749246	-5.718061
C	-1.384663	-2.076298	-8.424231
C	-1.896675	0.189524	-9.107760
C	1.396014	-1.057473	-7.409122
C	0.756421	-1.228214	-5.078992
Si	-3.599280	-0.598711	-5.916786
C	-1.775941	-2.543602	-9.681093

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	-9.899578
H	-2.657780	0.406008	-11.109599
C	2.953385	-1.952838	-5.787396
H	3.378806	-1.747099	-7.883489
H	2.249829	-2.039130	-3.758747
H	-4.156225	-1.626704	-8.102983
H	-3.774143	-2.884545	-6.847776
H	-5.374058	-2.040604	-6.844674
H	-4.035275	-0.110938	-3.533408
H	-5.448081	-0.929950	-4.311757
H	-3.984853	-1.893358	-3.849991
H	-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_2O** (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

C	4.276893	2.302185	-0.874343
C	5.212795	0.390834	-2.685516
H	3.380590	0.743550	-3.766104
C	5.513842	1.698332	-0.673427
H	3.903518	3.043849	-0.173261
C	5.980903	0.738250	-1.573254
H	5.573608	-0.356233	-3.386224
H	6.116130	1.977258	0.185456
H	6.943708	0.263849	-1.410057
O	4.426103	3.287522	-4.830922
H	4.741784	4.103316	-5.247443
H	5.183376	2.903640	-4.361326
C	-0.112420	0.944881	-3.107627
H	1.175712	-0.812783	-3.057925
C	0.731549	0.617648	-5.396919
C	-0.634520	2.584165	-4.900307
C	1.217086	1.749768	-6.294892
H	0.074259	-0.080543	-5.929891
H	1.542413	0.047487	-4.941834
C	0.059391	2.761660	-6.281309
H	-0.252576	3.359397	-4.232880
H	2.126049	2.187723	-5.872369
H	1.446669	1.398330	-7.303101
H	0.430560	3.784747	-6.375795
H	-0.591852	2.594603	-7.135607
H	-0.723299	1.571720	-2.460709
N	-0.047235	1.313095	-4.365840
H	-0.665697	0.019173	-0.733499
C	0.574537	-1.813064	-0.596227
H	1.571015	-2.114822	-0.931715
H	0.559995	-1.783963	0.494425
H	-0.134502	-2.589081	-0.912883
C	-2.202166	2.608422	-4.871371
C	-2.695804	3.798310	-5.739555
C	-2.695672	1.203407	-5.313225
O	-2.535672	2.850132	-3.502357
C	-3.749147	3.691601	-6.678993
C	-2.133312	5.080436	-5.532330
C	-2.674974	0.794218	-6.667812
C	-3.004470	0.219535	-4.343265
Si	-4.203196	3.211228	-3.081171
C	-4.167438	4.800877	-7.419466
H	-4.280448	2.768573	-6.839277
C	-2.556256	6.184286	-6.276463
H	-1.373506	5.238427	-4.779668
C	-3.023266	-0.508315	-7.034586
H	-2.411345	1.477691	-7.458605
C	-3.349093	-1.081649	-4.715841
H	-2.964905	0.444106	-3.286273
C	-5.513893	2.138453	-3.884018
C	-4.611405	5.014098	-3.364137

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

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	-2.900901	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

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	-4.734416
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	1.841422	1.978471	-6.177260
H	1.393604	0.623696	-4.504540
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	-1.322232	-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	-5.047299	0.392704	-7.204719
C	-5.059505	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

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-H_2O (Figure 5 in the main text)
E(M06-2X/6-311++G(d,p) = -2045.265914
Number of Negative Frequencies = 1

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	0.914692	-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

H	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	2.165267	1.196904	-7.280967
H	-0.048370	1.784641	-8.557619
H	-0.009565	0.255553	-7.690747
N	-0.442007	1.419358	-5.269207
C	-1.136095	-0.821190	-1.472703
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
H	-2.811409	3.532705	-10.958887
C	-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	-4.679265	5.350309	-6.725491
H	-5.215381	2.884160	-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 $Mo_{K\alpha}$ radiation, Confocal Max Flux optic and a Cryostream Plus low temperature device (*T* = 100K).

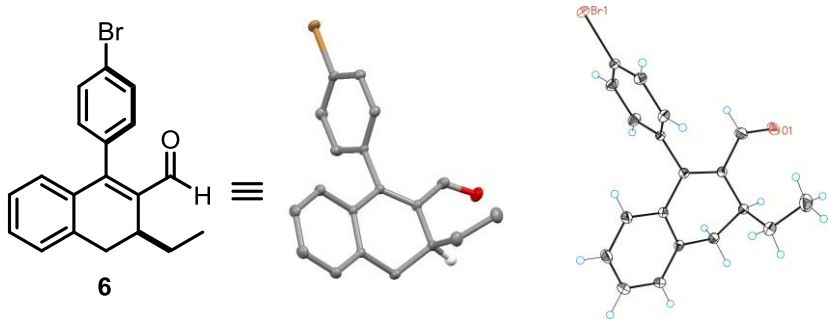


Table S2. Crystal data and structure refinement for **6** at 100 K: **CCDC 1417311**

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	α= 90°.
	b = 9.238(3)Å	β = 90°.
	c = 18.493(7)Å	γ = 90°.
Volume	1534.0(10) $Å^3$	
Z	4	
Density (calculated)	1.478 Mg/m^3	
Absorption coefficient	2.680 mm^{-1}	
F(000)	696	
Crystal size	0.20 x 0.20 x 0.20 mm^3	
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 F^2	
Data / restraints / parameters	7112/ 0/ 192	
Goodness-of-fit on F^2	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.$Å^{-3}$	

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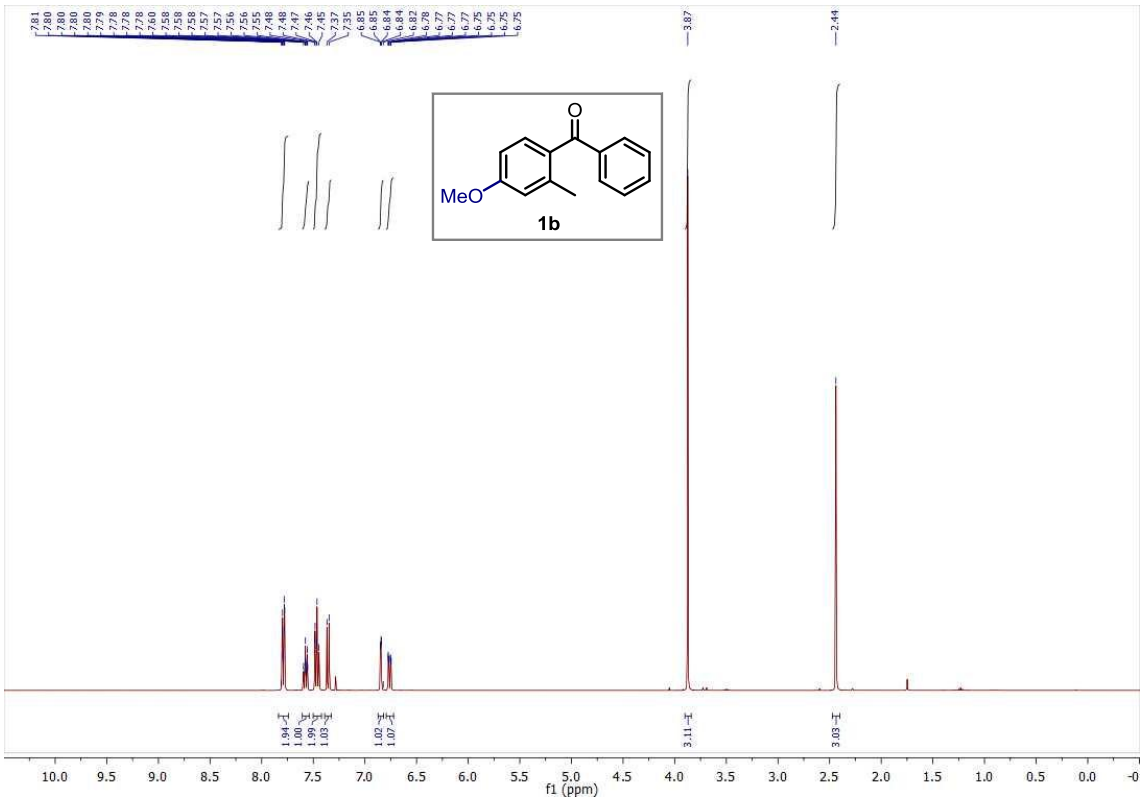
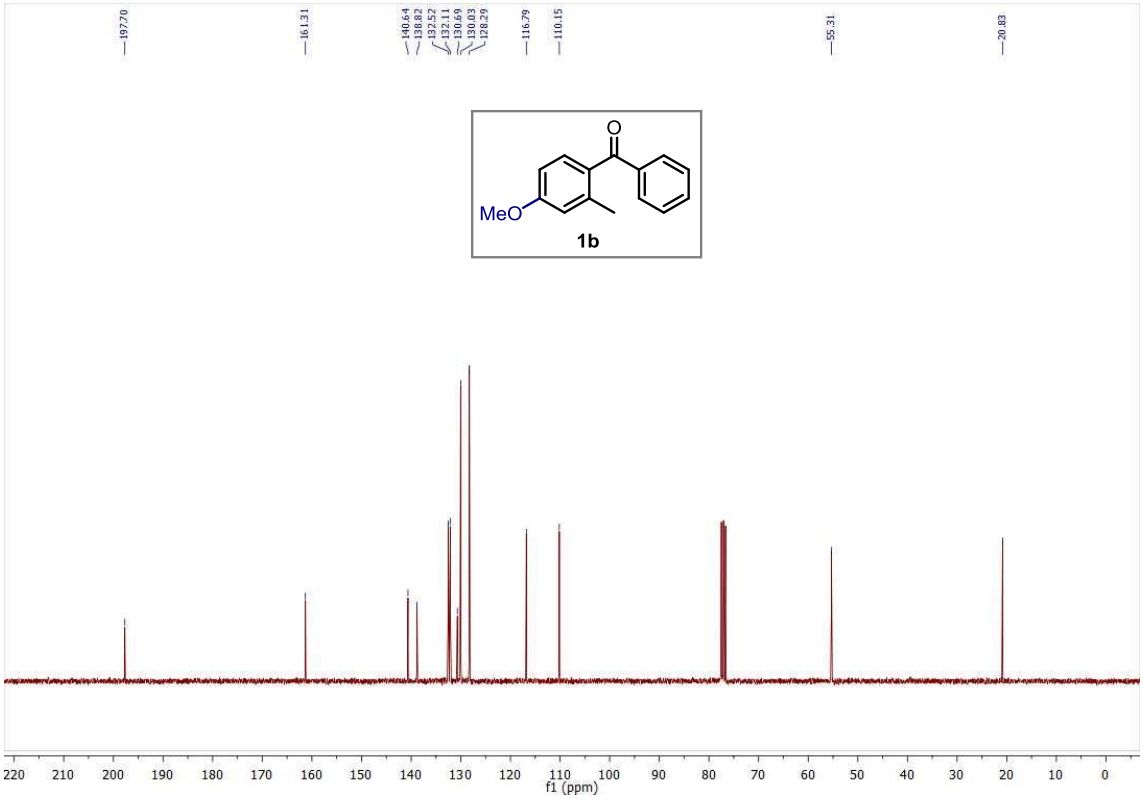
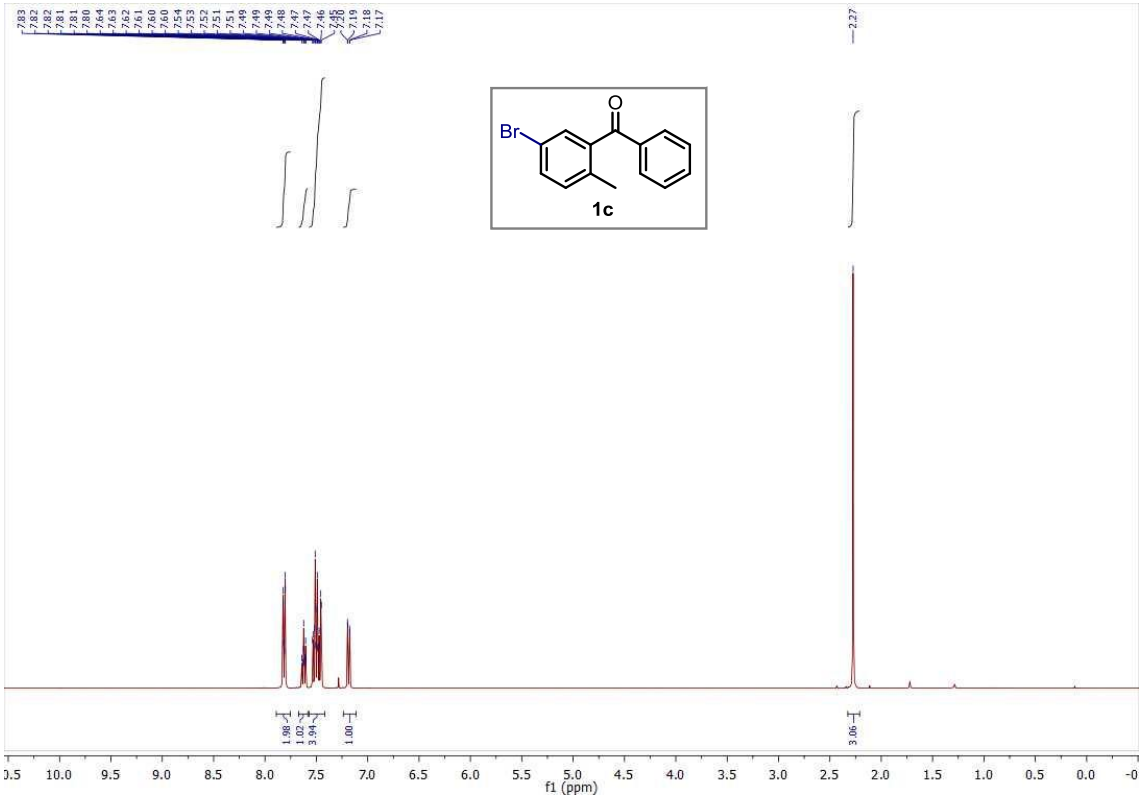
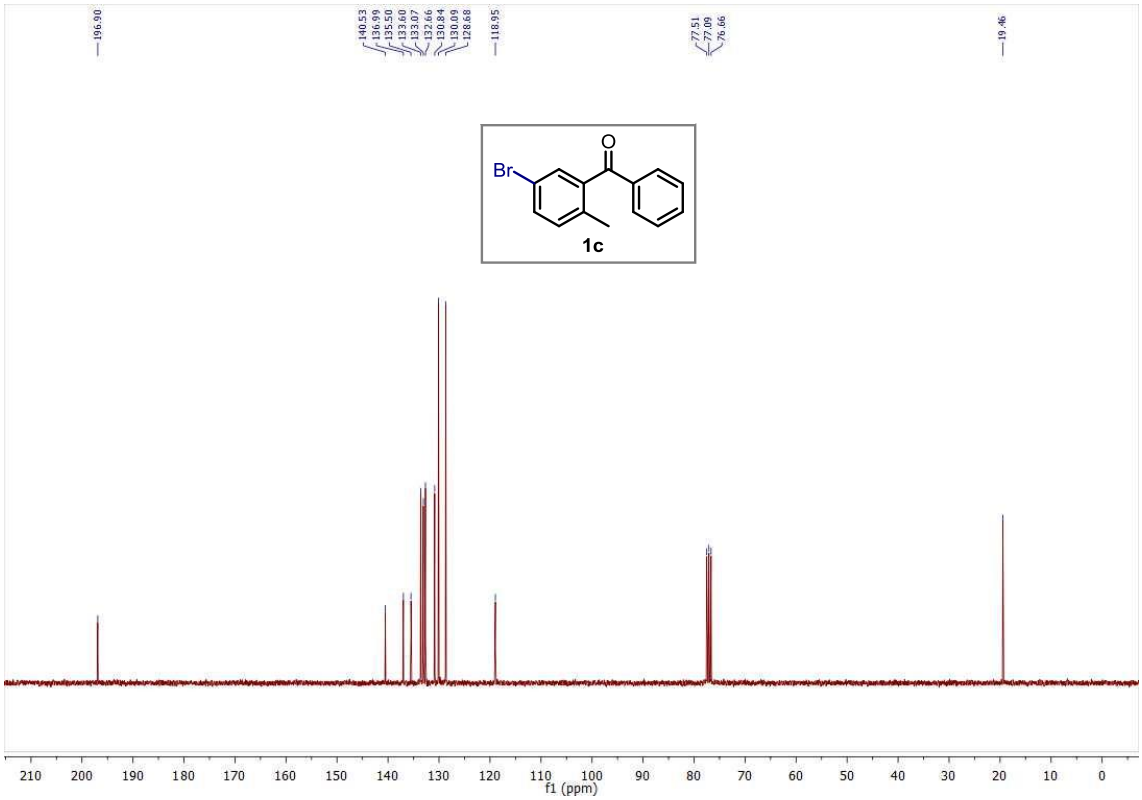
G. NMR Spectra






Br
O
1c
f1 (ppm)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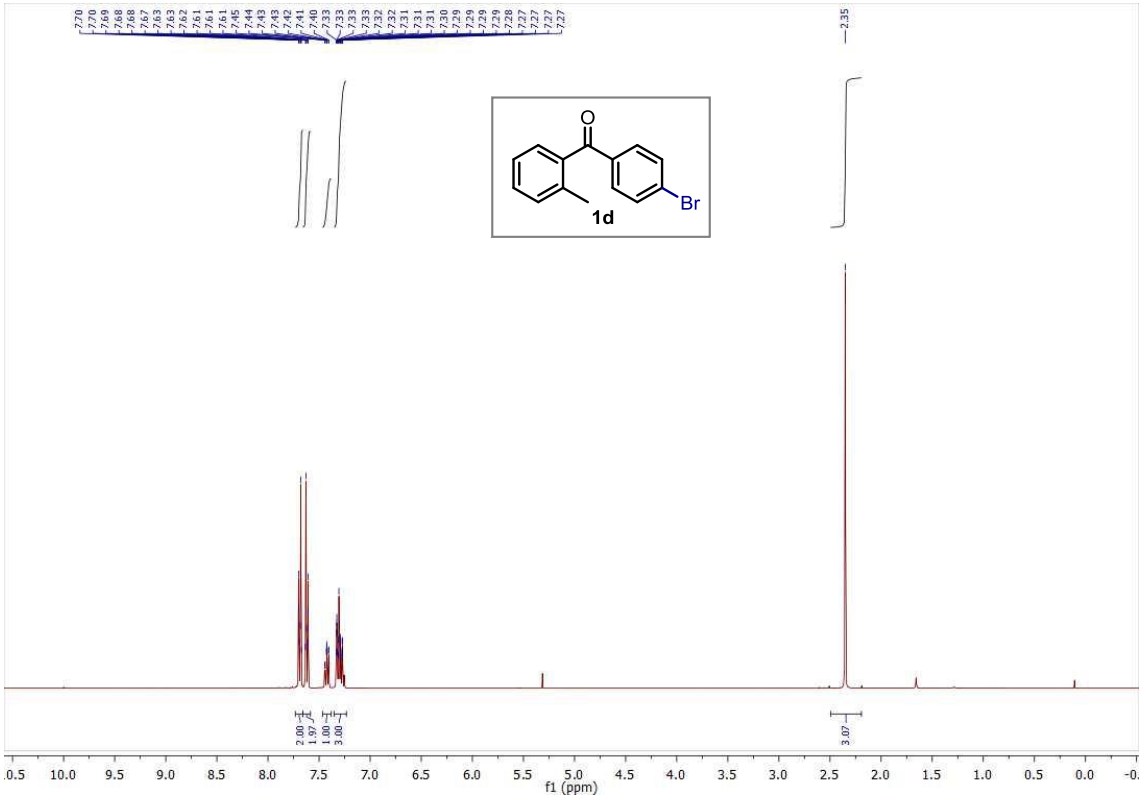
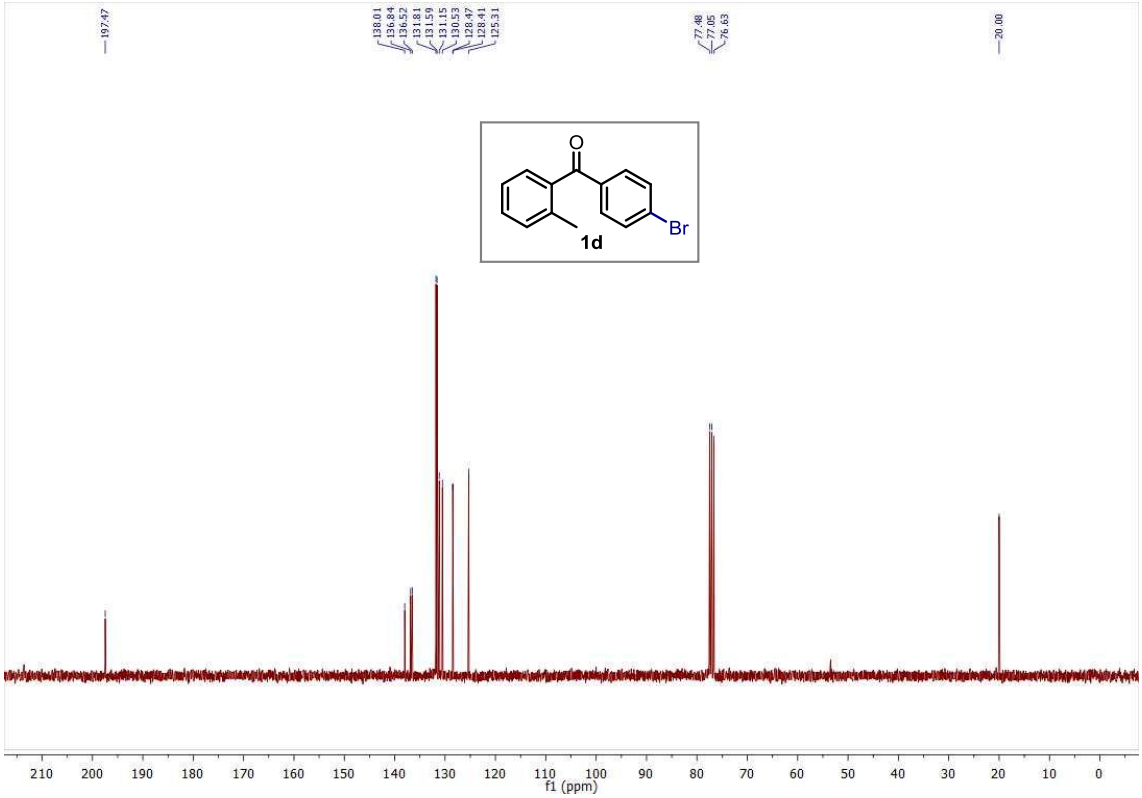
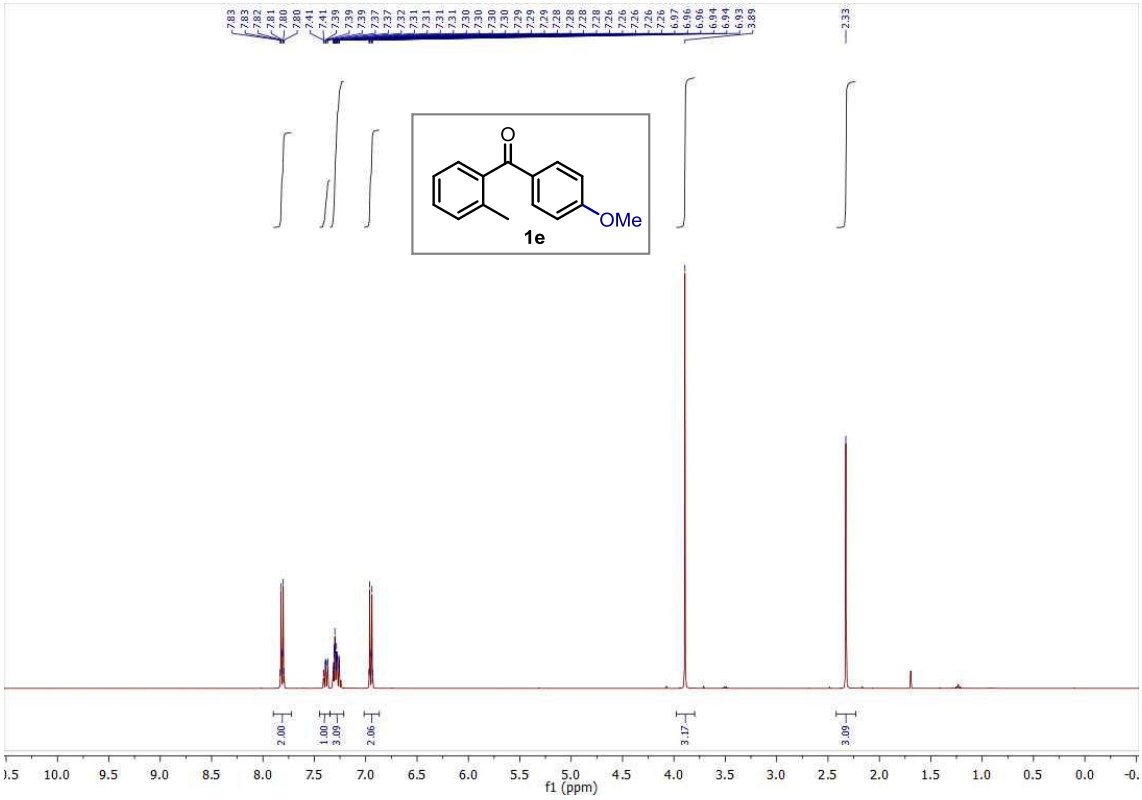

1d
Br
f1 (ppm)


1d
Br
f1 (ppm)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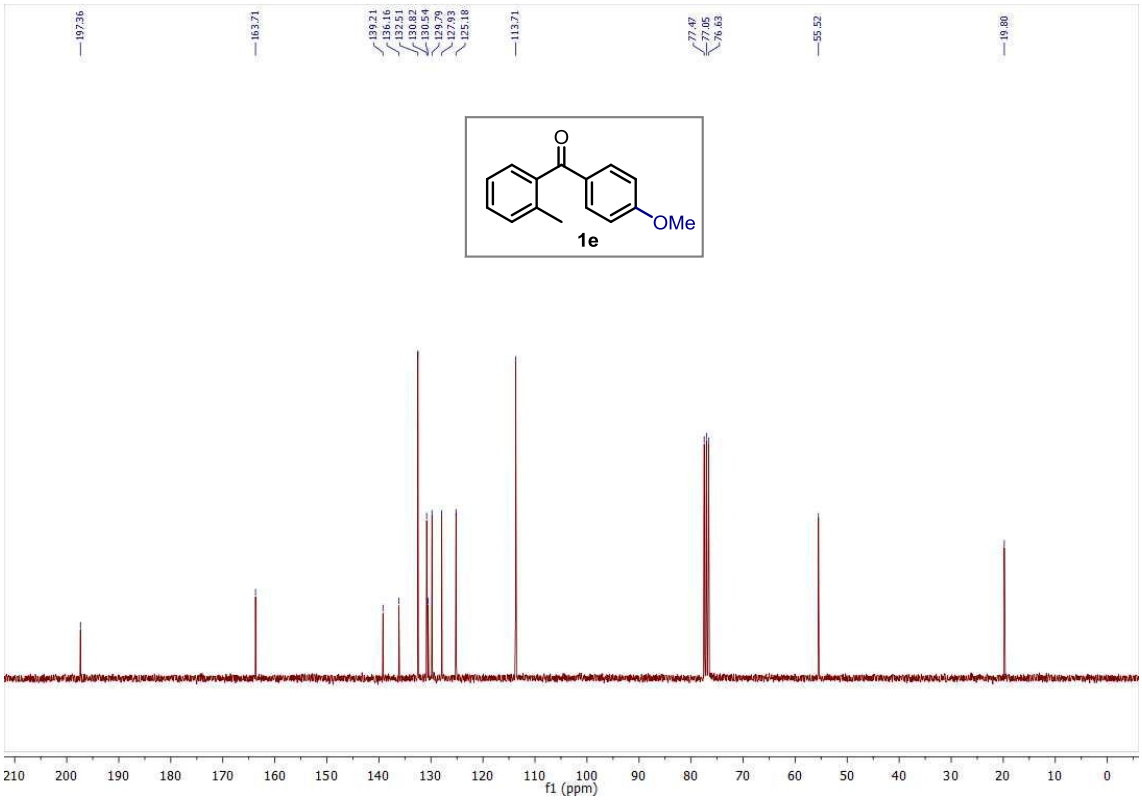
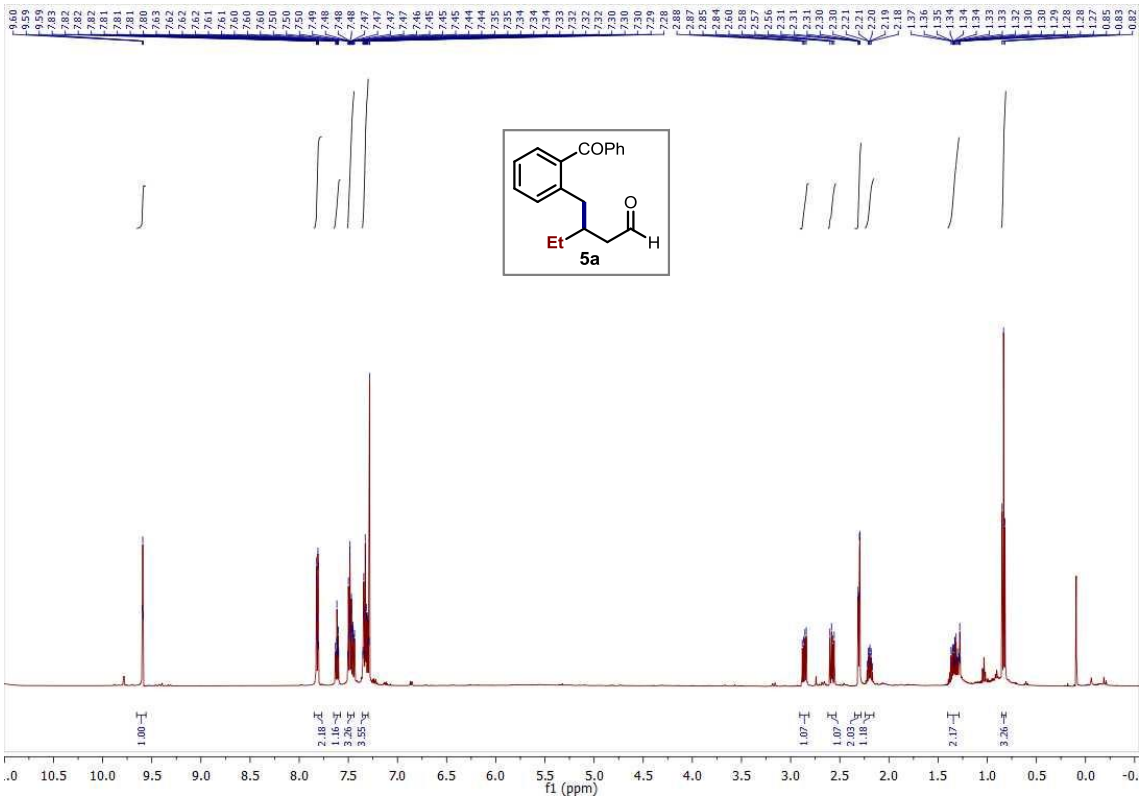
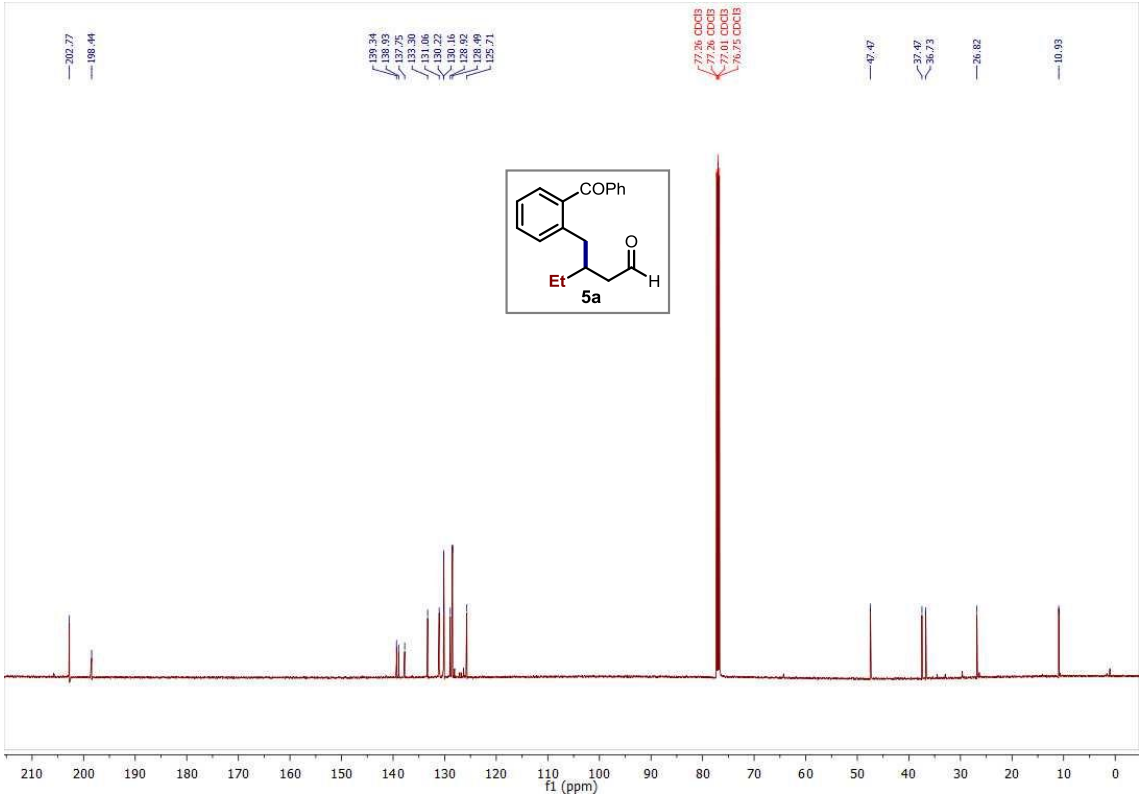
1e
f1 (ppm)


OMe
1e
f1 (ppm)


COPh
O
H
Et
5a
f1 (ppm)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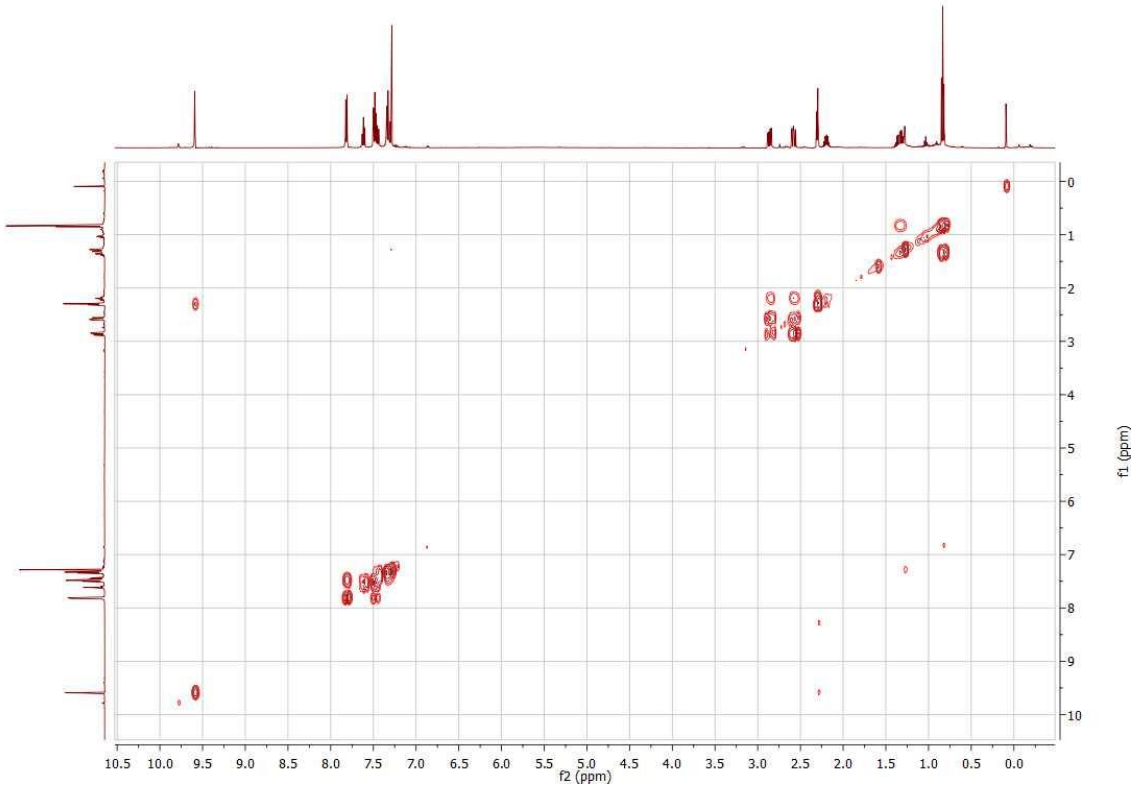
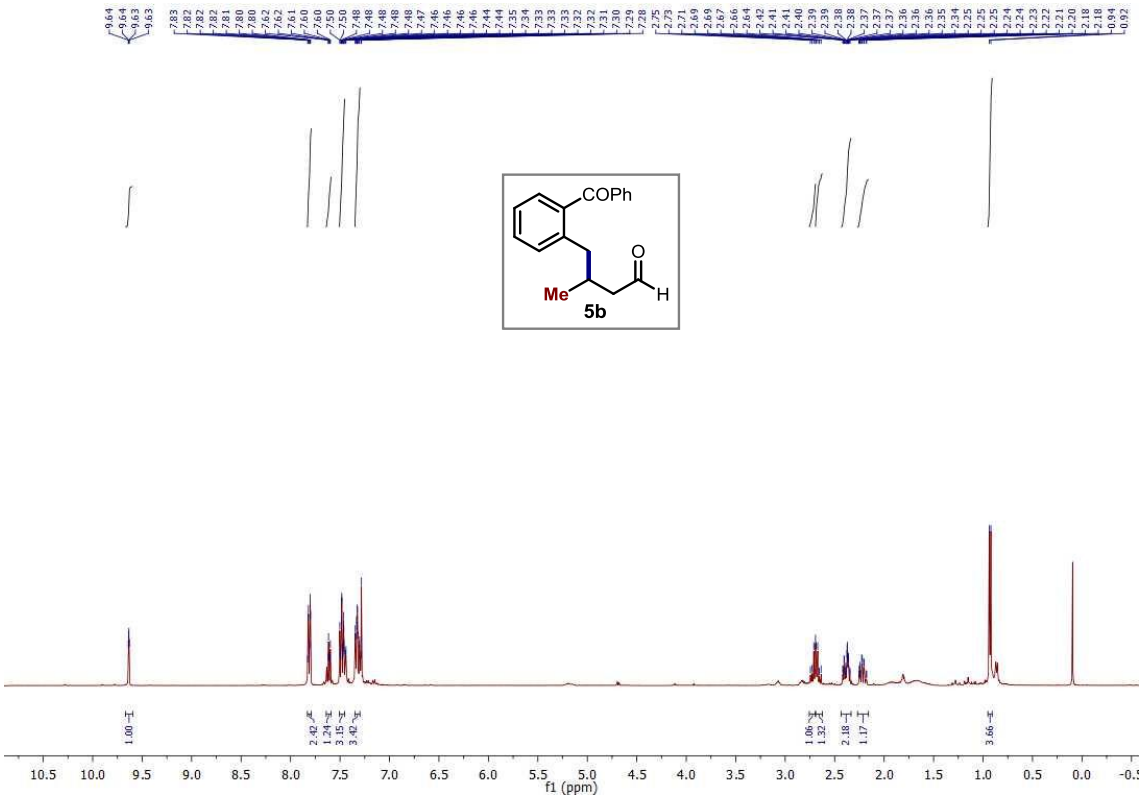
O
H
Et
5a
f1 (ppm)

H^1-H^1 COSY analysis of compound **5a**




COPh
O
Me
H
5b
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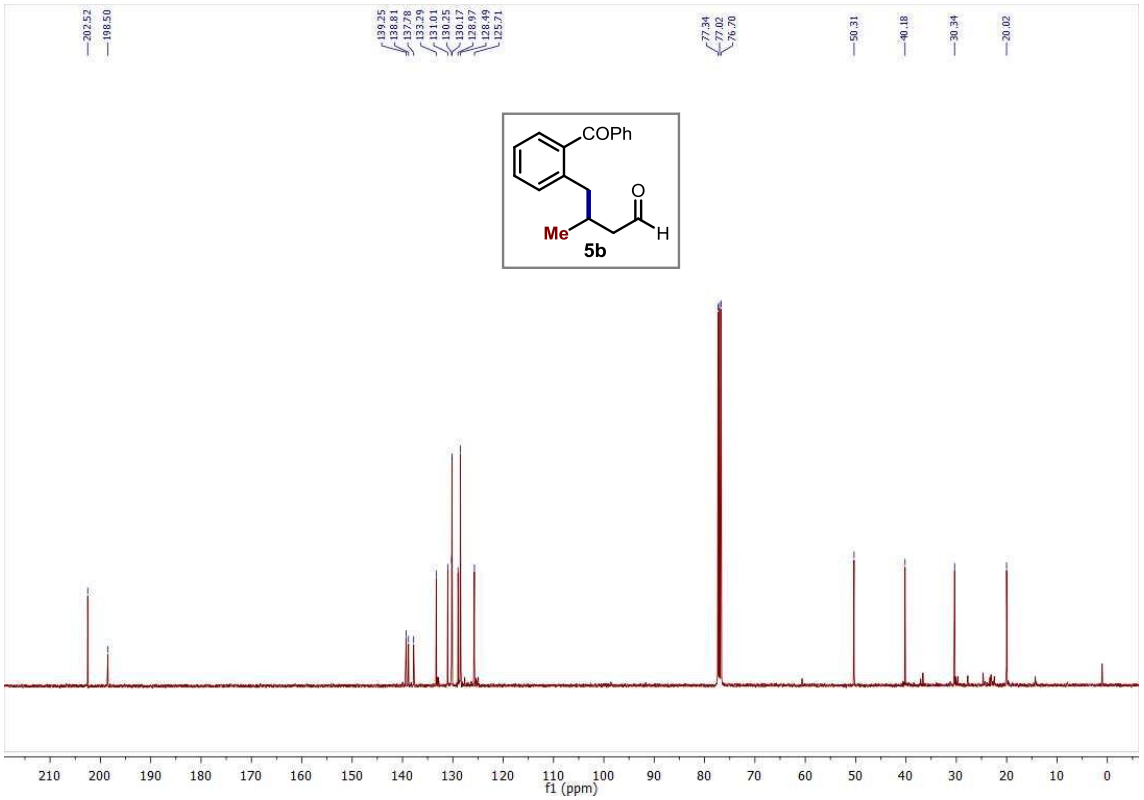
2.42
1.24
3.15
3.42
1.06
1.32
2.18
1.17
3.66
f1 (ppm)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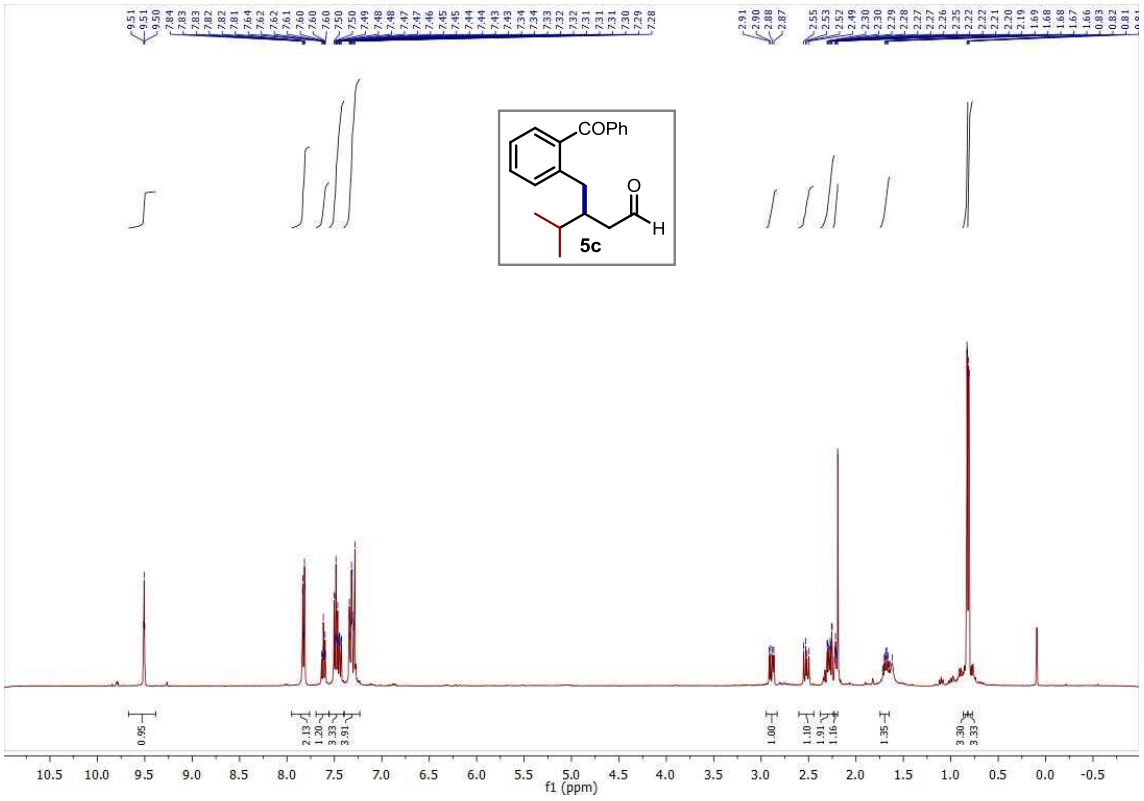
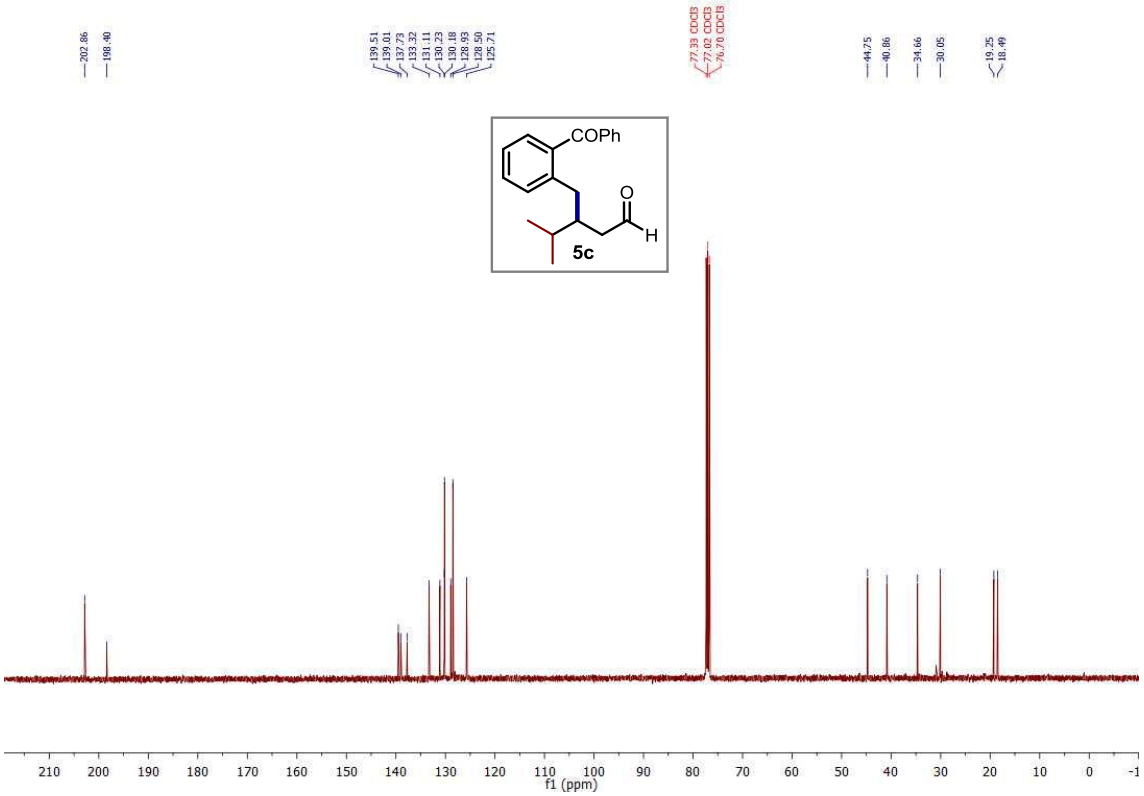
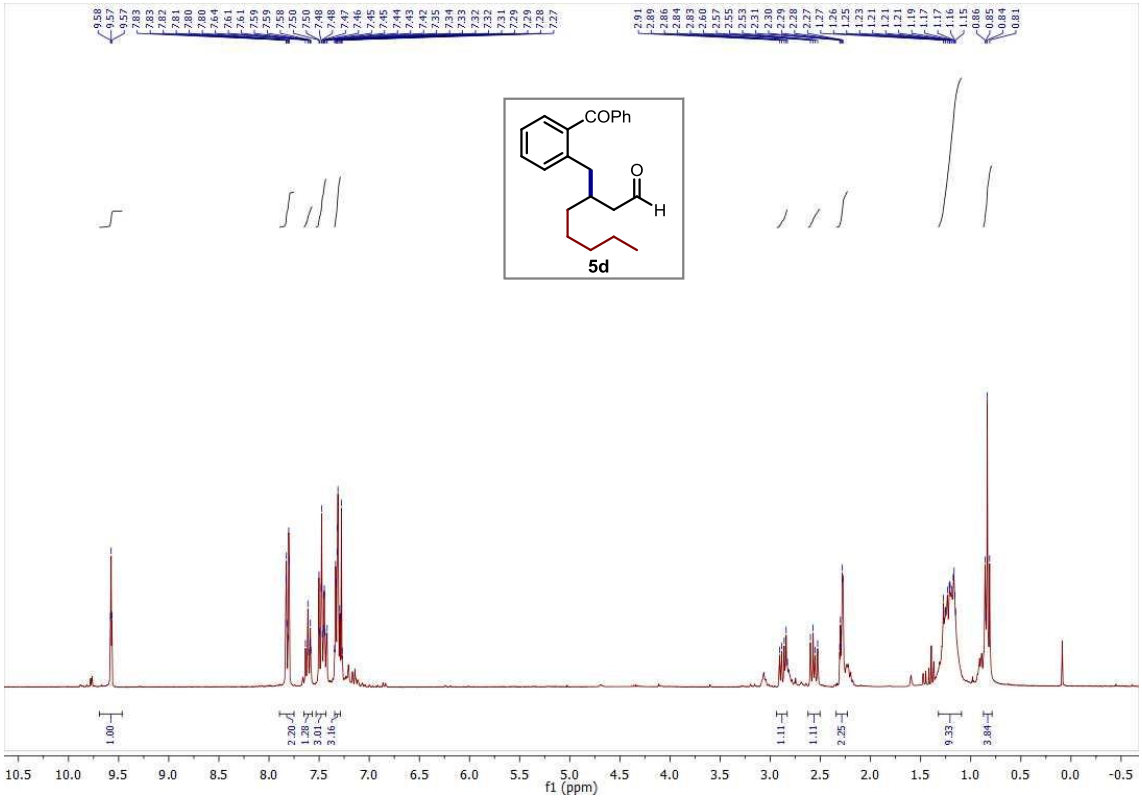
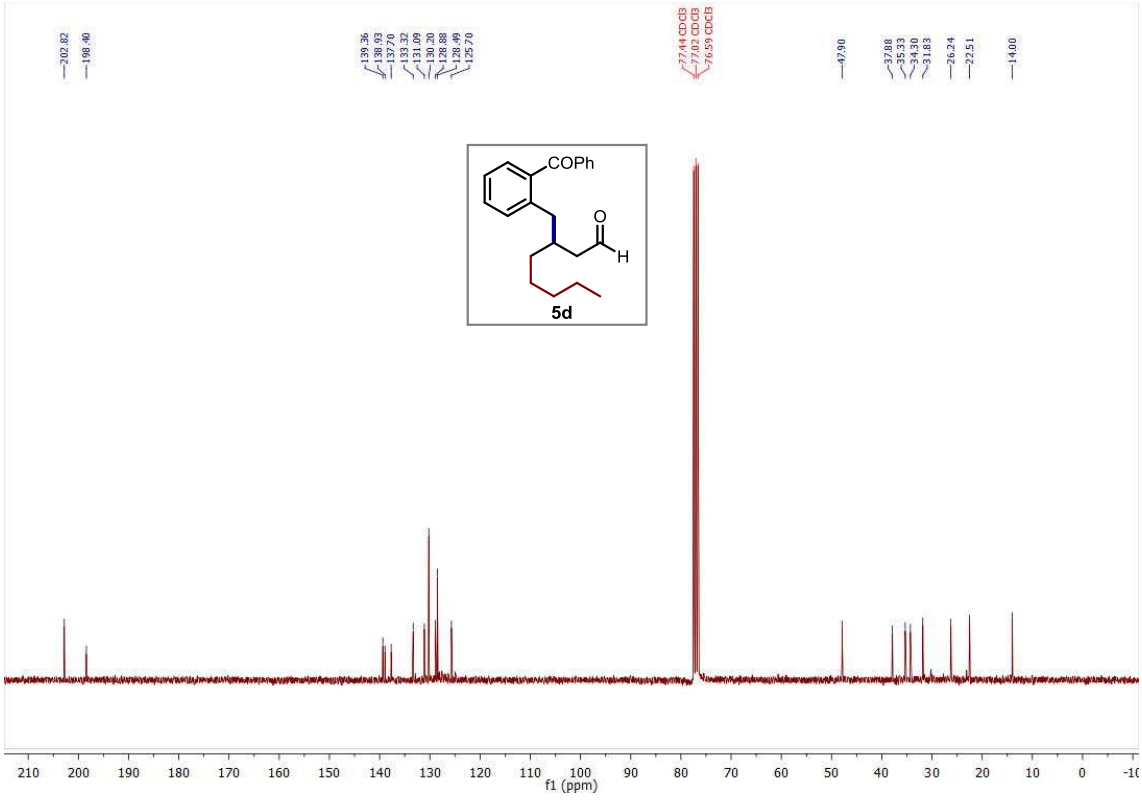
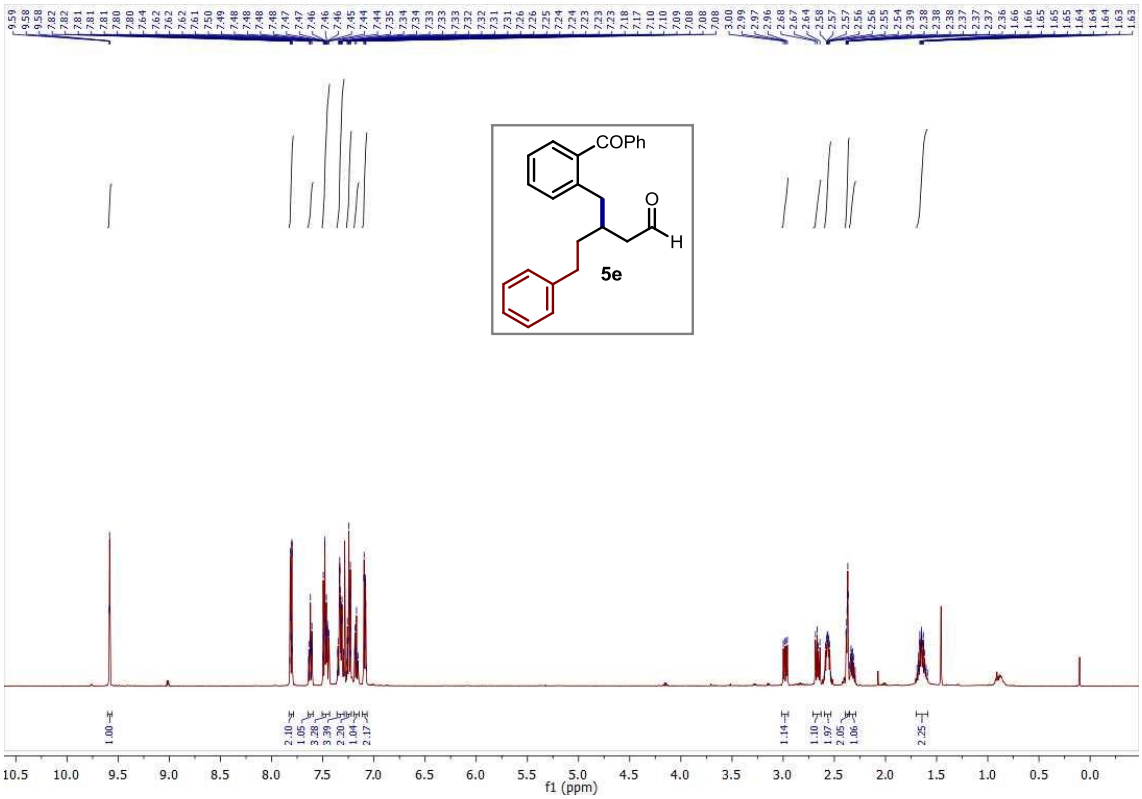
198.50
139.25
137.81
137.78
133.29
131.01
130.25
130.17
128.97
128.49
125.71
77.34
77.02
76.70
50.31
40.18
30.34
20.02
COPh
O
Me
H
5b
f1 (ppm)

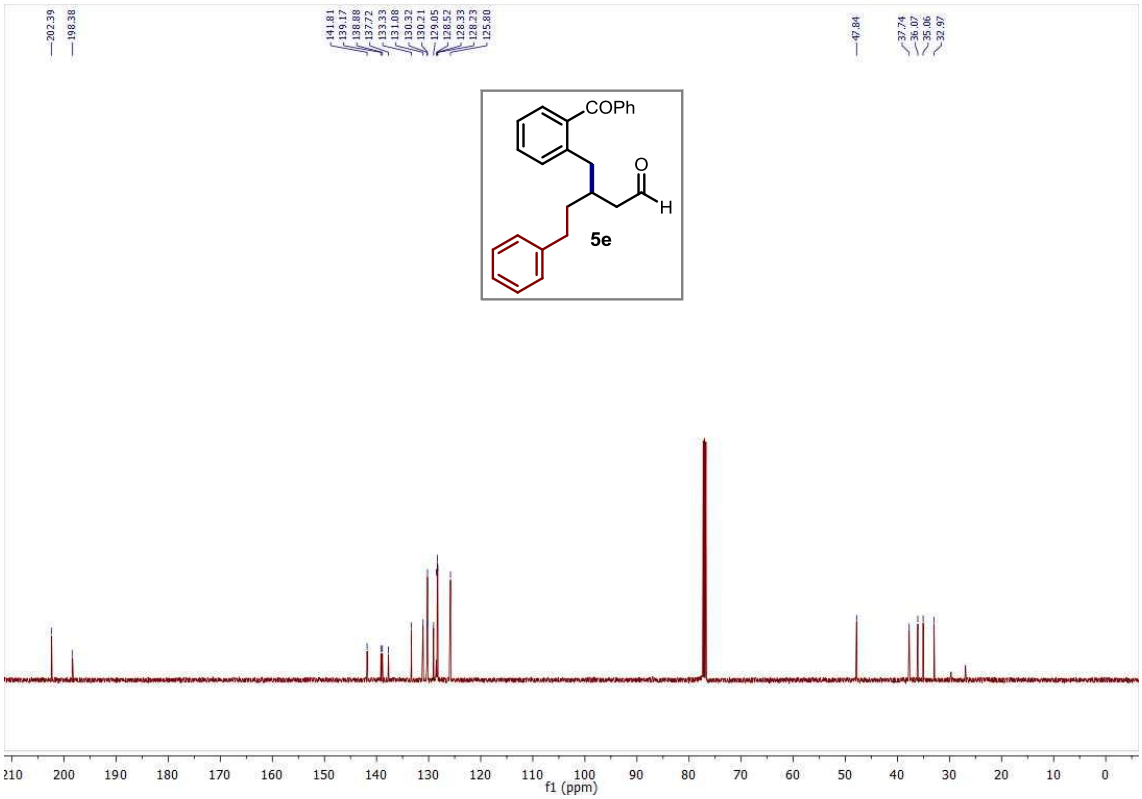

COPh
O
H
5c
f1 (ppm)


COPh
O
H
5c
f1 (ppm)


COPh
O
H
5d
f1 (ppm)


COPh
O
H
5d
f1 (ppm)


COPh
O
H
5e
f1 (ppm)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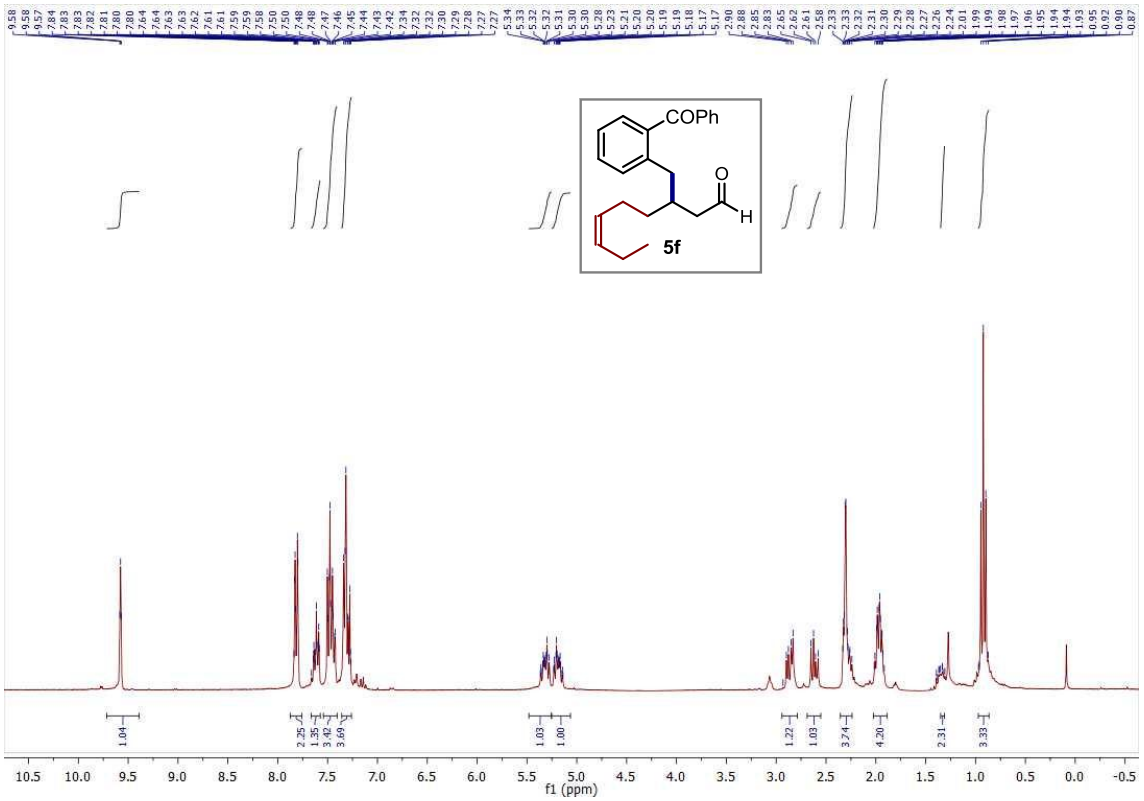
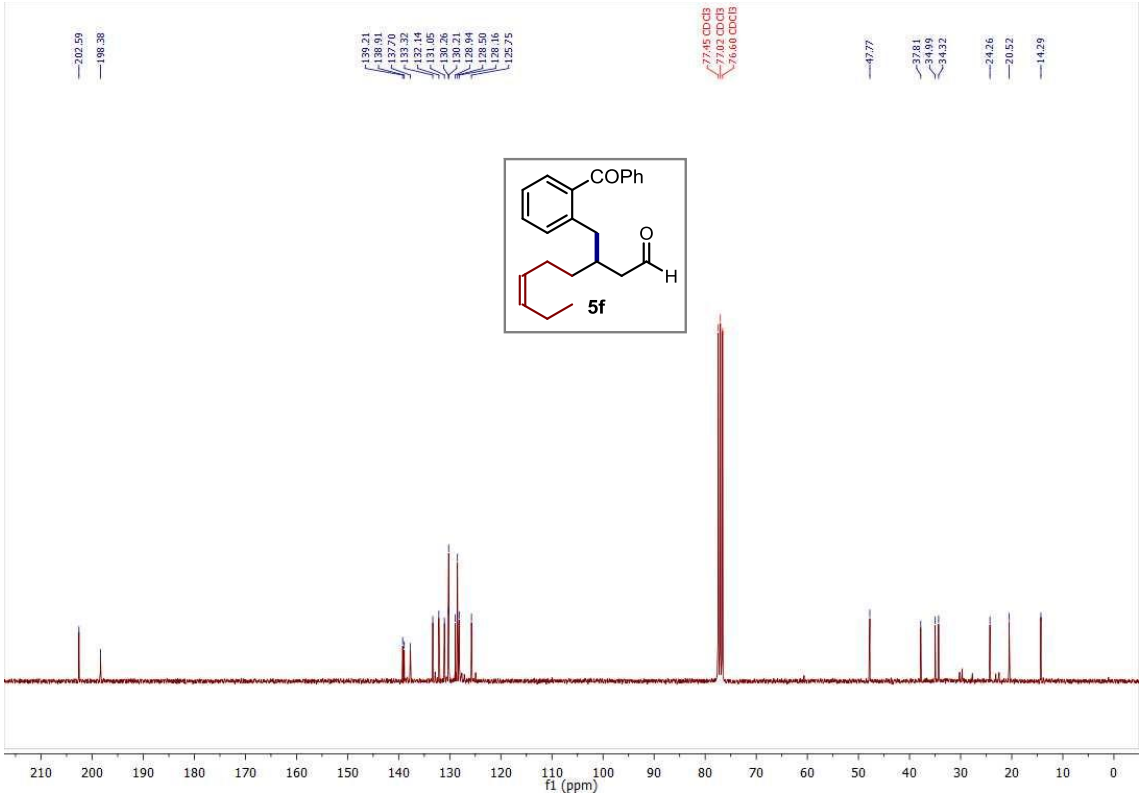
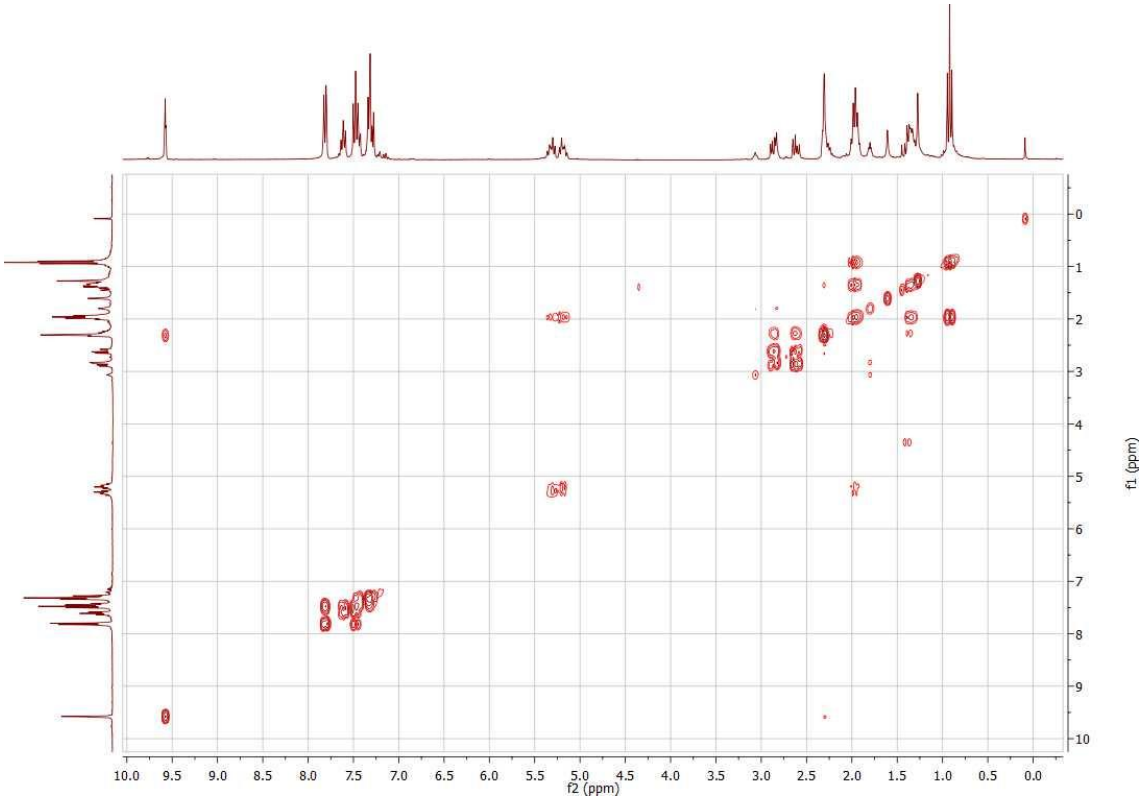
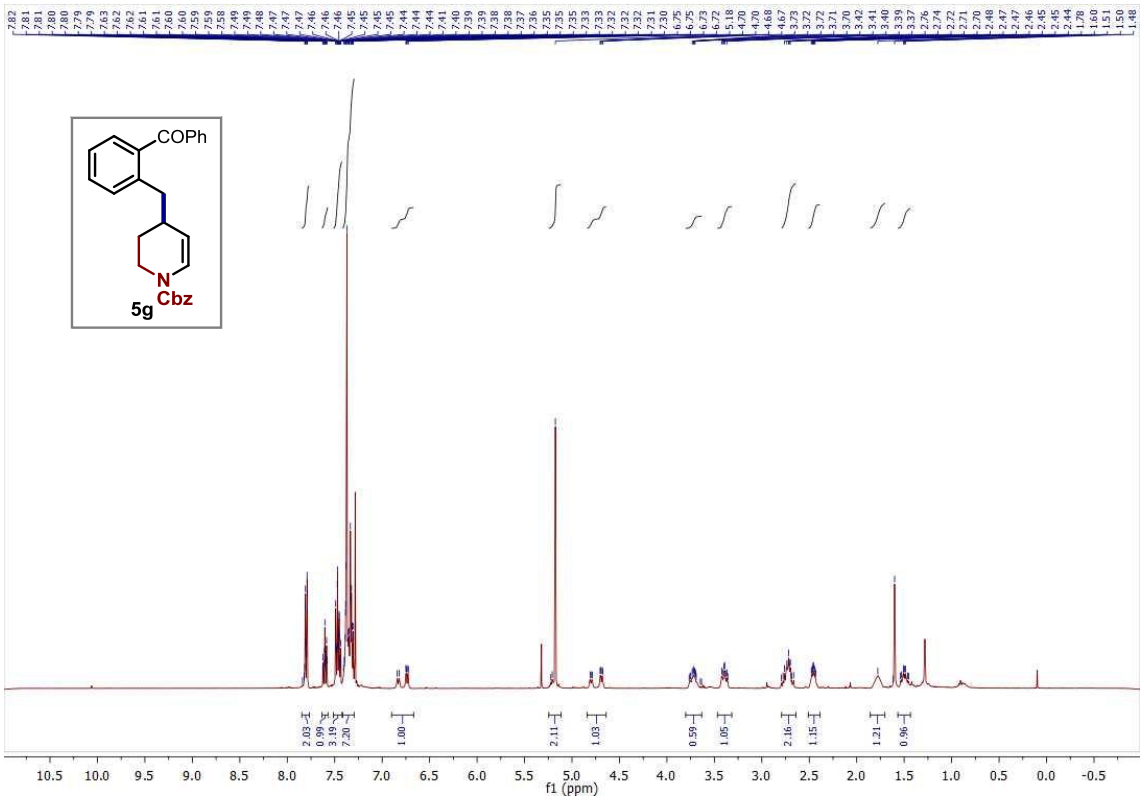
H
5e
f1 (ppm)

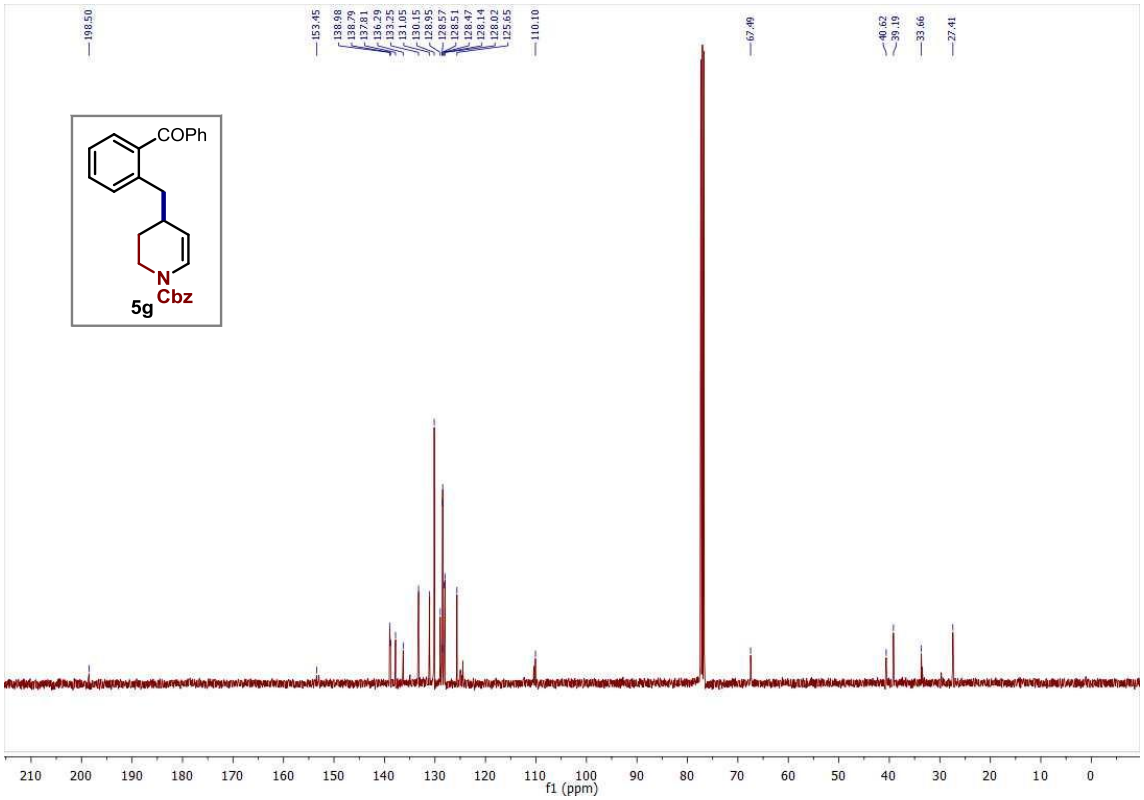

COPh
O
H
5f
f1 (ppm)

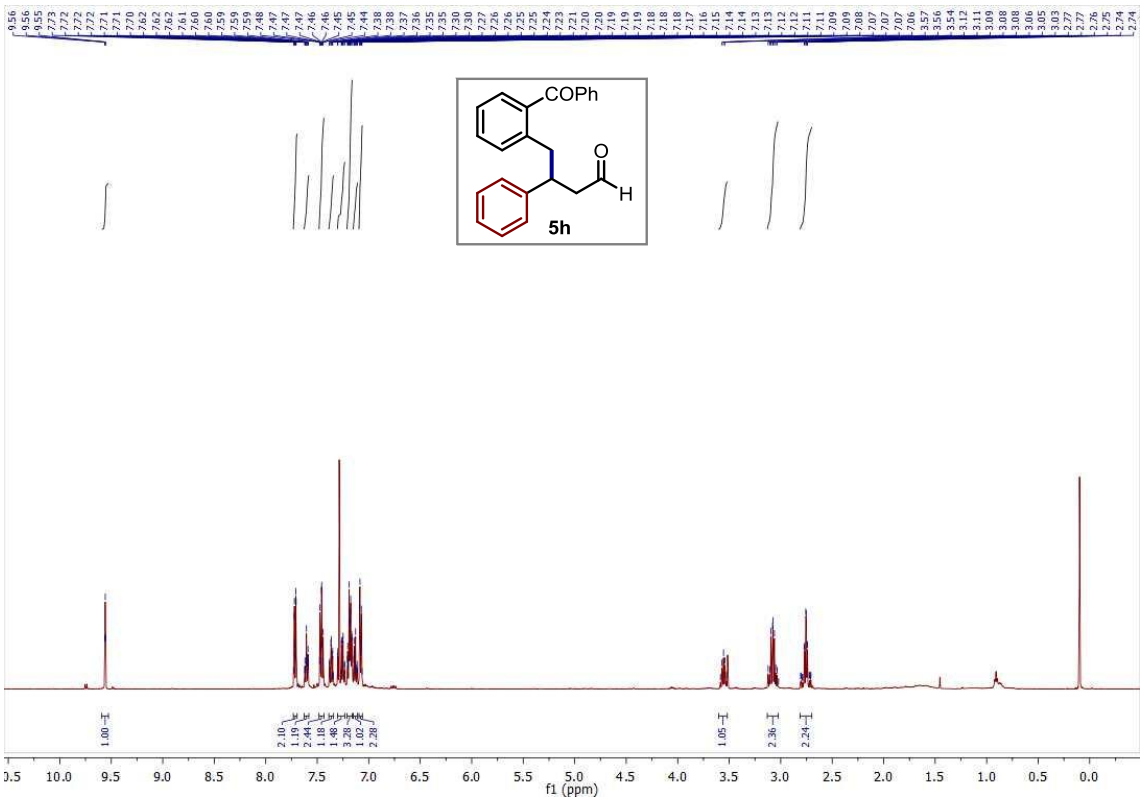

COPh
O
H
5f
f1 (ppm)

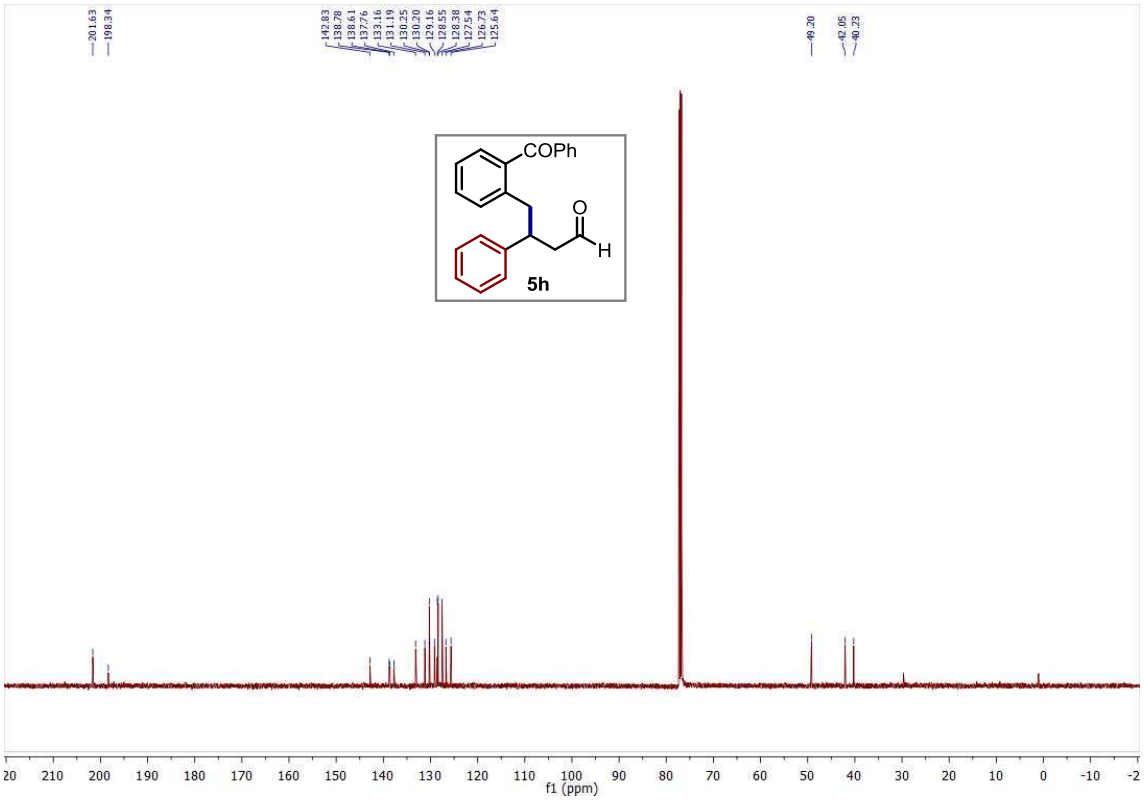
^{1}H-^{1}H COSY analysis of compound **5f**



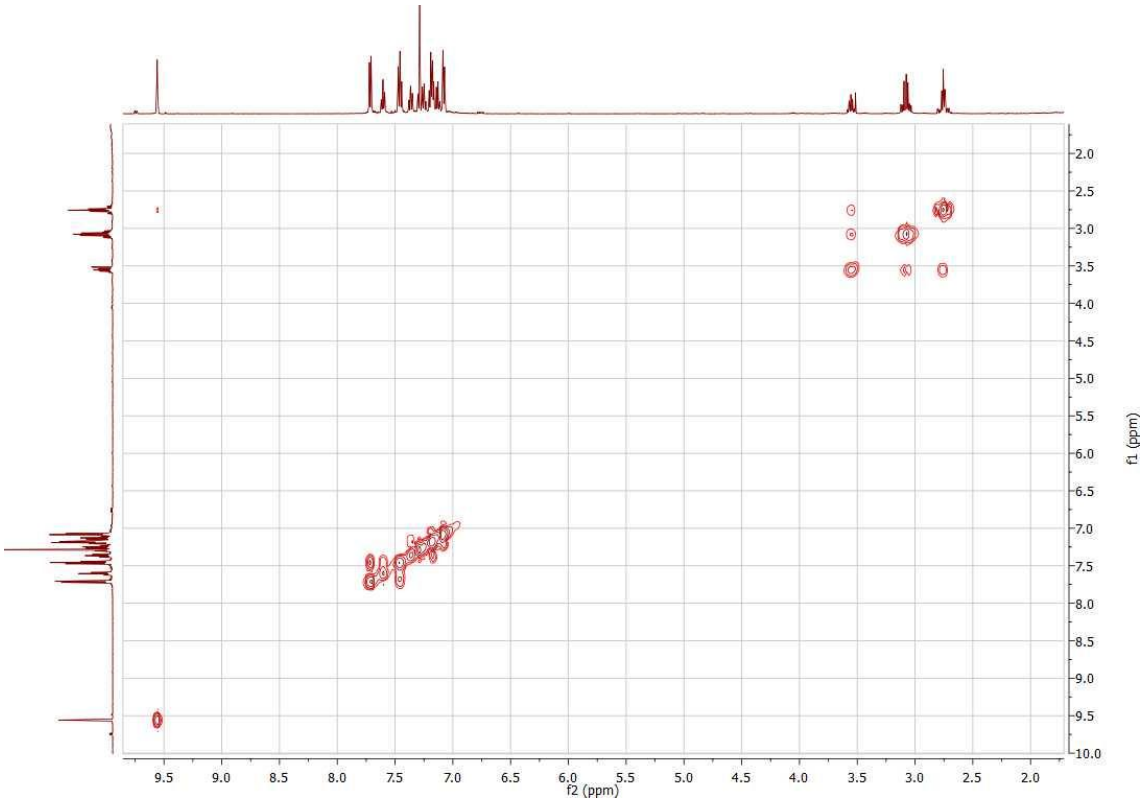

COPh
N
Cbz
5g
f1 (ppm)

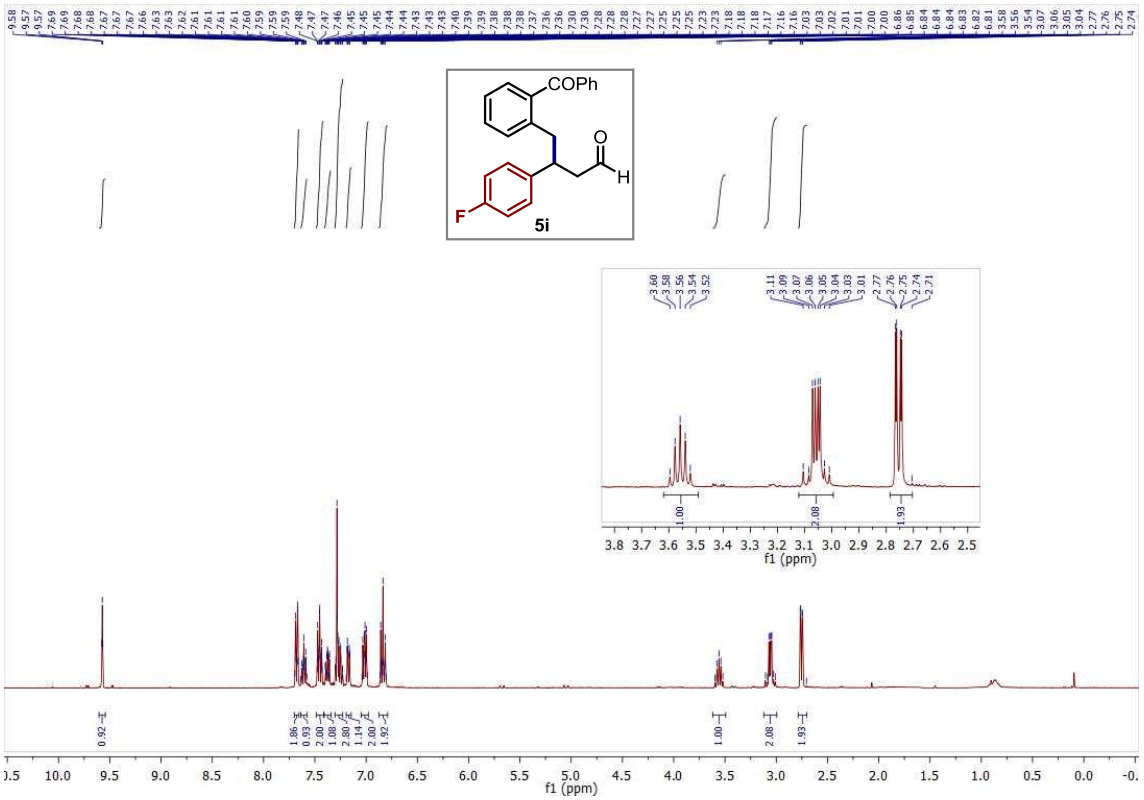

COPh
N
Cbz
5g
f1 (ppm)

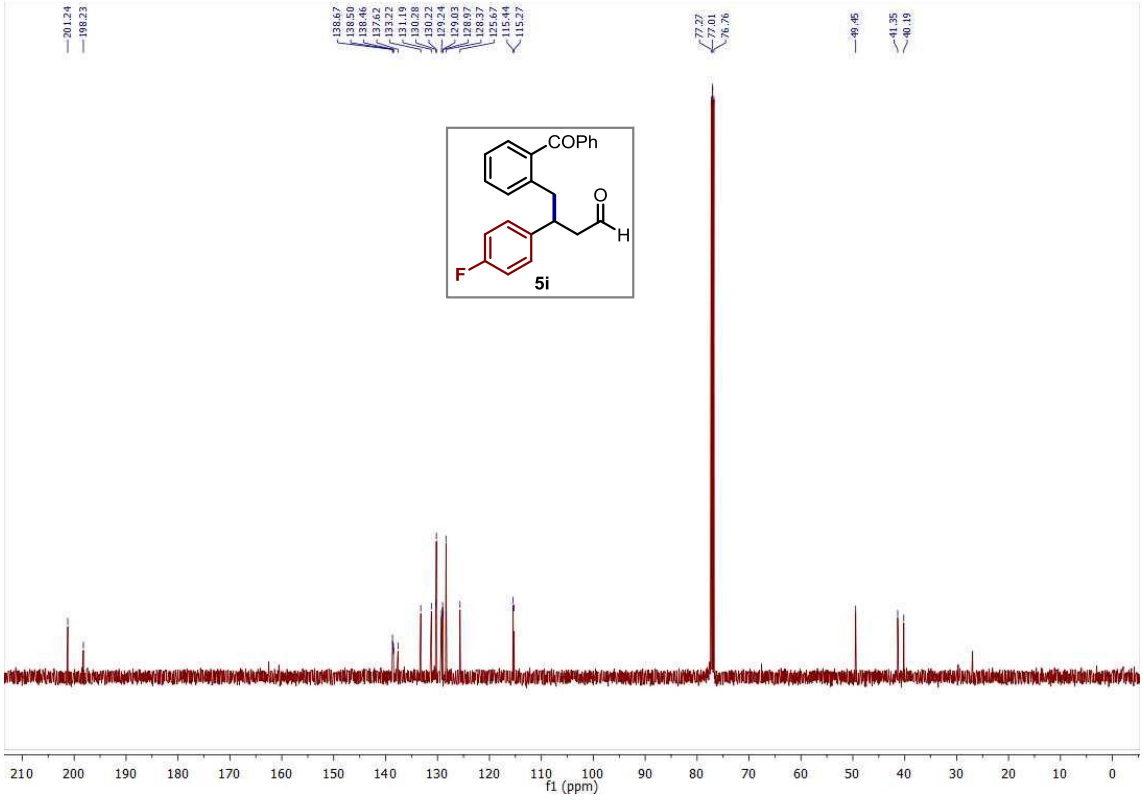

COPh
O
H
5h
f1 (ppm)

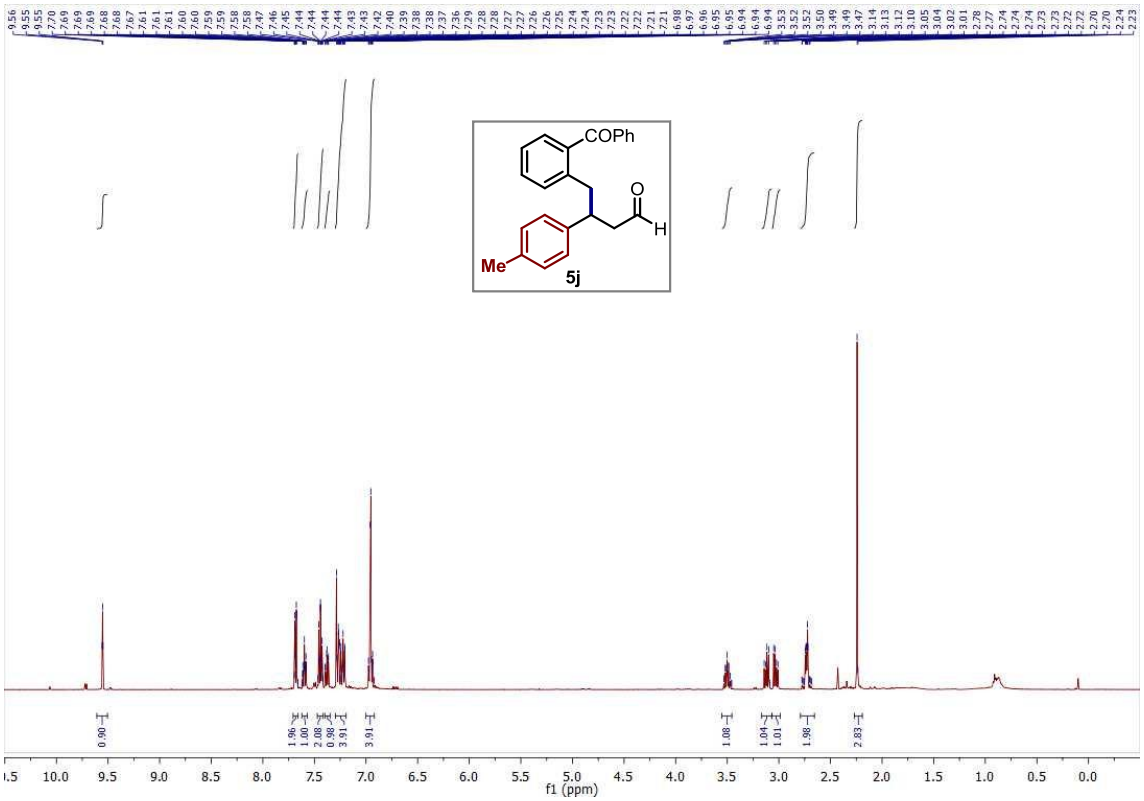

COPh
O
H
5h
f1 (ppm)

^{1}H-^{1}H COSY analysis of compound **5h**




COPh
O
H
F
5i
f1 (ppm)


COPh
O
H
F
5i
f1 (ppm)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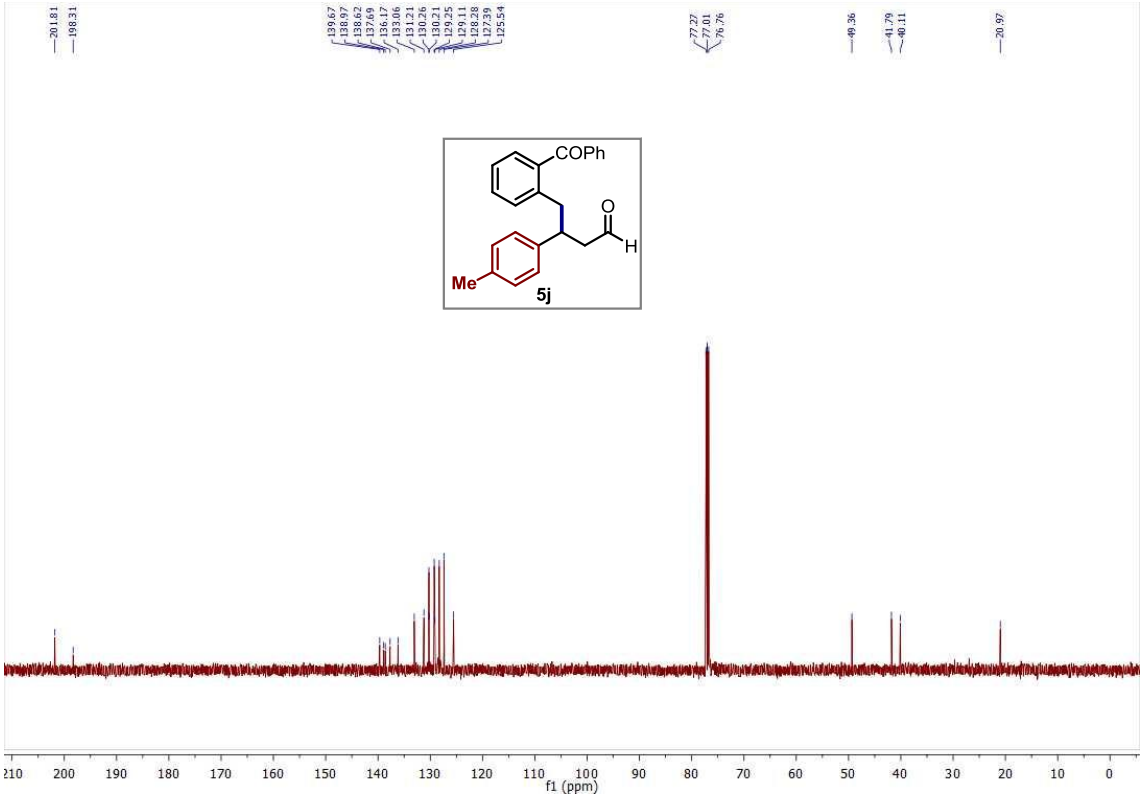
O
H
Me
5j
f1 (ppm)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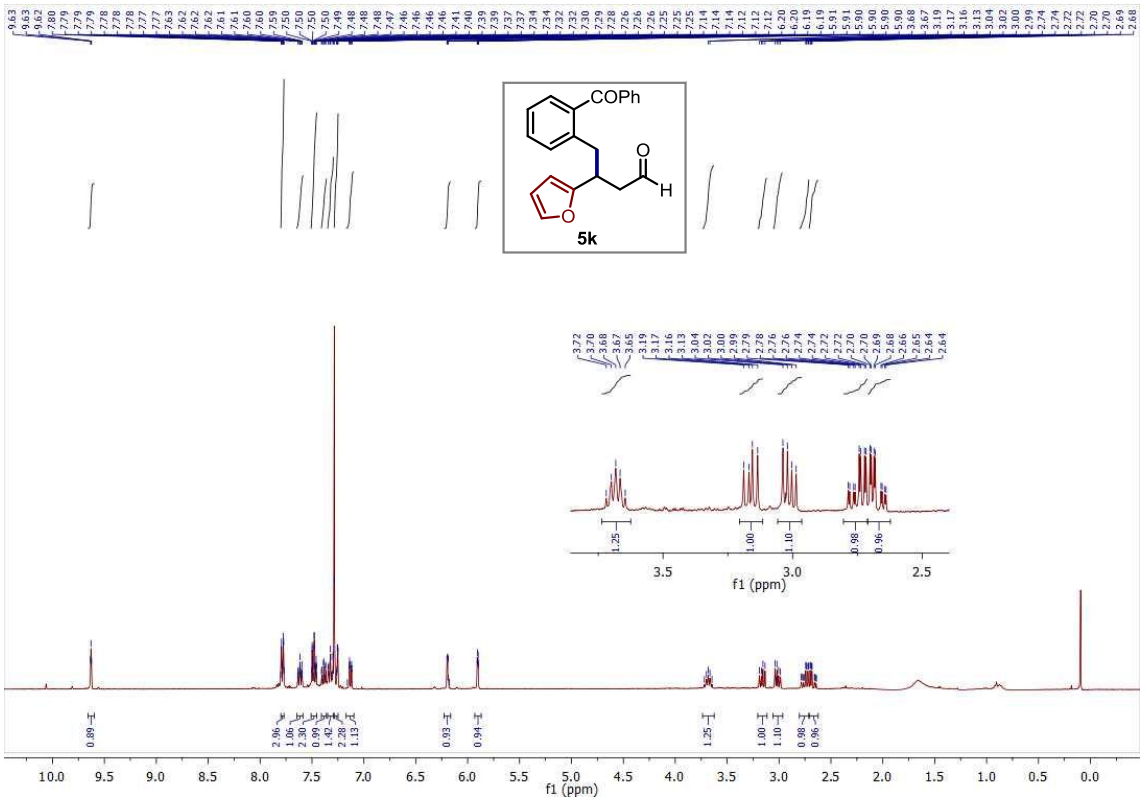
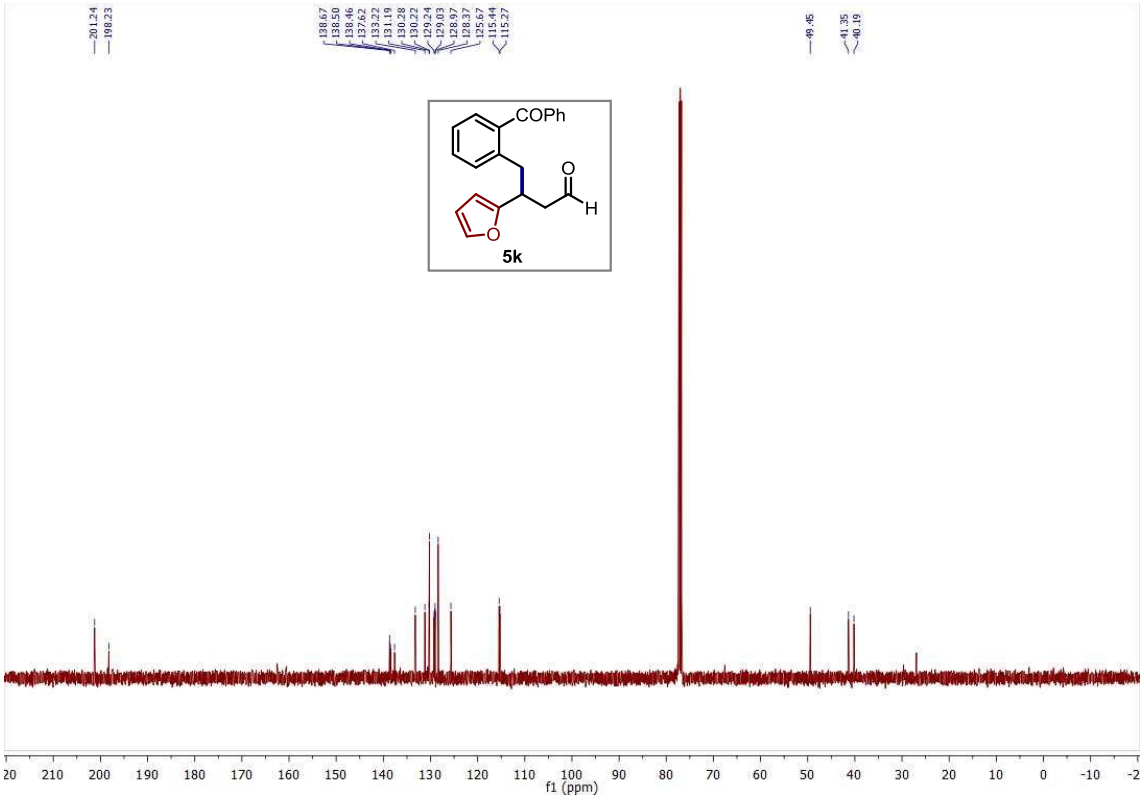
H
Me
5j
f1 (ppm)


COPh
O
H
O
5k
f1 (ppm)
f1 (ppm)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H
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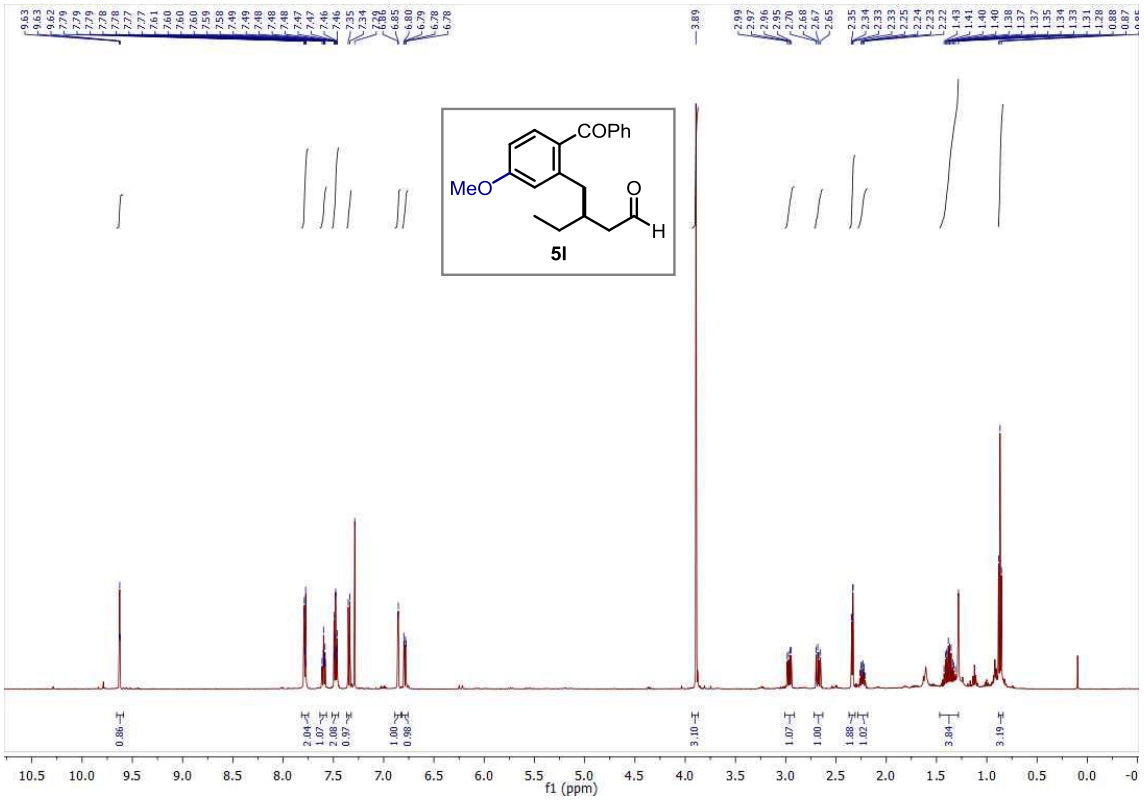
f1 (ppm)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O
H
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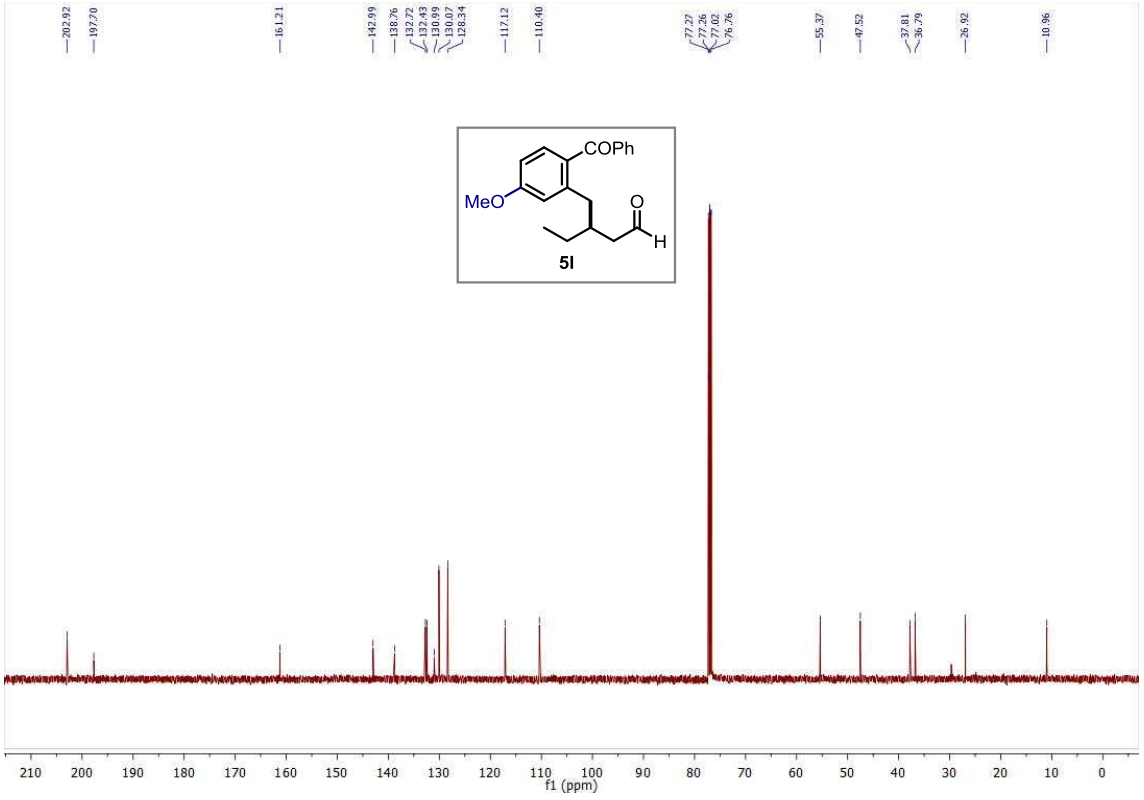
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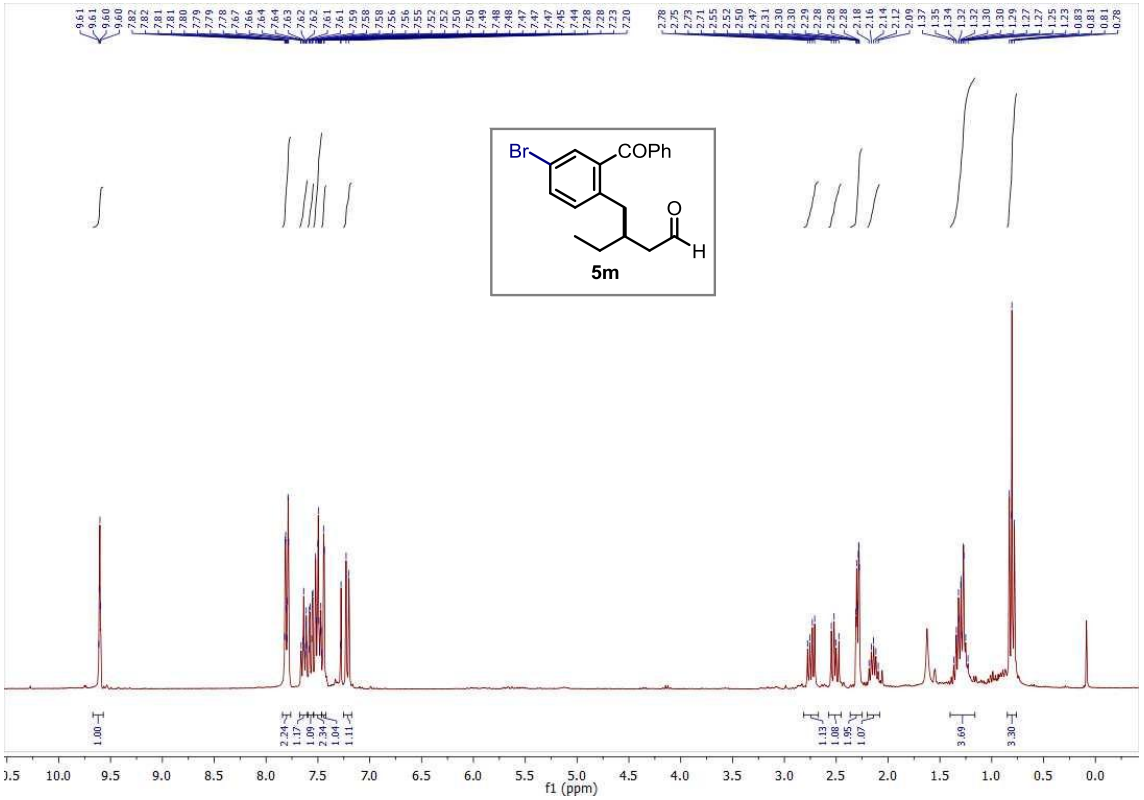
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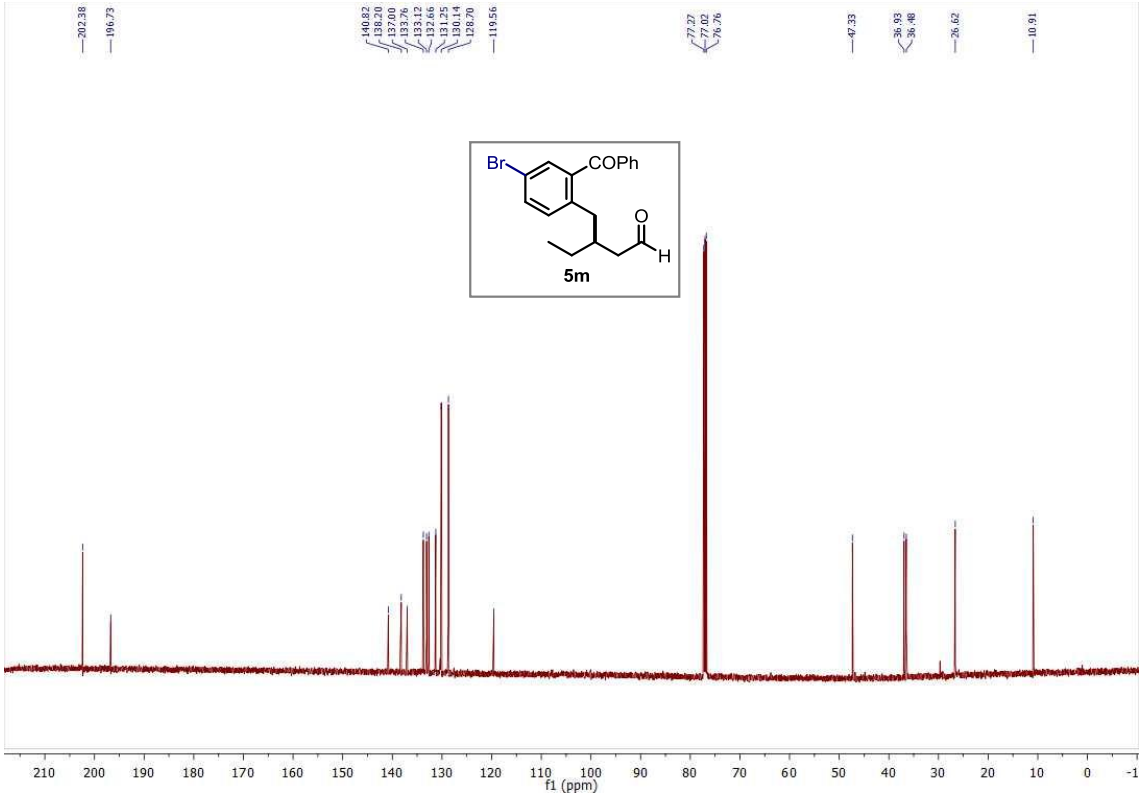
H
5m
f1 (ppm)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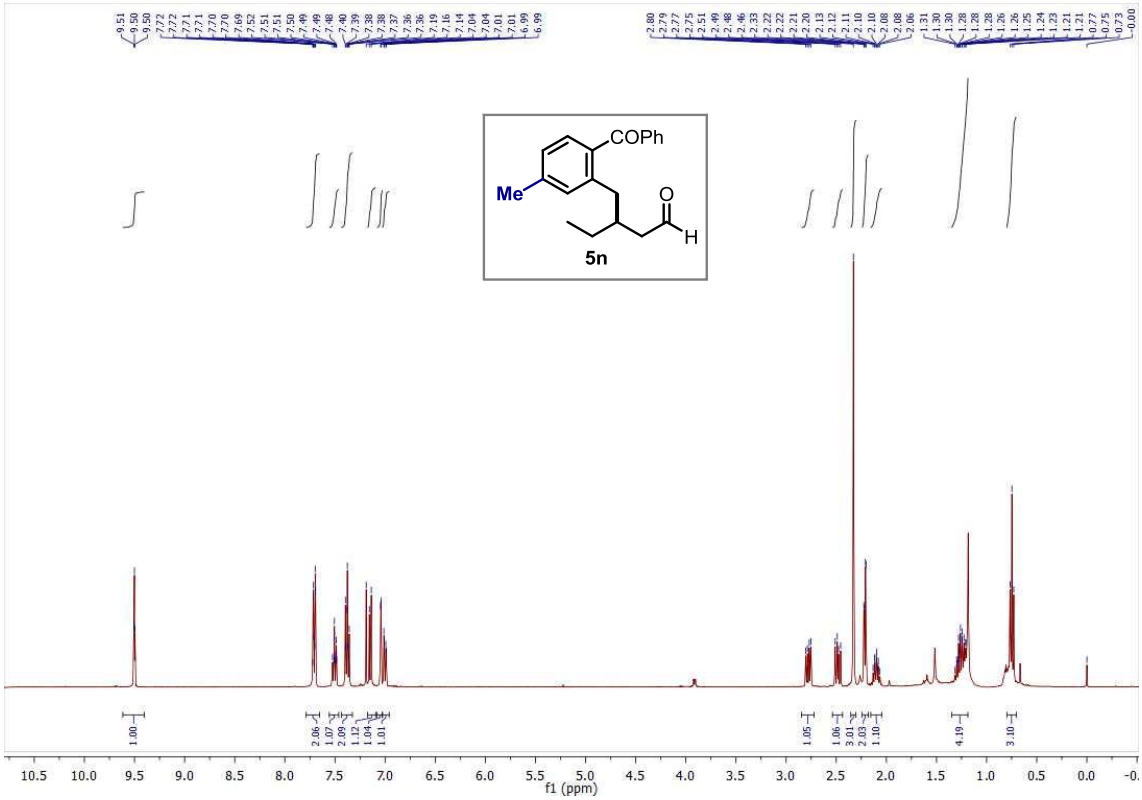
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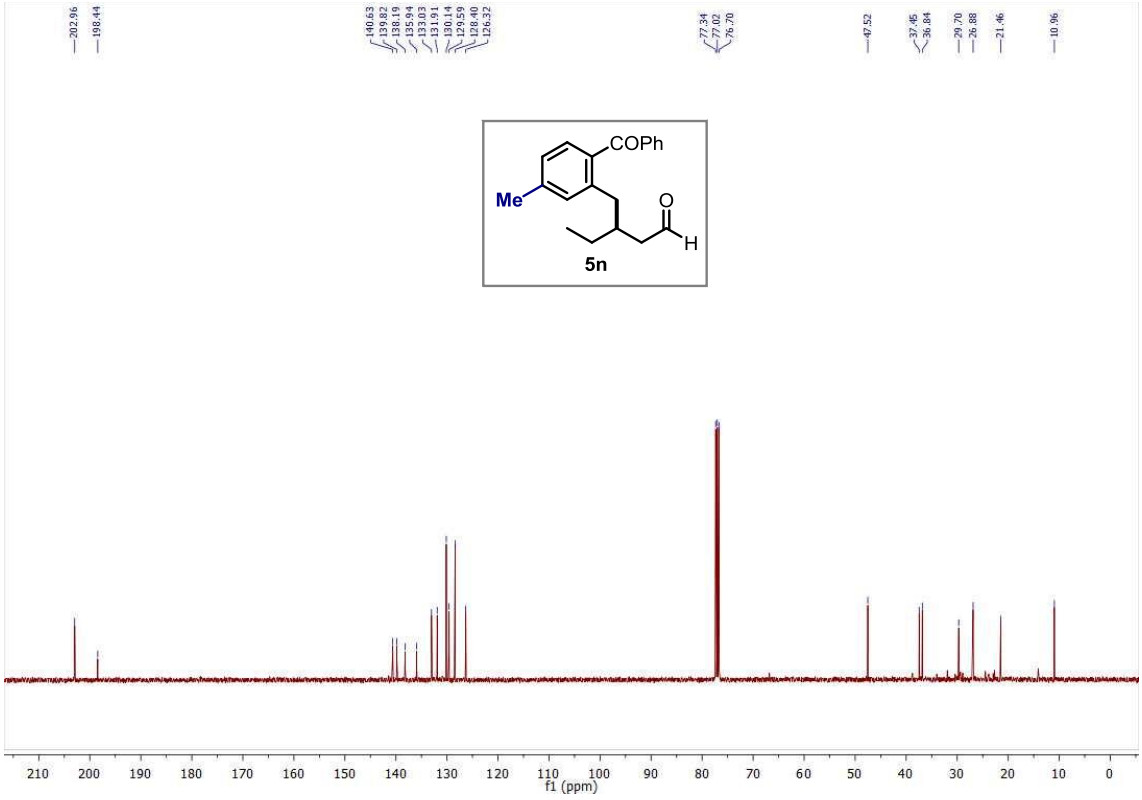
f1 (ppm)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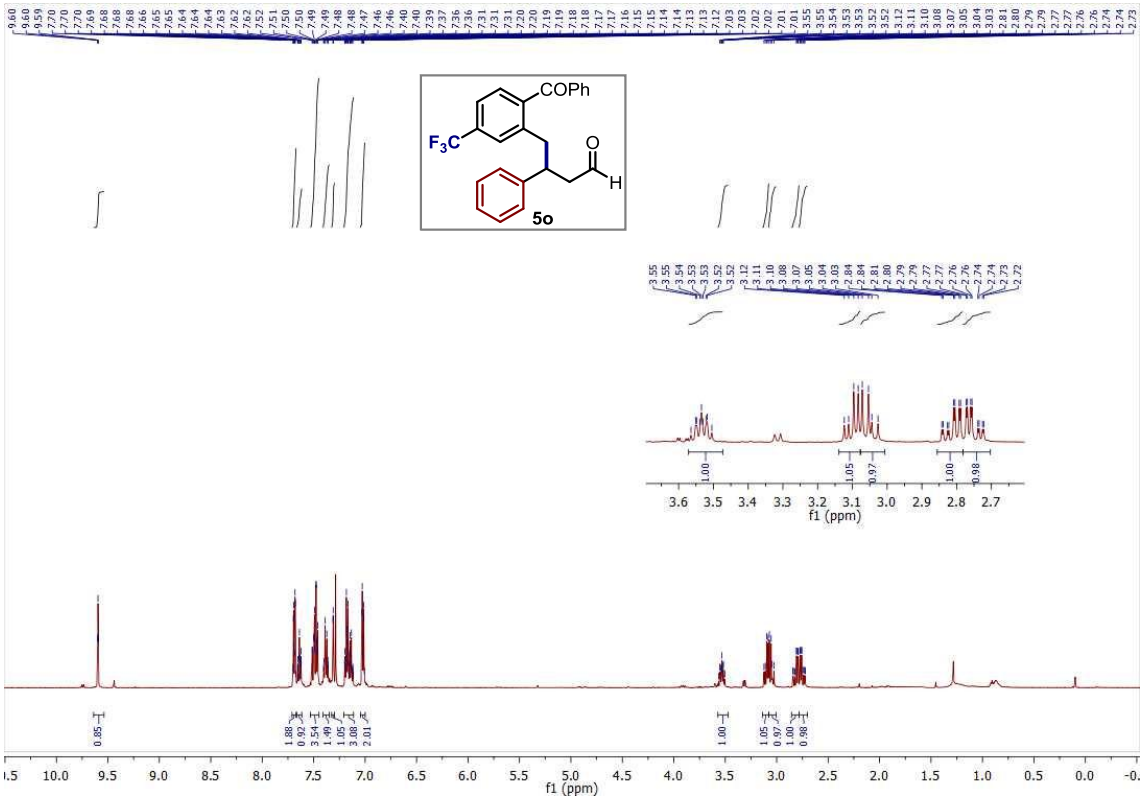
f1 (ppm)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F3C
O
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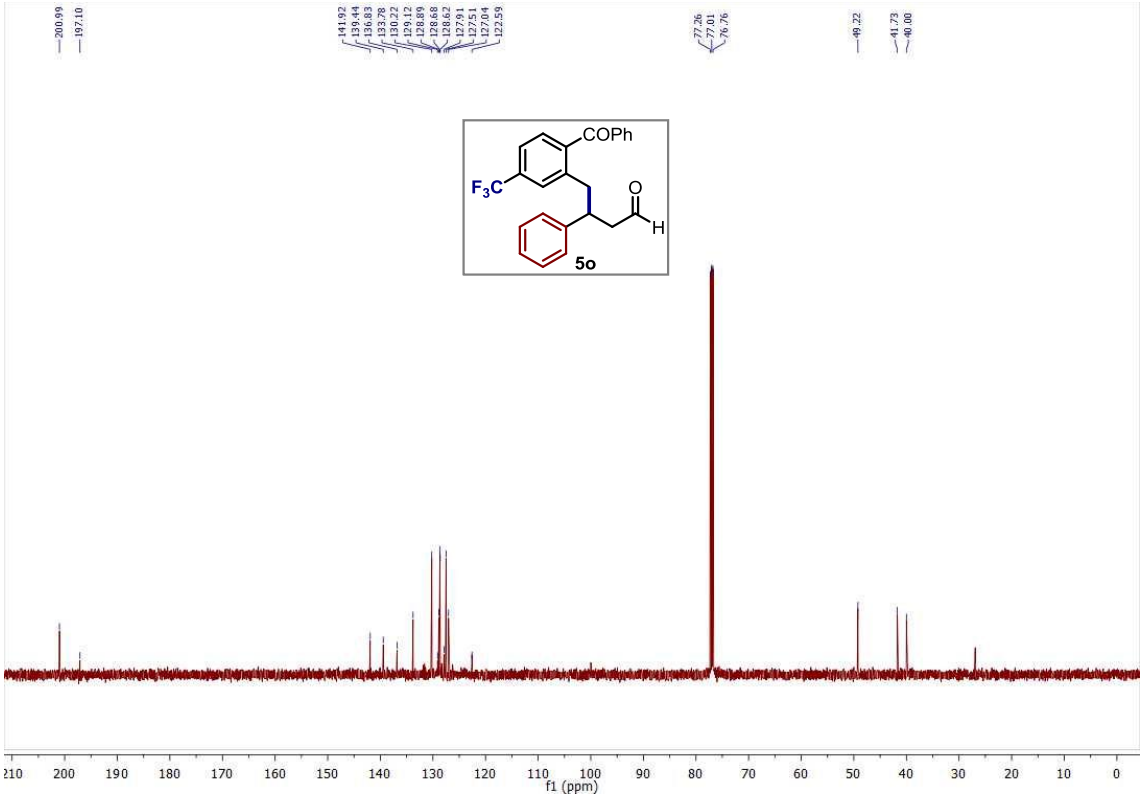
5o
f1 (ppm)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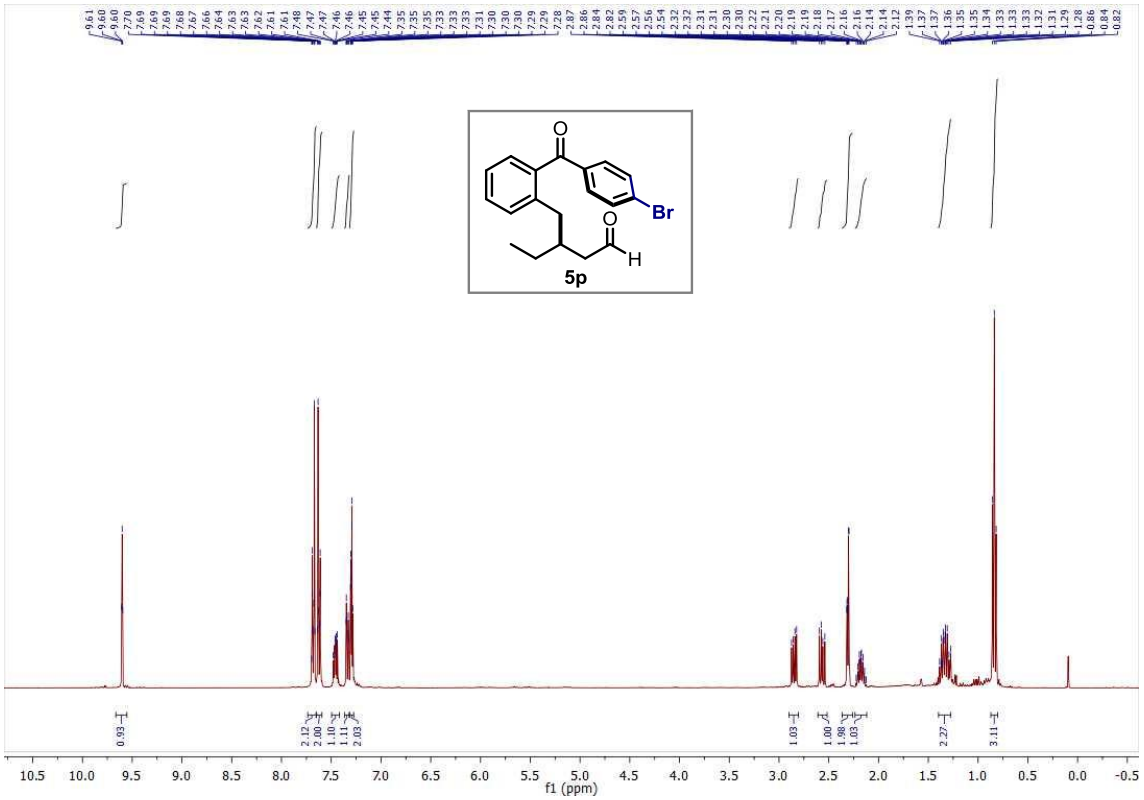
O
H
5o
f1 (ppm)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O
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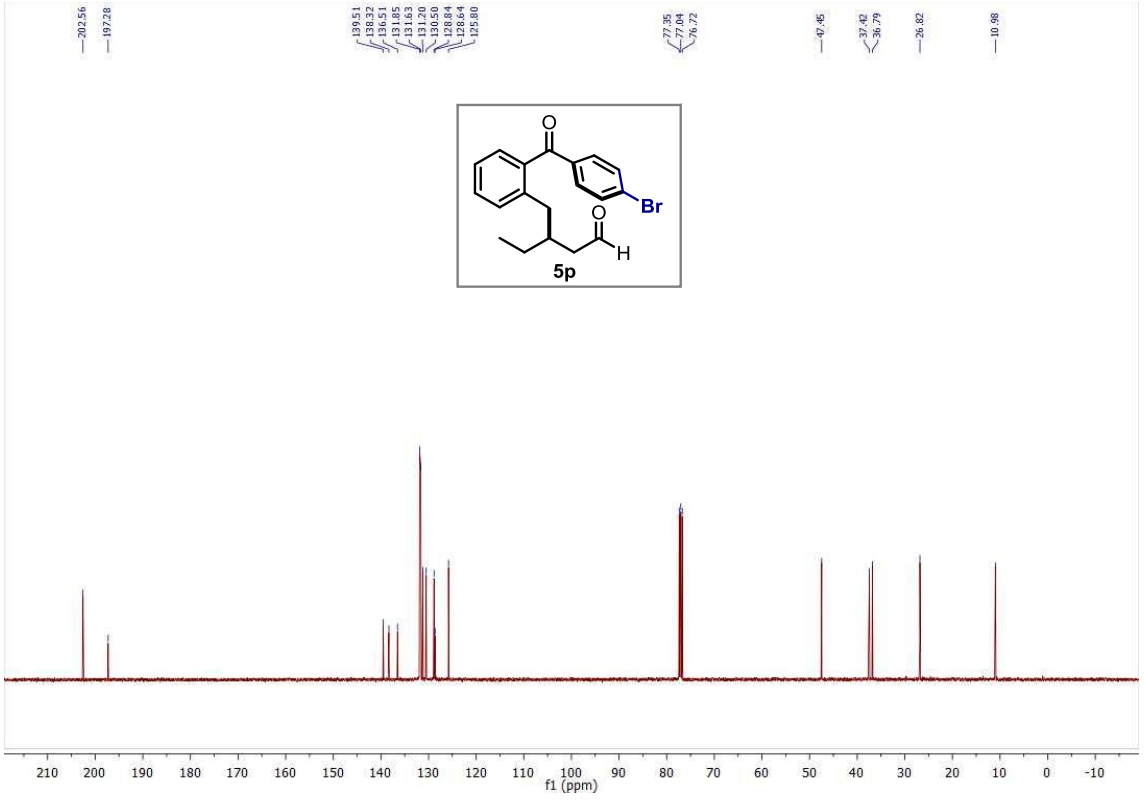
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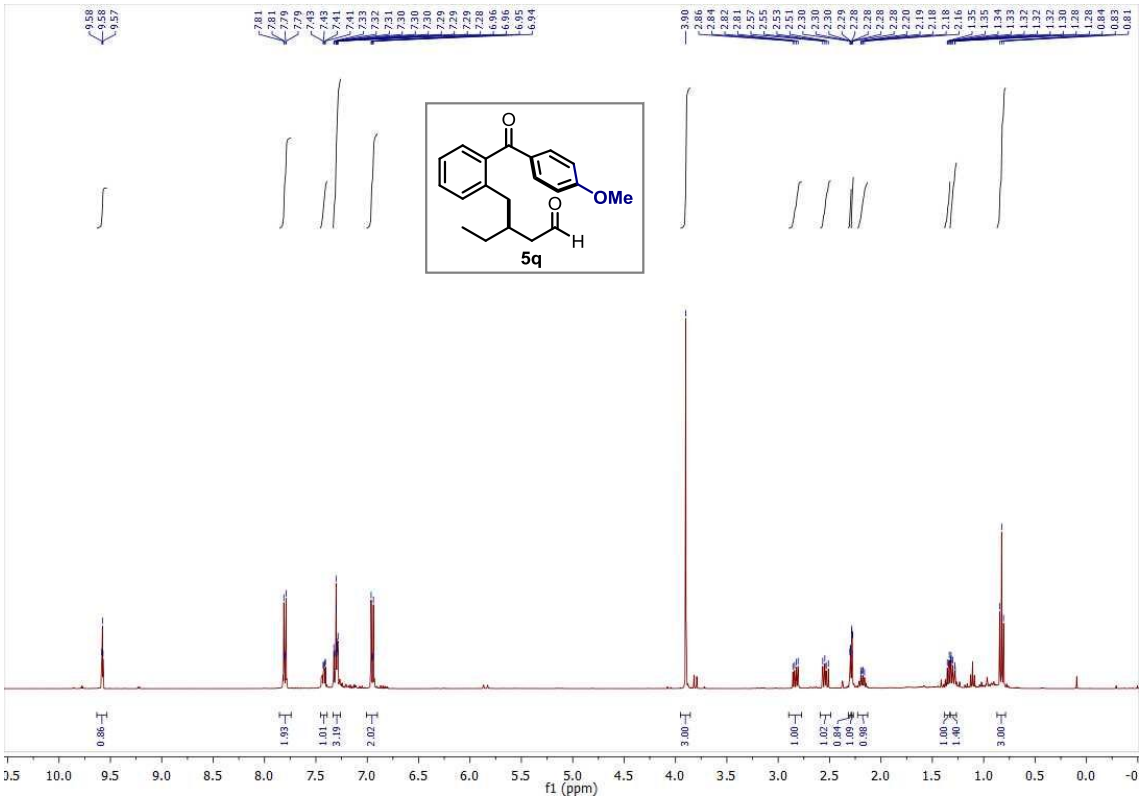
O
H
5p
f1 (ppm)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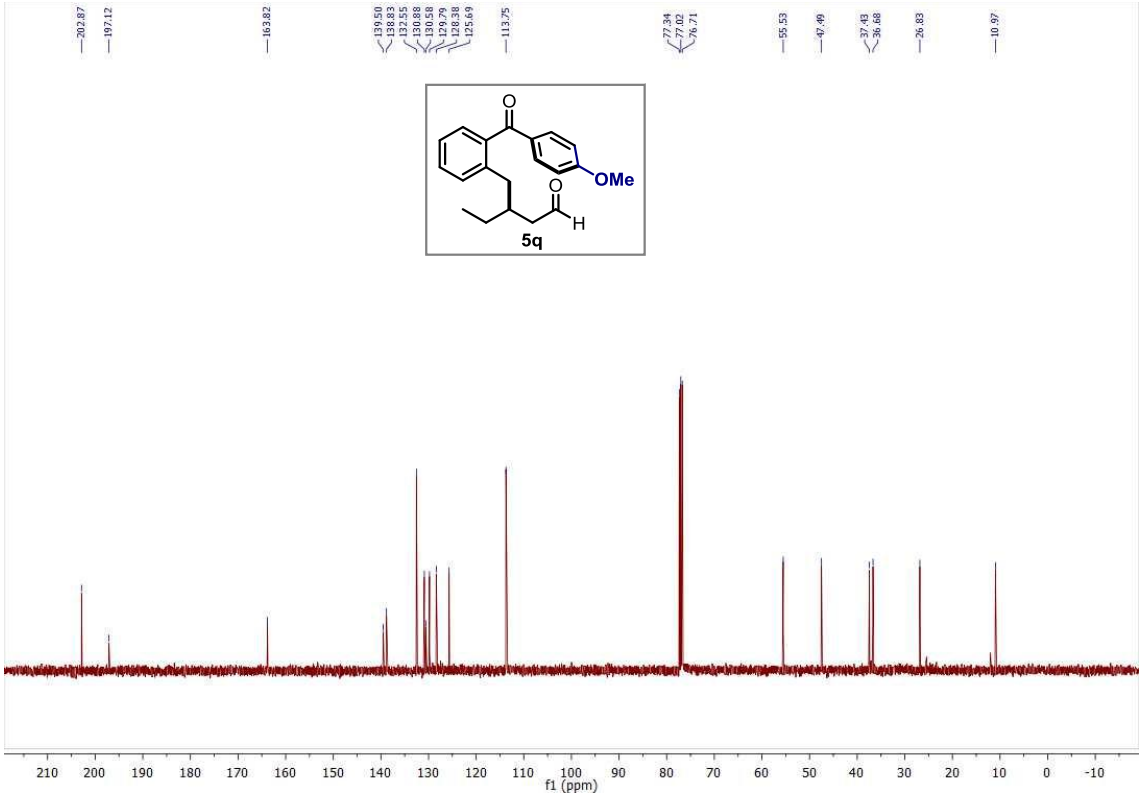
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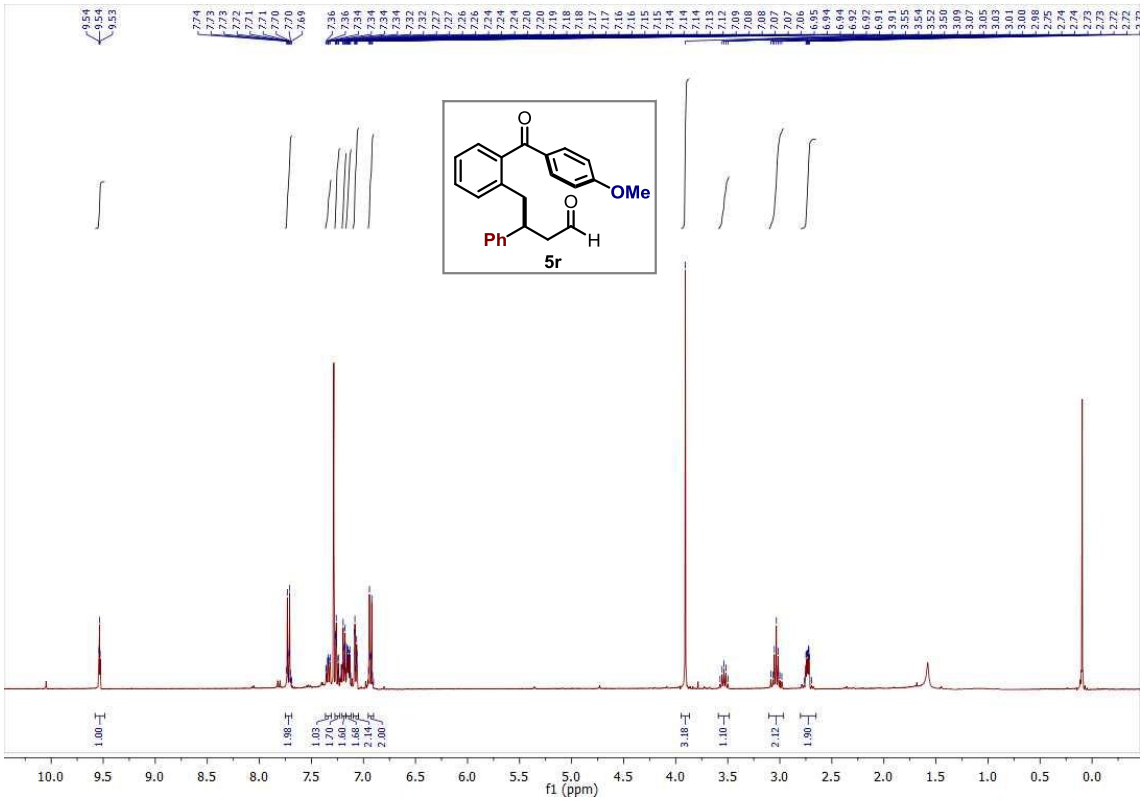
O
H
5q
f1 (ppm)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Ph
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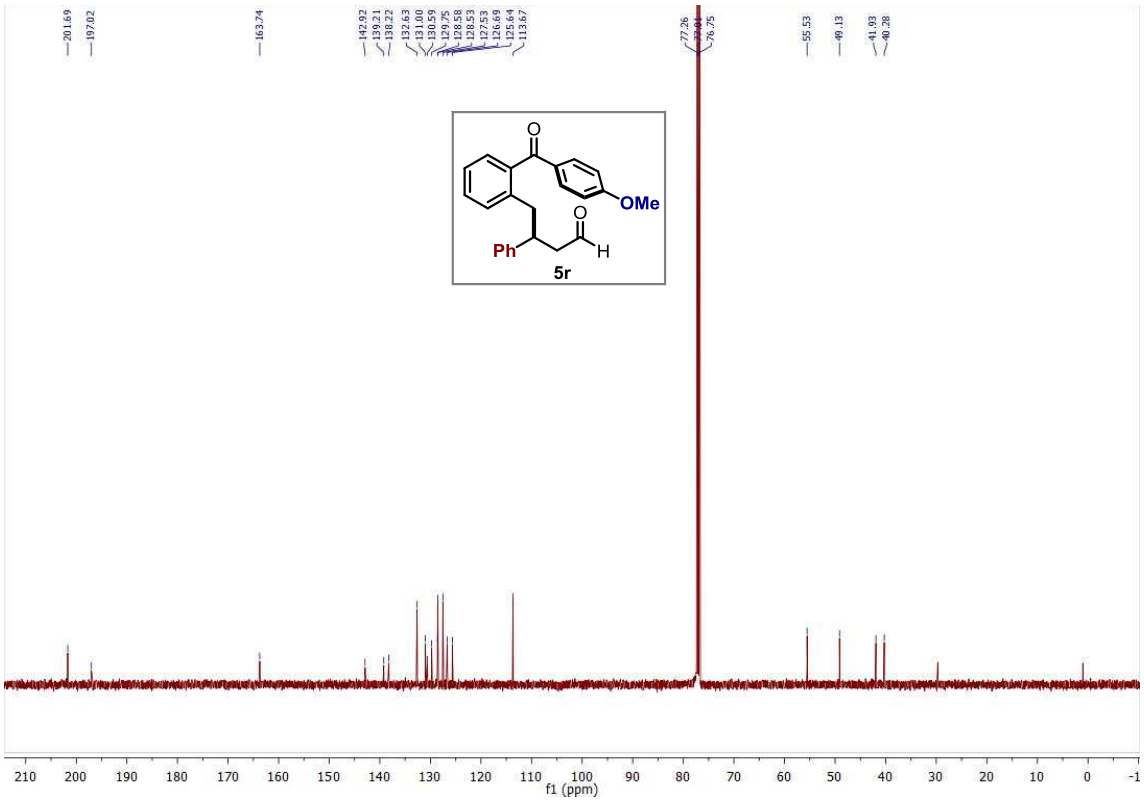
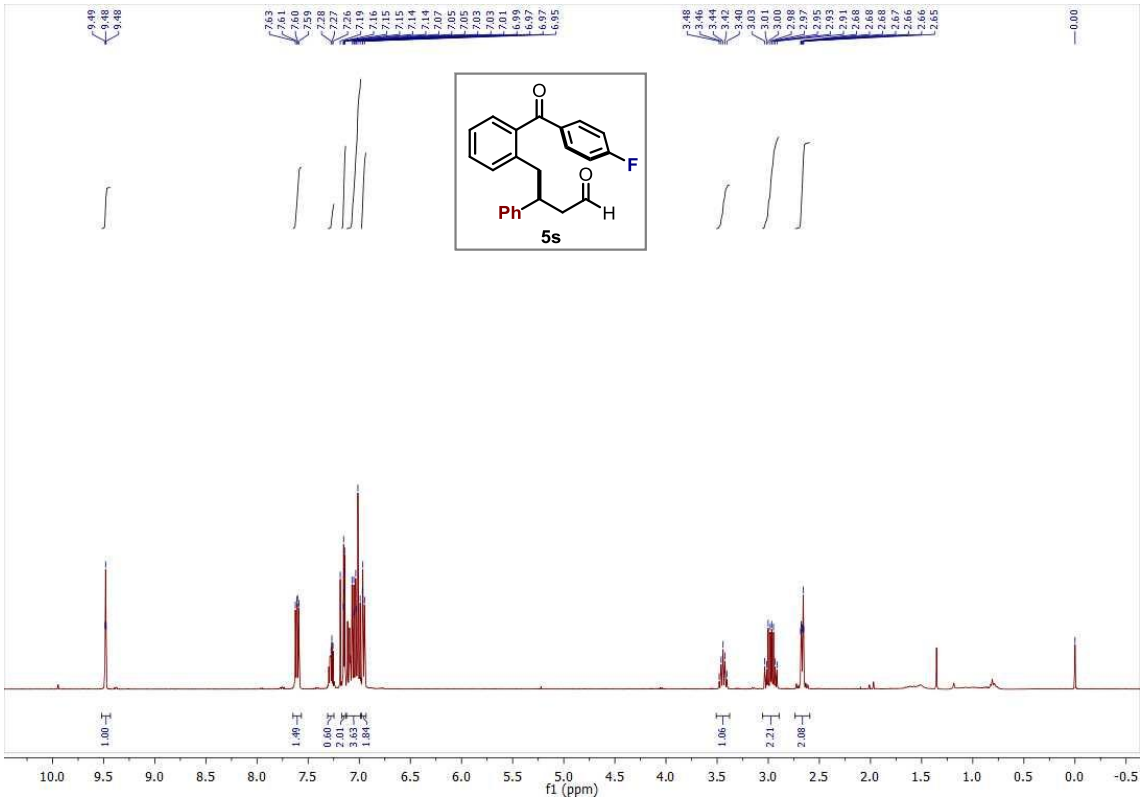
f1 (ppm)


OMe
Ph
5r
f1 (ppm)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7.15
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2.93
2.91
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2.68
2.67
2.67
2.66
2.66
2.65
0.00
O
F
O
Ph
H
5s
1.00
1.49
0.60
2.01
3.63
1.84
1.06
2.21
2.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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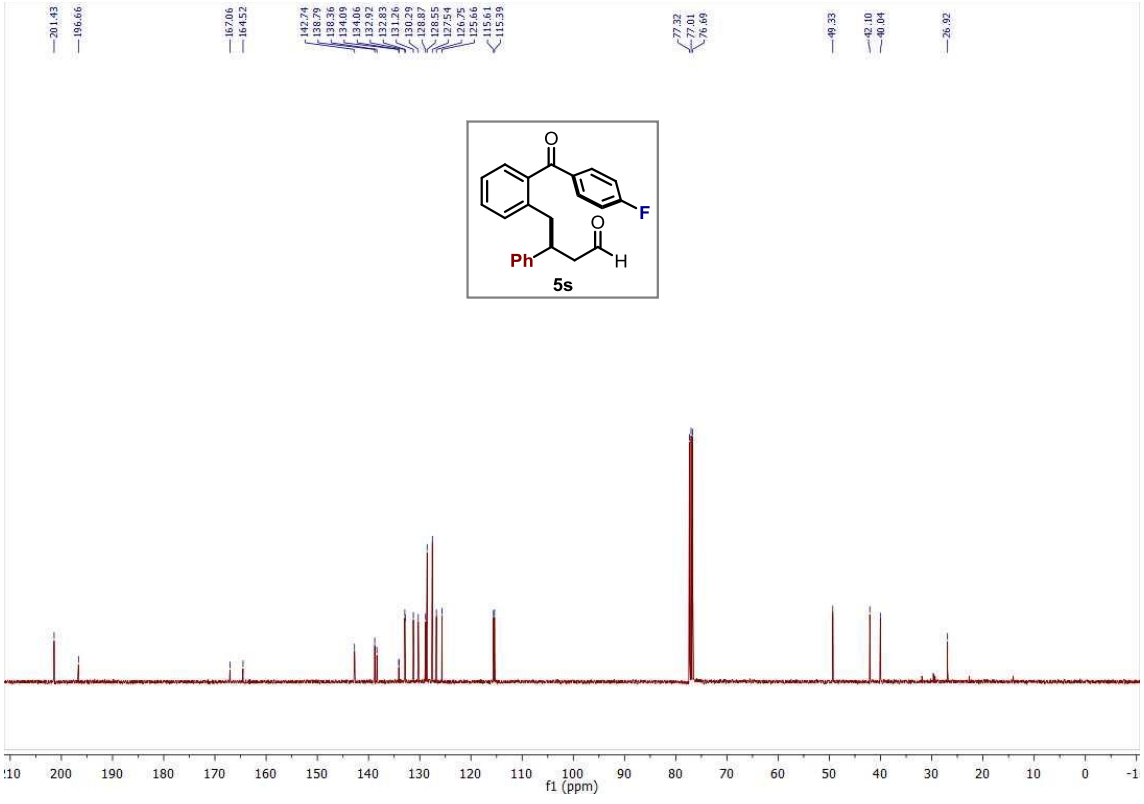
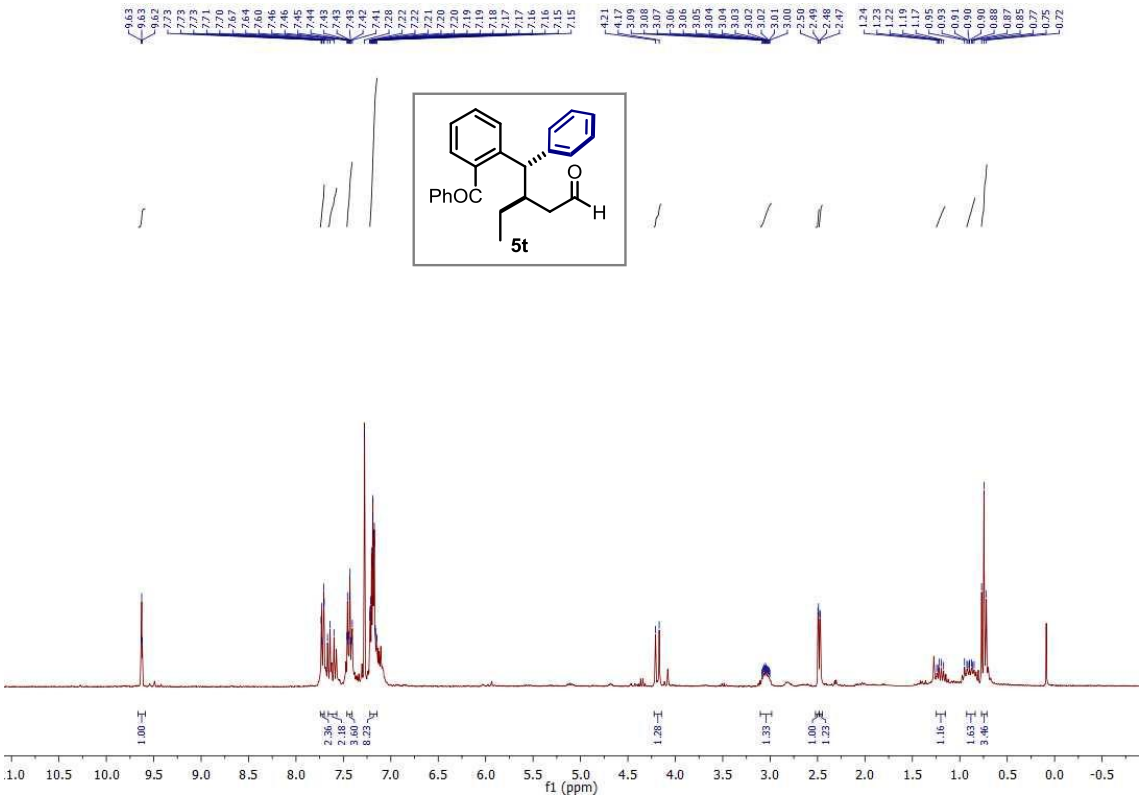
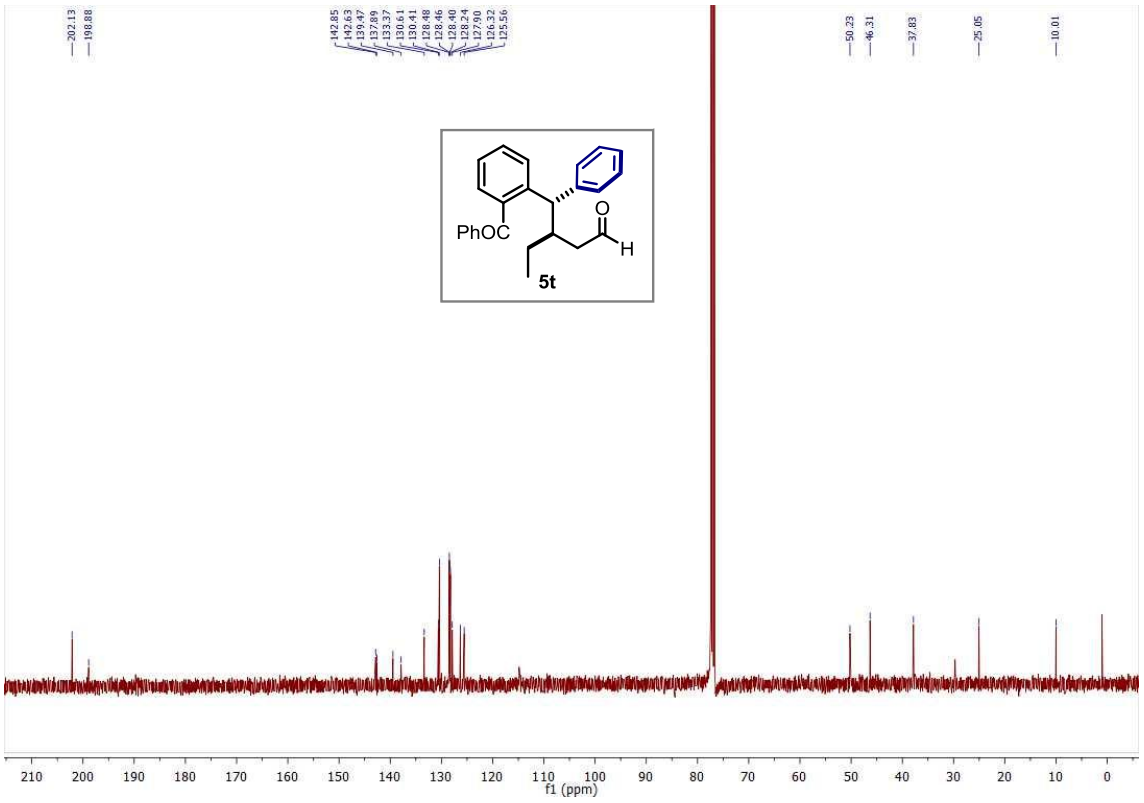
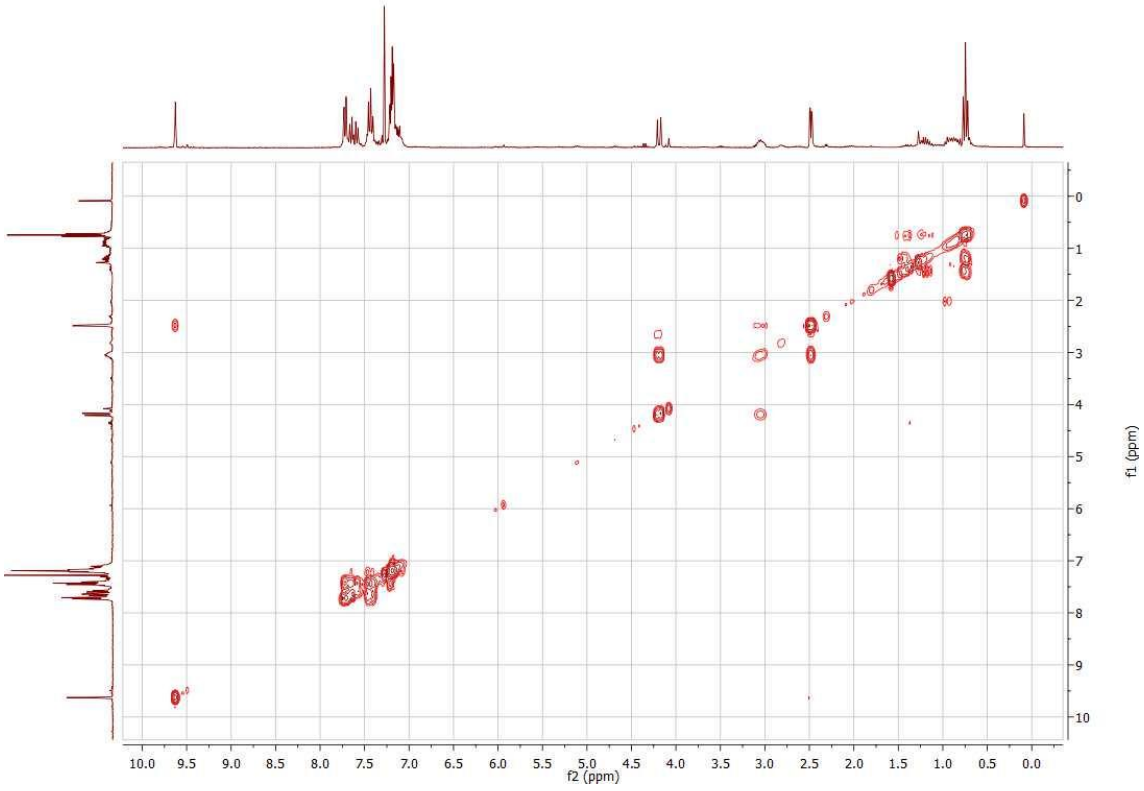
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

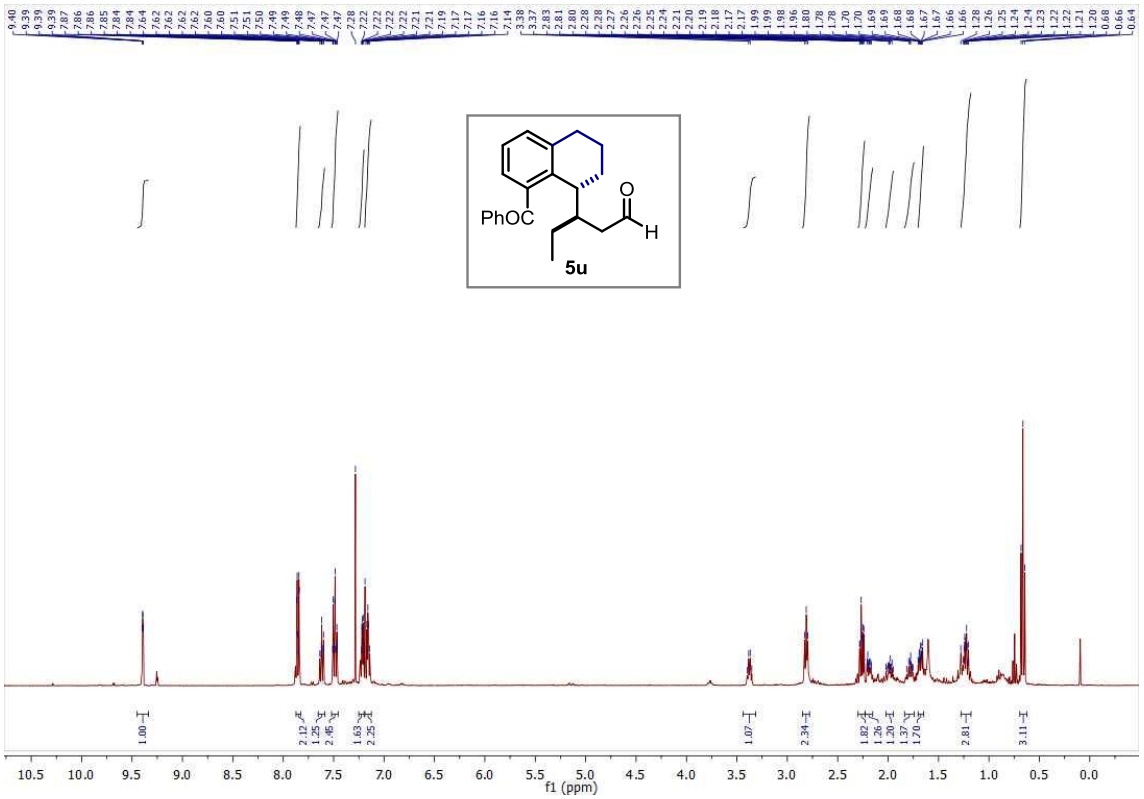

20.43
196.66
167.06
164.52
142.74
138.79
138.36
134.09
134.06
132.92
132.83
131.26
130.29
130.27
128.55
127.54
126.75
125.66
115.61
115.39
77.32
77.01
76.69
49.33
42.10
40.04
26.92
O
F
O
Ph
H
5s
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

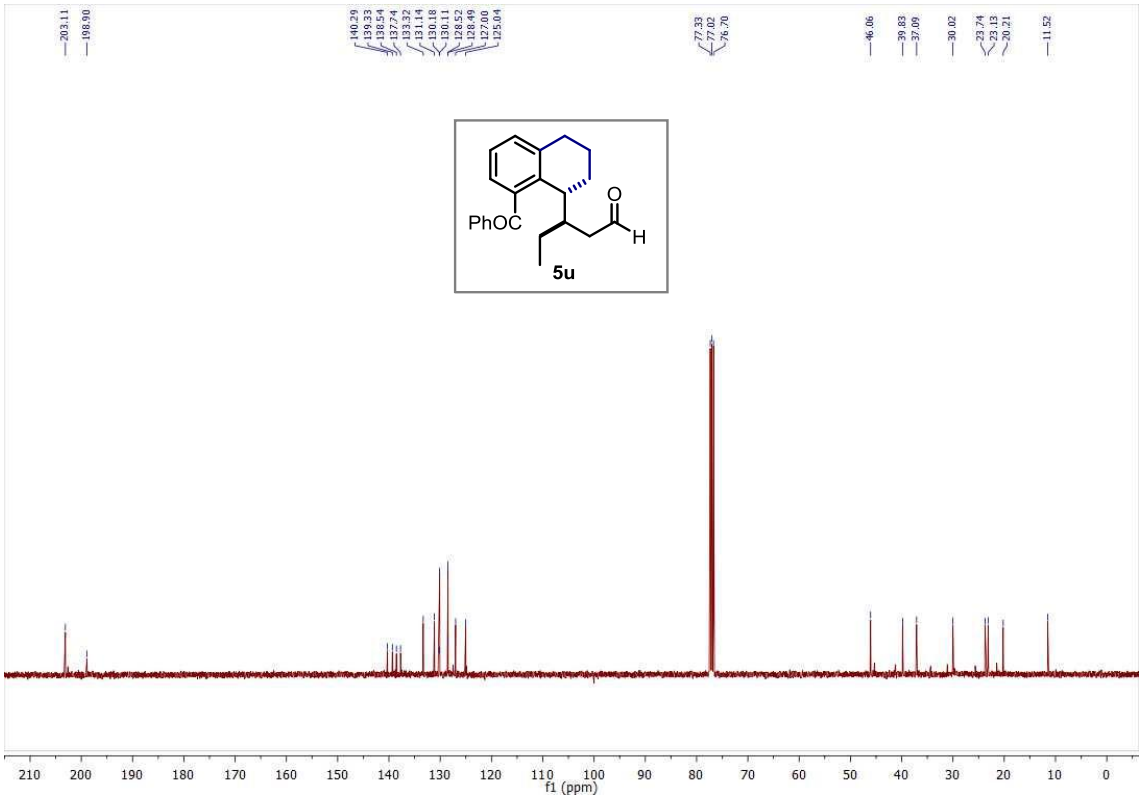

PhOC
O
H
5t
f1 (ppm)


PhOC
O
H
5t
f1 (ppm)

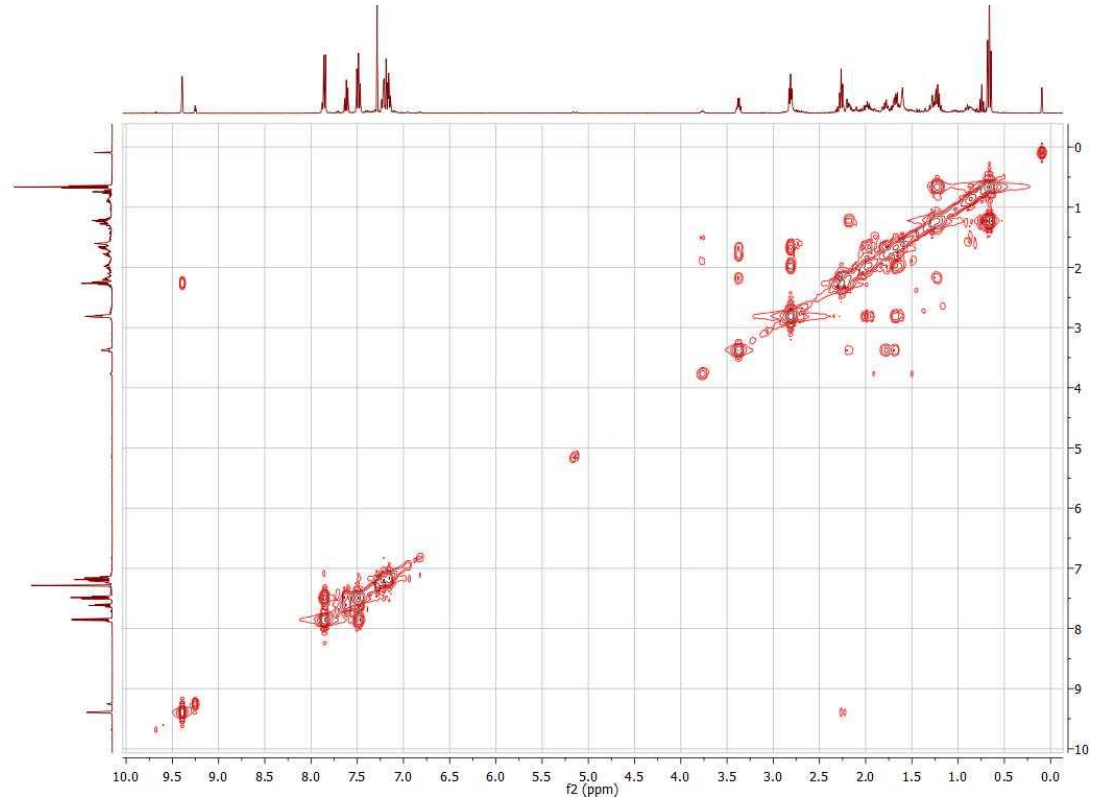
^{1}H-^{1}H COSY analysis of compound **5t**

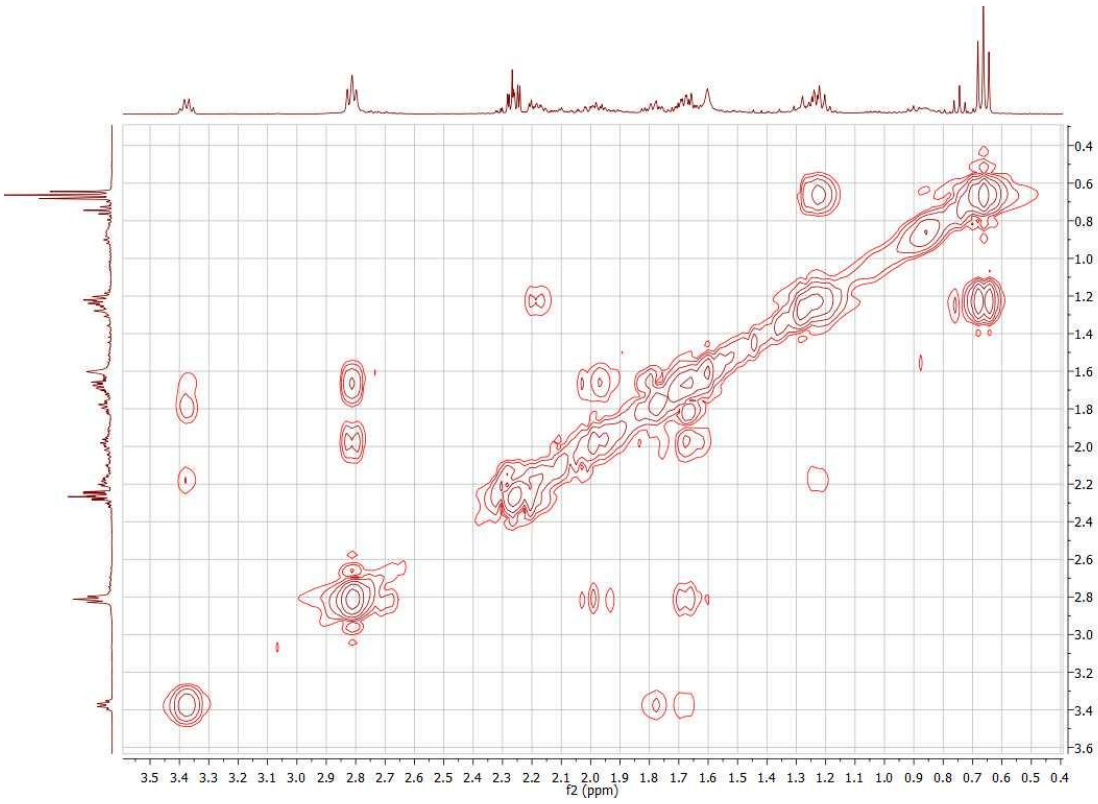


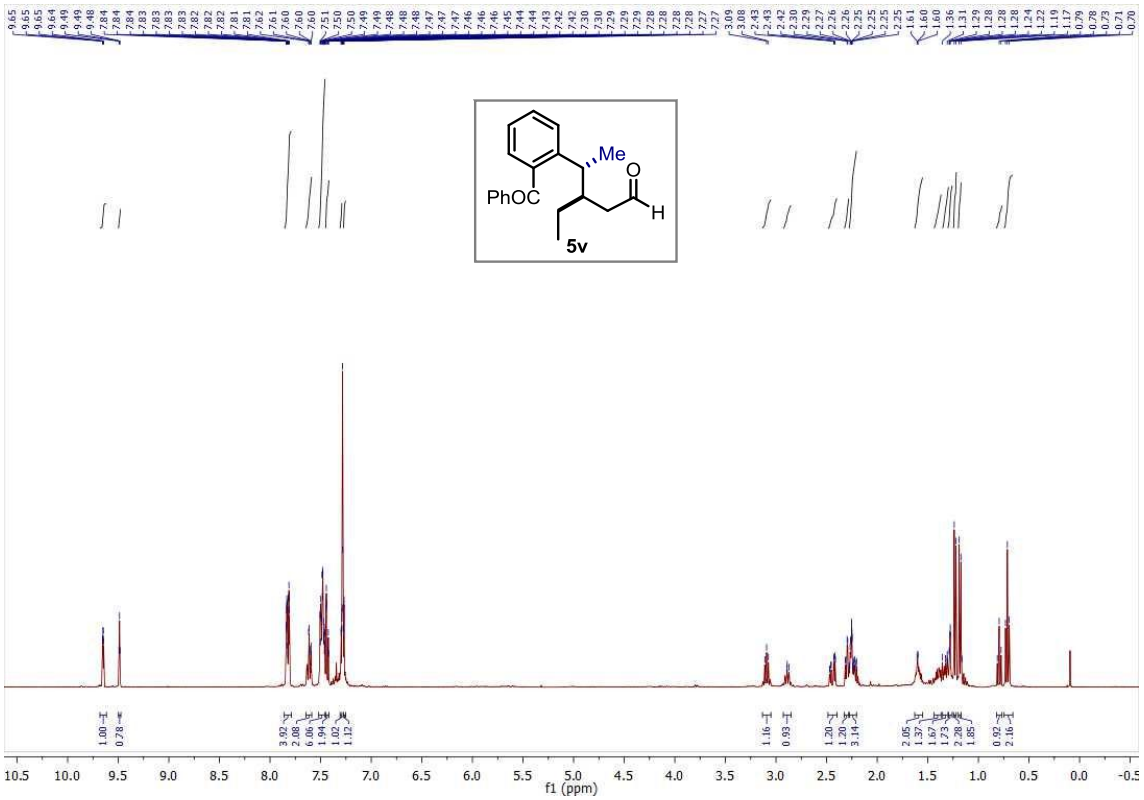

PhOC
O
H
5u
1.00
2.12
1.25
2.46
1.63
2.25
1.07
2.34
1.82
1.26
1.20
1.37
1.70
2.81
3.11
f1 (ppm)

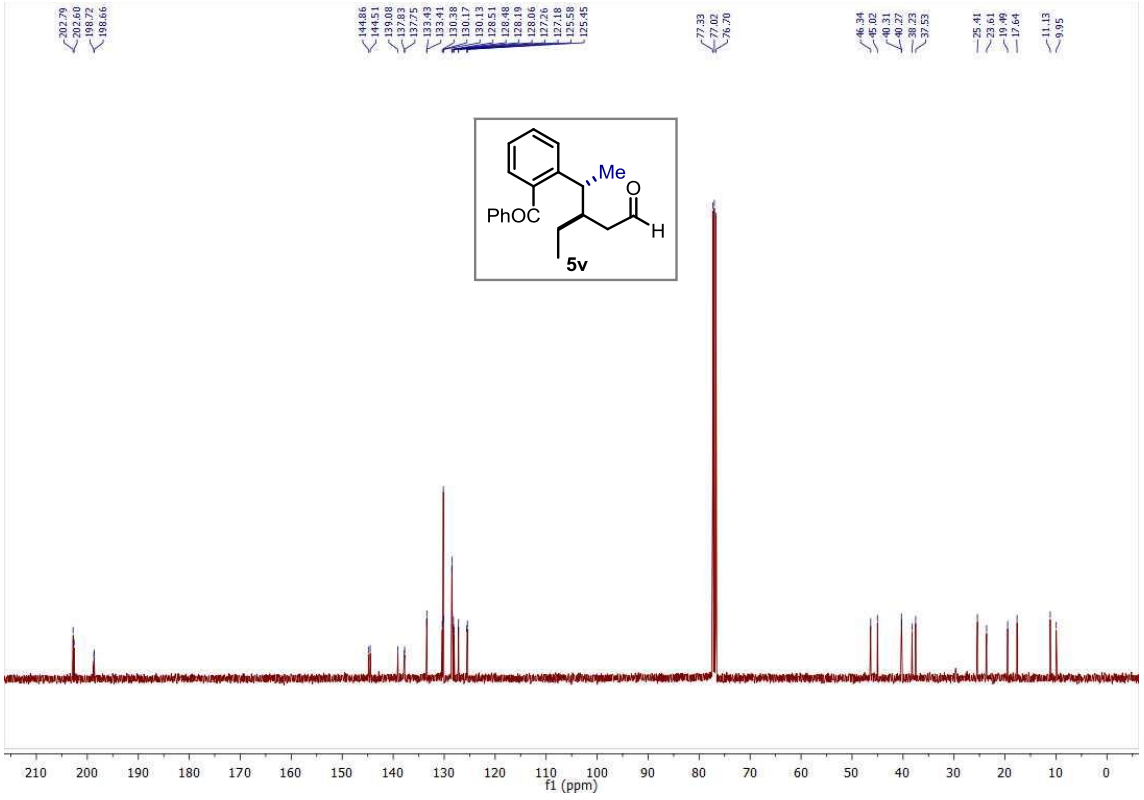

203.11
198.90
140.29
139.33
139.54
137.74
133.32
131.14
130.18
130.11
128.52
128.49
127.00
125.04
77.33
77.02
76.70
46.06
39.83
37.09
30.02
23.74
23.13
20.21
11.52
PhOC
O
H
5u
f1 (ppm)

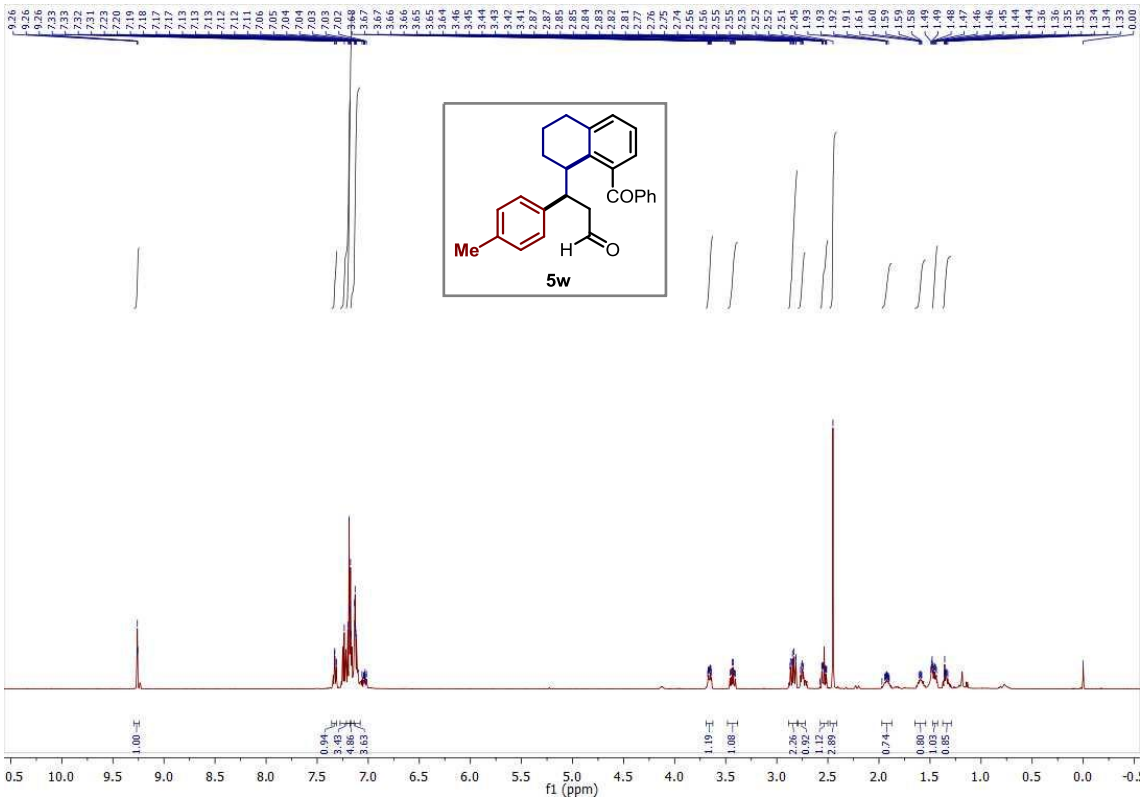
^{1}H-^{1}H COSY analysis for compound **5u**

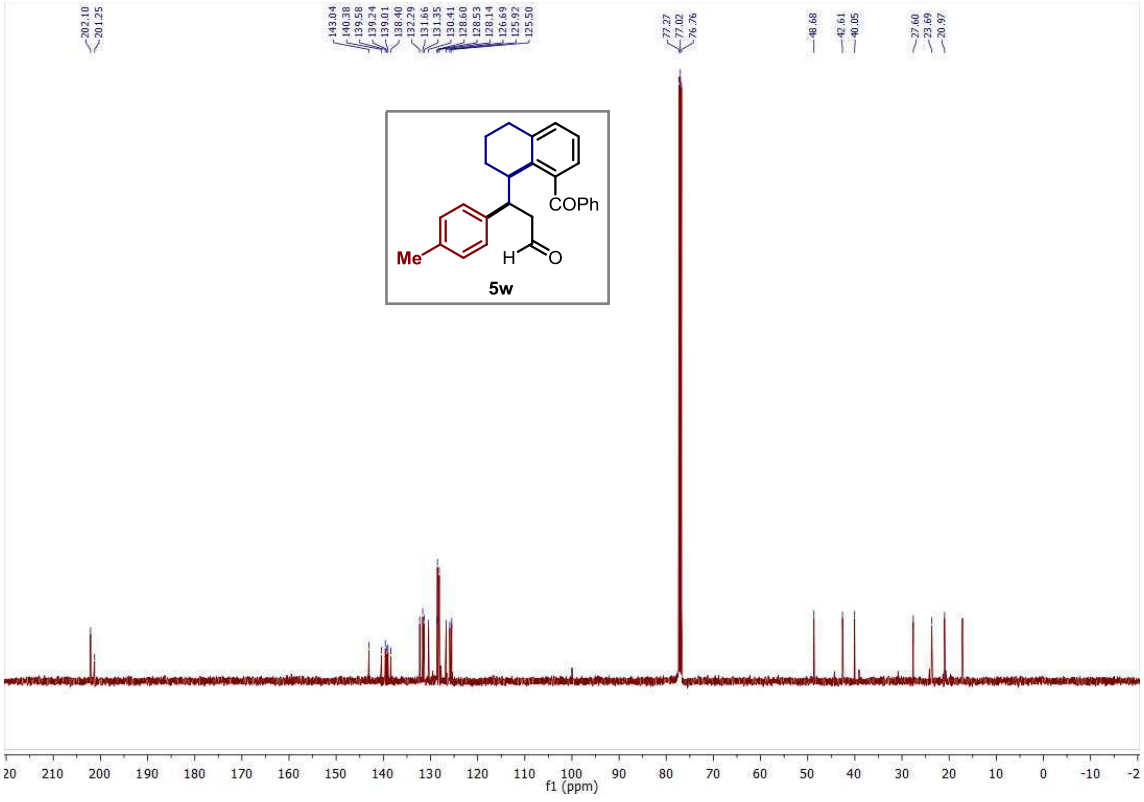




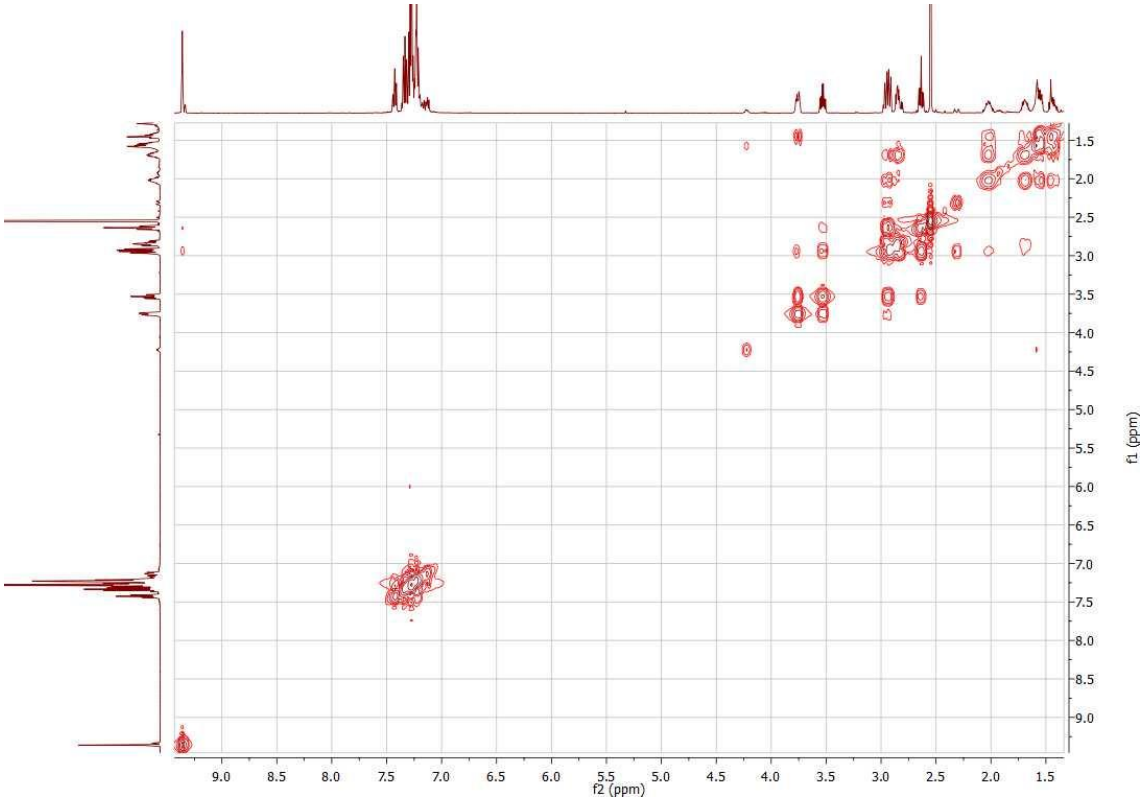

Me
O
PhOC
H
5v
f1 (ppm)

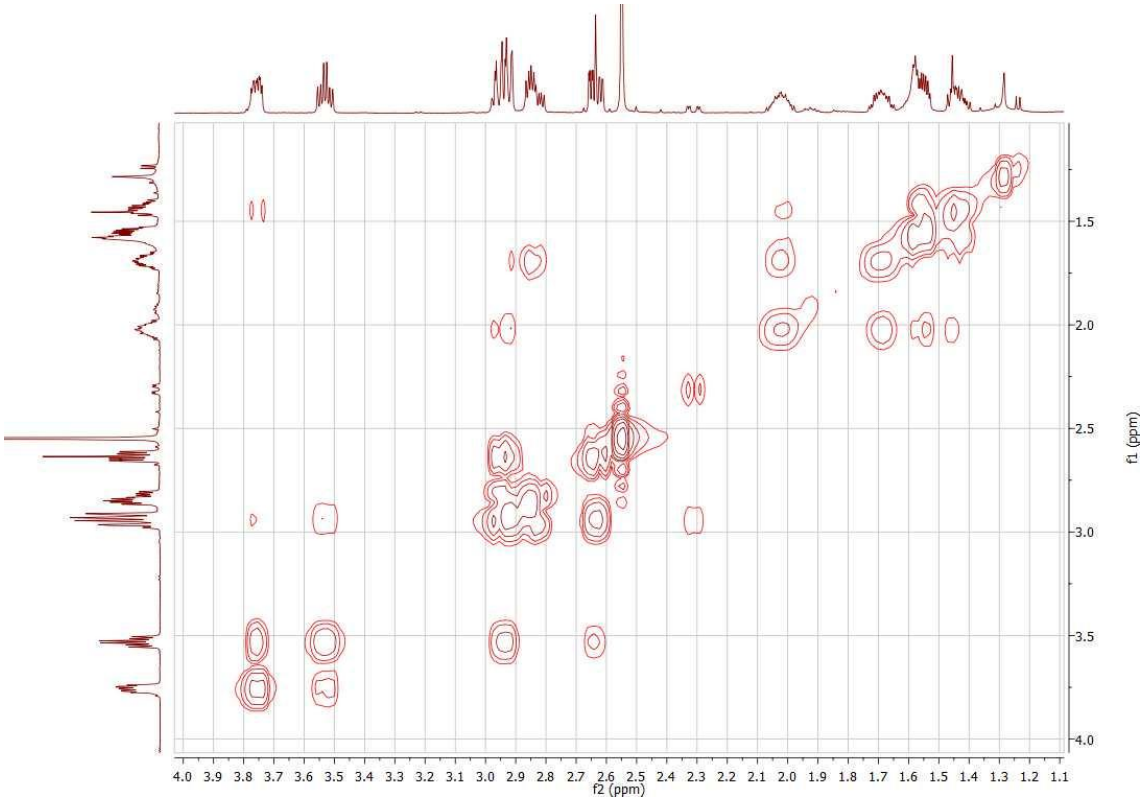

Me
O
PhOC
H
5v
f1 (ppm)

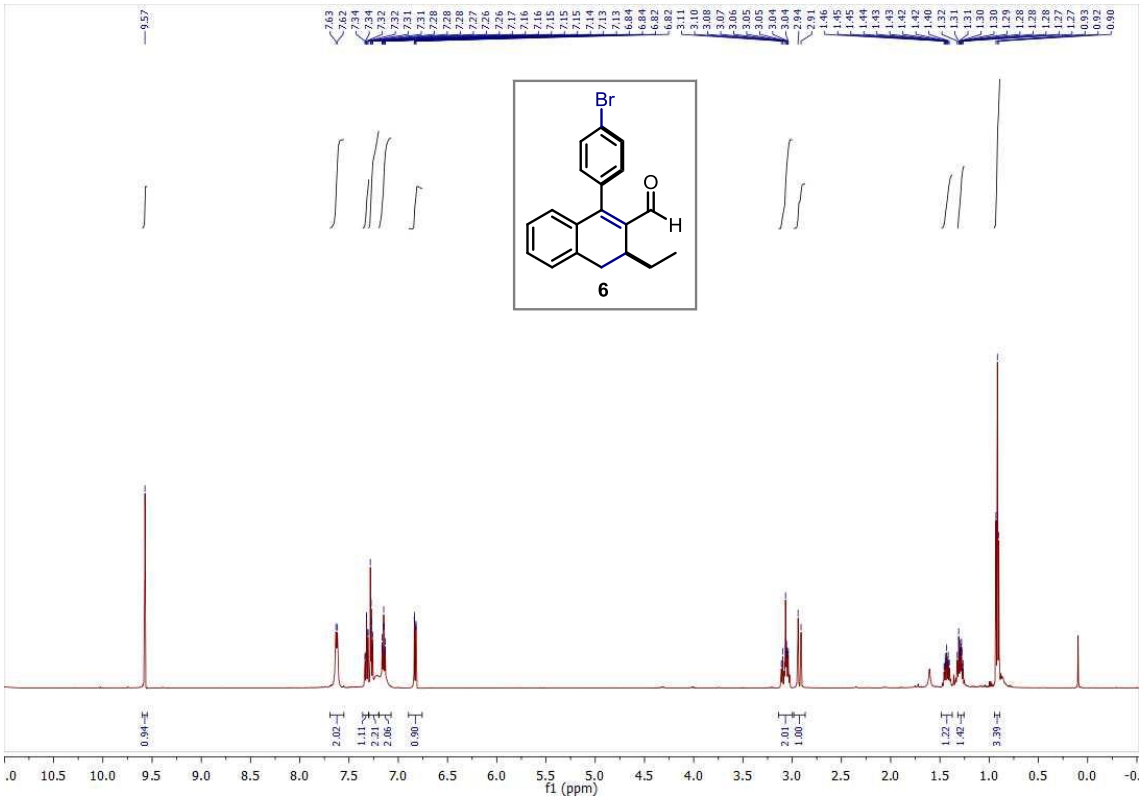

COPh
Me
H
O
5w
f1 (ppm)

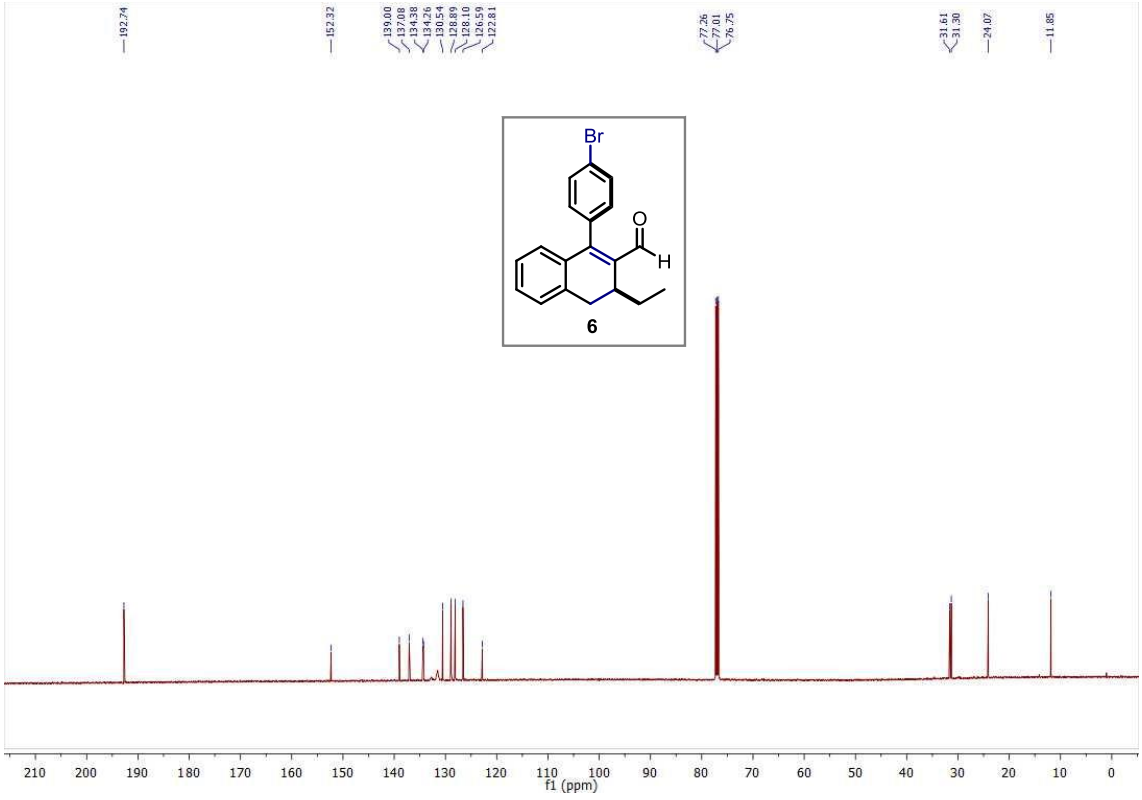

COPh
Me
H
O
5w
f1 (ppm)

^{1}H-^{1}H COSY analysis for compound **5W**





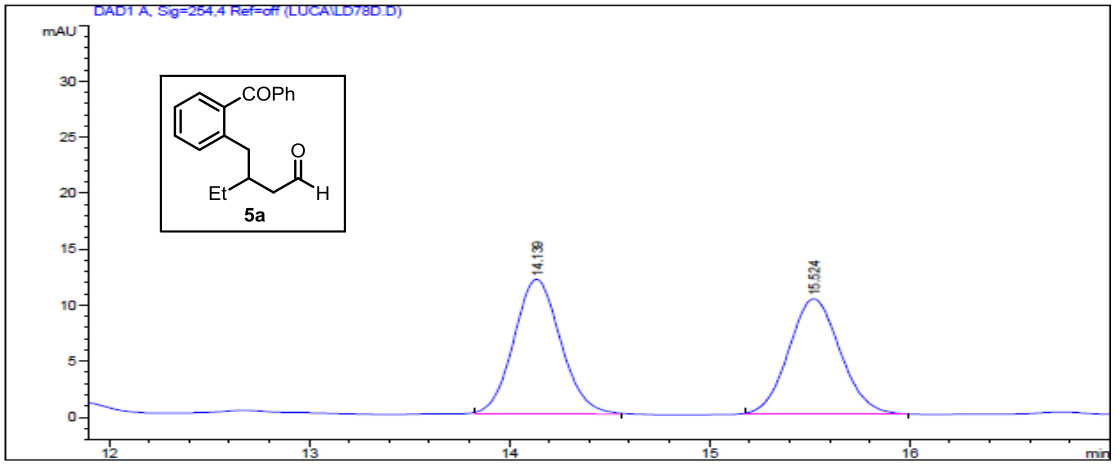

Br
O
H
6
f1 (ppm)


Br
O
H
6
f1 (ppm)

H. HPLC Traces

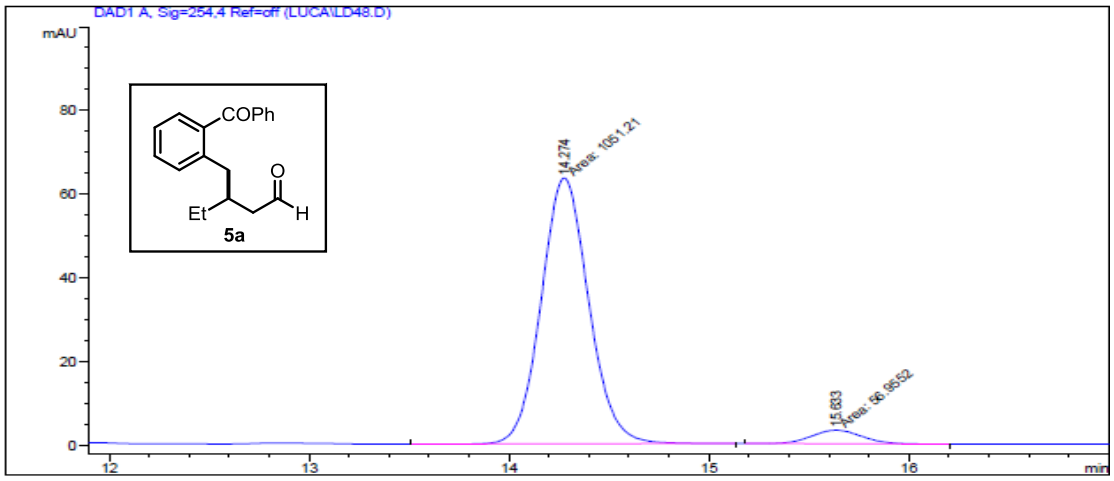
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 85:15), flow rate 1.0 mL/min; λ = 254 nm

Racemic sample 5a:



Peak #	RetTime [min]	Type	Width [min]	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

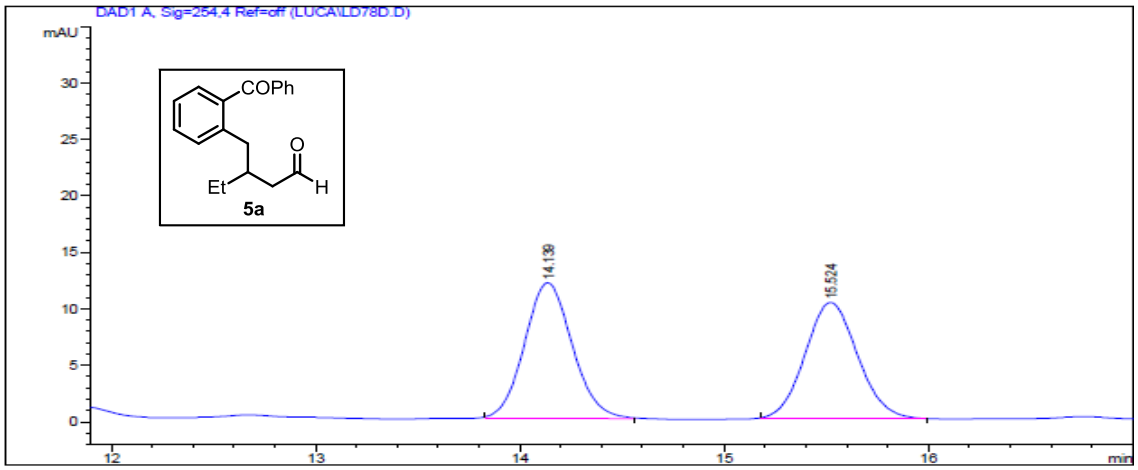
Enantioenriched sample 5a (0.2 mmol reaction scale):



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	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

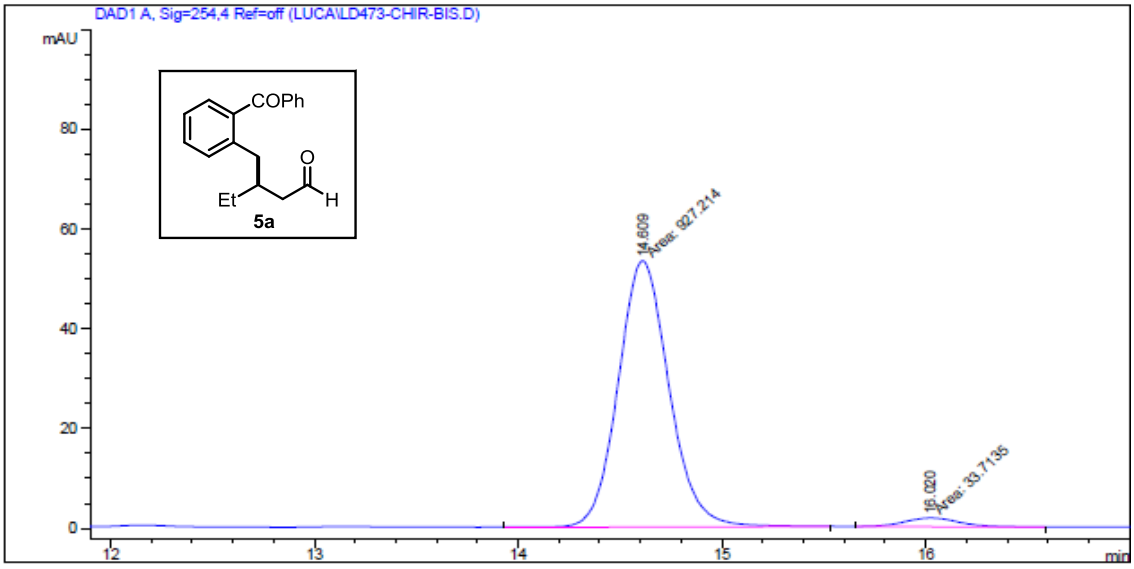
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 85:15), flow rate 1.0 mL/min; λ = 254 nm

Racemic sample 5a (1mmol reaction scale):



Peak #	RetTime [min]	Type	Width [min]	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

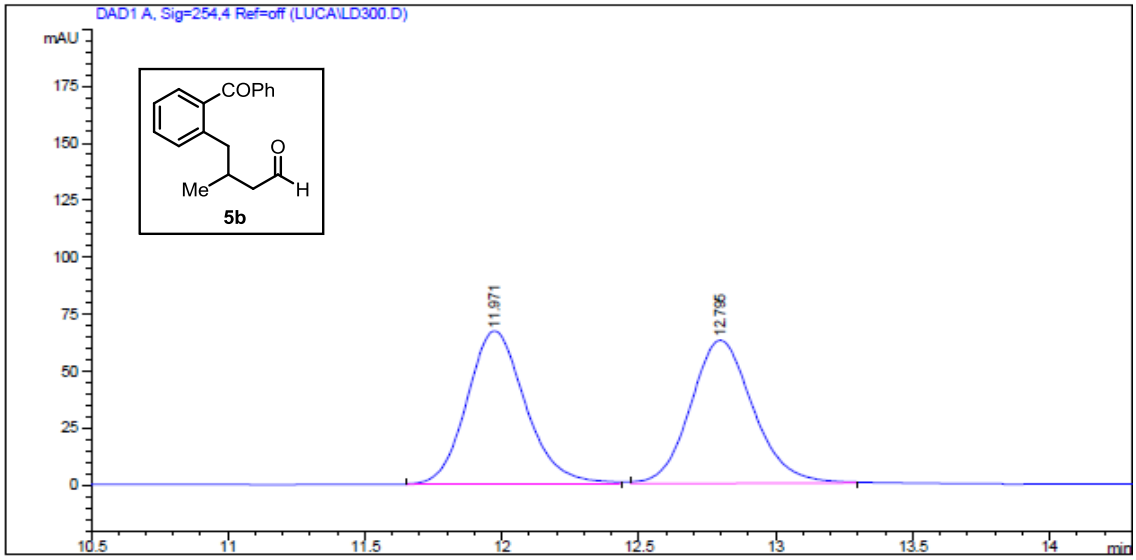
Enantioenriched sample 5a (1 mmol reaction scale):



Peak #	RetTime [min]	Type	Width [min]	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

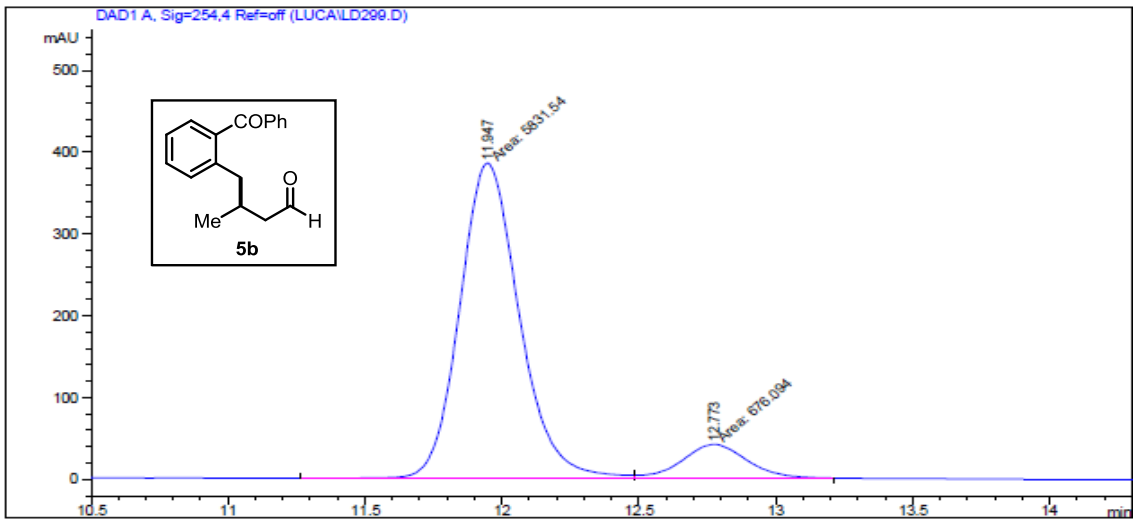
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 85:15), flow rate 1.0 mL/min; λ = 254 nm

Racemic sample 5b:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.971	BB	0.2273	997.54041	67.15819	50.0027
2	12.795	BB	0.2453	997.43158	62.79693	49.9973

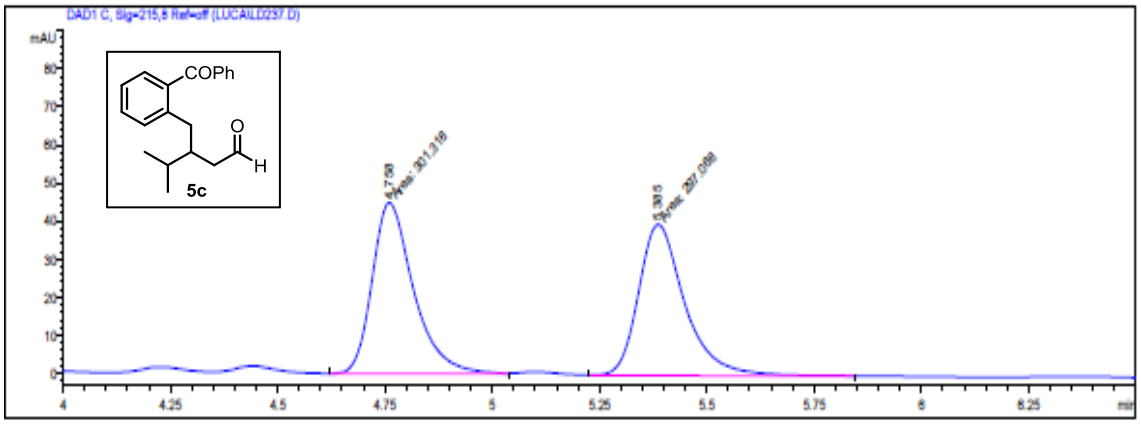
Enantioenriched sample 5b:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.947	MF	0.2520	5831.54297	385.67615	89.6108
2	12.773	FM	0.2735	676.09412	41.20249	10.3892

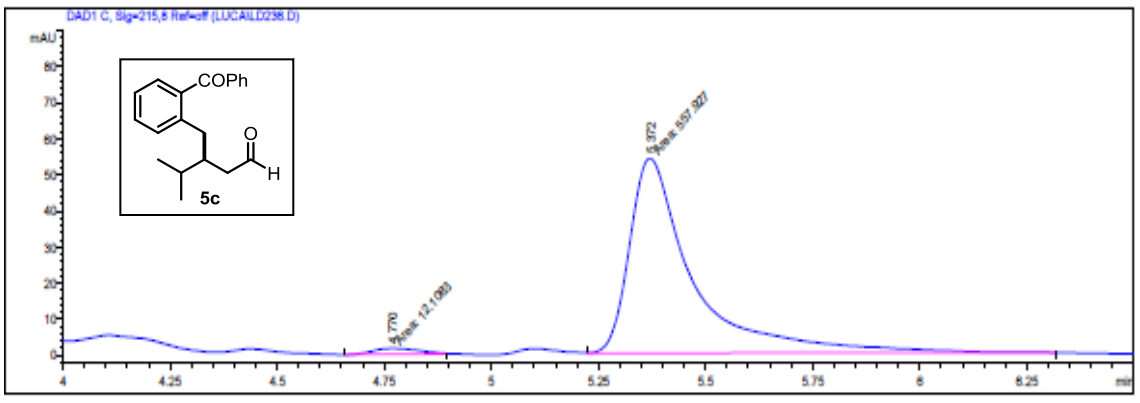
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 90:10), flow rate 1.0 mL/min; λ = 215 nm

Racemic sample 5c:



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

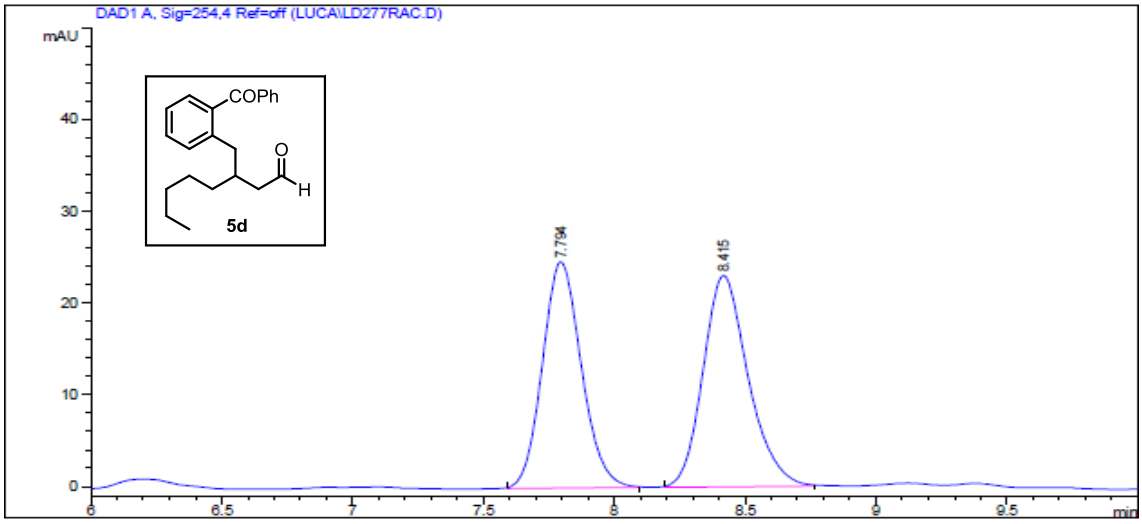
Enantioenriched sample 5c:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.770	MM	0.1223	12.10833	1.64966	2.1241
2	5.372	MM	0.1718	557.92670	54.11789	97.8759

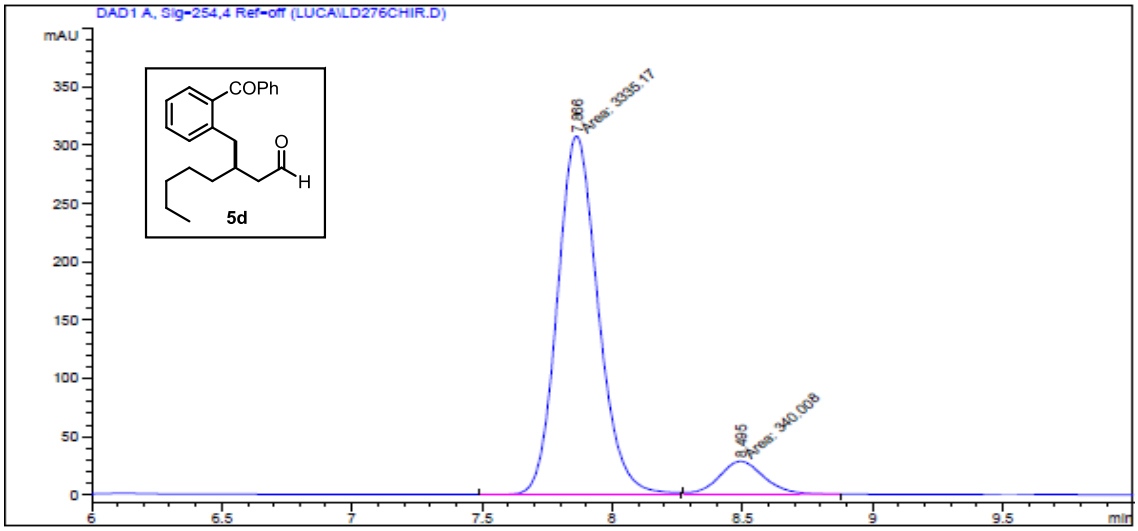
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 90:10), flow rate 1.0 mL/min; λ = 254 nm

Racemic sample 5e:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.794	BB	0.1610	255.80396	24.67247	48.0334
2	8.415	BB	0.1821	276.75043	23.05053	51.9666

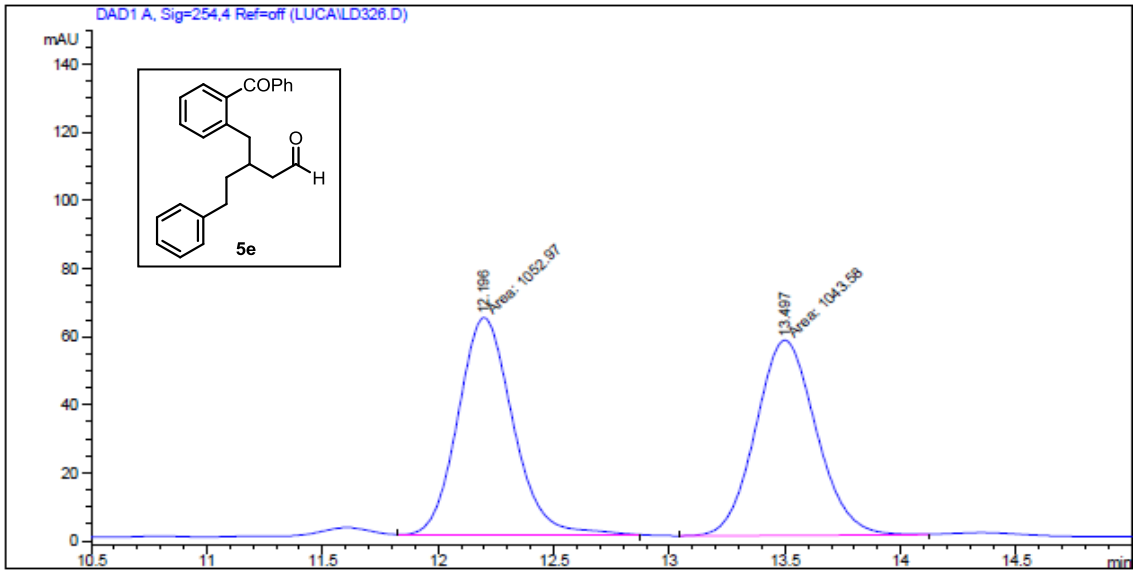
Enantioenriched sample 5e:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.866	MF	0.1807	3335.17310	307.64209	90.7485
2	8.495	FM	0.2002	340.00772	28.30513	9.2515

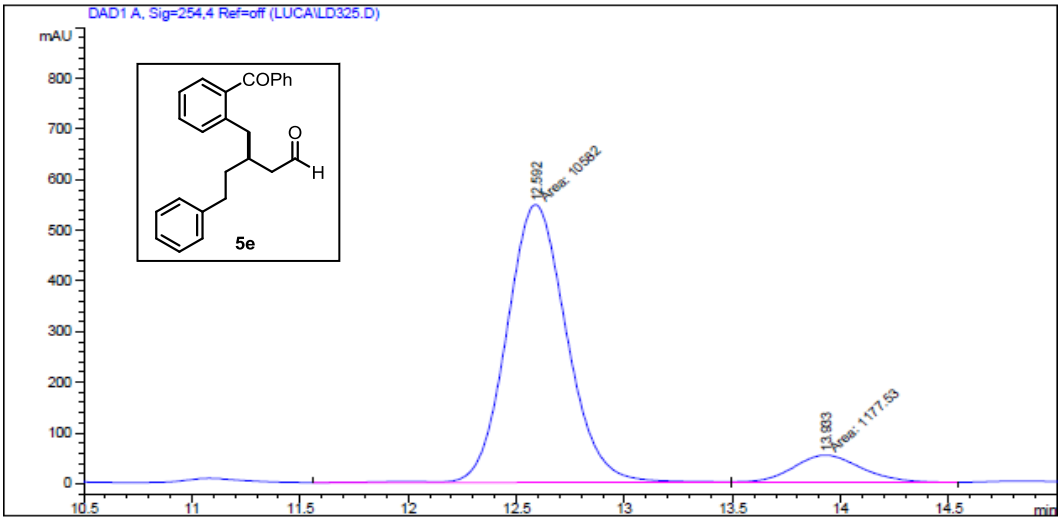
Condition: HPLC analysis on a Daicel Chiralpak IC column using an isocratic method (Hexane : i-PrOH, 85:15), flow rate 0.9 mL/min; λ = 254 nm

Racemic sample 5e:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	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

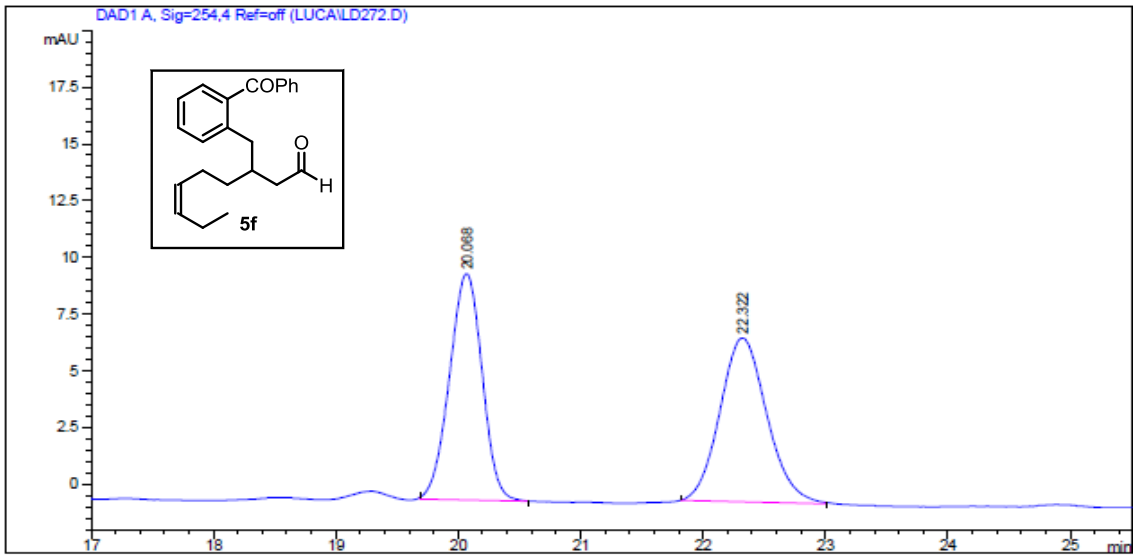
Enantioenriched sample 5e:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	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

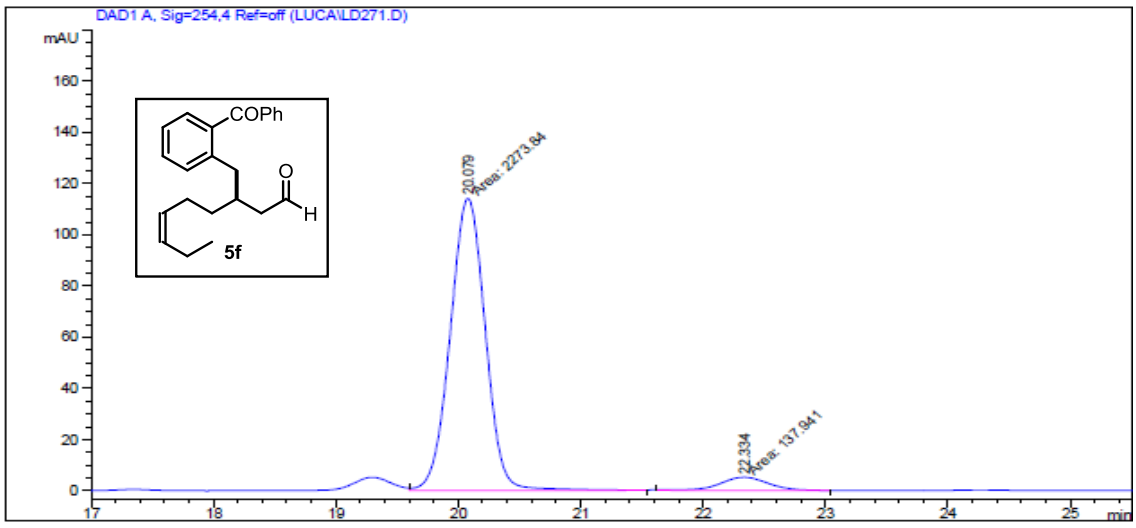
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 91:9), flow rate 0.5 mL/min; λ = 254 nm

Racemic sample 5f:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.068	BB	0.2926	185.21207	9.97773	49.0140
2	22.322	BB	0.4069	192.66386	7.23025	50.9860

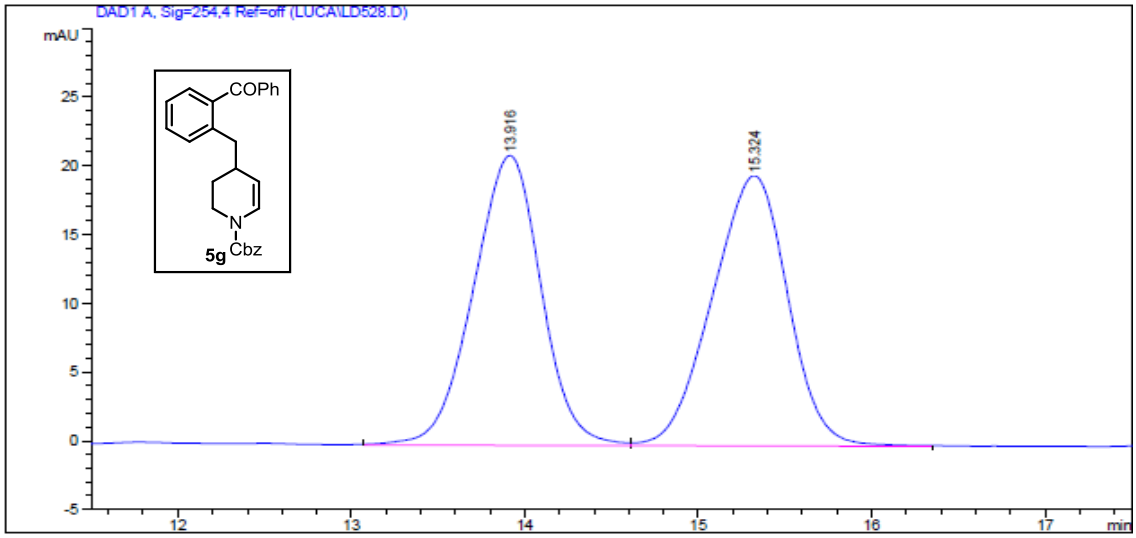
Enantioenriched sample 5f:



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

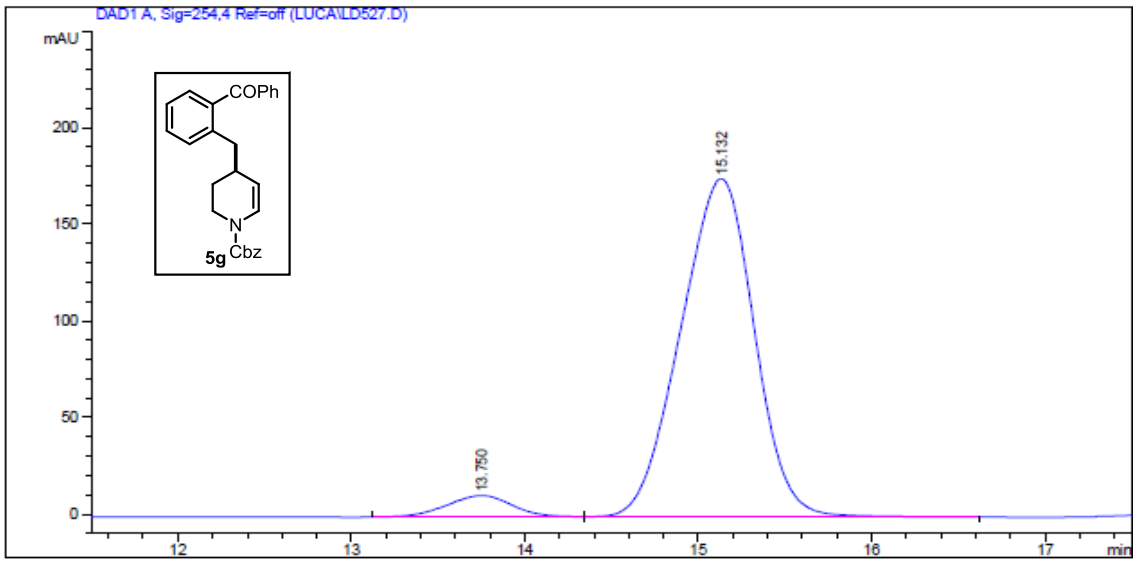
Condition: HPLC analysis on a Daicel Chiralpak ID-3 column using an isocratic method (Hexane : i-PrOH, 87:13), flow rate 0.9 mL/min; λ = 254 nm

Racemic sample 5g:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.916	BV	0.4223	575.03198	21.07978	49.1767
2	15.324	VB	0.4769	594.28571	19.64478	50.8233

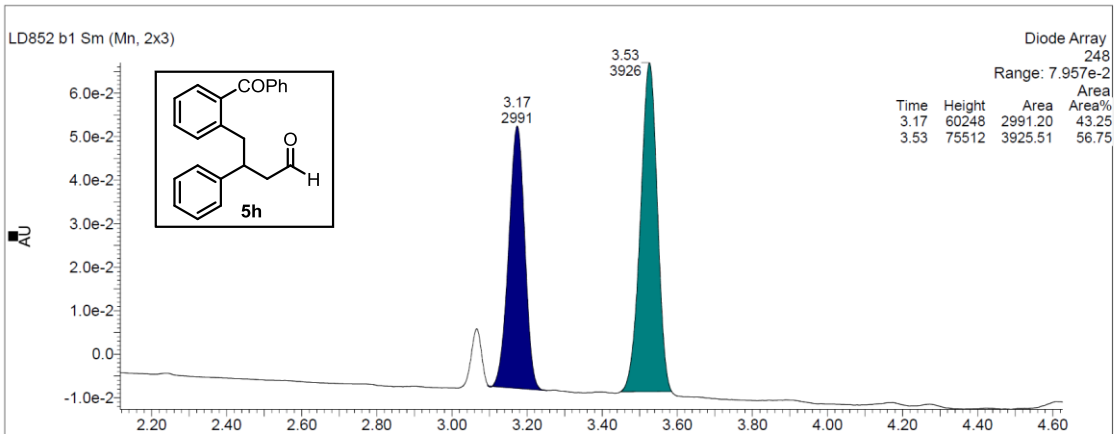
Enantioenriched sample 5g:



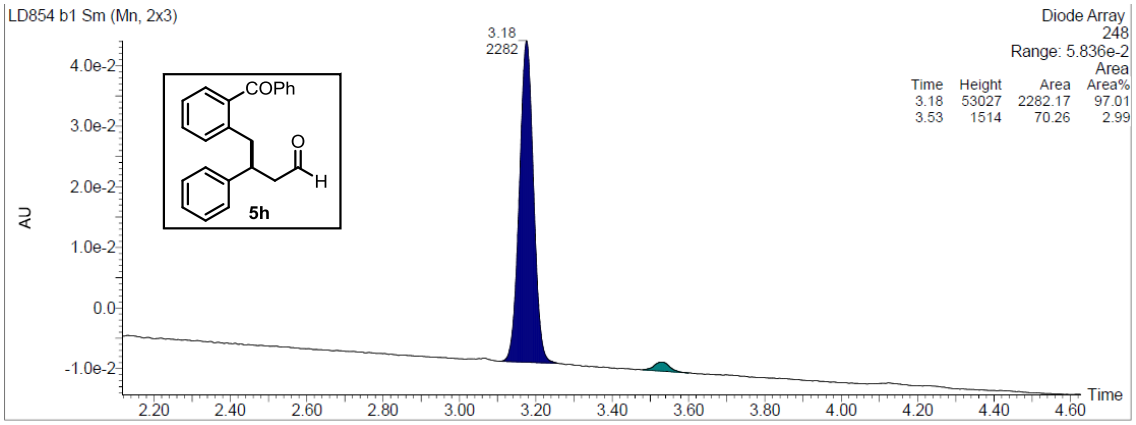
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.750	BV	0.4156	299.13678	11.20061	5.4673
2	15.132	VB	0.4645	5172.23975	175.13730	94.5327

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; λ = 248 nm

Racemic sample 5h:

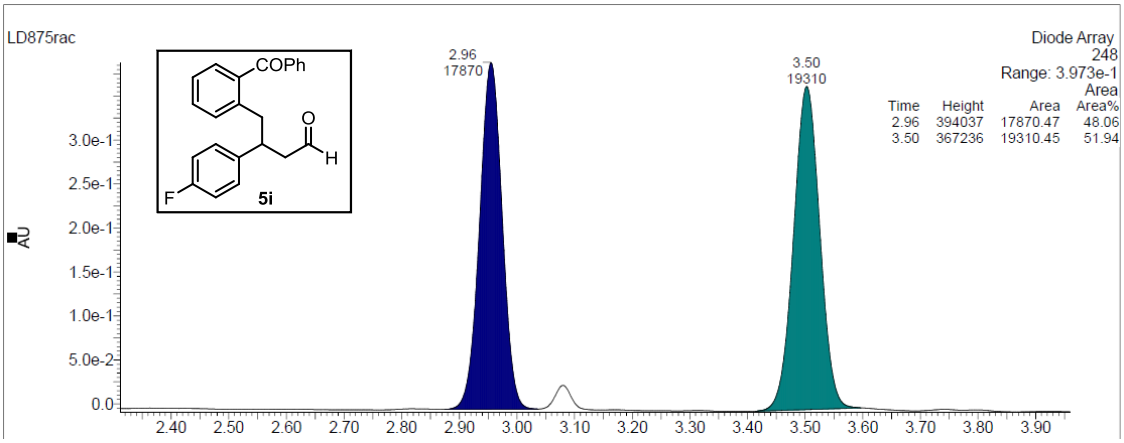


Enantioenriched sample 5h:

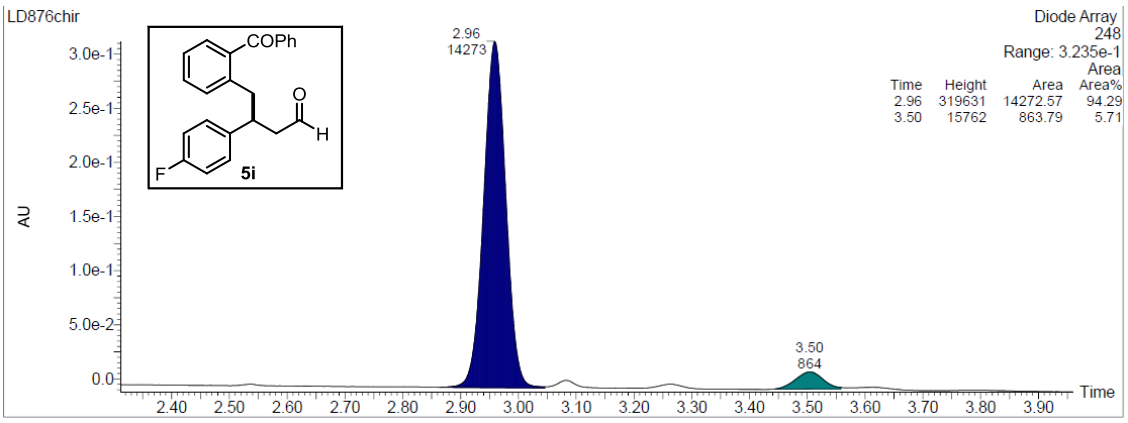


Condition: UPC^2 analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO^2 to 60:40 CO^2:ACN), flow rate 2.00 mL/min over 5 min; λ = 248 nm

Racemic sample 5i:

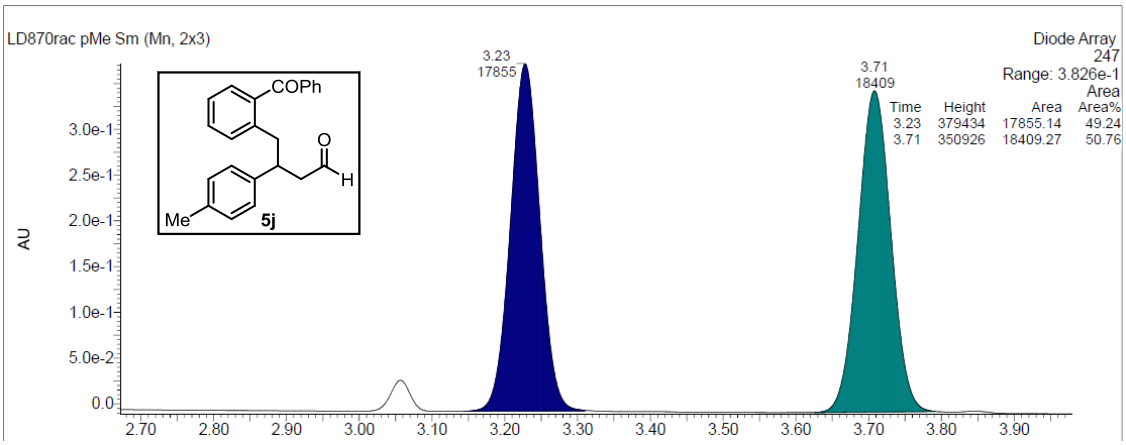


Enantioenriched sample 5i:

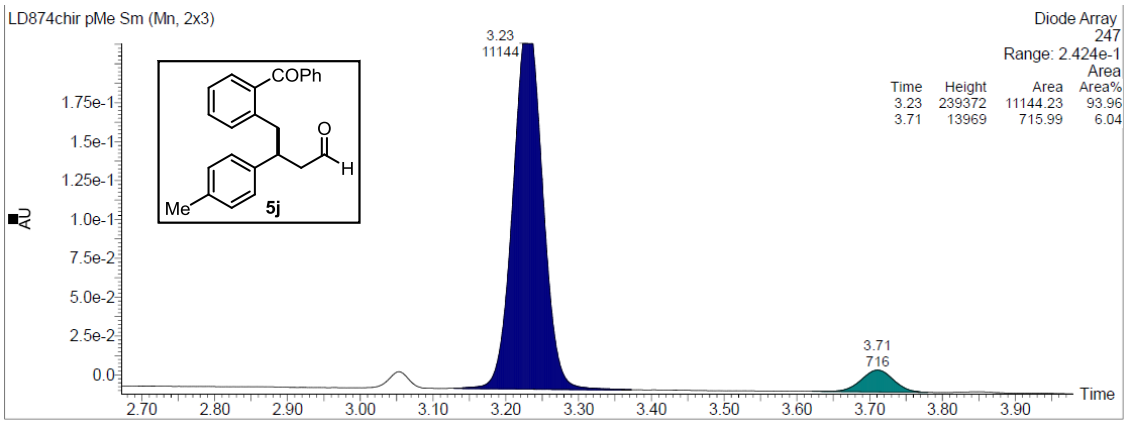


Condition: UPC^2 analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO^2 to 60:40 CO^2:ACN), flow rate 2.00 mL/min over 5 min; λ = 247 nm

Racemic sample 5j:

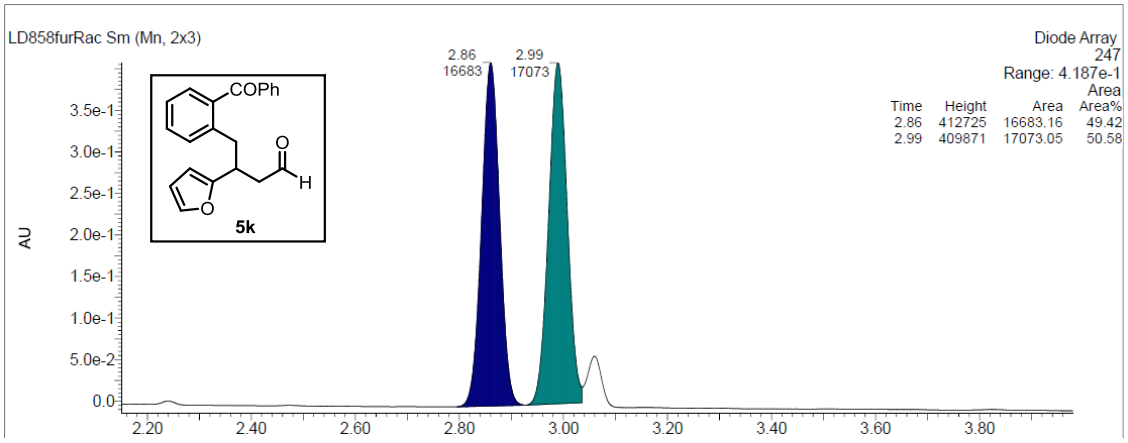


Enantioenriched sample 5j:

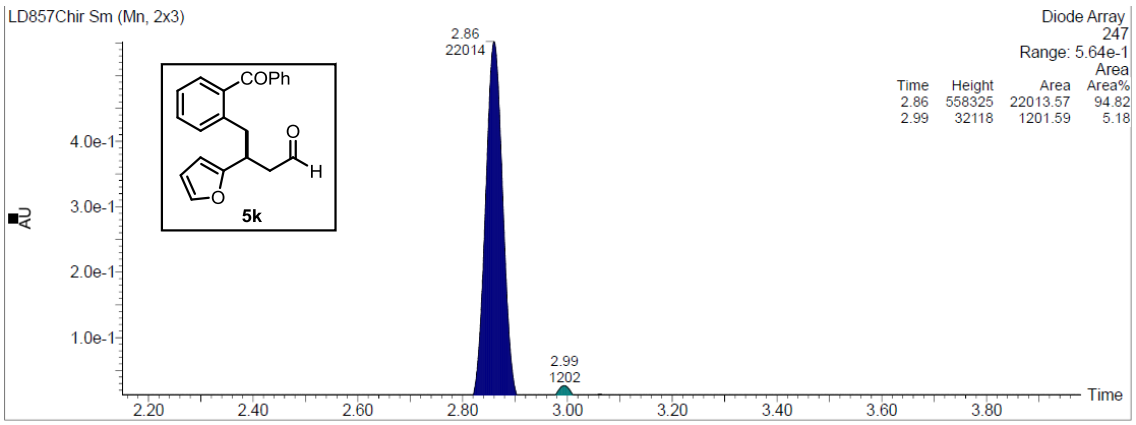


Condition: UPC^2 analysis on a Daicel Chiralpak IC column using a gradient method (from 100% CO^2 to 60:40 CO^2:ACN), flow rate 2.00 mL/min over 5 min; λ = 247 nm

Racemic sample 5k:

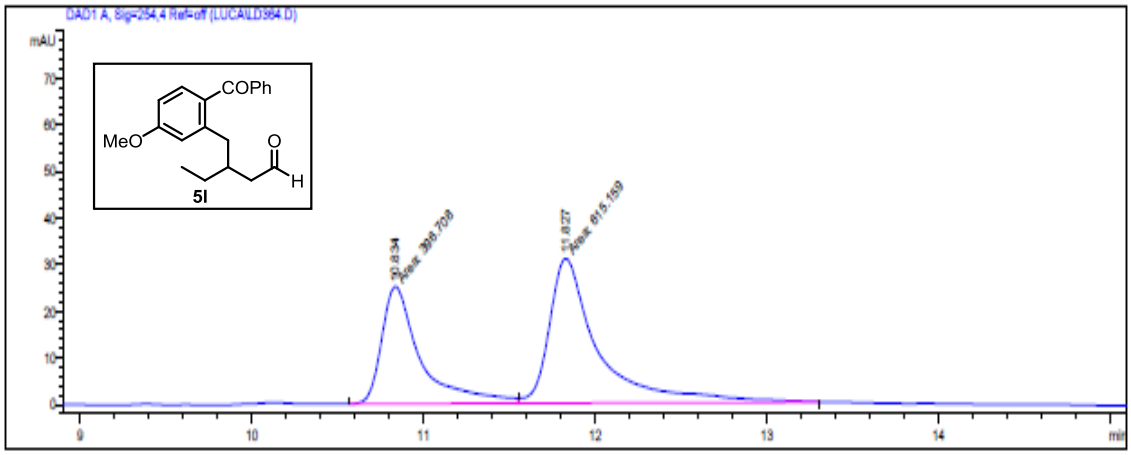


Enantioenriched sample 5k:



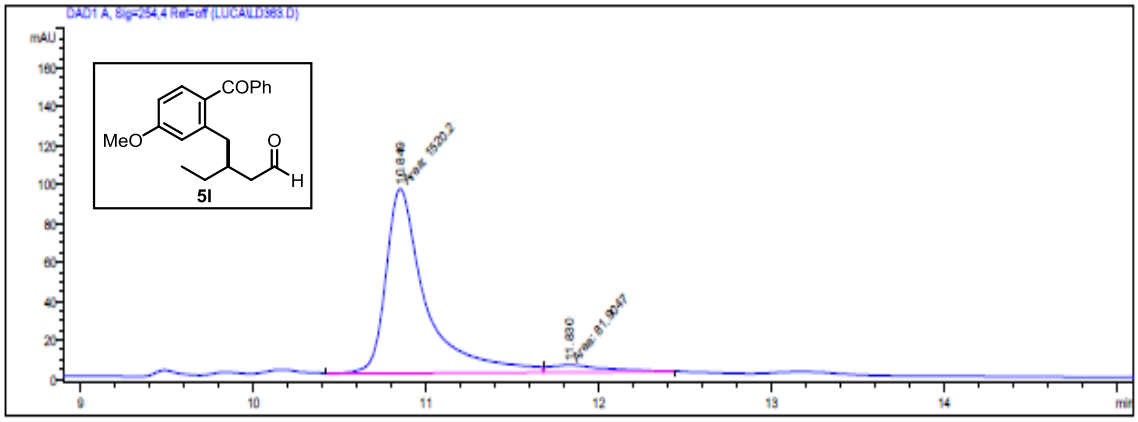
Condition: HPLC analysis on a Daicel Chiralpak IC column (55:42:3 hexane:iPrOH:DCM), flow rate 0.90 mL/min; λ = 254 nm

Racemic sample 5l:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.834	MF	0.2627	396.70798	25.16487	39.2056
2	11.827	FM	0.3300	615.15887	31.06535	60.7944

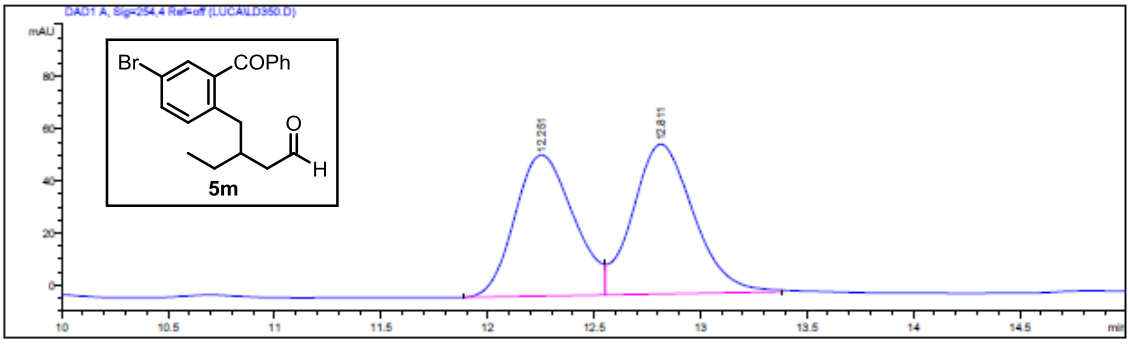
Enantioenriched sample 5l:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.849	MF	0.2668	1520.20410	94.96627	94.8877
2	11.830	FM	0.3703	81.90472	3.68627	5.1123

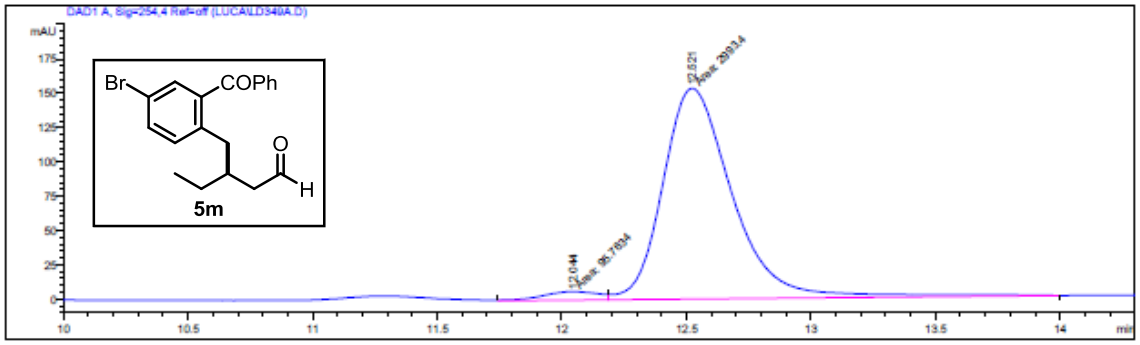
Condition: HPLC analysis on a Daicel Chiralpak IA column (96:2:2 hexane:iPrOH:DCM), flow rate 0.70 mL/min; λ = 254 nm

Racemic sample 5m:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.251	BV	0.2981	1040.54736	54.16446	47.6643
2	12.811	VB	0.3040	1142.52820	57.46648	52.3357

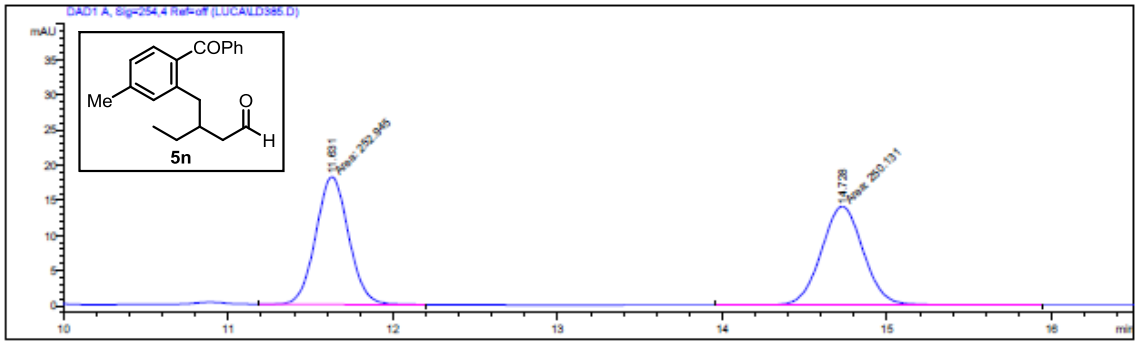
Enantioenriched sample 5m:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.044	MF	0.2597	95.76341	6.14630	3.1000
2	12.521	FM	0.3246	2993.40112	153.70894	96.9000

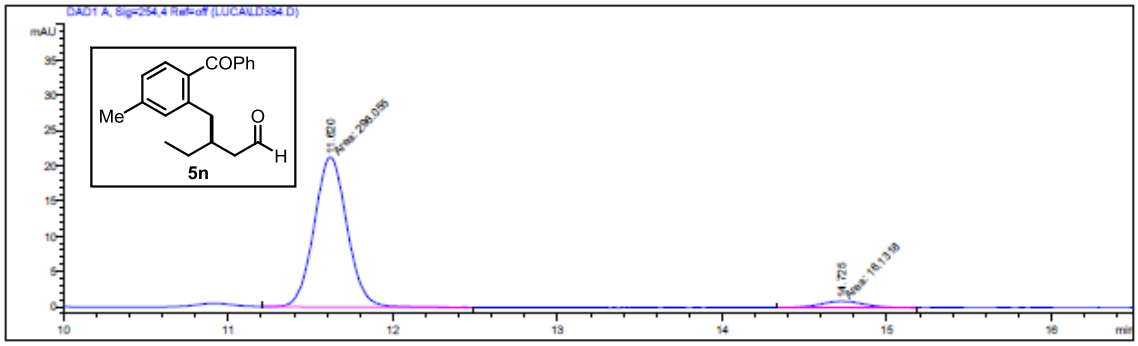
Condition: HPLC analysis on a Daicel Chiralpak IC column (85:15 hexane:iPrOH), flow rate 1.0 mL/min; λ = 254 nm

Racemic sample 5n:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.631	MM	0.2320	252.94456	18.17225	50.2796
2	14.728	MM	0.2967	250.13094	14.04841	49.7204

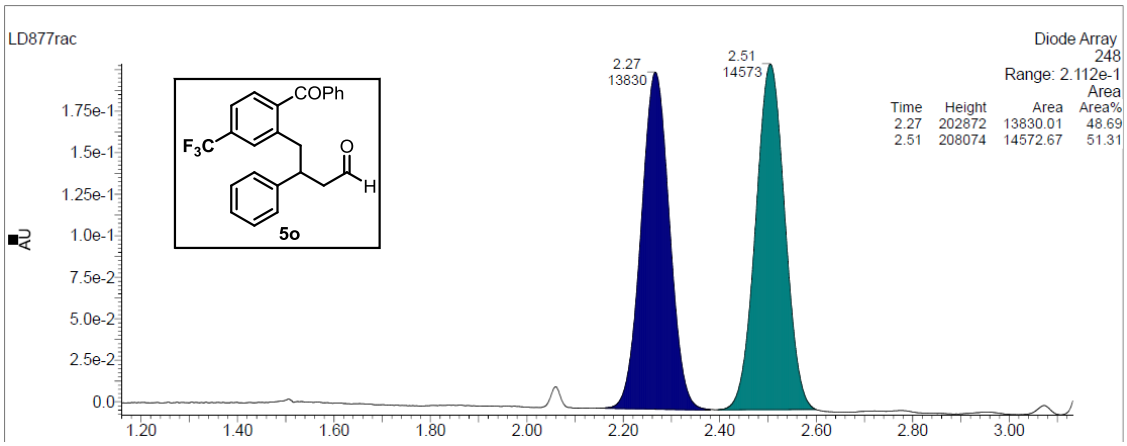
Enantioenriched sample 5n:



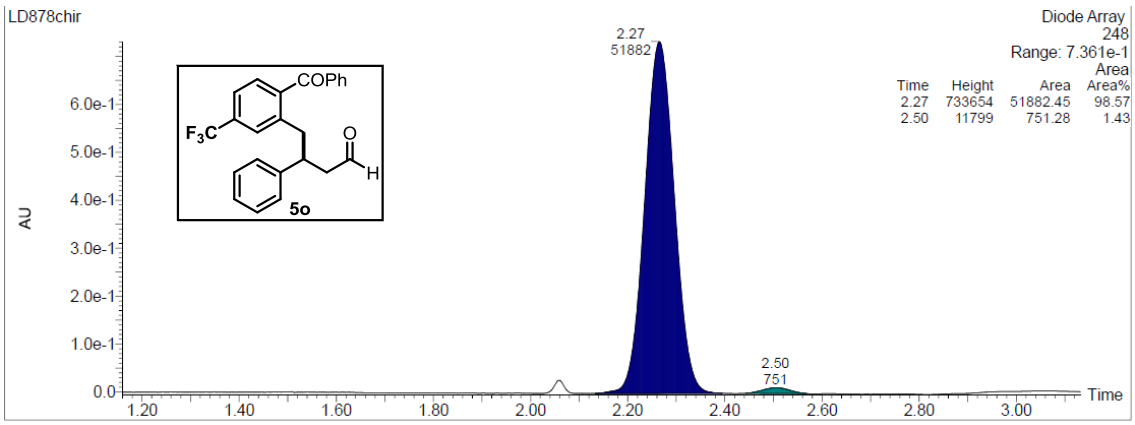
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.620	MM	0.2319	296.05478	21.27299	94.8326
2	14.725	MM	0.2977	16.13179	9.03017e-1	5.1674

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; λ = 248 nm

Racemic sample 5o:

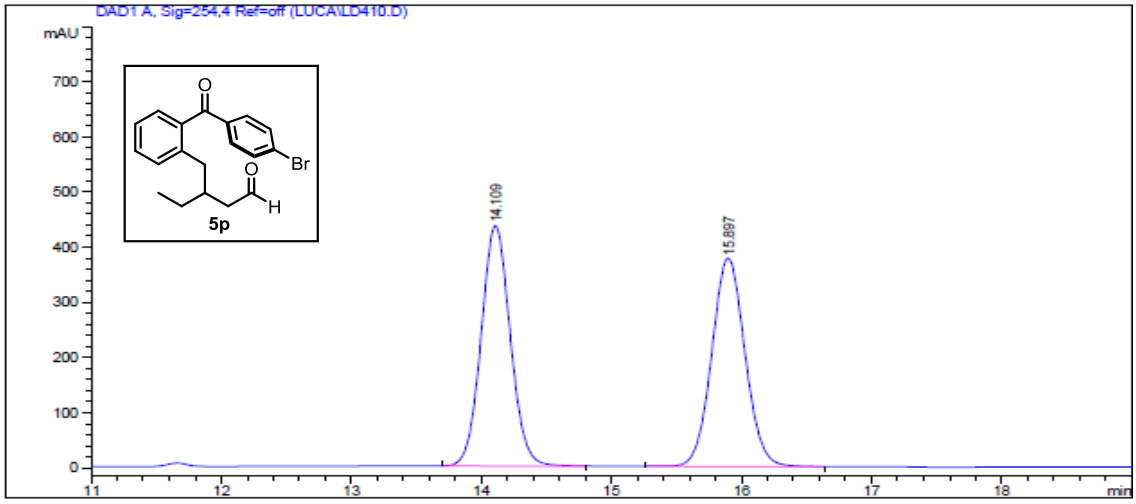


Enantioenriched sample 5o:



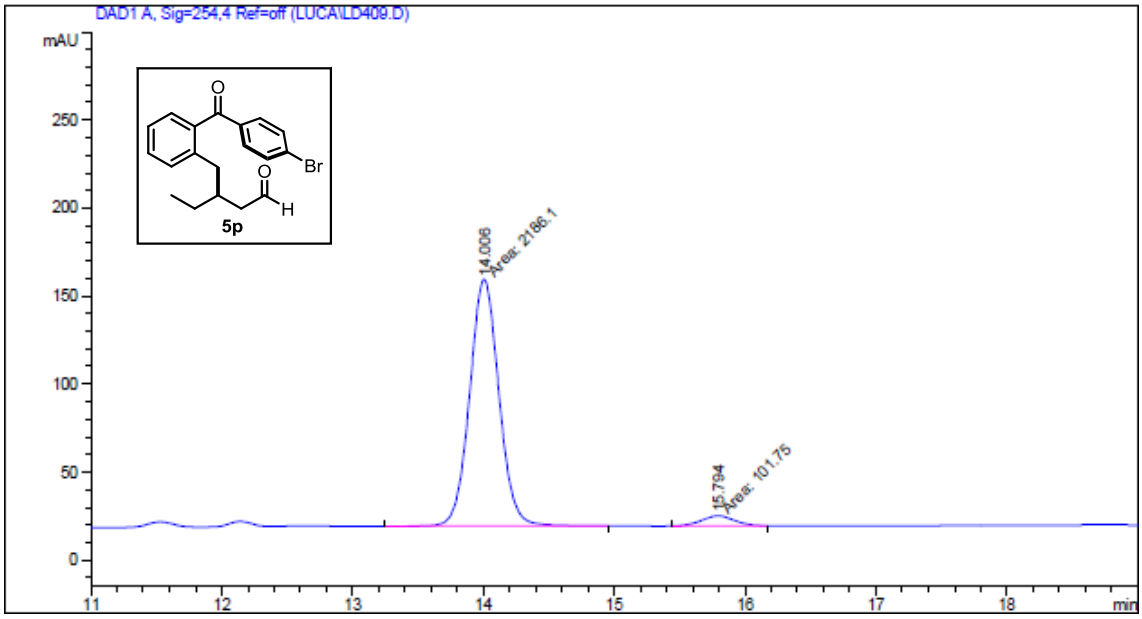
Condition: HPLC analysis on a Daicel Chiralpak IC column (97:03 hexane:iPrOH), flow rate 0.8 mL/min; λ = 254 nm

Racemic sample 5p:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.109	BB	0.2420	6801.81104	435.89511	50.2453
2	15.897	BB	0.2758	6735.38525	378.12573	49.7547

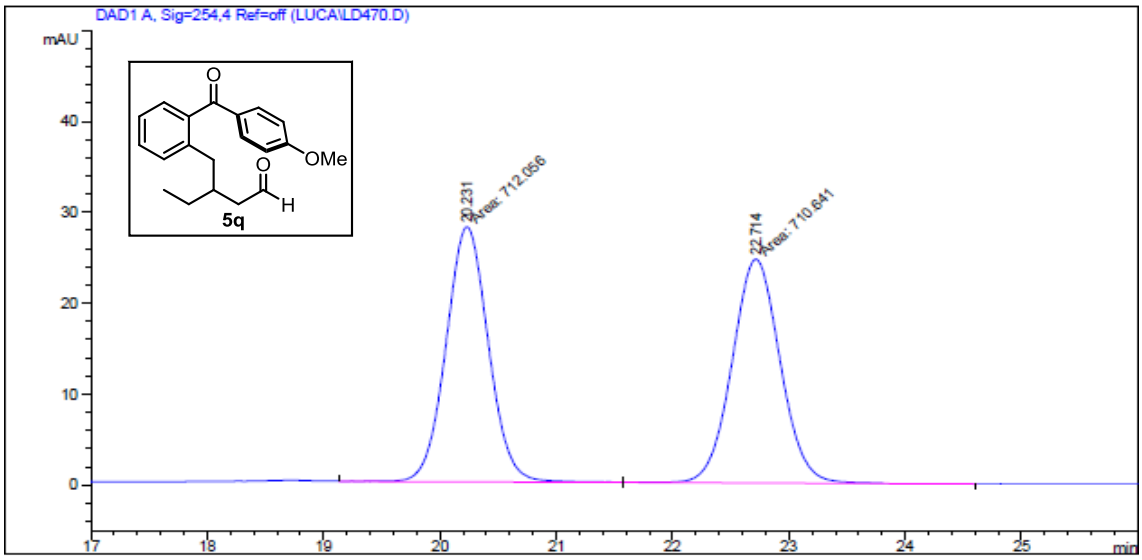
Enantioenriched sample 5p:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.006	MM	0.2600	2186.09985	140.12781	95.5526
2	15.794	MM	0.2978	101.75038	5.69487	4.4474

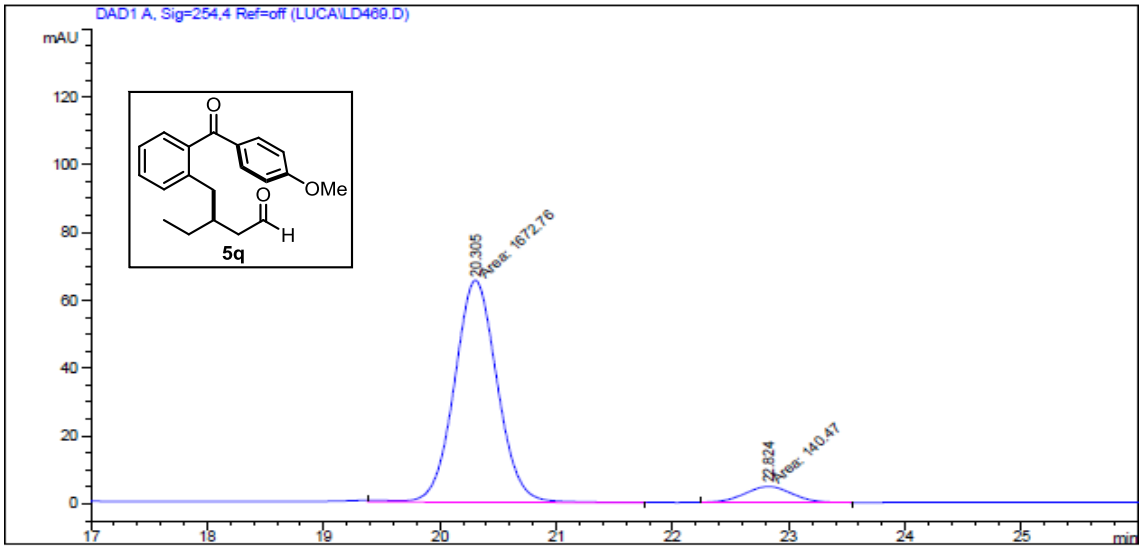
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column 85:15 hexane:*i*PrOH flow rate 1.00 mL/min; λ = 254 nm

Racemic sample 5q:



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

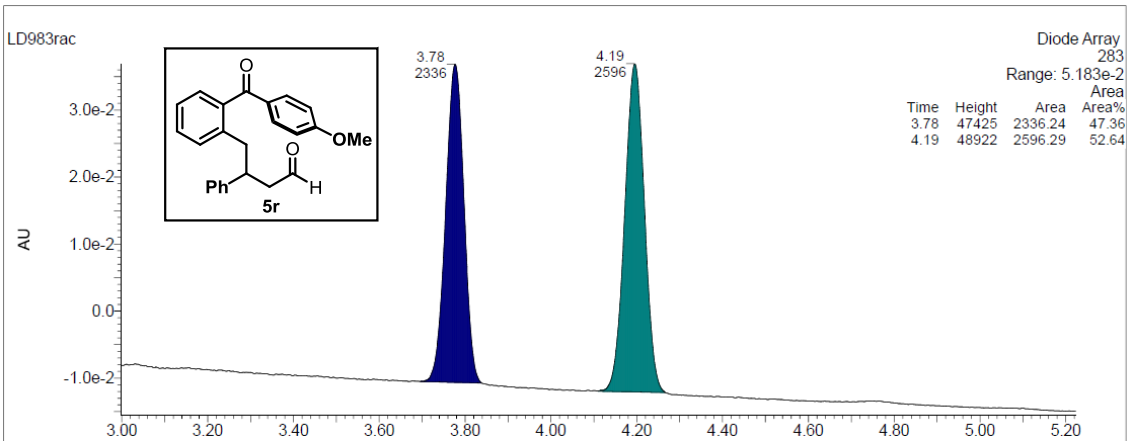
Enantioenriched sample 5q:



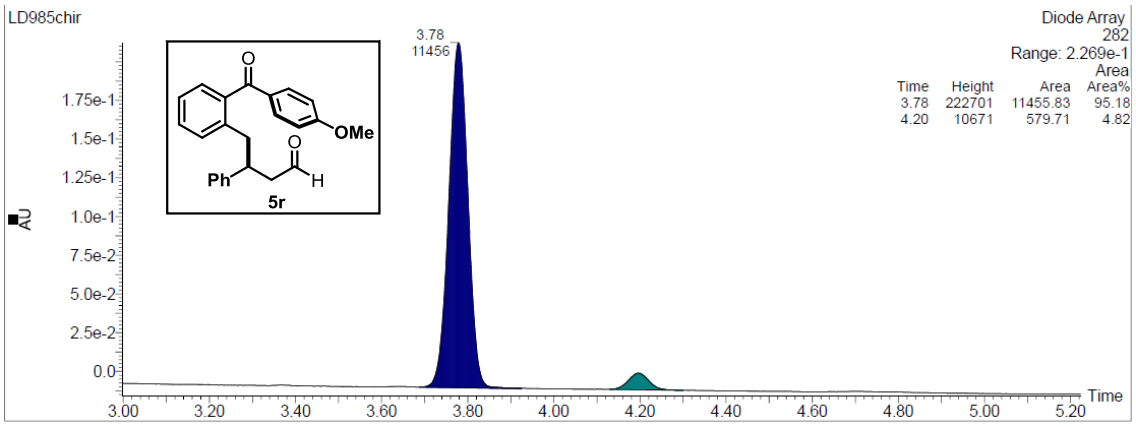
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.305	FM	0.4264	1672.75500	65.38972	92.2530
2	22.824	MM	0.4887	140.46997	4.79073	7.7470

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 6 min; λ = 283 nm

Racemic sample 5r:

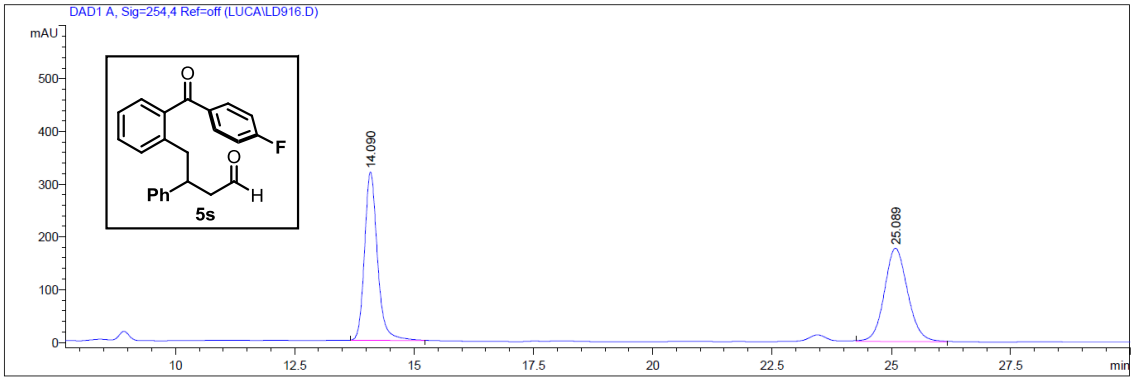


Enantioenriched sample 5r:



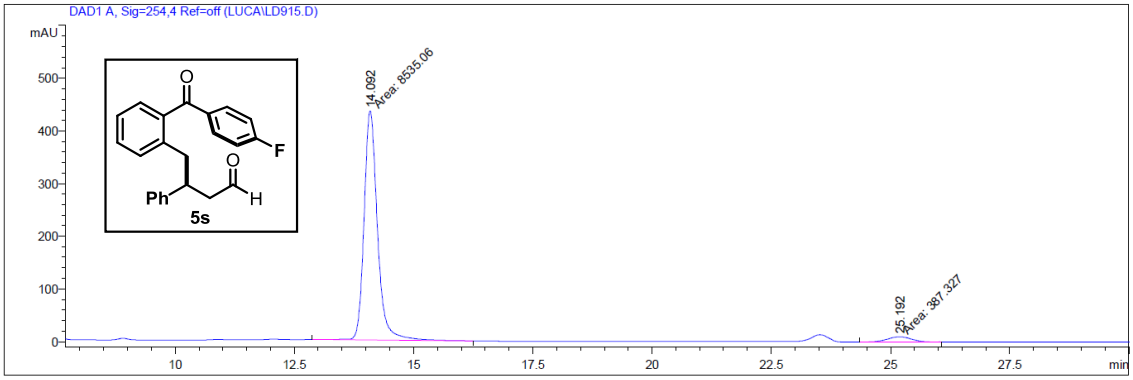
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column using an isocratic method (Hexane : i-PrOH, 98:2), flow rate 0.7 mL/min; λ = 254 nm

Racemic sample 5s:



Peak #	RetTime [min]	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

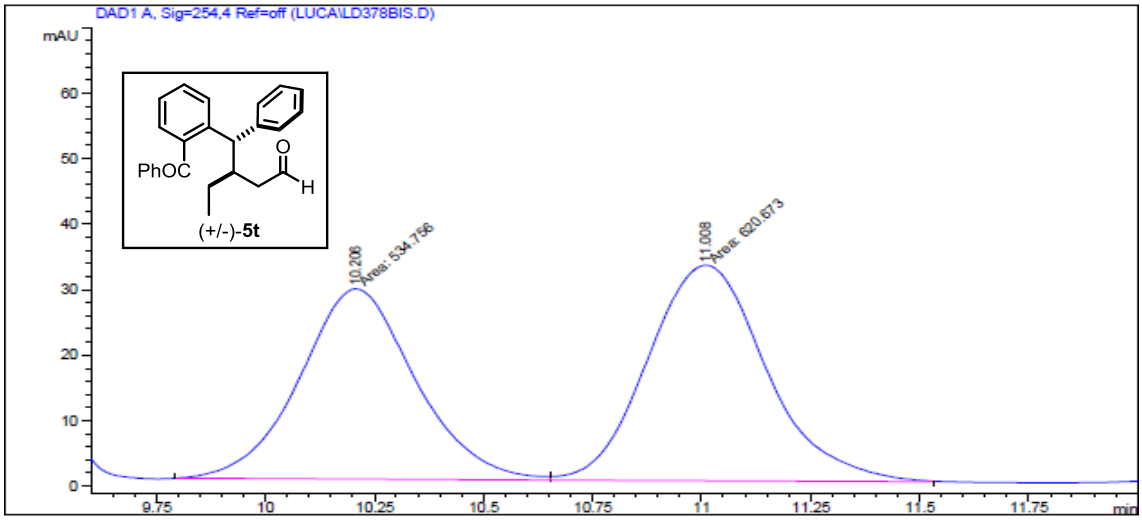
Enantioenriched sample 5s:



Peak #	RetTime [min]	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	387.32693	10.48334	4.3411

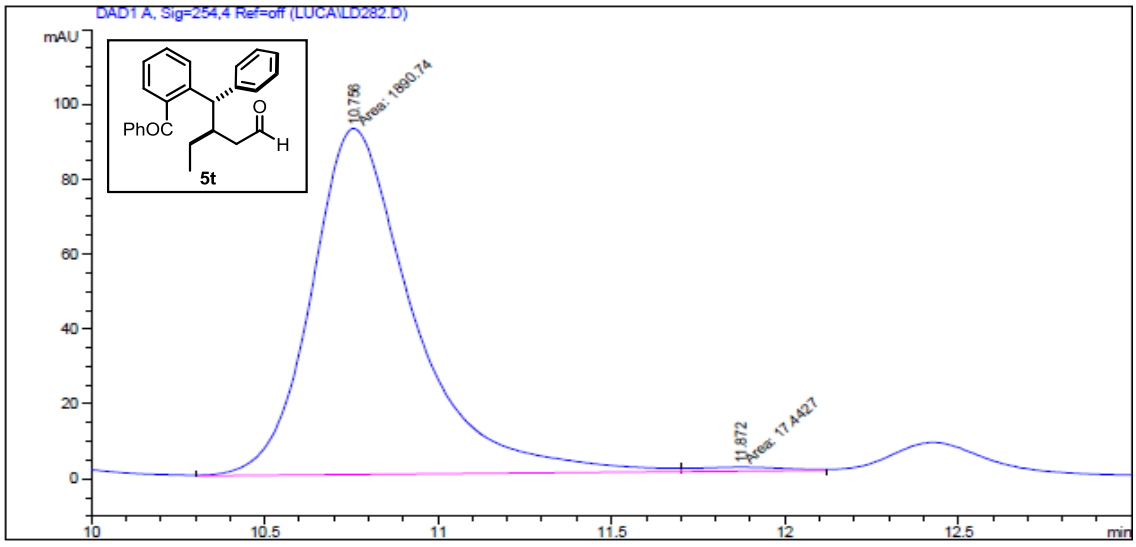
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column (85:15 hexane:*i*PrOH), flow rate 0.8 mL/min; λ = 254 nm

Racemic sample 5t:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.206	MF	0.3070	534.75592	29.02751	46.2820
2	11.008	FM	0.3144	620.67297	32.90187	53.7180

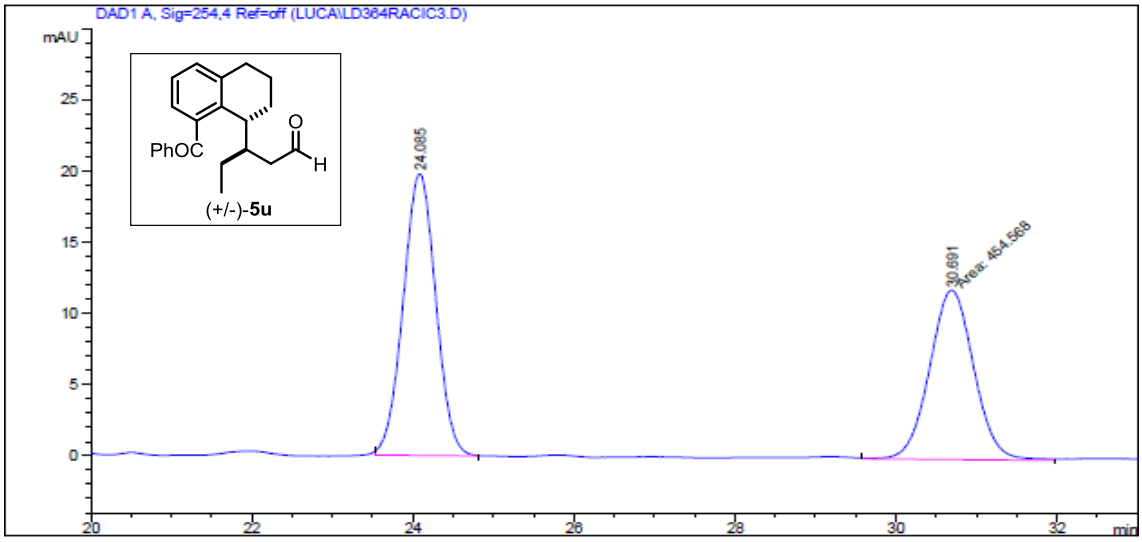
Enantioenriched sample 5t:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.756	MF	0.3411	1890.73657	92.38043	99.0859
2	11.872	FM	0.2888	17.44273	1.00669	0.9141

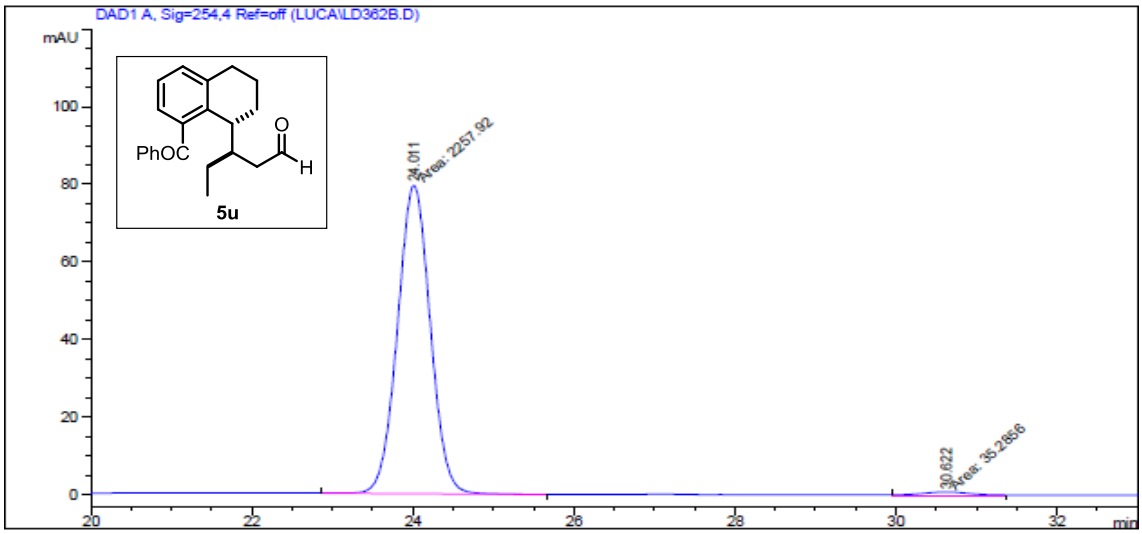
Condition: HPLC analysis on a Daicel Chiralpak IB column (85:15 hexane:*i*PrOH), flow rate 1.0 mL/min; λ = 254 nm

Racemic sample 5u:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.085	BB	0.4382	556.50024	19.78127	55.0408
2	30.691	MM	0.6367	454.56784	11.89833	44.9592

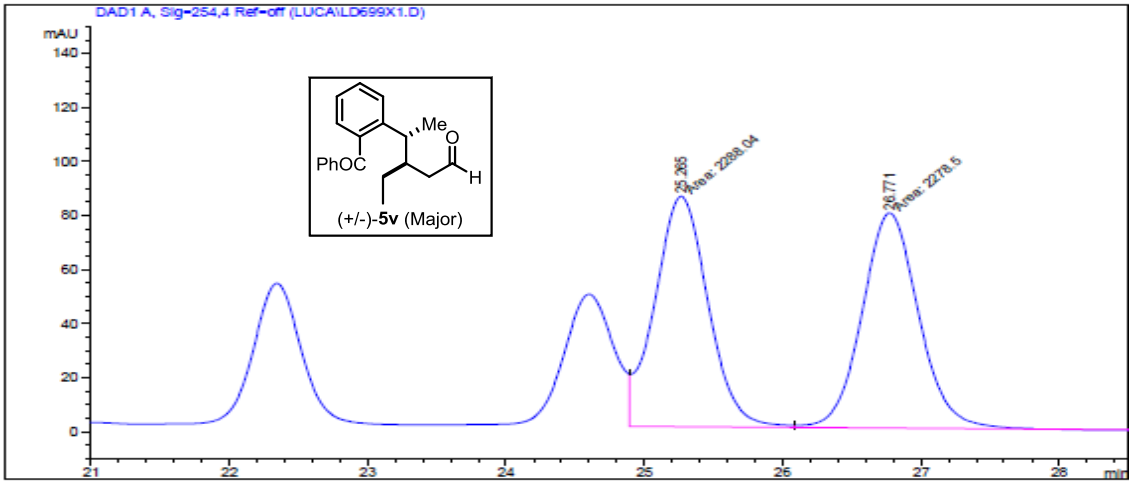
Enantioenriched sample 5u:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.011	MM	0.4732	2257.91821	79.52377	98.4613
2	30.622	MM	0.6682	35.28564	8.80142e-1	1.5387

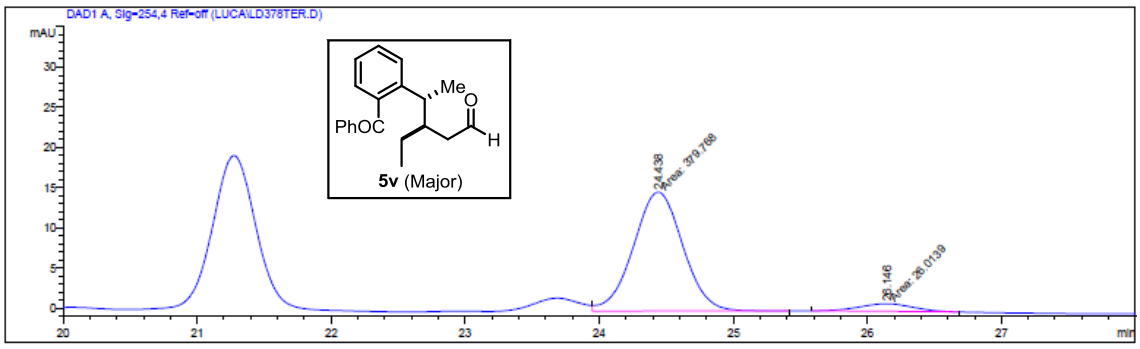
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column (95:5 hexane:*i*PrOH), flow rate 0.9 mL/min; λ = 254 nm

Racemic sample 5v (Major diastereoisomer):



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	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

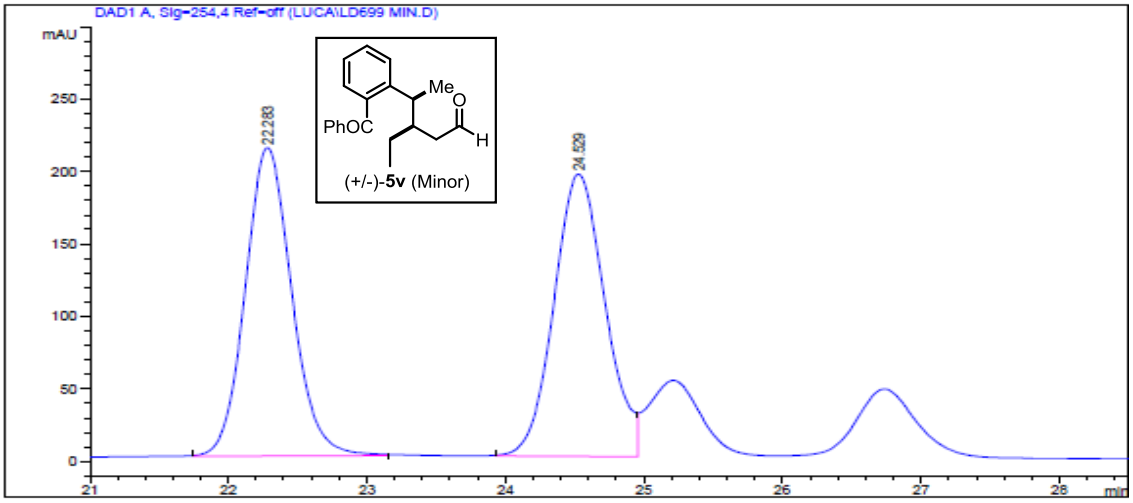
Enantioenriched sample 5v:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	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

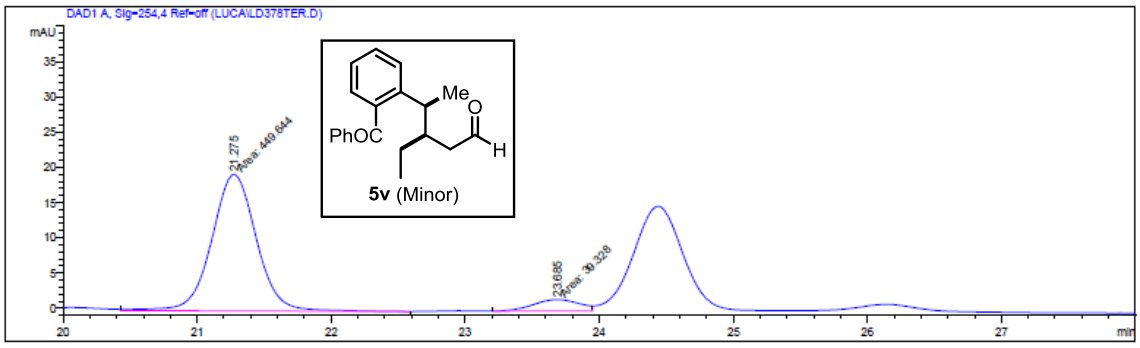
Condition: HPLC analysis on a Daicel Chiralpak IC-3 column (95:5 hexane:*i*PrOH), flow rate 0.9 mL/min; λ = 254 nm

Racemic sample 5v (Minor diastereoisomer):



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.283	BB	0.3599	4960.53516	212.82335	49.7805
2	24.529	BV	0.3958	5004.28760	194.75798	50.2195

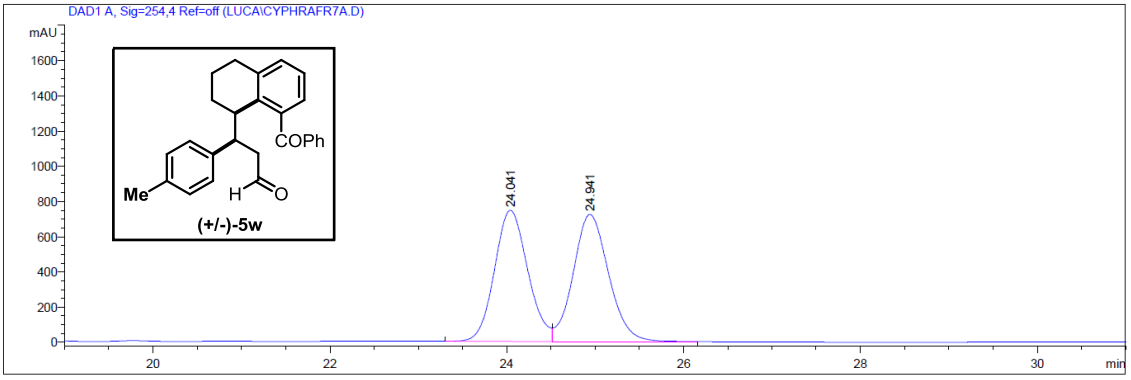
Enantioenriched sample 5v:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.275	FM	0.3870	449.64352	19.36314	91.9570
2	23.685	MF	0.3968	39.32801	1.65188	8.0430

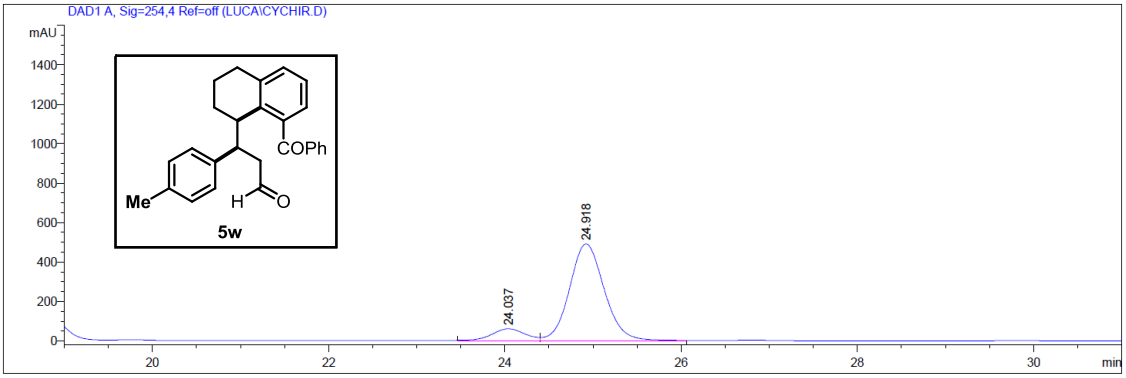
Condition: HPLC analisys on a Daicel Chiralpak IC-3 column using a isocratic method (80:20 Hexane:*i*PrOH), flow rate 0.4 mL/min; λ = 247 nm

Racemic sample 5w:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	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

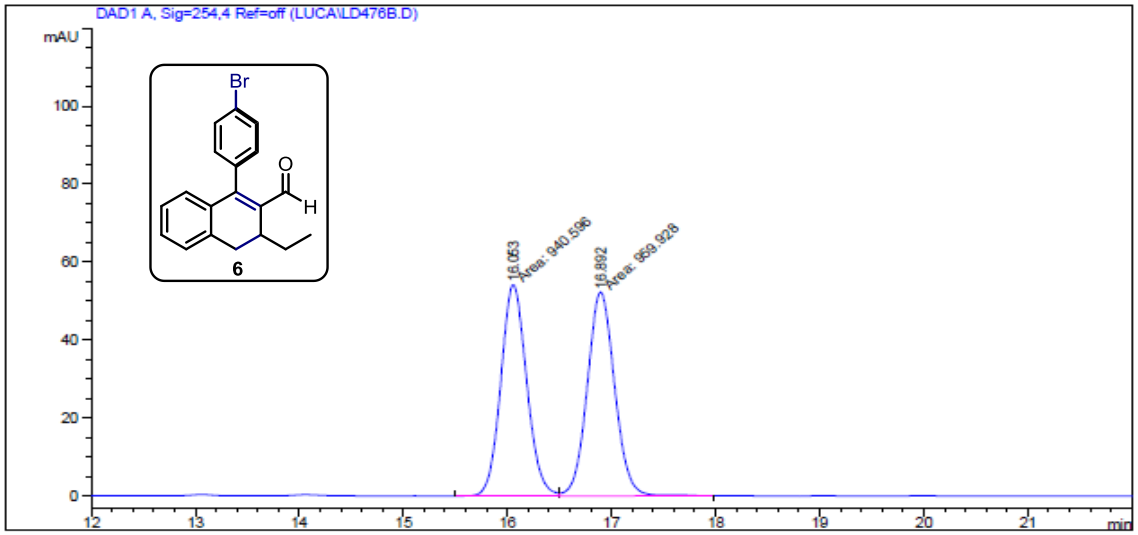
Enantioenriched sample 5w:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	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

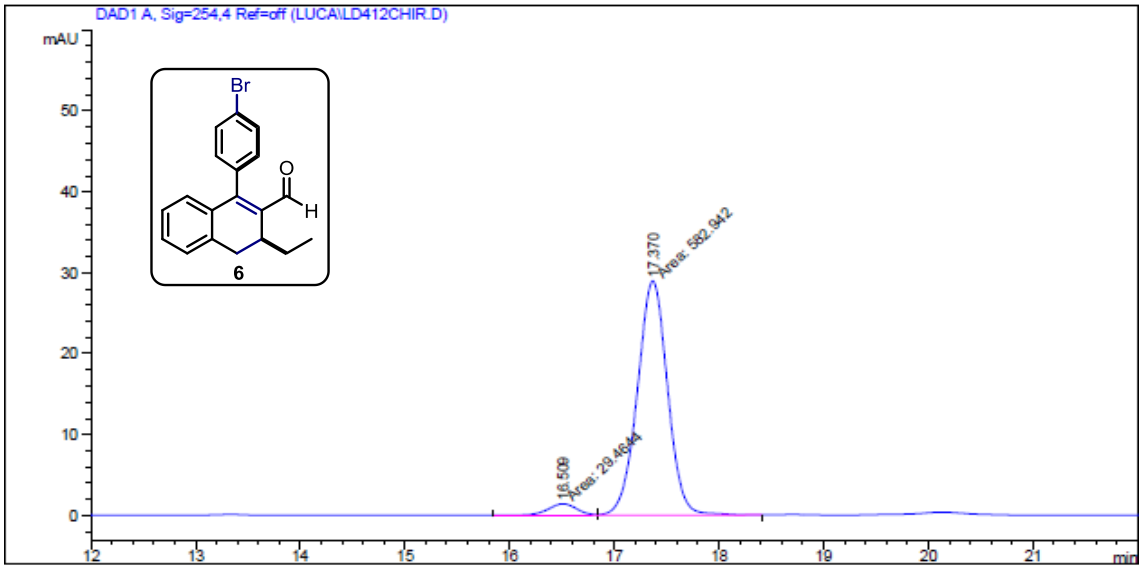
Condition: HPLC analisys on a Daicel Chiralpak IC-3 column using a isocratic method (98:2 hexane:*i*PrOH) flow rate 0.80 mL/min; λ = 254 nm

Racemic sample 6:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.053	MF	0.2891	940.59619	54.22182	49.4914
2	16.892	FM	0.3056	959.92847	52.34462	50.5086

Enantioenriched sample 6:



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.509	MF	0.3362	29.46443	1.46060	4.8113
2	17.370	FM	0.3351	582.94232	28.99752	95.1887