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Synthesis of *N*-alkylated lipopeptides and their application as organocatalyst in asymmetric Michael addition under aqueous environment

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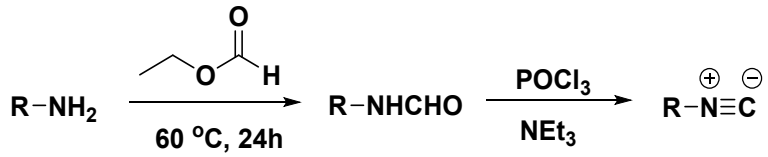
Contents

1. General Information

All solvents were dried and distilled before use by standard procedures and reagents were of the highest commercially available grade purchased from Sigma-Aldrich, Oakwood Chemicals, and Strem Chemicals and used as received or purified according to the procedures outlined in *Purification of Common Laboratory Chemicals.*[1] Glassware used was dried in oven or flame dried under vacuum and cooled under an inert atmosphere. Column flash chromatography was performed using silica gel 60 (230−400 mesh), and analytical thin-layer chromatography (TLC) was performed using silica gel aluminum sheets. Compounds were visualized on TLC by UV-light, $KMnO_4$, I_2, $H_3[P(Mo_3O_{10})_4]$ x H_2O (PMA) and Vanillin. Yields refer to chromatographically and spectroscopically pure compounds unless otherwise noted. ^1H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million relative to the residual solvent signals,[2] and coupling constants (J) are reported in hertz. the following abbreviations indicate the multiplicity of each signal: (s), singlet; (bs), broad singlet; (d), doublet; (t), triplet; (q), quartet; (p), pentet; (m), multiplet; (dd), doublet of doublets; (dt), doublet of triplets; (dq), doublet of quartet; (dp), doublet of pentet; (td), triplet of doublets; (ddt), doublet of doublet of triplets; (dtd), doublet of triplet of doublets; (ddd), doublet of doublet of doublets; (dddd), doublet of doublet of doublet of doublets; (heptd), heptet of doublets. High-resolution ESI mass spectra were obtained from a Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer, an RF-only hexapole ion guide and an external electrospray ion source. HPLC analysis were carried out on an analytical HPLC with a diode array detector SPD-M20A from Shimadzu using Chiralpak column OD-H (250 mm x 4.6 mm) from Daicel Chemical Ind. LTD. UPLC analysis was carried out on Acquity UPC^2 system from Waters with 2998 photodiode array (PDA) and Xevo TQD triple quadrupole mass spectrometry as detectors using Trefoil columns CEL2 and AMY1 (2.1 mm x 50 mm) from Waters. Optical rotations were measured on a Perkin Elmer Polarimeter.

2. Synthesis of lipidic isocyanides

General procedure A



1

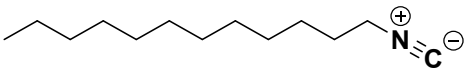
1a, R= *n*-$C_{12}H_{25}$
1b, R= *n*-C_6H_{13}
1c, R= *n*-$C_{18}H_{37}$

2

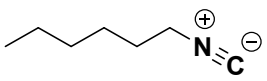
2a, R= *n*-$C_{12}H_{25}$
2b, R= *n*-C_6H_{13}
2c, R= *n*-$C_{18}H_{37}$

In a 50 mL bottom flask, aliphatic amine **1a-c** (11 mmol) was dissolved in HCOOEt (20 mL). The resulting solution was refluxed at 60 °C for 24 h in a silicone bath and the quantitative formation of formamide was verified by TLC (hexanes/EtOAc 1:1). The reaction was concentrated to dryness, the crude mixture was dissolved in NEt_3 (30 mL) and cooled to -70 °C. Then $POCl_3$ (3 mL, 33 mmol, 3 equiv.) was added dropwise during 15 min under argon atmosphere. The reaction mixture was stirred at room temperature for 48h. The resulting mixture was decanted; the solvent removed by reduced pressure and the resulting very viscous oil was directly purified by column chromatography (hexanes, until 10% of EtOAc). The fractions containing the product were combined and evaporated under reduced pressure to give the corresponding isocyanides **2a-c**.

3. Characterization data of compounds 2a-c

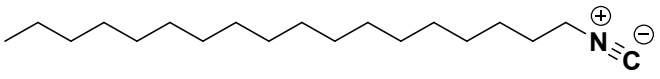


1-isocyanododecane (**2a**)[3]**:**The title compound was synthesized according to the general procedure A in 71% (1.50 g) isolated yield as a light yellow oil. R_f = 0.83 (hexanes/EtOAc 10:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 3.41 – 3.35 (m, 2H), 1.72 – 1.63 (m, 2H), 1.48 – 1.38 (m, 2H), 1.32 – 1.24 (m, 16H), 0.88 (t, *J* = 6.9 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 155.6, 60.5, 41.7, 32.0, 29.7, 29.6, 29.5, 29.5, 29.2, 28.8, 26.5, 22.8, 14.3.



1-isocyanohexane (**2b**)[4]**:** The title compound was synthesized according to the general procedure A in 65% (795 mg) isolated yield as a light yellow oil. R_f = 0.90 (hexanes/EtOAc 10:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 3.38 (td, *J* = 6.7, 2.1 Hz, 2H), 1.73 – 1.62 (m, 2H), 1.44 (p, *J* = 7.2 Hz, 2H), 1.37 –

1.27 (m, 4H), 0.90 (t, *J* = 6.7 Hz, 2H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 155.6, 41.7, 31.0, 29.2, 26.1, 22.6, 14.1.



1-isocyanooctadecane (**2c**)[3]**:** The title compound was synthesized according to the general procedure A in 76% (2.34 g) isolated yield as a light yellow solid. R_f = 0.65 (hexanes). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 3.40 – 3.34 (m, 2H), 1.71 – 1.62 (m, 2H), 1.48 – 1.37 (m, 1H), 1.32 – 1.21 (m, 29H), 0.88 (t, *J* = 6.6 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 155.7, 41.7, 32.1, 29.8, 29.7, 29.5, 29.3, 28.9, 26.5, 22.8, 14.3.

4. General procedures for the synthesis of prolyl pseudo-lipopeptides by Ugi-4CR

General Procedure B: A solution containing acetone (3 equiv.), amine (1.5 equiv.) and anhydrous sodium sulfate (3 equiv.) in MeOH was stirred at room temperature for 2 hours. After the addition of carboxylic acid (1.2 equiv.) and isocyanide (1 equiv.), the resulting mixture was allowed to stir at room temperature for 24 h. Finally, the solvent was removed under reduced pressure and the residue was subjected to deprotection procedure E and purified by column chromatography.

General Procedure C: A solution containing acetone (3 equiv.) and amine (1.5 equiv.) and anhydrous sodium sulfate (3 equiv.) in MeOH/THF (2:1 v/v) was stirred under microwave irradiation at 70 °C during 10 min. After the carboxylic acid (1.2 equiv.) and isocyanide (1 equiv.) were added, the resulting mixture was stirred under microwave irradiation (at 70 °C) for 30 min. Finally, the solvent was removed under reduced pressure and the residue was subjected to deprotection procedure E and purified by column chromatography.

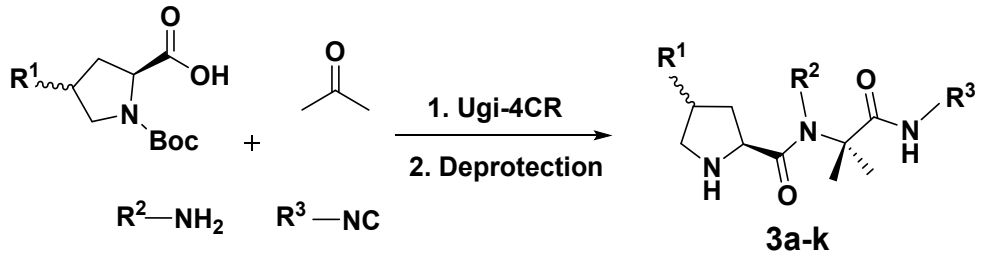
General Procedure D: A solution containing acetone (3 equiv.), amine (1.5 equiv.) and anhydrous sodium sulfate (3 equiv.) in MeOH/THF (2:1 v/v) was stirred under microwave irradiation at (70 °C) during 10 min to preform the imine. After carboxylic acid (1.2 equiv.) and isocyanide (1 equiv.) were added, the resulting mixture was allowed to stir at room temperature for 24-48 h. Finally, the solvent was removed under

reduced pressure and the residue was subjected to deprotection procedure E and purified by column chromatography.

5. *N*-Boc deprotection of prolyl *pseudo*-lipopeptides

General procedure E: The crude *N*-Boc product of the Ugi-4CR was dissolved in 1 mL of a mixture of TFA/DCM 9:1 v/v at 0 °C. The reaction mixture was allowed to stir for 30 min and then concentrated to reduced pressure (TFA was entirely removed by repetitive addition and evaporation of further DCM). The crude was dissolved in 10 mL of DCM and neutralized over anhydrous K_2CO_3, filtered and evaporated under reduced pressure afforded to the crude product.

TABLE 1. Synthesis of prolyl *pseudo*-lipopeptides by Ugi-4CR.

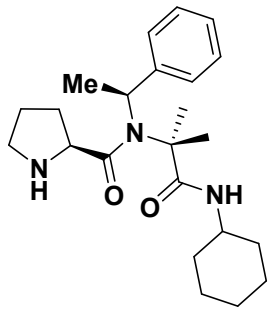


3a-k
prolyl *pseudo*-lipopeptides hybrid catalysts

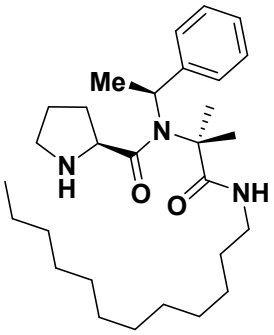
Entry	R^1/ R^2/ R^3	Catalyst	Yield (%)[a]
1	H/ (*S*)-α-MeBn/ Cy	**3a**	77
2	H/ (*S*)-α-MeBn/ *n*-$C_{12}H_{25}$	**3b**	54
3	*trans*-OH/ (*S*)-α-MeBn/ Cy	**3c**	73
4	*trans*-OH/ (*S*)-α-MeBn/ *n*-C_6H_{13}	**3d**	81
5	*trans*-OH/ (*S*)-α-MeBn/ *n*-$C_{12}H_{25}$	**3e**	50
6	*cis*-OH/ (*S*)-α-MeBn/ *n*-$C_{12}H_{25}$	**3f**	80
7	*trans*-OH/ (*S*)-α-MeBn/ *n*-$C_{18}H_{35}$	**3g**	35
8	*trans*-*n*-$C_{11}H_{23}COO$/ (*S*)-α-MeBn/ Cy	**3h**	48
9	H/ *n*-$C_{12}H_{25}$/ Cy	**3i**	70
10	H/ *n*-$C_{12}H_{25}$/ *n*-$C_{12}H_{25}$	**3j**	57
11	*trans*-OH/ α-PhBn / *n*-$C_{12}H_{25}$	**3k**	55

[a] Isolated yields after two step.

6. Characterization data of compounds 3a-k

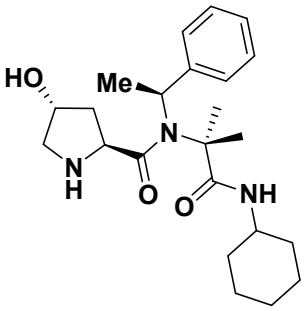


(*S*)-*N*-(1-(cyclohexylamino)-2-methyl-1-oxopropan-2-yl)-*N*-((*S*)-1-phenylethyl)pyrrolidine-2-carboxamide (**3a**)[5]: (*S*)-α-methylbenzylamine (39 μL, 0.3 mmol), acetone (44 μL, 0.6 mmol), *N*-Boc-proline (52 mg, 0.24 mmol), cyclohexyl isocyanide (25 µL, 0.2 mmol) and anhydrous sodium sulfate (85 mg, 0.6 mmol) were reacted in MeOH (200 μL) according to the general procedure C. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-peptoid hybrid **3a** in 77% (59 mg) as a colorless oil. R_f = 0.5 (DCM/MeOH 95:5). $[\alpha]_D^{23}$ = -5.0 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Methanol-d$_4$)** δ 7.64 (d, J = 7.7 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.31 (t, J = 7.4 Hz, 1H), 5.23 (q, J = 7.1 Hz, 1H), 3.91 (s, 1H), 3.62 (ddt, J = 9.8, 7.3, 3.6 Hz, 1H), 3.31 – 3.29 (m, 1H), 3.20 (dt, J = 11.2, 6.7 Hz, 1H), 2.92 (dt, J = 11.5, 7.3 Hz, 1H), 1.90 (d, J = 7.1 Hz, 3H), 1.87 – 1.70 (m, 5H), 1.69 – 1.42 (m, 9H), 1.38 – 1.13 (m, 6H). **NMR ^{13}C (100 MHz, Methanol-d$_4$)** δ 176.31, 173.88, 143.48, 129.92, 128.54, 128.18, 65.88, 61.37, 53.09, 50.35, 48.00, 33.49, 33.46, 30.52, 26.66, 26.40, 25.98, 25.64, 24.76, 20.22. **HRMS (ESI-Q-TOF)**: m/z: 386.2808. Calcd. for $[M+H]^+$:386.2802.

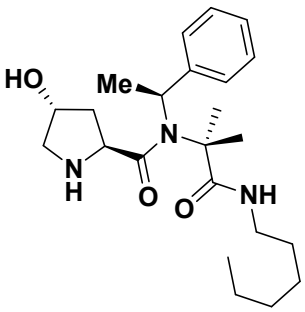


(*S*)-*N*-(1-(dodecylamino)-2-methyl-1-oxopropan-2-yl)-*N*-((*S*)-1-phenylethyl)pyrrolidine-2-carboxamide (**3b**): (*S*)-α-methylbenzylamine (39 μL, 0.3 mmol), acetone (44 μL, 0.6 mmol), *N*-Boc-proline (52 mg, 0.24 mmol), *n*-dodecyl isocyanide (45 μL, 0.2 mmol) and anhydrous sodium sulfate (85 mg, 0.6 mmol) were reacted in MeOH/THF (300 μL) according to the general procedure C. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-lipopeptoid hybrid **3b** in 54% (51 mg) as a colorless oil. R_f = 0.30 (EtOAc/MeOH 10:1). $[\alpha]_D^{23}$ = -1.2 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Methanol-d$_4$)** δ 7.65 (d, J = 7.7 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 5.25 (q, J = 7.2 Hz, 1H), 4.22 (s, 1H), 3.35 – 3.27 (m, 2H), 3.24 – 3.10 (m, 3H), 1.92 – 1.83 (m, 4H), 1.76 – 1.58 (m, 6H), 1.57 – 1.43 (m, 5H), 1.32 – 1.28 (m, 18H), 0.89 (t, J = 6.5 Hz, 3H). **NMR ^{13}C (100 MHz, Methanol-d$_4$)** δ 177.0, 171.4, 142.9, 130.0, 128.7, 128.4, 66.2, 61.2, 53.3, 47.6, 40.9, 33.1, 30.7, 30.5, 30.3, 30.0, 28.1,

25.6, 25.1, 24.9, 23.7, 20.0, 14.4. **HRMS (ESI-Q-TOF)**: m/z: 472.3876. Calcd. for $[M+H]^+$: 472.3898.

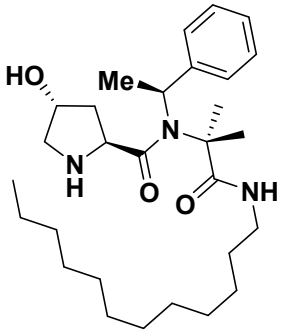


(2*S*,4*R*)-*N*-(1-(cyclohexylamino)-2-methyl-1-oxopropan-2-yl)-4-hydroxy-*N*-((*S*)-1-phenylethyl)pyrrolidine-2-carboxamide (**3c**): (*S*)-α-methylbenzylamine (39 μL, 0.3 mmol), acetone (44 μL, 0.6 mmol), *N*-Boc-*trans*-4-hydroxy-proline (56 mg, 0.24 mmol), cyclohexyl isocyanide (25 μL, 0.2 mmol) and anhydrous sodium sulfate (85 mg, 0.6 mmol) were reacted in MeOH/THF (300 μL) according to the general procedure D. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-peptoid hybrid **3c** in 73% (59 mg) as a colorless oil. $\boldsymbol{R_f}$ = 0.3 (DCM/MeOH 95:5). $\boldsymbol{[\alpha]_D^{23}}$ = 3.0 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Methanol-d$_4$)** δ 7.60 (d, J = 7.7 Hz, 2H), 7.41 (t, J = 7.6 Hz, 2H), 7.30 (t, J = 7.4 Hz, 1H), 5.20 (q, J = 7.2 Hz, 1H), 4.28 (bs, 2H), 3.59 (dp, J = 11.5, 4.1 Hz, 1H), 3.31 – 3.23 (m, 2H), 3.20 – 3.08 (m, 1H), 1.88 (d, J = 7.1 Hz, 3H), 1.85 – 1.70 (m, 4H), 1.69 – 1.49 (m, 8H), 1.37 – 1.09 (m, 6H). **NMR ^{13}C (100 MHz, Methanol-d$_4$)** δ 174.8, 170.8, 141.7, 128.7, 127.4, 126.8, 69.6, 64.8, 58.6, 54.1, 49.1, 38.4, 32.1, 25.2, 25.1, 24.1, 23.4, 18.8. **HRMS (ESI-Q-TOF)**: m/z: 402.2757. Calcd. for $[M+H]^+$: 402.2751.

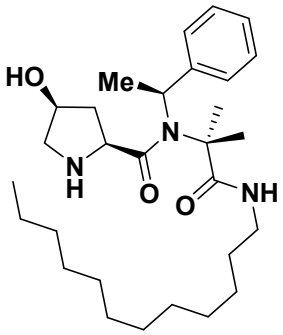


(2*S*,4*R*)-*N*-(1-(hexylamino)-2-methyl-1-oxopropan-2-yl)-4-hydroxy-*N*-((*S*)-1-phenylethyl)pyrrolidine-2-carboxamide (**3d**): (*S*)-α-methylbenzylamine (39 μL, 0.3 mmol), acetone (44 μL, 0.6 mmol), *N*-Boc-*trans*-4-hydroxy-proline (56 mg, 0.24 mmol), *n*-hexyl isocyanide (27 μL, 0.2 mmol) and anhydrous sodium sulfate (85 mg, 0.6 mmol) were reacted in MeOH/THF (300 μL) according to the general procedure D. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-peptoid hybrid **3d** in 81% (66 mg) as a colorless oil. $\boldsymbol{R_f}$ = 0.3 (DCM/MeOH 95:5). $\boldsymbol{[\alpha]_D^{23}}$ = -9.8 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Methanol-d$_4$)** δ 7.63 (d, *J* = 7.7 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 5.20 (q, *J* = 7.1 Hz, 1H), 4.26 (s, 1H), 4.18 (s, 1H), 3.24 (dd, J = 11.9, 3.9 Hz, 1H), 3.16 (q, *J* = 6.7 Hz, 2H), 3.00 (d, *J* = 11.8 Hz, 1H), 1.90 (d, *J* = 7.0 Hz, 3H), 1.69 – 1.46 (m, 9H), 1.38 – 1.26 (m, 6H), 0.88 (t, 3H). **NMR ^{13}C (100 MHz, Methanol-d$_4$)** δ 177.1, 173.5, 143.4, 130.0, 128.6, 128.1, 71.5, 65.9, 60.0, 55.6, 53.0,

40.9, 40.0, 32.7, 30.3, 27.8, 25.6, 24.8, 23.7, 20.4, 14.4. **HRMS (ESI-Q-TOF)**: m/z: 404.2906. Calcd. for $[M+H]^+$: 404.2908.

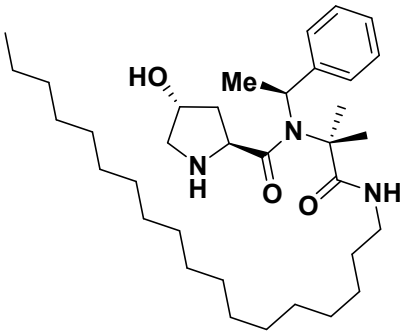


(2*S*,4*R*)-*N*-(1-(dodecylamino)-2-methyl-1-oxopropan-2-yl)-4-hydroxy-*N*-((*S*)-1-phenylethyl)pyrrolidine-2-carboxamide (**3e**): (*S*)-α-methylbenzylamine (39 μL, 0.3 mmol), acetone (44 μL, 0.6 mmol), *N*-Boc-*trans*-4-hydroxy-proline (56 mg, 0.24 mmol), *n*-dodecyl isocyanide (45 μL, 0.2 mmol) and anhydrous sodium sulfate (85 mg, 0.6 mmol) were reacted in MeOH/THF (300 μL) according to the general Ugi-4CR-based procedure D. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-lipopeptoid hybrid **3e** in 50% (49 mg) as a colorless oil. $\boldsymbol{R_f}$ = 0.4 (DCM/MeOH 95:5). $\boldsymbol{[\alpha]_D^{23}}$ = 3.2 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Methanol-d$_4$)** δ 7.65 (d, *J* = 7.7 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 5.24 (q, *J* = 7.1 Hz, 1H), 4.32 (s, 1H), 3.31 – 3.28 (m, 2H), 3.18 (dd, *J* = 8.9, 5.7 Hz, 2H), 1.92 (d, *J* = 7.0 Hz, 3H), 1.70 – 1.58 (m, 6H), 1.57 – 1.50 (m, 2H), 1.29 (s, 20H), 0.92 – 0.87 (m, 4H). **NMR ^{13}C (100 MHz, Methanol-d$_4$)** δ 177.0, 171.9, 143.0, 130.1, 128.8, 128.2, 70.8, 66.2, 60.0, 55.5, 53.2, 41.0, 39.8, 33.1, 30.7, 30.5, 30.4, 28.1, 25.4, 24.9, 23.7, 20.2, 14.4. **HRMS (ESI-Q-TOF)**: m/z: 488.3827. Calcd. for $[M+H]^+$: 488.3847.

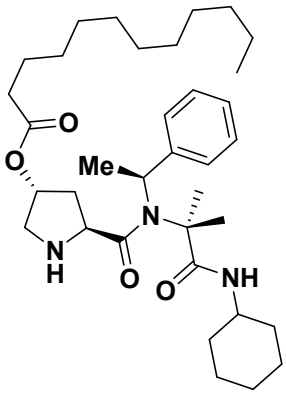


(2*S*,4*S*)-*N*-(1-(dodecylamino)-2-methyl-1-oxopropan-2-yl)-4-hydroxy-*N*-((*S*)-1-phenylethyl)pyrrolidine-2-carboxamide (**3f**): (*S*)-α-methylbenzylamine (39 μL, 0.3 mmol), acetone (44 μL, 0.6 mmol), *N*-Boc-*cis*-4-hydroxy-proline (56 mg, 0.24 mmol), *n*-dodecyl isocyanide (45 μL, 0.2 mmol) and anhydrous sodium sulfate (85 mg, 0.6 mmol) were reacted in MeOH/THF (300 μL) according to the general procedure D. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-lipopeptoid hybrid **3f** in 80% (78 mg) as a colorless oil. $\boldsymbol{R_f}$ = 0.45 (DCM/MeOH 95:5). $\boldsymbol{[\alpha]_D^{23}}$ = -21.2 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Methanol-d$_4$)** δ 7.65 (d, *J* = 7.7 Hz, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 5.17 (q, *J* = 7.2 Hz, 1H), 4.00 (s, 1H), 3.62 (s, 1H), 3.17 (td, *J* = 7.0, 3.9 Hz, 2H), 2.95 (d, *J* = 12.0 Hz, 1H), 2.60 (dd, *J* = 12.4, 4.2 Hz, 1H), 1.89 (d, *J* = 7.0 Hz, 3H), 1.62 – 1.49 (m, 8H), 1.28 (s, 20H), 0.89 (t, *J* = 6.7 Hz, 3H). **NMR ^{13}C (100 MHz, Methanol-d$_4$)** δ 177.3, 144.3, 129.8, 128.2, 127.8,

73.2, 65.5, 60.8, 56.9, 52.8, 40.9, 39.8, 33.1, 30.8, 30.7, 30.50, 30.48, 30.4, 28.1, 25.9, 24.6, 23.7, 20.9, 14.5. **HRMS (ESI-Q-TOF)**: m/z: 488.3863. Calcd. for $[M+H]^+$: 488.3847.

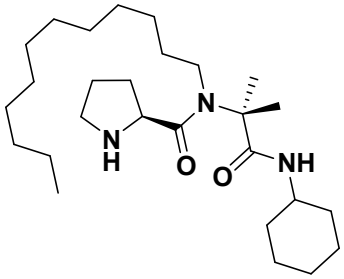


(2*S*,4*R*)-4-hydroxy-*N*-(2-methyl-1-(octadecylamino)-1-oxopropan-2-yl)-*N*-((*S*)-1-phenylethyl)pyrrolidine-2-carboxamide (**3g**): (*S*)-α-methylbenzylamine (39 μL, 0.3 mmol), acetone (44 μL, 0.6 mmol), *N*-Boc-*trans*-4-hydroxy-proline (56 mg, 0.24 mmol), *n*-octadecyl isocyanide (56 mg, 0.2 mmol) and anhydrous sodium sulfate (85 mg, 0.6 mmol) were reacted in MeOH/THF (300 μL) according to the general Ugi-4CR-based procedure D. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-lipopeptoid hybrid **3g** in 35% (40 mg) as a colorless oil. $\boldsymbol{R_f}$ = 0.2 (DCM/MeOH 95:5). $\boldsymbol{[\alpha]_D^{23}}$ = -38.4 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Methanol-d$_4$)** δ 7.52 – 7.26 (m, 5H), 5.29 – 5.12 (m, 1H), 4.64 (s, 1H), 4.04 – 3.63 (m, 1H), 3.54 – 3.31 (m, 2H), 3.20 – 3.13 (m, 2H), 2.58 – 1.82 (m, 3H), 1.78 – 1.39 (m, 6H), 1.27 (s, 30H), 1.16 – 0.71 (m, 5H). **NMR ^{13}C (100 MHz, Methanol-d$_4$)** δ 172.7, 169.6, 140.0, 129.9, 129.8, 129.5, 129.3, 129.2, 71.4, 61.8, 60.6, 59.8, 56.8, 55.0, 40.9, 40.8, 39.5, 33.1, 30.8, 30.5, 30.46, 30.43, 28.7, 28.1, 23.7, 17.1, 14.5. **HRMS (ESI-Q-TOF)**: m/z: 603.5006. Calcd. for $[M+CH_3OH]^+$: 603.4975.

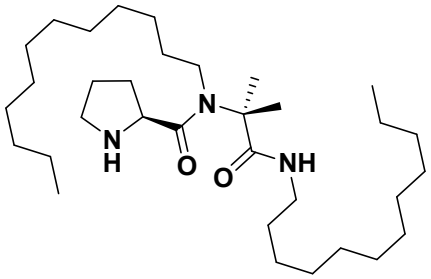


(3*R*,5*S*)-5-((1-(cyclohexylamino)-2-methyl-1-oxopropan-2-yl)((*S*)-1-phenylethyl)carbamoyl)pyrrolidin-3-yl dodecanoate (**3h**): (*S*)-α-methylbenzylamine (97 μL, 0.75 mmol), acetone (110 μL, 0.6 mmol), (2*S*,4*R*)-4-(dodecanoyloxy)pyrrolidine-2-carboxylic acid[6] (248 mg, 0.6 mmol), cyclohexyl isocyanide (62 μL, 0.5 mmol) and anhydrous sodium sulfate (213 mg, 1.5 mmol) were reacted in MeOH/THF (600 μL) according to the general procedure D. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-lipopeptoid hybrid **3h** in 48% (140 mg) as a colorless oil. $\boldsymbol{R_f}$ = 0.50 (hexanes/EtOAc 7:3). $\boldsymbol{[\alpha]_D^{23}}$ = 8.6 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Methanol-d$_4$)** δ 7.68 (d, *J* = 7.7 Hz, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.7 Hz, 1H), 5.27 (q, *J* = 7.1 Hz, 1H), 3.74 – 3.61 (m, 1H), 3.59 (dd, *J* = 12.9, 4.7

Hz, 2H), 3.40 – 3.31 (m, 1H), 2.34 – 2.19 (m, 2H), 1.94 (d, *J* = 7.0 Hz, 3H), 1.92 – 1.55 (m, 13H), 1.44 – 1.14 (m, 25H), 0.92 (t, *J* = 6.6 Hz, 3H). **NMR ^{13}C (100 MHz, Methanol-d_4)** δ 176.1, 173.7, 170.8, 143.2, 130.2, 128.9, 128.4, 73.8, 66.3, 60.3, 53.0, 52.7, 50.6, 37.1, 34.8, 33.5, 33.1, 30.7, 30.6, 30.5, 30.2, 26.6, 26.5, 25.9, 25.7, 25.5, 24.8, 23.7, 20.1, 14.4. **HRMS (ESI-Q-TOF)**: m/z: 584.4412. Calcd. for $[M+H]^+$: 584.4422.

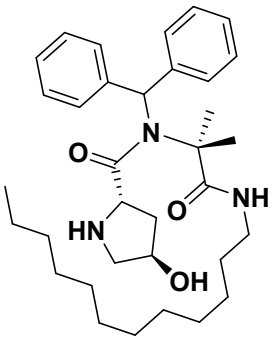


(*S*)-*N*-(1-(cyclohexylamino)-2-methyl-1-oxopropan-2-yl)-*N*-dodecylpyrrolidine-2-carboxamide (**3i**): *N*-dodecyl amine (56 mg, 0.3 mmol), acetone (44 *μ*L, 0.6 mmol), *N*-Boc-proline (52 mg, 0.24 mmol), cyclohexyl isocyanide (25 *μ*L, 0.2 mmol) and anhydrous sodium sulfate (85 mg, 0.6 mmol) were reacted in MeOH (200 *μ*L) according to the general procedure B. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-lipopeptoid hybrid **3i** in 70% (63 mg) as a colorless oil. R_f = 0.6 (DCM/MeOH 95:5). $[\alpha]_D^{23}$ = -11.2 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Chloroform-d_3)** δ 5.97 (d, *J* = 8.2 Hz, 1H), 4.66 (t, *J* = 7.6 Hz, 1H), 3.67 – 3.57 (m, 1H), 3.53 – 3.39 (m, 3H), 3.31 (ddd, *J* = 16.3, 11.7, 5.3 Hz, 1H), 2.44 – 2.33 (m, 1H), 2.17 – 1.93 (m, 3H), 1.83 (dt, *J* = 14.4, 7.2 Hz, 2H), 1.75 – 1.63 (m, 3H), 1.61 – 1.42 (m, 6H), 1.33 – 1.09 (m, 24H), 0.89 – 0.82 (m, 4H). **NMR ^{13}C (100 MHz, Chloroform-d_3)** δ 173.1, 168.8, 63.3, 58.9, 48.9, 46.5, 45.1, 32.9, 32.9, 32.0, 31.9, 29.8, 29.7, 29.67, 29.65, 29.4, 29.3, 27.2, 25.6, 25.2, 25.2, 25.0, 24.6, 24.5, 22.8, 14.2. **HRMS (ESI-Q-TOF)**: m/z: 450.4043. Calcd. for $[M+H]^+$: 450.4054.



(*S*)-*N*-dodecyl-*N*-(1-(dodecylamino)-2-methyl-1-oxopropan-2-yl)pyrrolidine-2-carboxamide (**3j**): *N*-dodecyl amine (56 mg, 0.3 mmol), acetone (44 *μ*L, 0.6 mmol), *N*-Boc-proline (52 mg, 0.24 mmol), *n*-dodecyl isocyanide (45 *μ*L, 0.2 mmol) and anhydrous sodium sulfate (85 mg, 0.6 mmol) were reacted in MeOH/THF (300 *μ*L) according to the general procedure C. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-lipopeptoid hybrid **3j** in 57% (61 mg) as a colorless oil. R_f = 0.5-0.6 (DCM/MeOH 95:5). $[\alpha]_D^{23}$ = -14.2 (c 0.1, MeOH, 23 ^{0}C). **NMR ^{1}H (400 MHz, Methanol-d_4)** δ 4.50 – 4.42 (m, 1H), 3.50 – 3.32 (m, 3H), 3.27 – 3.01 (m, 3H), 2.48 (dq, *J* = 13.0, 6.9, 5.4 Hz, 1H), 2.11 – 1.91 (m, 3H), 1.74 –

1.59 (m, 2H), 1.52 (s, 3H), 1.47 (s, 3H), 1.39 – 1.22 (m, 38H), 0.88 (t, *J* = 6.6 Hz, 6H). **NMR ^{13}C (100 MHz, Methanol-d$_4$)** δ 176.9, 169.8, 64.2, 60.4, 47.5, 45.6, 40.9, 33.1, 32.6, 30.8, 30.5, 30.4, 28.1, 27.9, 25.4, 24.8, 24.3, 23.7, 14.4. **HRMS (ESI-Q-TOF)**: m/z: 536.5145. Calcd. for $[M+H]^+$: 536.5150.



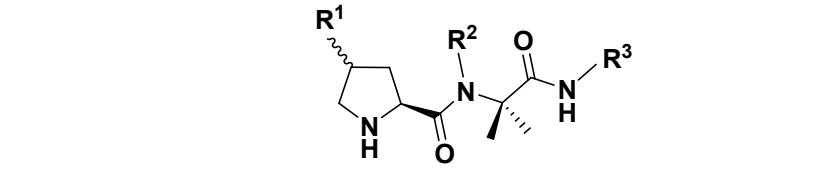
(2*S*,4*R*)-*N*-benzhydryl-*N*-(1-(dodecylamino)-2-methyl-1-oxopropan-2-yl)-4-hydroxypyrrolidine-2-carboxamide (**3k**): 2,2-diphenylglycine methyl ester hydrochloride (241 mg, 1 mmol), DIPEA (174 *μ*L, 1 mmol), acetone (110 *μ*L, 1.5 mmol), *N*-Boc-*trans*-4-hydroxy-proline (139 mg, 0.6 mmol), *n*-dodecyl isocyanide (98 *μ*L, 0.5 mmol) and anhydrous sodium sulfate (213 mg, 1.5 mmol) were reacted in MeOH/THF (600 μL) according to the general procedure D. Flash column chromatography purification 0-10% of MeOH in DCM afforded the peptide-lipopeptoid hybrid **3k** in 55% (151 mg) as a colorless oil. ***R$_f$*** **=** 0.5 (DCM/MeOH 95:5). **[α]$_D^{23}$** = 2.6 (c 0.1, MeOH, 23 °C). **NMR ^{1}H (400 MHz, Methanol-d$_4$)** δ 7.52 – 7.41 (m, 4H), 7.43 – 7.34 (m, 4H), 7.34 – 7.24 (m, 2H), 6.45 (bs, 1H), 4.12 (s, 1H), 3.88 (t, *J* = 7.8 Hz, 1H), 3.26 – 3.15 (m, 2H), 3.12 (dd, *J* = 11.8, 4.7 Hz, 1H), 2.63 (d, *J* = 11.8 Hz, 1H), 1.72 – 1.59 (m, 3H), 1.57 – 1.45 (m, 5H), 1.38 – 1.24 (m, 20H), 0.89 (t, *J* = 6.6 Hz, 3H). **NMR ^{13}C (100 MHz, Methanol-d$_4$)** δ 177.5, 177.1, 143.1, 139.9, 130.1, 130.0, 129.9, 129.5, 128.9, 128.8, 72.5, 66.0, 62.2, 61.6, 56.1, 40.9, 39.7, 33.1, 30.8, 30.7, 30.50, 30.47, 30.4, 28.1, 25.7, 24.5, 23.7, 14.5. **HRMS (ESI-Q-TOF)**: m/z: 550.4002. Calcd. for $[M+H]^+$: 550.4003.

7. General procedure for asymmetric 1,4-addition of butanal to *trans*-*β*-nitrostyrene: Catalyst Screening

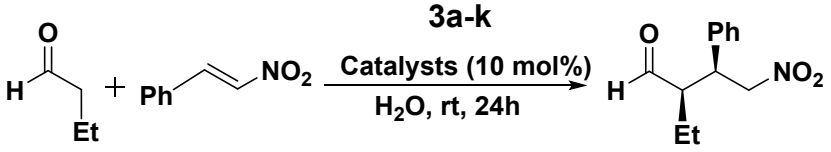
General procedure F: A vial was charged with the prolyl *pseudo*-lipopeptides hybrid catalyst **3a-k** (10 mol%), *trans*-*β*-nitrostyrene[7] (0.2 mmol, 1.0 equiv.) and 0.4 mL of water. The mixture was homogenized in an ultrasound bath, butanal (0.40 mmol, 2.0 equiv.) was added and this mixture was stirred for 24 h. After this period, the resulting reaction mixture was extracted with EtOAc, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The yield was determined by ^{1}H NMR analysis of crude product with 1.2.3-trimethoxybenzene (0.2 mmol, 1.0 equiv.) as internal standard. The crude product was purified by flash column chromatography on silica gel using hexanes/EtOAc (9:1 v/v) as eluent. The diastereoisomeric ratio was

determined by ^{1}H NMR analysis of crude of the reaction mixture. Enantiomeric excess (*e.e.*) was determined by chiral HPLC or UPC^2 analysis through comparison with the authentic racemic material.

TABLE 2. Catalysts Screening.



3a-k



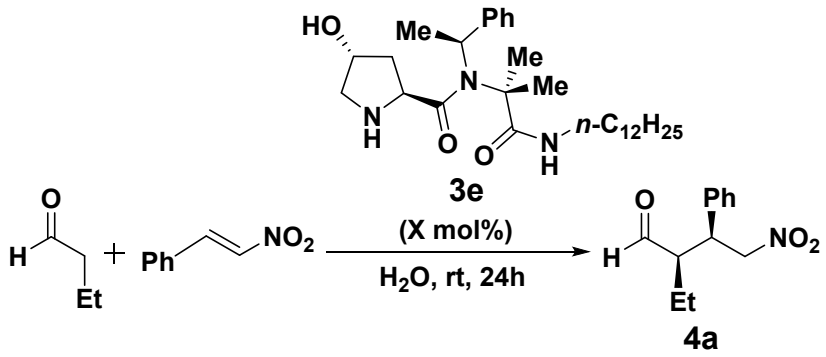
4a

Entry	Catalyst	Yield (%)[a]	*d.r.* (*syn/anti*)[c]	*e.e.* (%)[d]
1	**3a**	57	94:06	96
2	**3b**	90	89:11	94
3	**3c**	43	70:30	99
4	**3d**	72[b]	81:19	97
5	**3e**	**88**	**76:24**	**99**
6	**3f**	78[b]	79:21	94
7	**3g**	35[b]	87:13	92
8	**3h**	23	89:11	99
9	**3i**	75	76:24	88
10	**3j**	87	88:12	83
11	**3k**	84	79:21	89

[a] Yield determined by ^{1}H NMR spectroscopy analysis of crude of the reaction mixture with 1,2,3-trimethoxybenzene as standard; [b] Isolated yield; [c] *syn/trans* ratio determined by ^{1}H NMR; [d] Determined by chiral-stationary phase HPLC or UPC^2 analysis.

8. Optimization of asymmetric Michael reaction of butanal and *trans*-β-nitrostyrene catalyzed by compound 3e

TABLE 3. Optimization of the system.



Entry [a]	Catalyst (mol%)	Solvent	Yield (%) [b]	*d.r.* (*syn*/*anti*) [c]	*e.e.* (%) [d]
1	10	H_2O	88	76:24	99
2	5	H_2O	90	90:10	99
3	**2.5**	**H_2O**	**99(96)**	**93:7**	**99**
4	1	H_2O	65	98:2	99
5	2.5	Ethanol	26	85:15	98
6	2.5	Brine	84	95:5	99
7	2.5	PEG-300	54	82:18	98

[a] Reactions using 2 equivalents of butanal and 0.2 mmol of β-nitrostyrene in 0.4 mL of solvent; [b] Yield determined by ^{1}H NMR spectroscopy analysis of crude of the reaction mixture (yield of isolated product); [c] *syn/anti* ratio determined by ^{1}H NMR; [d] Determined by chiral-stationary phase HPLC or UPC2 analysis.

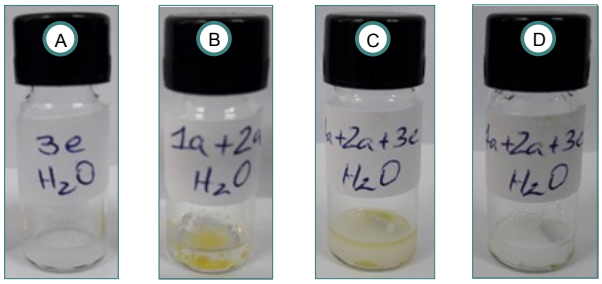


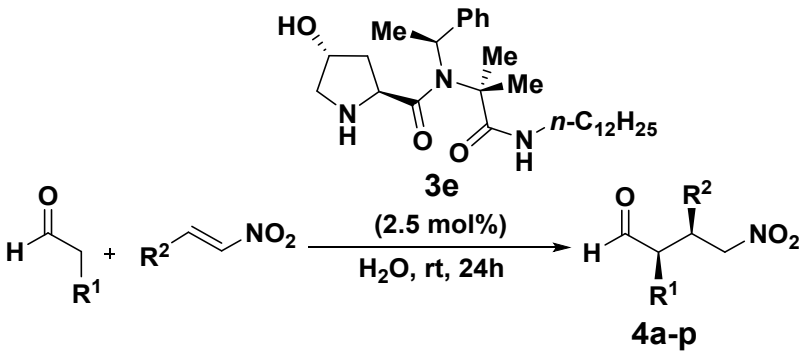
FIGURE 1. Visual schematic representation of the optimized condition in different stages. (***A***) Catalyst 3e in water; (***B***) mixture of butyraldehyde and trans-β-nitrostyrene in water; (***C***) mixture of butyraldehyde, trans-β-nitrostyrene and catalyst 3e in water; (***D***) mixture of butyraldehyde, trans-β-nitrostyrene and catalyst 3e in water after stirred for 24h.

9. General procedure for asymmetric 1,4-addition of aldehydes to nitrostyrenes

General procedure G: A vial was charged with the prolyl pseudo-lipopeptide hybrid catalyst **3e** (2.5 mol%), the nitrostyrene[7] (0.2 mmol, 1.0 equiv) and 0.4 mL of water. The mixture was homogenized in an ultrasound bath, the aldehyde (0.40 mmol, 2.0 equiv) was added and this mixture was stirred for 24 h. After this period, the resulting reaction mixture was extracted with EtOAc, dried over anhydrous Na_2SO_4 and

concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel using hexanes/EtOAc as eluent. The diastereoisomeric ratio was determined by ^{1}H NMR analysis of crude of the reaction mixture. Enantiomeric excess (*e.e.*) was determined by chiral HPLC or UPC^2 analysis through comparison with the authentic racemic material.

TABLE 4. Scope of catalyst **3e** in the asymmetric Michael reaction between different aldehydes and *trans*-*β*-nitrostyrenes.



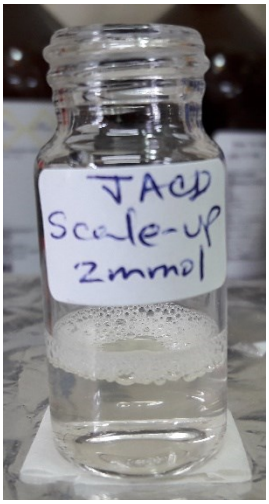
Entry[a]	R^1	R^2	Compound	Yield (%)[b]	*d.r.* (*syn*/*anti*)[c]	*e.e.* (%)[d]
1	Ethyl	Phenyl	**4a**	99(96)	93:07	99
2	*n*-Butyl	Phenyl	**4b**	91(n.d.)	92:08	99
3	*i*-Propyl	Phenyl	**4c**	79(n.d.)	99:01	99
4	6-(2-methylhept-2-ene)	Phenyl	**4d**	(64)	86:14	98
5	Ethyl	4-FC_6H_4	**4e**	91(86)	92:08	98
6	Ethyl	4-ClC_6H_4	**4f**	95(91)	92:08	99
7	Ethyl	4-BrC_6H_4	**4g**	96(94)	92:08	98
8	Ethyl	4-$NO_2C_6H_4$	**4h**	89(80)	89:11	97
9	Ethyl	4-$CF_3C_6H_4$	**4i**	(64)	91:09	98
10	Ethyl	4-$MeOC_6H_4$	**4j**	87(84)	93:07	96
11	Ethyl	4-MeC_6H_4	**4k**	(82)	91:09	98
12	Ethyl	4-*t*-BuC_6H_4	**4l**	(67)	79:21	97
13	Ethyl	2-$NO_2C_6H_4$	**4m**	(78)	75:25	97
14	Ethyl	2-$MeOC_6H_4$	**4n**	(71)	87:13	99
15	Ethyl	2-Furyl	**4o**	(83)	82:18	99
16	Ethyl	*n*-Pentyl	**4p**	(73)	99:01	96
17	Ethyl	*i*-Butyl	**4q**	(66)	99:01	99

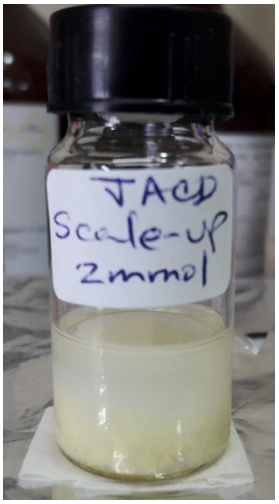
[a] All reactions were conducted using 2 equivalents of the aldehyde and 0.2 mmol of *β*-nitrostyrene in 0.4 mL of water; [b] Yield determined by ^{1}H-NMR analysis with 1,2,3-trimethoxybenzene as internal patron and (isolated product); [c] Determined by ^{1}H NMR of crude of the reaction mixture; [d] Determined by chiral-stationary phase HPLC or UPC^2 analysis.

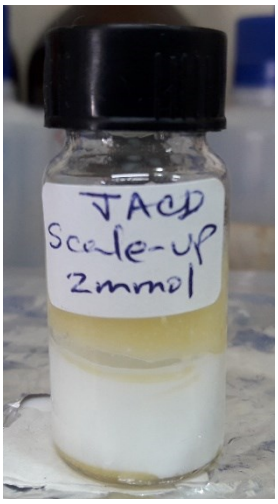
10. Scale-up

A vial was charged with the prolyl *pseudo*-lipopeptide hybrid catalyst **3e** (2.5 mol%, 24 mg), the nitrostyrene[7] (2 mmol, 298 mg, 1.0 equiv,) and 4 mL of water. The mixture was homogenized in an ultrasound bath, the butanal (4 mmol, 361 μL, 2.0 equiv) was added and this mixture was stirred for 72 h. After this period, the

resulting reaction mixture was extracted with EtOAc, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel using (hexanes/EtOAc 9:1) to afford **4a** in 90% (400.4 mg) as a colorless oil. The diastereoisomeric ratio was determined by ^{1}H NMR analysis of crude of the reaction mixture. Enantiomeric excess (*e.e.*) was determined by chiral UPC[2] analysis through comparison with the authentic racemic material.

a) 

b) 

c) 

a) Catalyst **3e** in water; b) After the addition of nitrostyrene and butanal; c) After 72h of reaction.

11. Catalyst recycle

A vial was charged with the prolyl pseudo-lipopeptide hybrid catalyst **3e** (10 mol%), the nitrostyrene[7] (0.2 mmol, 1.0 equiv), and 0.4 mL of water. The mixture was homogenized in an ultrasound bath, the aldehyde (0.40 mmol, 2.0 equiv) was added and this mixture was stirred for 24 h. After this period, the resulting reaction mixture was extracted with EtOAc, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was filtered by a small amount of silica flash using ethyl acetate to afford **4a** in as follows in Table 2, entry 5. After that, the catalyst remains in the silica, and it is recovered by passing 50 ml of methanol through the silica. Then, the solvent was removed by reduced pressure on rotovapory and transferred to the 5 ml vial, and dried under a high vacuum for 2 h. After this period, the nitrostyrene[7] (0.2 mmol, 1.0 equiv) and 0.4 mL of water were added into the vial containing the catalyst. The mixture was homogenized in an ultrasound bath, the aldehyde (0.40 mmol, 2.0 equiv) was added and this mixture was stirred for 24 h. The procedure was carried out over four times and the results

are depicted in Figure 2. The yield was determined by ^{1}H NMR analysis of the crude product with 1.2.3-trimethoxybenzene (0.2 mmol, 1.0 equiv.) as an internal standard. The diastereoisomeric ratio was determined by 1H NMR analysis of crude of the reaction mixture. Enantiomeric excess (*e.e.*) was determined by chiral UPC^2 analysis through comparison with the authentic racemic material.

Recycle [a]	**Yield (%)** [b]	***d.r.* (*syn*/*anti*)** [c]	***e.e.* (%)** [d]
1	90	80:20	99
2	87	91:9	99
3	88	92:8	99
4	88	93:2	99

[a] Reactions using 2 equivalents of butanal and 0.2 mmol of *β*-nitrostyrene in 0.4 mL of solvent; [b] Yield determined by ^{1}H NMR spectroscopy analysis of crude of the reaction mixture; [c] *syn/anti* ratio determined by ^{1}H NMR; [d] Determined by chiral-stationary phase HPLC or UPC2 analysis.

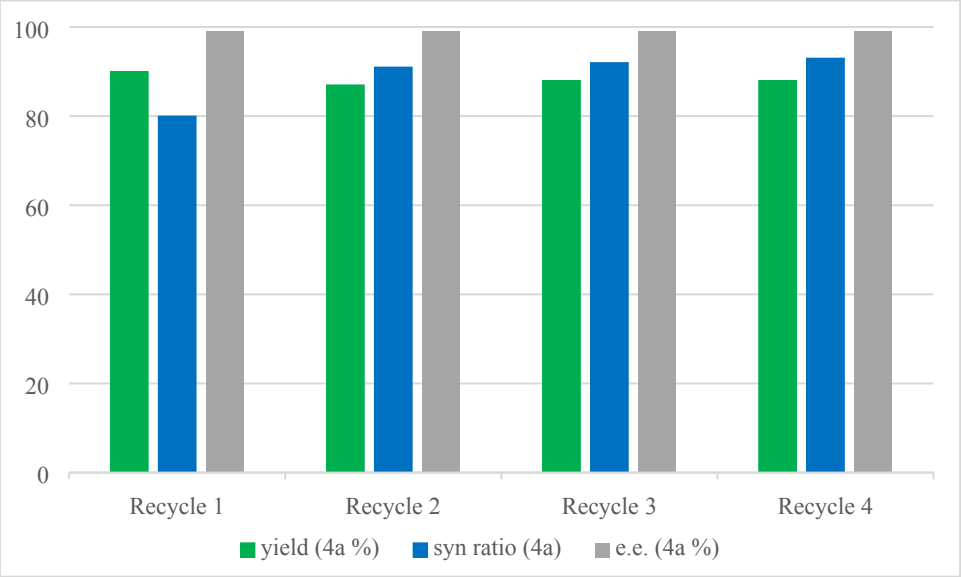
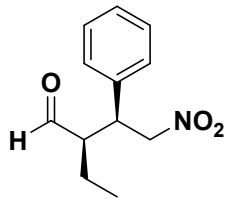


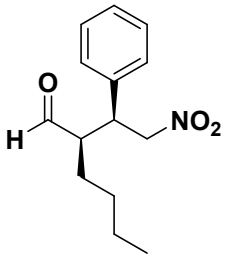
FIGURE 2. Catalyst recycled over four-times.

12. Characterization data of compounds 4a-q

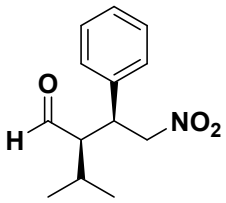


(2*R*,3*S*)-2-ethyl-4-nitro-3-phenylbutanal (**4a**)[8]: Prepared by reaction of butanal with t*rans*-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4a** in 96% (42 mg) as a colorless oil. The enantiomeric excess was determined by chiral-stationary phase UPC^2. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5% in 9 min; 100-0 % in 1 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 4.13 min, (syn, minor) = 3.93 min. $\boldsymbol{R_f}$ = 0.4 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz,**

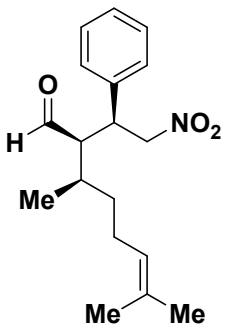
$CDCl_3$) δ 9.65 (s, 1H), 7.30 – 7.20 (m, 3H), 7.11 (d, *J* = 7.6 Hz, 2H), 4.77 – 4.52 (m, 2H), 3.72 (td, *J* = 10.1, 5.3 Hz, 1H), 2.61 (dddd, *J* = 10.1, 7.5, 4.7, 2.2 Hz, 1H), 1.48 – 1.39 (m, 2H), 0.76 (t, *J* = 7.3 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 203.4, 136.9, 129.3, 128.3, 128.1, 78.7, 55.1, 42.9, 20.5, 10.8.



(*R*)-2-((*S*)-2-nitro-1-phenylethyl)hexanal (**4b**)[9]: Prepared by reaction of hexanal with *trans*-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4b** in 91%. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5% in 9 min; 100-0 % in 1 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 6.95 min, (syn, minor) = 6.64 min. $\boldsymbol{R_f}$ = 0.5 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.70 (d, *J* = 2.8 Hz, 1H), 7.37 – 7.27 (m, 3H), 7.19 – 7.15 (m, 2H), 4.85 – 4.60 (m, 2H), 3.84 – 3.73 (m, 1H), 2.70 (dddd, *J* = 9.8, 8.9, 4.0, 2.8 Hz, 1H), 1.51 – 1.35 (m, 2H), 1.34 – 1.24 (m, 2H), 1.22 – 1.12 (m, 2H), 0.79 (t, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 203.4, 136.9, 129.2, 128.3, 128.1, 78.6, 54.0, 43.2, 28.6, 27.1, 22.6, 13.8.

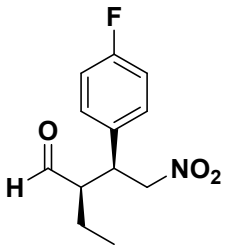


(2*R*,3*S*)-2-isopropyl-4-nitro-3-phenylbutanal (**4c**)[5]: Prepared by reaction of isovaleraldehyde with *trans*-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4c** in 79%. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5% in 9 min; 100-0 % in 1 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 3.97 min, (syn, minor) = 3.68 min. $\boldsymbol{R_f}$ = 0.45 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.93 (d, *J* = 2.4 Hz, 1H), 7.37 – 7.27 (m, 3H), 7.21 – 7.17 (m, 2H), 4.71 – 4.53 (m, 2H), 3.90 (td, *J* = 10.3, 4.4 Hz, 1H), 2.77 (ddd, *J* = 10.8, 4.1, 2.4 Hz, 1H), 1.72 (heptd, *J* = 7.1, 4.1 Hz, 1H), 1.10 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 204.4, 137.1, 129.2, 128.1, 128.0, 79.0, 58.8, 41.9, 27.9, 21.7, 17.0.

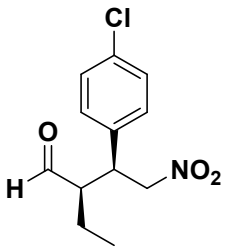


(2*R*,3*R*)-3,7-dimethyl-2-((*S*)-2-nitro-1-phenylethyl)oct-6-enal (**4d**): Prepared by reaction of (*R*)-(+)-Citronellal with *trans*-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4d** in 64% (38.6 mg) as a colorless oil.

The enantiomeric excess was determined by chiral-stationary phase UPC^2. Trefoil CEL1, **Grad:** CO_2/ACN 100-0% to 98-2% in 9 min; 100-0 % in 1 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 4.09 min, (syn, minor) = 3.70 min. $\boldsymbol{R_f}$ = 0.6-0.7 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.84 – 9.79 (m, 1H), 7.30 – 7.20 (m, 3H), 7.10 (d, *J* = 8.2 Hz, 2H), 4.72 (t, *J* = 6.5 Hz, 1H), 4.64 – 4.46 (m, 2H), 3.87 (td, *J* = 10.4, 4.4 Hz, 1H), 2.68 (dt, *J* = 10.7, 3.1 Hz, 1H), 1.90 – 1.79 (m, 1H), 1.64 – 1.52 (m, 2H), 1.51 (s, 3H), 1.48 – 1.43 (m, 2H), 1.42 (s, 3H), 1.00 (d, *J* = 7.1 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 204.14, 137.23, 132.29, 129.21, 128.19, 123.30, 79.22, 59.20, 41.70, 32.13, 31.48, 25.72, 25.70, 18.66, 17.67.

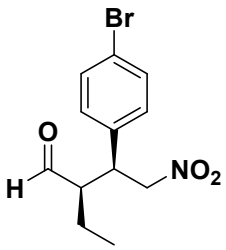


(2*R*,3*S*)-2-ethyl-3-(4-fluorophenyl)-4-nitrobutanal (**4e**)[8]: Prepared by reaction of butanal with *trans*-4-fluoro-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4f** in 86% (41 mg) as a colorless oil. The enantiomeric excess was determined by chiral-stationary phase UPC^2. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5% in 9 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 6.88 min, (syn, minor) = 6.30 min. $\boldsymbol{R_f}$ = 0.3 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.72 (d, *J* = 2.4 Hz, 1H), 7.19 – 7.15 (m, 2H), 7.07 – 7.00 (m, 2H), 4.83 – 4.56 (m, 2H), 3.85 – 3.75 (m, 1H), 2.66 (dddd, *J* = 10.3, 8.1, 4.3, 2.4 Hz, 1H), 1.54 – 1.47 (m, 2H), 0.84 (t, *J* = 7.5 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 202.9, 163.6, 161.1 (d, $^1J_{C\text{-}F}$ = 247.2 Hz), 132.58, 132.55 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 129.7, 129.6 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 116.3, 116.0 (d, $^2J_{C\text{-}F}$ = 21.6 Hz), 78.6, 54.9, 42.0, 20.3, 10.6. **^{19}F NMR (377 MHz, $CDCl_3$)** δ -113.42 – -113.76 (m).

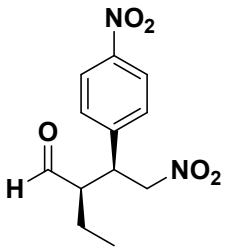


(2*R*,3*S*)-3-(4-chlorophenyl)-2-ethyl-4-nitrobutanal (**4f**)[8]: Prepared by reaction of butanal with *trans*-4-chloro-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4g** in 91% (46 mg) as a colorless oil. The enantiomeric excess was determined by chiral-stationary phase UPC^2. Trefoil AMY1, **Grad:** CO_2/MeOH 100-0% to 90-10 % in 6 min; 90-10 % in 3 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 3.45 min, (syn, minor) = 4.21 min. $\boldsymbol{R_f}$ = 0.25 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.71 (d, *J* = 2.3 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.16 – 7.11 (m, 2H), 4.82 – 4.55 (m, 2H), 3.79 (td, *J* = 9.9, 4.9 Hz, 2H), 2.67 (dddd, *J* = 10.3, 8.2, 4.2, 2.3 Hz, 1H), 1.55 – 1.45 (m,

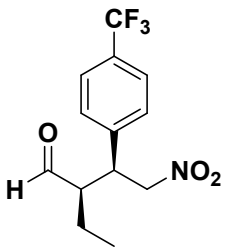
2H), 0.83 (t, *J* = 7.5 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 202.9, 135.5, 129.6, 129.5, 129.4, 78.5, 54.8, 42.1, 20.4, 10.7.



(2*R*,3*S*)-3-(4-bromophenyl)-2-ethyl-4-nitrobutanal (**4g**)[8]: Prepared by reaction of butanal with *trans*-4-bromo-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4h** in 94% (57 mg) as a light yellow oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil AMY1, **Grad:** CO_2/MeOH 100-0% to 90-10 % in 6 min; 90-10 % in 3 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 3.98 min, (syn, minor) = 6.71min. $\boldsymbol{R_f}$ = 0.3 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.71 (d, *J* = 2.3 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.10 – 7.05 (m, 2H), 4.82 – 4.55 (m, 2H), 3.83 – 3.74 (m, 1H), 2.67 (dddd, J = 10.3, 8.2, 4.2, 2.3 Hz, 1H), 1.54 – 1.47 (m, 2H), 0.84 (t, *J* = 7.5 Hz, 2H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 202.8, 136.0, 132.4, 129.8, 122.3, 78.4, 54.8, 42.2, 20.5, 10.7.

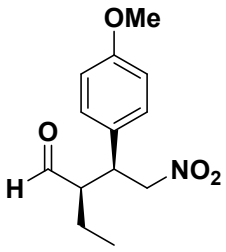


(2*R*,3*S*)-2-ethyl-4-nitro-3-(4-nitrophenyl)butanal (**4h**): Prepared by reaction of butanal with *trans*-4-nitro-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 8:2) afforded **4i** in 80% (43 mg) as a light yellow oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil AMY1, **Grad:** CO_2/IPA 100-0% to 90-10 % in 18 min; 90-10 % in 2 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 8.84 min, (syn, minor) = 10.04 min. $\boldsymbol{R_f}$ = 0.4 (hexanes/EtOAc 8:2). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.74 (d, *J* = 1.9 Hz, 1H), 8.26 – 8.18 (m, 2H), 7.45 – 7.39 (m, 2H), 4.86 – 4.65 (m, 2H), 4.02 – 3.92 (m, 1H), 2.82 – 2.70 (m, 1H), 1.61 – 1.44 (m, 2H), 0.87 (t, *J* = 7.5 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 202.1, 147.8, 144.7, 129.3, 124.4, 77.9, 54.4, 42.3, 20.5, 10.5.

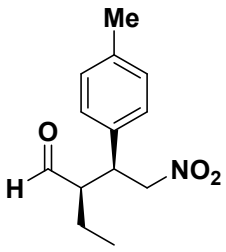


(2*R*,3*S*)-2-ethyl-4-nitro-3-(4-(trifluoromethyl)phenyl)butanal (**4i**): Prepared by reaction of butanal with *trans*-4-trifluoromethyl-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4j** in 64% (37 mg) as a light yellow oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, **Grad:** CO_2/IPA 100- 0% to 95-05 % in 14 min; 100-0 % in 1 min

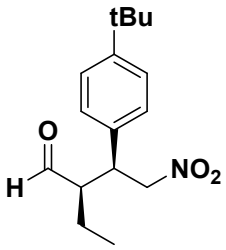
at 1.5 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 10.69 min, (syn, major) = 11.18 min. $\boldsymbol{R_f}$ = 0.3 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ = 9.73 (d, *J* = 2.0 Hz, 1H), 7.62 (d, J = 8.1 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 4.83 – 4.63 (m, 2H), 3.89 (td, *J* = 10.0, 4.8 Hz, 1H), 2.78 – 2.69 (m, 1H), 1.57 – 1.44 (m, 2H), 0.85 (t, *J* = 7.5 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 202.6, 141.3, 131.1, 130.8, 130.4, 130.1 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 128.7, 128.0, 126.30, 126.26, 126.22, 126.18 (q, $^3J_{C\text{-}F}$ = 4.0 Hz), 125.3, 122.6, 119.9 (q, $^1J_{C\text{-}F}$ = 272.2 Hz)., 78.2, 54.7, 42.4, 20.5, 10.6. **^{19}F NMR (377 MHz, $CDCl_3$)** δ -62.52 – -62.90 (m).



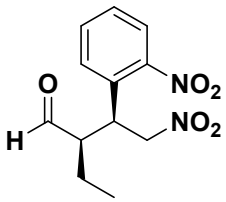
(2*R*,3*S*)-2-ethyl-3-(4-methoxyphenyl)-4-nitrobutanal (**4j**)[8]: Prepared by reaction of butanal with *trans*-4-methoxy-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 8:2) afforded **4k** in 84% (42 mg) as a light yellow oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 98-2 % in 19 min; 100-0 % in 1 min at 2.5 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 15.43 min, (syn, minor) = 14.88 min. $\boldsymbol{R_f}$ = 0.2 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.71 (d, *J* = 2.7 Hz, 1H), 7.11 – 7.07 (m, 2H), 6.89 – 6.83 (m, 2H), 4.81 – 4.54 (m, 2H), 3.79 (s, 3H), 3.73 (dt, *J* = 10.0, 5.1 Hz, 1H), 2.67 – 2.59 (m, 1H), 1.56 – 1.46 (m, 2H), 0.83 (t, *J* = 7.5 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 203.5, 159.4, 129.4, 129.2, 114.6, 78.9, 55.4, 42.1, 20.5, 10.8.



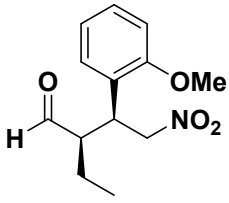
(2*R*,3*S*)-2-ethyl-4-nitro-3-(p-tolyl)butanal (**4k**): Prepared by reaction of butanal with *trans*-4-methyl-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4l** in 82% (39 mg) as a colorless oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, **Grad:** CO_2/ACN 100- 0% to 90-10 % in 5 min; 90-10 % in 4 min; 100-0 % in 1 min at 1 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 5.85 min, (syn, major) = 6.17 min. $\boldsymbol{R_f}$ = 0.45-0.50 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.70 (d, *J* = 2.3 Hz, 1H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 4.81 – 4.56 (m, 2H), 3.75 (td, *J* = 9.8, 5.1 Hz, 1H), 2.65 (dddd, *J* = 10.2, 7.7, 4.5, 2.4 Hz, 1H), 2.32 (s, 3H), 1.57 – 1.44 (m, 2H), 0.82 (t, *J* = 7.5 Hz, 4H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 203.5, 138.0, 133.8, 129.9, 128.0, 78.8, 55.2, 42.5, 21.2, 20.5, 10.8.



(2*R*,3*S*)-3-(4-(tert-butyl)phenyl)-2-ethyl-4-nitrobutanal (**4l**): Prepared by reaction of butanal with *trans*-4-*tert*-butyl-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4m** in 67% (37 mg) as a light yellow oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 98-02 % in 19 min; 100-0 % in 1 min at 3 ml/min at 40°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 9.30 min, (syn, major) = 9.65 min. $\boldsymbol{R_f}$ = 0.5 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.71 (d, *J* = 2.6 Hz, 1H), 7.35 – 7.29 (m, 2H), 7.14 – 7.05 (m, 2H), 4.84 – 4.58 (m, 2H), 3.77 (td, J = 9.6, 5.3 Hz, 1H), 2.65 (dtd, *J* = 9.3, 6.4, 2.7 Hz, 1H), 1.51 (p, *J* = 7.2 Hz, 2H), 1.29 (s, 9H), 0.84 (t, *J* = 7.5 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 203.6, 151.1, 133.7, 127.7, 126.1, 78.6, 55.4, 42.4, 34.6, 31.4, 20.5, 11.0.

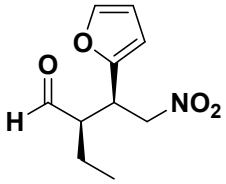


(2*R*,3*S*)-2-ethyl-4-nitro-3-(2-nitrophenyl)butanal (**4m**): Prepared by reaction of butanal with *trans*-2-nitro-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 7:3) afforded **4n** in 78% (42 mg) as a light yellow oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, **Grad:** CO_2/ACN 100-0% to 90-10 % in 5 min; 90-10 % in 4 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 5.77 min, (syn, major) = 7.14 min. $\boldsymbol{R_f}$ = 0.6 (hexanes/EtOAc 7:3). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ = 9.73 (d, *J* = 2.2 Hz, 1H), 7.90 – 7.86 (m, 1H), 7.64 – 7.58 (m, 1H), 7.50 – 7.36 (m, 2H), 4.92 – 4.70 (m, 2H), 4.42 (td, *J* = 9.2, 4.2 Hz, 1H), 3.00 – 2.84 (m, 1H), 1.74 – 1.44 (m, 2H), 0.88 (t, *J* = 7.5 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ = 202.6, 150.7, 133.4, 132.0, 129.1, 125.4, 77.4, 54.4, 37.2, 21.1, 11.1.

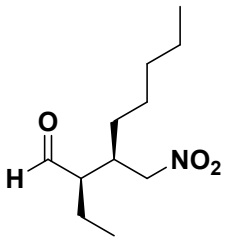


(2*R*,3*S*)-2-ethyl-3-(2-methoxyphenyl)-4-nitrobutanal (**4n**)[8]: Prepared by reaction of butanal with *trans*-2-methoxy-*β*-nitrostyrene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4o** in 71% (36 mg) as a light yellow oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, **Grad:** CO_2/EtOH 100- 0% to 98-02 % in 19 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 11.37 min, (syn, major) = 12.03 min. $\boldsymbol{R_f}$ = 0.4

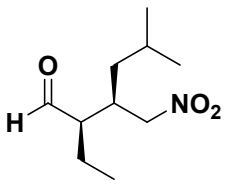
(hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.63 (d, *J* = 2.6 Hz, 1H), 7.24 – 7.15 (m, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.86 – 6.80 (m, 2H), 4.80 – 4.55 (m, 2H), 3.95 (td, *J* = 9.7, 4.9 Hz, 1H), 2.95 – 2.82 (m, 1H), 1.45 – 1.35 (m, 2H), 0.73 (t, *J* = 7.5 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 203.9, 157.6, 130.6, 129.4, 121.1, 111.3, 55.5, 53.6, 39.6, 20.6, 10.9.



(2*R*,3*R*)-2-ethyl-3-(furan-2-yl)-4-nitrobutanal (**4o**)[5]: Prepared by reaction of butanal with *trans-β*-nitrovinylfuran according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4p** in 83% (35 mg) as a light yellow oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, CO_2/MeOH 98.5-1.5 in 8 min at 1 ml/min at 35°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 5.53 min, (syn, major) = 5.78 min. $\boldsymbol{R_f}$ = 0.5 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ = 9.71 (s, 1H), 7.37 (d, *J* = 0.9 Hz, 1H), 6.34 – 6.28 (m, 1H), 6.20 (d, *J* = 3.3 Hz, 1H), 4.76 – 4.63 (m, 2H), 4.05 – 3.95 (m, 1H), 2.76 (dtd, *J* = 8.6, 6.9, 1.5 Hz, 1H), 1.62 – 1.52 (m, 2H), 0.90 (t, *J* = 7.5 Hz, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 202.5, 150.2, 142.8, 110.6, 108.9, 76.3, 53.5, 36.7, 20.1, 11.0.



(2*R*,3*R*)-2-ethyl-3-(nitromethyl)octanal (**4p**): Prepared by reaction of butanal with (*E*)-1-nitrohept-1-ene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4q** in 73% (31 mg) as a colorless oil. The enantiomeric excess was determined by chiral-stationary phase UPC[2]. Trefoil CEL2, CO_2/IPA 99-1 in 8 min at 1 ml/min at 35°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 5.71 min, (syn, major) = 6.71 min. $\boldsymbol{R_f}$ = 0.8 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.69 (s, 1H), 4.49 – 4.31 (m, 2H), 2.68 – 2.53 (m, 1H), 2.43 – 2.31 (m, 1H), 1.84 – 1.70 (m, 1H), 1.59 – 1.43 (m, 1H), 1.42 – 1.20 (m, 8H), 1.03 – 0.94 (m, 3H), 0.90 – 0.84 (m, 3H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 203.3, 54.0, 36.9, 31.7, 29.2, 26.5, 22.5, 18.7, 14.1, 12.2.



(2*R*,3*R*)-2-ethyl-5-methyl-3-(nitromethyl)hexanal (**4q**)[8]: Prepared by reaction of butanal with (E)-4-methyl-1-nitropent-1-ene according to the procedure G. Flash chromatography (hexanes/EtOAc 9:1) afforded **4r** in 66% (27 mg) as a colorless oil. The enantiomeric

excess was determined by chiral-stationary phase UPC^2. Trefoil CEL2, CO_2/MeOH 99-1 in 8 min at 1 ml/min at 35°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 5.34 min. $\boldsymbol{R_f}$ = 0.75 (hexanes/EtOAc 9:1). **NMR ^{1}H (400 MHz, $CDCl_3$)** δ 9.70 (s, 1H), 4.50 – 4.29 (m, 2H), 2.76 – 2.61 (m, 1H), 2.41 (dt, *J* = 9.0, 4.7 Hz, 1H), 1.85 – 1.72 (m, 1H), 1.64 – 1.44 (m, 2H), 1.30 – 1.17 (m, 2H), 1.04 – 0.95 (m, 3H), 0.89 (dt, *J* = 5.8 Hz, 6H). **NMR ^{13}C (100 MHz, $CDCl_3$)** δ 203.2, 77.2, 54.2, 38.4, 34.8, 25.3, 22.8, 22.2, 18.6, 12.3.

13. NMR Spectra: Isocyanides

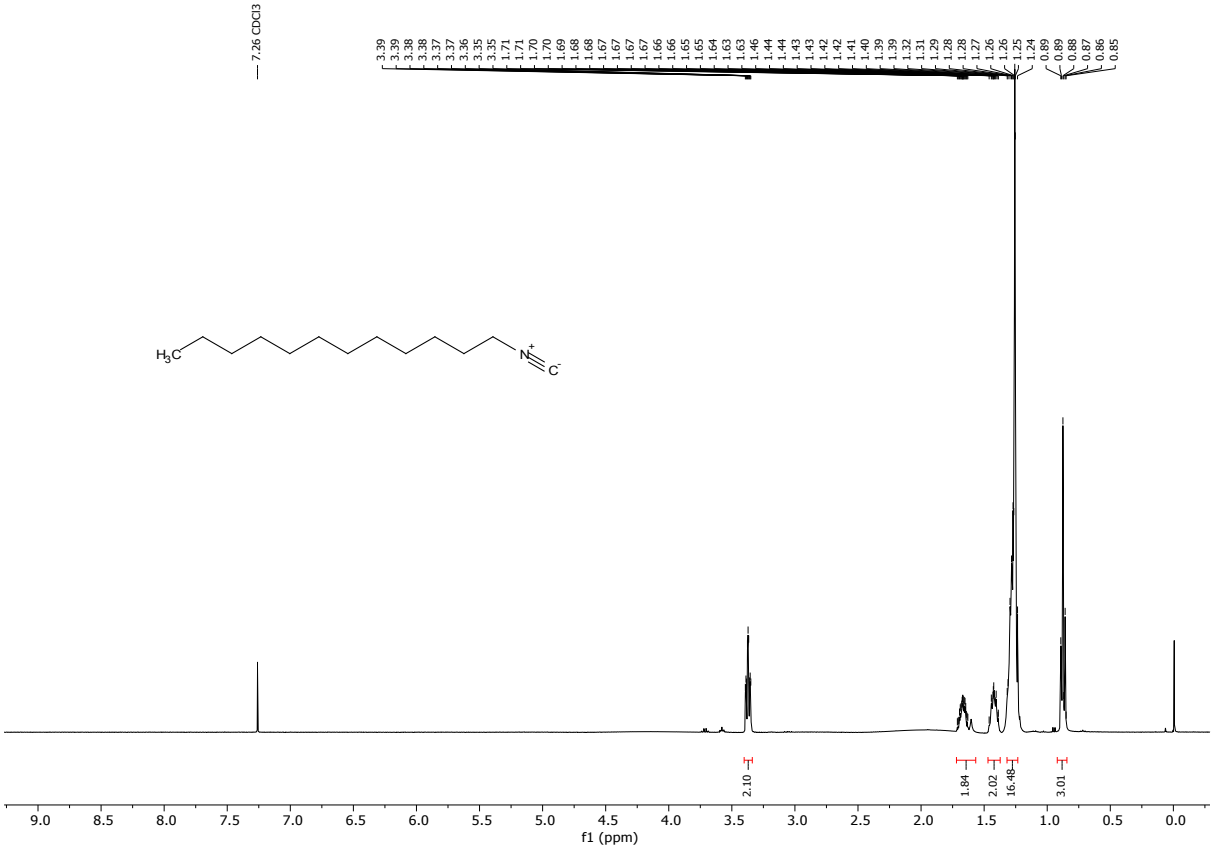


FIGURE 3. ^{1}H NMR of compound **2a** (400 MHz, $CDCl_3$).

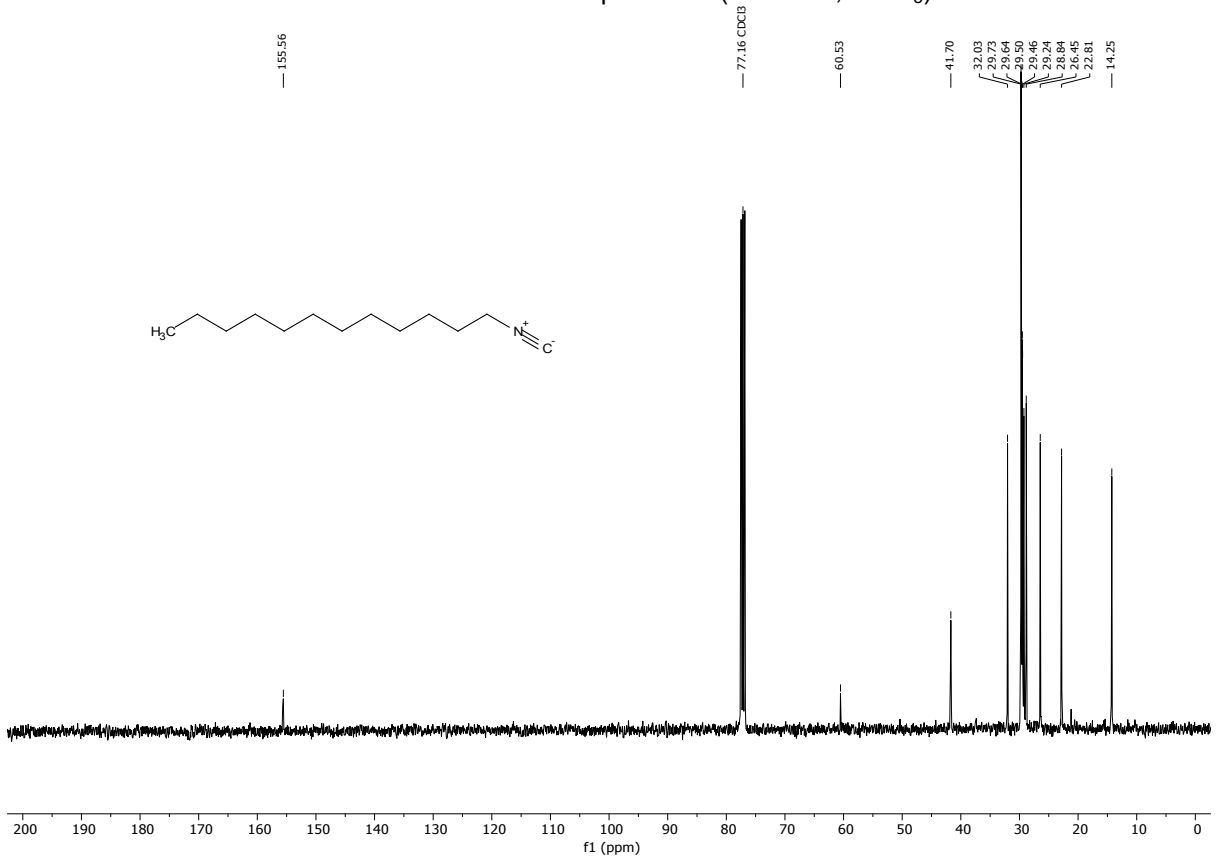


FIGURE 4. ^{13}C NMR of compound **2a** (100 MHz, $CDCl_3$).

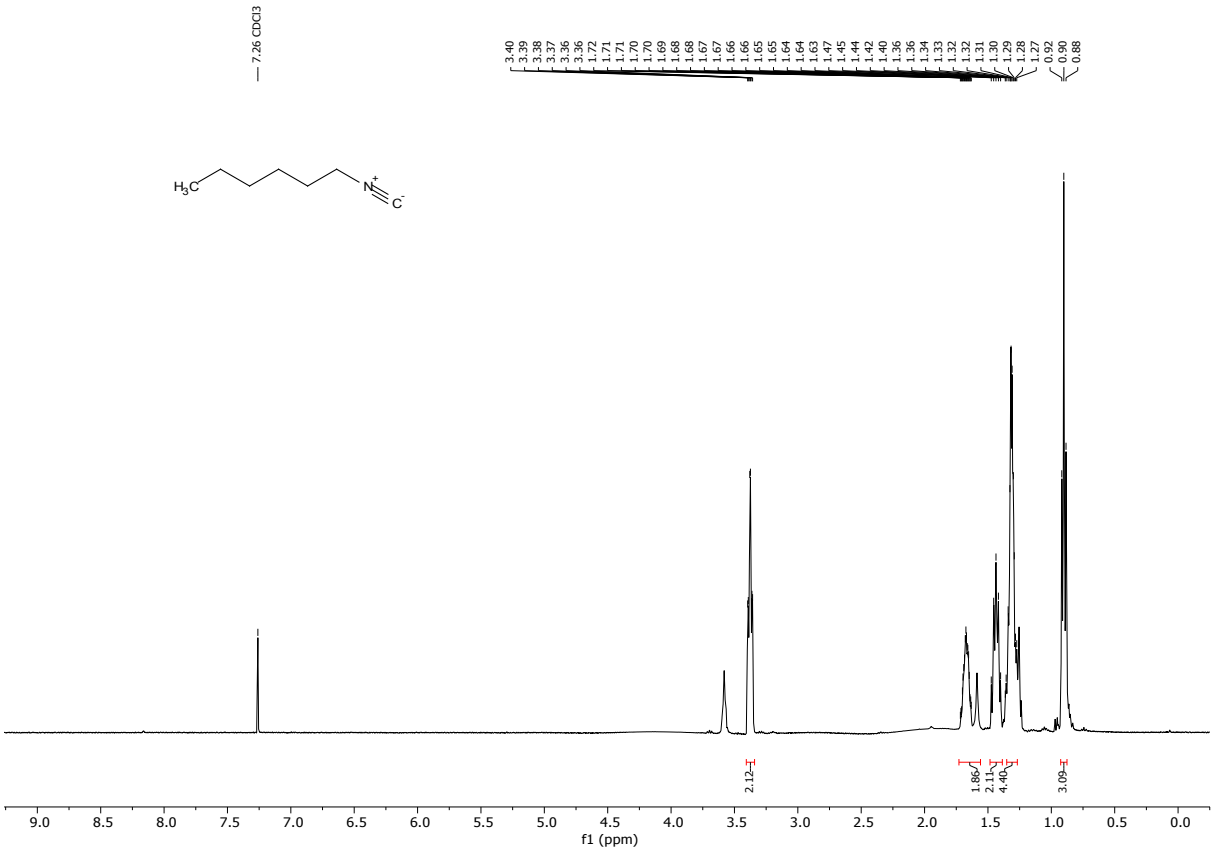


FIGURE 5. ^{1}H NMR of compound **2b** (400 MHz, $CDCl_3$).

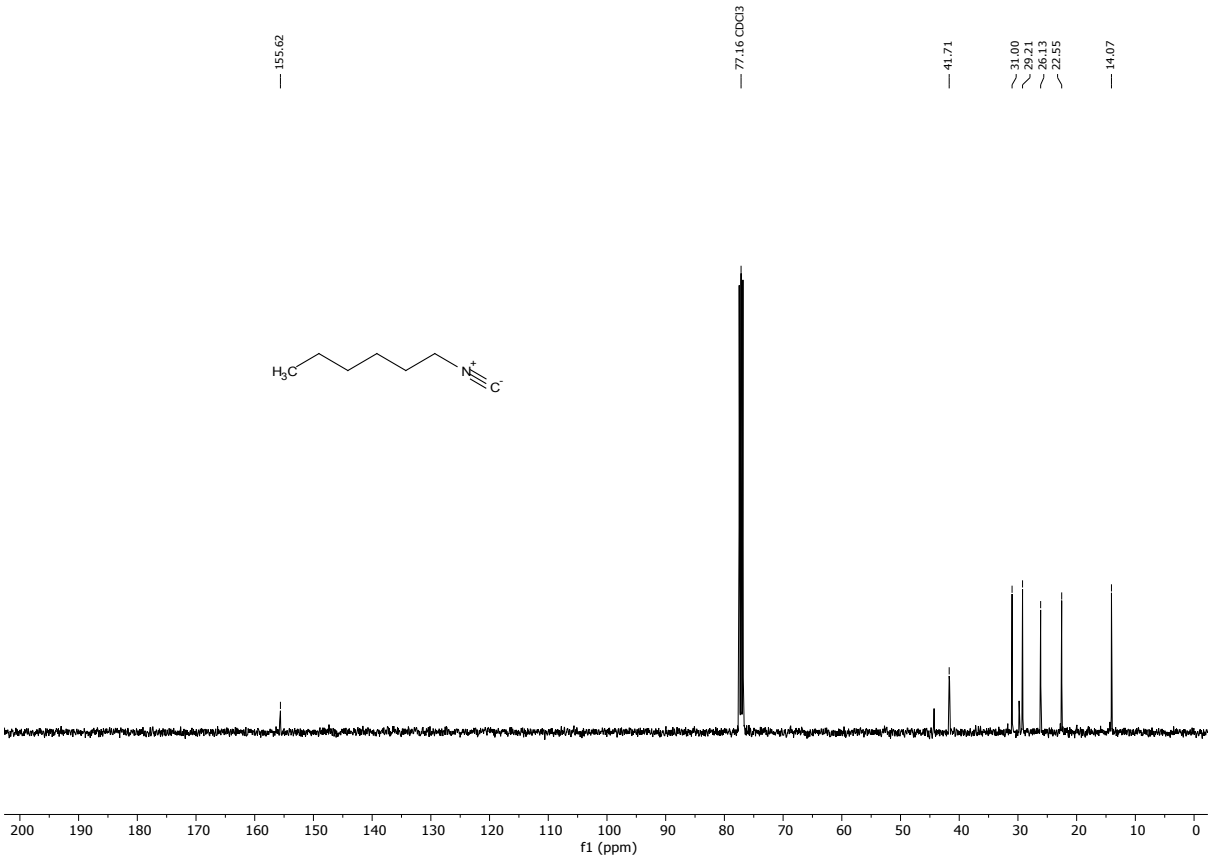


FIGURE 6. ^{13}C NMR of compound **2b** (100 MHz, $CDCl_3$).

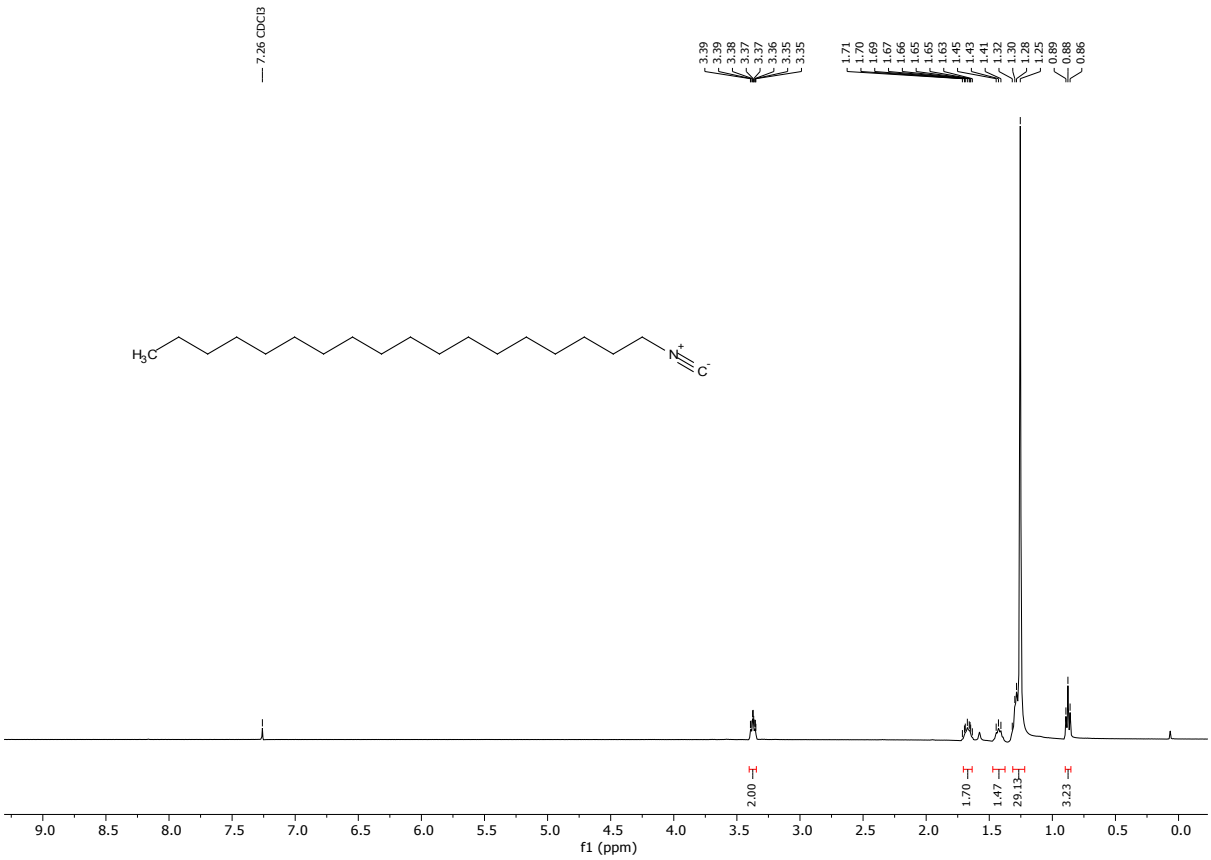


FIGURE 7. ^{1}H NMR of compound **2c** (400 MHz, $CDCl_3$).

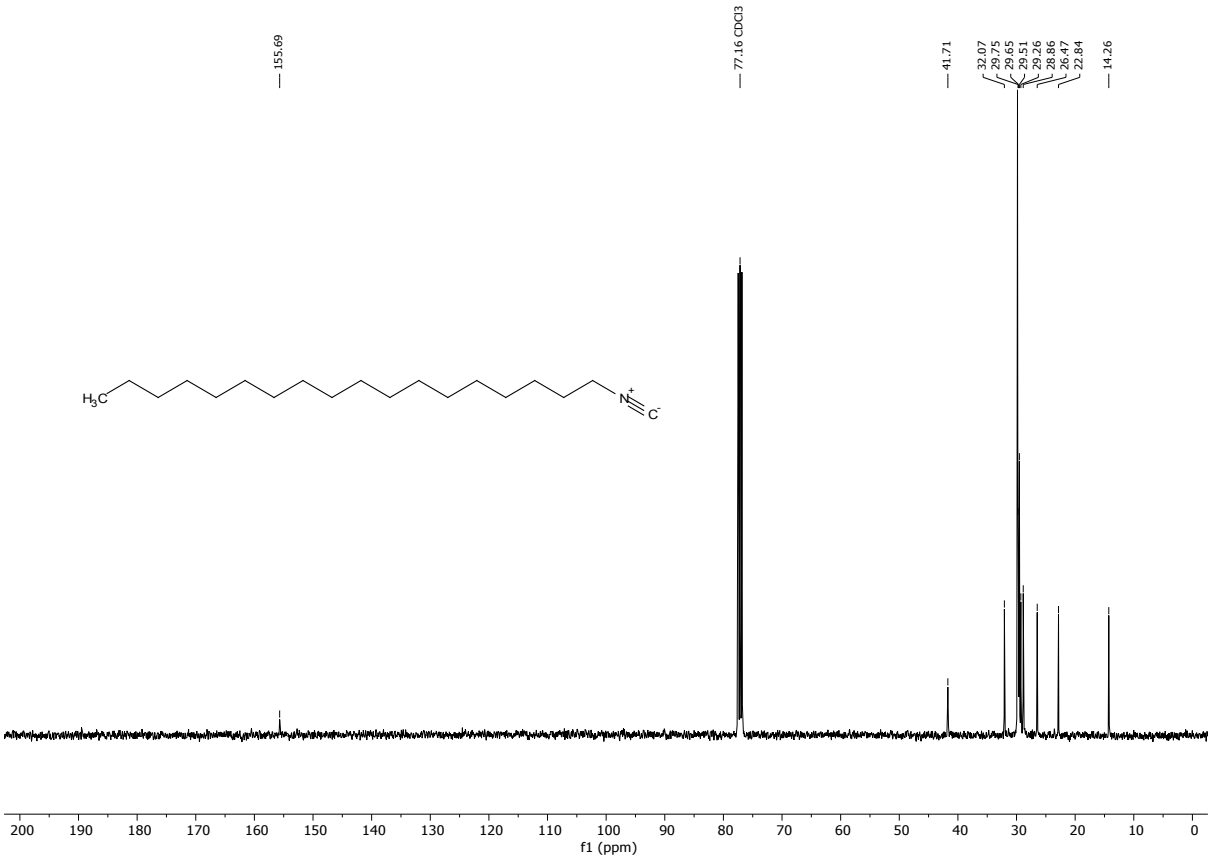


FIGURE 8. ^{13}C NMR of compound **2c** (100 MHz, $CDCl_3$).

14. NMR Spectra: Catalysts

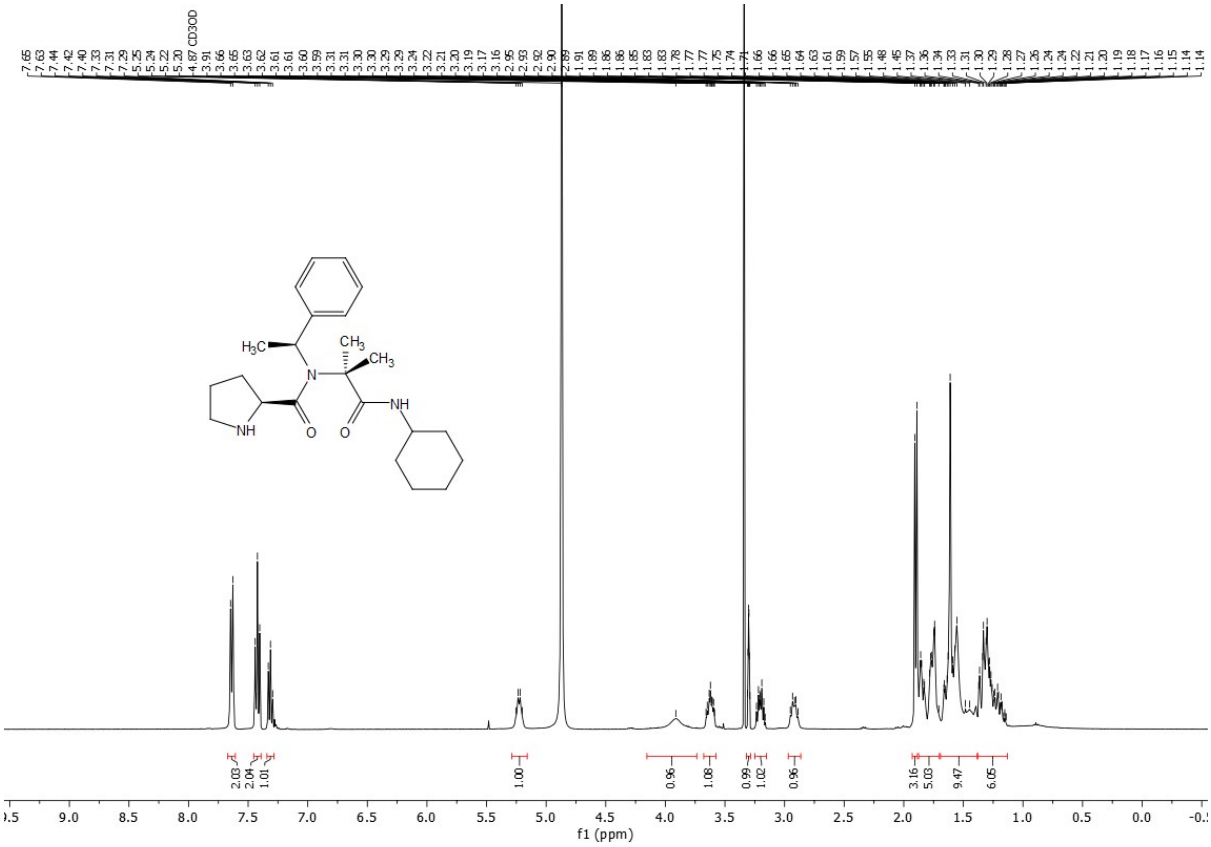


FIGURE 9. ^{1}H NMR of compound **3a** (400 MHz, CD_3OD).

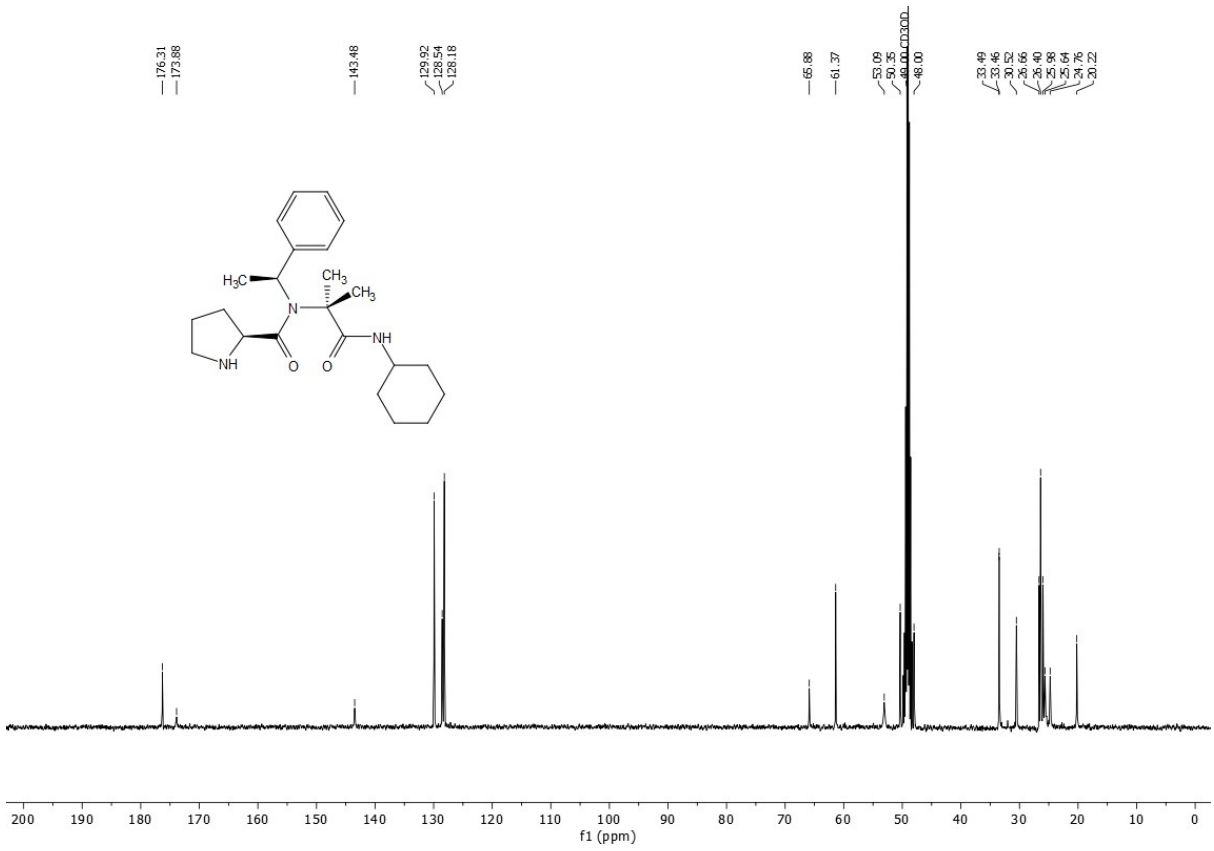


FIGURE 10. ^{13}C NMR of compound **3a** (100 MHz, CD_3OD).

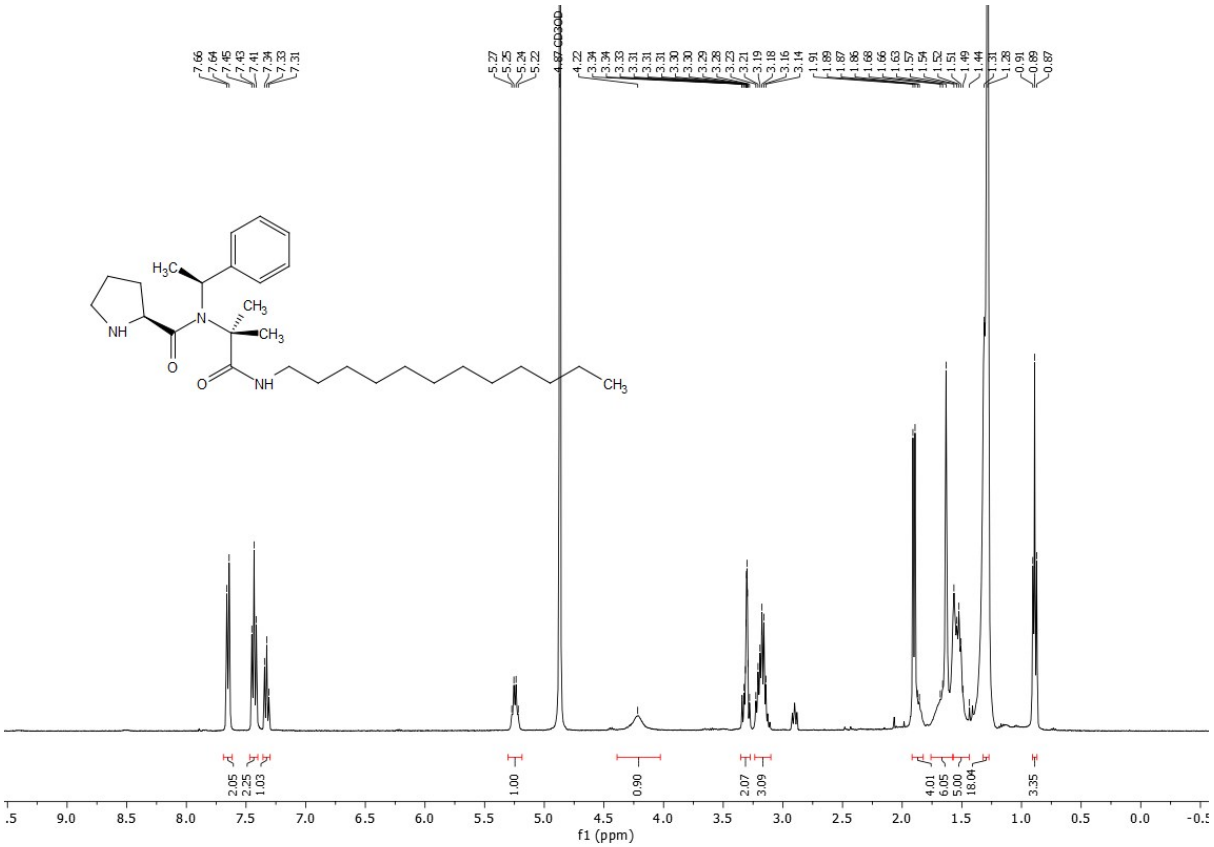


FIGURE 11. ^{1}H NMR of compound **3b** (400 MHz, CD_3OD).

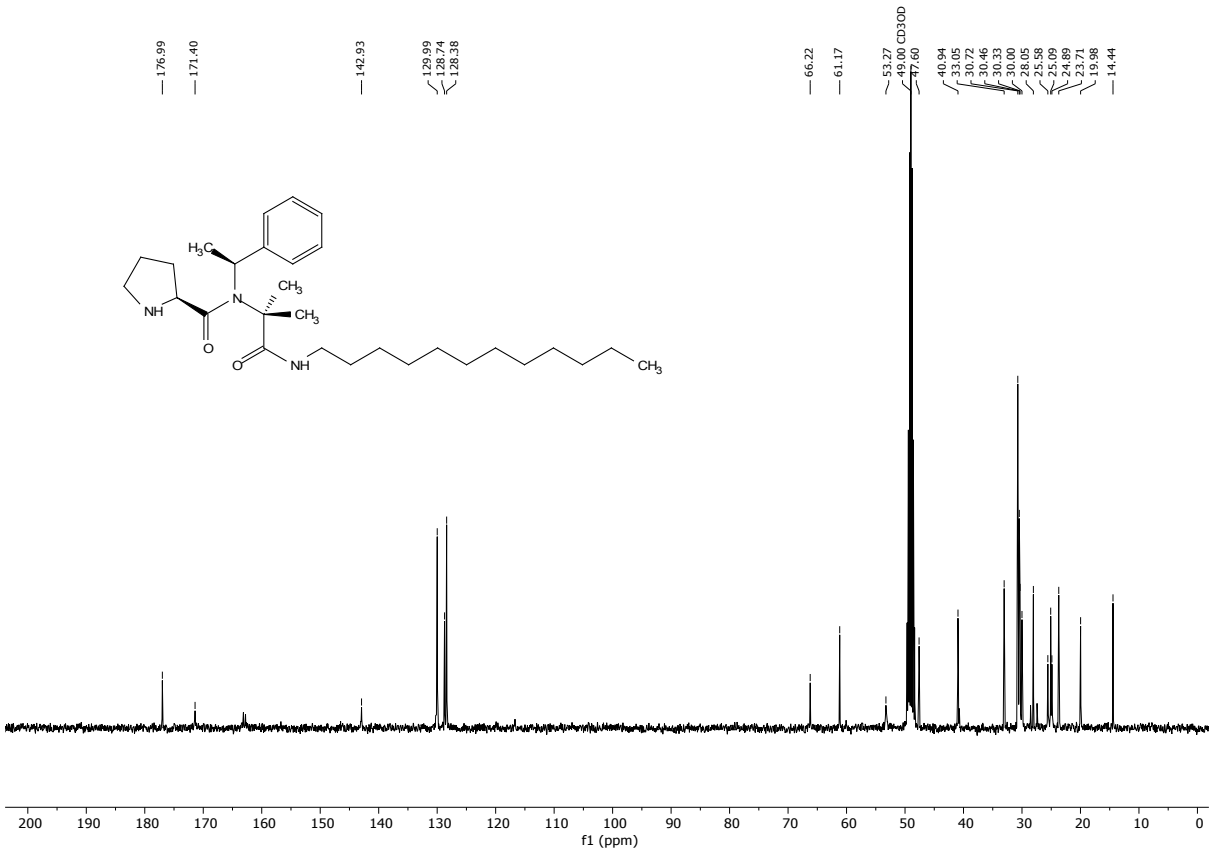


FIGURE 12. ^{13}C NMR of compound **3b** (100 MHz, CD_3OD).

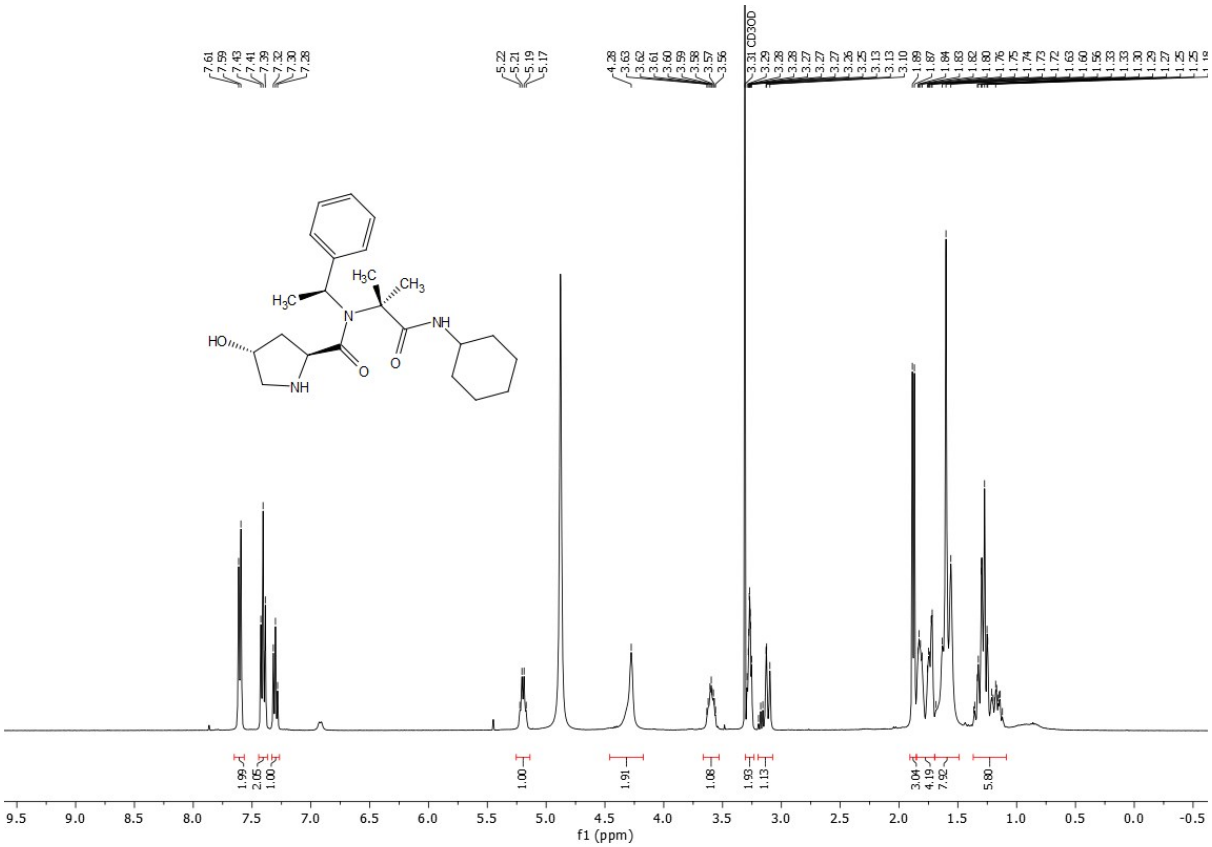


FIGURE 13. ^{1}H NMR of compound **3c** (400 MHz, CD_3OD).

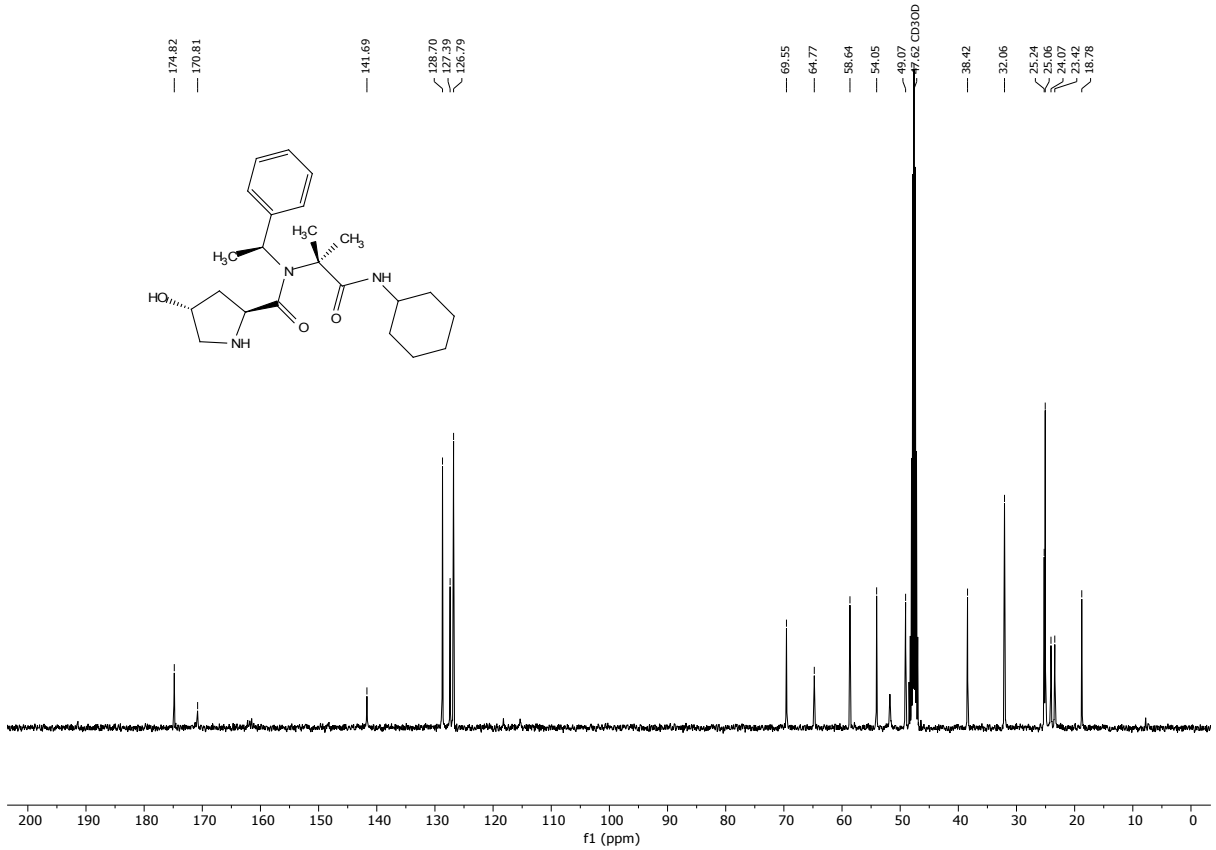


FIGURE 14. ^{13}C NMR of compound **3c** (100 MHz, CD_3OD).

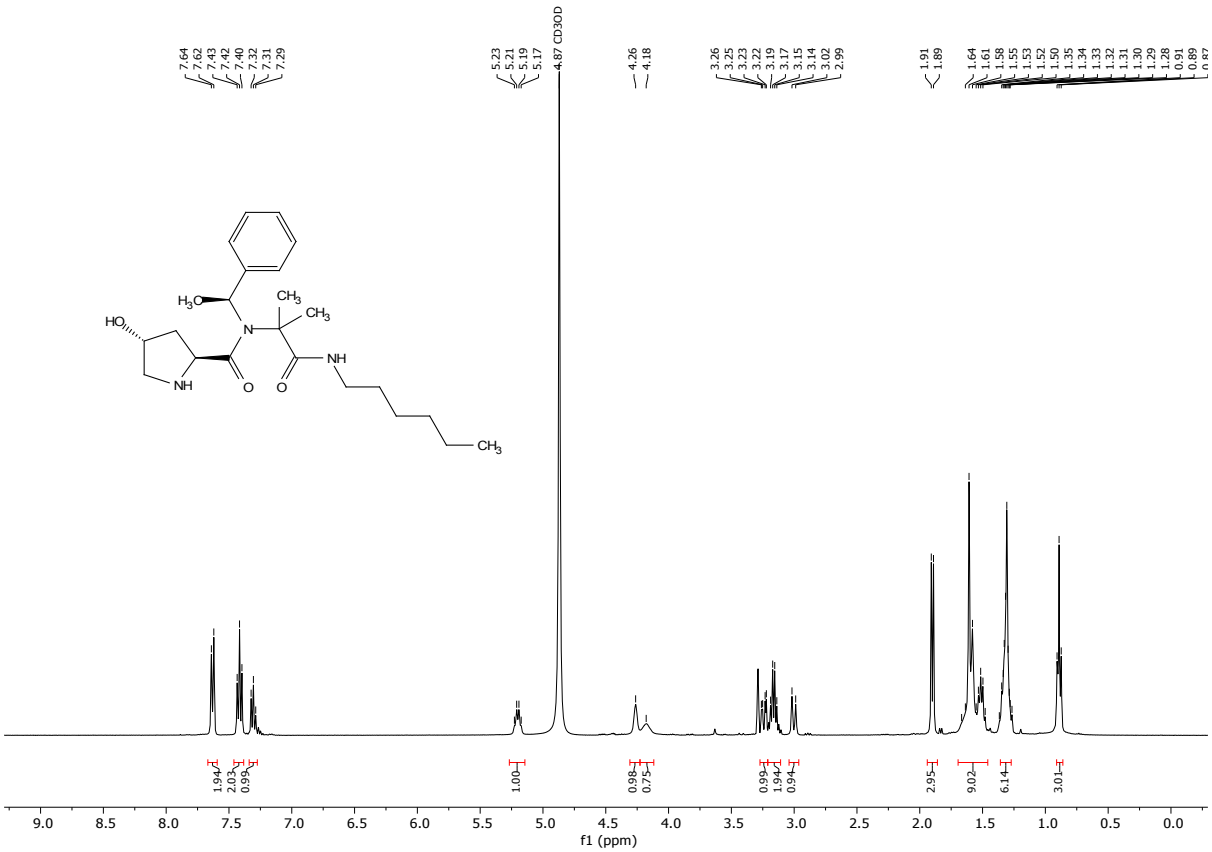


FIGURE 15. ^{1}H NMR of compound **3d** (400 MHz, CD_3OD).

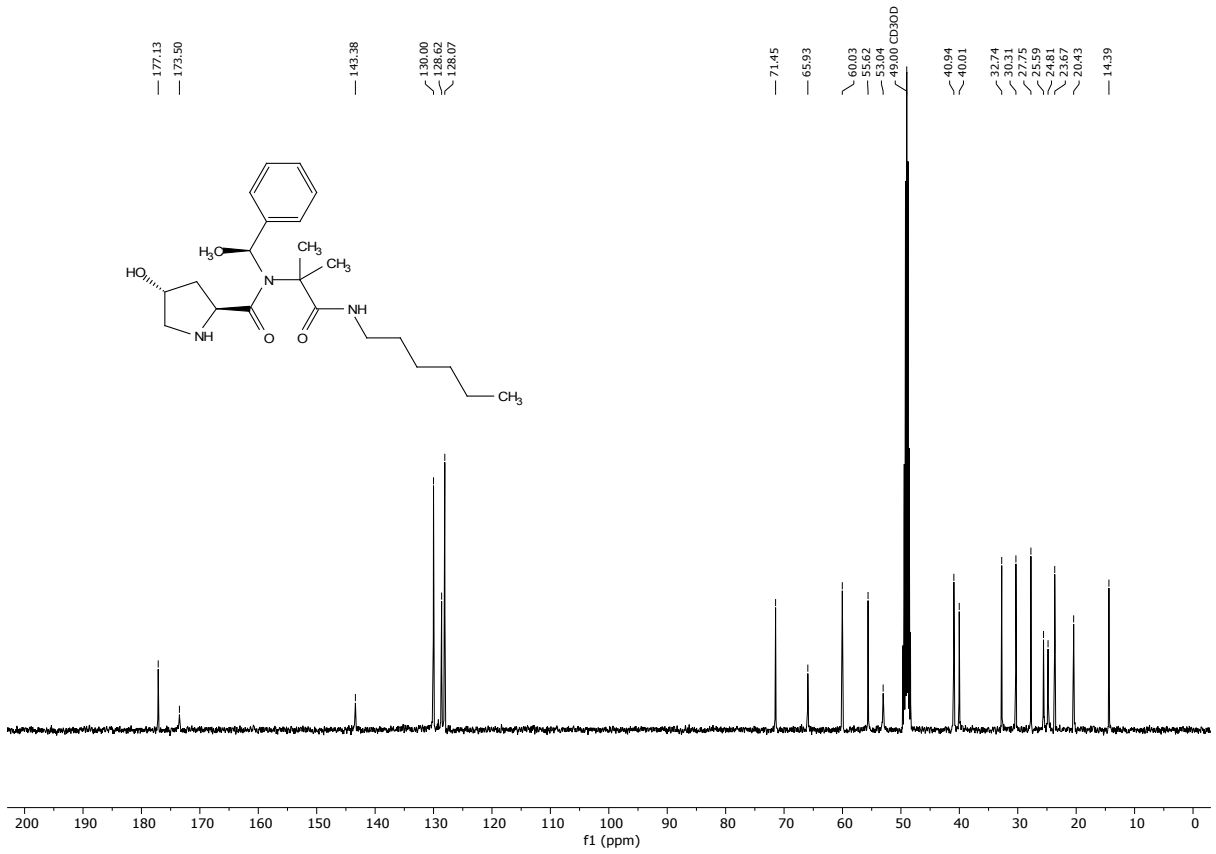


FIGURE 16. ^{13}C NMR of compound **3d** (100 MHz, CD_3OD).

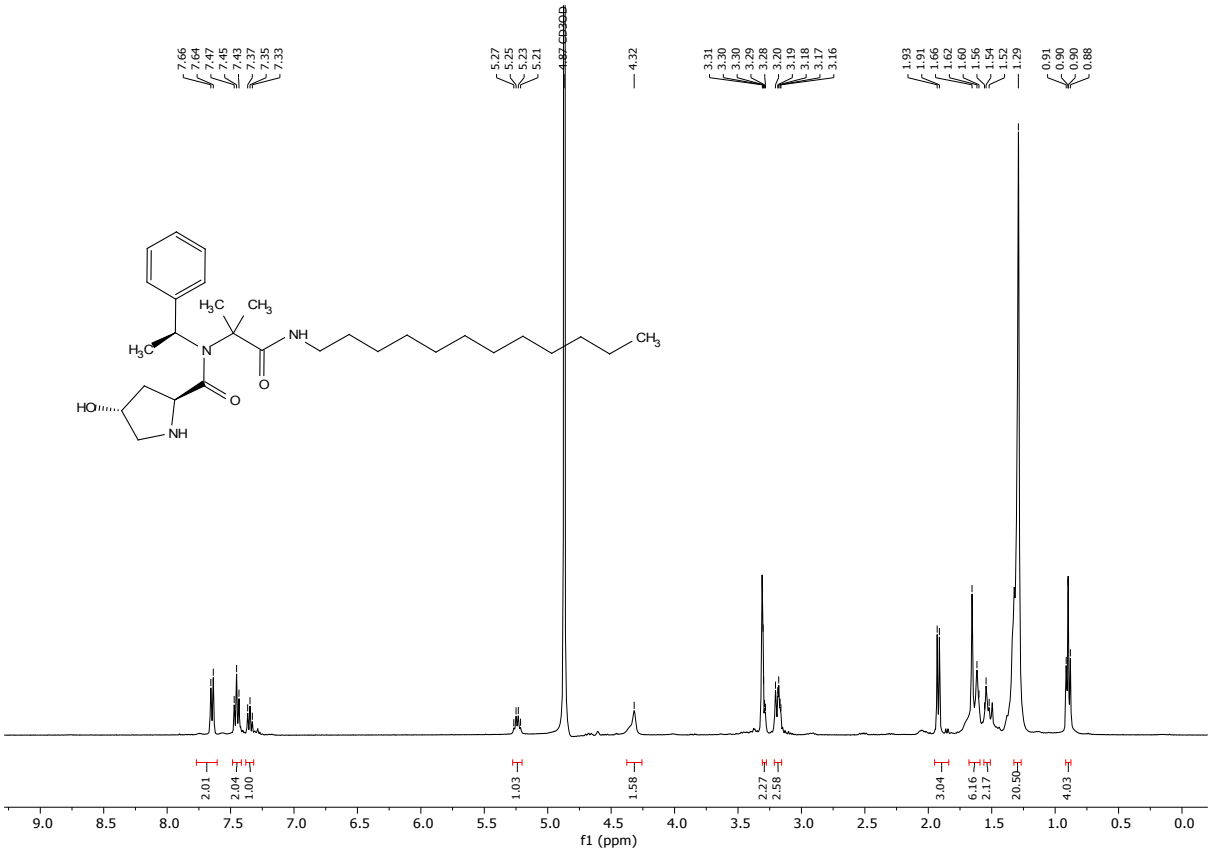


FIGURE 17. ^{1}H NMR of compound **3e** (400 MHz, CD_3OD).

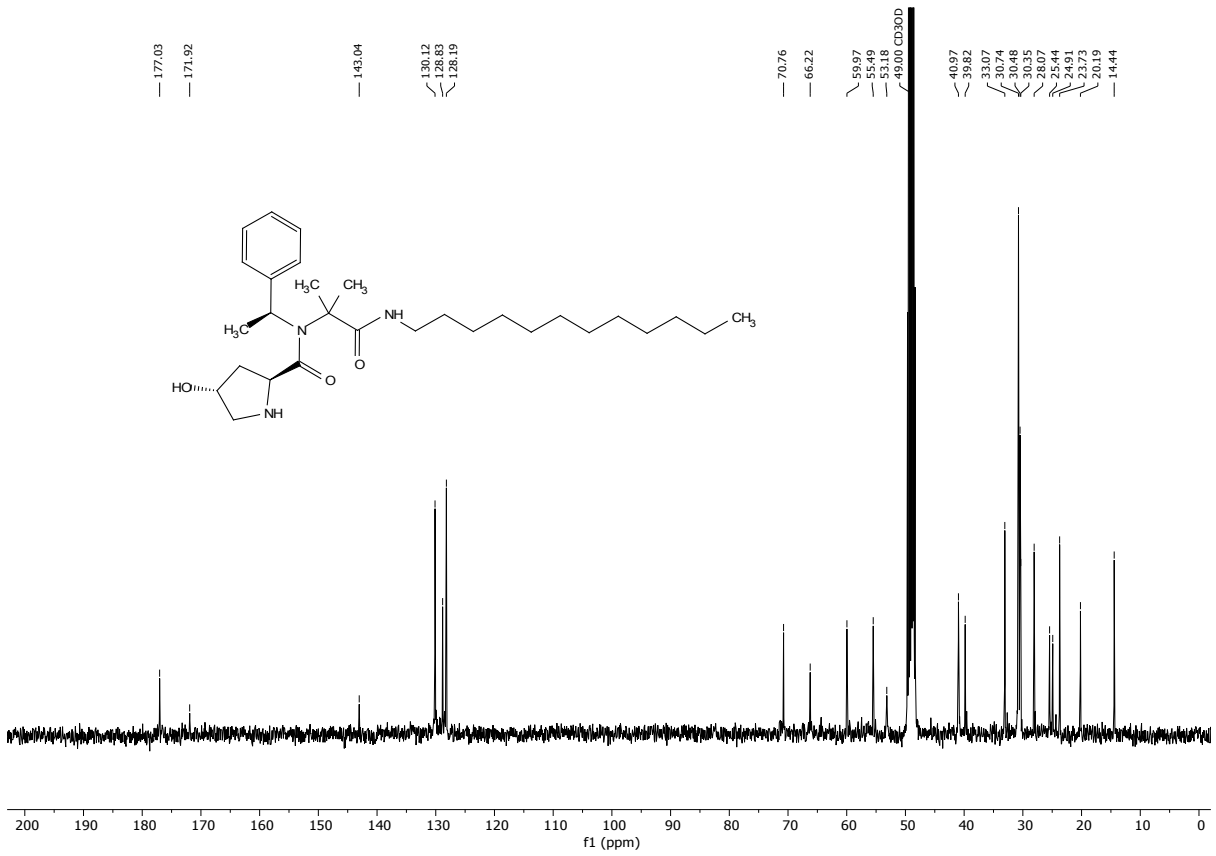


FIGURE 18. ^{13}C NMR of compound **3e** (100 MHz, CD_3OD).

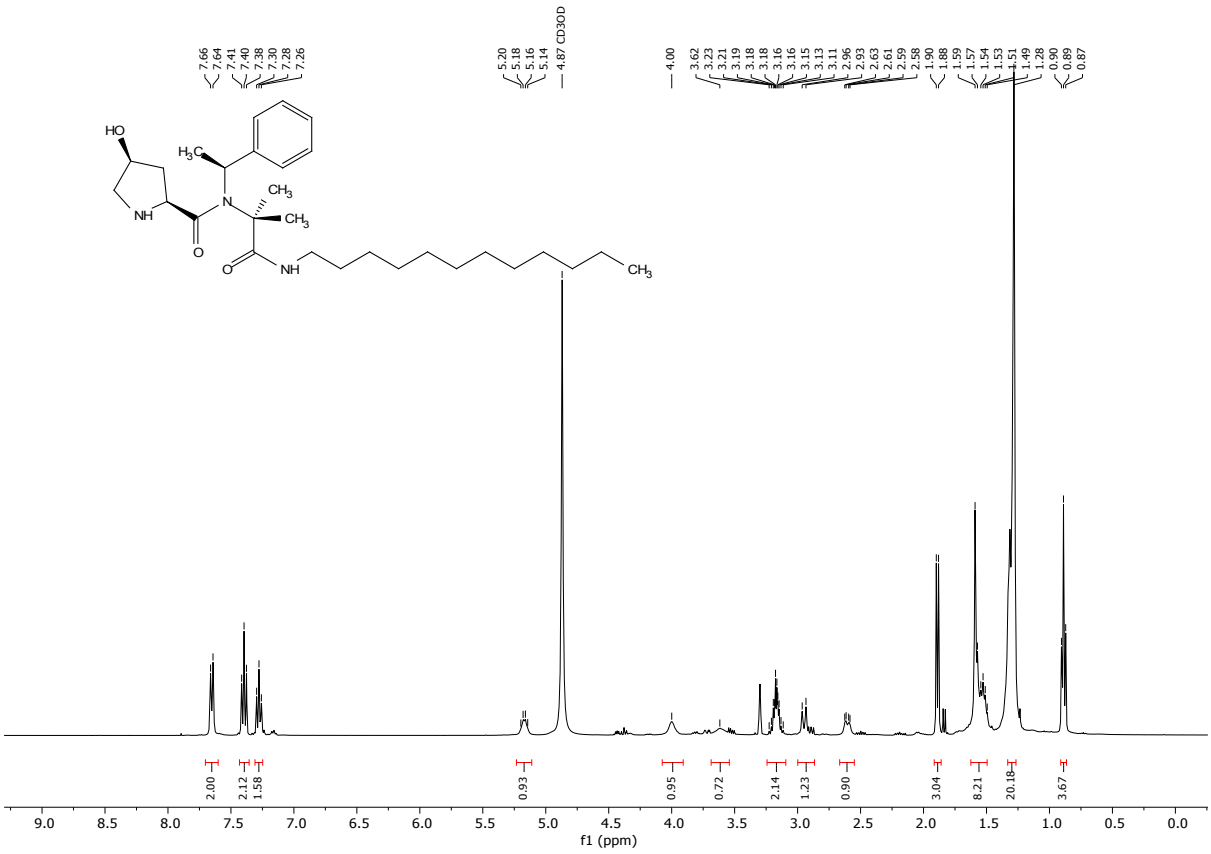


FIGURE 19. ^{1}H NMR of compound **3f** (400 MHz, CD_3OD).

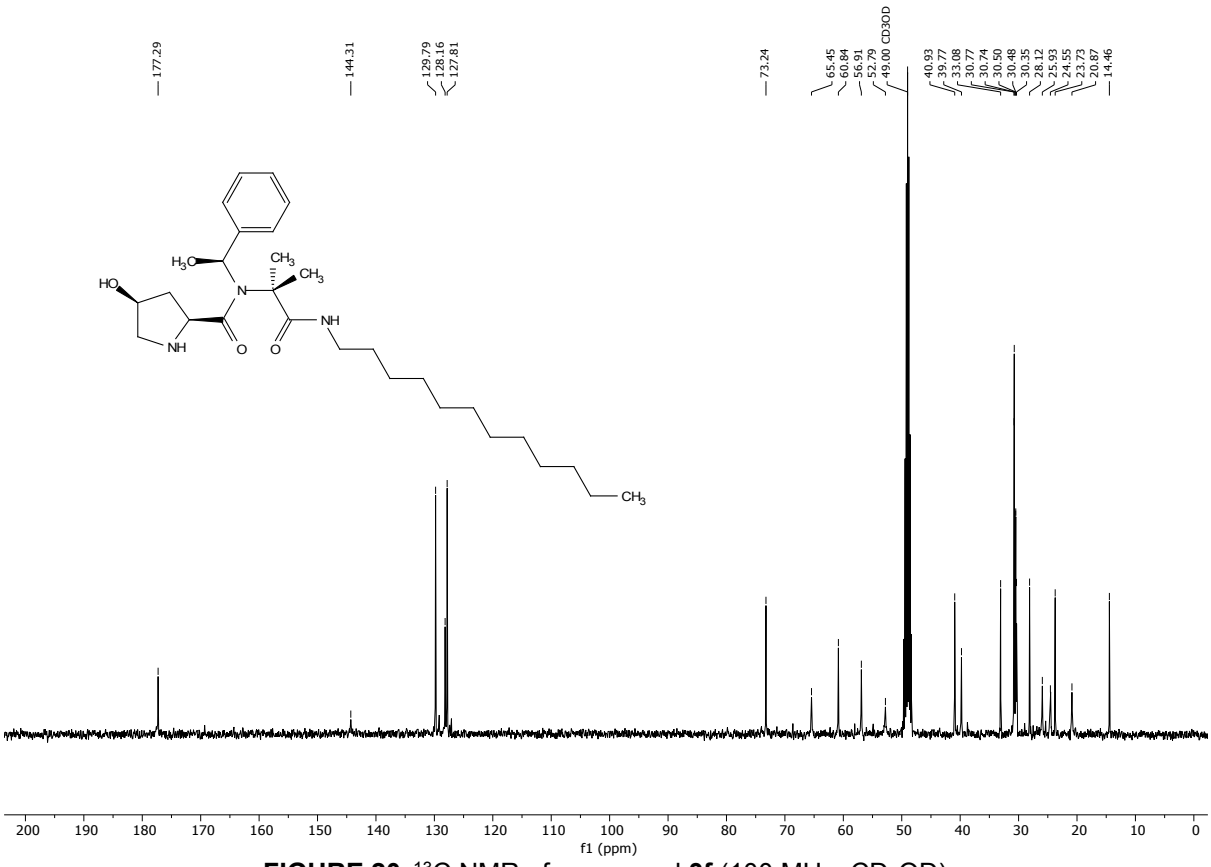


FIGURE 20. ^{13}C NMR of compound **3f** (100 MHz, CD_3OD).

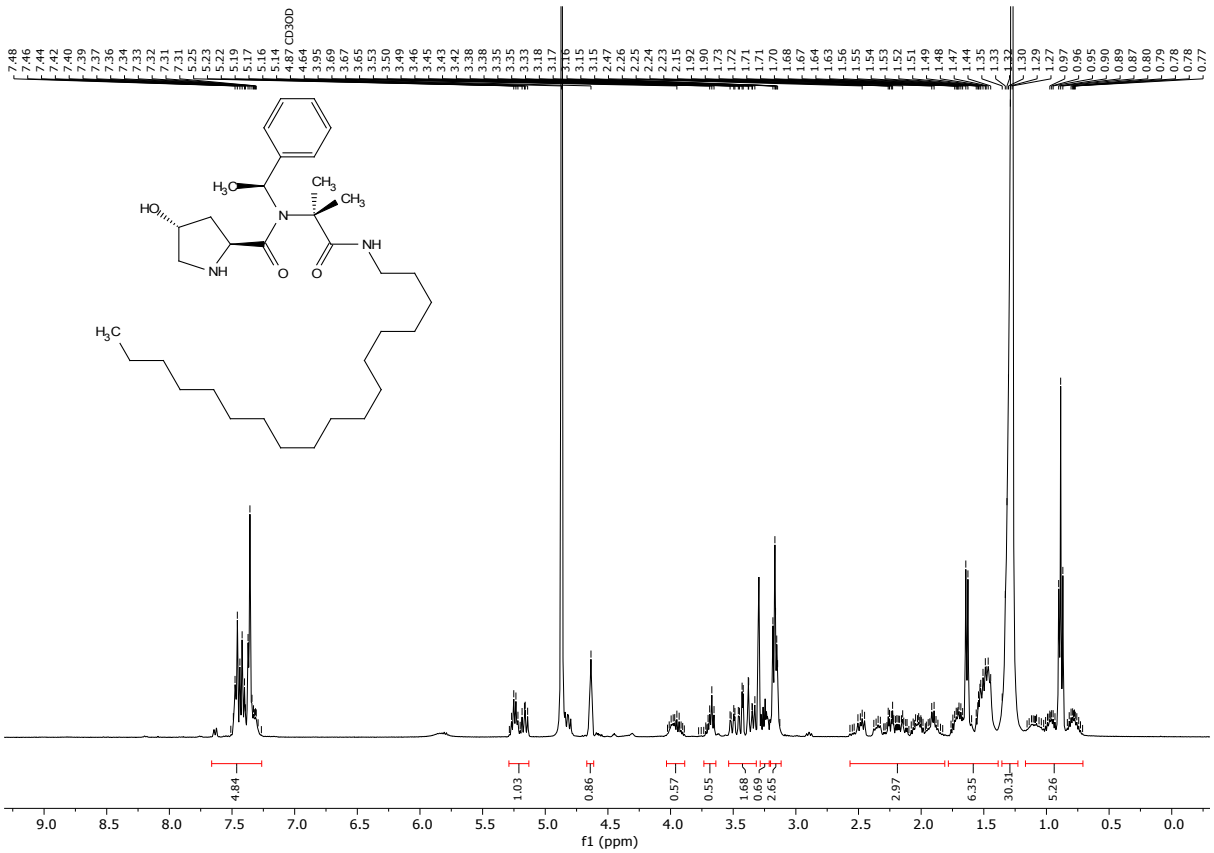


FIGURE 21. ^{1}H NMR of compound **3g** (400 MHz, CD_3OD).

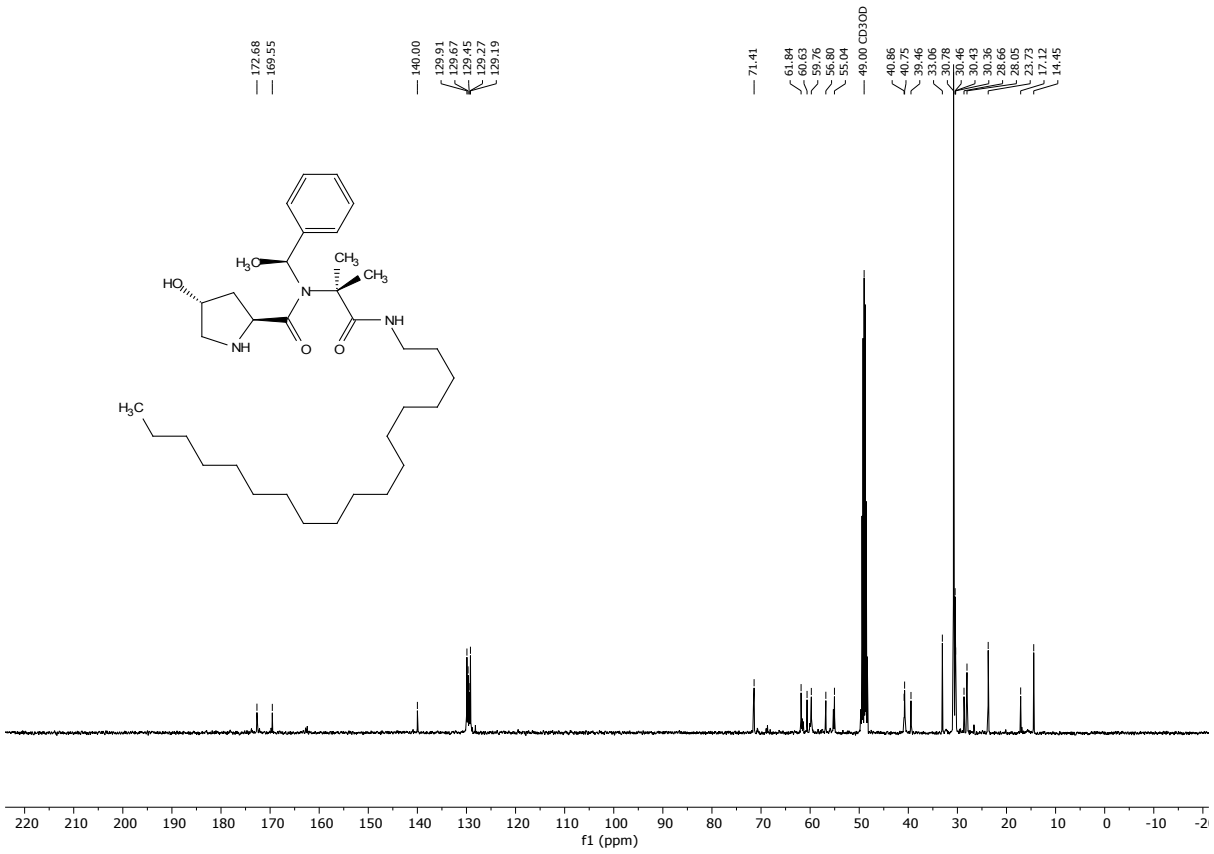


FIGURE 22. ^{13}C NMR of compound **3g** (100 MHz, CD_3OD).

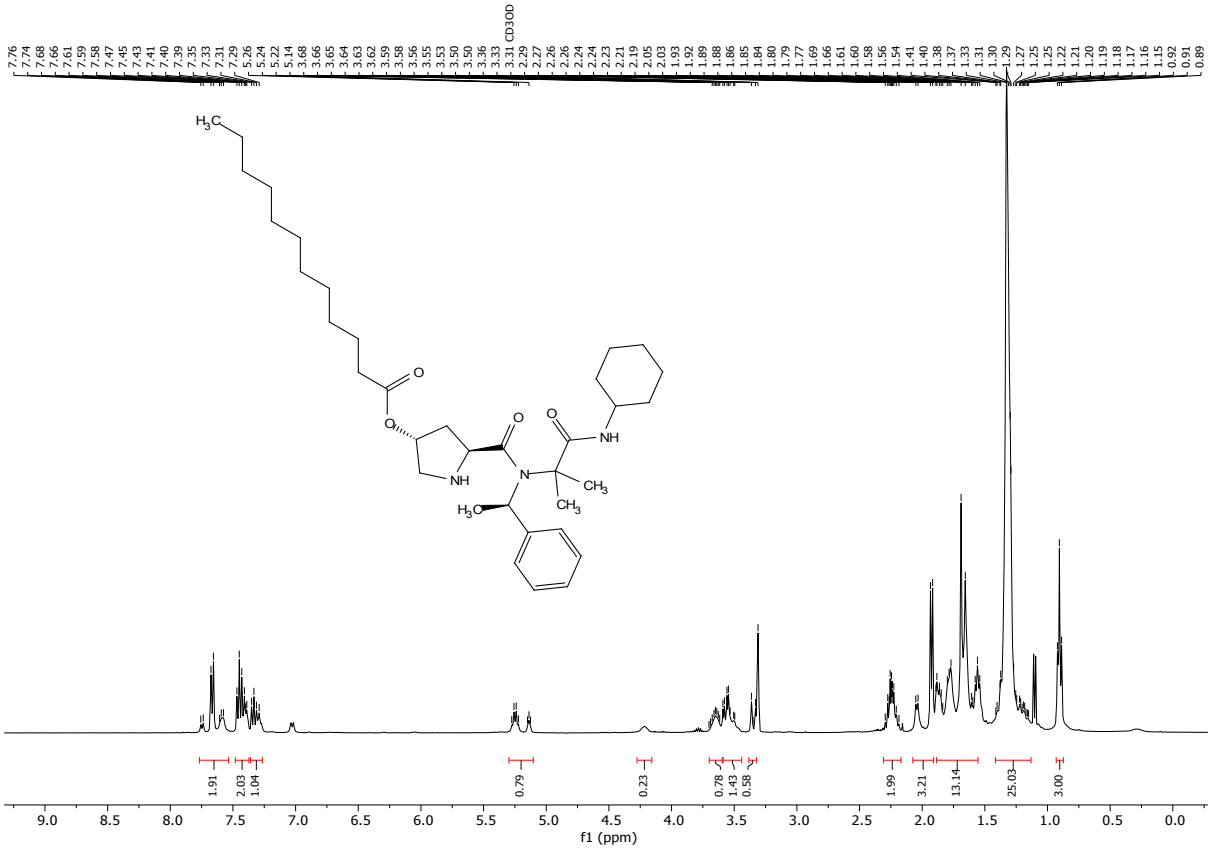


FIGURE 23. ^{1}H NMR of compound **3h** (400 MHz, CD_3OD).

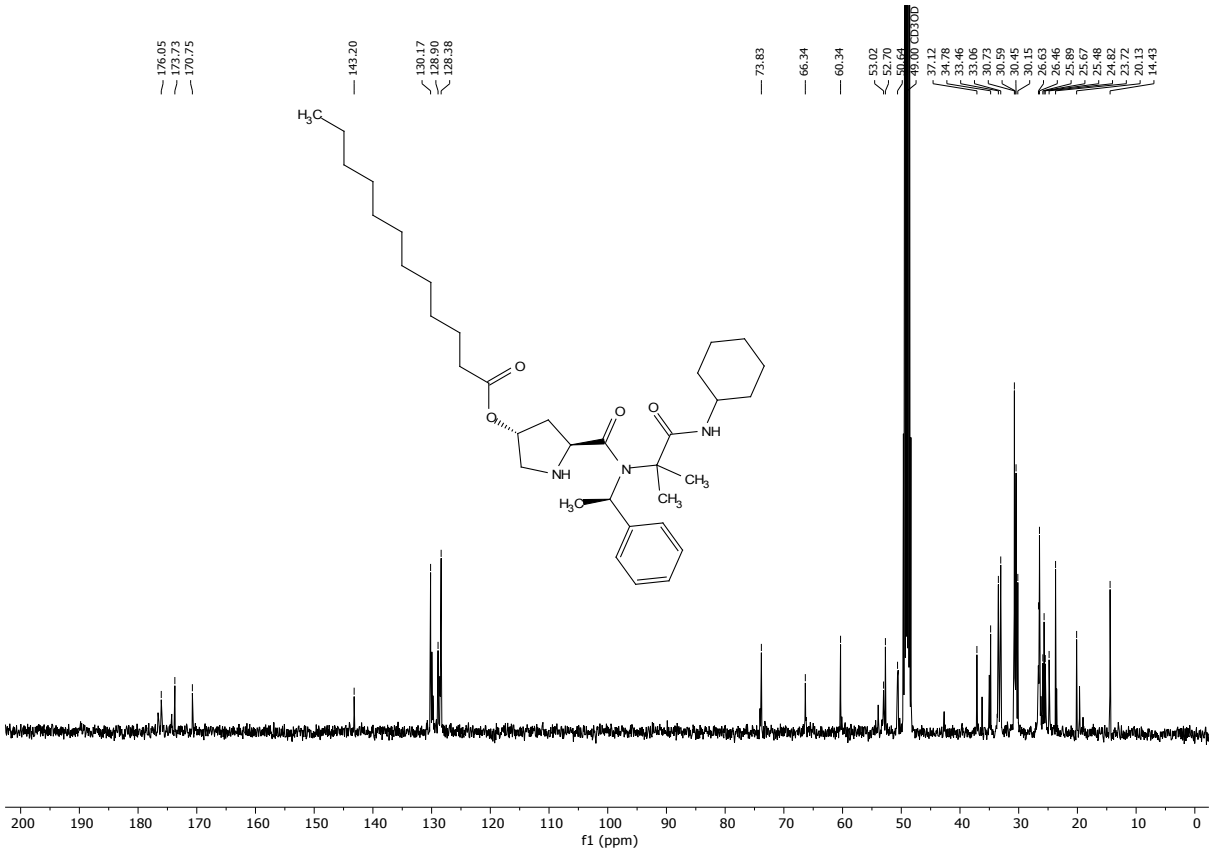


FIGURE 24. ^{13}C NMR of compound **3h** (100 MHz, CD_3OD).

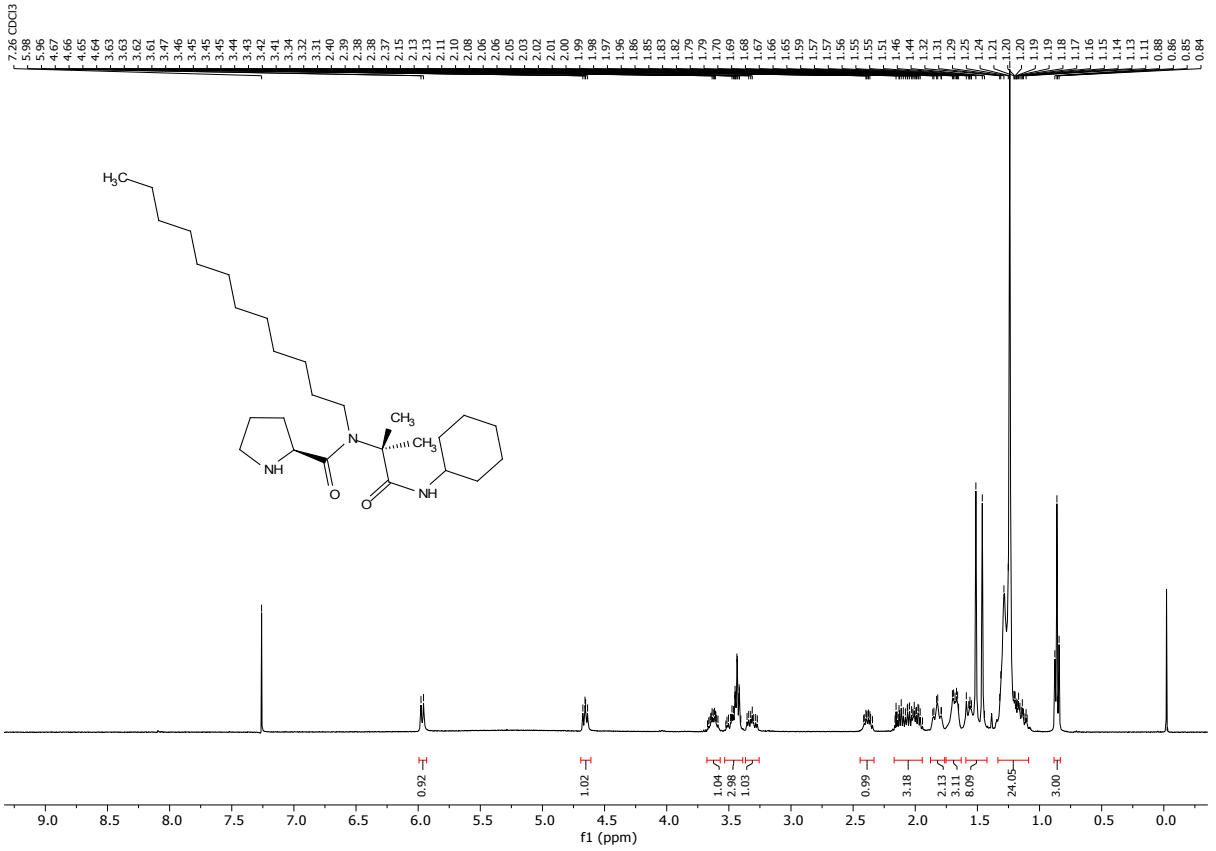


FIGURE 25. ^{1}H NMR of compound **3i** (400 MHz, $CDCl_3$).

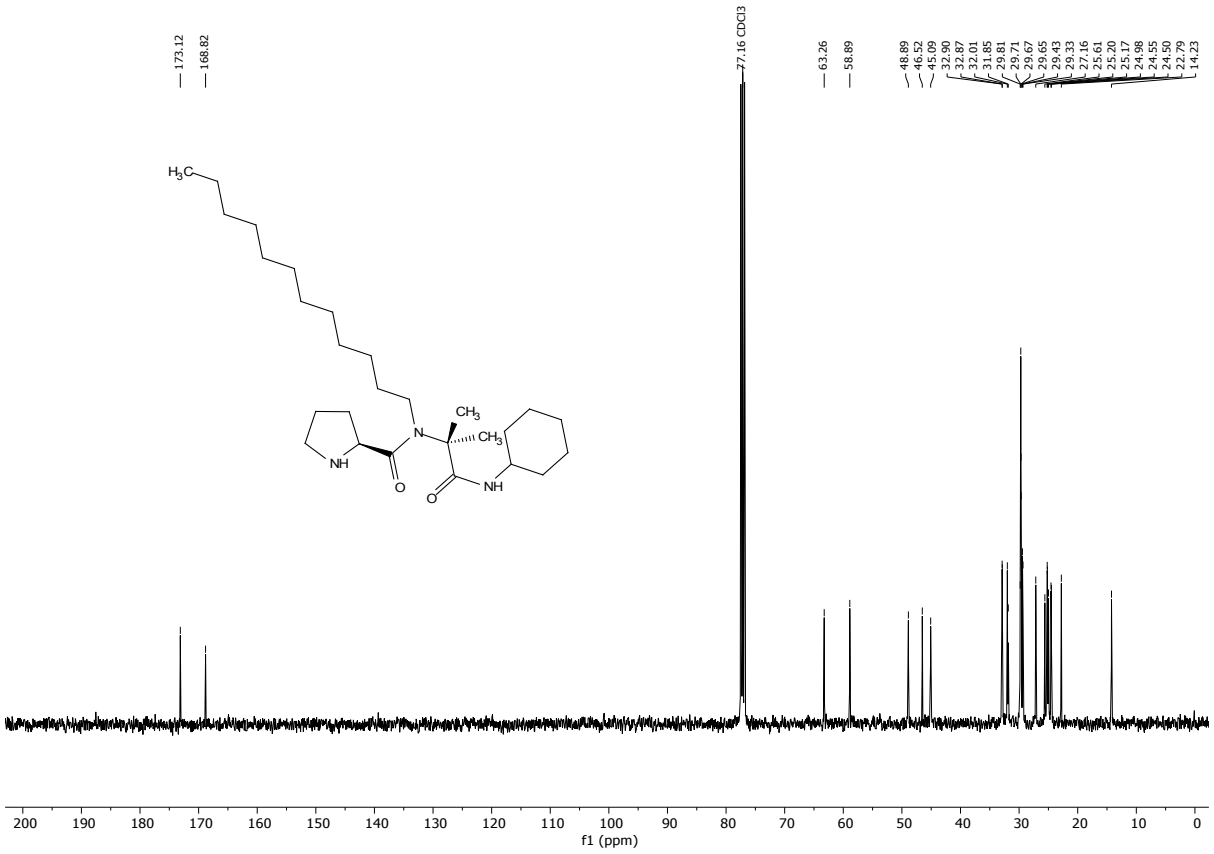


FIGURE 26. ^{13}C NMR of compound **3i** (100 MHz, $CDCl_3$).

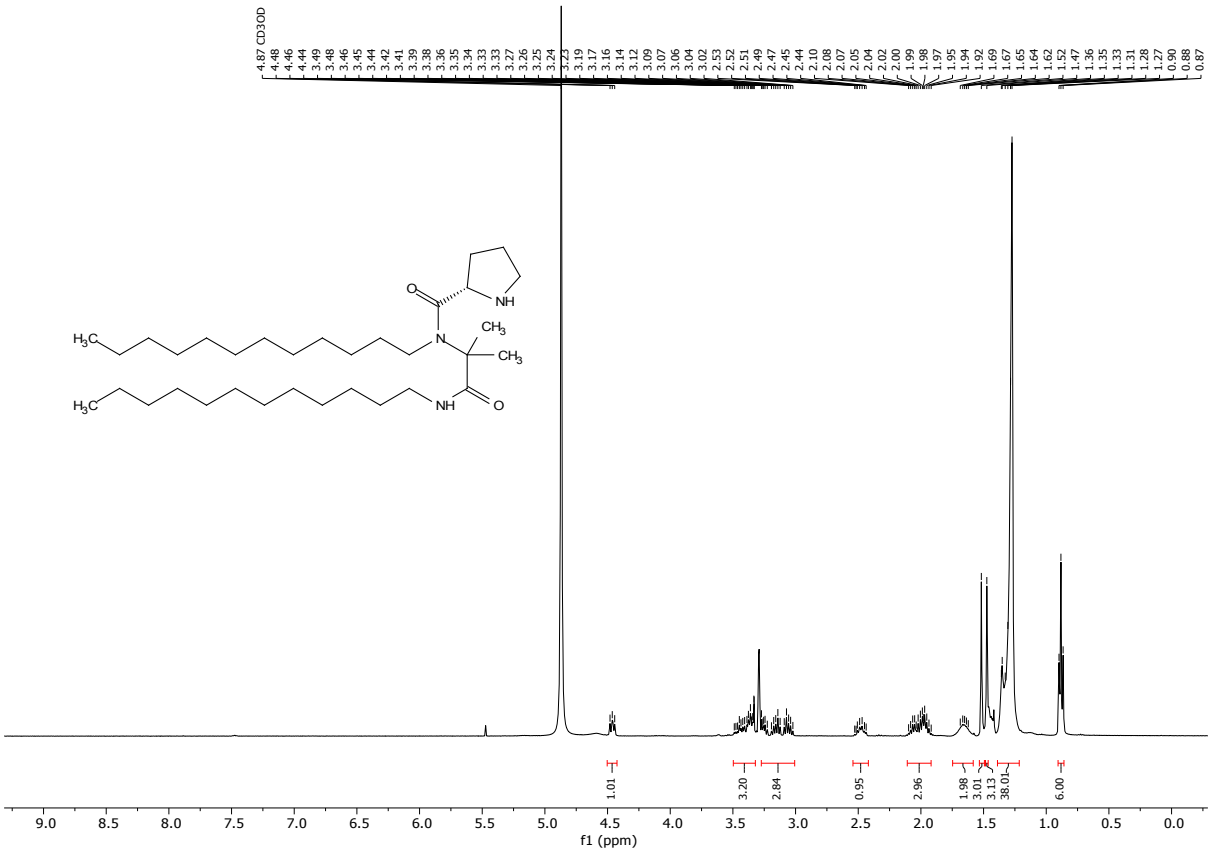


FIGURE 27. ^{1}H NMR of compound **3j** (400 MHz, CD_3OD).

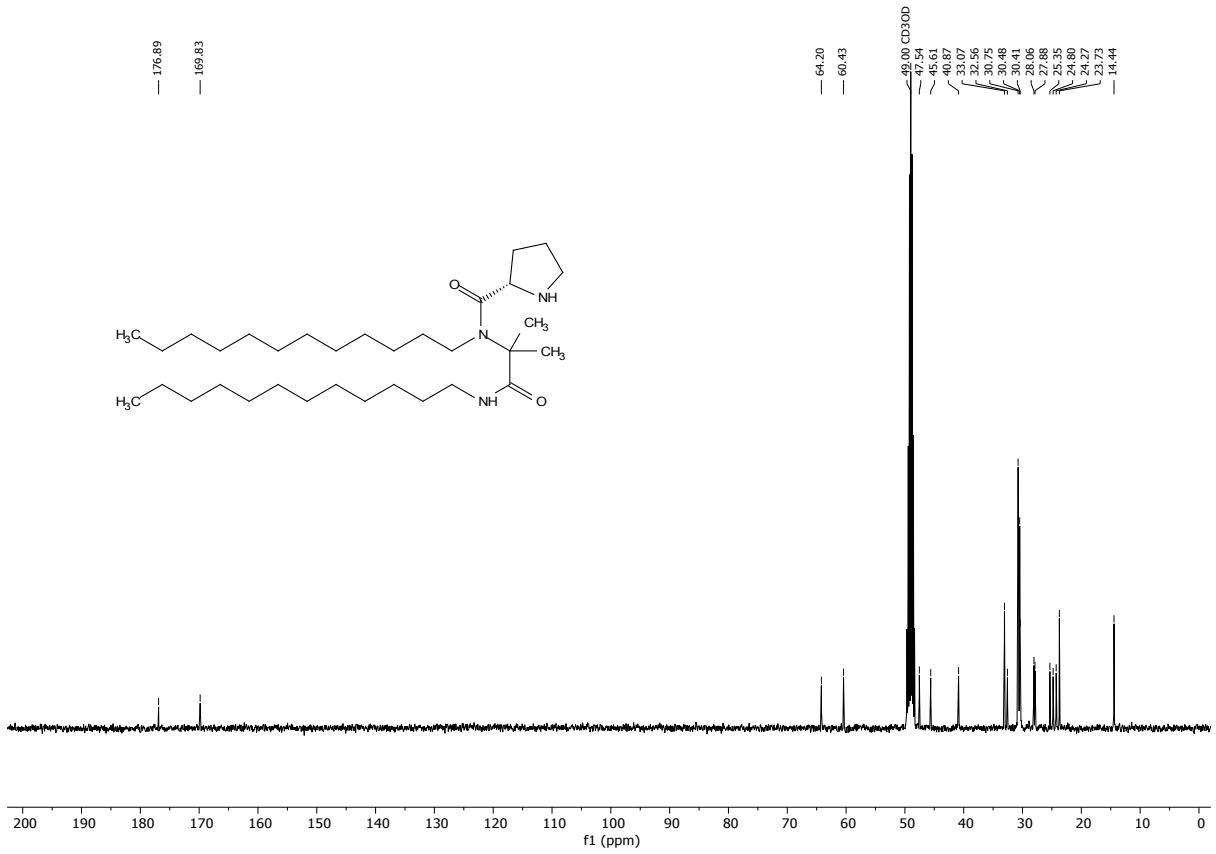


FIGURE 28. ^{13}C NMR of compound **3j** (100 MHz, CD_3OD).

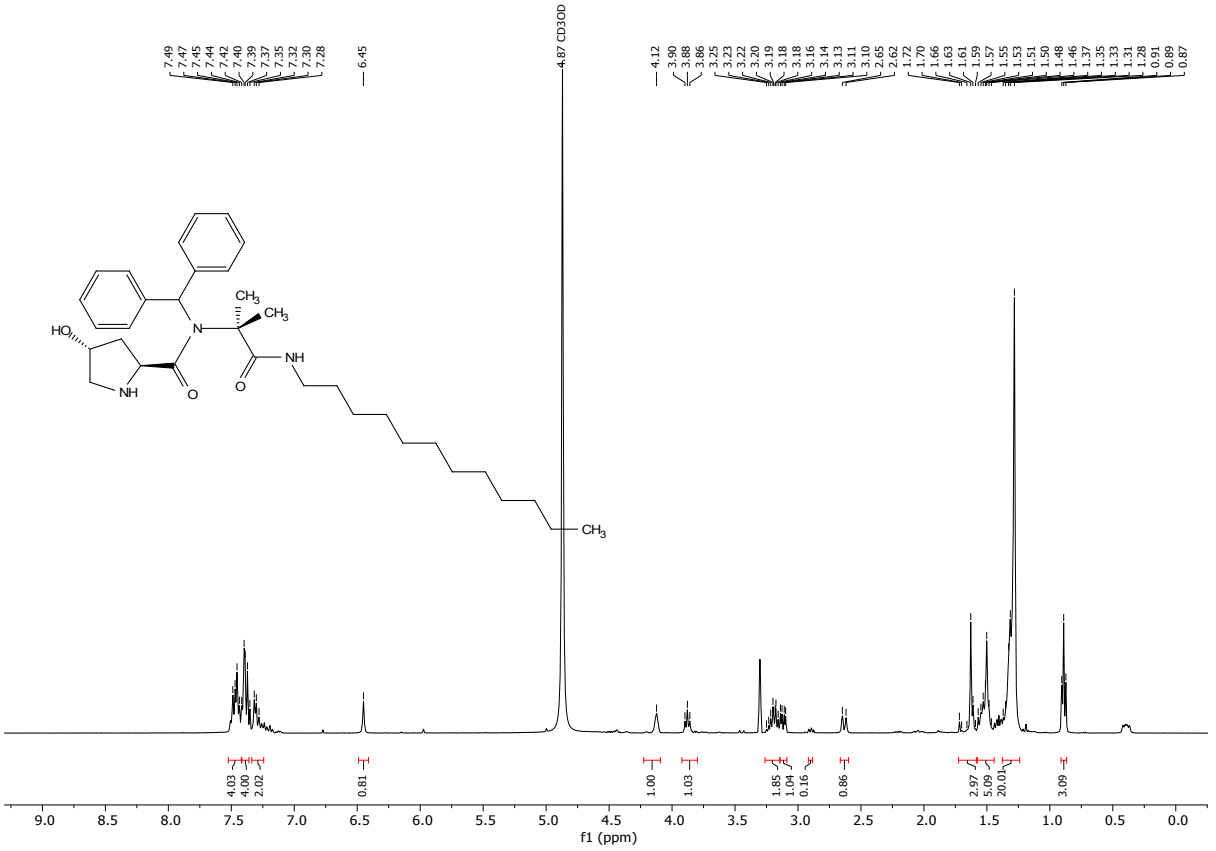


FIGURE 29. ^{1}H NMR of compound **3k** (400 MHz, CD_3OD).

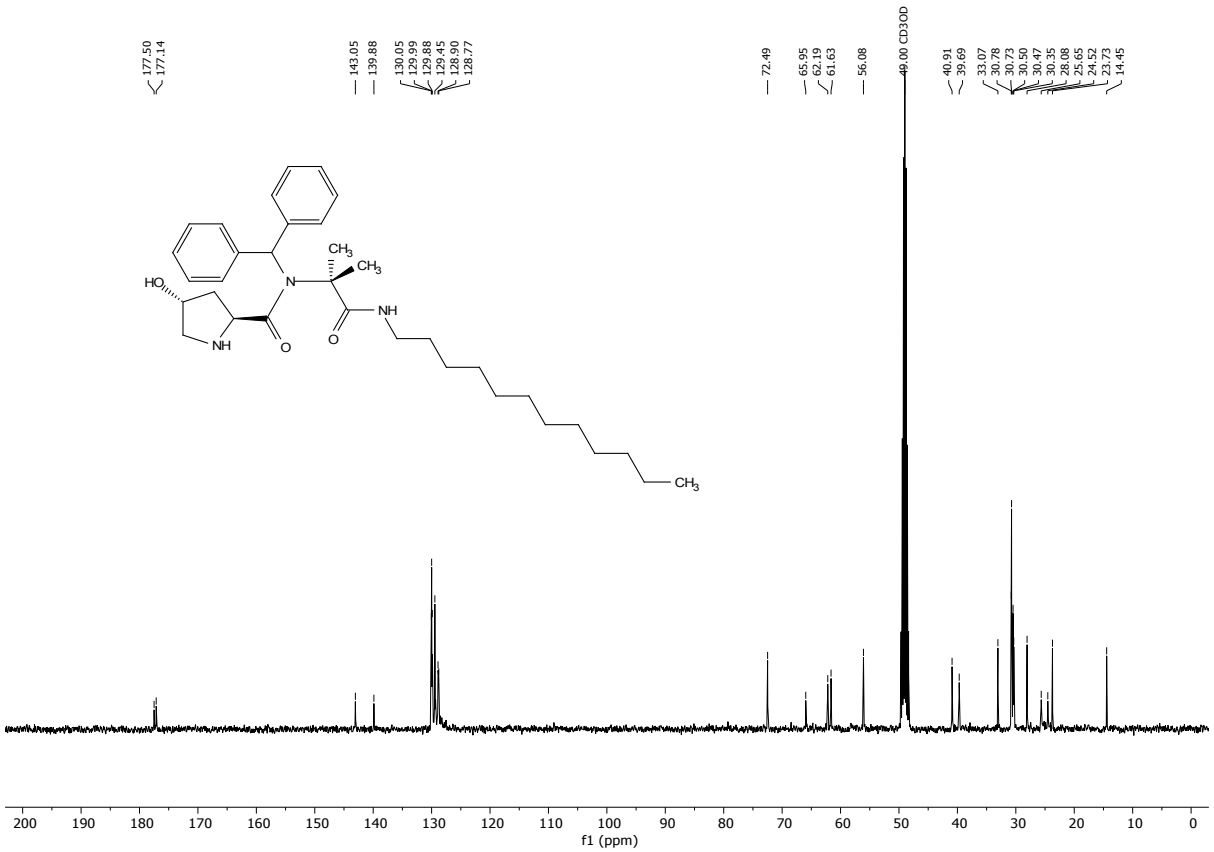


FIGURE 30. ^{13}C NMR of compound **3k** (100 MHz, CD_3OD).

15. NMR Spectra and Chromatograms: Catalyst Screening

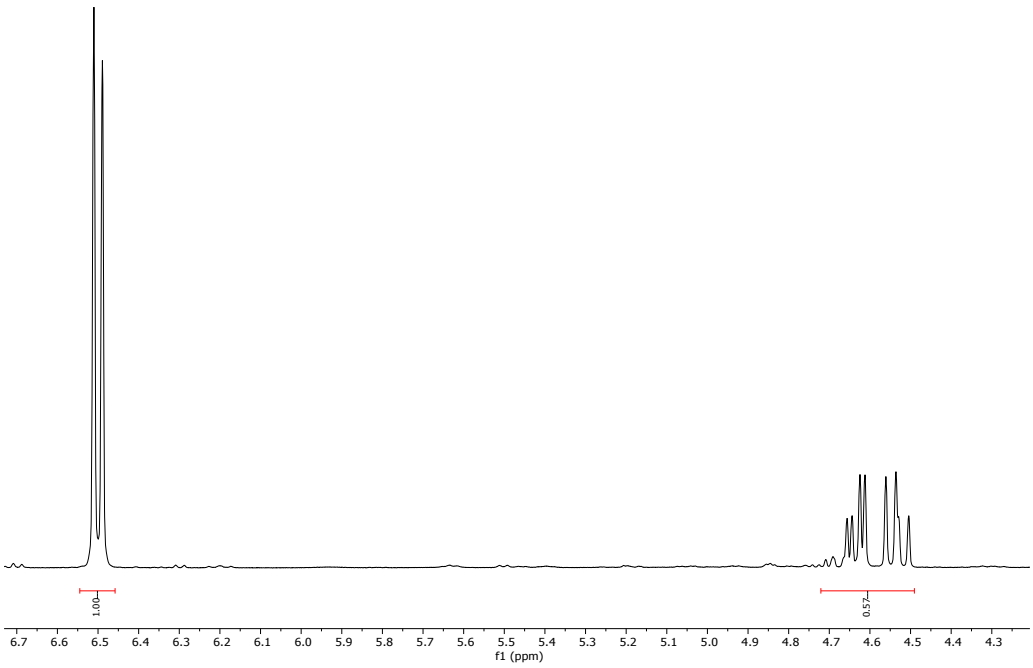


FIGURE 31. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3a** with 1, 2, 3-trimethoxybenzene as standard. Yield: 57%. TABLE 2, Entry 1.

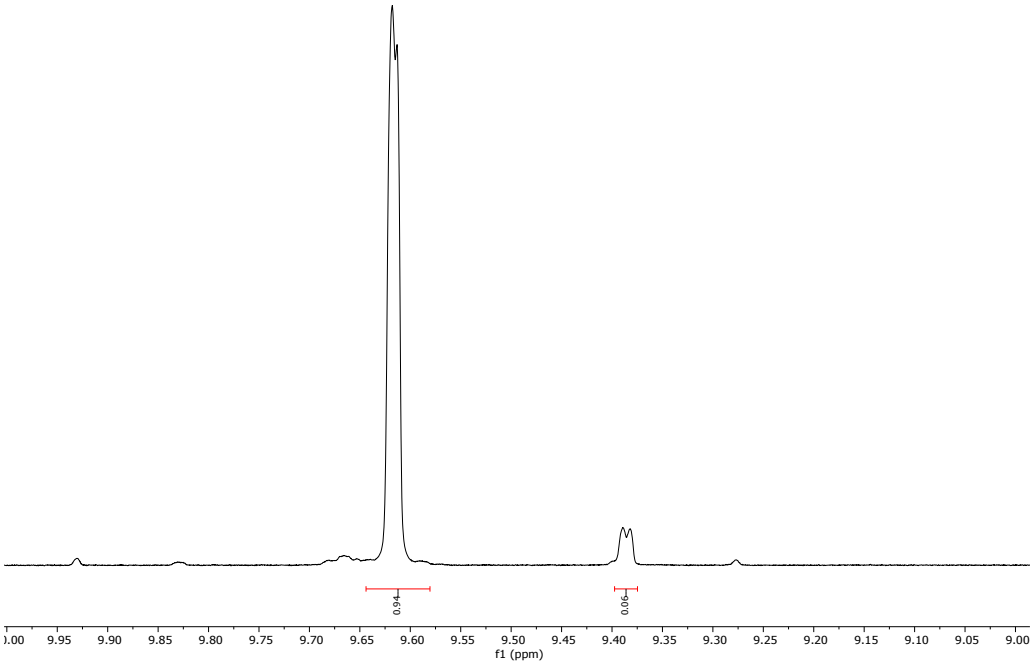


FIGURE 32. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3a**. Diastereoisomeric ratio (*syn/anti*): 94:06. TABLE 2, Entry 1.

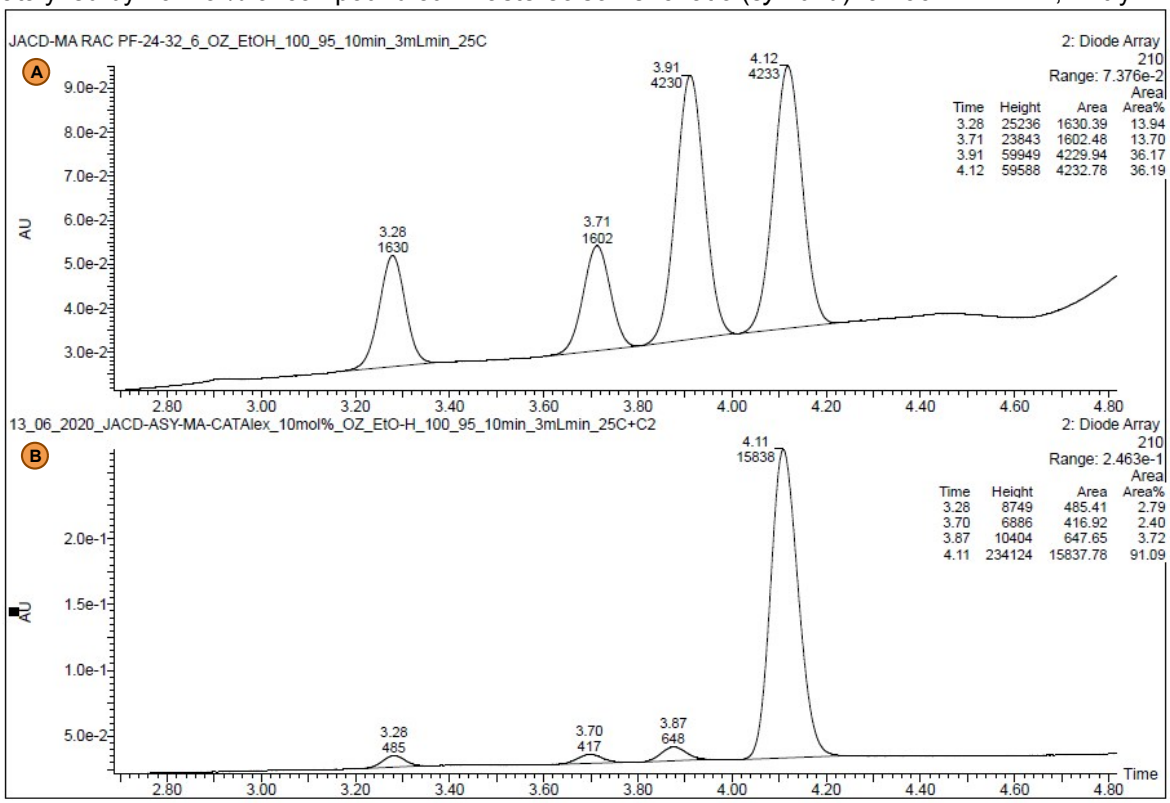


FIGURE 33. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3a**. Trefoil CEL2, Grad: CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.87 min, (syn, major) = 4.11 min. TABLE 2, Entry 1

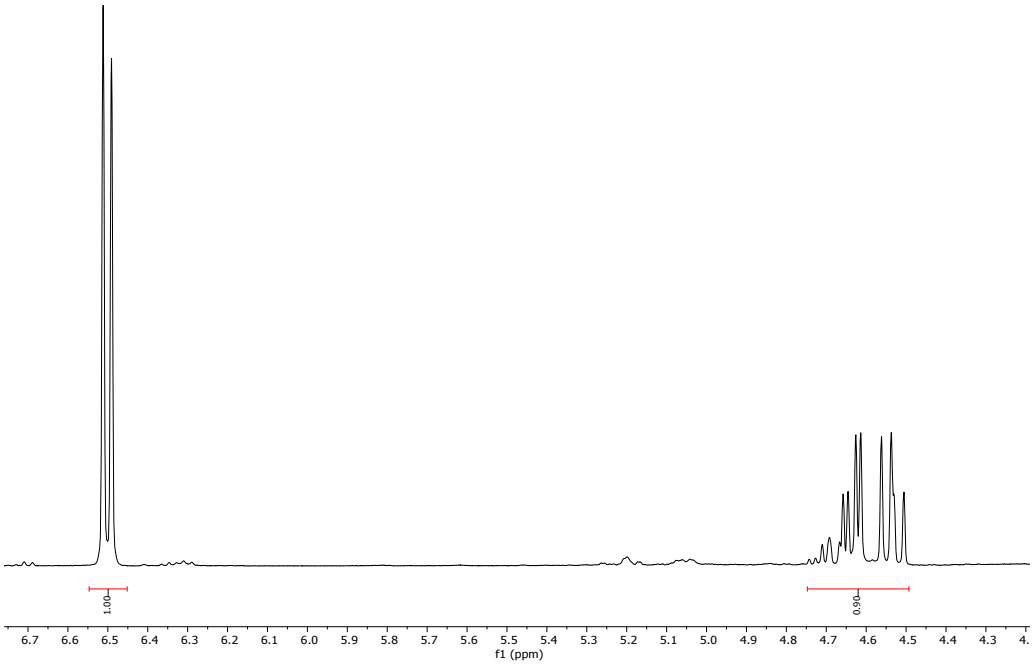


FIGURE 34. ^{1}H NMR of crude compound **4a** (400 MHz, CDCl3) obtained by the Michael reaction catalyzed by 10 mol% of compound **3b** with 1, 2, 3-trimethoxybenzene as standard. Yield: 90%. TABLE 2, Entry 2.

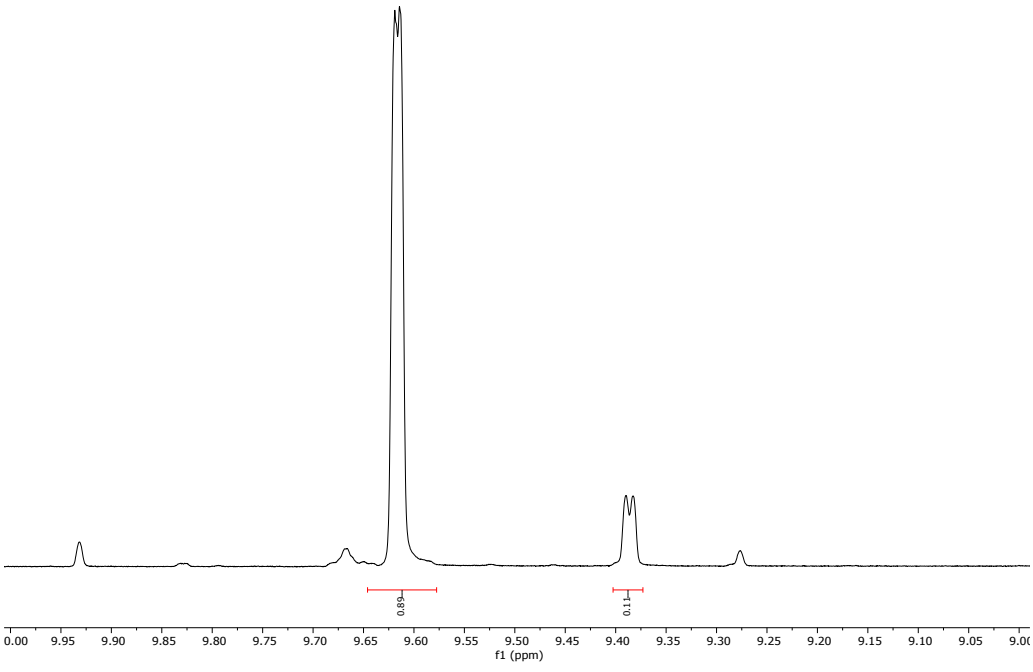


FIGURE 35. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3b**. Diastereoisomeric ratio (*syn/anti*): 89:11. TABLE 2, Entry 2.

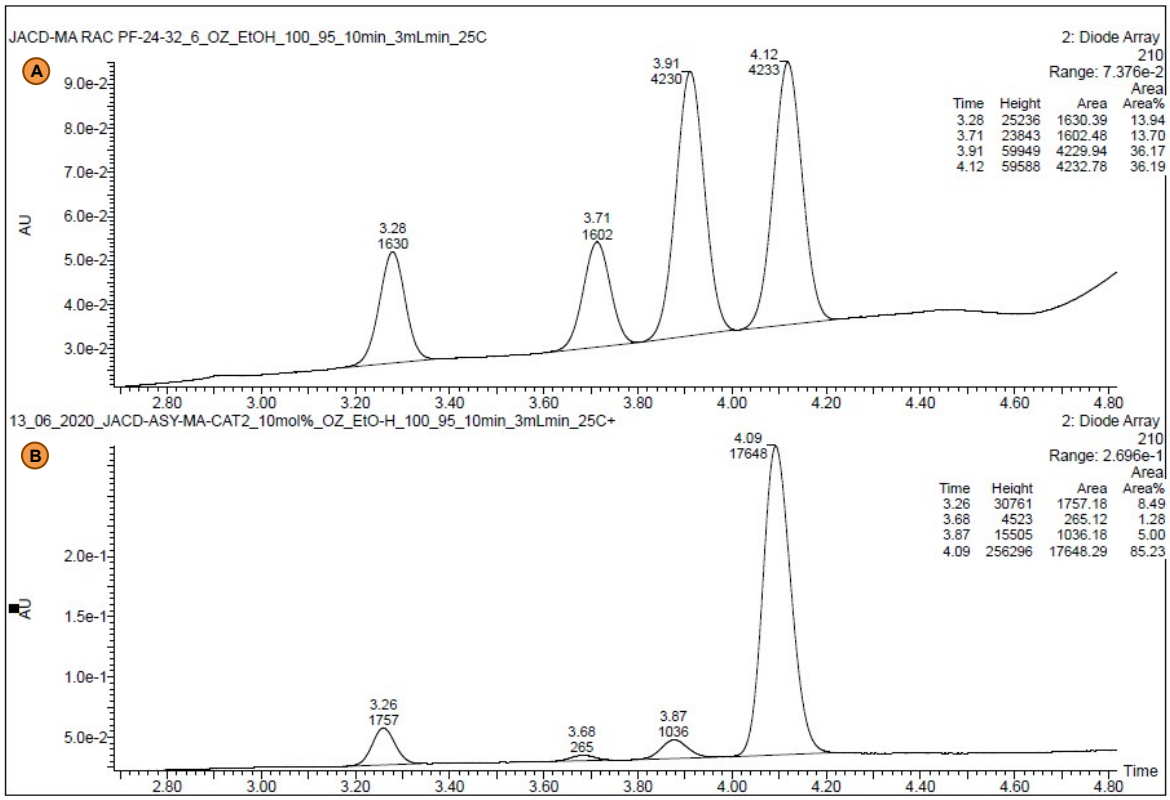


FIGURE 36. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3b**. Trefoil CEL2, Grad: CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.87 min, (syn, major) = 4.09 min. TABLE 2, Entry 2.

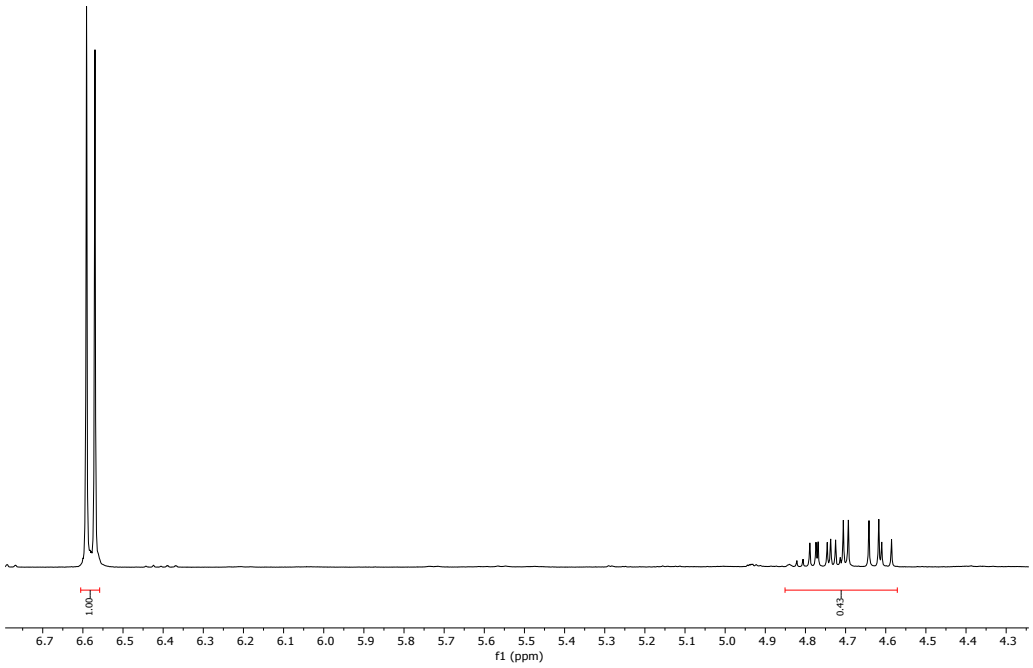


FIGURE 37. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3c** with 1, 2, 3-trimethoxybenzene as standard. Yield: 43%. TABLE 2, Entry 3.

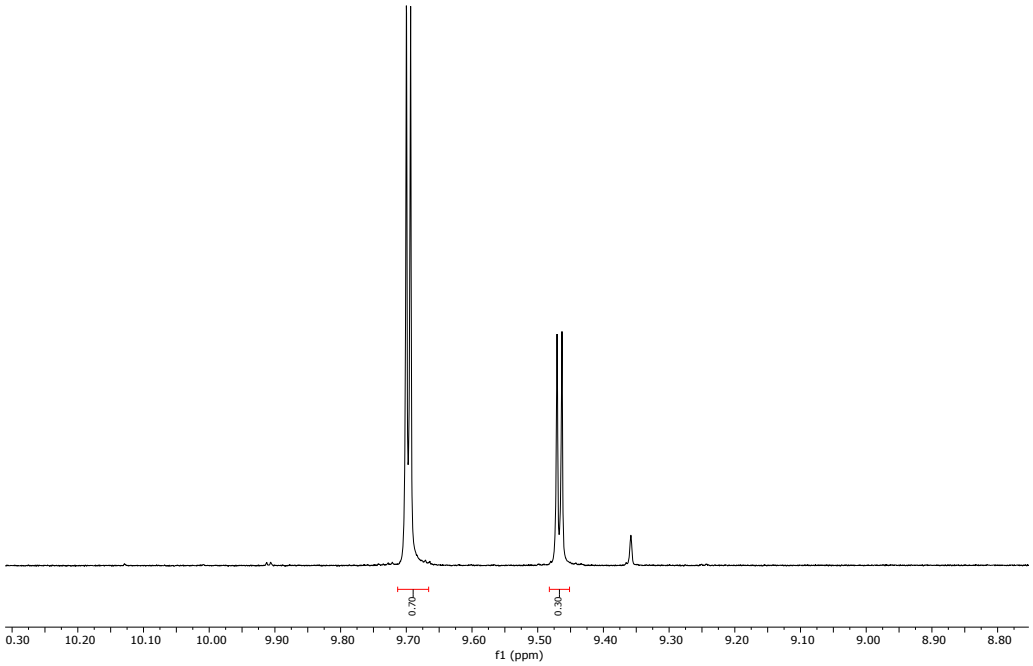


FIGURE 38. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3c**. Diastereoisomeric ratio (*syn/anti*): 70:30. TABLE 2, Entry 3.

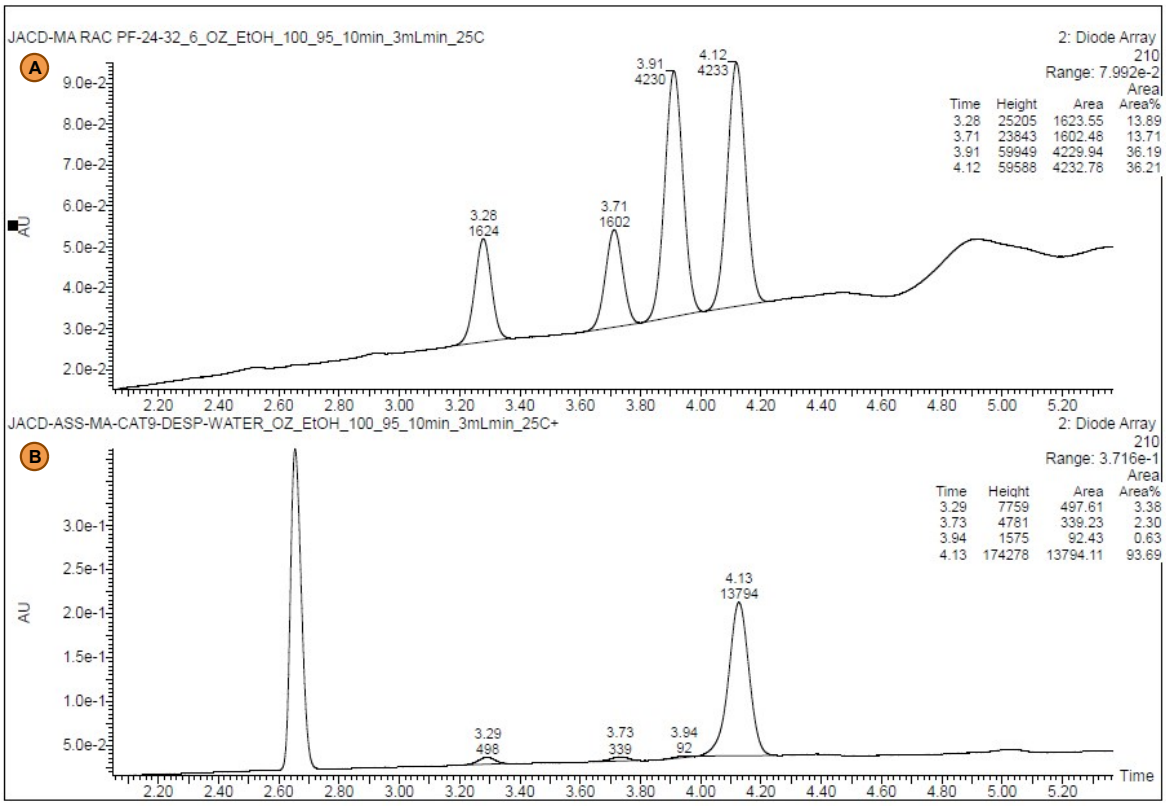


FIGURE 39. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3c**. Trefoil CEL2**, Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.94 min, (syn, major) = 4.13 min. TABLE 2, Entry 3.

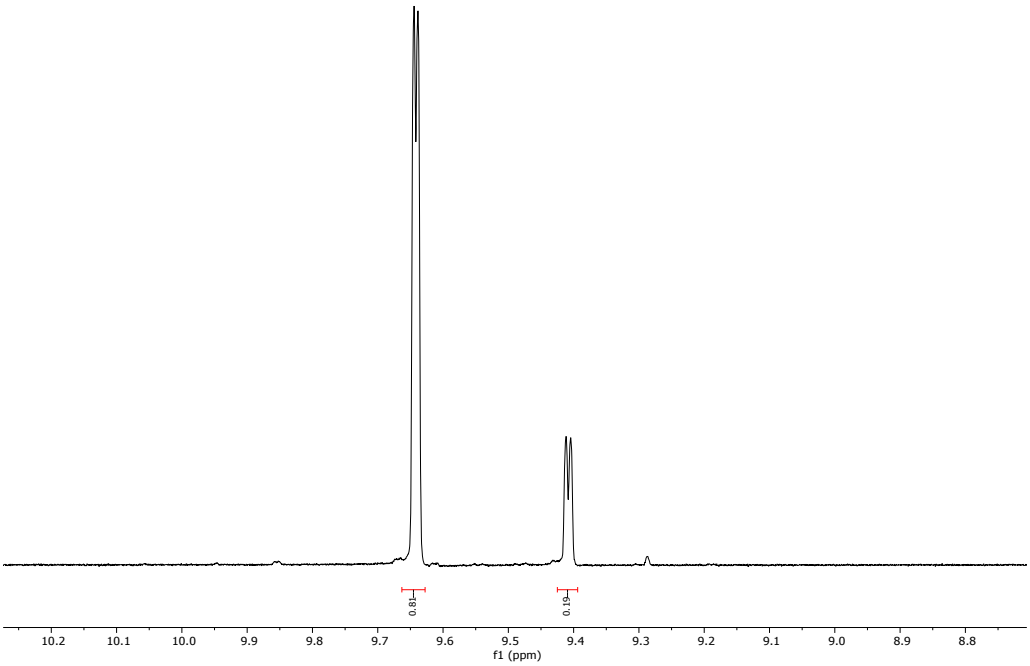


FIGURE 40. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3d**. Diastereoisomeric ratio (*syn/anti*): 81:19. TABLE 2, Entry 4.

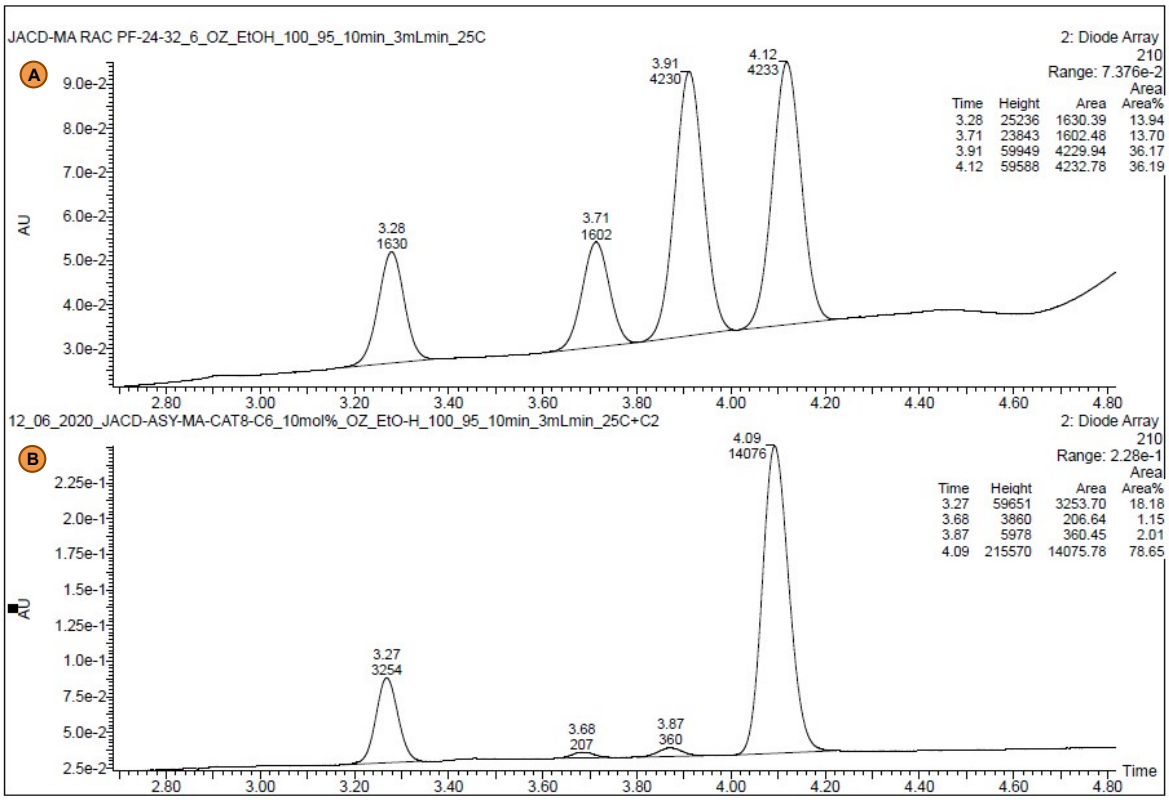


FIGURE 41. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3d**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 4.84min, (syn, major) = 5.18 min. TABLE 2, Entry 4.

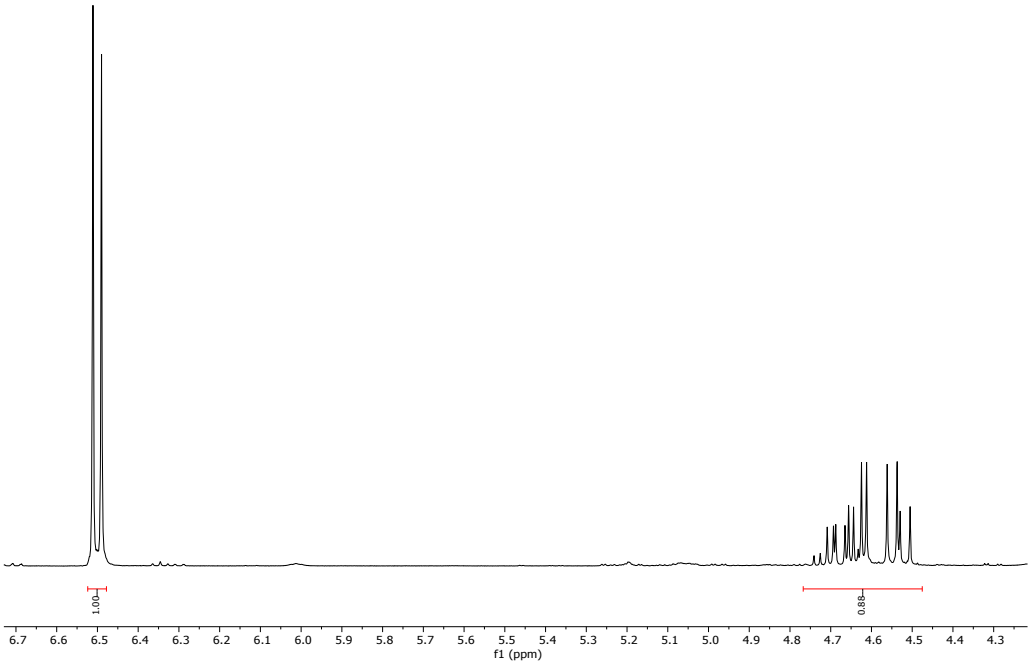


FIGURE 42. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3e** with 1, 2, 3-trimethoxybenzene as standard. Yield: 88%. TABLE 2, Entry 5.

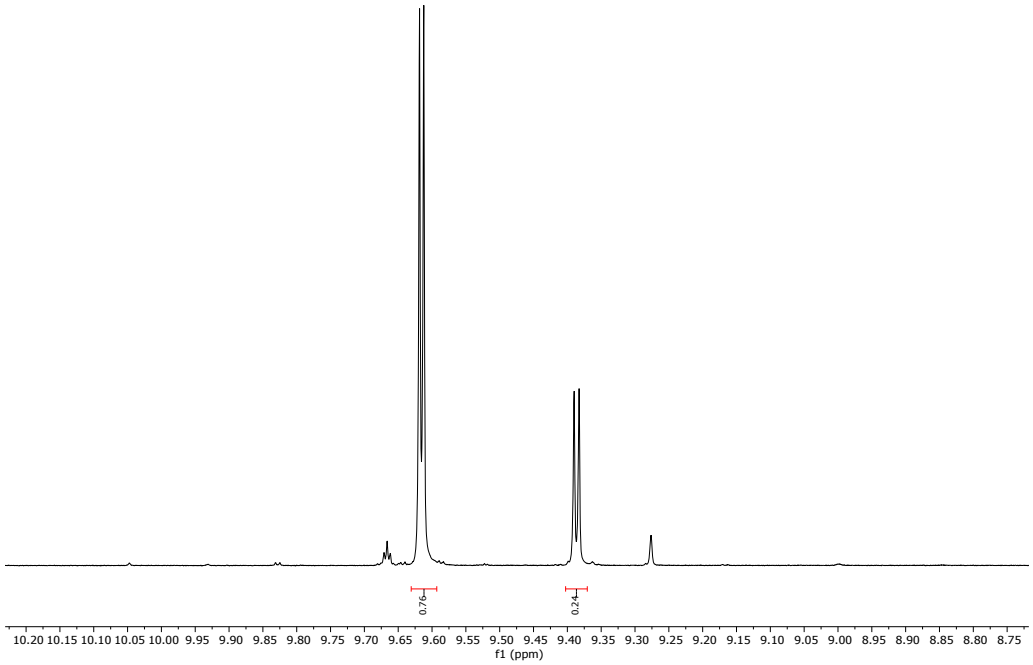


FIGURE 43. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 76:24. TABLE 2, Entry 5.

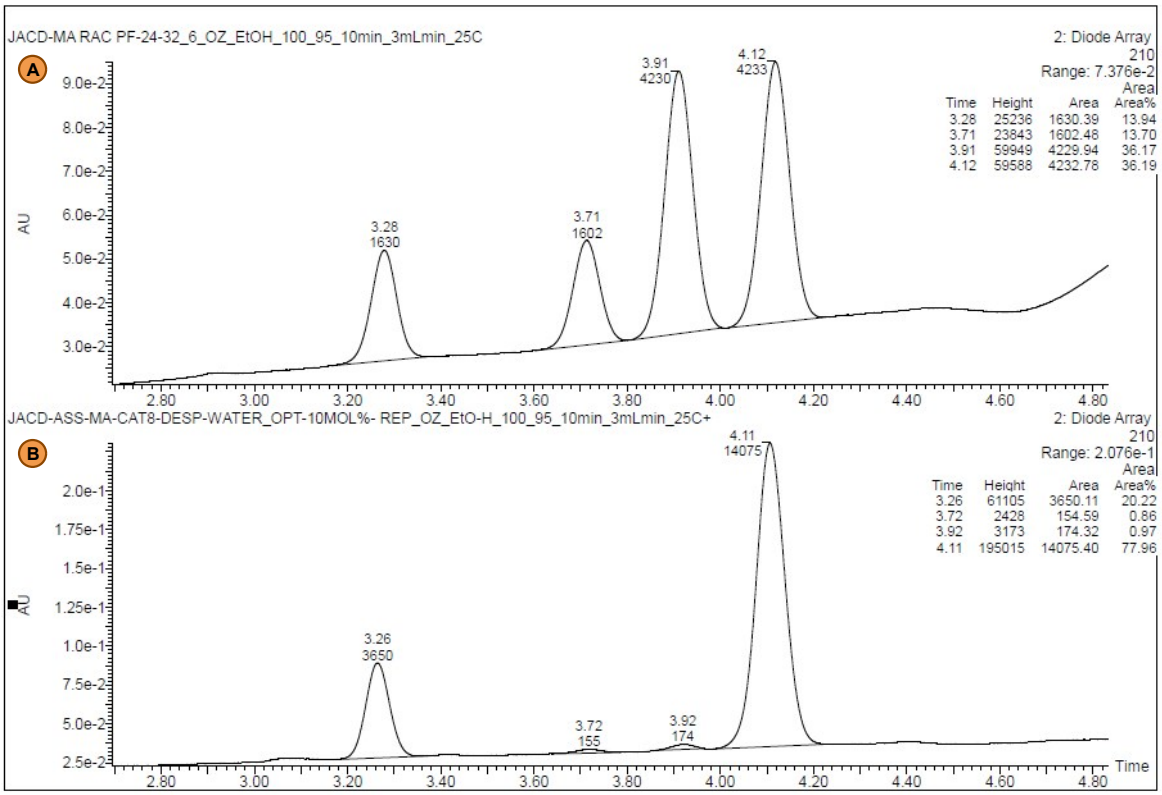


FIGURE 44. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.92 min, (syn, major) = 4.11 min. TABLE 2, Entry 5.

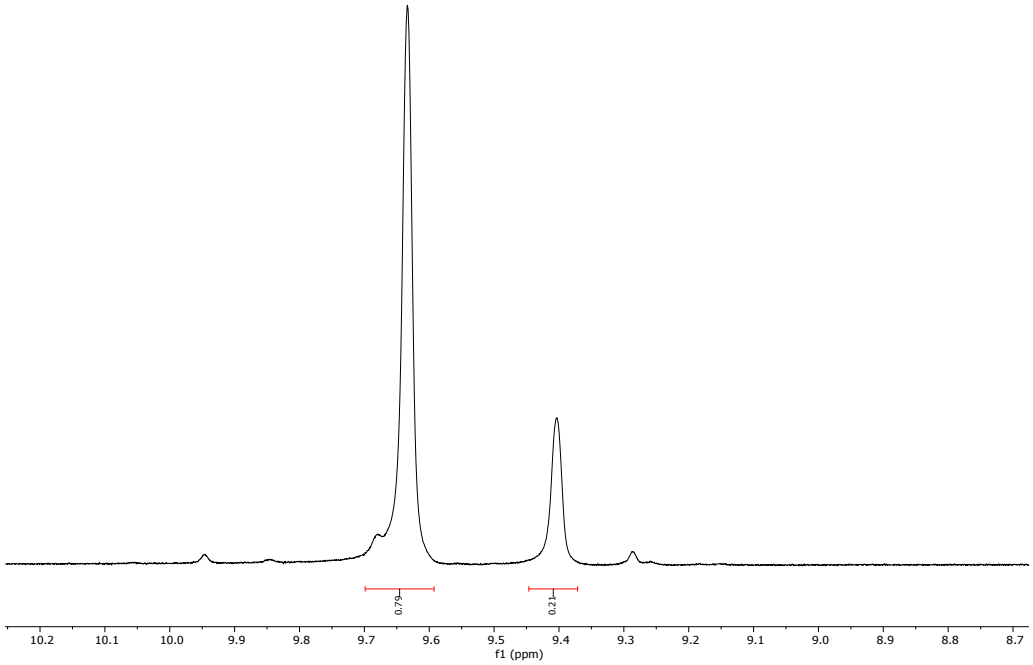


FIGURE 45. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3f**. Diastereoisomeric ratio (*syn/anti*): 79:21. TABLE 2, Entry 6.

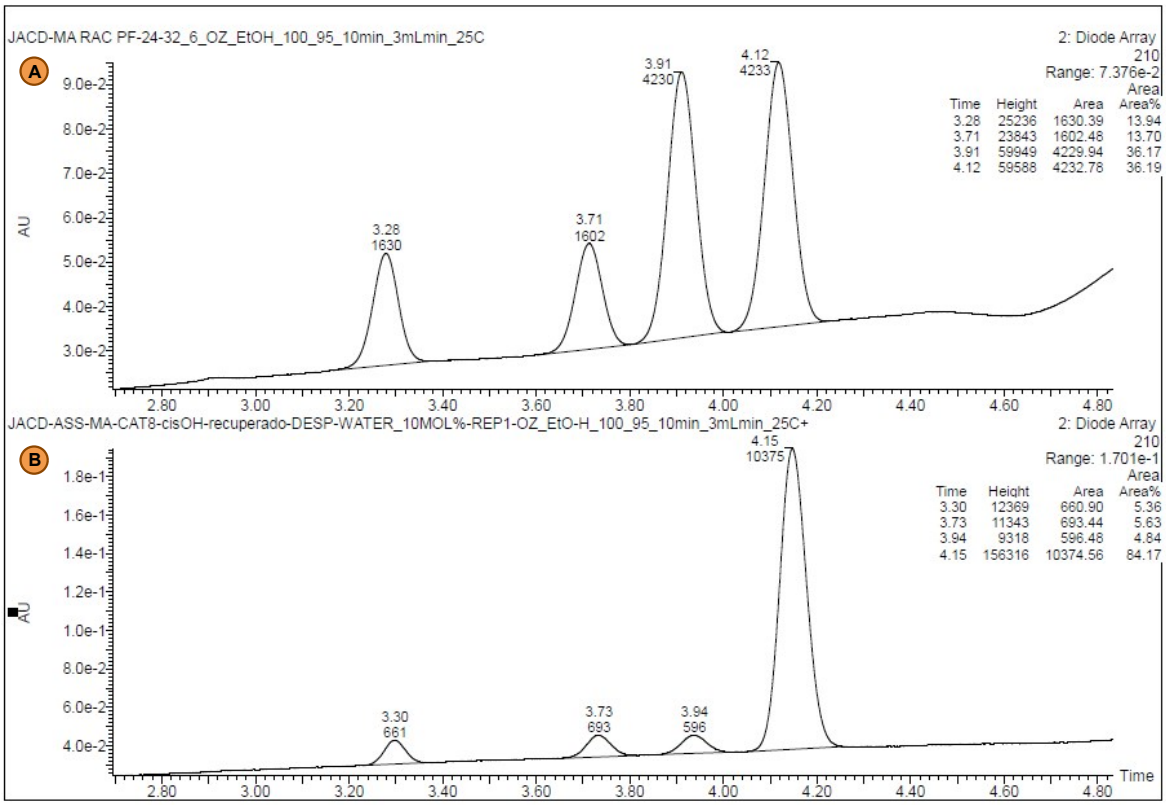


FIGURE 46. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3f**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.94 min, (syn, major) = 4.15 min. TABLE 2, Entry 6.

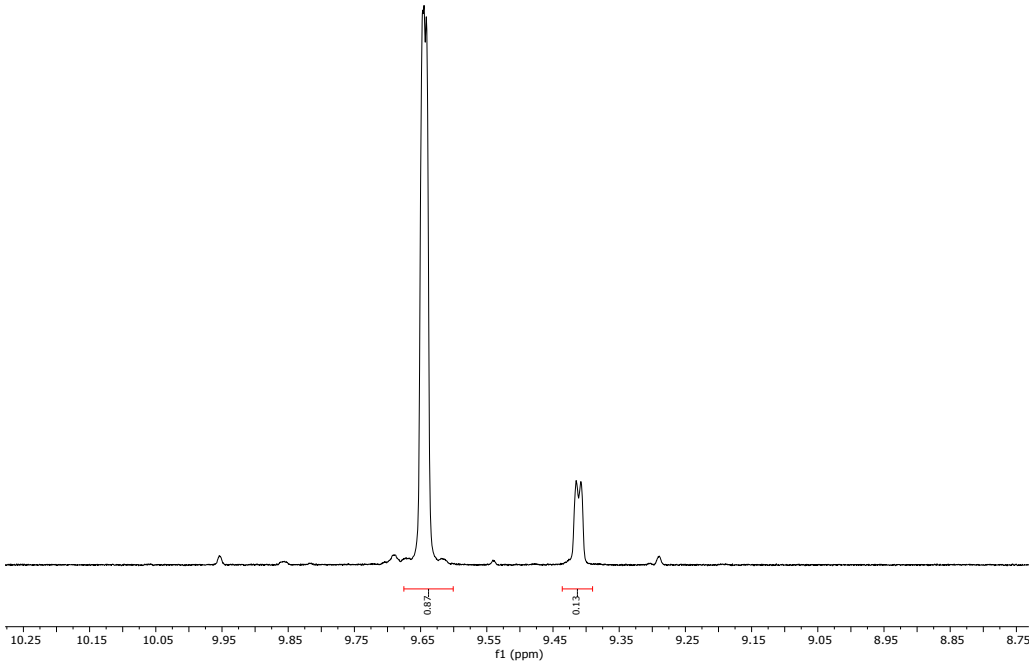


FIGURE 47. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3g**. Diastereoisomeric ratio (*syn/anti*): 87:13. TABLE 2, Entry 7.

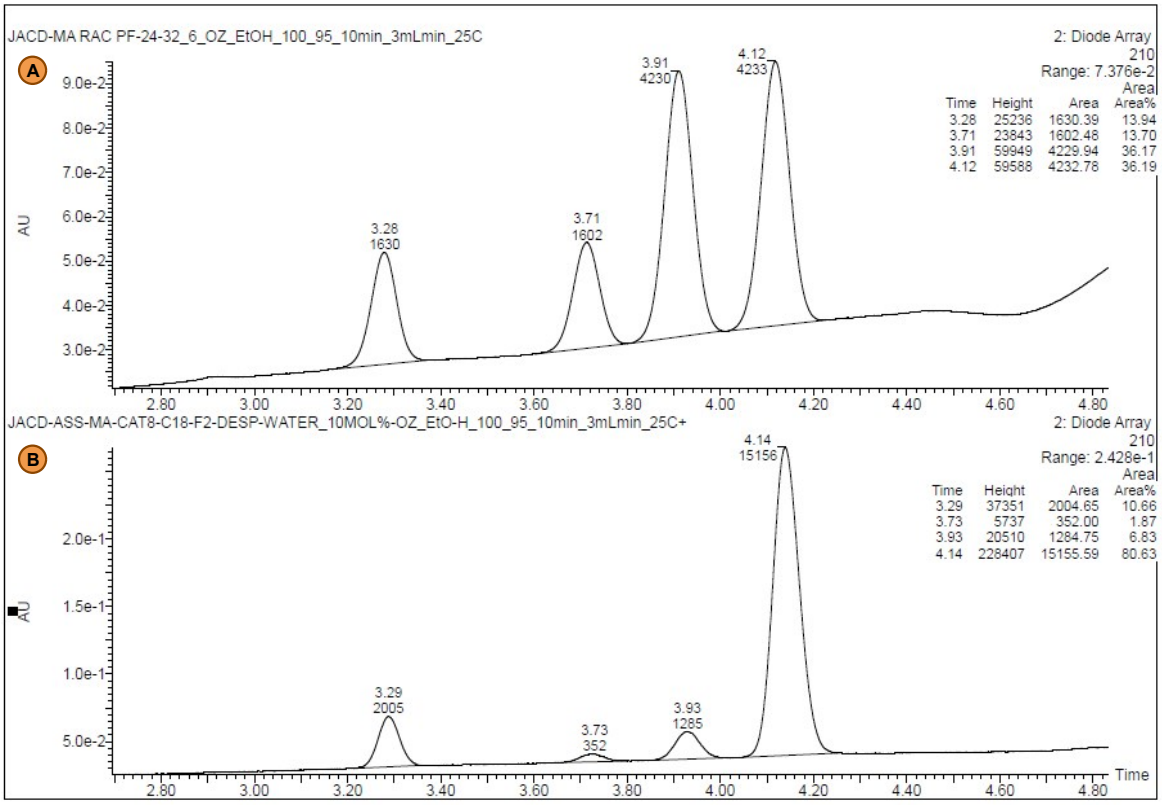


FIGURE 48. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3g**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.93 min, (syn, major) = 4.14 min. TABLE 2, Entry 7.

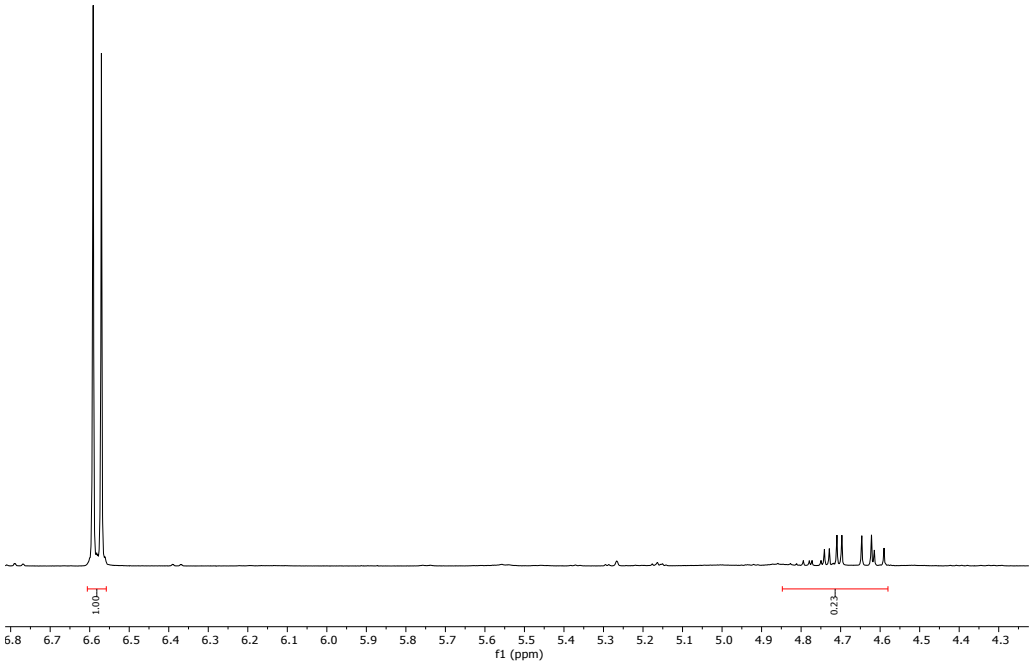


FIGURE 49. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3h** with 1, 2, 3-trimethoxybenzene as standard. Yield: 23%. TABLE 2, Entry 8.

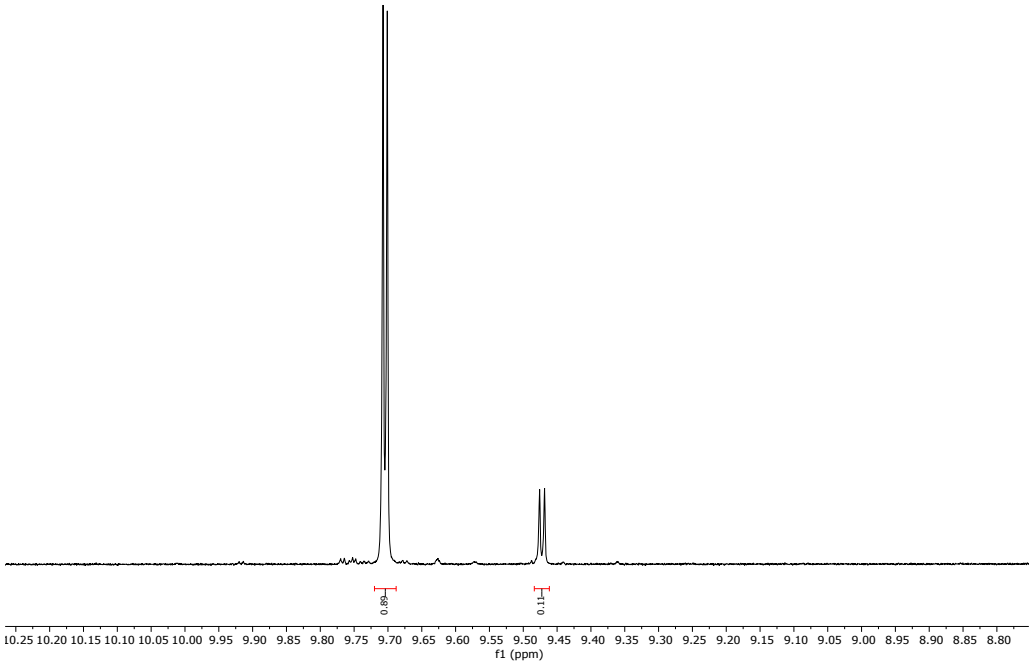


FIGURE 50. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3h**. Diastereoisomeric ratio (*syn/anti*): 89:11. TABLE 2, Entry 8.

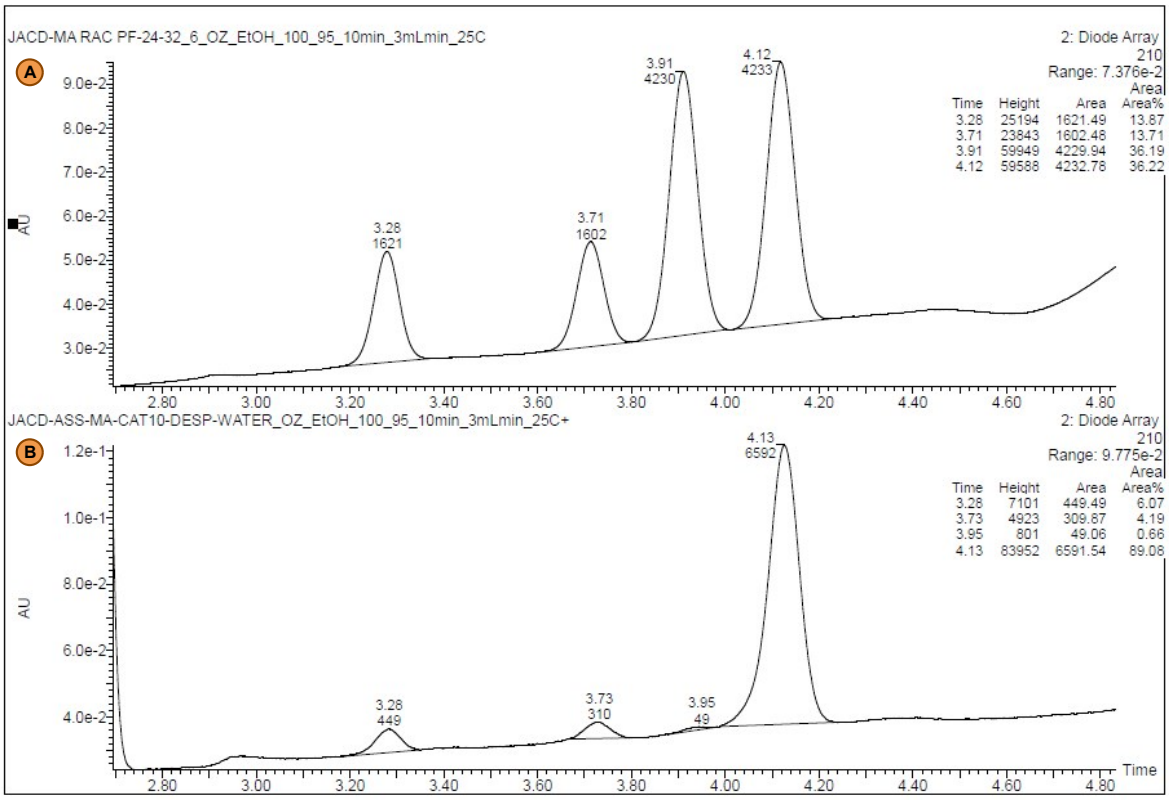


FIGURE 51. (a) Chiral UPC² of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC² of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3h**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.95 min, (syn, major) = 4.13 min. TABLE 2, Entry 8.

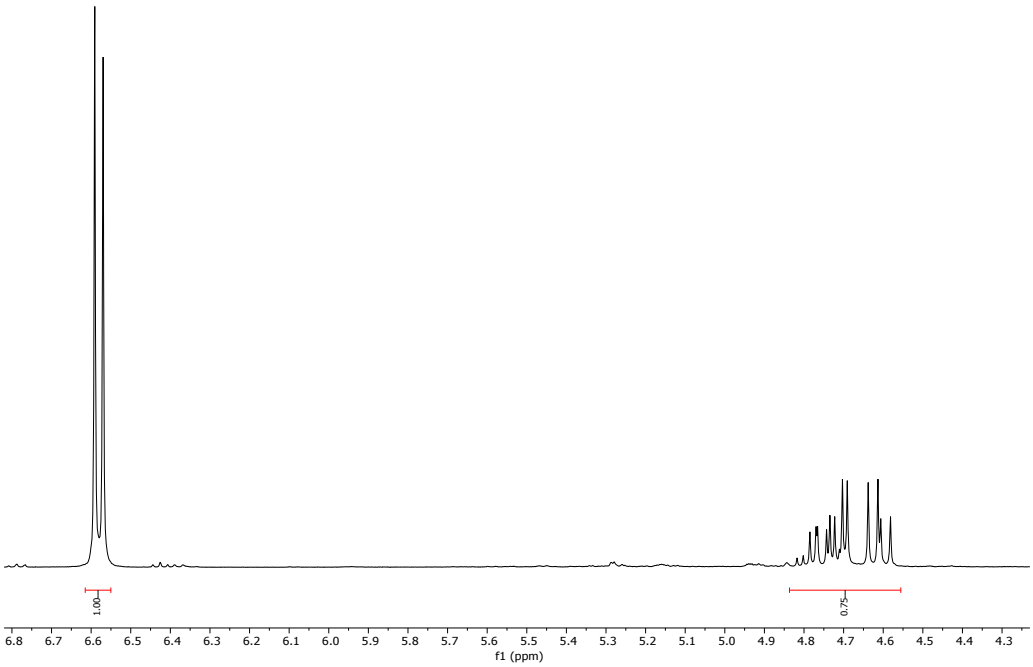


FIGURE 52. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3i** with 1, 2, 3-trimethoxybenzene as standard. Yield: 75%. TABLE 2, Entry 9.

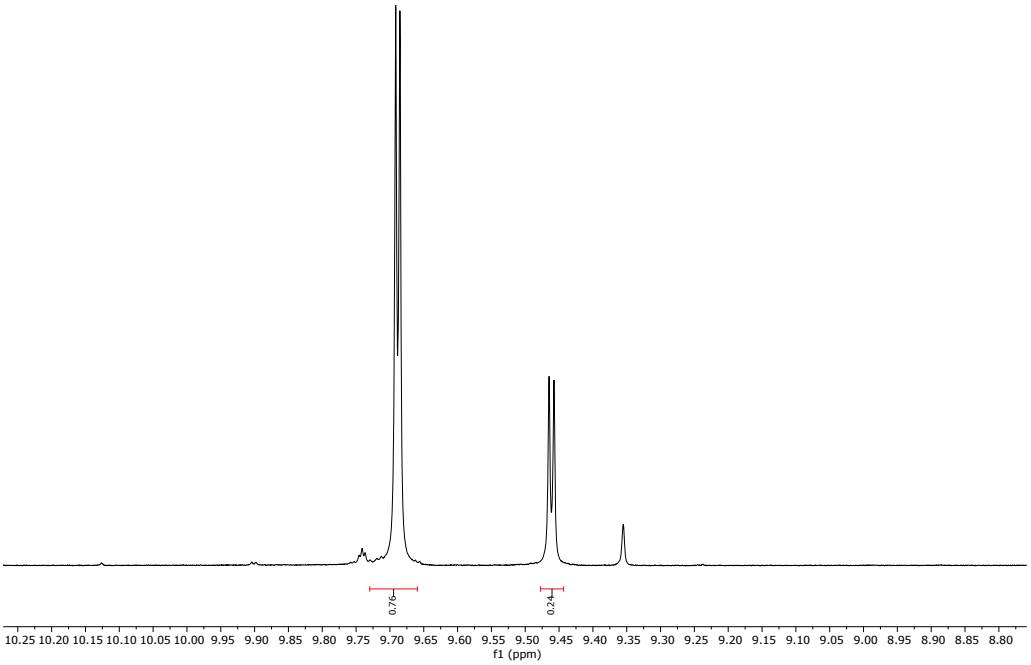


FIGURE 53. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3i**. Diastereoisomeric ratio (*syn/anti*): 76:24. TABLE 2, Entry 9.

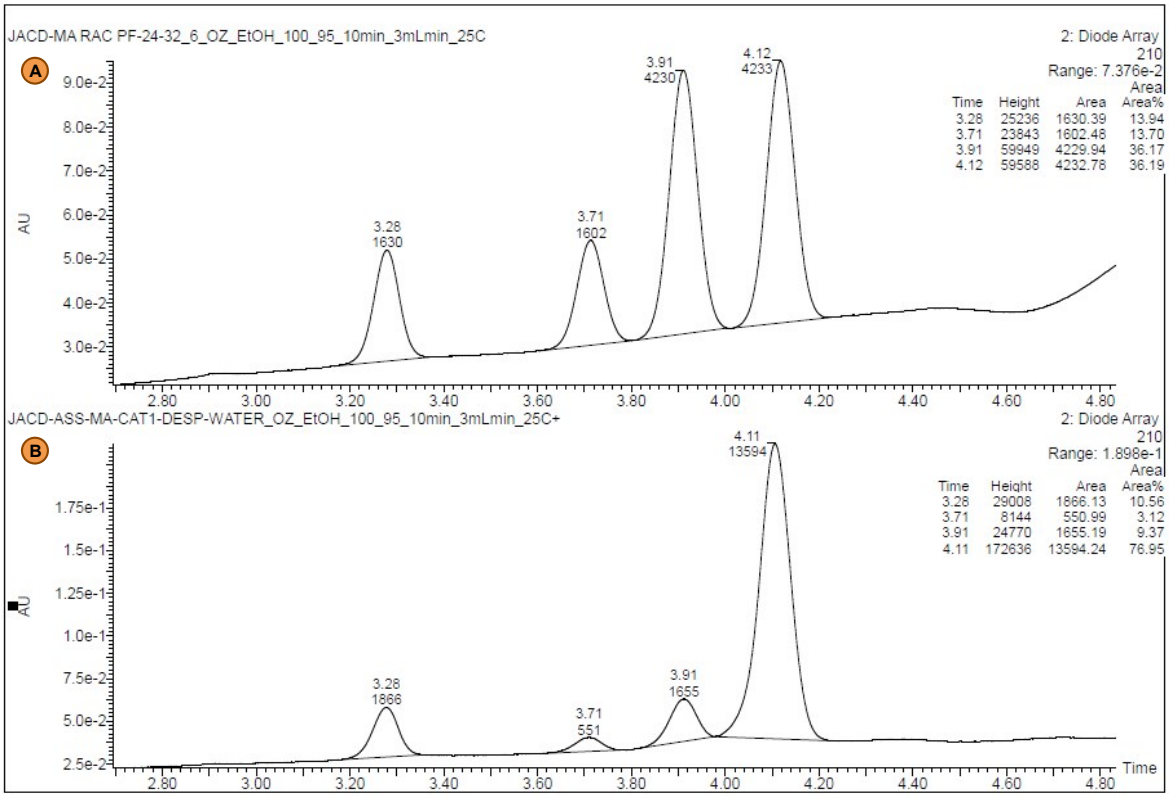


FIGURE 54. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3i**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.91 min, (syn, major) = 4.11 min. TABLE 2, Entry 9.

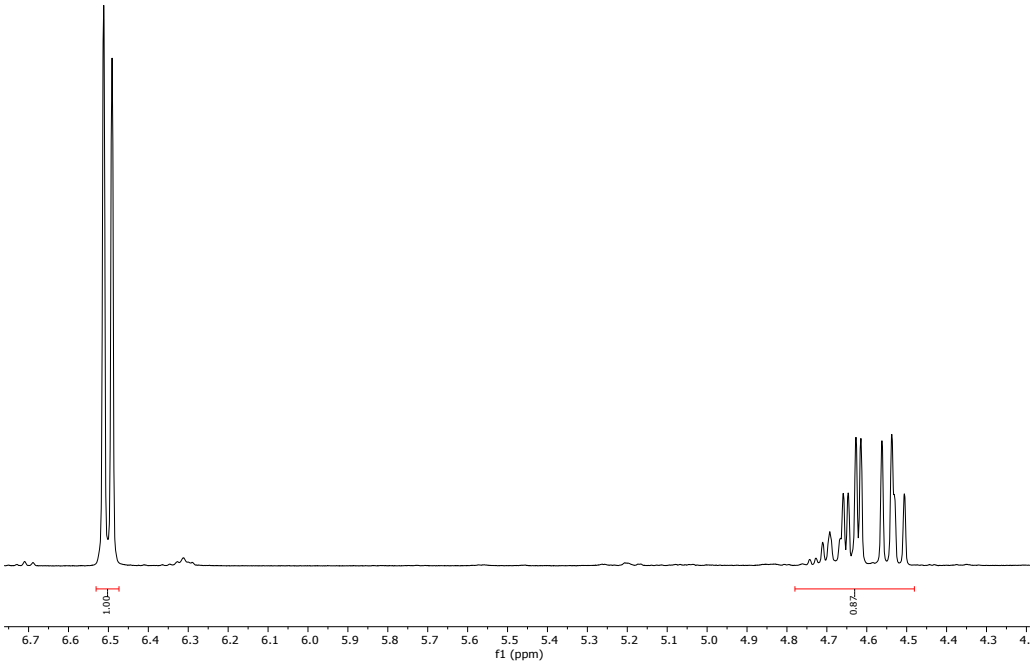


FIGURE 55. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3j** with 1, 2, 3-trimethoxybenzene as standard. Yield: 87%. TABLE 2, Entry 10.

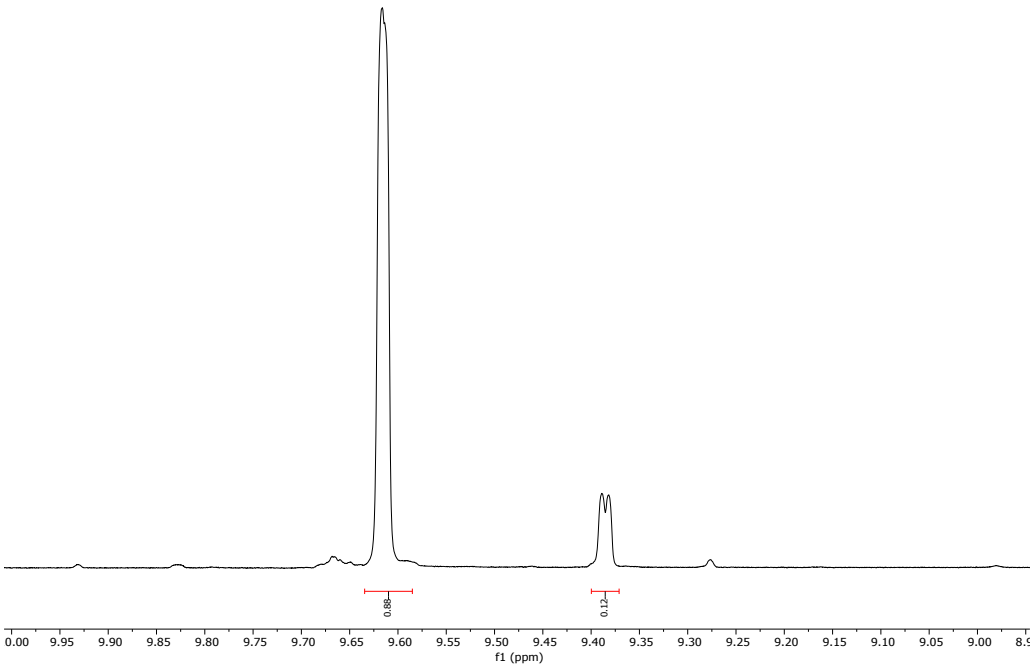


FIGURE 56. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3j**. Diastereoisomeric ratio (*syn/anti*): 88:12. TABLE 2, Entry 10.

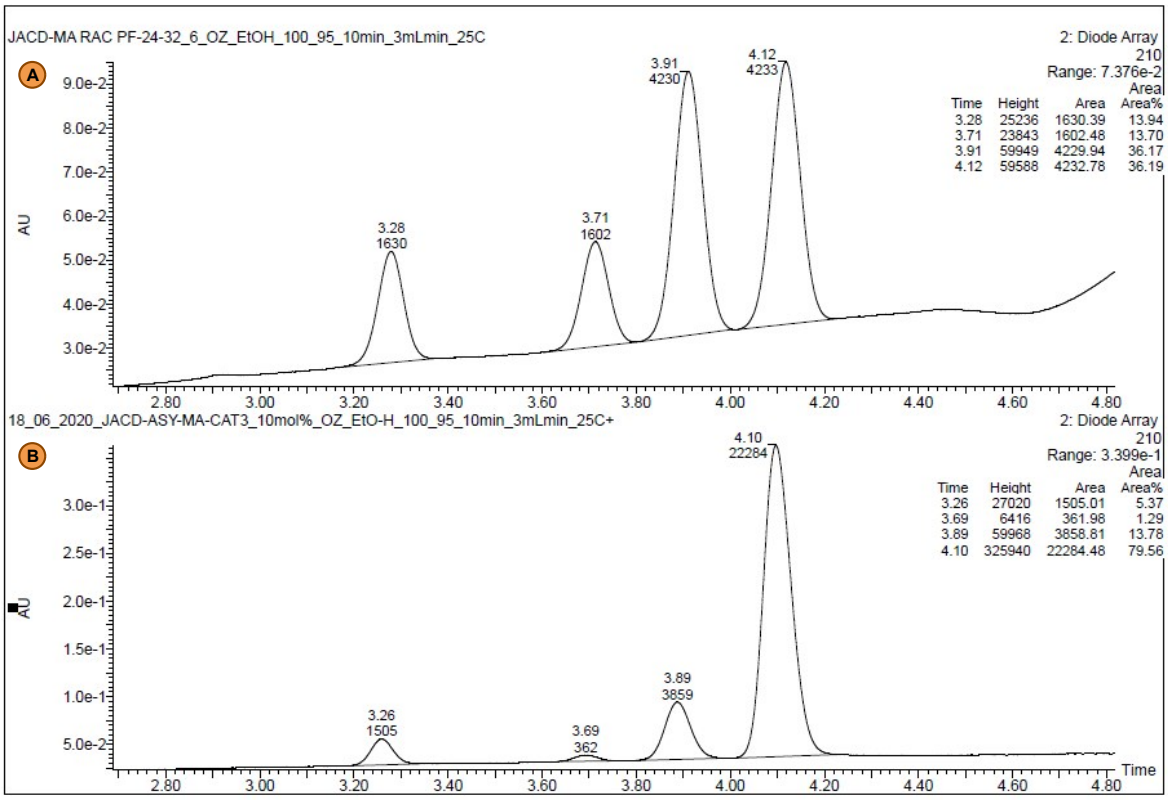


FIGURE 57. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3j**. Trefoil CEL2, Grad: CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: Rt: (syn, minor) = 3.89 min, (syn, major) = 4.10 min. TABLE 2, Entry 10.

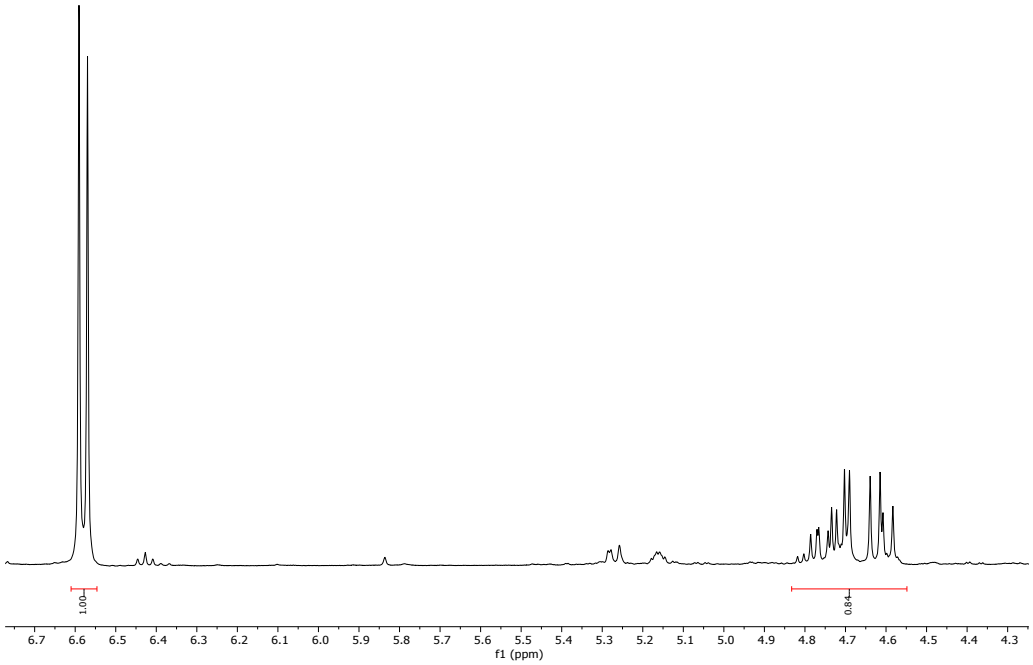


FIGURE 58. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3k** with 1, 2, 3-trimethoxybenzene as standard. Yield: 84%. TABLE 2, Entry 11.

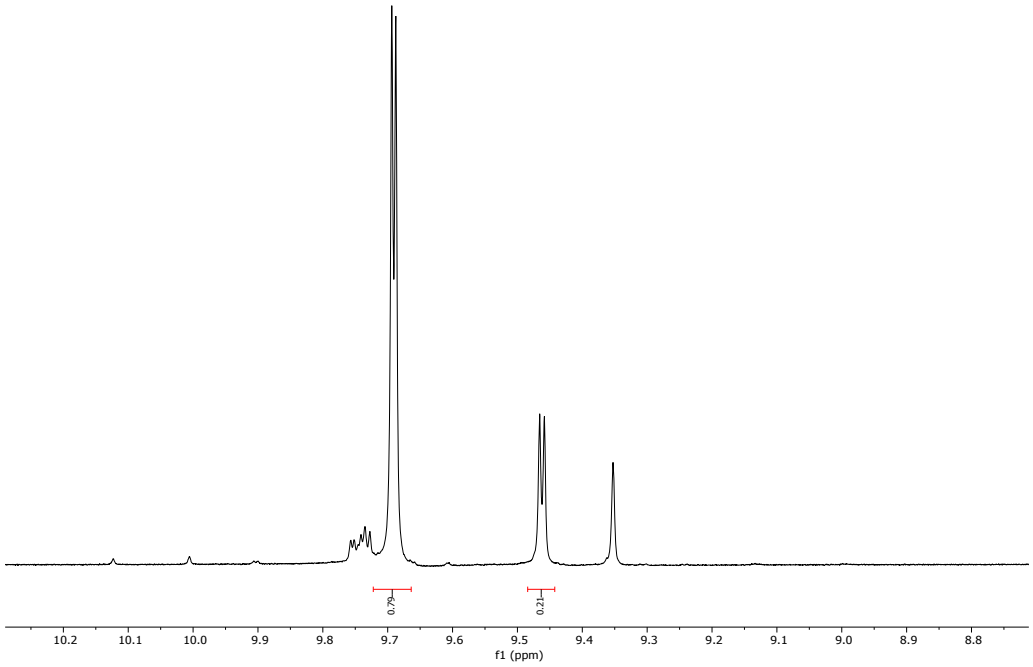


FIGURE 59. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 10 mol% of compound **3k**. Diastereoisomeric ratio (*syn/anti*): 79:21. TABLE 2, Entry 11.

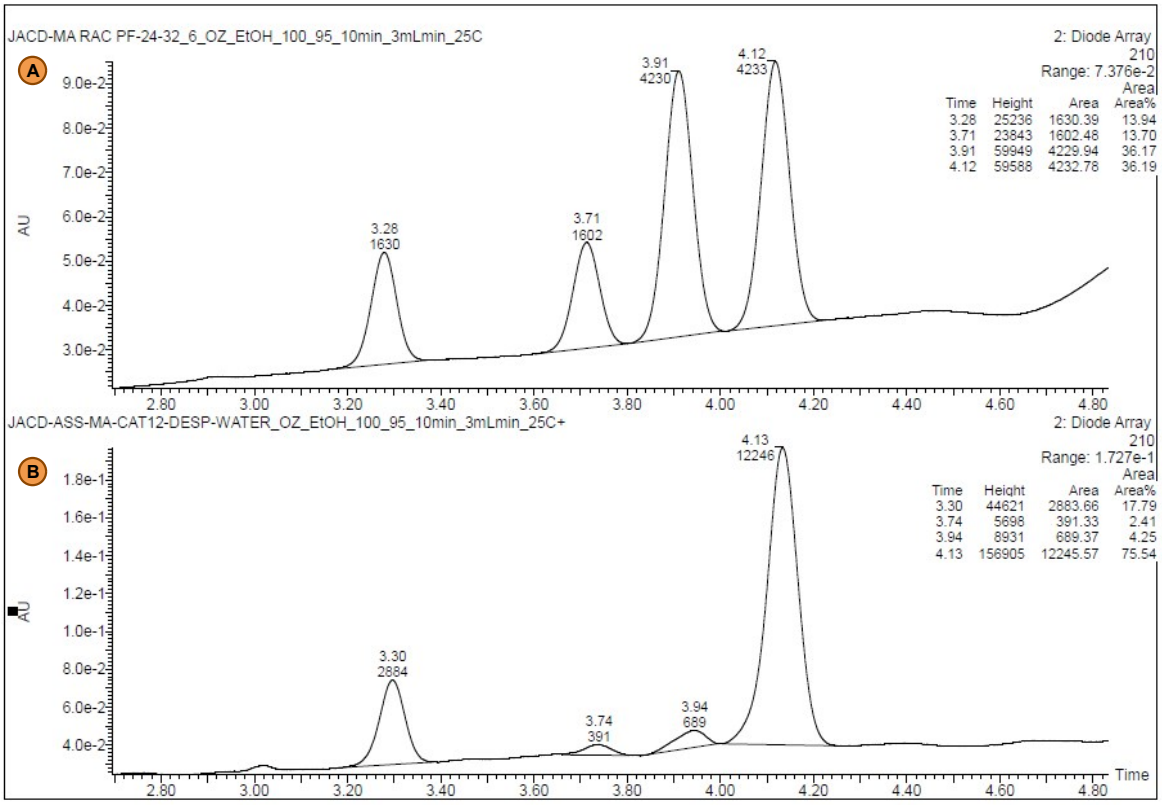


FIGURE 60. (a) Chiral UPC² of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC² of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 10 mol% of compound **3k**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.94 min, (syn, major) = 4.13 min. TABLE 2, Entry 11.

16. NMR Spectra and Chromatograms: Optimization

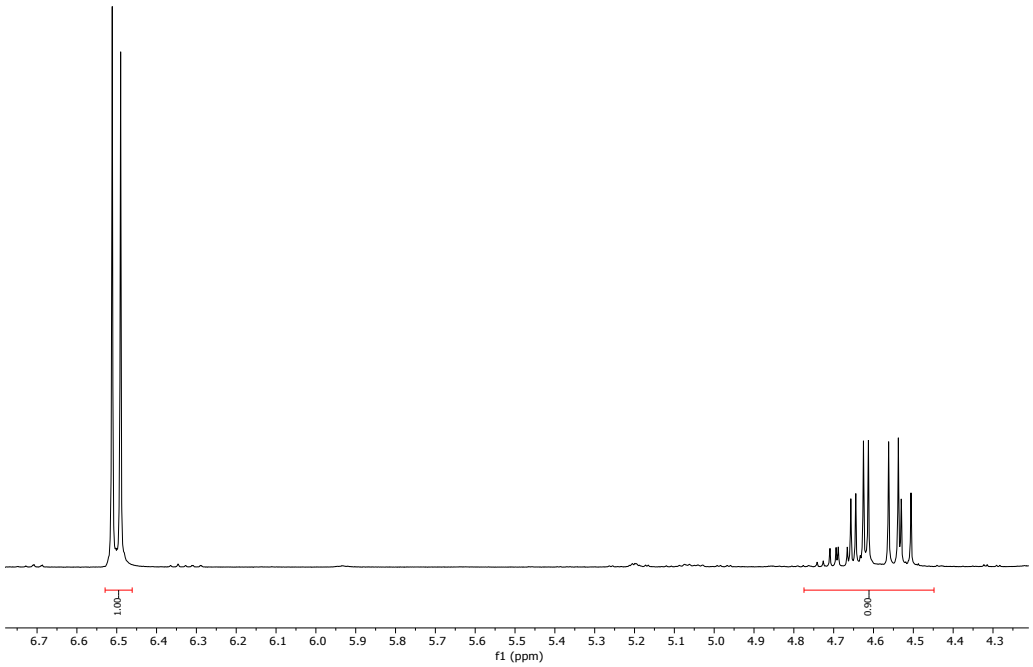


FIGURE 61. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 5 mol% of compound **3e** with 1, 2, 3-trimethoxybenzene as standard. Yield: 90%. TABLE 3, Entry 1.

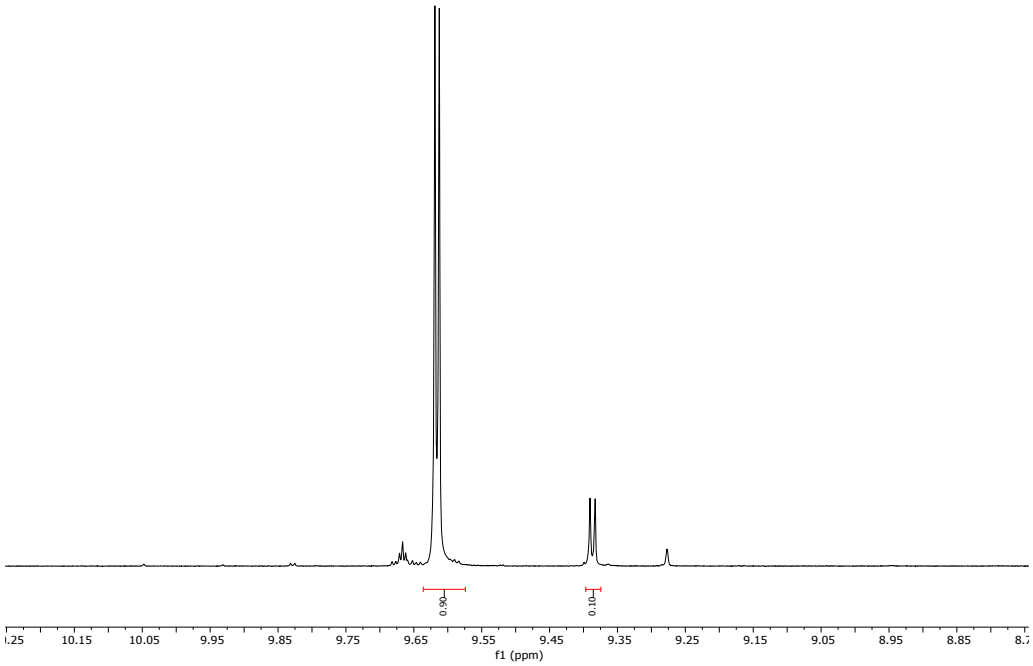


FIGURE 62. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 90:10. TABLE 3, Entry 1.

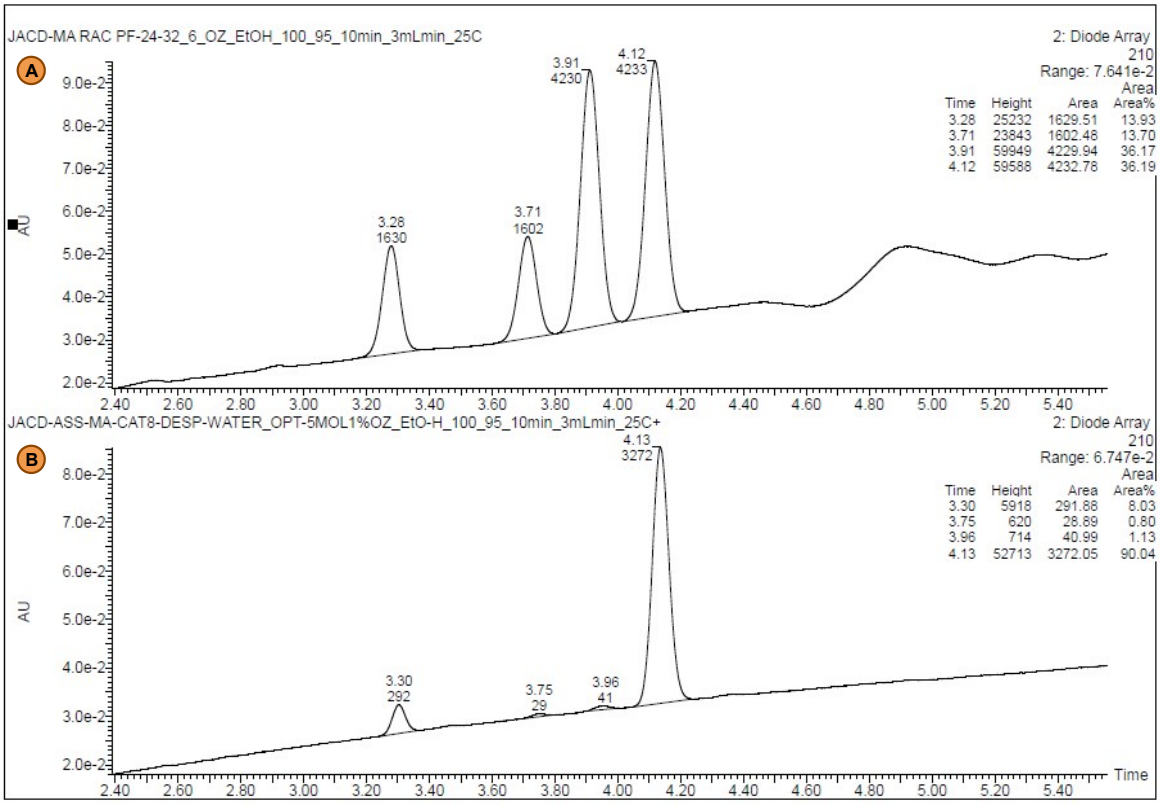


FIGURE 63. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.96 min, (syn, major) = 4.13 min. TABLE 3, Entry 1.

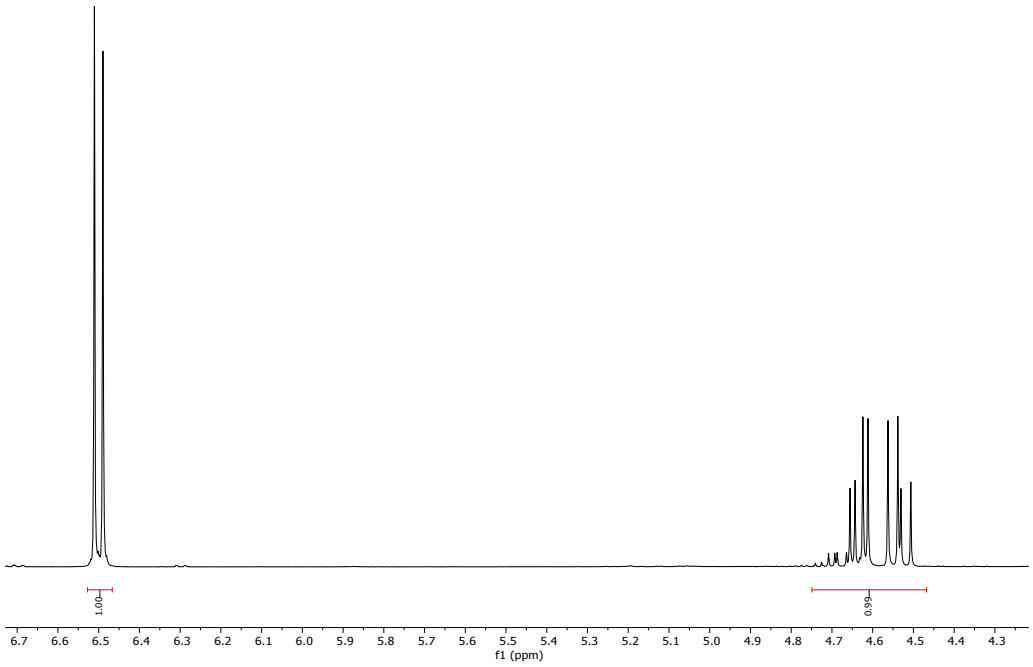


FIGURE 64. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** with 1, 2, 3-trimethoxybenzene as standard. Yield: 99%. TABLE 3, Entry 2.

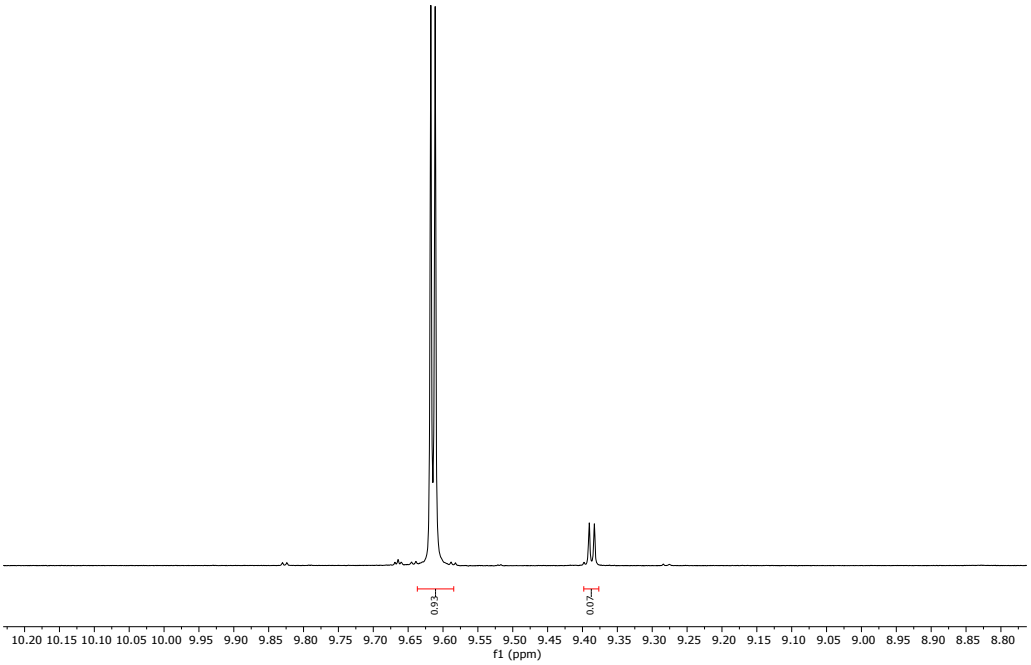


FIGURE 65. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 93:07. TABLE 3, Entry 2. TABLE 4, Entry 1.

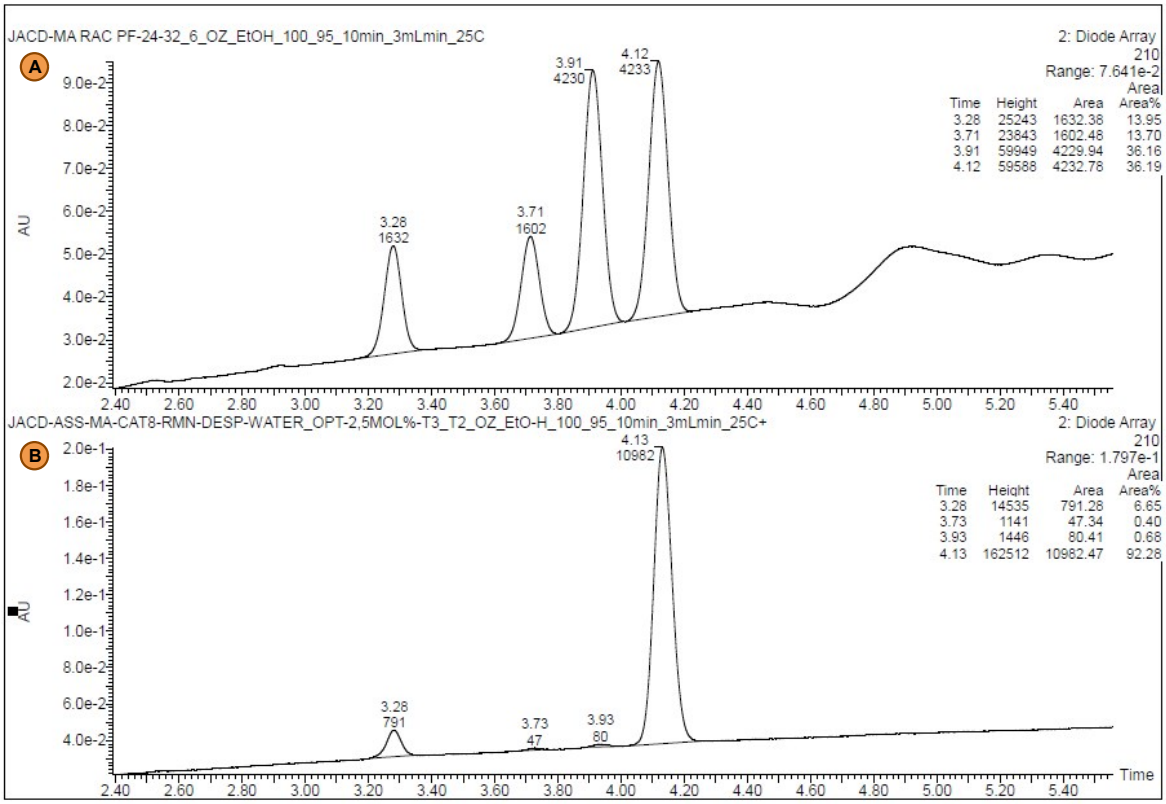


FIGURE 66. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.93 min, (syn, major) = 4.13 min. TABLE 3, Entry 2. TABLE 4, Entry 1.

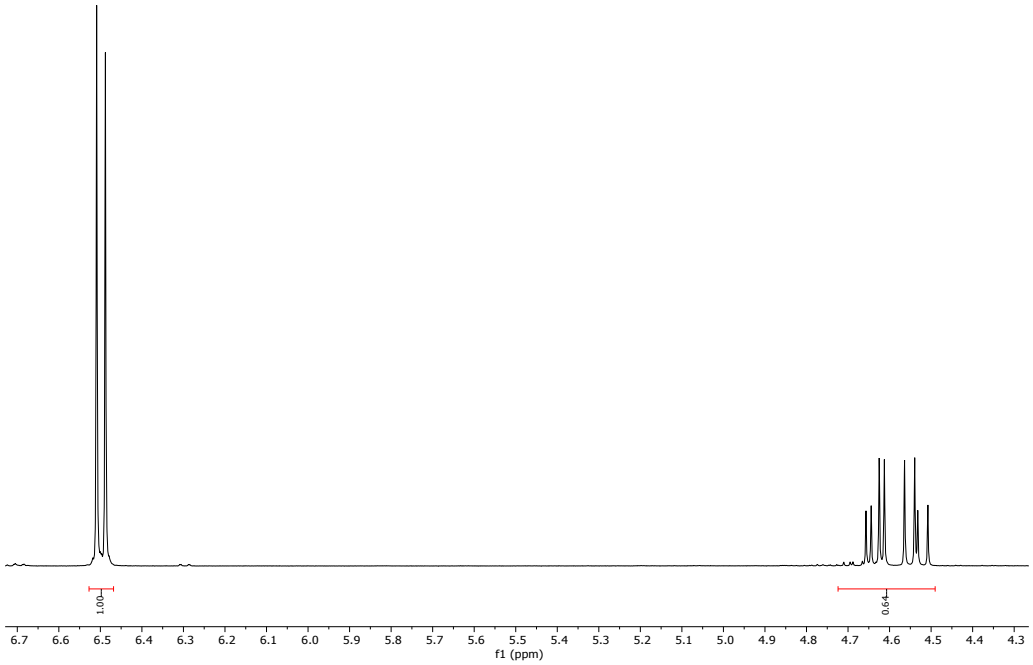


FIGURE 67. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 1 mol% of compound **3e** with 1, 2, 3-trimethoxybenzene as standard. Yield: 64%. TABLE 3, Entry 3.

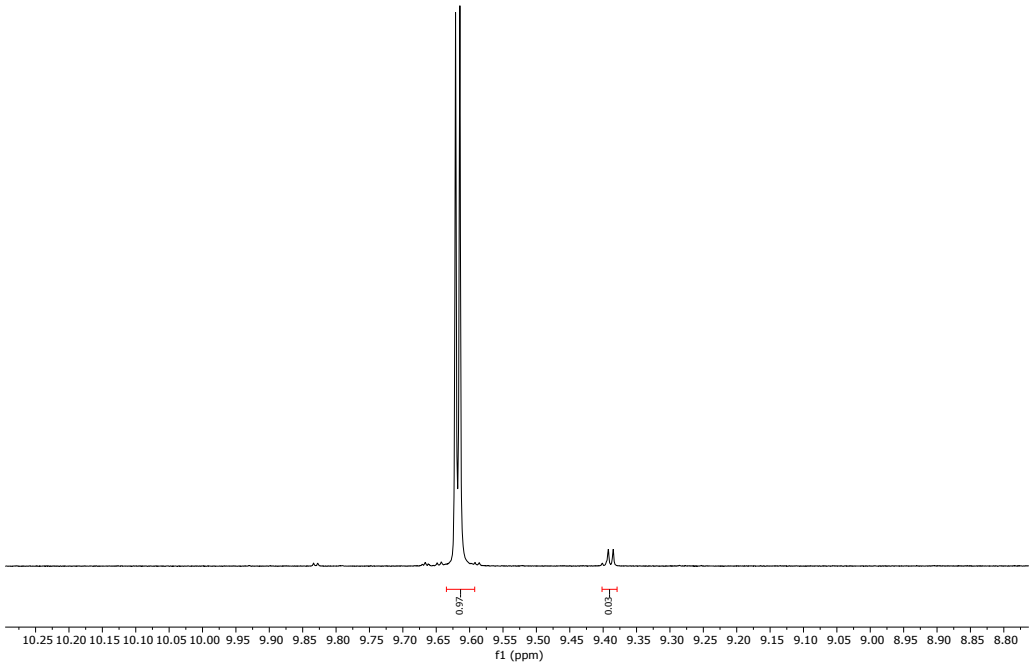


FIGURE 68. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 1 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 97:03. TABLE 3, Entry 3.

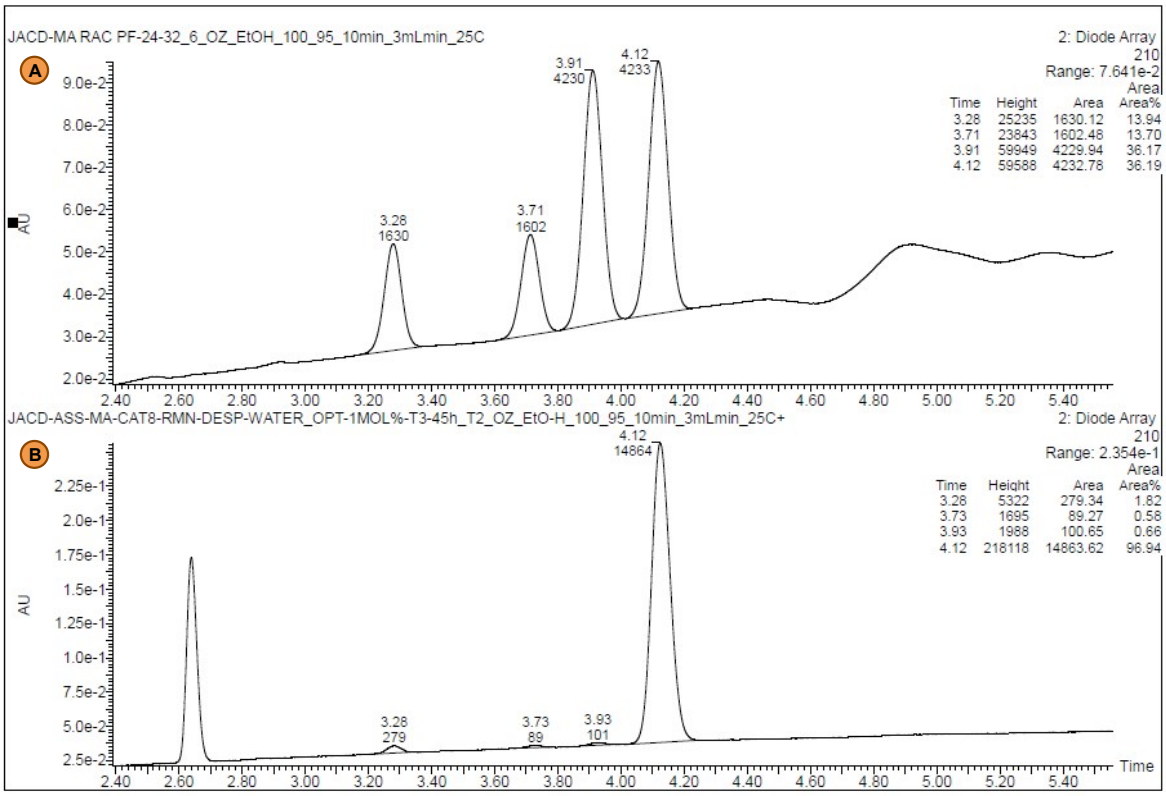


FIGURE 69. (a) Chiral UPC² of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC² of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 1 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.93 min, (syn, major) = 4.12 min. TABLE 3, Entry 3.

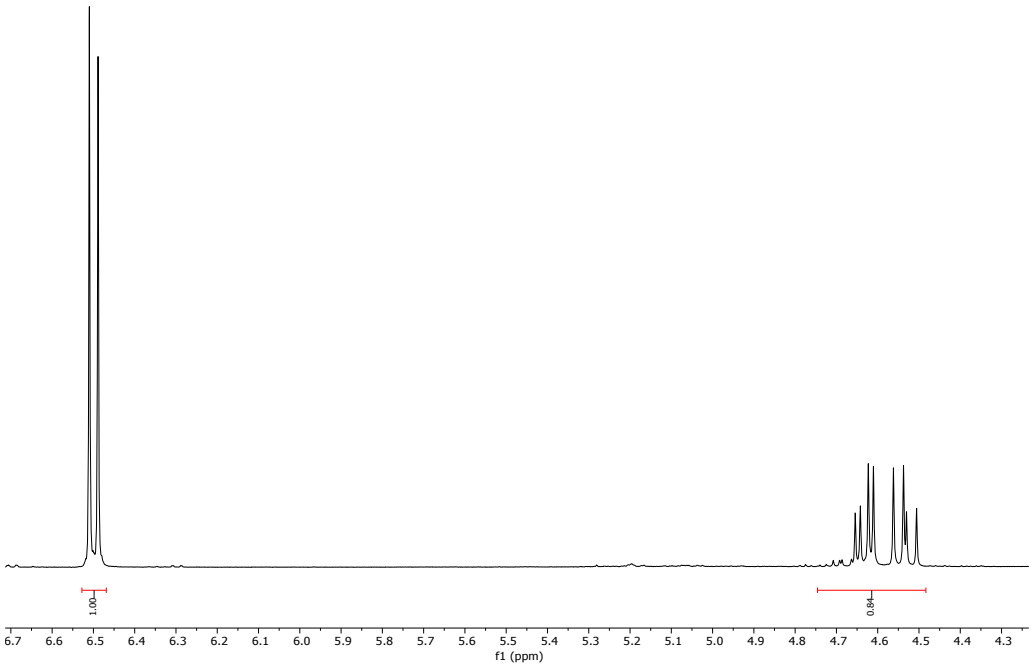


FIGURE 70. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in Brine as a solvent; 1, 2, 3-trimethoxybenzene as standard. Yield: 84%. TABLE 3, Entry 4.

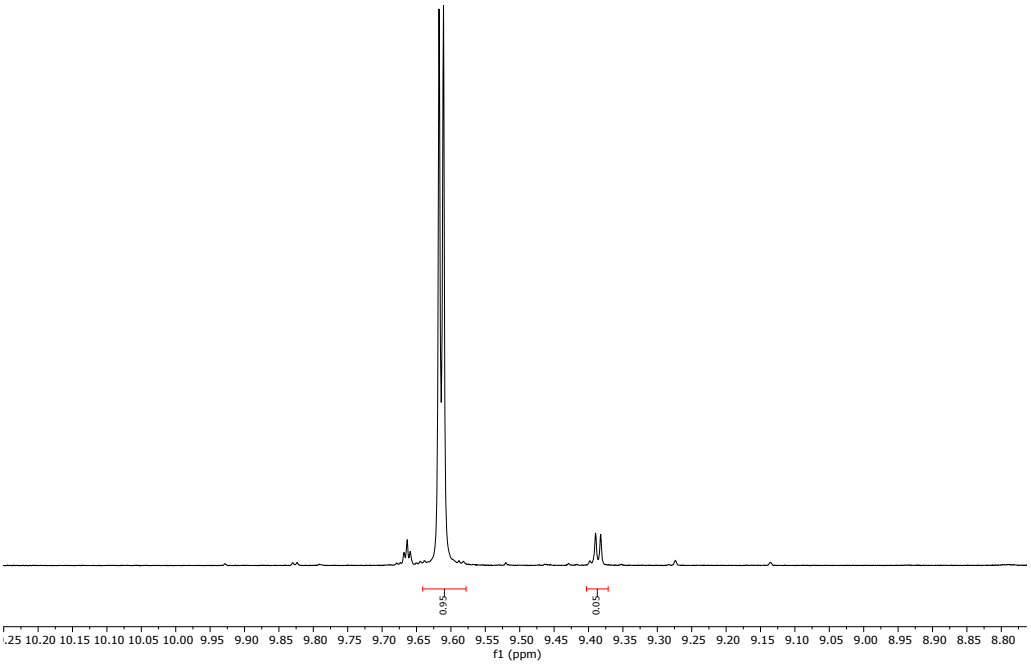


FIGURE 71. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in Brine as a solvent. Diastereoisomeric ratio (*syn/anti*): 95:05. TABLE 3, Entry 4.

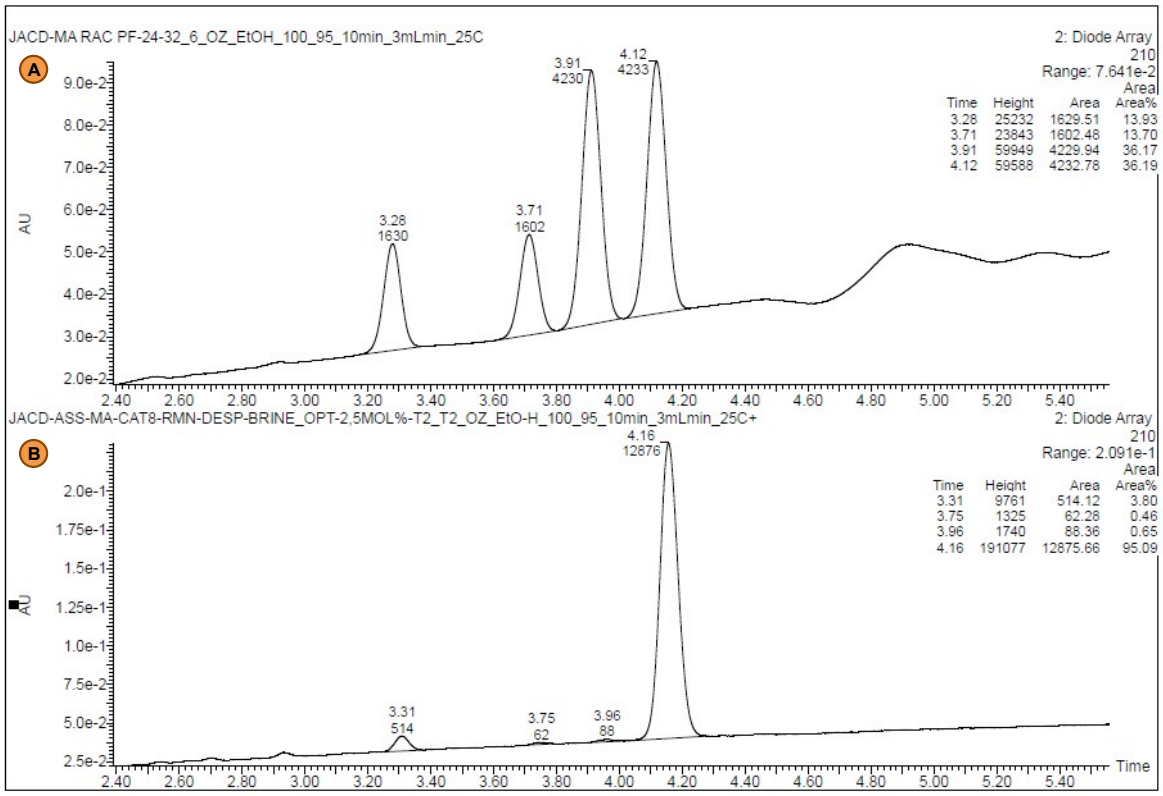


FIGURE 72. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in Brine as a solvent. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.96 min, (syn, major) = 4.16 min. TABLE 3, Entry 4.

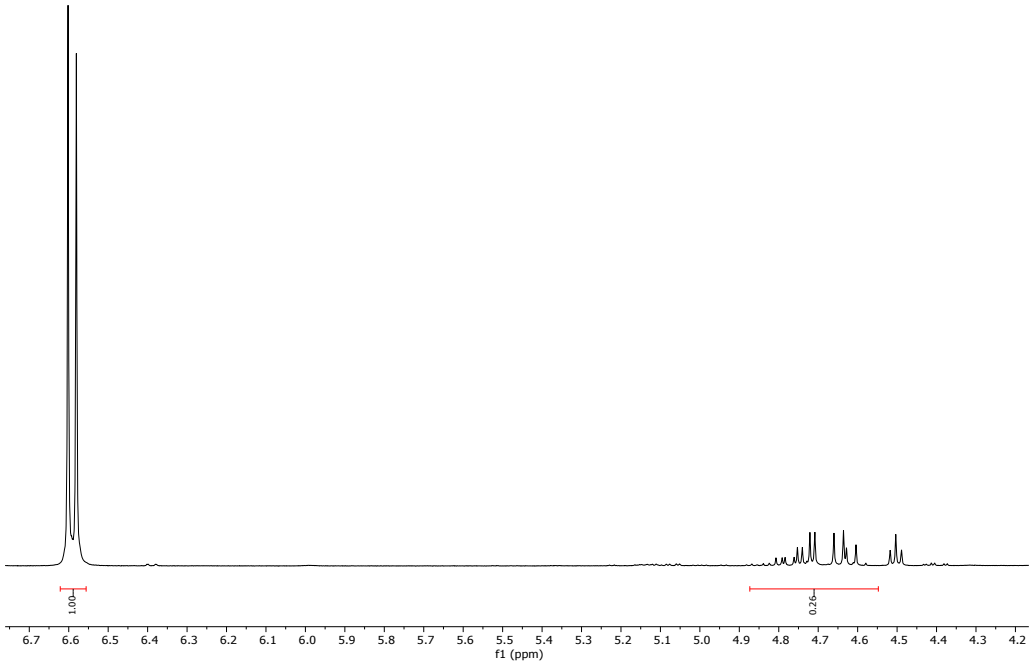


FIGURE 73. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in Ethanol as a solvent; 1, 2, 3-trimethoxybenzene as standard. Yield: 26%. TABLE 3, Entry 5.

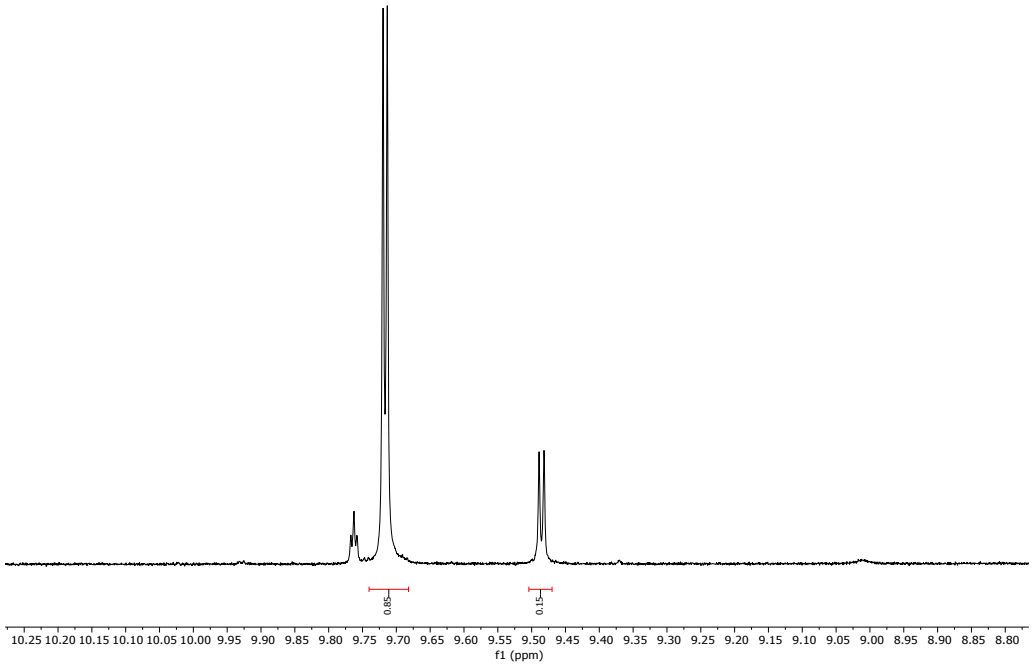


FIGURE 74. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in Ethanol as a solvent. Diastereoisomeric ratio (*syn/anti*): 85:15. TABLE 3, Entry 5.

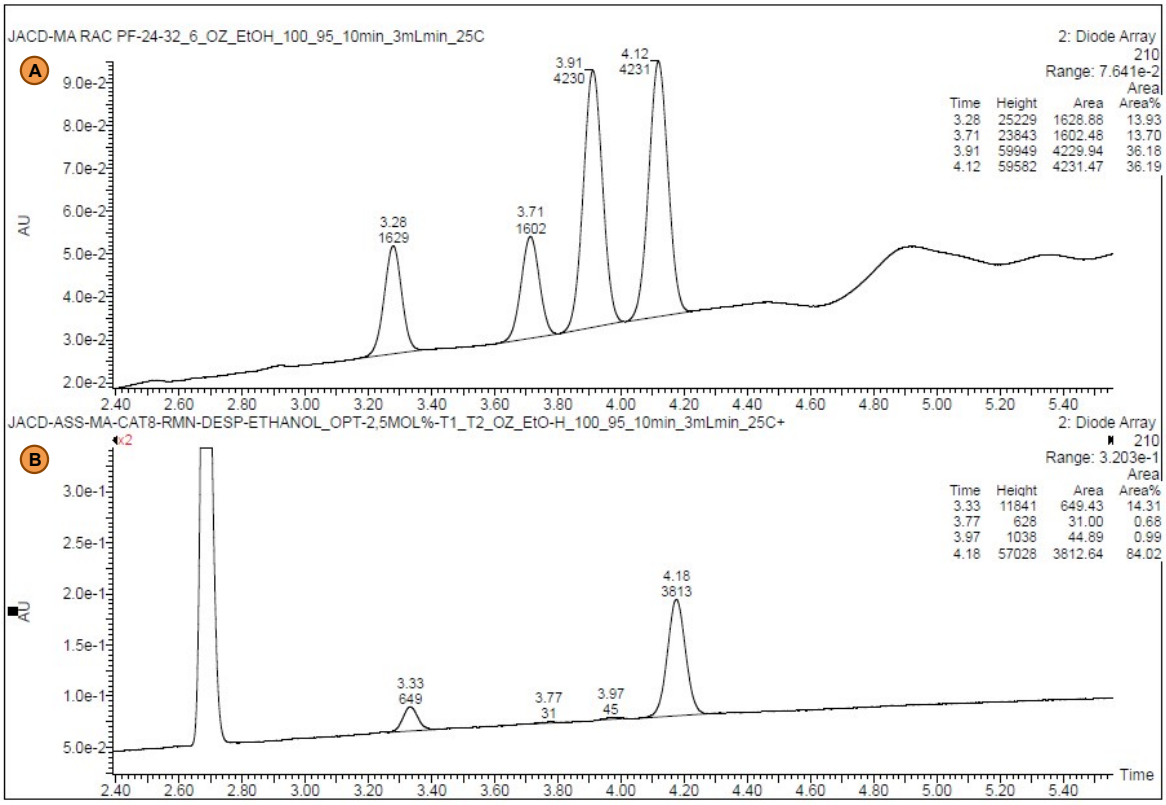


FIGURE 75. (a) Chiral UPC² of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC² of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in Ethanol as a solvent. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.97 min, (syn, major) = 4.18 min. TABLE 3, Entry 5.

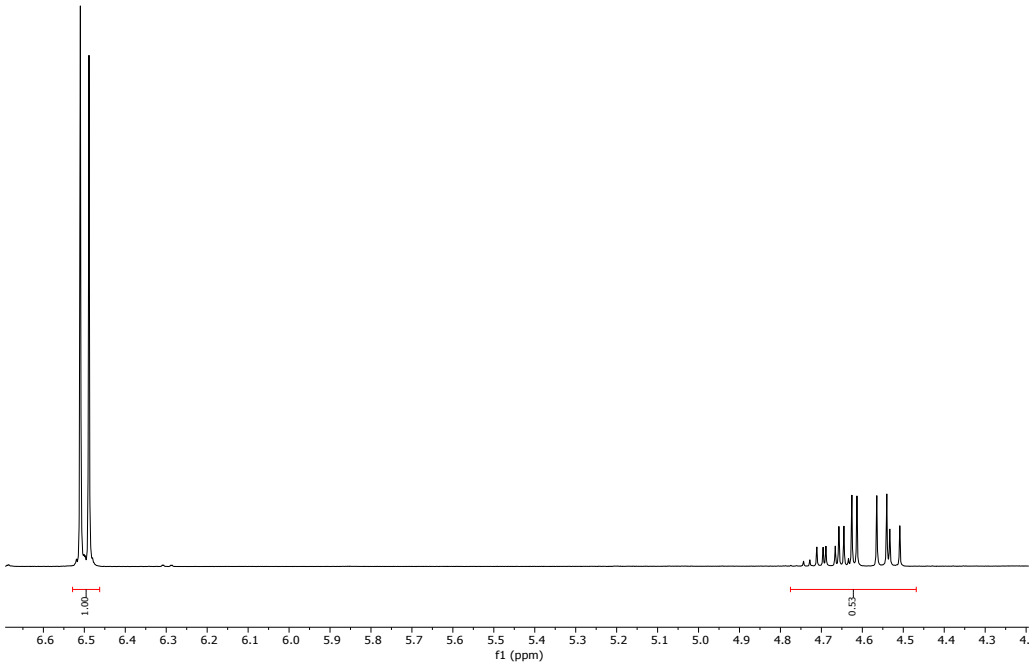


FIGURE 76. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in PEG-300 as a solvent; 1, 2, 3-trimethoxybenzene as standard. Yield: 53%. TABLE 3, Entry 6.

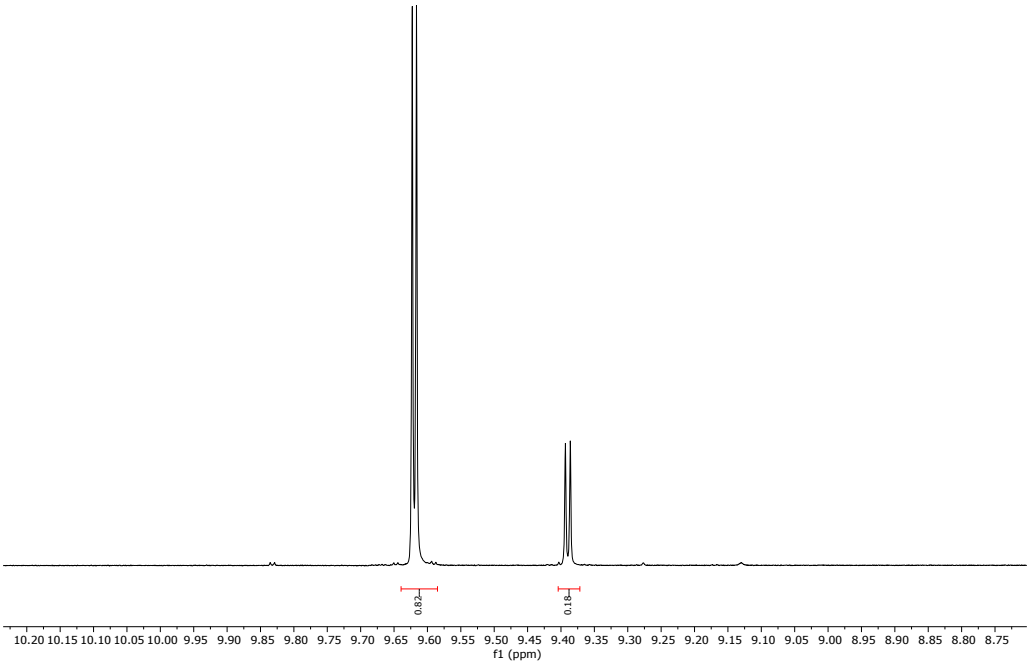


FIGURE 77. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in PEG-300 as a solvent. Diastereoisomeric ratio (*syn/anti*): 82:18. TABLE 3, Entry 6.

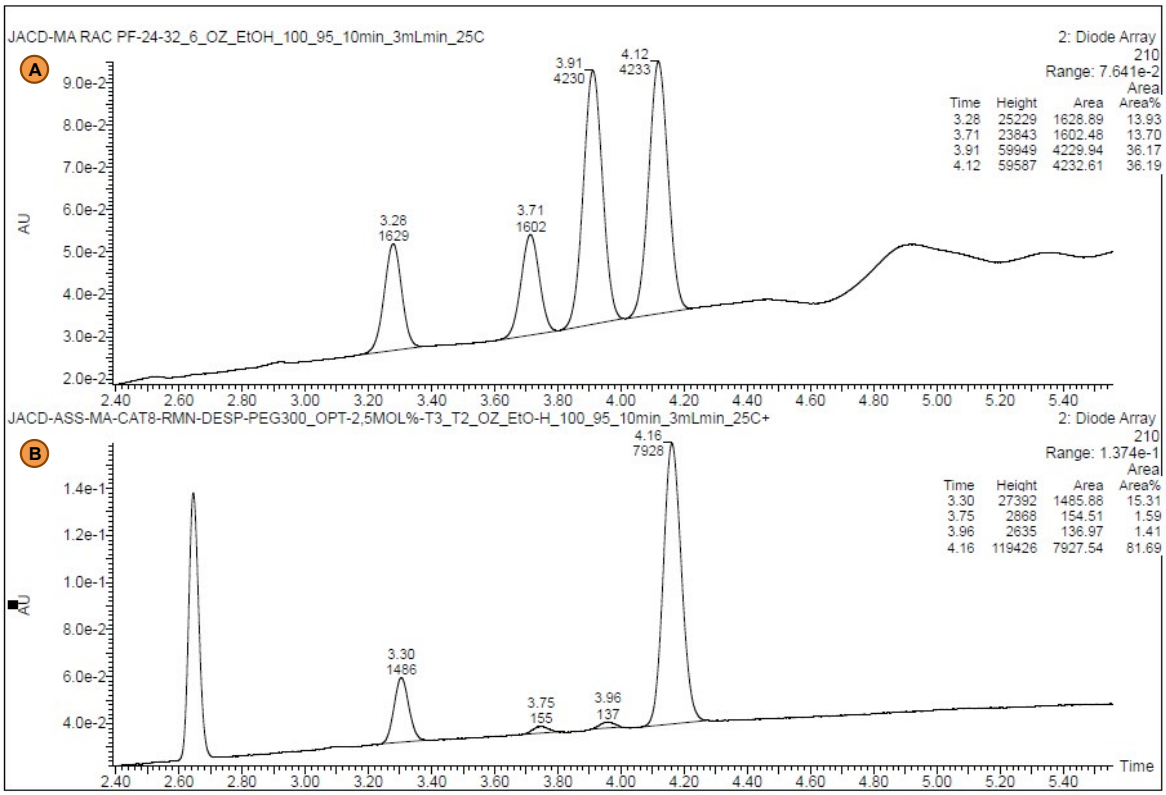


FIGURE 78. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in PEG-300 as a solvent. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.96 min, (syn, major) = 4.16 min. TABLE 3, Entry 6.

17. NMR Spectra: Scope

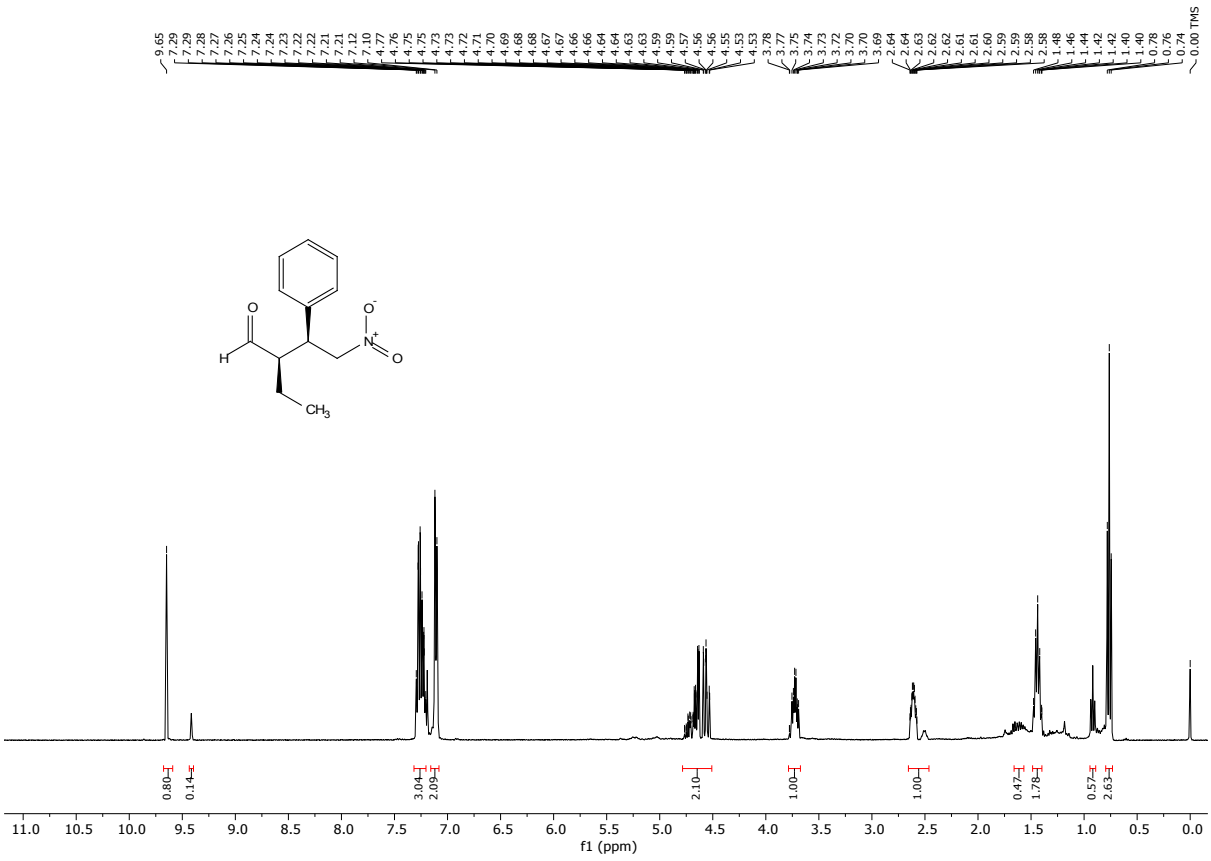


FIGURE 79. ^{1}H NMR of compound **4a** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 85:15.

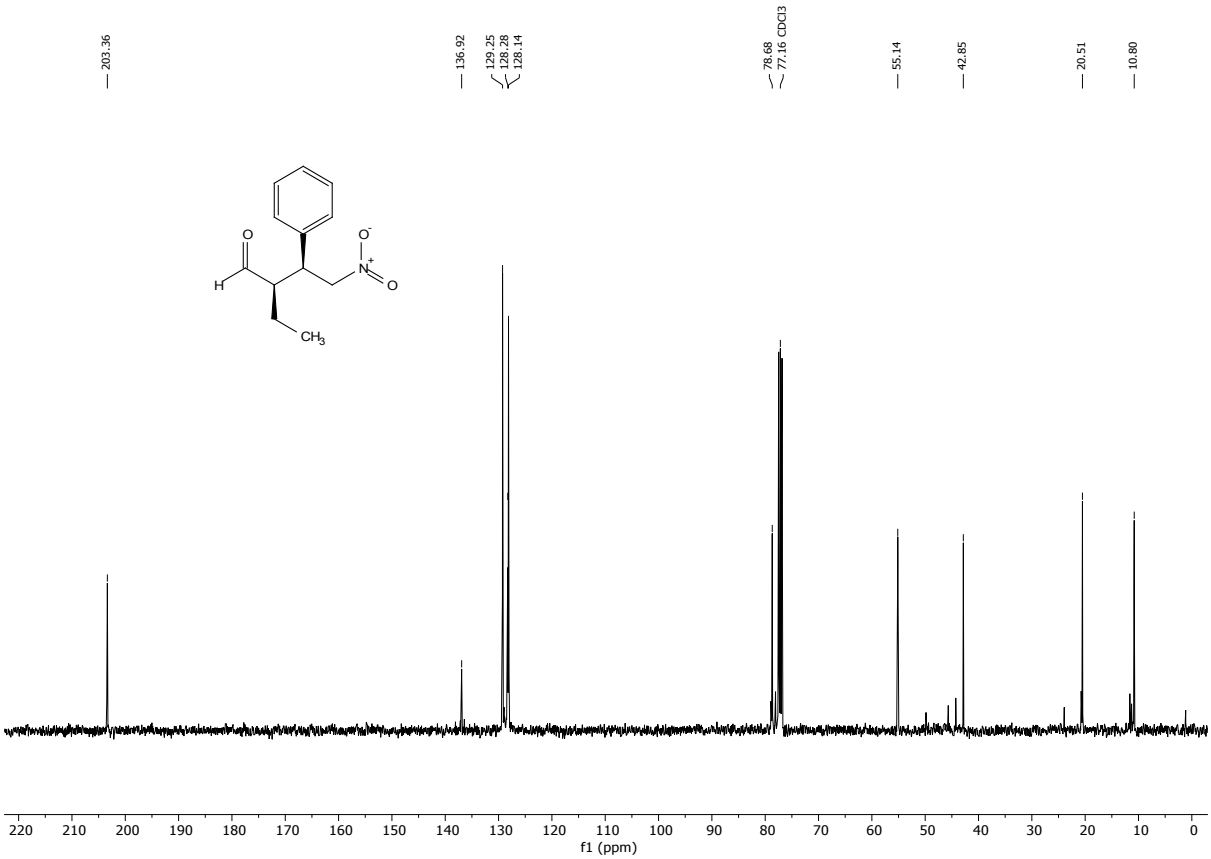


FIGURE 80. ^{13}C NMR of compound **4a** (100 MHz, $CDCl_3$).

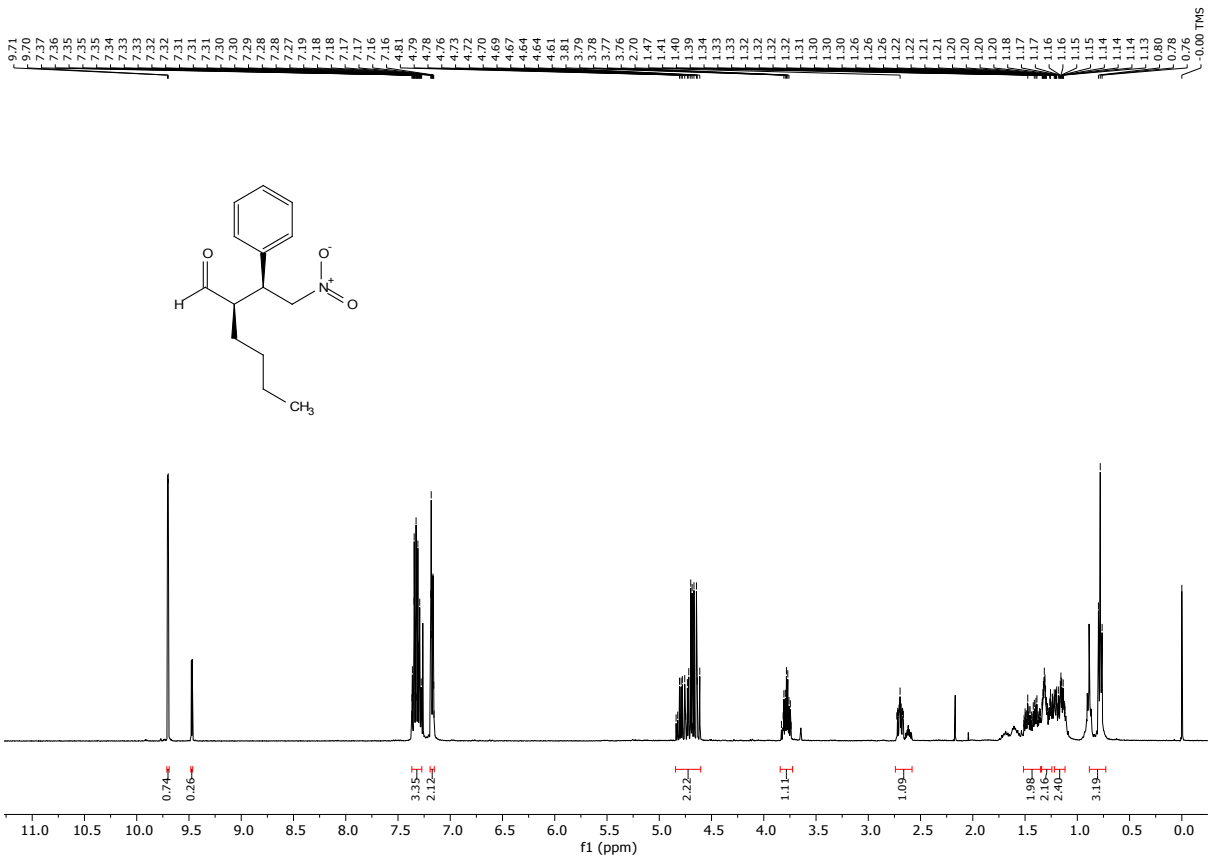


FIGURE 81. ^{1}H NMR of compound **4b** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 74:26.

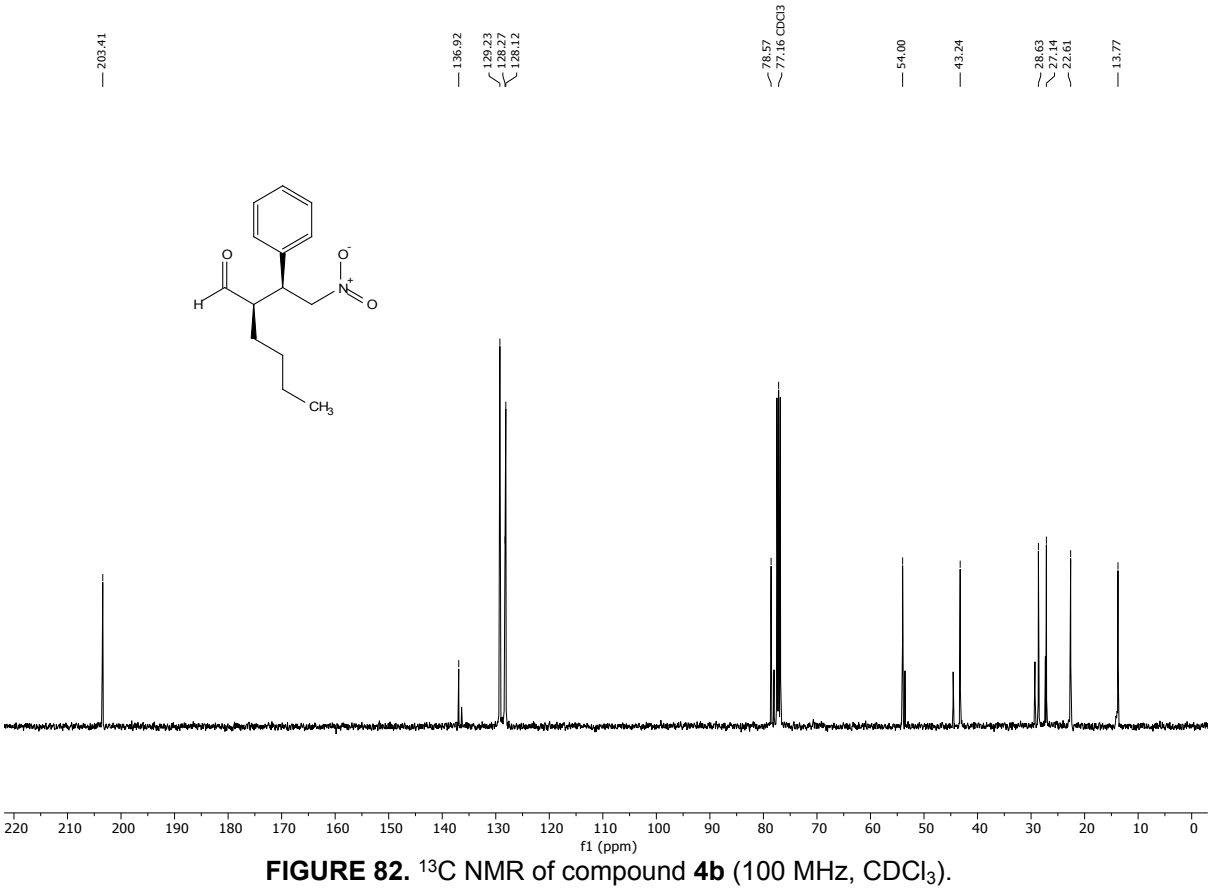


FIGURE 82. ^{13}C NMR of compound **4b** (100 MHz, $CDCl_3$).

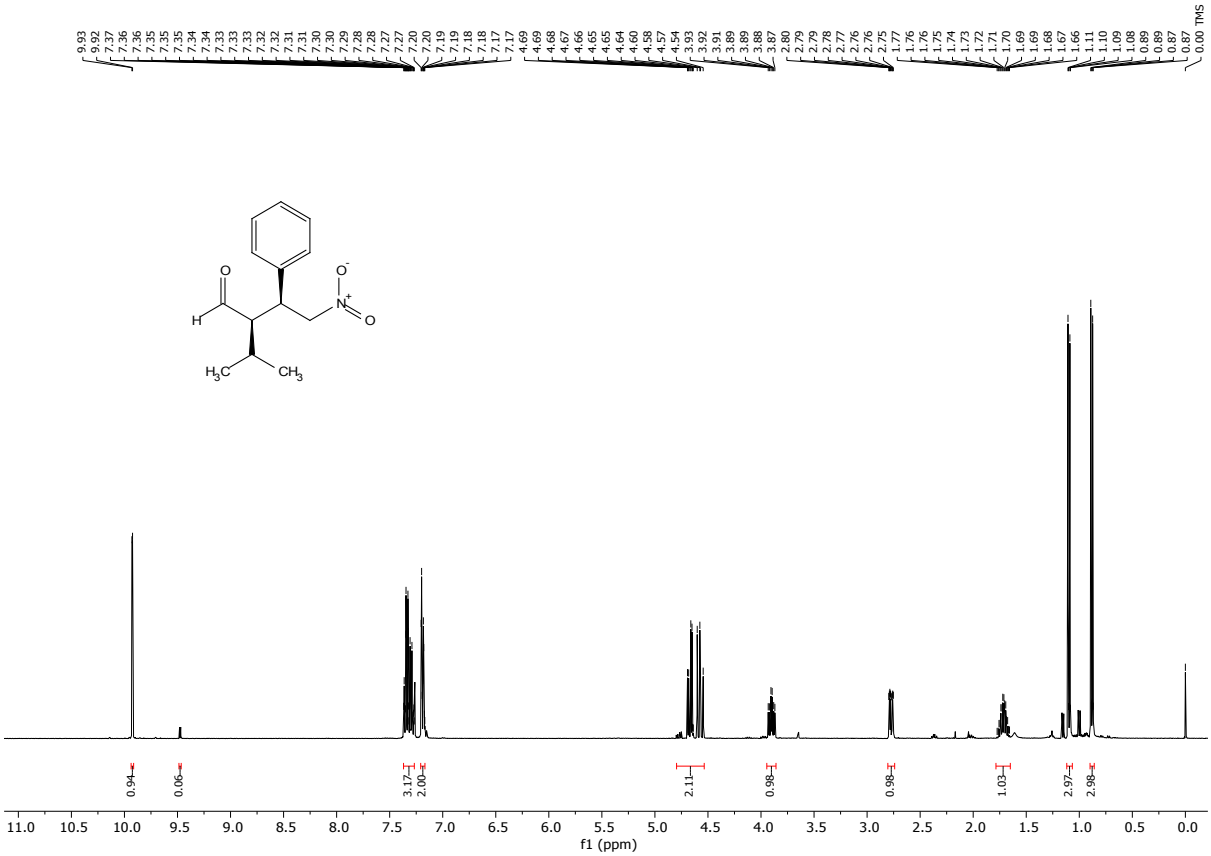


FIGURE 83. ^{1}H NMR of compound **4c** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 94:06.

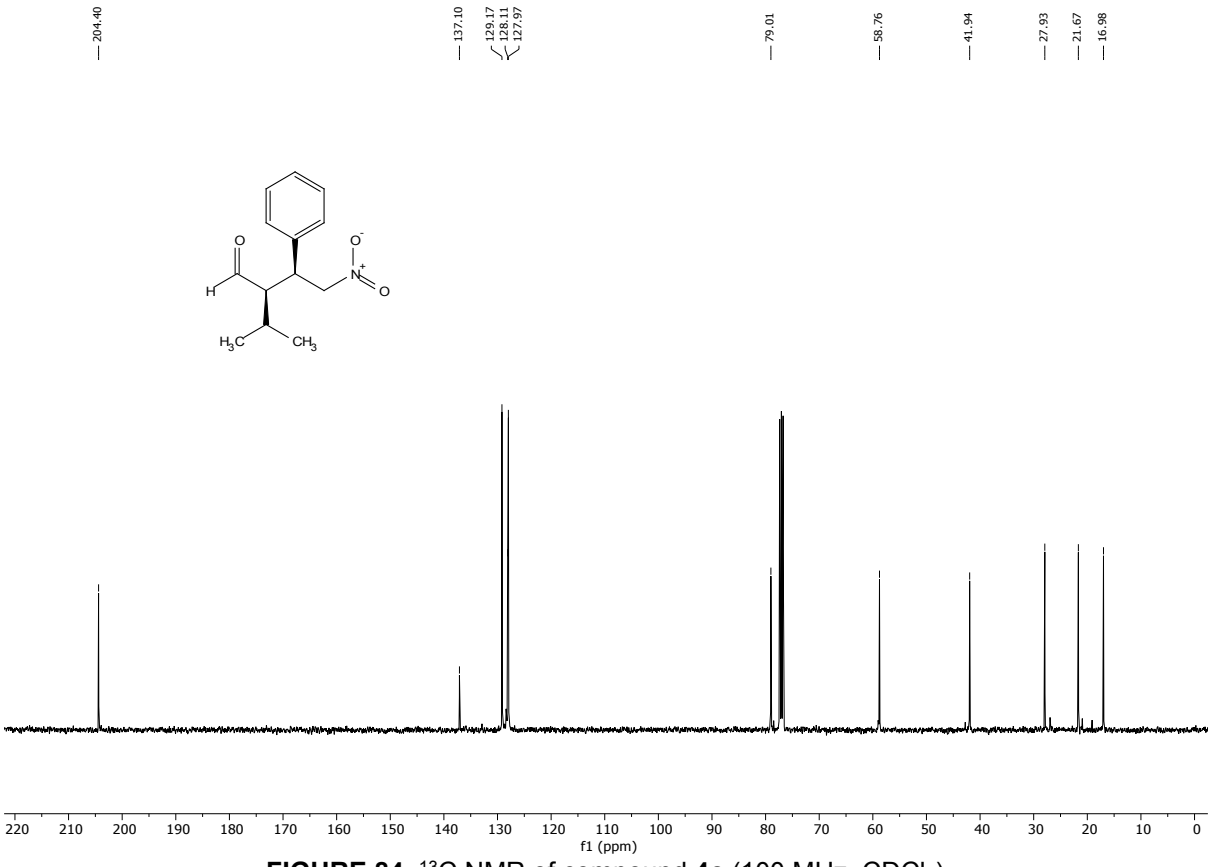


FIGURE 84. ^{13}C NMR of compound **4c** (100 MHz, $CDCl_3$).

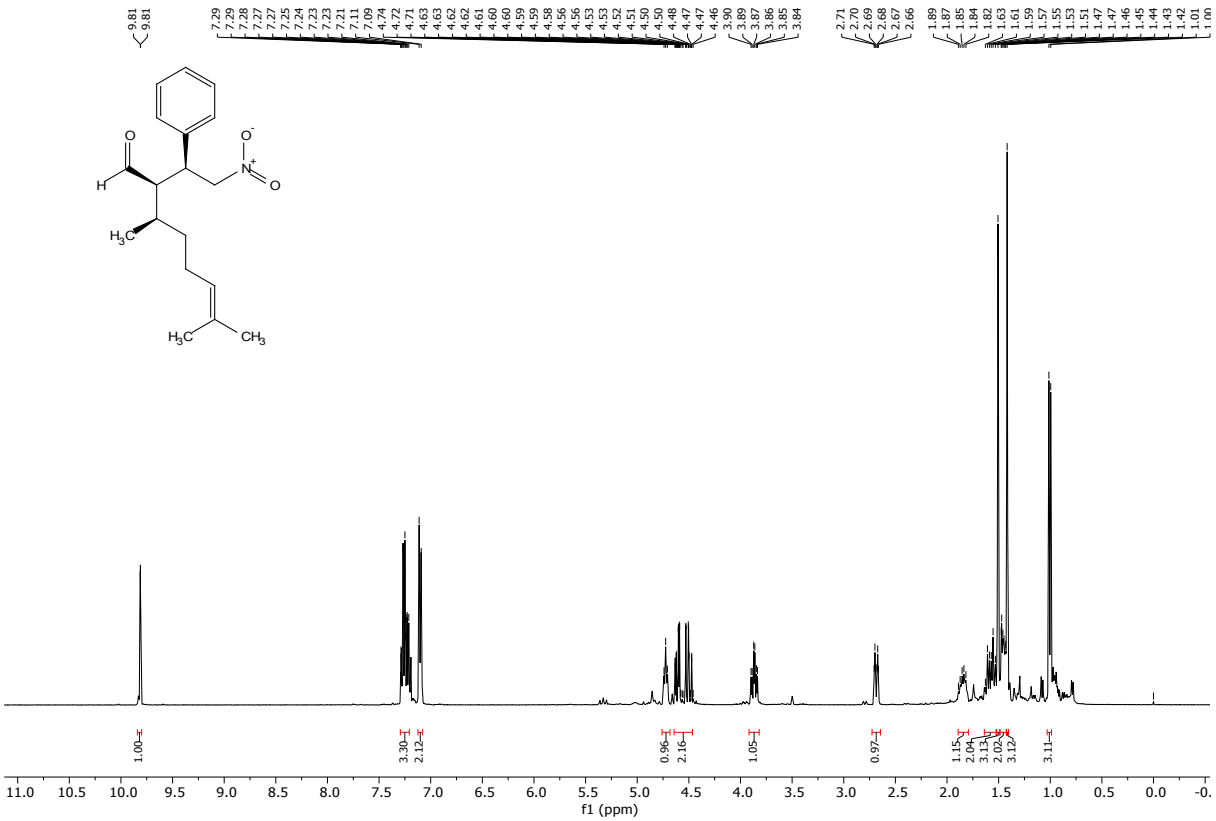


FIGURE 85. ^{1}H NMR of compound **4d** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 92:08.

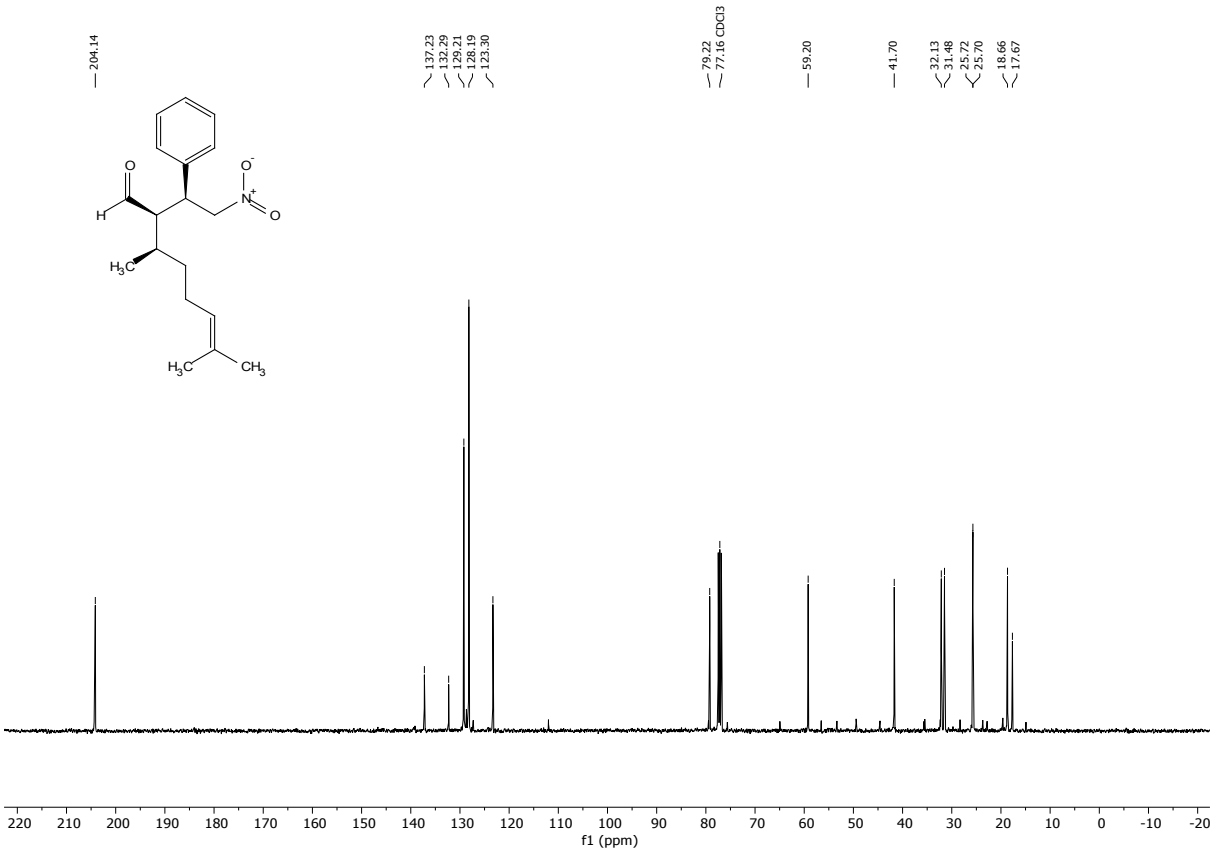


FIGURE 86. ^{13}C NMR of compound **4d** (100 MHz, $CDCl_3$).

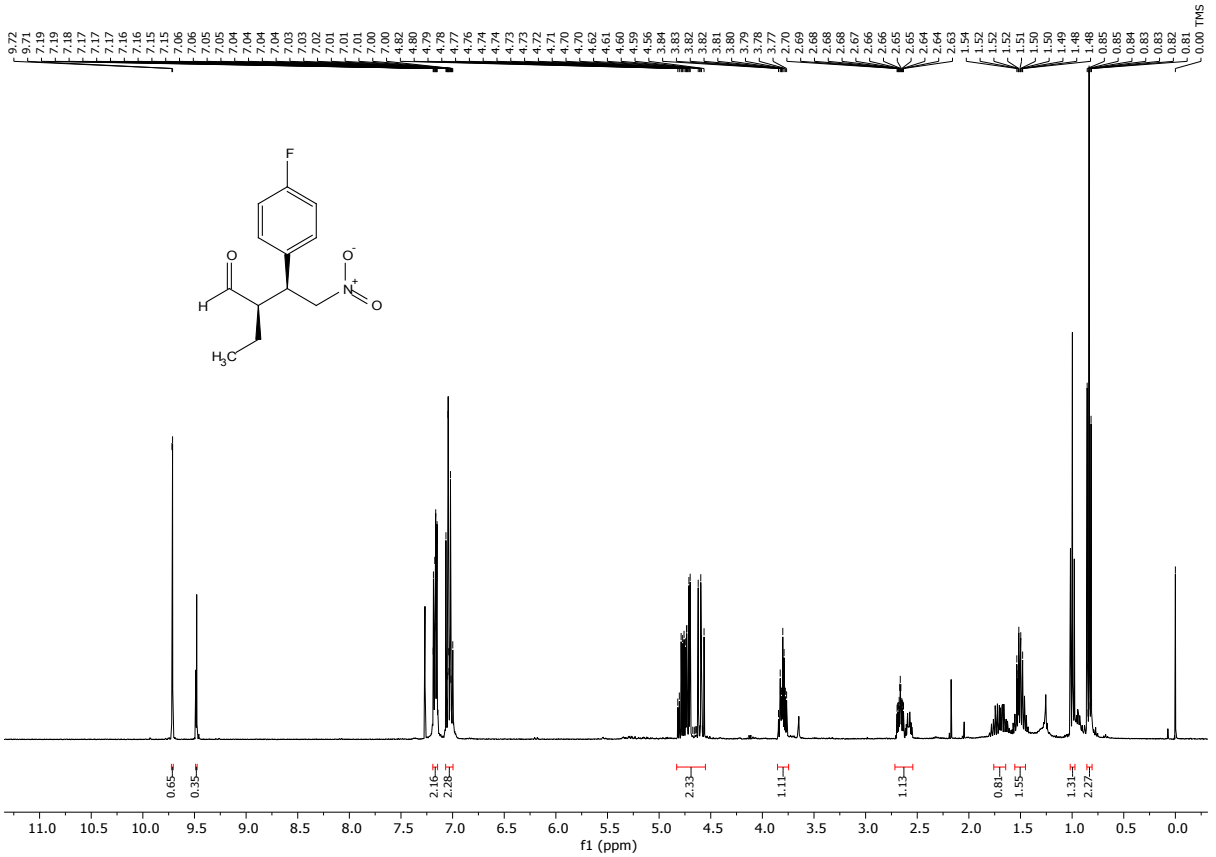


FIGURE 87. ^{1}H NMR of compound **4e** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 65:35.

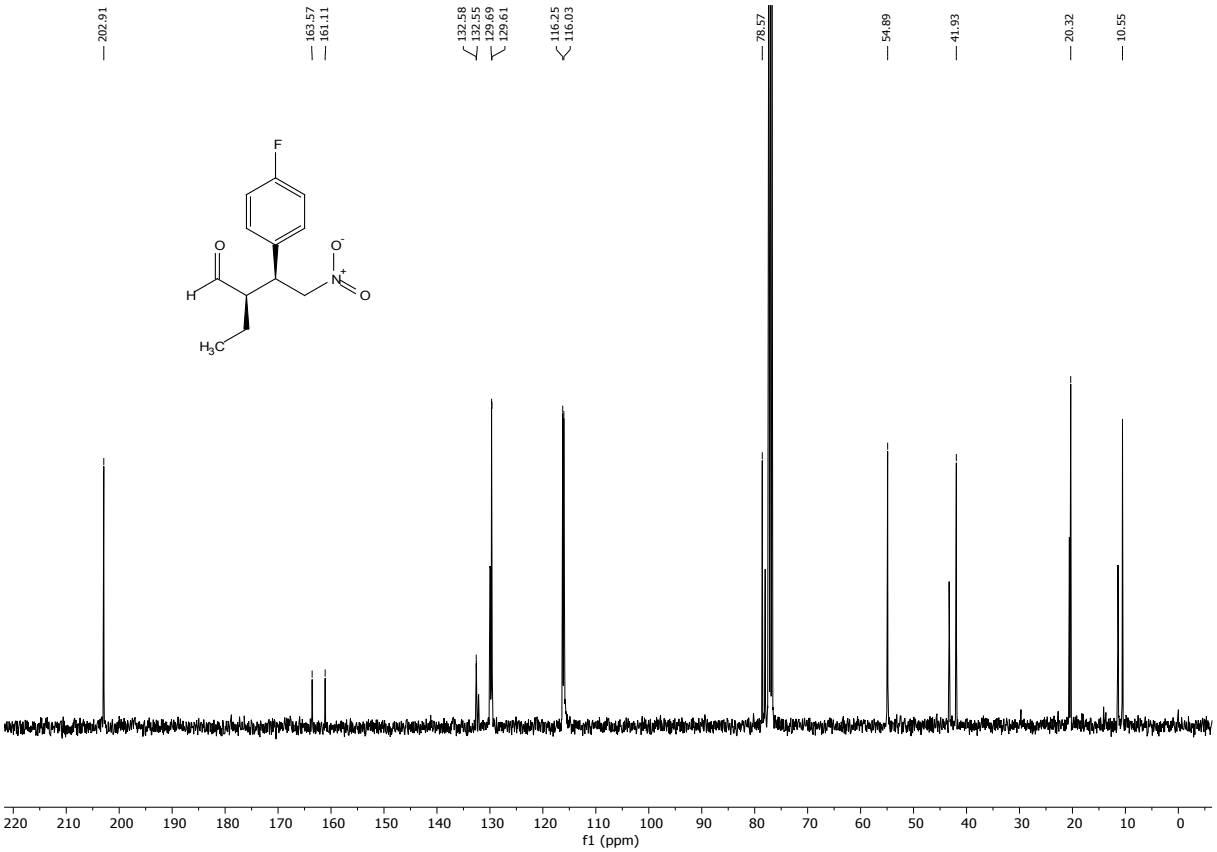


FIGURE 88. ^{13}C NMR of compound **4e** (100 MHz, $CDCl_3$).

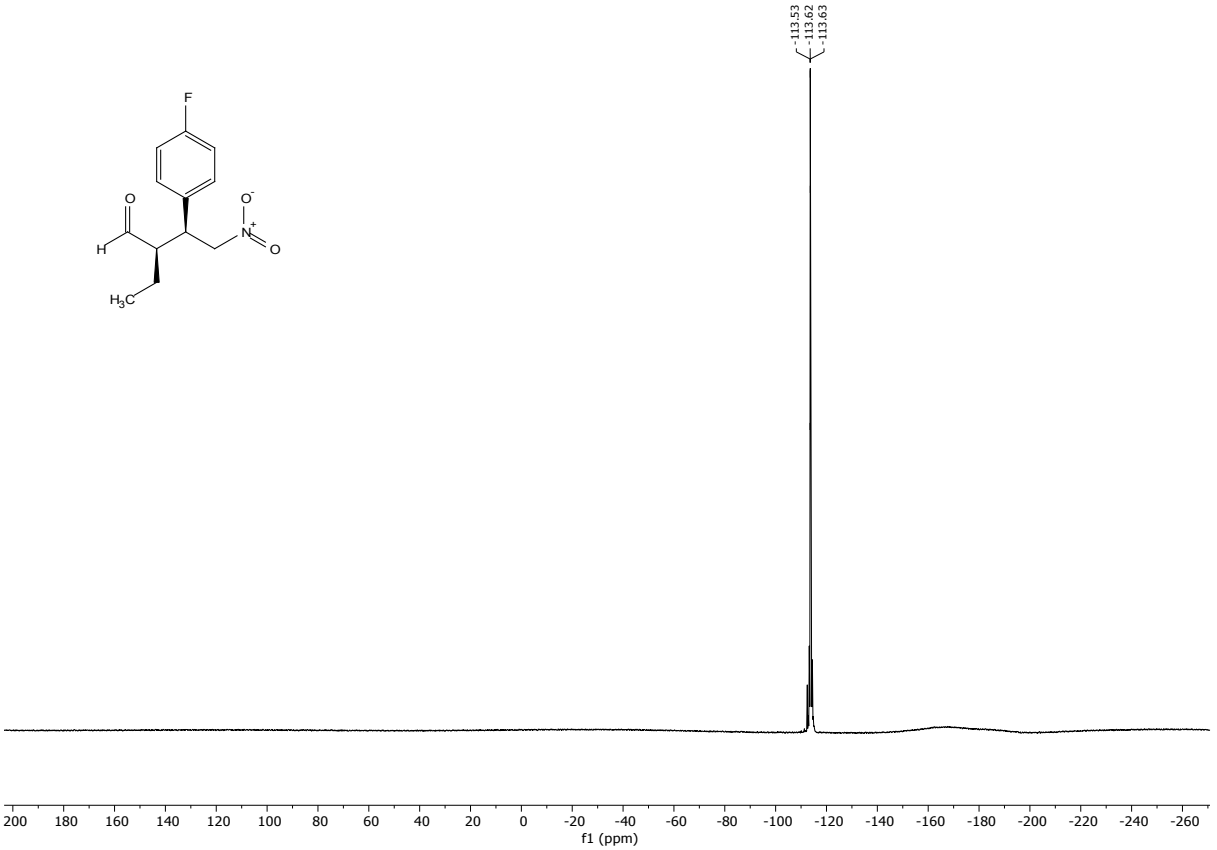


FIGURE 89. ^{19}F NMR of compound **4e** (377 MHz, $CDCl_3$).

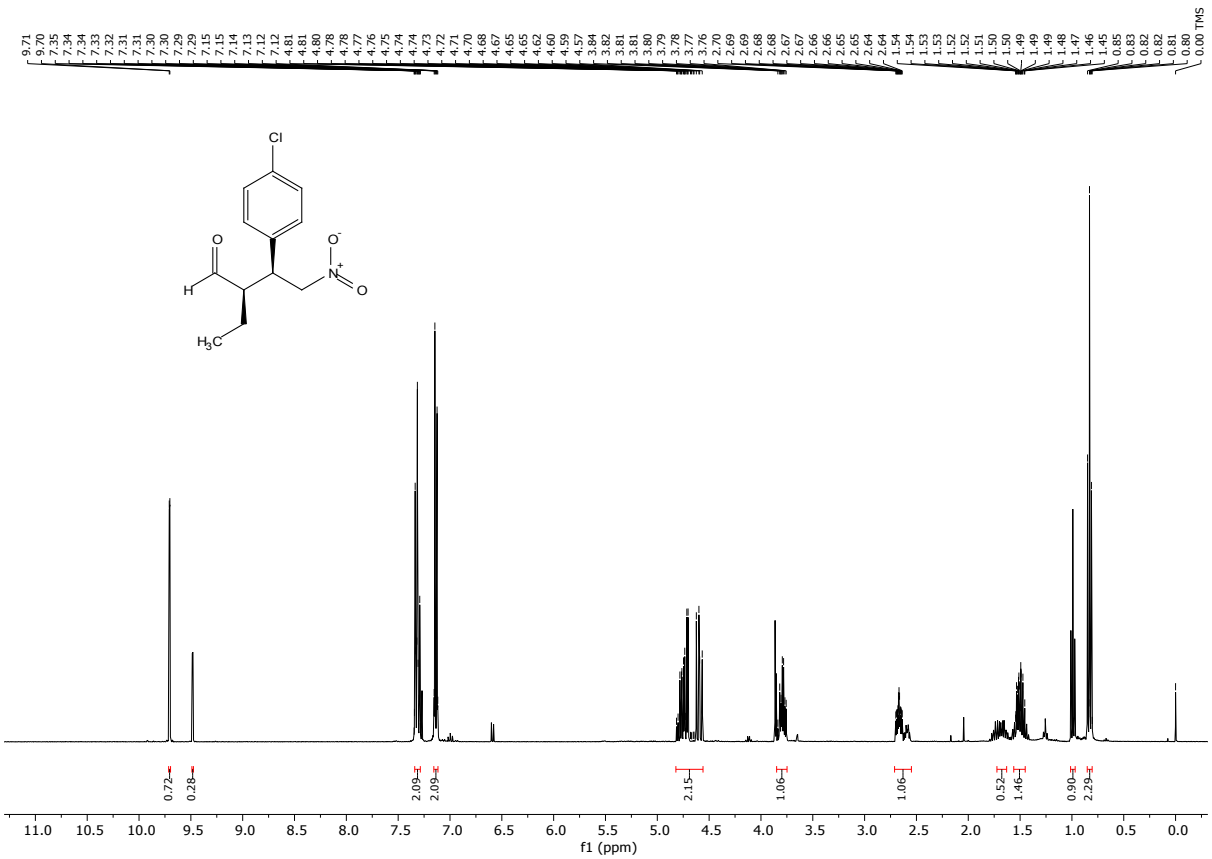


FIGURE 90. ^{1}H NMR of compound **4f** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 72:28.

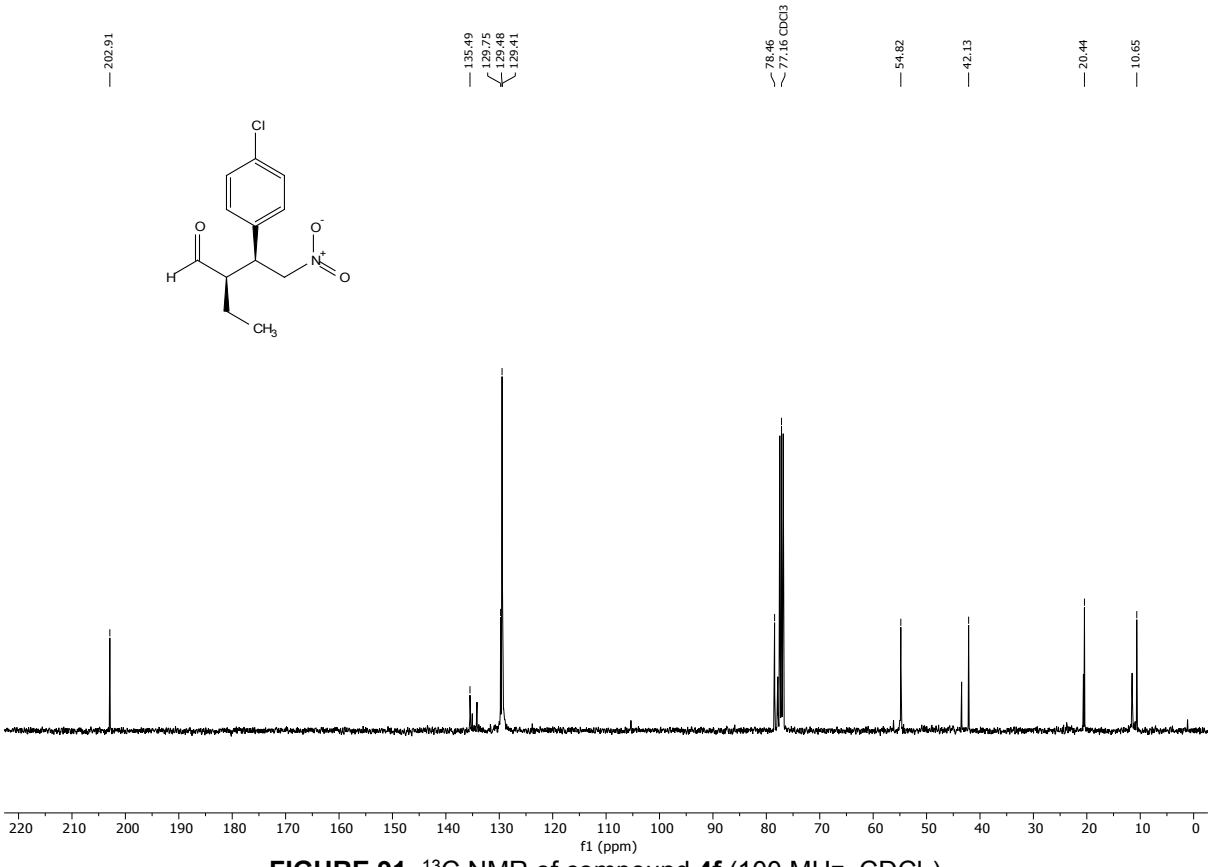


FIGURE 91. ^{13}C NMR of compound **4f** (100 MHz, $CDCl_3$).

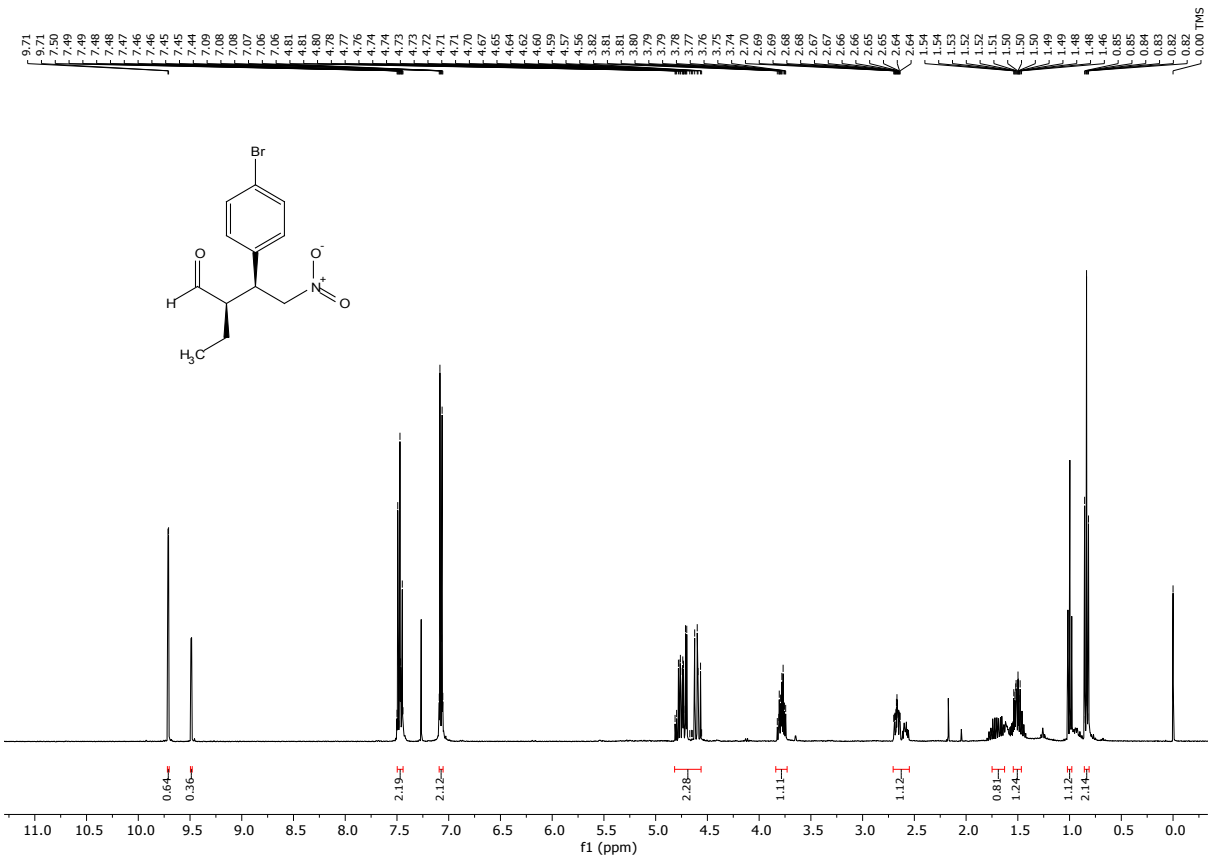


FIGURE 92. ^{1}H NMR of compound **4g** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 64:36.

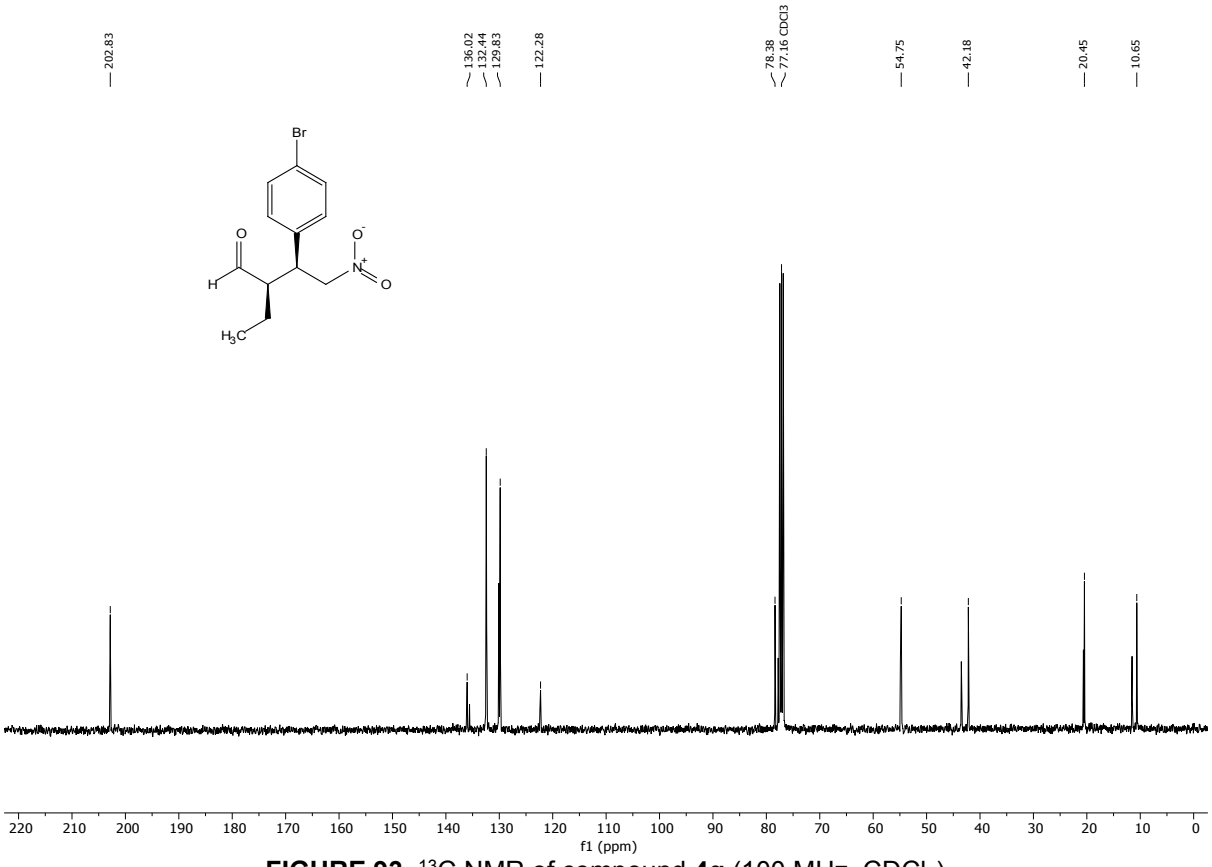


FIGURE 93. ^{13}C NMR of compound **4g** (100 MHz, $CDCl_3$).

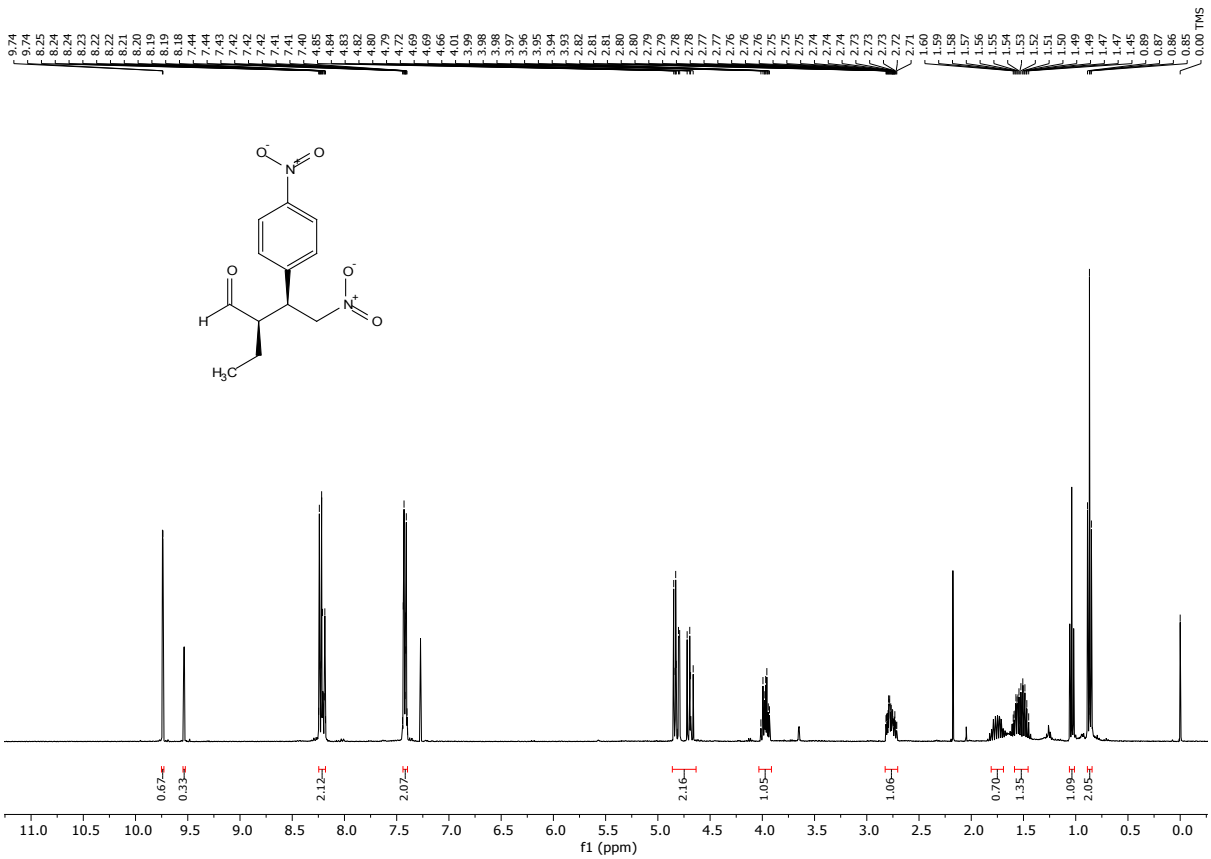


FIGURE 94. ^{1}H NMR of compound **4h** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 67:33.

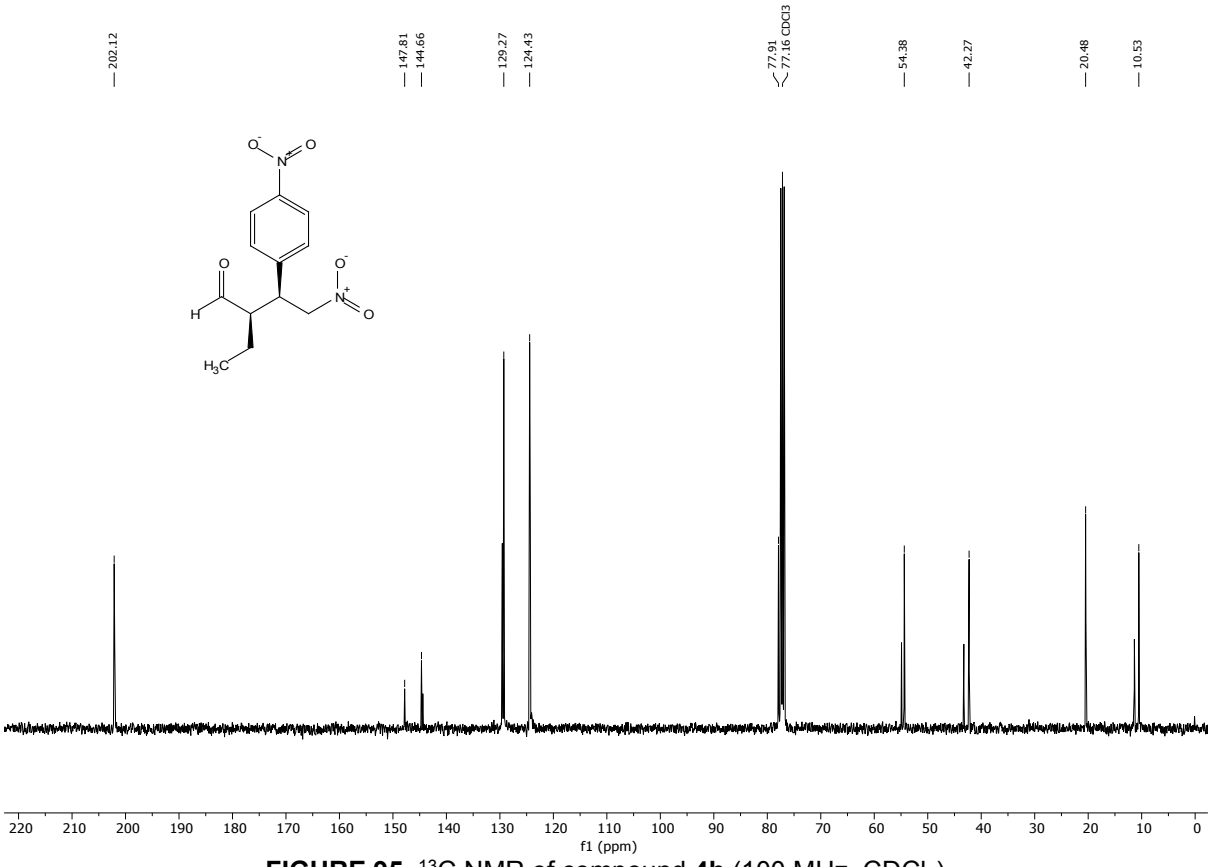


FIGURE 95. ^{13}C NMR of compound **4h** (100 MHz, $CDCl_3$).

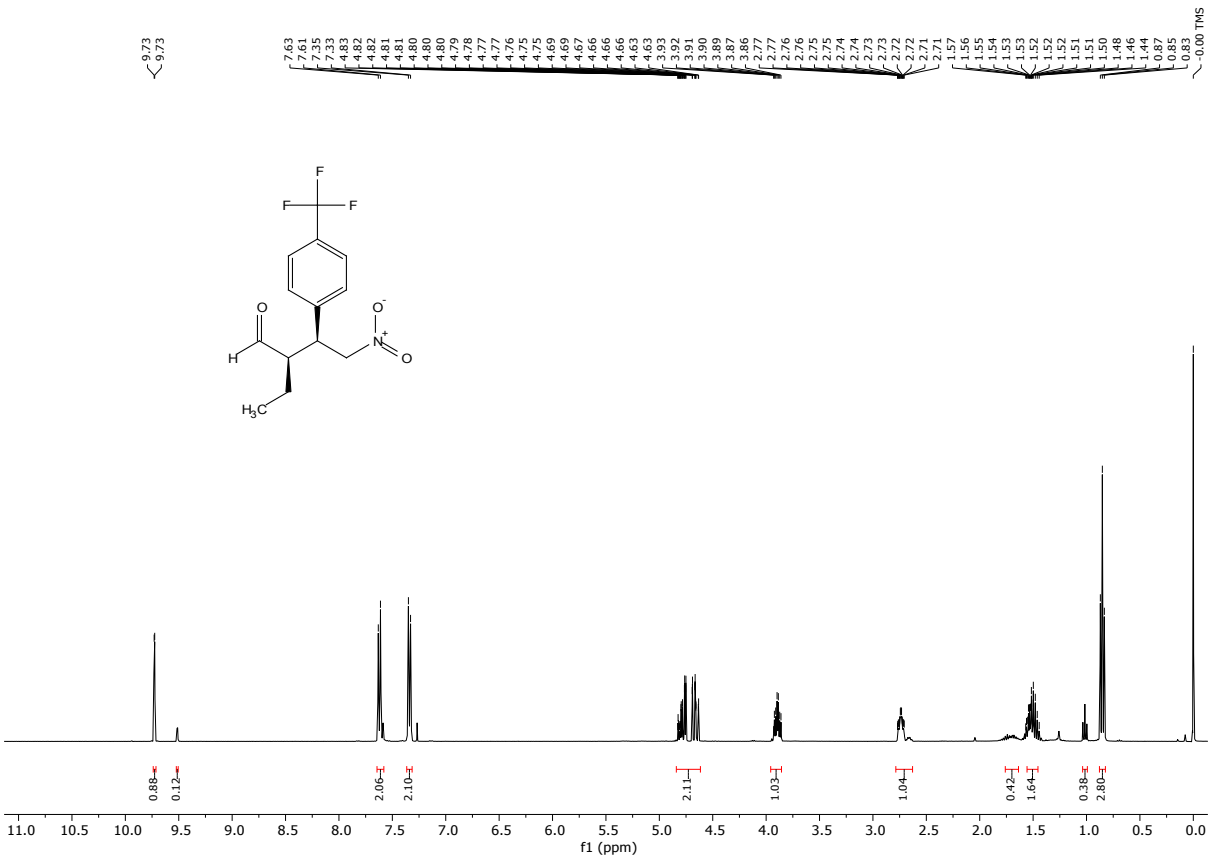


FIGURE 96. ^{1}H NMR of compound **4i** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 88:12.

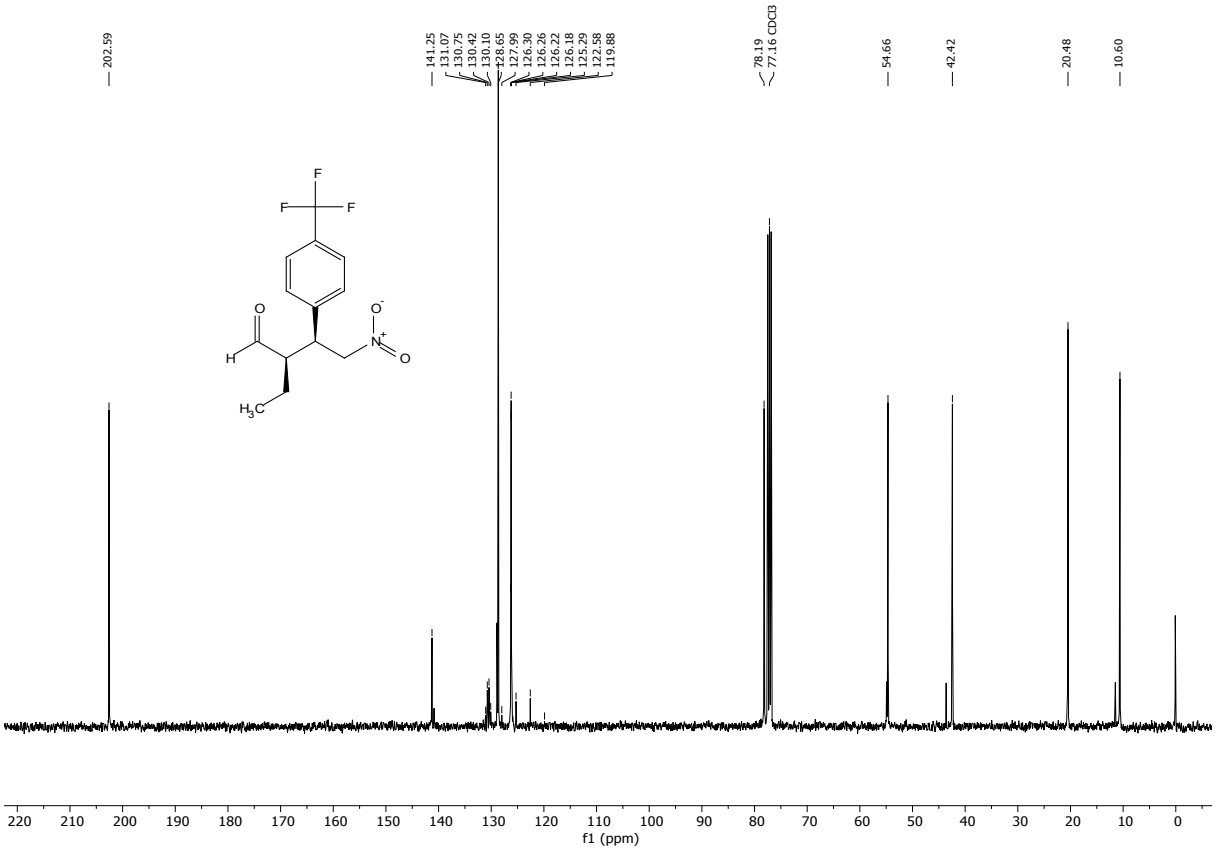


FIGURE 97. ^{13}C NMR of compound **4i** (100 MHz, $CDCl_3$).

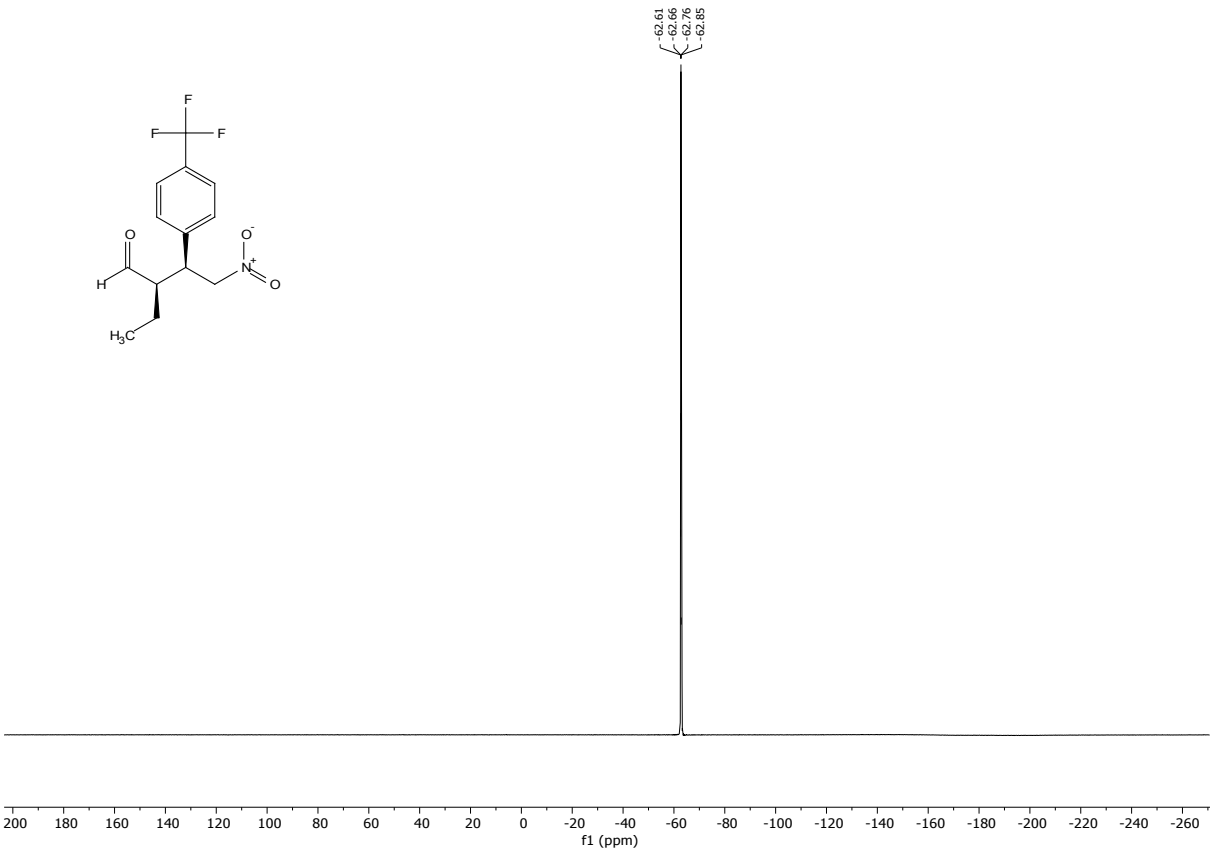


FIGURE 98. ^{19}F NMR of compound **4i** (377 MHz, $CDCl_3$).

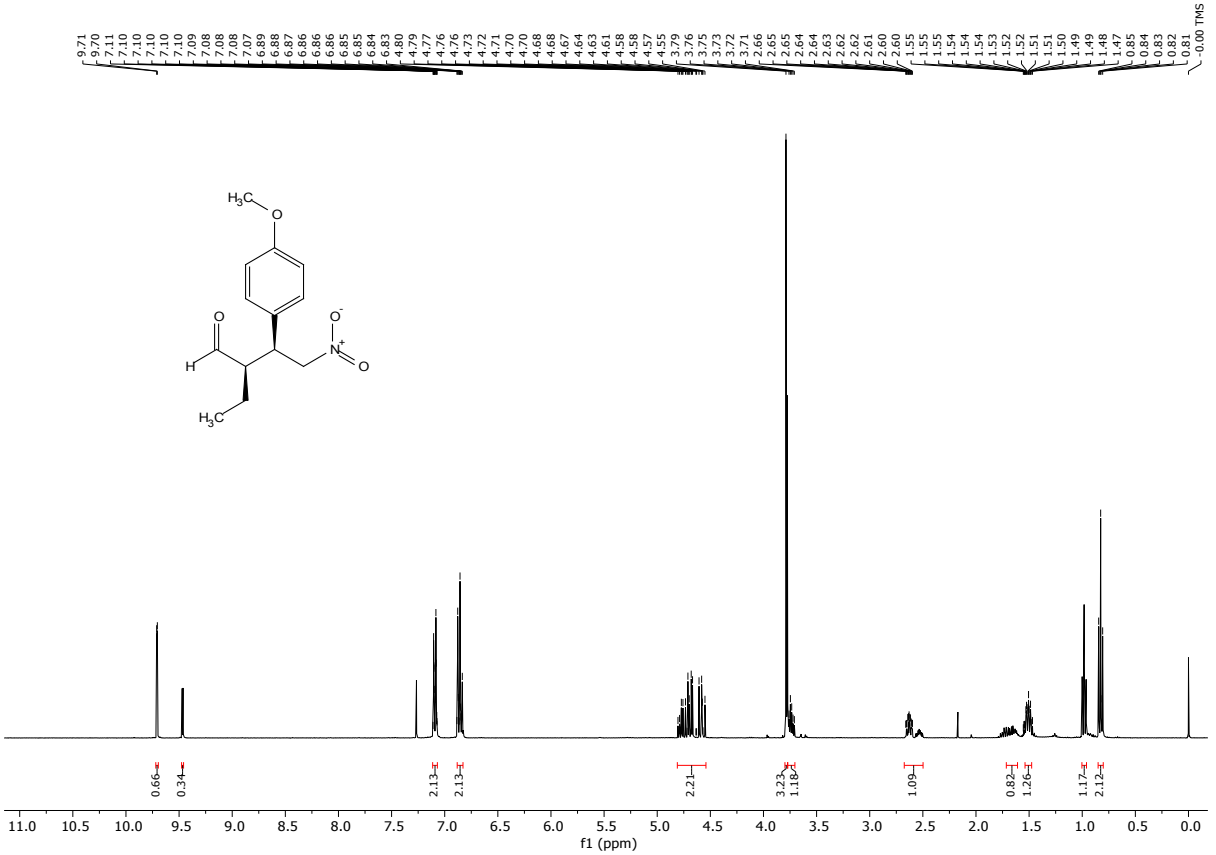


FIGURE 99. ^{1}H NMR of compound **4j** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 66:34.

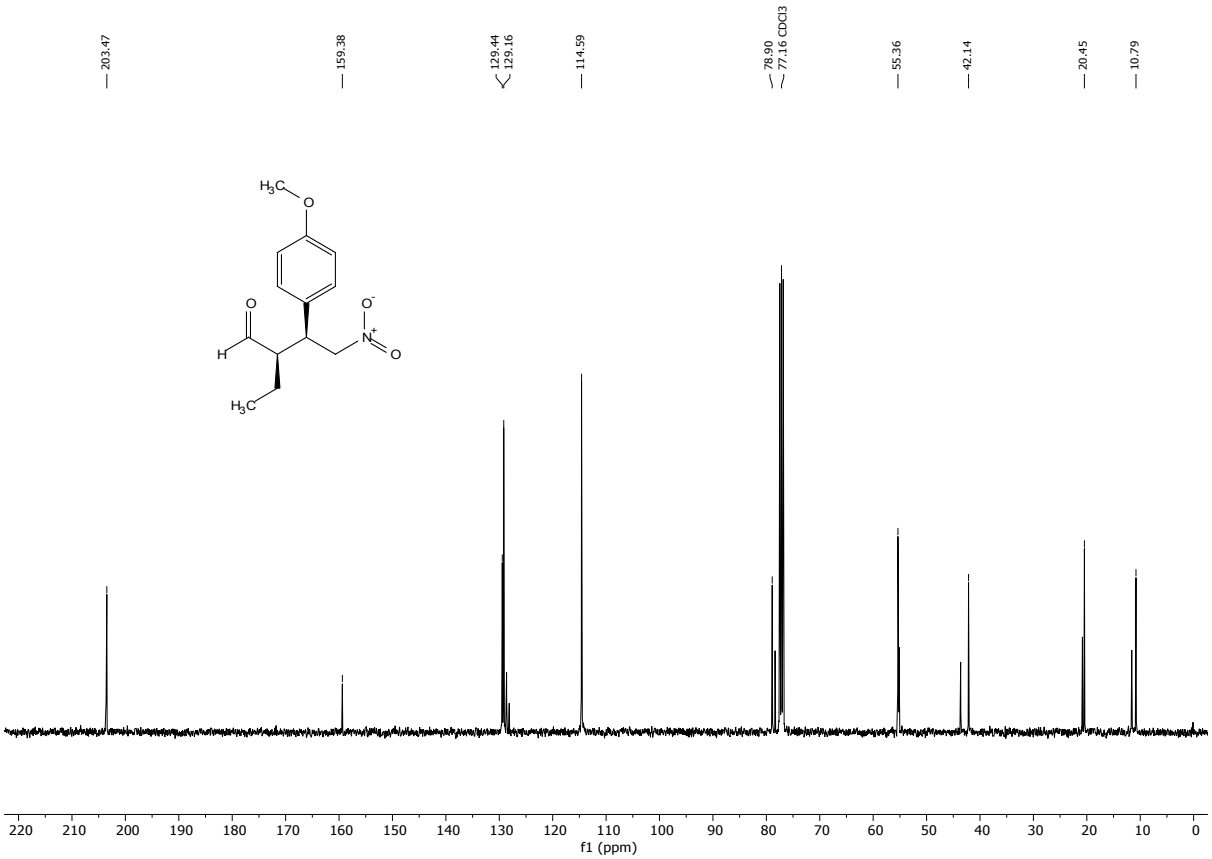


FIGURE 100. ^{13}C NMR of compound **4j** (100 MHz, $CDCl_3$).

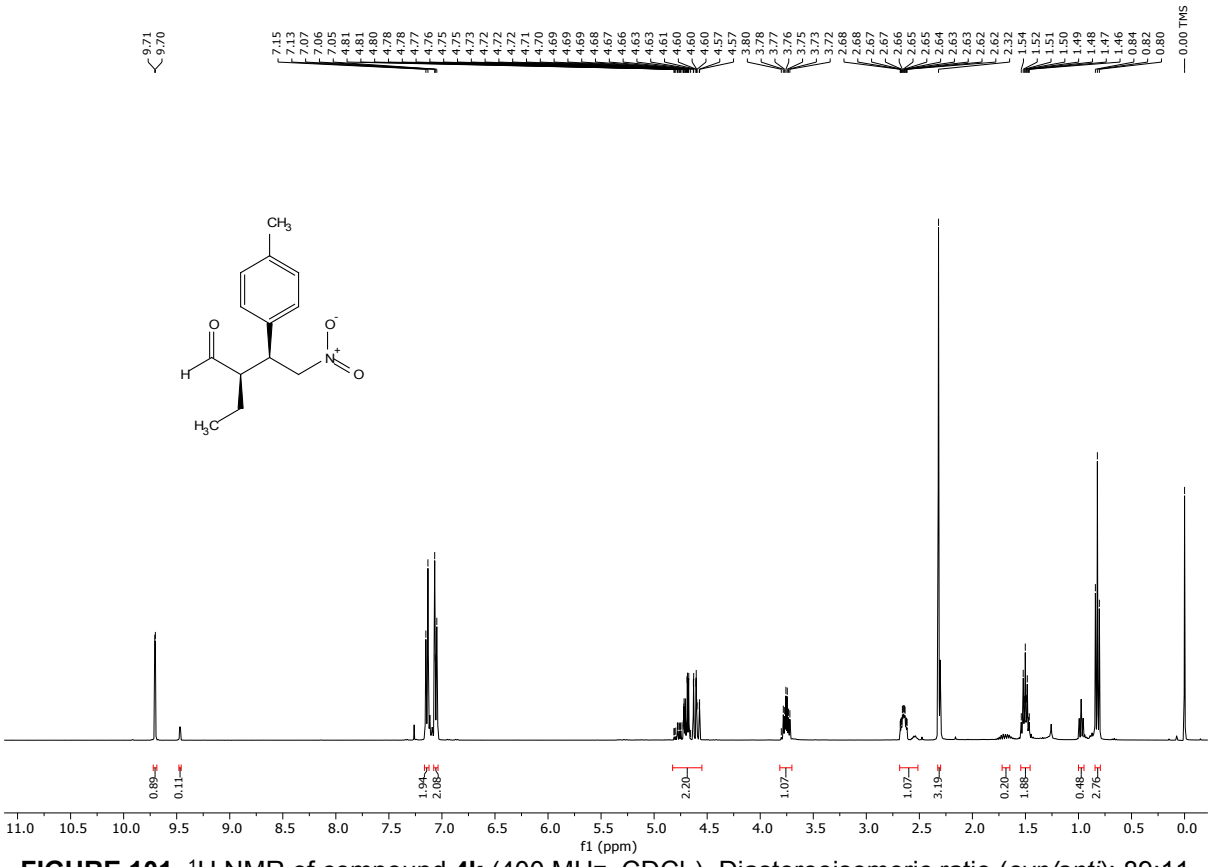


FIGURE 101. ^{1}H NMR of compound **4k** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 89:11.

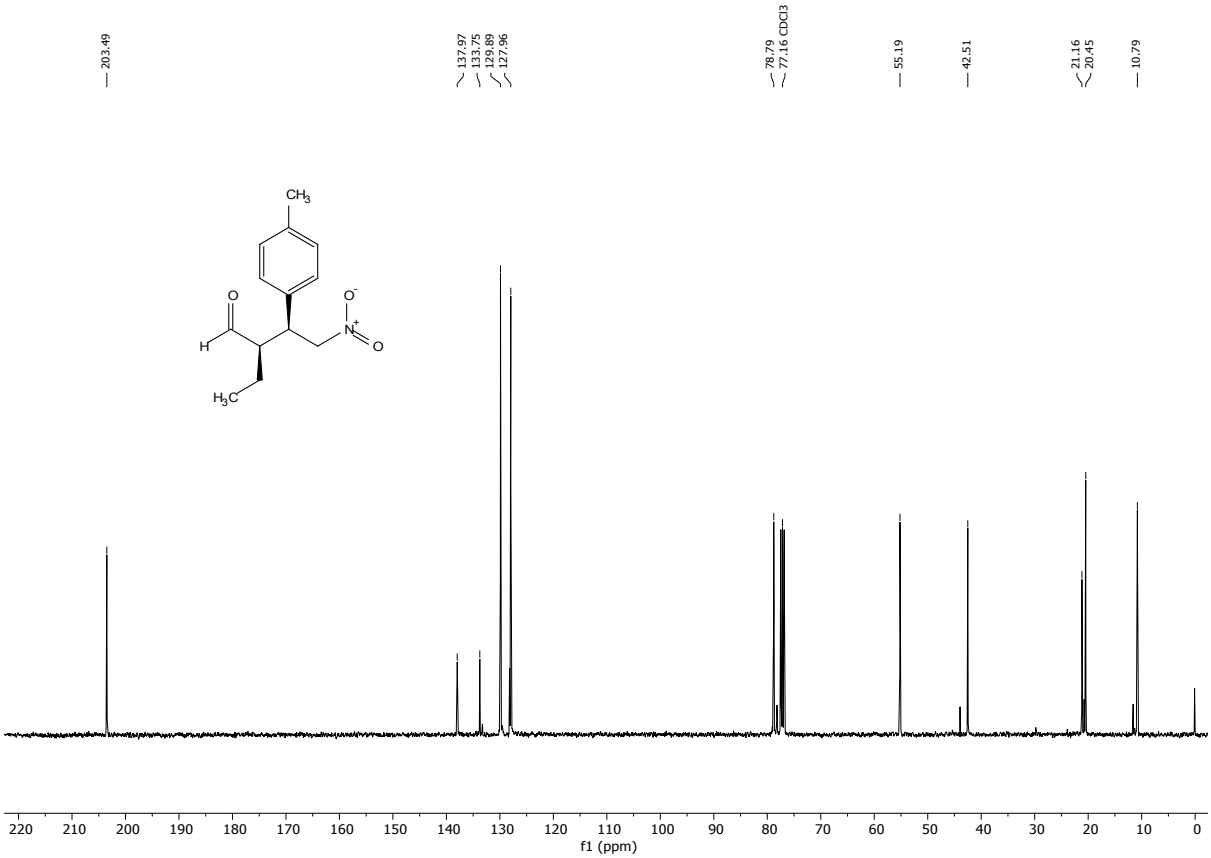


FIGURE 102. ^{13}C NMR of compound **4k** (100 MHz, $CDCl_3$).

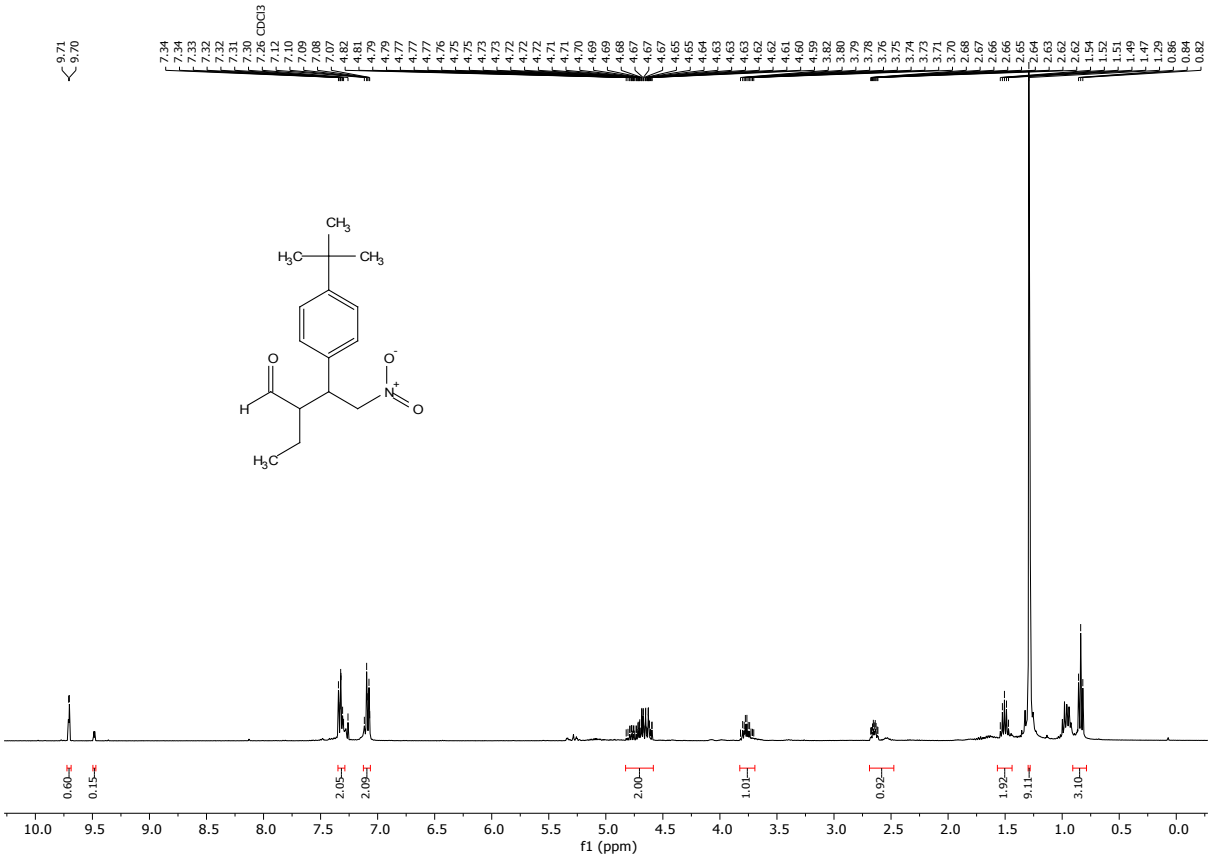


FIGURE 103. ^{1}H NMR of compound **4l** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 80:20.

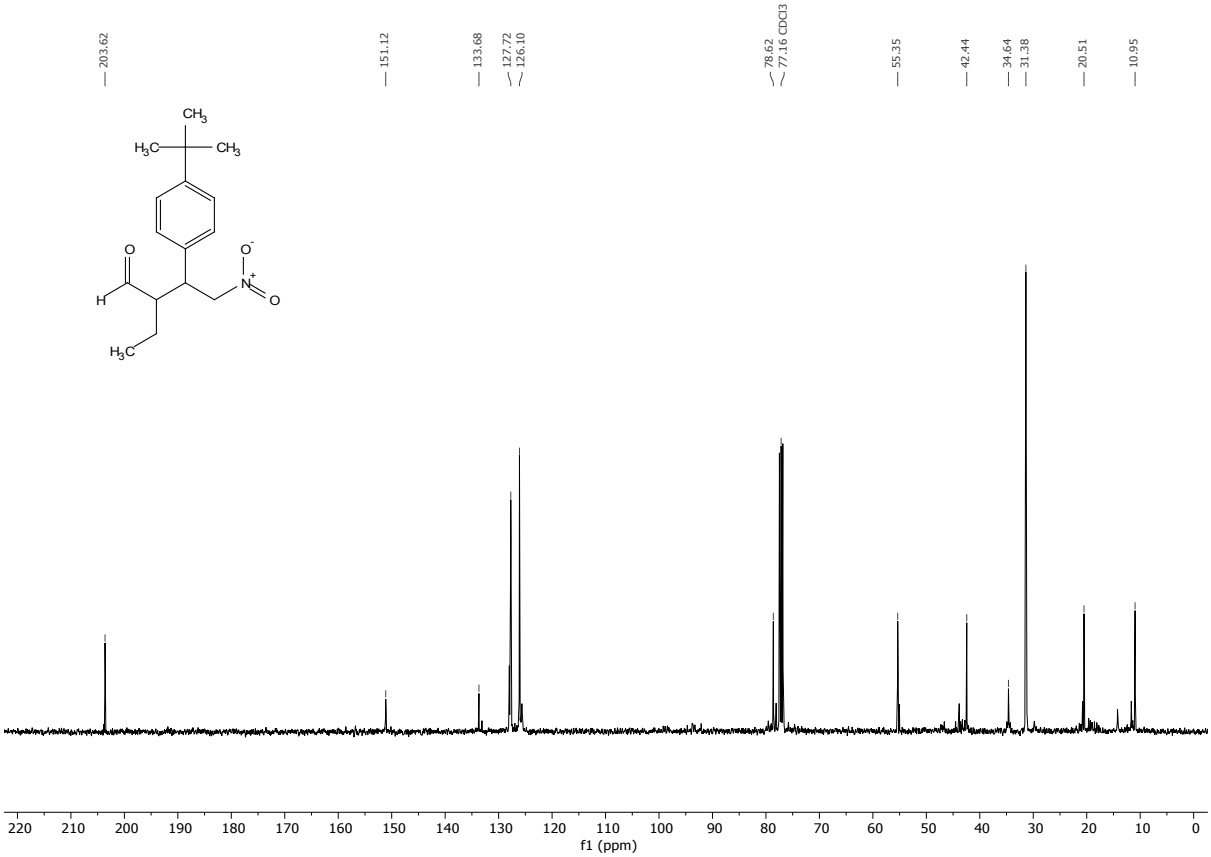


FIGURE 104. ^{13}C NMR of compound **4l** (100 MHz, $CDCl_3$).

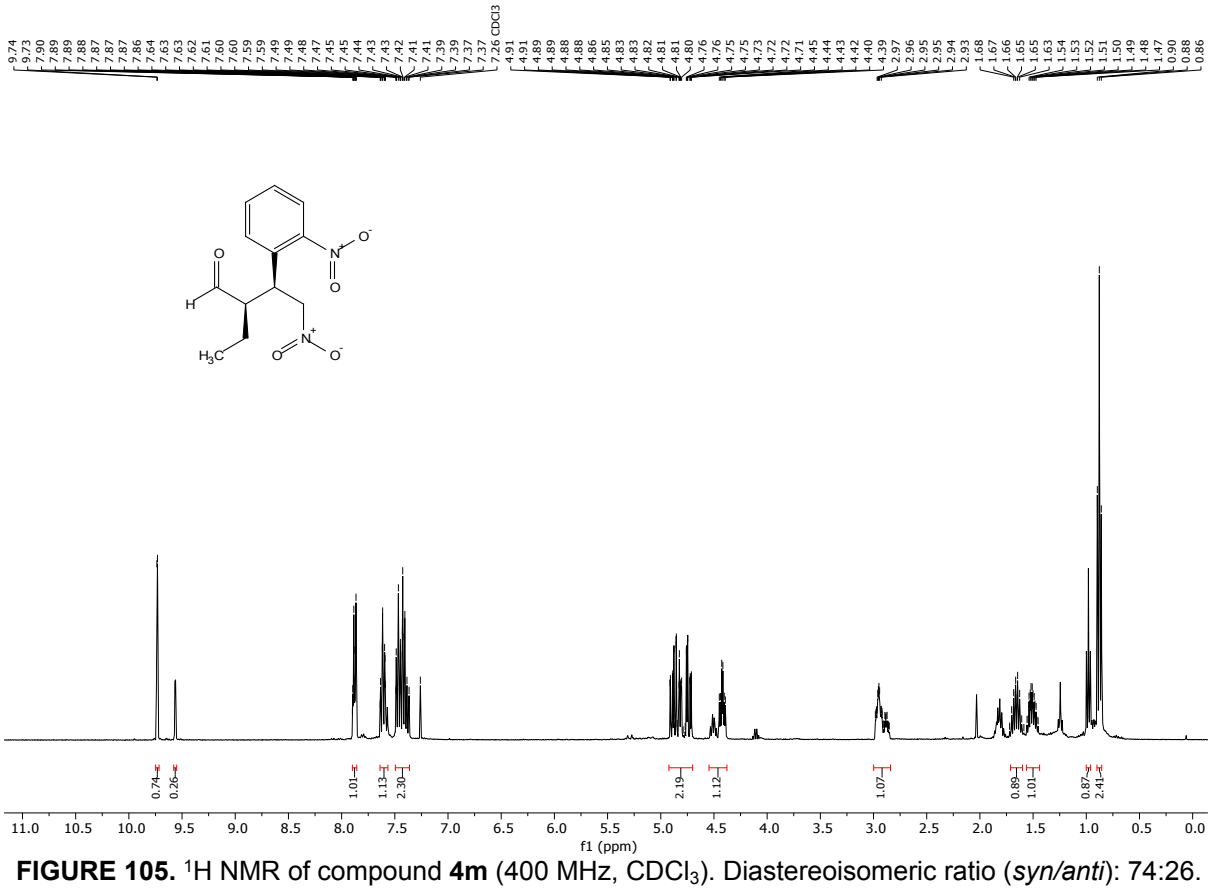


FIGURE 105. ^{1}H NMR of compound **4m** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 74:26.

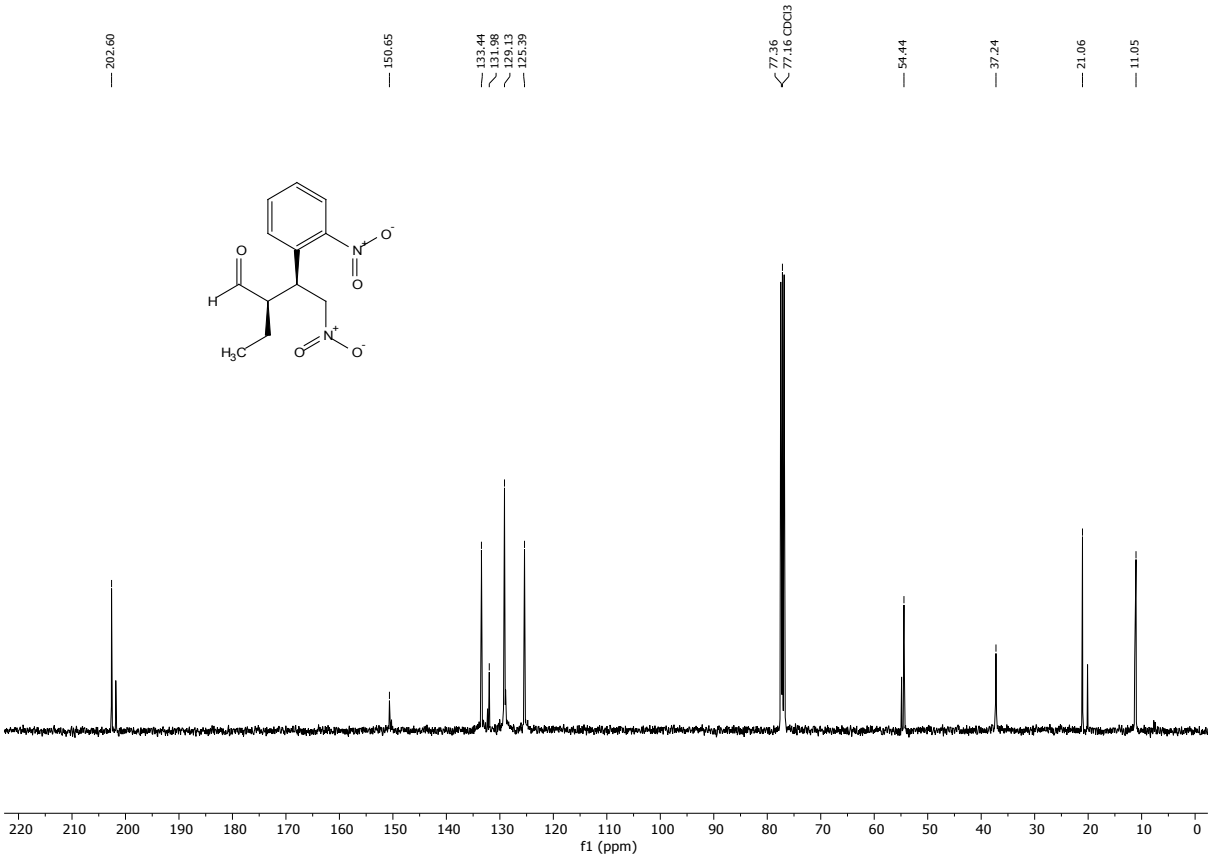


FIGURE 106. ^{13}C NMR of compound **4m** (100 MHz, $CDCl_3$).

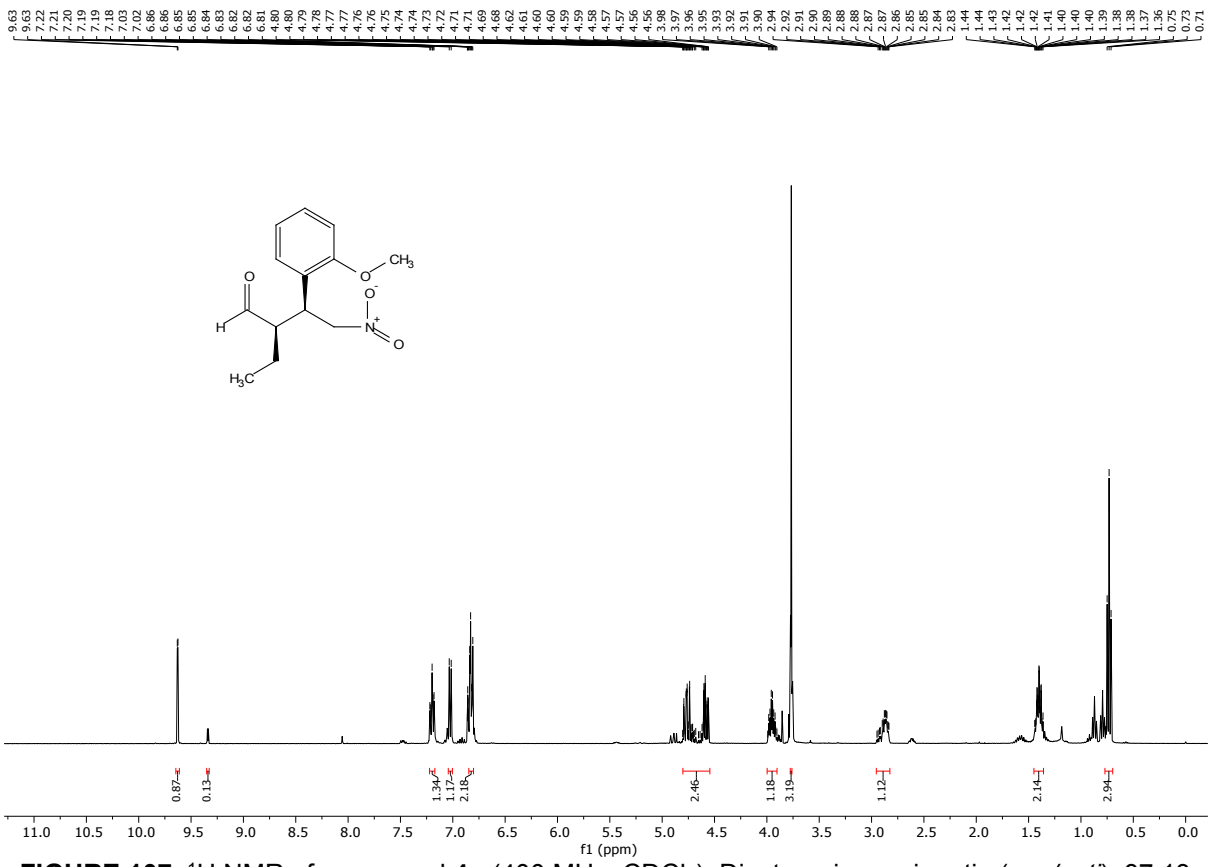


FIGURE 107. ^{1}H NMR of compound **4n** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 87:13.

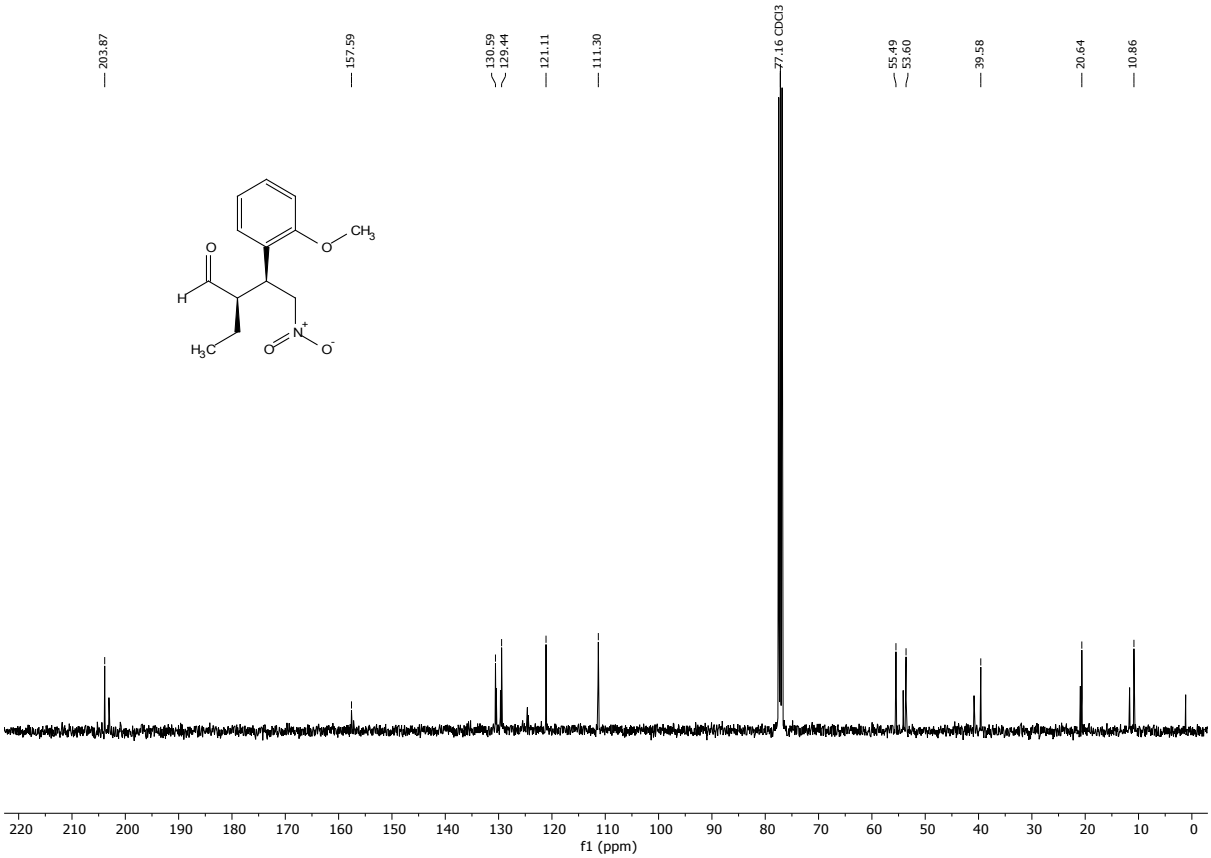


FIGURE 108. ^{13}C NMR of compound **4n** (100 MHz, $CDCl_3$).

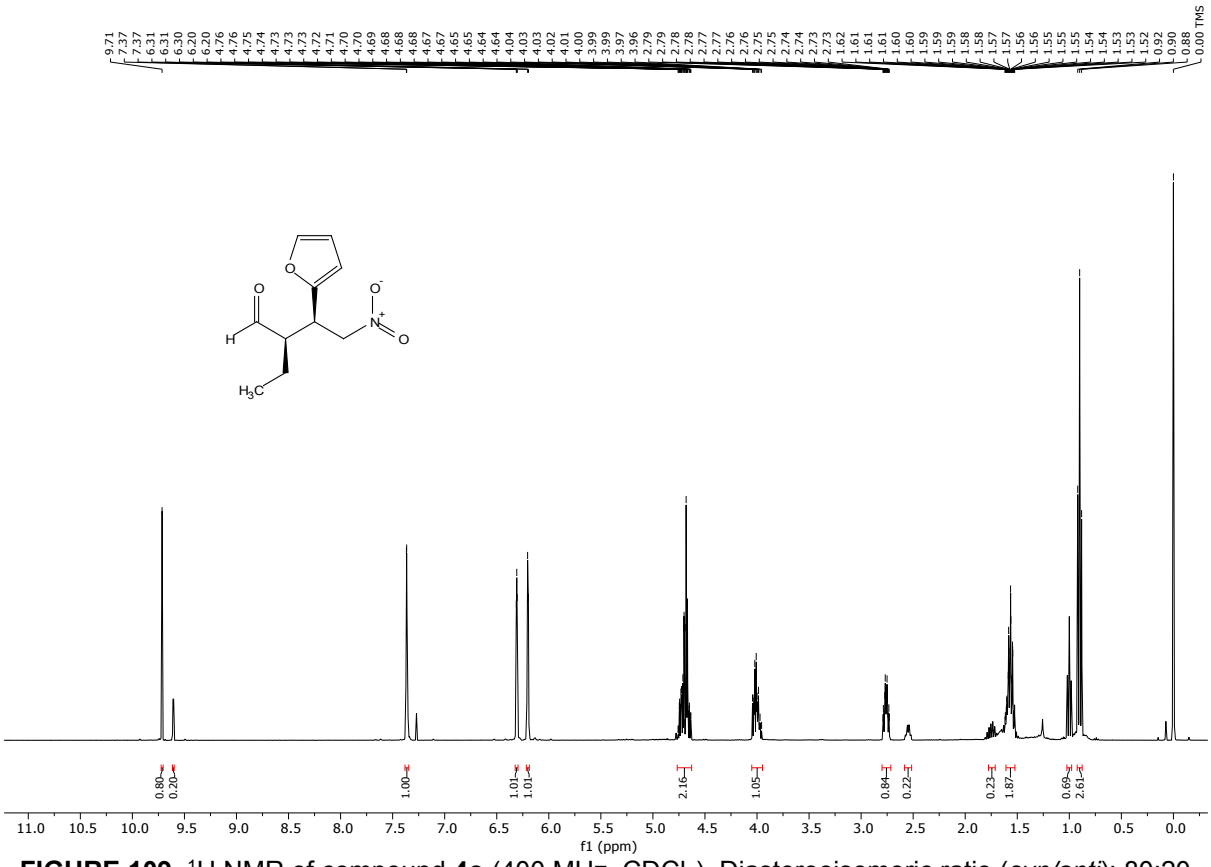


FIGURE 109. ^{1}H NMR of compound **4o** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 80:20.

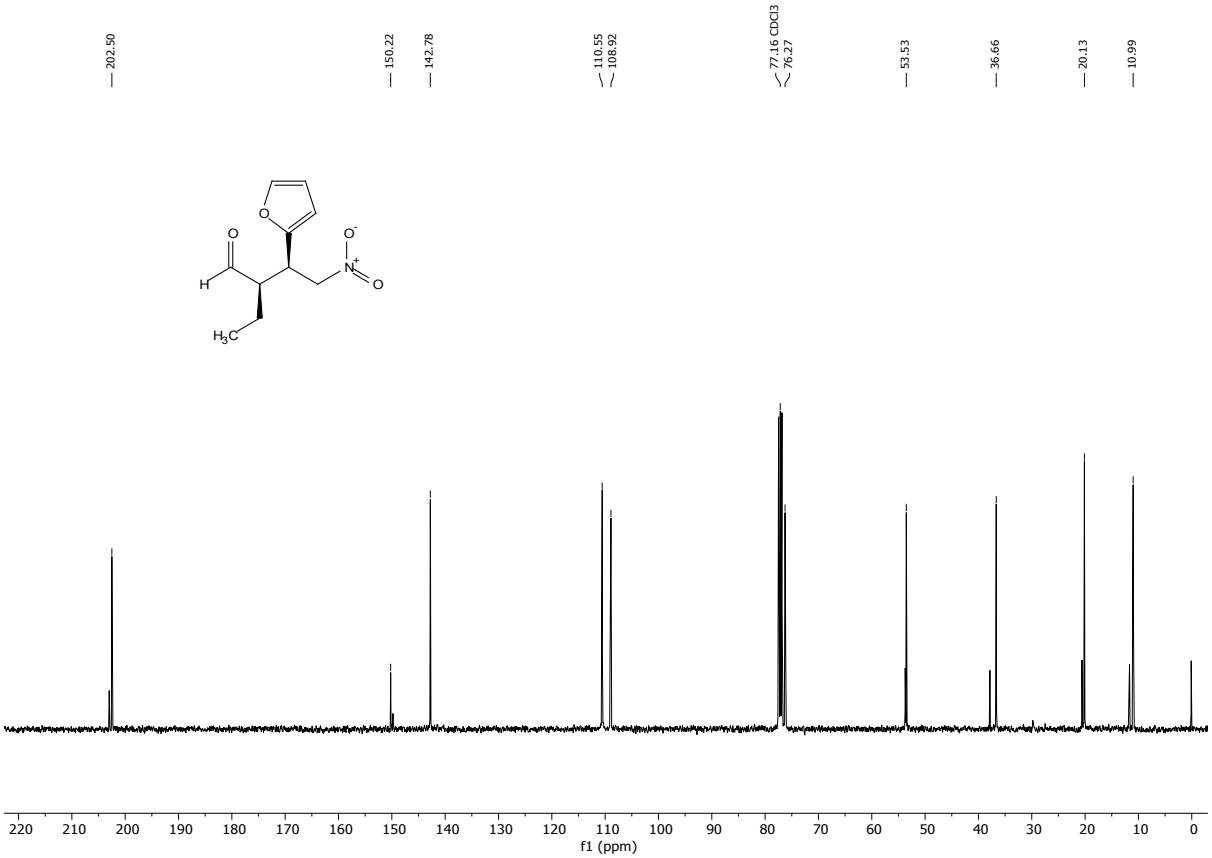


FIGURE 110. ^{13}C NMR of compound **4o** (100 MHz, $CDCl_3$).

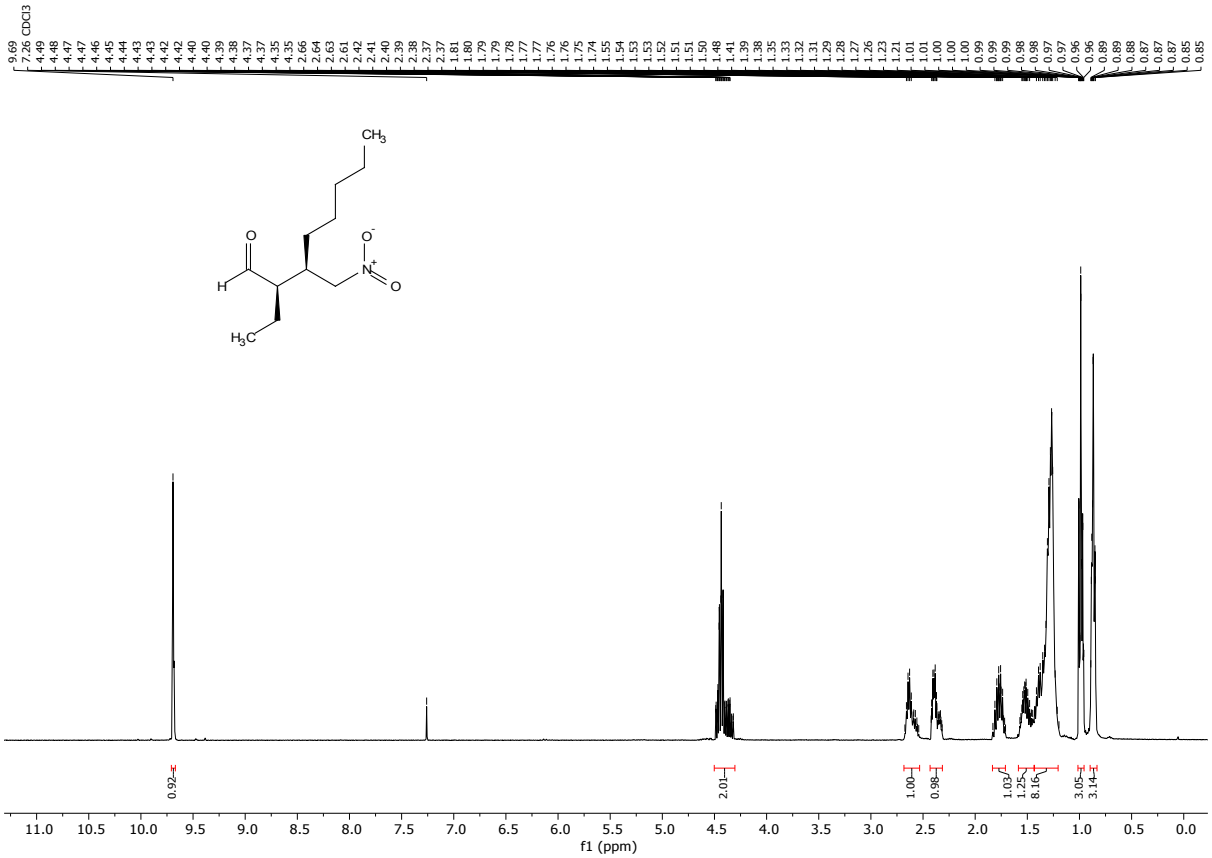


FIGURE 111. ^{1}H NMR of compound **4p** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 81:19.

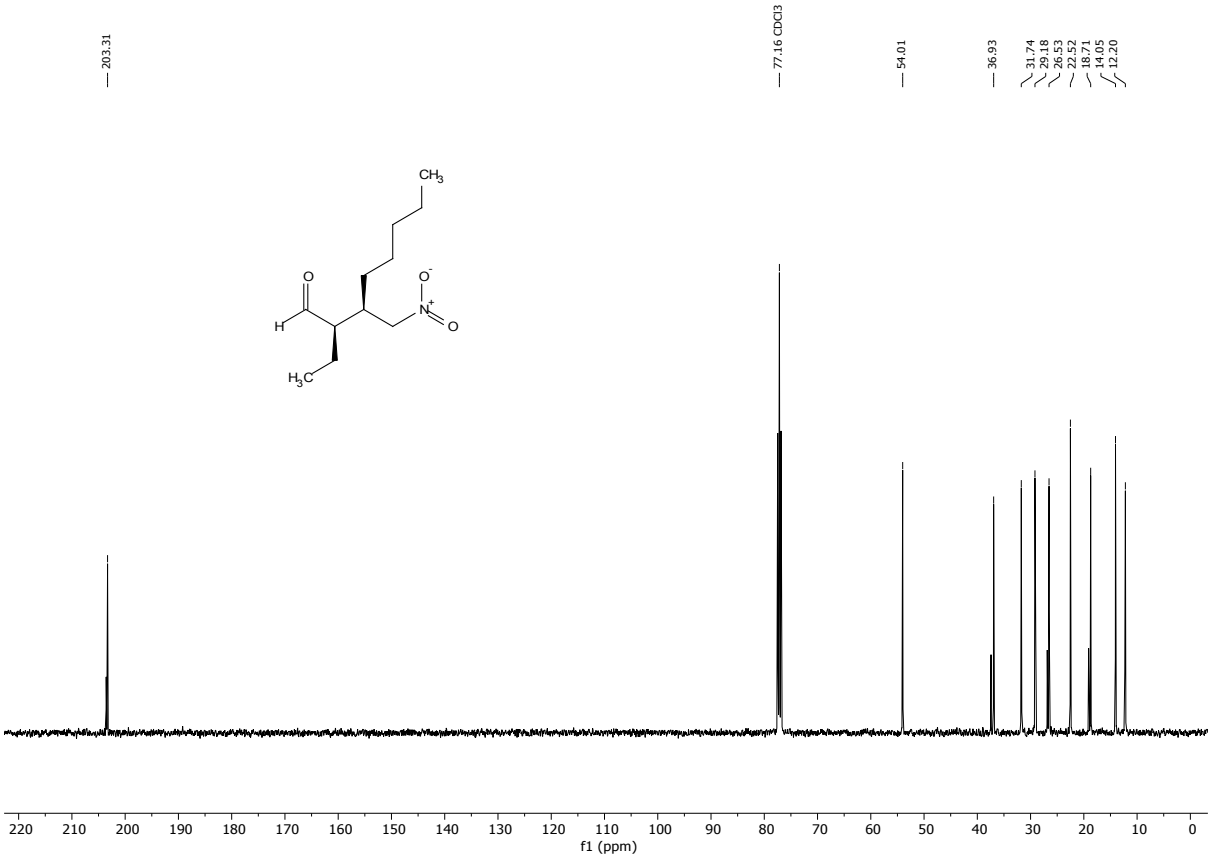


FIGURE 112. ^{13}C NMR of compound **4p** (100 MHz, $CDCl_3$).

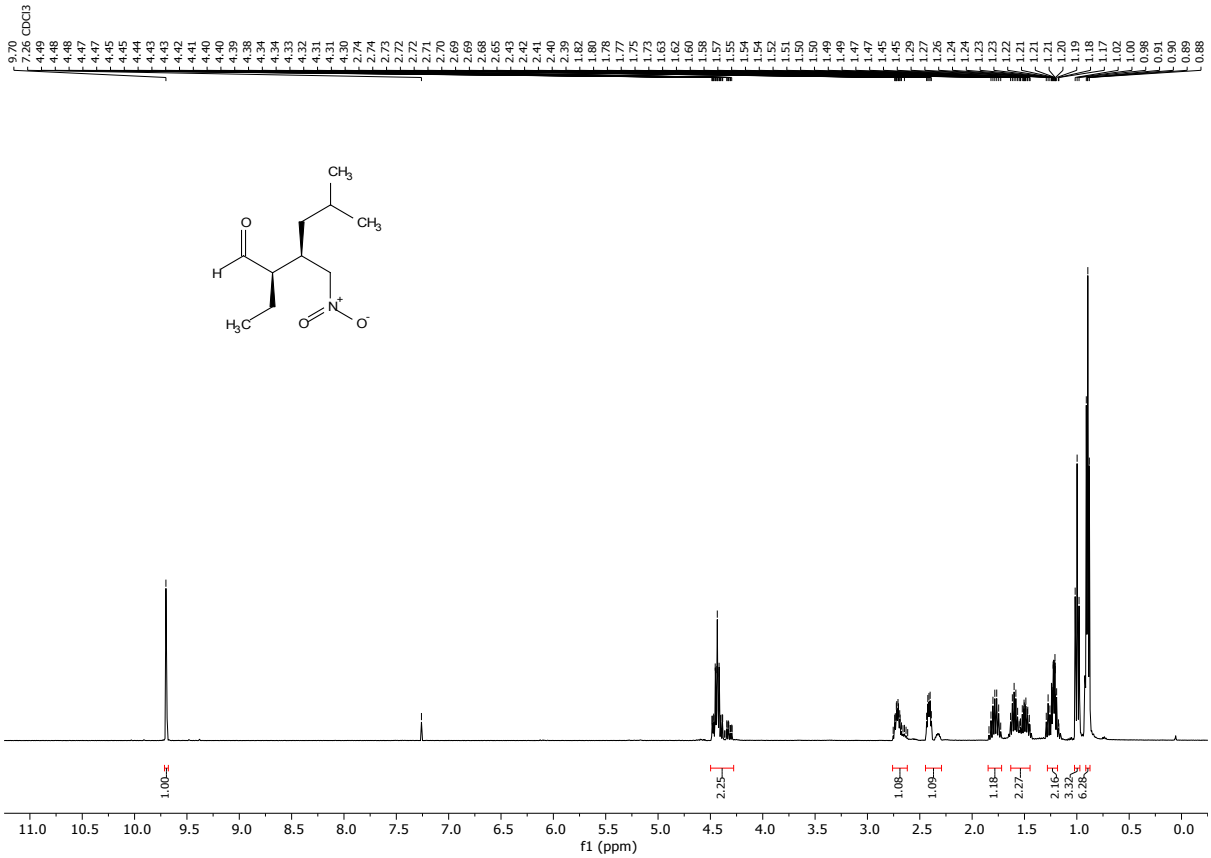


FIGURE 113. ^{1}H NMR of compound **4q** (400 MHz, $CDCl_3$). Diastereoisomeric ratio (*syn/anti*): 88:12.

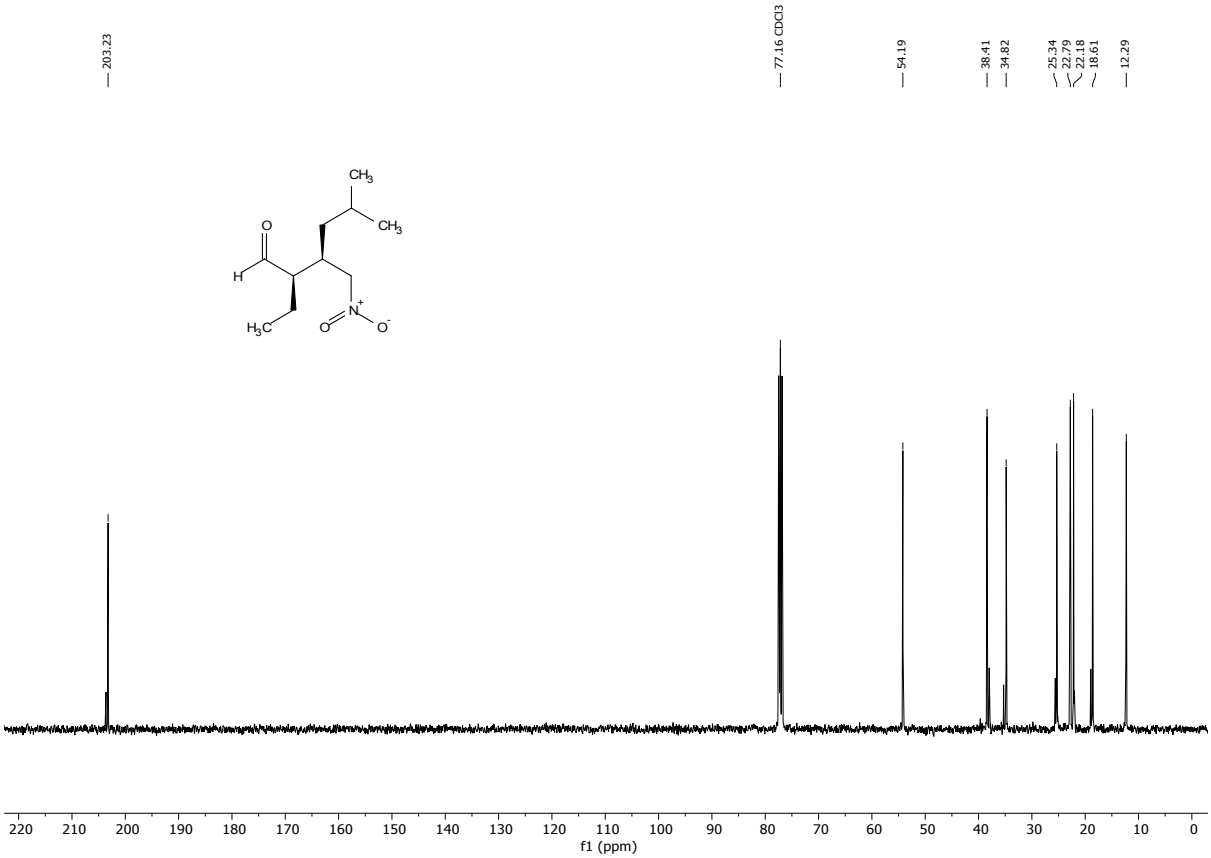


FIGURE 114. ^{13}C NMR of compound **4q** (100 MHz, $CDCl_3$).

18. NMR Spectra and Chromatograms: Scope

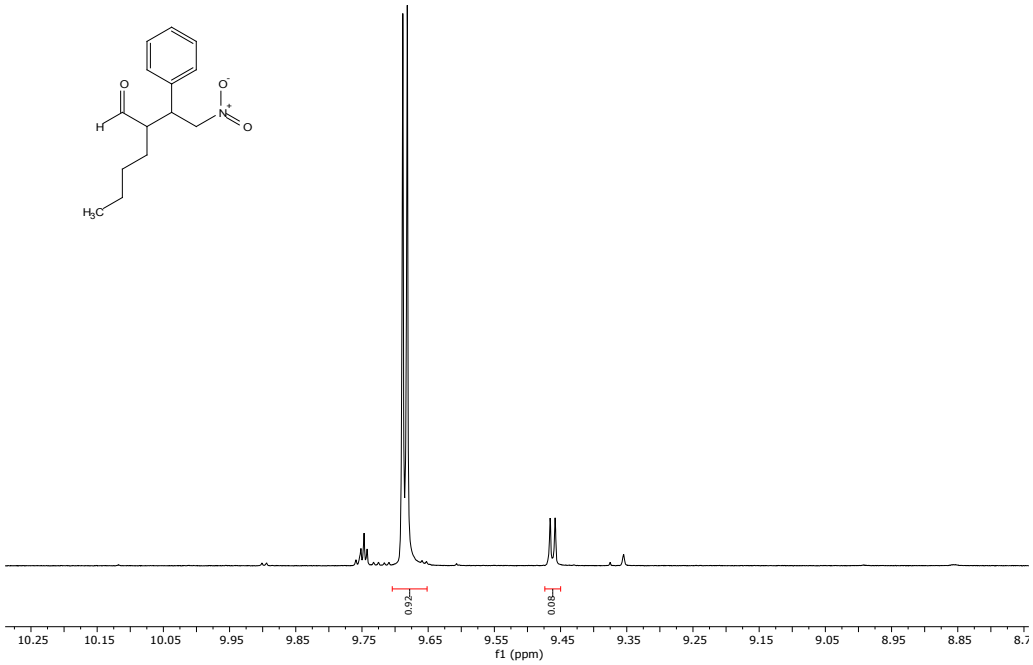


FIGURE 115. ^{1}H NMR of crude compound **4b** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 92:08. TABLE 4, Entry 2.

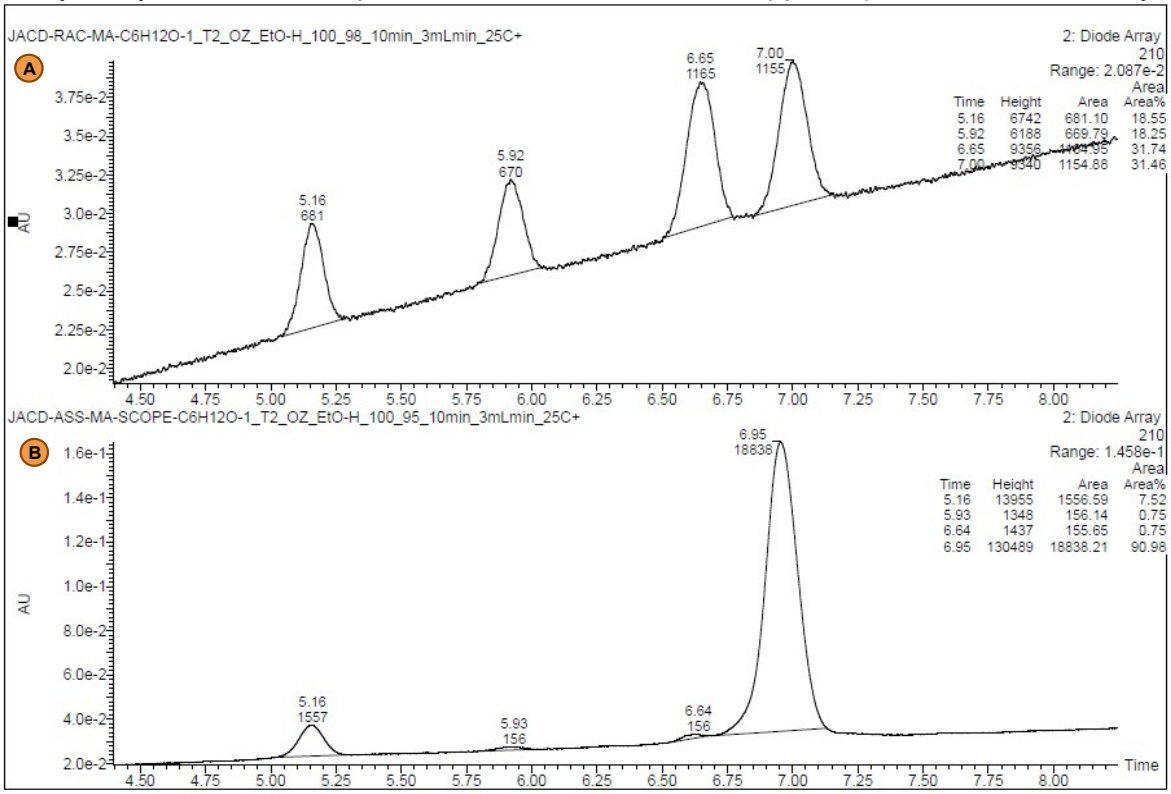


FIGURE 116. (a) Chiral UPC^2 of racemic 2-(2-nitro-1-phenylethyl) hexanal (**4b**); (b) Chiral UPC^2 of 2-(2-nitro-1-phenylethyl) hexanal (**4b**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, Grad: CO2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UVdetection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 6.64 min, (syn, major) = 6.95 min. TABLE 4, Entry 2.

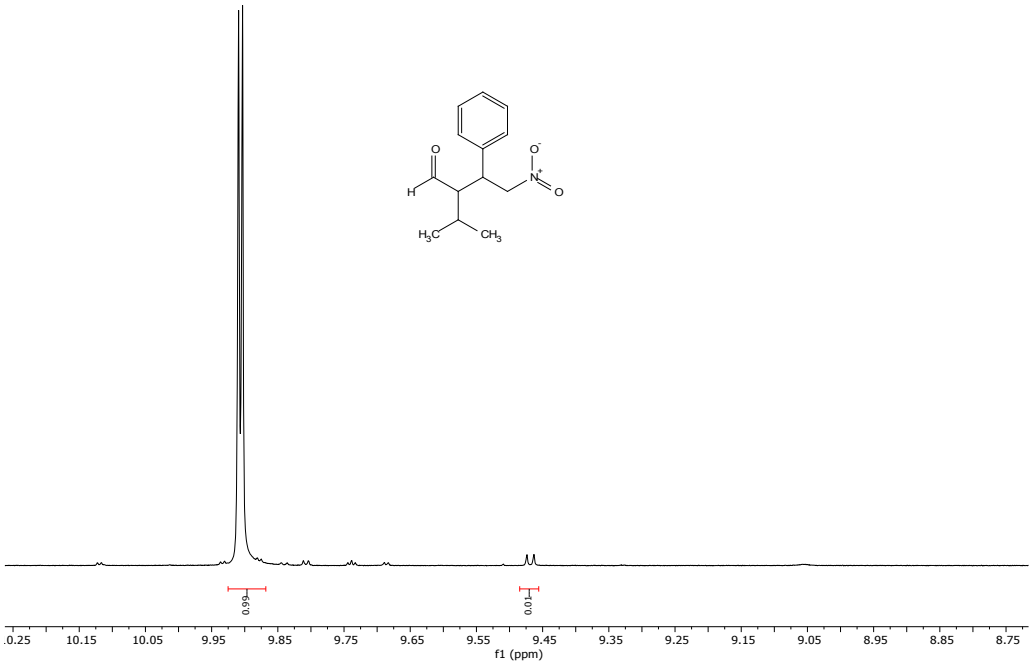


FIGURE 117. 1H NMR of crude compound **4c** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 99:01. TABLE 4, Entry 3.

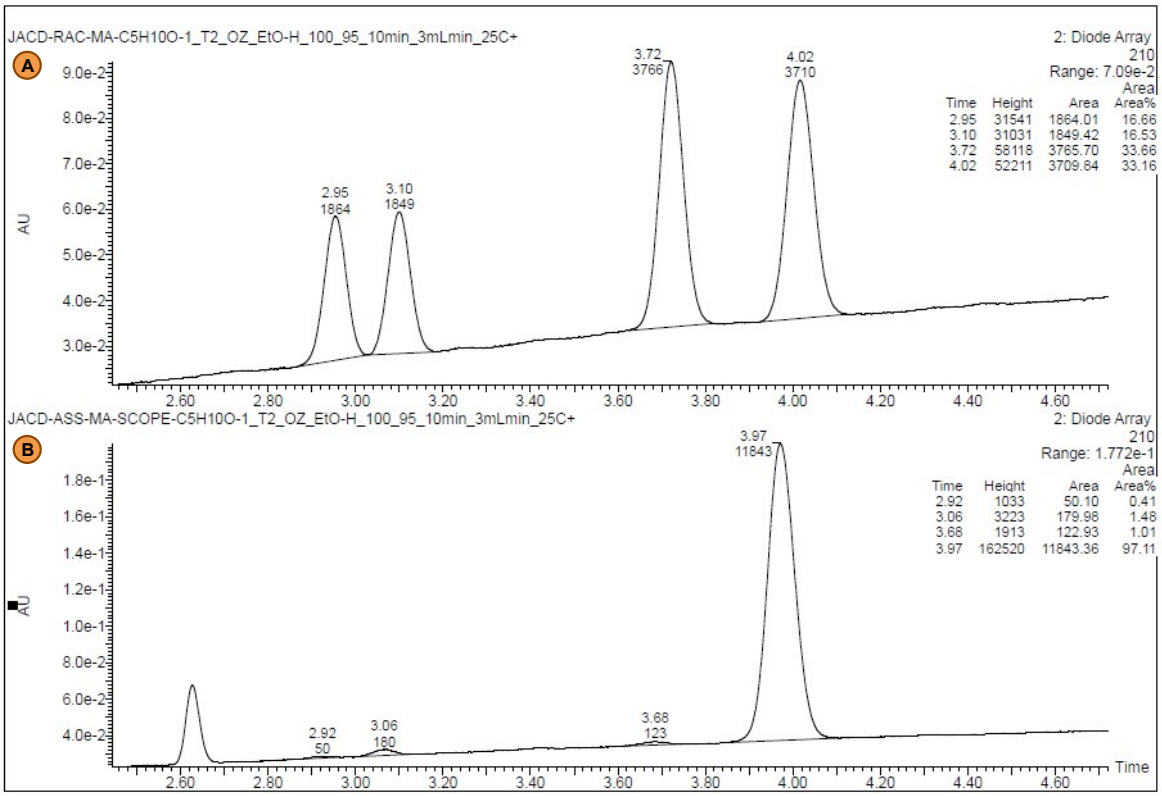


FIGURE 118. (a) Chiral UPC^2 of racemic 2-isopropyl-4-nitro-3-phenylbutanal (**4c**); b) Chiral UPC^2 of 2-isopropyl-4-nitro-3-phenylbutanal **4c** obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.68 min, (syn, major) = 3.97 min. TABLE 4, Entry 3.

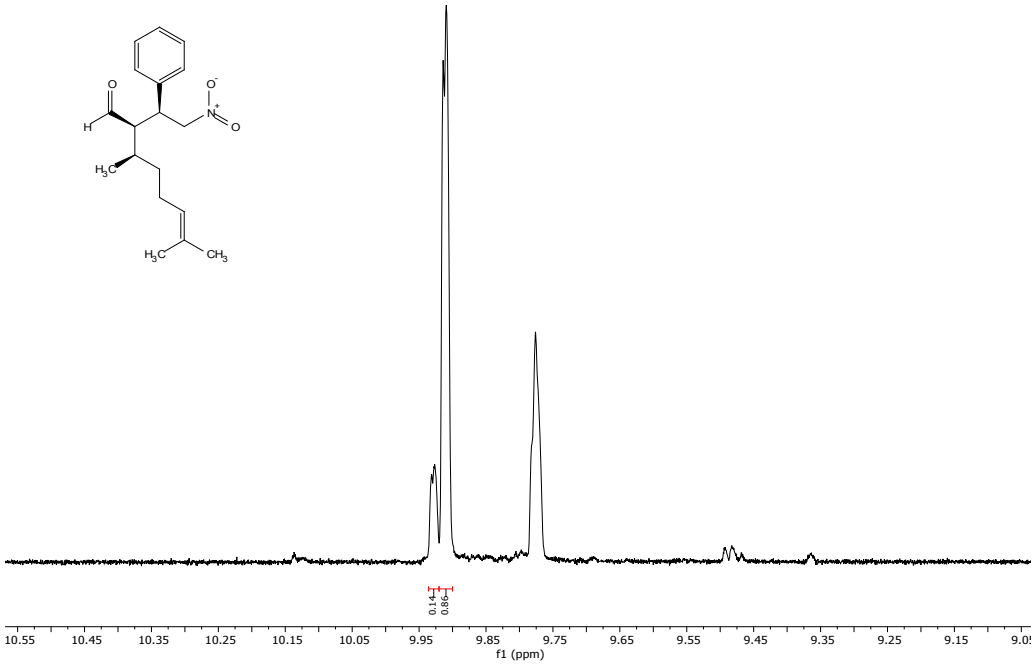


FIGURE 119. ^{1}H NMR of crude compound **4d** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 86:14. TABLE 4, Entry 4.

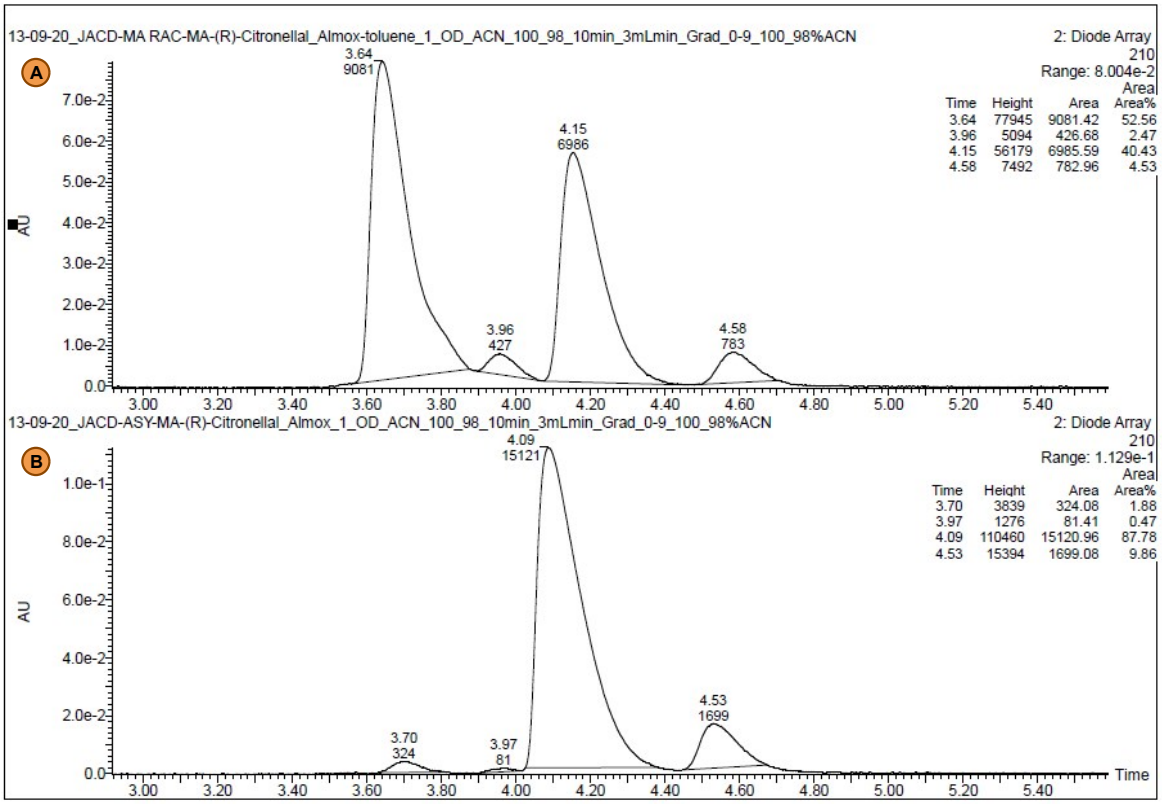


FIGURE 120. (a) Chiral UPC^2 of racemic 3,7-dimethyl-2-(2-nitro-1-phenylethyl)oct-6-enal (**4d**); (b) Chiral UPC^2 of 3,7-dimethyl-2-(2-nitro-1-phenylethyl)oct-6-enal (**4d**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL1, Grad: CO_2/ACN 100-0% to 98-2 % in 9 min; 100-0% in 1 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.70 min, (syn, major) = 4.09 min. TABLE 4, Entry 4.

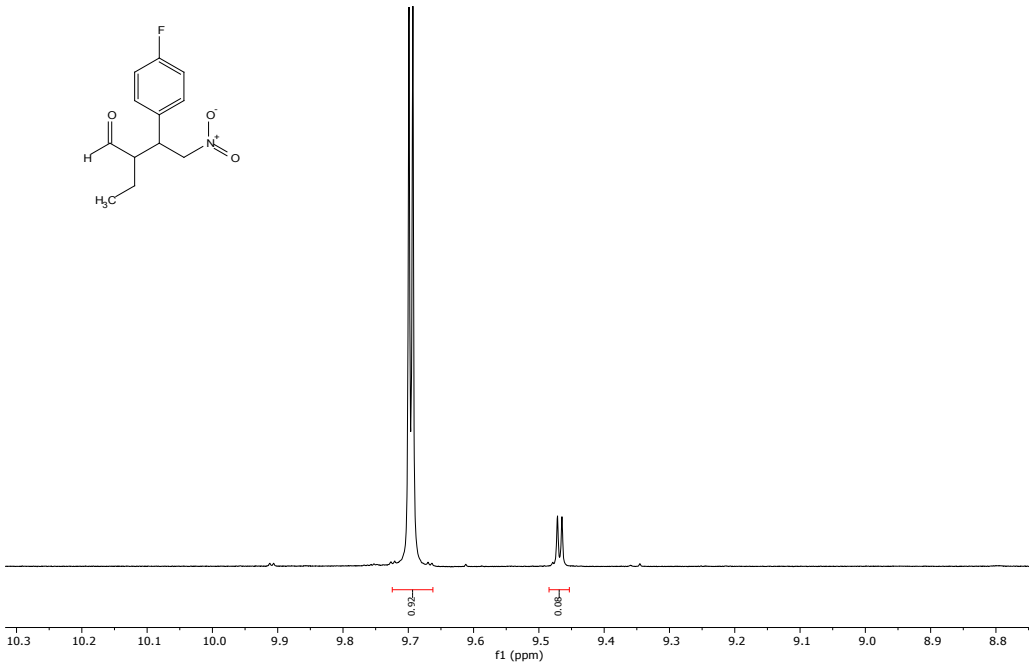


FIGURE 121. ^{1}H NMR of crude compound **4e** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 92:08. TABLE 4, Entry 5.

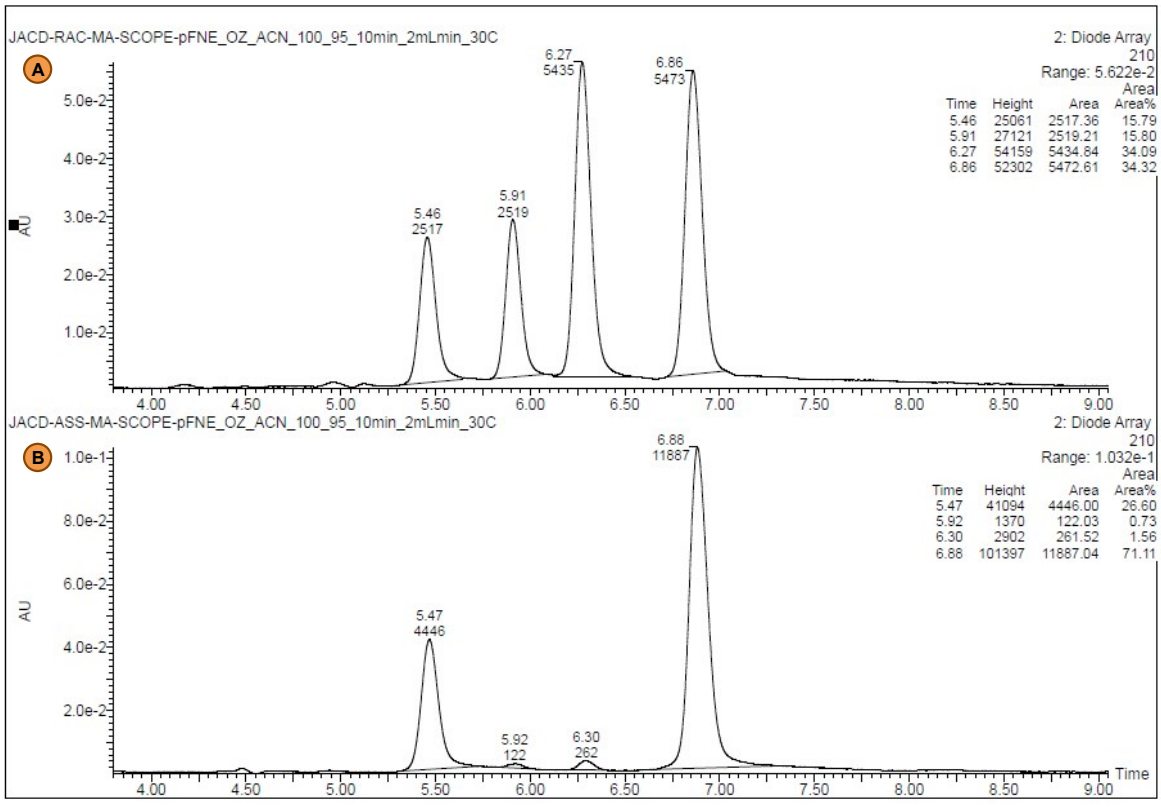


FIGURE 122. (a) Chiral UPC^2 of racemic 2-ethyl-3-(4-fluorophenyl)-4-nitrobutanal (**4e**); (b) Chiral UPC^2 of 2-ethyl-3-(4-fluorophenyl)-4-nitrobutanal (**4e**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5% in 9 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 6.30 min, (syn, major) = 6.88 min. TABLE 4, Entry 5.

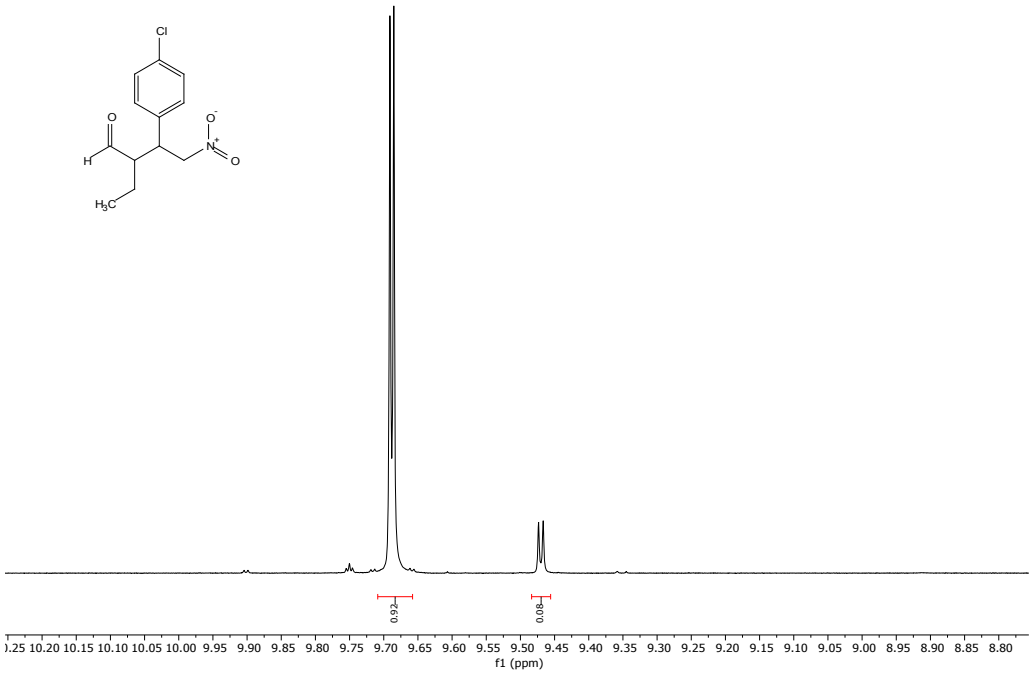


FIGURE 123. ^{1}H NMR of crude compoundcrude compound **4f** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 92:08. TABLE 4, Entry 6.

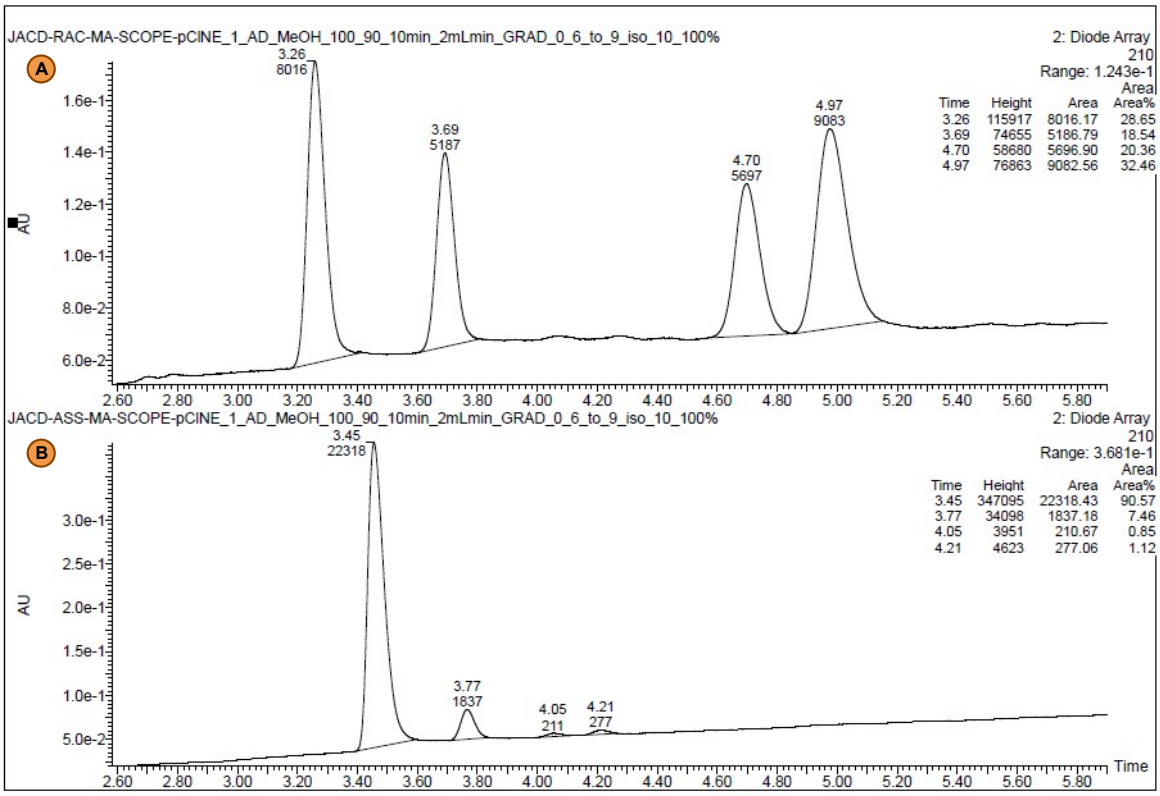


FIGURE 124. (a) Chiral UPC^2 of racemic 3-(4-chlorophenyl)-2-ethyl-4-nitrobutanal (**4f**); (b) Chiral UPC^2 of 3-(4-chlorophenyl)-2-ethyl-4-nitrobutanal (**4f**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil AMY1, **Grad:** CO_2/MeOH 100-0% to 90-10 % in 6 min; 90-10 % in 3 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 3.45 min, (syn, minor) = 4.21 min. TABLE 4, Entry 6.

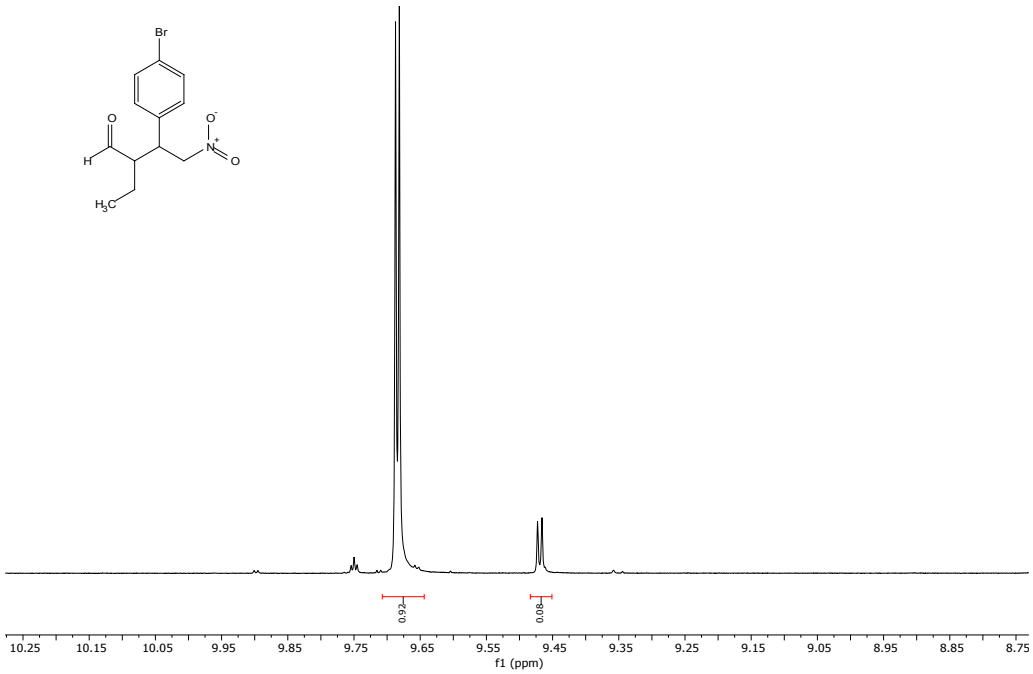


FIGURE 125. ^{1}H NMR of crude compound **4g** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 92:08. TABLE 4, Entry 7.

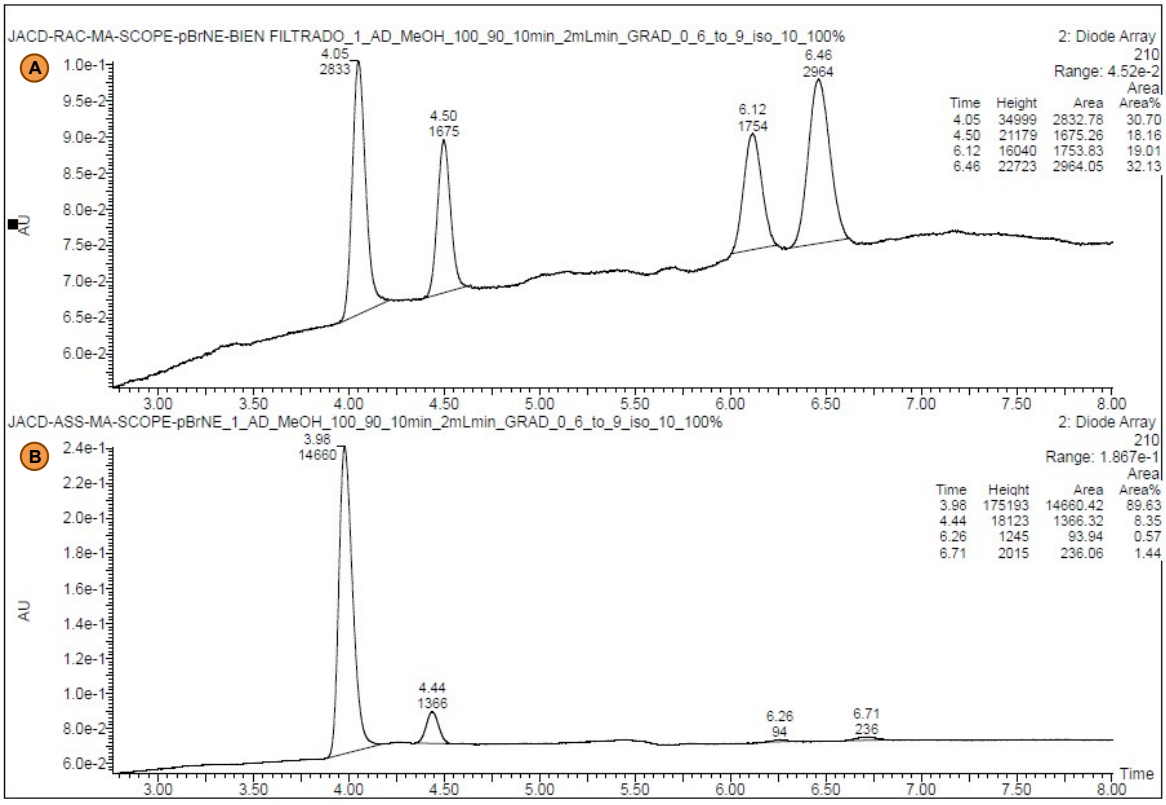


FIGURE 126. (a) Chiral UPC^2 of racemic 3-(4-bromophenyl)-2-ethyl-4-nitrobutanal (**4g**); (b) Chiral UPC^2 of 3-(4-bromophenyl)-2-ethyl-4-nitrobutanal (**4g**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil AMY1, **Grad:** CO_2/MeOH 100-0% to 90-10 % in 6 min; 90-10 % in 3 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 3.98 min, (syn, minor) = 6.71min. TABLE 4, Entry 7.

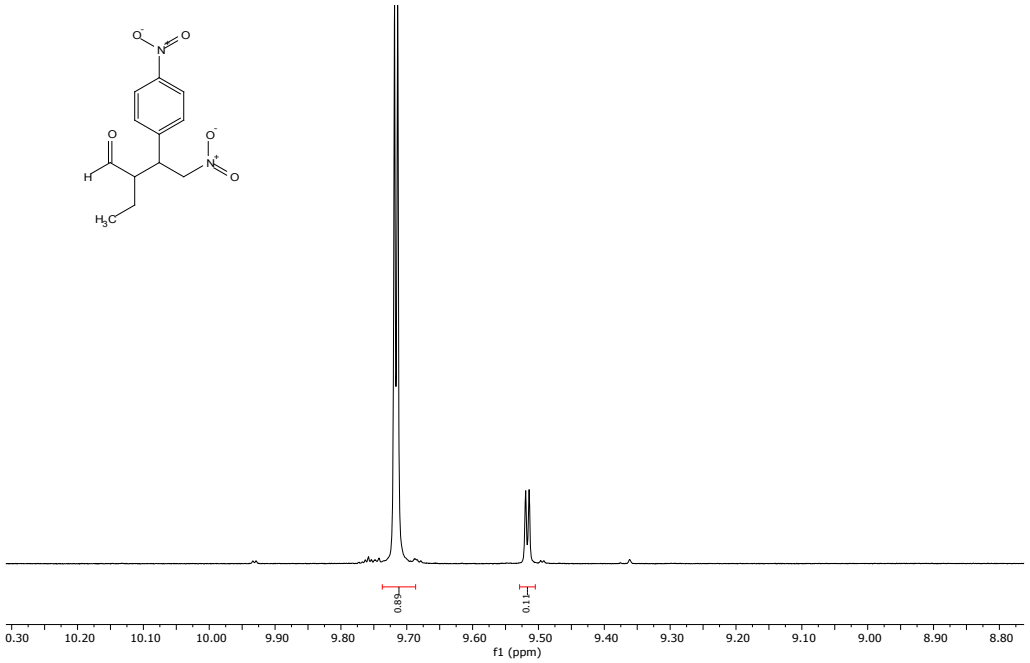


FIGURE 127. ^{1}H NMR of crude compound **4h** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 89:11. TABLE 4, Entry 8.

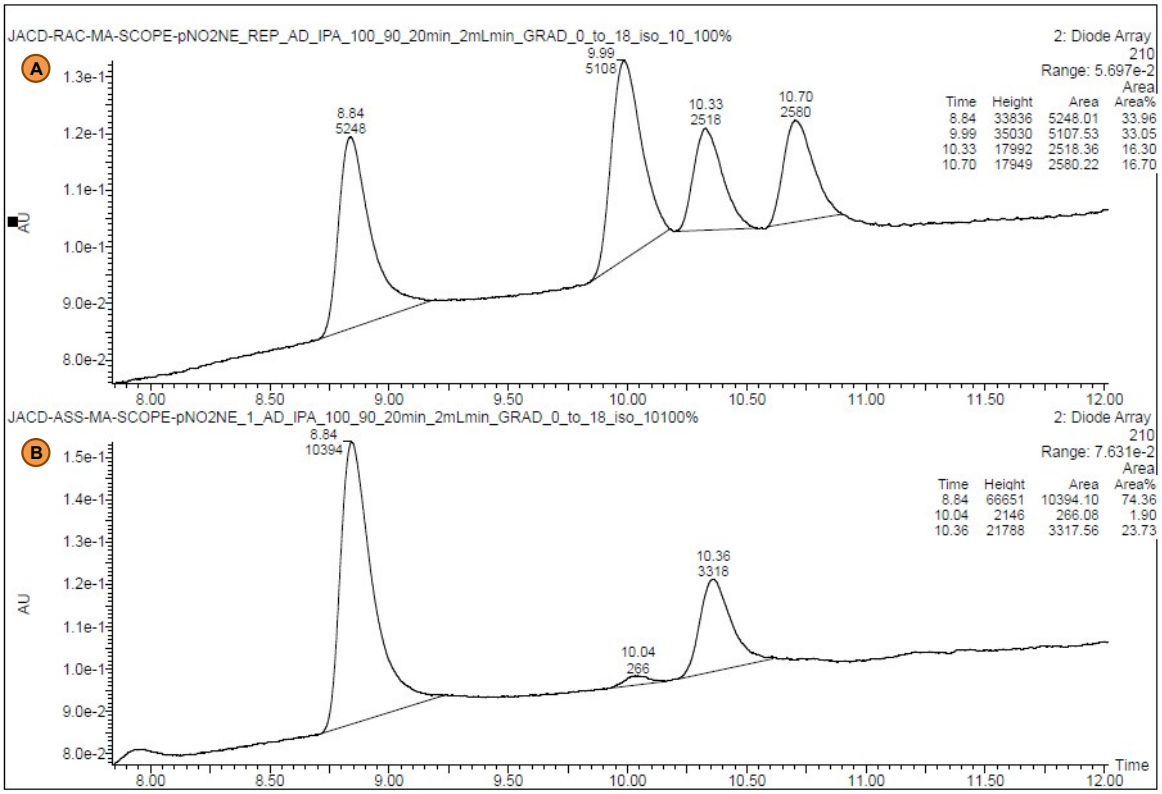


FIGURE 128. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-(4-nitrophenyl) butanal (**4h**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-(4-nitrophenyl) butanal (**4h**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil AMY1, **Grad:** CO_2/IPA 100-0% to 90-10 % in 18 min; 90-10 % in 2 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 8.84 min, (syn, minor) = 10.04 min. TABLE 4, Entry 8.

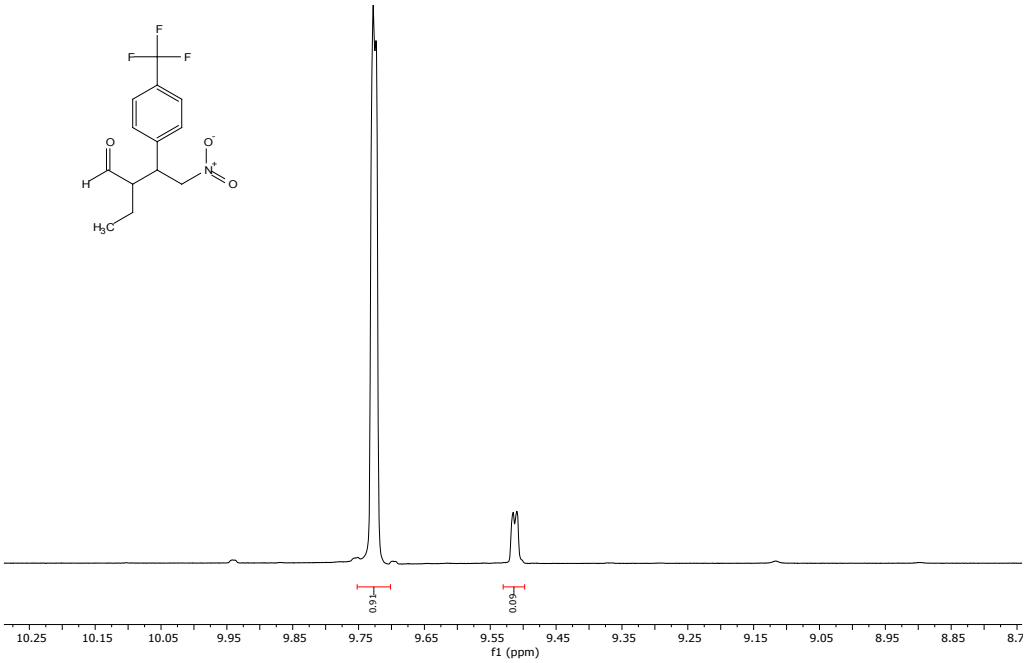


FIGURE 129. ^{1}H NMR of crude compound **4i** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 91:09. TABLE 4, Entry 9.

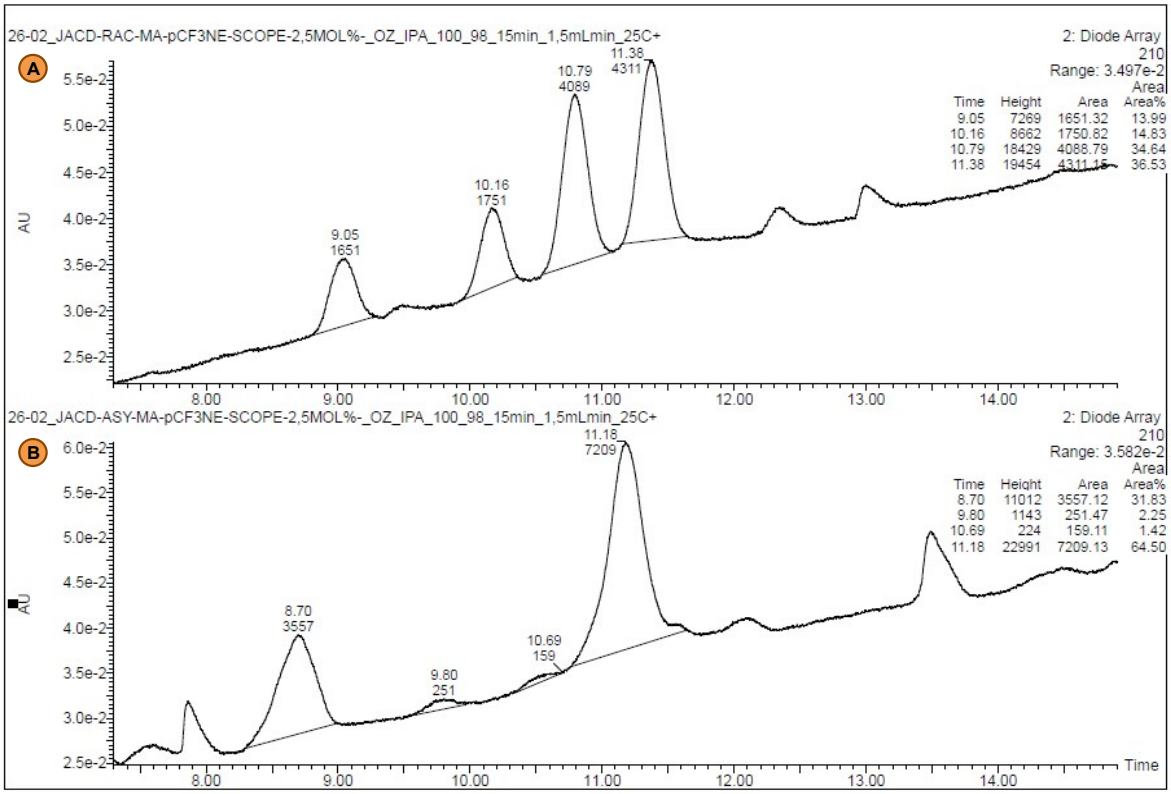


FIGURE 130. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-(4-(trifluoromethyl)phenyl)butanal (**4i**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-(4-(trifluoromethyl)phenyl)butanal (**4i**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/IPA 100- 0% to 95-05 % in 14 min; 100-0 % in 1 min at 1.5 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 10.69 min, (syn, major) = 11.18 min. TABLE 4, Entry 9.

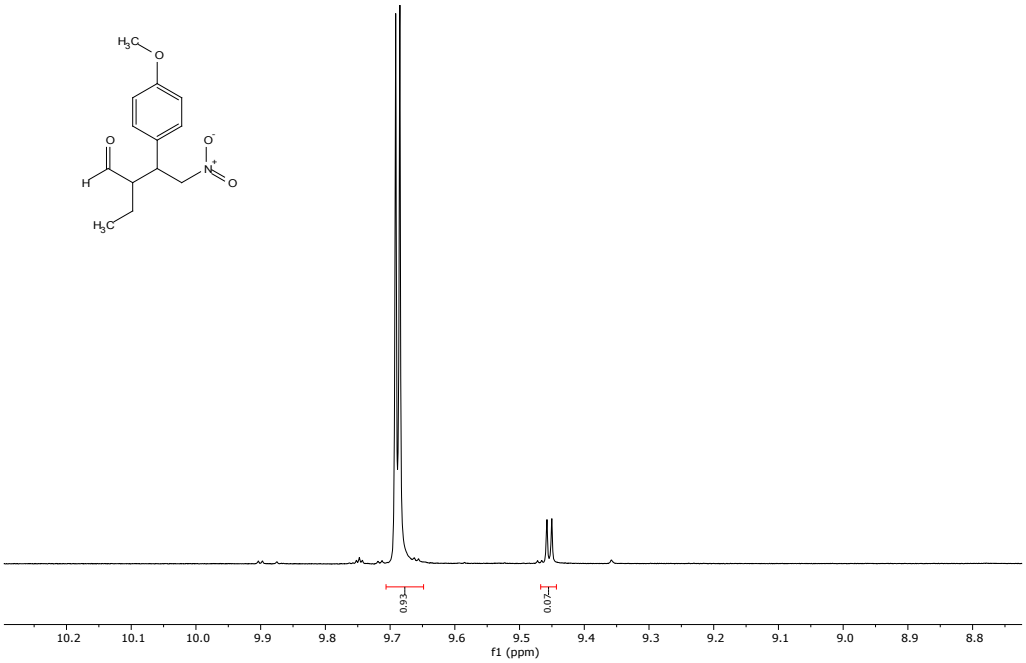


FIGURE 131. ^{1}H NMR of crude compound **4j** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn*/*anti*): 93:07. TABLE 4, Entry 10.

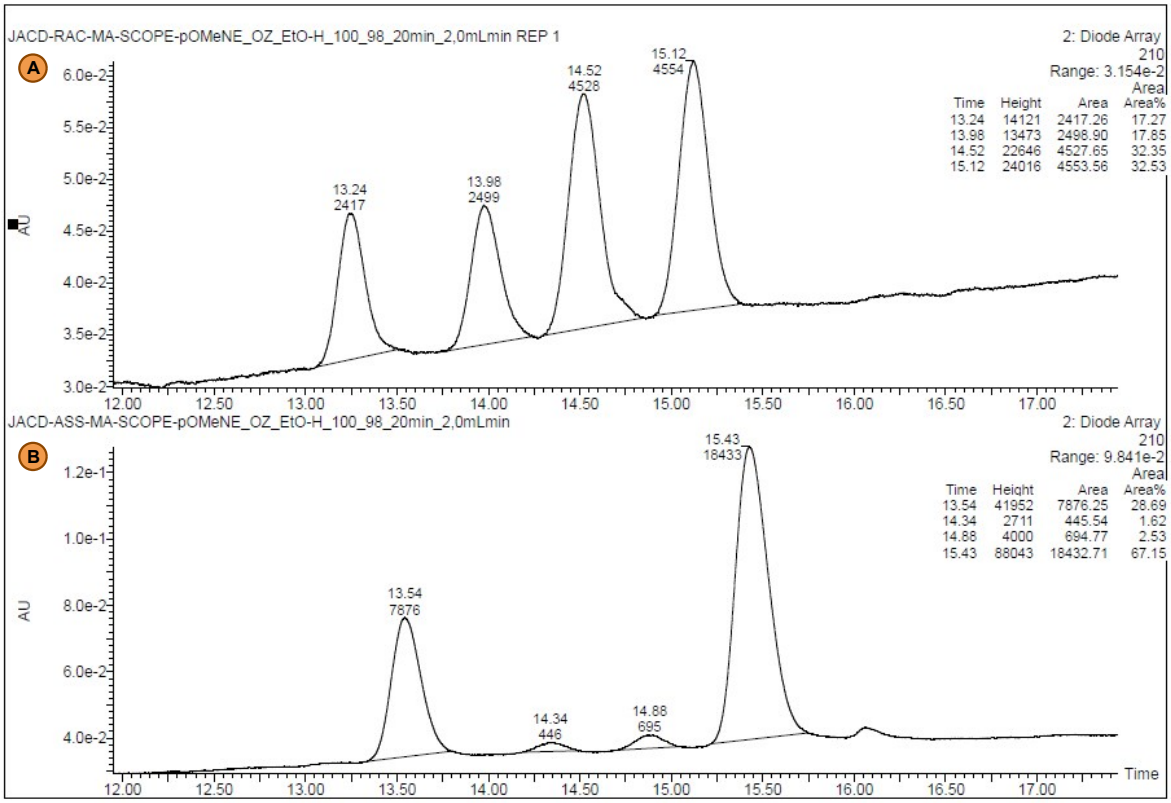


FIGURE 132. (a) Chiral UPC^2 of racemic 2-ethyl-3-(4-methoxyphenyl)-4-nitrobutanal (**4j**); (b) Chiral UPC^2 of 2-ethyl-3-(4-methoxyphenyl)-4-nitrobutanal (**4j**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 98-2 % in 19 min; 100-0 % in 1 min at 2.5 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 14.88 min, (syn, major) = 15.43 min. TABLE 4, Entry 10.

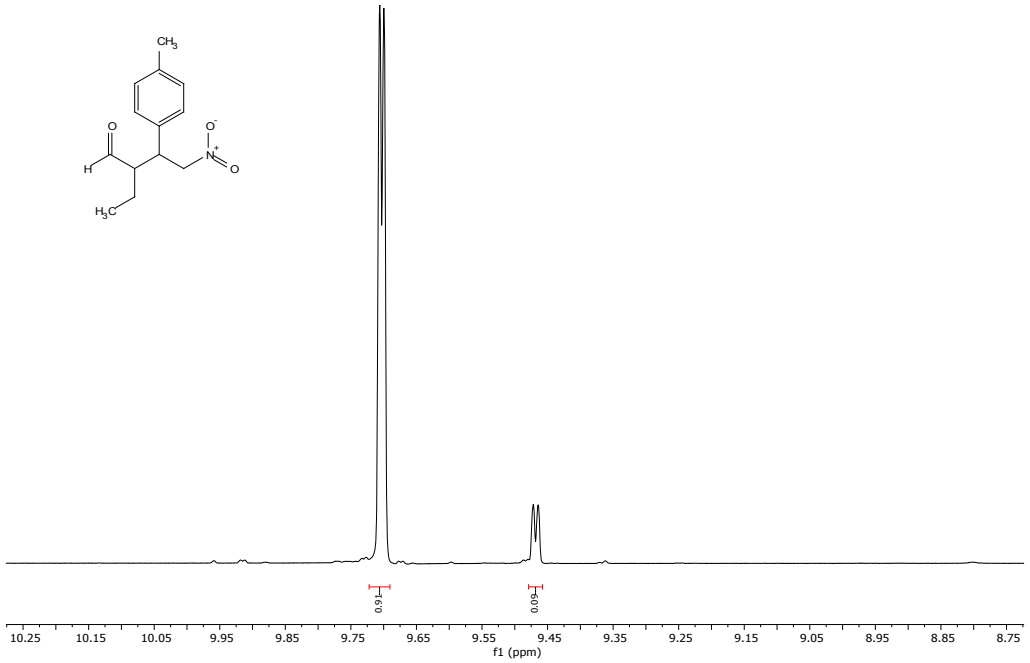


FIGURE 133. ^{1}H NMR of crude compound **4k** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 91:09. TABLE 4, Entry 11.

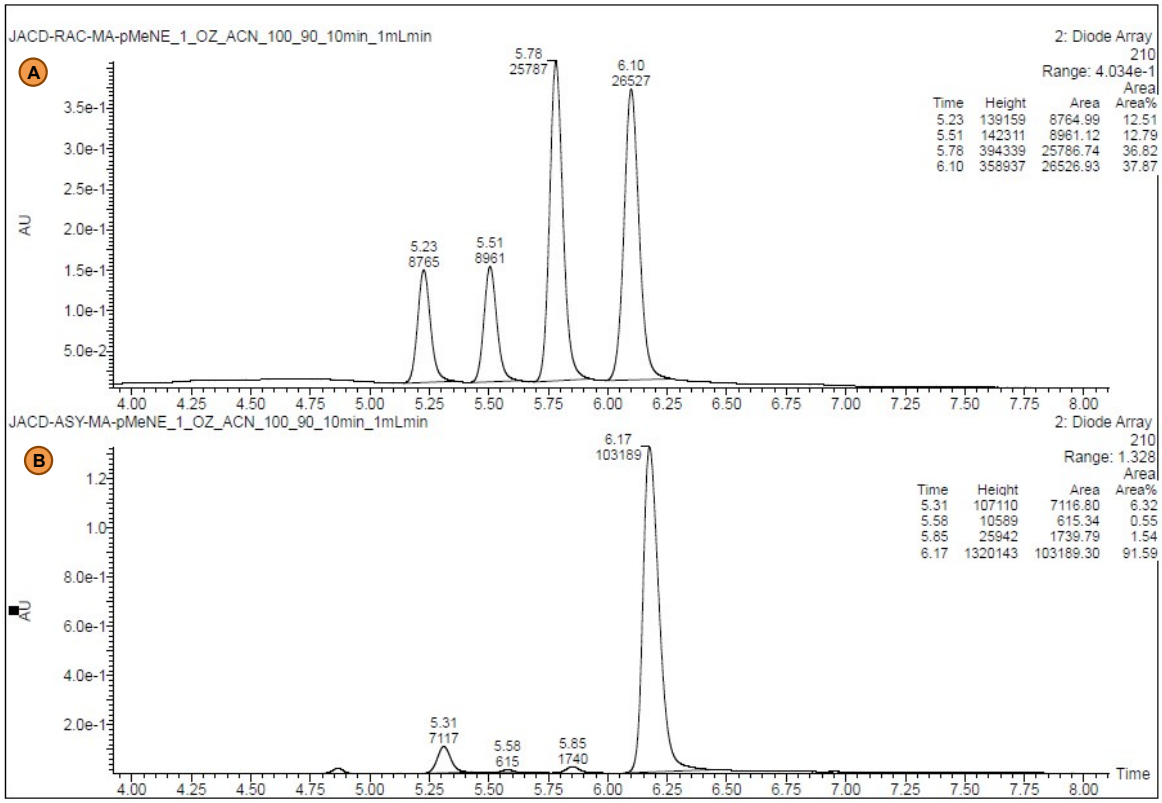


FIGURE 134. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-(p-tolyl)butanal (**4k**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-(p-tolyl)butanal (**4k**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/ACN 100- 0% to 90-10 % in 5 min; 90-10 % in 4 min; 100-0 % in 1 min at 1 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 5.85 min, (syn, major) = 6.17 min. TABLE 4, Entry 11.

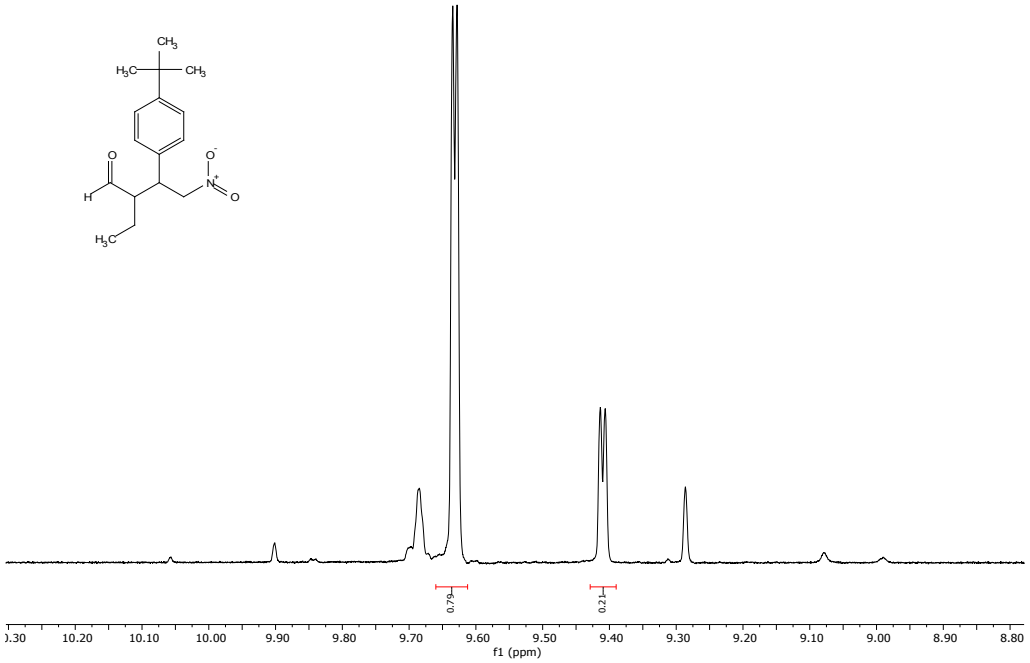


FIGURE 135. ^{1}H NMR of crude compound **4l** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 79:21. TABLE 4, Entry 12.

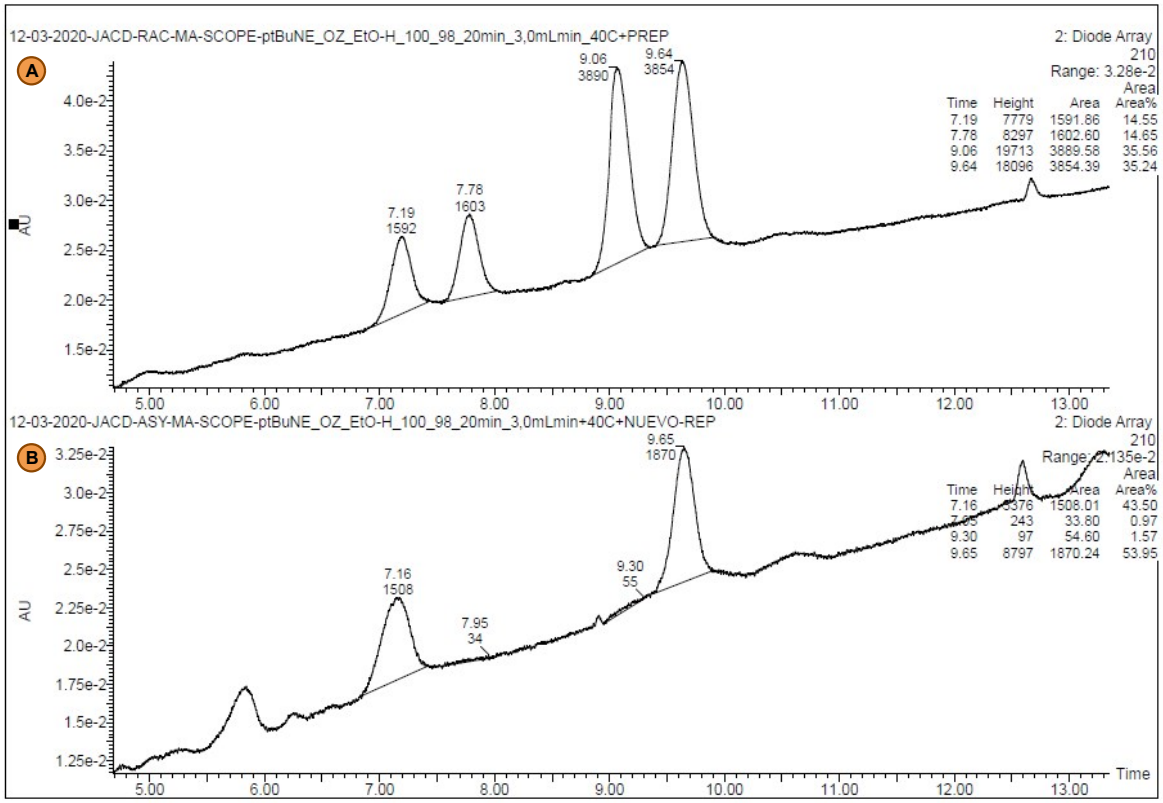


FIGURE 136. (a) Chiral UPC^2 of racemic 3-(4-(tert-butyl)phenyl)-2-ethyl-4-nitrobutanal (**4l**); (b) Chiral UPC^2 of 3-(4-(tert-butyl)phenyl)-2-ethyl-4-nitrobutanal (**4l**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 98-02 % in 19 min; 100-0 % in 1 min at 3 ml/min at 40°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 9.30 min, (syn, major) = 9.65 min. TABLE 4, Entry 12.

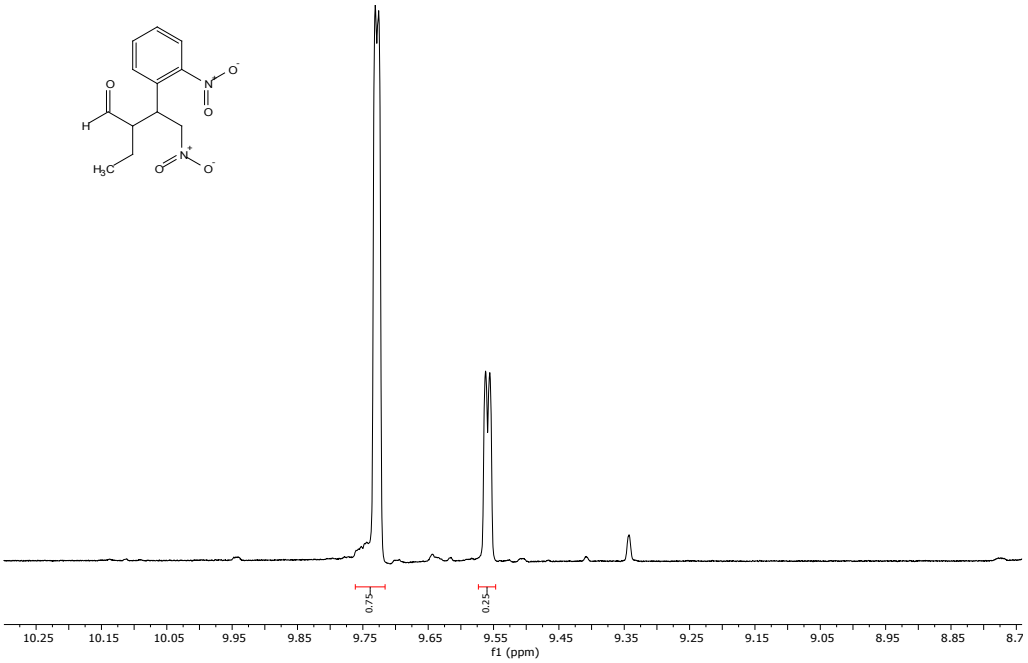


FIGURE 137. ^{1}H NMR of crude compound **4m** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 75:25. TABLE 4, Entry 13.

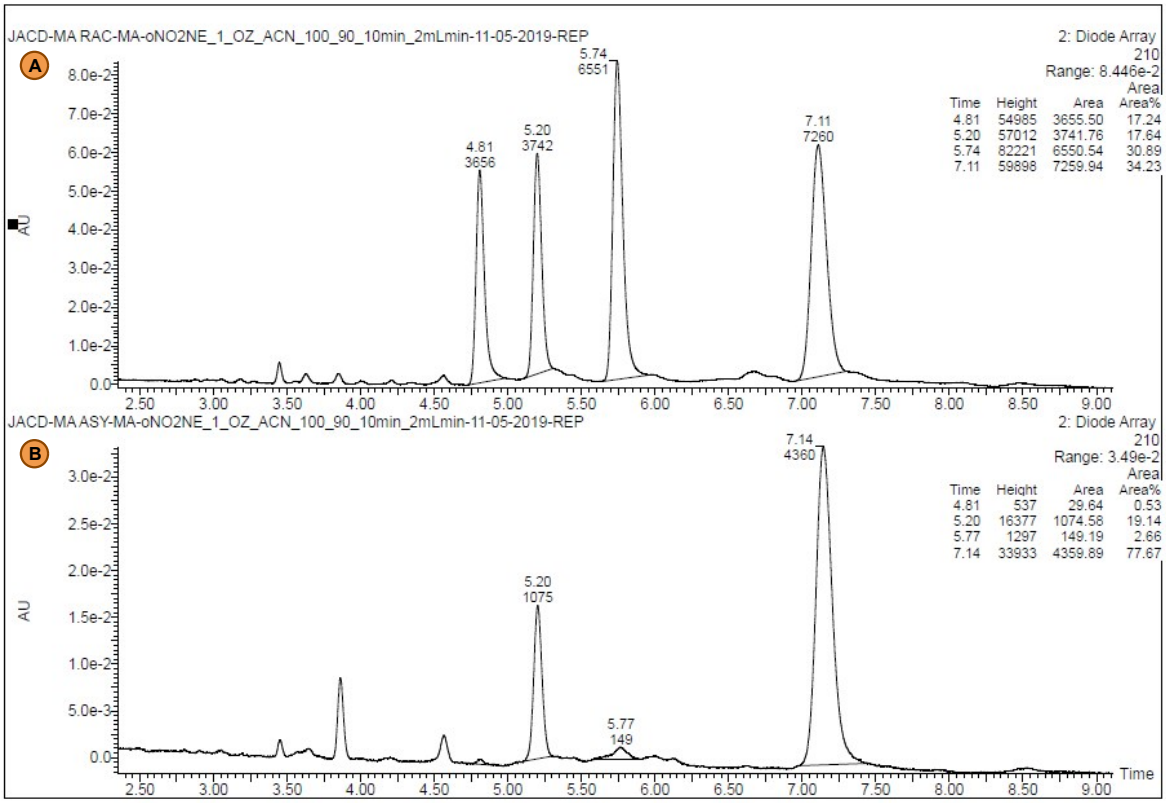


FIGURE 138. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-(2-nitrophenyl)butanal (**4m**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-(2-nitrophenyl)butanal (**4m**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/ACN 100-0% to 90-10 % in 5 min; 90-10 % in 4 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 5.77 min, (syn, major) = 7.14 min. TABLE 4, Entry 13.

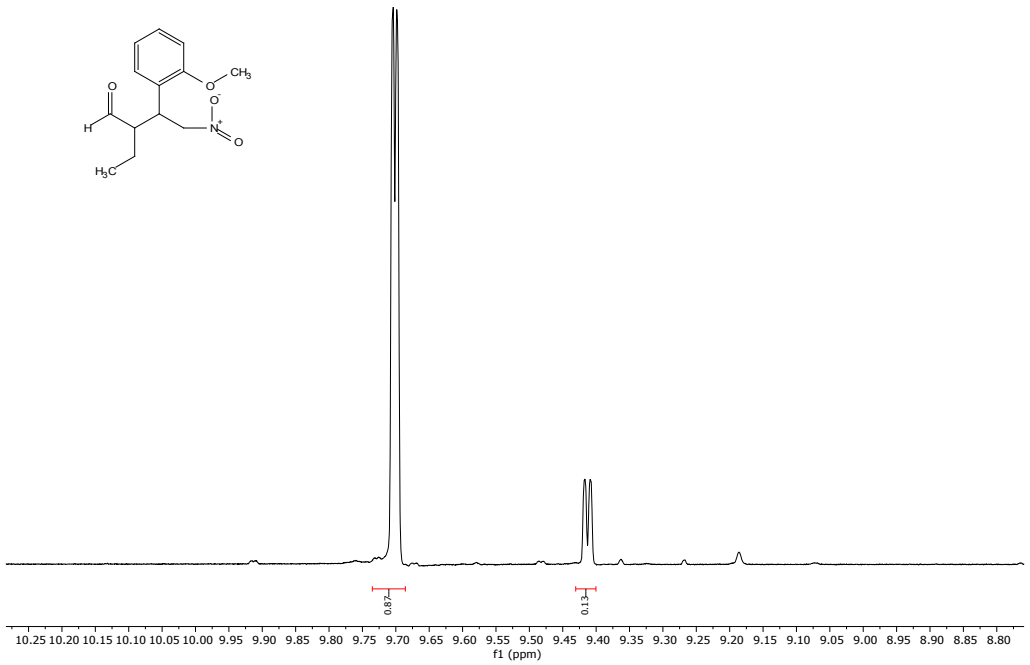


FIGURE 139. ^{1}H NMR of crude compound **4n** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 87:13. TABLE 4, Entry 14.

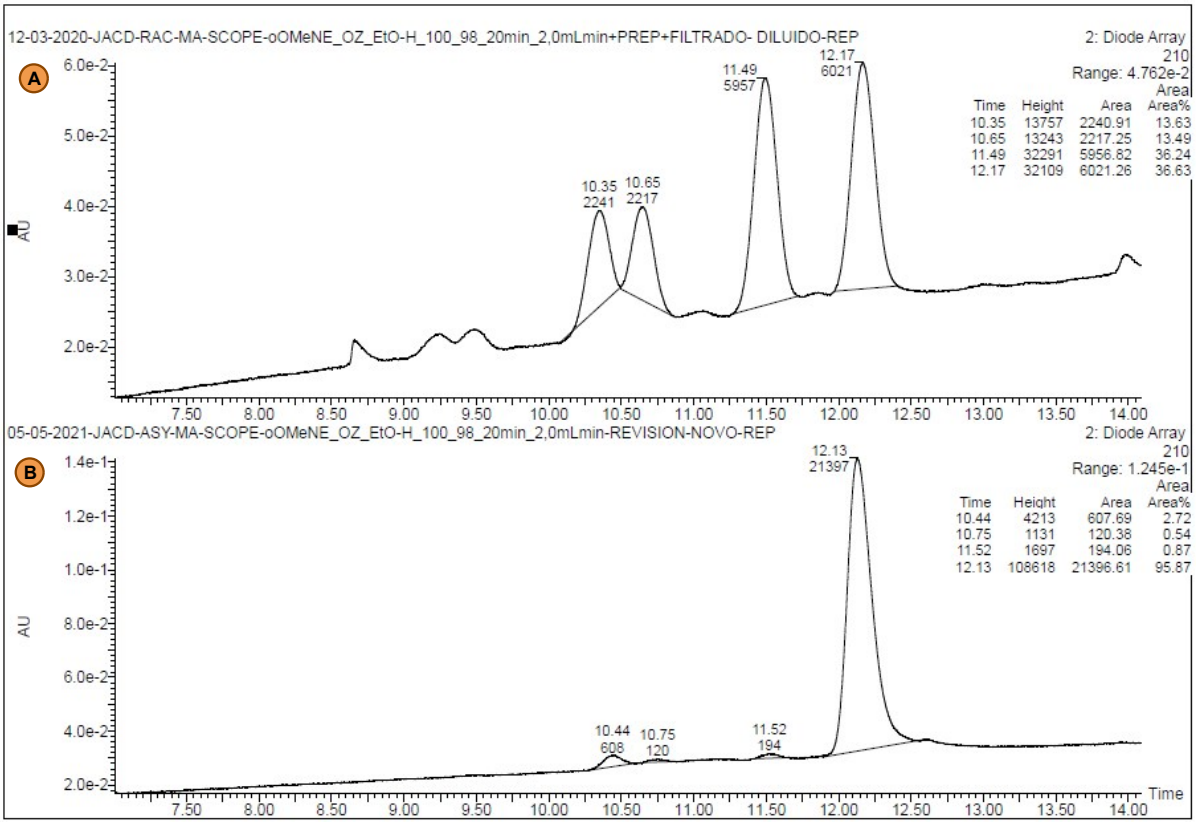


FIGURE 140. (a) Chiral UPC^2 of racemic 2-ethyl-3-(2-methoxyphenyl)-4-nitrobutanal (**4n**); (b) Chiral UPC^2 of 2-ethyl-3-(2-methoxyphenyl)-4-nitrobutanal (**4n**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100- 0% to 98-02 % in 19 min; 100-0 % in 1 min at 2 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 11.52 min, (syn, major) = 12.13 min. TABLE 4, Entry 14.

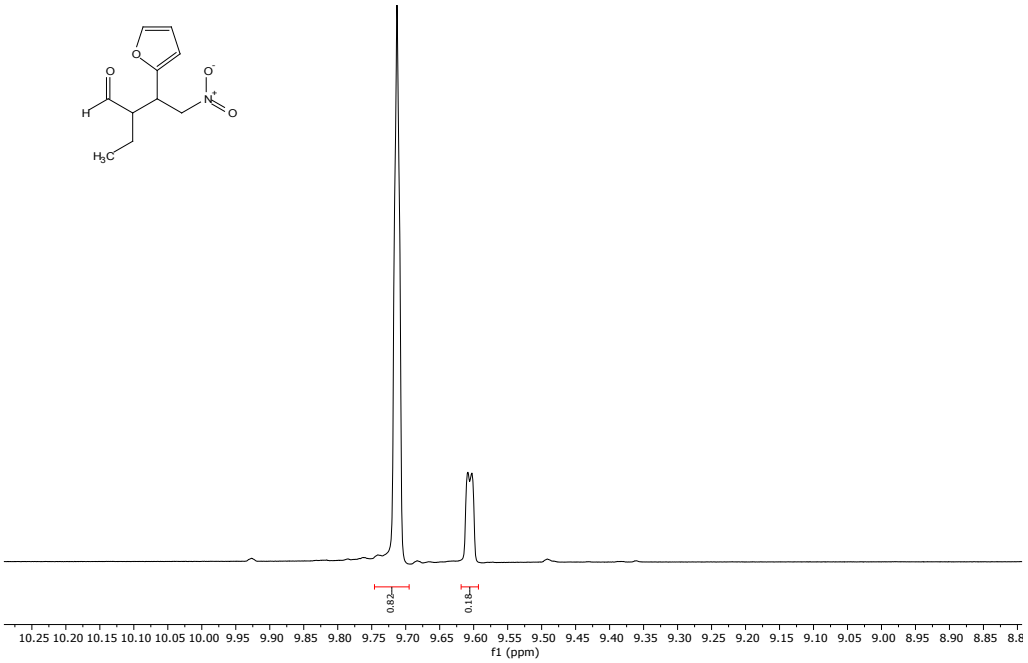


FIGURE 141. ^{1}H NMR of crude compound **4o** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): 82:18. TABLE 4, Entry 15.

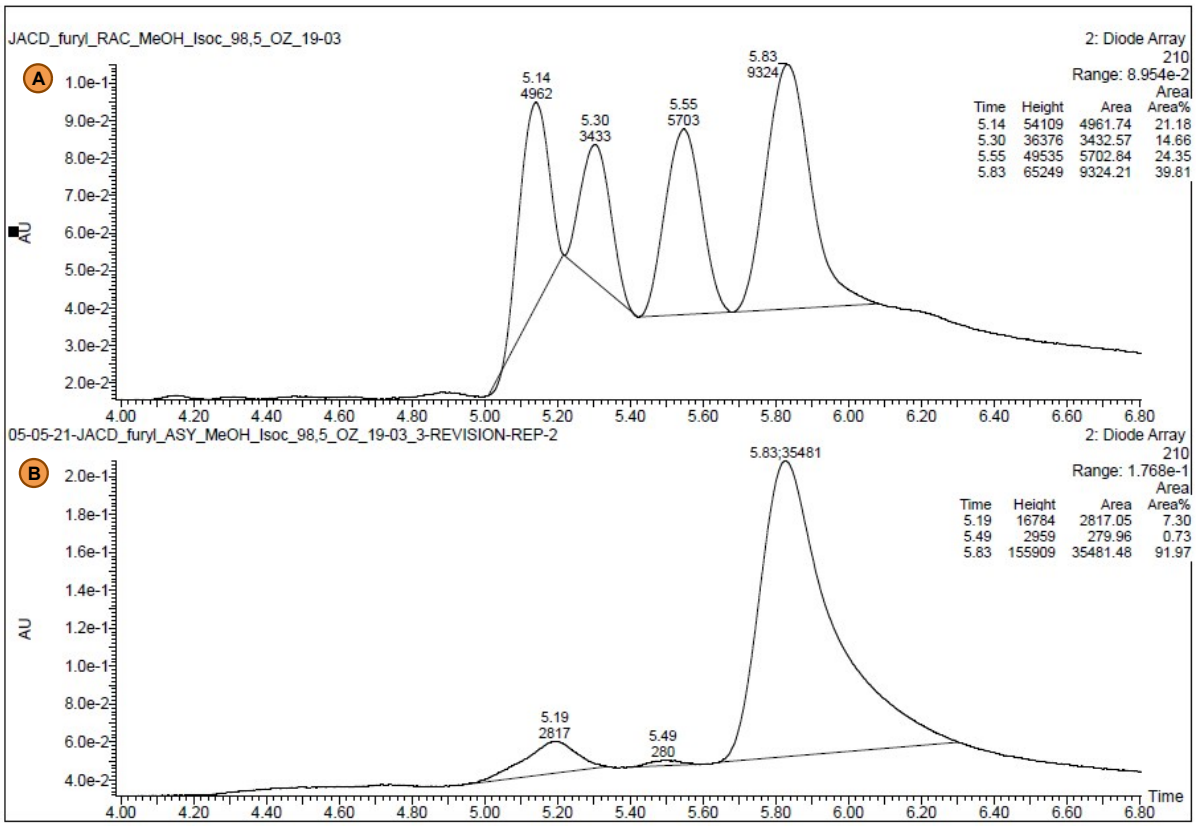


FIGURE 142. (a) Chiral UPC^2 of racemic 2-ethyl-3-(furan-2-yl)-4-nitrobutanal (**4o**); (b) Chiral UPC^2 of 2-ethyl-3-(furan-2-yl)-4-nitrobutanal (**4o**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, CO_2/MeOH 98.5-1.5 in 8 min at 1 ml/min at 35°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 5.49 min, (syn, major) = 5.83 min. TABLE 4, Entry 15.

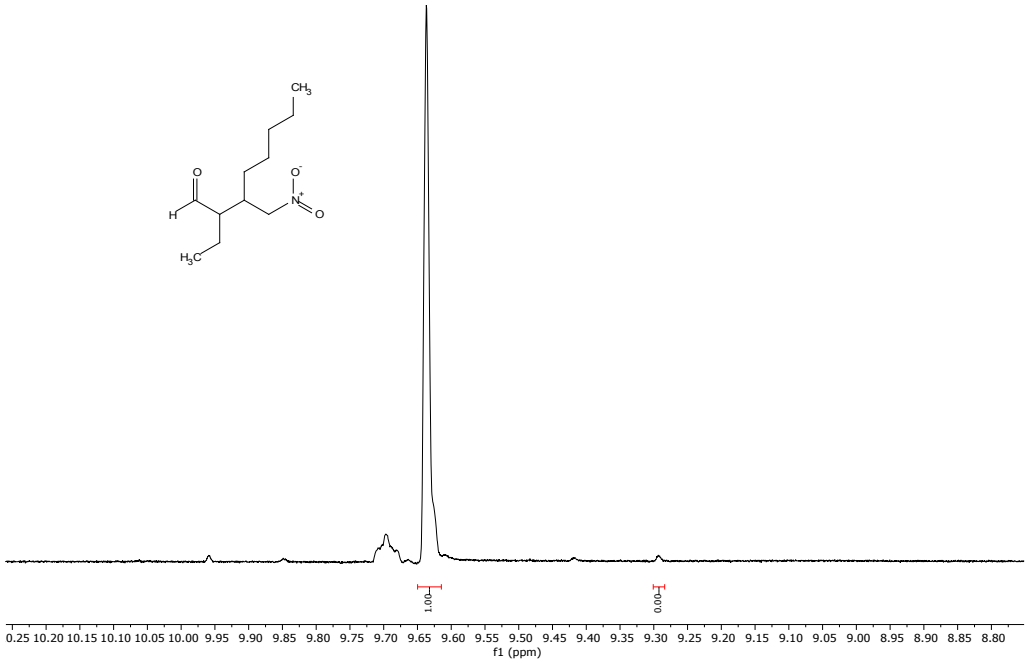


FIGURE 143. ^{1}H NMR of crude compound **4p** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Diastereoisomeric ratio (*syn/anti*): >99:1. TABLE 4, Entry 16.

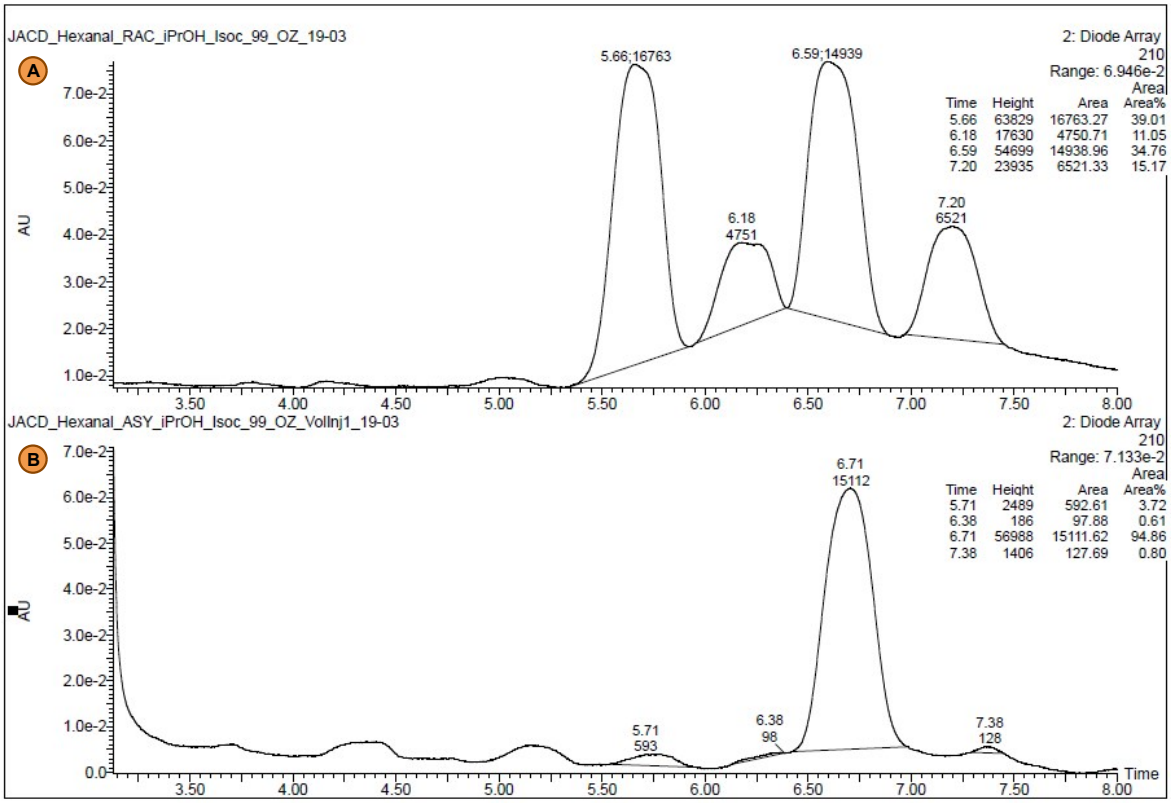


FIGURE 144. (a) Chiral UPC^2 of racemic 2-ethyl-3-(nitromethyl)octanal (**4p**); (b) Chiral UPC^2 of 2-ethyl-3-(nitromethyl)octanal (**4p**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, CO_2/IPA 99-1 in 8 min at 1 ml/min at 35°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 5.71 min, (syn, major) = 6.71 min. TABLE 4, Entry 16.

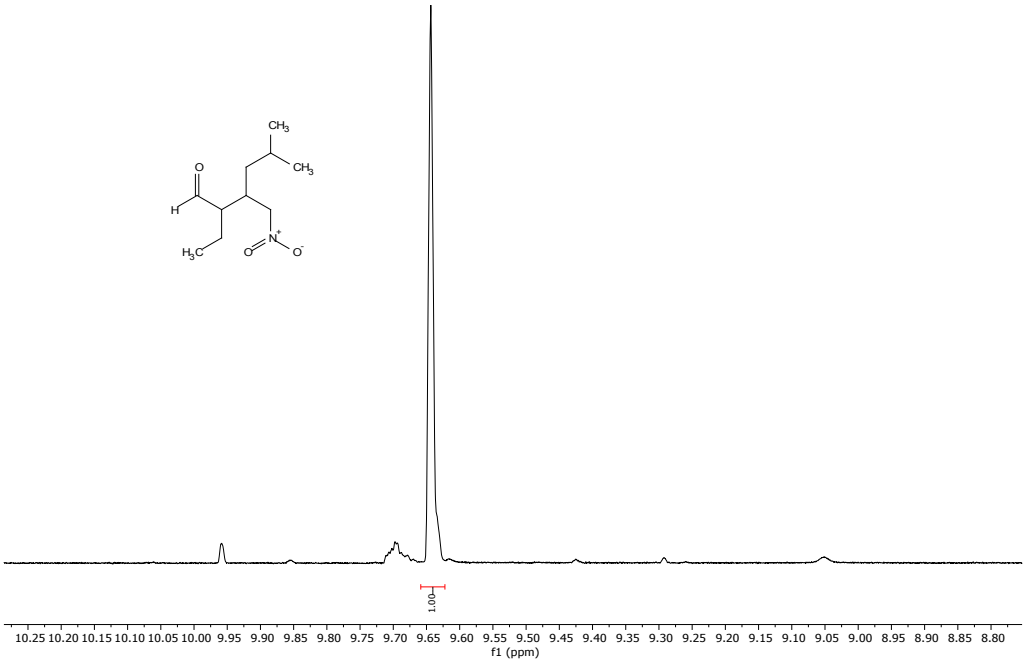


FIGURE 145. ^{1}H NMR of crude of crude **4q** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound 3e. Diastereoisomeric ratio (*syn/anti*): >99:1. TABLE 4, Entry 17.

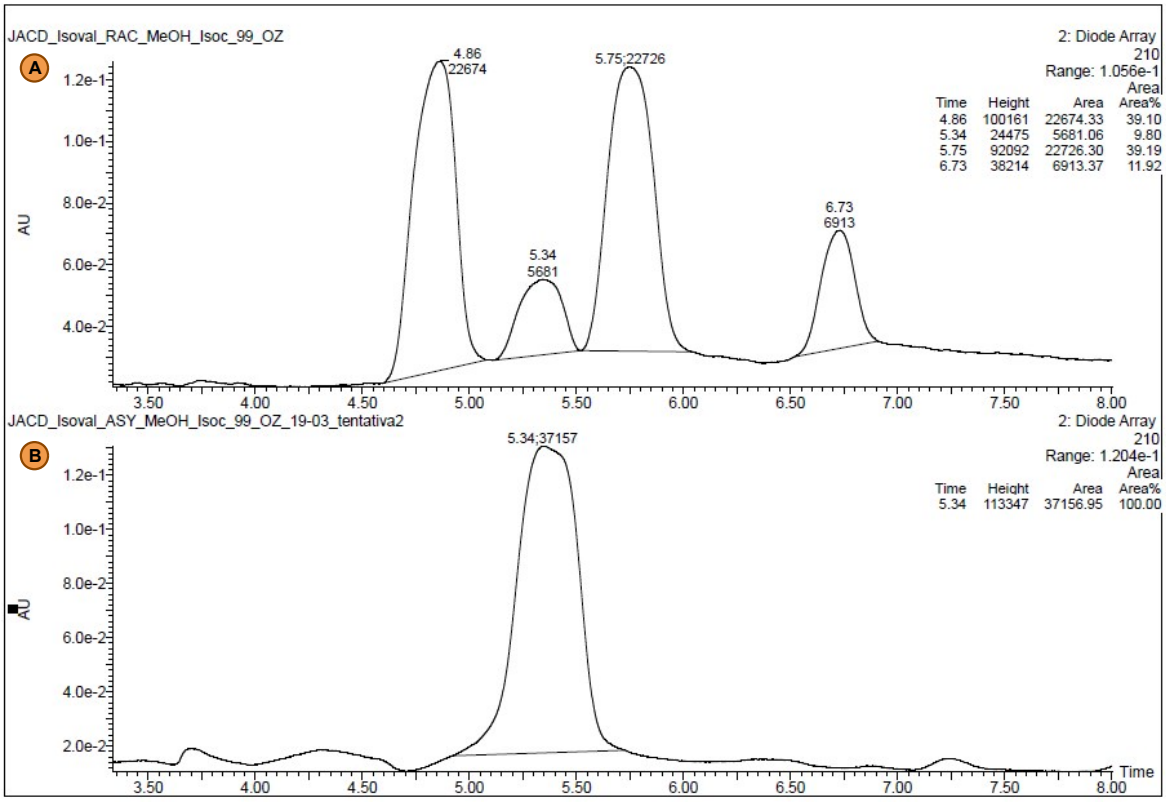


FIGURE 146. (a) Chiral UPC² of racemic 2-ethyl-5-methyl-3-(nitromethyl)hexanal (**4q**); (b) Chiral UPC² of 2-ethyl-5-methyl-3-(nitromethyl)hexanal (**4q**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e**. Trefoil CEL2, CO_2/MeOH 99-1 in 8 min at 1 ml/min at 35°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, major) = 5.34 min. TABLE 4, Entry 17.

19. NMR Spectra and Chromatograms: Scale-Up

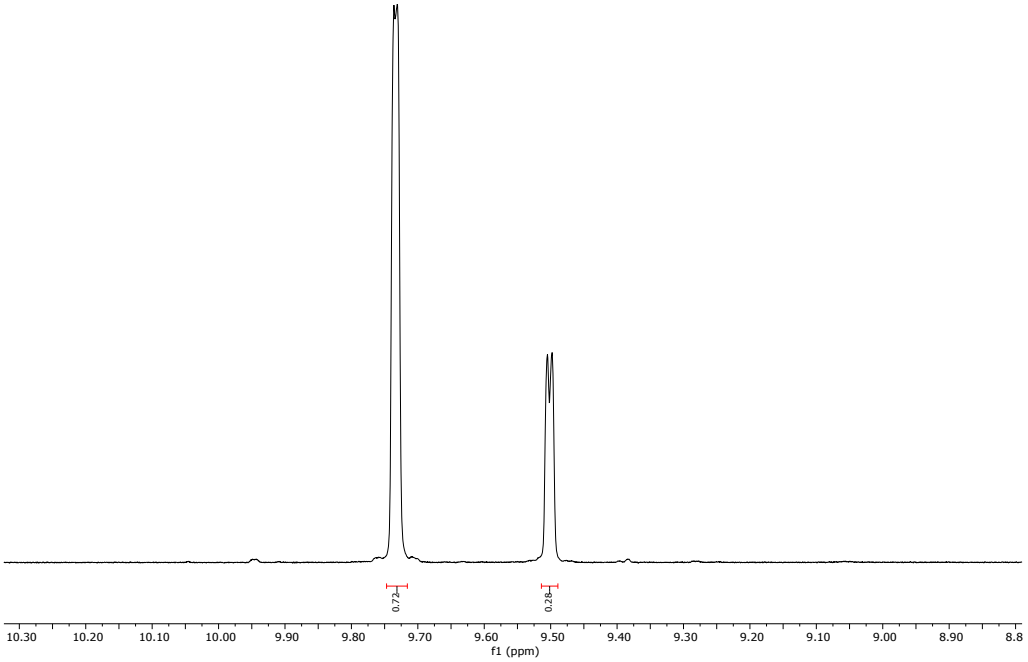


FIGURE 147. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in a 2 mmol scale. Diastereoisomeric ratio (*syn/anti*): 72:28.

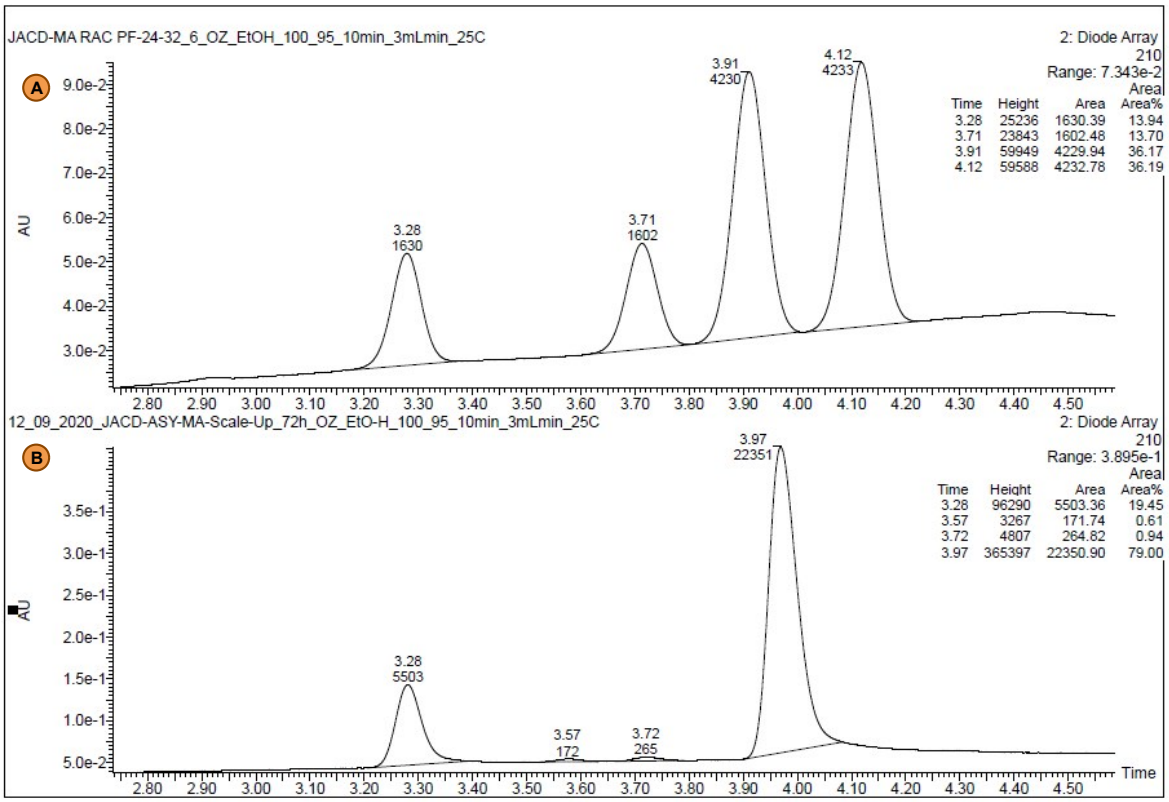


FIGURE 148. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by 2.5 mol% of compound **3e** in a 2 mmol scale. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.72 min, (syn, major) = 3.97 min.

20. NMR Spectra and Chromatograms: Catalyst recycle

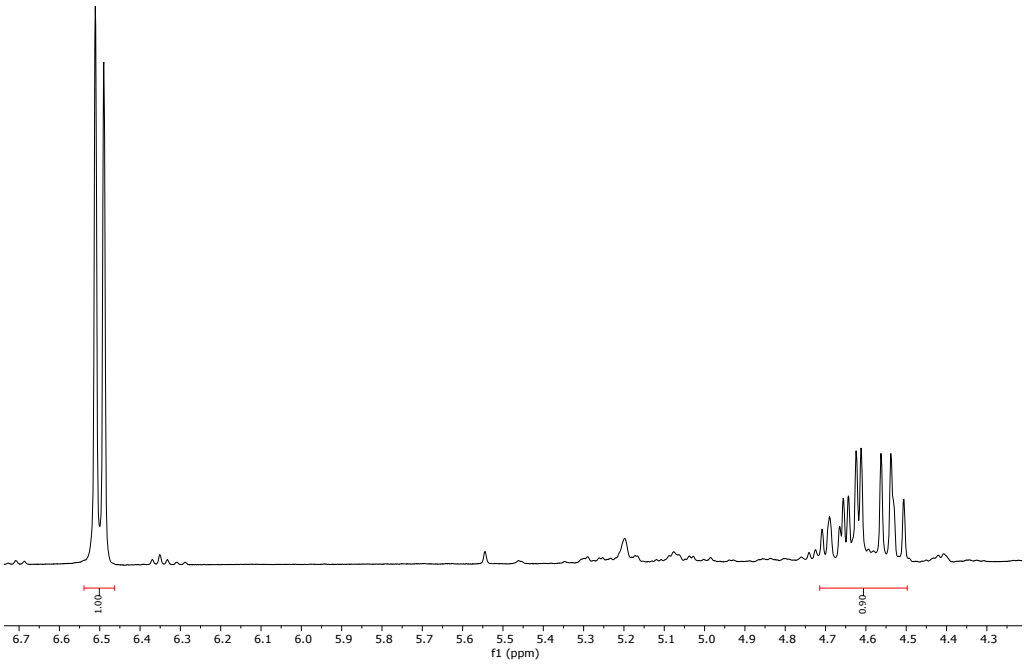


FIGURE 149. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by one-time recovered compound **3a** with 1, 2, 3-trimethoxybenzene as standard. Yield: 90%.

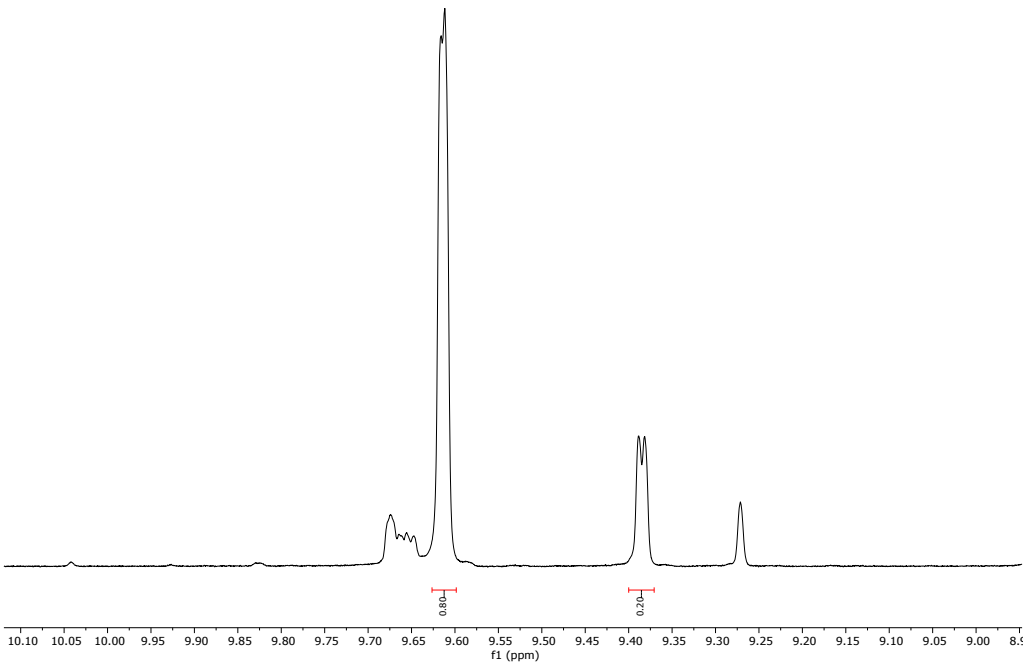


FIGURE 150. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by one-time recovered compound **3a**. Diastereoisomeric ratio (syn/anti): 80:20.

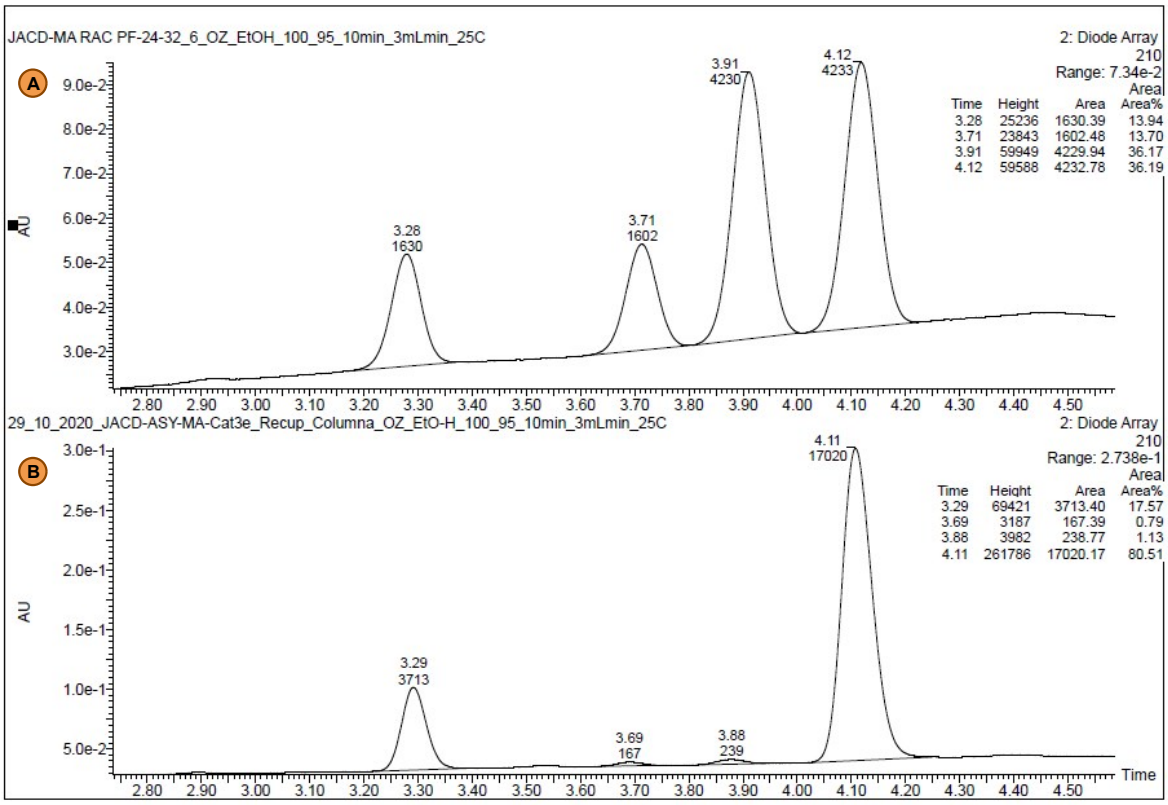


FIGURE 151. (a) Chiral UPC² of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC² of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by one-time recovered compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.88 min, (syn, major) = 4.11 min.

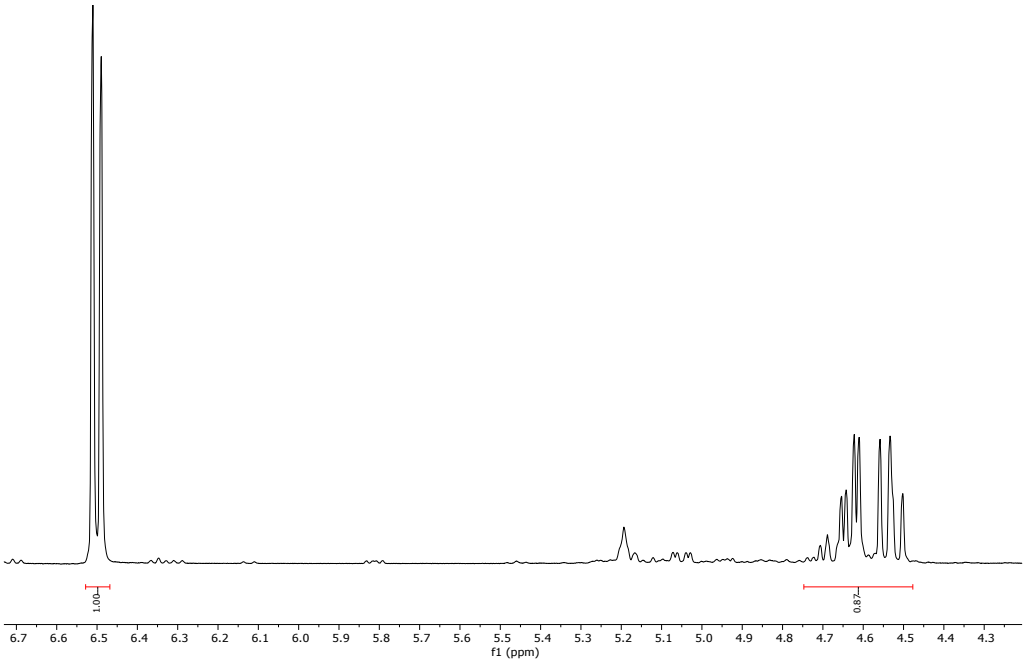


FIGURE 152. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by two-times recovered compound **3a** with 1, 2, 3-trimethoxybenzene as standard. Yield: 87%.

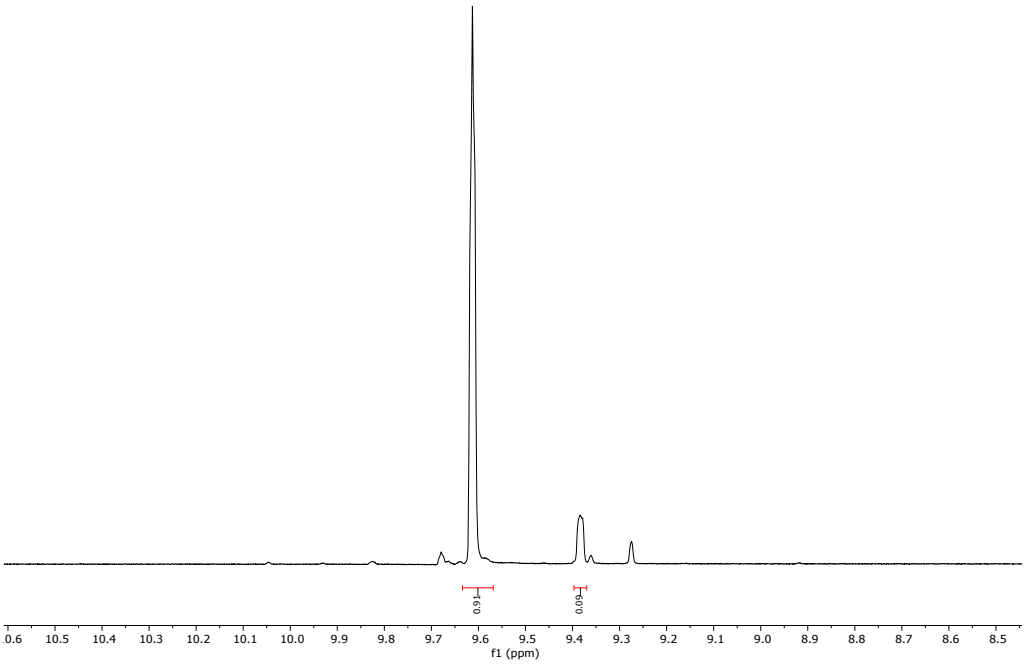


FIGURE 153. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by two-times recovered compound **3a**. Diastereoisomeric ratio (syn/anti): 91:09.

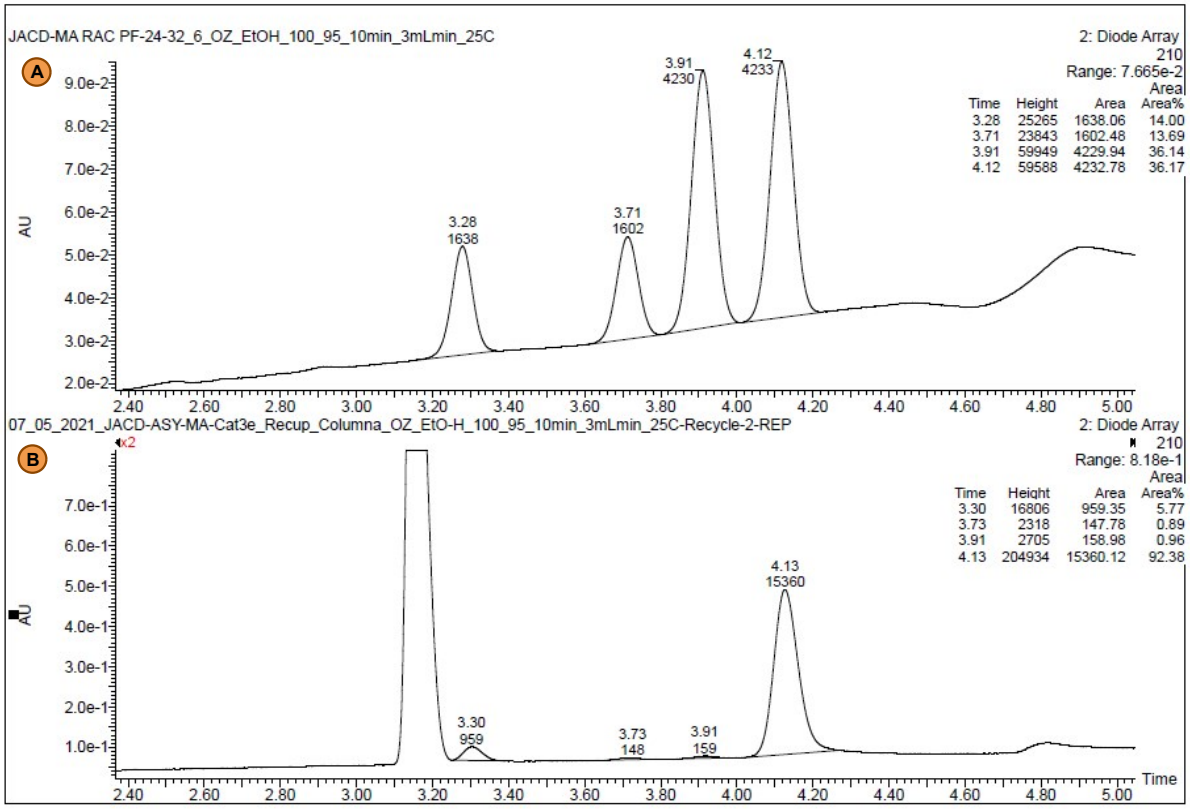


FIGURE 154. (a) Chiral UPC² of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC² of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by two-times recovered compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.91 min, (syn, major) = 4.13 min.

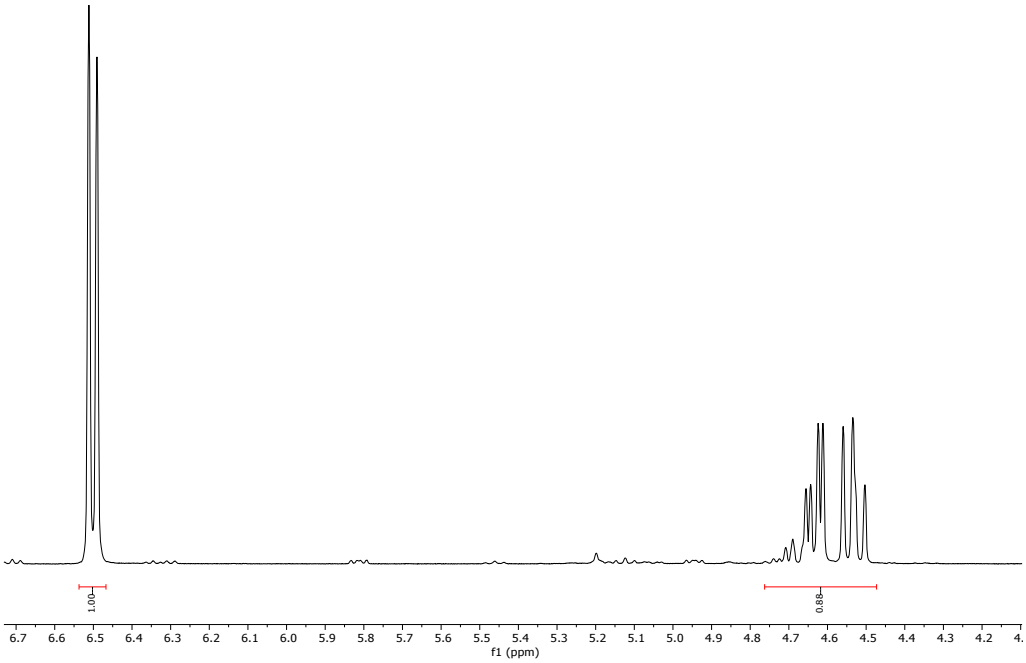


FIGURE 155. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by three-times recovered compound **3a** with 1, 2, 3-trimethoxybenzene as standard. Yield: 88%.

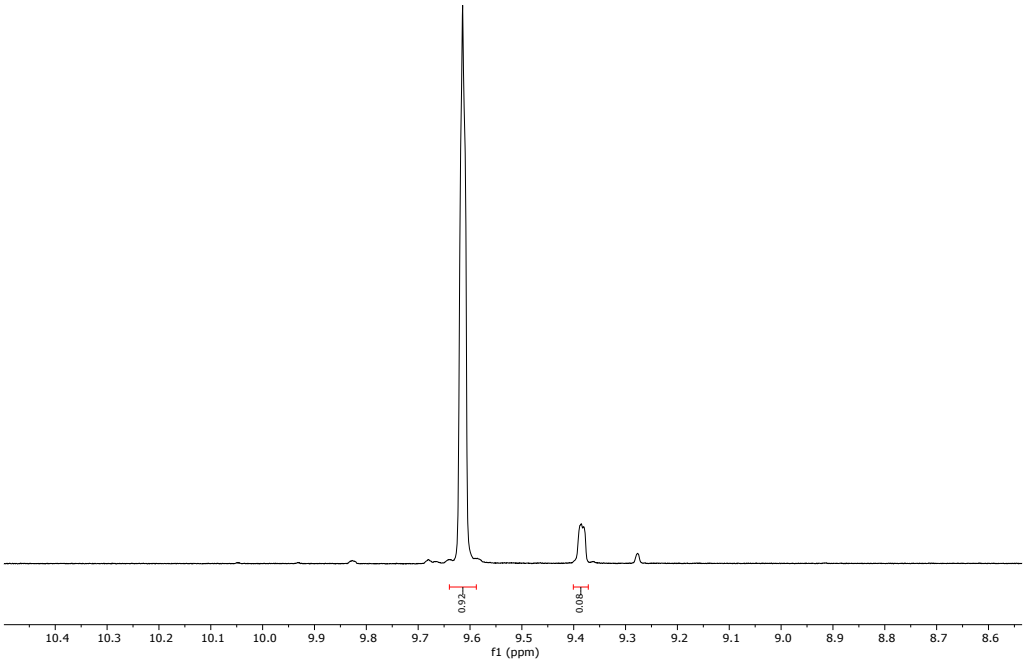


FIGURE 156. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by three-times recovered compound **3a**. Diastereoisomeric ratio (syn/anti): 92:08.

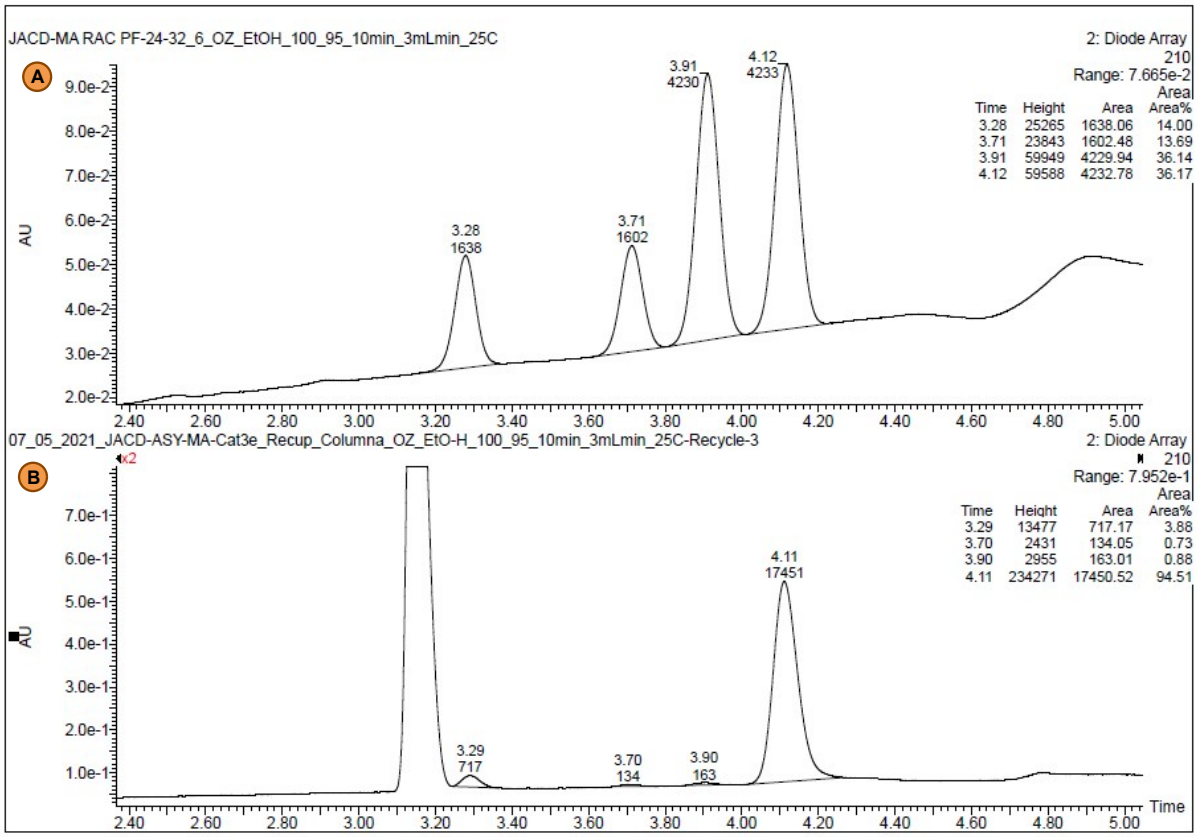


FIGURE 157. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by three-times recovered compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.90 min, (syn, major) = 4.11 min.

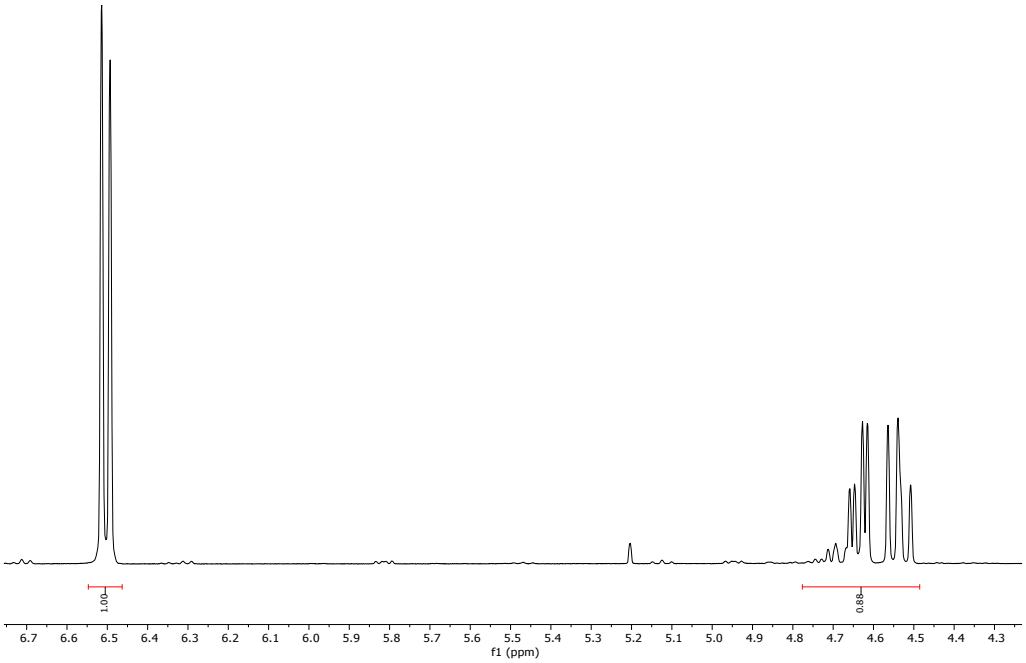


FIGURE 158. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by four-times recovered compound **3a** with 1, 2, 3-trimethoxybenzene as standard. Yield: 88%.

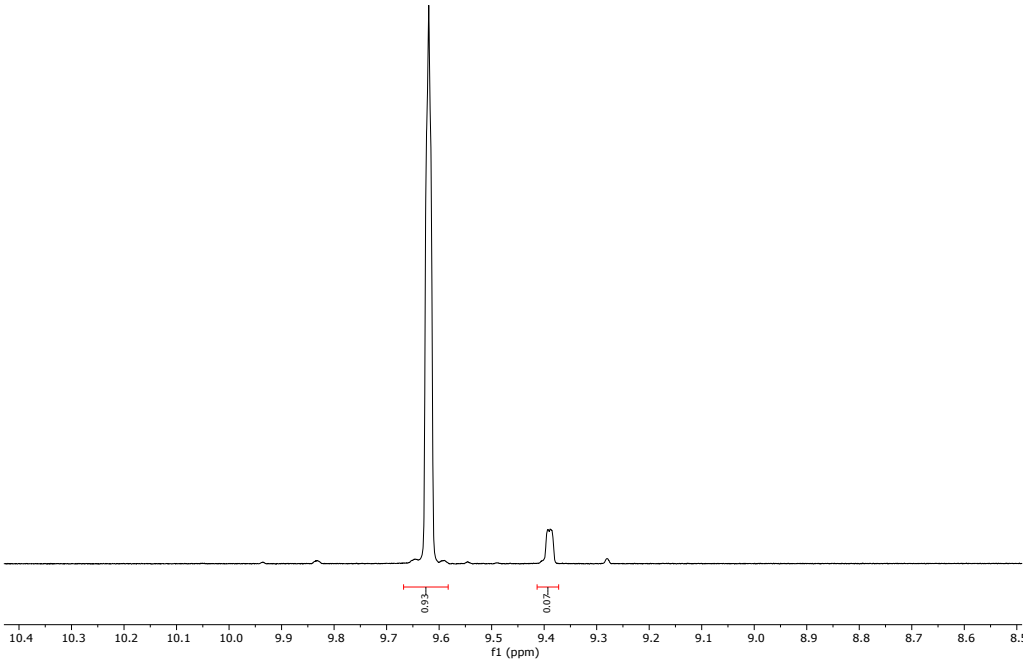


FIGURE 159. ^{1}H NMR of crude compound **4a** (400 MHz, $CDCl_3$) obtained by the Michael reaction catalyzed by four-times recovered compound **3a**. Diastereoisomeric ratio (syn/anti): 93:07.

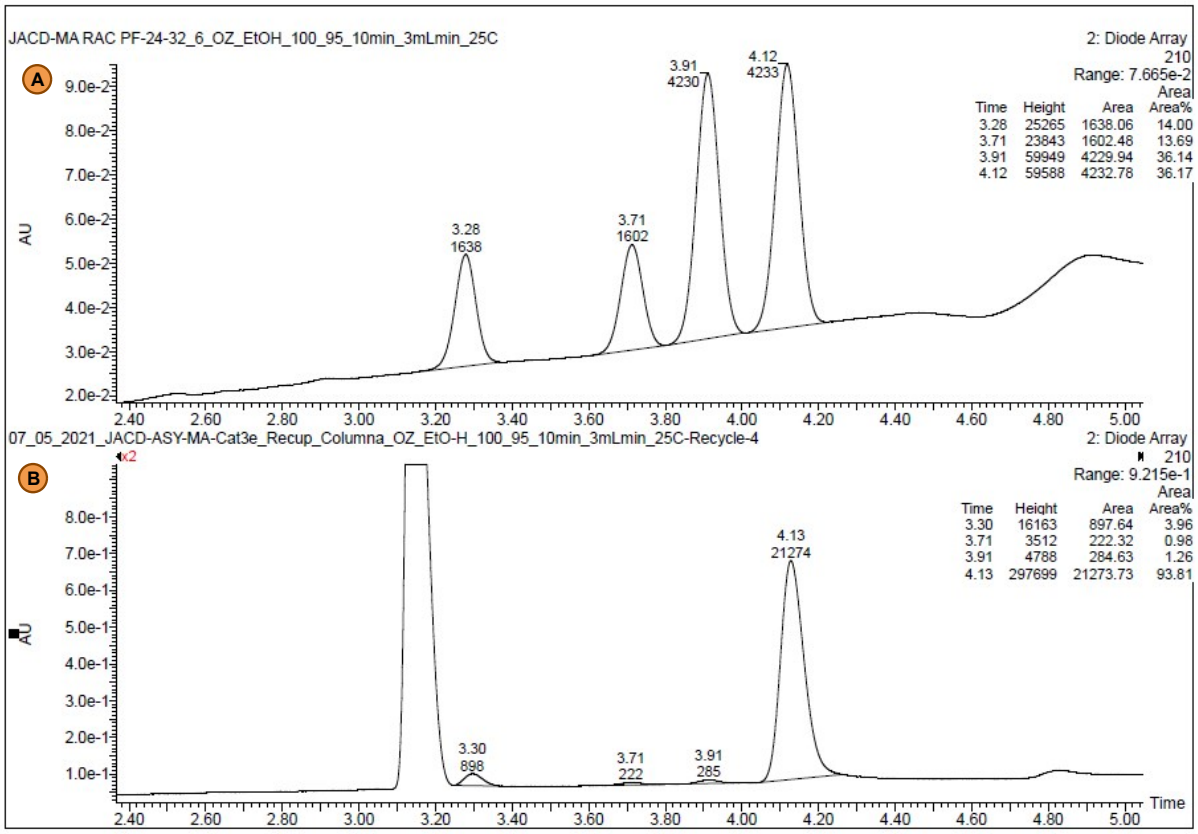


FIGURE 160. (a) Chiral UPC^2 of racemic 2-ethyl-4-nitro-3-phenylbutanal (**4a**); (b) Chiral UPC^2 of 2-ethyl-4-nitro-3-phenylbutanal (**4a**) obtained by the Michael reaction catalyzed by four-times recovered compound **3e**. Trefoil CEL2, **Grad:** CO_2/EtOH 100-0% to 95-5 % in 10 min at 3 ml/min at 25°C. UV detection at 210 nm: $\mathbf{R_t}$: (syn, minor) = 3.91 min, (syn, major) = 4.13 min.

21. HRMS Spectra: Catalysts

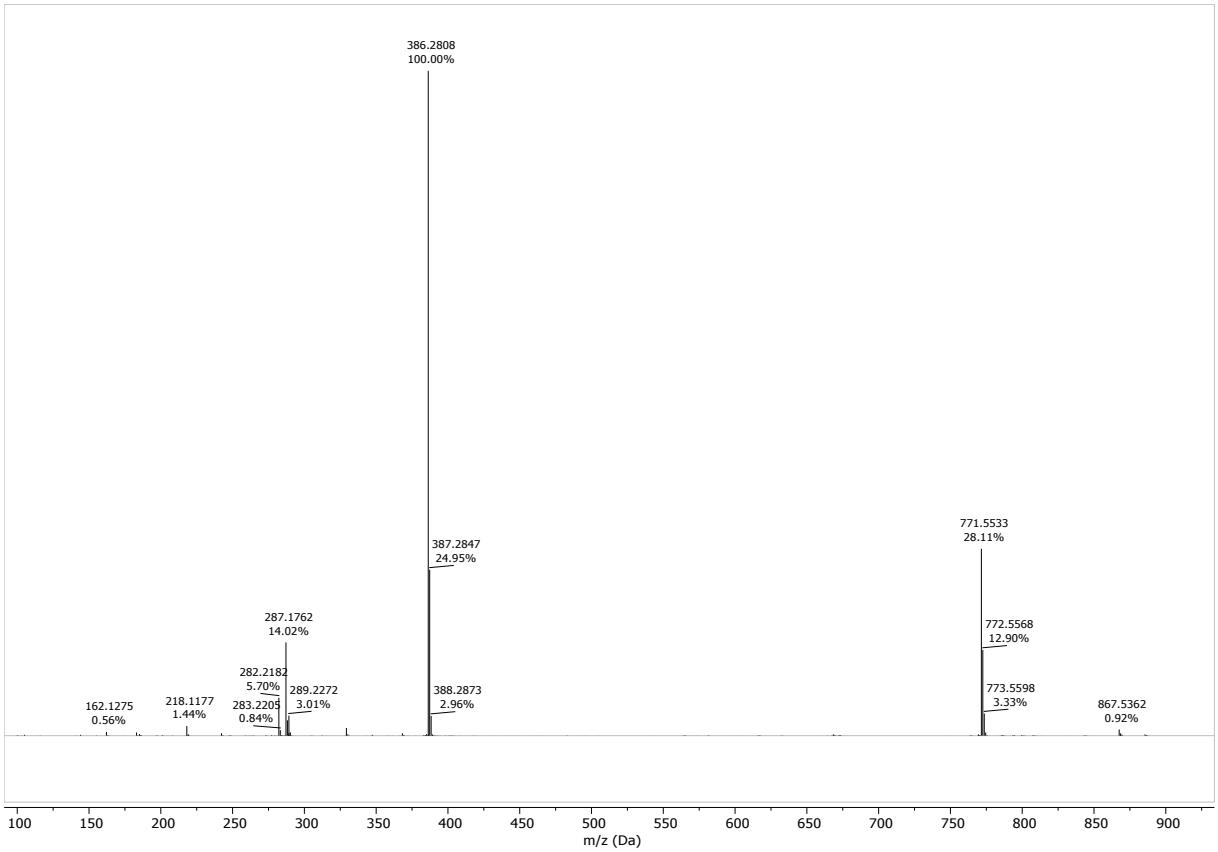


FIGURE 161. HRMS (ESI-Q-TOF) of compound **3a**; m/z: 386.2808. Calcd. for $[M+H]^+$:386.2802.

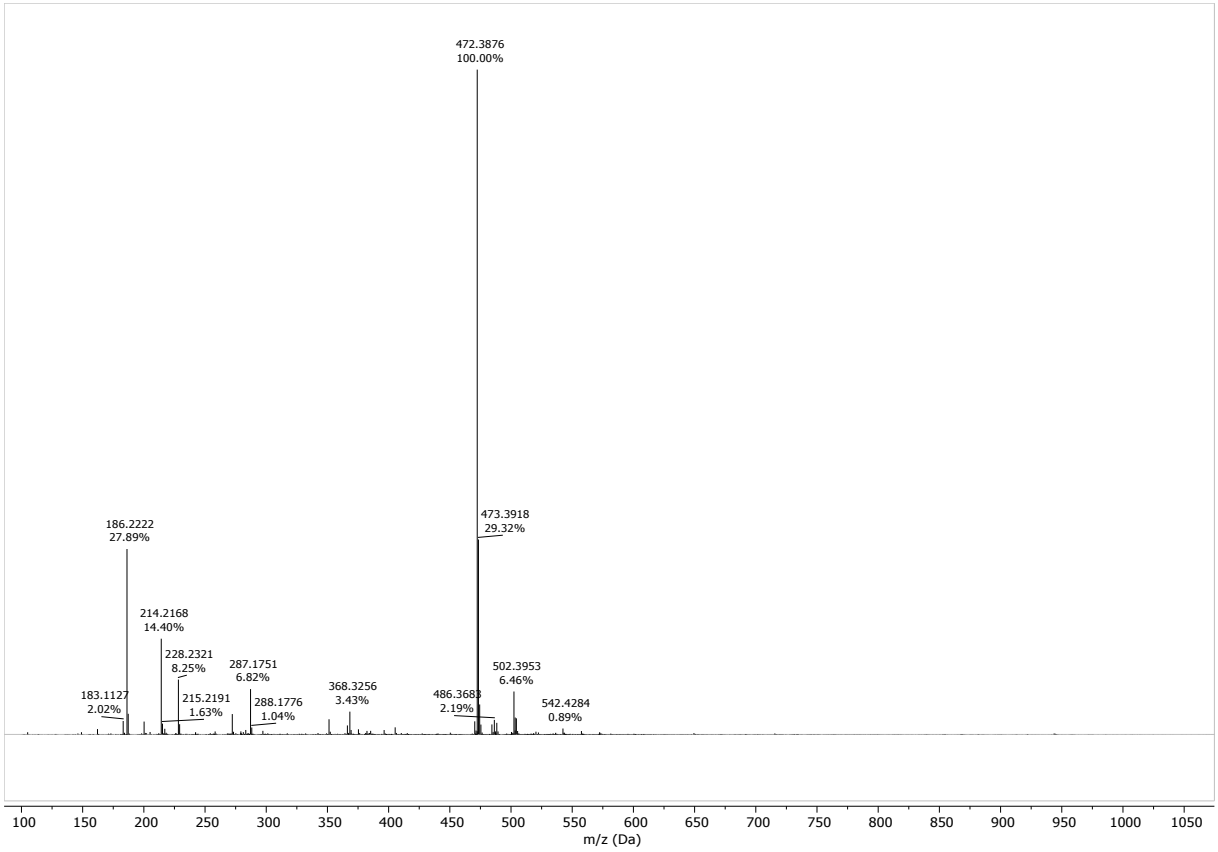


FIGURE 162. HRMS (ESI-Q-TOF) of compound **3b**; m/z: 472.3876. Calcd. for $[M+H]^+$: 472.3898.

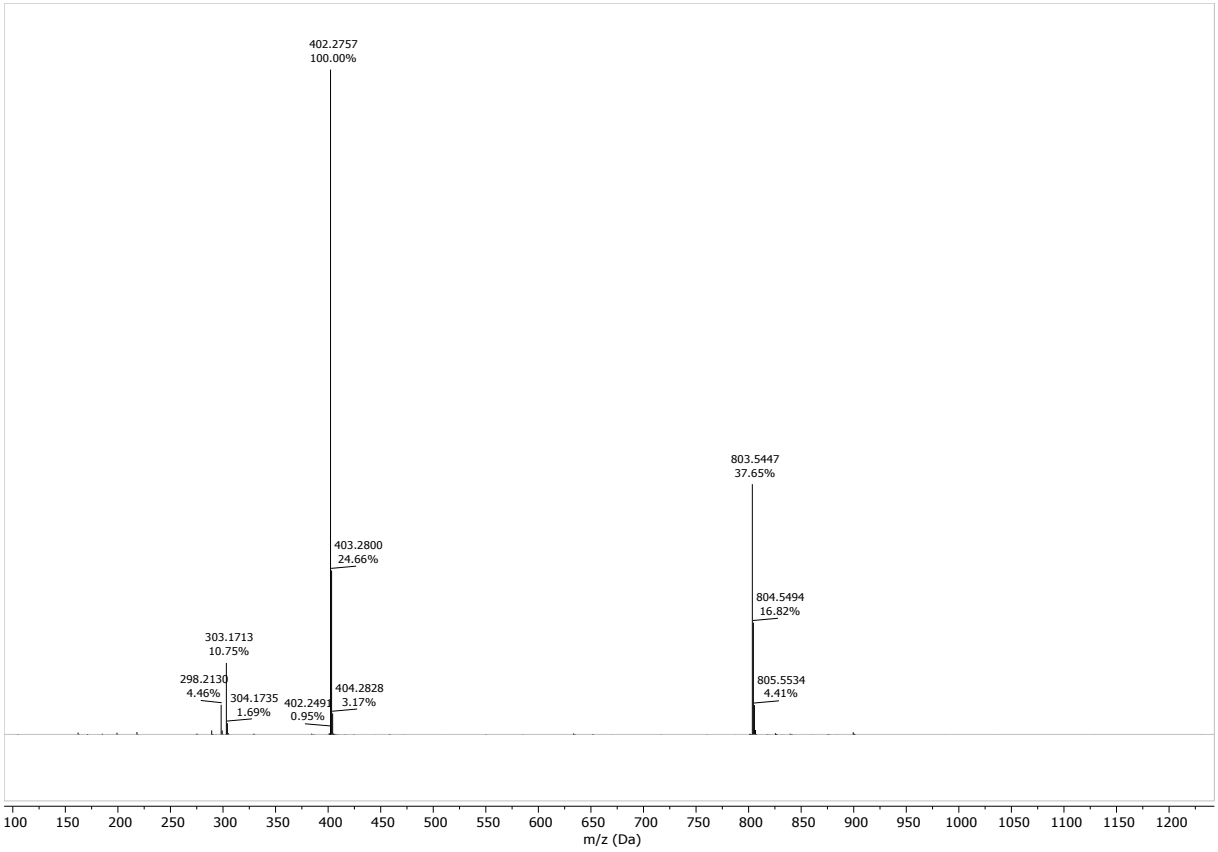


FIGURE 163. HRMS (ESI-Q-TOF) of compound **3c**; m/z: 402.2757. Calcd. for $[M+H]^+$: 402.2751.

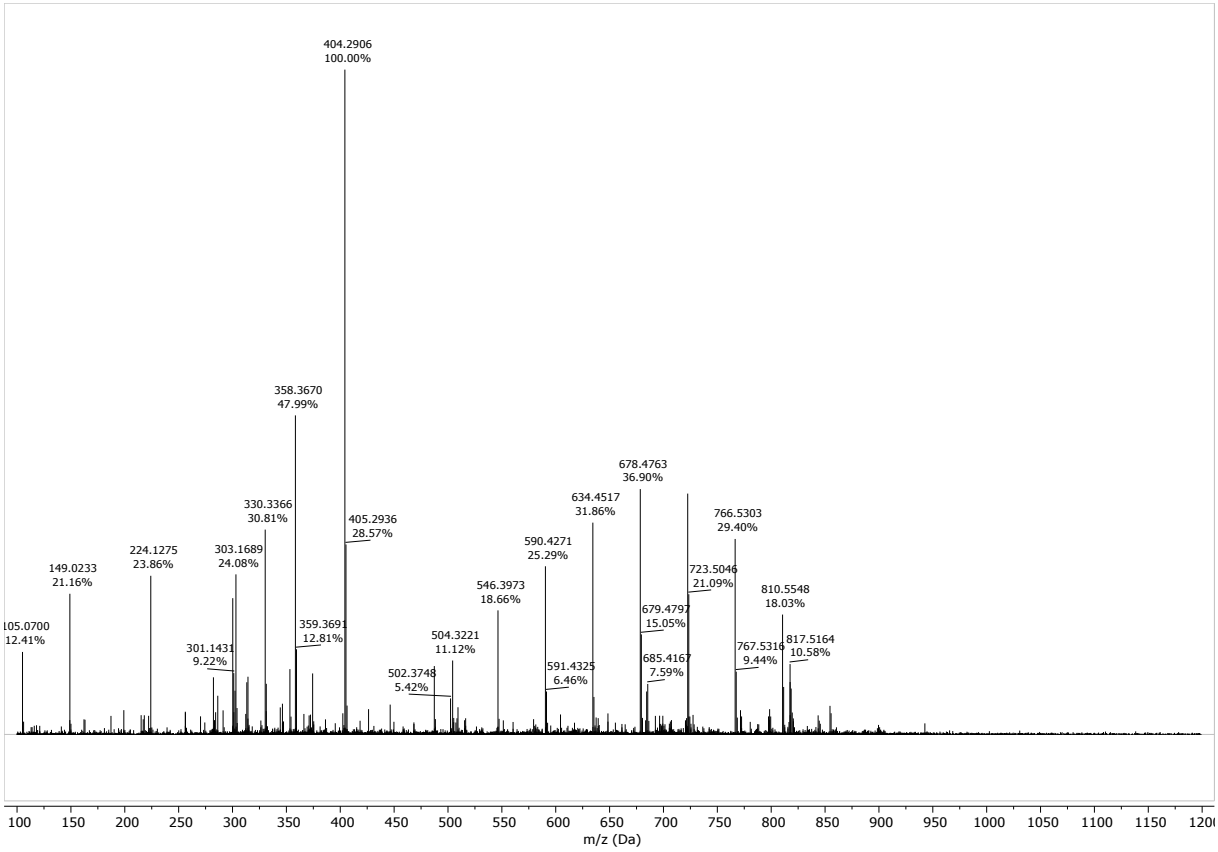


FIGURE 164. HRMS (ESI-Q-TOF) of compound **3d**; m/z: 404.2906. Calcd. for $[M+H]^+$: 404.2908.

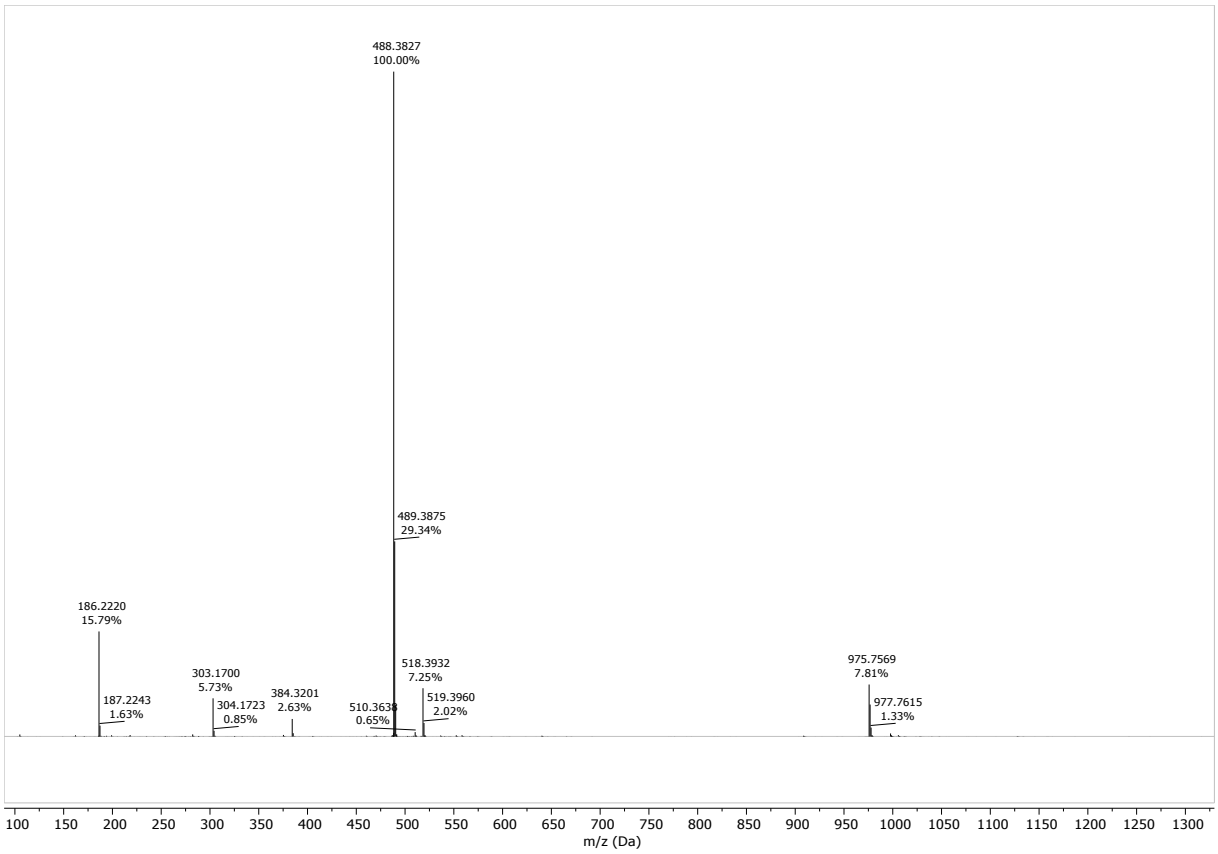


FIGURE 165. HRMS (ESI-Q-TOF) of compound **3e**; m/z: 488.3827. Calcd. for $[M+H]^+$: 488.3847.

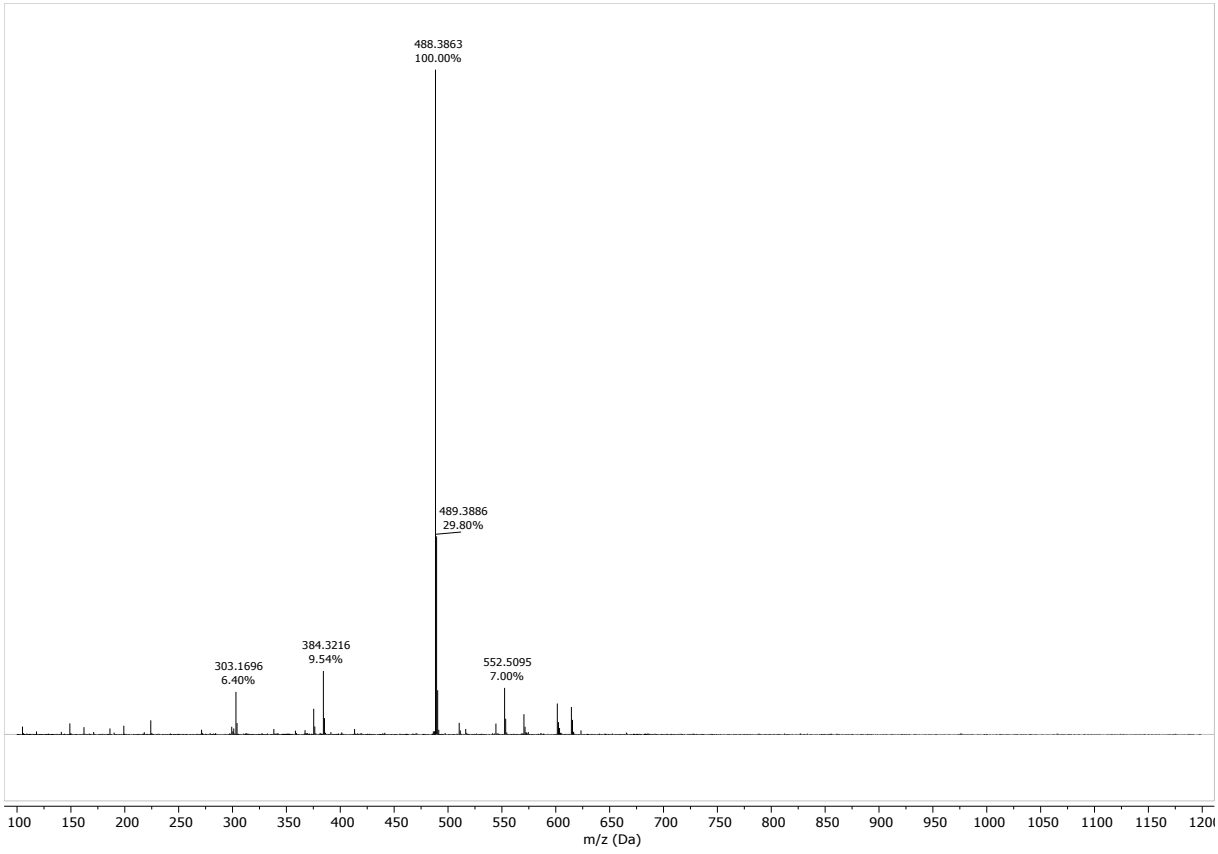


FIGURE 166. HRMS (ESI-Q-TOF) of compound **3f**; m/z: 488.3863. Calcd. for $[M+H]^+$: 488.3847.

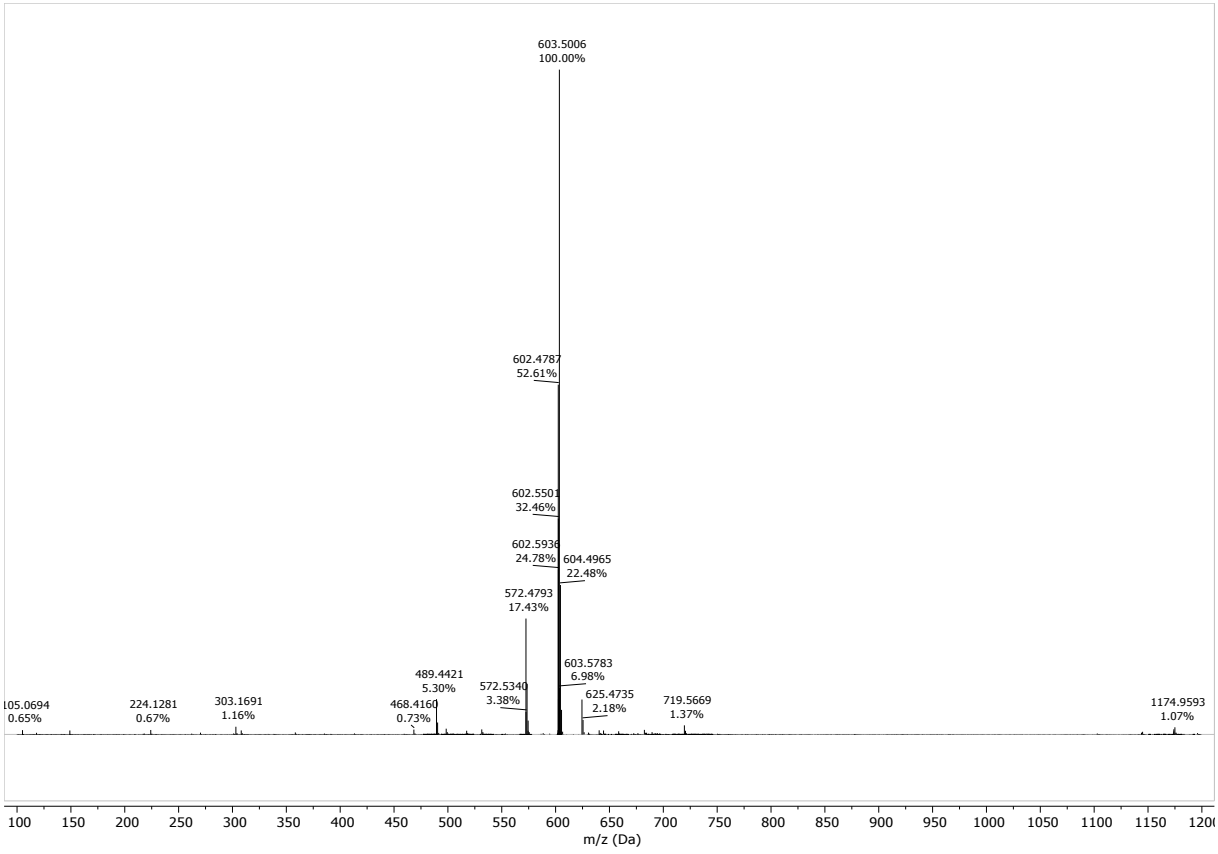


FIGURE 167. HRMS (ESI-Q-TOF) of compound **3g**; m/z: 603.5006. Calcd. for $[M+CH_3OH]^+$: 603.4975.

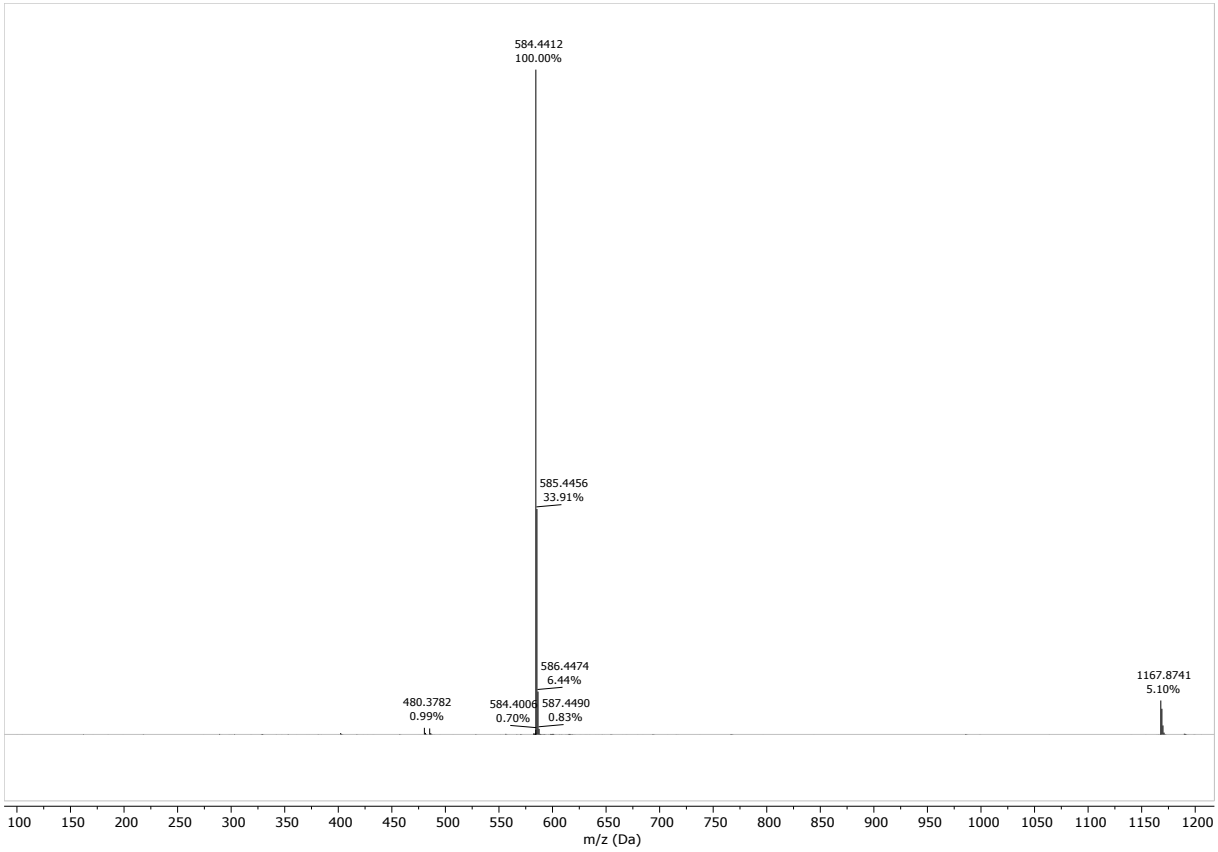


FIGURE 168. HRMS (ESI-Q-TOF) of compound **3h**; m/z: 584.4412. Calcd. for $[M+H]^+$: 584.4422.

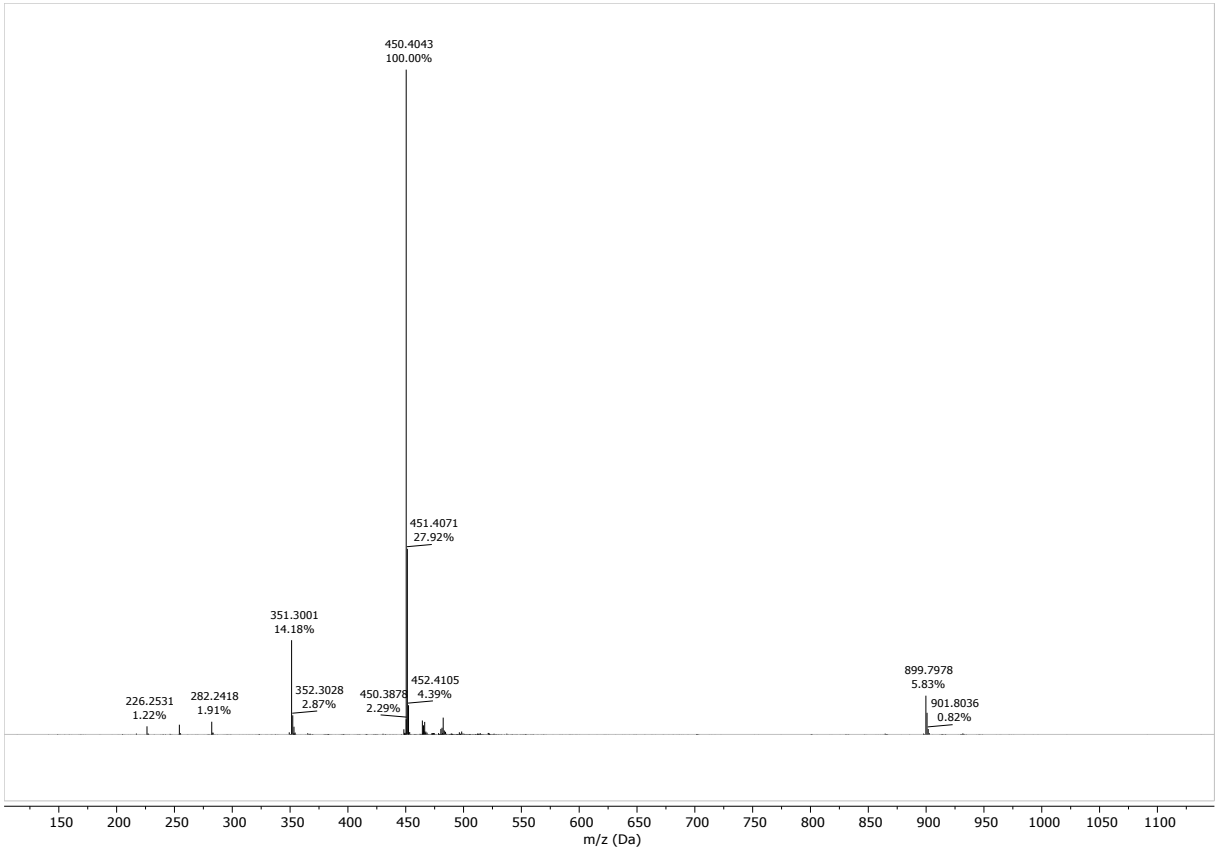


FIGURE 169. HRMS (ESI-Q-TOF) of compound **3i**; m/z: 450.4043. Calcd. for $[M+H]^+$: 450.4054.

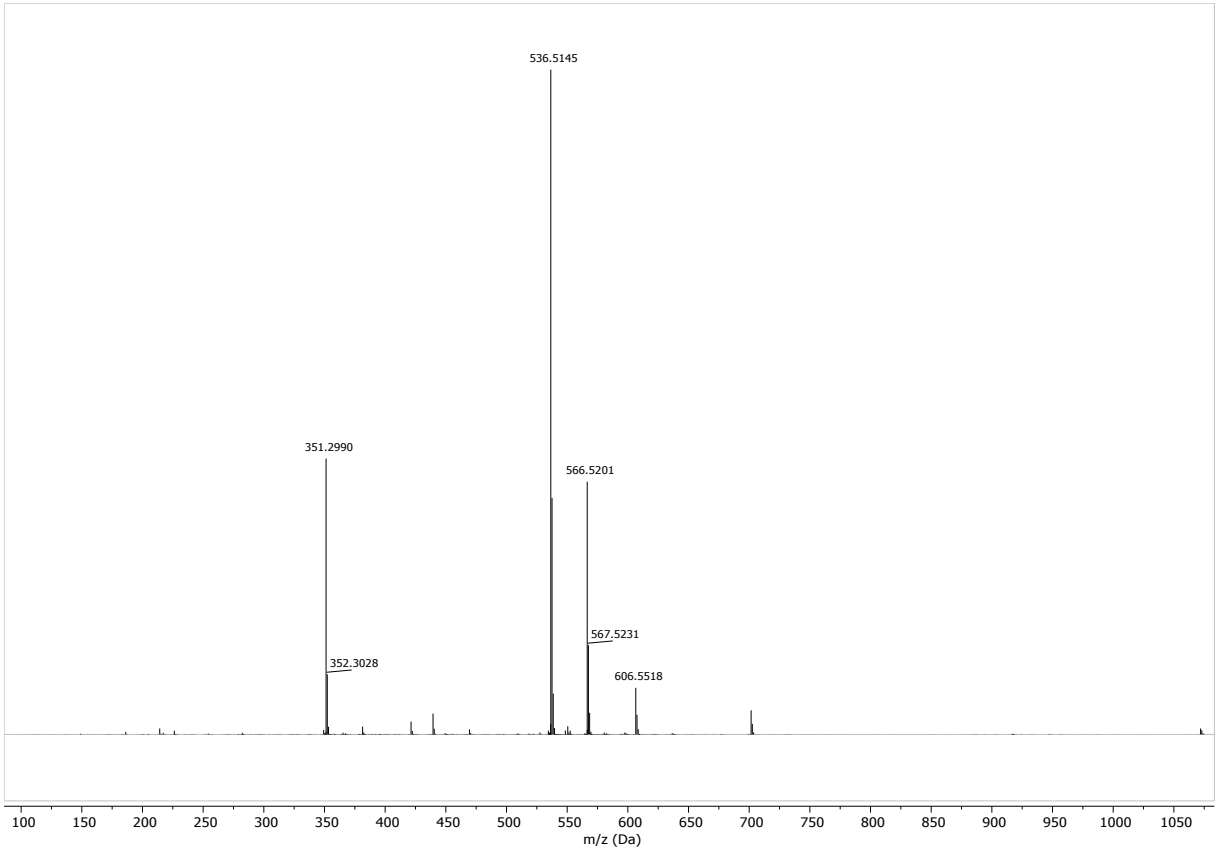


FIGURE 170. HRMS (ESI-Q-TOF) of compound **3j**; m/z: 536.5145. Calcd. for $[M+H]^+$: 536.5150.

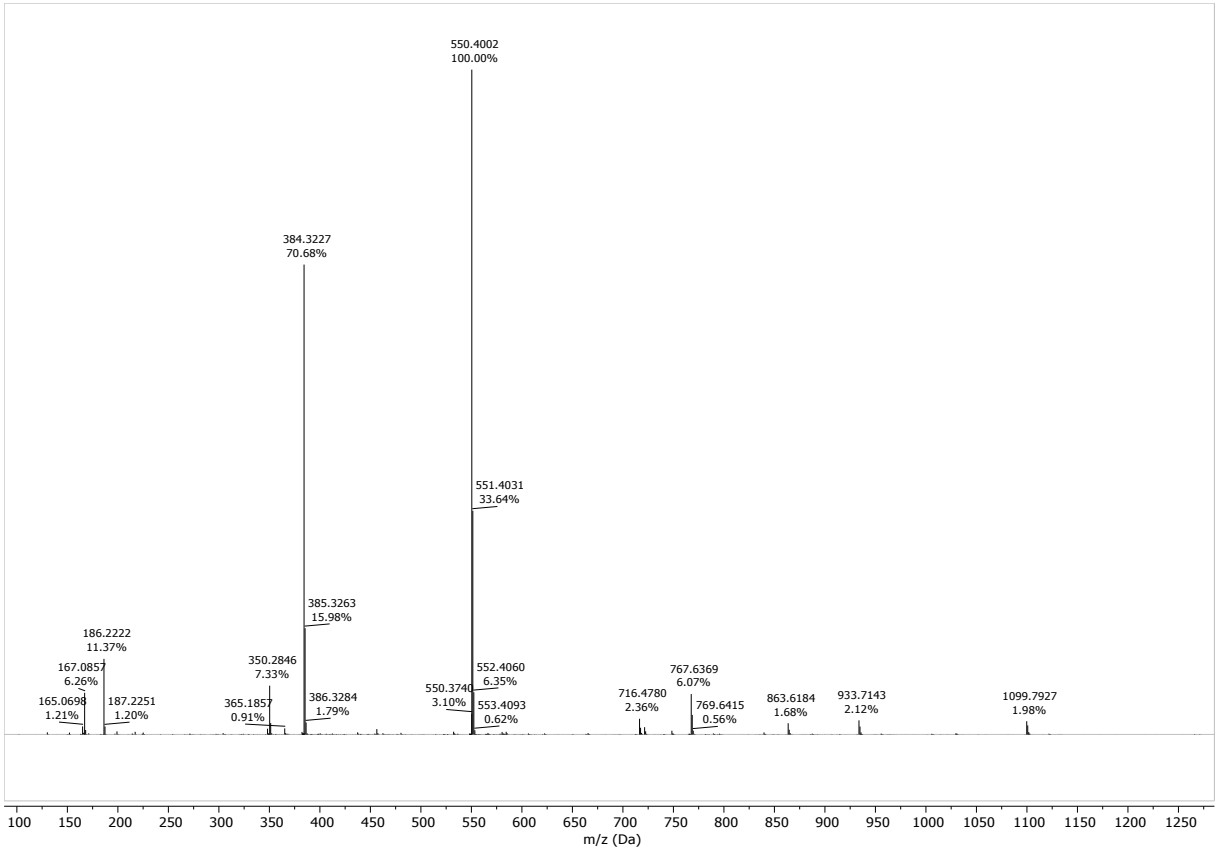


FIGURE 171. HRMS (ESI-Q-TOF) of compound **3k**; m/z: 550.4002. Calcd. for $[M+H]^+$: 550.4003.

22. References

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