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Supporting Information

Stereocontrolled Synthesis of 1,4-Dicarbonyl Compounds by Photochemical Organocatalytic Acyl Radical Addition to Enals

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Author Contributions

G.G. Investigation: Lead; Methodology: Lead; Writing—original draft: Supporting
B.B. Investigation: Lead; Methodology: Lead; Writing—original draft: Supporting
A.V. Investigation: Supporting; Methodology: Supporting; Writing—review & editing: Supporting
P.M. Funding acquisition: Lead; Investigation: Supporting; Supervision: Lead; Writing—original draft: Lead; Writing—review & editing: Lead.

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A. General Information

The NMR spectra were recorded at 300 MHz, 400 MHz and 500 MHz for ^{1}H, 101 MHz or 126 MHz for ^{13}C and 376 MHz or 471 MHz for ^{19}F. The chemical shift (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 and 77.16 ppm ^{13}C NMR, CD_3CN @ 1.94 ppm ^{1}H NMR and 118.26, 1.32 ppm ^{13}C NMR and tetramethylsilane @ 0 ppm). Coupling constants are given in Hertz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; sept, septet; m, multiplet; bs, broad signal.
GC-MS analysis were performed by an Agilent Technology (7890A) equipped with an HP-5 column and MS spectrometer Agilent Technology 5975C.
High-resolution mass spectra (HRMS) were obtained from the ICIQ High Resolution Mass Spectrometry Unit on MicroTOF Focus and Maxis Impact (Bruker Daltonics) with electrospray ionization. X-ray data were obtained from the ICIQ X-Ray unit using a Bruker DUO diffractometer equipped with an APEX II detector using Cu Kα radiation from a Microfocus source E025 IuS anode. Optical rotations were measured on a Polarimeter Jasco P-1030 and are reported as follows: $[\alpha]_D^T$ (c in g per 100 mL, solvent).
UV-vis measurements were carried out on a Shimadzu UV-2401PC spectrophotometer equipped with photomultiplier detector, double beam optics and D2 and W light sources.
Cyclic voltammetry studies were carried out on a Princeton Applied Research PARSTAT 2273 potentiostat offering compliance voltage up to ± 100 V (available at the counter electrode), ± 10 V scan range and ± 2 A current range.
Continuous wave (CW) EPR spectra were obtained on a Bruker EMX Micro X-band bridge of 9.1 - 9.9 GHz, using a Bruker ER 1164 HS resonator.

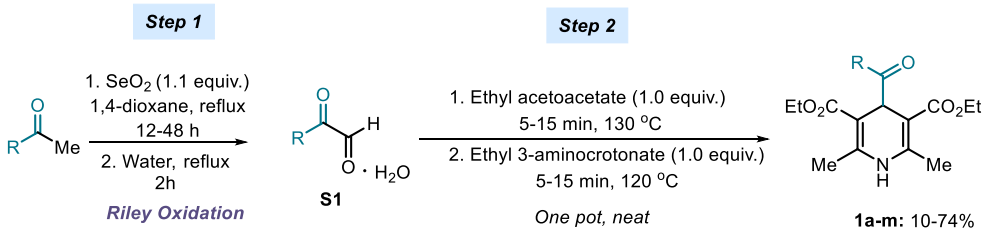
The authors are indebted to the team of the Research Support Area at ICIQ. Grace Fox is thanked for proofreading the manuscript.

General Procedures. All reactions were set up under argon atmosphere in oven-dried glassware using standard Schlenk techniques, unless otherwise stated. Synthesis grade solvents were used as purchased. Anhydrous solvents were taken from a commercial SPS solvent dispenser. 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 pre-coated TLC plates (silica gel 60 GF254, 0.25 mm) were employed, using UV light as the visualizing agent and acid solution of 2,4-dinitophenylhydrazine or basic aqueous potassium permanganate ($KMnO_4$) stain solutions and heat as developing agents. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator (in vacuo at 40 ºC, ≈5 mbar).

Determination of Enantiomeric Purity. UPC[2] analysis on chiral stationary phase was performed on an Waters Acquity instrument, employing IA, IC and IG chiral columns. The exact conditions for the analyses are specified within the characterization section. UPC[2] traces were compared to racemic samples prepared performing the reaction in the presence of the racemic amine catalyst **A**.

Materials. Commercial grade reagents and solvents were purchased at the highest commercial quality from Sigma-Aldrich, Apollo Scientific, Fluka, Alfa Aesar, Fluorochem, SynQuest and used without further purification, unless otherwise stated. The chiral secondary amine catalysts **A** and **B** are commercially available (Sigma-Aldrich). The aminocatalysts **C** was synthesized according to a procedure reported in the literature.[1] The majority of enals **2** are commercially available. Enals **2o,q**[1] and **2u**[2] were prepared according to literature procedures. Enal **2a** and **2t** were distilled prior to use. Acyl DHPs **1a-m** were prepared from the corresponding glyoxals or glyoxal hydrates according to the procedure described in Section B.

B. Preparation of Acyl DHPs 1



Scheme S1. General procedure for the preparation of substrates **1a-m**.

Glyoxal hydrates **S1** were purchased from Sigma-Aldrich, Apollo Scientific or prepared using literature protocols via the Riley oxidation (vide infra), unless stated otherwise.[3] 3,3-Dimethyl-2-oxobutanal monohydrate[4] and 2-cyclohexyl-2-oxoacetaldehyde monohydrate[5] were prepared according to literature procedures. Substrates **S1** were recrystallized from boiling water before use in the next step.

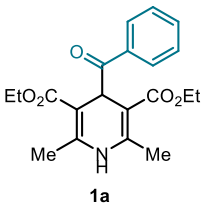
General Procedure for the Preparation of Glyoxal Hydrates via the Riley Oxidation (Step 1)

To a 250 mL round bottom flask, equipped with a magnetic stirrer and a reflux condenser, SeO_2 (1.2 equiv.) was added, followed by 1,4-dioxane/water (5 vol., 10:1 mixture) and the ketone (1.0 equiv.). The reaction mixture was refluxed under argon for 5-48 h until completion, as inferred by TLC analysis, and then cooled to ambient temperature. The suspension was filtered through a plug of celite and the solvent was removed by rotary evaporator. The residue was dried under high vacuum and dissolved in a minimum amount of boiling water. The mixture was slowly cooled to 0 °C and then the crystallized glyoxal hydrates were filtered off and dried.

General Procedure 1 for the Preparation of Acyl DHPs (Step 2)

Ethyl acetoacetate (1.0 equiv.) and the glyoxals or glyoxal hydrates (2 g, 1.0 equiv.) prepared in step 1 were added to a 50 mL round bottom flask equipped with a magnetic stirrer. The mixture was heated to 130 °C and kept under stirring for 5-30 min, until the condensation reaction was completed (as monitored by TLC analysis). The solution was then cooled to 80 °C. Ethyl 3-aminocrotonate (1.0 equiv.) was slowly added (exothermic reaction), then the mixture was heated at 120 °C for 5-15 min and monitored by TLC. After completion, the reaction mixture was cooled to ambient temperature and the solid residue was dissolved in a minimum amount of hot cyclohexane/ethyl acetate (8:2, approximately 10 vol.). The solution was slowly cooled to 0 °C and the product (bright yellow or orange crystalline solid) was filtered off, washed with cold cyclohexane/ethyl acetate (8:2) and dried. In specific cases (**1i-m**, vide infra), the substrates **1** were initially purified on silica gel (pentane/diethyl ether, gradient from 80:20 to 50:50), prior to recrystallization from cyclohexane/ethyl acetate (8:2).

Diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1a)

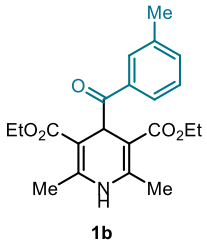


1a

Prepared using the *General Procedure 1* from phenylglyoxal hydrate to yield 10.1 g (10 g scale, 43% yield) of pure product **1a** (yellow crystalline solid).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 8.24 – 8.12 (m, 2H), 7.59 – 7.51 (m, 1H), 7.51 – 7.39 (m, 2H), 6.39 (s, 1H), 5.74 (s, 1H), 4.08 – 3.91 (m, 4H), 2.34 (s, 6H), 1.06 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 204.2, 167.3, 147.1, 137.4, 133.0, 130.0, 128.3, 100.2, 60.2, 42.1, 19.8, 14.5.

Diethyl 2,6-dimethyl-4-(3-methylbenzoyl)-1,4-dihydropyridine-3,5-dicarboxylate (1b)

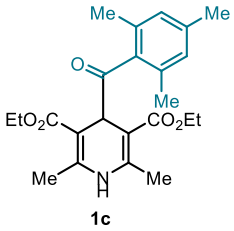


1b

2-Oxo-2-(*m*-tolyl)acetaldehyde monohydrate was prepared via Riley oxidation from 3'-methylacetophenone and **1b** was prepared using the *General Procedure 1* to yield 594 mg (1 g scale, 27% yield) of pure product (yellow crystalline solid).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.96 – 7.91 (m, 1H), 7.90 – 7.84 (m, 1H), 7.36 – 7.29 (m, 2H), 6.41 (s, 1H), 5.68 (s, 1H), 4.08 – 3.84 (m, 4H), 2.39 (s, 3H), 2.30 (s, 6H), 1.04 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): δ 204.1, 167.3, 147.1, 137.8, 137.4, 133.8, 130.3, 128.2, 127.3, 100.2, 60.2, 42.1, 21.7, 19.8, 14.4; HRMS: Calculated for $C_{21}H_{24}NO_5$ $[M-H]^-$: 370.1660, found: 370.1663.

Diethyl 2,6-dimethyl-4-(2,4,6-trimethylbenzoyl)-1,4-dihydropyridine-3,5-dicarboxylate (1c)

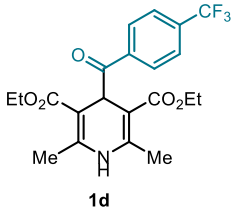


1c

2-Mesityl-2-oxoacetaldehyde monohydrate was prepared via Riley oxidation from 1-mesitylethan-1-one. **1c** was synthesized using the *General Procedure 1* to yield 824 mg (1 g scale, 44% yield) of pure product (orange crystalline solid).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 6.77 (s, 2H), 6.12 (s, 1H), 5.34 (s, 1H), 3.93 (m, 4H), 2.37 (s, 6H), 2.24 (s, 3H), 2.18 (s, 6H), 1.17 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 205.4, 167.3, 146.5, 138.5, 137.7, 134.5, 128.4, 97.7, 60.3, 48.3, 21.3, 19.8, 19.5, 14.5; HRMS: Calculated for $C_{23}H_{28}NO_5$ $[M-H]^-$: 398.1973, found: 398.1975.

Diethyl 2,6-dimethyl-4-(4-(trifluoromethyl)benzoyl)-1,4-dihydropyridine-3,5-dicarboxylate (1d)

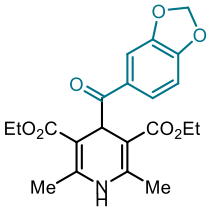


1d

2-Oxo-2-(4-(trifluoromethyl)phenyl)acetaldehyde monohydrate was prepared via Riley oxidation from 4'-(trifluoromethyl) acetophenone. **1d** was synthesized using the *General Procedure 1* to yield 3.76 g (5.0 g scale, 39% yield) of pure product (yellow solid).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 8.26 – 8. 21 (m, 2H), 7.74 – 7.63 (m, 2H), 6.37 (s, 1H), 5.66 (s, 1H), 4.06 – 3.83 (m, 4H), 2.29 (s, 6H), 1.01 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 203.6, 167.2, 147.1, 140.5, 134.2 (q, *J* = 32.5 Hz), 130.1, 125.3 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 272.7 Hz), 100.2, 60.4, 42.6, 19.9, 14.4; ^{19}F NMR (471 MHz, $CDCl_3$), δ (ppm): -63.16; HRMS: Calculated for $C_{21}H_{21}F_3NO_5$ $[M-H]^-$: 424.1377, found: 424.1382.

Diethyl 4-(benzo[d][1,3]dioxole-5-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1e)

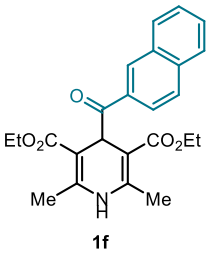


1e

Prepared using the *General Procedure 1* from 3,4-(methylenedioxy)phenylglyoxal hydrate to yield 1.9 g (1.0 g scale, 57% yield) of pure product **1e** (pale yellow solid).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.88 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.62 (d, *J* = 1.7 Hz, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.79 (s, 1H), 6.04 (s, 2H), 5.64 (s, 1H), 4.19 – 3.89 (m, 4H), 2.30 (s, 6H), 1.13 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 201.6, 167.3, 151.9, 148.0, 146.9, 131.7, 126.6, 109.8, 107.8, 102.0, 100.4, 60.3, 41.7, 20.0, 14.5; HRMS: Calculated for $C_{21}H_{22}NO_7$ $[M-H]^-$: 400.1402, found: 400.1410.

Diethyl 4-(2-naphthoyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1f)

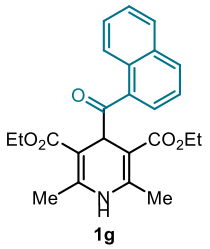


1f

2-(Naphthalen-2-yl)-2-oxoacetaldehyde monohydrate monohydrate was prepared via Riley oxidation from 1-acetonaphthone and **1f** was synthesized using the *General Procedure 1* to yield 705 mg (3.5 g scale, 10% yield) of pure product (orange solid).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 8.79 – 8.67 (m, 1H), 8.12 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.98 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.91 – 7.84 (m, 2H), 7.63 - 7.47 (m, 2H), 6.33 (s, 1H), 5.87 (s, 1H), 4.05 – 3.80 (m, 4H), 2.33 (s, 6H), 0.96 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 203.2, 166.9, 146.7, 135.5, 134.1, 132.4, 131.5, 129.9, 129.6, 128.1, 127.7, 126.4, 125.3, 100.0, 59.9, 41.7, 19.6, 14.1; HRMS: Calculated for $C_{24}H_{24}NO_5$ $[M-H]^-$: 406.1660, found: 406.1653.

Diethyl 4-(1-naphthoyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1g)

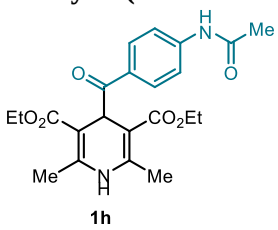


1g

2-(Naphthalen-1-yl)-2-oxoacetaldehyde monohydrate was prepared via Riley oxidation from 1-acetonaphthone and **1g** was synthesized using the *General Procedure 1* to yield 1.27 g (3.7 g scale, 17% yield) of pure product (yellow solid).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 8.19 – 8.05 (m, 1H), 7.94 – 7.79 (m, 3H), 7.59 – 7.45 (m, 3H), 5.96 (s, 1H), 5.66 (s, 1H), 4.00 – 3.70 (m, 4H), 2.41 (s, 6H), 0.98 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 203.2, 166.8, 146.4, 137.4, 133.4, 130.7, 130.5, 128.1, 127.0, 126.5, 126.1, 125.4, 124.4, 98.5, 59.9, 46.9, 19.6, 13.9; HRMS: Calculated for $C_{24}H_{24}NO_5$ $[M-H]^-$: 406.1660, found: 406.1671.

Diethyl 4-(4-acetamidobenzoyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1h)

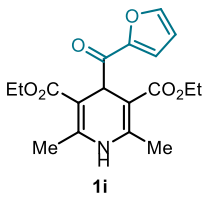


1h

Prepared using the *General Procedure 1* from *N*-(4-(2-oxoacetyl)phenyl)acetamide hydrate to yield 1.33 g (1.0 g scale, 67% yield) of pure product **1h** (yellow solid).

^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 10.20 (s, 1H), 8.80 (s, 1H), 7.99 – 7.89 (m, 2H), 7.72 – 7.59 (m, 2H), 5.45 (s, 1H), 3.91 – 3.72 (m, 4H), 2.19 (s, 6H), 2.05 (s, 3H), 0.93 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, DMSO-d_6), δ (ppm): δ 201.2, 169.7, 167.2, 148.2, 144.1, 131.8, 131.1, 118.4, 98.9, 59.9, 31.5, 27.2, 19.0, 14.8; HRMS: Calculated for $C_{22}H_{26}N_2NaO_6$ $[M+Na]^+$: 437.1683, found: 437.1674.

Diethyl 4-(furan-2-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1i)

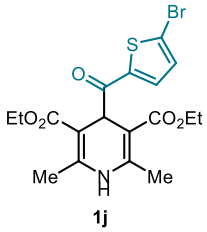


1i

2-(furan-2-yl)-2-oxoacetaldehyde monohydrate was prepared via Riley oxidation from 1-(furan-2-yl)ethan-1-one and **1i** was synthesized using modified *General Procedure 1* to yield 484 mg (1.8 g scale, 11% yield) of pure product (dark yellow solid). The crude reaction mixture was purified on silica gel (pentane/diethyl ether, gradient from 80:20 to 50:50), prior to recrystallization from cyclohexane/ethyl acetate (8:2).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.67 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.53 (dd, *J* = 3.6, 0.8 Hz, 1H), 6.87 (s, 1H), 6.61 – 6.53 (m, 1H), 5.46 (s, 1H), 4.17 – 3.87 (m, 4H), 2.30 (s, 6H), 1.13 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 191.9, 166.9, 152.0, 147.0, 147.0, 120.4, 112.2, 99.3, 59.9, 42.7, 19.4, 14.2; HRMS: Calculated for $C_{18}H_{21}NaO_6$ $[M+Na]^+$: 370.1261, found: 370.1258.

Diethyl 4-(5-bromothiophene-2-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1j)

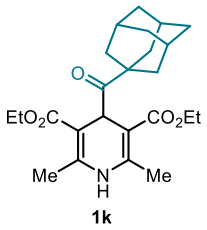


1j

Prepared using the *General Procedure 1* from (5-bromothien-2-yl)glyoxal hydrate to yield 437 mg (1 g scale, 13% yield) of pure product **1j** (yellow crystalline solid). The crude reaction mixture was purified on silica gel (pentane/diethyl ether, gradient from 80:20 to 50:50), prior to recrystallization from cyclohexane/ethyl acetate (8:2).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.84 (d, *J* = 4.0 Hz, 1H), 7.10 (d, *J* = 4.1 Hz, 1H), 6.34 (s, 1H), 5.42 (s, 1H), 4.11 – 3.97 (m, 4H), 2.28 (s, 6H), 1.12 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 195.2, 167.2, 147.2, 145.4, 135.3, 131.5, 123.7, 99.7, 60.4, 43.2, 20.0, 14.6; HRMS: Calculated for $C_{18}H_{19}BrNO_5S$ $[M-H]^-$: 440.0173, found: 440.0165.

Diethyl 4-((3r,5r,7r)-adamantane-1-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1k)

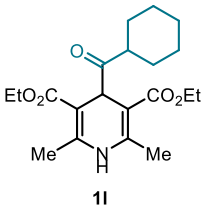


1k

2-((1*r*,3*r*,5*r*,7*r*)-adamantan-2-yl)-2-oxoacetaldehyde monohydrate was prepared via Riley oxidation from 1-adamantyl methyl ketone and **1k** was synthesized using the *General Procedure 1* to yield 294 mg (1.0 g scale, 15% yield) of pure product (pale yellow solid). The crude reaction mixture was purified on silica gel (pentane/diethyl ether, gradient from 80:20 to 50:50), prior to recrystallization from cyclohexane/ethyl acetate (8:2).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 5.94 (s, 1H), 5.21 (s, 1H), 4.32 – 4.10 (m, 4H), 2.31 (s, 6H), 2.1 – 1.96 (bs, 3H), 1.96 - 1.88 (bs, 6H), 1.77 - 1.64 (bs, 6H), 1.33 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 215.8, 167.1, 146.2, 99.2, 60.1, 46.0, 40.7, 38.2, 36.6, 28.2, 26.9, 19.6, 14.5; HRMS: Calculated for $C_{24}H_{32}NO_5$ $[M-H]^-$: 414.2286, found: 414.2290.

Diethyl 4-(cyclohexanecarbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1l)

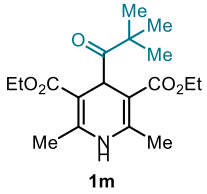


1l

2-cyclohexyl-2-oxoacetaldehyde monohydrate was prepared via Riley oxidation from cyclohexyl methyl ketone and **1l** was synthesized using the *General Procedure 1* to yield 322 mg (1.0 g scale, 14%) of pure product (pale yellow solid). The crude reaction mixture was purified on silica gel (pentane/diethyl ether, gradient from 80:20 to 50:50), prior to recrystallization from cyclohexane/ethyl acetate (8:2).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 5.98 (s, 1H), 5.02 (s, 1H), 4.34 – 4.06 (m, 4H), 2.74 - 2.61 (m, 1H), 2.34 (s, 6H), 1.92 – 1.75 (m, 4H), 1.72 – 1.49 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 6H), 1.29 – 1.21 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 211.4, 167.0, 146.4, 98.3, 60.0, 47.1, 44.5, 28.8, 26.9, 25.9, 19.5, 14.4; HRMS: Calculated for $C_{20}H_{29}NNaO_5$ $[M+Na]^+$: 386.1938, found: 386.1931.

Diethyl 2,6-dimethyl-4-pivaloyl-1,4-dihydropyridine-3,5-dicarboxylate (1m)



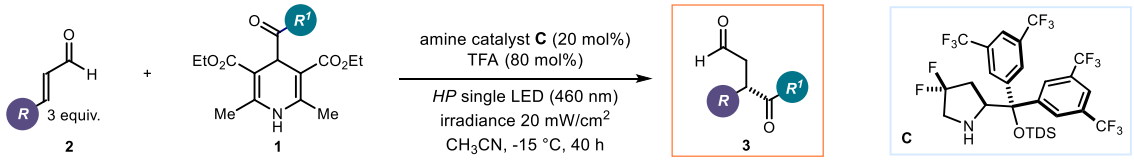
1m

3,3-dimethyl-2-oxobutanal monohydrate was prepared via Riley oxidation from pinacolone and **1m** was synthesized using the *General Procedure 1* to yield 920 mg (2 g scale, 18% yield) of pure product (pale yellow crystalline solid). The crude reaction mixture was purified on silica gel (pentane/diethyl ether, gradient from 80:20 to 50:50), prior to recrystallization from cyclohexane/ethyl acetate (8:2).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 6.13 (s, 1H), 5.27 (s, 1H), 4.30 - 4.10 (m, 4H), 2.30 (s, 6H), 1.32 (t, *J* = 7.1 Hz, 6H), 1.21 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 217.6, 167.1, 146.5, 99.2, 60.0, 43.7, 41.2, 27.1, 19.4, 14.4; HRMS: Calculated for $C_{18}H_{26}NO_5$ $[M-H]^-$: 336.1816, found: 336.1831.

C. Enantioselective Photochemical β-Acylation of Enals

C.1 General Procedure 2 for the Photochemical Asymmetric Acyl Radical Addition



To a 8 mL vial, the acyl DHP **1** (0.1 mmol, 1 equiv.) and the chiral amine catalyst **C** (0.02 mmol, 0.2 equiv.) were sequentially added. The vial was put under vacuum and backfilled with argon three times, finally enal **2** (0.3 mmol, 3 equiv.) and a TFA solution in CH_3CN degassed with argon (200 µL, 0.2 M) was added. The vial was sealed with parafilm and placed inside a steel reactor fixed over an aluminum block equipped with a High Power single LED (λ = 460 nm), irradiance = 20 mW/cm^2 (unless otherwise stated) as controlled by external power supply. The temperature was kept at -15 °C using a chiller connected to the steel reactor. To prevent moisture condensation, the reactor was placed inside a glass bell, which assured continuous air flow during the whole experiment (Figure S1).

The reaction was irradiated at -15 °C for 40 h. Finally, the solvent was evaporated on the rotary evaporator, the residue was dissolved in DCM and filtered through a plug of silica to remove the pyridine byproduct and the unreacted substrate **1**. The silica was washed with 250 mL of DCM. The washings were combined and the solvent was removed by rotary evaporator. The residue was purified by flash chromatography (Ø = 1.5 cm, h SiO_2 = 13 cm, gradient from hexane 95% - EtOAc 5% to hexane 85% - EtOAc 15%) to get products **3** in the stated yield and enantiomeric purity.

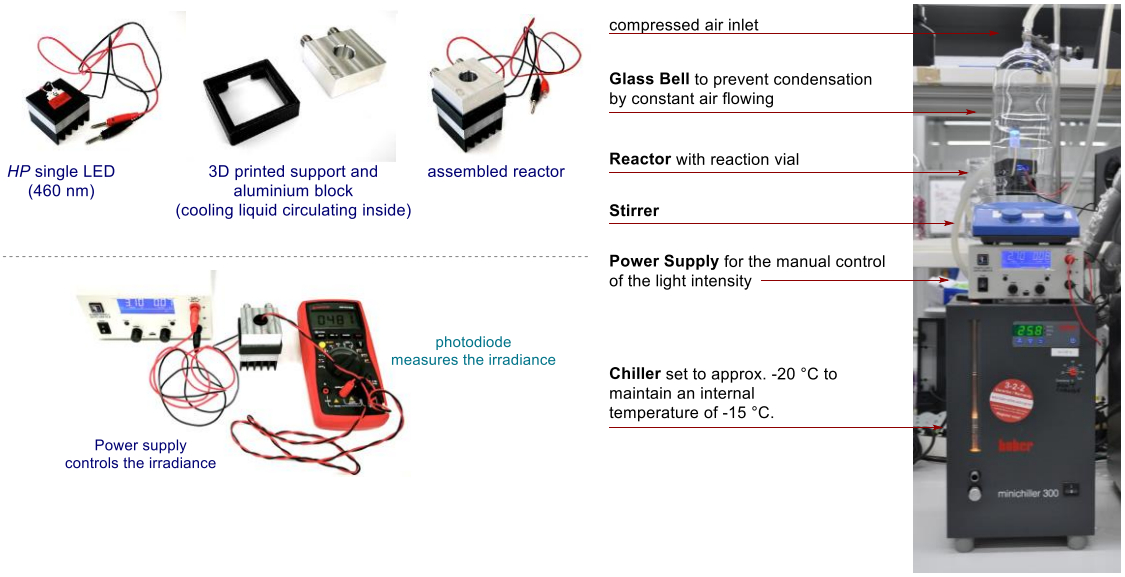
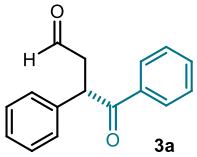


Figure S1. Detailed set-up and illumination system. The light source for illuminating the reaction vessel consisted of a 460 nm high-power single LED (OCU-440 UE420-X-T) purchased from OSA Opto Light (more information [here]).

C.2 Characterization of Products 3a-u

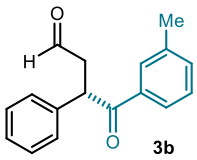
(*S*)-4-oxo-3,4-diphenylbutanal (3a)



Prepared according to the *General Procedure 2* mixing diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), cinnamaldehyde (0.3 mmol, 38 µL), trifluoroacetic acid (0.8 mmol, 6 µL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 95:5 to 85:15) to give **3a** as a yellow solid (21.6 mg, 90% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ = 242 nm: τ_{Minor} = 2.8 min, τ_{Major} = 3.1 min (74% ee); $[\alpha]_D^{26}$ = +52.9 (c = 1.15, $CHCl_3$, 74% ee). The absolute configuration for **3a** was unambiguously determined by X-ray crystallographic analysis, see X-ray Crystallographic Data section.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 9.80 (s, 1H), 8.04 – 7.85 (m, 2H), 7.50 – 7.43 (m, 1H), 7.40 – 7.33 (m, 2H), 7.31 – 7.24 (m, 4H), 7.23 – 7.17 (m, 1H), 5.12 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.60 (ddd, *J* = 18.6, 9.6, 0.7 Hz, 1H), 2.82 (dd, *J* = 18.6, 4.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 200.3, 198.5, 138.6, 136.4, 133.4, 129.6, 129.3, 128.9, 128.4, 127.8, 48.6, 48.0.

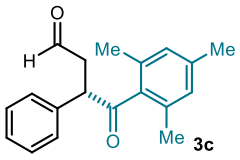
(*S*)-4-oxo-3-phenyl-4-(m-tolyl)butanal (3b)



Prepared according to the *General Procedure 2* mixing diethyl 2,6-dimethyl-4-(3-methylbenzoyl)-1,4-dihydropyridine-3,5-dicarboxylate **1b** (0.1 mmol, 37 mg), cinnamaldehyde (0.3 mmol, 38 µL), trifluoroacetic acid (0.8 mmol, 6 µL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 30 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 95:5 to 85:15) to give **3b** as a yellow solid (21 mg, 84% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% ACN, flow rate 2 mL/min, λ = 250 nm: τ_{Minor} = 2.9 min, τ_{Major} = 3.2 min (74% ee); $[\alpha]_D^{26}$ = +34.2 (c = 1.00, $CHCl_3$, 74% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.83 (s, 1H), 7.87 – 7.71 (m, 2H), 7.39 – 7.18 (m, 7H), 5.15 (dd, *J* = 9.6, 4.3 Hz, 1H), 3.63 (ddd, *J* = 18.5, 9.6, 0.7 Hz, 1H), 2.86 (ddd, *J* = 18.5, 4.3, 0.5 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 200.0, 198.3, 138.3, 138.3, 136.0, 133.9, 129.4, 129.2, 128.4, 128.0, 127.4, 126.2, 48.3, 47.6, 21.3; HRMS: Calculated for $C_{17}H_{16}NaO_2$ $[M+Na]^+$: 275.1043, found: 275.1055.

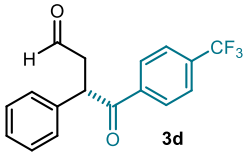
(*S*)-4-mesityl-4-oxo-3-phenylbutanal (3c)



Prepared according to the *General Procedure 2* mixing diethyl 2,6-dimethyl-4-(2,4,6-trimethylbenzoyl)-1,4-dihydropyridine-3,5-dicarboxylate **1c** (0.1 mmol, 40 mg), cinnamaldehyde (0.3 mmol, 38 µL), trifluoroacetic acid (0.8 mmol, 6 µL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 30 mW/cm^2 The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 95:5 to 90:10) to give **3c** as a yellow solid (18 mg, 64% yield, 74% ee isolated, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ = 240 nm: τ_{Major} = 2.9 min, τ_{Minor} = 3.0 min, (74% ee); $[\alpha]_D^{26}$ = +40.8 (c = 0.45, $CHCl_3$, 74% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 9.87 (s, 1H), 7.27 – 7.19 (m, 3H), 7.16 – 7.09 (m, 2H), 6.73 (s, 2H), 4.72 (dd, *J* = 7.6, 6.5 Hz, 1H), 3.67 – 3.48 (m, 1H), 3.12 – 2.99 (m, 1H), 2.24 (s, 3H), 1.95 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 206.9, 200.3, 139.1, 137.8, 136.0, 134.1, 129.4, 129.1, 128.8, 128.1, 54.1, 44.8, 21.4, 19.7; HRMS: Calculated for $C_{19}H_{20}NaO_2$ $[M+Na]^+$: 303.1356, found 303.1353.

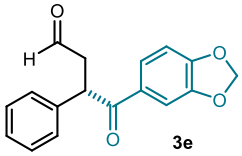
(*S*)-4-oxo-3-phenyl-4-(4-(trifluoromethyl)phenyl)butanal (3d)



Prepared according to the *General Procedure 2* mixing diethyl 2,6-dimethyl-4-(4-(trifluoromethyl)benzoyl)-1,4-dihydropyridine-3,5-dicarboxylate **1d** (0.1 mmol, 43 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 30 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 95:5 to 85:15) to give **4d** as a yellow solid (17 mg, 55% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IG column, gradient: 1 min 100% CO_2, 8 min from 100% CO_2 to 40% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ = 242 nm: τ_{Minor} = 3.9 min, τ_{Major} = 4.4 min (73% ee); $[\alpha]_D^{26}$ = +71.5 (c = 0.25, $CHCl_3$, 73% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.84 (s, 1H), 8.15 – 8.00 (m, 2H), 7.77 – 7.62 (m, 2H), 7.36 – 7.24 (m, 5H), 5.12 (dd, *J* = 9.9, 3.9 Hz, 1H), 3.80 – 3.61 (m, 1H), 2.89 (dd, *J* = 18.8, 4.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 199.8, 197.5, 139.0, 137.6, 134.4 (q, *J* = 32.5 Hz), 129.6, 129.3, 128.2, 127.9, 125.7 (q, *J* = 3.6 Hz), 123.7 (q, *J* = 272.6 Hz), 48.5, 48.1; ^{19}F NMR (376 MHz, $CDCl_3$), δ (ppm): -63.34; HRMS: Calculated for $C_{18}H_{17}F_3NaO_3$ $[M+Na+MeOH]^+$: 361.1022, found 361.1015.

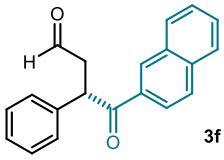
(*S*)-4-(benzo[d][1,3]dioxol-5-yl)-4-oxo-3-phenylbutanal (3e)



Prepared according to the *General Procedure 2* mixing diethyl 4-(benzo[d][1,3]dioxole-5-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1e** (0.1 mmol, 40 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 30 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 95:5 to 80:20) to give **3e** as a yellow oil (18.8 mg, 67% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ = 306 nm: τ_{Minor} = 3.3 min, τ_{Major} = 3.5 min, 54% ee); $[\alpha]_D^{26}$ = +51.9 (c = 0.5, $CHCl_3$, 54% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.82 (s, 1H), 7.61 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.45 (d, *J* = 1.7 Hz, 1H), 7.35 – 7.22 (m, 5H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.01 (s, 2H), 5.05 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.60 (dd, *J* = 18.5, 9.6 Hz, 1H), 2.82 (dd, *J* = 18.5, 4.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 200.4, 196.5, 148.4, 138.9, 131.1, 129.6, 128.3, 127.8, 125.7, 109.1, 108.3, 102.2, 48.7, 47.8; HRMS: Calculated for $C_{17}H_{14}NaO_4$ $[M+Na]^+$: 305.0784, found 305.0792.

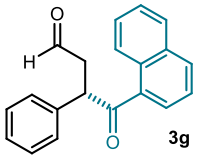
(*S*)-4-(naphthalen-2-yl)-4-oxo-3-phenylbutanal (3f)



Prepared according to the *General Procedure 2* mixing diethyl 4-(2-naphthoyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1f** (0.1 mmol, 41 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 30 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 95:5 to 90:10) to give **3f** as a yellow solid (26 mg, 92% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, 91:9 CO_2/ACN, flow rate 2 mL/min, λ = 290 nm: τ_{Minor} = 2.2 min, τ_{Major} = 2.4 min (68% ee); $[\alpha]_D^{26}$ = +31.9 (c = 1.0, $CHCl_3$, 68% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 9.88 (s, 1H), 8.54 (d, *J* = 1.8 Hz, 1H), 8.03 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.84 (dd, *J* = 8.5, 3.5 Hz, 2H), 7.67-7.47 (m, 2H), 7.42 – 7.19 (m, 5H), 5.33 (dd, *J* = 9.5, 4.3 Hz, 1H), 3.70 (dd, *J* = 18.6, 4.3 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 200.1, 198.1, 138.4, 135.5, 133.3, 132.4, 130.8, 129.7, 129.3, 128.5, 128.4, 128.1, 127.7, 127.5, 126.7, 124.5, 48.3, 47.7; HRMS: Calculated for $C_{20}H_{16}NaO_2$ $[M+Na]^+$: 311.1043, found: 311.1053.

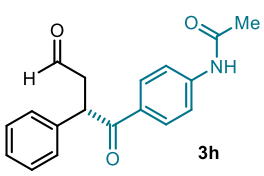
(*S*)-4-(naphthalen-1-yl)-4-oxo-3-phenylbutanal (3g)



Prepared according to the *General Procedure 2* mixing diethyl 4-(1-naphthoyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1g** (0.1 mmol, 41 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 30 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 95:5 to 90:10) to give **3g** as a yellow solid (19 mg, 66% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, 90:10 CO_2/IPA, flow rate 2 mL/min, λ = 290 nm: τ_{Minor} = 2.44 min, τ_{Major} = 2.69 min (76% ee); $[\alpha]_D^{26}$ = +65.4 (c = 0.75, $CHCl_3$, 76% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 9.92 (s, 1H), 8.43 – 8.23 (m, 1H), 8.01 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.93 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.88 – 7.78 (m, 1H), 7.60 – 7.38 (m, 4H), 7.28 – 7.13 (m, 4H), 5.17 (dd, *J* = 10.1, 3.9 Hz, 1H), 3.81 (dd, *J* = 18.7, 10.1 Hz, 1H), 2.92 (dd, *J* = 18.7, 3.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 201.8, 200.1, 137.4, 135.9, 133.8, 132.4, 130.6, 129.1, , 128.5, 128.2, 128.2, 127.7, 127.5, 126.3, 125.5, 124.3, 50.9, 47.9; HRMS: Calculated for $C_{20}H_{16}NaO_2$ $[M+Na]^+$: 311.1043, found 311.1044.

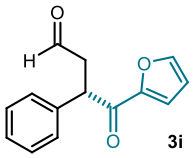
(*S*)-*N*-(4-(4-oxo-2-phenylbutanoyl)phenyl)acetamide (3h)



Prepared according to the *General Procedure 2* mixing diethyl 4-(4-acetamidobenzoyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1h** (0.1 mmol, 41 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 96 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 90:10 to 75:25) to give **3h** as a yellow solid (20.7 mg, 69% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% ACN, flow rate 2 mL/min, λ = 290 nm: τ_{Minor} = 4.8 min, τ_{Major} = 5.0 min (64% ee); $[\alpha]_D^{26}$ = +47.7 (c = 0.75, $CHCl_3$, 64% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.83 (s, 1H), 8.01 – 7.90 (m, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.47 (bs, 1H), 7.38 – 7.20 (m, 5H), 5.10 (dd, *J* = 9.6, 4.2 Hz, 1H), 3.61 (dd, *J* = 18.5, 9.6 Hz, 1H), 2.84 (dd, *J* = 18.6, 4.2 Hz, 1H), 2.20 – 2.17 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 200.2, 196.8, 168.5, 142.2, 138.3, 130.4, 129.3, 128.0, 127.5, 126.0, 118.8, 48.2, 47.4, 30.9; HRMS: Calculated for $C_{18}H_{16}NO_3$ $[M-H]^-$: 294.1136, found: 294.1128.

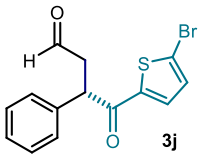
(*S*)-4-(furan-2-yl)-4-oxo-3-phenylbutanal phenylbutanal (3i)



Prepared according to the *General Procedure 2* mixing diethyl 4-(furan-2-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1i** (0.1 mmol, 35 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 90:10 to 75:25) to give **3i** as a yellow oil (15.6 mg, 68% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% ACN, flow rate 2 mL/min, λ = 270 nm: τ_{Minor} = 2.9 min, τ_{Major} = 3.1 min (70% ee); $[\alpha]_D^{26}$ = +85.2 (c = 0.65, DCM, 70% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 9.91 – 9.64 (m, 1H), 7.55 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.38 – 7.15 (m, 6H), 6.48 (dd, *J* = 3.6, 1.7 Hz, 1H), 4.95 (dd, *J* = 9.8, 4.4 Hz, 1H), 3.61 (ddd, *J* = 18.6, 9.7, 0.7 Hz, 1H), 2.86 (ddd, *J* = 18.6, 4.5, 0.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 200.1, 187.3, 152.2, 146.9, 138.1, 129.4, 128.5, 127.9, 118.8, 112.7, 47.8, 47.5; HRMS: Calculated for $C_{14}H_{12}NaO_3$ $[M+Na]^+$: 251.0679, found: 251.0681.

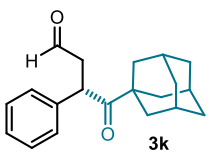
(*S*)-4-(5-bromothiophen-2-yl)-4-oxo-3-phenylbutanal (3j)



Prepared according to the *General Procedure 2* mixing diethyl 4-(5-bromothiophene-2-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1j** (0.1 mmol, 44 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 95:5 to 85:15) to give **1j** as a yellow solid (18.2 mg, 57% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, 95:5 CO_2/ACN, flow rate 2 mL/min, λ = 290 nm: τ_{Minor} = 2.9 min, τ_{Major} = 3.4 min (57% ee); $[\alpha]_D^{26}$ = +60.3 (c = 0.5, $CHCl_3$, 57% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 9.81 (s, 1H), 7.47 (d, *J* = 4.1 Hz, 1H), 7.39 – 7.24 (m, 5H), 7.03 (d, *J* = 4.1 Hz, 1H), 4.87 (dd, *J* = 9.6, 4.3 Hz, 1H), 3.60 (ddd, *J* = 18.7, 9.6, 0.6 Hz, 1H), 2.84 (dd, *J* = 18.7, 4.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 199.5, 189.8, 144.3, 137.9, 133.1, 131.2, 129.3, 128.0, 127.8, 122.9, 48.4, 47.8; HRMS: Calculated for $C_{15}H_{15}BrNaO_3S$ $[M+Na+MeOH]^+$: 376.9817, found 376.9808.

(*S*)-4-((3r,5r,7r)-adamantan-1-yl)-4-oxo-3-phenylbutanal (3k)

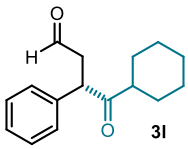


Prepared according to the *General Procedure 2* mixing diethyl 4-((1r,3r,5r,7r)adamantane-2-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1k** (0.1 mmol, 42 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 30 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 98:2 to 90:10) to give **3k** as colourless oil (28.2 mg, 94% yield, average of two runs). The enantiomeric excess was

determined by UPC^2 analysis on a Daicel Chiralpak IA column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% EtOH, flow rate 2 mL/min, λ = 215 nm: τ_{Major} = 3.2 min, τ_{Minor} = 3.0 min, (64% ee); $[\alpha]_D^{26}$ = +23.0 (c = 0.9, DCM, 64% ee). Absolute inferred in analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.70 (s, 1H), 7.38 – 7.15 (m, 5H), 4.66 (dd, *J* = 10.0, 4.1 Hz, 1H), 3.43 (ddd, *J* = 18.5, 10.0, 0.7 Hz, 1H), 2.65 (dd, *J* = 18.5, 4.1 Hz, 1H), 1.99 (p, *J* = 3.2 Hz, 3H), 1.83 – 1.63 (m, 12H).; ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 213.4, 200.1, 138.0, 129.0, 128.2, 127.2, 49.3, 47.3, 46.1, 38.8, 36.4, 29.7, 28.0; HRMS: Calculated for $C_{20}H_{24}NaO_2$ $[M+Na]^+$: 319.1669, found 319.1662.

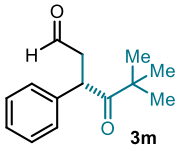
(*S*)-4-cyclohexyl-4-oxo-3-phenylbutanal (3l)



Prepared according to the *General Procedure 2* mixing diethyl 4-(cyclohexanecarbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1l** (0.1 mmol, 36 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 97:3 to 90:10) to give **3l** as a colourless oil (14.6 mg, 61% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ = 220 nm: τ_{Major} = 2.5 min, τ_{Minor} = 2.6 min, (52% ee); $[\alpha]_D^{26}$ = +50.8 (c = 0.5, $CHCl_3$, 52% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 9.76 (s, 1H), 7.40 – 7.13 (m, 5H), 4.40 (dd, *J* = 9.9, 4.1 Hz, 1H), 3.45 (ddd, *J* = 18.5, 9.9, 0.7 Hz, 1H), 2.78 – 2.58 (m, 1H), 2.50 -2.31 (m, 1H), 2.01 - 2.10 (m, 1H), 1.88 – 1.74 (m, 1H), 1.70 – 1.49 (m, 4H), 1.36 – 1.16 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 211.6, 200.0, 137.6, 129.1, 128.3, 127.6, 50.6, 49.5, 47.2, 29.5, 28.3, 25.9, 25.7, 25.2; HRMS: Calculated for $C_{16}H_{10}NaO_2$ $[M+Na]^+$: 267.1356, found 267.1348.

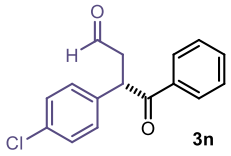
(*S*)-5,5-dimethyl-4-oxo-3-phenylhexanal (3m)



Prepared according to the *General Procedure 2* mixing diethyl 2,6-dimethyl-4-pivaloyl-1,4-dihydropyridine-3,5-dicarboxylate **1m** (0.1 mmol, 34 mg), cinnamaldehyde (0.3 mmol, 38 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 97:3 to 90:10) to give **3m** as a colourless oil (20 mg, 91% yield, average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IG column, 95:5 CO_2/ACN, flow rate 2 mL/min, λ = 218 nm: τ_{Major} = 1.90 min ,τ_{Minor} = 2.06 min, (76% ee); $[\alpha]_D^{26}$ = +113.1 (c = 0.7, DCM, 76% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 9.78 – 9.56 (m, 1H), 7.39 – 7.14 (m, 5H), 4.65 (dd, *J* = 9.9, 4.2 Hz, 1H), 3.43 (ddd, *J* = 18.6, 10.0, 0.7 Hz, 1H), 2.66 (ddd, *J* = 18.6, 4.2, 0.5 Hz, 1H), 1.10 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 214.5, 200.3, 138.5, 129.4, 128.5, 127.7, 49.7, 47.2, 45.4, 27.7; HRMS: Calculated for $C_{15}H_{22}NaO_3$ $[M+H+Na]^+$: 273.1461, found: 273.1459.

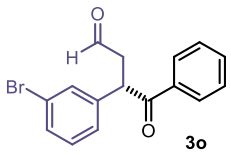
(*S*)-3-(4-chlorophenyl)-4-oxo-4-phenylbutanal (3n)



Prepared according to the *General Procedure 2* using diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), *p*-chloro cinnamaldehyde (0.15 mmol, 25 mg), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (*n*-hexane/EtOAc, gradient from 99:1 to 90:10) to give **3n** as a pale yellow oil (22.1 mg, 81% yield, 74% ee average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% CH_3CN, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm: τ_{Major} = 2.84 min, τ_{Minor} = 2.70 min. $[\alpha]_D^{28}$ = +162.2 (c = 0.40, CH_2Cl_2, 74% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.80 (s, 1 H), 7.96 – 7.91 (m, 2H), 7.50 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.29 – 7.24 (m, 2H), 7.23 – 7.18 (m, 2H), 5.12 (dd, *J* = 9.4, 4.5 Hz, 1H), 3.59 (dd, *J* = 18.6, 9.6 Hz, 1H), 2.82 (dd, *J* = 18.7, 4.5 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 199.7, 198.0, 136.9, 135.9, 133.6, 133.4, 129.6, 129.6, 129.0, 128.8, 48.2, 46.9; HRMS: Calculated for $C_{16}H_{13}ClNaO_2$ $[M+Na]^+$: 295.0496, found 295.0501.

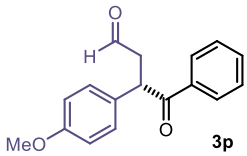
(*S*)-3-(3-bromophenyl)-4-oxo-4-phenylbutanal (3o)



Prepared according to the *General Procedure 2* using diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), *m*-bromo cinnamaldehyde (0.15 mmol, 32 mg), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (*n*-hexane/EtOAc, gradient from 99:1 to 90:10) to give **3o** as a pale yellow oil (25.0 mg, 78% yield, 74% ee average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% CH_3CN, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm: τ_{Major} = 2.9 min, τ_{Minor} = 2.7 min. $[\alpha]_D^{28}$ = +164.7 (c = 0.29, CH_2Cl_2, 74% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.79 (s, 1 H), 7.98 – 7.93 (m, 2H), 7.50 (tt, *J* = 7.3, 1.3 Hz, 1H), 7.45 – 7.34 (m, 3H), 7.35 (ddd, *J* = 7.7, 1.9, 1.4 Hz, 1H), 7.20 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.16 (t, *J* = 7.7 Hz, 1H), 5.09 (dd, *J* = 9.6, 4.3 Hz, 1H), 3.60 (dd, *J* = 18.6, 9.6 Hz, 1H), 2.83 (dd, *J* = 18.8, 4.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 199.5, 197.7, 140.6, 135.9, 133.5, 131.2, 130.9, 130.8, 129.0, 128.80, 126.9, 123.4, 48.3, 47.1; HRMS: Calculated for $C_{16}H_{13}BrNaO_2$ $[M+Na]^+$: 338.9991, found 338.9985.

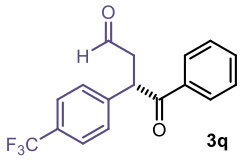
(*S*)-3-(4-methoxyphenyl)-4-oxo-4-phenylbutanal (3p)



Prepared according to the *General Procedure 2* using diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), *p*-methoxy cinnamaldehyde (0.15 mmol, 24 mg), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 99:1 to 90:10) to give **3p** as a pale yellow oil (26.0 mg, 90% yield). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% CH_3CN, flow rate 2 mL/min, column T = 40 °C, λ = 243 nm: τ_{Minor} = 3.0 min, τ_{Major} = 3.2 min. $[\alpha]_D^{28}$ = +88.6 (c = 0.95, CH_2Cl_2, 60% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 9.79 (s, 1H), 8.01 – 7.89 (m, 2H), 7.49 – 7.31 (m, 3H), 7.20 – 7.13 (m, 2H), 6.84 – 6.76 (m, 2H), 5.06 (dd, *J* = 9.4, 4.4 Hz, 1H), 3.73 (s, 3H), 3.62 – 3.48 (m, 1H), 2.80 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 200.5, 198.7, 159.2, 136.4, 133.3, 130.5, 129.5, 129.3, 128.9, 115.0, 55.6, 48.7, 47.1; HRMS: Calculated for $C_{17}H_{16}NaO_3$ $[M+Na]^+$: 291.0992, found 291.0996.

(*S*)-4-oxo-4-phenyl-3-(4-(trifluoromethyl)phenyl)butanal (3q)

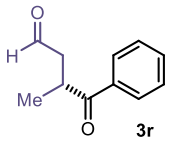


3q

Prepared according to the *General Procedure 2* using diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), *p*-trifluoromethyl cinnamaldehyde (0.15 mmol, 30 mg), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (cyclohexane/EtOAc, gradient from 99:1 to 90:10) to give **3q** as a pale yellow oil (25.0 mg, 83% yield). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, column T = 40 °C, λ = 244 nm: τ_{Minor} = 2.2 min, τ_{Major} = 2.4 min. $[\alpha]_D^{28}$ = +81.5 (c = 0.29, CH_2Cl_2, 70% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.83 (s, 1H), 8.02 – 7.91 (m, 2H), 7.65 – 7.50 (m, 3H), 7.48 – 7.35 (m, 4H), 5.24 (dd, *J* = 9.4, 4.4 Hz, 1H), 3.66 (m, 1H), 2.88 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 199.4, 197.7, 142.4, 135.8, 133.6, 130.0 (q, *J* = 32.6 Hz), 129.0, 128.8, 128.6, 126.4 (q, *J* = 3.7 Hz), 124.0 (q, *J* = 271.8 Hz), 48.2, 47.2; ^{19}F NMR (376 MHz, $CDCl_3$), δ (ppm): -65.71; HRMS: Calculated for $C_{17}H_{13}F_3NaO_2$ $[M+Na]^+$: 329.0760, found 329.0751.

(*R*)-3-methyl-4-oxo-4-phenylbutanal (3r)

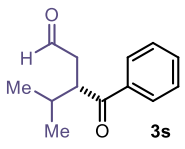


3r

Prepared according to the *General Procedure 2* using diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), (*E*)-but-2-enal (0.2 mmol, 7 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 16 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (*n*-hexane/EtOAc, gradient from 95:5 to 90:10) to give **3r** as a pale yellow oil (5.5 mg, 31% yield, 69% ee average of two runs). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% CH_3CN, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm: τ_{Major} = 2.42 min, τ_{Minor} = 2.22 min. $[\alpha]_D^{28}$ = +28.9 (c = 0.30, CH_2Cl_2, 74% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.81 (s, 1 H), 8.01 – 7.96 (m, 2H), 7.58 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.520 – 7.45 (m, 2H), 4.00 (dtd, *J* = 7.6, 7.3, 5.2 Hz, 1H), 3.16 (ddd, *J* = 18.5, 8.3, 0.5 Hz, 1H), 2.62 (ddd, *J* = 18.5, 5.3, 0.8 Hz, 1H), 1.24 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 202.6, 200.6, 135.8, 133.3, 128.9, 128.6, 47.3, 35.3, 18.1; HRMS: Calculated for $C_{12}H_{16}NaO_3$ $[M+MeOH+Na]^+$: 231.0992, found 231.0988.

(*S*)-3-benzoyl-4-methylpentanal (3s)



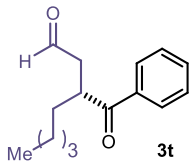
3s

Prepared according to the *General Procedure 2* using diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), (*E*)-4-methylpent-2-enal (0.2 mmol, 23 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 16 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (*n*-hexane/EtOAc, gradient from 95:5 to 90:10) to give **3s** as a pale yellow oil (10.3 mg, 51% yield, 62% ee average

of two runs). The enantiomeric excess was determined by UPC[2] analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm: τ_{Major} = 2.8 min, τ_{Minor} = 2.6 min. $[\alpha]_D^{28}$ = +74.2 (c = 0.33, CH_2Cl_2, 58% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 9.82 (s, 1 H), 8.00 – 7.95 (m, 2H), 7.57 (tt, *J* = 7.5, 1.3 Hz, 1H), 7.51 – 7.45 (m, 2H), 3.87 (ddd, *J* = 10.2, 4.8, 3.1 Hz, 1H), 3.22 (dd, *J* = 18.5, 10.2 Hz, 1H), 2.60 (dd, *J* = 18.5, 3.2 Hz, 1H), 2.11 (septd *J* = 6.8, 5.0 Hz, 1H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.81 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 202.5, 201.1, 137.2, 133.1, 128.8, 128.5, 46.0, 41.7, 30.0, 21.4, 18.5; HRMS: Calculated for $C_{13}H_{16}NaO_2$ $[M+Na]^+$: 227.1043, found 227.1032.

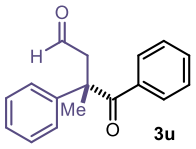
(*R*)-3-benzoyloctanal (3t)



Prepared according to the *General Procedure 2* using diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), (*E*)-oct-2-enal (0.2 mmol, 30 μL), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 16 hours (460 nm, 20 mW/cm^2). The product mixture was purified by column chromatography (*n*-hexane/EtOAc, 90:10) to give **3t** as a pale yellow oil (9.8 mg, 42% yield, 73% ee average of two runs). The enantiomeric excess was determined by UPC[2] analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm: τ_{Major} = 2.97 min, τ_{Minor} = 2.66 min. $[\alpha]_D^{28}$ = +68.1 (c = 0.25, CH_2Cl_2, 75% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 9.80 (s, 1 H), 8.00 – 7.96 (m, 2H), 7.58 (tt, *J* = 7.5, 1.3 Hz, 1H), 7.50 – 7.46 (m, 2H), 3.95 (dddd, *J* = 13.2, 7.6, 5.6, 4.8 Hz, 1H), 3.16 (dd, *J* = 18.6, 8.9 Hz, 1H), 2.66 (ddd, *J* = 18.3, 4.4, 0.7 Hz, 1H), 1.76 – 1.67 (m, 1H), 1.52 – 1.44 (m, 1H), 1.31 – 1.18 (m, 6H), 0.84 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$), δ (ppm): 202.7, 200.9, 136.6, 133.2, 128.8, 128.5, 45.5, 40.3, 32.5, 31.9, 26.9, 22.5, 14.1; HRMS: Calculated for $C_{13}H_{16}NaO_2$ $[M+Na]^+$: 227.1043, found 227.1032.

(*S*)-3-methyl-4-oxo-3,4-diphenylbutanal (3u)



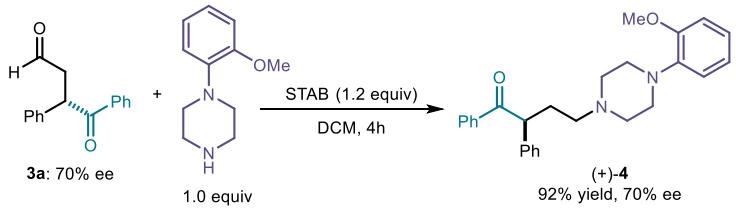
Prepared according to the *General Procedure 2* using diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), (*E*)-3-phenylbut-2-enal (0.2 mmol, 29.2 mg), trifluoroacetic acid (0.8 mmol, 6 μL) and aminocatalyst **C** (0.02 mmol, 14 mg). Time of irradiation: 40 hours (460 nm, 20 mW/cm^2). The product mixture was purified on silica gel (*n*-hexane/EtOAc, gradient from 99:1 to 90:10) to give **3u** as a pale yellow oil (5.5 mg, 39% yield, 57% ee average of two runs). The enantiomeric excess was determined by UPC[2] analysis on a Daicel Chiralpak IG column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm: τ_{Major} = 5.24 min, τ_{Minor} = 5.15 min. $[\alpha]_D^{25}$ = +214 (c = 0.27, CH_2Cl_2, 57% ee). Absolute configuration inferred in analogy to compound **3a**.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 9.69 (t, *J* = 2.2 Hz, 1 H), 7.49 – 7.45 (m, 2H), 7.43 – 7.38 (m, 3H), 7.37 – 7.30 (m, 3H), 7.27 – 7.22 (m, 2H), 3.08 (dd, *J* = 15.9, 2.2 Hz, 1H), 2.82 (dd, *J* = 16.0, 2.2 Hz, 1H), 1.83 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$), δ (ppm): 202.2, 201.2, 142.4, 135.8, 132.3, 129.8, 129.5, 128.3, 127.8, 126.2, 54.8, 53.7, 23.6; HRMS: Calculated for $C_{17}H_{16}NaO_2$ $[M+Na]^+$: 275.1043, found 275.1052.

C.3 Scale up Procedure for the synthesis of 3a

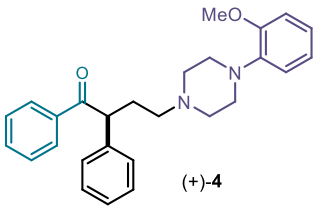
To a 8 mL vial, **1a** (357 mg, 1 mmol, 1 eq.), the amino catalyst **C** (140 mg, 0.2 mmol, 0.2 eq.) and cinnamaldehyde **2a** (0.38 mL, 3 mmol, 3 eq.) were added. The vial was put under vacuum and backfilled with argon three times and finally a TFA solution in CH_3CN degassed with argon (2 mL, 0.2 M) was added. The vial was sealed with parafilm and placed inside a steel reactor fixed over an aluminum block equipped with a High Power single LED (λ = 460 nm), irradiance = 20 mW/cm^2 as controlled by external power supply. The temperature was kept at -15 °C using a chiller connected to the steel reactor. To prevent moisture condensation, the reactor was placed inside a glass bell, which assured continuous air flow during the whole experiment. The reaction was irradiated at -15 °C for 48 h. Finally, the solvent was evaporated on the rotary evaporator, the residue was dissolved in DCM and filtered through a plug of silica to remove pyridine byproduct and unreacted DHP. The silica was washed with 500 mL of DCM. The washings were combined and the solvent was removed by rotary evaporator. The mixture purified by flash chromatography gradient from Hex 95% - EtOAc 5% to Hex 85% - EtOAc 15%) to get product **3a** as yellow solids (178 mg, 74% yield, 70% ee).

C.4 Synthesis of (*S*)-(+)-4-(4-(2-methoxyphenyl)piperazin-1-yl)-1,2-diphenylbutan-1-one (4)



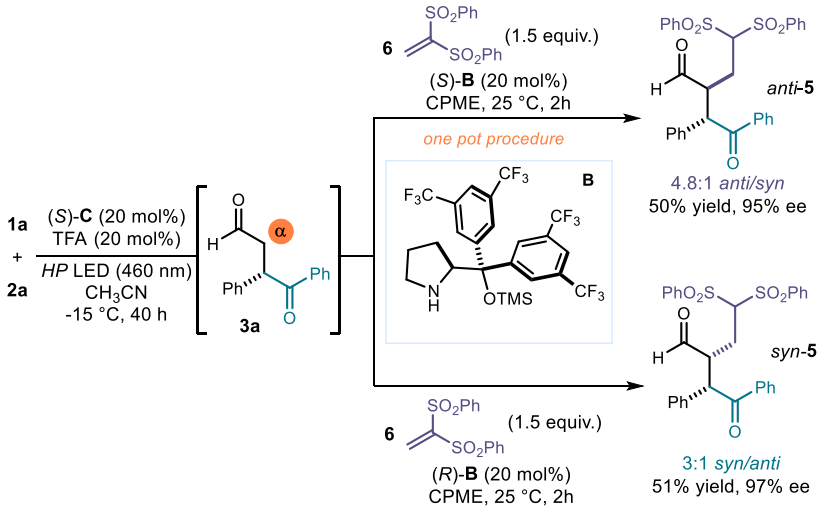
Scheme S2. Synthesis of serotonin 5HT$_{1A}$ receptor antagonist **4**; STAB = sodium triacetoxyborohydride.

To a 10 mL round bottom flask, equipped with a magnetic stirrer, **3a** (100 mg, 0.42 mmol, 1.0 eq.) was added, followed by DCM (1 mL) and 1-(2-methoxyphenyl)piperazine (97 mg, 0.5 mmol, 1.2 eq.). Sodium triacetoxyborohydride (107 mg, 0.5 mmol, 1.2 eq.) was added in portions at 0 ^oC and the mixture was allowed to warm to r.t. and stirred under nitrogen for 4 h, monitored by TLC. After completion, the reaction was quenched with aq. $NaHCO_3$ (sat., 1 mL) and the product was extracted by diethyl ether (3 x 25 mL), washed with water (25 mL), brine (25 mL) and dried over anhydrous Na_2SO_4. The ether extracts were combined and the solvent was removed by rotary evaporator. The mixture was purified by silica chromatography (cyclohexane/EtOAc, 70:30) to get product **4** as a white solid (160 mg, 92% yield, 70% ee). Enantiomeric excess was determined by UPC^2 analysis using a Daicel Chiralpak IC chiral column, 85:15 CO_2/EtOH, flow rate 2 mL/min, λ = 242 nm: τ_{Minor} = 3.02 min, τ_{Major} = 3.69 min. $[\alpha]_D^{27}$ = +52 (c = 1.0, CH_2Cl_2, 70% ee). Absolute configuration determined in comparison to compound **3a**.



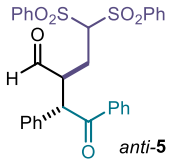
^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 8.97 – 7.94 (m, 2H), 7.52 - 7.17 (m, 8H), 7.04-6.83 (m, 4H), 7.04 – 6.83 (m, 4H), 4.74 (t, *J* = 6.7 Hz, 1H), 3.86 (s, 3H), 3.07 (bs, 4H), 2.76 (bs, 4H), 2.61 – 2.43 (m, 3H), 2.01 – 2.13 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 199.3, 175.7, 152.2, 141.0, 139.4, 136.8, 132.8, 129.0, 128.8, 128.5, 128.2, 127.1, 123.1, 121.0, 118.3, 111.2, 55.9, 55.4, 52.8, 51.4, 49.9, 22.1.

C.5 One-pot Preparation of 2,3-Disubstituted 1,4-dicarbonyls (*anti*-5, *syn*-5)



Scheme S3. One-pot stereodivergent synthesis of 2,3-difunctionalized 1,4-dicarbonyl compounds.

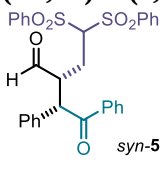
(2*S*,3*S*)-2-(2,2-bis(phenylsulfonyl)ethyl)-4-oxo-3,4-diphenylbutanal (*anti*-5)



The radical conjugate addition was performed following the *General Procedure 2* mixing diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), cinnamaldehyde (0.3 mmol, 38 µL), trifluoroacetic acid (0.2 mmol, 1.5 µL) and aminocatalyst (*S*)-**C** (0.02 mmol, 14 mg). After an irradiation time of 40 hours (460 nm, 20 mW/cm^2), the reaction was allowed to reach room temperature. The enamine specific aminocatalyst (*S*)-**B** (0.02 mmol, 12 mg), CPME (1 mL) and 1,1-bis(phenylsulfonyl)ethylene **6** (0.15 mmol, 46 mg) were added in the order and the reaction stirred for 2 h at room temperature. The crude mixture was filtered through a pad of neutral silica, which was then washed with EtOAc, and the solvent was removed under reduced pressure. The diastereomeric ratio (dr) was determined to be 4.8:1 (*anti/syn*) by ^{1}H NMR analysis of the crude mixture. The crude was first purified by flash chromatography on neutral silica gel (Hex/EtOAc, gradient from 8:2 to 7:3) and then by preparative TLC (hexane:EtOAc, 7:3, R_f = 0.21), to afford *anti*-**5** as a colorless oil (27.3 mg, 50% yield). The enantiomeric excess was determined by UPC^2 analysis on a Daicel Chiralpak IA column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ = 240 nm: *Major diastereomer*: τ_{Major} = 6.1 min, τ_{Minor} = 6.4 min; minor diastereomer (-42% ee): τ_{Major} = 6.7 min, τ_{Minor} = 7.2 min. $[\alpha]_D^{24}$ = +178.7 (c = 0.26, CH_2Cl_2, 95% ee_{anti}, 4.8:1 *anti*/*syn*).

^{1}H NMR (500 MHz, CD_3CN), δ (ppm): 9.54 (d, *J* = 1.2 Hz, 1H), 7.89-7.84 (m, 4H), 7.79-7.75 (m, 3H), 7.70-7.66 (tt, 7.6, 1.3, 1H), 7.64-7.59 (m), 7.57-7.51 (m), 7.43-7.39 (m), 7.34-7.26 (m), 7.22-7.19 (m), 5.14 (d, *J* = 6.9 Hz, 1H), 4.97 (dd, *J* = 6.9, 5.4 Hz, 1H), 3.66-3.61 (m, 1H), 2.77 (ddd, *J* = 15.7, 8.2, 5.3 Hz, 1H), 2.18 (ddd, *J* = 15.9, 6.9, 4.8 Hz, 1H); ^{13}C NMR (126 MHz, CD_3CN), δ (ppm): 203.3, 199.2, 138.9, 138.4, 136.6, 136.4, 135.9, 135.8, 134.5, 130.4, 130.4, 130.3, 130.3, 130.3, 130.2, 129.9, 129.7, 129.0, 81.1, 55.6, 51.6, 24.1; HRMS: Calculated for $C_{30}H_{26}NaO_6S_2$ $[M+Na]^+$: 569.1063, found: 569.1067.

(2*R*,3*S*)-2-(2,2-bis(phenylsulfonyl)ethyl)-4-oxo-3,4-diphenylbutanal (*syn*-5)



The radical conjugate addition was performed following the *General Procedure 2* mixing diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate **1a** (0.1 mmol, 36 mg), cinnamaldehyde (0.3 mmol, 38 µL), trifluoroacetic acid (0.2 mmol, 1.5 µL) and aminocatalyst (*S*)-**C** (0.02 mmol, 14 mg). After an irradiation time of 40 hours (460 nm, 20 mW/cm^2), the reaction was allowed to reach room temperature. The aminocatalyst (*R*)-**B** (0.02 mmol, 12 mg), CPME (1 mL) and 1,1-

bis(phenylsulfonyl)ethylene **6** (0.15 mmol, 46 mg) were added in the order and the reaction stirred for 2 h at room temperature. The crude mixture was filtered through a pad of neutral silica, which was then washed with EtOAc, and the solvent was removed under reduced pressure. The d.r. was determined to be 3:1 (*syn/anti*) by ^{1}H NMR analysis of the crude mixture. The crude was purified first by flash chromatography on neutral silica gel (Hex/EtOAc, gradient from 8:2 to 7:3) and then by preparative TLC (hexane:EtOAc, 7:3, R_f = 0.21), to give *syn*-**5** as a colorless oil (27.9 mg, 51% yield). The enantiomeric excess was determined by UPC[2] analysis on a Daicel Chiralpak IA column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ = 240 nm: *syn diastereomer*: τ_{Major} = 7.24 min, τ_{Minor} = 6.72 min; Minor diastereomer (-17% ee): τ_{Major} = 6.42 min, τ_{Minor} = 6.12 min. $[\alpha]_D^{24}$ = +146 (c = 0.3, CH_2Cl_2, 97% ee, 3:1 *syn/anti*).

^{1}H NMR (400 MHz, CD_3CN), δ (ppm): 9.66 (d, *J* = 1.2 Hz, 1H), 7.92-7.47 (m, 13H), 7.45-7.25 (m, 7H), 5.05 (d, *J* = 9.0 Hz, 1H), 4.89 (dd, *J* = 6.9, 4.7 Hz, 1H), 3.61-3.54 (m, 1H), 2.52 (ddd, *J* = 14.2, 9.5, 4.7 Hz, 1H), 2.00 (ddd, *J* = 15.9, 6.8, 4.8 Hz, 1H); ^{13}C NMR (126 MHz, CD_3CN), δ (ppm): 202.8, 199.3, 138.0, 136.8, 136.7, 136.4, 135.8, 135.7, 134.4, 130.5, 130.4, 130.4, 130.3, 130.3, 130.2, 130.1, 129.7, 129.1, 80.3, 54.9, 52.2, 24.4; HRMS: Calculated for $C_{30}H_{25}O_6S_2$ [M-H]$^-$: 545.1098, found: 545.1101.

The relative configuration of products **5** was inferred considering the known absolute configuration of intermediate **3a**, formed upon iminium-ion-mediated acyl radical conjugate addition, and on the basis of the stereochemical induction inferred by the silyl prolinol catalyst of type **B** in the enamine-mediated addition of aldehydes to 1,1-bis(phenylsulfonyl)ethylene **6**, as reported by Alexakis *et al*.[6]

D. Cyclic Voltammetry

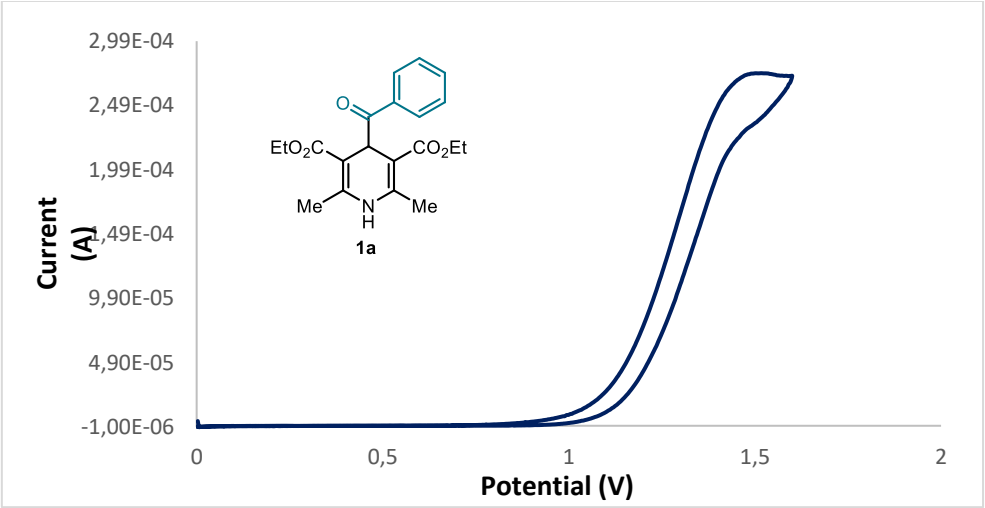


Figure S2. Cyclic voltammogram of **1a** [0.02 M] in [0.1 M] $TBAPF_6$ in CH_3CN. Sweep rate: 20 mV/s. glassy carbon working electrode, Ag/AgCl (KCl 3.5 M) reference electrode, Pt wire auxiliary electrode. Irreversible oxidation. $E_p^A = E_{ox}$ (**1a**$^{\cdot+}$/**1a**) = +1.51 V; E_p^A is the anodic peak potential, while E_{ox} value describes the electrochemical properties of **1a**.

E. UV-vis Absorption Spectra

Solutions at different concentrations of **1a**, obtained by opportunely diluting an original stock solution ([**1a**] = 0.3 mM in CH_3CN) with acetonitrile, were introduced to a 1 cm path length quartz cuvette equipped with a Teflon® septum. The solution were analyzed using a Shimadzu 2401PC UV-Vis spectrophotometer. The absorption spectra (Figure S3) show a typical Lambert-Beer linear correlation with the concentrations (Figure S4).

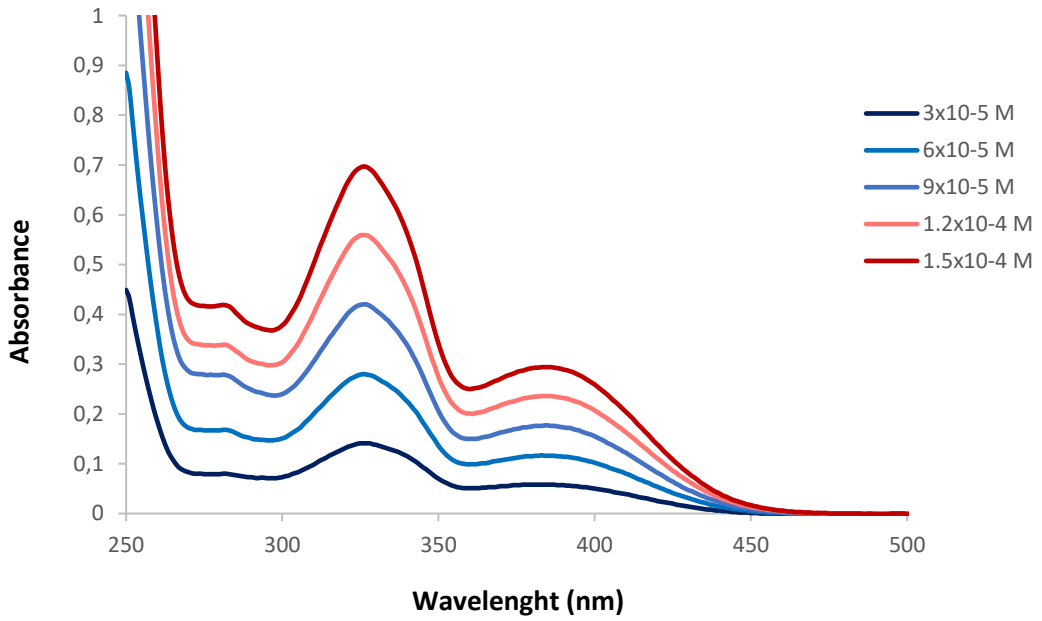


Figure S3. Absorption spectra of **1a** at different concentrations in CH_3CN. The tail wavelength of absorption was considered at 475 nm.

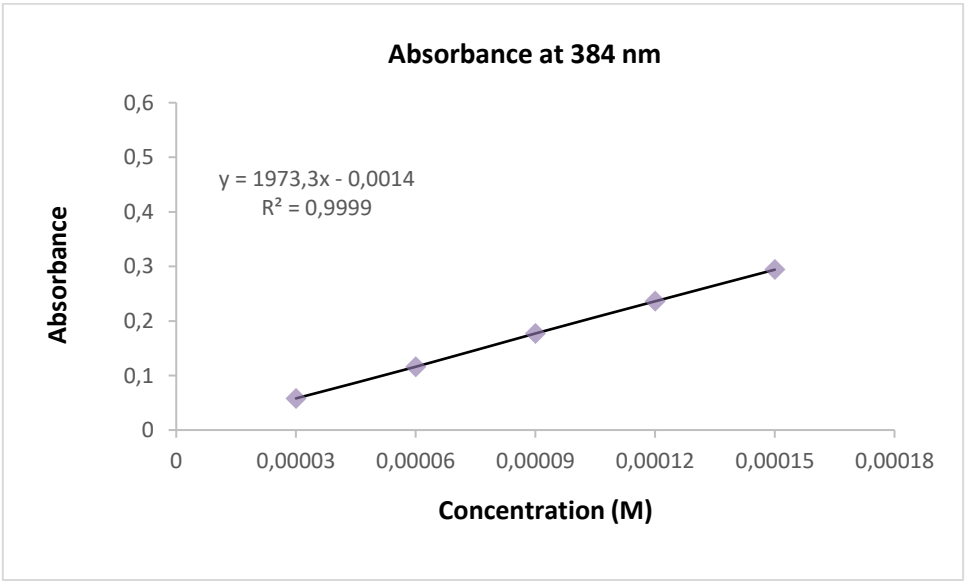


Figure S4. Lambert-Beer linear correlation between absorbance and concentration at 384 nm for **1a**. The slope of the line is the molar extinction coefficient ε at 384 nm ($M^{-1}cm^{-1}$).

F. Evaluation of the Excited State Potential of 1a

Using the data collected from the cyclic voltammetry studies (Section D) and from the absorption spectra (Section E) of the **1a**, we could estimate the redox potential of the excited **1a** employing the following Equation 1:

$$E(\mathbf{1a}^{\cdot+}/\mathbf{1a^*}) = E(\mathbf{1a}^{\cdot+}/\mathbf{1a}) - E_{0\text{-}0}(\mathbf{1a^*}/\mathbf{1a}) \quad \text{[Eq. 1]}$$

Since the electrochemical oxidation of **1a** was irreversible (see Figure S2), the irreversible peak potential E_p^{Anode} was used for ($\mathbf{1a}^{\cdot+}$/**1a**). $E_{0\text{-}0}$(**1a***/**1a**), which is the excited state energy of the **1a**, was estimated spectroscopically from the position of the long wavelength tail of the absorption spectrum (Figure S3) recorded in acetonitrile, the solvent used for the electrochemical analysis.

For **1a**, the E_p^{Anode}, which provides the $E(\mathbf{1a}^{\cdot+}/\mathbf{1a})$, is +1.51 V (Figure S2), while the position of the long wavelength tail of the absorption spectrum corresponds to 475 nm (Figure S3), which translates into an $E_{0\text{-}0}$(**1a***/**1a**) of 2.61 eV.

$$E(\mathbf{1a}^{\cdot+}/\mathbf{1a^*}) = +1.51 - 2.61 = -1.10 \text{ V (vs Ag/AgCl)}$$

G. EPR Experiment

Continuous wave (CW) EPR spectra were obtained on a Bruker EMX Micro X-band spectrometer operating at 9.3495 GHz using a Bruker ER 1164 HS resonator and equipped with a Nitrogen Dewar Flask supplied from Wildman-LabGlass. The spectral data were collected at 77 K with the following spectrometer settings: microwave power = 0.5 mW; center field = 3348 G, sweep width = 1000 G, sweep time = 30 s, modulation frequency = 100 KHz, modulation amplitude = 5 G, power attenuation = 25 dB, time constant = 0.01 ms.

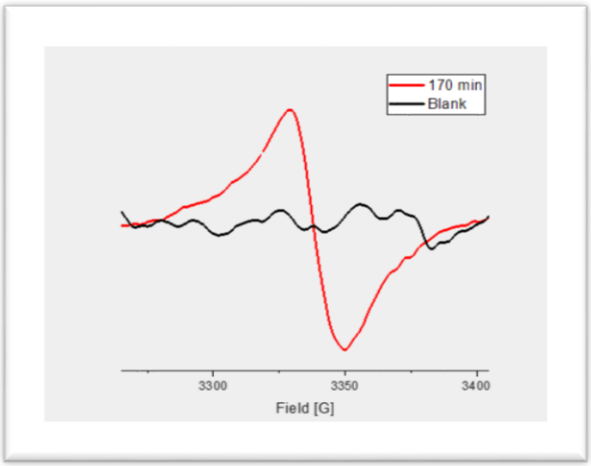


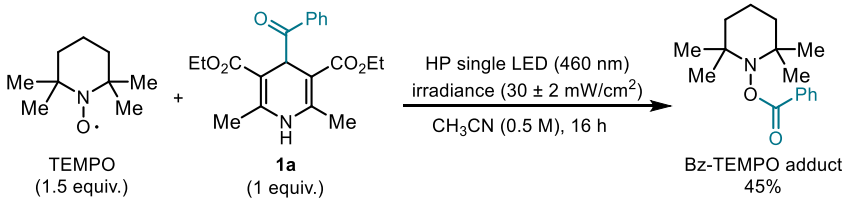
Figure S5. EPR signal of Bz-DHP **1a** at 170 min of acquisition.

The samples were prepared as follow: **1a** (36 mg, 0.1 mmol) was dissolved in CH_3CN (1 mL, [**1a**] = 100 mM). This solution was transferred into EPR Low Pressure/Vacuum Tube (more information [here]). The reaction mixture was degassed via a freeze-pump-thaw procedure, and kept frozen with liquid nitrogen under argon in the EPR tube. The tube was then inserted inside the EPR cavity for the EPR measurements.

Before acquiring the spectra, a 460 nm high power LED purchased from LEDENGIN was used to irradiate the samples. The LED was connected to the EPR cavity using an optical fiber supplied with the equipment from Bruker. EPR spectra were recorded after 0 and 170 minutes of irradiation

(Figure S5). The spectrum at 170 min showed an isotropic X-band absorption and afforded a *g*-value of 2.0008, which is consistent with literature data for the characterization of acyl radicals.[7]

H. Radical Trapping Experiment



Bz-DHP **1a** (36 mg, 0.1 mmol) and TEMPO (16 mg, 0.1 mmol) were transferred in a vial which was put under vacuum and backfilled with argon three times. Then, CH_3CN degassed with argon (200 µL, 0.5 M) was added and the reaction placed above a 460 nm high-power single LED (λ = 460 nm, irradiance = 30 mW/cm^2, as controlled by an external power supply). The reaction was stirred under light irradiation at ambient temperature for 16 hours. ^{1}H NMR analysis of the reaction crude mixture revealed the formation of Bz-TEMPO adduct (45%), as determined by adding trichloroethylene as internal standard. Diagnostic signals: ^{1}H NMR (400 MHz) δ (ppm): 8.05 (d, *J* = 8.0 Hz, 2H), 7.56 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.48-7.42 (m, 2H), 1.26 (s, 6H), 1.10 (s, 6H). The spectroscopic data are in agreement with those already reported in the literature.[8] The presence of benzaldehyde (41%) was also detected, which is likely arising by hydrogen abstraction by the benzoyl radical.

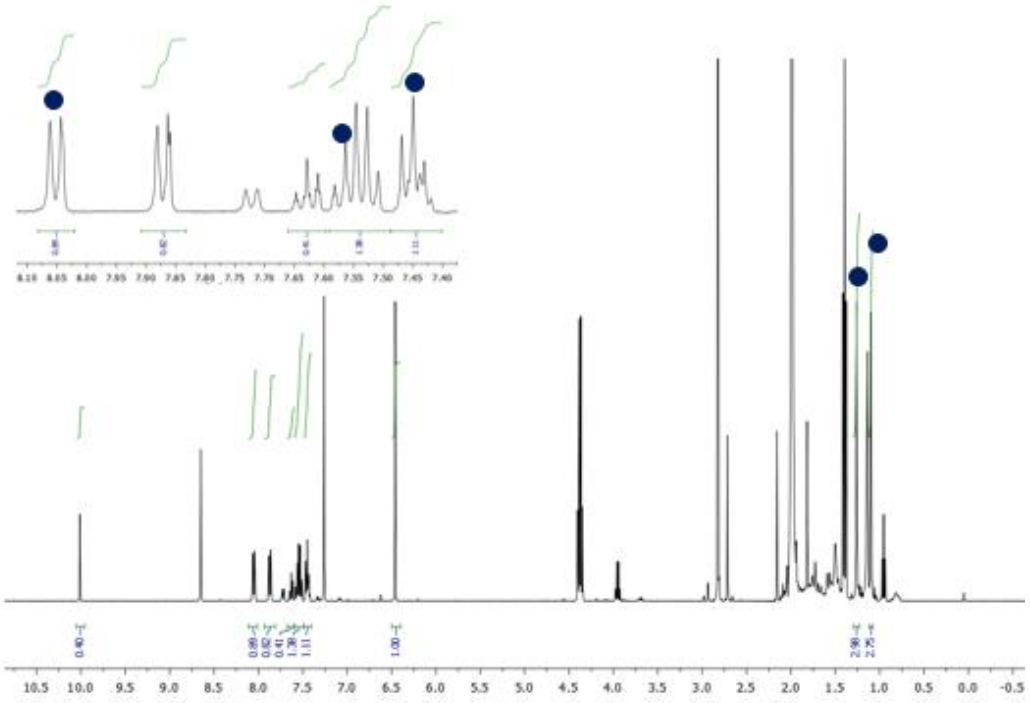


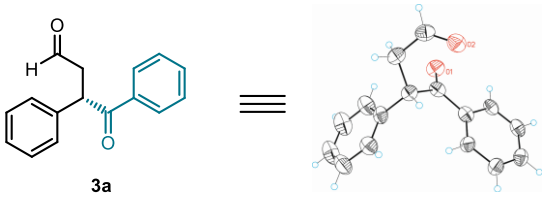
Figure S6. ^{1}H NMR spectrum of the crude reaction mixture after 16 h of irradiation of **1a** in presence of TEMPO. The Bz-TEMPO adduct was formed in 45% yield as determined by using trichloroethylene as internal standard. The diagnostic signals of Bz-TEMPO adduct are indicated by the blue circles.

The presence of the Bz-TEMPO adduct was further confirmed by GC-MS analysis: 5 min at 50 °C, followed by a gradient until 300 °C in 12.5 min, then 15 min at 300 °C; τ = 12.908 min. MS: *m/z* (%): 261.1 (0.2), 246.1 (17.3), 126.1 (4.6), 105.0 (100), 77.0 (14.1), 55.1 (13.1).

I. X-ray Crystallographic Data

Single Crystal X-ray Diffraction Data for compound 3a.

Crystals of the compound **3a** were obtained as 91:1 *S*:*R* ratio by slow evaporation of a cyclohexane solution. *Data Collection*. Measurements were made on a Bruker DUO diffractometer equipped with an APEX II detector using Cu Kα radiation from a Microfocus source E025 IuS anode. Cryostream Plus low temperature device (T = 100K). Full-sphere data collection was used with φ and ω scans. According to the absolute structure parameters (Flack and Parsons parameters), the absolute configuration of **1a** are in good agreement with the obtained ee (91:1 S:R).



CCDC1867805

Supplementary Table 1. Crystal data and structure refinement for **3a**. CCDC1867805

Empirical formula	C16 H14 O2	
Formula weight	238.27	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 5.3671(3)Å	α= 90°.
	b = 9.1746(7)Å	β = 90°.
	c = 25.5676(16)Å	γ = 90°.
Volume	1258.97(14) $Å^3$	
Z	4	
Density (calculated)	1.257 Mg/m^3	
Absorption coefficient	0.626 mm^{-1}	
F(000)	504	
Crystal size	? x ? x ? mm^3	
Theta range for data collection	3.457 to 66.583°.	
Index ranges	-6<=h<=6,-9<=k<=10,-30<=l<=28	
Reflections collected	5224	
Independent reflections	2186[R(int) = 0.0395]	
Completeness to theta =66.583°	99.6%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.940 and 0.649	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2186/ 303/ 302	
Goodness-of-fit on F^2	1.117	
Final R indices [I>2sigma(I)]	R1 = 0.0595, wR2 = 0.1514	
R indices (all data)	R1 = 0.0615, wR2 = 0.1527	
Flack parameter	x =0.19(19)	
Largest diff. peak and hole	0.320 and -0.210 e.$Å^{-3}$	

J. Proposed Mechanism

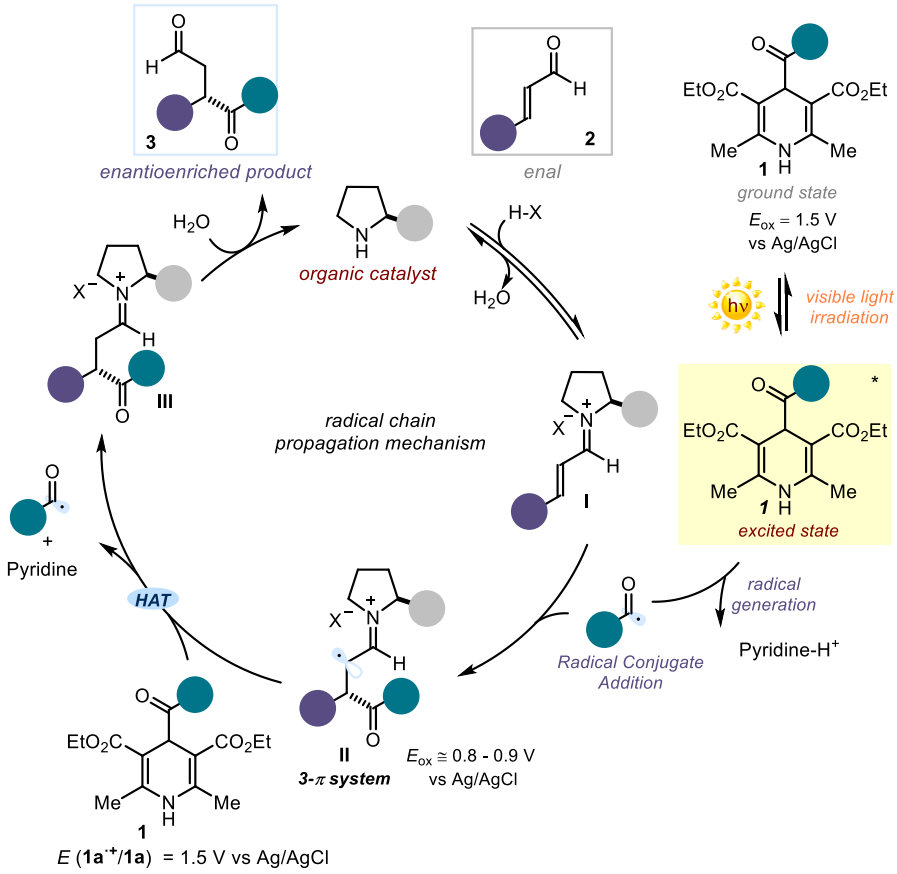
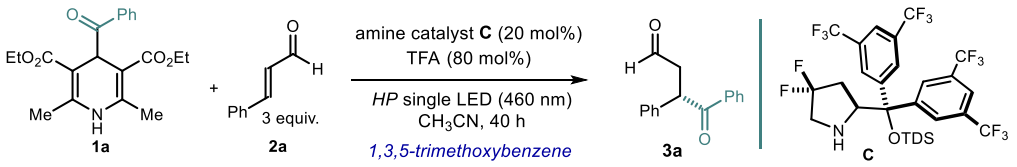


Figure S7. **Proposed mechanism.** Upon visible light excitation of **1**, the emerging acyl radical is trapped by the ground-state iminium ion **I**, affording the 3-π system **II**. This intermediate could then participate in a hydrogen atom transfer (HAT) process with a second molecule of **1a**. This induces the generation of a new acyl radical and the closed shell intermediate **III**. The possibility of a SET event from a second molecule of DHP **1** (E (**1a**$^{\cdot+}$/**1a**) = 1.5 V vs Ag/AgCl for **1a**, see Section D) to the 3-π intermediate **II** (estimated E (**II**/**II**$^{\cdot-}$) = 0.8-0.9 V vs Ag/AgCl)[1] was excluded because thermodynamically unfeasible.

Light on/off experiments.

The model reaction between cinnamaldehyde **2a** and Bz-DHP **1a** catalyzed by amine **C** was performed under optimized conditions on 0.2 mmol scale in the presence of 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) as the internal standard.



Irradiation was provided by a single High Power LED (λ = 460 nm, irradiance = 20 mW/cm^2), which was alternatively turned on and off upon intervals of 1 hour, during a total of 6 hours. Aliquots of the reaction were collected after each period of irradiation or dark and quenched by filtering on a small silica gel pad eluting with $CDCl_3$ (0.6 mL). Finally, the samples were analyzed by ^{1}H NMR to get the corresponding yields.

The results, depicted in Figure S8, show that the reaction does not proceed at all in absence of irradiation, while the reactivity is restored when switching the light on again. This experiment

unambiguously demonstrates that light is a fundamental requisite for the reaction to occur. However, the fact that the reaction is terminated in absence of irradiation is not sufficient to discard a chain propagation mechanism. Indeed, a similar trend has been observed for on/off experiments even for reactions known to proceed through relatively long radical chains (average chain length of 150).[9] This is because radical chains are likely to decay too fast to be detected on lab scale times.[10] Accordingly, also in the present reaction, fast radical chain terminations could explain the observed behavior, which can be therefore consistent with the mechanism proposed in Figure S7.

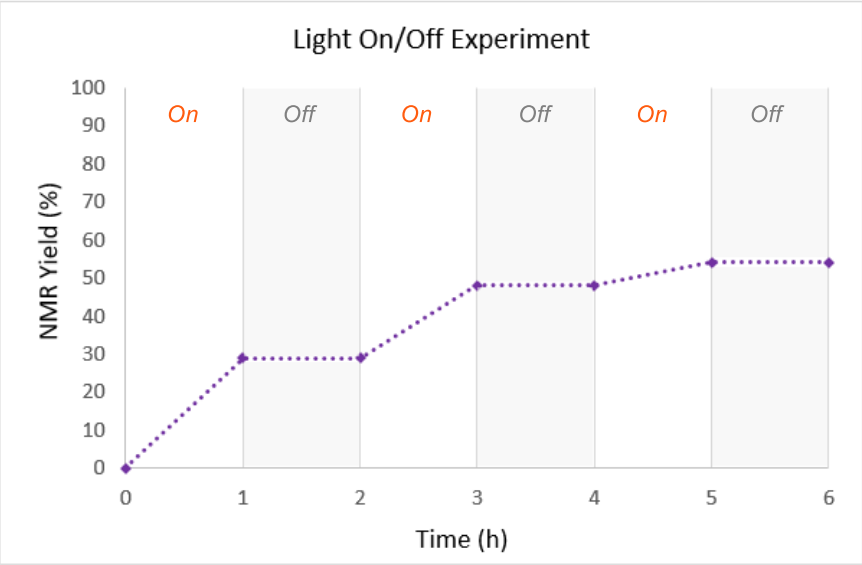


Figure S8. Light on/off experiments.

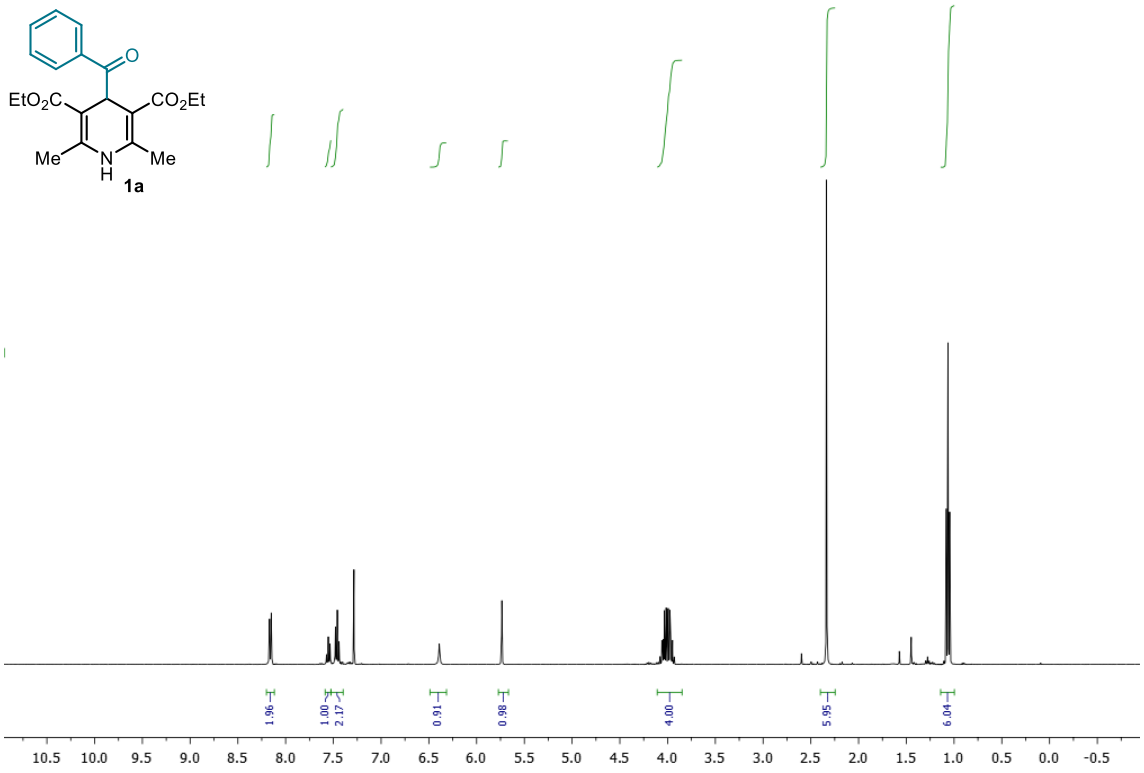
K. References

1. M. Silvi, C. Verrier, Y. P. Rey, L. Buzzetti, P. Melchiorre, *Nat. Chem.* **2017** *9*, 868.
2. D. J. Miller, F. Yu, N. J. Young, R. K. Allemann, *Org. Biomol. Chem.* **2007**, *5*, 3287.
3. H. L. Riley, J. F. Morley, N. A. Child Friend, *J. Chem. Soc.* **1932**, 1875.
4. R. C. Fuson, H. Gray, J. J. Gouza, *J. Am. Chem. Soc.* **1939,** *61*, 1937.
5. G. B. Barlin, L. P. Davies, S. J. Ireland, J. K. Zhang, *Aust. J. Chem.* **1992**, *48*, 1281.
6. S. Sulzer-Mossé, A. Alexakis, J. Mareda, G. Bollot, G. Bernardinelli, Y. Filinchuk, *Chem. Eur. J.* **2009**, *15*, 3204.
7. P. J. Krusic, T. A. Rettig, *J. Am. Chem. Soc.* **1970**, *92*, 722.
8. K. Jing, J.-P. Yao, Z.-Y. Li, Q.-L. Li, H.-S. Lin, G.-W. Wang, *J. Org. Chem.* **2017**, *82*, 12715.
9. M. A. Cismesia, T. P. Yoon, *Chem. Sci.* **2015**, *6*, 5426.
10. A. Studer, D. P. Curran, *Angew. Chem. Int. Ed.* **2016**, *55*, 58.

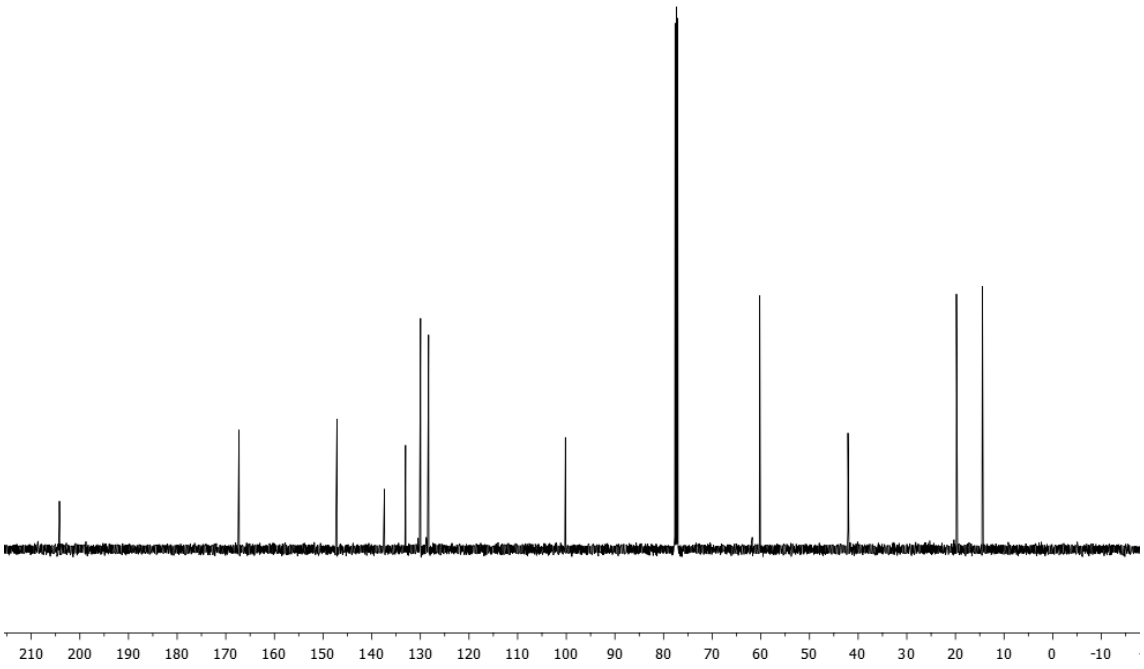
L. NMR Spectra

Diethyl 4-benzoyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1a)

^{1}H NMR (500 MHz, $CDCl_3$)

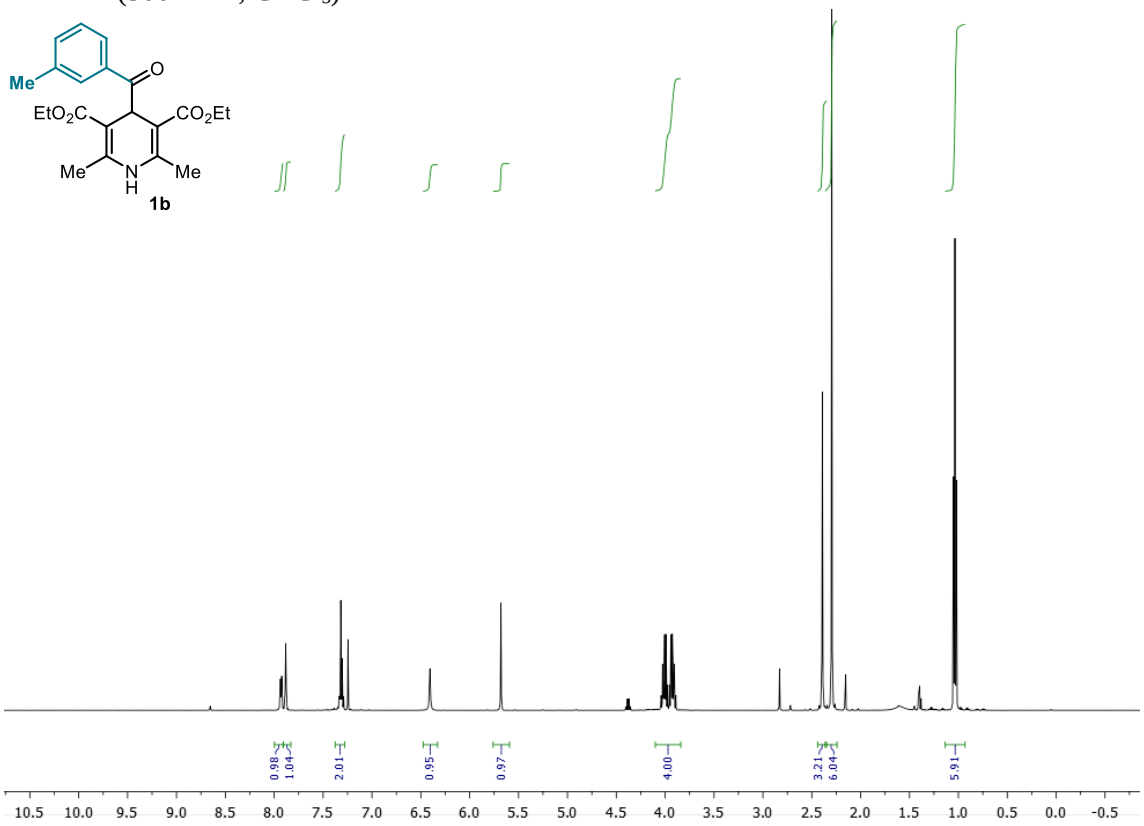


^{13}C NMR (126 MHz, $CDCl_3$)

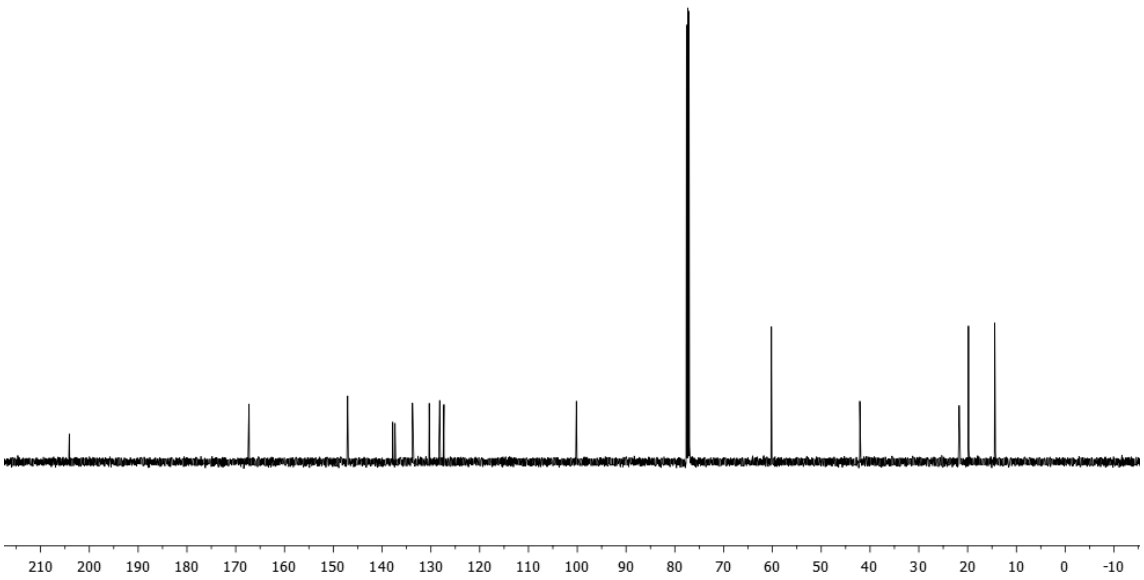


Diethyl 2,6-dimethyl-4-(3-methylbenzoyl)-1,4-dihydropyridine-3,5-dicarboxylate (1b)

^{1}H NMR (500 MHz, $CDCl_3$)

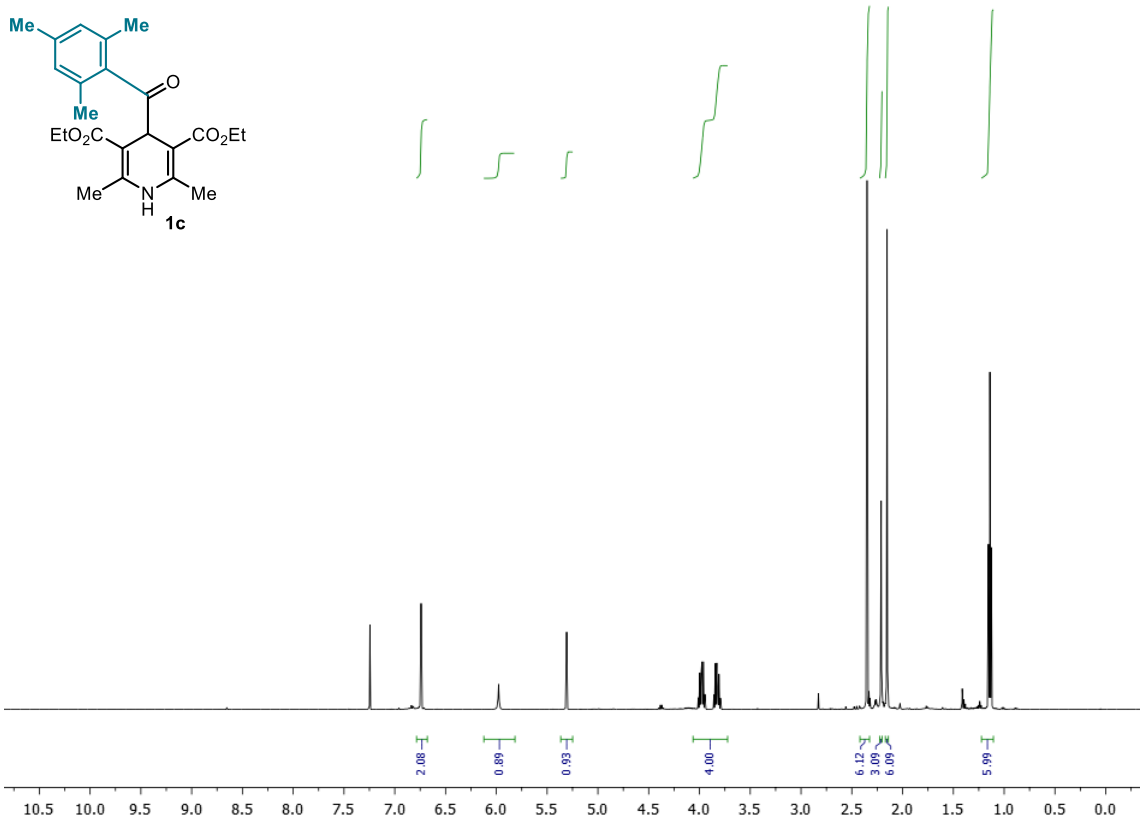


^{13}C NMR (126 MHz, $CDCl_3$)

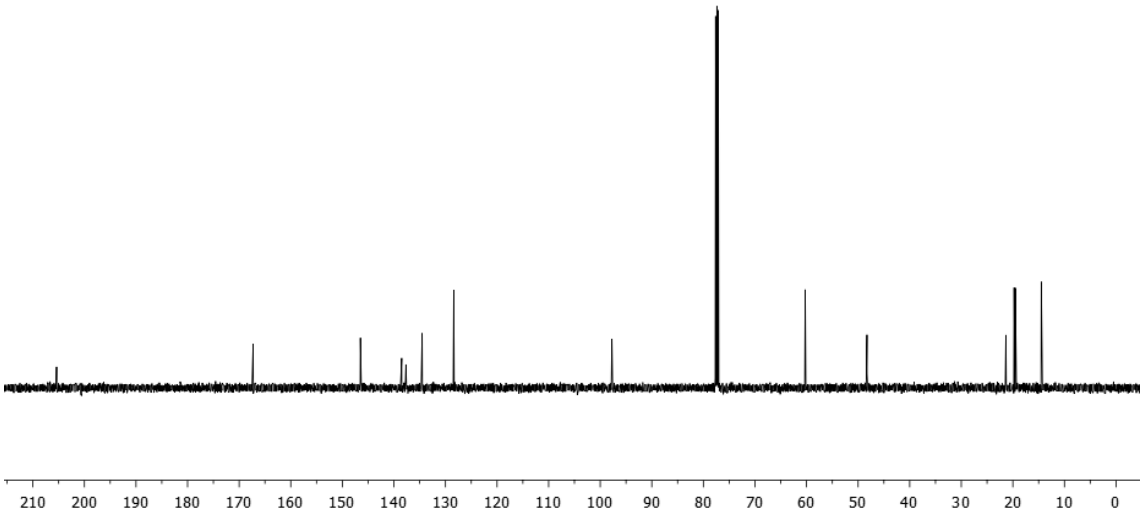


Diethyl 2,6-dimethyl-4-(2,4,6-trimethylbenzoyl)-1,4-dihydropyridine-3,5-dicarboxylate (1c)

^{1}H NMR (400 MHz, $CDCl_3$)

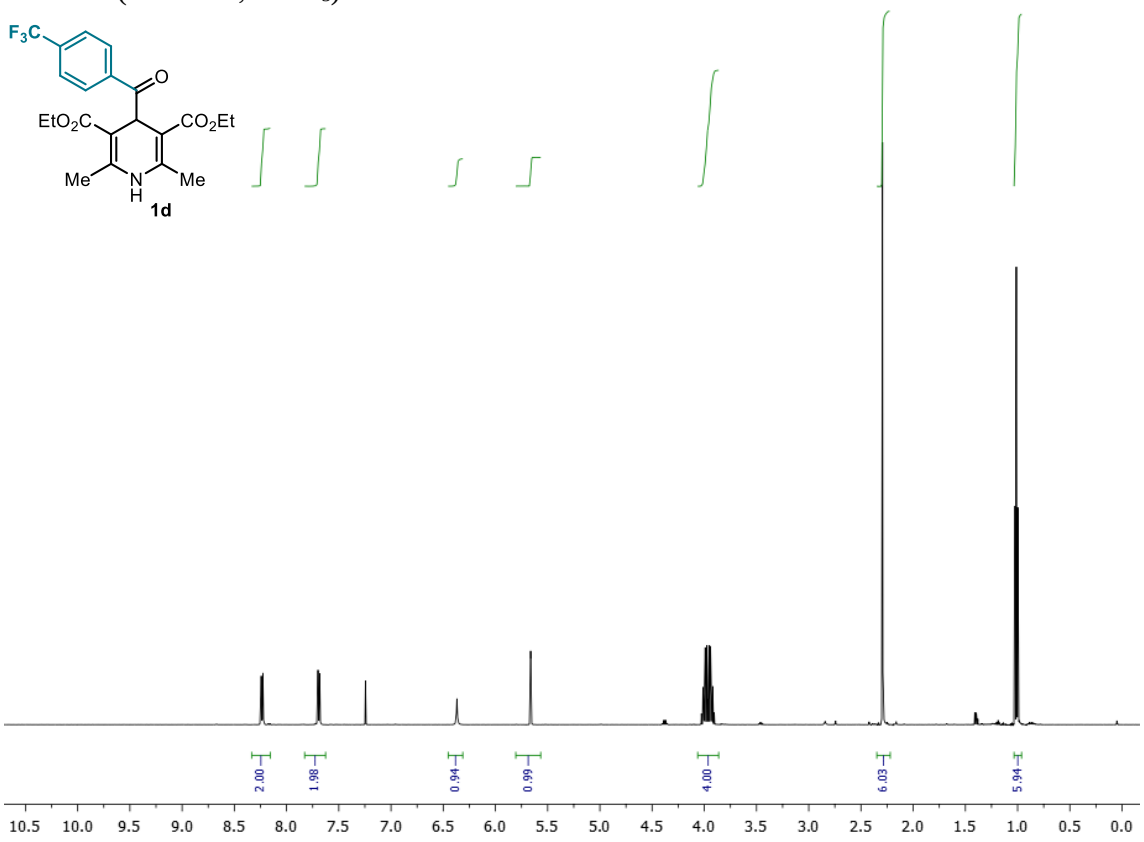


^{13}C NMR (126 MHz, $CDCl_3$)

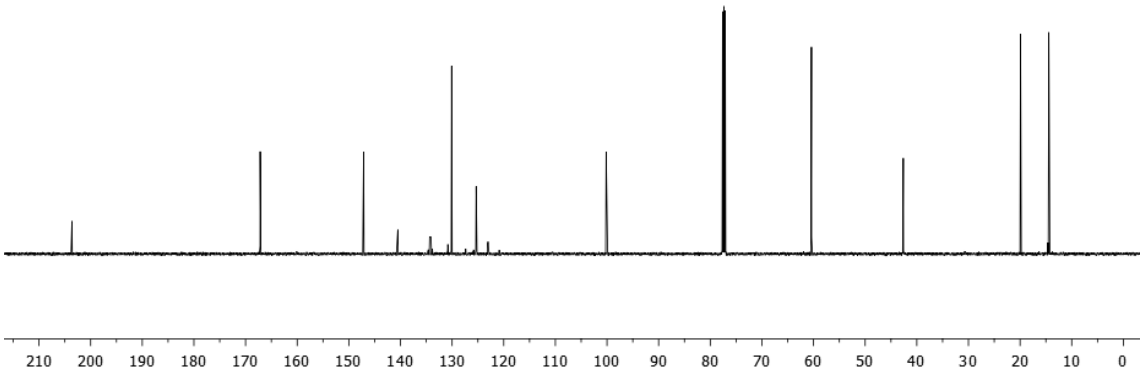


Diethyl 2,6-dimethyl-4-(4-(trifluoromethyl)benzoyl)-1,4-dihydropyridine-3,5-dicarboxylate (1d)

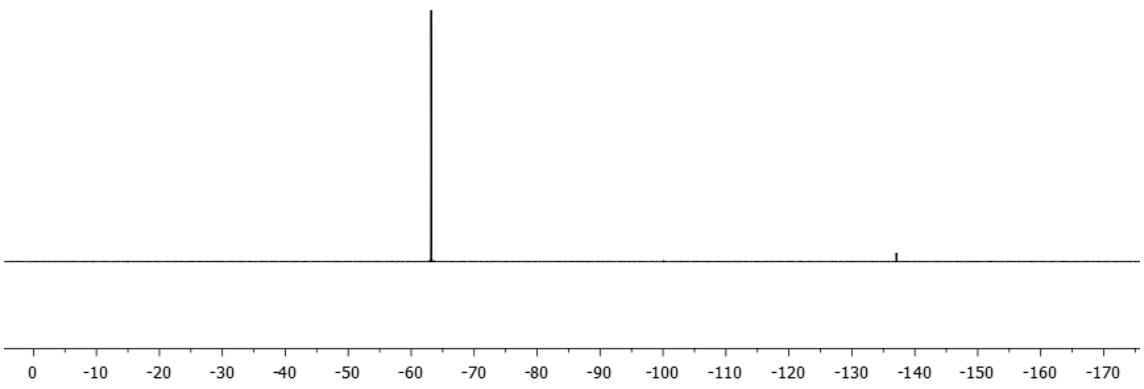
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

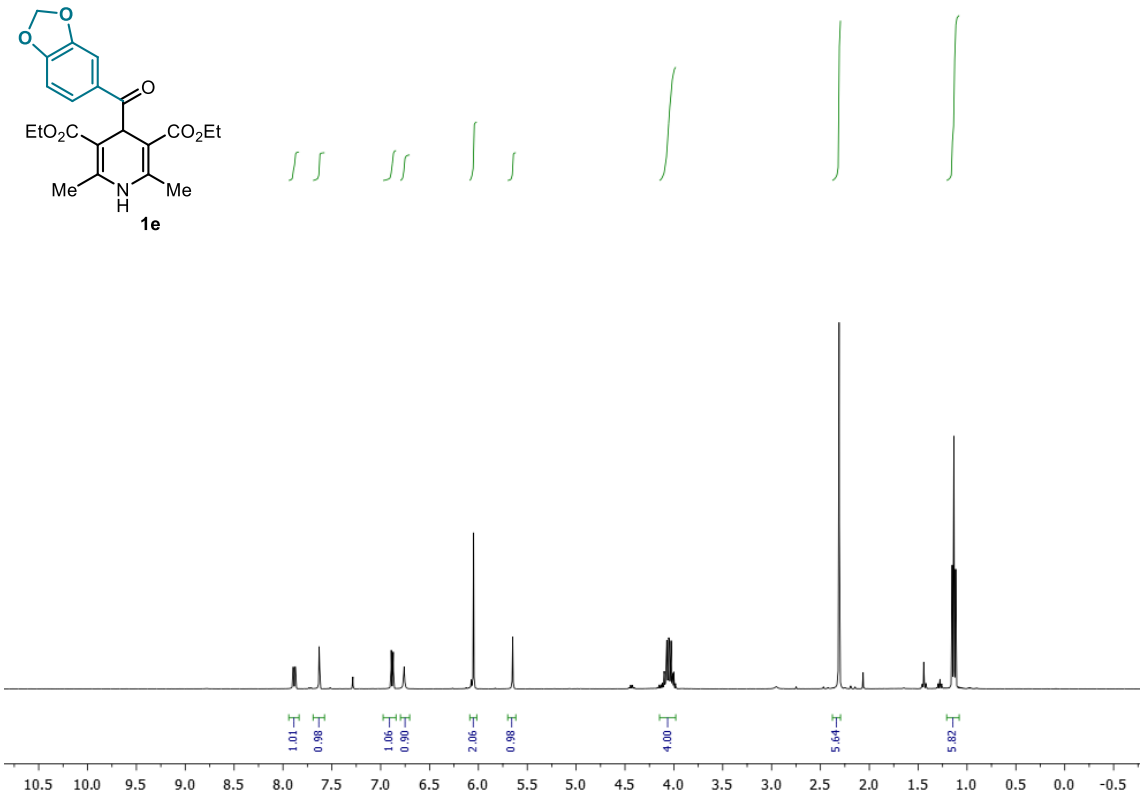


^{19} F NMR (471 MHz, $CDCl_3$)

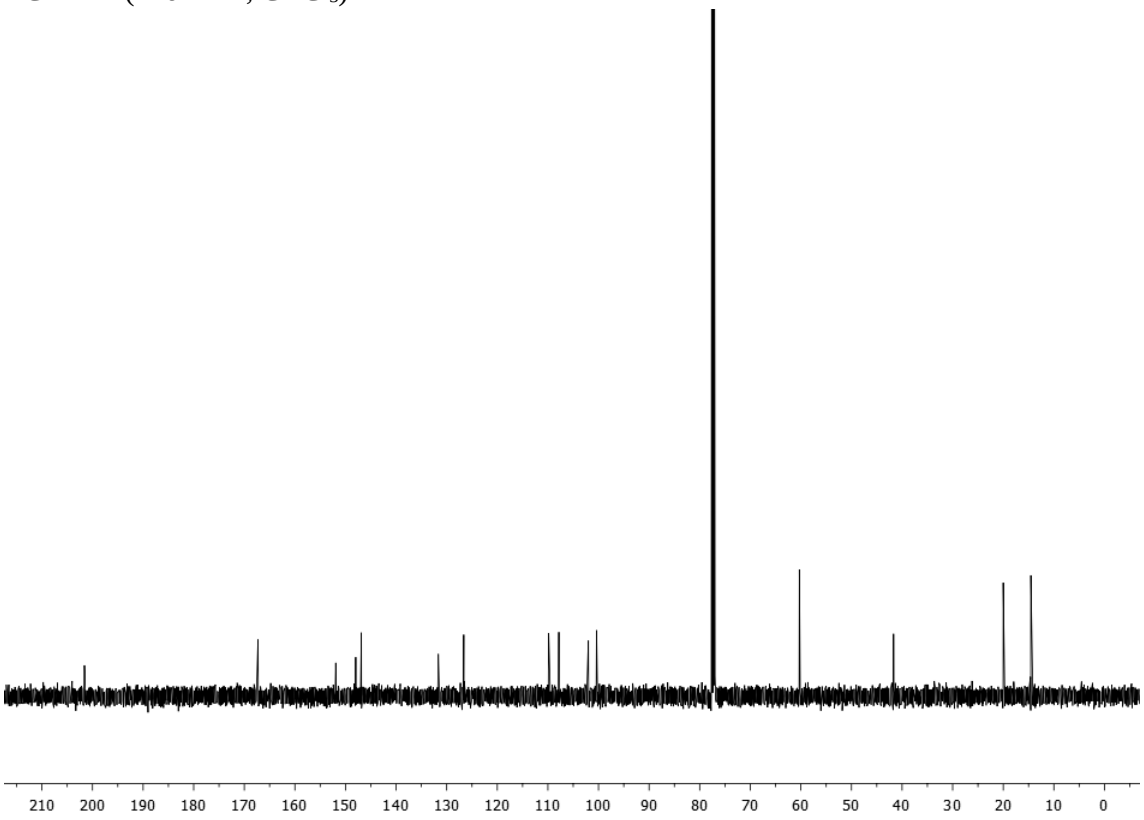


Diethyl 4-(benzo[d][1,3]dioxole-5-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1e)

^{1}H NMR (500 MHz, $CDCl_3$)

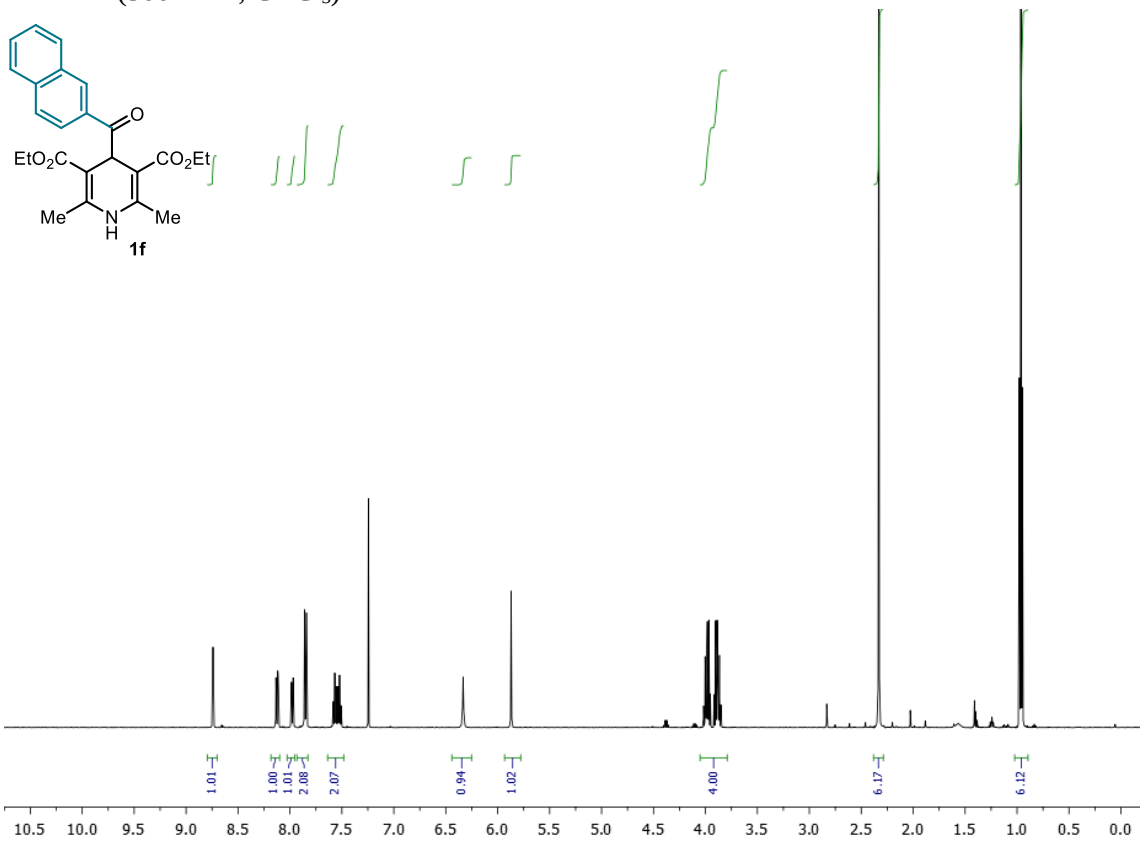


^{13}C NMR (126 MHz, $CDCl_3$)

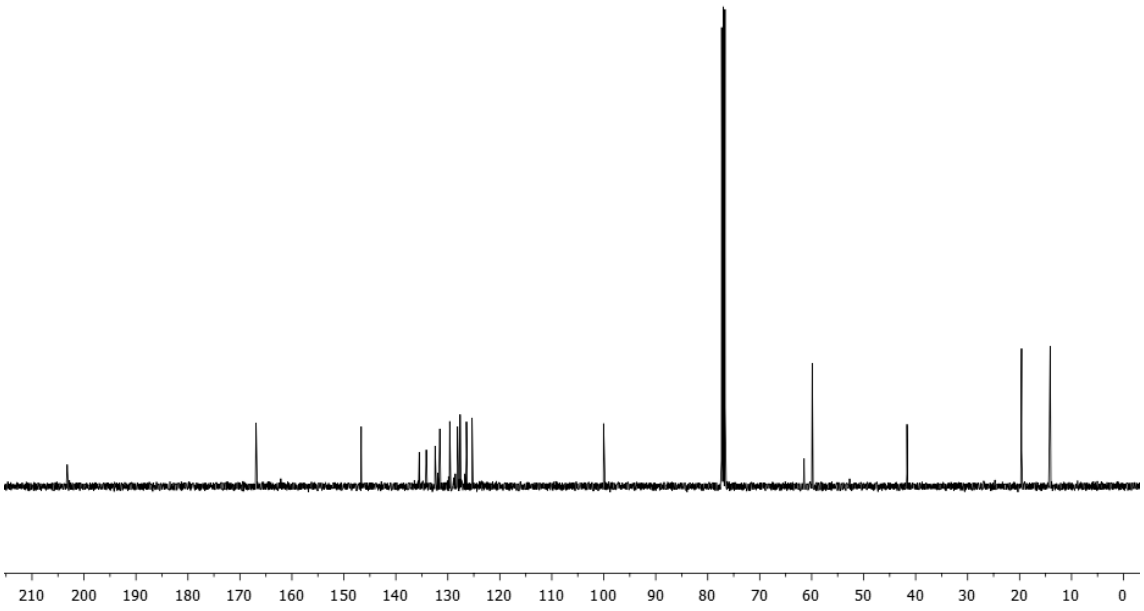


Diethyl 4-(2-naphthoyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1f)

^{1}H NMR (500 MHz, $CDCl_3$)

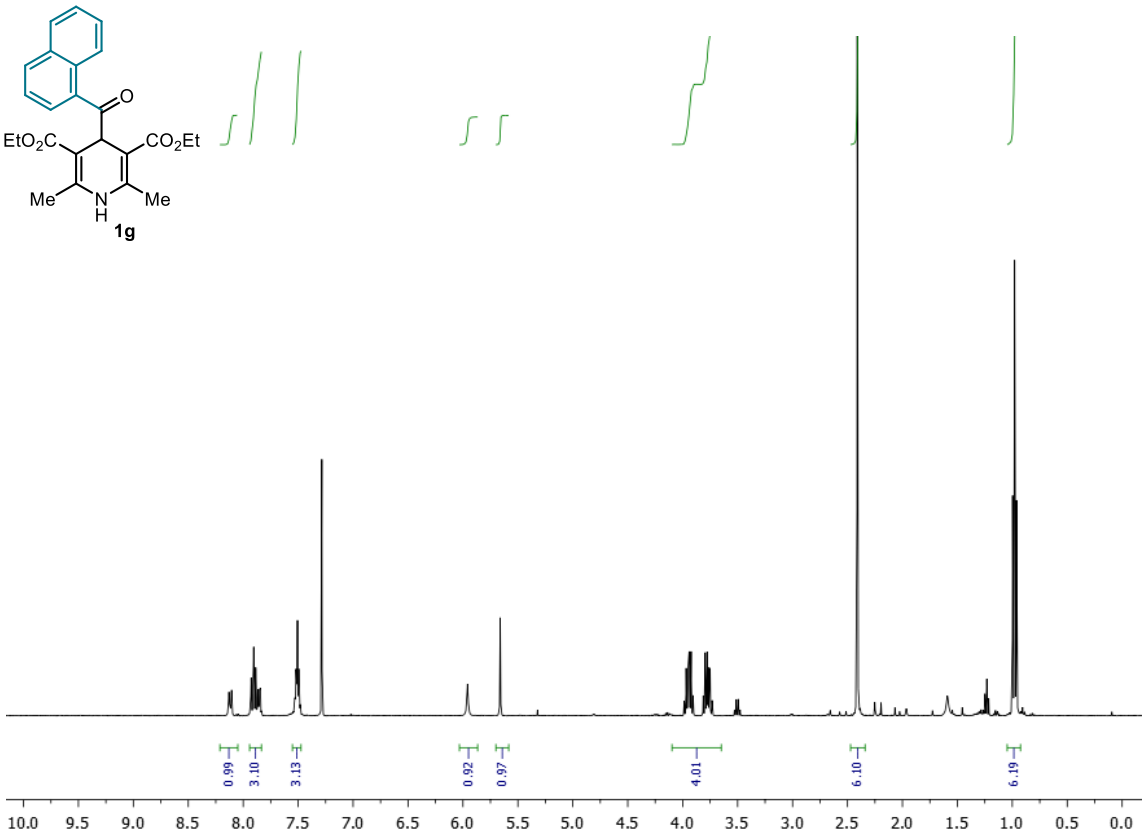


^{13}C NMR (101 MHz, $CDCl_3$)

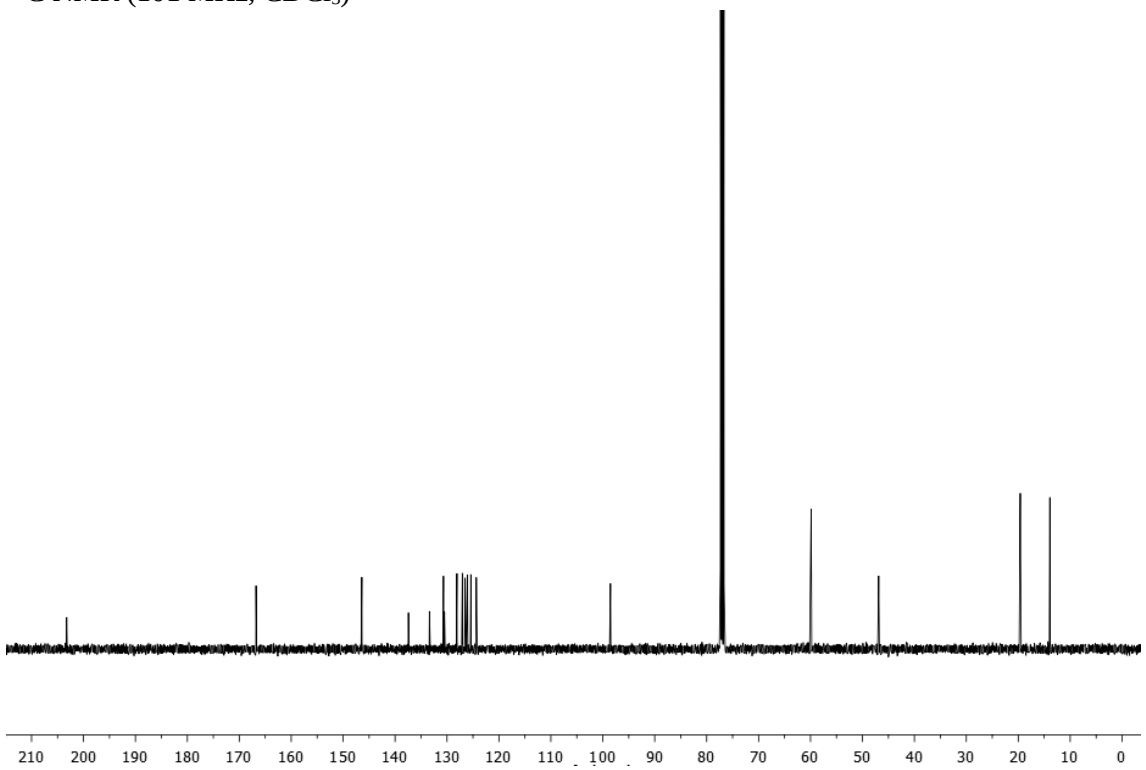


Diethyl 4-(1-naphthoyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1g)

^{1}H NMR (500 MHz, $CDCl_3$)

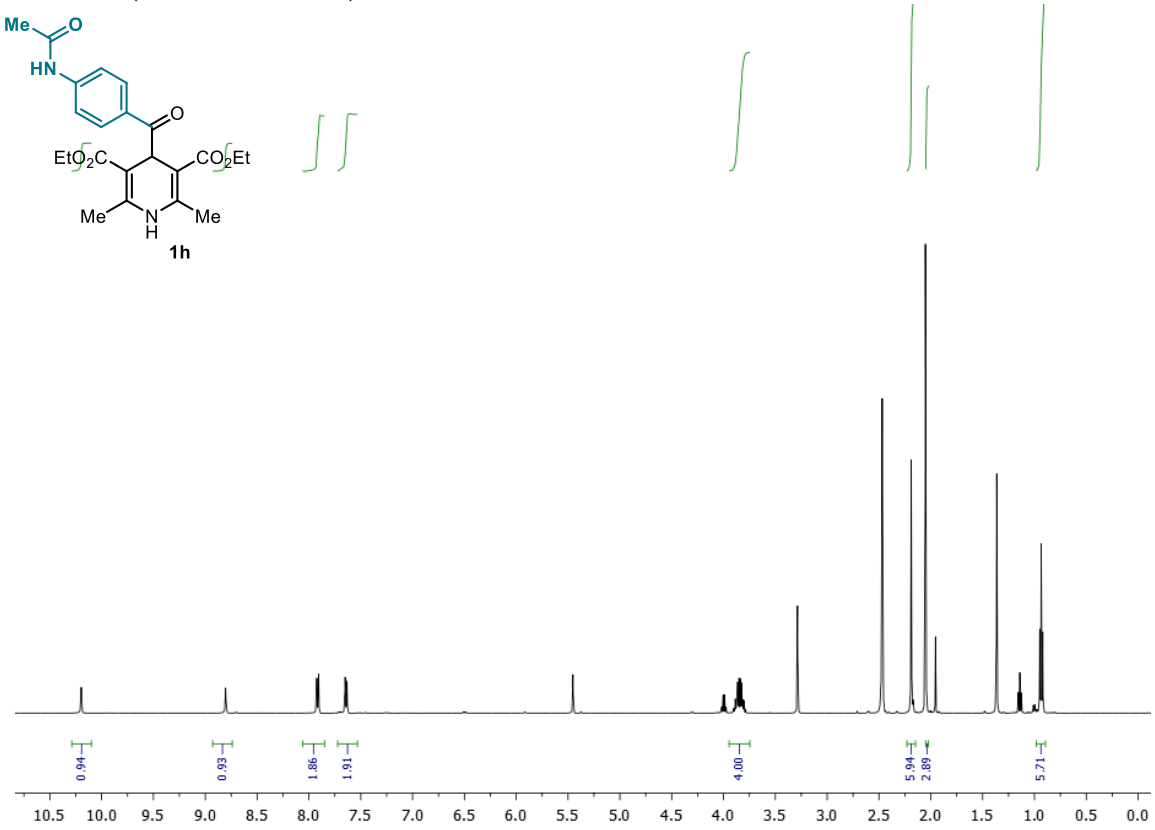


^{13}C NMR (101 MHz, $CDCl_3$)

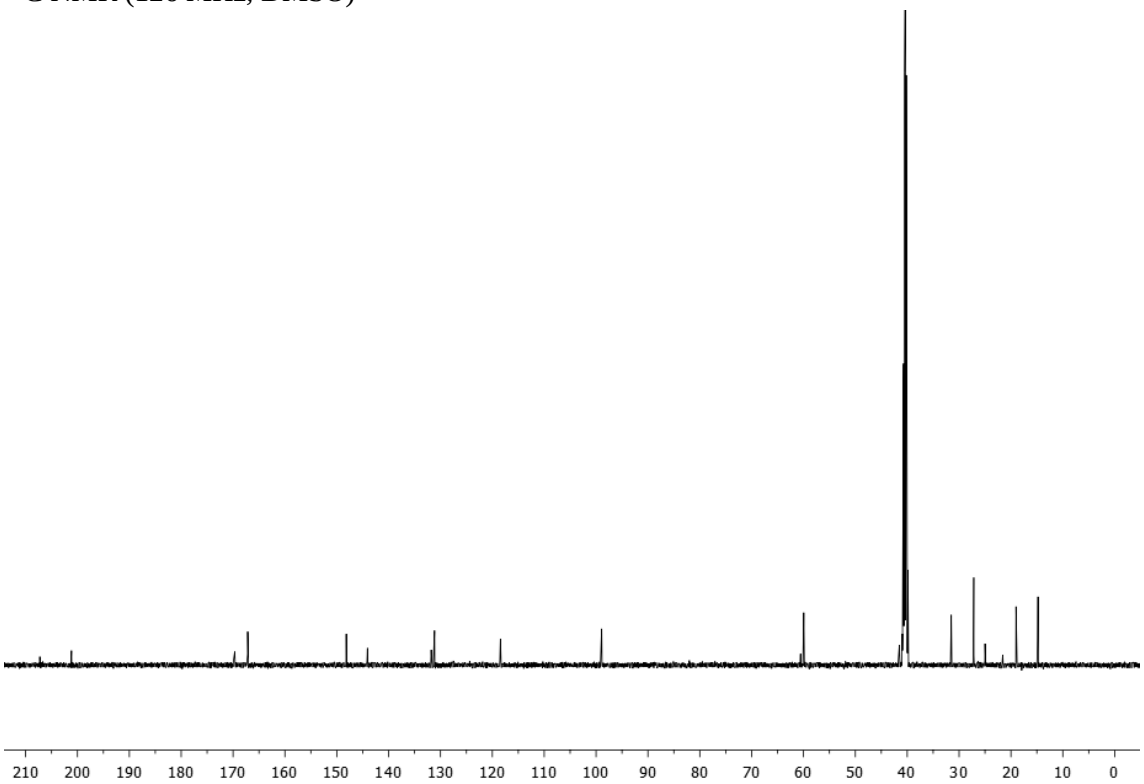


Diethyl 4-(4-acetamidobenzoyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1h)

^{1}H NMR (500 MHz, DMSO)

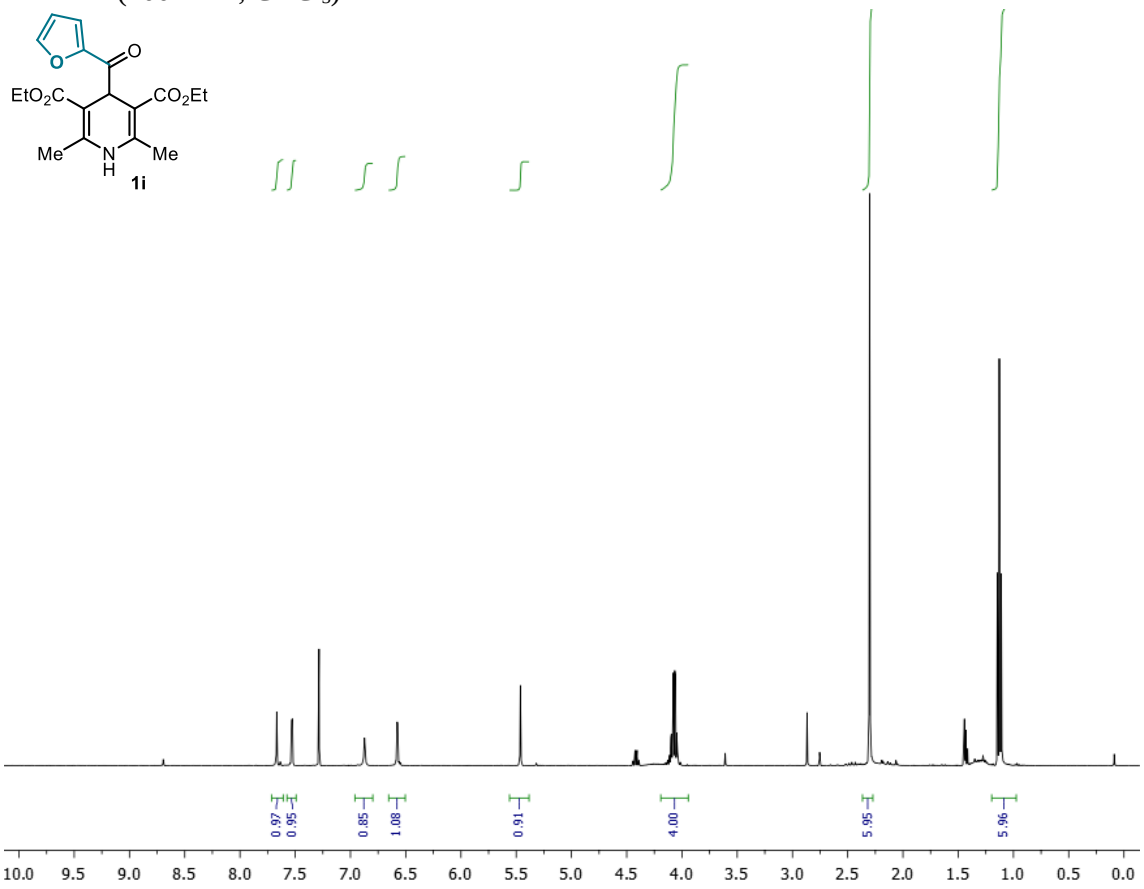


^{13}C NMR (126 MHz, DMSO)

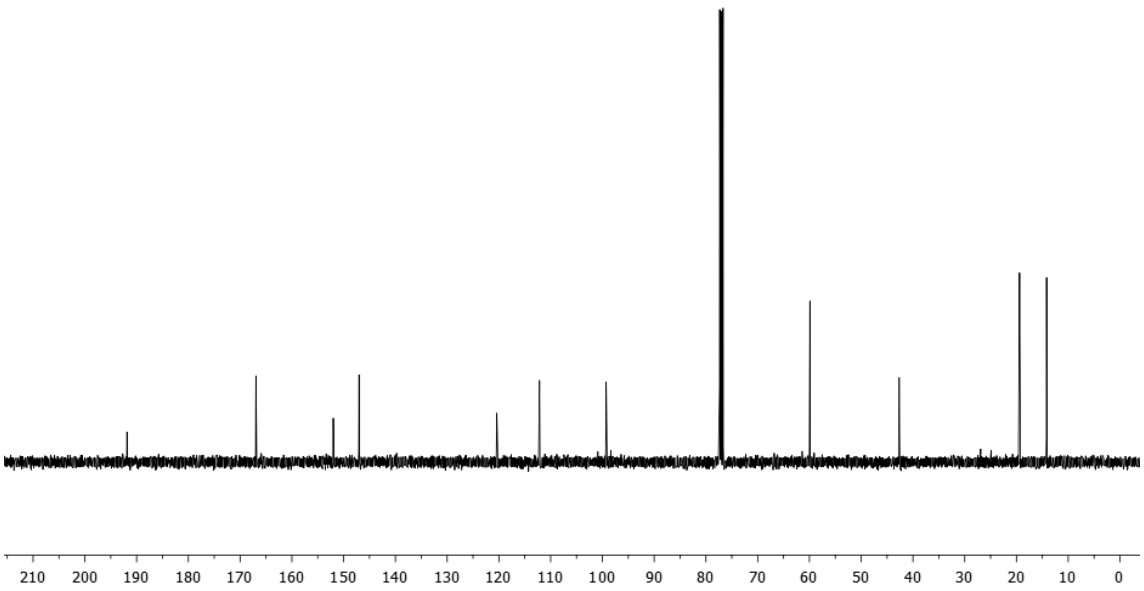


Diethyl 4-(furan-2-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1i)

^{1}H NMR (400 MHz, $CDCl_3$)

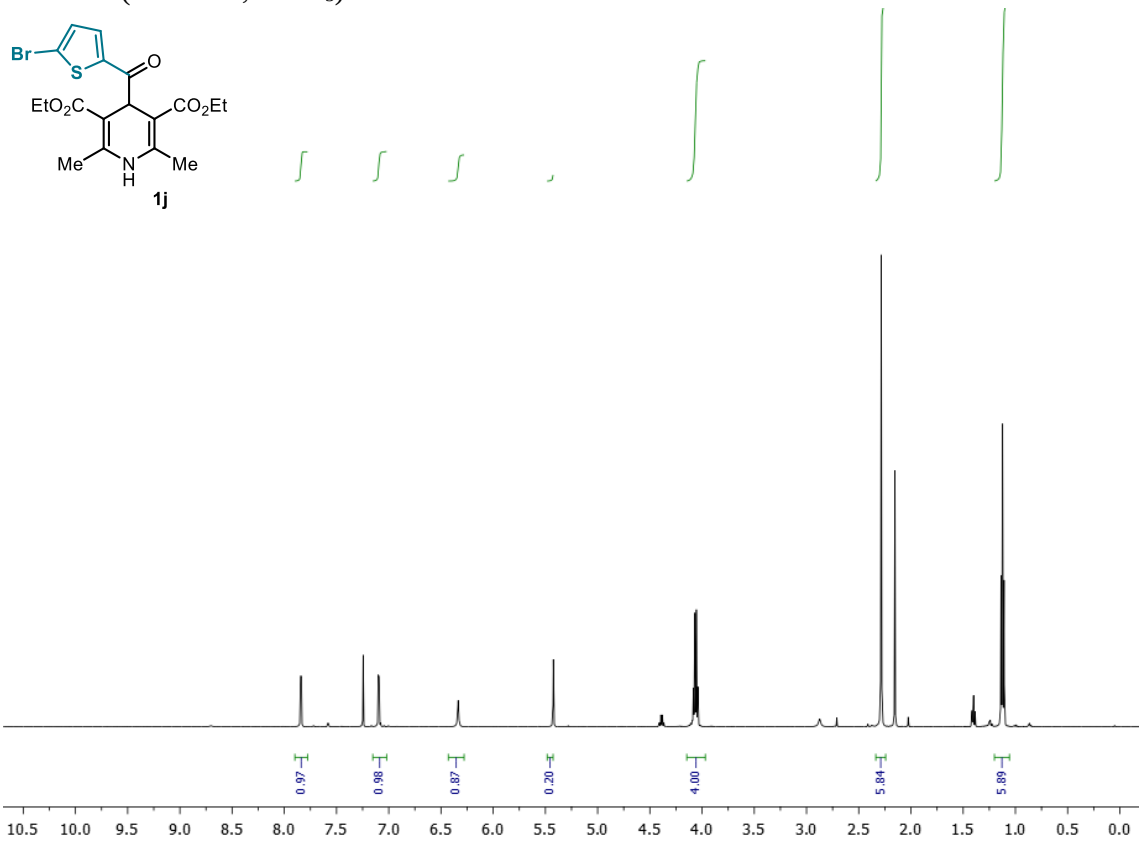


^{13}C NMR (126 MHz, $CDCl_3$)

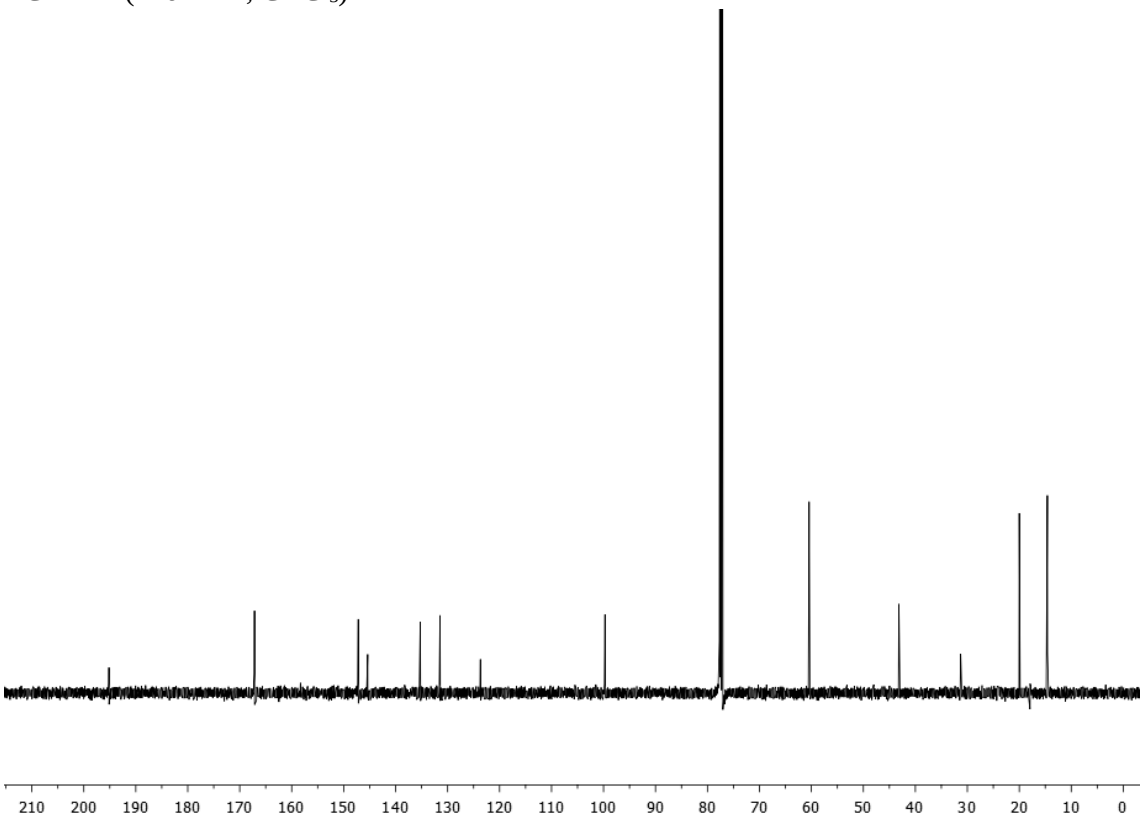


Diethyl 4-(5-bromothiophene-2-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1j)

^{1}H NMR (500 MHz, $CDCl_3$)

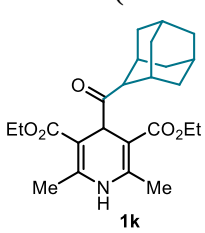


^{13}C NMR (126 MHz, $CDCl_3$)



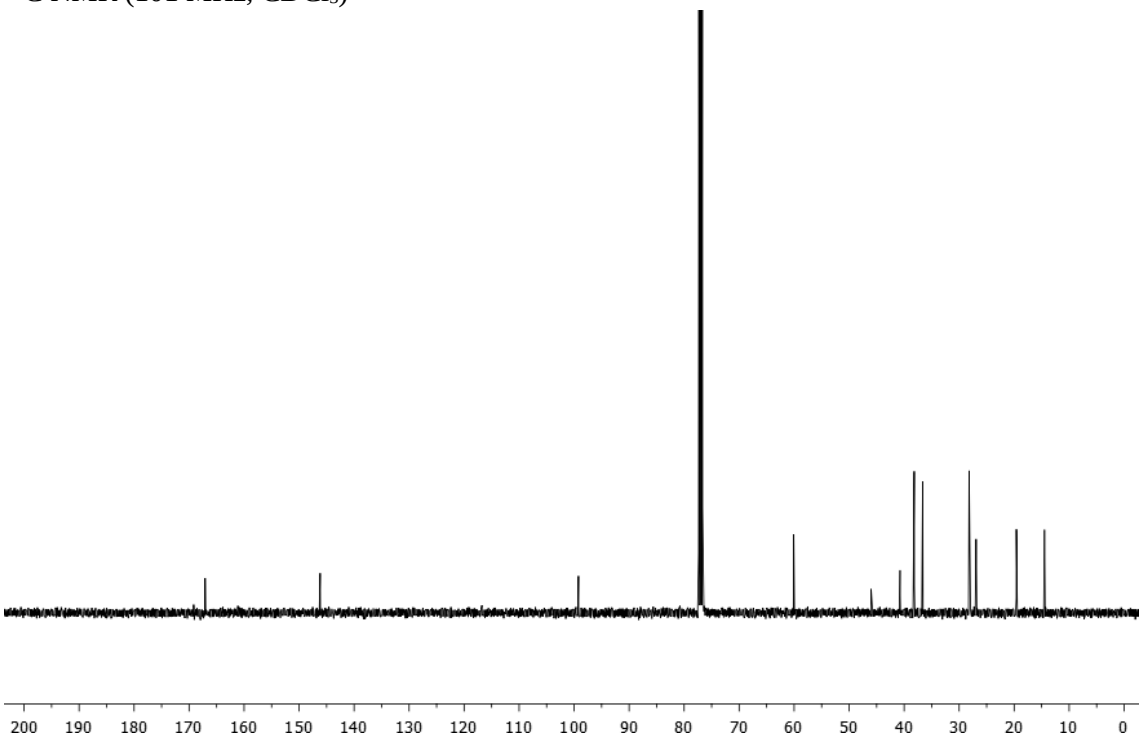
Diethyl 4-((1r,3r,5r,7r)-adamantane-2-carbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1k)

^{1}H NMR (400 MHz, $CDCl_3$)



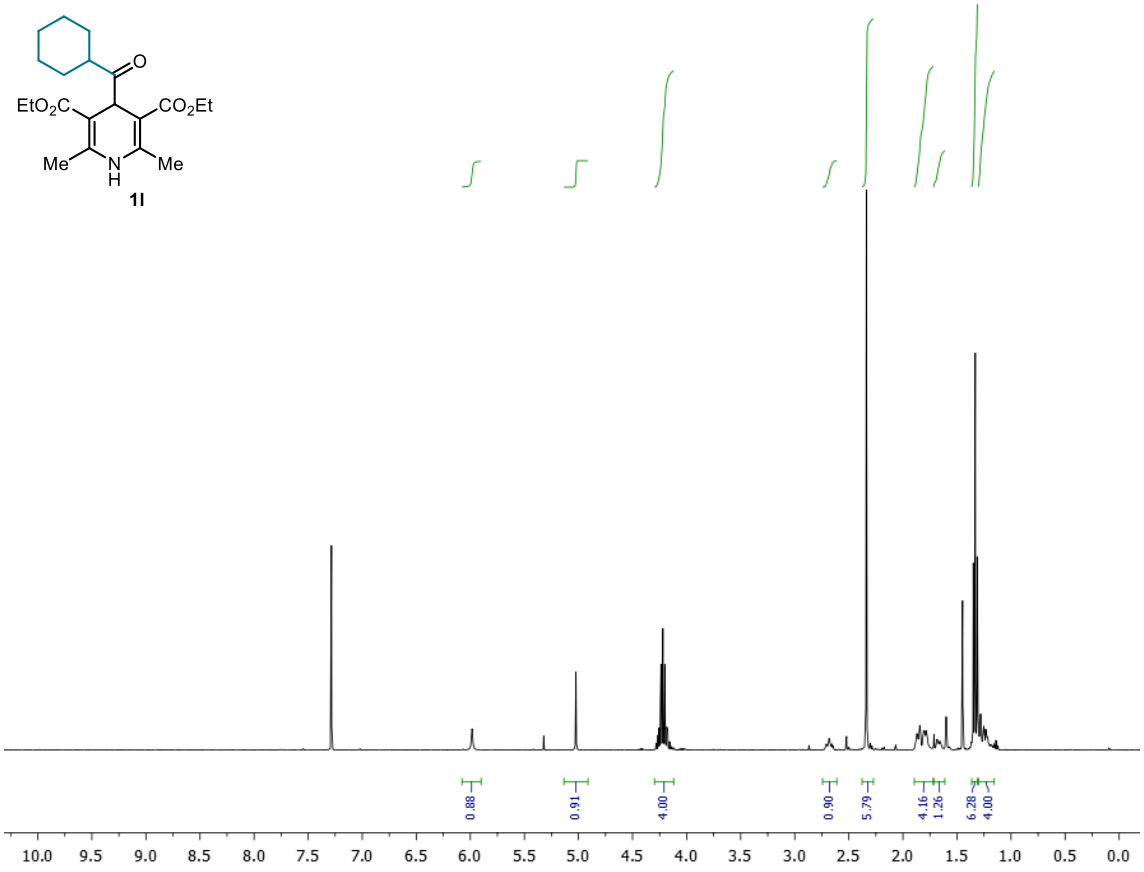
1k

^{13}C NMR (101 MHz, $CDCl_3$)

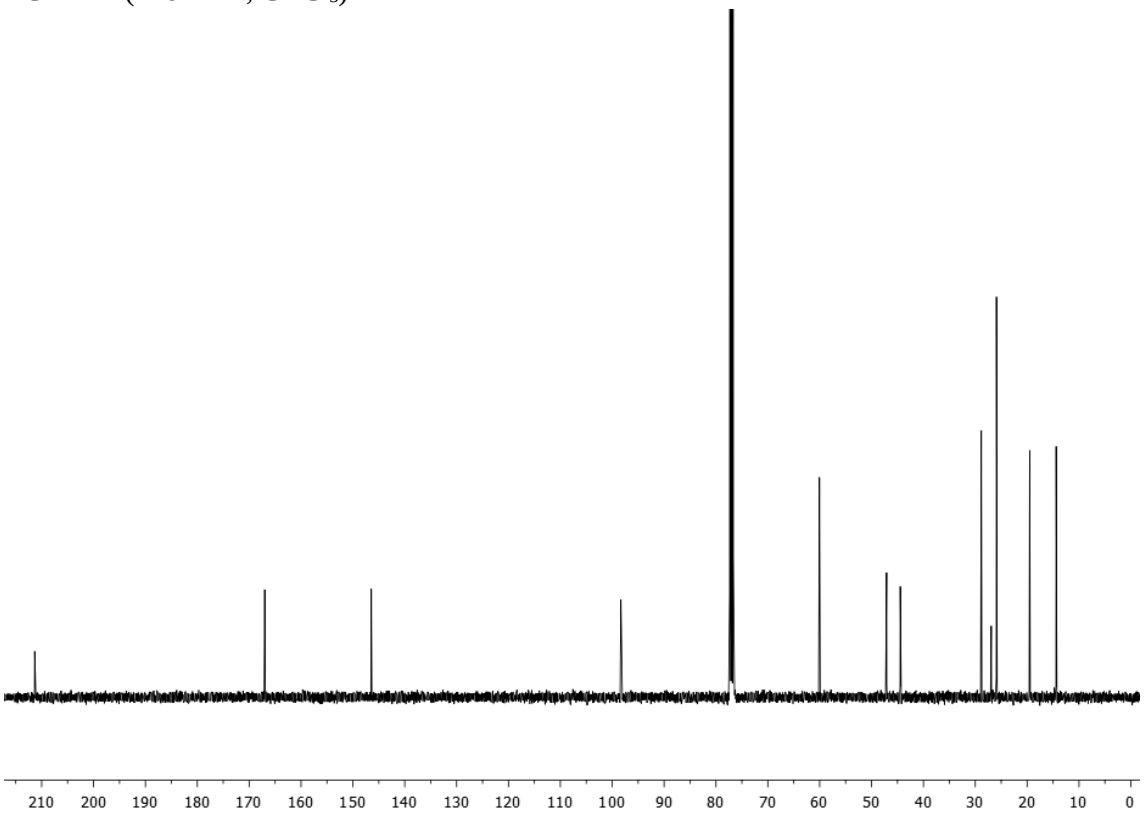


Diethyl 4-(cyclohexanecarbonyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (1l)

^{1}H NMR (500 MHz, $CDCl_3$)

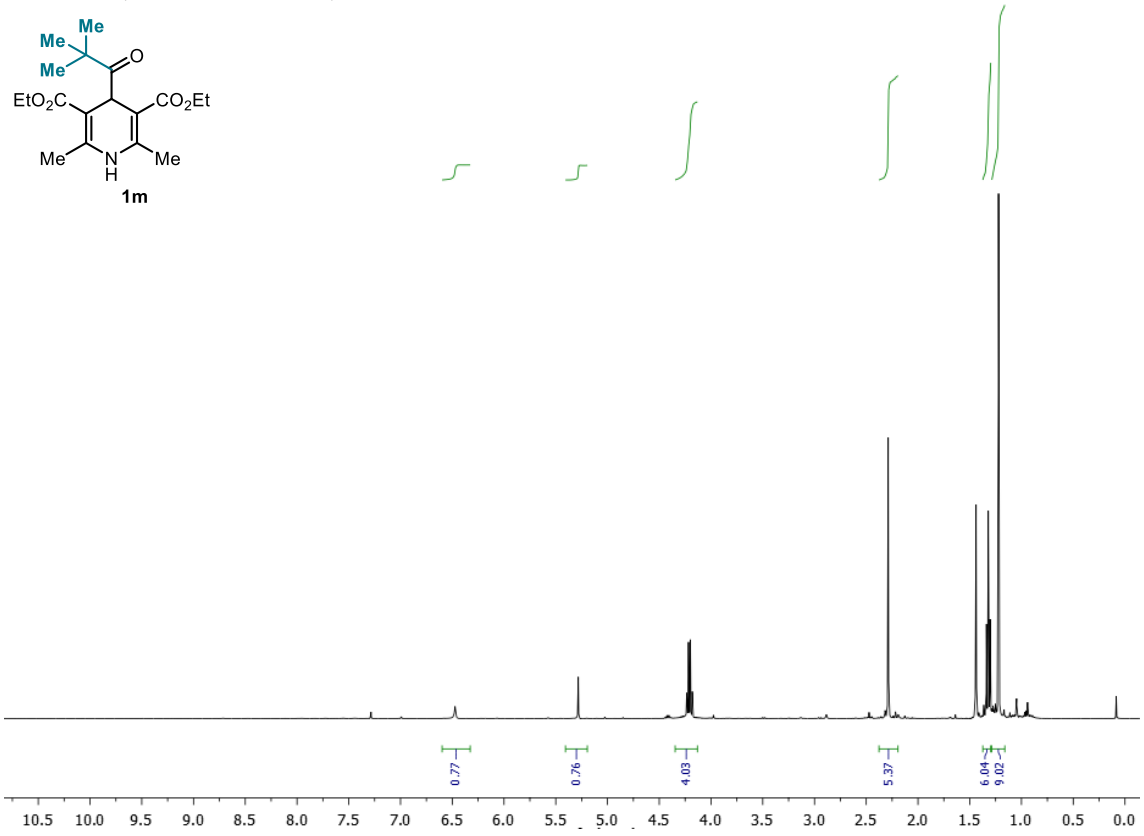


^{13}C NMR (126 MHz, $CDCl_3$)

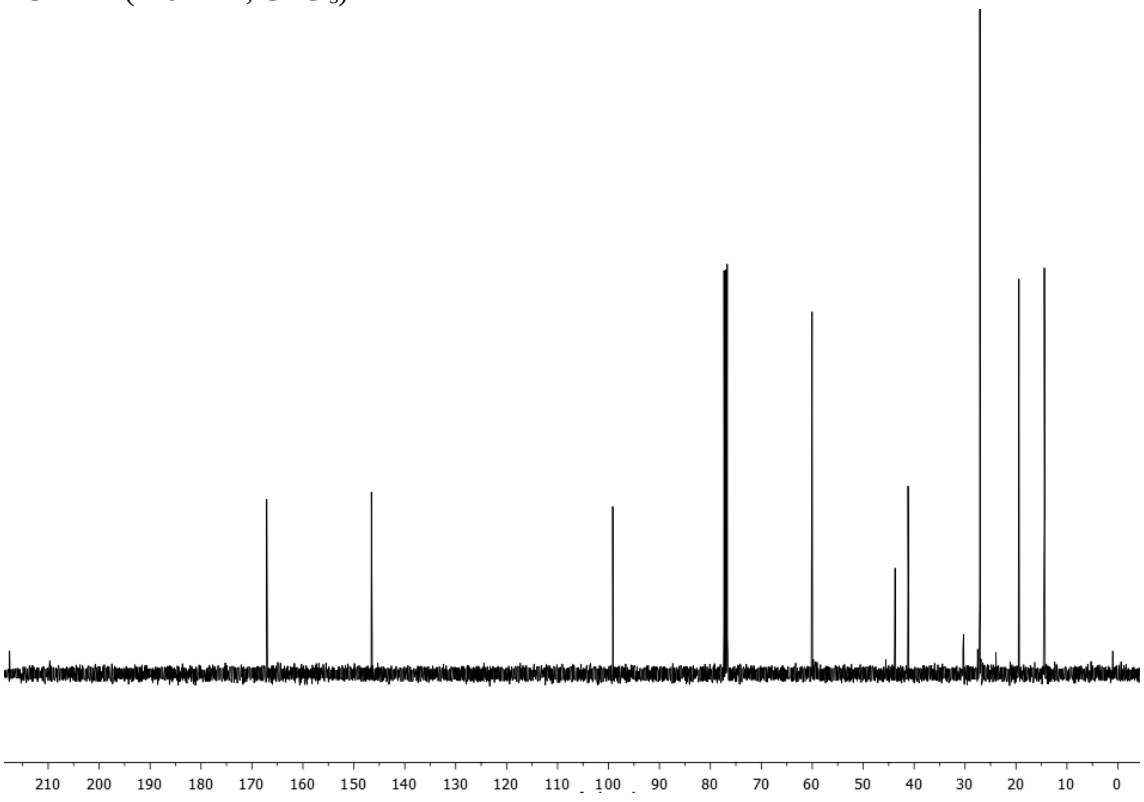


Diethyl 2,6-dimethyl-4-pivaloyl-1,4-dihydropyridine-3,5-dicarboxylate (1m)

^{1}H NMR (500 MHz, $CDCl_3$)

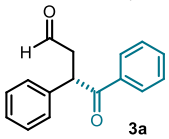


^{13}C NMR (126 MHz, $CDCl_3$)

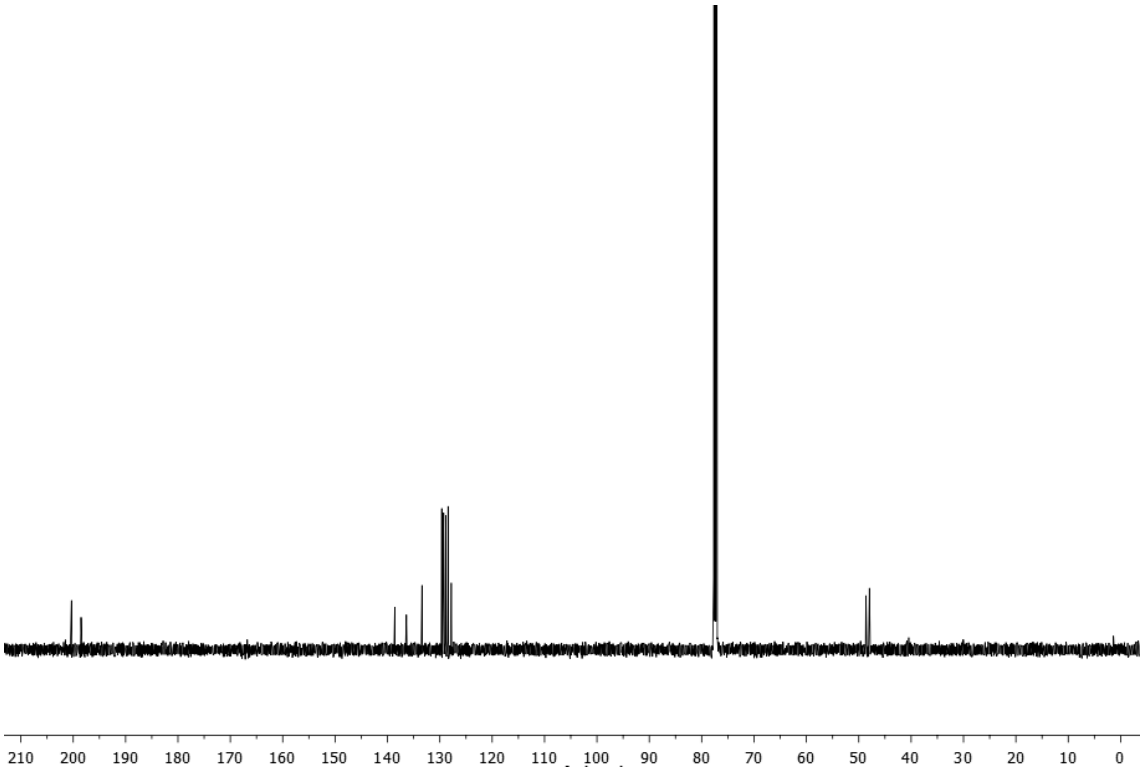


(*S*)-4-Oxo-3,4-diphenylbutanal (3a)

^{1}H NMR (500 MHz, $CDCl_3$)

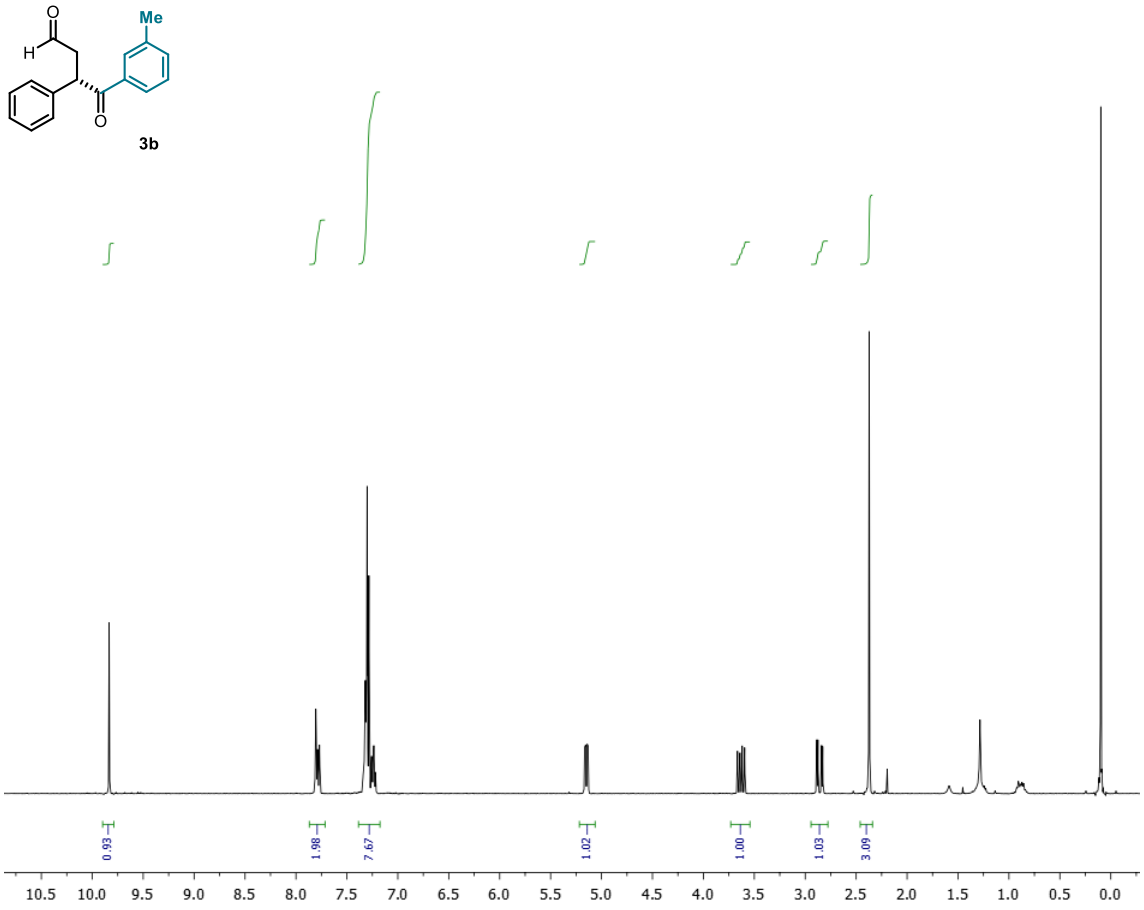


^{13}C NMR (126 MHz, $CDCl_3$)

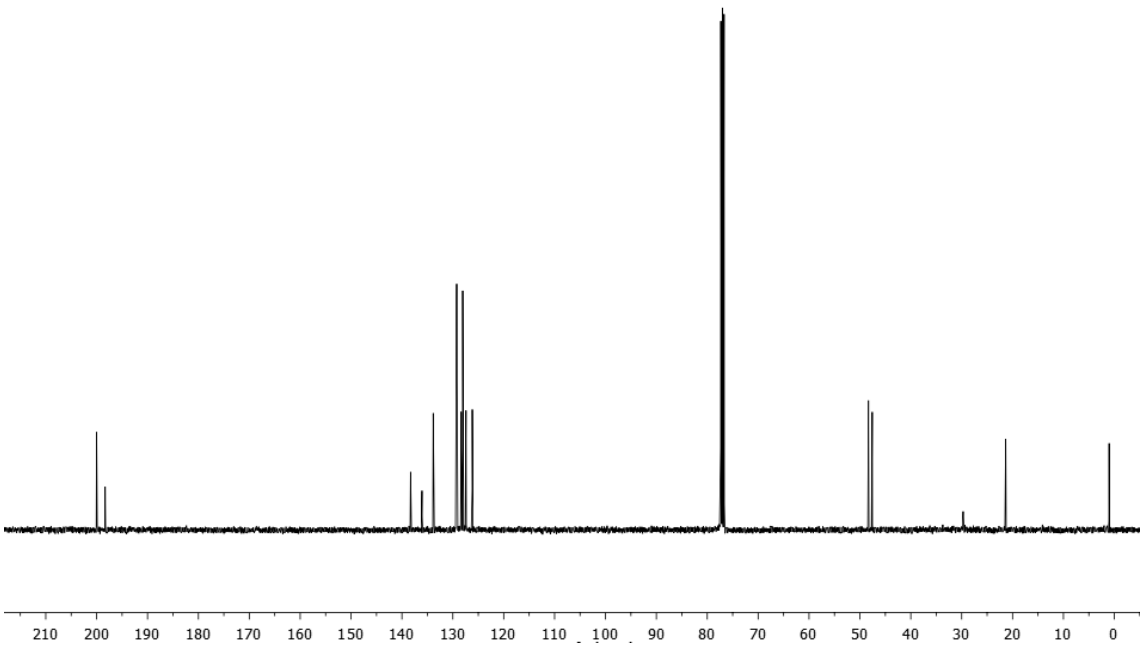


(*S*)-4-Oxo-3-phenyl-4-(m-tolyl)butanal (3b)

^{1}H NMR (400 MHz, $CDCl_3$)

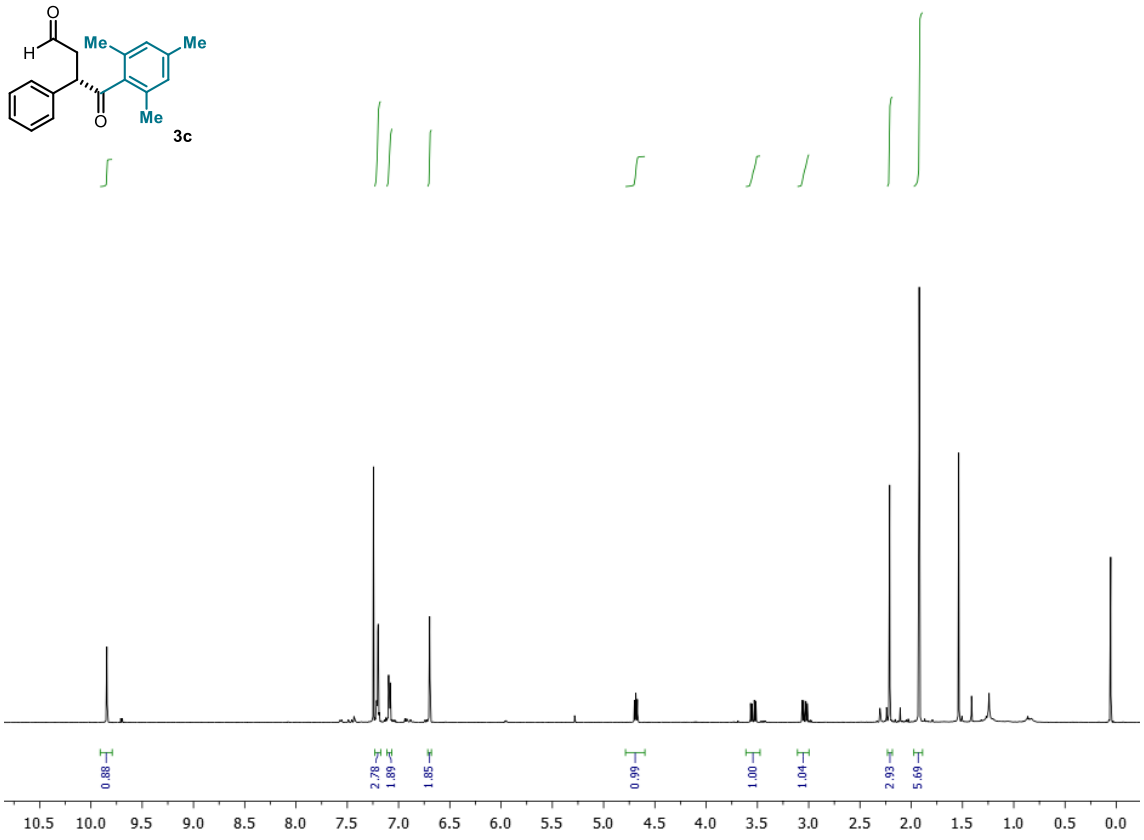


^{13}C NMR (100 MHz, $CDCl_3$)

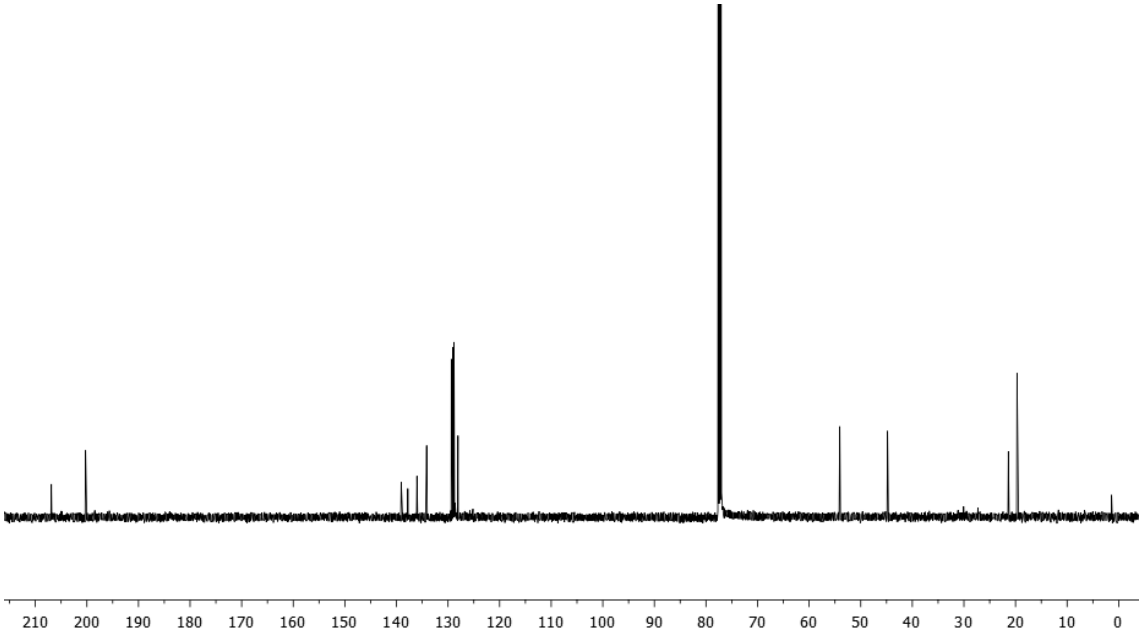


(*S*)-4-Mesityl-4-oxo-3-phenylbutanal (3c)

^{1}H NMR (300 MHz, $CDCl_3$)

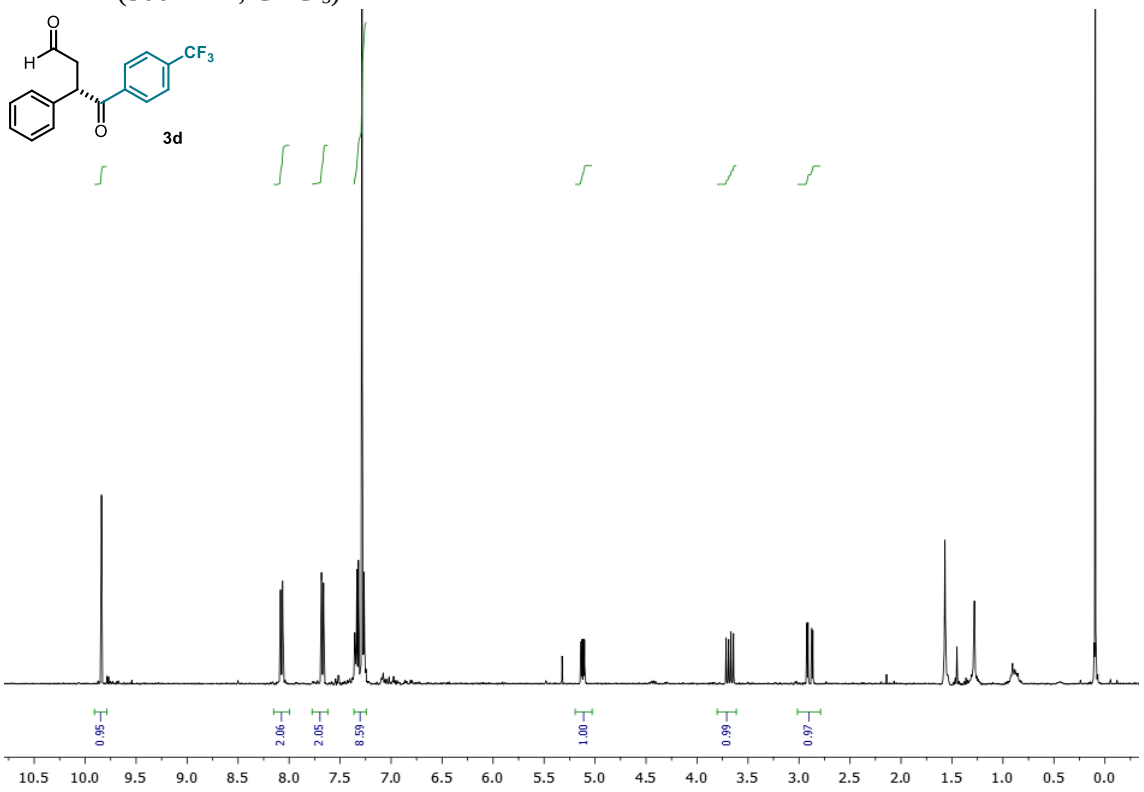


^{13}C NMR (101 MHz, $CDCl_3$)

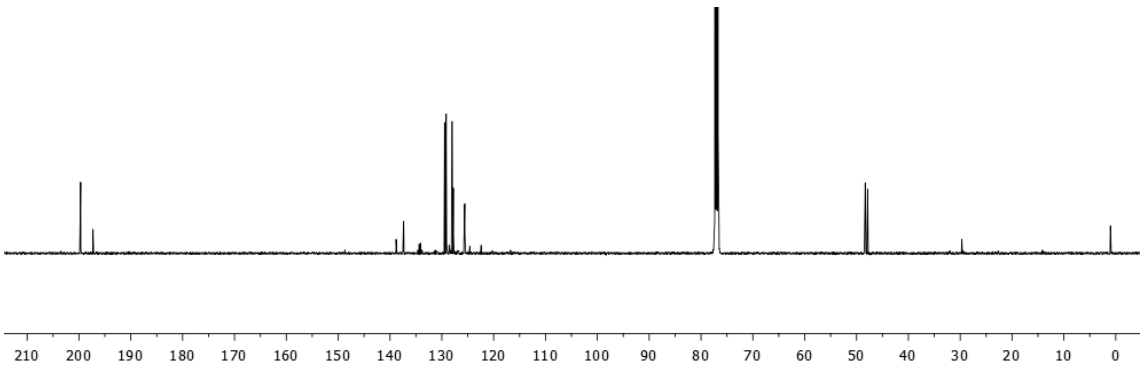


(*S*)-4-Oxo-3-phenyl-4-(4-(trifluoromethyl)phenyl)butanal (3d)

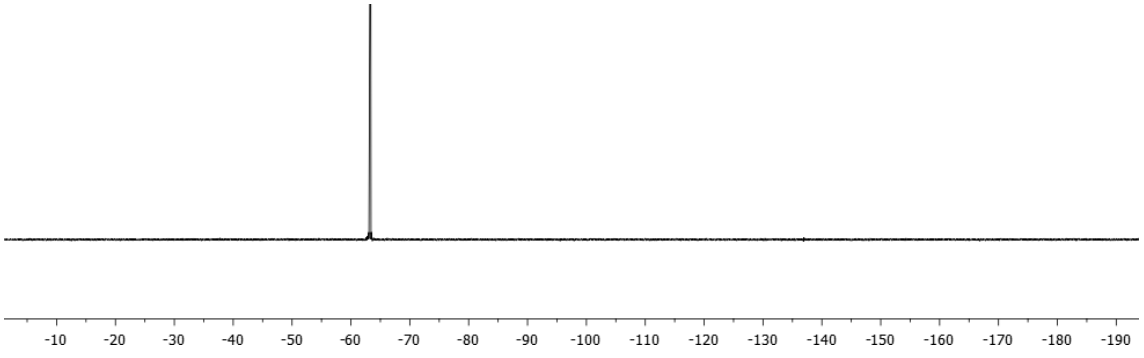
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)

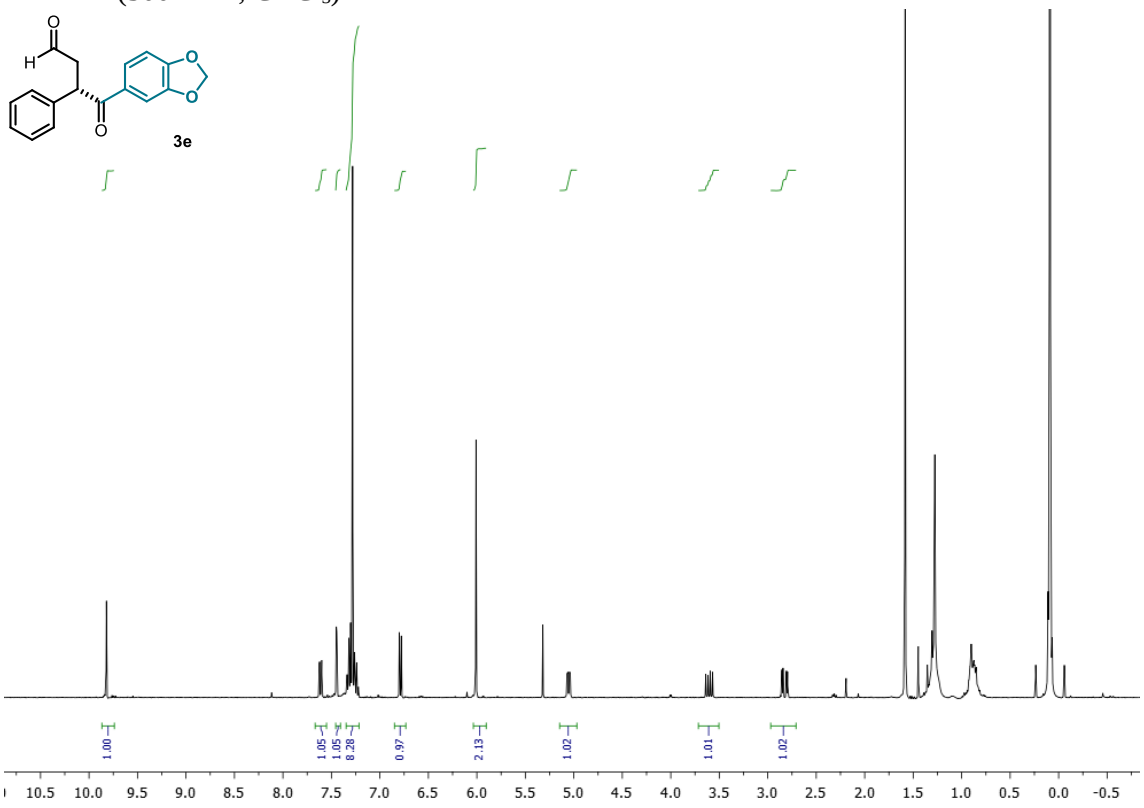


^{19}F NMR (376 MHz, $CDCl_3$)

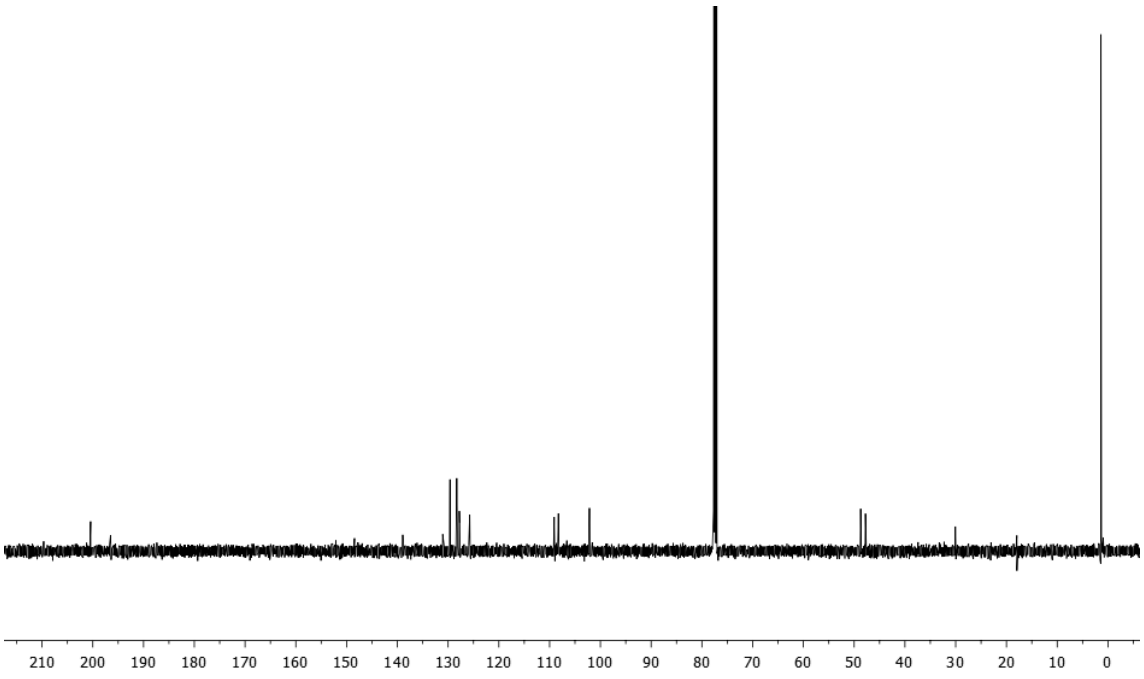


(*S*)-4-(Benzo[d][1,3]dioxol-5-yl)-4-oxo-3-phenylbutanal (3e)

^{1}H NMR (300 MHz, $CDCl_3$)

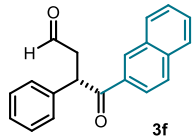


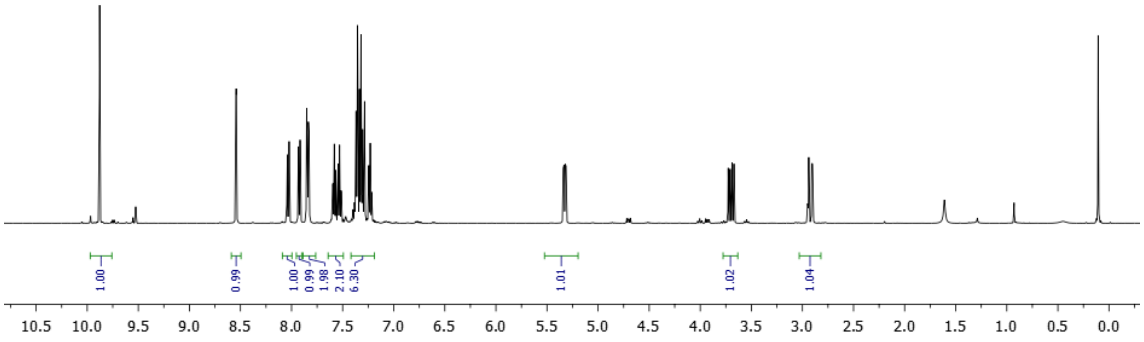
^{13}C NMR (101 MHz, $CDCl_3$)



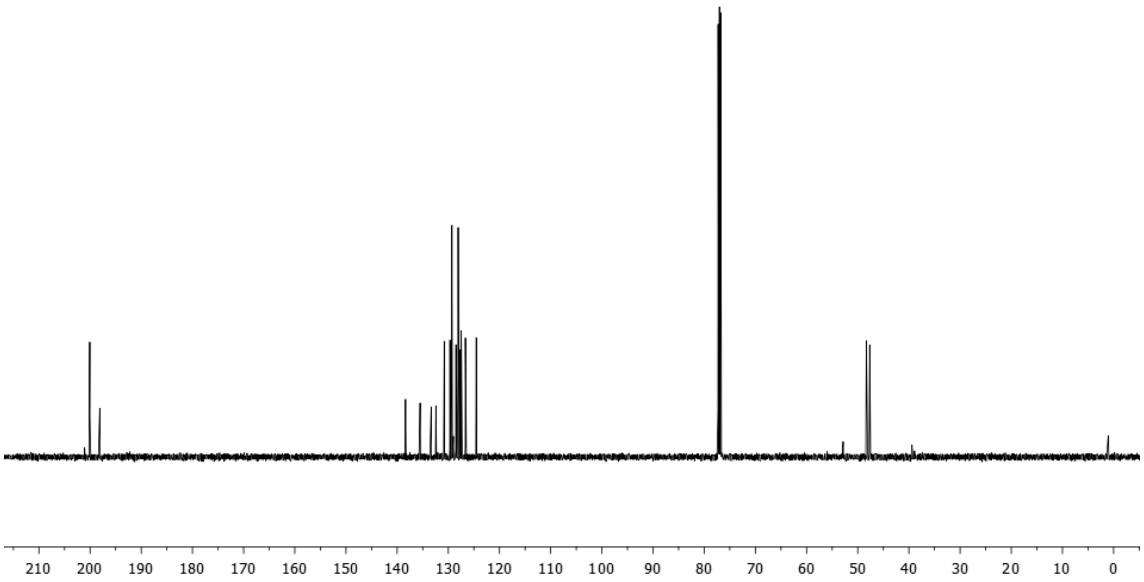
(*S*)-4-(Naphthalen-2-yl)-4-oxo-3-phenylbutanal (3f)

^{1}H NMR (500 MHz, $CDCl_3$)



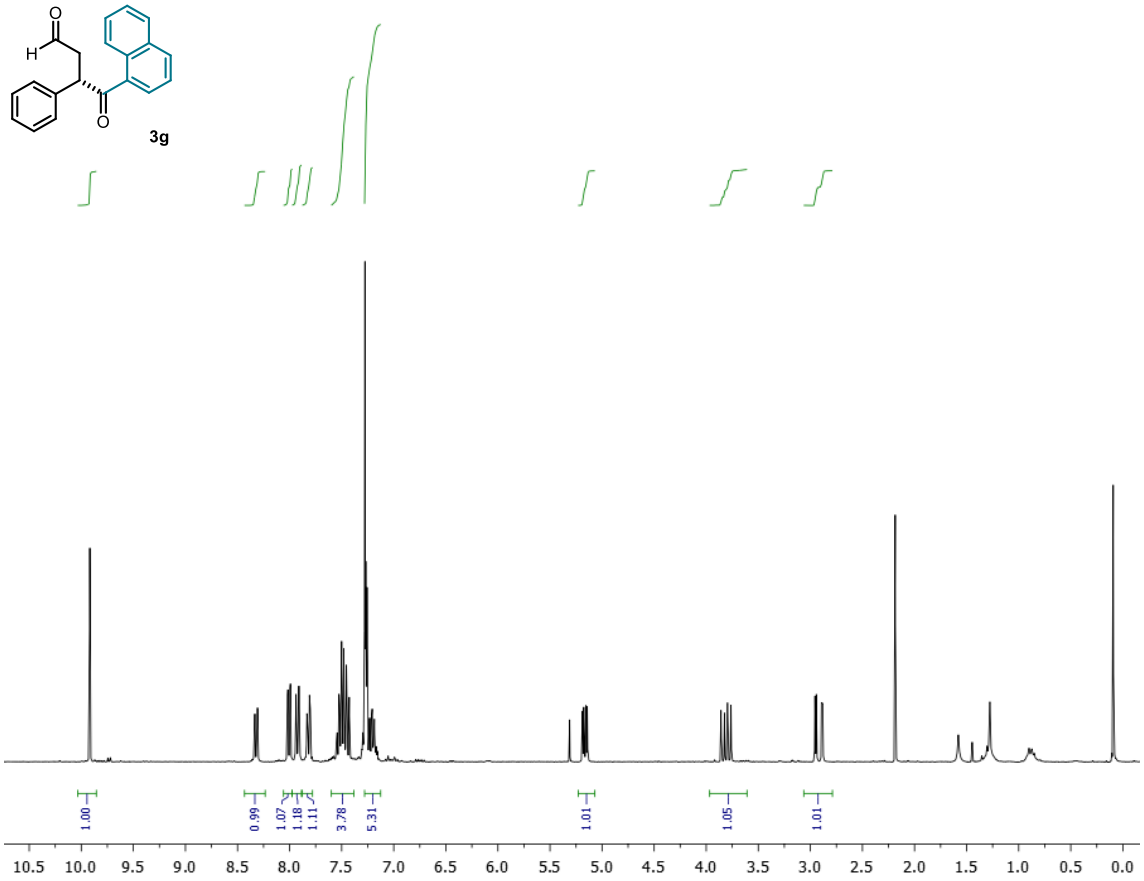


^{13}C NMR (126 MHz, $CDCl_3$)

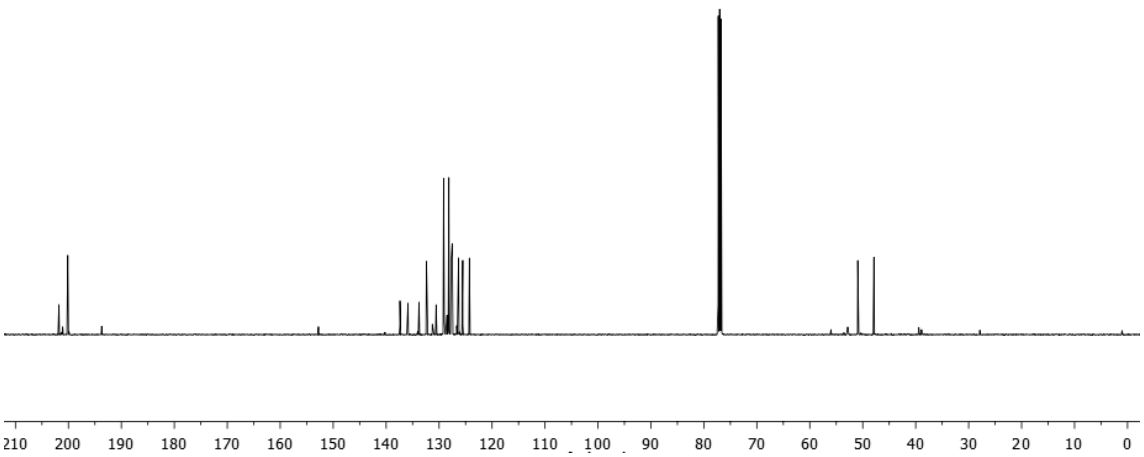


(*S*)-4-(Naphthalen-1-yl)-4-oxo-3-phenylbutanal (3g)

^{1}H NMR (300 MHz, $CDCl_3$)

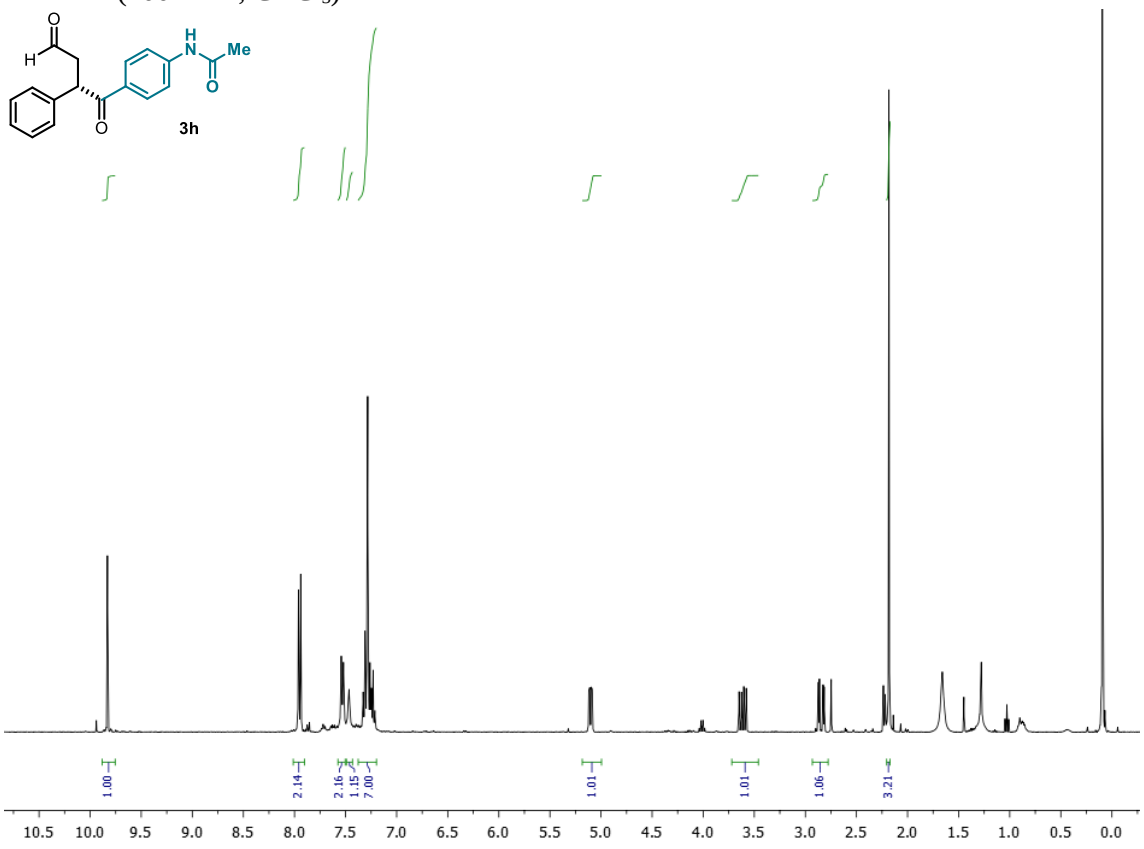


^{13}C NMR (101 MHz, $CDCl_3$)

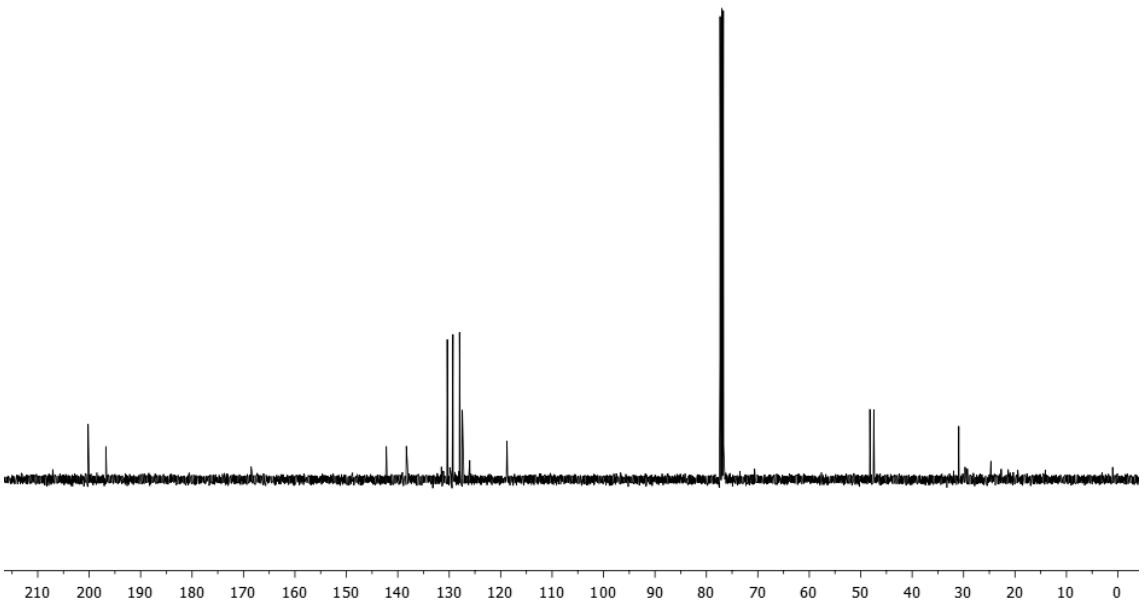


(*S*)-N-(4-(4-Oxo-2-phenylbutanoyl)phenyl)acetamide (3h)

^{1}H NMR (400 MHz, $CDCl_3$)

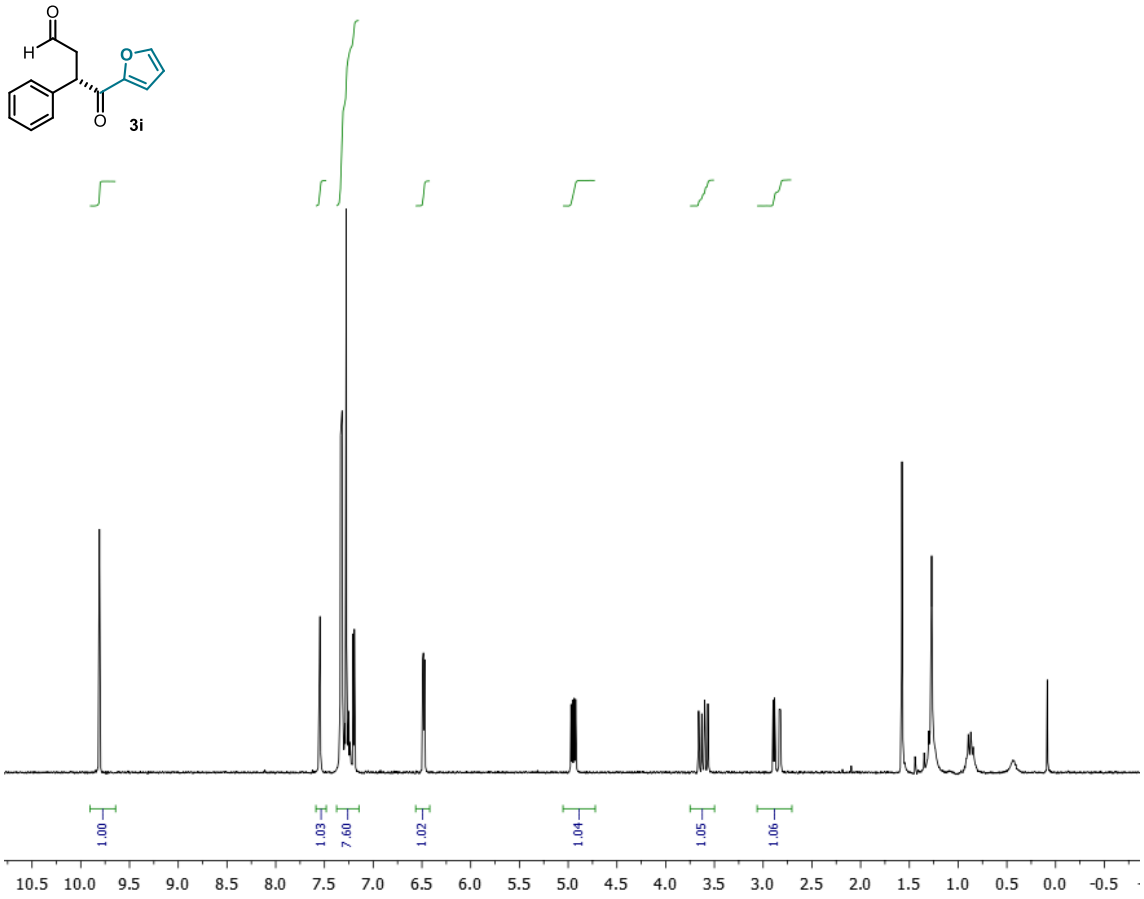


^{13}C NMR (101 MHz, $CDCl_3$)

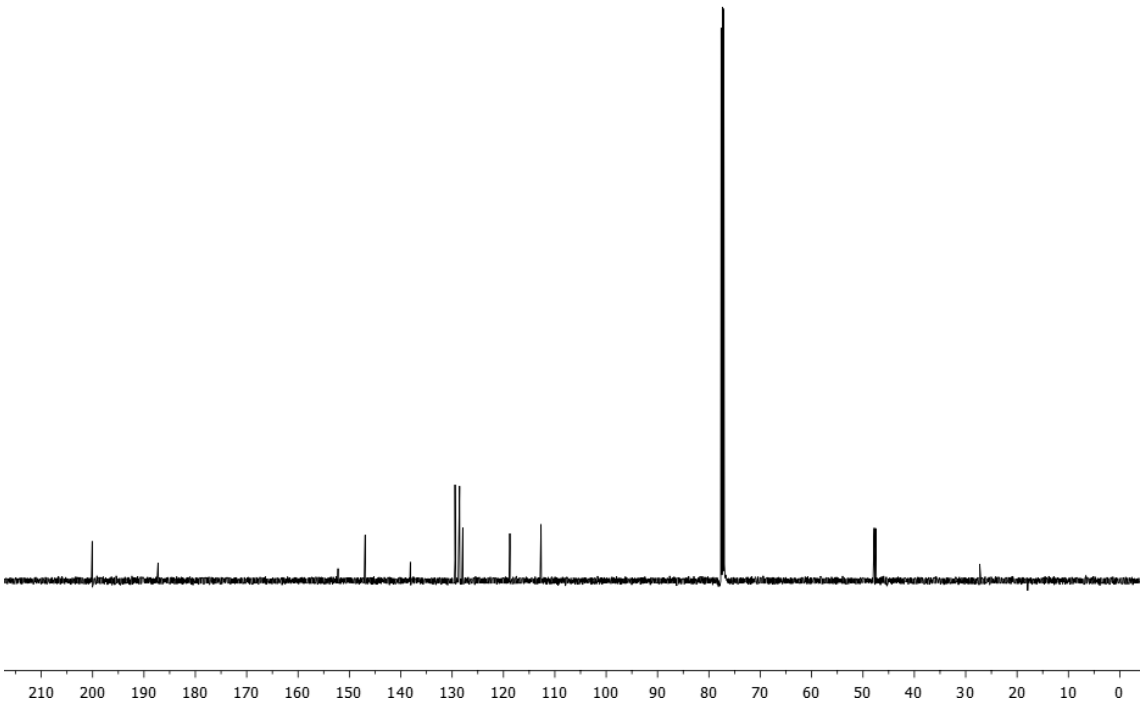


(*S*)-4-(Furan-2-yl)-4-oxo-3-phenylbutanal phenylbutanal (3i)

^{1}H NMR (300 MHz, $CDCl_3$)

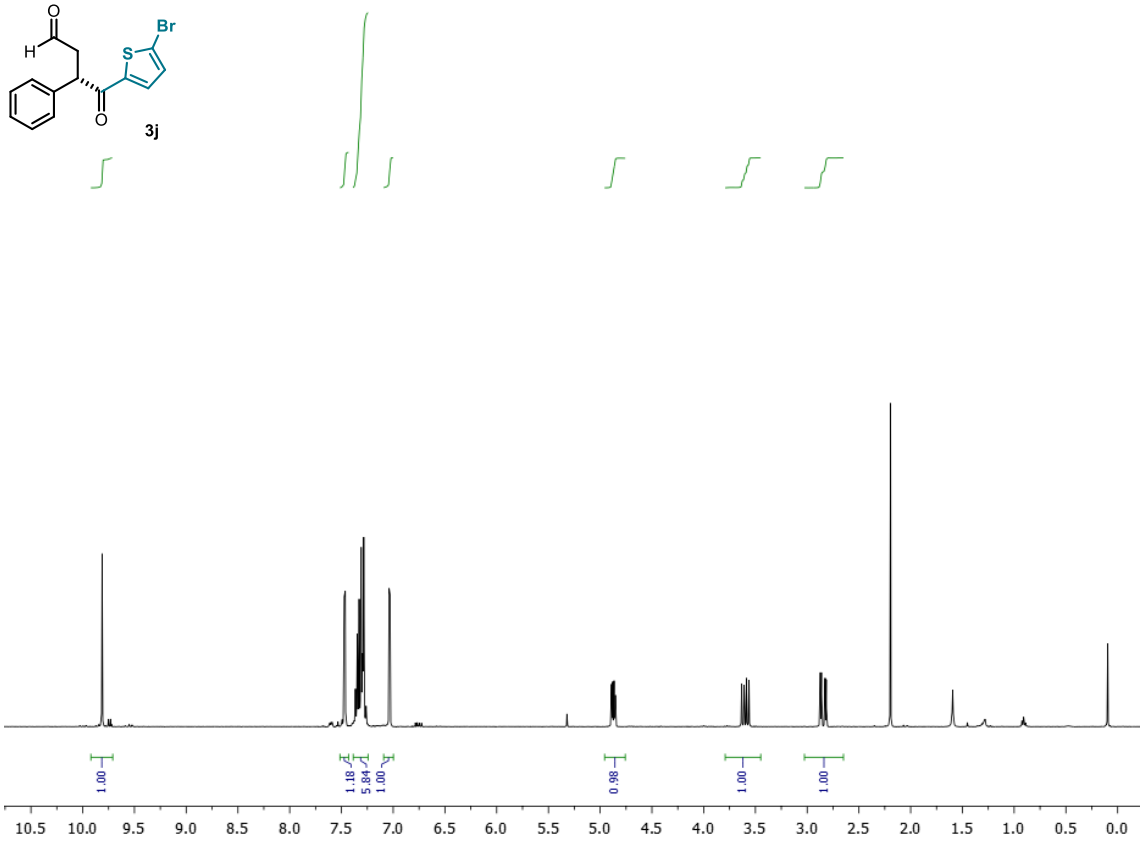


^{13}C NMR (101 MHz, $CDCl_3$)

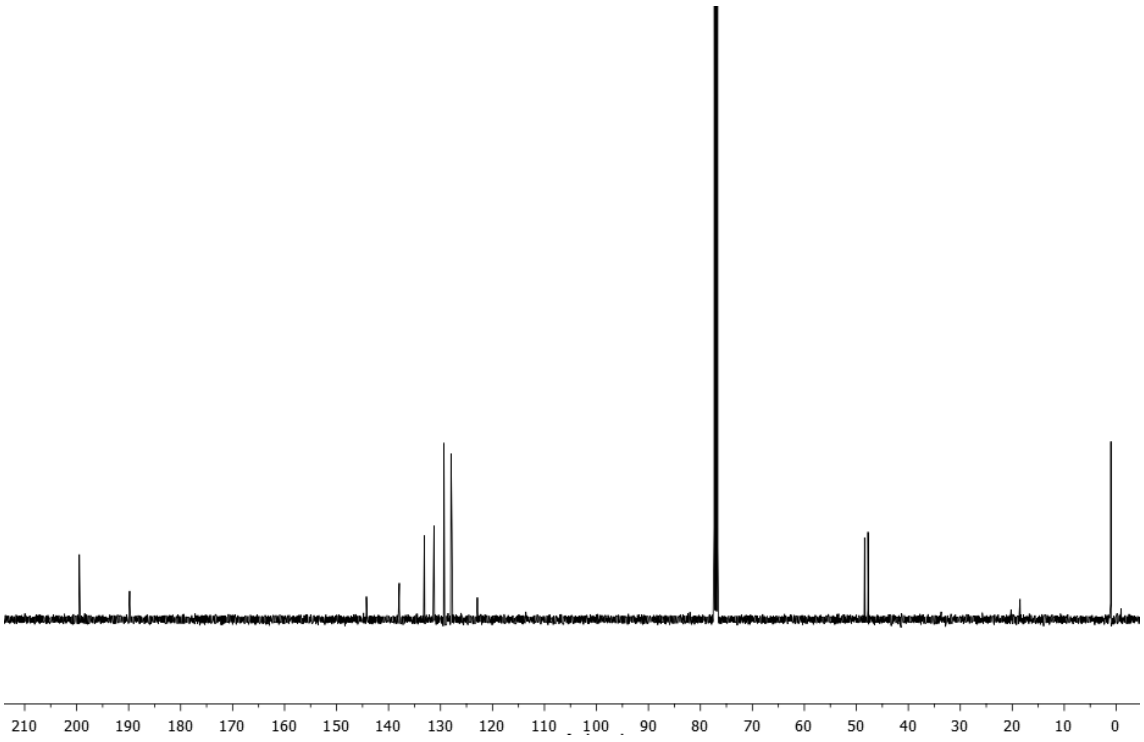


(*S*)-4-(5-Bromothiophen-2-yl)-4-oxo-3-phenylbutanal (3j)

^{1}H NMR (400 MHz, $CDCl_3$)

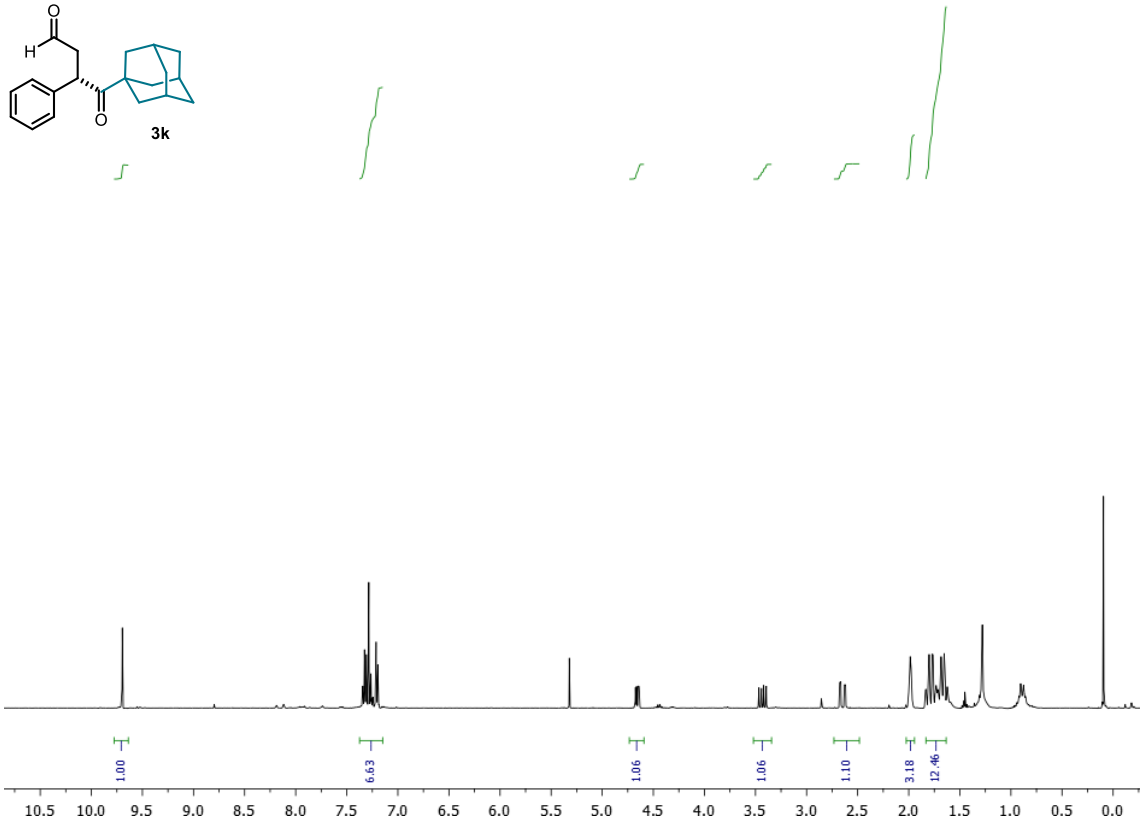


^{13}C NMR (101 MHz, $CDCl_3$)

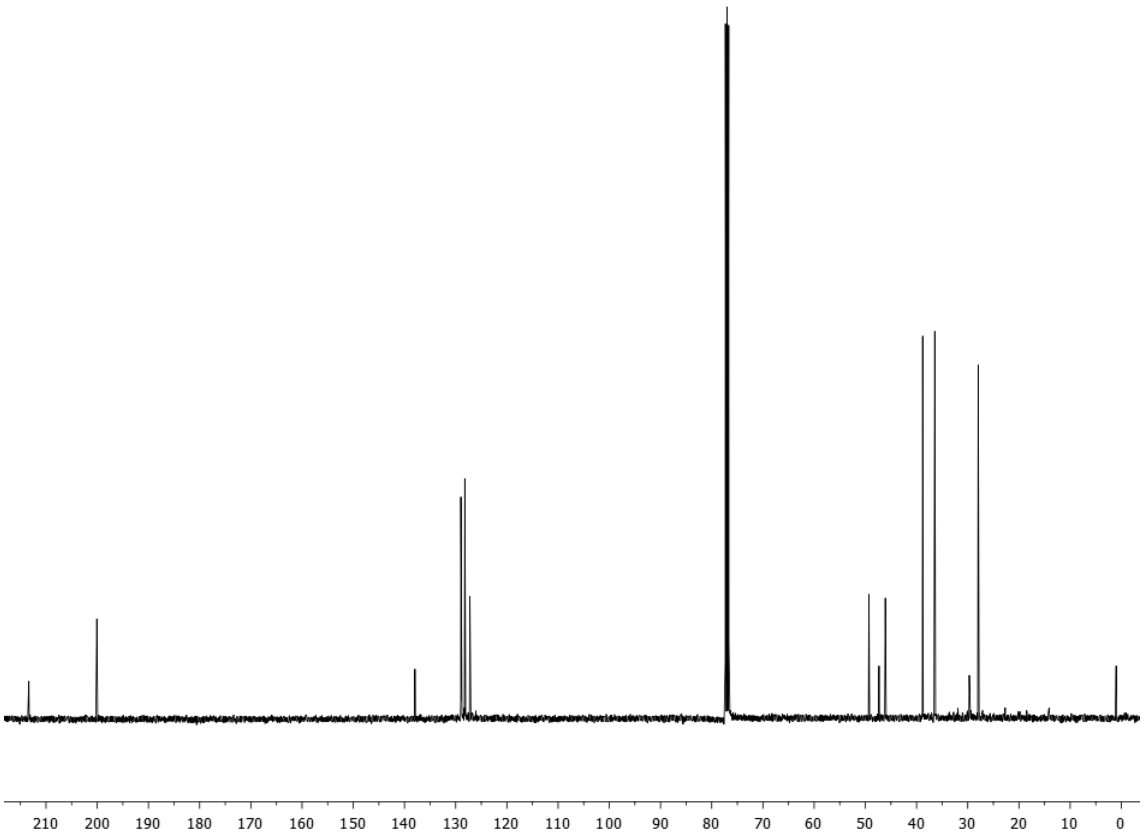


(*S*)-4-((3r,5r,7r)-Adamantan-1-yl)-4-oxo-3-phenylbutanal (3k)

^{1}H NMR (500 MHz, $CDCl_3$)

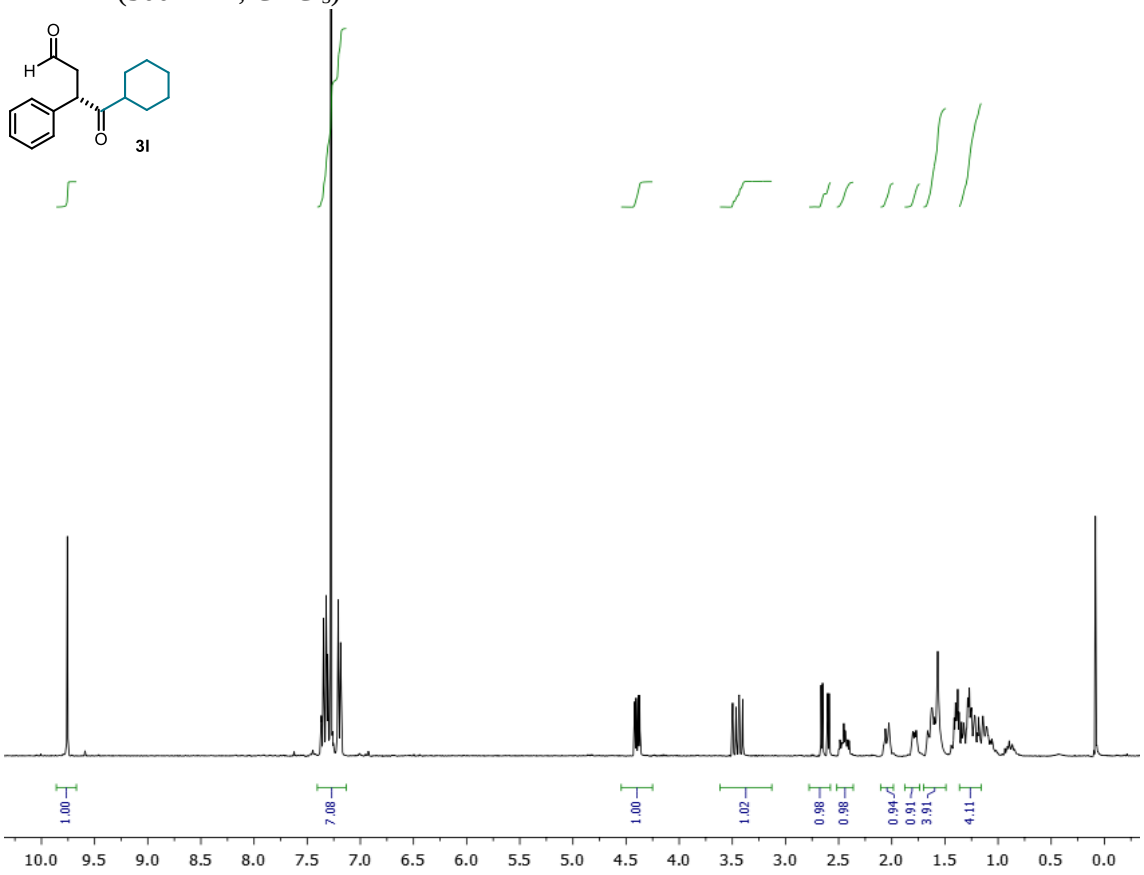


^{13}C NMR (101 MHz, $CDCl_3$)

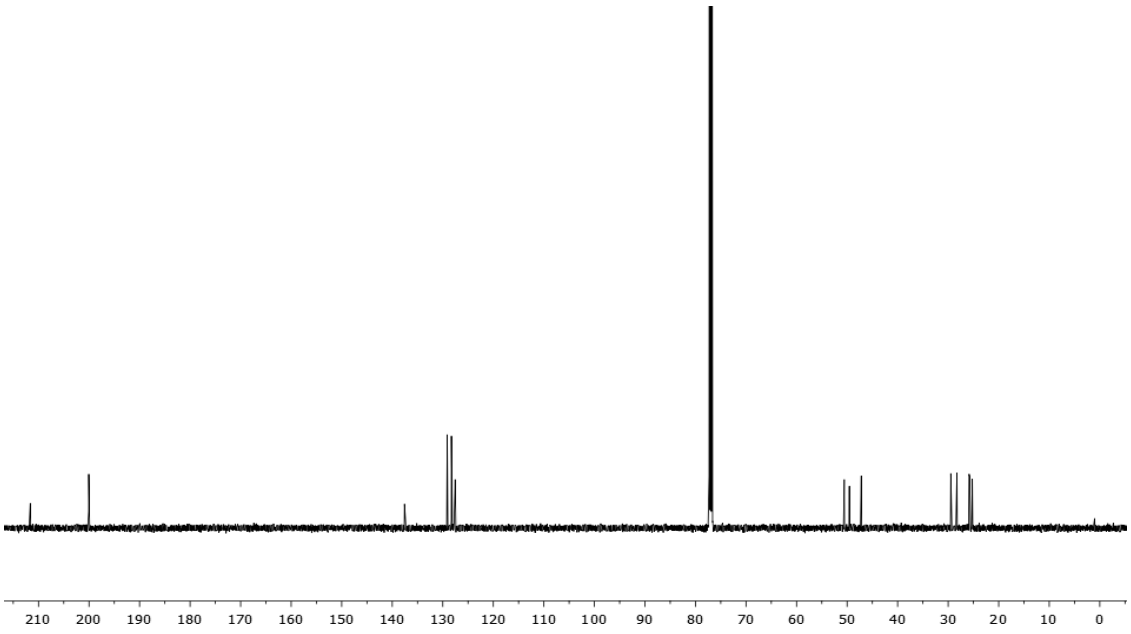


(*S*)-4-Cyclohexyl-4-oxo-3-phenylbutanal (3l)

^{1}H NMR (300 MHz, $CDCl_3$)

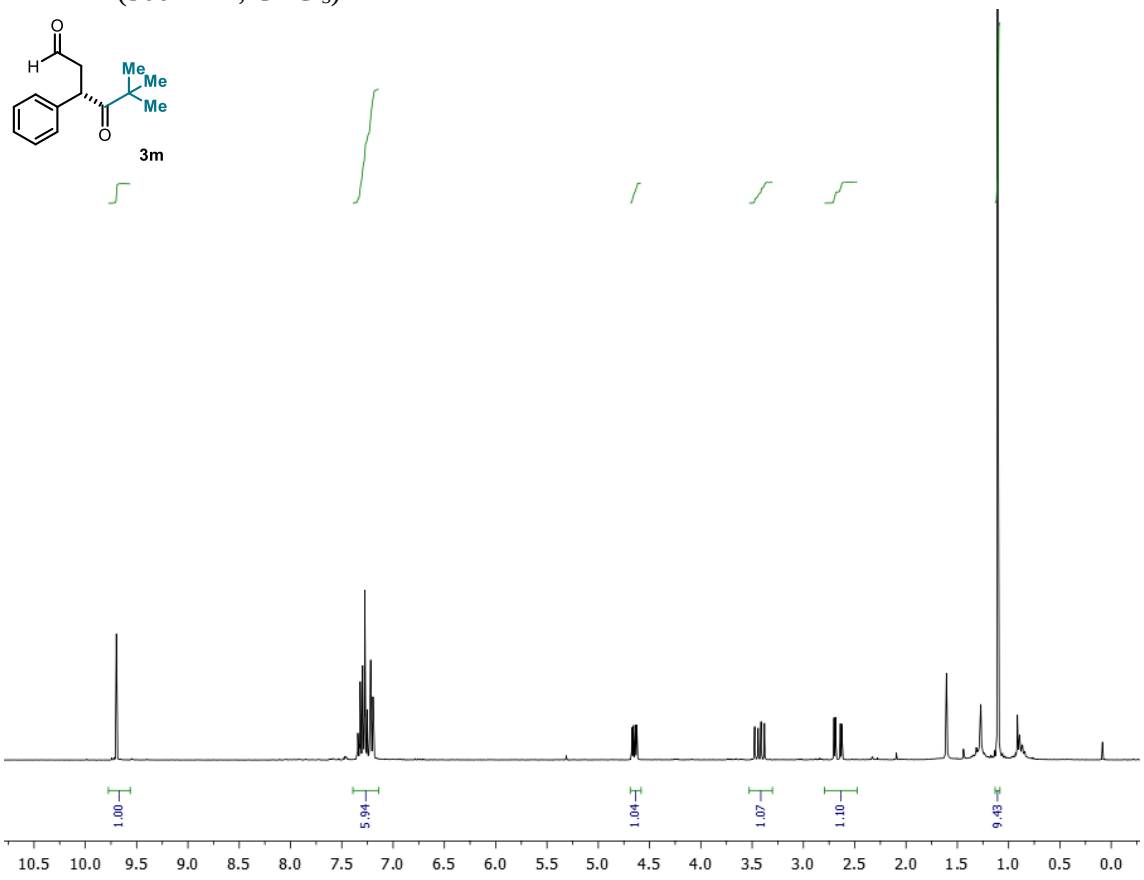


^{13}C NMR (126 MHz, $CDCl_3$)

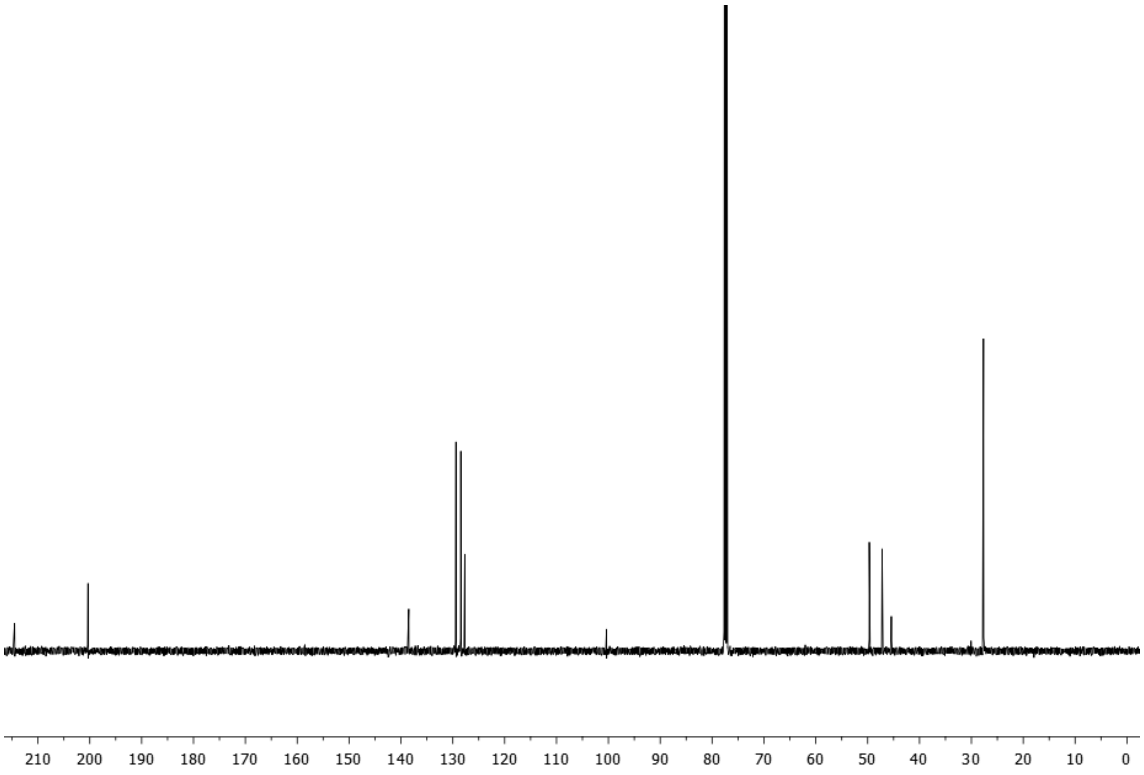


(*S*)-5,5-Dimethyl-4-oxo-3-phenylhexanal (3m)

^{1}H NMR (300 MHz, $CDCl_3$)

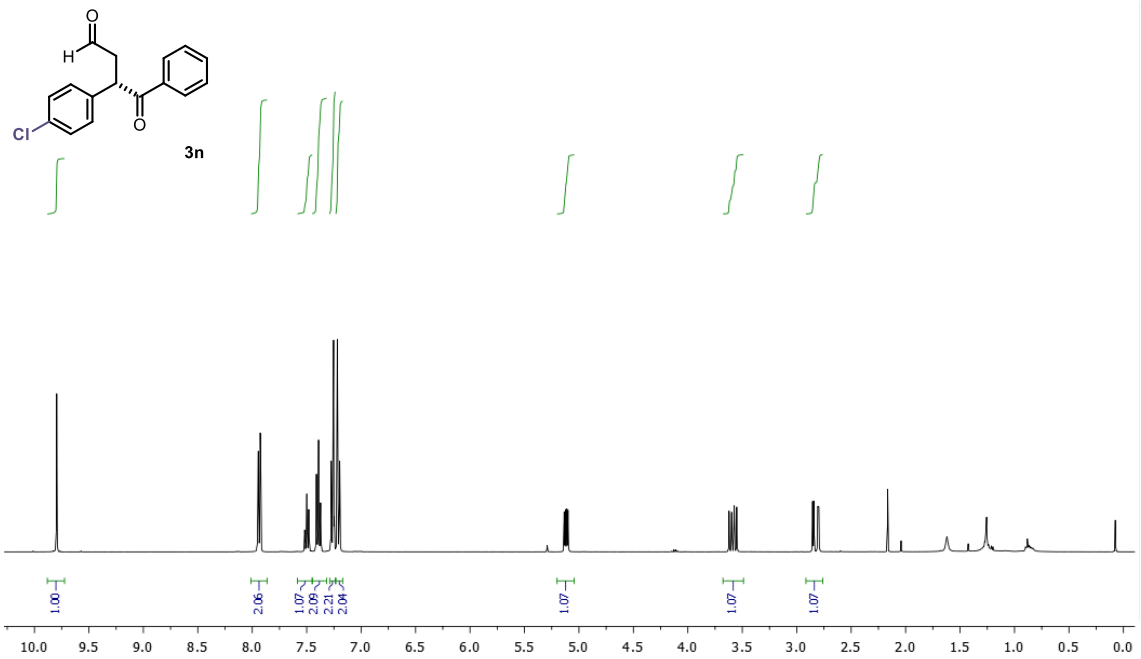


^{13}C NMR (126 MHz, $CDCl_3$)

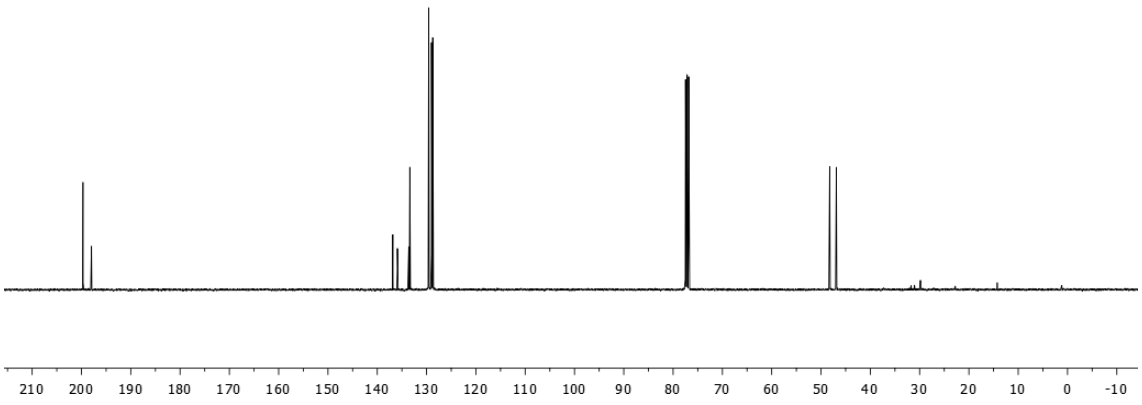


(*S*)-3-(4-chlorophenyl)-4-oxo-4-phenylbutanal (3n)

^{1}H NMR (400 MHz, $CDCl_3$)

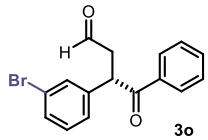


^{13}C NMR (101 MHz, $CDCl_3$)

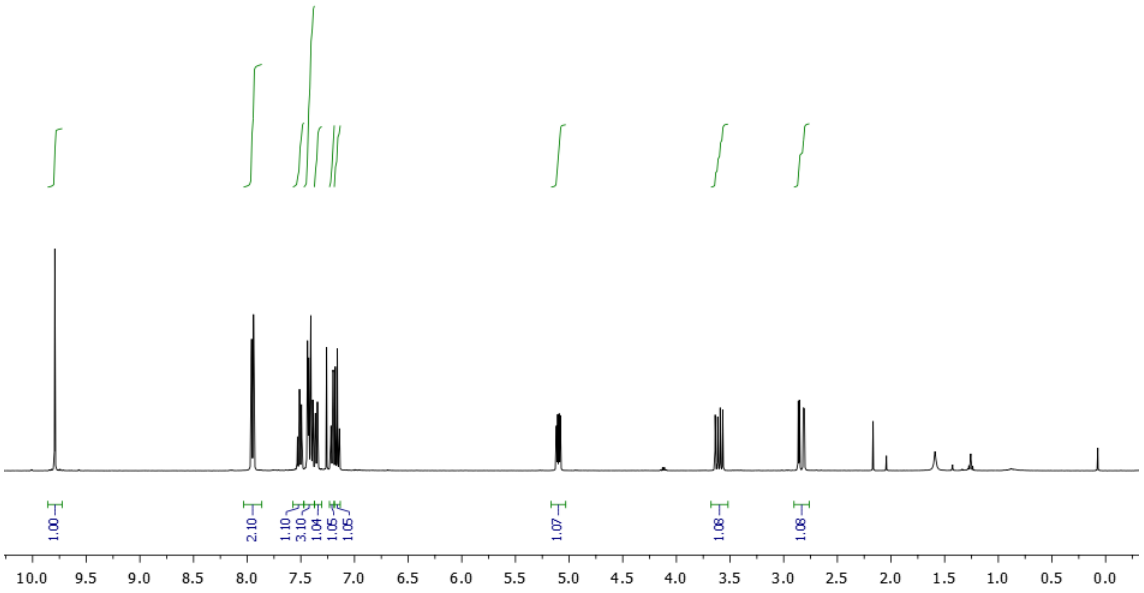


(*S*)-3-(3-bromophenyl)-4-oxo-4-phenylbutanal (3o)

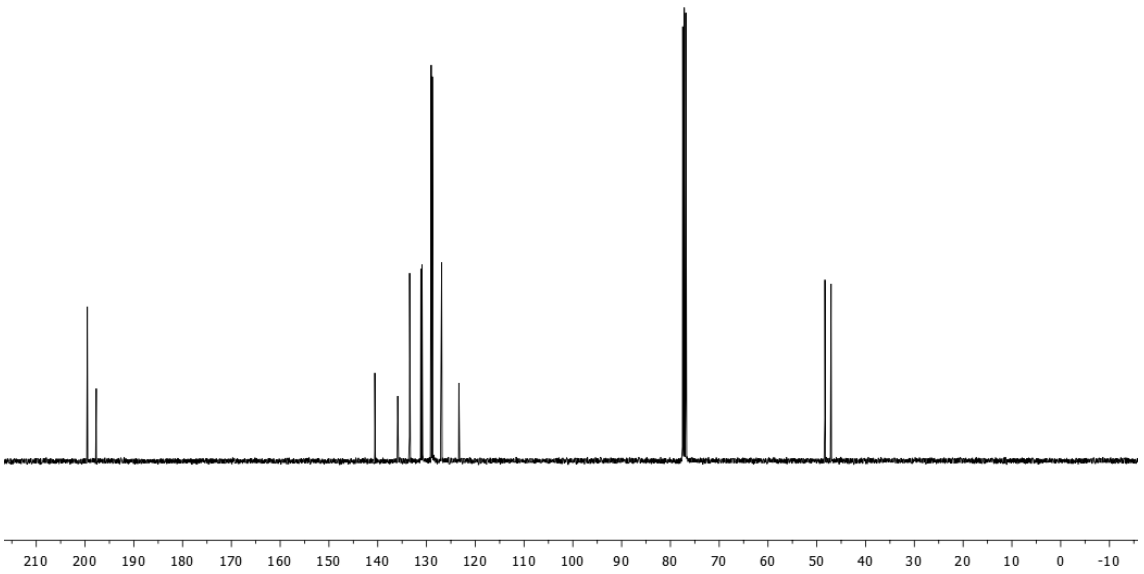
^{1}H NMR (400 MHz, $CDCl_3$)



3o

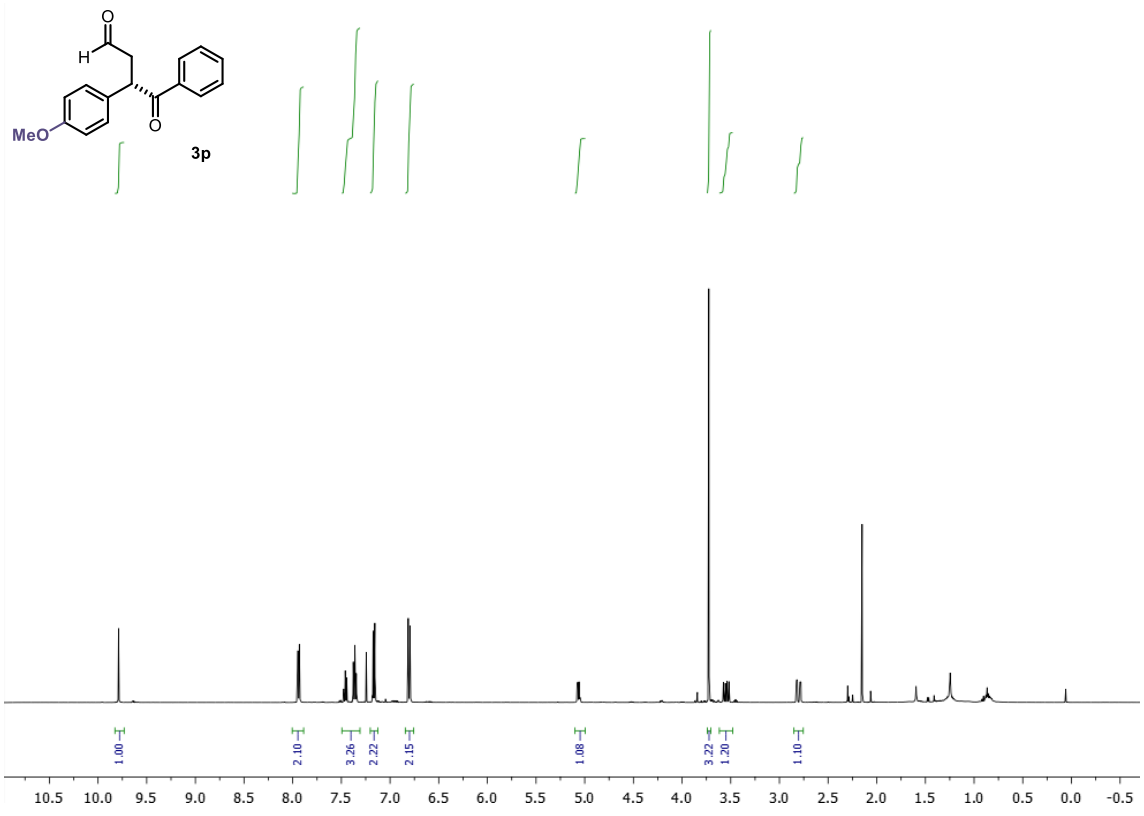


^{13}C NMR (101 MHz, $CDCl_3$)

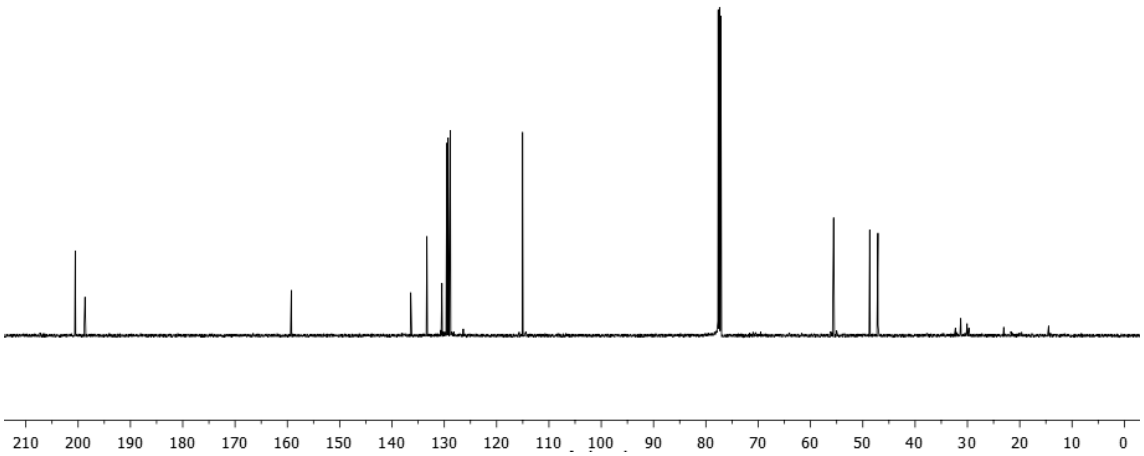


(*S*)-3-(4-methoxyphenyl)-4-oxo-4-phenylbutanal (3p)

^{1}H NMR (500 MHz, $CDCl_3$)

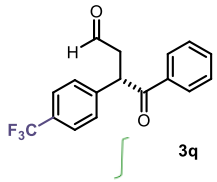


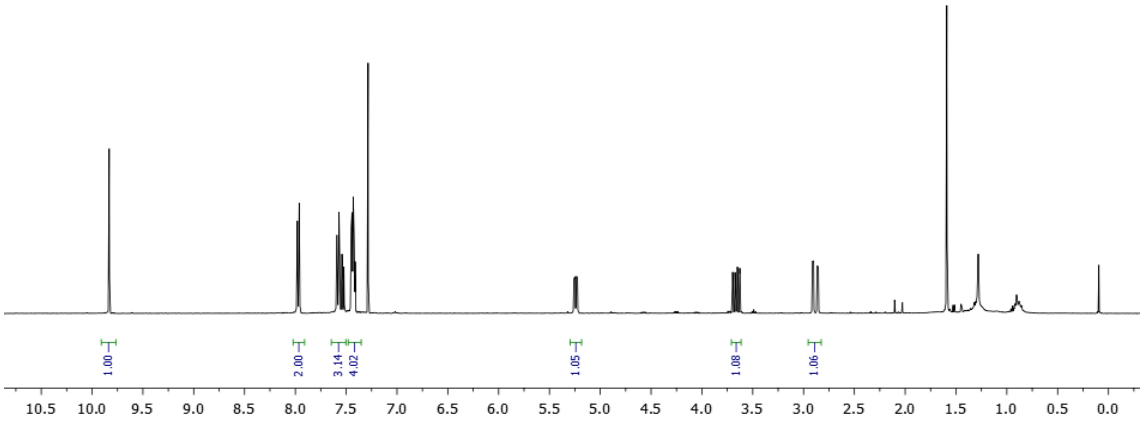
^{13}C NMR (126 MHz, $CDCl_3$)



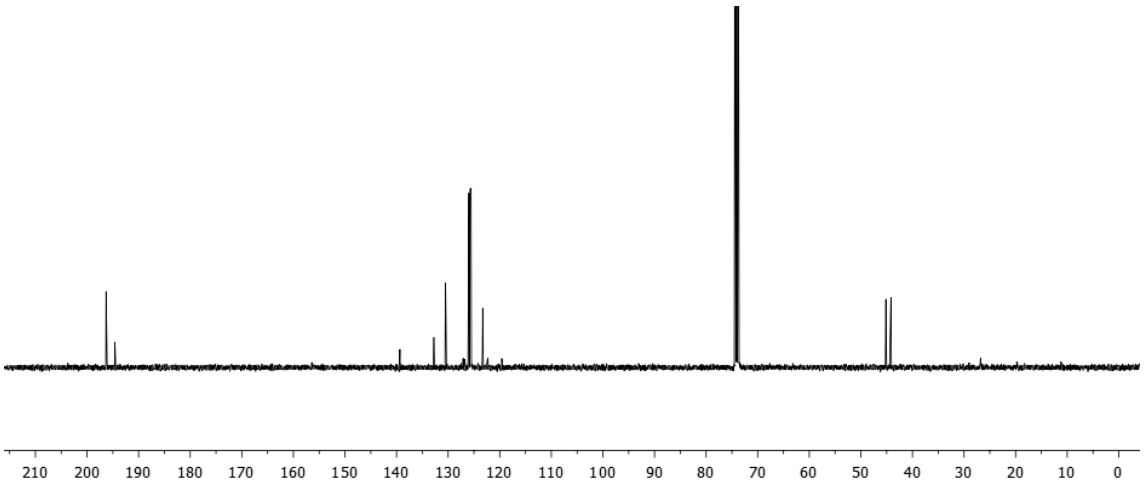
(*S*)-4-oxo-4-phenyl-3-(4-(trifluoromethyl)phenyl)butanal (3q)

^{1}H NMR (400 MHz, $CDCl_3$)

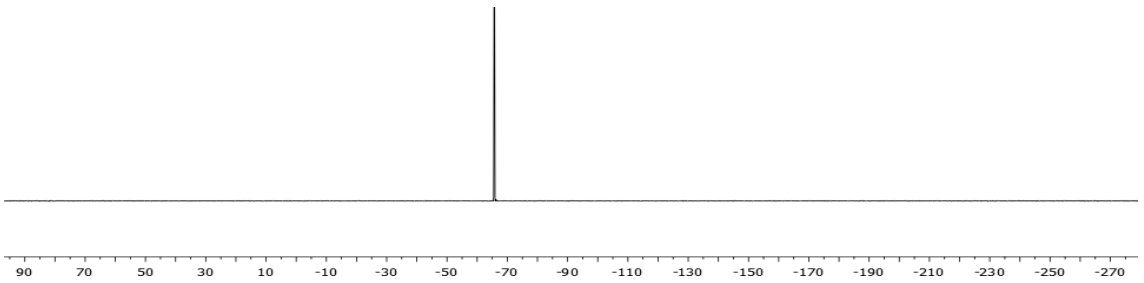




^{13}C NMR (101 MHz, $CDCl_3$)

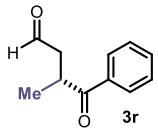


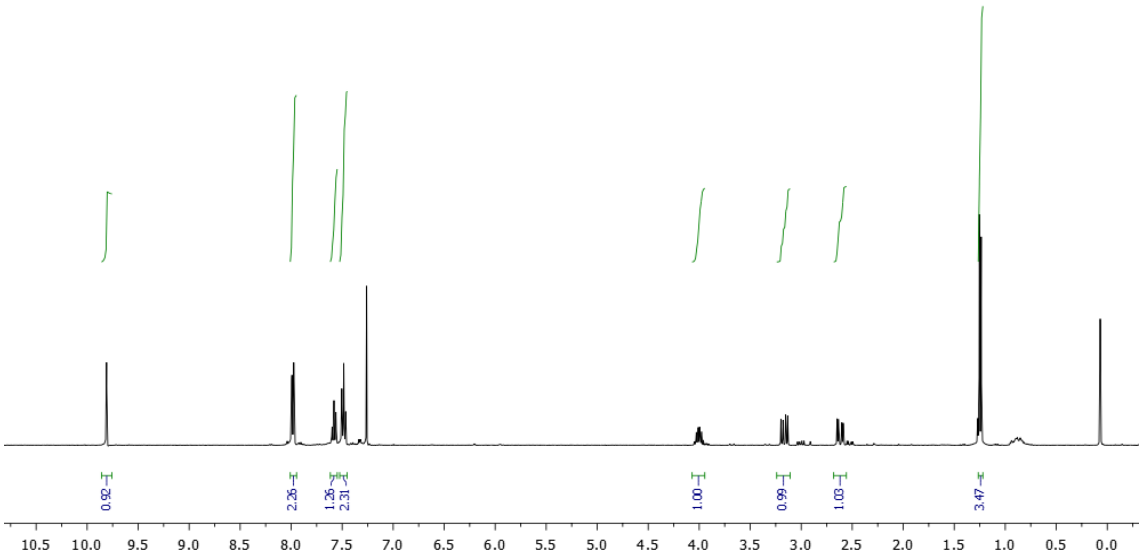
^{19}F NMR (376 MHz, $CDCl_3$).



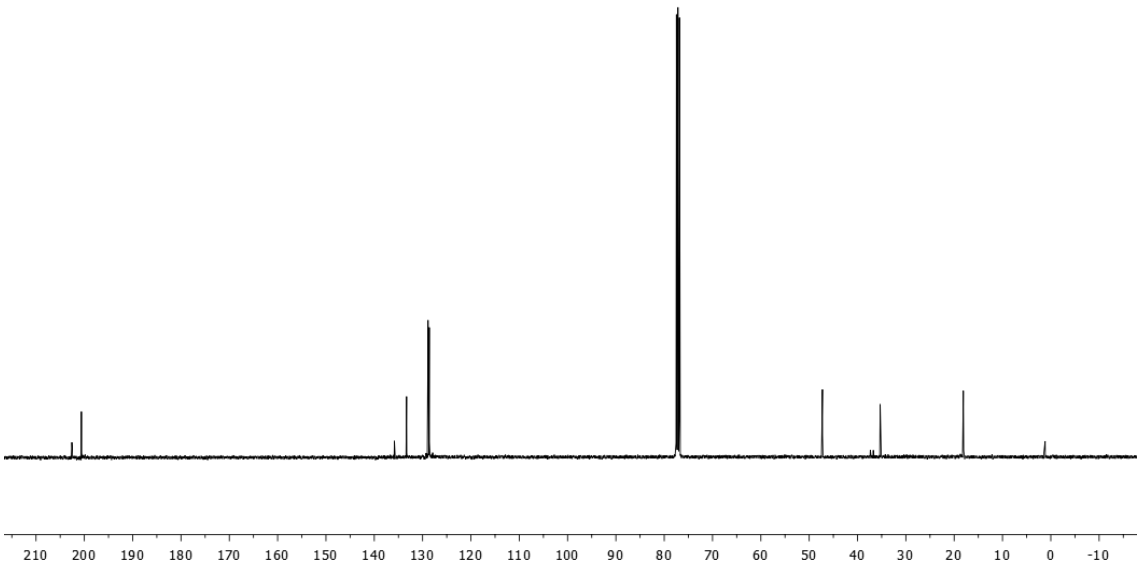
(*R*)-3-methyl-4-oxo-4-phenylbutanal (3r)

^{1}H NMR (500 MHz, $CDCl_3$)



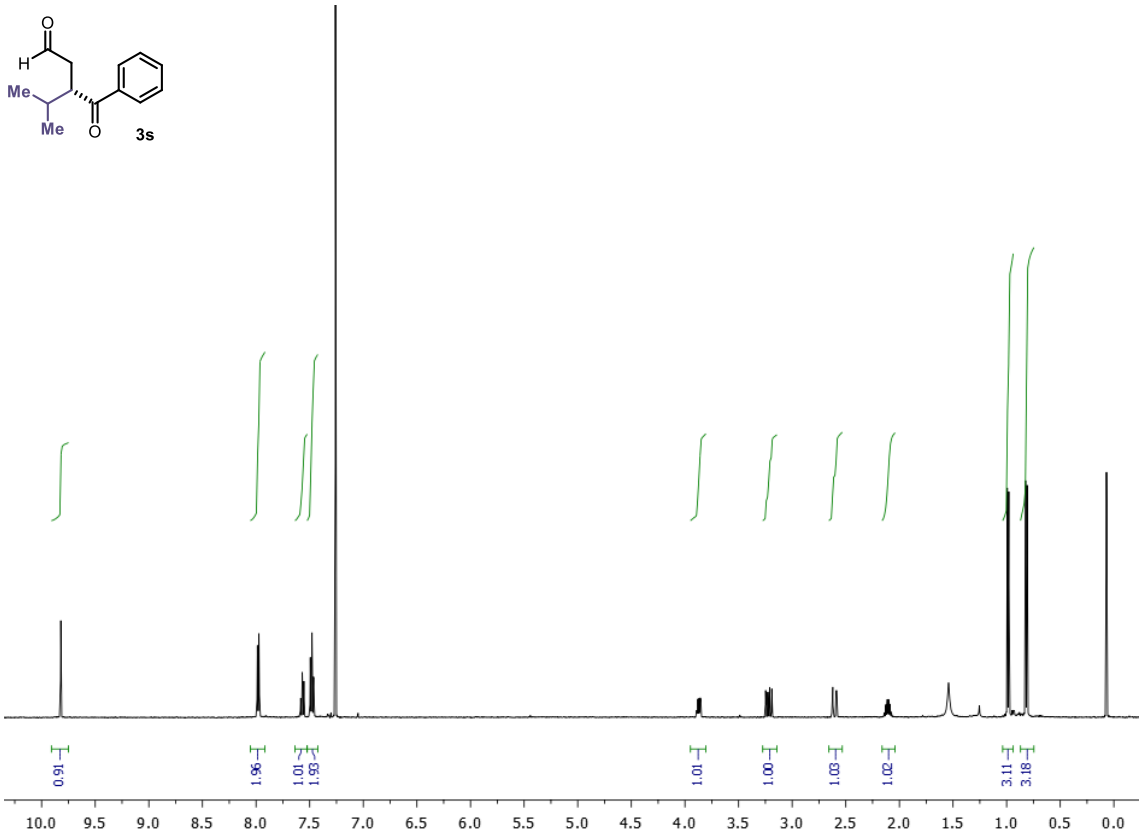


^{13}C NMR (101 MHz, $CDCl_3$)

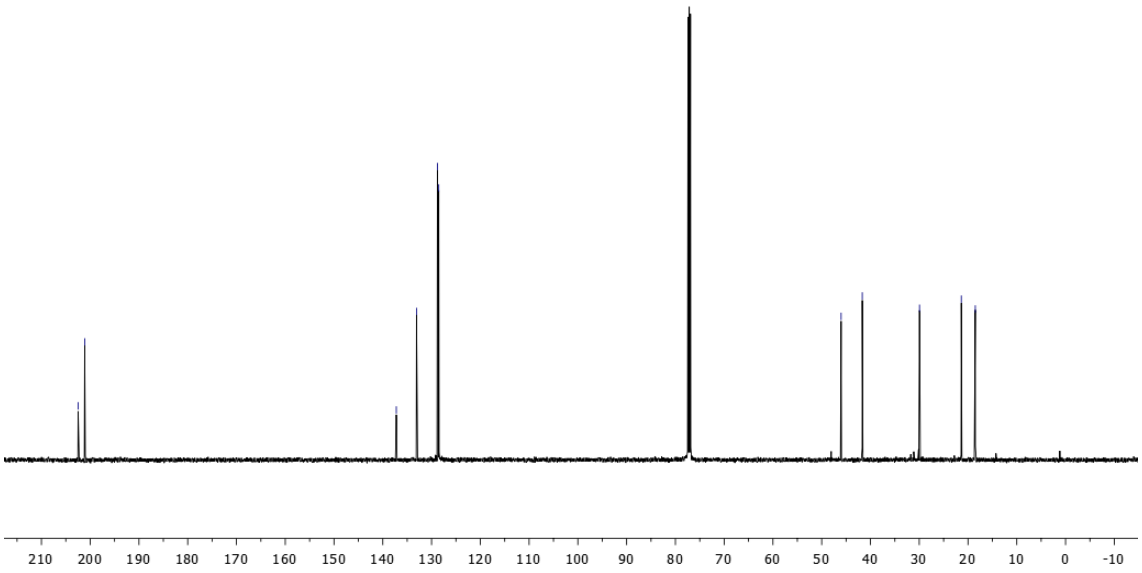


(*S*)-3-benzoyl-4-methylpentanal (3s)

^{1}H NMR (500 MHz, $CDCl_3$)

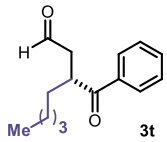


^{13}C NMR (126 MHz, $CDCl_3$)

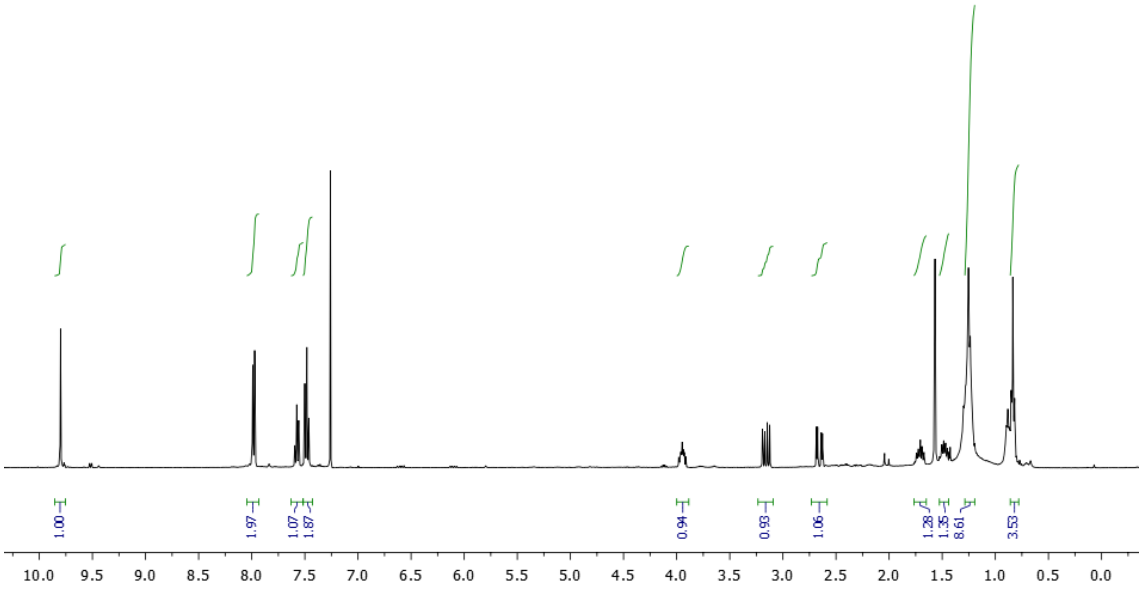


(*R*)-3-benzoyloctanal (3t)

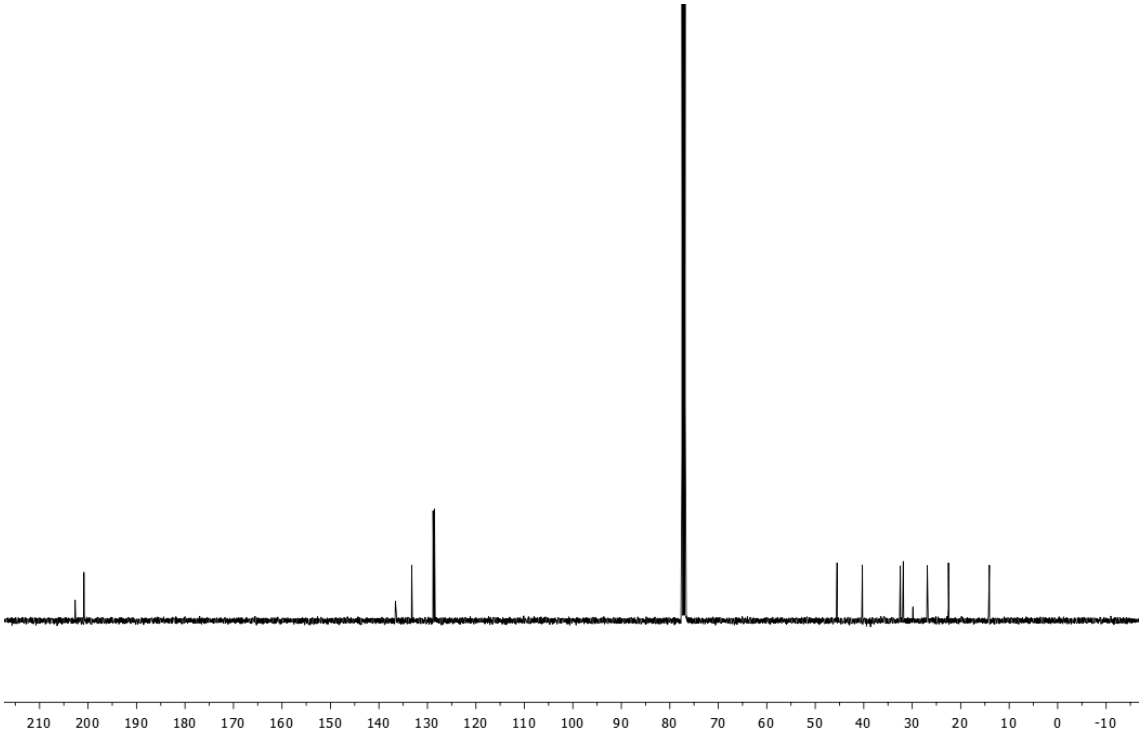
^{1}H NMR (500 MHz, $CDCl_3$)



3t

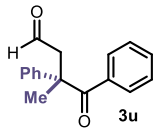


^{13}C NMR (101 MHz, $CDCl_3$)

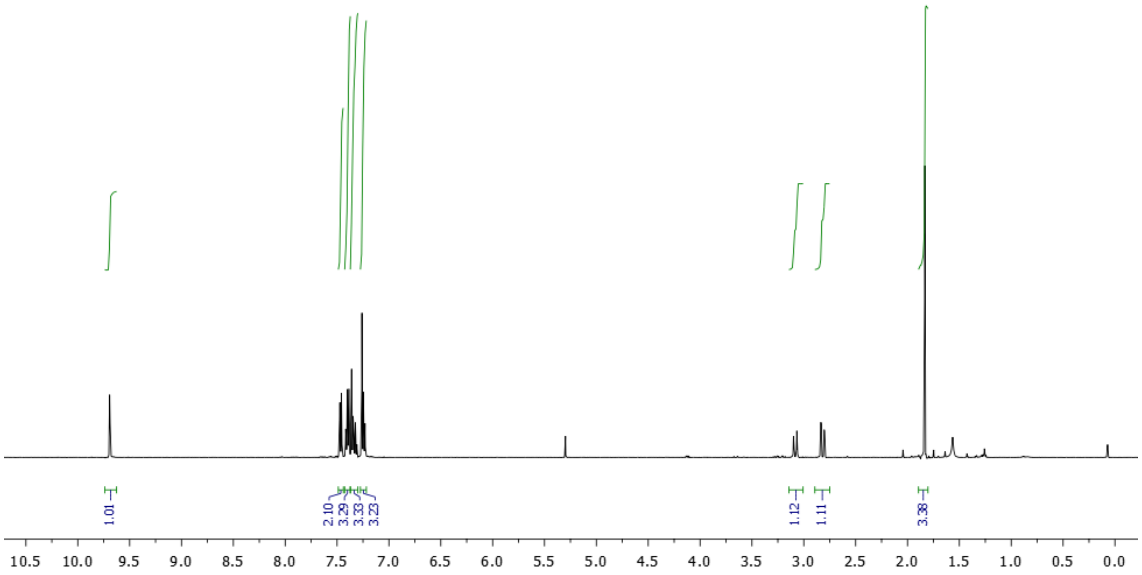


(*S*)-3-methyl-4-oxo-3,4-diphenylbutanal (3u)

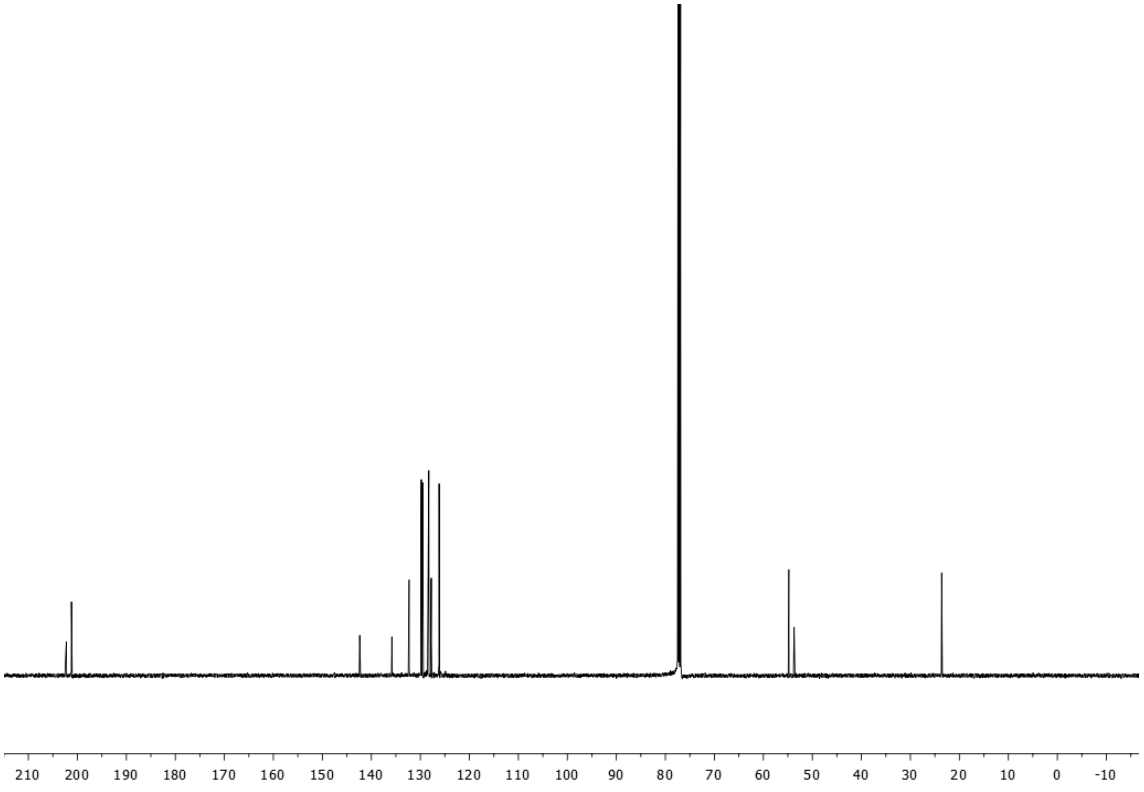
^{1}H NMR (500 MHz, $CDCl_3$)



3u

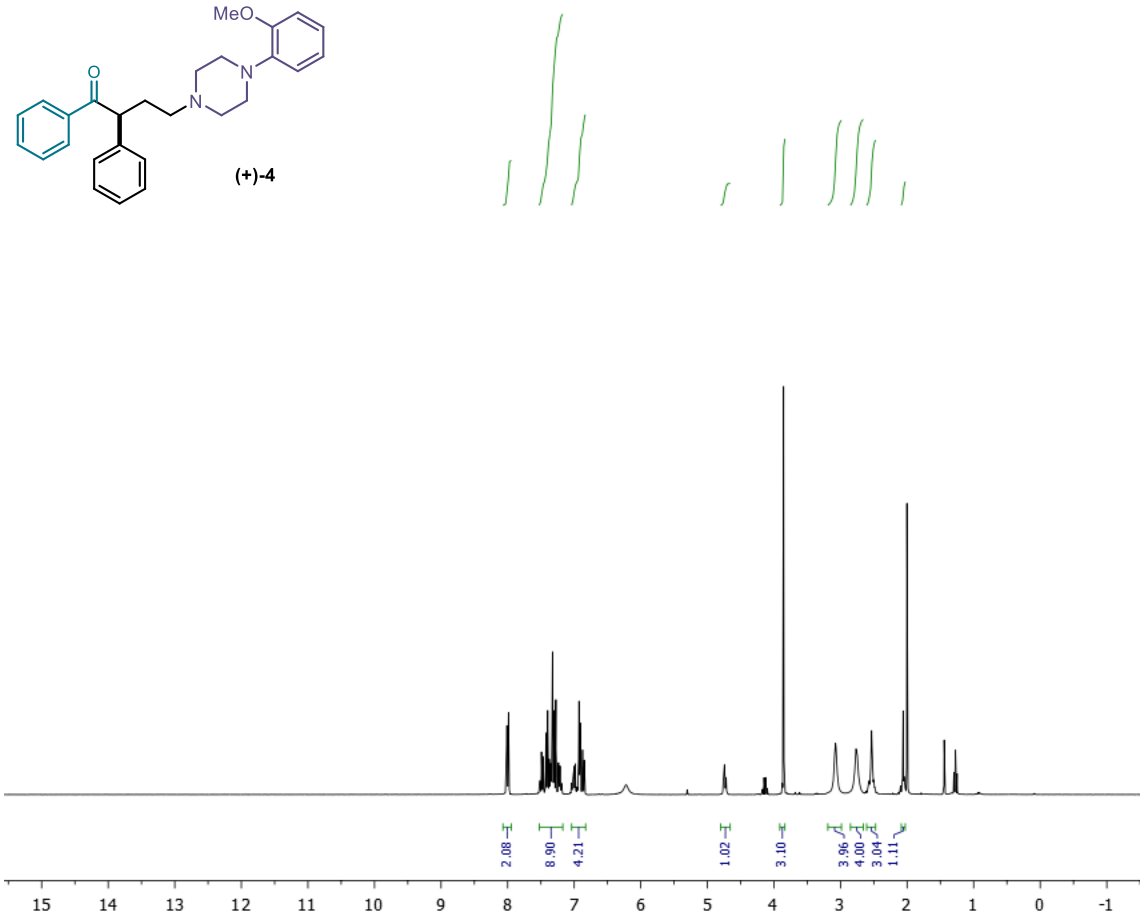


^{13}C NMR (126 MHz, $CDCl_3$)

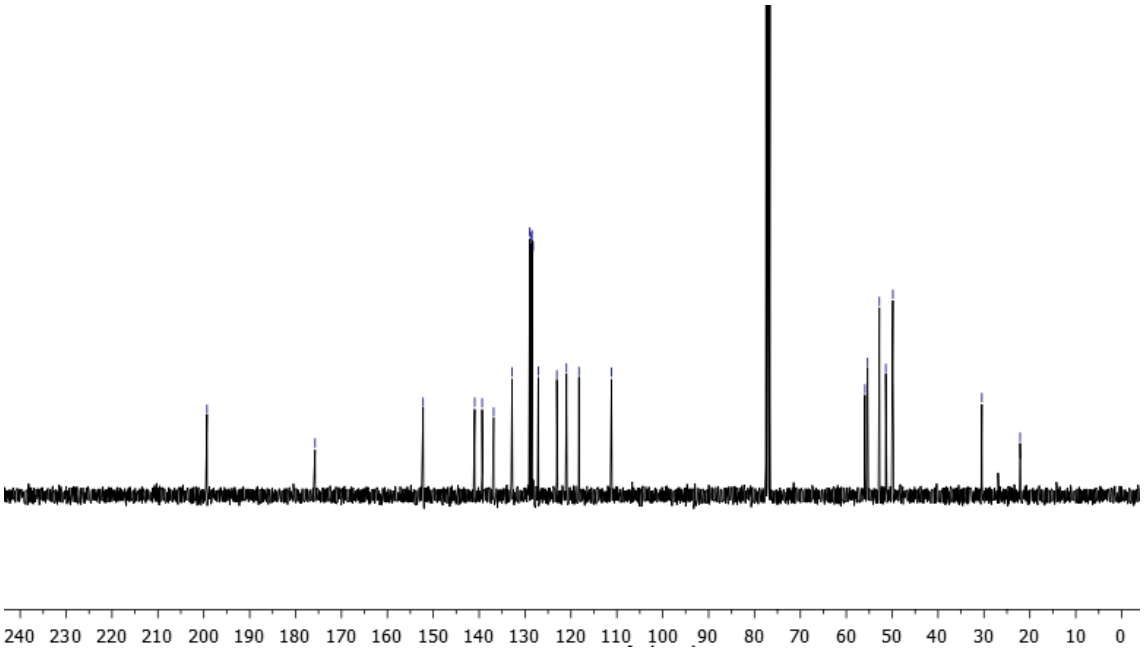


(*S*)-(+)-4-(4-(2-methoxyphenyl)piperazin-1-yl)-1,2-diphenylbutan-1-one (4)

^{1}H NMR (300 MHz, $CDCl_3$)

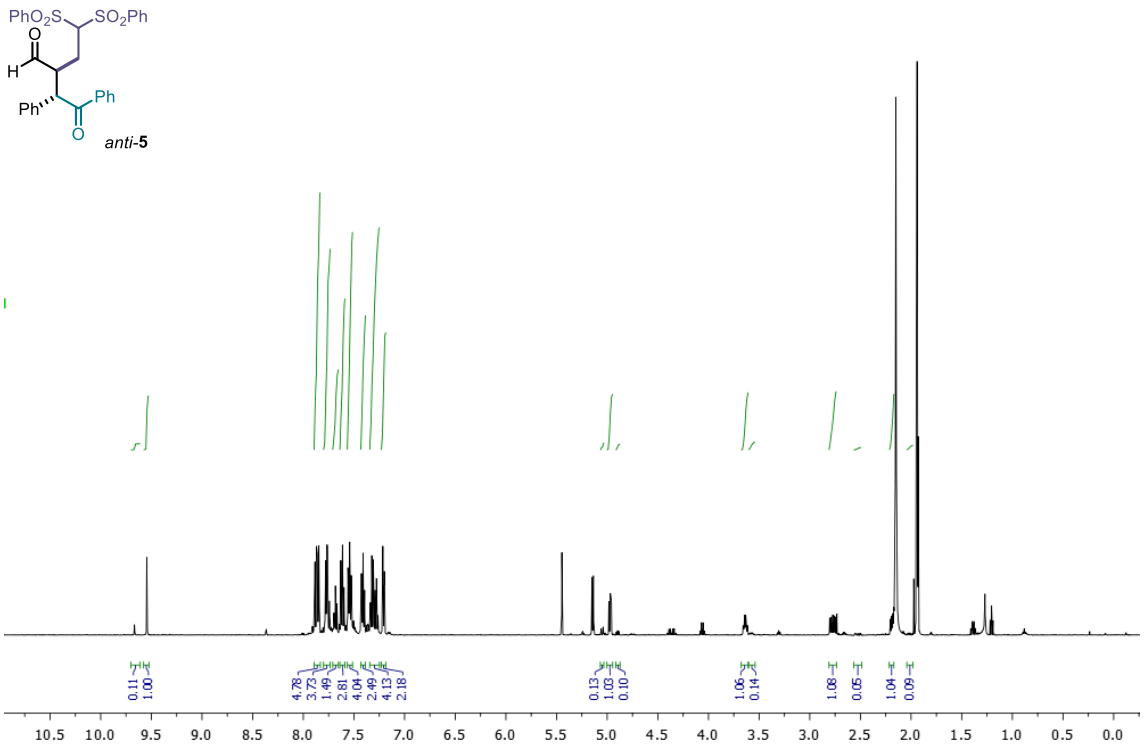


^{13}C NMR (75 MHz, $CDCl_3$)

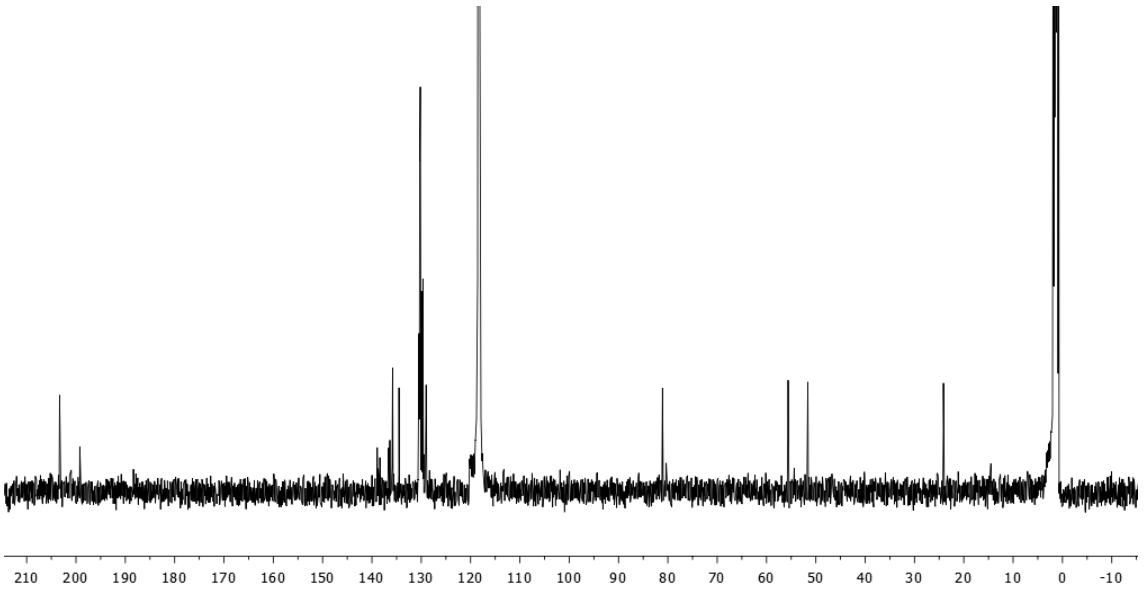


(2*S*,3*S*)-2-(2,2-bis(phenylsulfonyl)ethyl)-4-oxo-3,4-diphenylbutanal (*anti*-5)

^{1}H NMR (500 MHz, CD_3CN, 9:1 d.r.)

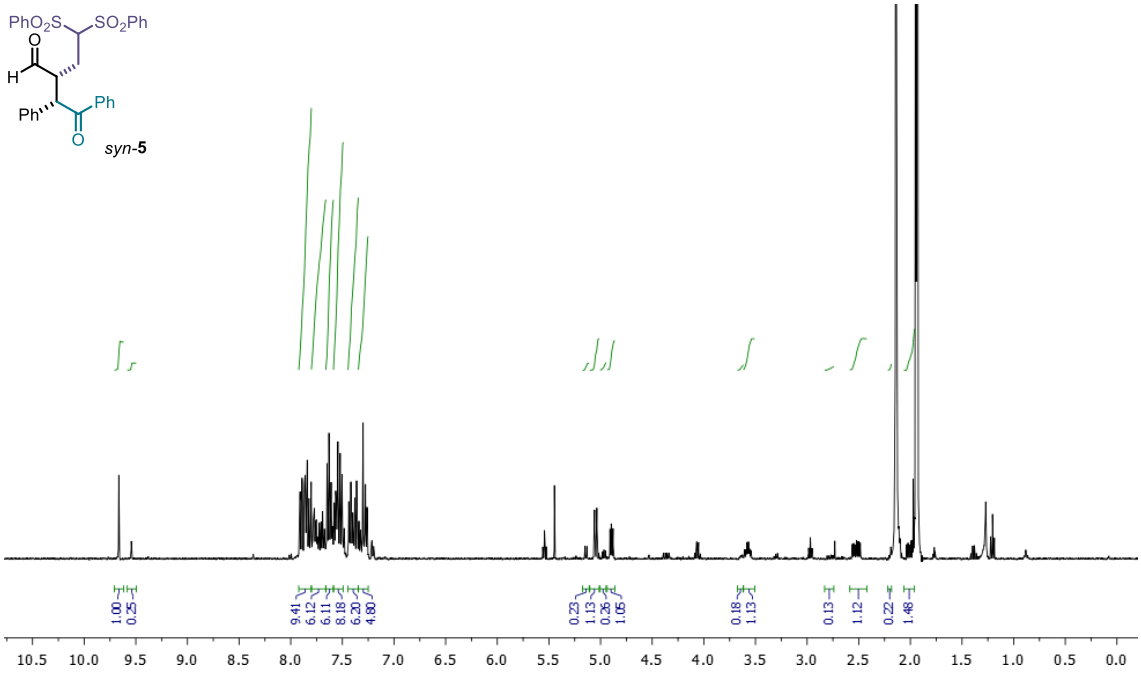


^{13}C NMR (126 MHz, CD_3CN)

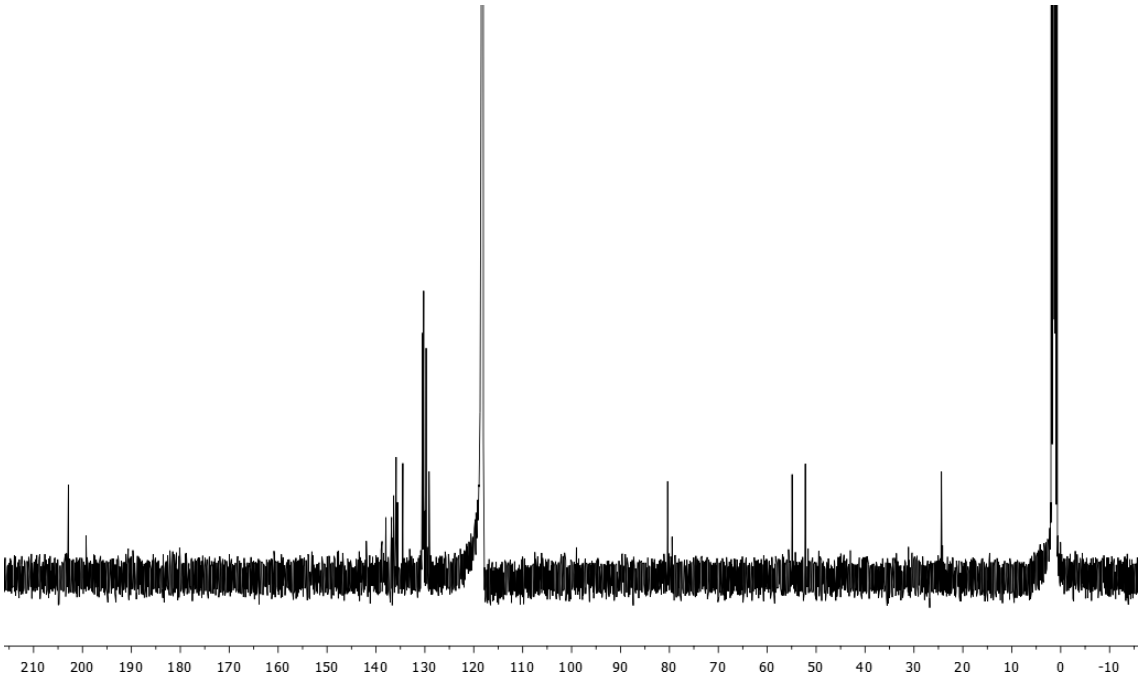


(2*S*,3*S*)-2-(2,2-bis(phenylsulfonyl)ethyl)-4-oxo-3,4-diphenylbutanal (*syn*-5)

^{1}H NMR (400 MHz, CD_3CN, 4:1 d.r.)

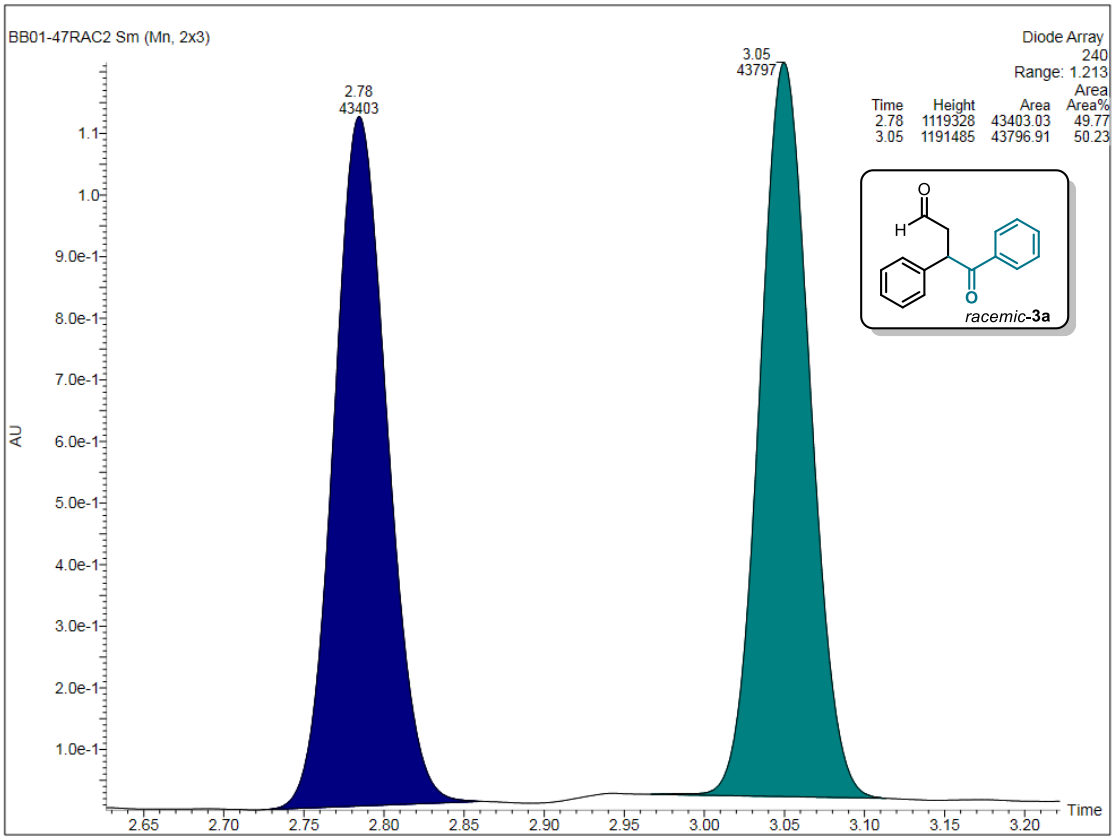


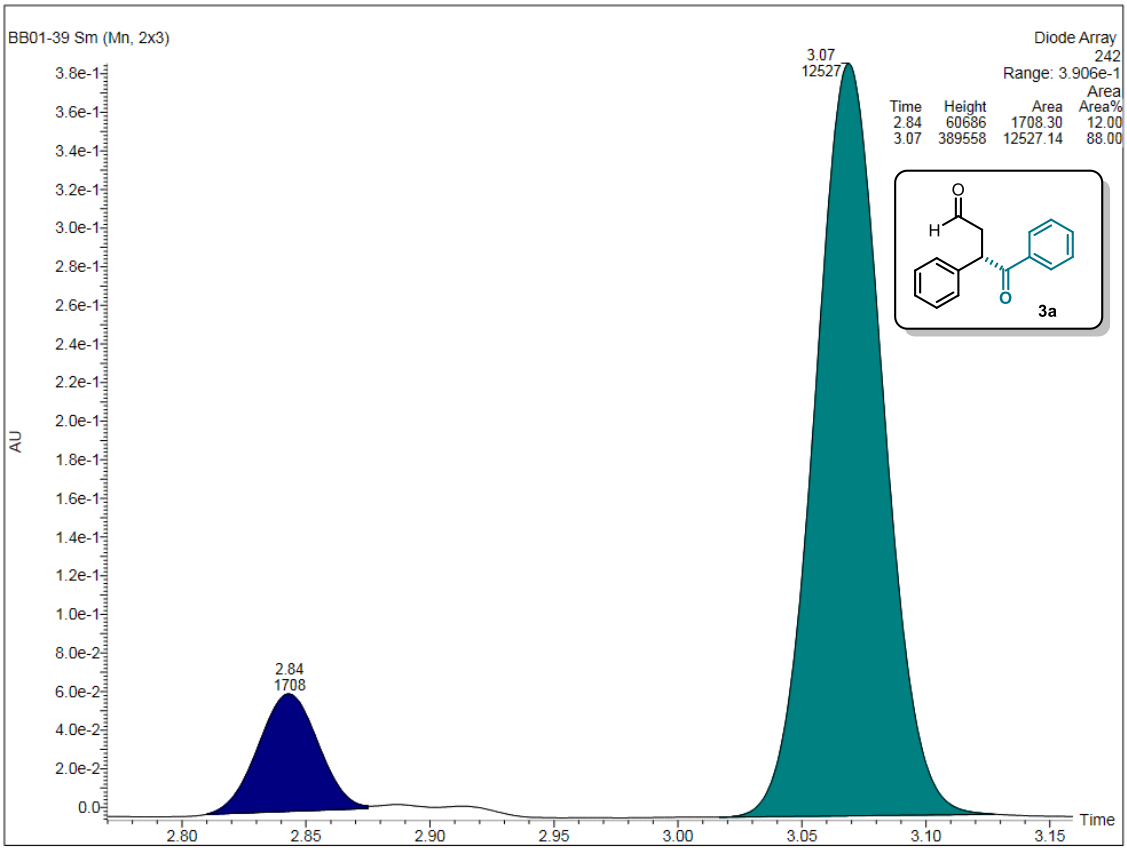
^{13}C NMR (126 MHz, CD_3CN)



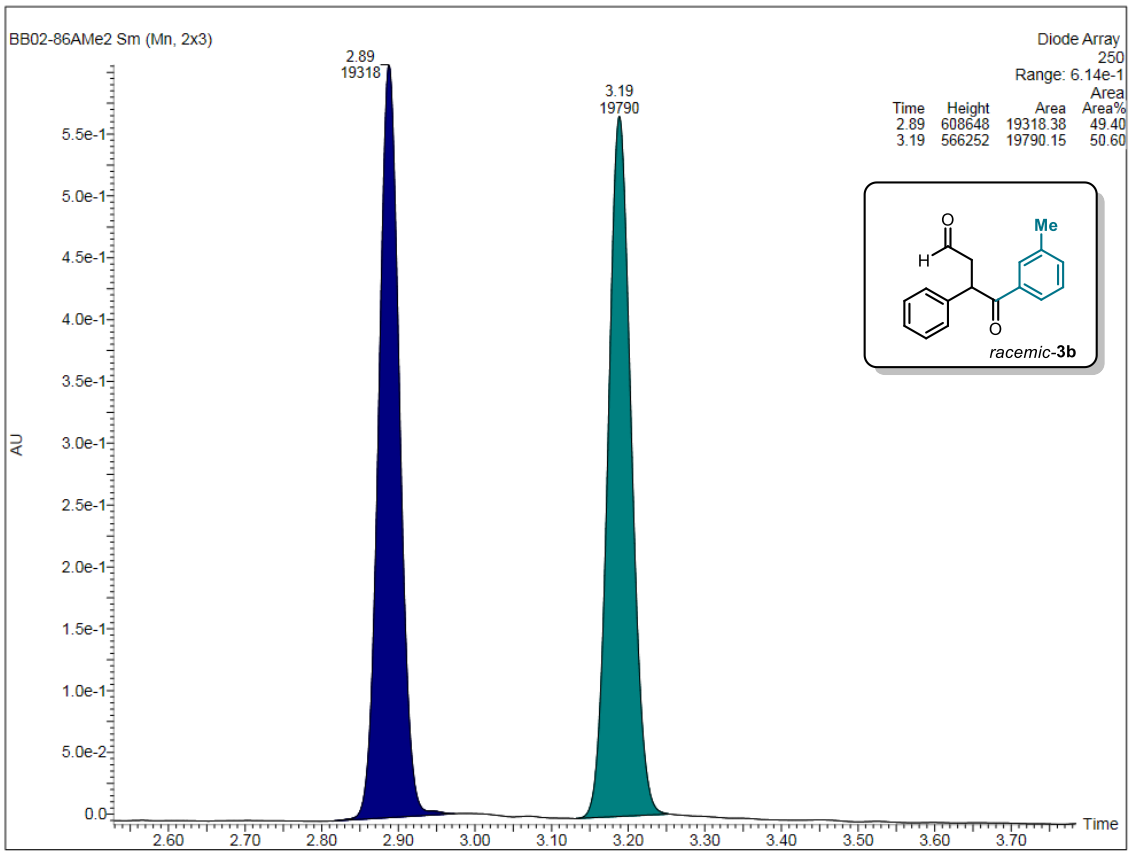
M. UPC^2 Traces

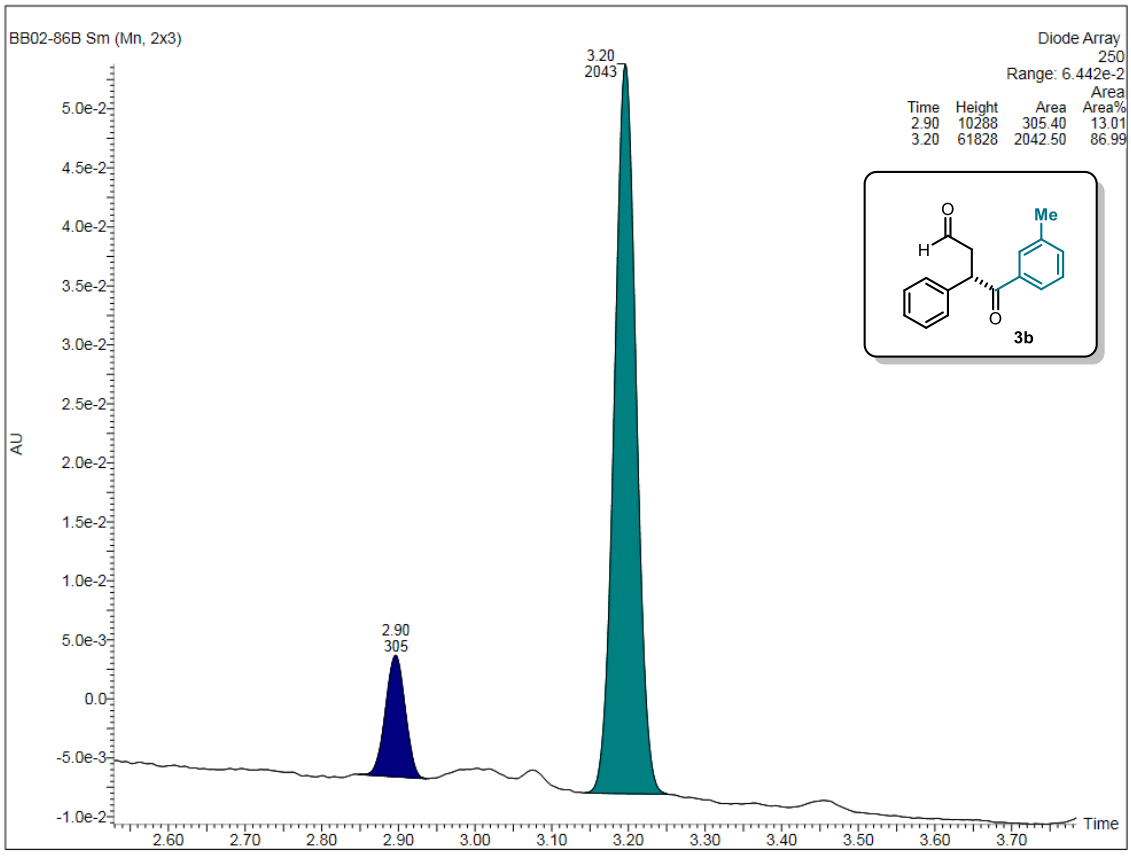
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ = 240 nm.



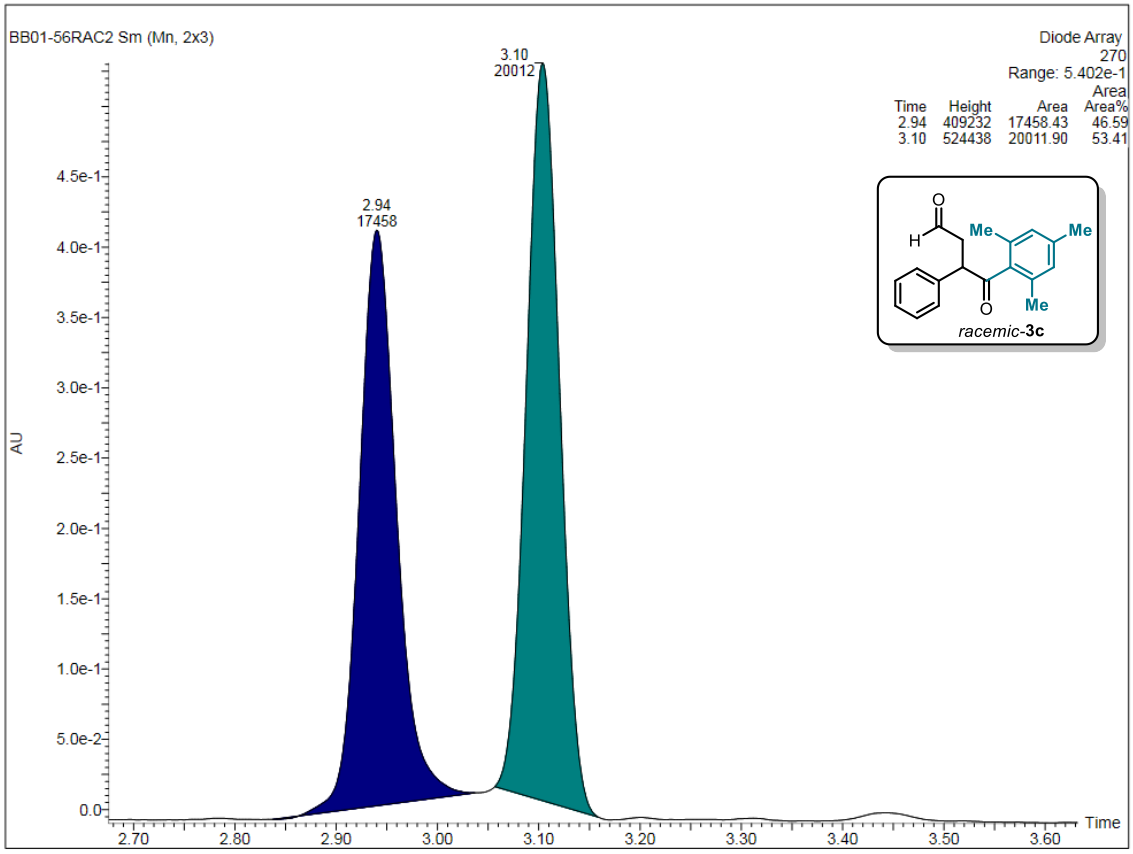


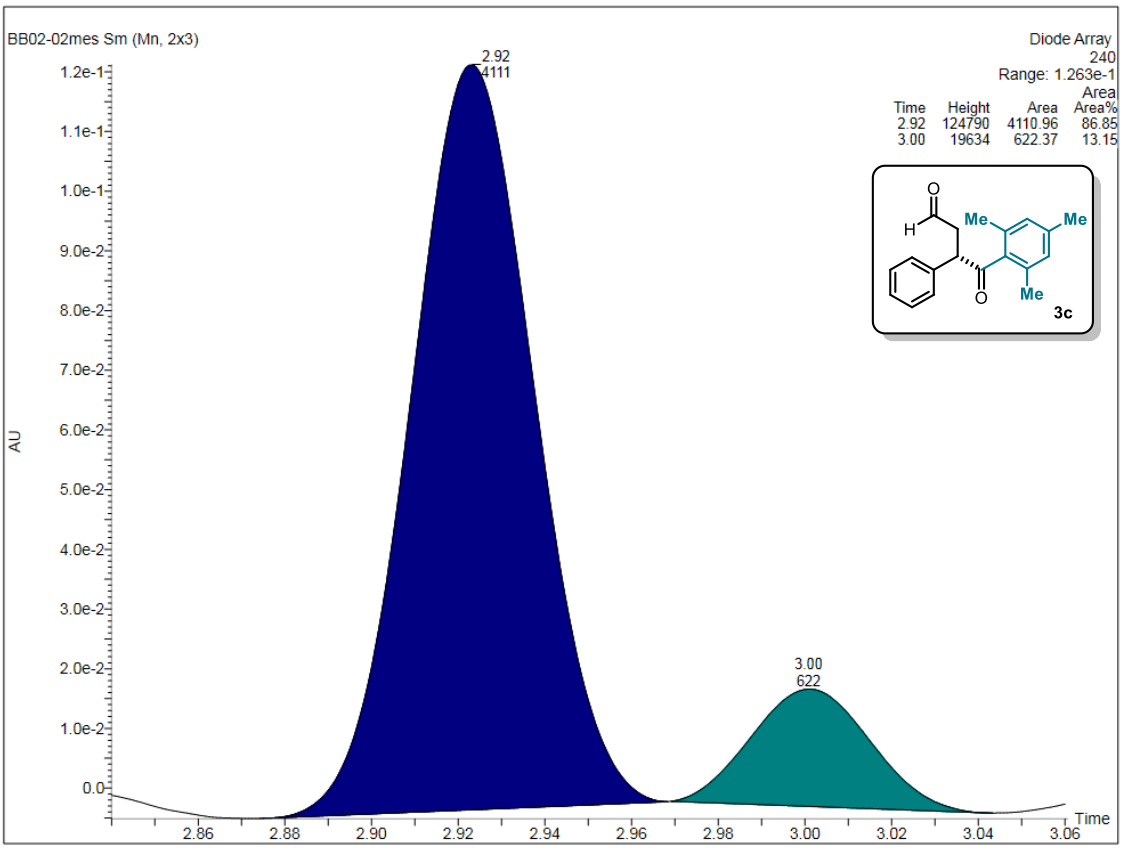
Conditions: : UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% ACN, flow rate 2 mL/min, λ=250 nm.



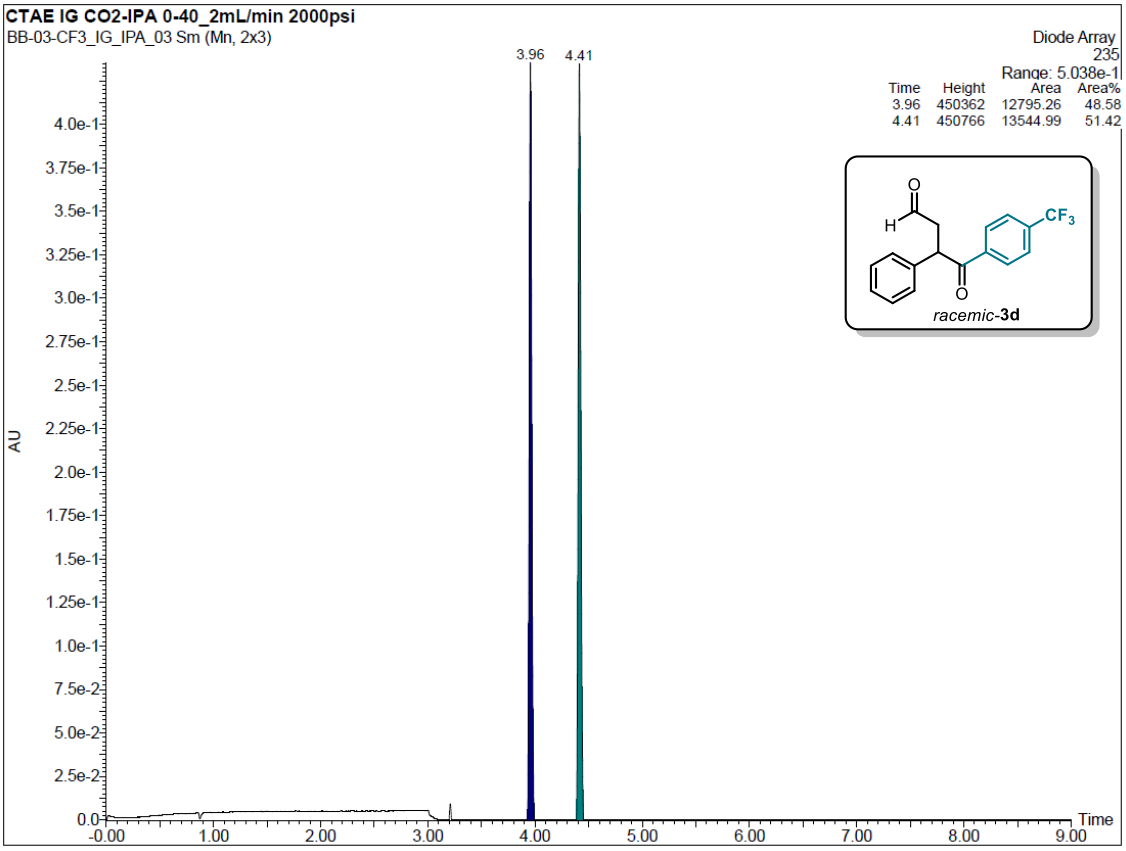


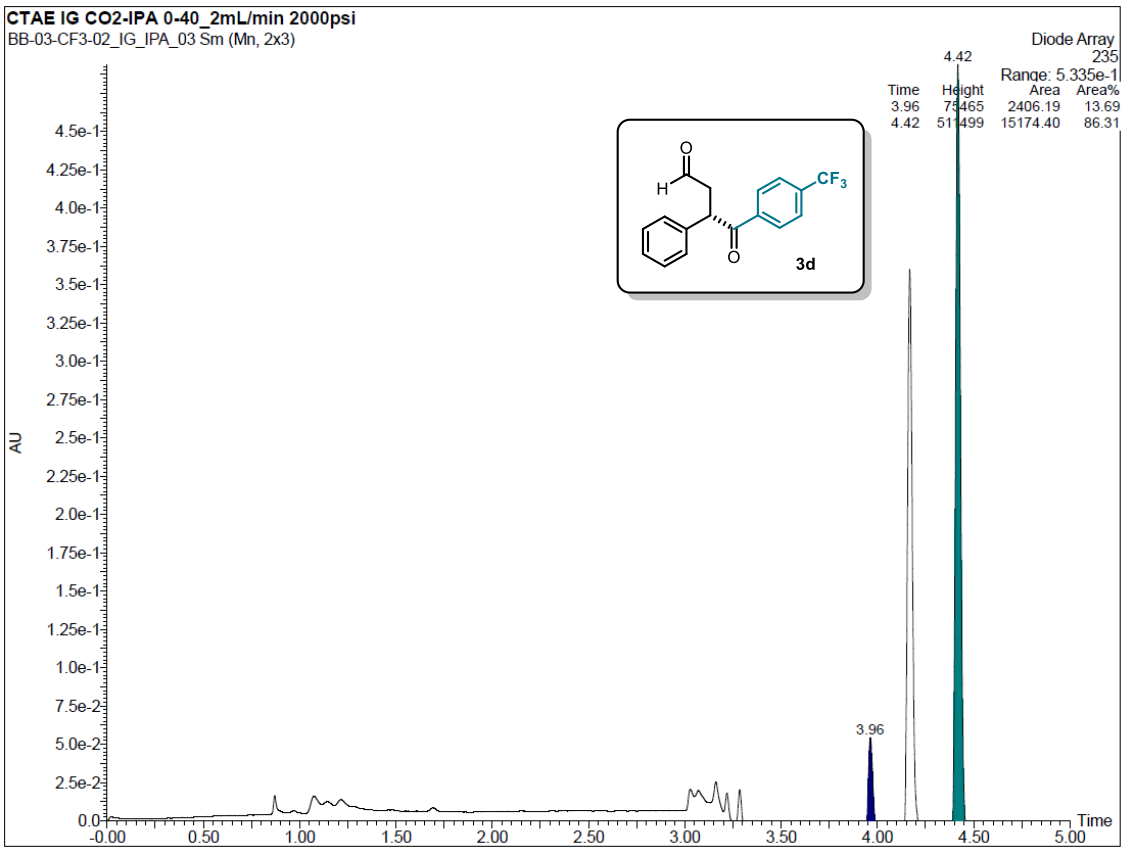
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ=270 nm).



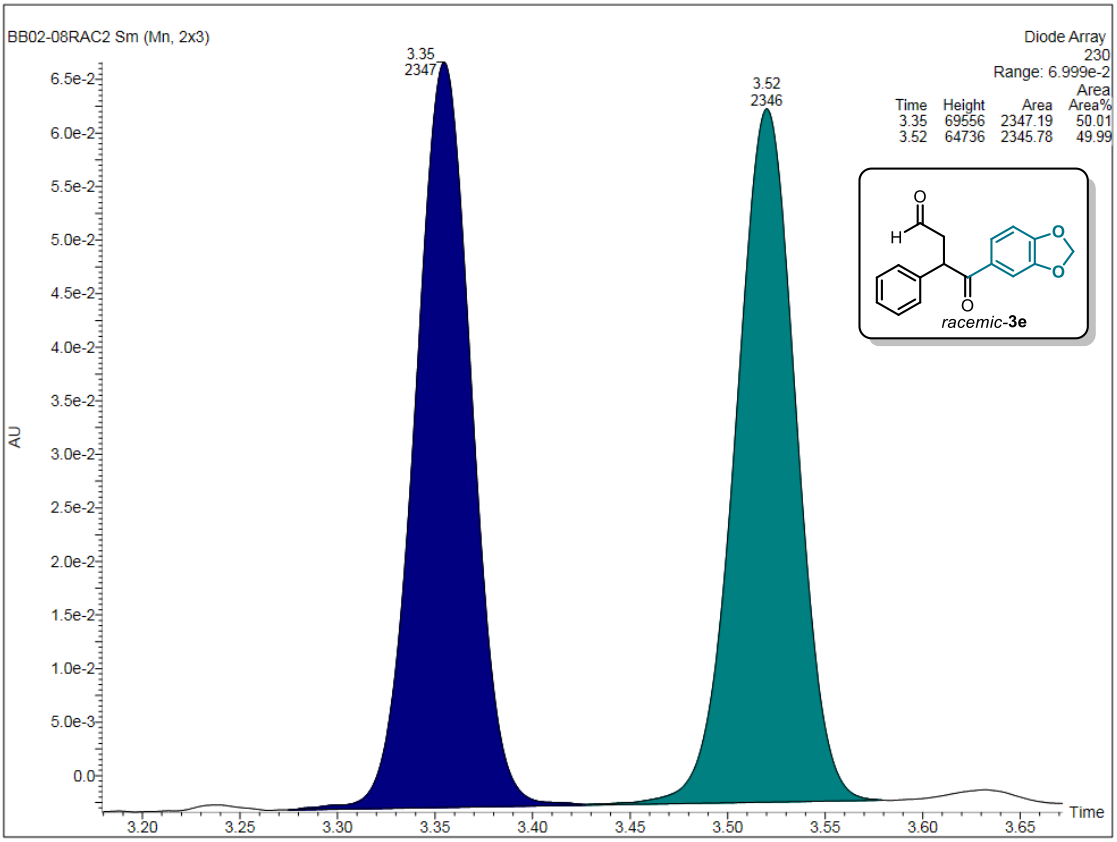


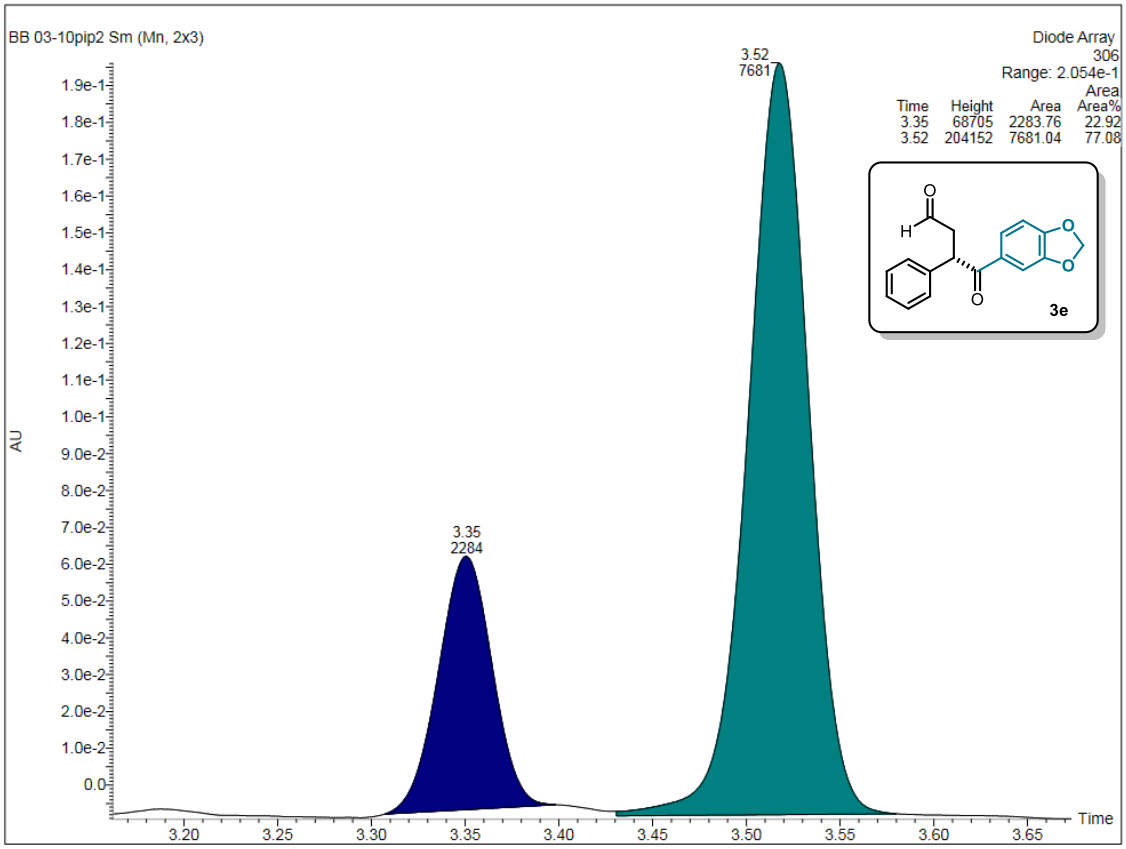
Conditions: UPC^2 analysis on a Daicel Chiralpak IG column, gradient: 1 min 100% CO_2, 8 min from 100% CO_2 to 40% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ=235 nm.



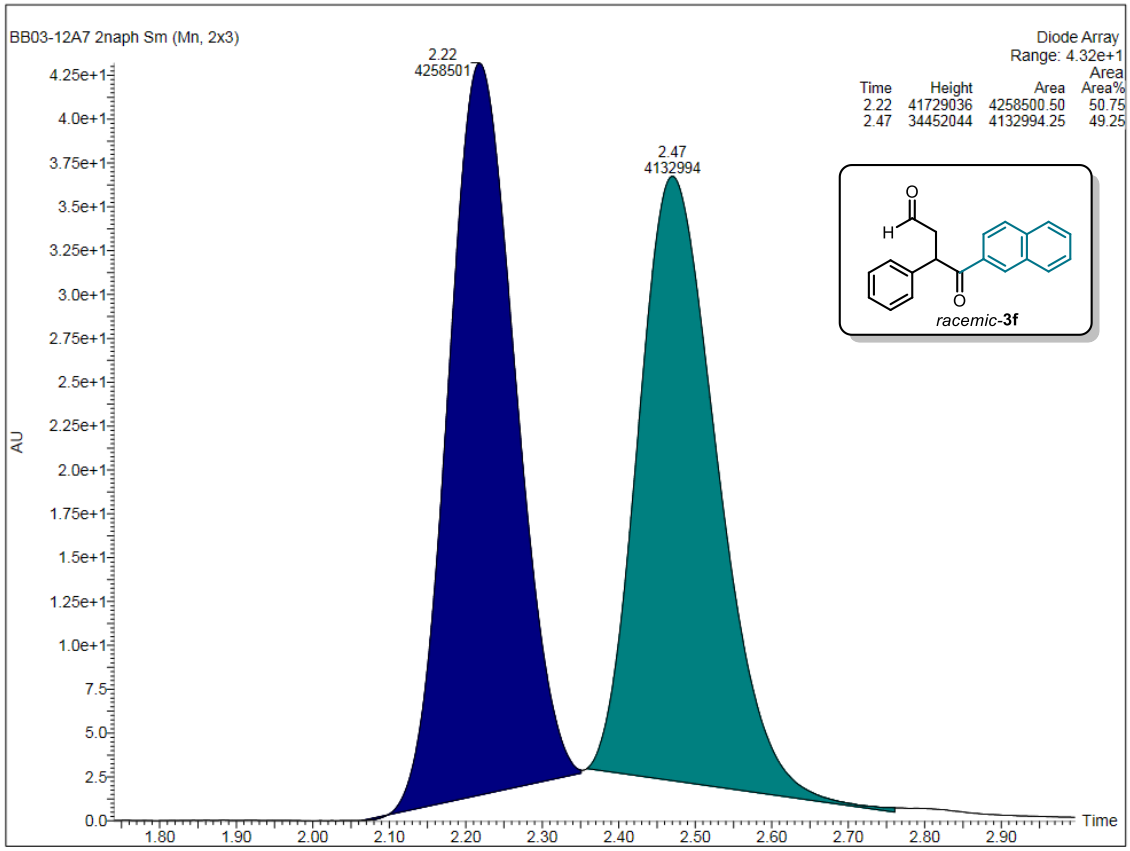


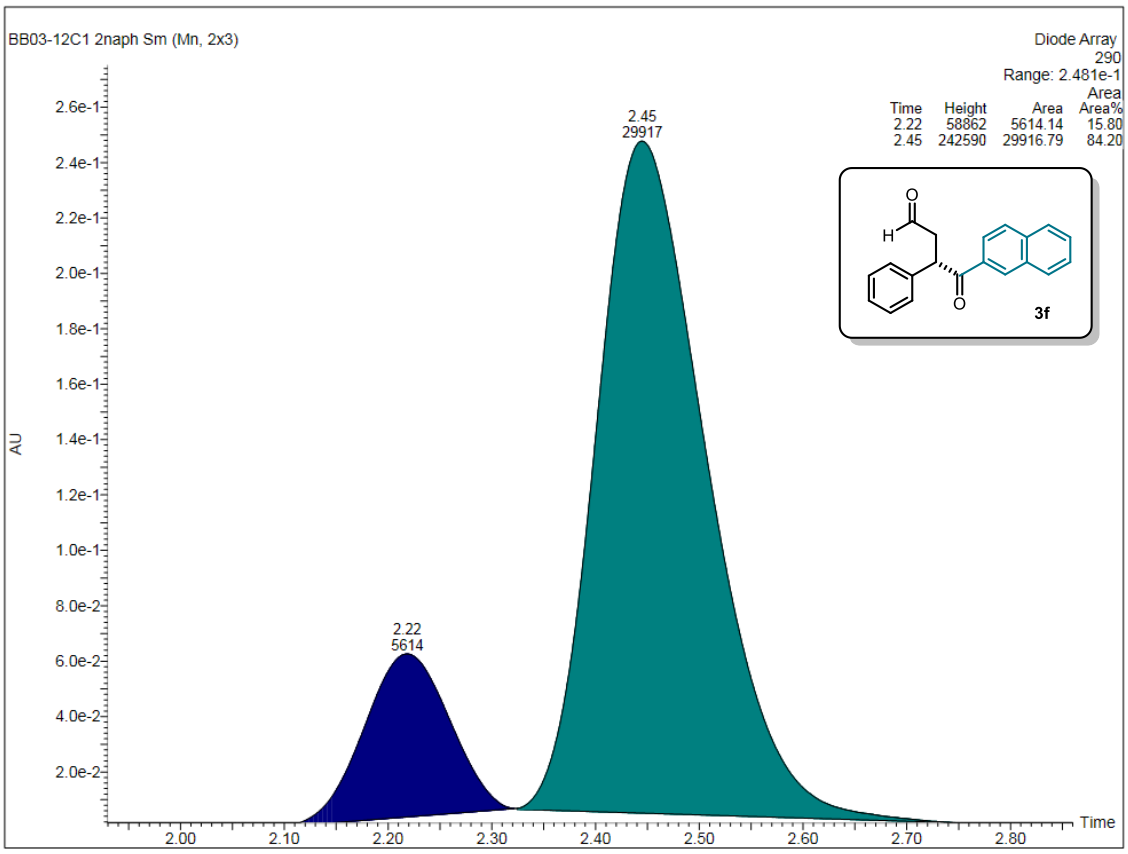
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ=230 nm.



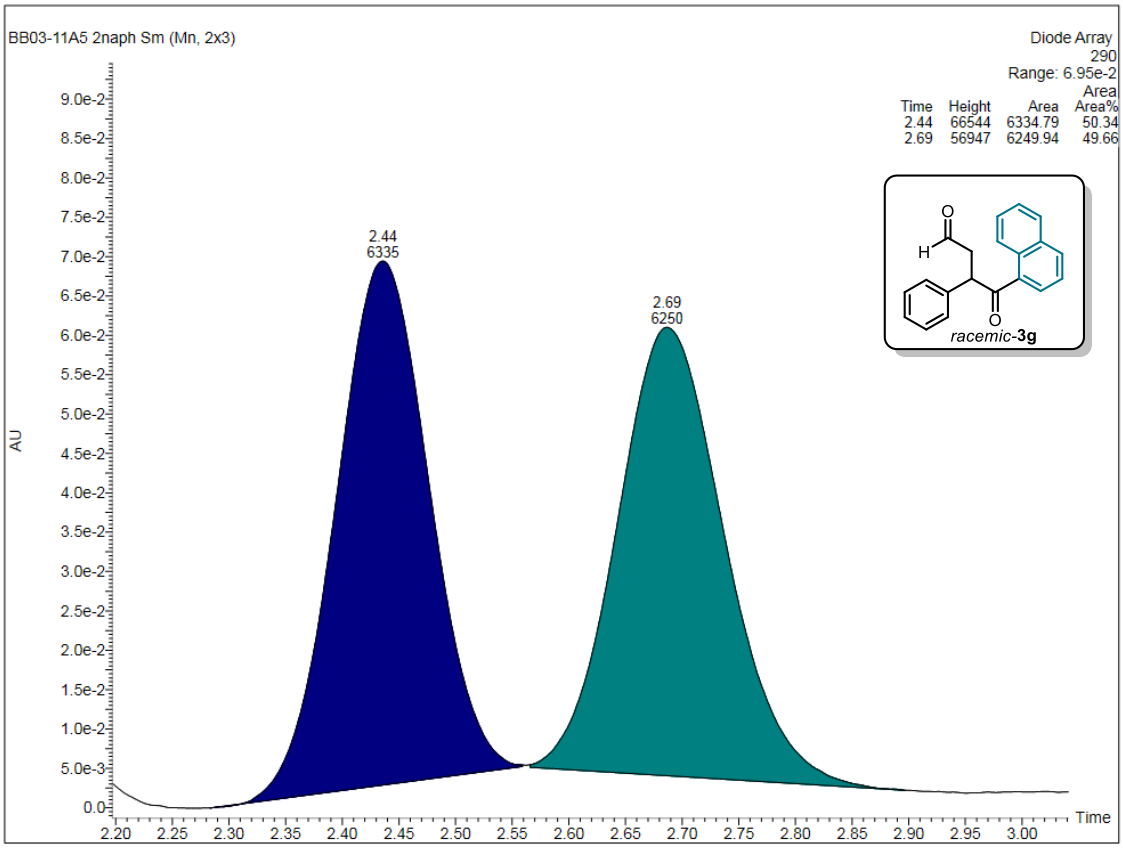


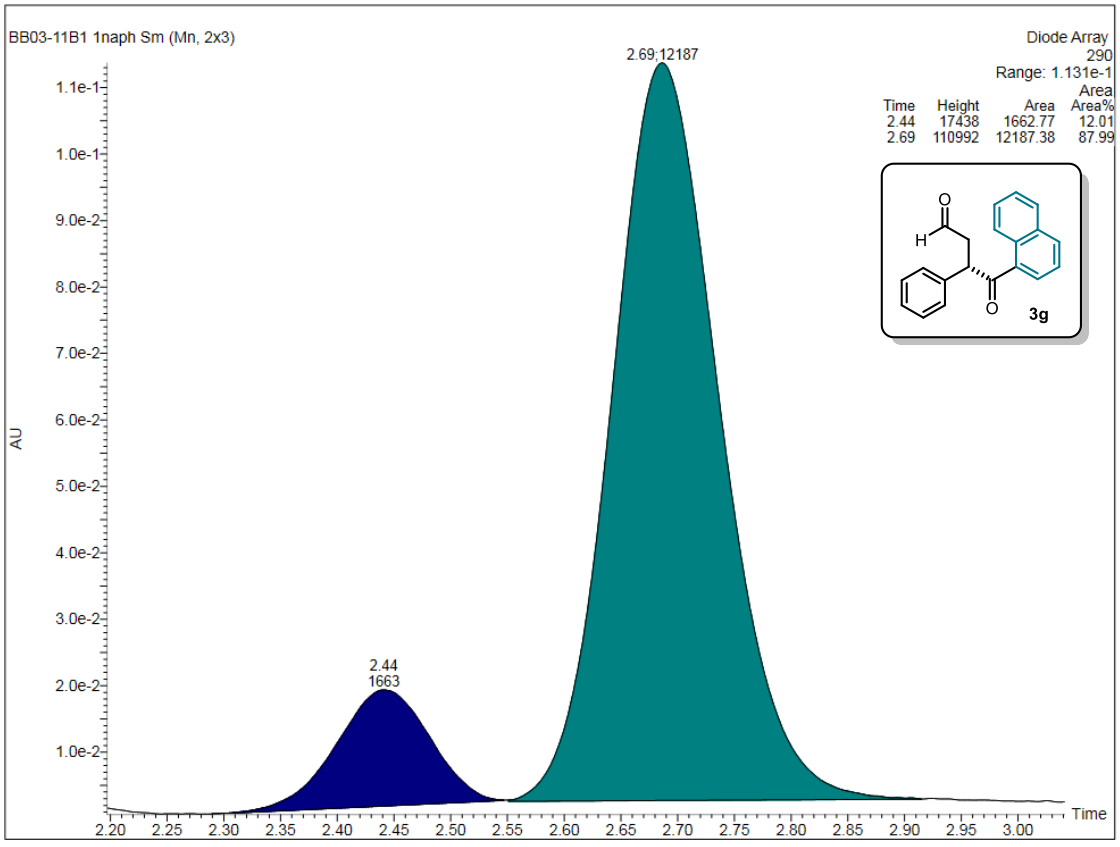
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, 91:9 CO_2/ACN, flow rate 2 mL/min, λ=290 nm.



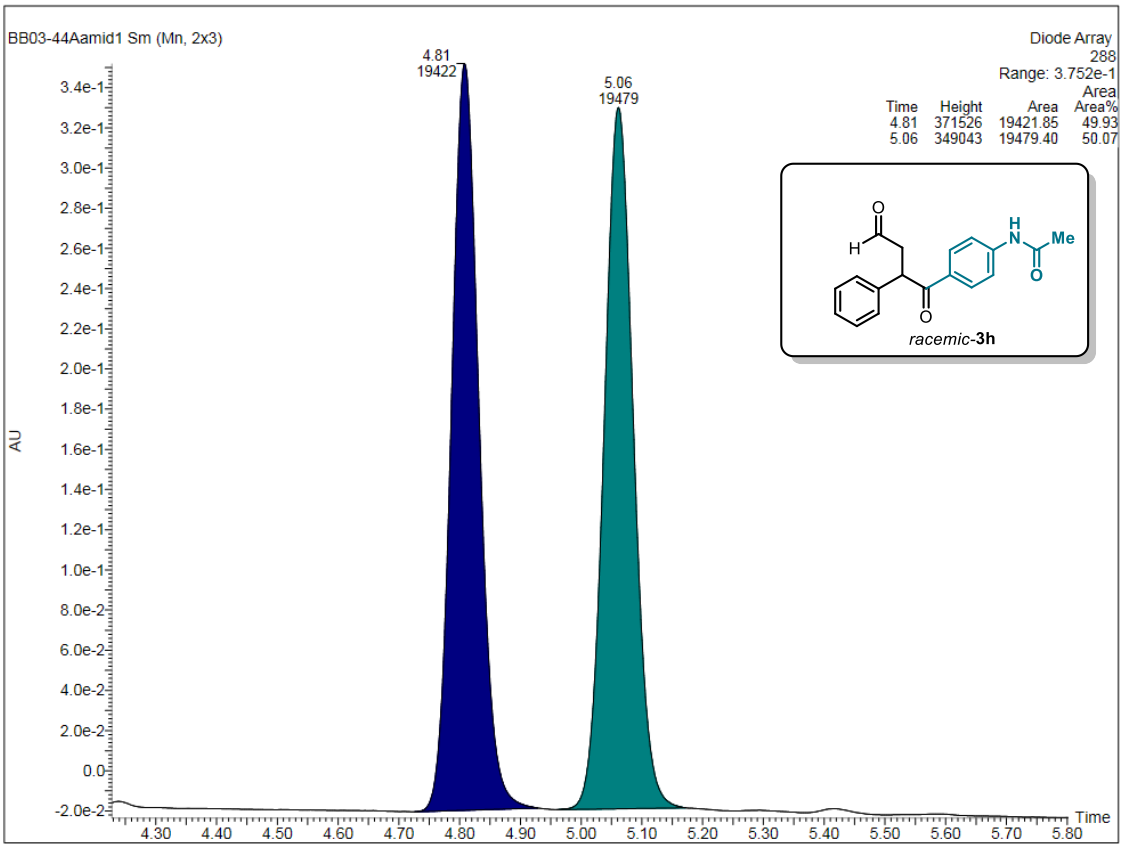


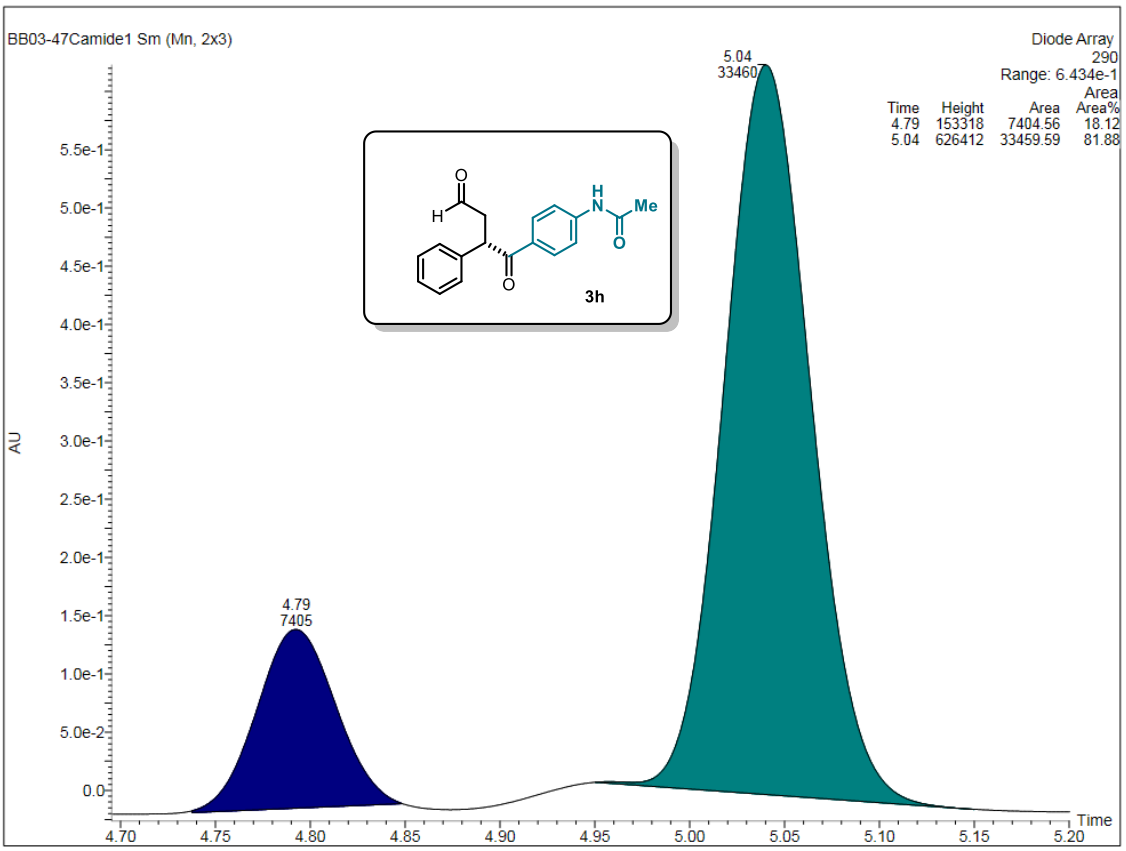
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, 90:10 CO_2/IPA, flow rate 2 mL/min, λ=290 nm.



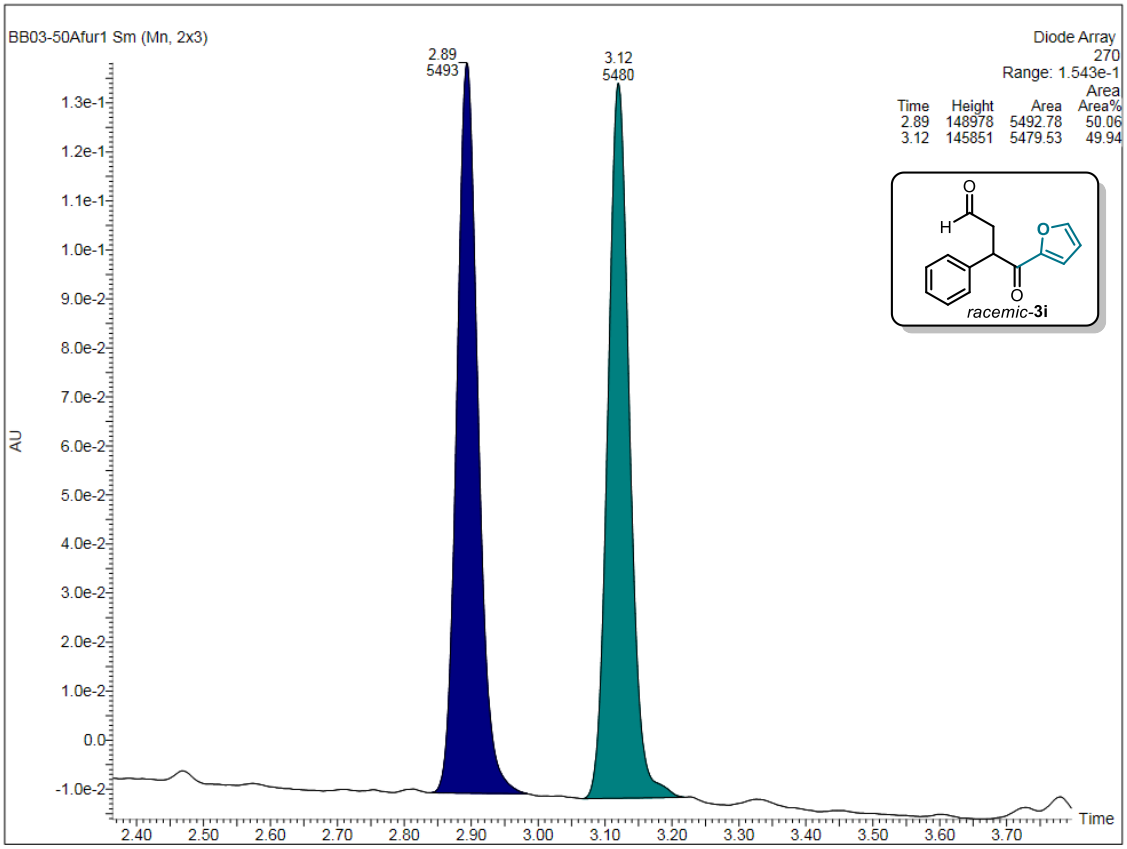


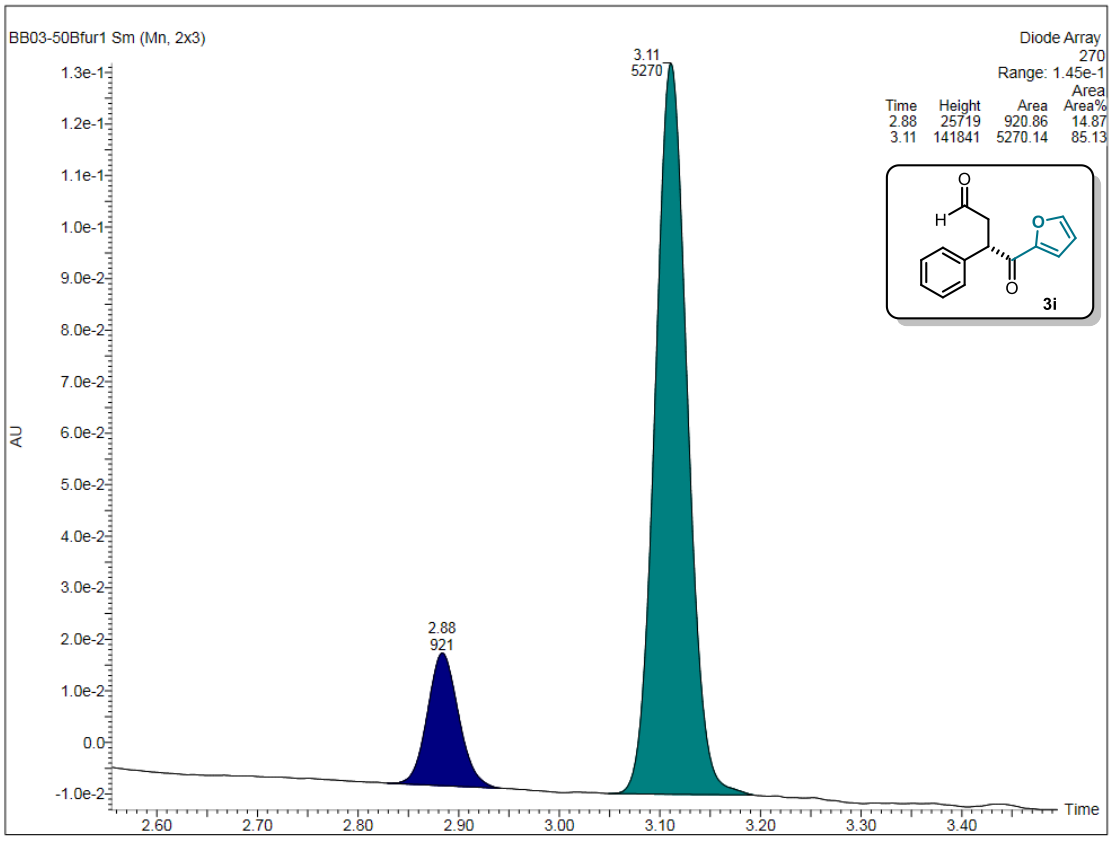
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% ACN, flow rate 2 mL/min, λ = 288 nm.



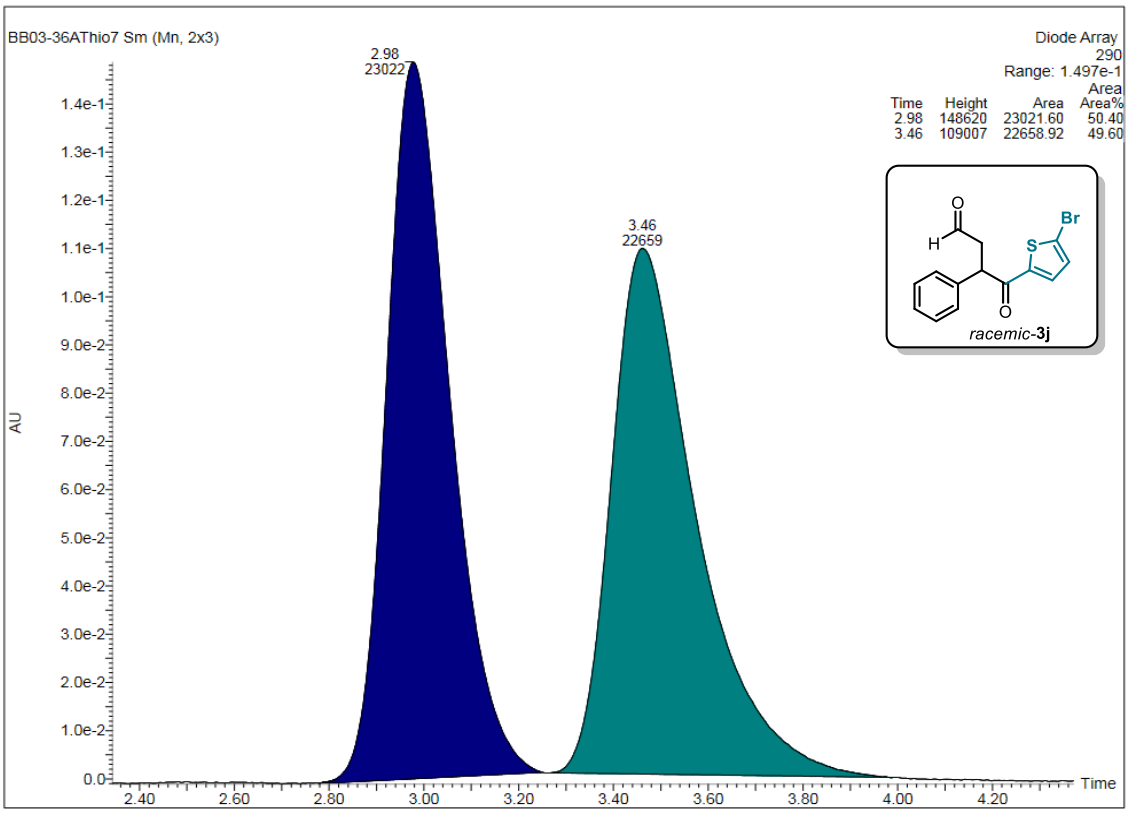


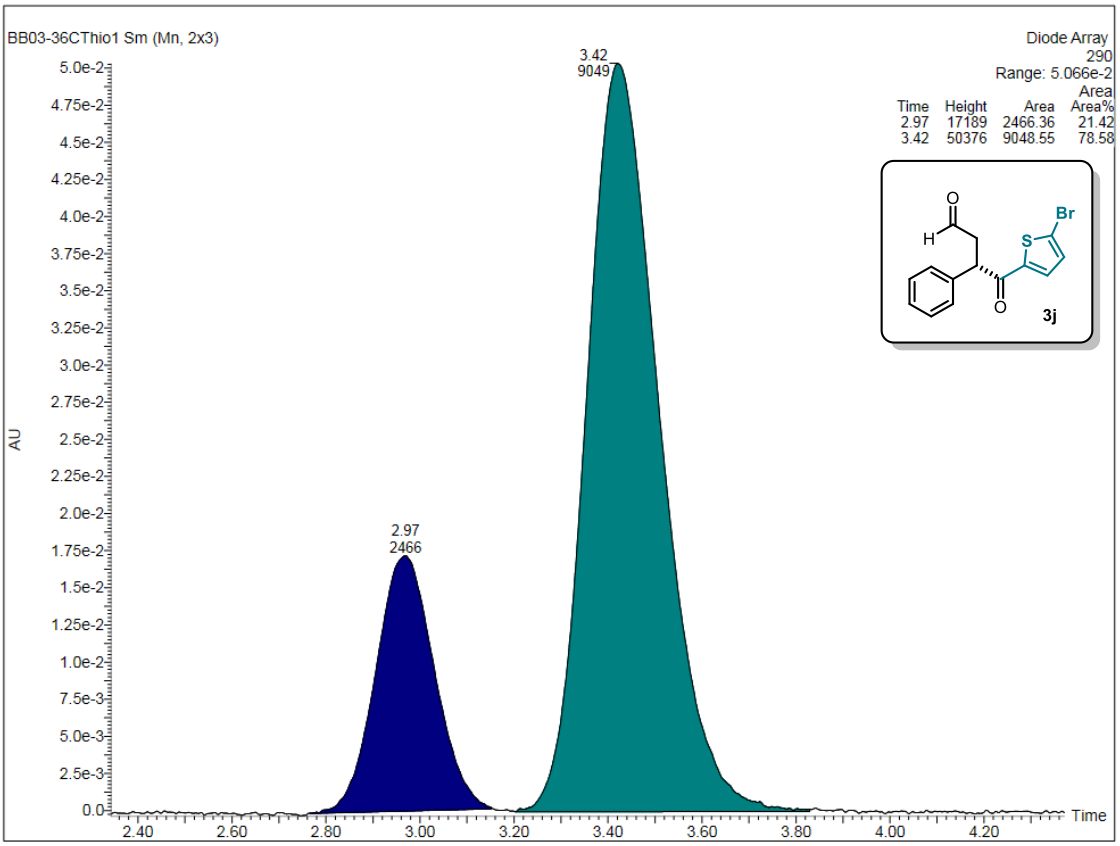
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% ACN, flow rate 2 mL/min, λ=270 nm.



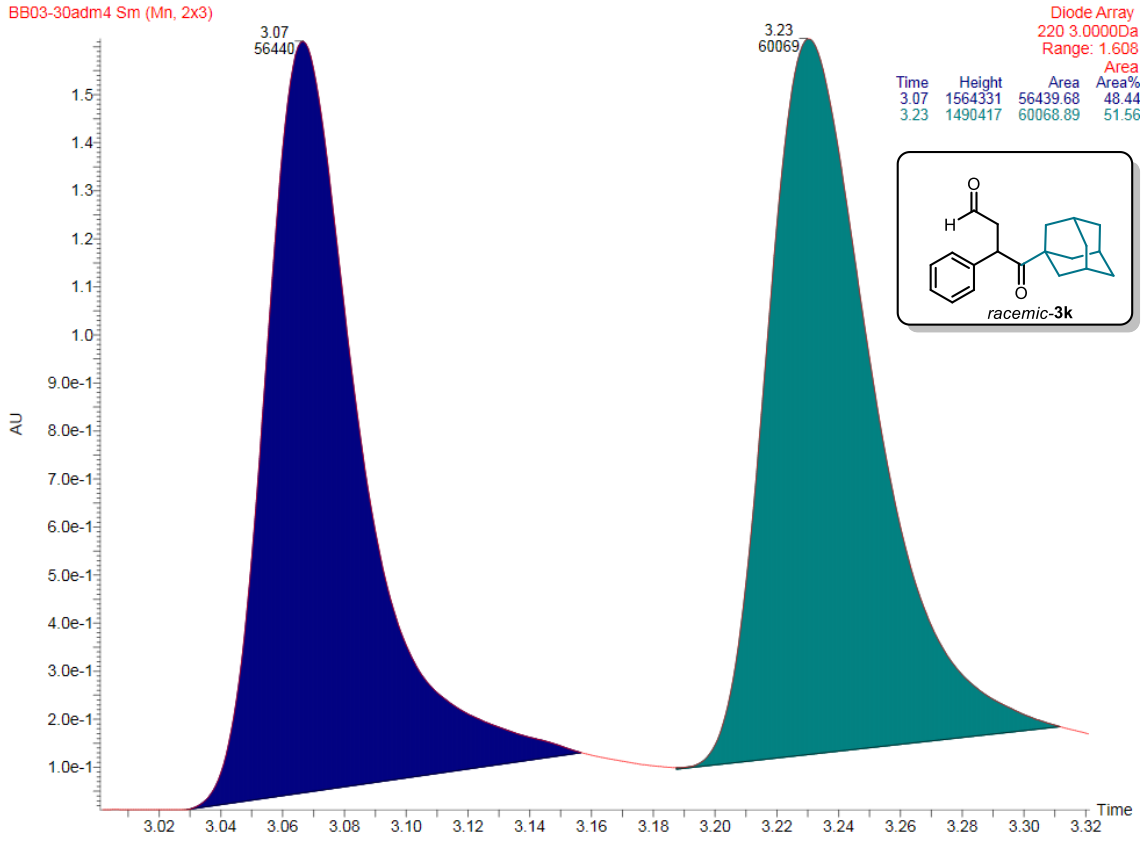


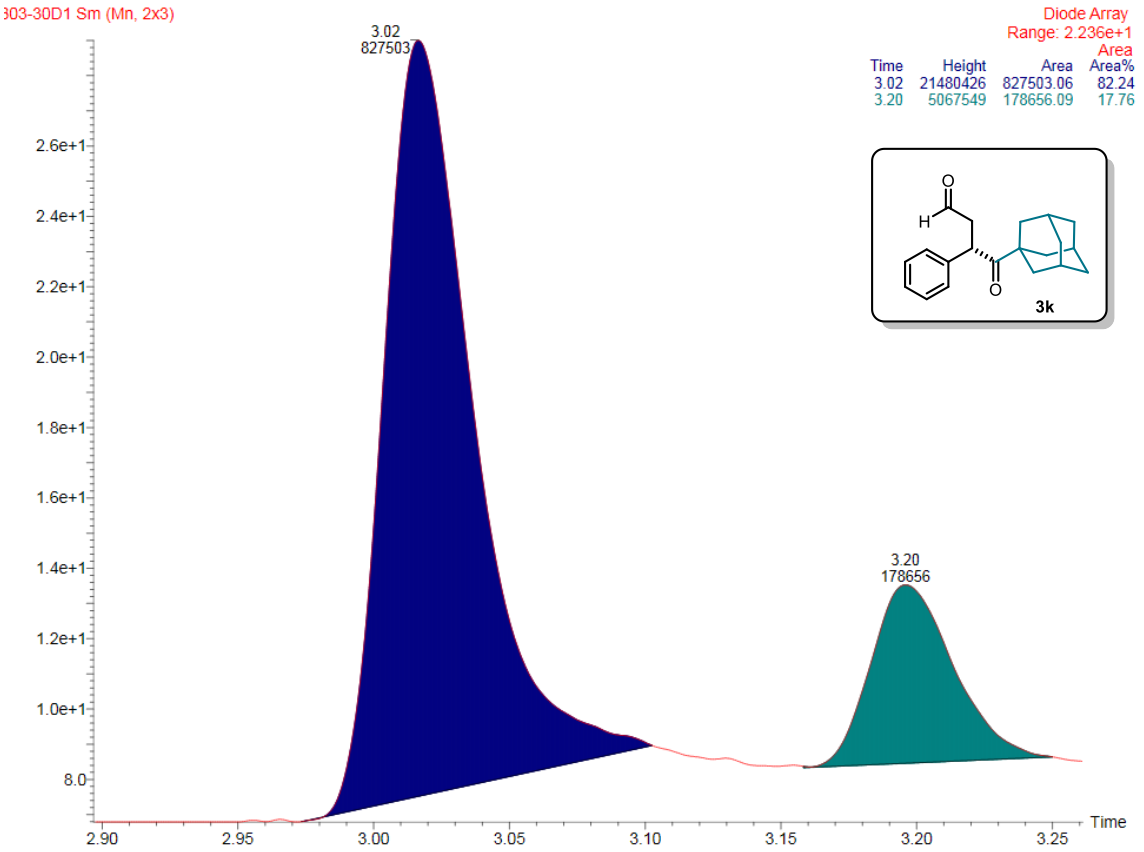
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, 95:5 CO_2/ACN, flow rate 2 mL/min, λ=290 nm.



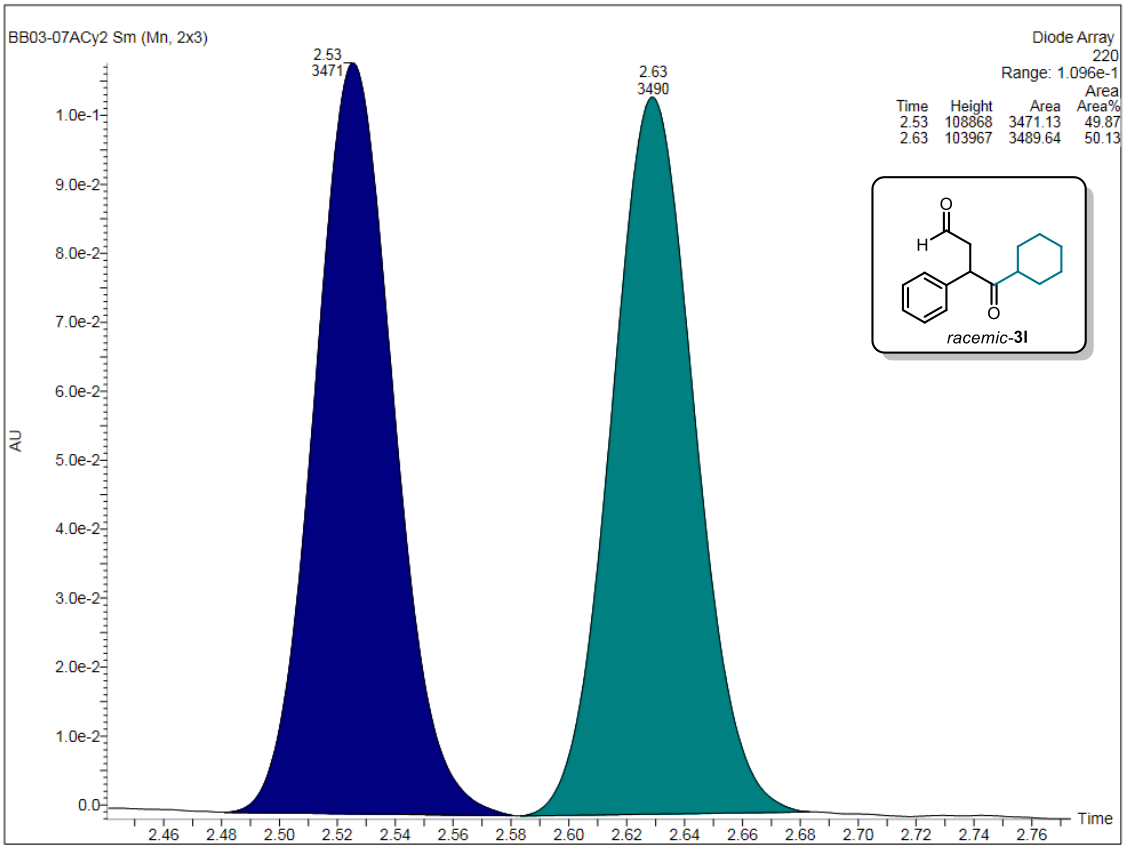


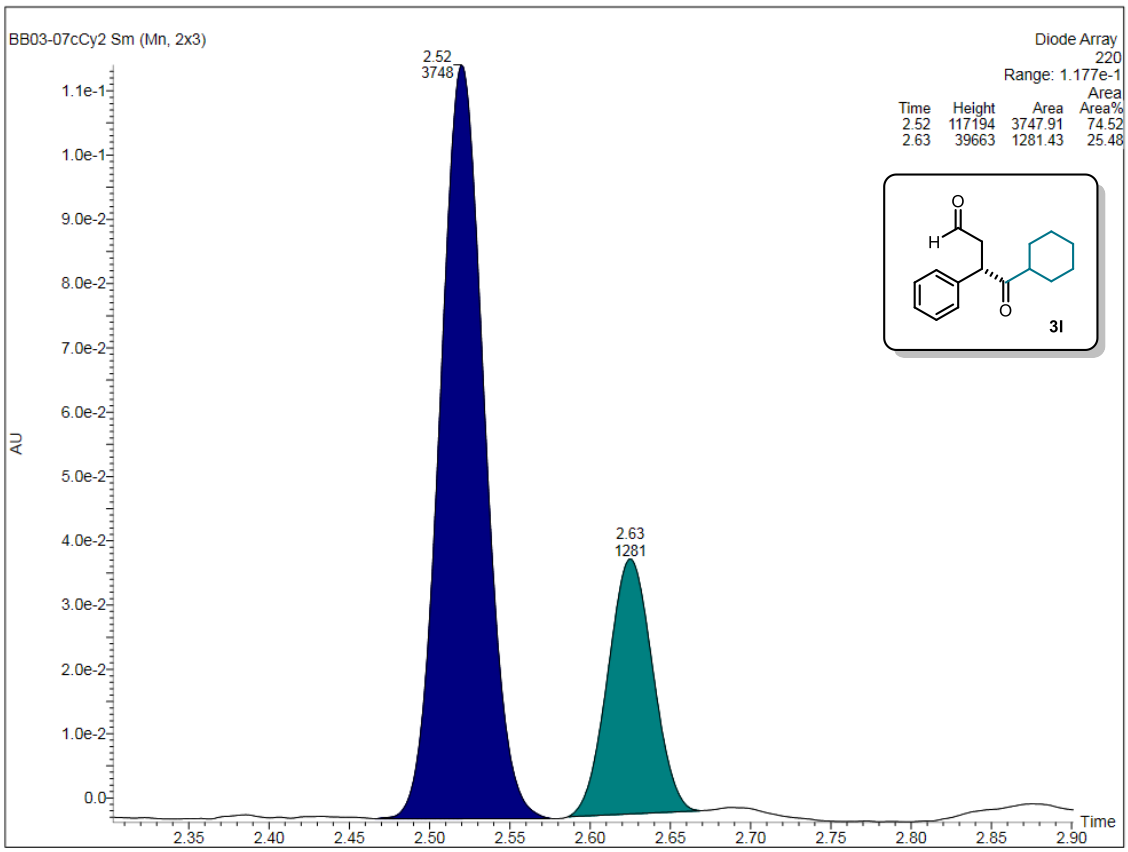
Conditions: UPC^2 analysis on a Daicel Chiralpak IA column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% EtOH, flow rate 2 mL/min, λ=220 nm.



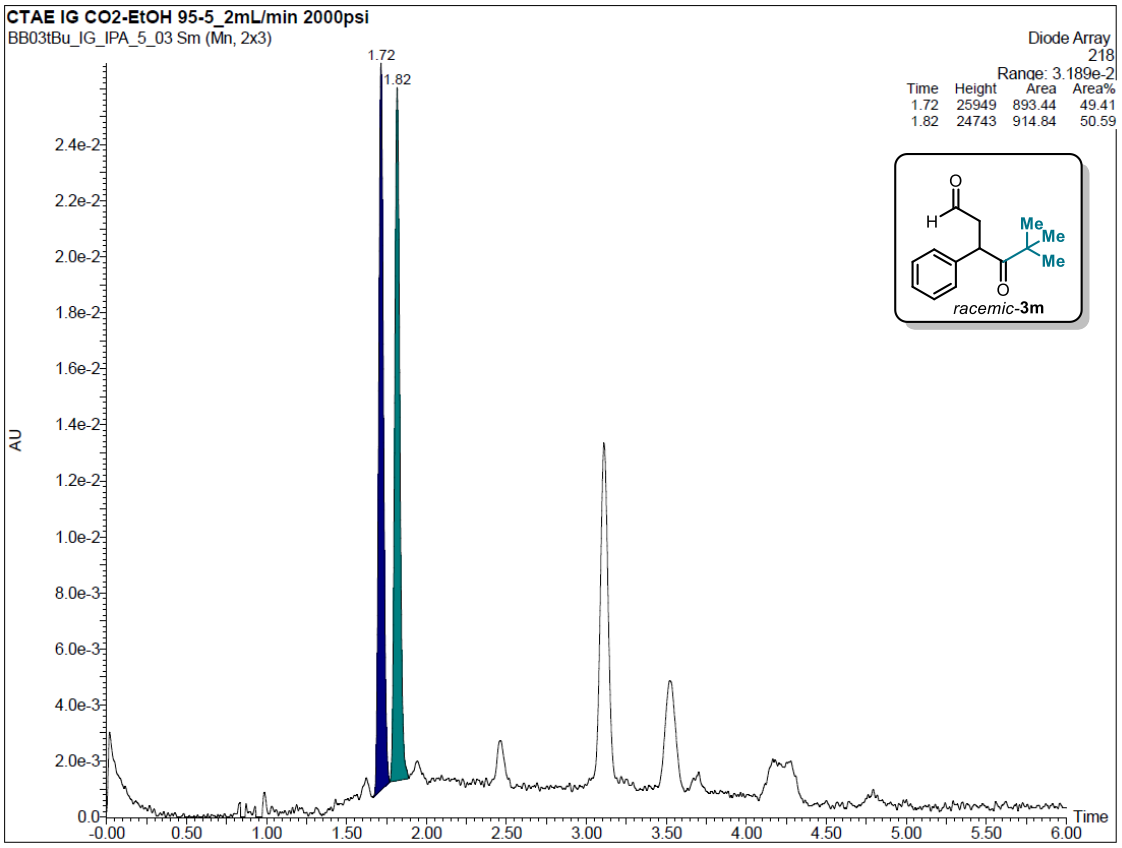


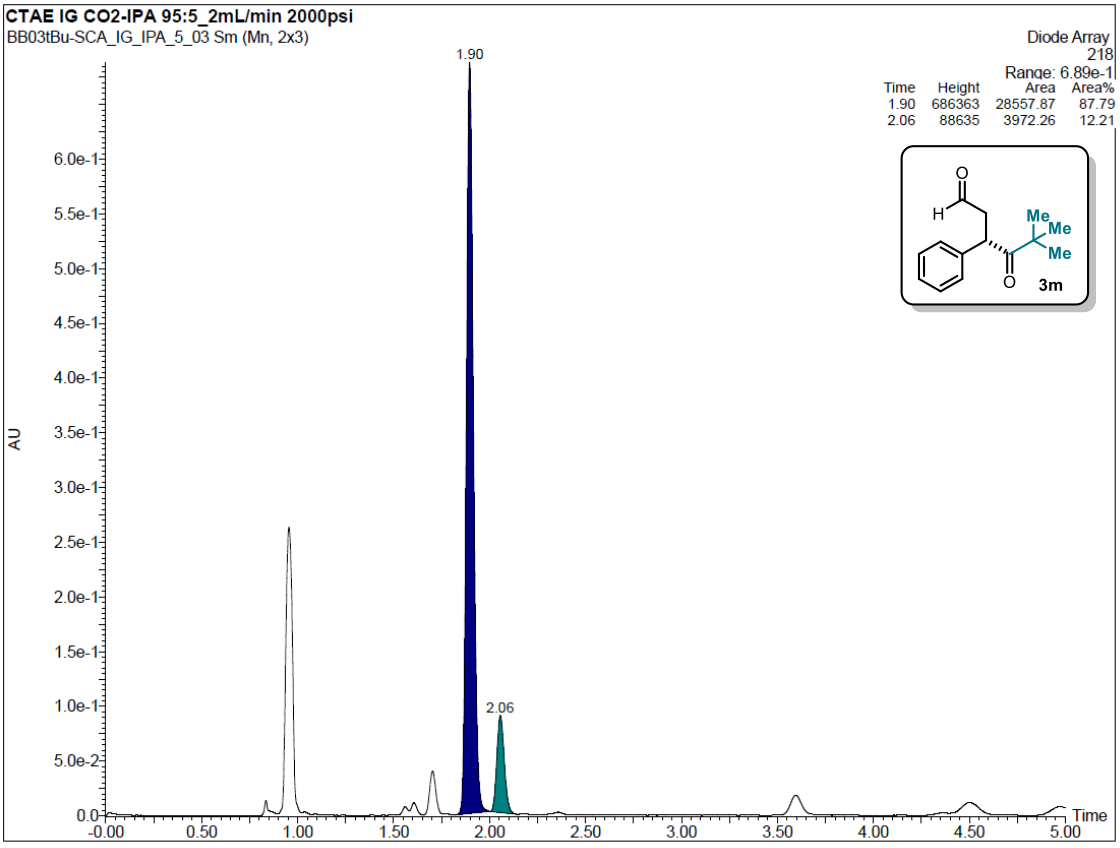
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, λ=220 nm.



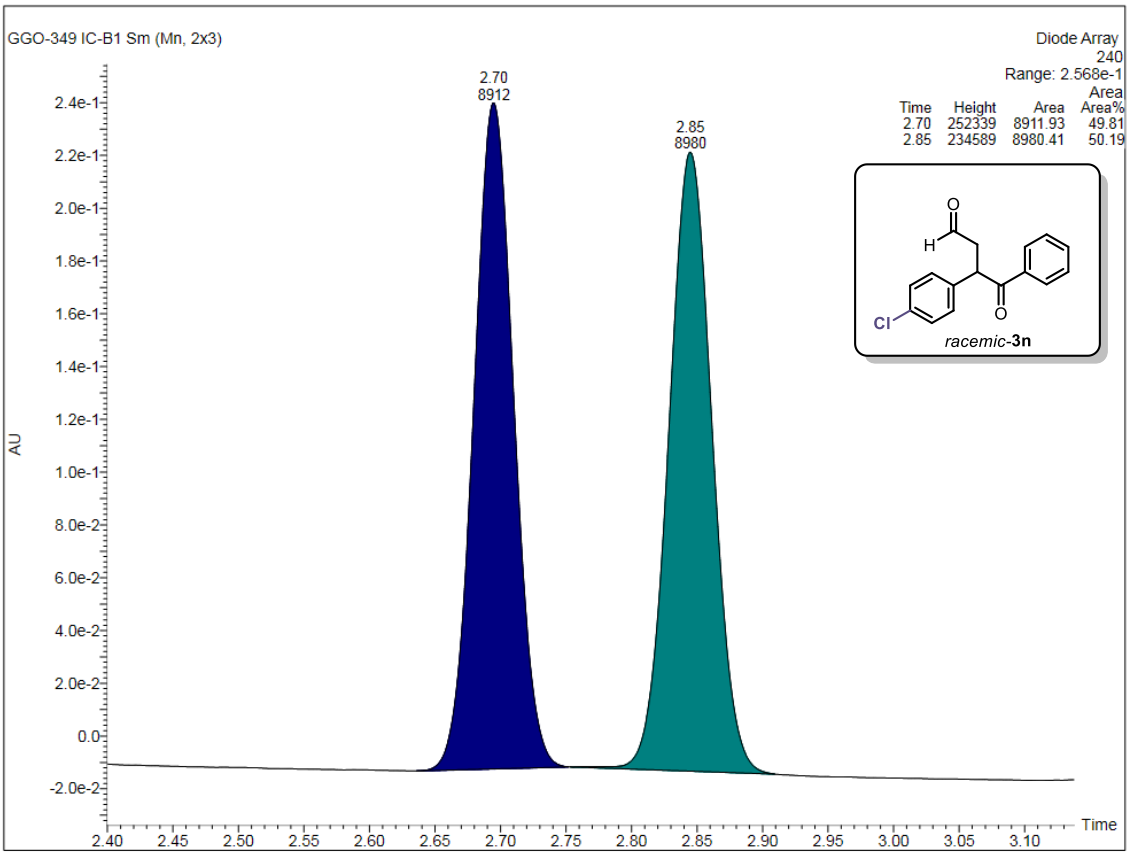


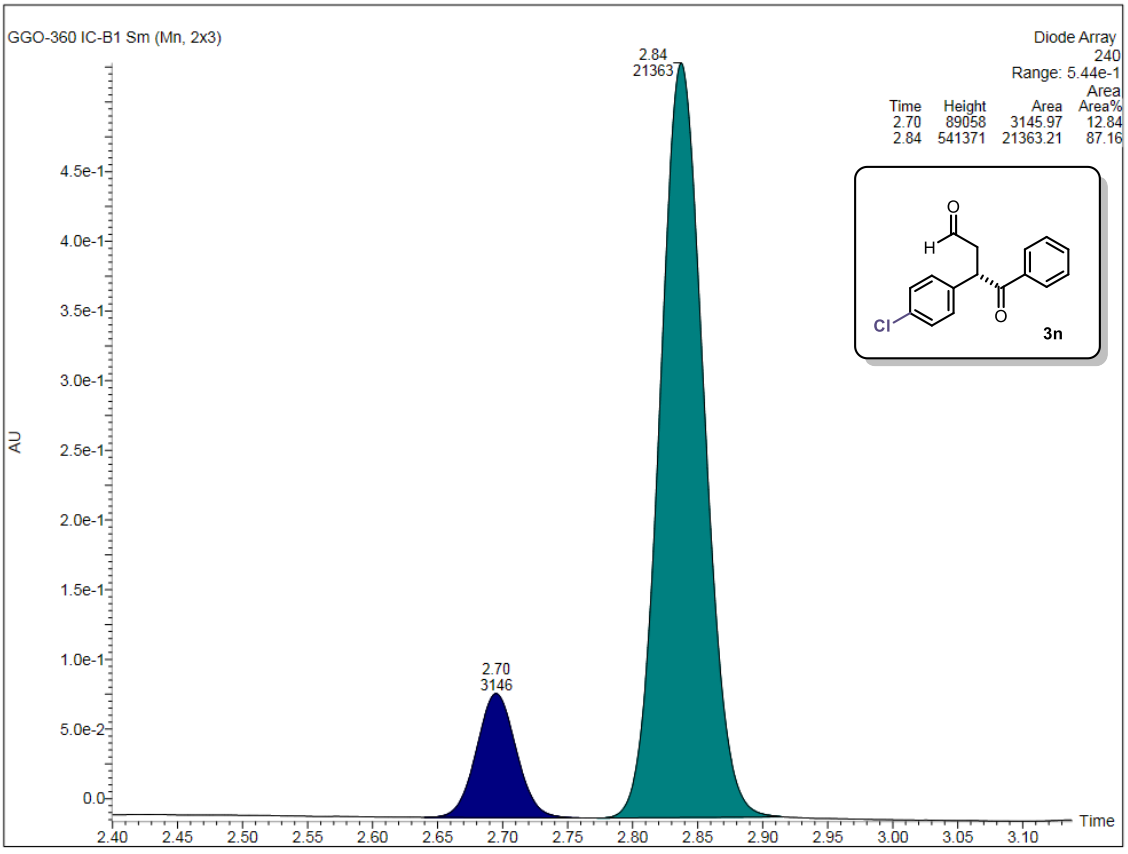
Conditions: UPC^2 analysis on a Daicel Chiralpak IG column, 95:5 CO_2/ACN, flow rate 2 mL/min, λ=218 nm.



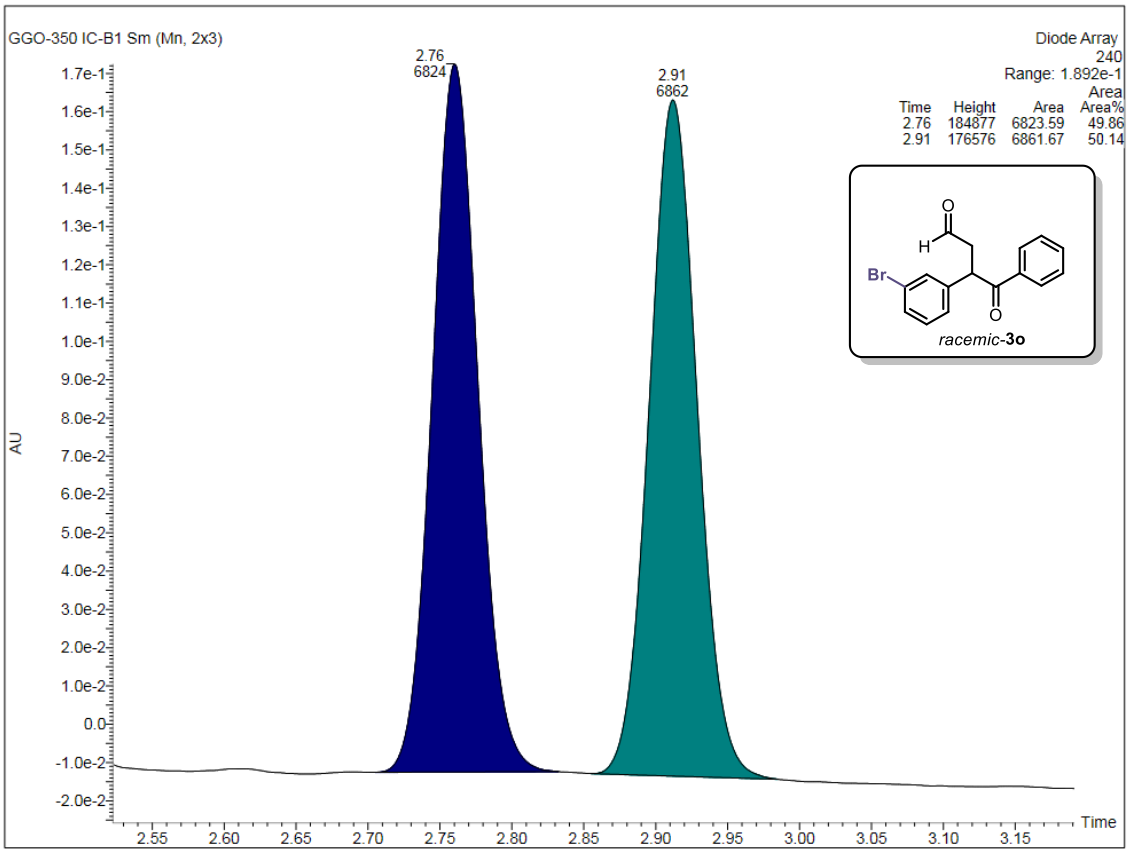


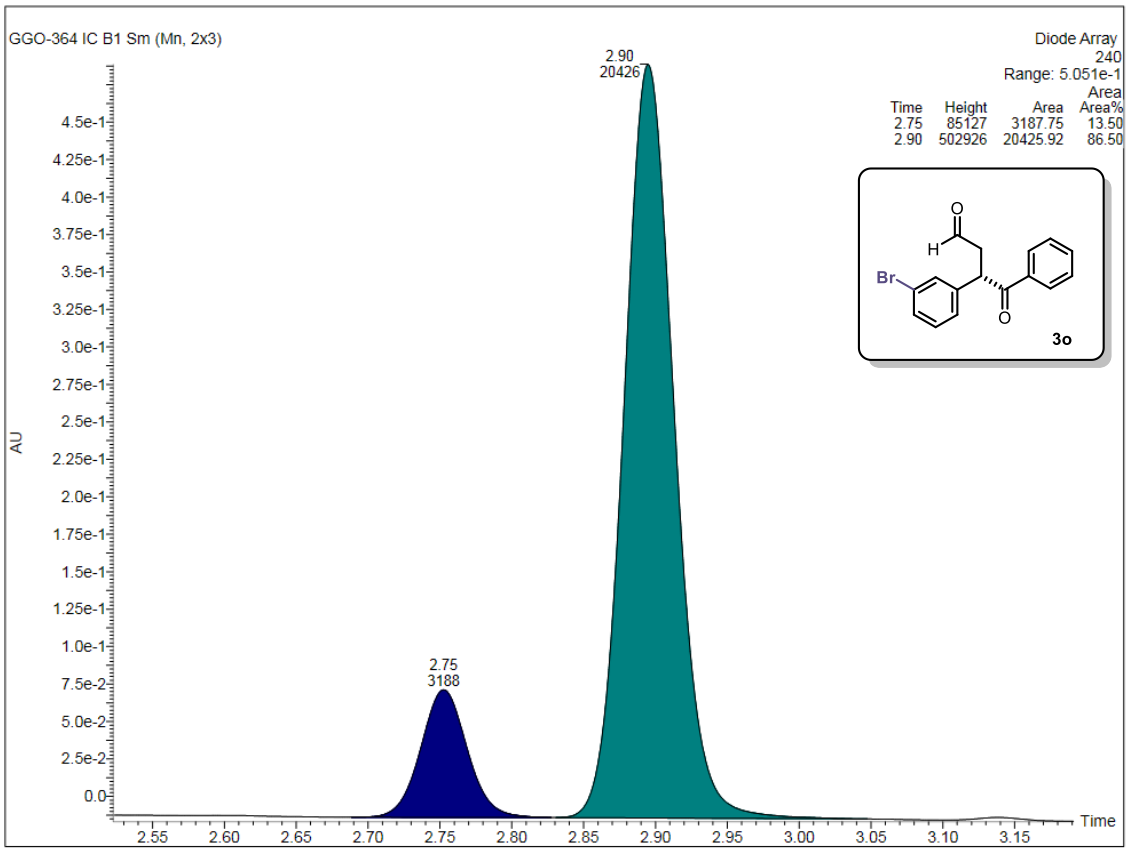
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% CH_3CN, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm.



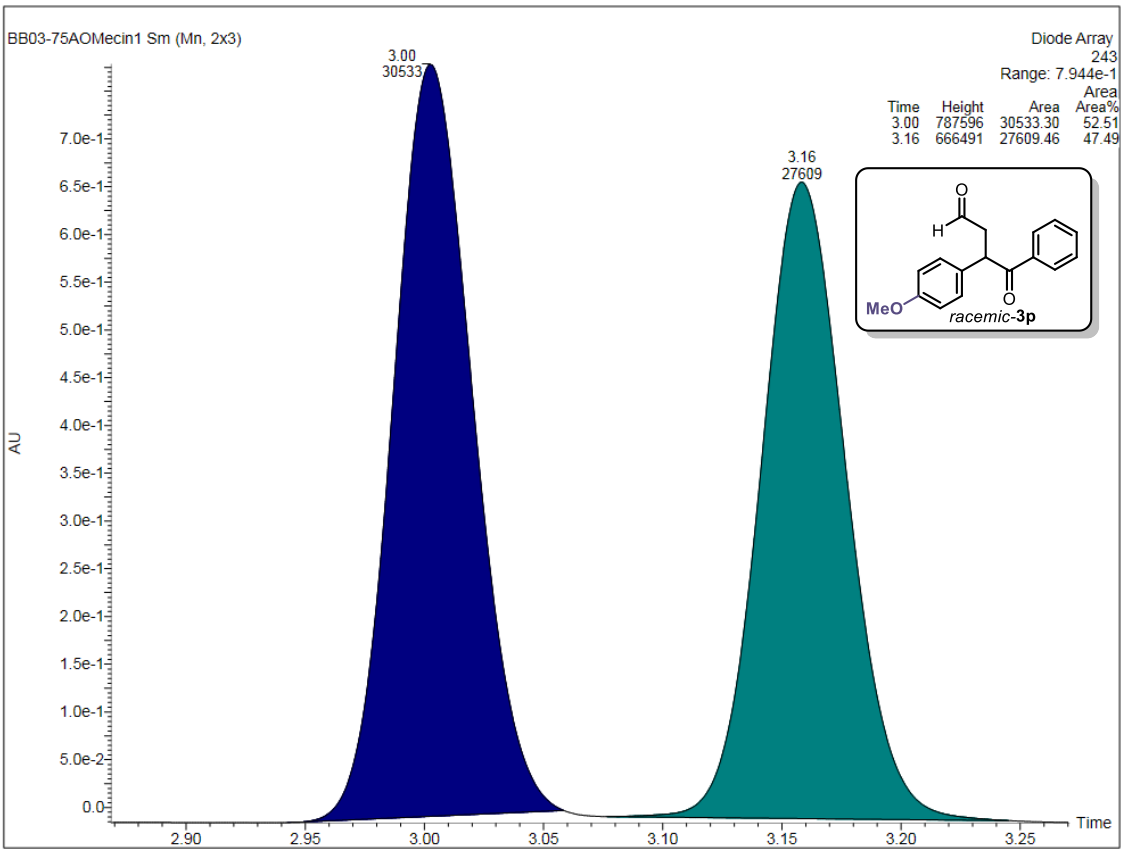


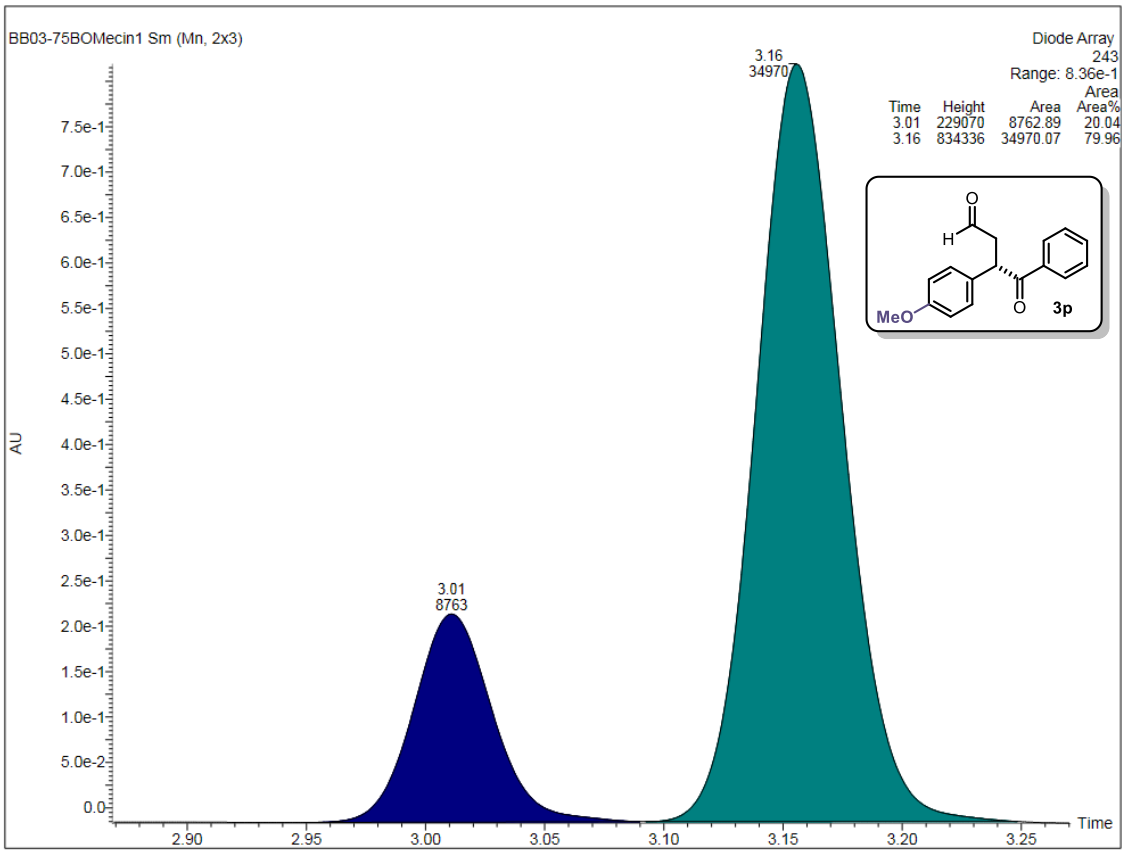
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% CH_3CN, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm.



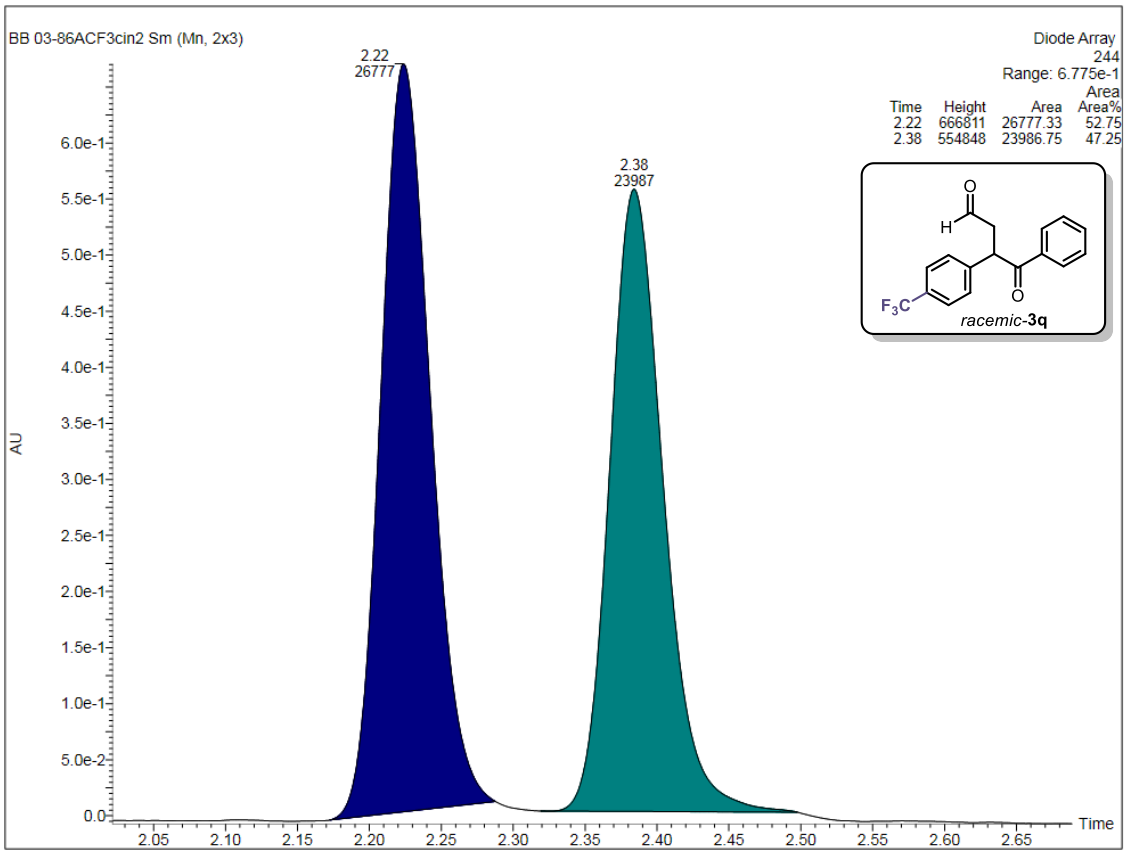


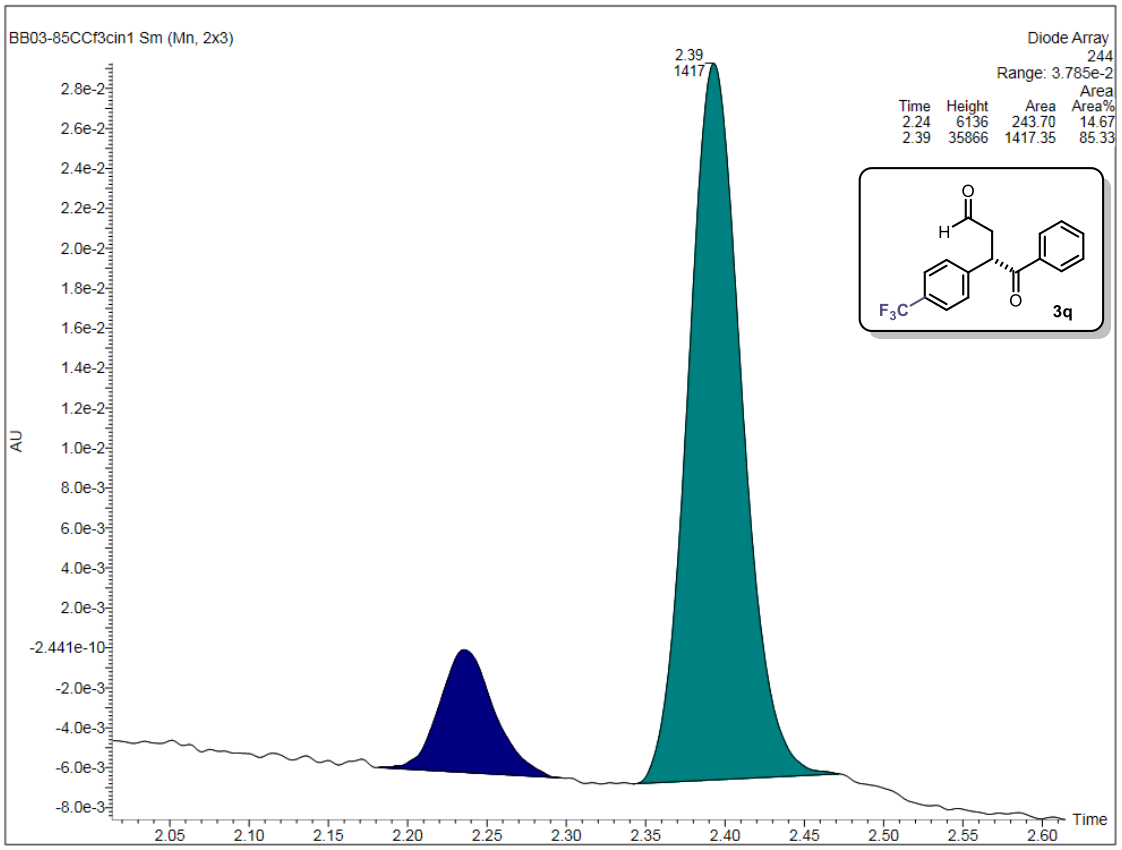
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% ACN, flow rate 2 mL/min, column T = 40 °C, λ = 243 nm.



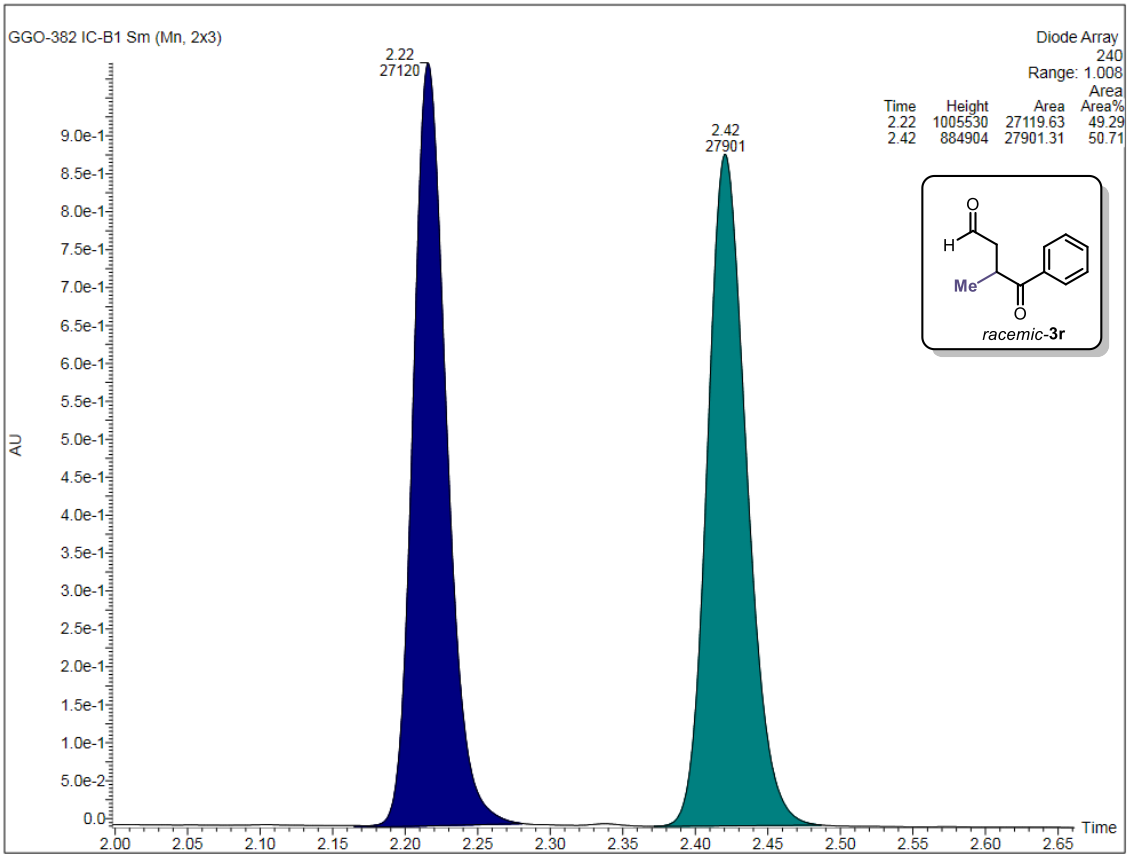


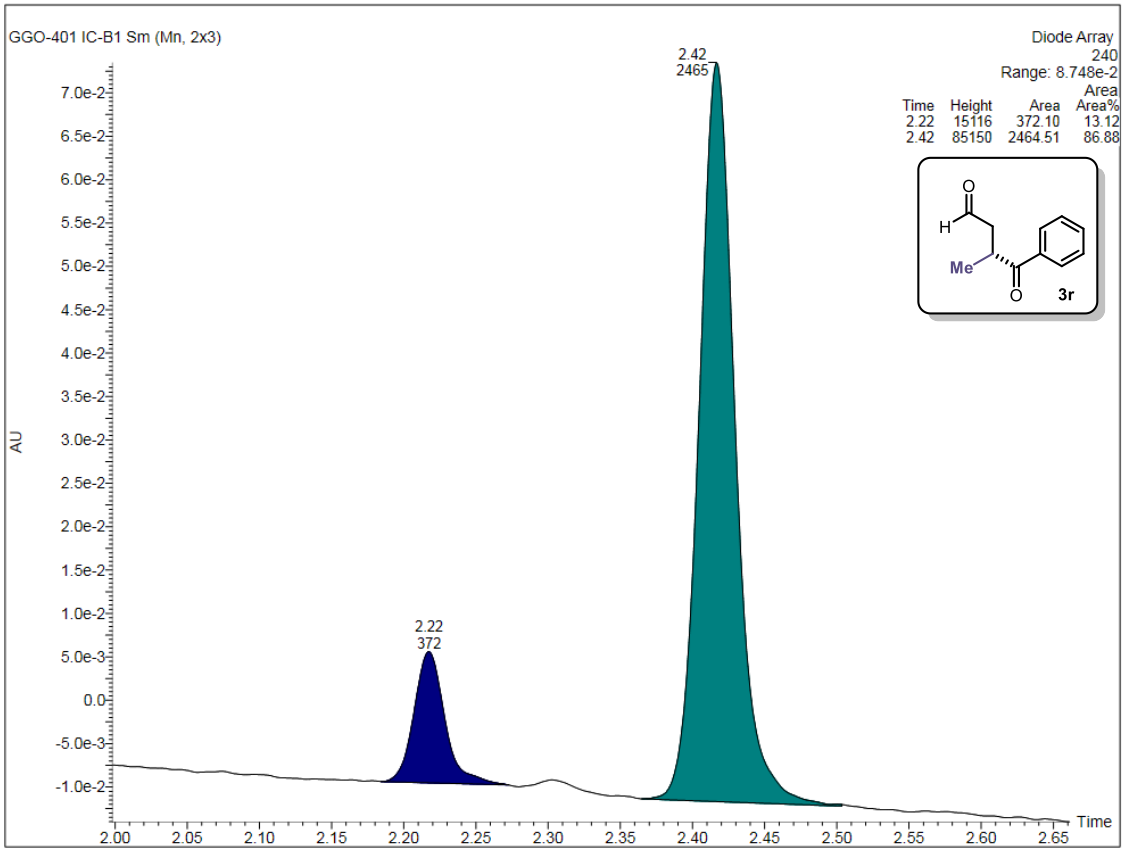
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, column T = 40 °C, λ = 244 nm.



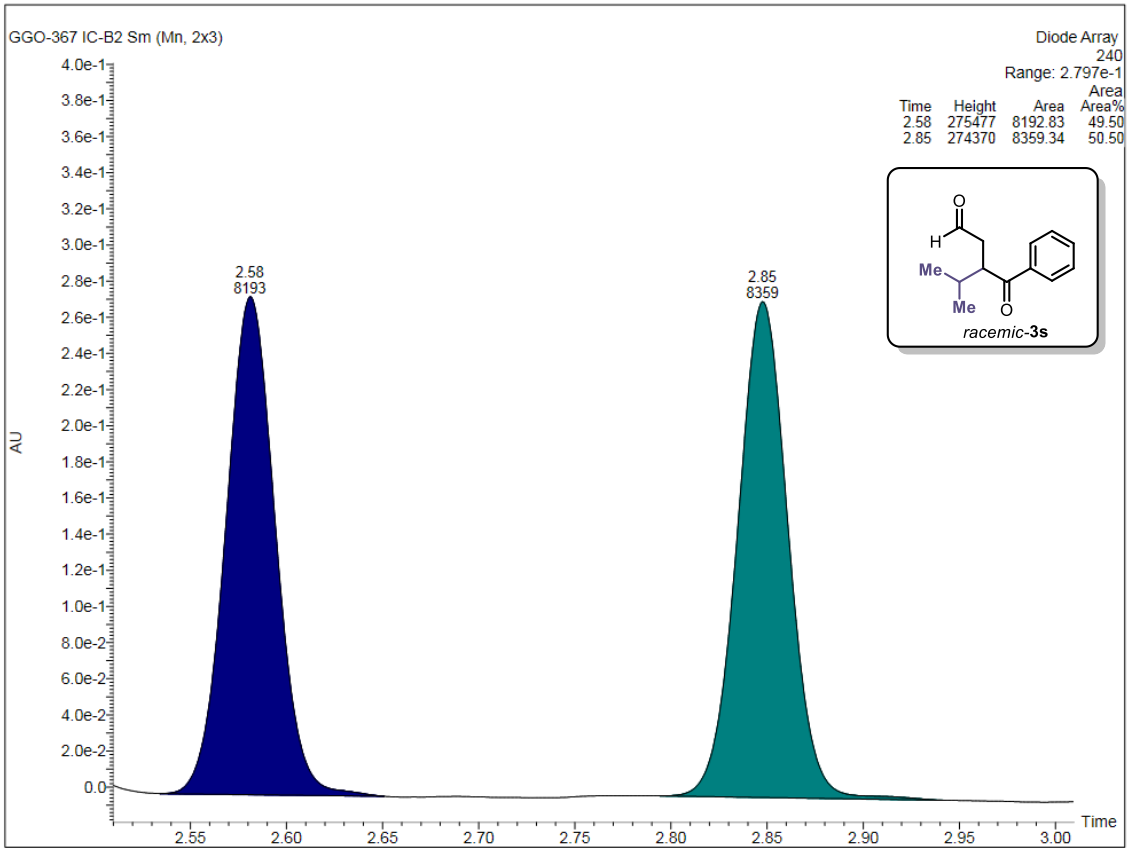


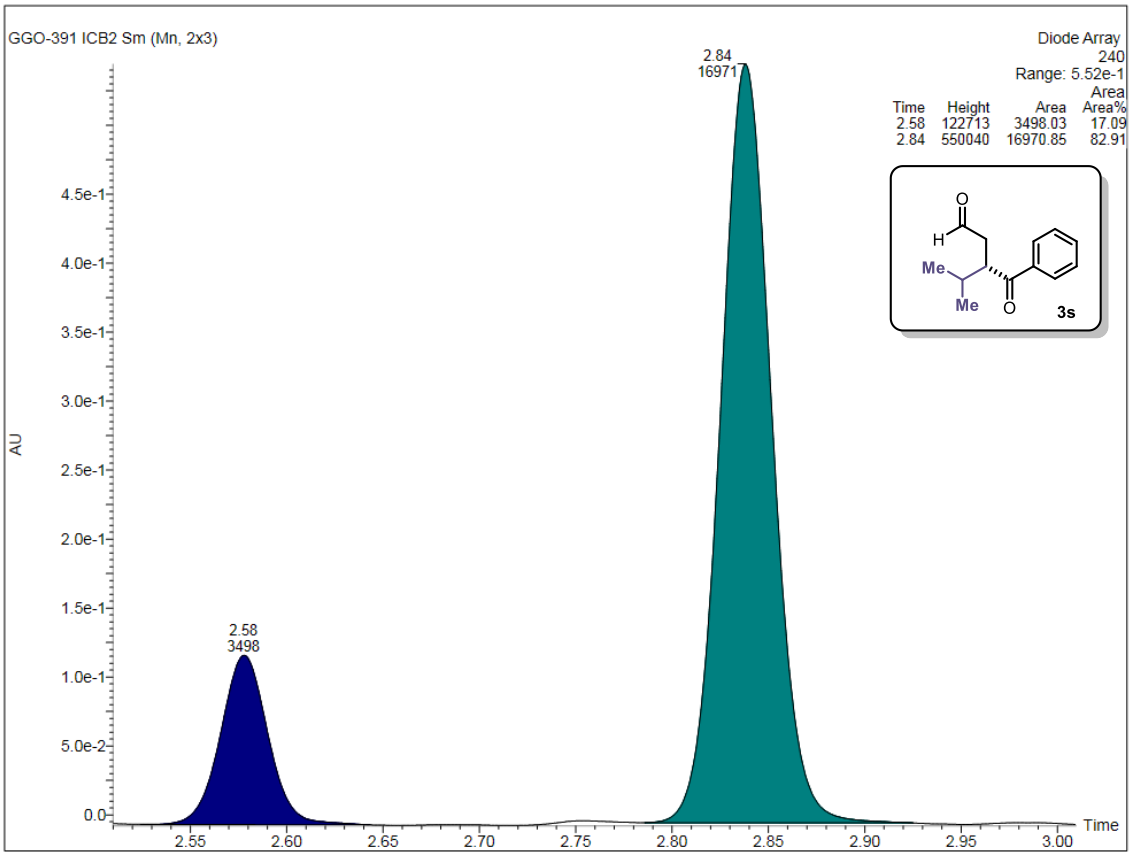
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% CH_3CN, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm.



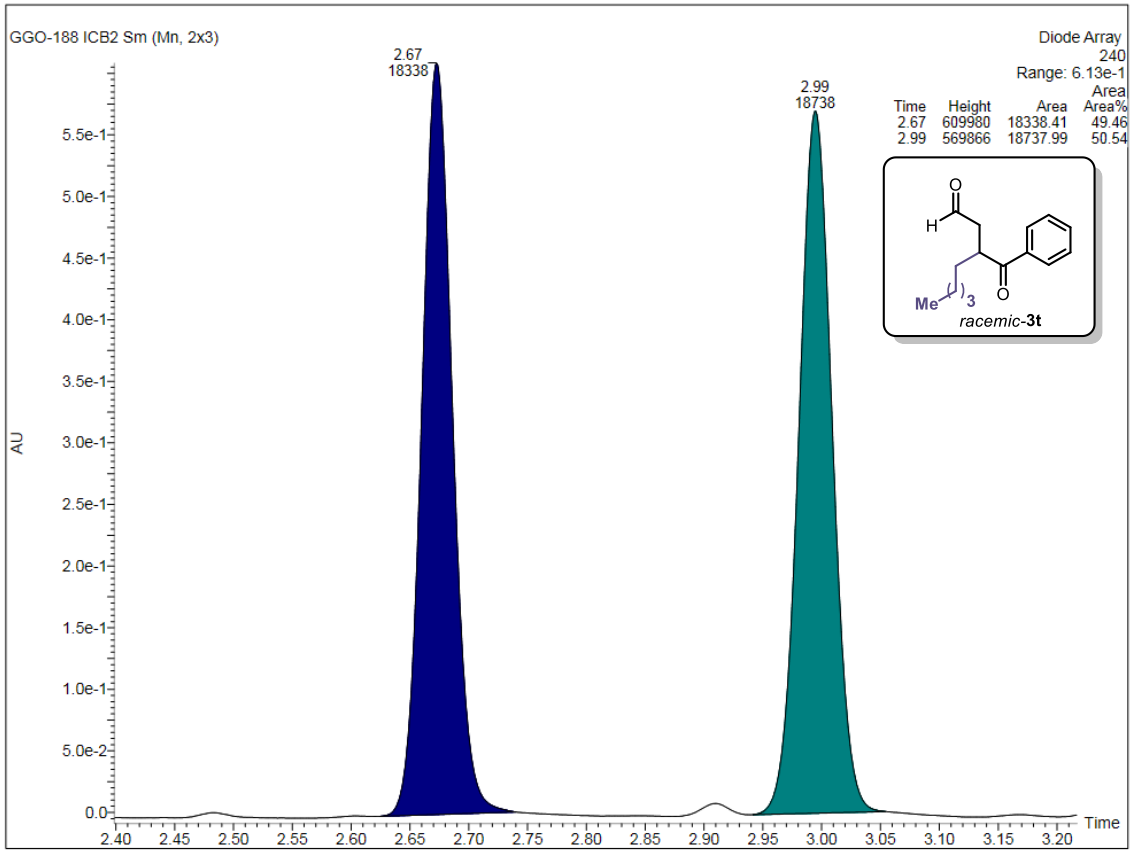


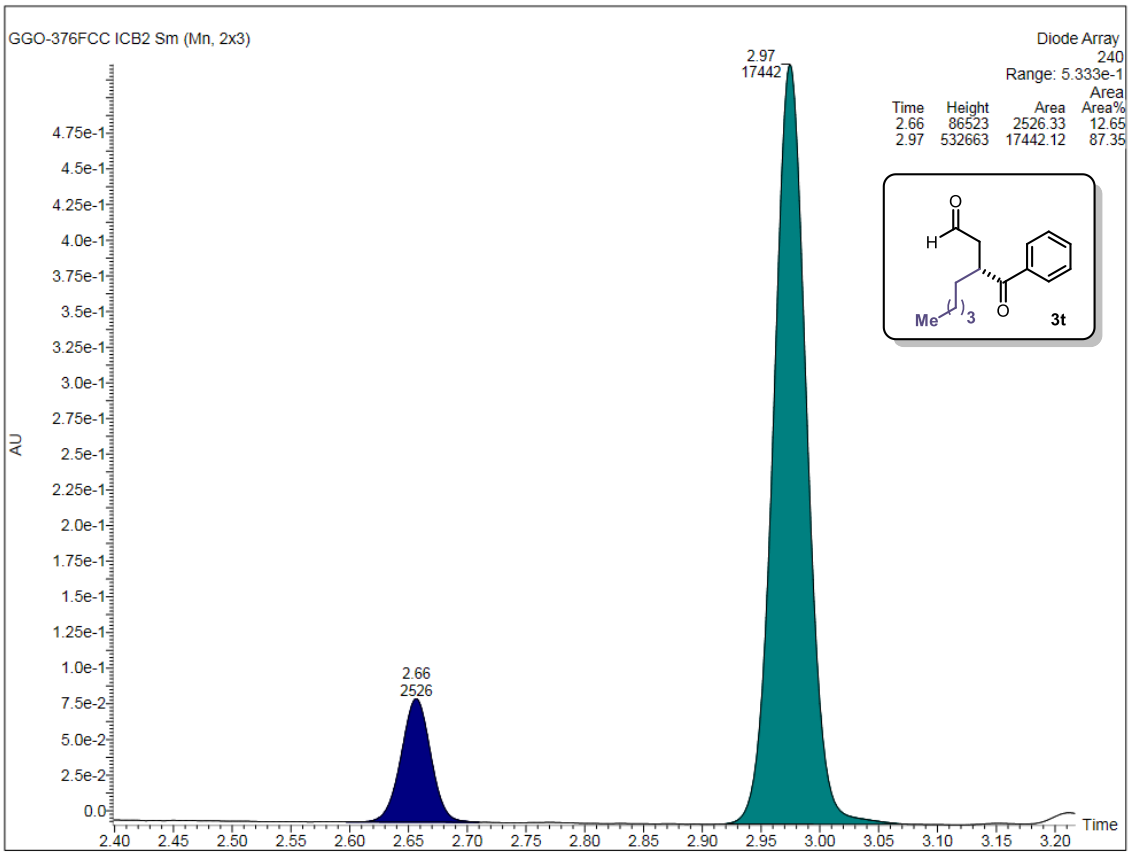
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm.



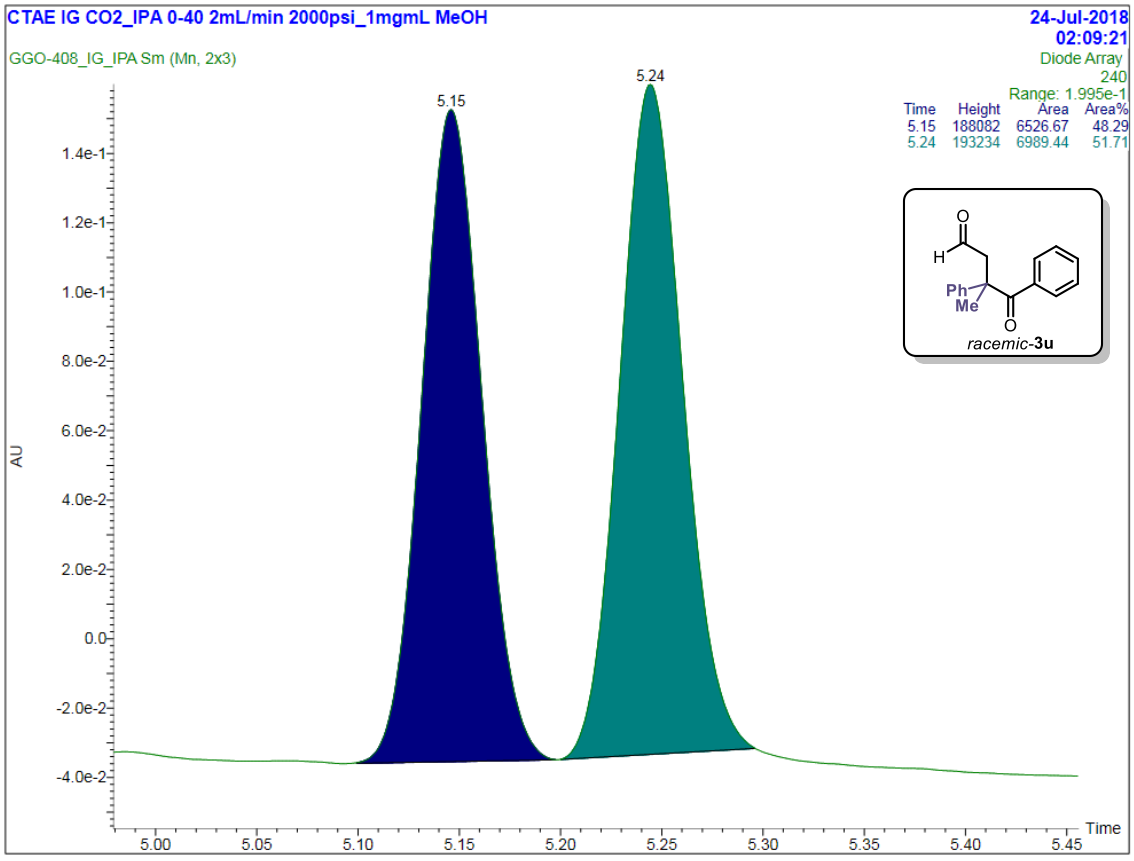


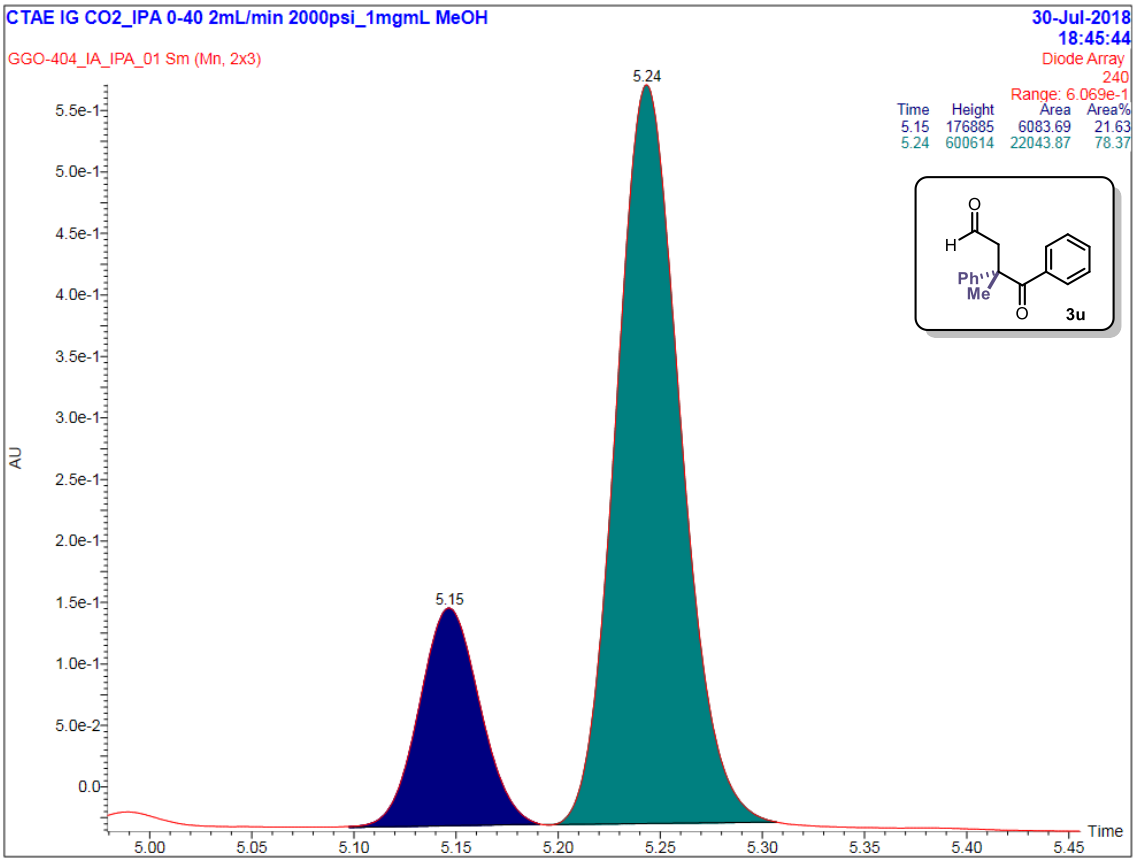
Conditions: UPC^2 analysis on a Daicel Chiralpak IC column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm.



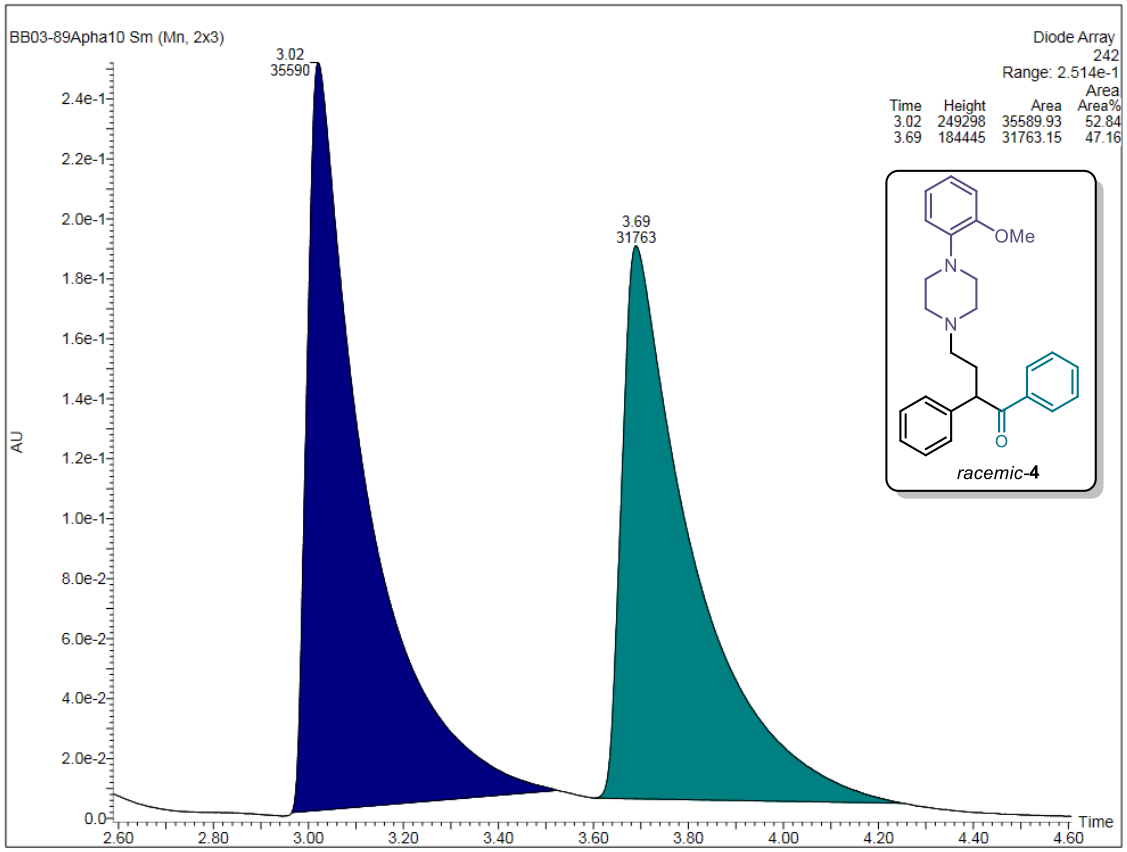


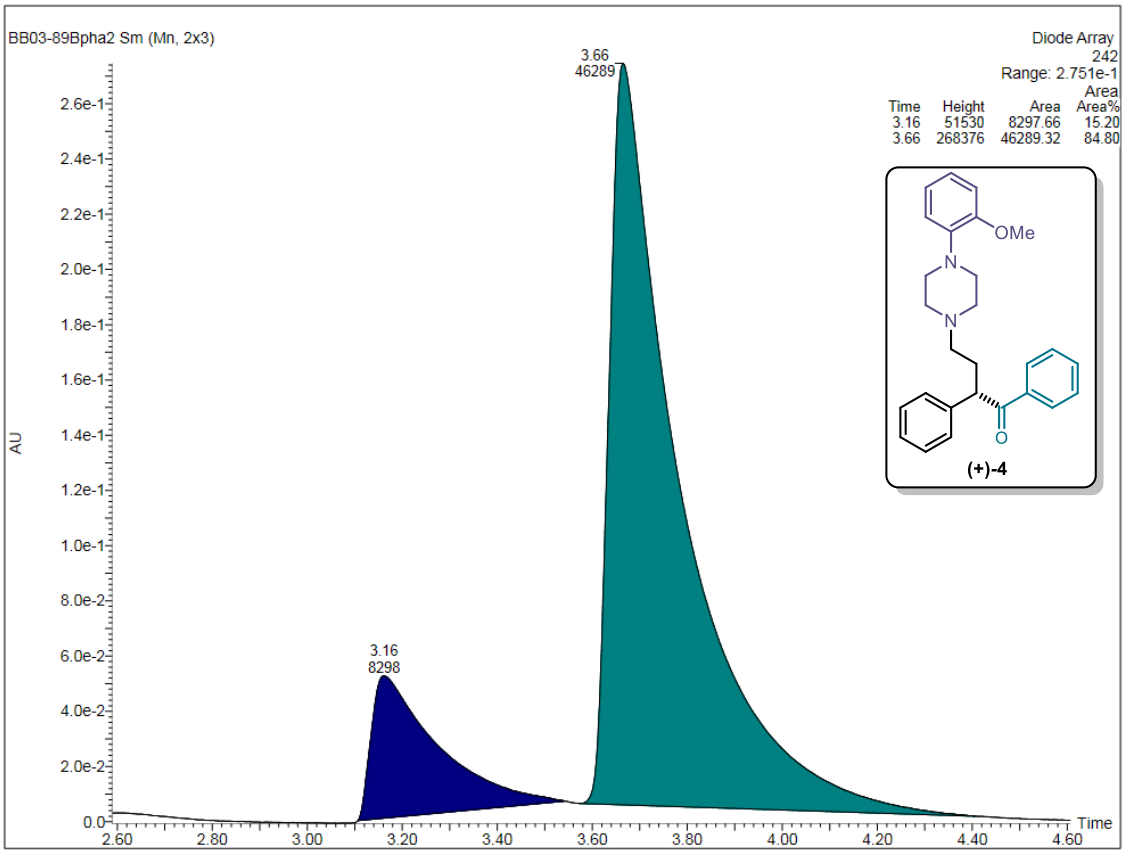
Conditions: UPC^2 analysis on a Daicel Chiralpak IG column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm.



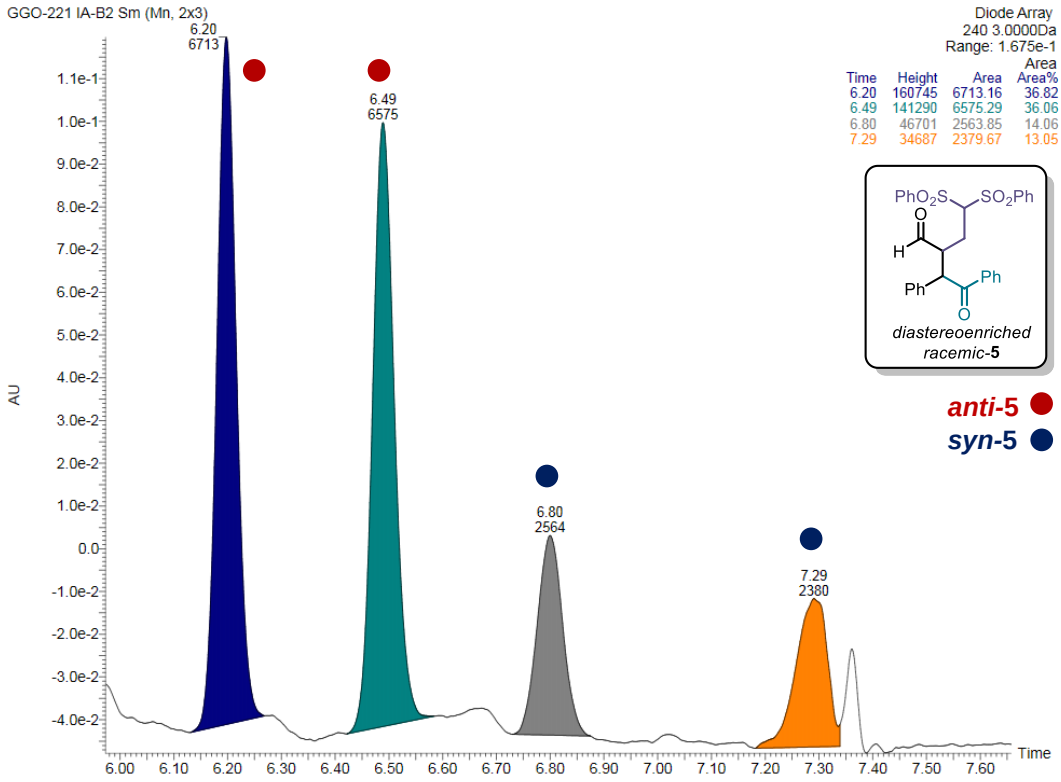


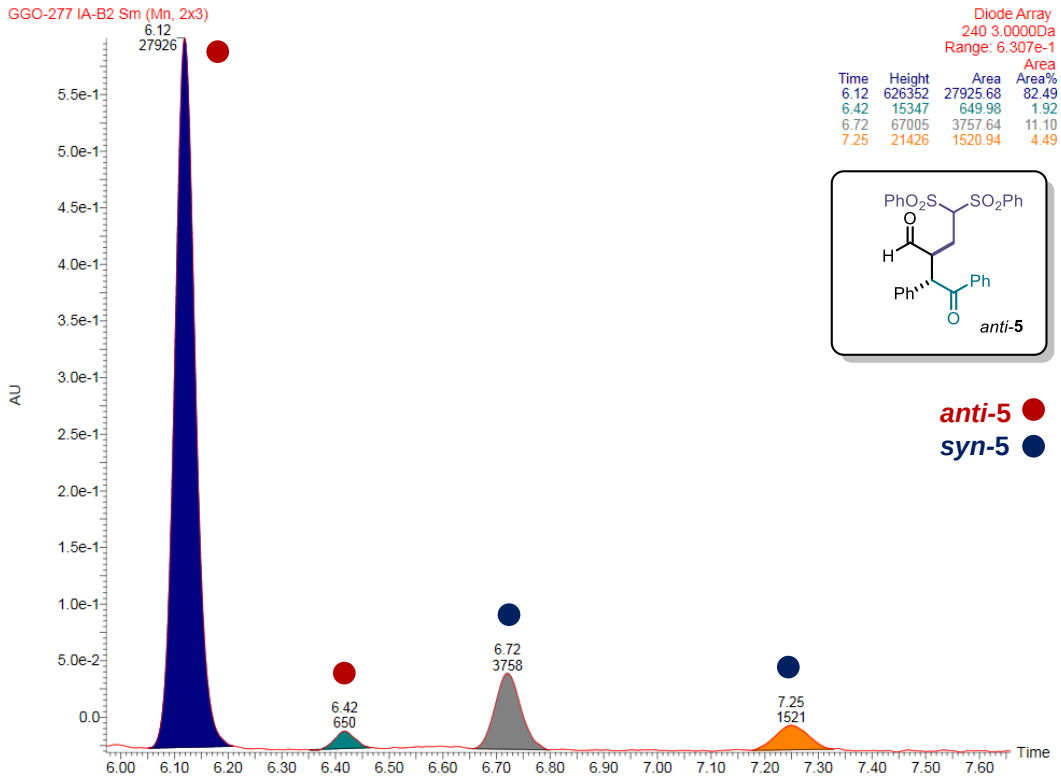
Conditions: UPC^2 analysis a Daicel Chiralpak IC column, 85:15 CO_2/EtOH, flow rate 2 mL/min, λ = 242 nm.

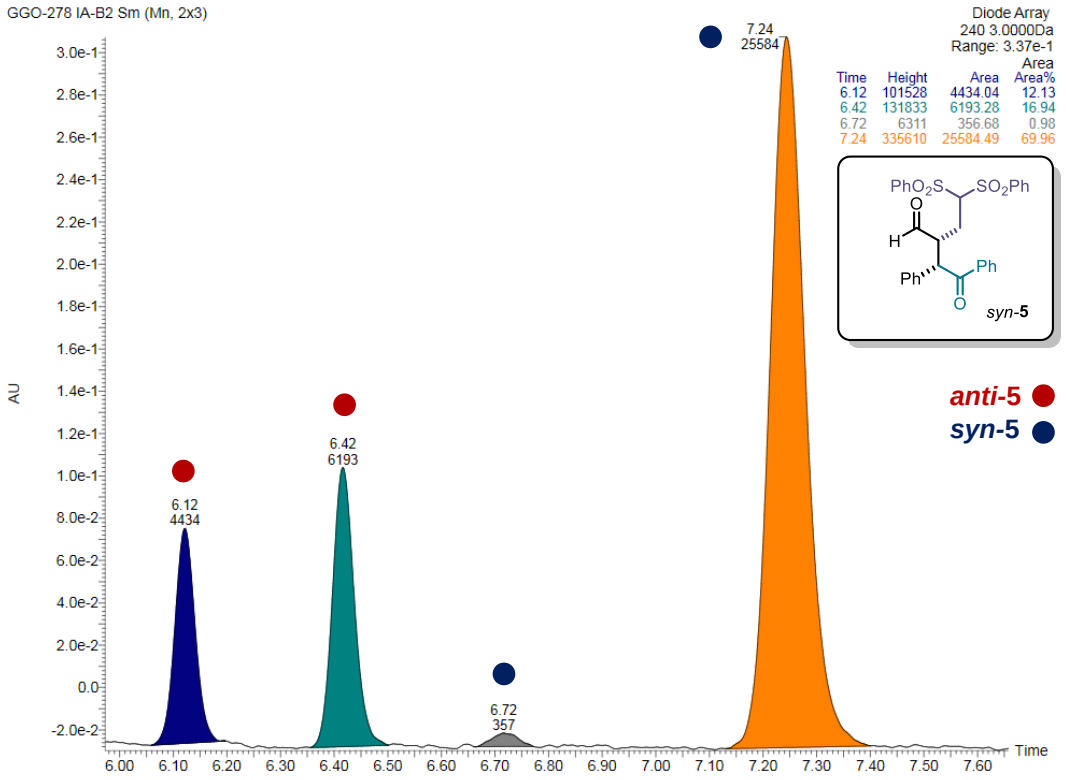




Conditions: UPC^2 analysis on a Daicel Chiralpak IA column, gradient: 1 min 100% CO_2, 5 min from 100% CO_2 to 60% CO_2 - 40% *i*PrOH, flow rate 2 mL/min, column T = 40 °C, λ = 240 nm.






GGO-278 IA-B2 Sm (Mn, 2x3)
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Range: 3.37e-1
Area
Time Height Area Area%
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6.42 131833 6193.28 16.94
6.72 6311 356.68 0.98
7.24 335610 25584.49 69.96
PhO2S SO2Ph
O
H
Ph
Ph
O
syn-5
anti-5
syn-5
7.24
25584
6.42
6193
6.12
4434
6.72
357
AU
Time
3.0e-1
2.8e-1
2.6e-1
2.4e-1
2.2e-1
2.0e-1
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1.4e-1
1.2e-1
1.0e-1
8.0e-2
6.0e-2
4.0e-2
2.0e-2
0.0
-2.0e-2
6.00 6.10 6.20 6.30 6.40 6.50 6.60 6.70 6.80 6.90 7.00 7.10 7.20 7.30 7.40 7.50 7.60