A Polystyrene-Supported 9-amino(9-deoxy)*epi* Quinine for Continuous Flow Asymmetric Michael Reactions

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Electronic Supplementary Information

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1. GENERAL INFORMATION

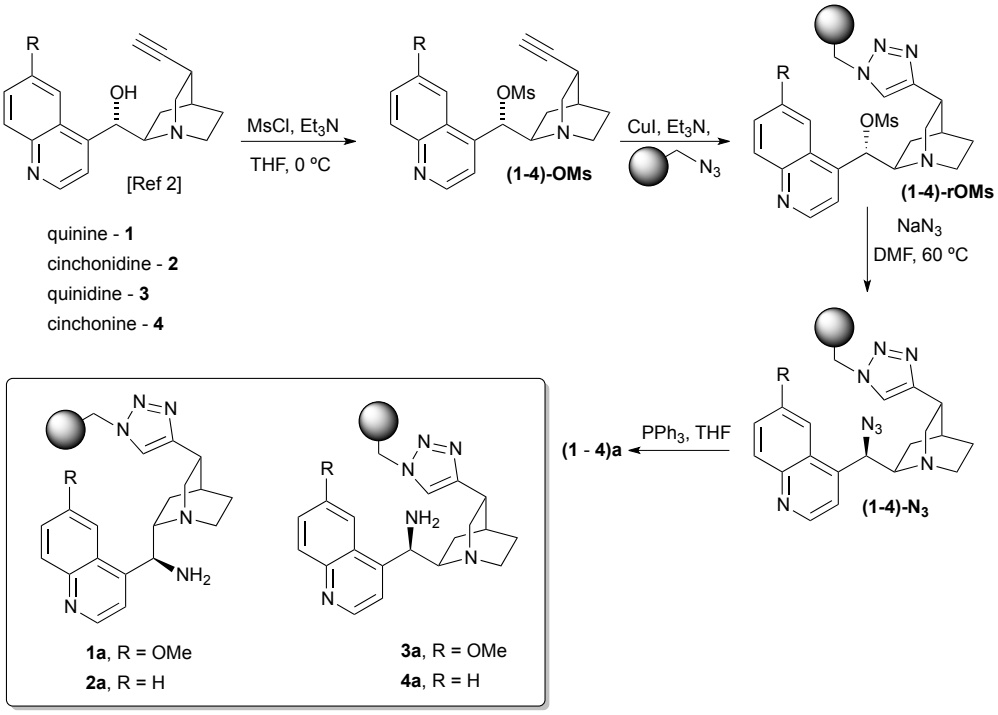
Unless otherwise stated, all commercial reagents were used as received and all reactions were carried out directly under open air. In each case the extent of the supporting process and the functionalization of the final resin was determined by elemental analysis. All flash chromatography was carried out using 60-mesh silica gel and dry-packed columns. Thin layer chromatography was carried out using Merck TLC Silica gel 60 F254 aluminium sheets. Components were visualized by UV light (λ = 254 nm) or by staining with potassium permanganate solution. NMR spectra were recorded on a Bruker Advance 300, 400 or 500 Ultrashield NMR spectrometer for ^{1}H NMR at 300, 400 or 500 MHz, and ^{13}C at 75, 101 or 126 MHz. All samples were recorded in $CDCl_3$. Chemical shifts (δ) for protons are quoted in parts per million (ppm) downfield from tetramethylsilane and were referenced to residual proton resonances of the NMR solvent. IR spectra were recorded on a Bruker Tensor 27 / Diamond ATR FT-IR spectrometer. Melting points were determined in open capillary tubes using a Büchi Melting Point B-540 apparatus. High resolution mass spectrometry analyses (HRMS) were performed in a Waters LCD PremierTM instrument operating in ESI (Electro-Spray Ionization) mode or APCI (Atmospheric-Pressure Chemical Ionization) mode. Elemental analyses (EA) of resins **1**-**4** were performed on a LECO CHNS 932- micro-analyzer at the Universidad Complutense de Madrid, Spain. The ee of the compounds was determined by High performance liquid chromatography (HPLC) through Agilent Technologies chromatograph (Serie1200), using Chiralcel OD-H or Chiralpak IA, IB, IC, AD-H or AS-H columns and chiral stationary phase Waters ACQUITY UPC^2 (Daicel Chiralpak IC column). 4-Phenylbutan-2-one was purchased from Sigma-Aldrich laboratories and used as received without further purification. Other enones were prepared according to reported procedures.[1] Racemic reference samples were prepared using DABCO 50 mol% following the same conditions that as the asymmetric reaction. Scalemic reference samples were prepared using a 1:1 mixture of 9-amino(9-deoxy)*epi* quinine and 9-amino(9-deoxy)*epi* quinidine following the same conditions as for the asymmetric reaction. New compounds have been fully characterized. NMR characterization was performed on reported ones. The continuous flow experiments were carried out using an Asia120® flow chemistry system developed by Syrris. The packed-bed reactor was a 1⁄4 inch Teflon tube of 30 cm length. Conversion was monitored by real time IR spectroscopy using the Mettler Toledo FlowIR.

Calculation of the functionalization of the polystyrene-supported catalysts on the basis of nitrogen elemental analysis

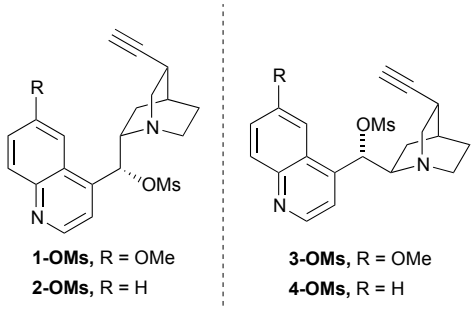
The level of functionalization of the polystyrene-supported catalysts *ƒ* (mmol of monomeric catalyst/gram of resin) can be calculated based on the results of nitrogen elemental analysis by the following formula as previously reported in our group (See: A. Bastero, D. Font and M. A. Pericàs *J. Org. Chem.* **2007**, *72*, 2460-2468).

$$f\ (\text{mmol g}^{-1}) = \%\text{N} \times 1000 \times (\text{number of N atoms})^{-1} \times \text{MW(N)}^{-1} \times 100^{-1}$$

2. PREPARATION AND CHARACTERIZATION OF RESINS 1-4

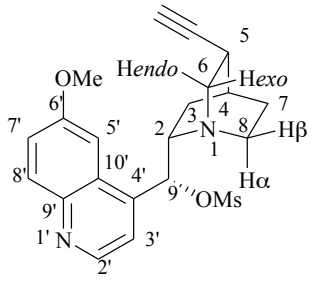


Mesylation reaction of alkyne cinchona (1-4)-OMs



General procedure: MsCl (4.6 equiv.) and Et_3N (5.7 equiv.) were added to a cool (0 ºC) solution of alkyne cinchona[2] (1 equiv.) in dry THF and the reaction mixture was stirred at this temperature for 30 min. Saturated aqueous $NaHCO_3$ solution was added and the layers were separated. The aqueous layer was extracted 3 times with AcOEt and the combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give mesylated product (**1**-**4**)-**OMs** which was purified by column chromatography.

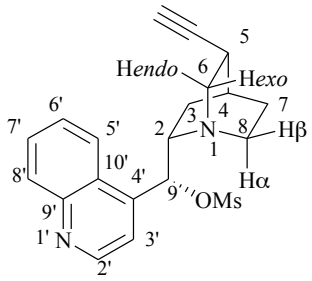
Synthesis of (1S,2S,4S,5S,9R)-5-(Ethynylquinuclidin-2-yl)-(6-methoxyquinolin-4-yl)methyl methanesulfonate **1-OMs**



1-OMs

A solution of quinine alkyne[2] (2.2 g, 6.8 mmol), MsCl (2.4 mL, 31.3 mmol) and Et_3N (5.4 mL, 38.8 mmol) in dry THF (40 mL) gave following the general procedure a brown foam (3.2 g) which was submitted to flash silica gel column chromatography (mixtures AcOEt / MeOH 99:1) to give the mesylated quinine **1-OMs** (2.3 g, 83% yield) as a yellow foam. Product was purified by crystallization from AcOEt:*n*-hexane to obtain a white solid. Mp= 130.5-131.5 ºC, IR (ATR): 3650, 3285, 2938, 2109, 1621, 1509, 1358, 1226, 1174, 1029, 941, 914, 867, 732, 636, 526 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.40–1.47 (m, 1 H, H7β), 1.64–1.69 (m, 1 H, H3α), 1.71–1.77 (m, 1 H, H7α), 2.05 (d, *J* = 2.5 Hz, 1 H, ≡CH), 2.08–2.09 (m, 1 H, H4), 2.30–2.41 (m, 1 H, H3β), 2.48–2.50 (m, 1 H, H5), 2.56–2.60 (m, 1 H, H8β), 2.60 (s, 3 H, OMs), 2.70–2.72 (m, 1 H, H6*endo*), 3.02 (dd, *J* = 13.5 and 10.0 Hz, 1 H, H6*exo*), 3.07–3.12 (m, 1 H, H8α), 3.64 (br s, 1 H, H2), 3.96 (s, 3 H, OMe), 6.14 (br s, 1 H, H9), 7.37 (br s, 1 H, H5'), 7.41 (dd, *J* = 9.5 and 2.5 Hz, 1 H, H 7'), 7.46 (br s, 1 H, H 3'), 8.05 (d, *J* = 9.5 Hz, 1 H, H8'), 8.80 (d, *J* = 4.5 Hz, 1 H, H2'). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 25.5 (t, C3), 26.0 (t, C7), 26.5 (d, C4), 27.4 (d, C5), 39.2 (q, OMs), 41.8 (t, C8), 55.7 (q, OMe), 57.5 (t, C6), 59.5 (d, C2), 68.8 (d, ≡CH), 80.1 (d, C9), 87.5 (s, ≡C), 100.9 (d, C5'), 119.2 (d, C3'), 122.2 (d, C7'), 126.5 (s, C10'), 132.1 (d, C8'), 141.4 (s, C4'), 144.9 (s, C9'), 147.4 (d, C2'), 158.3 (s, C6') ppm. $[\alpha]_D^{24}$ = –94.12 (*c* 0.505, $CHCl_3$). MS (ESI+), *m*/*z* (%): 401 ($[M+H]^+$, 100), 402 ($[M+2H]^{\cdot+}$, 30). HRMS (ESI+) calcd for $[C_{21}H_{24}N_2O_4S+H]^+$: 401.1529. Found: 401.1540.

Synthesis of (1S,2S,4S,5S,9R)-5-(Ethynylquinuclidin-2-yl)-(quinolin-4-yl)methyl methanesulfonate **2-OMs**

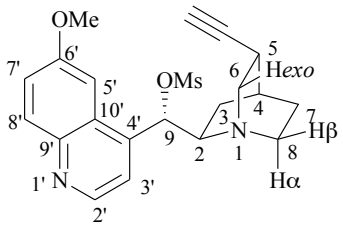


2-OMs

A solution of corresponding alkyne cinchonidine[2] (1.0 g, 3.42 mmol), MsCl (1.2 mL, 15.73 mmol) and Et_3N (2.7 mL, 19.5 mmol) in dry THF (20 mL) gave following the general procedure a brown foam (1.3 g) which was submitted to flash silica gel column chromatography (mixtures AcOEt / MeOH 99:1) to give the mesylated cinchonidine **2-OMs** (0.89 g, 70% yield) as a yellow foam. Product was purified by crystallization from DCM:*n*-pentane to obtain a yellow solid. Mp= 156-158 ºC, IR (ATR): 3649, 3288, 3010, 2956, 2884, 2104, 1458, 1347, 1166, 970, 925, 872, 761, 741, 656, 628, 524, 491 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.40–1.46 (m, 1 H, H7β), 1.64–1.68 (m, 1 H, H3α), 1.70–1.76 (m, 1 H, H7α), 2.05 (d, *J* = 2.5 Hz, 1 H, ≡CH), 2.08 (m, 1 H, H4), 2.33–2.42 (m, 1 H, H3β), 2.47-2.49 (m, 1 H, H5), 2.51–2.55 (m, 1 H, H8β), 2.59 (s, 3 H, OMs), 2.67–2.70 (m, 1 H, H6*endo*), 3.0 (dd, *J* = 13.5 and 10.0 Hz, 1 H, H6*exo*), 3.04–3.11 (m, 1 H, H8α), 3.62 (br s, 1 H, H2), 6.20 (br s, 1 H, H9), 7.50 (br s, 1 H,

H3'), 7.63 (td, *J* = 8.5 and 1.0 Hz, 1 H, H 6'), 7.75 (td, *J* = 8.5 and 1.0 Hz, 1 H, H 7'), 8.17 (dd, *J* = 8.5 and 1.0 Hz, 2 H, H5' and H8'), 8.96 (d, *J* = 4.5 Hz, 1 H, H2'). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.7 (t, C3), 26.0 (t, C7), 26.6 (d, C4), 27.4 (d, C5), 39.1 (q, OMs), 41.7 (t, C8), 57.5 (t, C6), 59.7 (d, C2), 68.9 (d, ≡CH), 80.9 (d, C9), 87.5 (s, ≡C), 119.5 (d, C3'), 122.8 (d, C5'), 125.5 (s, C10'), 127.4 (d, C6'), 129.6 (d, C7'), 130.8 (d, C8'), 143.1 (s, C4'), 148.7 (s, C9'), 150.0 (d, C2') ppm. $[\alpha]_D^{28}$ = −120.1 (*c* 0.505, MeOH). MS (ESI−), *m*/*z* (%): 369 ([M−H]$^-$, 100). HRMS (ESI−) calcd for $[C_{20}H_{22}N_2O_3S-H]^-$: 369.1273. Found: 369.1267.

Synthesis of (1S,2R,4S,5S,9S)-5-(Ethynylquinuclidin-2-yl)-(6-methoxyquinolin-4-yl)methyl methanesulfonate **3-OMs**

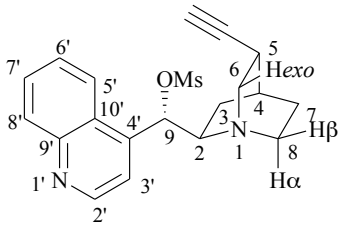


3-OMs

A solution of corresponding alkyne quinidine[2] (1.3 g, 4.12 mmol), MsCl (1.5 mL, 18.93 mmol) and Et_3N (3.3 mL, 23.5 mmol) in dry THF (25 mL) gave following the general procedure an orange oil (1.5 g) which was submitted to flash silica gel column chromatography (mixtures AcOEt / MeOH 90:10) to give the mesylated quinidine **3-OMs** (1.2 g, 73% yield) as a white foam. Product was purified by crystallization from AcOEt to obtain a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.46−1.52 (m, 2 H, H3α and 3β), 1.55−1.63 (m, 2 H, H7α and H7β), 2.06−2.08 (m, 1 H, H4), 2.26 (d, *J* = 2.5 Hz, 1 H, ≡CH), 2.50−2.70 (m, 3 H, H5, H8α and H8β), 2.66 (s, 3 H, OMs), 2.93−3.05 (m, 2 H, H6*endo* and H6*exo*), 3.38 (br s, 1 H, H2), 3.98 (s, 3 H, OMe), 6.43 (br s, 1 H, H9), 7.40−7.42 (m, 2 H, H5' and H 7'), 7.48 (br s, 1 H, H 3'), 8.06 (d, *J* = 9.5 Hz, 1 H, H8'), 8.81 (d, *J* = 4.5 Hz, 1 H, H2').

Compound **3-OMs** was characterized by comparing its ^{1}H NMR spectra to the previously reported data described in the literature.[2b]

Synthesis of (1S,2R,4S,5S,9S)-5-(Ethynylquinuclidin-2-yl)-(quinolin-4-yl)methyl methanesulfonate **4-OMs**

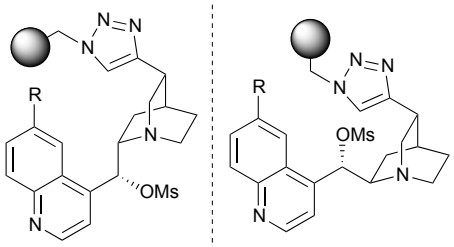


4-OMs

A solution of alkyne cinchonine (1.0 g, 3.42 mmol), MsCl (1.2 mL, 15.73 mmol) and Et_3N (2.7 mL, 19.5 mmol) in dry THF (20 mL) gave following the general procedure a brown foam (1.03 g) which was submitted to flash silica gel column chromatography (mixtures AcOEt / MeOH 6:1) to give the mesylated cinchonine **4-OMs** (0.56 g, 44% yield) as a white foam. The analytic sample was purified by recrystallization from AcOEt to give a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.45−1.51 (m, 2 H, H3α and 3β), 1.53−1.60 (m, 2 H, H7α and H7β), 2.06−2.07 (m, 1 H, H4), 2.26 (d, *J* = 2.5 Hz, 1 H, ≡CH), 2.49−2.61 (m, 3 H, H5, H8α and H8β), 2.67 (s, 3 H, OMs), 2.94−3.05 (m, 2 H, H6*endo* and H6*exo*), 3.41 (br s, 1 H, H2), 6.39 (br s, 1 H, H9), 7.52 (br s, 1 H, H3'), 7.6 (td, *J* = 8.5 and 1.0 Hz, 1 H, H 6'), 7.76 (td, *J* = 8.5 and 1.0 Hz, 1 H, H 7'), 8.17 (dd, *J* = 8.5 and 1.0 Hz, 1 H, H8'), 8.19 (br s, 1 H, H5'), 8.96 (d, *J* = 4.5 Hz, 1 H, H2').

Compound **4-OMs** was characterized by comparing its ^{1}H NMR spectra to the previously reported data described in the literature.[2b]

Cycloaddition of alkyne MsO-cinchona, (1-4)-OMs with azidomethyl polystyrene[3]

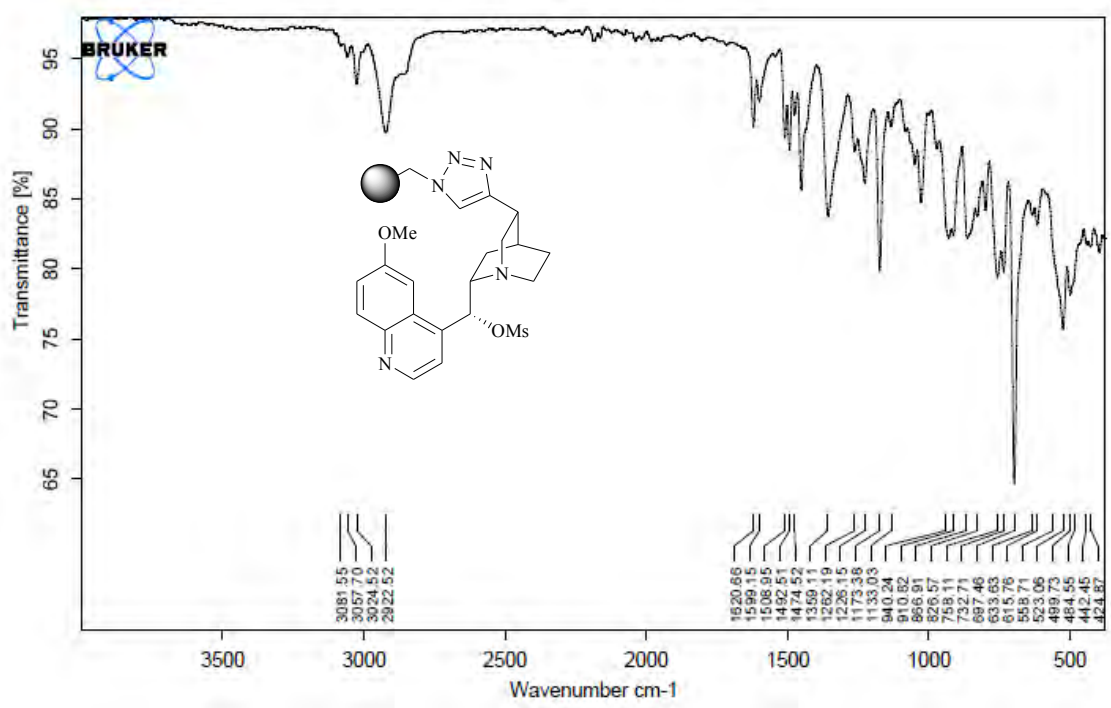


1-rOMs, R = OMe
2-rOMs, R = H

3-rOMs, R = OMe
4-rOMs, R = H

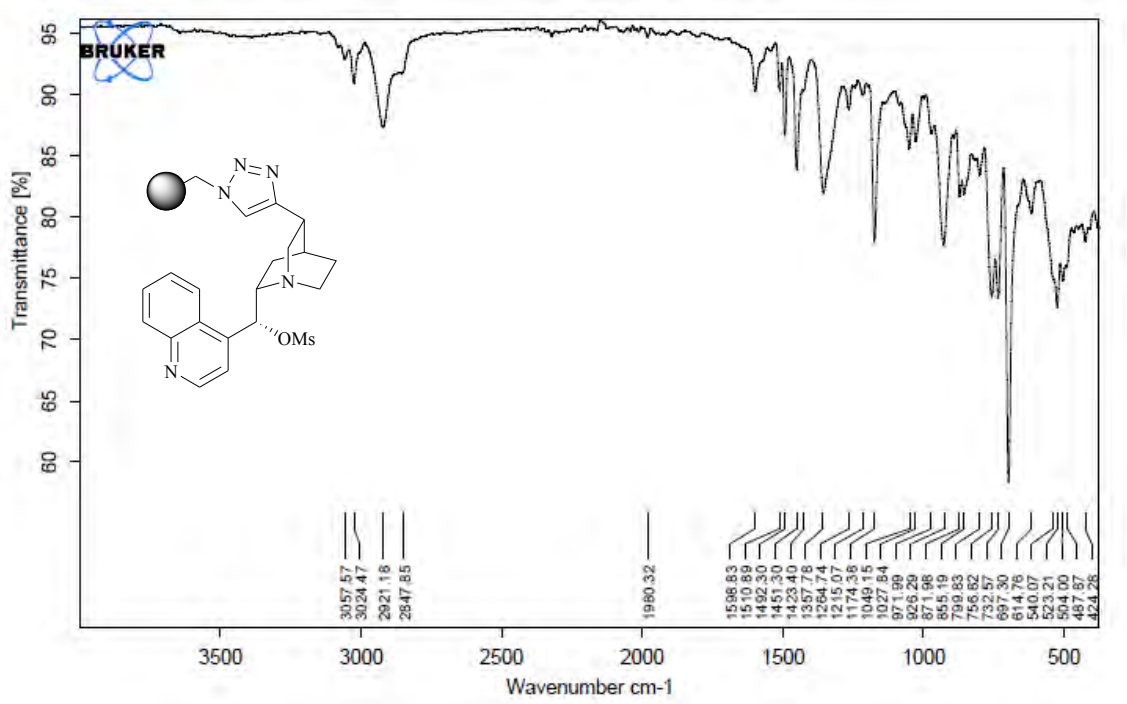
General procedure: alkyne MsO-cinchone **(1-4)-OMs** (1.4 equiv.), Et_3N (0.5 equiv.) and CuI (8 mol%) were added to a suspension of azidomethyl polystyrene[3] (1 eq, 1% DVB) in a solvent mixture of THF:DMF (1:1) and the mixture was shaken at 40 ºC for 24 h. After filtration, the mixture was monitored by IR. When the azide band was disappeared, the solid was filtered and washed with THF (100 mL), H_2O (100 mL), H_2O-MeOH (100 mL), MeOH (100 mL), MeOH-THF (1:1) (100 mL), THF (100 mL) and DCM (100 mL). The solid was dried in vacuo at 40 ºC for 24 h.

With quinine: a suspension of alkyne MsO-quinine **1-OMs** (420 mg, 1.05 mmol), Et_3N (0.05 mL, 0.38 mmol), CuI (11 mg, 0.06 mmol) and azidomethyl polystyrene[3] (580 mg, 0.75 mmol, f = 1.3 mmol/g) in a solvent mixture of THF:DMF (1:1) (10 mL) gave following the general procedure resin **1-rOMs**. IR (ATR): 3024, 2922, 1621, 1474, 1359, 1226, 1173, 940, 911, 867, 758, 733, 697, 523 cm^{-1}. Elemental analysis (%) = N, 5.94; C, 75.61; H, 6.50; S, 2.49. f = 0.85 mmol/g.

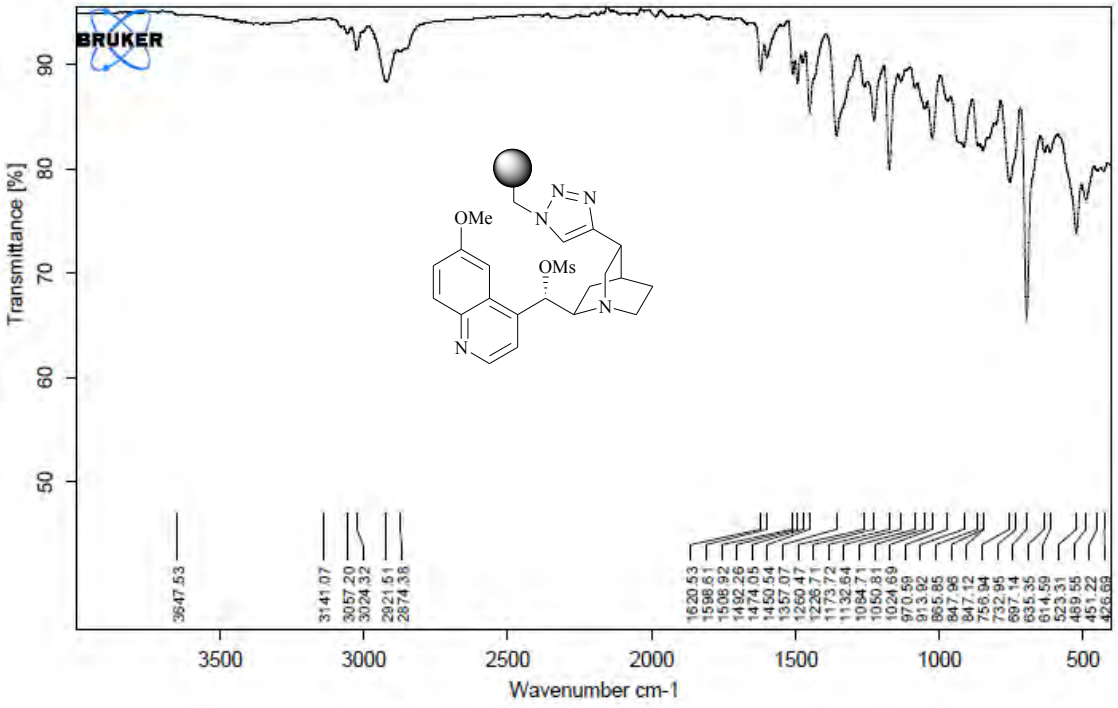


With cinchonidine: a suspension of alkyne MsO-cinchonidine **2-OMs** (460 mg, 1.26 mmol), Et_3N (0.06 mL, 0.45 mmol), CuI (14 mg, 0.07 mmol) and azidomethyl polystyrene[3] (690 mg, 0.90 mmol, f = 1.3 mmol/g) in a solvent mixture of THF:DMF (1:1) (12 mL) gave following the general procedure resin **2-**

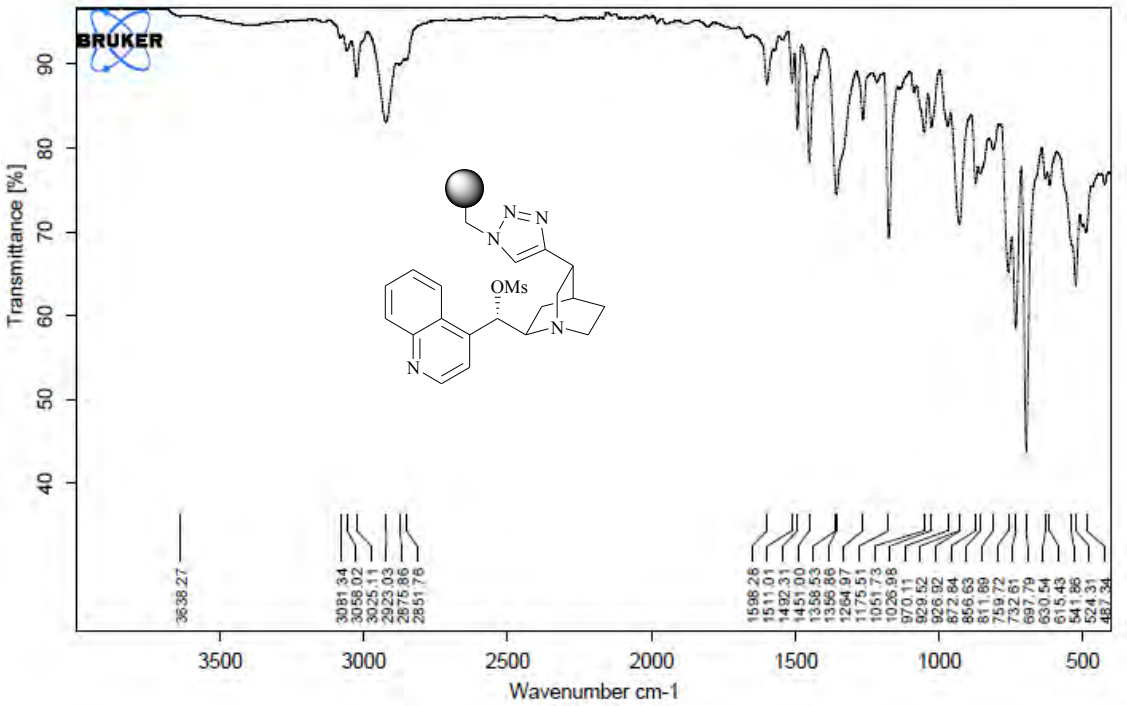
rOMs. IR (ATR): 3024, 2921, 1599, 1492, 1423, 1358, 11174, 926, 757, 733, 697, 523 cm^{-1}. Elemental analysis (%) = N, 6.28; C, 76.68; H, 6.66; S, 2.45. f = 0.90 mmol/g.



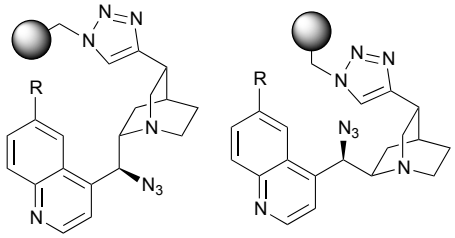
With quinidine: a suspension of alkyne MsO-quinidine **3-OMs** (496 mg, 1.24 mmol), Et_3N (0.06 mL, 0.44 mmol), CuI (13 mg, 0.07 mmol) and azidomethyl polystyrene[3] (680 mg, 0.88 mmol, f = 1.3 mmol/g) in a solvent mixture of THF:DMF (1:1) (12 mL) gave following the general procedure resin **3-rOMs**. IR (ATR): 3025, 2921, 1620, 1450, 1357, 1227, 1174, 914, 847, 757, 697, 523 cm^{-1}. Elemental analysis (%) = N, 5.93; C, 75.75; H, 6.57; S, 2.56. f = 0.85 mmol/g.



With cinchonine: a suspension of alkyne MsO-cinchonine **4-OMs** (380 mg, 1.04 mmol), Et_3N (0.05 mL, 0.37 mmol), CuI (11 mg, 0.06 mmol) and azidomethyl polystyrene[3] (570 mg, 0.74 mmol, f = 1.3 mmol/g) in a solvent mixture of THF:DMF (1:1) (10 mL) gave following the general procedure resin **4-rOMs**. IR (ATR): 3025, 2923, 1598, 1492, 1451, 1358, 1175, 929, 927, 760, 733, 698, 524 cm^{-1}. Elemental analysis (%) = N, 6.14; C, 74.76; H, 6.88; S, 2.60. f = 0.88 mmol/g.



Synthesis of polymer-supported azide cinchona, *epi*-(1-4)-N_3

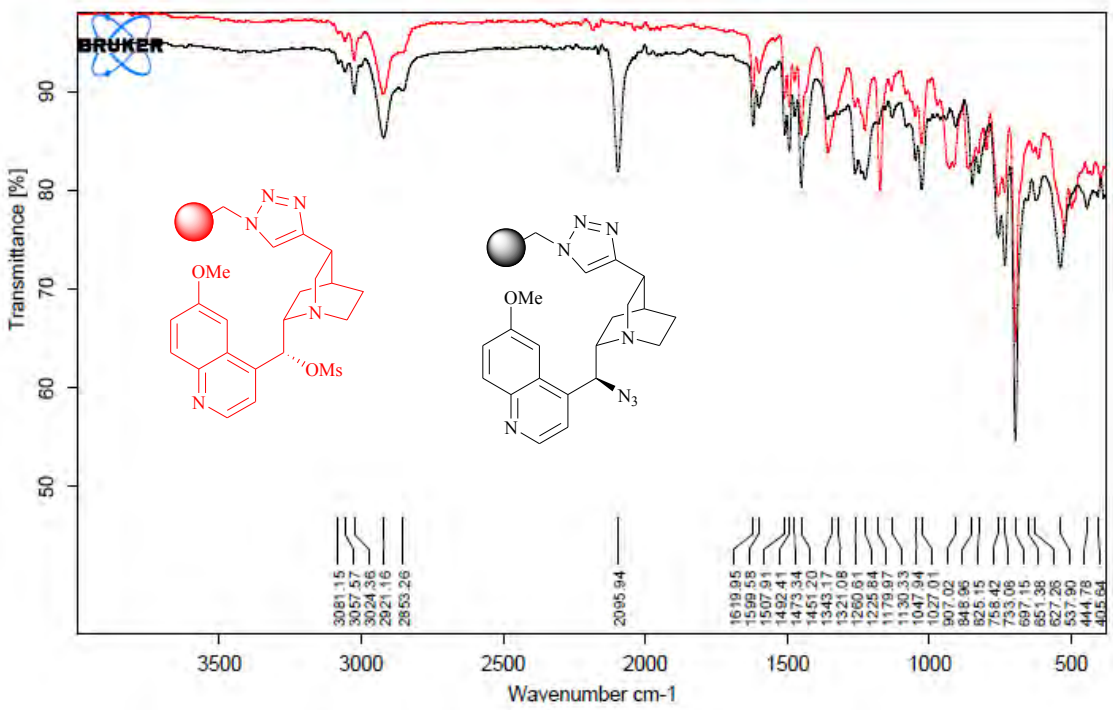


1-N_3, R = OMe
2-N_3, R = H

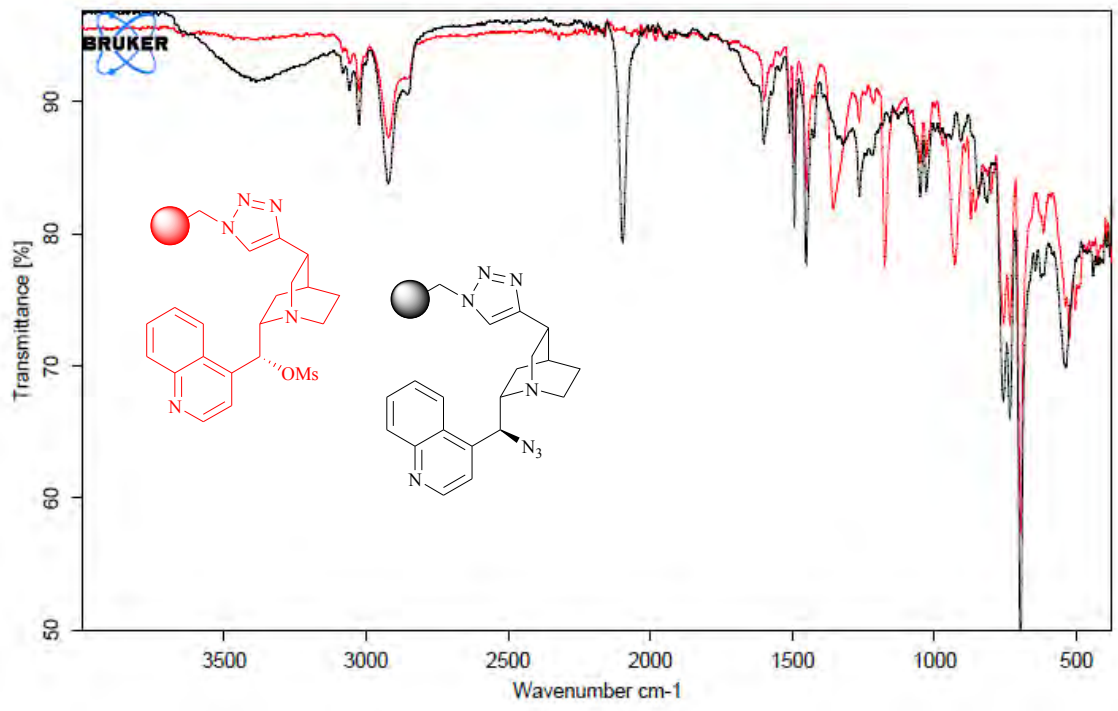
3-N_3, R = OMe
4-N_3, R = H

General procedure: polymer-supported MsO-cinchone **(1-4)-rOMs** (1 equiv.) was swollen with DMF and was shaken for 10 min. NaN_3 (5 equiv.) was added and the mixture was shaken at 60 ºC for 3-4 days. After filtration, the mixture was monitored by IR. When the SO_2 band was disappeared, the solid was filtered and washed with H_2O (100 mL), H_2O-MeOH (100 mL), MeOH (100 mL), MeOH-THF (100 mL), THF (100 mL) and DCM (100 mL). The solid was dried in vacuo at 40 ºC for 24 h.

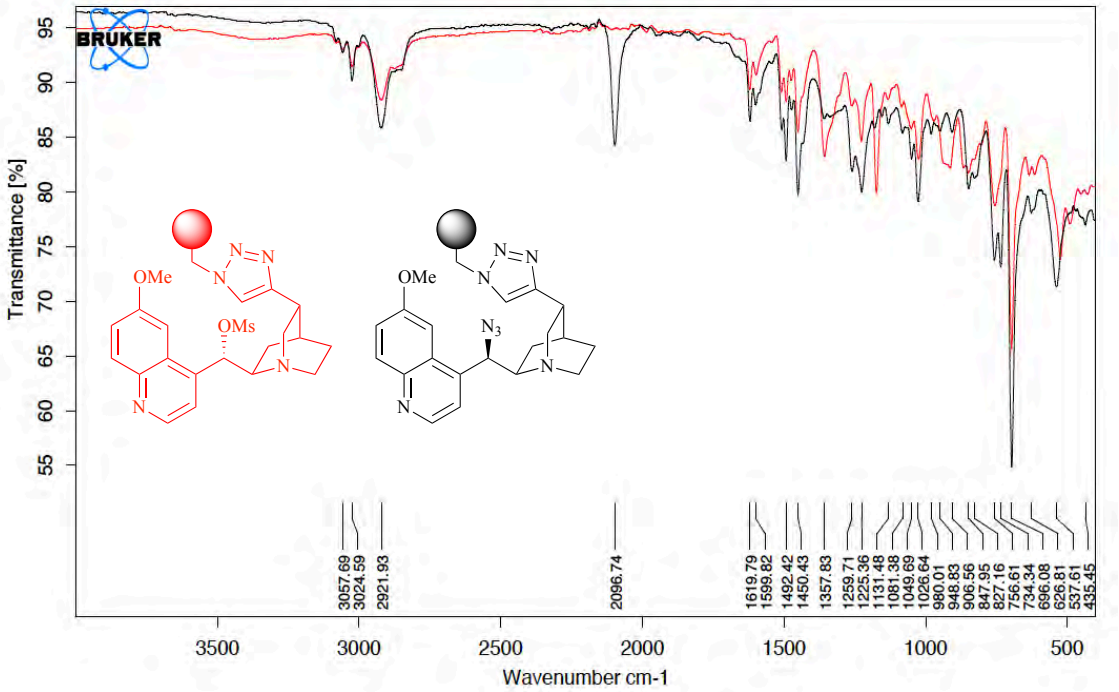
With MsO-quinine: a suspension of polymer-supported MsO-quinine **1-rOMs** (0.82 g, 0.70 mmol) and NaN_3 (0.23 g, 3.52 mmol) in DMF (10 mL) gave after shaking for 3 days and following the general procedure resin **1-N_3**. IR (ATR): 3024, 2921, 2853, 2096, 1620, 1600, 1451, 1261, 1226, 1027, 849, 825, 758, 733, 697, 538 cm^{-1}. Elemental analysis (%) = N, 9.41; C, 79.60; H, 6.71; S, 0.04. f = 0.84 mmol/g.



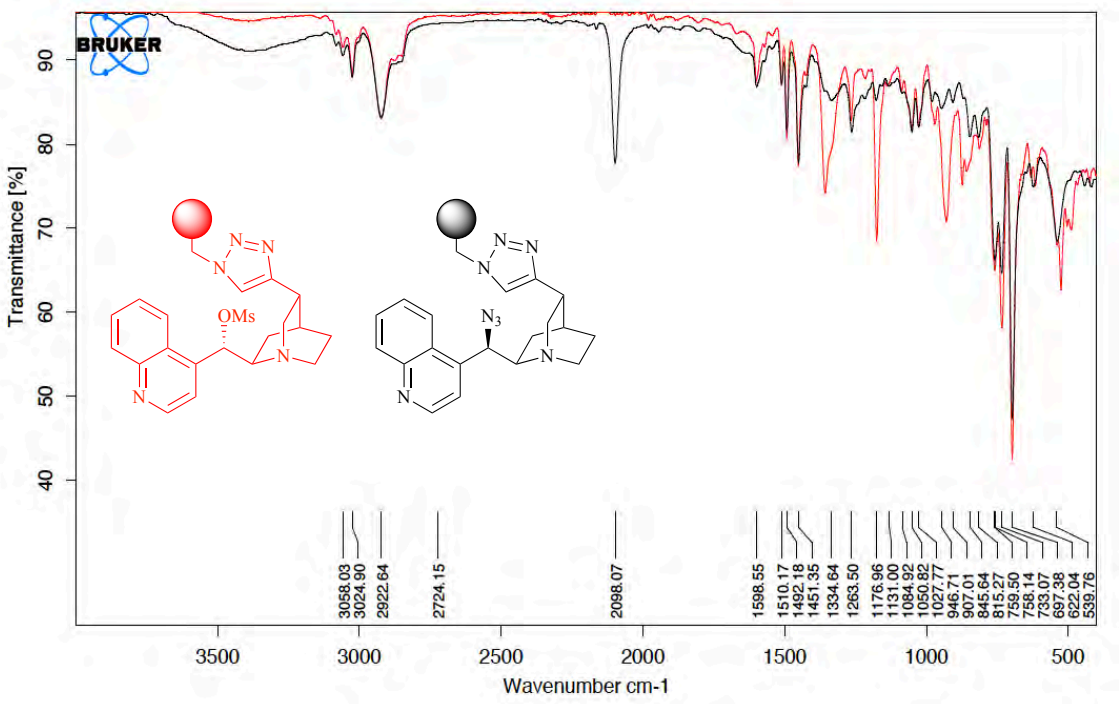
With MsO-cinchonidine: a suspension of polymer-supported MsO-cinchonidine **2-rOMs** (0.92 g, 0.81 mmol) and NaN_3 (0.26 g, 4.07 mmol) in DMF (10 mL) gave after shaking for 3 days and following the general procedure resin **2-N_3**. IR (ATR): 3025, 2922, 2847, 2098, 1600, 1492, 1451, 1264, 1049, 1028, 759, 733, 697, 536 cm^{-1}. Elemental analysis (%) = N, 9.69; C, 80.89; H, 6.84; S, 0.09. f = 0.86 mmol/g.



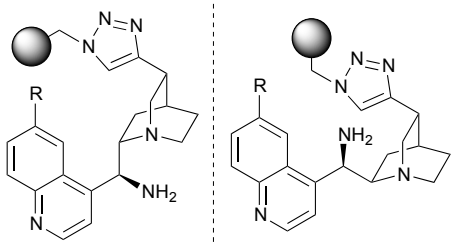
With MsO-quinidine: a suspension of polymer-supported MsO-quinidine **3-rOMs** (1.01 g, 0.86 mmol) and NaN_3 (0.28 g, 4.30 mmol) in DMF (10 mL) gave after shaking for 4 days and following the general procedure resin **3-N_3**. IR (ATR): 3025, 2922, 2097, 1620, 1492, 1450, 1225, 1027, 848, 757, 734, 696 cm^{-1}. Elemental analysis (%) = N, 8.84; C, 78.44; H, 6.70; S, 0.06. f = 0.79 mmol/g.



With MsO-cinchonine: a suspension of polymer-supported MsO-cinchonine **4-rOMs** (0.85 g, 0.75 mmol) and NaN_3 (0.24 g, 3.75 mmol) in DMF (10 mL) gave after shaking for 4 days and following the general procedure resin **4-N_3**. IR (ATR): 3024, 2923, 2873, 2097, 1598, 1492, 1451, 1264, 1051, 758, 734, 697 cm^{-1}. Elemental analysis (%) = N, 9.36; C, 80.17; H, 6.82; S, 0.09. f = 0.84 mmol/g.



Synthesis of polymer-supported amino cinchona (1-4)a

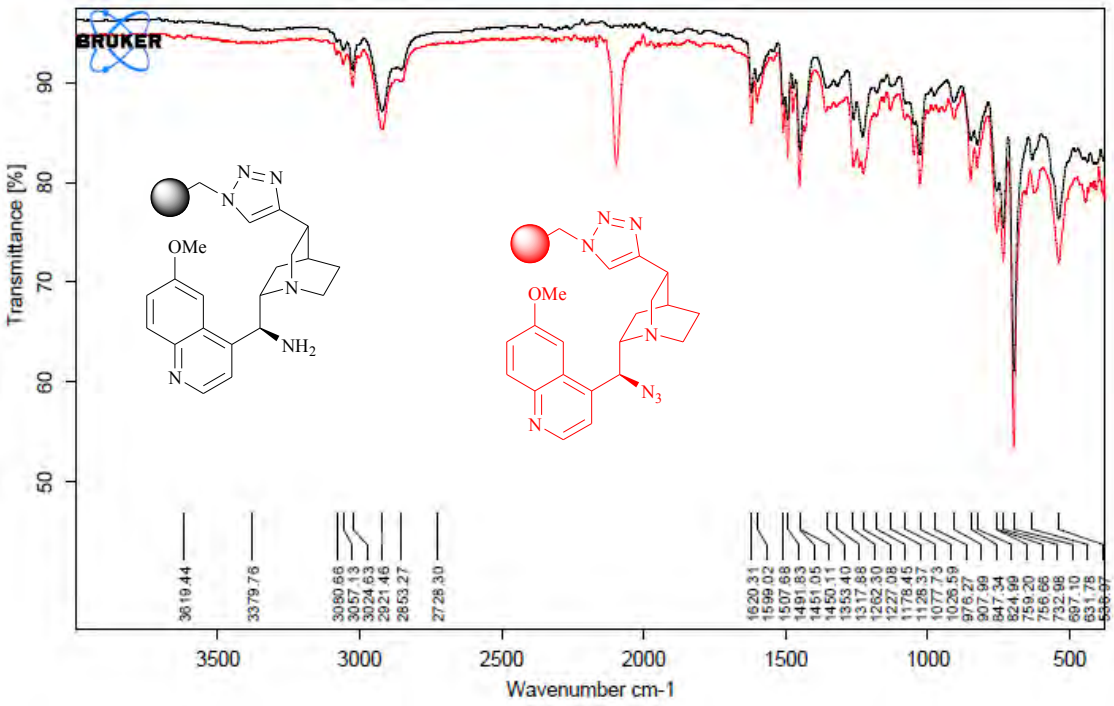


1a, R = OMe
2a, R = H

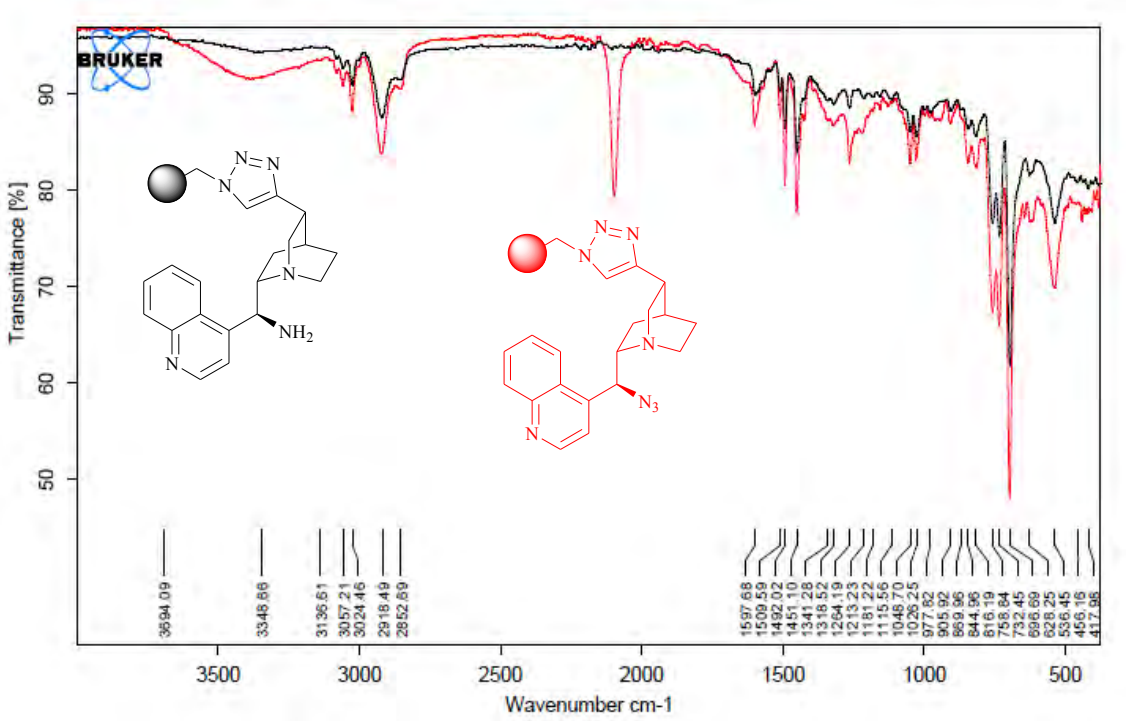
3a, R = OMe
4a, R = H

General procedure: polymer-supported azide-cinchone *epi*-**(1-4)-N$_3$** (1 equiv.) was swollen with dry THF and was shaken for 10 min. PPh_3 (3 equiv.) and deionized water (12 equiv.) were added and the mixture was shaken at room temperature for 24 h. After filtration, the mixture was monitored by IR. When the azide band was disappeared, the solid was filtered and washed with THF. The solid was taken with ethylenediamine shaking for 30 min and filtered. After that, the solid was washed with HCl 0.5N (50 mL), NaOH 0.5N, H_2O (until pH neutral), H_2O-MeOH, MeOH, MeOH-THF, THF and DCM. The solid was dried in vacuo at 40 ºC for 24 h.

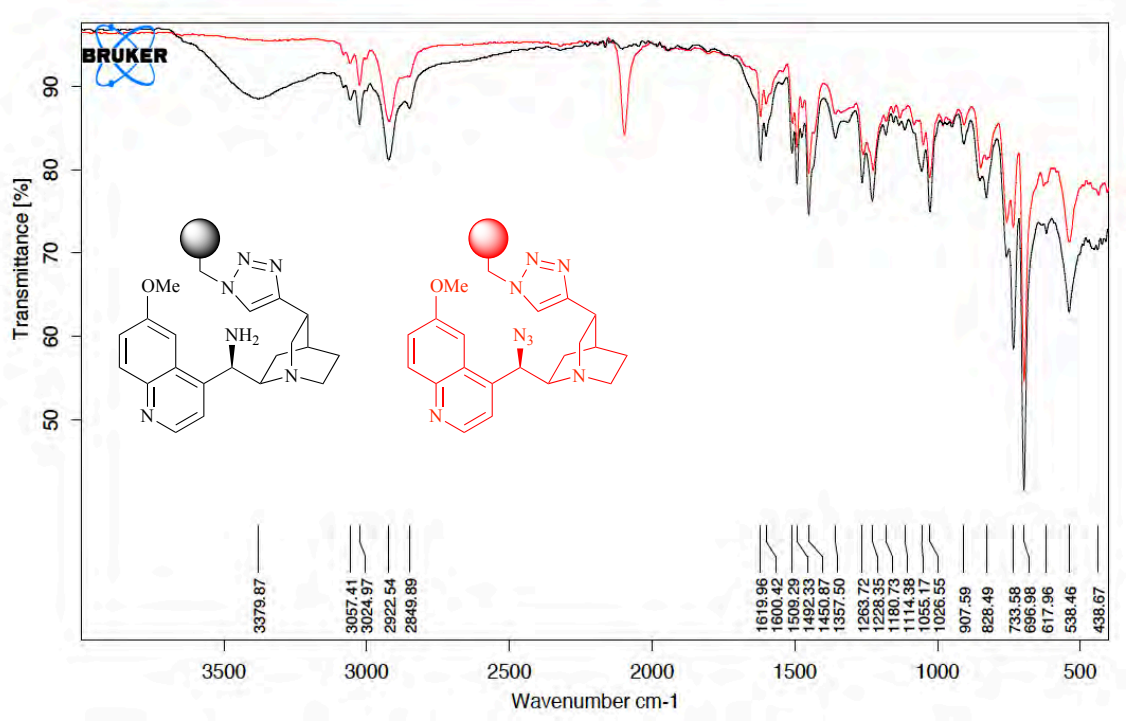
With azide-quinine: a suspension of polymer-supported azide-quinine *epi*-**1-N$_3$** (0.70 g, 0.59 mmol), PPh_3 (0.46 g, 1.77 mmol) and deionized water (0.13 mL, 7.08 mmol) in dry THF (12 mL) gave following the general procedure resin **1a**. IR (ATR): 3380, 3025, 2921, 2853, 1620, 1599, 1492, 1451, 1262, 1227, 1027, 847, 825, 733, 697, 539 cm^{-1}. Elemental analysis (%) = N, 7.24; C, 77.10; H, 6.89. f = 0.87 mmol/g.



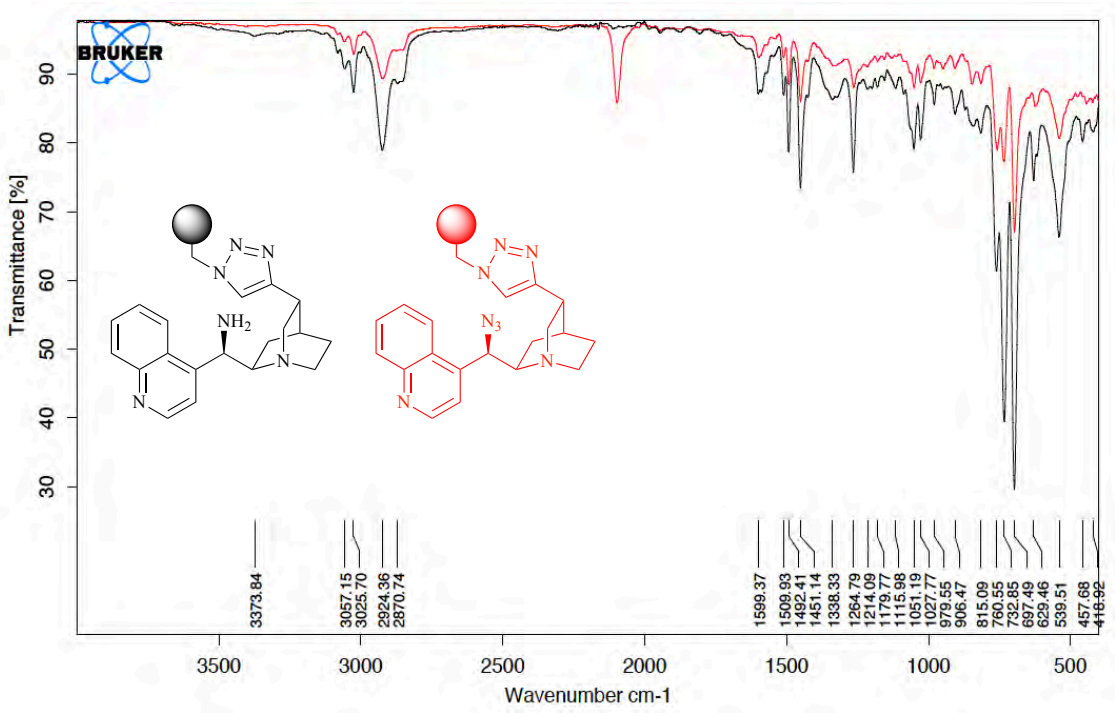
With azide-cinchonidine: a suspension of polymer-supported azide-cinchonidine *epi*-**2-N$_3$** (0.80 g, 0.67 mmol), PPh_3 (0.53 g, 2.02 mmol) and deionized water (0.15 mL, 8.09 mmol) in dry THF (15 mL) gave following the general procedure resin **2a**. IR (ATR): 3349, 3024, 2918, 2853, 1598, 1492, 1451, 1049, 1026, 759, 732, 697, 536 cm^{-1}. Elemental analysis (%) = N, 7.68; C, 81.57; H, 6.97. f = 0.91 mmol/g.



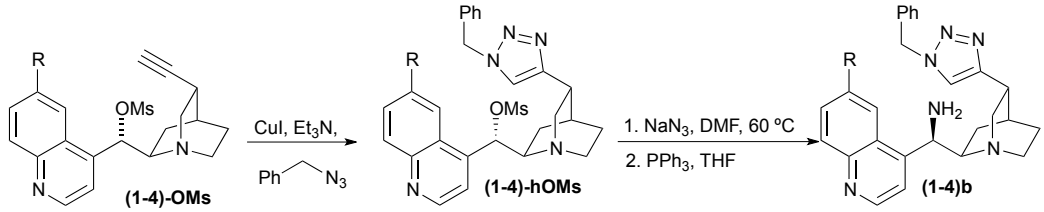
With azide-quinidine: a suspension of polymer-supported azide-quinidine *epi*-**3-N$_3$** (0.91 g, 0.72 mmol), PPh_3 (0.57 g, 2.15 mmol) and deionized water (0.15 mL, 8.64 mmol) in dry THF (15 mL) gave following the general procedure resin **3a**. IR (ATR): 3380, 3025, 2922, 1620, 1492, 1451, 1264, 1228, 1055, 1026, 828, 734, 697, 538 cm^{-1}. Elemental analysis (%) = N, 7.32; C, 78.28; H, 6.87. f = 0.87 mmol/g.



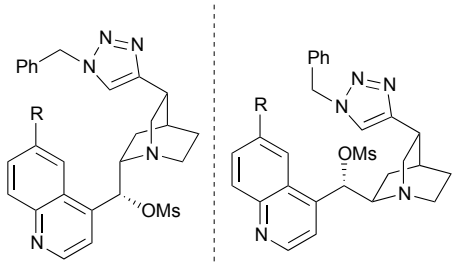
With azide-cinchonine: a suspension of polymer-supported azide-cinchonine *epi*-**4-N$_3$** (0.70 g, 0.59 mmol), PPh_3 (0.46 g, 1.76 mmol) and deionized water (0.13 mL, 7.08 mmol) in dry THF (12 mL) gave following the general procedure resin **4a**. IR (ATR): 3374, 3026, 2924, 1599, 1492, 1451, 1265, 1051, 761, 733, 697, 539 cm^{-1}. Elemental analysis (%) = N, 7.42; C, 81.01; H, 7.10. f = 0.88 mmol/g.



3. PREPARATION AND CHARACTERIZATION OF HOMOGENEOUS COUNTERPARTS OF RESINS (1-4)a. SYNTHESIS OF (1-4)b



Cycloaddition of alkyne MsO-cinchona (1-4)-OMs with benzyl azide

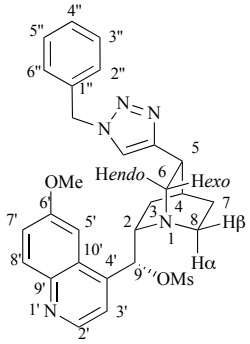


1-hOMs, R = OMe
2-hOMs, R = H

3-hOMs, R = OMe
4-hOMs, R = H

General procedure: $Cu(AcO)_2 \cdot H_2O$ (10 mol%) and L-ascorbic sodium salt (20 mol%) were added to a solution of alkyne MsO-cinchona **(1-4)-OMs** (1 equiv.) and benzyl azide (1.02 equiv.) in MeOH and the mixture was stirred at room temperature for 2 h. Water and AcOEt were added and the layers were separated. The aqueous layer was washed 3 times with AcOEt and the combined organic layers were washed 2 times with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give triazole **(1-4)-hOMs** which was purified by column chromatography.

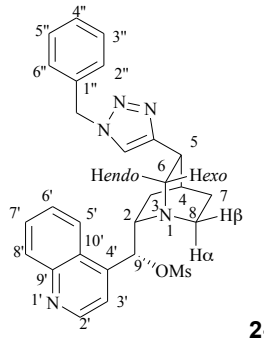
Synthesis of (1S,2S,4S,5R,9R)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(6-methoxyquinolin-4-yl)methyl methanesulfonate **1-hOMs**



1-hOMs

A solution of MsO-quinine **1-OMs** (0.76 g, 1.91 mmol), benzyl azide (0.24 mL, 1.95 mmol), $Cu(AcO)_2{\cdot}H_2O$ (35 mg, 0.19 mmol) and L-ascorbic sodium salt (76 mg, 0.38 mmol) in MeOH (20 mL) gave following the general procedure a green oil (1.10 g) which was submitted to flash silica gel column chromatography (mixtures AcOEt / MeOH 90:10) to give the triazole MsO-quinine **1-hOMs** (716 mg, 70% yield) as a yellow foam. IR (ATR): 2935, 2879, 1620, 1509, 1455, 1353, 1226, 1172, 1027, 928, 913, 866, 798, 717, 523, 500 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.55–1.71 (m, 2 H, H3α and H7β), 1.79-1.84 (m, 1 H, H7α), 1.92–2.02 (m, 1 H, H3β), 2.09–2.15 (m, 1 H, H4), 2.57 (s, 3 H, OMs), 2.68–2.76 (m, 1 H, H8β), 2.92–3.00 (m, 1 H, H5), 3.06–3.21 (m, 2 H, H6*exo* and H8α), 3.22–3.31 (m, 1 H, H6*endo*), 3.72 (br s, 1 H, H2), 3.98 (s, 3 H, OMe), 5.46 (d, 1 H, *J* = 15.0 Hz, CH_2Ph), 5.50 (d, 1 H, *J* = 15.0 Hz, CH_2Ph), 6.17 (br s, 1 H, H9), 7.18 (s, 1 H, H*triazole*), 7.21–7.24 (m, 2 H, H2" and 6"), 7.33–7.38 (m, 3 H, H3" and 5" and H4"), 7.39–7.43 (m, 2 H, H 5' and H 7'), 7.45 (br s, 1 H, H3'), 8.05 (d, *J* = 9.0 Hz, 1 H, H 8'), 8.79 (br s, 1 H, H2'). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.2 (t, C3), 25.2 (t, C7), 27.8 (d, C4), 33.0 (d, C5), 39.2 (q, OMs), 42.3 (t, C8), 54.0 (t, CH_2Ph), 55.5 (t, C6), 55.8 (q, OMe), 59.5 (d, C2), 79.8 (d, C9), 100.9 (d, C5'), 119.2 (d, C3'), 120.6 (d, CH*triazole*), 122.3 (d, C7'), 126.7 (s, C10'), 127.9 (d, C2" and 6"), 128.7 (d, C4"), 129.1 (d, C3" and 5"), 132.1 (d, C8'), 134.7 (s, C1"), 141.4 (s, C4'), 145.2 (s, C9'), 147.4 (d, C2'), 150.8 (s, C*triazole*), 158.4 (s, C6') ppm. $[\alpha]_D^{25}$ = –92.7 (*c* 0.51, $CHCl_3$). MS (ESI+), *m*/*z* (%): 534 ($[M+H]^+$, 100), 535 ($[M+2H]^{\cdot+}$, 27). HRMS (ESI+) calcd for $[C_{28}H_{31}N_5O_4S+H]^+$: 534.2170. Found: 534.2167.

Synthesis of (1S,2S,4S,5R,9R)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(quinolin-4-yl)methyl methanesulfonate **2-hOMs**

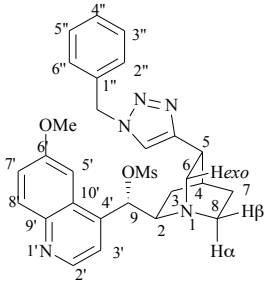


2-hOMs

A solution of MsO-cinchonidine **2-OMs** (0.7 g, 1.89 mmol), benzyl azide (0.24 mL, 1.93 mmol), $Cu(AcO)_2{\cdot}H_2O$ (34 mg, 0.19 mmol) and L-ascorbic sodium salt (75 mg, 0.38 mmol) in MeOH (20 mL) gave following the general procedure an orange foam (0.98 g) which was submitted to column chromatography (mixtures AcOEt / MeOH 92:8) to give the triazole MsO-cinchonidine **2-hOMs** (670 mg, 71% yield) as a yellow foam. IR (ATR): 2933, 2870, 1506, 1455, 1347, 1170, 1050, 928, 866, 764, 720, 515, 497 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.61–1.65 (m, 2 H, H3α and H7β), 1.78–1.84 (m, 1 H,

H7α), 1.91–2.00 (m, 1 H, H3β), 2.11–2.12 (m, 1 H, H4), 2.55 (s, 3 H, OMs), 2.63–2.69 (m, 1 H, H8β), 2.94–2.96 (m, 1 H, H5), 3.09–3.24 (m, 3 H, H6*endo* and H6*exo* and H8α), 3.62–3.81 (br s, 1 H, H2), 5.46 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 5.51 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 6.25 (br s, 1 H, H9), 7.19 (s, 1 H, H*triazole*), 7.22-7.24 (m, 2 H, H2" and 6"), 7.34-7.38 (m, 3 H, H3" and 5" and H4"), 7.52 (br s, 1 H, H3'), 7.62 (t, *J* = 7.5 Hz, 1 H, H 6'), 7.75 (t, *J* = 7.5 Hz, 1 H, H 7'), 8.16 (d, *J* = 7.5 Hz, 1 H, H 8'), 8.20 (br s, 1 H, H 5'), 8.95 (br s, 1H, H2'). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 25.4 (t, C3), 27.4 (t, C7), 27.7 (2d, C4 and C5), 32.9 (q, OMs), 42.2 (t, C8), 54.0 (t, CH_2Ph), 55.6 (t, C6), 59.9 (d, C2), 80.2 (d, C9), 119.7 (d, C3'), 120.5 (d, CH*triazole*), 122.7 (d, C5'), 125.5 (s, C10'), 127.5 (d, C6'), 127.9 (d, C2" and 6"), 128.7 (d, C4"), 129.1 (d, C3" and 5"), 129.6 (d, C7'), 130.7 (d, C8'), 134.7 (s, C1"), 143.0 (s, C4'), 148.7 (s, C9'), 150.0 (d, C2'), 150.8 (s, C*triazole*) ppm. $[\alpha]_D^{26}$ = −101.2 (*c* 0.51, $CHCl_3$). MS (ESI+), *m*/*z* (%): 504 ($[M+H]^+$, 100), 505 ($[M+2H]^{\cdot+}$, 30). HRMS (ESI+) calcd for $[C_{27}H_{29}N_5O_3S+H]^+$: 504.2064. Found: 504.2075.

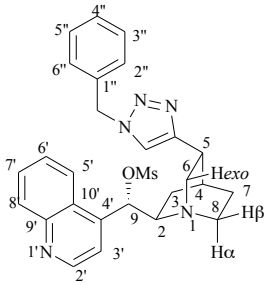
Synthesis of (1S,2R,4S,5R,9S)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(6-methoxyquinolin-4-yl)methyl methanesulfonate **3-hOMs**



3-hOMs

A solution of MsO-quinidine **3-OMs** (0.70 g, 1.75 mmol), benzyl azide (0.22 mL, 1.78 mmol), $Cu(AcO)_2 \cdot H_2O$ (32 mg, 0.17 mmol) and L-ascorbic sodium salt (70 mg, 0.35 mmol) in MeOH (20 mL) gave following the general procedure a yellow foam (1.11 g) which was submitted to flash silica gel column chromatography (mixtures AcOEt / MeOH 8:1) to give the triazole MsO-quinidine **3-hOMs** (790 mg, 85% yield) as a yellow foam. IR (ATR): 2934, 2870, 1620, 1508, 1354, 1226, 1172, 1023, 920, 868, 849, 717, 524, 491 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.58–1.66 (m, 3 H, H3α, H7α and H7β), 1.87–1.91 (m, 1 H, H3β), 2.05–2.06 (m, 1 H, H4), 2.64 (s, 3 H, OMs), 2.78–2.81 (m, 2 H, H8α and 8β), 3.01–3.08 (m, 2 H, H5 and H6*exo*), 3.34–3.40 (m, 1 H, H2), 3.51–3.60 (m, 1H, H6*endo*), 3.96 (s, 3 H, OMe), 5.53 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 5.57 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 6.54 (br s, 1 H, H9), 7.31-7.34 (m, 2 H, H2" and H6"), 7.36–7.44 (m, 5 H, H3', H7', H3" and 5" and H4"), 7.48 (s, 1 H, H*triazole*), 7.54 (d, *J* = 2.5 Hz, 1 H, H 5'), 8.03 (d, *J* = 9.2 Hz, 1 H, H 8'), 8.79 (br s, 1H, H2'). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 24.1 (t, C3), 26.0 (t, C7), 28.3 (d, C4), 33.3 (d, C5), 38.9 (q, OMs), 48.2 (t, C6), 50.0 (t, C8), 54.1 (t, CH_2Ph), 55.9 (q, OMe), 60.0 (d, C2), 81.0 (d, C9), 100.8 (d, C5'), 118.7 (d, C3'), 121.0 (d, CH*triazole*), 122.5 (d, C7'), 126.6 (s, C10'), 128.1 (d, C2" and 6"), 128.6 (d, C4"), 129.1 (d, C3" and 5"), 132.0 (d, C8'), 135.0 (s, C1"), 141.9 (s, C4'), 144.9 (s, C9'), 147.4 (d, C2'), 150.4 (s, C*triazole*), 158.5 (s, C6') ppm. $[\alpha]_D^{28}$ = +148.2 (*c* 0.76, $CHCl_3$). MS (ESI+), *m*/*z* (%): 534 ($[M+H]^+$, 100), 535 ($[M+2H]^{\cdot+}$, 30). HRMS (ESI+) calcd for $[C_{28}H_{31}N_5O_4S+H]^+$: 534.2175. Found: 534.2197.

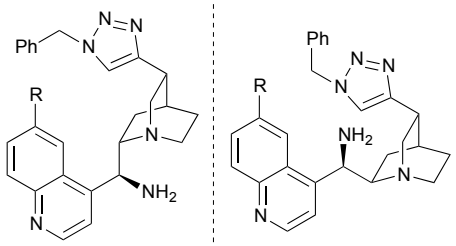
Synthesis of (1S,2R,4S,5R,9S)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(quinolin-4-yl)methyl methanesulfonate **4-hOMs**



4hOMs

A solution of MsO-cinchonine **4-OMs** (0.56 g, 1.51 mmol), benzyl azide (0.2 mL, 1.54 mmol), $Cu(AcO)_2 \cdot H_2O$ (27 mg, 0.15 mmol) and L-ascorbic sodium salt (60 mg, 0.30 mmol) in MeOH (15 mL) gave following the general procedure an orange foam (0.89 g) which was submitted to flash silica gel column chromatography (mixtures AcOEt / MeOH 8:1) to give the triazole MsO-cinchonine **4-hOMs** (600 mg, 79% yield) as a yellow foam. IR (ATR): 2934, 2870, 1592, 1455, 1350, 1214, 1083, 927, 867, 762, 721, 621, 524, 493 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.57–1.67 (m, 3 H, H3α, H7α and H7β), 1.88–1.93 (m, 1 H, H3β), 2.08–2.09 (m, 1 H, H4), 2.68 (s, 3 H, OMs), 2.74–2.77 (m, 2 H, H8α and 8β), 3.03-3.06 (m, 1 H, H5), 3.06–3.12 (m, 1 H, H6*exo*), 3.30–3.41 (m, 1 H, H2), 3.44–3.48 (m, 1H, H6*endo*), 5.54 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 5.57 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 6.40 (br s, 1 H, H9), 7.33–7.36 (m, 2 H, H3" and H5"), 7.37–7.4 (m, 3 H, H2" and 6" and H4"), 7.47 (br s, 1 H, H3'), 7.51 (s, 1 H, H*triazole*), 7.62 (t, *J* = 8.0 Hz, 1 H, H 6'), 7.75 (t, *J* = 8.0 Hz, 1 H, H 7'), 8.16 (d, *J* = 8.0 Hz, 1 H, H 8'), 8.20 (d, *J* = 8.0 Hz, 1 H, H 5'), 8.94 (br s, 1H, H2'). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 23.8 (t, C3), 26.0 (t, C7), 28.2 (d, C4), 33.3 (d, C5), 38.8 (q, OMs), 48.4 (t, C6), 49.9 (t, C8), 54.2 (t, CH_2Ph), 60.2 (d, C2), 80.7 (d, C9), 119.1 (d, C3'), 120.9 (d, CH*triazole*), 123.1 (d, C5'), 125.4 (s, C10'), 127.4 (d, C6'), 128.1 (d, C3" and 5"), 128.6 (d, C4"), 129.1 (d, C2" and 6"), 129.6 (d, C7'), 130.7 (d, C8'), 134.9 (s, C1"), 143.6 (s, C4'), 148.7 (s, C9'), 150.0 (d, C2'), 150.4 (s, C*triazole*) ppm. $[\alpha]_D^{25}$ = +138.0 (*c* 1.01, $CHCl_3$). MS (ESI+), *m*/*z* (%): 504 ($[M+H]^+$, 100), 505 ($[M+2H]^{\cdot+}$, 30). HRMS (ESI+) calcd for $[C_{27}H_{29}N_5O_3S+H]^+$: 504.2069. Found: 504.2066.

Synthesis of amino cinchona, *epi*-(1-4)b



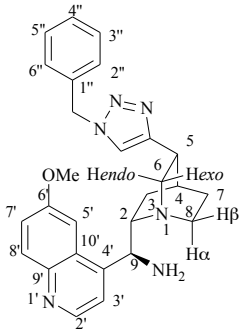
1b, R = OMe
2b, R = H

3b, R = OMe
4b, R = H

General procedure: A solution of triazole MsO-cinchona **(1-4)-hOMs** (1 equiv.) and sodium azide (3 equiv.) in dry DMF was stirred at 60 ºC for 22 h. The reaction was allowed to cool to room temperature, water was added and the organic layer was extracted 3 times with AcOEt and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give the azide. This compound was treated with PPh_3 (3 equiv.) and deionized water (12

equiv.) in distilled THF and the reaction mixture was stirred at room temperature for 16 h. Aqueous 1N HCl solution was added and extracted 3 times with AcOEt. The aqueous layer was made alkaline (pH = 10) with excess of NH_4OH and was extracted 3 times with AcOEt. The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give the amine *epi*-(**1-4)b** which was purified by column chromatography.

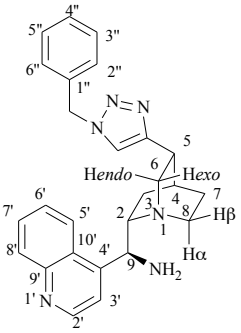
Synthesis of (1S,2S,4S,5R,9S)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(6-methoxyquinolin-4-yl)methanamine **1b**



1b

A solution of triazole MsO-quinine **1-hOMs** (0.65 g, 1.22 mmol) and sodium azide (0.24 g, 3.65 mmol) in dry DMF (12 mL) gave following the general procedure the azide as a green oil (0.81 g). The above green oil (0.81 g), PPh_3 (0.96 g, 3.66 mmol) and deionized water (0.26 mL, 14.6 mL) in distilled THF (25 mL) following the general procedure gave a yellow foam (0.52 g) which was submitted to flash silica gel column chromatography (mixtures from AcOEt / MeOH 2:1 to AcOEt / MeOH / NH_4OH 50:50:1) to give the amine quinine **1b** (0.44 g, 79% yield) as a yellow foam. IR (ATR): 3690-2741 (max. at 3379, 2941, 2915), 1620, 1507, 1474, 1454, 1430, 1357, 1228, 1026, 849, 825, 718, 634, 459 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.72 (dd, 1 H, *J* = 13.5 and 7.5 Hz H3α), 1.21–1.33 (m, 1 H, H3β), 1.57–1.63 (m, 1H, H7α), 1.64–1.71 (m, 1 H, H7β), 1.89–1.90 (m, 1 H, H4), 1.96 (br s, 2 H, NH_2), 2.85–2.91 (m, 1 H, H8β), 3.01–3.03 (m, 1 H, H5), 3.18–3.31 (m, 2 H, H2 and H8α), 3.38 (ddd, 1 H, *J* = 14.0, 5.0 and 2.5 Hz, H6*endo*), 3.48 (dd, 1 H, *J* = 14.0, and 10.5 Hz, H6*exo*), 3.95 (s, 3 H, OMe), 4.58 (br s, 1 H, H9), 5.43 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 5.47 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 7.14 (s, 1 H, H*triazole*), 7.18–7.19 (m, 2 H, H2" and 6"), 7.33–7.34 (m, 4 H, H3', H3" and 5" and H4"), 7.36 (dd, *J* = 9.5 and 3.0 Hz, 1 H, H 7'), 7.61 (br s, 1 H, H 5'), 8.01 (d, *J* = 9.5 Hz, 1 H, H 8'), 8.68 (d, 1 H, *J* = 4.5 Hz, H2'). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.0 (t, C3), 27.6 (d, C4), 28.0 (t, C7), 33.2 (d, C5), 41.0 (t, C8), 50.9 (d, C9), 54.0 (t, CH_2Ph), 55.5 (q, OMe), 55.8 (t, C6), 61.5 (d, C2), 102.0 (d, C5'), 119.7 (d, C3'), 120.1 (d, CH*triazole*), 121.2 (d, C7'), 127.9 (d, C2" and 6"), 128.6 (d, C4"), 128.7 (s, C10'), 129.0 (d, C3" and 5"), 131.8 (d, C8'), 134.8 (s, C1"), 144.7 (s, C9'), 146.9 (s, C4'), 147.8 (d, C2'), 151.3 (s, C*triazole*), 157.6 (s, C6') ppm. $[\alpha]_D^{25}$ = +65.5 (*c* 0.705, $CHCl_3$). MS (ESI+), *m*/*z* (%): 455 ($[M+H]^+$, 100). HRMS (ESI+) calcd for $C_{27}H_{30}N_6O+H]^+$: 455.2554. Found: 455.2548.

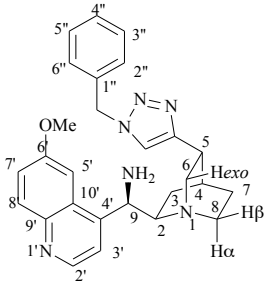
*Synthesis of (1S,2S,4S,5R,9S)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(quinolin-4-yl)methanamine epi-***2b**



2b

A solution of triazole MsO-cinchonidine **2-hOMs** (0.62 g, 1.23 mmol) and sodium azide (0.24 g, 3.69 mmol) in dry DMF (12 mL) gave following the general procedure the azide as a green oil (0.69 g). The above green oil (0.69 g), PPh_3 (0.97 g, 3.69 mmol) and deionized water (0.27 mL, 14.8 mL) in distilled THF (25 mL) following the general procedure gave an orange foam (0.50 g) which was submitted to column chromatography (mixtures from AcOEt / MeOH 5:1 to AcOEt / MeOH / NH_4OH 50:50:1) to give the amine cinchonidine **2b** (430 mg, 83% yield) as a yellow foam. IR (ATR): 3709-2736 (max. at 3367, 2937, 2865), 1589, 1509, 1454, 1342, 1320, 1214, 1051, 909, 819, 764, 723, 630 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.68–0.72 (m, 1 H, H3α), 1.24–1.32 (m, 1 H, H3β), 1.59–1.69 (m, 2 H, H7α and H7β), 1.88–1.89 (m, 1 H, H4), 2.09 (br s, 2 H, NH_2), 2.84–2.90 (m, 1 H, H8β), 3.01–3.03 (m, 1 H, H5), 3.22–3.30 (m, 2 H, H2 and H8α), 3.37–3.41 (m, 1 H, H6*endo*), 3.48 (dd, 1 H, *J* = 13.8 and 10.3 Hz, H6*exo*), 4.70 (br s, 1 H, H9), 5.42 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 5.46 (d, 1 H, *J* = 14.5 Hz, CH_2Ph), 7.15 (s, 1 H, H*triazole*), 7.18–7.20 (m, 2 H, H2" and 6"), 7.33–7.34 (m, 3 H, H3" and 5" and H4"), 7.42 (d, 1 H, *J* = 4.5 Hz, H3'), 7.57 (dt, *J* = 8.5 and 1.0 Hz, 1 H, H 6'), 7.69 (dt, *J* = 8.5 and 1.3 Hz, 1 H, H 7'), 8.11 (dd, *J* = 8.5 and 1.0 Hz, 1 H, H 8'), 8.32 (br s, 1 H, H 5'), 8.83 (d, 1 H, *J* = 4.5 Hz, H2'). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.1 (t, C3), 27.6 (d, C4), 27.8 (t, C7), 33.2 (d, C5), 41.0 (t, C8), 51.3 (d, C9), 54.0 (t, CH_2Ph), 55.8 (t, C6), 61.6 (d, C2), 119.4 (d, C3'), 120.2 (d, CH*triazole*), 123.2 (d, C5'), 126.4 (d, C6'), 127.8 (s, C10'), 127.8 (d, C2" and 6"), 128.6 (d, C4"), 128.9 (d, C7'), 129.0 (d, C3" and 5"), 130.4 (d, C8'), 134.7 (s, C1"), 148.5 (s, C9'), 150.2 (s, C4'), 150.3 (d, C2'), 151.3 (s, C*triazole*) ppm. $[\alpha]_D^{24}$ = +63.3 (*c* 0.58, $CHCl_3$). MS (ESI+), *m*/*z* (%): 425 ($[M+H]^+$, 100). HRMS (ESI+) calcd for $[C_{26}H_{28}N_6+H]^+$: 425.2448. Found: 425.2450.

Synthesis of (1S,2R,4S,5R,9R)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(6-methoxyquinolin-4-yl)methanamine **3b**

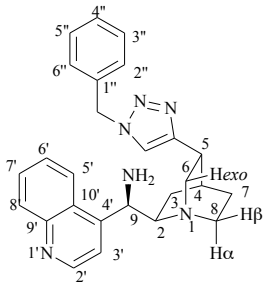


3b

A solution of triazole MsO-quinidine **3-hOMs** (0.75 g, 1.40 mmol) and sodium azide (0.27 g, 4.22 mmol) in dry DMF (15 mL) gave following the general procedure the azide as a yellow solid (0.83 g). The above yellow solid (0.83 g), PPh_3 (1.11 g, 4.22 mmol) and deionized water (0.30 mL, 16.9 mL) in

distilled THF (25 mL) following the general procedure gave a yellow foam (0.56 g) which was submitted to flash silica gel column chromatography (mixtures from AcOEt / MeOH 2:1 to AcOEt / MeOH / NH_4OH 50:50:1) to give the amine quinidine **3b** (0.48 g, 75% yield) as a yellow foam. IR (ATR): 3690-2830 (max. at 3364, 2936, 2870), 1620, 1507, 1473, 1454, 1432, 1353, 1226, 1087, 1051, 910, 828, 719, 634, 459 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.89–0.92 (m, 1 H, H3α), 1.17–1.22 (m, 1 H, H3β), 1.54–1.66 (m, 2H, H7α and H7β), 1.71–1.72 (m, 1 H, H4), 2.08 (br s, 2 H, NH_2), 2.91–2.95 (m, 1 H, H5), 2.97–3.06 (m, 2 H, H2 and H8α) 3.06–3.14 (m, 1 H, H8β), 3.22 (dd, 1 H, *J* = 14.0 and 10.3 Hz, H6*exo*), 3.77–3.81 (m, 1 H, H6*endo*), 4.01 (s, 3 H, OMe), 4.89 (br s, 1 H, H9), 5.43 (d, 1 H, *J* = 14.8 Hz, CH_2Ph), 5.48 (d, 1 H, *J* = 14.8 Hz, CH_2Ph), 7.13 (s, 1 H, H*triazole*), 7.18–7.19 (m, 2 H, H2" and 6"), 7.29–7.32 (m, 3 H, H3" and 5" and H4"), 7.34 (dd, *J* = 9.2 and 2.7 Hz, 1 H, H 7'), 7.50 (br s, 1 H, H3'), 7.70 (br s, 1 H, H 5'), 7.98 (d, *J* = 9.2 Hz, 1 H, H 8'), 8.70 (d, 1 H, *J* = 4.3 Hz, H2'). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 24.9 (t, C3), 26.5 (t, C7), 28.9 (d, C4), 33.3 (d, C5), 46.4 (t, C6), 49.4 (t, C8), 50.9 (d, C9), 54.0 (t, CH_2Ph), 55.8 (q, OMe), 62.3 (d, C2), 101.6 (d, C5'), 119.8 (d, C3'), 120.8 (d, CH*triazole*), 121.8 (d, C7'), 127.9 (d, C2" and 6"), 128.6 (d, C4"), 128.8 (s, C10'), 129.0 (d, C3" and 5"), 131.4 (d, C8'), 134.7 (s, C1"), 144.6 (s, C9'), 147.6 (d, C2'), 147.9 (s, C4'), 150.5 (s, C*triazole*), 157.7 (s, C6') ppm. $[\alpha]_D^{25}$ = +26.4 (*c* 0.92, $CHCl_3$). MS (ESI+), *m/z* (%): 455 ($[M+H]^+$, 100). HRMS (ESI+) calcd for $[C_{27}H_{30}N_6O+H]^+$: 455.2559. Found: 455.2549.

Synthesis of (1S,2R,4S,5R,9R)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(quinolin-4-yl)methanamine **4b**



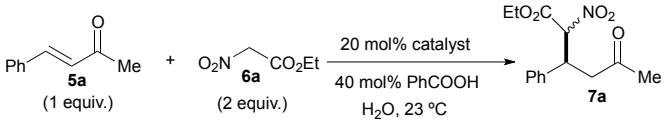
4b

A solution of triazole MsO-cinchonine **4-hOMs** (0.54 g, 1.07 mmol) and sodium azide (0.2 g, 3.22 mmol) in dry DMF (10 mL) gave following the general procedure the azide as a green oil (0.50 g). The above green oil (0.50 g), PPh_3 (0.84 g, 3.22 mmol) and deionized water (0.23 mL, 12.9 mL) in distilled THF (20 mL) following the general procedure gave an orange foam (0.35 g) which was submitted to flash silica gel column chromatography (mixtures from AcOEt / MeOH 2:1 to AcOEt / MeOH / NH_4OH 50:50:1) to give the amine cinchonine **4b** (300 mg, 66% yield) as a white foam. IR (ATR): 3694-2684 (max. at 3362, 3283, 2935, 2868), 1588, 1569, 1509, 1455, 1337, 1321, 1212, 1050, 1028, 821, 762, 718, 697, 629, 458 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.82–0.87 (m, 1 H, H3α), 1.11–1.15 (m, 1 H, H3β), 1.53–1.60 (m, 1H, H7α), 160–1.67 (m, 1 H, H7β), 1.72–1.73 (m, 1 H, H4), 2.01 (br s, 2 H, NH_2), 2.93–2.97 (m, 1 H, H5), 3.00–3.12 (m, 3 H, H2 and H8α and H8β), 3.22 (dd, 1 H, *J* = 14.0 and 10.5 Hz, H6*exo*), 3.80–3.84 (m, 1 H, H6*endo*), 4.99 (br s, 1 H, H9), 5.45 (d, 1 H, *J* = 14.8 Hz, CH_2Ph), 5.54 (d, 1 H, *J* = 14.8 Hz, CH_2Ph), 7.15 (s, 1 H, H*triazole*), 7.21–7.23 (m, 2 H, H2" and 6"), 7.33–7.34 (m, 3 H, H3" and 5" and H4"), 7.45 (dt, *J* = 8.3 and 0.9 Hz, 1 H, H 6'), .57 (br s, 1 H, H3'), 7.65 (dt, *J* = 8.3 and 1.3 Hz, 1 H, H 7'), 8.08 (dd, *J* = 8.3 and 0.9 Hz, 1 H, H 8'), 8.41 (br s, 1 H, H 5'), 8.84 (d, 1 H, *J* = 4.4 Hz, H2'). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 24.7 (t, C3), 26.5 (t, C7), 28.8 (d, C4), 33.3 (d, C5), 46.3 (t, C6), 49.5 (t, C8), 50.5 (d, C9), 54.1 (t, CH_2Ph), 62.4 (d, C2), 119.7 (d, C3'), 120.8 (d, CH*triazole*), 124.0 (d, C5'),

126.2 (d, C6'), 127.90 (s, C10'), 127.91 (d, C2" and 6"), 128.6 and 128.9 (2d, C7' and C4"), 129.1 (d, C3" and 5"), 130.0 (d, C8'), 134.8 (s, C1"), 148.4 (s, C9'), 149.5 (s, C4'), 150.2 (d, C2'), 150.6 (s, C*triazole*) ppm. $[\alpha]_D^{25}$ = +87.6 (*c* 0.995, $CHCl_3$). MS (ESI+), *m*/*z* (%): 425 ([M+H]$^+$, 100). HRMS (ESI+) calcd for $[C_{26}H_{28}N_6+H]^+$: 425.2454. Found: 425.2471.

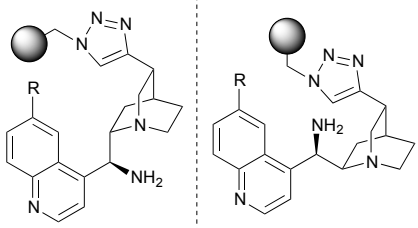
4. MICHAEL ADDITION CATALYZED BY RESINS 1-4

Michael addition of ethyl nitroacetate to enones[4] was selected as a model to check the catalytic activity of the prepared resins. Catalyst **1a** afforded better results than the other cinchona alkaloid family, therefore was selected as the catalyst for the rest of the study.



Entry	Catalyst	Time	Conversion (%)[a]	d.r.[a]	ee (%)[b]
1	4a	2 h	91	1.3:1	-81/-80
2	3a	2 h	51	1.4:1	-87/-83
3	3a	19 h	100	1.5:1	-85/-84
4	2a	2 h	87	1.3:1	91/91
5	1a	2 h	87	1.3:1	92/92

[a]Conversion was determined by ^{1}H NMR spectroscopy.
[b]Enantiomeric excess was determined by chiral HPLC analysis.

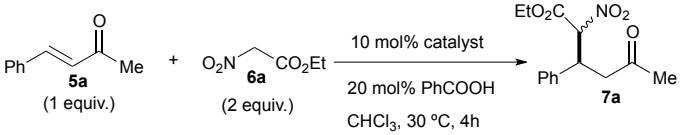


1a, R = OMe
2a, R = H

3a, R = OMe
4a, R = H

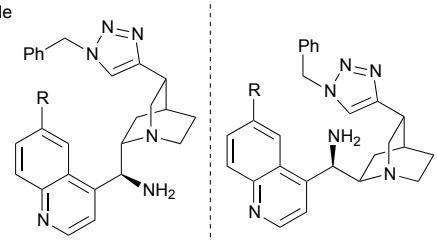
Michael addition catalyzed by homogeneous amino cinchones, *epi*-(1-4)b

Cinchona derivatives **(1-4)b** (4.5 mg, 0.01 mmol, 10 mol%) were added to a vial with a mixture of (*E*)-4-phenylbut-3-en-2-one **5a** (14.6 mg, 0.1 mmol, 1 equiv.), ethyl nitroacetate, **6a** (22 µL, 0.2 mmol, 2 equiv.) and benzoic acid (2.4 mg, 0.02 mmol, 20 mol%) in $CHCl_3$ (0.1 mL) and the mixture was stirred at 30 ºC in a sand bath for 4 h. An aliquot was taken and the conversion was measured by ^{1}H NMR. The reaction crude was directly purified through column chromatography eluting with cyclohexane and (1-20%) AcOEt. A summary of the results can be observed in the following table.



Entry	Catalyst	Conversion (%)[a]	d.r.[a]	ee (%)[b]
1	1b	100	1:1	97/95
2	3b	100	1:1	-90/-91
3	2b	100	1.1:1	90/93
4	4b	100	1.1:1	-89/-90

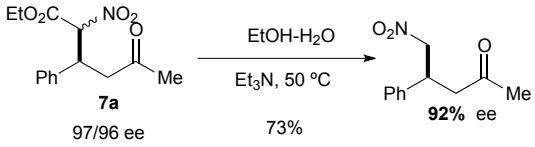
[a]Conversion was determined by ^{1}H NMR spectroscopy.
[b]Enantiomeric excess was determined by chiral HPLC analysis.



1b, R = OMe
2b, R = H

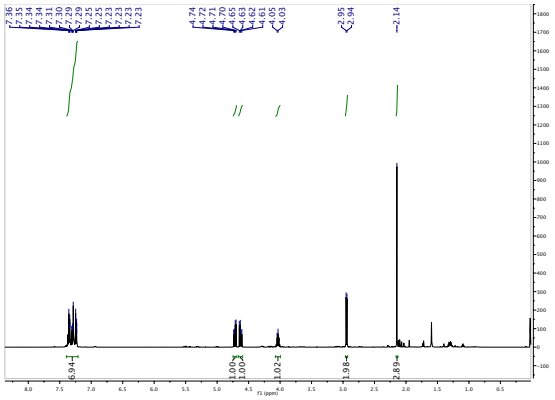
3b, R = OMe
4b, R = H

Decarboxylation of nitroester 7 to eliminate the γ-stereocenter.

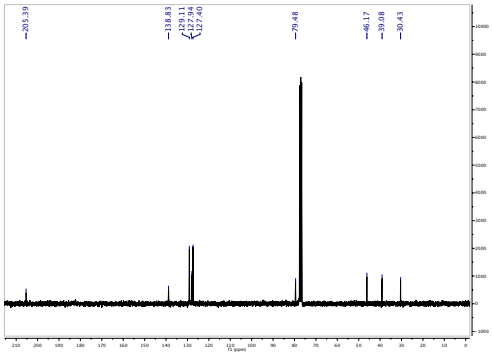


δ-ketoester **7a** (279 mg, 1mmol) was solved in EtOH (4 mL). Then H_2O (4 mL) and Et_3N (1.2 mL) were added and the reaction mixture was stirred at 50 ºC for 9h. Brine was added and the aqueous mixture was extracted 2x20 mL of EtOAc. Combined organic layers were dried over $MgSO_4$, filtrated and concentrated in the rotatory evaporator. The reaction crude was directly purified through column chromatography eluting with cyclohexane and (1- 30) % AcOEt. 151 mg of the nitroester were obtained as a white solid . The ee value was 92%: tR (major) = 14.56 min, tR (minor) = 20.36 (Chiralpak AS-H, λ = 220 nm, 25% iPrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.14 (s, 3H), 2.94 (d, *J* = 7.0 Hz, 2H), 4.03 (p, *J* = 7.1 Hz), 4.63 (dd, *J* = 12.4, 7.7 Hz, 1H), 4.72 (dd, *J* = 12.4, 6.9 Hz, 1H), 7.21-7.40 (m, 5H). ^{13}C NMR (75 MHz, CDCl3): δ = 30.4, 39.1, 46.2, 79.5, 127.4, 127.9, 129.1, 138.8, 205.4. ppm.

^{1}H NMR 500 MHz

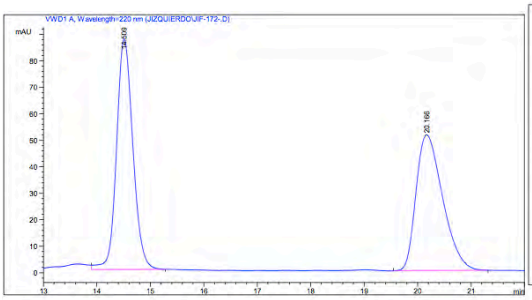


^{13}C NMR 75 MHz



(Chiralpak AS-H, λ = 220 nm, 25% iPrOH/hexane, flow rate = 1 mL/min)

RACEMIC



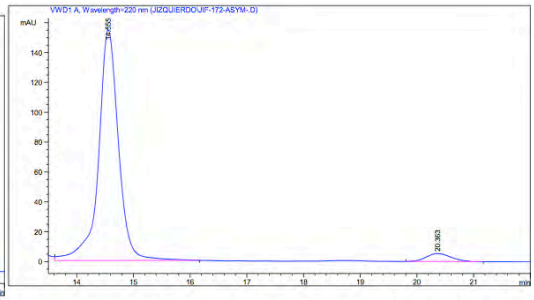
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.509	VB	0.3284	1854.51294	87.11607	51.1065
2	20.166	BB	0.5375	1774.21057	51.29480	48.8935

ENANTIOPURE



Area Percent Report

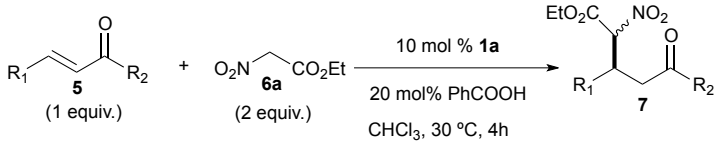
Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=220 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.555	VB	0.3685	3802.12646	154.55257	95.8439
2	20.363	BB	0.4728	164.87215	5.37684	4.1561

5. GENERAL PROCEDURE FOR MICHAEL ADDITIONS. CHARACTERIZATION OF MICHAEL ADDUCTS

Procedure for the Michael addition of ethyl nitroacetate to enones catalyzed by resin 1.



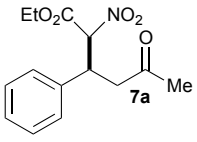
Entry	Product	R_1	R_2	Conversion (%)[a]	Yield (%)	d.r.[a]	ee (%)[b]
1	**7a**	Ph	Me	98	96	1:1	97/96
2	**7b**	2-Me-C_6H_4	Me	92	89	1:1.1	96/96
3	**7c**	3-Me-C_6H_4	Me	89	85	1:1	95/98
4	**7d**	4-Me-C_6H_4	Me	90	89	1.1:1	96/95
5	**7e**	4-Cl-C_6H_4	Me	87	85	1.1:1	>99/>99
6	**7f**	4-Br-C_6H_4	Me	97	96	1.1:1	97/98
7	**7g**	4-OMe-C_6H_4	Me	78	78	1:1	95/95
8	**7h**	4-NO_2-C_6H_4	Me	97	93	1.2:1	96/96
9	**7i**	4-CN-C_6H_4	Me	99	94	1.1:1	93/98
10	**7j**	2-F-C_6H_4	Me	99	92	1:1.1	97/97
11	**7k**	3,5-Cl_2-C_6H_4	Me	99	99	1:2	97/96
12	**7l**	2-furyl	Me	79	60	1:1	98/98
13	**7m**	C_2H_2Ph	Me	89	89	1.3:1	95/95
14	**7n**	C_2H_4Ph	Me	85	77	1:1	98/99
15	**7o**	CHex	Me	77	63	1:1.1	98/98
16[c]	**7p**	2-Cyclopentenone		57	56	1:1	66/65
17	**7q**	2-Cyclohexenone		75	52	1:1	95/93
18	**7r**	2-Cycloheptenone		65	65	1:1.1	97/96
19	**7s**	Ph	Et	80	62	1:1	97/96

[a]Conversion was determined by ^{1}H NMR spectroscopy. [b]Enantiomeric excess was determined by chiral HPLC analysis. [c]Conditions: (2 equiv.) 2-cyclopentenone, (1 equiv.) ethyl nitroacetate, 16 h.

Polymer-supported quinine derivative **1a** (11.2 mg, 0.01 mmol, 10 mol%) was added to a vial with a mixture of α,β-unsaturated ketone (0.1 mmol, 1 equiv.), ethyl nitroacetate, **6a** (22 μL, 0.2 mmol, 2 equiv.) and benzoic acid (2.4 mg, 0.02 mmol, 20 mol%) in $CHCl_3$ (0.1 mL) and the mixture was stirred at 30 ºC in a sand bath for 4 h. Then, the resin was filtered off, washed with $CHCl_3$ (3 x 1 mL) and dried under vacuum. The combined liquid phases were concentrated under reduced pressure. The reaction crude was directly purified through column chromatography eluting with cyclohexane and (1- 20) % AcOEt.

Characterization of compounds 7a–7s.

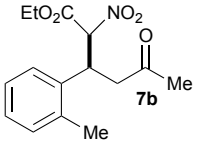
(3*S*)-Ethyl 2-nitro-5-oxo-3-phenylhexanoate **7a**[5,6]



The diastereomeric mixture (*anti*:*syn*) (dr = 1:1) was isolated as a white solid; The ee value were 97% and 96%. *Syn* isomer: tR (major) = 18.91 min, tR (minor) = 20.72 min and *anti* isomer: tR (minor) = 29.51 min, tR (major) = 36.51 min (Chiralpak IC, λ = 254 nm, 20% iPrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.29 (t, *J* = 7.2 Hz, 3 H, *anti* diastereoisomer), 2.08 (s, 3 H, *syn* diastereoisomer), 2.09 (s, 3 H, *anti* diastereoisomer),

2.92–3.16 (m, 4 H, both diastereomers), 4.07 (dq, *J* = 7.1 and 2.6 Hz, 2 H, *syn* diastereoisomer), 4.21–4.34 (m, 4 H, both diastereomers), 5.43 (d, *J* = 8.7 Hz, 1 H, *syn* diastereoisomer), 5.50 (d, *J* = 9.8 Hz, 1 H, *anti* diastereoisomer), 7.25–7.35 (m, 10 H, both diastereoisomers). ^{13}C NMR (101 MHz, CDCl3): δ = 13.6, 13.8, 30.3, 30.4, 41.3, 41.6, 45.2, 45.5, 62.9, 63.3, 91.2, 91.3, 128.0, 128.1, 128.2, 128.4, 128.8, 129.0, 136.9, 137.8, 163.1, 163.6, 204.7, 204.9 ppm.

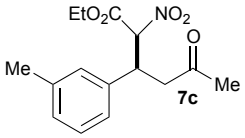
(3*S*)-Ethyl 2-nitro-5-oxo-3-(*o*-tolyl)hexanoate **7b**



7b

The diastereomeric mixture (*anti*:*syn*) (dr = 1:1.1) was isolated as a colorless oil; The ee value were 96% and 96%. *Syn* isomer: tR (major) = 13.51 min, tR (minor) = 20.85 min and *anti* isomer: tR (major) = 14.66 min, tR (minor) = 18.76 min (Chiralpak AD-H, λ = 210 nm, 10% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.32 (t, *J* = 7.1 Hz, 3 H, *anti* diastereoisomer), 2.05 (s, 3 H, *syn* diastereoisomer), 2.06 (s, 3 H, *anti* diastereoisomer), 2.49 (s, 3 H, *anti* diastereoisomer), 2.52 (s, 3 H, *syn* diastereoisomer), 2.88–2.98 (m, 2 H, *syn* diastereoisomer), 3.04 (dd, *J* = 17.6 and 5.5 Hz, 1 H, *anti* diastereoisomer), 3.14 (dd, *J* = 17.4 and 9.4 Hz, 1 H, *anti* diastereoisomer), 4.05 (q, *J* = 7.1 Hz, 2 H, *syn* diastereoisomer), 4.28 (qd, *J* = 7.2 and 3.8 Hz, 2 H, *anti* diastereoisomer), 4.49–4.66 (m, 2 H, both diastereosimers), 5.38 (d, *J* = 9.3 Hz, 1 H, *syn* diastereoisomer), 5.48 (d, *J* = 10.2 Hz, 1 H, *anti* diastereoisomer), 7.10–7.20 (m, 8 H, both diastereoisomers). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.5, 13.8, 19.6, 19.8, 30.3, 30.5, 36.3, 36.6, 45.7, 45.8, 62.9, 63.3, 90.9, 91.3, 125.5, 126.3, 126.4, 126.5, 127.7, 127.8, 131.2, 131.3, 135.4, 136.5, 137.1, 137.4, 163.2, 163.8, 204.7, 204.8 ppm. IR (film) 2984, 1745, 1717, 1559, 1359, 1161, 1114, 1020, 756 cm^{-1}. HRMS (ESI+) *m/z* calcd for $C_{15}H_{19}NNaO_5$ $[M+Na]^+$: 316.1155. Found: 316.1148.

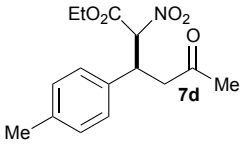
(3*S*)-Ethyl 2-nitro-5-oxo-3-(*m*-tolyl)hexanoate **7c**



7c

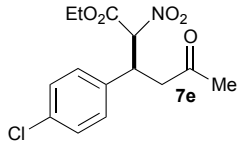
The diastereomeric mixture (*anti*:*syn*) (dr = 1:1) was isolated as a colorless oil; The ee value were 95% and 98%. *Anti* isomer: tR (major) = 16.56 min, tR (minor) = 17.84 min and *syn* isomer: tR (major) = 17.28 min, tR (minor) = 19.44 min (Chiralpak AD-H, λ = 254 nm, 10% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.31 (t, *J* = 7.1 Hz, 3 H, *anti* diastereoisomer), 2.09 (s, 6 H, both diastereoisomers), 2.34 (s, 6 H, both diastereoisomers), 2.88–3.18 (m, 4 H, both diastereoisomers), 4.09 (qd, *J* = 7.1 and 2.1 Hz, 2 H, *syn* diastereoisomer), 4.19–4.32 (m, 4 H, CH_2 ester both diastereoisomers, *anti* diastereoisomer), 5.41 (d, *J* = 8.6 Hz, 1 H, *syn* diastereoisomer), 5.47 (d, *J* = 9.7 Hz, 1 H, *anti* diastereoisomer), 7.01–7.12 (m, 6 H, both diastereoisomers), 7.19–7.24 (m, 2 H, both diastereoisomers). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.6, 13.8, 21.4, 21.5, 30.3, 30.4, 41.2, 41.5, 45.2, 45.5, 62.9, 63.2, 91.3, 91.4, 124.9, 125.2, 128.7, 128.8, 128.9, 129.0, 129,1, 136.8, 137.8, 138.6, 138.7, 163.2, 163.7, 204.8, 204.9 ppm. IR (film) 2985, 2921, 1746, 1717, 1559, 1359, 1305, 1189, 1159, 1021, 786, 703 cm^{-1}. HRMS (ESI+) *m/z* calcd for $C_{15}H_{19}NNaO_5$ $[M+Na]^+$: 316.1155. Found 316.1155.

(3*S*)-Ethyl 2-nitro-5-oxo-3-(*p*-tolyl)hexanoate **7d**[6]



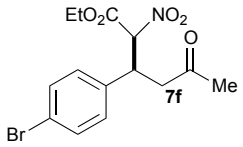
The diastereomeric mixture (*anti*:*syn*) (dr = 1.1:1) was isolated as a colorless oil; The ee value were 96% and 95%. *Anti* isomer: tR (major) = 21.08 min, tR (minor) = 25.52 min and *syn* isomer: tR (major) = 22.33 min, tR (minor) = 25.98 min (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.28 (t, *J* = 7.1 Hz, 3 H, *anti* diastereoisomer), 2.05 (s, 3 H, *syn* diastereoisomer), 2.06 (s, 3 H, *anti* diastereoisomer), 2.28 (s, 3 H, *anti* diastereoisomer), 2.29 (s, 3 H, *syn* diastereoisomer), 2.88–2.97 (m, 2 H, both diastereoisomers), 2.98–3.14 (m, 2 H, both enantiomers), 4.03–4.10 (m, 2 H, both diastereoisomers), 4,18–4,29 (m, 4 H, both diastereoisomers), 5.38 (d, *J* = 8.3 Hz, 1 H, *syn* diastereoisomer), 5.44 (d, *J* = 9.6 Hz, 1 H, *anti* diastereoisomer), 7.11 (m, 8 H, both diastereoisomers). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.6, 13.8, 21.1, 30.3, 30.4, 41.0, 41.3, 45.2, 45.5, 62.9, 63.2, 91.3, 91.5, 127.9, 128.2, 129.5, 129.6, 133.7, 134.7, 137.8, 163.1, 163.6, 204.8, 205.0 ppm.

(3*S*)-Ethyl 3-(4-cyanophenyl)-2-nitro-5-oxohexanoate **7e**[5,6]



The diastereomeric mixture (*anti*:*syn*) (dr = 1.1:1) was isolated as a colorless oil; The ee value were >99% and >99%. *Anti* isomer: tR (minor) = 46.34 min, tR (major) = 52.67 min and *syn* isomer: tR (minor) = 50.87 min, tR (major) = 76.52 min (Chiralpak IC, λ = 210 nm, 7% CH_2Cl_2/ 3% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.31 (t, *J* = 7.2 Hz, 3 H, *anti* diastereoisomer), 2.09 (s, 3 H, *syn* diastereoisomer), 2.10 (s, 3 H, *anti* diastereoisomer. 2.93–3.02 (m, 2 H, both enantiomers), 3.03–3.13 (m, 2 H, both diastereoisomers), 4.07–4.15 (m, 2 H, both diastereoisomers), 4.22–4.33 (m, 4 H, both diastereoisomers), 5.41 (d, *J* = 8.5 Hz, 1 H, *syn* diastereoisomer), 5.47 (d, *J* = 9.5 Hz, 1 H, *anti* diastereoisomer), 7.22 (d, *J* = 3.7 Hz, 2 H, *syn* diastereoisomer), 7.23 (d, *J* = 3.6 Hz, 2 H, *anti* diastereoisomer), 7.29 (d, *J* = 4.7 Hz, 2 H, *anti* diastereoisomer), 7.31 (d, *J* = 4.6 Hz, 2 H, *syn* diastereoisomer). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.6, 13.8, 30.2, 30.3, 40.6, 40.8, 45.1, 45.3, 63.1, 63.4, 90.89, 90.90, 128.5, 129.1, 129.5, 129.8, 130.2, 134.0, 134.1, 135.5, 136.30, 162.9, 163.3, 204.4, 204.6 ppm.

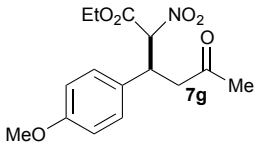
(3*S*)-Ethyl 3-(4-bromophenyl)-2-nitro-5-oxohexanoate **7f**[5]



The diastereomeric mixture (*anti*:*syn*) (dr = 1.1:1) was isolated as a white solid; The ee value were 97% and 98%. *Anti* isomer: tR (major) = 22.59 min, tR (minor) = 25.53 min and *syn* isomer: tR (major) = 28.67 min, tR (minor) = 31.09 min (UPC^2, Chiralpak IC, gradient: 1-5% MeOH/CO_2, flow rate = 1 mL/min). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.28 (t, *J* = 7.2 Hz, 3 H, *anti* diastereoisomer), 2.07 (s, 3 H, *syn* diastereoisomer), 2.08 (s, 3 H, *anti* diastereoisomer),

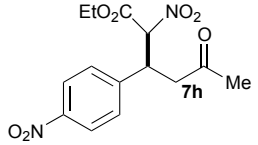
2.85–3.15 (m, 4 H, both diastereoisomers), 4.09 (qd, *J* = 7.2 and 1.1 Hz, 2 H, *syn* diastereoisomer), 4.17–4.31 (m, 4 H, CH_2 ester *anti* diastereoisomer, both diastereoisomers), 5.38 (d, *J* = 8.5 Hz, 1 H, *syn* diastereoisomer), 5.45 (d, *J* = 9.5 Hz, 1 H, *anti* diastereoisomer), 7.13 (d, *J* = 2.4 Hz, 2 H, *syn* diastereoisomer), 7.16 (d, *J* = 2.4 Hz, 2 H, *anti* diastereoisomer), 7.42 (d, *J* = 2.6 Hz, 2 H, *anti* diastereoisomer), 7.45 (d, *J* = 2.7 Hz, 2 H, *syn* diastereoisomer). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.7, 13.8, 30.3, 30.4, 40.7, 40.9, 45.0, 45.2, 63.2, 63.4, 90.8, 90.9, 122.1, 122.2, 129.9, 130.1, 132.1, 136.1, 136.8, 162.9, 163.3, 204.4, 204.5 ppm.

(3*S*)-Ethyl 3-(4-methoxyphenyl)-2-nitro-5-oxohexanoate **7g**[5]



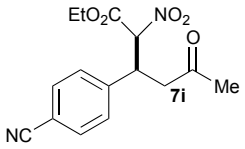
The diastereomeric mixture (*anti*:*syn*) (dr = 1:1) was isolated as a white solid; The ee value were 95% and 95%. *Anti* isomer: tR (major) = 29.82 min, tR (minor) = 38.04 min and *syn* isomer: tR (major) = 27.55 min, tR (minor) = 35.01 min (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.12 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.31 (t, *J* = 7.1 Hz, 3 H, *anti* diastereoisomer), 2.08 (s, 3 H, *syn* diastereoisomer), 2.09 (s, 3 H, *anti* diastereoisomer), 2.89–2.99 (m, 2 H, both diastereoisomers), 3.00–3.14 (m, 2 H, both diastereoisomers), 3.78 (s, 3 H, *anti* diastereoisomer), 3.791 (s, 3 H, *syn* diastereoisomer), 4.10 (qd, *J* = 7.1 and 2.6 Hz, 2 H), 4.29–4.33 (m, 3H+1H, *anti*+*syn* diastereoisomers), 5.39 (d, *J* = 8.7 Hz, 1 H, *syn* diastereoisomer), 5.44 (d, *J* = 9.5 Hz, 1 H, *anti* diastereoisomer), 6.84 (d, *J* = 2.7 Hz, 2 H, *syn* diastereoisomer), 6.96 (d, *J* = 2.7 Hz, 2 H, *anti* diastereoisomer), 7.18 (d, *J* = 3.2 Hz, 2 H, *anti* diastereoisomer), 7.20 (d, *J* = 3.3 Hz, 2 H, *syn* diastereoisomer). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.7, 13.8, 26.9, 30.3, 30.4, 40.7, 45.6, 55.2, 62.9, 63.2, 91.4, 91.5, 114.3, 128.6, 129.2, 129.5, 159.2, 159.3, 163.6, 204.9, 205.0 ppm.

(3*S*)-Ethyl 2-nitro-3-(4-nitrophenyl)-5-oxohexanoate **7h**[5, 6]



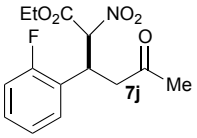
The diastereomeric mixture (*anti*:*syn*) (dr = 1.2:1) was isolated as a white solid; The ee value were 96% and 96%. *Anti* isomer: tR (major) = 29.84 min, tR (minor) = 48.37 min and *syn* isomer: tR (major) = 44.91 min, tR (minor) = 56.43 min (Chiralpak AD-H, λ = 210 nm, 10% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.15 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.31 (t, *J* = 7.1 Hz, 3 H, *anti* diastereoisomer), 2.12 (s, 3 H, minor diastereoisomer), 2.132 (s, 3 H, *anti* diastereoisomer.), 2.95–3.22 (m, 4 H, both diastereoisomers), 4.14 (qd, *J* = 7.1 and 4.3 Hz, 2 H, *syn* diastereoisomer), 4.30 (qq, *J* = 7.1 and 3.6 Hz, 2 H, *anti* diastereoisomer), 4.35–4.44 (m, 2 H, both diastereoisomers), 5.49 (d, *J* = 8.2 Hz, 1 H, *syn* diastereoisomer), 5.55 (d, *J* = 9.4 Hz, 1 H, *anti* diastereoisomer), 7.49 (d, *J* = 3.4 Hz, 2 H, *syn* diastereoisomer), 7.51 (d, *J* = 3.4 Hz, 2 H, *anti* diastereoisomer), 8.18 (d, *J* = 3.1 Hz, 2 H, major diastereoisomer), 8.20 (d, *J* = 3.2 Hz, 2 H, *syn* diastereoisomer). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.7, 13.8, 30.2, 30.3, 40.8, 41.0, 44.8, 45.0, 63.4, 63.6, 90.3, 90.4, 123.9, 124.0, 124.1, 129.4, 129.5, 129.6, 144.7, 145.2, 147.6, 162.6, 163.0, 203.9, 204.0 ppm.

(3*S*)-Ethyl 3-(4-cyanophenyl)-2-nitro-5-oxohexanoate **7i**



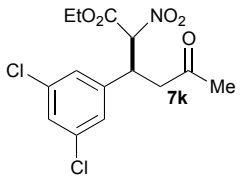
The diastereomeric mixture (*anti*:*syn*) (dr = 1.1:1) was isolated as a colorless oil. The ee value were 93% and 98%. *Anti* isomer: tR (major) = 13.24 min, tR (minor) = 19.56 min and *syn* isomer: tR (major) = 17.67 min, tR (minor) = 18.23 min (Chiralpak AD-H, λ = 210 nm, 20% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.30 (t, *J* = 7.2 Hz, 3 H, *anti* diastereoisomer), 2.11 (s, 3 H, *syn* diastereoisomer), 2.12 (s, 3 H, *anti* diastereoisomer), 2.91–3.20 (m, 4 H, both diastereoisomers), 4.12 (dtt, *J* = 10.7, 7.1 and 3.7 Hz, 2 H, *syn* diastereoisomer), 4.24–4.36 (m, 4 H, CH_2 ester *anti* diastereoisomer, both diastereoisomers), 5.45 (d, *J* = 8.3 Hz, 1 H, *syn* diastereoisomer), 5.52 (d, *J* = 9.4 Hz, 1 H, *anti* diastereoisomer), 7.41 (d, *J* = 3.3 Hz, 2 H, *syn* diastereoisomer), 7.43 (d, *J* = 3.3 Hz, 2 H, *anti* diastereoisomer), 7.61 (d, *J* = 3.3 Hz, 2 H, *anti* diastereoisomer), 7.64 (d, *J* = 3.3 Hz, 2 H, *syn* diastereoisomer). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.6, 13.8, 30.1, 30.2, 41.0, 44.7, 45.0, 63.3, 63.6, 90.3, 112.1, 118.2, 129.2, 129.4, 132.6, 142.6, 143.2, 162.7, 163.1, 204.0, 204.1 ppm. IR (film) 2986, 2230, 1746, 1716, 1559, 1360, 1162, 1017, 842, 565 cm^{-1}. HRMS (ESI+) *m/z* calcd for $C_{15}H_{15}N_2O_5$ $[M+H]^+$: 303.0986. Found: 303.0997.

(3*S*)-Ethyl 3-(2-fluorophenyl)-2-nitro-5-oxohexanoate **7j**



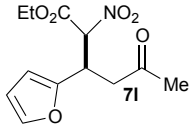
The diastereomeric mixture (*anti*:*syn*) (dr = 1:1.1) was isolated as a colorless oil; The ee value were 97% and 97%. *Anti* isomer: tR (minor) = 18.53 min, tR (major) = 20.16 min and *syn* isomer: tR (minor) = 21.66 min, tR (major) = 26.92 min (Chiralpak AS-H, λ = 210 nm, 20% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.29 (t, *J* = 7.1 Hz, 3 H, *anti* diastereoisomer), 2.08 (s, 3 H, *syn* diastereoisomer), 2.09 (s, 3 H, *anti* diastereoisomer), 2.87–3.27 (m, 4 H, both diastereoisomers), 4.06 (qd, *J* = 7.2 and 1.1 Hz, 2 H, *syn* diastereoisomer), 4.26 (qd, *J* = 7.1 and 2.8 Hz, 2 H, *anti* diastereoisomer), 4.40–4.52 (m, 2 H, both diastereoisomers), 5.55 (d, *J* = 9.4 Hz, 1 H, *syn* diastereoisomer), 5.59 (d, *J* = 10.4 Hz, 1 H, *anti* diastereoisomer), 6.99–7.15 (m, 4 H, both diastereoisomers), 7.21–7.35 (m, 4 H, both diastereoisomers). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.6, 13.8, 30.1, 30.2, 37.1, 37.2, 43.9, 44.0, 44.1, 63.0, 63.4, 89.4, 89.5, 115.8, 116.0, 116.1, 116.2, 124.5, 124.6, 124.7, 129.8, 129.9, 130.0, 130.1, 131.0, 131.1, 131.2, 163.0, 163.5, 204.3, 204.5 ppm. IR (film) 2986, 2926, 1747, 1718, 1560, 1493, 1360, 1233, 1192, 1162, 1197, 1021, 758, cm^{-1}. HRMS (ESI+) *m/z* calcd for $C_{14}H_{16}FNNaO_5$ $[M+Na]^+$: 320.0905. Found: 320.0919.

(3*S*)-Ethyl 3-(3,5-dichlorophenyl)-2-nitro-5-oxohexanoate **7k**



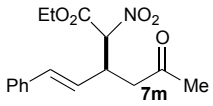
The diastereomeric mixture (*anti*:*syn*) (dr = 1:1.2) was isolated as a colorless oil; The ee value were 96% and 97%. *Anti* isomer: tR (minor) = 15.13 min, tR (major) = 16.38 min and *syn* isomer: tR (major) = 17.93 min, tR (minor) = 18.78 min (Chiralpak IA, λ = 240 nm, 5% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.01 = (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.33 (t, *J* = 7.2 Hz, 3 H, minor diastereoisomer), 2.13 (s, 3 H, *syn* diastereoisomer), 2.15 (s, 3 H, *anti* diastereoisomer), 2.93 (dd, *J* = 17.5 and 4.1 Hz, 1 H, *syn* diastereoisomer), 3.08 (dd, *J* = 17.9 and 6.2 Hz, 1 H, *anti* diastereoisomer), 3.33 (dd, *J* = 17.9 and 6.3 Hz, 1 H, *anti* diastereoisomer), 3.51 (dd, *J* = 17.5 and 9.1 Hz, 1 H, *syn* diastereoisomer), 4.01 (qd, *J* = 7.1 and 2.0 Hz, 2 H, *syn* diastereoisomer), 4.29 (qq, *J* = 7.0 and 3.6 Hz, 2 H, *anti* diastereoisomer), 5.22–5.49 (m, 2 H, both diastereoisomers), 5.97 (d, *J* = 11.4 Hz, 1 H, *syn* diastereoisomer), 6.13 (d, *J* = 11.6 Hz, 1 H, *anti* diastereoisomer), 7.20–7.41 (m, 6 H, both diastereoisomers). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.4, 13.8, 29.7, 29.9, 36.7, 37.4, 43.4, 44.0, 63.0, 63.6, 88.0, 88.2, 129.2, 129.5, 129.7, 129.8, 130.0, 132.6, 133.3, 134.2, 162.6, 163.5, 203.8, 203.9 ppm. IR (film) 2985, 2921, 1748, 1721, 1561, 1434, 1358, 1303, 1163, 1020, 768 cm^{-1}. HRMS (ESI+) *m/z* calcd for $C_{14}H_{15}Cl_2NNaO_5$ $[M+Na]^+$: 370.0219. Found: 370.0212.

(3*R*)-Ethyl 3-(furan-2-yl)-2-nitro-5-oxohexanoate **7l**



The diastereomeric mixture (*anti*:*syn*) (dr = 1:1) was isolated as a light brown oil; The ee value were 98% and 98%. *Syn* isomer: tR (major) = 19.65 min, tR (minor) = 21.20 min and *anti* isomer: tR (major) = 18.74 min, tR (minor) = 20.39 min (Chiralpak AD-H, λ = 210 nm, 10% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.28 (t, *J* = 7.2 Hz, 3 H, *anti* diastereoisomer), 2.14 (s, 3 H, *anti* diastereoisomer), 2.18 (s, 3 H, *syn* diastereoisomer), 2.95 (dd, *J* = 17.8 and 4.4 Hz, 1 H, *syn* diastereoisomer), 2.99–3.08 (m, 2 H, both diastereoisomers), 3.13 (dd, *J* = 17.9 and 8.7 Hz, 1 H, *anti* diastereoisomer), 4.19 (qd, *J* = 7.1 and 3.3 Hz, 2 H, *anti* diastereoisomer), 4.26 (d, *J* = 7.2 Hz, 2 H, *syn* diastereoisomer), 4.35–4.44 (m, 2 H, both diastereoisomers), 5.49 (d, *J* = 6.9 Hz, 1 H, *syn* diastereoisomer), 5.50 (d, *J* = 7.9, 1 H, *anti* diastereoisomer), 6.18–6.20 (m, 2 H, both diastereoisomers), 6.25–6.31 (m, 2 H, both diastereoisomers), 7.29–7.35 (m, 2 H, both diastereoisomers). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.8, 13.9, 30.1, 30.2, 35.1, 35.2, 42.7, 42.8, 63.2, 63.3, 88.8, 88.9, 108.4, 108.5, 110.6, 110.7, 142.4, 142.5, 150.1, 150.4, 163.1, 163.2, 204.4, 204.5 ppm. IR (film) 2986, 1714, 1718, 1560, 1362, 1191, 1163, 1014, 885, 813, 740 cm^{-1}. HRMS (ESI+) *m/z* calcd for $C_{12}H_{15}NNaO_6$ $[M+Na]^+$: 292.0797. Found: 292.0788.

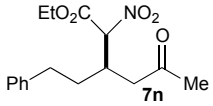
(3*S*)-Ethyl 2-nitro-5-oxo-3-((*E*)-styryl)hexanoate **7m**



7m

The diastereomeric mixture (*anti*:*syn*) (dr = 1.3:1) was isolated as a white solid; The ee value were 95% and 95%. *Anti* isomer: tR (major) = 4.17 min, tR (minor) = 4.92 min and *syn* isomer: tR (minor) = 4.67 min, tR (major) = 5.45 min (UPC^2, Chiralpak IC, 10% *i*PrOH/CO_2, flow rate = 1 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.30 (t, *J* = 7. Hz, 3 H, *anti* diastereoisomer), 2.18 (s, 3 H, *syn* diastereoisomer), 2.19 (s, 3 H, *anti* diastereoisomer), 2.83–2.91 (m, 4 H, both diastereoisomers), 3.65–3.84 (m, 2 H, both diastereoisomers), 4.21–4.33 (m, 4 H, both diastereoisomers), 5.45 (d, *J* = 7.0 Hz, 1 H, *syn* diastereoisomer), 5.53 (d, *J* = 6.7 Hz, 1 H, *anti* diastereoisomer), 6.13 (dd, *J* = 15.8 and 9.0 Hz, 1 H, *syn* diastereoisomer), 6.23 (dd, *J* = 15.8 and 9.2 Hz, 1 H, *anti* diastereoisomer), 6.53–6.63 (m, 2 H, both diastereoisomers), 7.22–7.40 (m, 10 H, both diastereoisomers). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.9, 14.0, 30.4, 30.5, 39.5, 44.3, 63.0, 63.1, 89.6, 89.9, 124.4, 126.5, 126.6, 128.2, 128.6, 128.7, 134.8, 134.9, 136.0, 136.1, 163.4, 163.5, 205.3, 205.4 ppm. IR (film) 2978, 2913, 1747, 1710, 1554, 1358, 1239, 1190, 1164, 1019, 972, 744, 692 cm^{-1}. HRMS (ESI+) *m/z* calcd for $C_{16}H_{19}NNaO_5$ [M+Na]$^+$: 328.1155. Found: 328.1150.

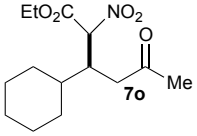
(3*R*)-Ethyl 2-nitro-5-oxo-3-phenethylhexanoate **7n**



7n

The diastereomeric mixture (*anti*:*syn*) (dr = 1:1) was isolated as a colorless oil; The ee value were 98% and 99%. Major isomer: tR (major) = 24.64 min, tR (minor) = 28.19 min and minor isomer: tR (major) = 32.05 min, tR (minor) = 38.27 min (UPC^2, Chiralpak IC, 2% acetonitrile/CO_2, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.13 Hz, 3 H), 1.29 (t, *J* = 7.13 Hz, 3 H), 1.69–1.79 (m, 3 H, both diastereoisomers), 1.81–1.90 (m, 1 H), 2.14 (s, 3 H), 2,15 (s, 3 H), 2.58–2.76 (m, 7 H, both diastereoisomers), 2.85 (dd, *J* = 18.6 and 4.8 Hz, 1 H), 2.93–3.02 (m, 2 H, both diastereoisomers), 4.21–4.31 (m, 4 H, both diastereoisomers), 5.38 (d, *J* = 5.35 Hz, 1 H), 5.39 (d, *J* = 4.88 Hz, 1 H), 7.13–7.17, (m, 4 H, both diastereoisomers), 7.18–7.22 (m, 2 H, both diastereoisomers), 7.2–7.31 (m, 4 H, both diastereoisomers). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.9, 30.3, 32.1, 32.6, 33.3, 33.5, 34.6, 34.7, 43.3, 43.6, 62.9, 63.1, 89.3, 89.5, 126.3, 128.3, 128.6, 140.5, 140.6, 163.8, 164.0, 206.0, 206.2 ppm. IR (film) 2867,1745, 1715, 1556, 1363, 1192, 1021, 747, 670 cm^{-1}. HRMS (ESI+) *m/z* calcd for $C_{16}H_{21}NNaO_5$ [M+Na]$^+$: 330.1312. Found: 330.1303.

(3*S*)-Ethyl 3-cyclohexyl-2-nitro-5-oxohexanoate **7o**

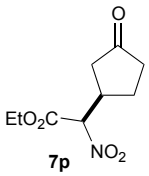


7o

The diastereomeric mixture (*anti*:*syn*) (dr = 1:1.1) was isolated as a colorless oil The ee value were 98% and 98%. *Syn* isomer: tR (minor) = 16.21 min, tR (major) = 17.96 min and *anti* isomer: tR (major) = 14.72 min, tR (minor) = 19.81 min (Chiralpak IC, λ = 210 nm, 20% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89–1.4 (m, 14 H, both diastereoisomers), 1.28 (t, *J* = 7.1 Hz, 3 H, *anti* diastereoisomer), 1.29 (t, *J* = 7.2 Hz, 3 H, *syn* diastereoisomer), 1.48–1.78 (m, 12 H, both

diastereoisomers), 2.15 (s, 3 H, *syn* diastereoisomer), 2.17 (s, 3 H, *anti* diastereoisomer), 2.59 (dd, *J* = 18.6 and 5.0 Hz, 1 H, *syn* diastereoisomer), 2.65–2.76 (m, 2 H, both diastereoisomers), 2.79–2.89 (m, 2 H, both diastereoisomers), 3.01–3.09 (m, 1 H, *syn* diastereoisomer), 4.18–4.28 (m, 4 H, both diastereoisomers), 5.22 (d, *J* = 7.5 Hz, 1 H, *syn* diastereoisomer), 5.44 (d, *J* = 4.4 Hz, 1 H, *anti* diastereoisomer). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.8, 13.9, 26.0, 26.1, 26.2, 26.3, 26.4, 28.8, 29.9, 30.0, 30.4, 30.7, 31.1, 39.2, 39.4, 39.5, 39.7, 40.1, 42.6, 63.0, 63.1, 88.7, 88.9 ppm. IR (film) 2931, 1747, 1718, 1557, 1364, 1314, 1282, 1207, 1116, 854 cm^{-1}. HRMS (ESI+) *m/z* calcd for $C_{14}H_{23}NNaO_5$ $[M+Na]^+$: 308.1468. Found: 308.1466.

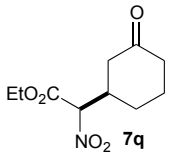
(*S*)-Ethyl 2-nitro-2-((*R*)-3-oxocyclopentyl)acetate **7p**[7]



7p

The diastereomeric mixture (*anti*:*syn*) (dr = 1:1) was isolated as a colorless oil; The ee value were 66% and 65%. *Syn* isomer: tR (minor) = 28.56 min, tR (major) = 44.27 min and *anti* isomer: tR (major) = 29.46 min, tR (minor) = 35.25 min (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.33 (t, *J* = 7.2 Hz, 3 H, *anti* diastereoisomer), 1.72–1.85 (m, 2 H, both diastereoisomers), 2.04–2.24 (m, 2 H, both diastereoisomers), 2.25–2.36 (m, 2 H, both diastereoisomers), 2.37–2.47 (m, 2 H**,** both diastereoisomers), 2.50–2.63 (m, 2 H**,** both diastereoisomers), 4.27–4.63 (m, 4 H, both diastereomers), 5.06 (d, *J* = 9.4 Hz, 1 H, *syn* diastereoisomer), 5.08 (d, *J* = 9.0 Hz, 1 H, *anti* diastereoisomer). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 13.9, 14.0, 25.8, 26.5, 37.4, 37.5, 37.6, 38.0, 41.2, 41.6, 63.3, 63.4, 90.9, 91.1, 163.2, 214.5, 214.7 ppm. IR (film) 2954, 2921, 1744, 1561, 1461, 1375, 1263, 1161, 1020 cm^{-1}.

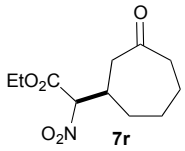
(*S*)-Ethyl 2-nitro-2-((*R*)-3-oxocyclohexyl)acetate **7q**[5]



7q

The diastereomeric mixture (*anti*:*syn*) (dr = 1:1) was isolated as a colorless oil; The ee value were 95% and 93%. *Syn* isomer: tR (minor) = 16.84 min, tR (major) = 19.49 min and *anti* isomer: tR (minor) = 17.74 min, tR (major) = 26.38 min (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.32 (t, *J* = 7.1 Hz, 3 H, *anti* diastereoisomer), 1.50–1.79. (m, 4 H, both diastereoisomers), 1.90–2.07 (m, 2 H, both diastereoisomers), 2.08–2.18 (m, 2 H, both diastereoisomers), 2.20–2.34 (m, 2 H**,** both diastereoisomers), 2.36–2.57 (m, 6 H**,** both diastereoisomers), 2.70–2.87 (m, 2 H, both diastereoisomers), 4.25–4.35 (m, 2 H, both diastereomers), 5.02 (d, *J* = 7.8 Hz, 1 H, *syn* diastereoisomer), 5.06 (d, *J* = 6.9 Hz, 1 H, *anti* diastereoisomer). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.9, 14.0, 24.0, 24.2, 27.2, 27.3 39.0, 39.1, 40.8, 43.1, 43.2, 63.2, 63.3, 91.1, 91.2, 162.9, 163.0, 207.6, 207.7 ppm.

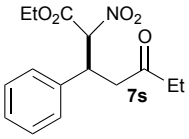
(*S*)-Ethyl 2-nitro-2-((*R*)-3-oxocycloheptyl)acetate **7r**[5]



7r

The diastereomeric mixture (*anti*:*syn*) (dr = 1:1.1) was isolated as a colorless oil; The ee value were 97% and 96%. *anti* isomer: tR (major) = 26.08 min, tR (minor) = 32.09 min and *syn* isomer: tR (minor) = 42.24 min, tR (major) = 46.40 min (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 7.2 Hz, 3 H, *syn* diastereoisomer), 1.31 (t, *J* = 7.2 Hz, 3 H, *anti* diastereoisomer), 1.35–1.65 (m, 6 H, both diastereoisomers), 1.83–2.06 (m, 6 H, both diastereoisomers), 2.45–2.60 (m, 6 H, both diastereoisomers), 2.65–2.85 (m, 4 H, both diastereoisomers), 4.26–4.33 (m, 4 H, both diastereomers), 5.01 (d, *J* = 7.5 Hz, 1 H, *syn* diastereoisomer), 5.05 (d, *J* = 6.1 Hz, 1 H, *anti* diastereoisomer). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 14.0, 24.1, 24.26, 28.2, 28.3, 32.4, 36.9, 37.0, 43.5, 43.6, 45.2, 45.3, 63.3, 91.8, 163.2, 163.3, 210.8, 210.9 ppm.

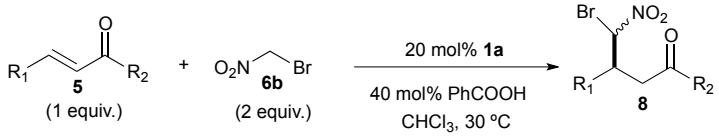
(3*S*)-Ethyl 2-nitro-5-oxo-3-phenylheptanoate **7s**[6]



7s

The diastereomeric mixture (dr = 1:1) was isolated as a colorless oil; The ee value were 97% and 96%. *Anti* isomer: tR (major) = 26.03 min, tR (minor) = 32.09 min and *syn* isomer: tR (minor) = 42.23 min, tR (major) = 46.40 min (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.98 (q, *J* = 7.4 Hz, 4 H, both diastereoisomers), 1.09 (t, *J* = 7.1 Hz, 3 H, *syn* diastereoisomer), 1.31 (t, *J* = 7.1 Hz, 3 H, *anti* diastereoisomer), 2.23–2.48 (m, 4 H, both diastereoisomers), 2.90–2.99 (m, 2 H, both diastereomers), 3.04 (dd, *J* = 17.4 and 5.8 Hz, 1 H, *syn* diastereoisomer), 3.11 (dd, *J* = 17.2 and 9.1 Hz, 1 H, *anti* diastereoisomer), 4.08 (dq, *J* = 7.1 and 4.1 Hz, 2 H, *syn* diastereoisomer), 4.21–4.35 (m, 3+1 H, both diastereomers), 5.45 (d, *J* = 8.8 Hz, 1 H, *syn* diastereoisomer), 5.52 (d, *J* = 9.7 Hz, 1 H, *anti* diastereoisomer), 7.24–7.36 (m, 10 H, both diastereoisomers). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 7.5, 7.6, 13.6, 13.8, 36.4, 36.5, 41.4, 41.7, 44.0, 44.3, 63.0, 63.3, 91.3, 91.4, 128.0, 128.1, 128.2, 128.4, 128.9, 129.0, 137.0, 137.9, 163.2, 163.6, 207.5, 207.7 ppm.

Procedure for the Michael addition of bromonitromethane to enones catalyzed by resin 1a.



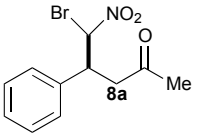
Entry	Product	R_1	R_2	Time (h)	Conversion (%)[a]	Yield (%)[a]	d.r.[a]	ee (%)[b]
1	**8a**	Ph	Me	15	94	89	1.2:1	97/96
2	**8b**	2-furyl	Me	36	69	46	1.1:1	94/93
3	**8c**	Ph	Ph	36	81	51	1.4:1	97/96
4	**8d**	4-OMe-C_6H_4	Me	15	99	92	1.4:1	93/91
5	**8e**	4-Br-C_6H_4	Me	15	99	75	1.3:1	96/96

[a]Conversion was determined by ^{1}H NMR spectroscopy. [b]Enantiomeric excess was determined by chiral HPLC analysis.

Polymer-supported quinine derivative **1a** (20 mol%) was added to a vial with a mixture of α,β-unsaturated ketone (0.1 mmol), bromo nitromethane, **6b** (0.2 mmol) and benzoic acid (40 mo%) in $CHCl_3$ (0.1 mL) and the mixture was stirred at 30 ºC. After the indicated time shown in table above, the resin was filtered off, washed with $CHCl_3$ (3 x 1 mL) and dried under vacuum. The combined liquid phases were concentrated under reduced pressure. Purification by column chromatography (eluting with cyclohexane/AcOEt) gave the corresponding Michael products **8**.

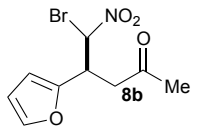
Description of compounds 8a–8e.[8]

(4*S*)-5-Bromo-5-nitro-4-phenylpentan-2-one **8a**



The diastereomeric mixture (dr = 1.2:1) was isolated as a white solid; The ee value were 97% and 96%. Major isomer: tR (minor) = 19.03 min, tR (major) = 1975 min and minor isomer: tR (major) = 21.19 min, tR (minor) = 23.73 min (Chiralopak AS-H, λ = 220 nm, 25% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.13 (s, 3 H, major diastereoisomer), 2.14 (s, 3 H, minor diastereoisomer), 3.00–3.14 (m, 3 H, both diastereoisomers), 3.21 (dd, J = 17.6 and 4.5 Hz, 1 H, major diastereoisomer), 4.09–4.22 (m, 4 H, both diastereoisomers), 6.26 (d, *J* = 8.6 Hz, 1 H, major diastereoisomer), 6.35 (d, *J* = 6.7 Hz, 1 H, minor diastereoisomer), 7.20–7.39 (m, 10 H, both diastereoisomers).^{13}C NMR (75 MHz, $CDCl_3$): δ = 30.4, 30.6, 45.2, 45.6, 46.1, 46.5, 83.7, 84.8, 128.3, 128.4, 128.7, 129.0, 129.2, 136.0, 136.2, 204.3, 204.4 ppm.

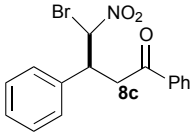
(4*S*)-5-Bromo-4-(furan-2-yl)-5-nitropentan-2-one **8b**



The diastereomeric mixture (dr = 1.1:1) was isolated as a yellow oil; The ee value were 94% and 93%. Major isomer: tR (major) = 17.06 min, tR (minor) = 14.34 min and minor isomer, tR (major) = 18.59 min, tR (minor) = 20.65 min (Daicel Chiralpak AS-H, 10% *i*PrOH/hexane, flow rate 1.0 mL/min, λ = 220 nm). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.18 (s, 6 H, both diastereoisomers), 3.03 (dd, *J* = 18.0 and 5.5 Hz, 1 H,

major diastereoisomer), 3.07–3.14 (m, 3 H, both diastereoisomers), 4.29 (td, *J* = 7.5 and 5.5 Hz, 1 H, major diastereoisomer), 4.33–4.37 (m, 1 H, minor diastereoisomer), 6.22–6.24 (m, 1 H, both diastereoisomers), 6.27 (d, *J* = 7.5 Hz, 1 H, major diastereoisomer), 6.30 (dd, *J* = 3.5 and 2.0 Hz, 1 H, major diastereoisomer), 6.32 (dd, *J* = 3.0 and 1.5 Hz, 1 H, minor diastereoisomer), 6.35 (d, *J* = 6.0 Hz, 1 H, minor diastereoisomer), 7.34 (dd, *J* = 2.0 and 1.0 Hz, 1 H, major diastereoisomer), 7.35 (dd, *J* = 1.5 and 1.0 Hz, 1 H, minor diastereoisomer). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 30.2, 30.3, 40.3, 40.4, 42.9, 43.0, 81.7, 82.5, 109.3, 109.5, 110.6, 110.8, 142.8, 142.9, 148.7, 149.0, 203.9, 204.0 ppm

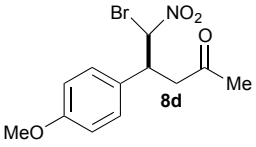
(3*S*)-4-bromo-4-nitro-1,3-diphenylbutan-1-one **8c**



8c

The diastereomeric mixture (dr = 1.4:1) was isolated as a yellow oil; The ee value were 97% and 96%. Major isomer, tR (major) = 14.76 min, tR (minor) = 19.56 min and minor isomer, tR (major) = 11.91 min, tR (minor) = 16.78 min (Daicel Chiralpak AD-H, 10 % *i*PrOH/hexane, flow rate 1.0 mL/min, λ = 208 nm). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.65–3.77 (m, 4 H, both diastereoisomers), 4.33–4.43 (m, 4 H, both diastereoisomers), 6.38 (d, *J* = 8.4 Hz, 1 H, major diastereoisomer), 6.49 (d, *J* = 6.4 Hz, 1 H, minor diastereoisomer), 7.21–7.35 (m, 10 H, both diastereoisomers), 7.44–7.49 (m, 4 H, both diastereoisomers), 7.55–7.60 (m, 2 H, both diastereoisomers), 7.89–7.92 (m, 4 H, both diastereoisomers). ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.5, 40.9, 46.2, 46.7, 84.1, 85.1, 128.0, 128.1, 128.3, 128.5, 128.6, 128.7, 128.8, 128.9, 129.1, 133.6, 133.7, 136.1, 136.2, 136.3, 136.4, 195.9, 196.0 ppm.

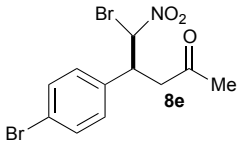
(4*S*)-5-Bromo-4-(4-methoxyphenyl)-5-nitropentan-2-one **8d**



8d

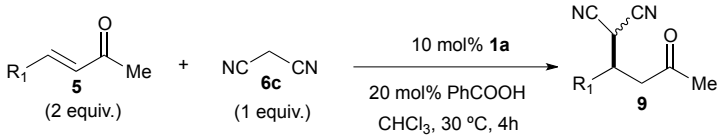
The diastereomeric mixture (dr = 1.4:1) was isolated as a yellow oil; The ee value were 93% and 91%. Major isomer, tR (major) = 27.76 min, tR (minor) = 31.08 min and minor isomer, tR (major) = 23.81 min, tR (minor) = 43.57 min (Daicel Chiralpak AS-H, 10% *i*PrOH/hexane, flow rate 1.0 mL/min, λ = 220 nm). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.10 (s, 3 H, major diastereoisomer), 2.12 (s, 3 H, minor diastereoisomer), 2.98–3.07 (m, 3 H, both diastereoisomers), 3.15 (dd, *J* = 17.5 and 4.0 Hz, 1 H, major diastereoisomer), 3.77 (s, 3 H, major diastereoisomer), 3.78 (s, 3 H, minor diastereoisomer), 4.04–4.13 (m, 4 H, both diastereoisomers), 6.19 (d, *J* = 8.5 Hz, 1 H, major diastereoisomer), 6.31 (d, *J* = 6.5 Hz, 1 H, minor diastereoisomer), 6.83 (d, *J* = 9.0 Hz, 2 H, major diastereoisomer), 6.85 (d, *J* = 9.0 Hz, 2 H, minor diastereoisomer), 7.13 (d, *J* = 9.0 Hz, 2 H, minor diastereoisomer), 7.15 (d, *J* = 9.0 Hz, 2 H, major diastereoisomer). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.4, 30.5, 45.2, 45.3, 45.6, 45.8, 55.2, 55.3, 83.7, 85.2, 114.3, 114.5, 127.6, 127.7, 129.3, 129.4, 159.6, 159.7, 204.5, 204.6 ppm.

(4*S*)-5-Bromo-4-(4-bromophenyl)-5-nitropentan-2-one **8e**



The diastereomeric mixture (dr = 1.3:1) was isolated as a colorless oil; The ee value were 96% and 96%. Major isomer, tR (major) = 12.36 min, tR (minor) = 10.68 min and minor isomer, tR (major) = 13.25 min, tR (minor) = 11.64 min (Daicel Chiralpak IA, 10% *i*PrOH/hexane, flow rate 0.8 mL/min, λ = 254 nm). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.12 (s, 3 H, major diastereoisomer), 2.13 (s, 3 H, minor diastereoisomer), 2.99–3.07 (m, 3 H, both diastereoisomers), 3.17 (dd, *J* = 18.0 and 4.5 Hz, 1 H, major diastereoisomer), 4.09 (td, *J* = 8.5 and 4.5 Hz, 1 H, major diastereoisomer), 4.12 (q, *J* = 7.0 Hz, 1 H, minor diastereoisomer), 6.22 (d, *J* = 8.5 Hz, 1 H, major diastereoisomer), 6.32 (d, *J* = 7.0 Hz, 1 H, minor diastereoisomer), 7.10 (d, *J* = 8.5 Hz, 2 H, minor diastereoisomer), 7.13 (d, *J* = 8.5 Hz, 2 H, major diastereoisomer), 7.45 (d, *J* = 8.5 Hz, 2 H, major diastereoisomer), 7.47 (d, *J* = 8.5 Hz, 2 H, minor diastereoisomer). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3, 30.4, 45.1, 45.3, 45.4, 45.9, 83.1, 84.4, 122.8, 122.9, 129.9, 130.1, 132.1, 132.3, 134.9, 135.1, 204.0, 204.1 ppm.

Procedure for the Michael addition of malonitrile to enones catalyzed by resin 1a.



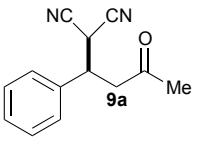
Entry	Product	R_1	Conversion (%)[a]	Yield (%)	ee (%)[b]
1	**9a**	Ph	99	66	92
2	**9b**	4-Me-C_6H_4	99	70	91
3	**9c**	4-Cl-C_6H_4	99	64	99

[a]Conversion was determined by ^{1}H NMR spectroscopy.
[b]Enantiomeric excess was determined by chiral HPLC analysis.

Supported quinine derivative **1a** (11.2 mg, 0.01 mmol, 10 mol%) was added to a vial with a mixture of α,β-unsaturated ketone (0.2 mmol, 2 equiv.), malonitrile **6c** (6.6 mg, 0.1 mmol, 1 equiv.) and benzoic acid (2.4 mg, 0.02 mmol, 20 mol%) in $CHCl_3$ (0.1 mL) and the mixture was stirred at 30 ºC in a sand bath for 4 h. Then, the resin was filtered off, washed with $CHCl_3$ (3 x 1 mL) and dried under vacuum. The combined liquid phases were concentrated under reduced pressure. The reaction crude was directly purified through column chromatography eluting with cyclohexane and (1- 20) % AcOEt.

Description of compounds 9a–9c[9]

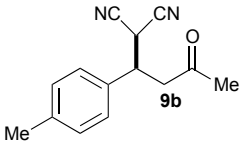
(*R*)-2-(3-Oxo-1-phenylbutyl)malononitrile **9a**



Product isolated as colorless oil. The ee value was 92%; tR (minor) = 15.51 min, tR (major) = 18.22 min (Chiralpak AS-H, λ = 210 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.24 (s, 3H), 3.12 (dd, *J* = 18.5 and 5.4 Hz, 1 H), 3.20 (dd, *J* = 18.6 and 8.6 Hz, 1 H), 3.77 (dt, *J* = 8.6

and 5.3 Hz, 1 H), 4.51 (d, *J* = 5.3 Hz, 1 H), 7.25–7.56 (m, 5 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 28.6, 30.4, 40.9, 44.8, 111.6, 111.7, 127.9, 129.2, 129.3, 136.2, 205.4 ppm.

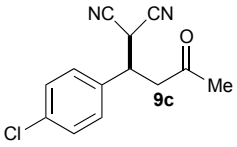
(*R*)-2-(3-Oxo-1-(*p*-tolyl)butyl)malononitrile **9b**



9b

Product isolated as colorless oil. The ee value was 91%; tR (major) = 11.66 min, tR (minor) = 15.22 min (Chiralcel OD-H, λ = 210 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (s, 3 H), 2.38 (s, 3 H), 3.09 (dd, *J* = 18.6 and 5.4 Hz, 1 H), 3.20 (dd, *J* = 18.6 and 8.6 Hz, 1 H), 3.73 (dt, *J* = 8.5 and 5.4 Hz, 1 H), 4.48 (d, *J* = 5.3 Hz, 1 H), 7.17–7.35 (m, 4 H). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 21.1, 28.7, 30.4, 40.6, 44.9, 111.7, 111.8, 127.7, 130.0, 130.2, 133.2, 139.1, 205.5 ppm.

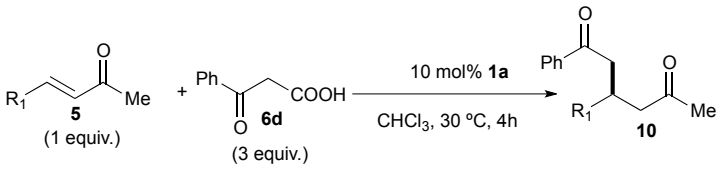
(*R*)-2-(1-(4-Chlorophenyl)-3-oxobutyl)malononitrile **9c**



9c

Product isolated as colorless oil yellow oil. The ee value was 99%; tR (major) = 15.09 min, tR (major) = 16.02 min (Chiralpak AS-H, λ = 210 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.22 (s, 3 H), 3.05 (dd, *J* = 18.7 and 5.3 Hz, 1 H), 3.17 (dd, *J* = 18.7 and 8.6 Hz, 1 H), 3.72 (dt, *J* = 8.6 and 5.3 Hz, 1 H), 4.47 (d, *J* = 5.3 Hz, 1 H), 7.30 (d, *J* = 8.5 Hz, 2 H), 7.39 (d, *J* = 8.5 Hz, 2 H), ^{13}C NMR (101 MHz, $CDCl_3$): δ = 28.5, 30.3, 40.3, 44.7, 111.4, 111.6, 129.3, 129.6, 134.7, 135.3, 205.1 ppm.

Procedure for the Michael addition of Phenylacetylenacetic acid to enones catalyzed by resin 1a.



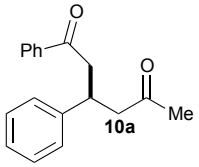
Entry	Product	R_1	Conversion (%)[a]	Yield (%)	ee (%)[b]
1	**10a**	Ph	80	80	75
2	**10b**	4-OMe-C_6H_4	68	64	69
3	**10c**	4-Cl-C_6H_4	92	86	93

[a]Conversion was determined by ^{1}H NMR spectroscopy.
[b]Enantiomeric excess was determined by chiral HPLC analysis.

Supported quinine derivative **1a** (11.2 mg, 0.01 mmol, 10 mol%) was added to a vial with a mixture of α,β-unsaturated ketone (0.1 mmol, 1 equiv.), 3-oxo-3-phenylpropanoic acid **6d** (0.3 mmol, 3 equiv.) in $CHCl_3$ (0.1 mL) and the mixture was stirred at 30 ºC in a sand bath for 4 h. Then, the resin was filtered off, washed with $CHCl_3$ (3 x 1 mL) and dried under vacuum. The combined liquid phases were concentrated under reduced pressure. The reaction crude was directly purified through column chromatography eluting with cyclohexanes and (1- 20) % AcOEt.

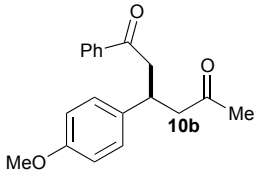
Description of compounds 10a–10c[10]

(*R*)-1,3-Diphenylhexane-1,5-dione **10a**



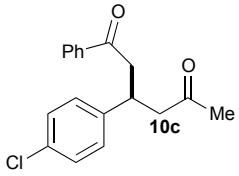
Product isolated as a white solid. ; The ee value was 75%; tR (major) = 17.60 min, tR (minor) = 27.18 min (Chiralpak IC, λ = 254 nm, 20% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.11 (s, 3 H), 2.86 (dd, *J* = 16.5 and 7.5 Hz, 1 H), 2.96 (dd, *J* = 16.6 and 6.7 Hz, 1 H), 3.31 (dd, *J* = 16.6 and 6.7 Hz, 1 H), 3.37 (dd, *J* = 16.5 and 7.5 Hz, 1 H), 3.91 (p, *J* = 7.1 Hz, 1 H), 7.19–7.24 (m, 1 H), 7.26–7.34 (m, 4 H), 7.43–7.58 (m, 2 H), 7.54–7.59 (m, 1 H), 7.91–7.96 (m, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 30.3, 36.8, 44.9, 49.7, 126.7, 127.4, 128.1, 128.6, 128.7, 133.1, 136.9, 143.7, 198.5, 207.2 ppm.

(*R*)-3-(4-Methoxyphenyl)-1-phenylhexane-1,5-dione **10b**



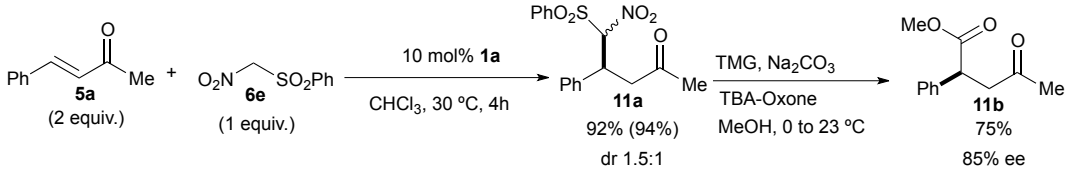
Product isolated as a pale yellow oil; The ee value was 69%; tR (minor) = 9.22 min, tR (major) = 10.06 min (Chiralpak IA, λ = 254 nm, 20% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.07 (s, 3 H), 2.79 (dd, *J* = 16.4 and 7.6 Hz, 1 H), 2.89 (dd, *J* = 16.4 and 6.7 Hz, 1 H), 3.24 (dd, *J* = 16.4 and 7.0 Hz, 1 H), 3.32 (dd, *J* = 16.4 and 7.1 Hz, 1 H), 3.76 (s, 3 H), 3.87–3.80 (m, 1 H), 6.81 (d, *J* = 8.6 Hz, 2 H), 7.16 (d, *J* = 8.6 Hz, 2 H), 7.40–7.47 (m, 2 H), 7.50–7.57 (m, 1 H), 7.88–7.94 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.9, 30.4, 36.2, 45.1, 49.9, 55.2, 114.0, 128.1, 128.3, 128.6, 133.1, 135.6, 136.9, 158.3, 198.7, 207.5 ppm.

(*R*)-3-(4-Chlorophenyl)-1-phenylhexane-1,5-dione **10c**



Product isolated as a yellow solid; The ee value was 93%; tR (minor) = 8.24 min, tR (major) = 11.84 min (Chiralpak IA, λ = 254 nm, 20% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.11 (s, 3 H), 2.83 (dd, *J* = 16.9 and 7.5 Hz, 1 H), 2.94 (dd, *J* = 16.9 and 6.6 Hz, 1 H), 3.27 (dd, *J* = 16.7 and 7.2 Hz, 1 H), 3.36 (dd, *J* = 16.7 and 6.8 Hz, 1 H), 3.89 (p, *J* = 7.0 Hz, 1 H), 7.25–7.18 (m, 2 H), 7.29–7.25 (s, 2 H), 7.44–7.49 (m, 2 H), 7.55–7.60 (m, 1 H), 8.01–7.98 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 30.4, 36.1, 44.6, 49.5, 128.1, 128.6, 128.7, 128.8, 133.2, 142.2, 198.2, 206.8 ppm.

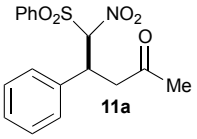
Procedure for the Michael addition of Phenylsulfonyl nitromethane to (*E*)-4-phenylbut-3-en-2-one catalyzed by resin 1a.



Supported quinine derivative **1a** (16.8 mg, 0.015 mmol, 10 mol%) was added to a vial with a mixture of (*E*)-4-phenylbut-3-en-2-one (43.8 mg, 0.3 mmol, 2 equiv.), phenylsulfonyl nitromethane **6e**[11] (30.1 mg, 0.15 mmol, 1 equiv.) and benzoic acid (3.6 mg, 0.03 mmol, 20 mol%) in $CHCl_3$ (0.15 mL) and the mixture was stirred at 30 ºC in a sand bath for 4 h. Then, the resin was filtered off, washed with $CHCl_3$ (3 x 1 mL) and dried under vacuum. The combined liquid phases were concentrated under reduced pressure. The reaction crude was directly purified through column chromatography eluting with cyclohexanes and (1- 20) % AcOEt. The product was derivatized to the corresponding 1,4-dicarbonyl compound in order to measure the ee.[11]

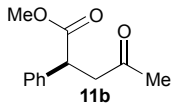
Methyl ketone **11a** (42 mg, 0.12 mmol, 1 equiv.) was suspended in MeOH (2 mL) at 0 ºC. To this suspension, 1,1,3,3-tetramethylguanidine (20 µL, 0.16 mmol, 1.3 equiv.) was added dropwise. The solution formed was stirred for 15 min at 0 ºC and TBA-Oxone (640 mg, 2 mmol active oxidizing agent Bu_4NHSO_5, ca. 5.0 equiv.) was added in one portion, followed by the addition of Na_2CO_3 (64 mg, 0.6 mmol, 5 equiv.). The reaction mixture was stirred for 12 h achieving room temperature gradually. Solvent was then removed under vacuum and the viscous oil was passed through a short pad of SiO_2 (silica gel) using CH_2Cl_2-cyclohexane (1:1) as eluent to remove tetra-*n*-butyl ammonium salts and other inorganic salts. The organic solution was evaporated on a rotatory evaporator and the mixture was purified by column chromatography using cyclohexane:AcOEt 2-40% to afford product **11b** as a colorless oil (20 mg. 75% yield).

(4*S*)-5-Nitro-4-phenyl-5-(phenylsulfonyl)pentan-2-one **11a**



The diastereomeric mixture (dr = 1:1.5) was isolated as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.03 (s, 3 H, minor diastereoisomer), 2.09 (s, 3 H, major diastereoisomer), 3.04–3.19 (m, 2 H, minor diastereoisomer), 3.34 (dd, *J* = 18.0 and 8.7 Hz, 1 H, major diastereoisomer), 3.43 (dd, *J* = 18.0 and 3.2 Hz, 1 H, major diastereoisomer), 4.22 (ddd, *J* = 11.6, 8.7 and 3.2 Hz, major diastereoisomer), 4.40 (td, *J* = 8.1 and 4.3 Hz, minor diastereoisomer), 5.98 (d, *J* = 7.8 Hz, minor diastereoisomer), 6.29 (d, *J* = 11.3 Hz, major diastereoisomer), 7.15–7.20 (m, 2 H, minor diastereoisomer), 7.22–7.30 (m, 10 H, both diastereoisomers), 7.59–7.81 (m, 6 H, both diastereoisomers), 7.90–7.97 (m, 2 H, major diastereoisomer). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.9, 30.4, 30.5, 40.7, 41.1, 44.9, 45.6, 103.9, 104.7, 128.3, 128.3, 128.4, 128.5, 128.6, 129.0, 129.1, 129.4, 129.5, 129.6, 129.9, 130.1, 134.1, 135.1, 135.6, 135.7, 136.0, 136.9, 204.1, 204.6 ppm. IR (film) 2986, 2920, 1713, 1551, 1336, 1158, 1083, 921, 758 cm^{-1}. HRMS (ESI–) *m/z* calcd for $C_{17}H_{16}NO_5S$ $[M-H]^-$: 346.0749. Found: 346.0757.

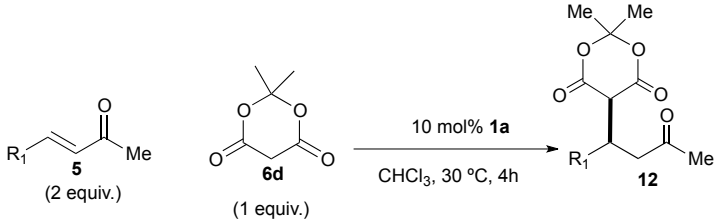
Methyl (*S*)-4-oxo-2-phenylpentanoate **11b**



11b

Product isolated as colorless oil. The ee value was 85%; tR (major) = 21.20 min, tR (minor) = 24.53 min (Chiralcel OD-H, λ = 210 nm, 7% *i*PrOH/hexane, flow rate = 0.5 mL/min). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.19 (s, 3 H), 2.73 (dd, *J* = 18.0 and 4.2 Hz, 1 H), 3.41 (dd, *J* = 18.0 and 10.4 Hz, 1 H), 3.68 (s, 3 H), 4.12 (dd, *J* = 10.4 and 4.2 Hz), 7.22–7.39 (m, 5 H, minor diastereoisomer). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 29.0, 46.1, 47.1, 52.3, 127.5, 127.7, 128.9, 138.1, 173.8, 206.2 ppm.

Procedure for the Michael addition of Meldrum's acid to enones catalyzed by resin 1a.

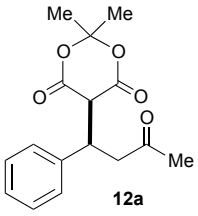


Entry	Product	R_1	Conversion (%)[a]	Yield (%)	ee (%)[b]
1	**12a**	Ph	99	99	96
2	**12b**	2-F-C_6H_4	97	97	85

[a]Conversion was determined by ^{1}H NMR spectroscopy.
[b]Enantiomeric excess was determined by chiral HPLC analysis.

Supported quinine derivative **1a** (16.8 mg, 0.015 mmol, 10 mol%) was added to a vial with a mixture of α,β-unsaturated ketone (0.3 mmol, 2 equiv.), Meldrum's acid, **6d** (21.6 mg, 0.15 mmol, 1 equiv.) and benzoic acid (3.6 mg, 0.03 mmol, 20 mol%) in $CHCl_3$ (0.15 mL) and the mixture was stirred at 30 ºC in a sand bath for 4 h. Then, the resin was filtered off, washed with $CHCl_3$ (3 x 1 mL) and dried under vacuum. The combined liquid phases were concentrated under reduced pressure. The reaction crude was directly purified through column chromatography eluting with cyclohexane and (1- 40) % AcOEt.

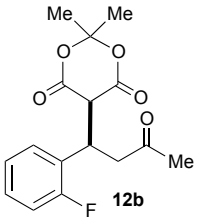
(*R*)-2,2-Dimethyl-5-(3-oxo-1-phenylbutyl)-1,3-dioxane-4,6-dione **12a**



12a

Product isolated as a white solid; The ee value was 96%; tR (major) = 5.70 min, tR (minor) = 9.74 min (Chiralpak IA, λ = 210 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.34 (s, 3 H), 1.68 (s, 3 H), 2.21 (s, 3 H), 3.05 (dd, *J* = 18.5 and 5.1 Hz, 1 H), 3.73 (dd, *J* = 18.6 and 10.3 Hz, 1 H), 4.24–4.33 (m, 1 H), 7.21–7.41 (m, 5 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.9, 27.9, 28.1, 30.4, 39.7, 45.5, 49.0, 105.3, 127.8, 128.5, 128.7, 128.8, 130.2, 139.7, 165.2, 165.5, 207.9 ppm. IR (film) 2909, 1780, 1739, 1712, 1291, 1260, 1203, 1178, 1123, 1057, 919, 708 cm^{-1}. HRMS (ESI–) *m/z* calcd for $C_{16}H_{17}O_5$ $[M-H]^-$: 289.1076. Found: 289.1087.

(*R*)-5-(1-(2-Fluorophenyl)-3-oxobutyl)-2,2-dimethyl-1,3-dioxane-4,6-dione **12b**

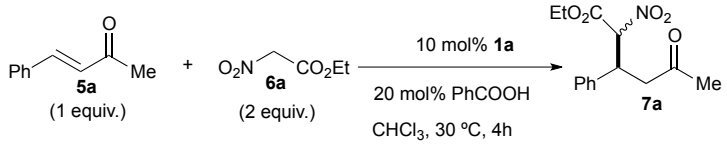


12b

Product isolated as a pale yellow oil; The ee value was 85%; tR (minor) = 14.39 min, tR (major) = 19.96 min (Chiralpak IC, λ = 254 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.66 (s, 3 H), 1.74 (s, 3 H), 2.18 (s, 3 H), 3.07 (dd, *J* = 18.3 and 6.3 Hz, 1 H), 3.41 (dd, *J* = 18.3 and 9.1 Hz, 1 H), 4.17 (d, *J* = 4.0 Hz, 1 H), 4.51–4.61 (m, 1 H), 7.04 (ddd, *J* = 10.6, 8.2 and 1.3 Hz, 1 H), 7.10 (td, *J* = 8.5 Hz, 2 H), ^{13}C NMR (126 MHz, $CDCl_3$): δ = 26.9, 27.4, 28.3, 30.2, 32.0, 44.1, 48.2, 105.3, 115.7, 115.9, 124.5, 124.6, 129.0, 129.1, 129.2, 129.3, 164.4, 165.1, 207.4 ppm. IR (film) 2972, 1741, 1492, 1383, 1295, 1201, 1021, 910, 759 cm^{-1}. HRMS (ESI–) *m/z* calcd for $C_{16}H_{16}FO_5$ [M–H]$^-$: 307.0987. Found: 307.0987.

6. GENERAL PROCEDURE FOR THE RECYCLING EXPERIMENTS

Polymer-supported catalyst **1a** (22.4 mg, 0.020 mmol, 10 mol%), (*E*)-4-phenylbut-3-en-2-one, **5a** (29.2 mg, 0.2 mmol, 1 equiv.) ethyl nitroacetate, **6a** (44 µL, 0.4 mmol, 2 equiv.) and benzoic acid (4.8 mg, 0.04 mmol, 20 mol%) in $CHCl_3$ (0.2 mL) were stirred in a previously weighted 2 mL-vial at 30 ºC sand bath for 4h. Then, the resin was filtered off and washed with $CHCl_3$ (3 x 1mL). The recovered catalyst was gently dried under vacuum at 30 ºC for 2-3 h. The dried catalyst was directly used in the next recycling run. Conversion was determined by NMR spectrometry of the crude mixture whilst the enantiomeric excess by HPLC after chromatography column purification.



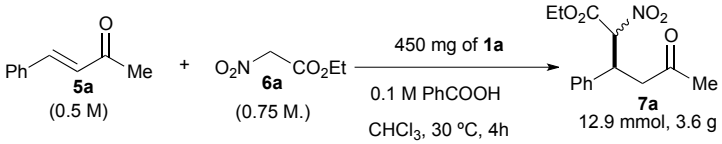
Cycle	Time (h)	Conversion (%)[a]	ee (%)[b]
1	4	98	97/96
2	4	93	97/96
3	4	89	97/96
4	4.33	80	97/96
5	4	68	96/94
6	4.5	52	97/95

[a]Conversion was determined by ^{1}H NMR spectroscopy.
[b]Enantiomeric excess was determined by chiral HPLC analysis.

7. DESCRIPTION OF THE CONTINUOUS FLOW PROCESS

The packed-bed reactor consisted of a vertically mounted 30 cm Teflon® tube limited by glass wool in the inlet and the outlet loaded with the resin **1a** (450 mg; *f* = 0.87 mmol·g^{-1}). The tube was assembled to an Asia120® flow chemistry system developed by Syrris. Resin **1** was swollen by circulation of $CHCl_3$ at 500 µL·min^{-1} flow rate for 10 min. The Teflon® tube was coated with a jacket allowing the circulation of a heating fluid at 30 ºC. After conditioning of the resin, a single solution of (*E*)-4-phenylbut-3-en-2-one

5a 0.5 M, benzoic acid 0.1 M and ethyl nitroacetate **6a** 0.75 M in $CHCl_3$ was flushed through the system at 50 µl/min flow rate. The reactor outlet was connected to FTIR inline analysis to monitorize the reaction and the solution was collected in a receiving flask.[12] Conversion and enantiomeric ratio of the final product were determined by ^1H NMR and HPLC analysis respectively of periodically collected samples. The experiment was run for 22 h. Samples were collected from 2 h (where the experiment was stabilized) to 22 h. The solvent from the collected samples was removed under reduce pressure. Column chromatography, using the same conditions for batch experiments, afforded the pure product (3.6 g, 13 mmol) as a white solid with slightly better enantioselectivity than the batch process.



Entry	Time (Δt)	Conversion (%)[a]	Entry	Time	Conversion (%)[a]
1	1 h	51	7	7 h (+1h)	60
2	2 h (+1h)	68	8	8 h (+1h)	58
3	3 h (+1h)	66	9	9 h (+1h)	57
4	4 h (+1h)	66	10	12 h (+3h)	60
5	5 h (+1h)	59	11	22 h (+10h)	49
6	6 h (+1h)	60			

TON = 32 mmol product/mmol catalyst
Residence time = 40 min

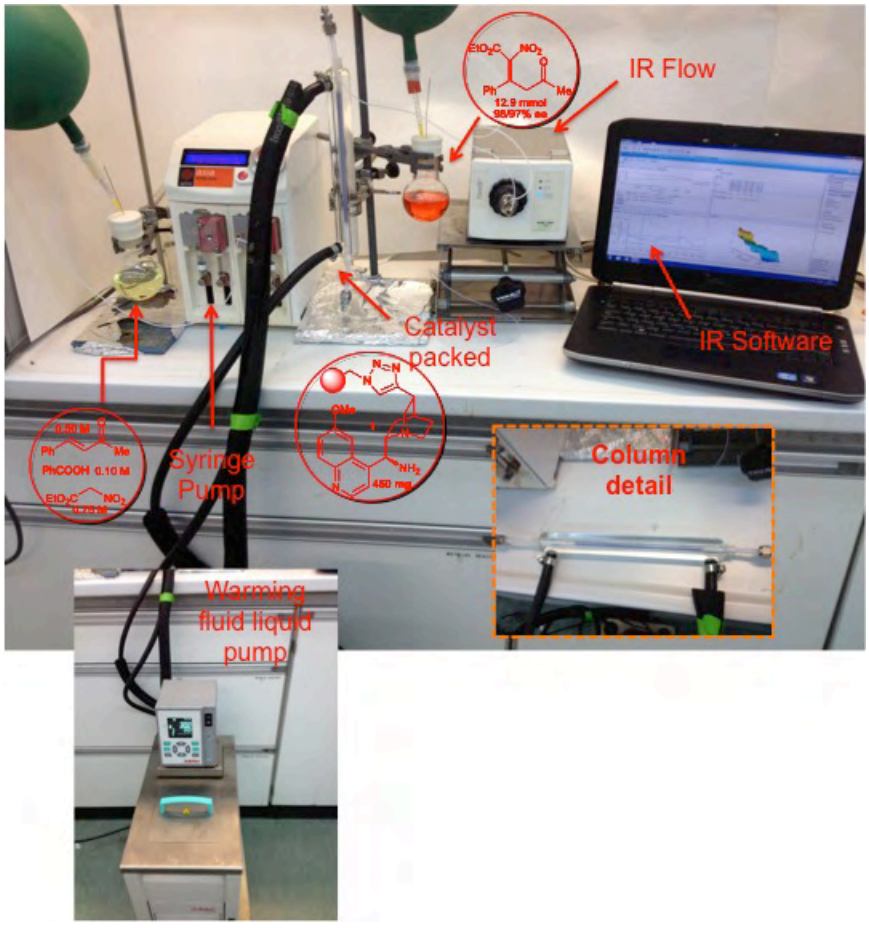


Figure 1. Set-up for the continuous system.

8. CONTINUOUS FLOW PRODUCTION OF A LIBRARY OF MICHAEL ADDUCTS

The Teflon® tube was filled with swollen polymer-supported quinine **1a** (500 mg; f = 0.87 mmol·g^{-1}). The column was assembled to an Asia120® flow chemistry system developed by Syrris. $CHCl_3$ was flushed through the column at 500 μL·min^{-1} flow rate for 10 min. When the resin has been conditioned, a solution of ethyl nitroacetate 0.75 M, (*E*)-4-(3,5-dichlorophenyl)but-3-en-2-one 0.5 M and benzoic acid 0.1 M in $CHCl_3$ was pumped with a flow rate of 500 μL·min^{-1} through the system until the solution filled the column. Then the flow rate was reduced to 50 μL·min^{-1} and the system was run for 1h to be stabilized. After that, the process was run for 1 h, the collected sample was evaporated and analyzed by ^{1}H NMR spectroscopy to determine both conversion and diastereoselectivity of the final product. The system was flushed with $CHCl_3$ for 1 h at 500 μL·min^{-1} flow rate to clean the resin. The same procedure was repeated four more times using the same resin with different substrates.

1. Continuous flow reaction of (*E*)-4-(3,5-dichlorophenyl)but-3-en-2-one 0.5 M, ethyl nitroacetate 0.75 M and benzoic acid 0.1 M in $CHCl_3$.
The solvent was removed from the collected sample to give a yellow oil which was submitted to column chromatography cyclohexane/ethyl acetate 1-40% to give pure product **7k** (0.47 g, 1.39 mmol, productivity: 3.2 mmol product · mmol resin^{-1}· h^{-1} with 99/99% ee).

2. Continuous flow reaction of 2,2-dimethyl-1,3-dioxane-4,6-dione 0.5 M, (*E*)-4-(2-fluorophenyl)but-3-en-2-one 0.75 M and benzoic acid 0.1 M in $CHCl_3$.
The solvent was removed from the collected sample to give orange oil, which was submitted to column chromatography cyclohexane/ethyl acetate 1-40% to give pure product **12b** (0.36 g, 1.15 mmol, productivity: 2.6 mmol product · mmol resin^{-1}· h^{-1} with 91% ee).

3. Continuous flow reaction of 2,2-dimethyl-1,3-dioxane-4,6-dione 0.5 M, (*E*)-4-phenylbut-3-en-2-one 0.75 M and benzoic acid 0.1 M in $CHCl_3$.
The solvent was removed from the collected sample to give yellow oil, which was submitted column chromatography cyclohexane/ethyl acetate 1-40% to give pure product **12a** (0.33 g, 1.14 mmol, productivity: 2.6 mmol product · mmol resin^{-1}· h^{-1} with 96% ee).

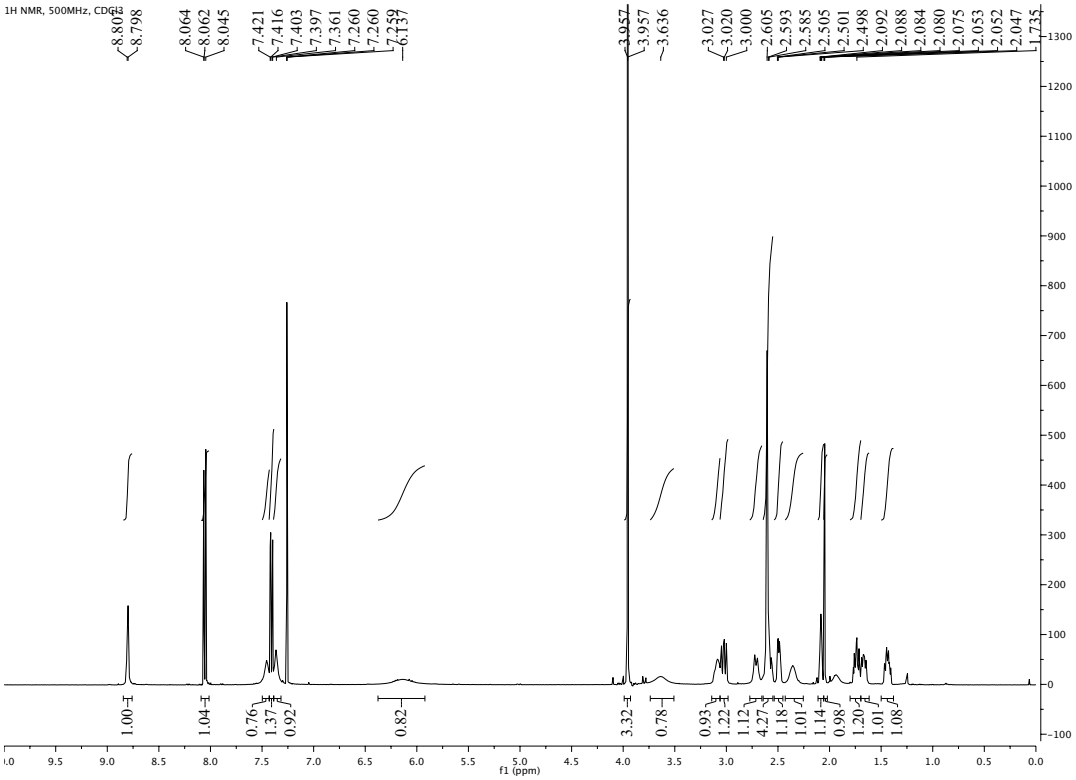
4. Continuous flow reaction of (*E*)-4-(*m*-tolyl)but-3-en-2-one 0.5 M, ethyl nitroacetate 0.75 M and benzoic acid 0.1 M in $CHCl_3$.
The solvent was removed from the collected sample to give colorless oil, which was submitted to column chromatography cyclohexane/ethyl acetate 1-40% to give pure product **7c** (0.24 g, 0.83 mmol, productivity: 1.9 mmol product · mmol resin^{-1}· h^{-1} with 98/99% ee).

5. Continuous flow reaction of ((nitromethyl)sulfonyl)benzene 0.5 M, (*E*)-4-phenylbut-3-en-2-one 0.75 M and benzoic acid 0.1 M in $CHCl_3$.
The solvent was removed from the collected sample to give colourless oil, which was submitted column chromatography cyclohexane/ethyl acetate 1-40% to give pure product **11a** (0.21 g, 0.60 mmol, productivity: 1.4 mmol product · mmol resin^{-1}· h^{-1} with 85% ee).

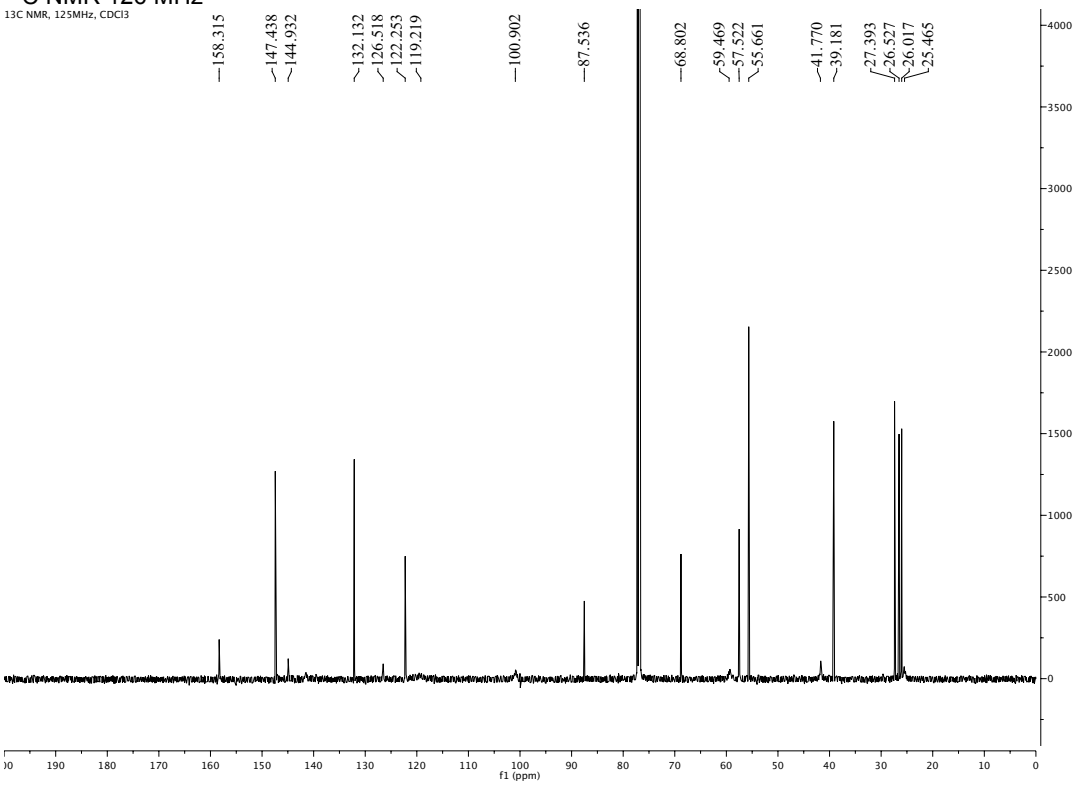
9. NMR SPECTRA

(1*S*,2*S*,4*S*,5*S*,9*R*)-5-(Ethynylquinuclidin-2-yl)-(6-methoxyquinolin-4-yl)methyl methanesulfonate **1-OMs**

^{1}H NMR 500 MHz

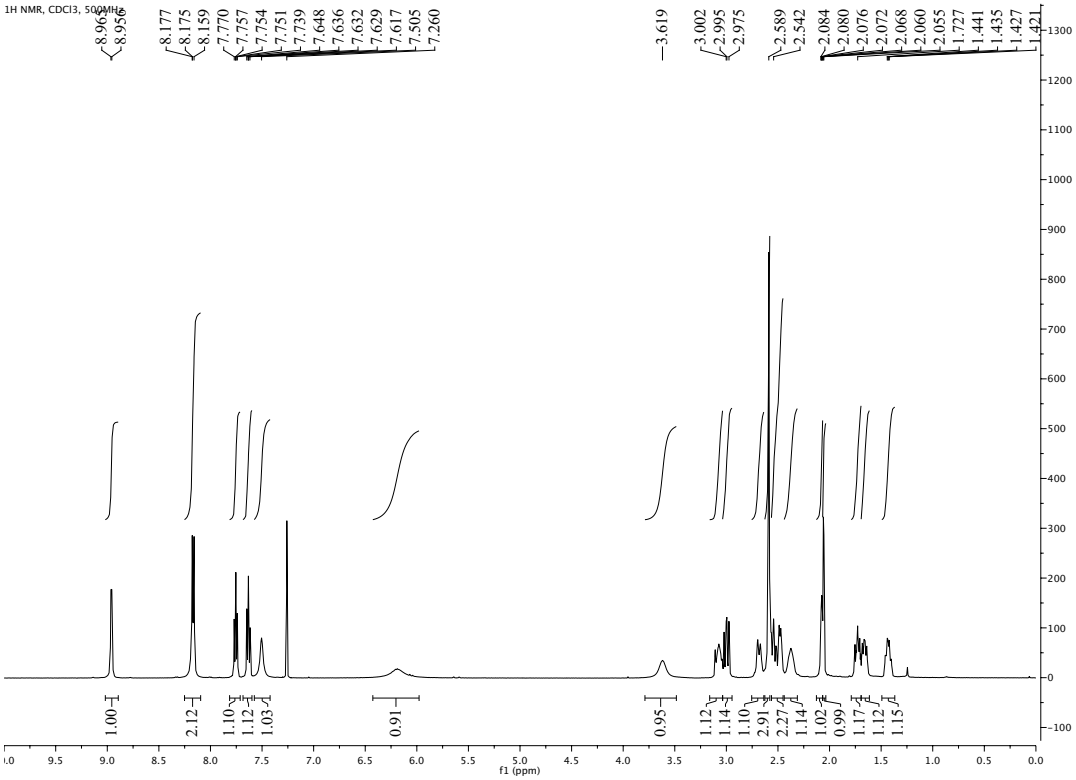


^{13}C NMR 126 MHz

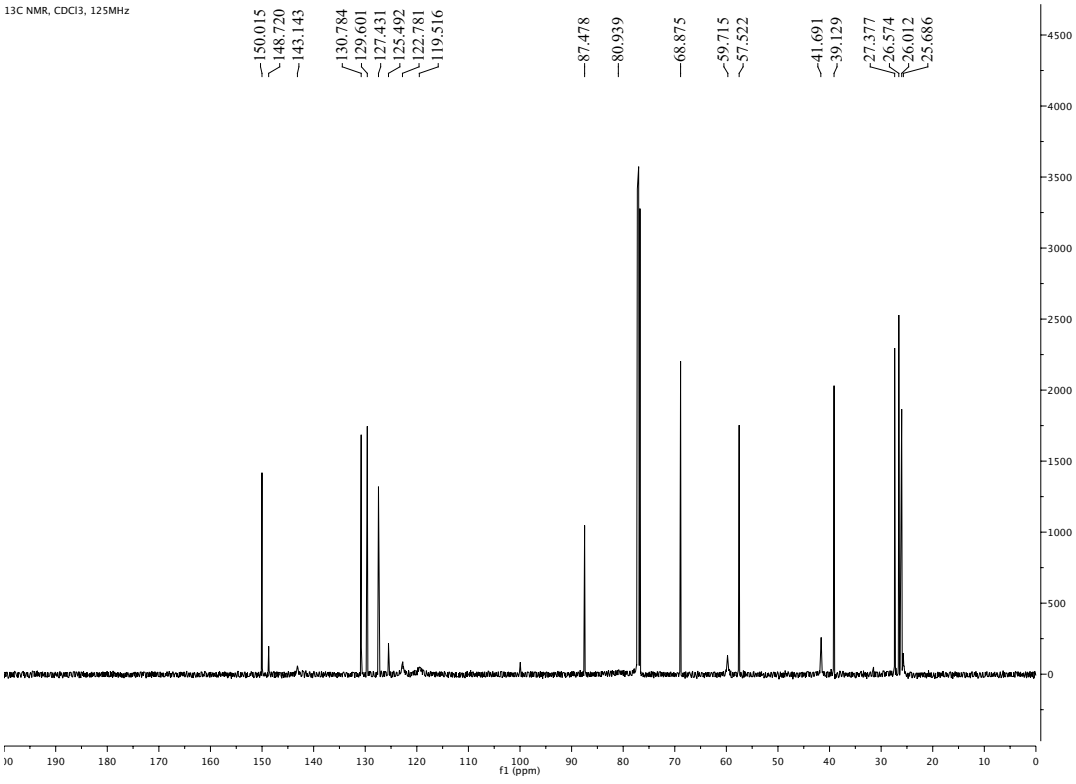


(1*S*,2*S*,4*S*,5*S*,9*R*)-5-(Ethynylquinuclidin-2-yl)-(quinolin-4-yl)methyl methanesulfonate **2-OMs**

^{1}H NMR 500 MHz

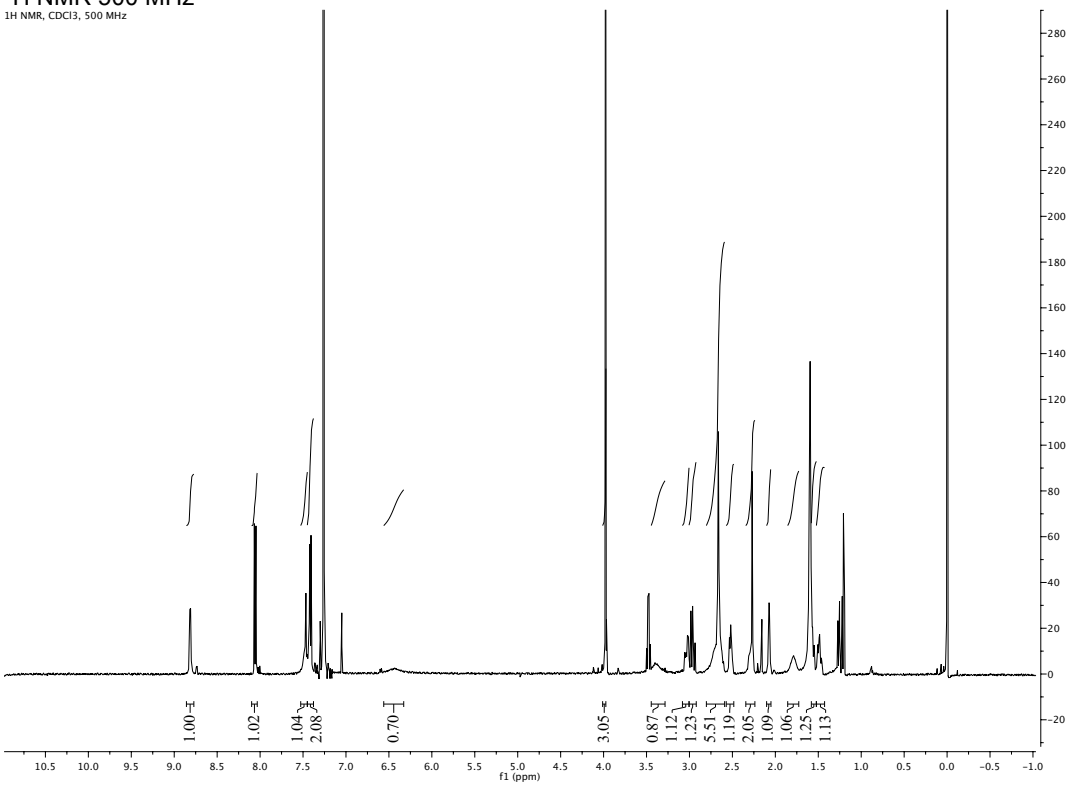


^{13}C NMR 126 MHz



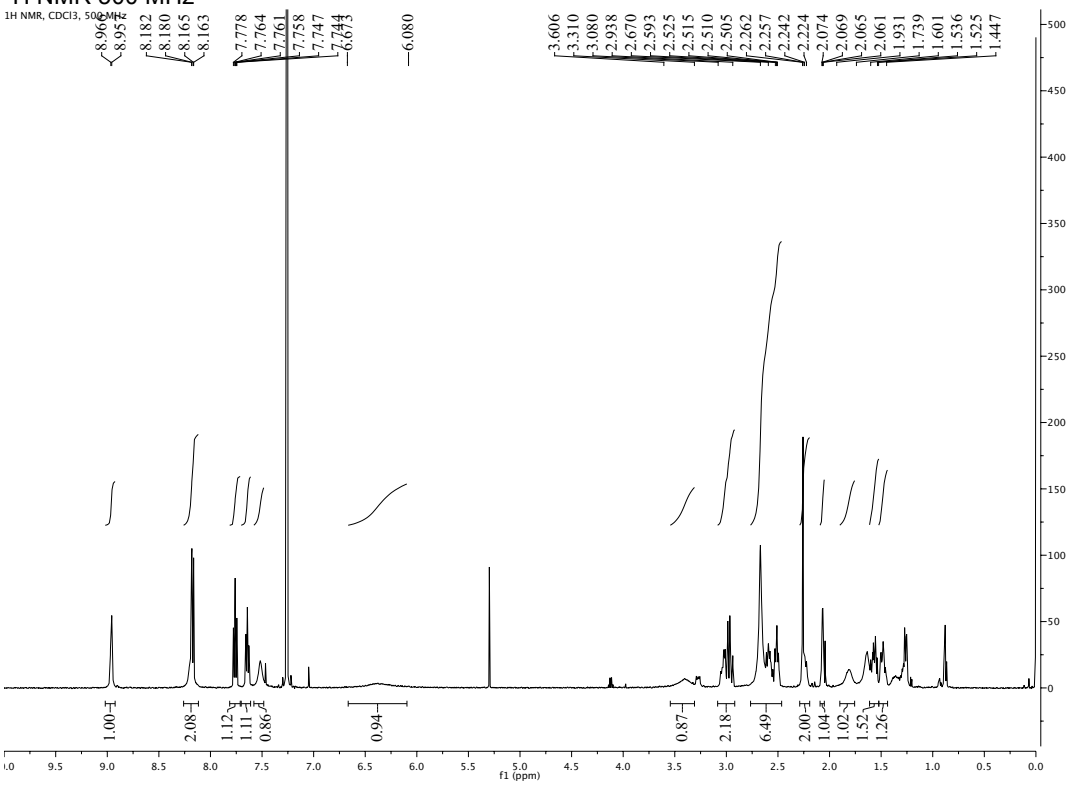
(1*S*,2*R*,4*S*,5*S*,9*S*)-5-(Ethynylquinuclidin-2-yl)-(6-methoxyquinolin-4-yl)methyl methanesulfonate **3-OMs**

^{1}H NMR 500 MHz



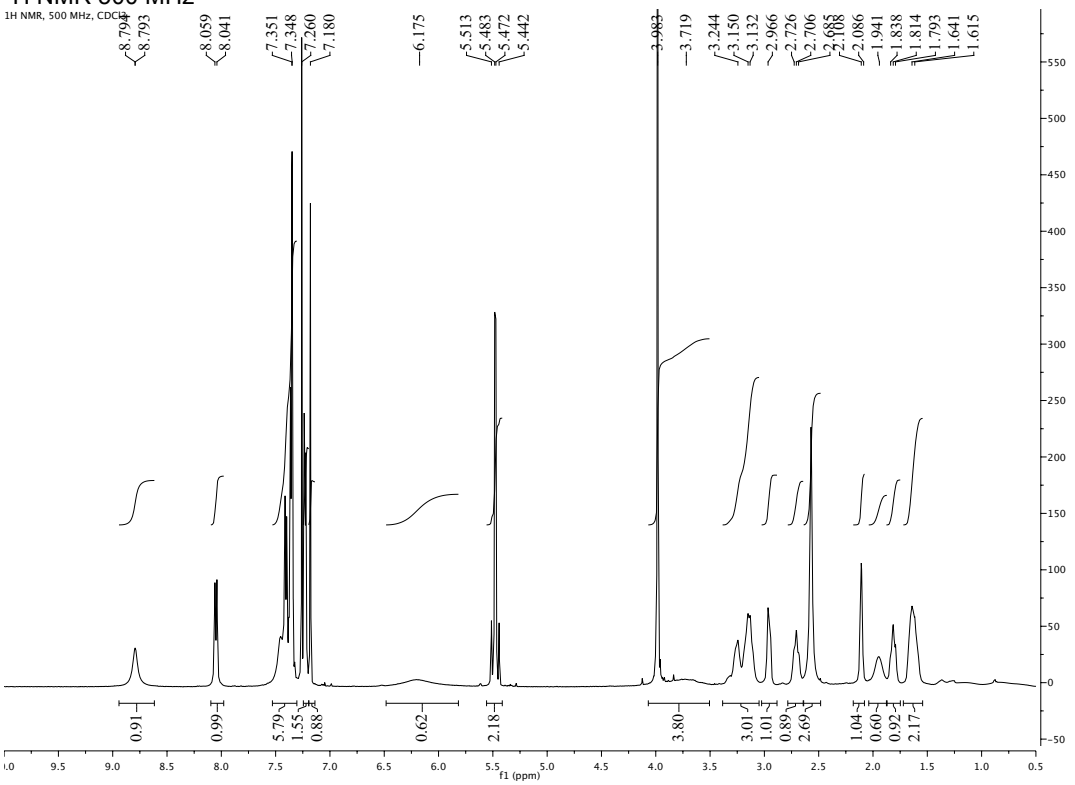
(1*S*,2*R*,4*S*,5*S*,9*S*)-5-(Ethynylquinuclidin-2-yl)-(quinolin-4-yl)methyl methanesulfonate **4-OMs**

^{1}H NMR 500 MHz

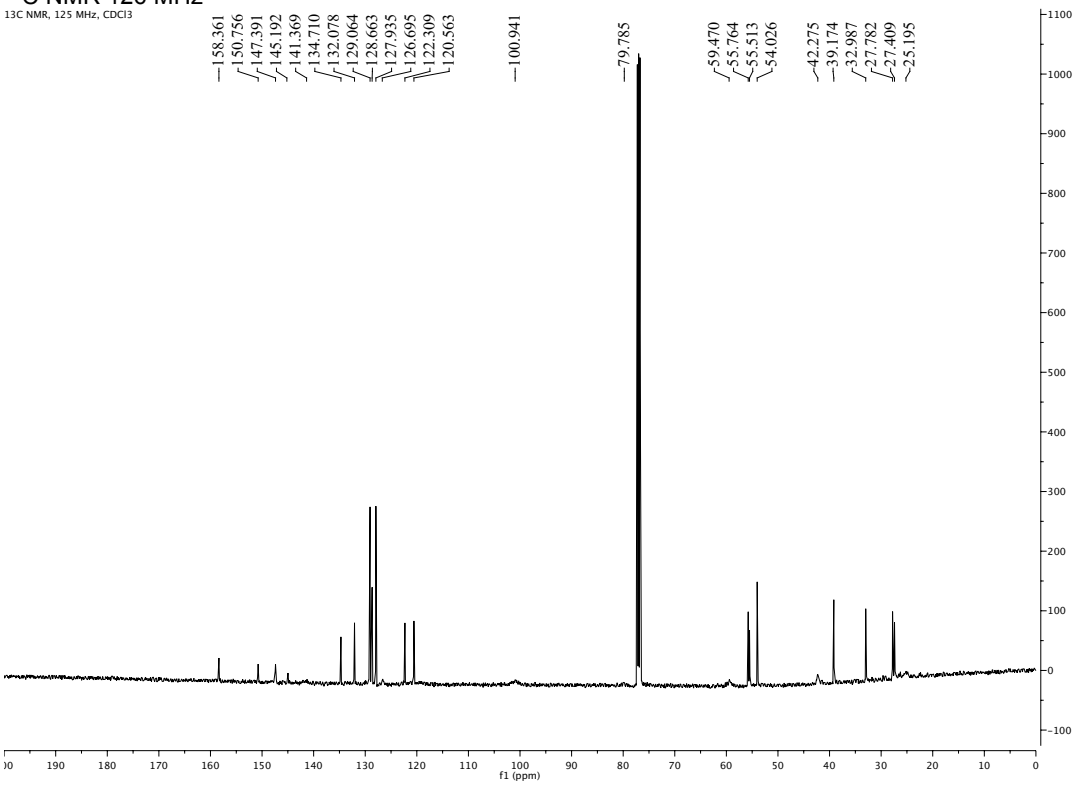


(1*S*,2*S*,4*S*,5*R*,9*R*)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(6-methoxyquinolin-4-yl)methyl methanesulfonate **1-hOMs**

^{1}H NMR 500 MHz

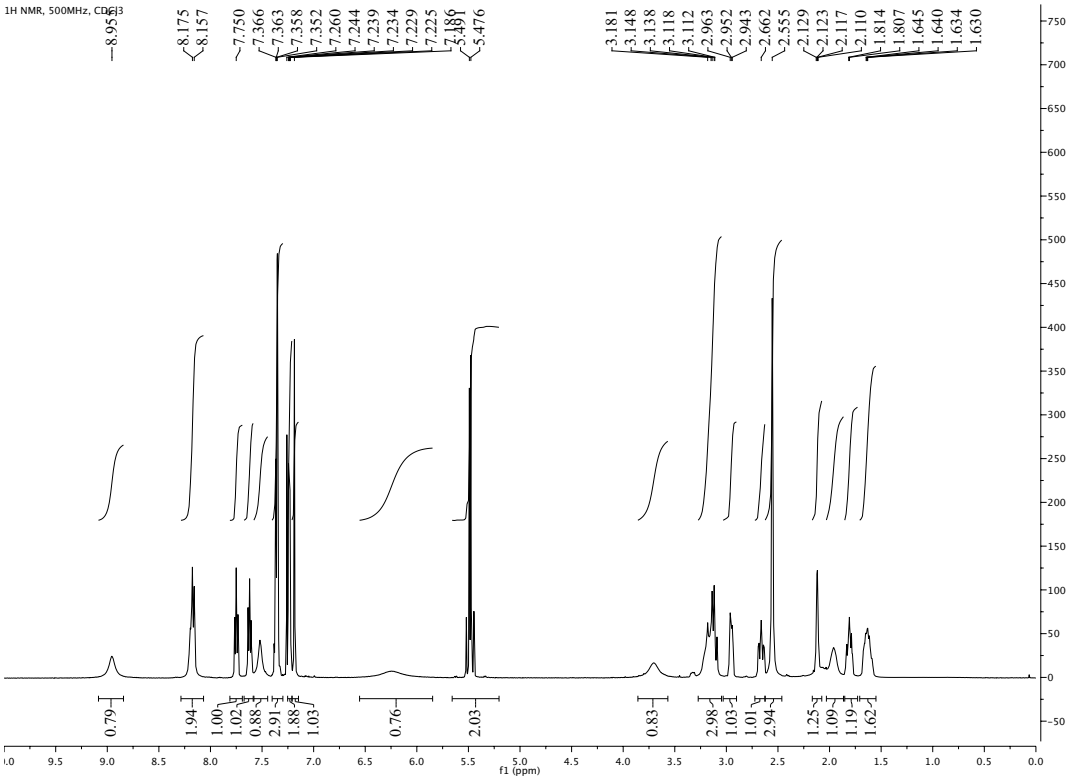


^{13}C NMR 126 MHz

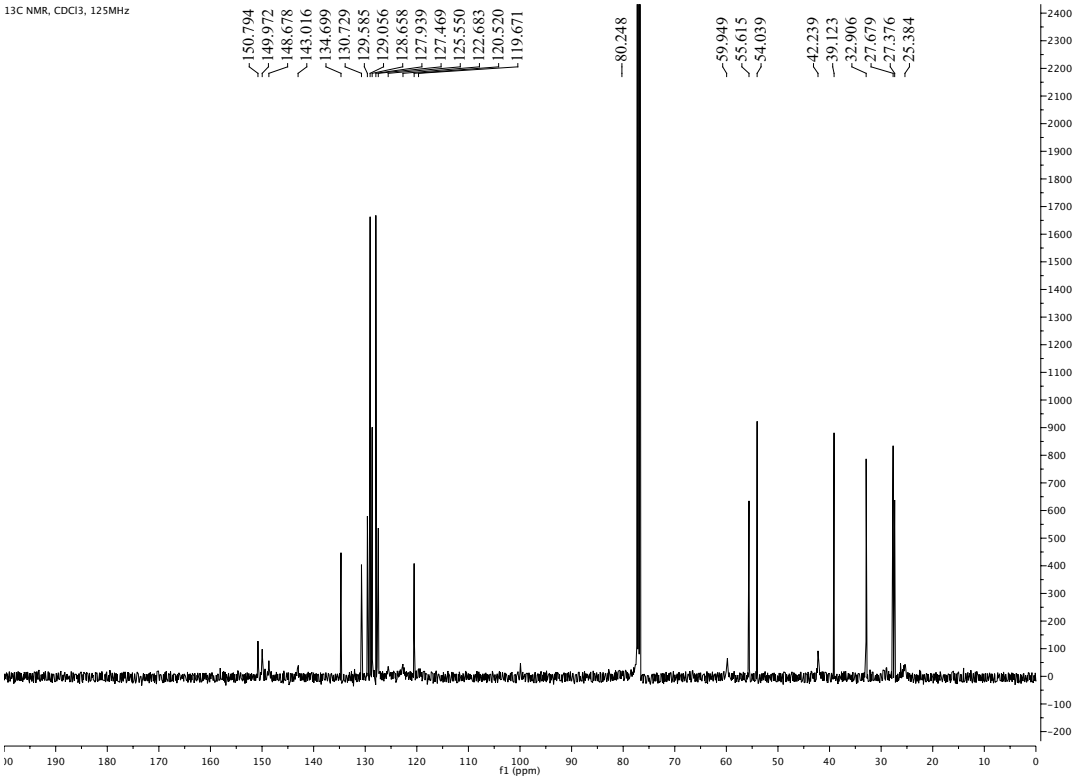


(1*S*,2*S*,4*S*,5*R*,9*R*)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(quinolin-4-yl)methyl methanesulfonate **2-hOMs**

^{1}H NMR 500 MHz

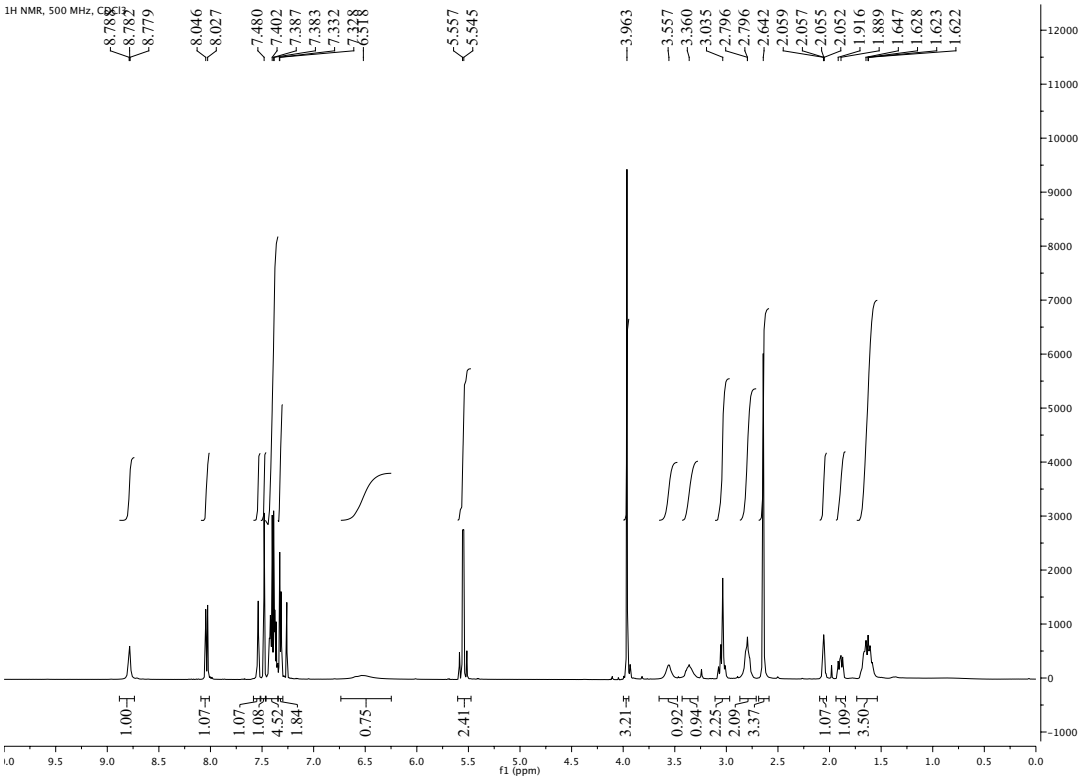


^{13}C NMR 126 MHz

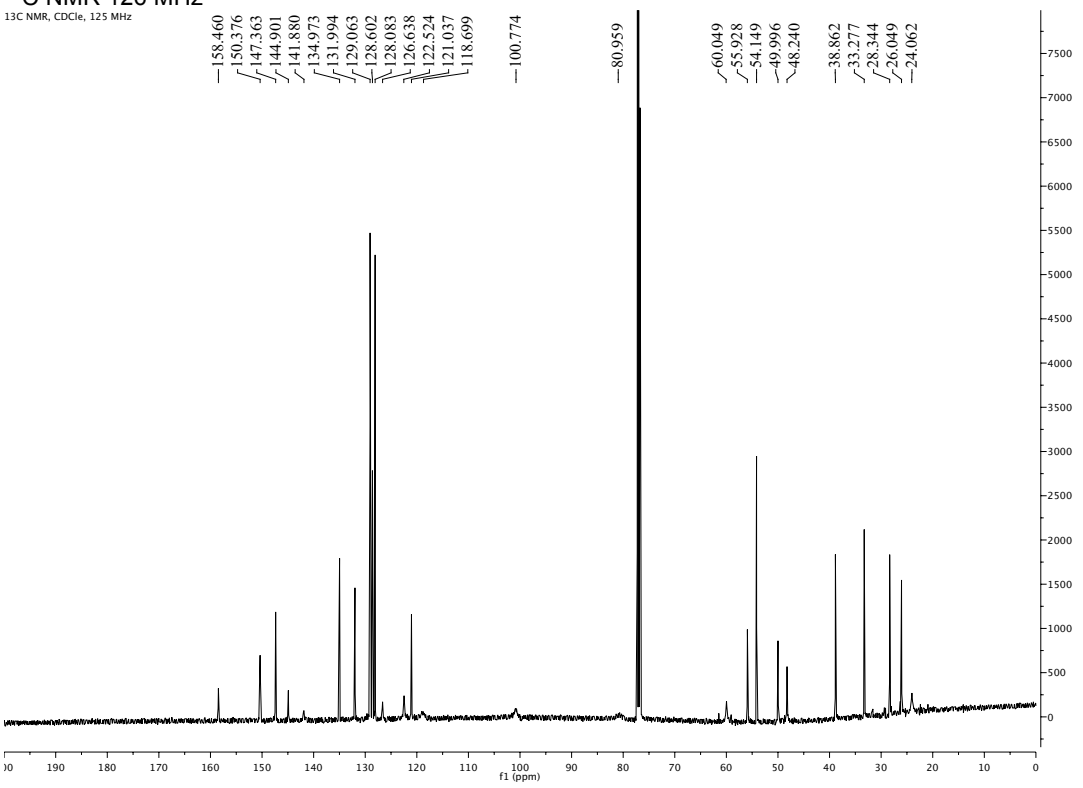


(1*S*,2*R*,4*S*,5*R*,9*S*)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(6-methoxyquinolin-4-yl)methyl methanesulfonate **3-hOMs**

^{1}H NMR 500 MHz

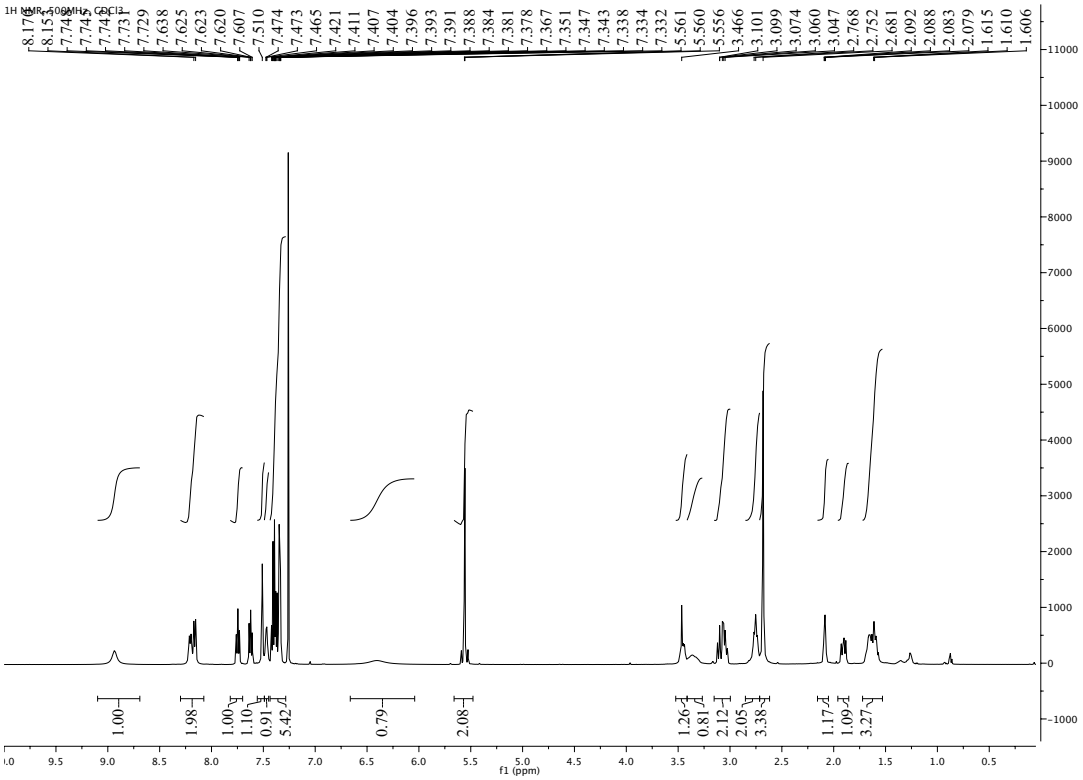


^{13}C NMR 126 MHz

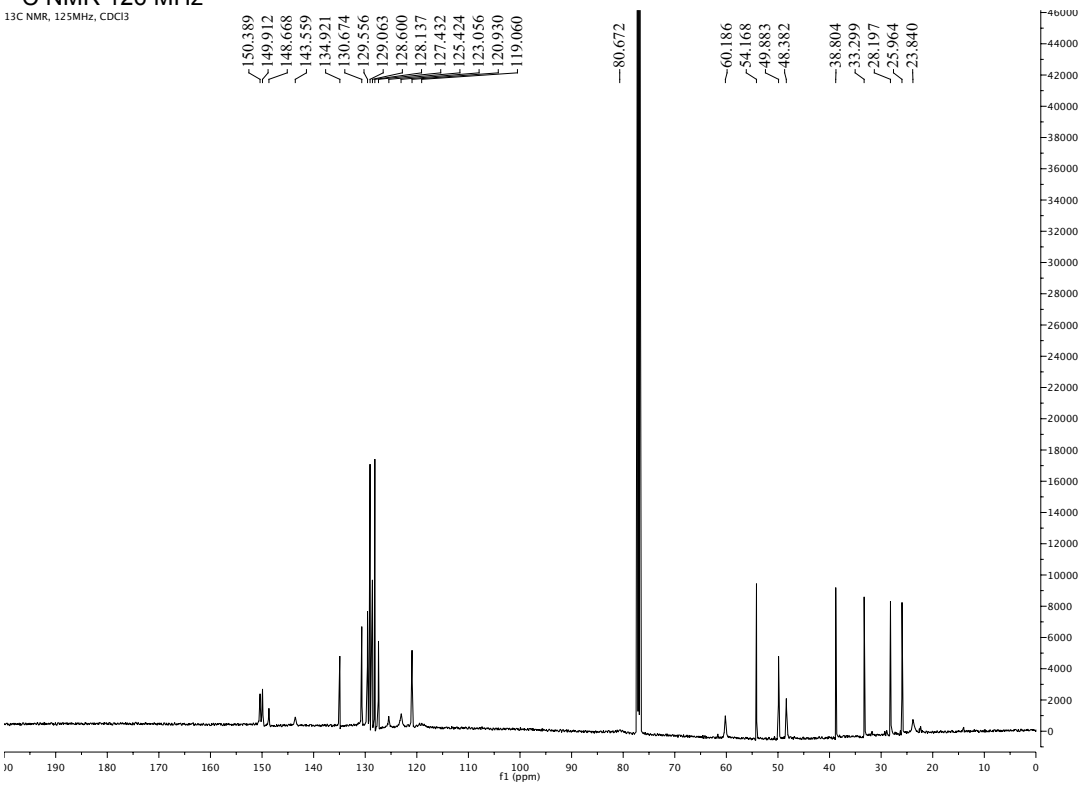


(1*S*,2*R*,4*S*,5*R*,9*S*)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(quinolin-4-yl)methyl methanesulfonate **4-hOMs**

^{1}H NMR 500 MHz

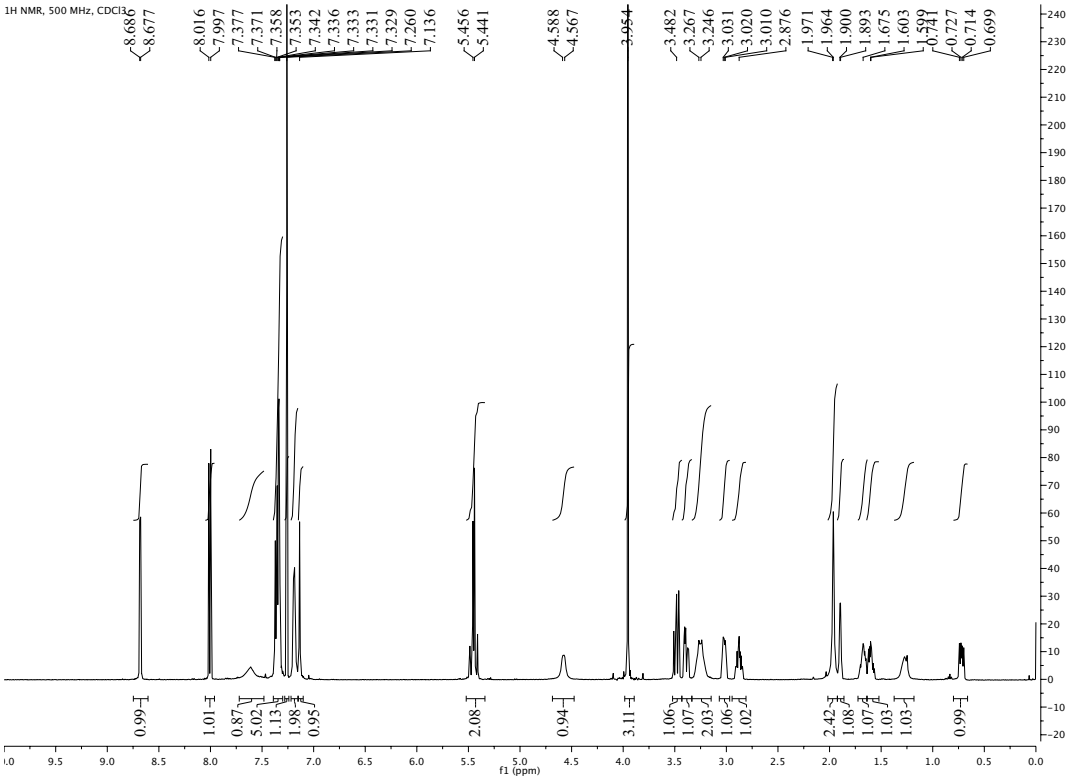


^{13}C NMR 126 MHz

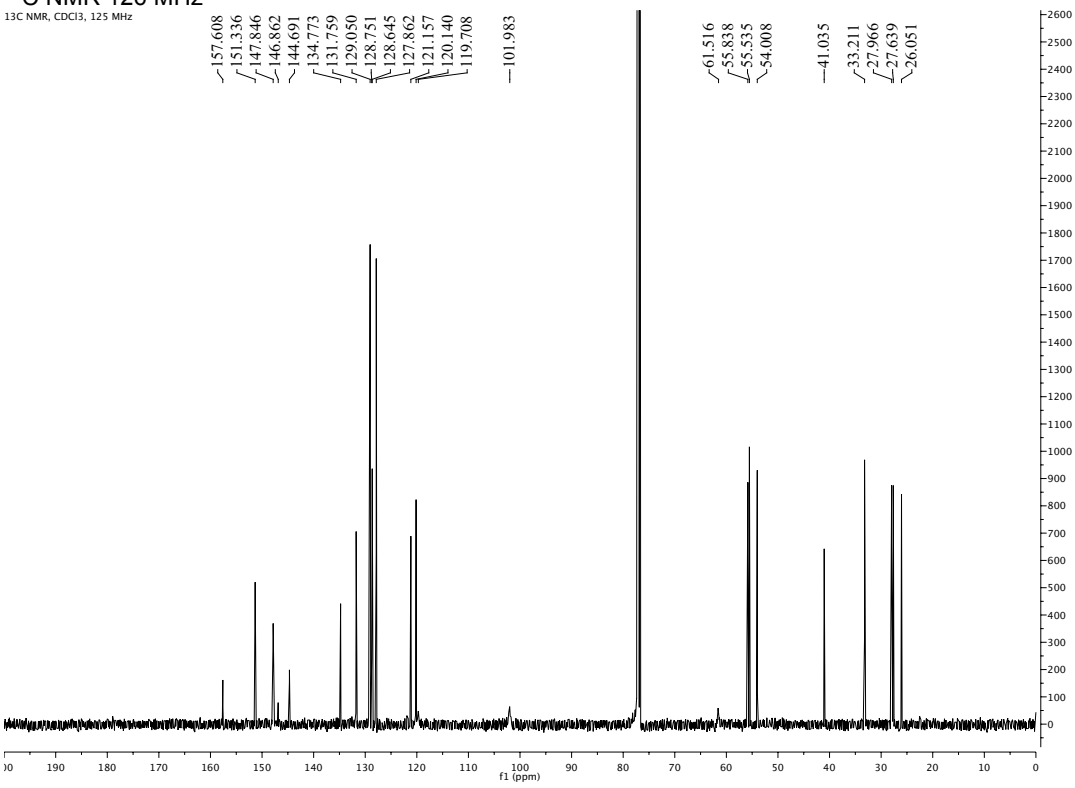


(1*S*,2*S*,4*S*,5*R*,9*S*)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(6-methoxyquinolin-4-yl)methanamine, **1b**

^{1}H NMR 500 MHz

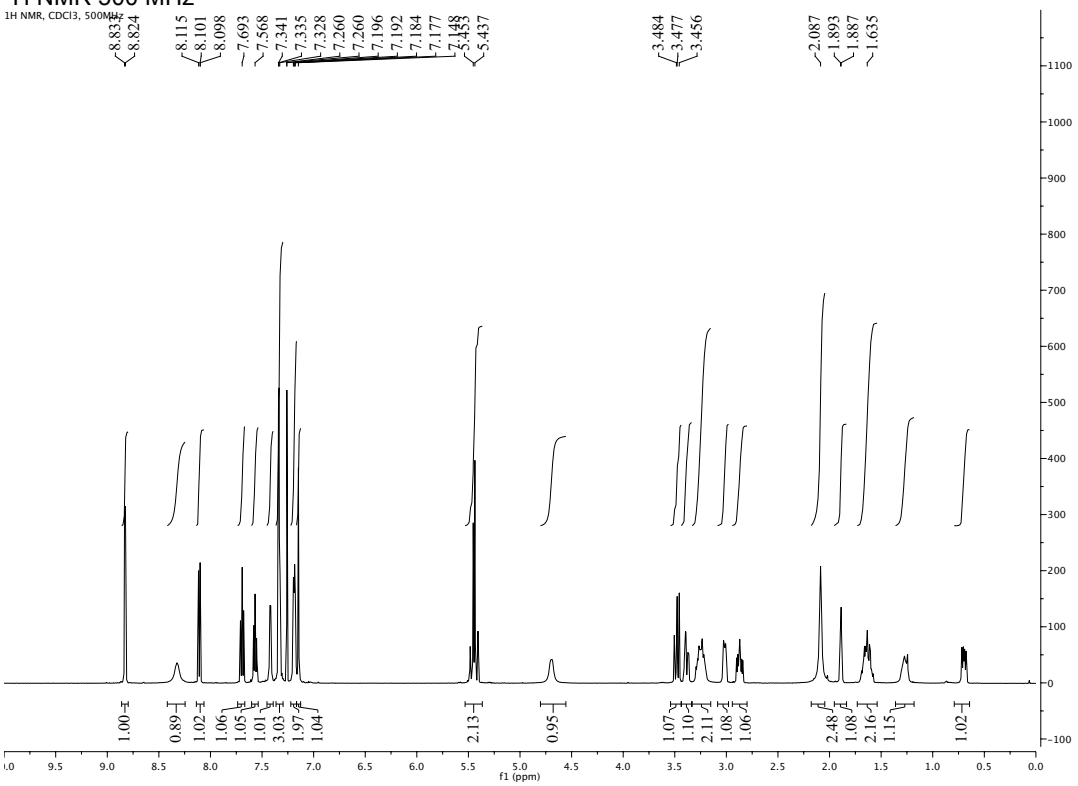


^{13}C NMR 126 MHz

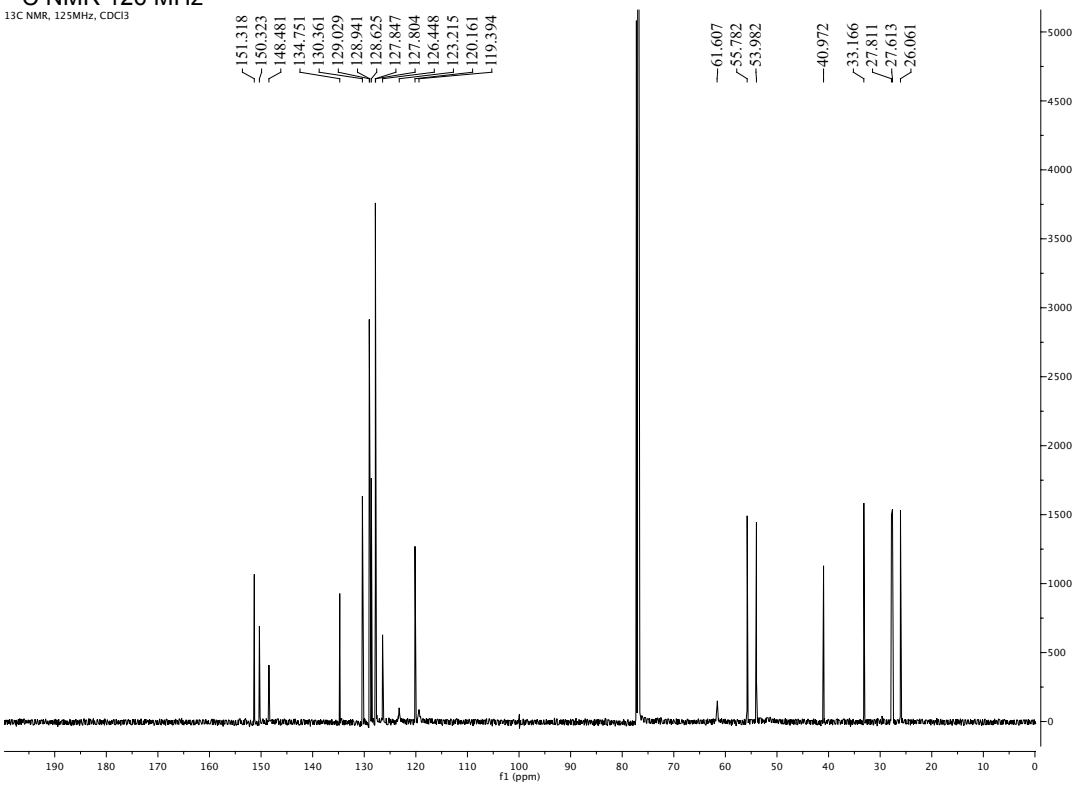


(1*S*,2*S*,4*S*,5*R*,9*S*)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(quinolin-4-yl)methanamine **2b**

^{1}H NMR 500 MHz

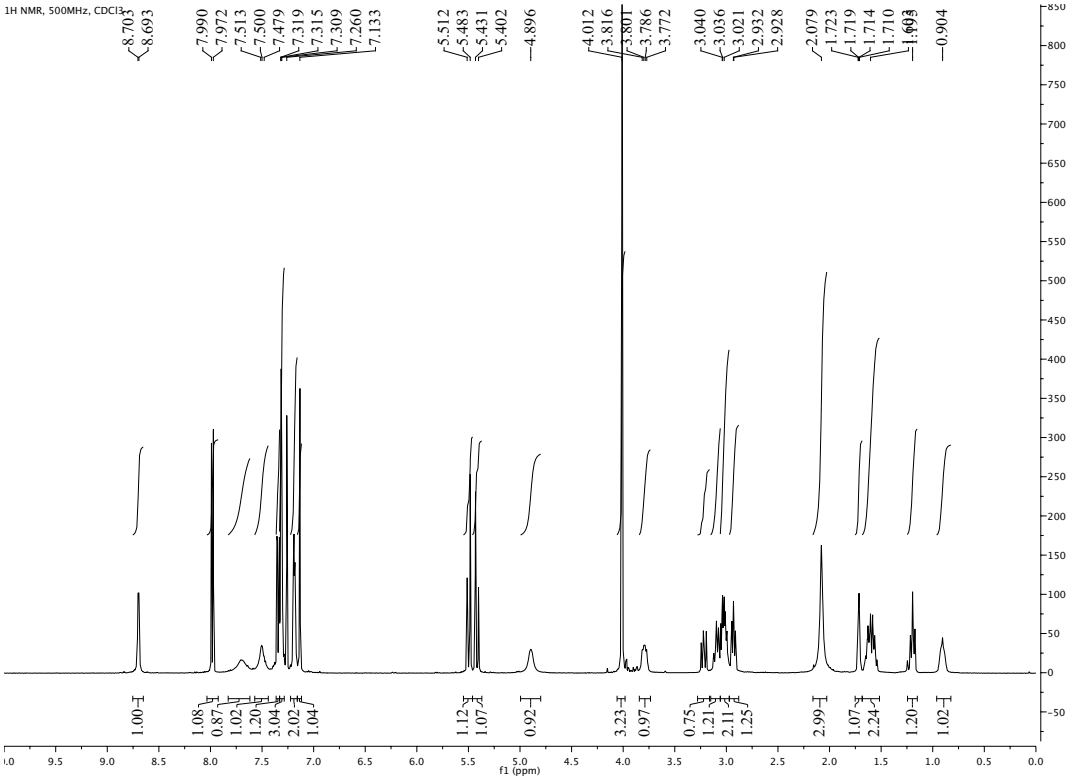


^{13}C NMR 126 MHz

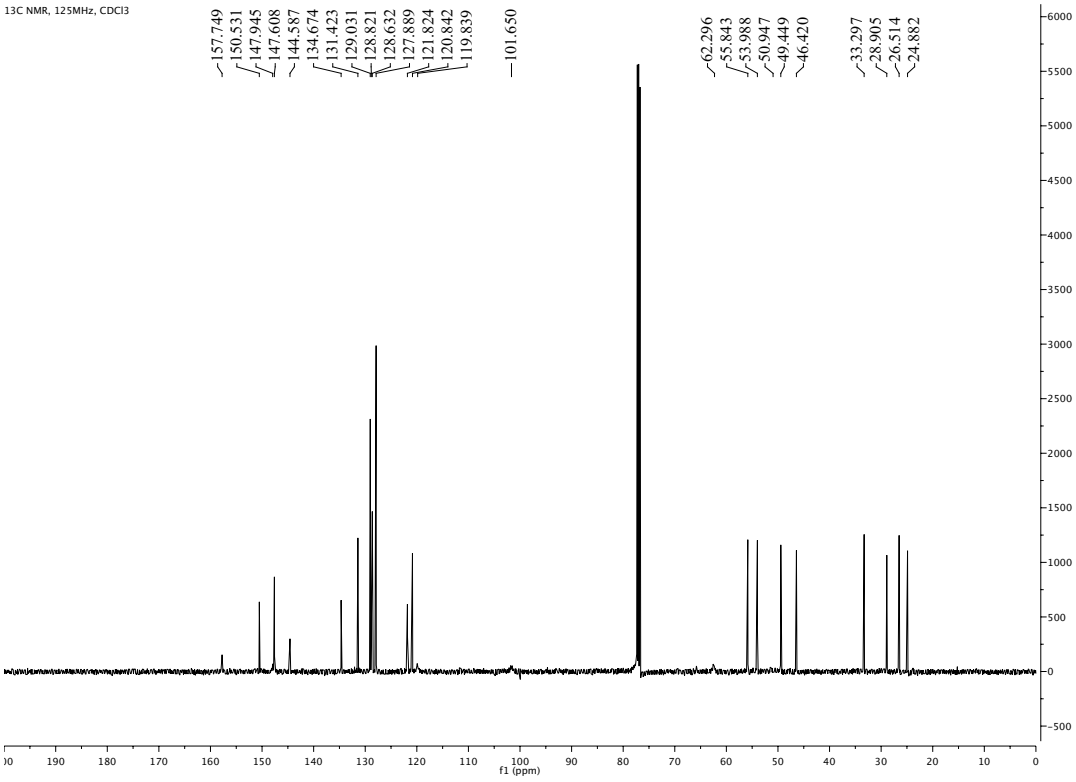


(1*S*,2*R*,4*S*,5*R*,9*R*)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(6-methoxyquinolin-4-yl)methanamine **3b**

^{1}H NMR 500 MHz

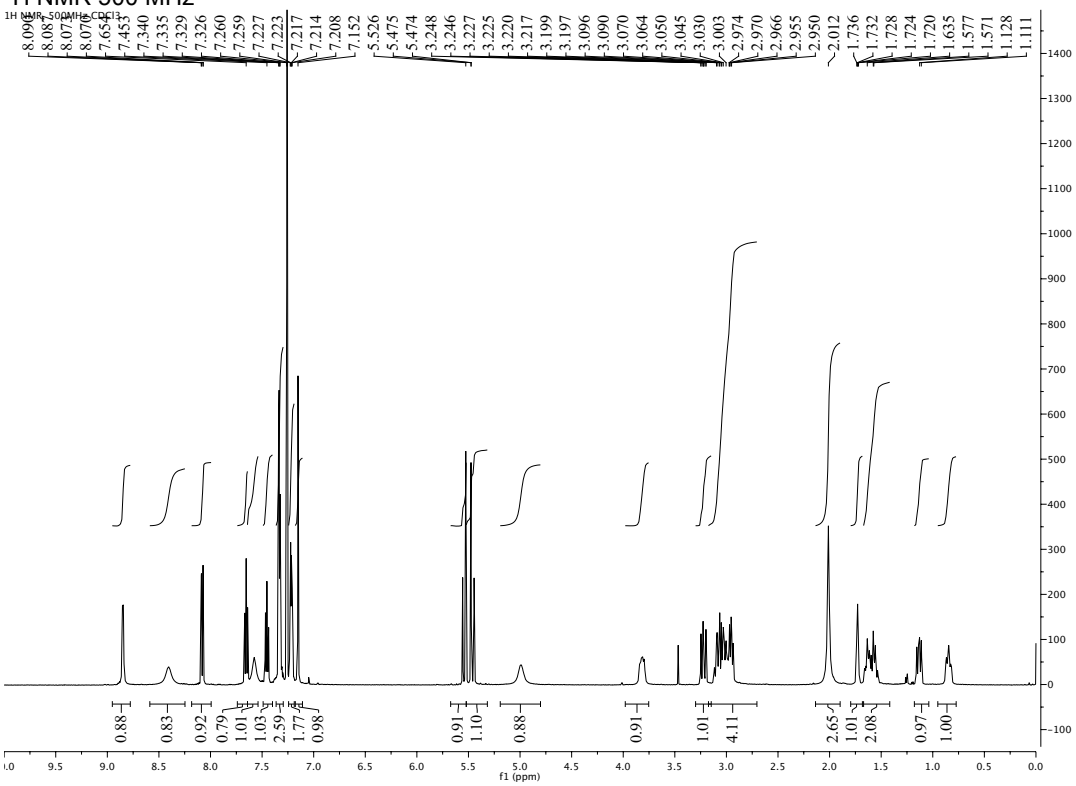


^{13}C NMR 126 MHz

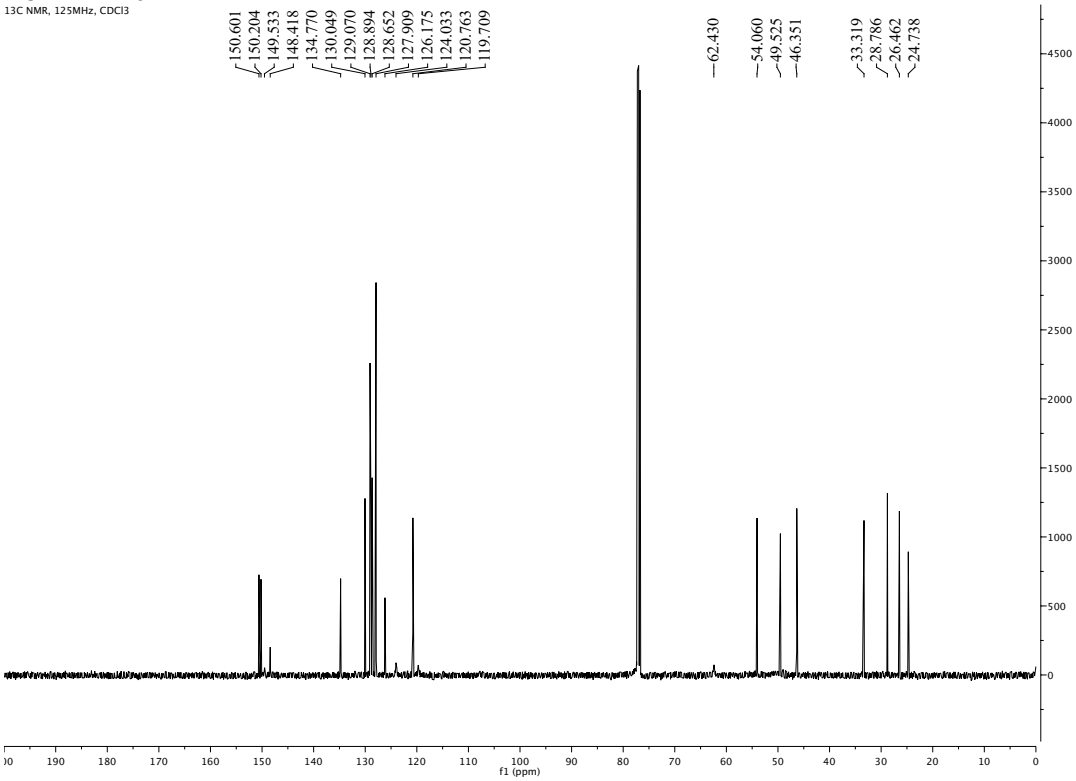


(1*S*,2*R*,4*S*,5*R*,9*R*)-[5-(1-benzyl-1H-1,2,3-triazol-4-yl)quinuclidin-2-yl]-(quinolin-4-yl)methanamine **4b**

^{1}H NMR 500 MHz

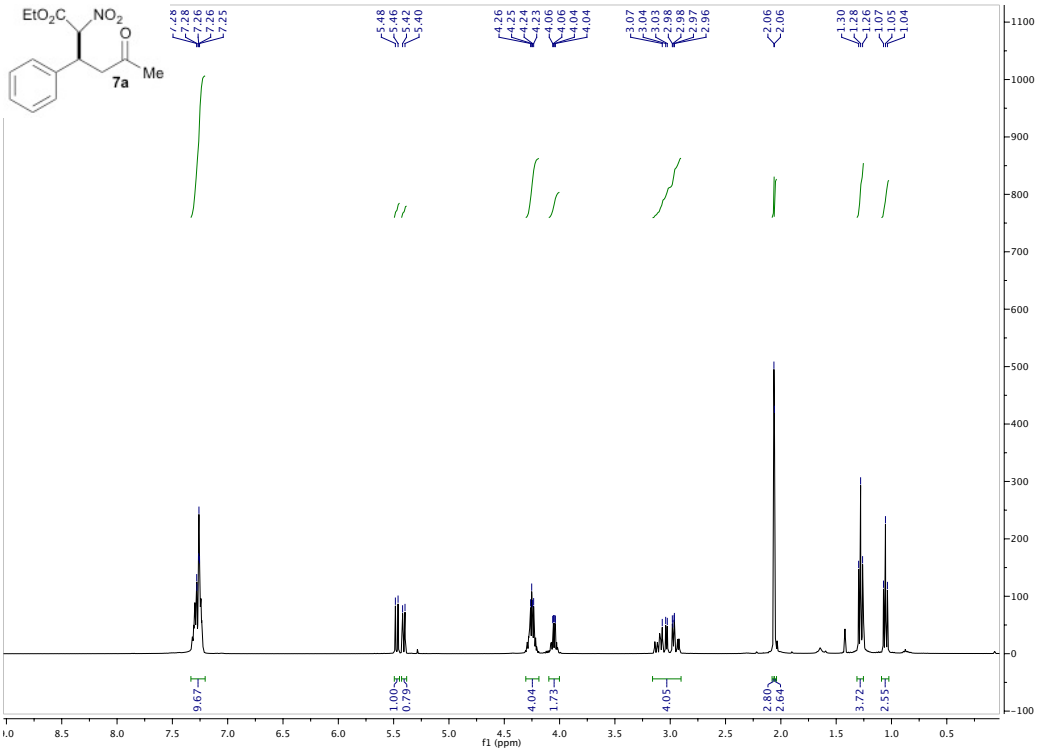


^{13}C NMR 126 MHz

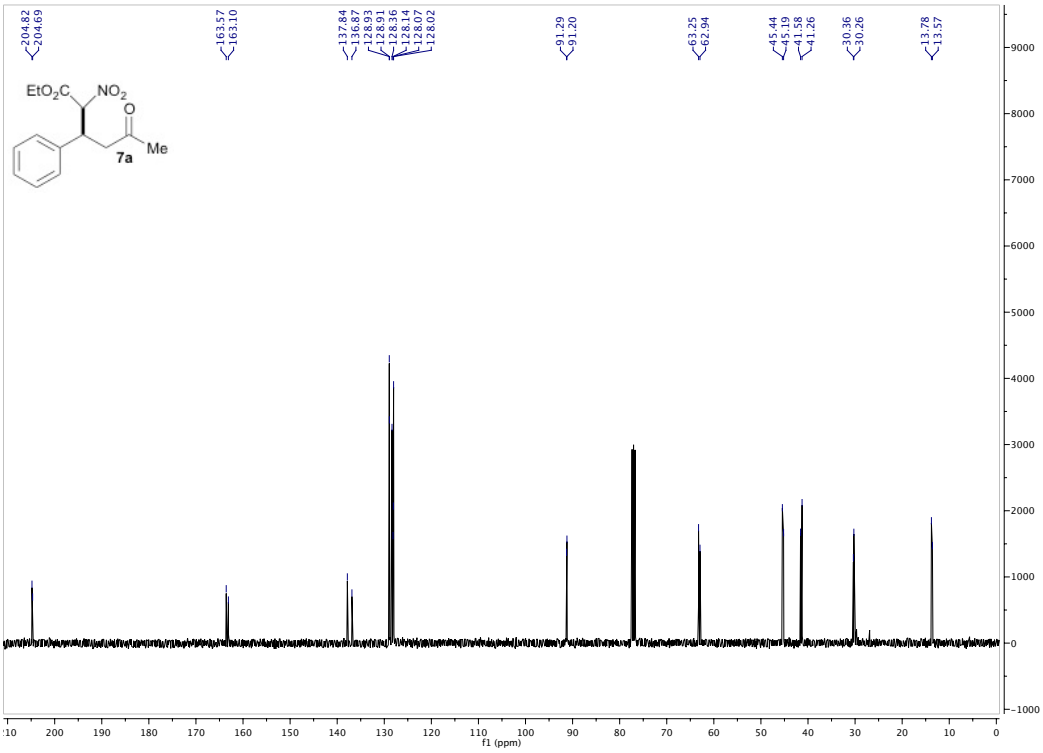


(3*S*)-Ethyl 2-nitro-5-oxo-3-phenylhexanoate **7a**

^{1}H NMR 400 MHz

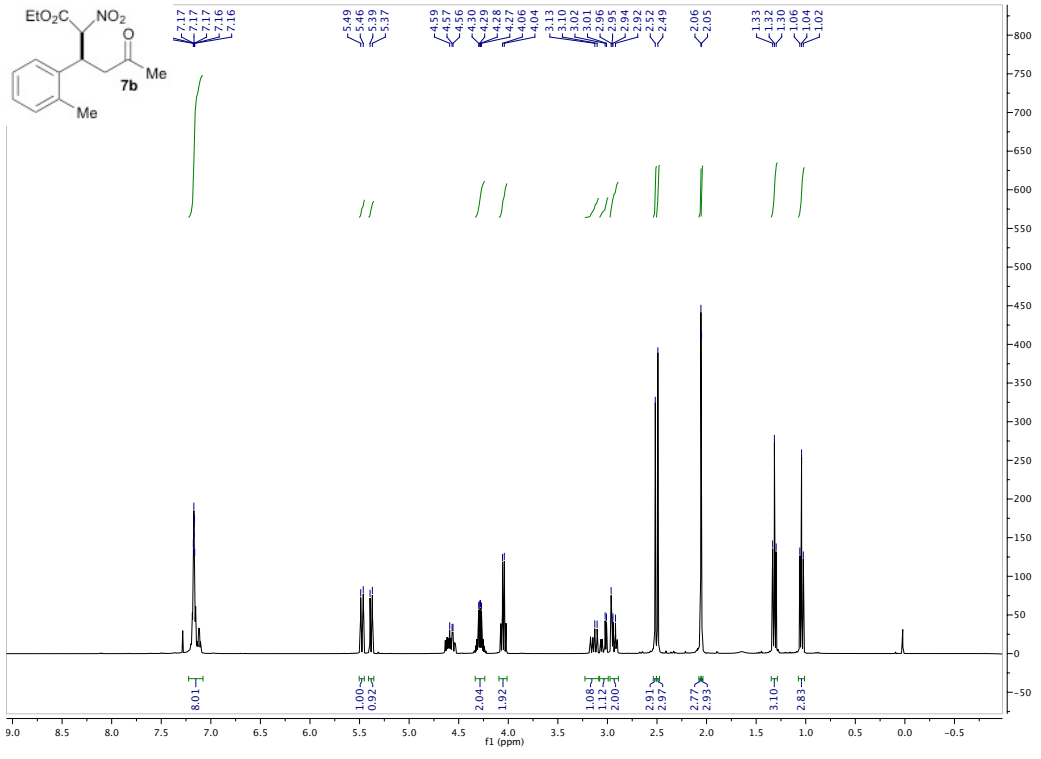


^{13}C NMR 101 MHz

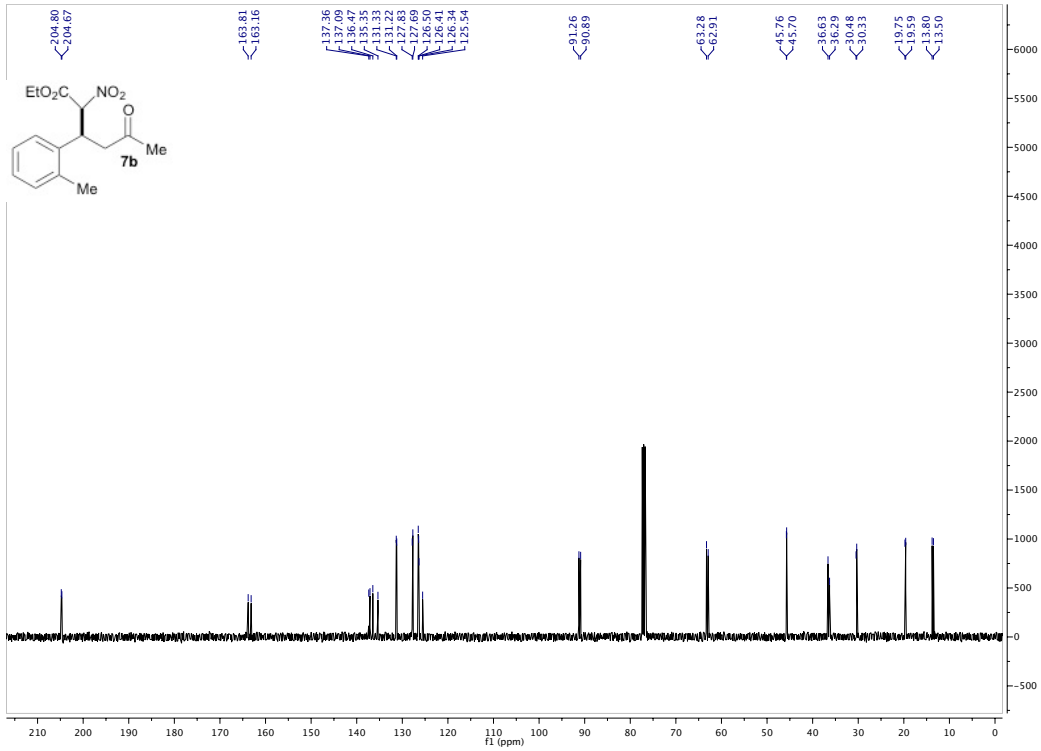


(3*S*)-Ethyl 2-nitro-5-oxo-3-(*o*-tolyl)hexanoate **7b**

^{1}H NMR 400 MHz

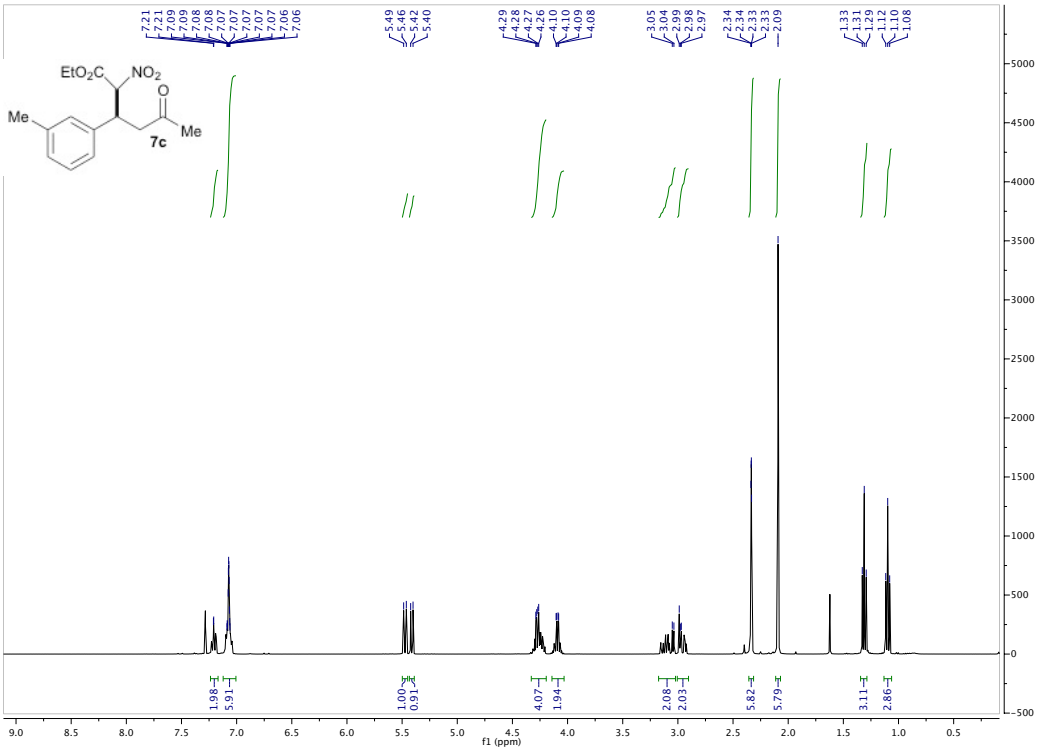


^{13}C NMR 101 MHz

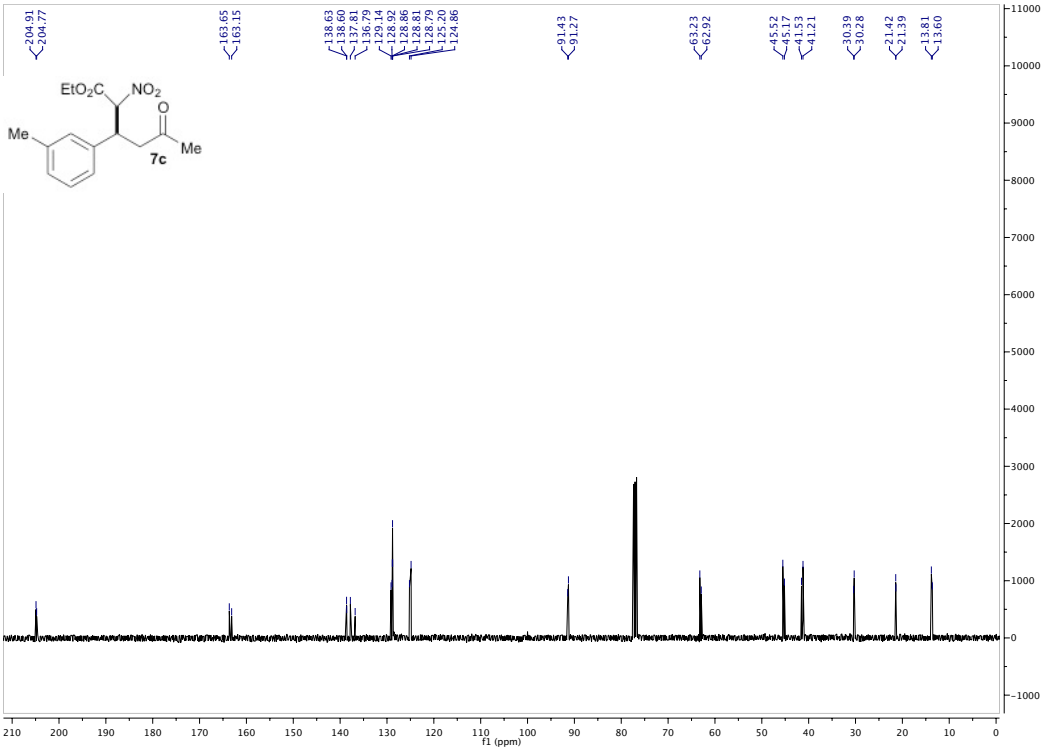


(3*S*)-Ethyl 2-nitro-5-oxo-3-(*m*-tolyl)hexanoate **7c**

^{1}H NMR 400 MHz

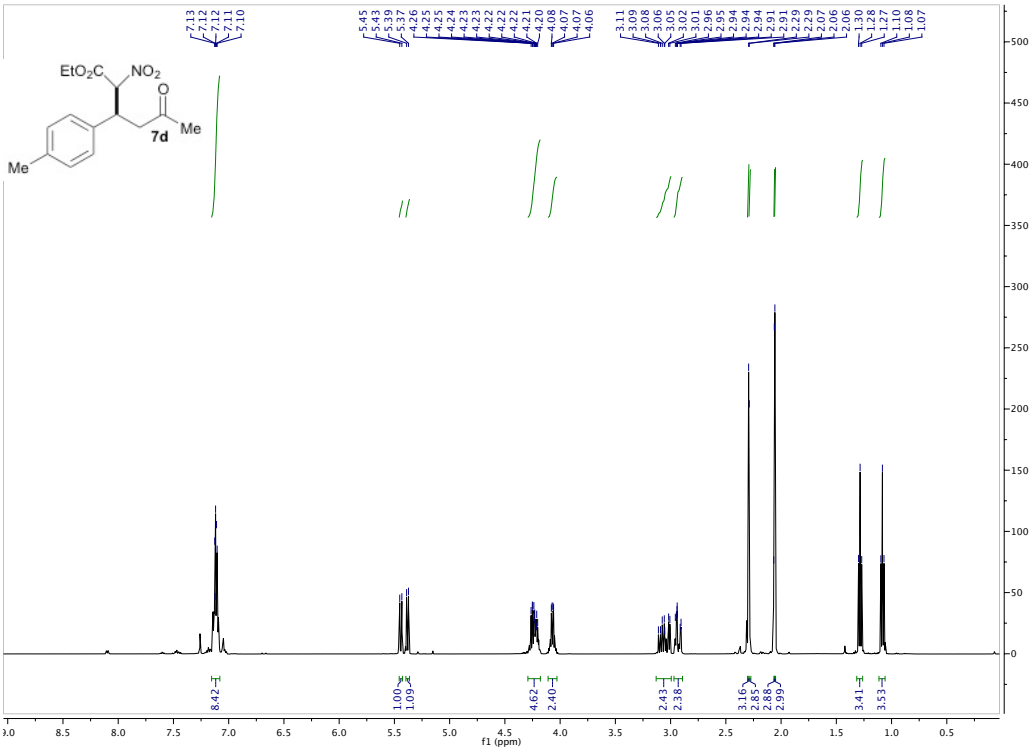


^{13}C NMR 101 MHz

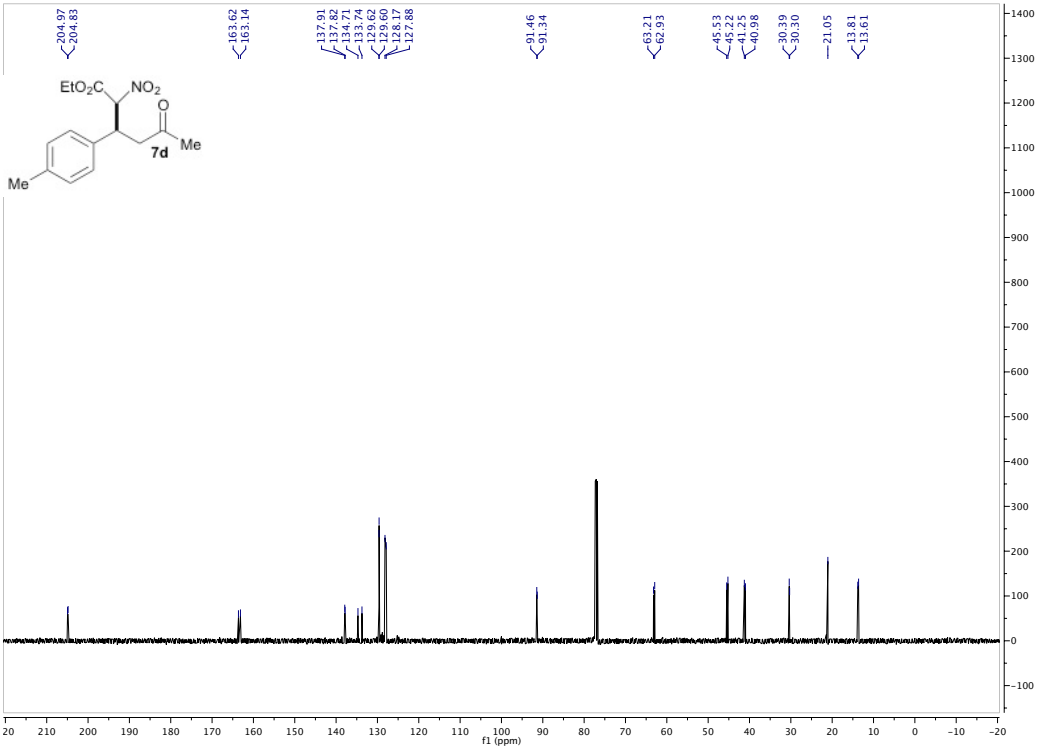


(3*S*)-Ethyl 2-nitro-5-oxo-3-(*p*-tolyl)hexanoate **7d**

^{1}H NMR 500 MHz

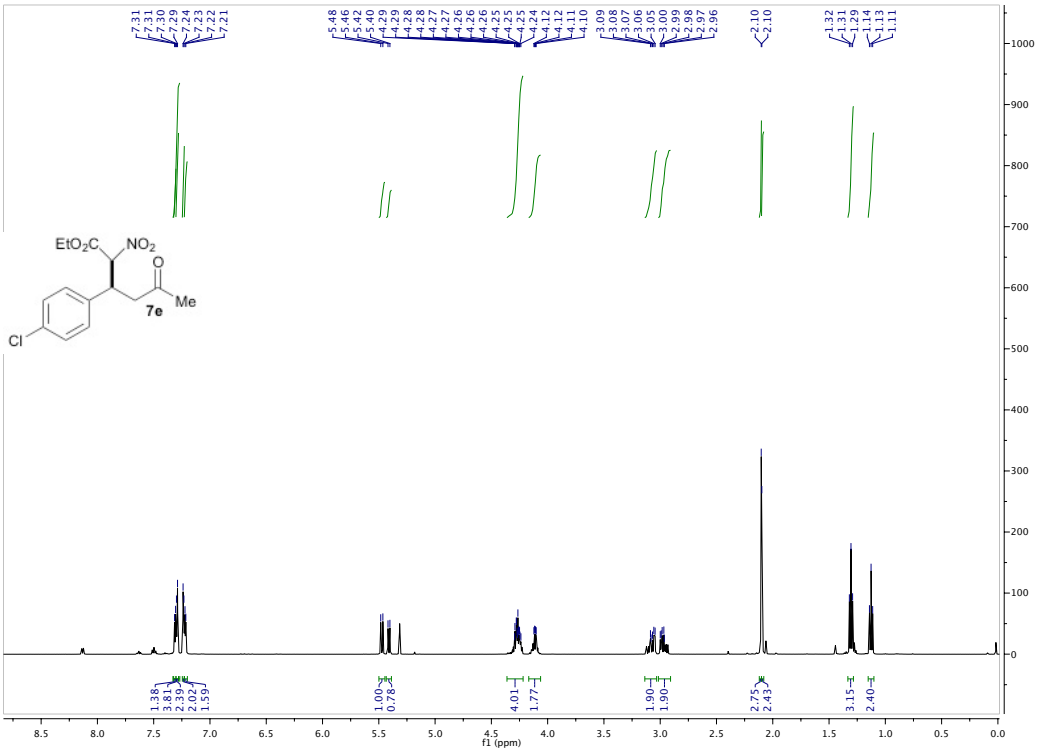


^{13}C NMR 126 MHz

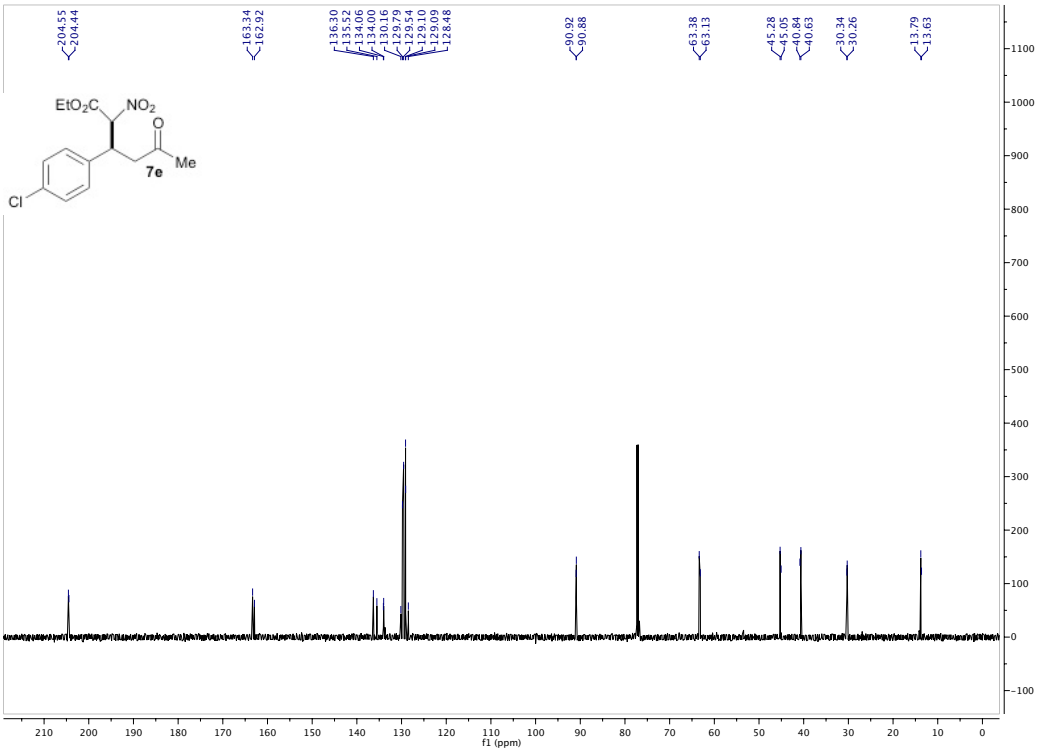


(3*S*)-Ethyl 3-(4-cyanophenyl)-2-nitro-5-oxohexanoate **7e**

^{1}H NMR 500 MHz

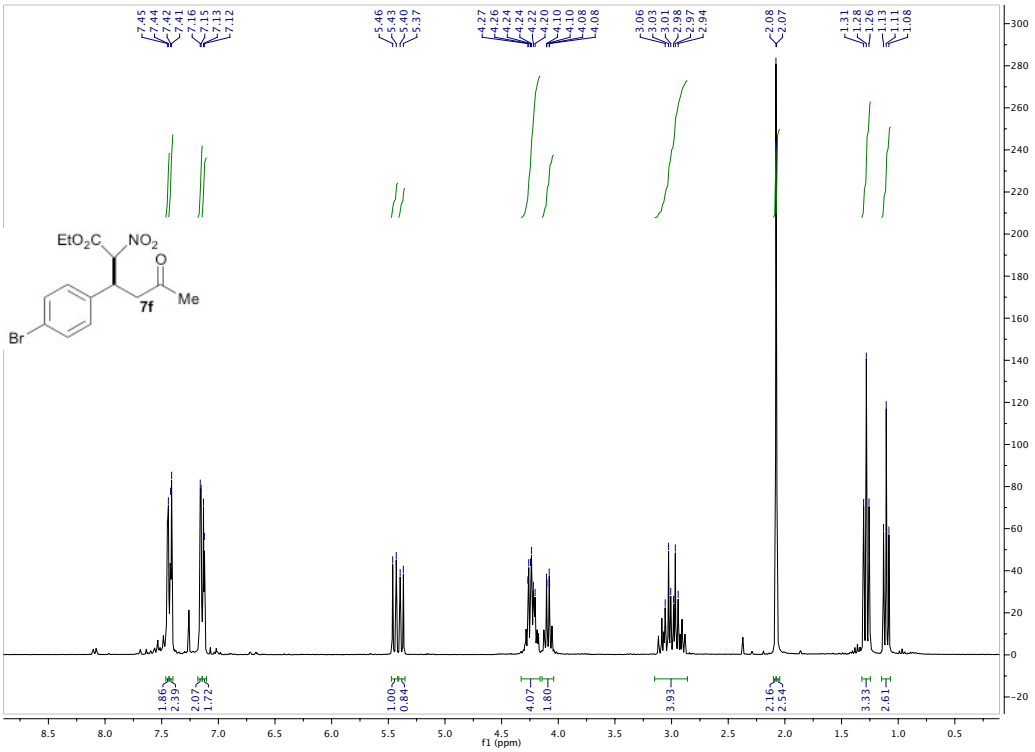


^{13}C NMR 126 MHz

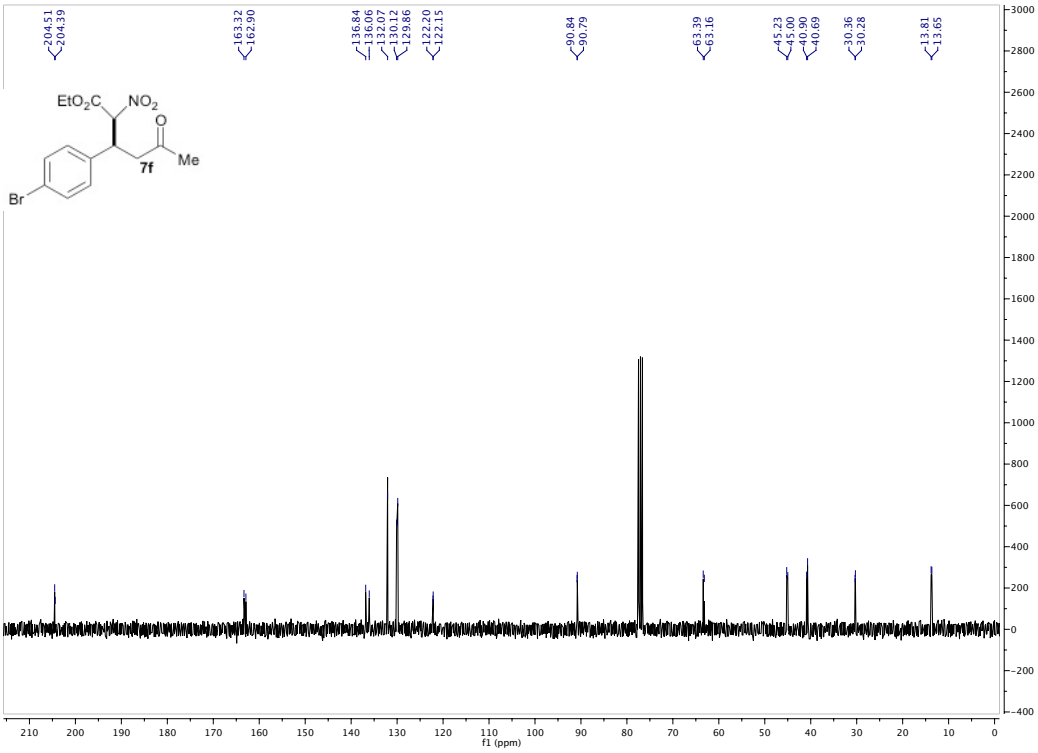


(3*S*)-Ethyl 3-(4-bromophenyl)-2-nitro-5-oxohexanoate **7f**

^{1}H NMR 300 MHz

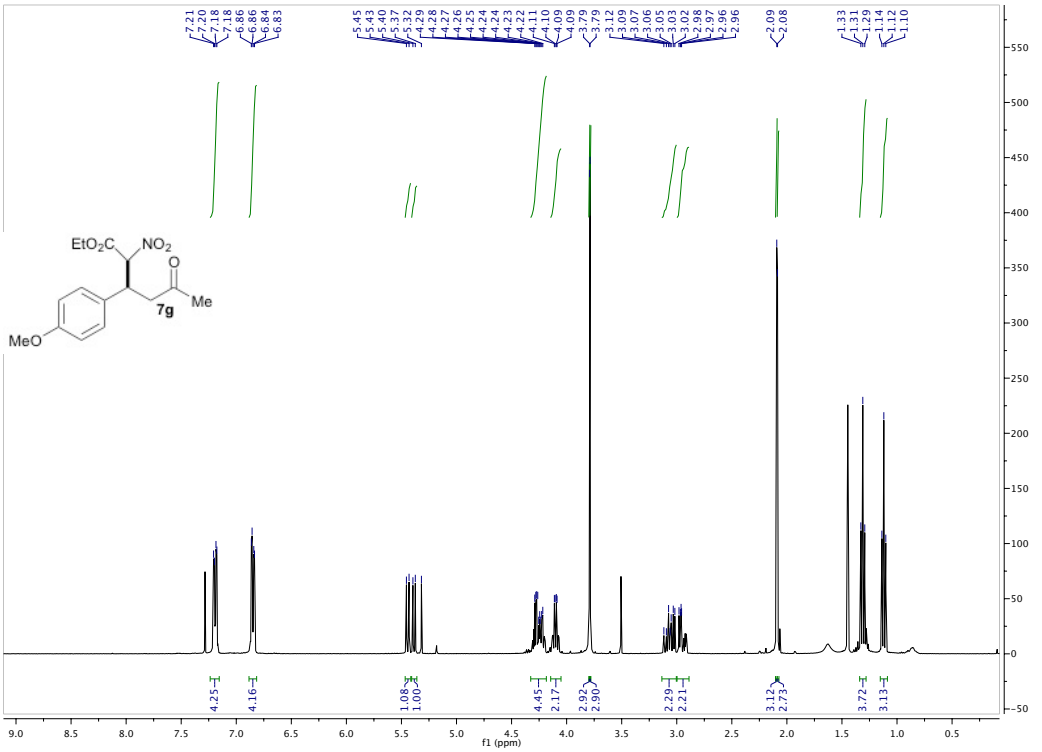


^{13}C NMR 75 MHz

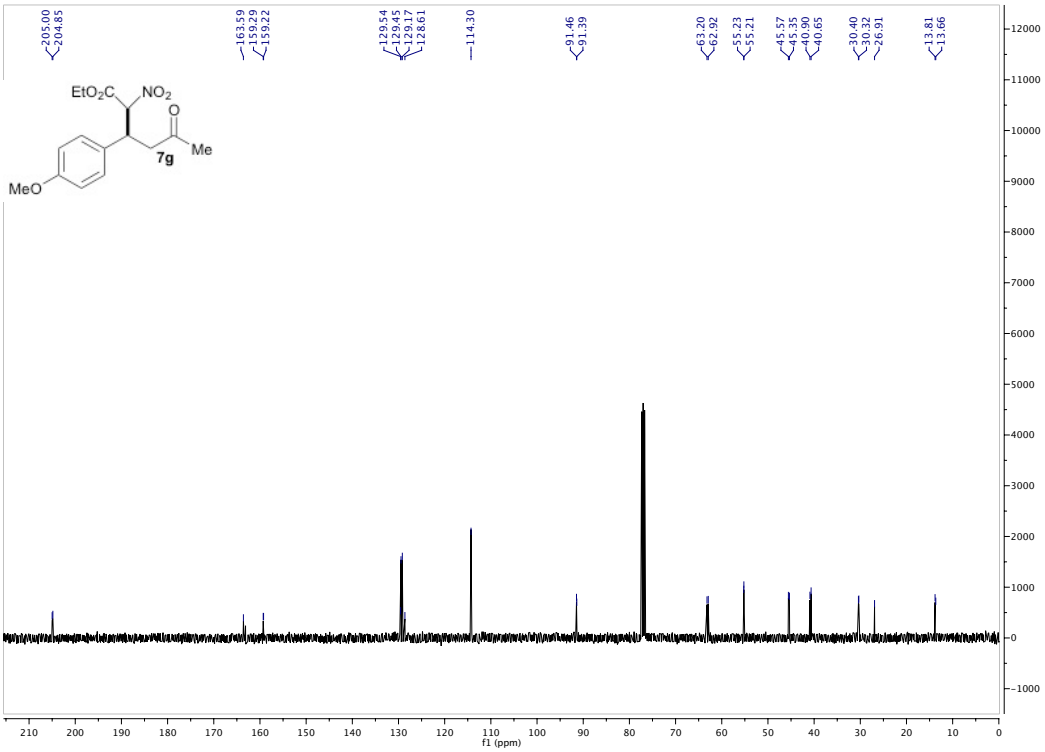


(3*S*)-Ethyl 3-(4-methoxyphenyl)-2-nitro-5-oxohexanoate **7g**

^{1}H NMR 400 MHz

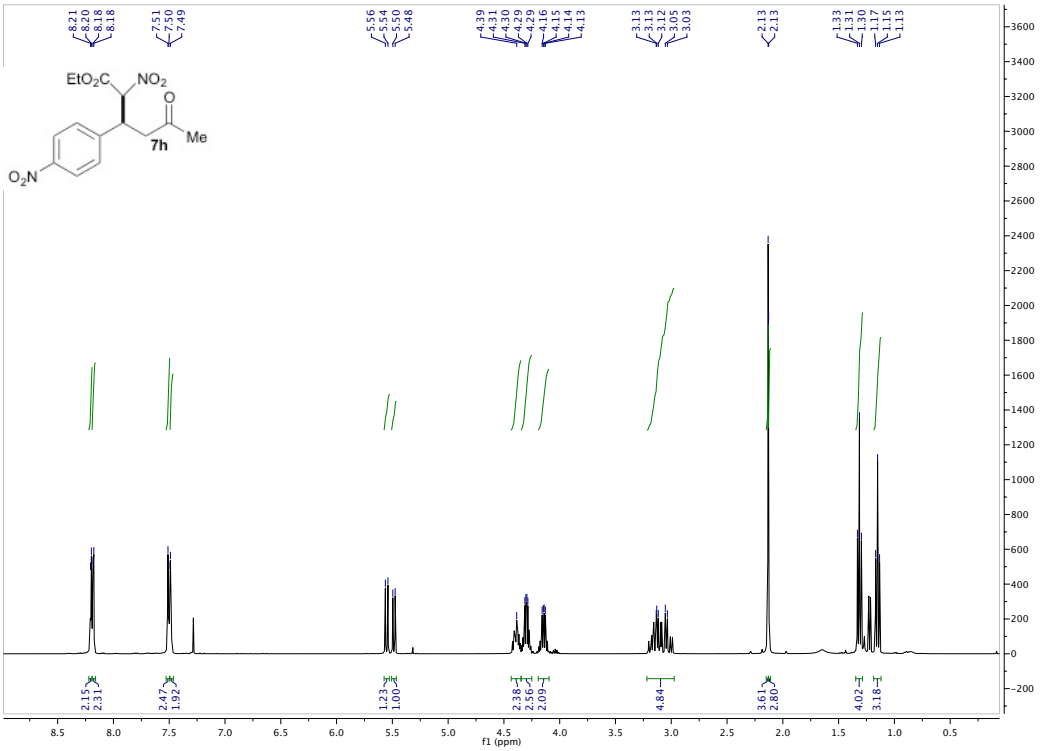


^{13}C NMR 101 MHz

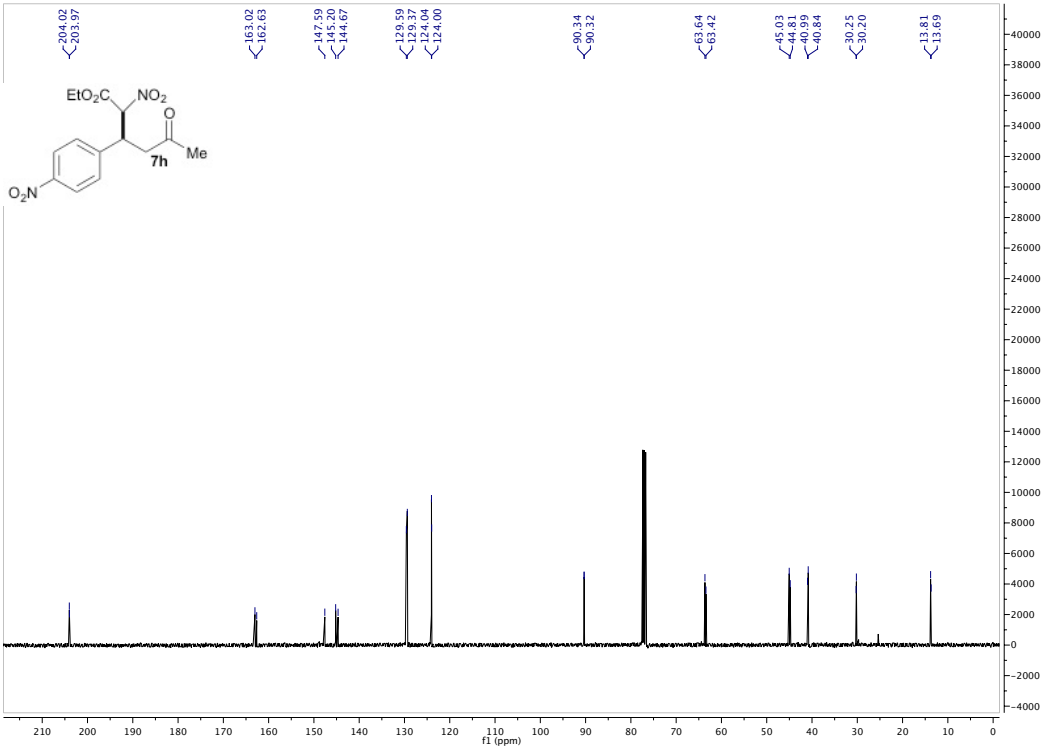


(3*S*)-Ethyl 2-nitro-3-(4-nitrophenyl)-5-oxohexanoate **7h**

^{1}H NMR 400 MHz

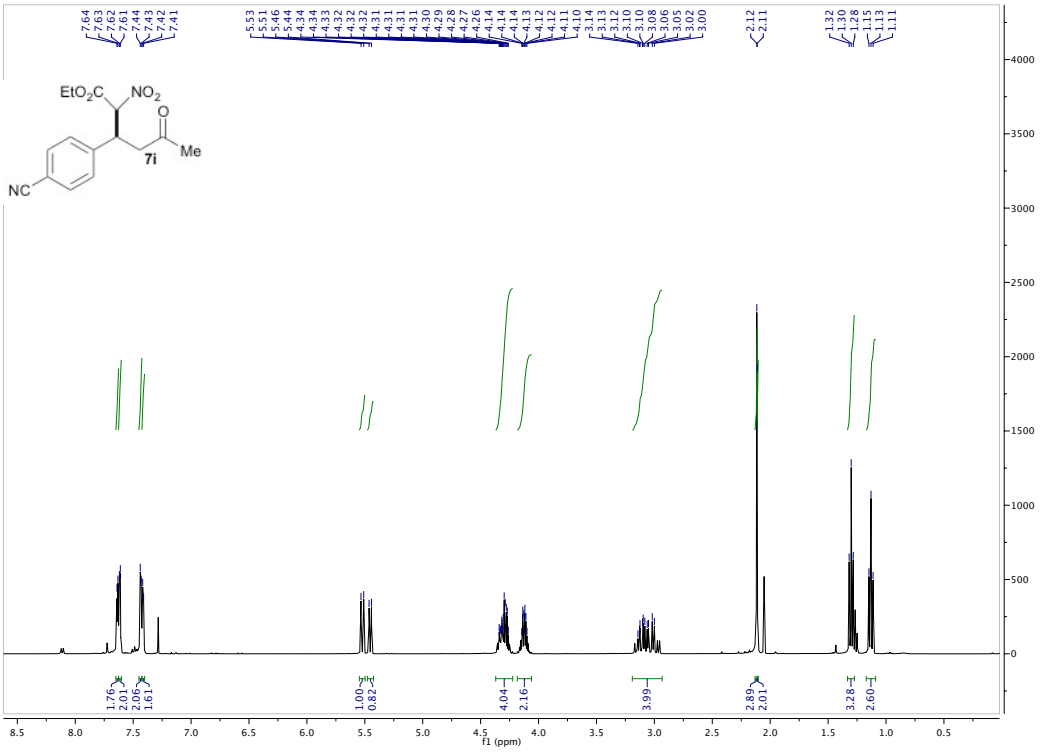


^{13}C NMR 101 MHz

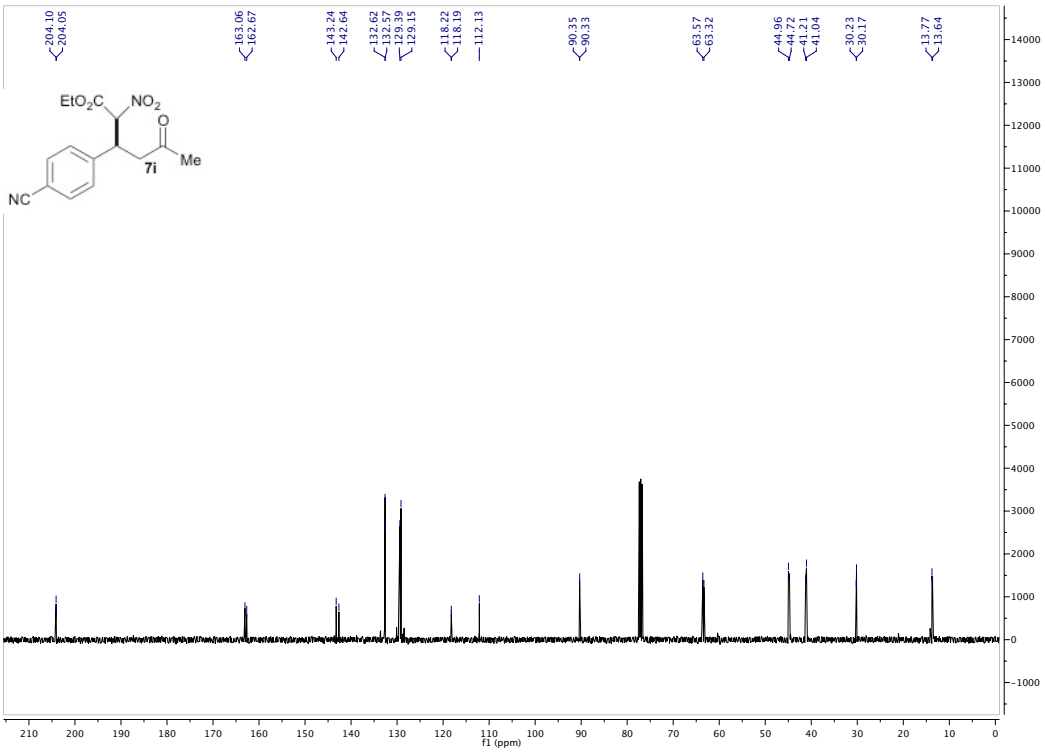


(3*S*)-Ethyl 3-(4-cyanophenyl)-2-nitro-5-oxohexanoate **7i**

^{1}H NMR 400 MHz

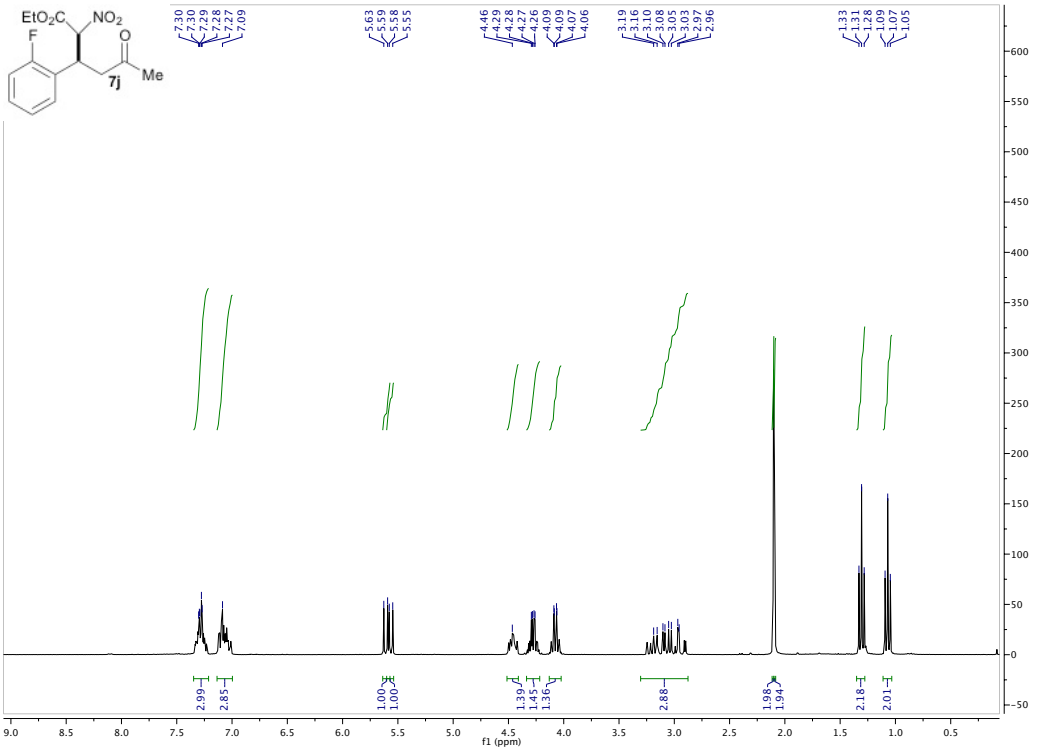


^{13}C NMR 101 MHz

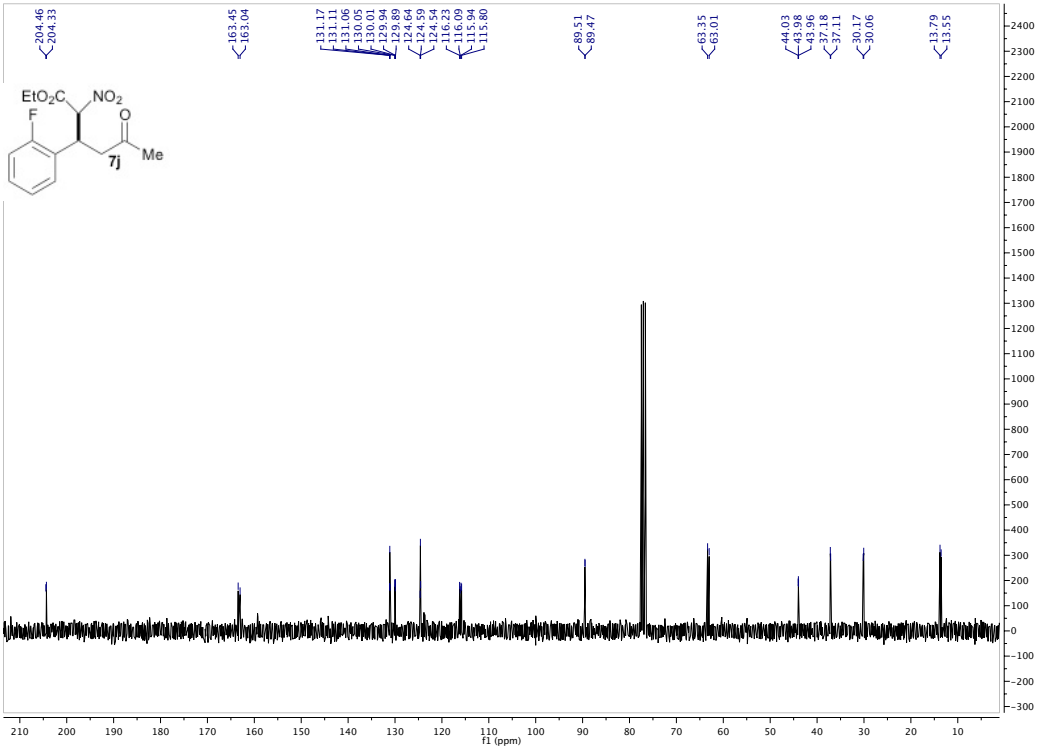


(3*S*)-Ethyl 3-(2-fluorophenyl)-2-nitro-5-oxohexanoate **7j**

^{1}H NMR 300 MHz

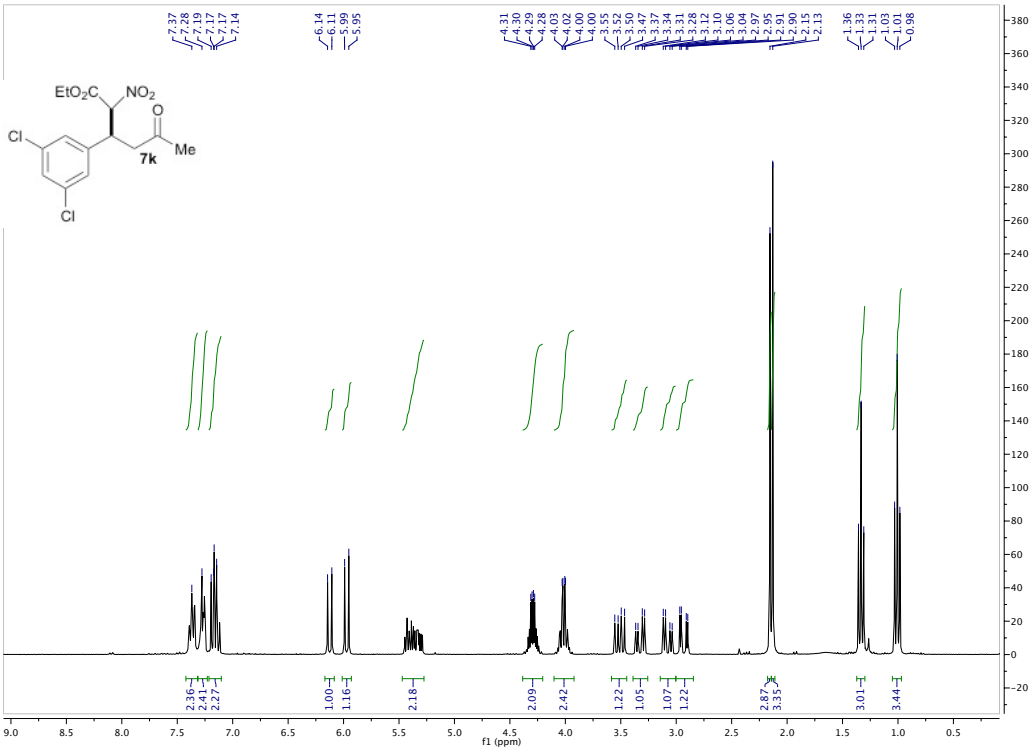


^{13}C NMR 75 MHz

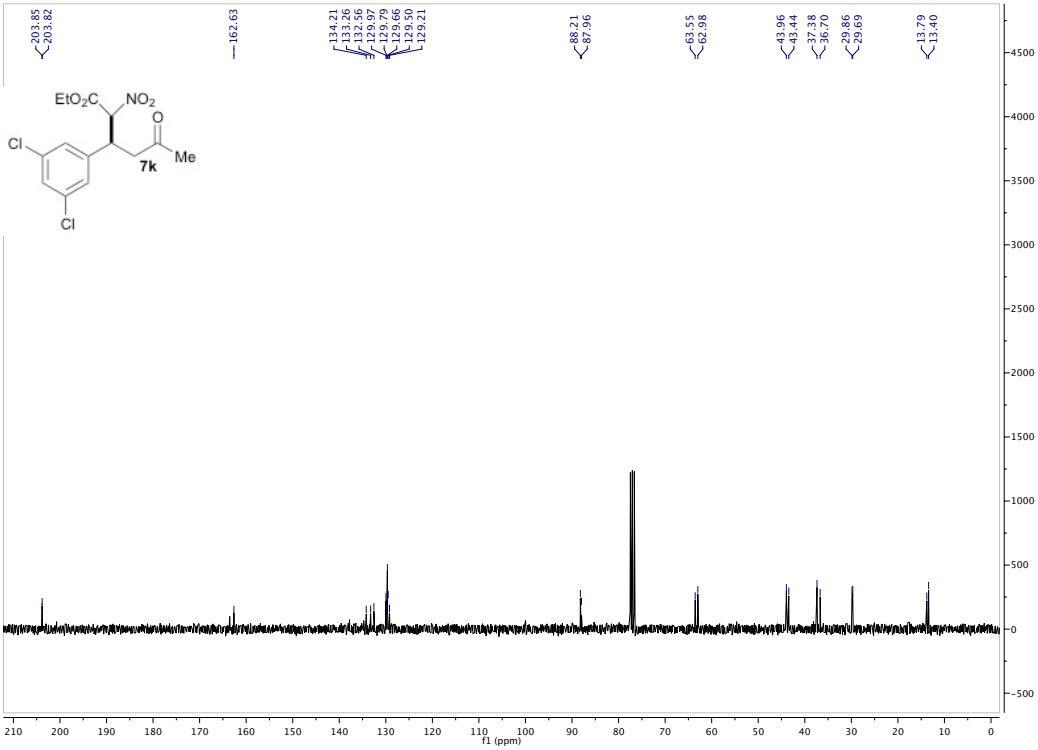


(3*S*)-Ethyl 3-(3,5-dichlorophenyl)-2-nitro-5-oxohexanoate **7k**

^{1}H NMR 300 MHz

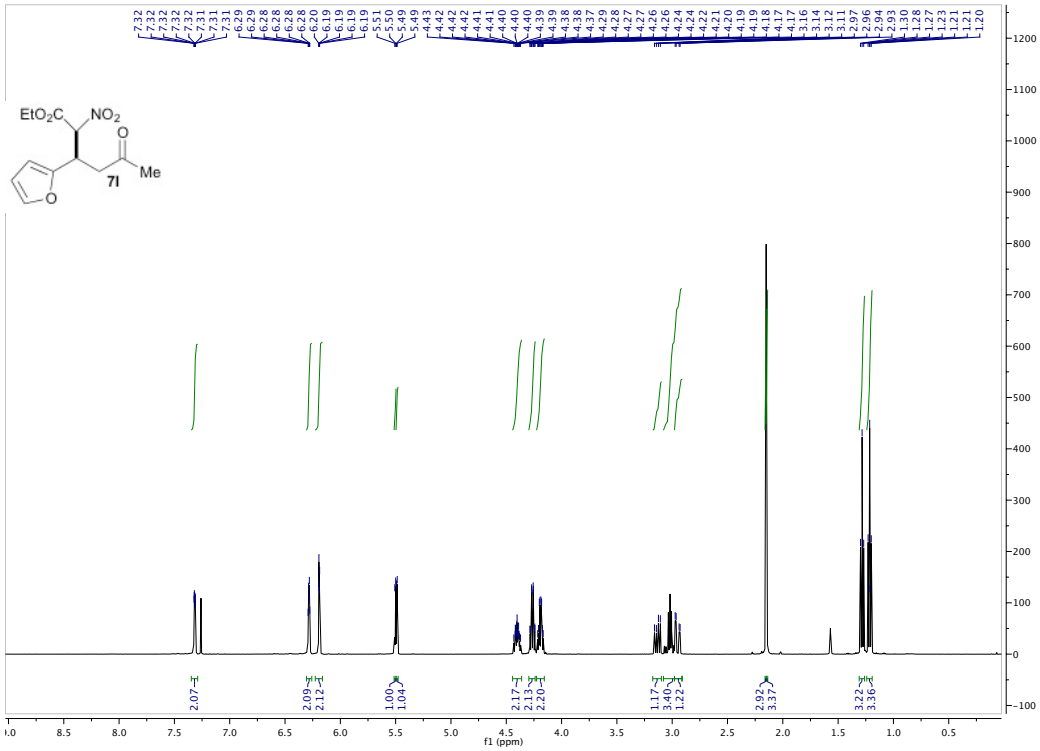


^{13}C NMR 75 MHz

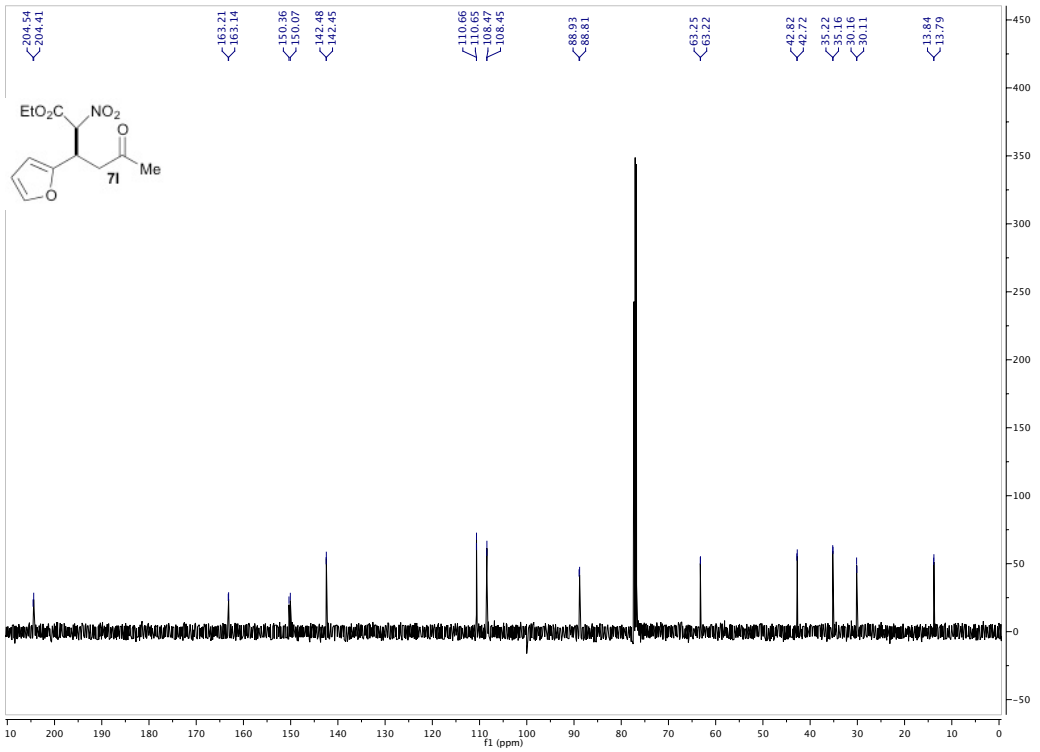


(3*R*)-Ethyl 3-(furan-2-yl)-2-nitro-5-oxohexanoate **7l**

^{1}H NMR 500 MHz

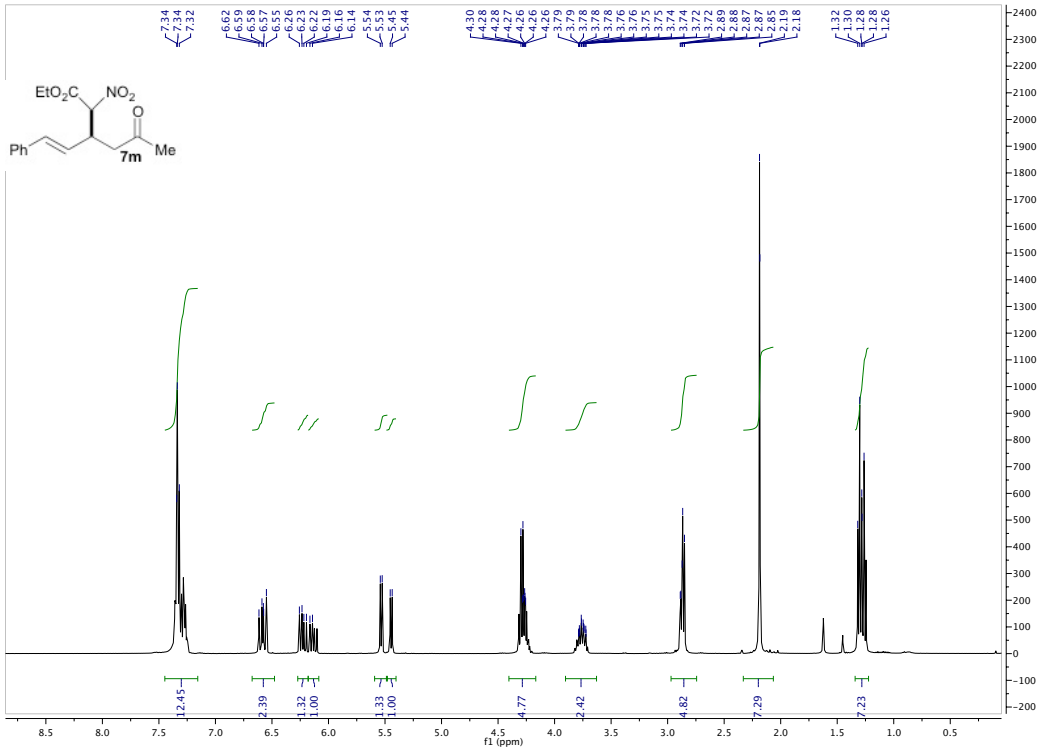


^{13}C NMR 126 MHz

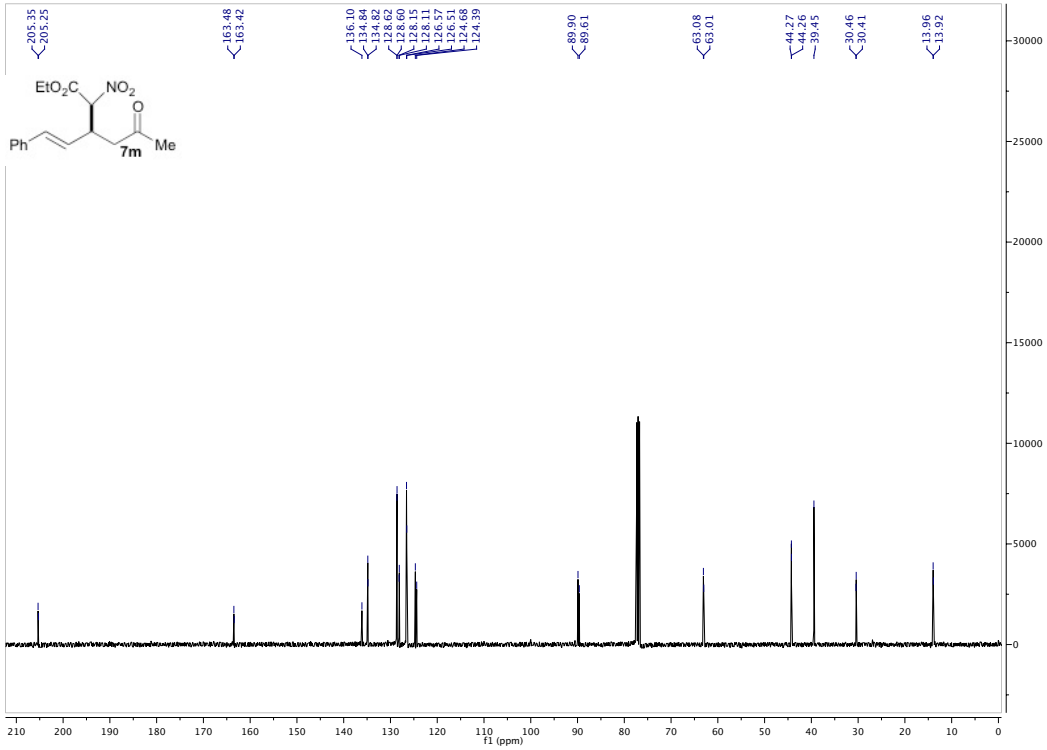


(3*S*)-Ethyl 2-nitro-5-oxo-3-((*E*)-styryl)hexanoate **7m**

^{1}H NMR 400 MHz

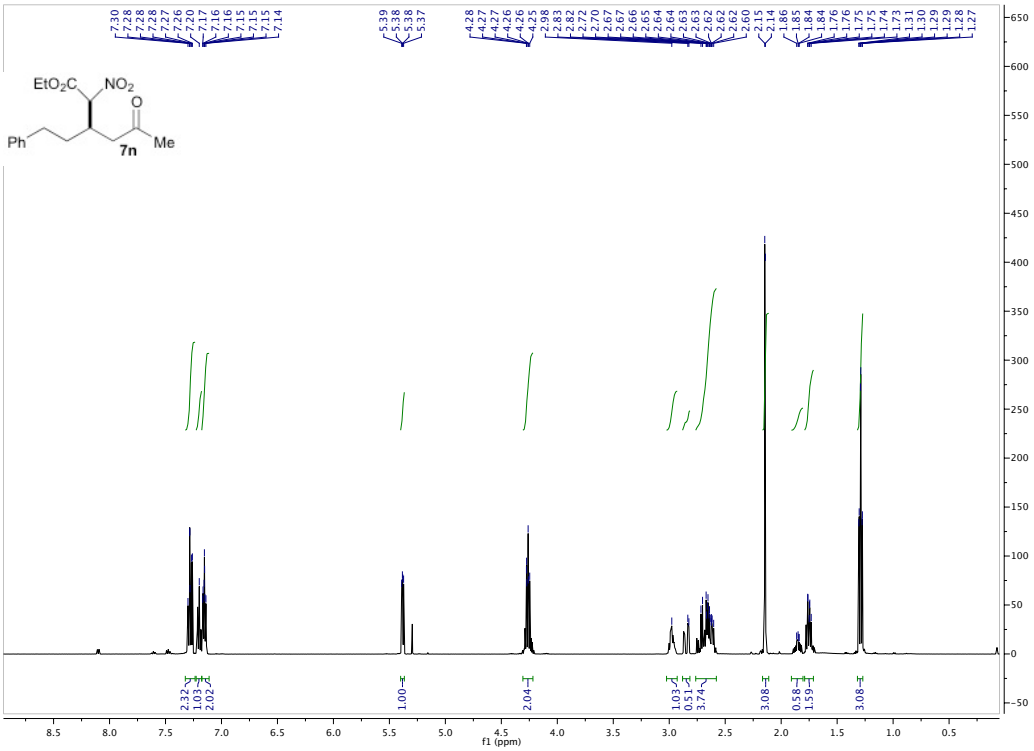


^{13}C NMR 101 MHz

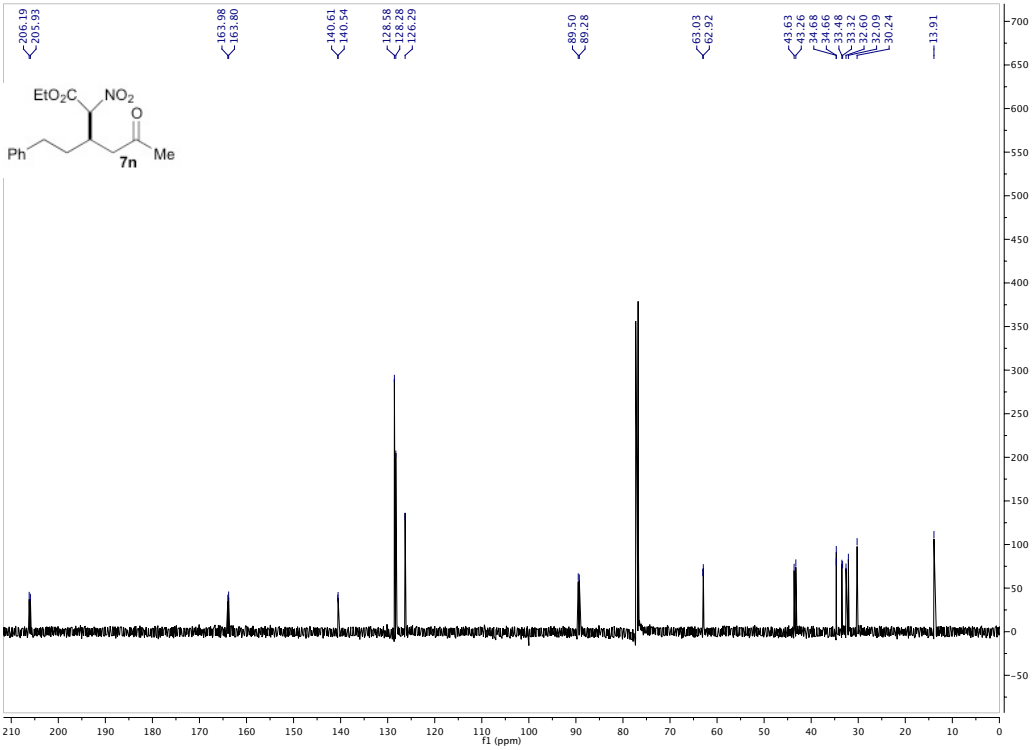


(3*R*)-Ethyl 2-nitro-5-oxo-3-phenethylhexanoate **7n**

^{1}H NMR 500 MHz

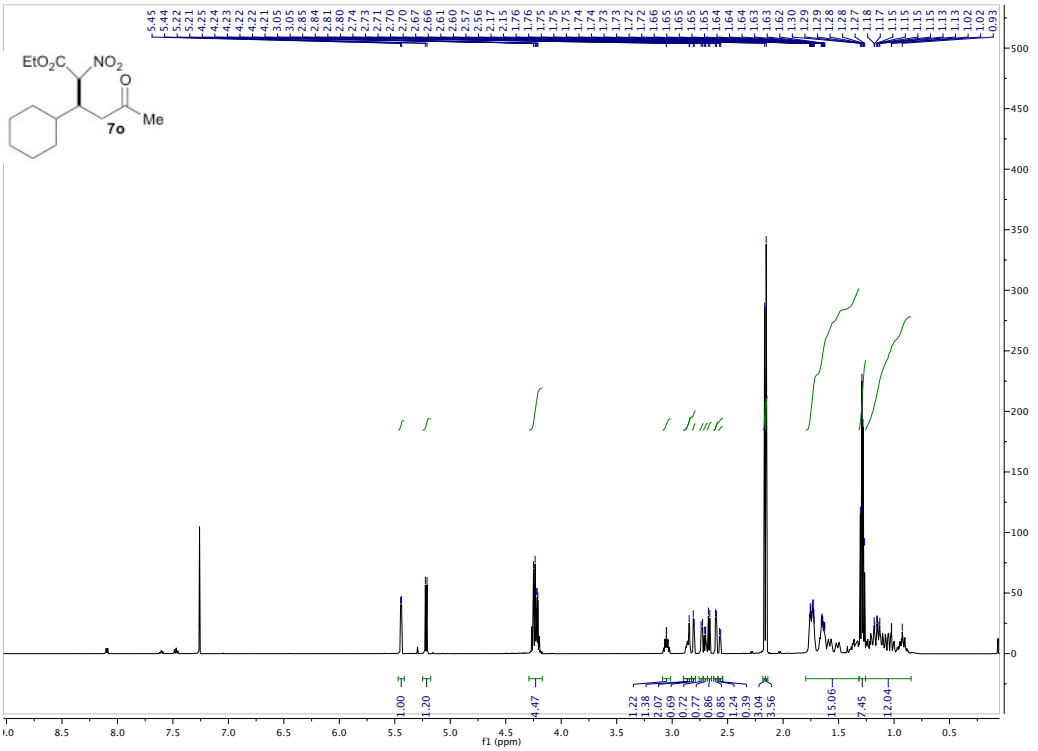


^{13}C NMR 126 MHz

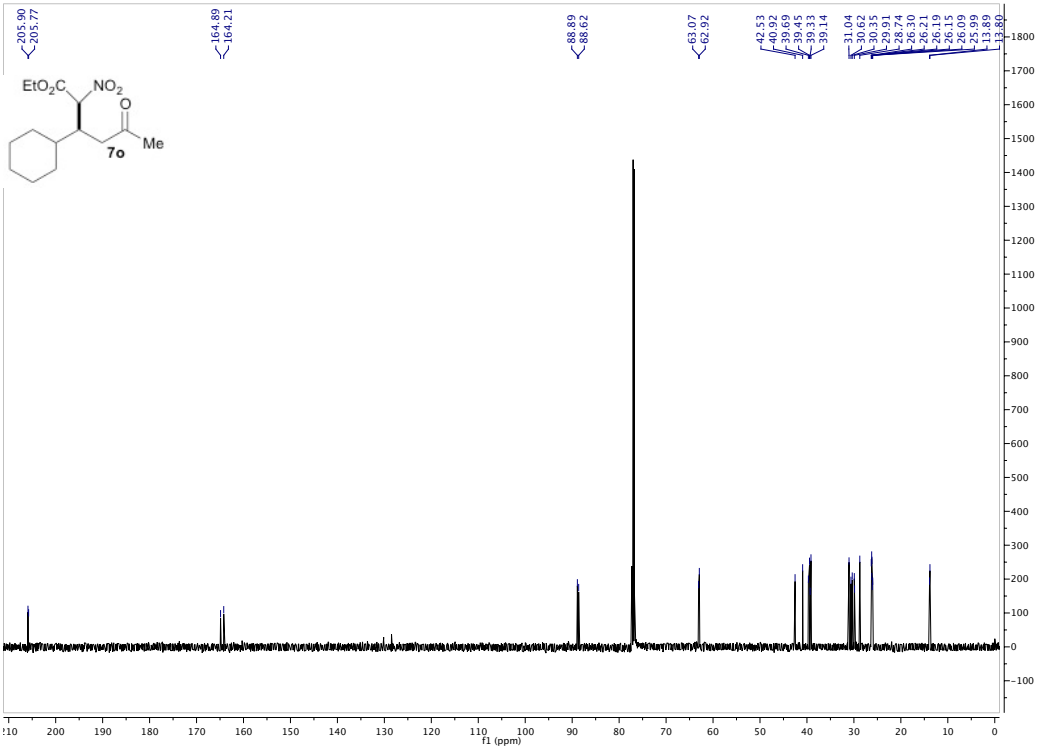


(3*S*)-Ethyl 3-cyclohexyl-2-nitro-5-oxohexanoate **7o**

^{1}H NMR 500 MHz

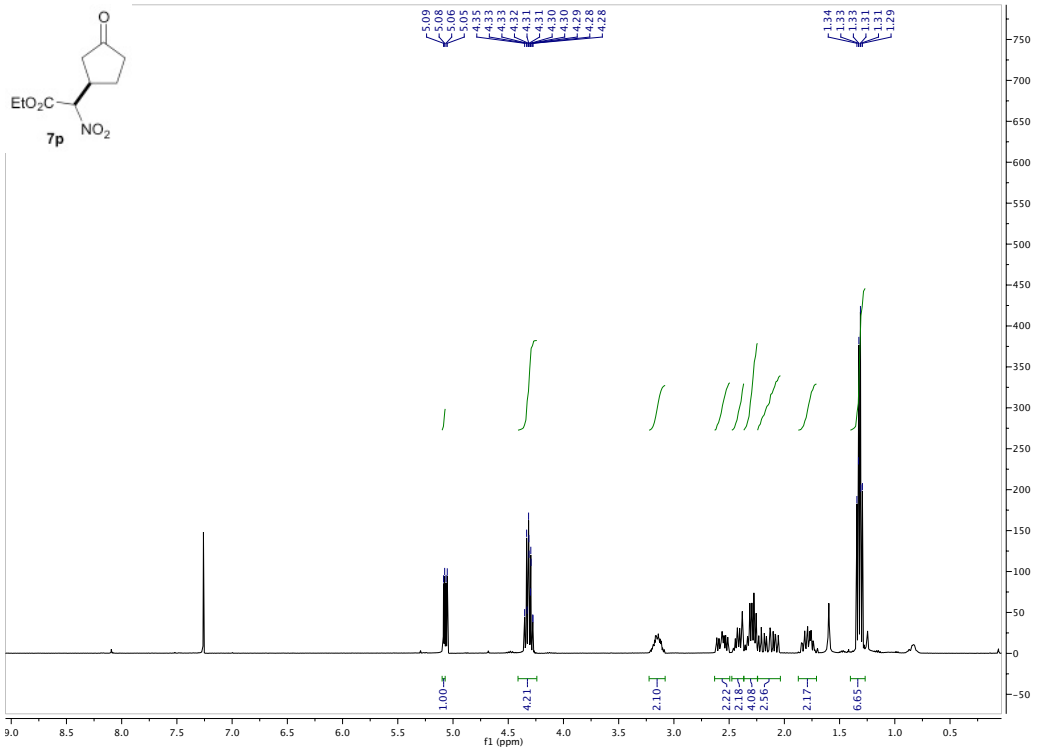


^{13}C NMR 126 MHz

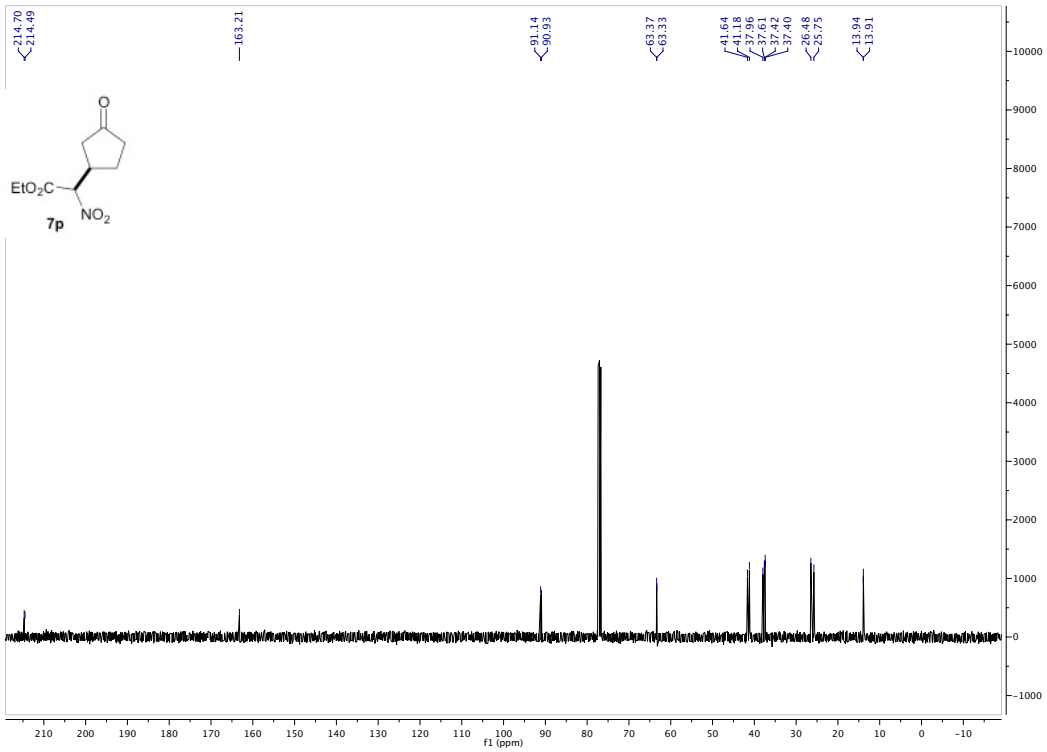


(*S*)-Ethyl 2-nitro-2-((*R*)-3-oxocyclopentyl)acetate **7p**

^{1}H NMR 400 MHz

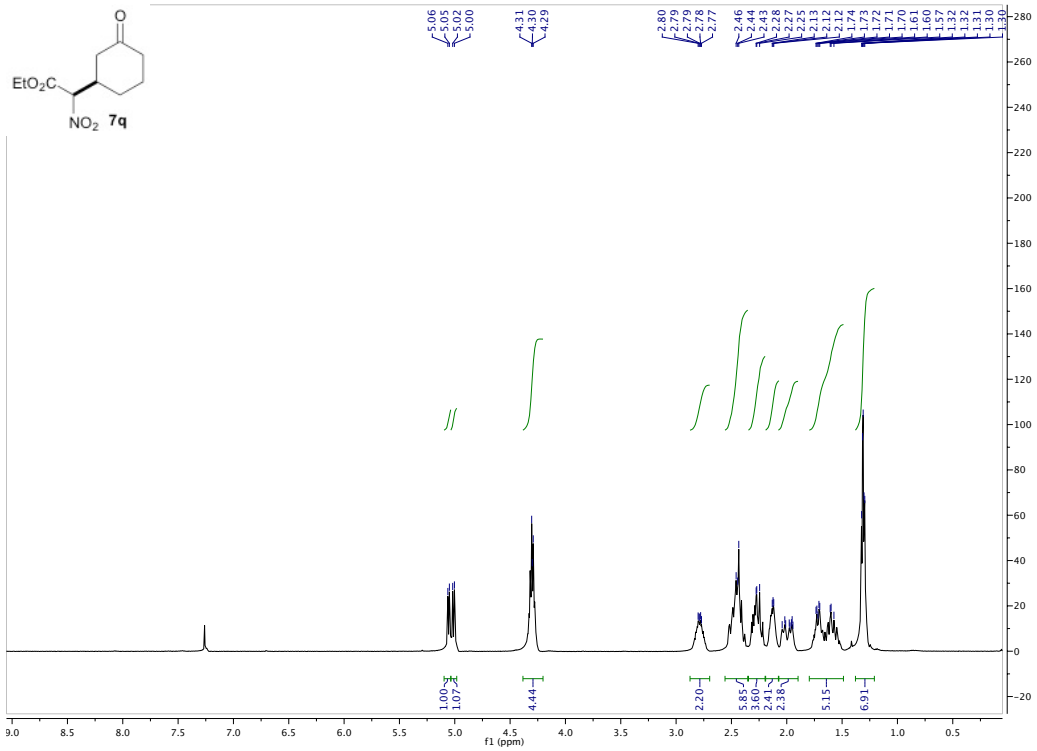


^{13}C NMR 101 MHz

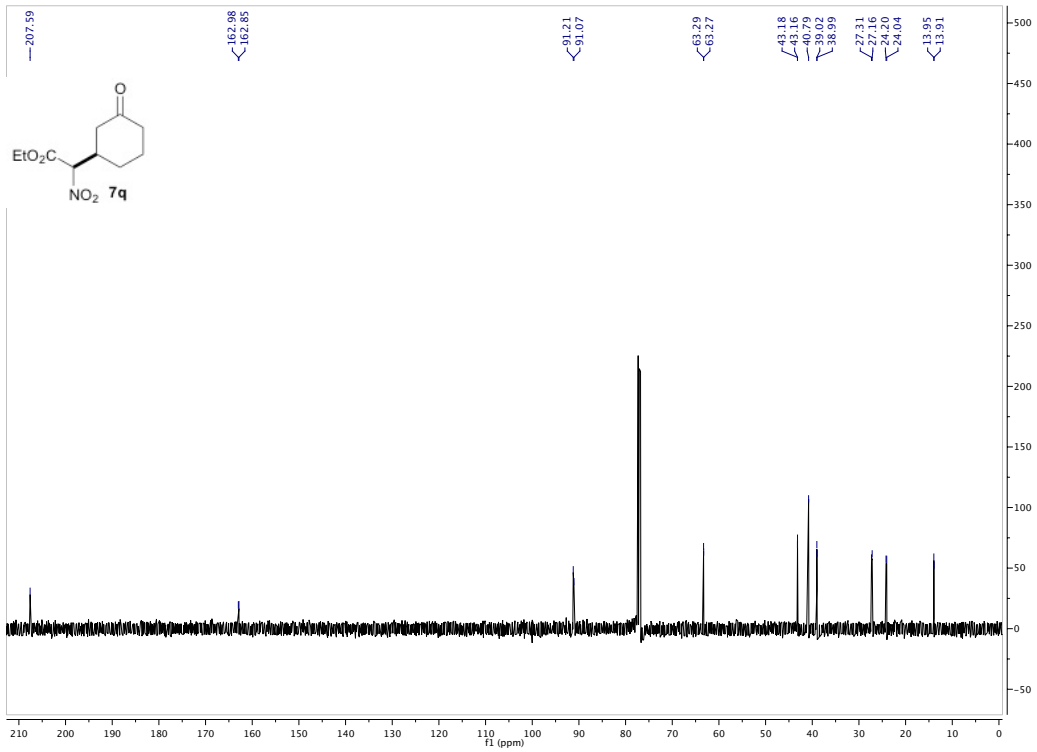


(*S*)-Ethyl 2-nitro-2-((*R*)-3-oxocyclohexyl)acetate **7q**

^{1}H NMR 500 MHz

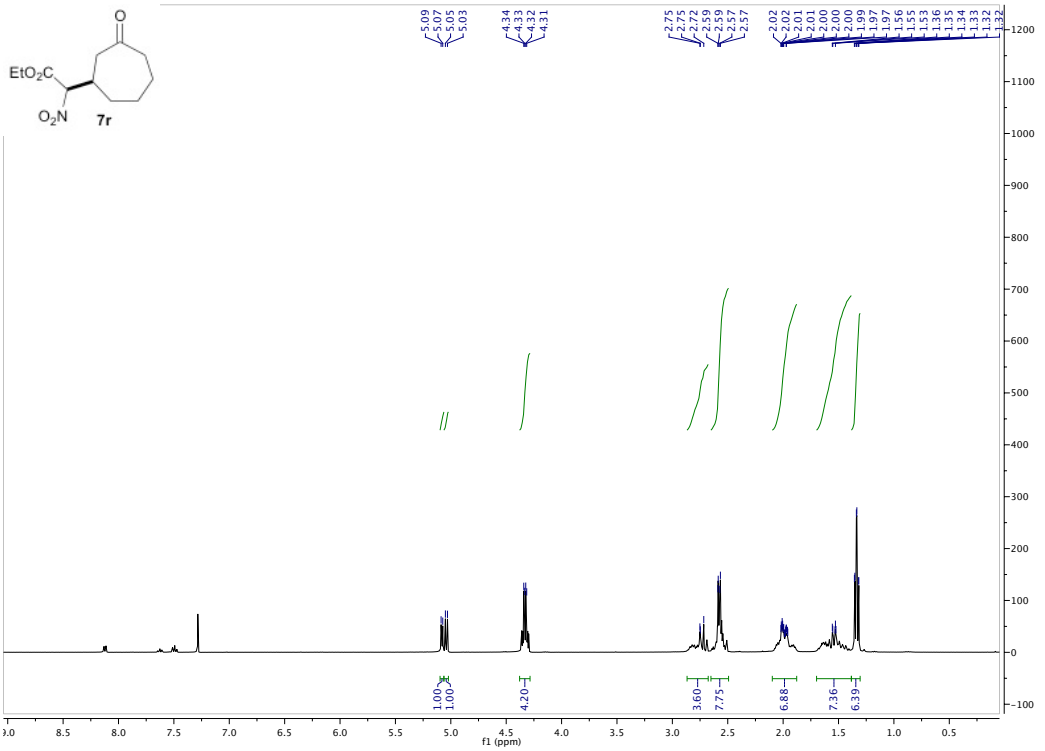


^{13}C NMR 126 MHz

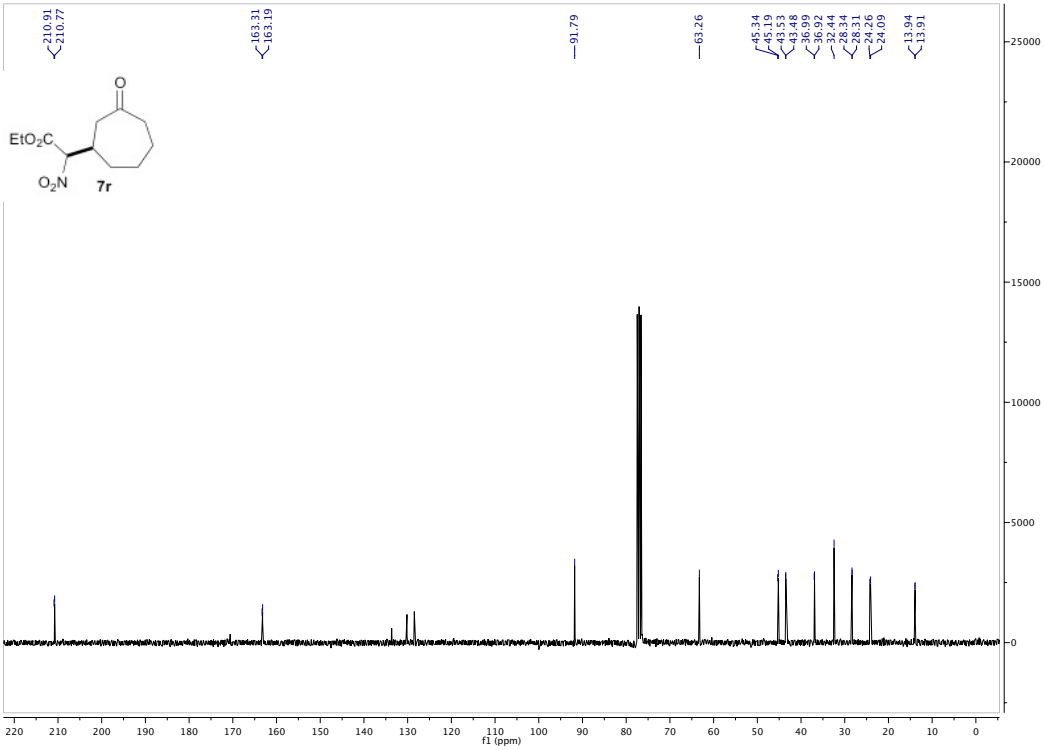


(*S*)-Ethyl 2-nitro-2-((*R*)-3-oxocycloheptyl)acetate **7r**

^{1}H NMR 400 MHz

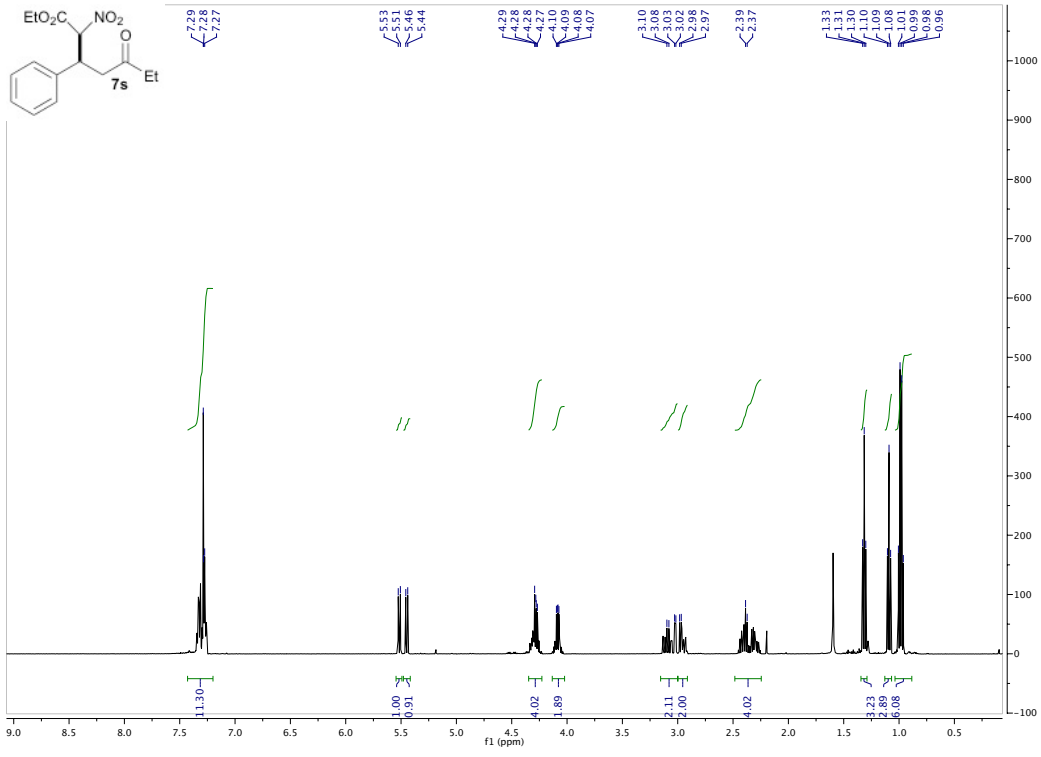


^{13}C NMR 101 MHz

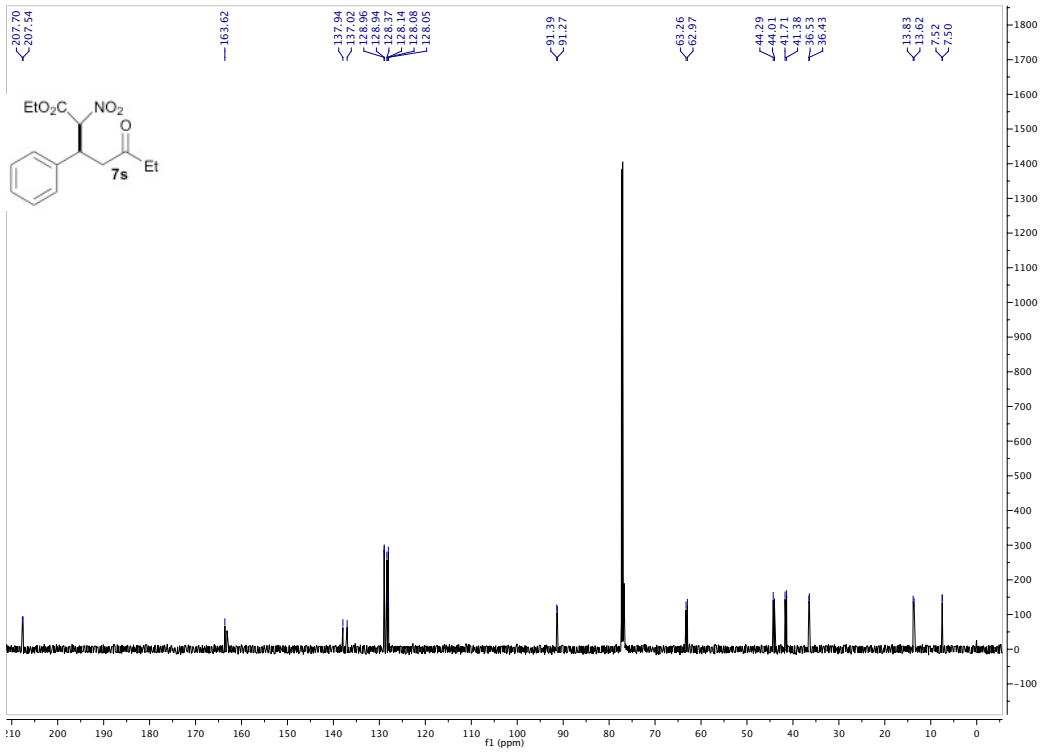


(3*S*)-Ethyl 2-nitro-5-oxo-3-phenylheptanoate **7s**

^{1}H NMR 500 MHz

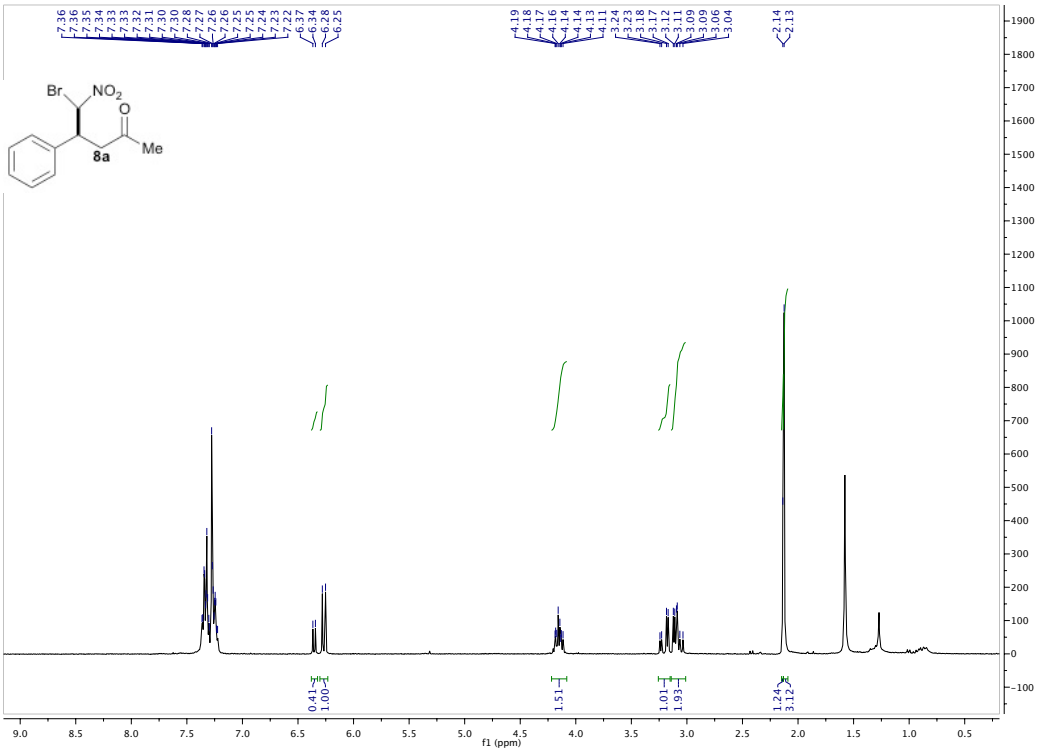


^{13}C NMR 126 MHz

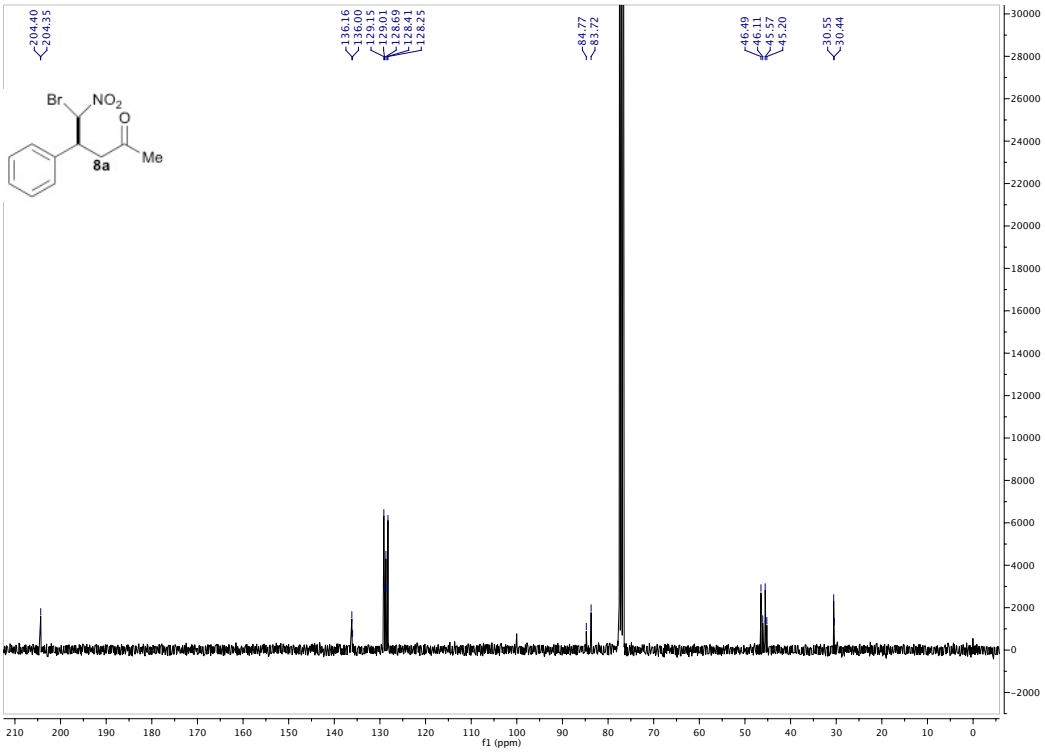


(4*S*)-5-Bromo-5-nitro-4-phenylpentan-2-one **8a**

^{1}H NMR 400 MHz

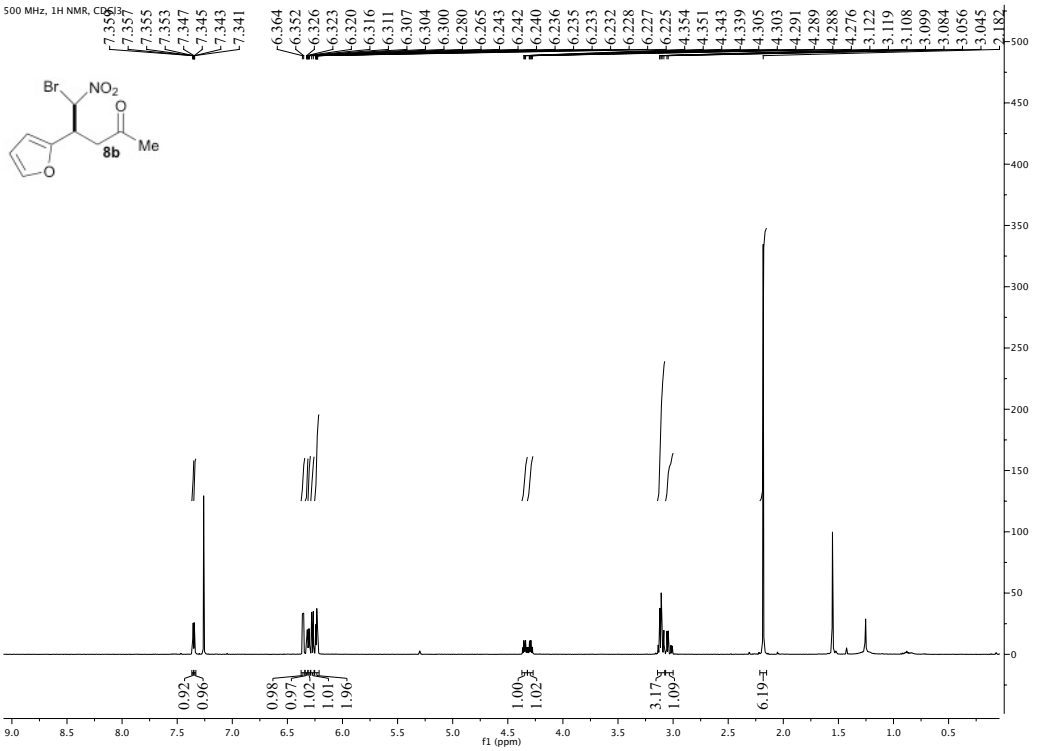


^{13}C NMR 101 MHz

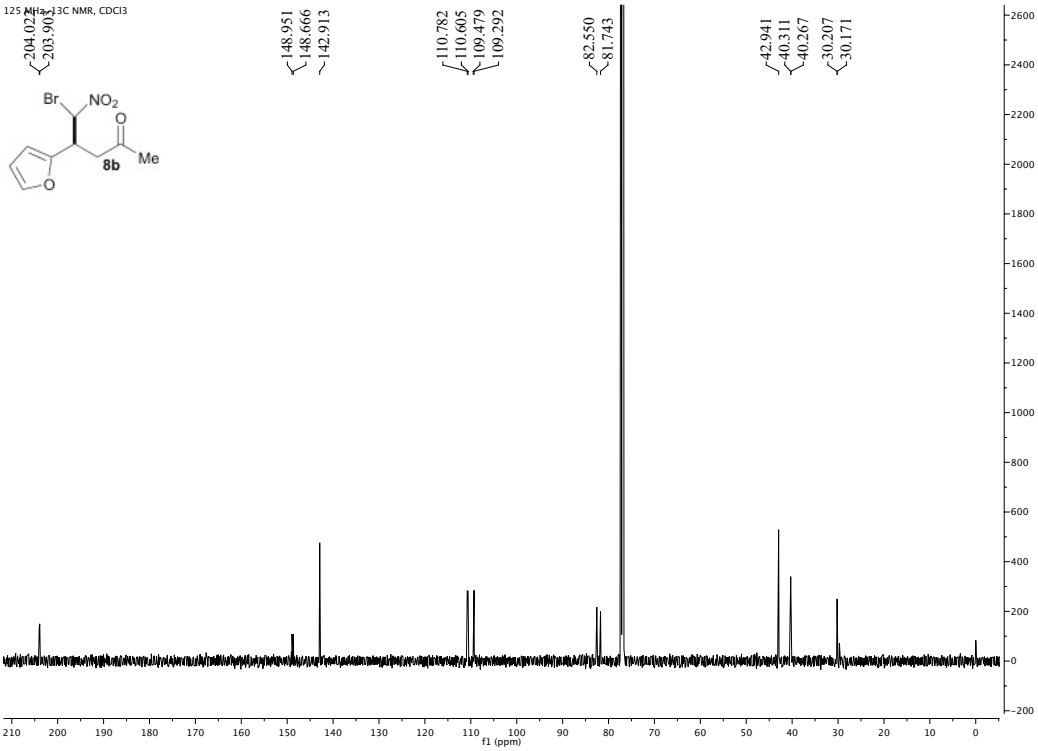


(4*S*)-5-Bromo-4-(furan-2-yl)-5-nitropentan-2-one **8b**

^{1}H NMR 500 MHz

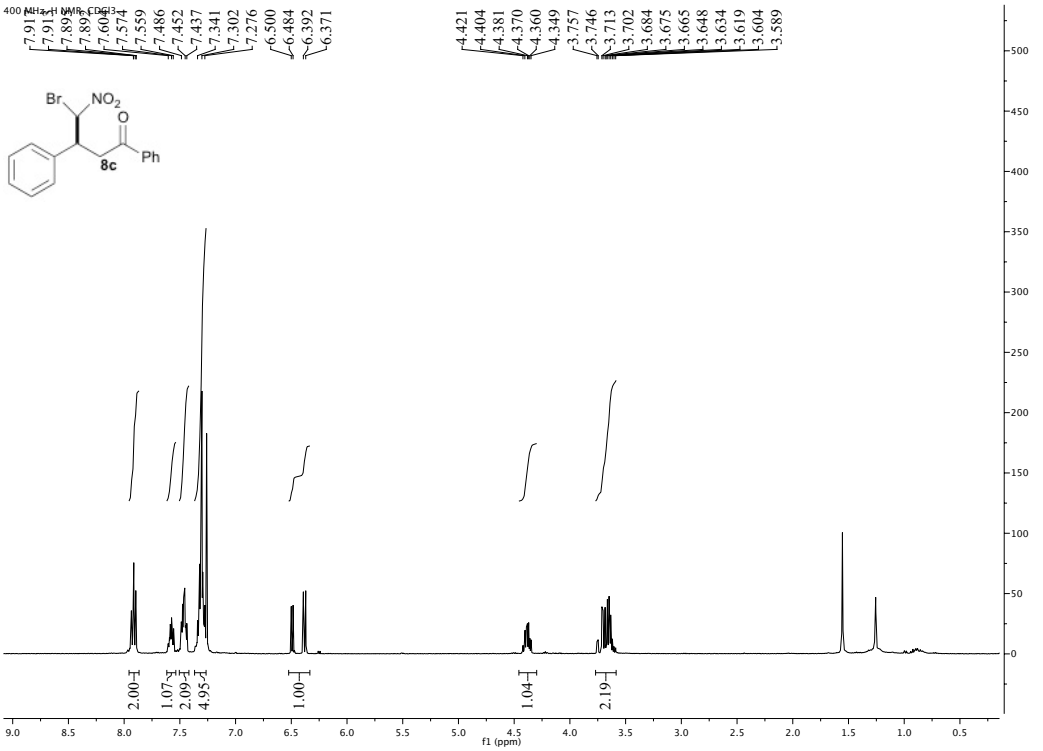


^{13}C NMR 126 MHz

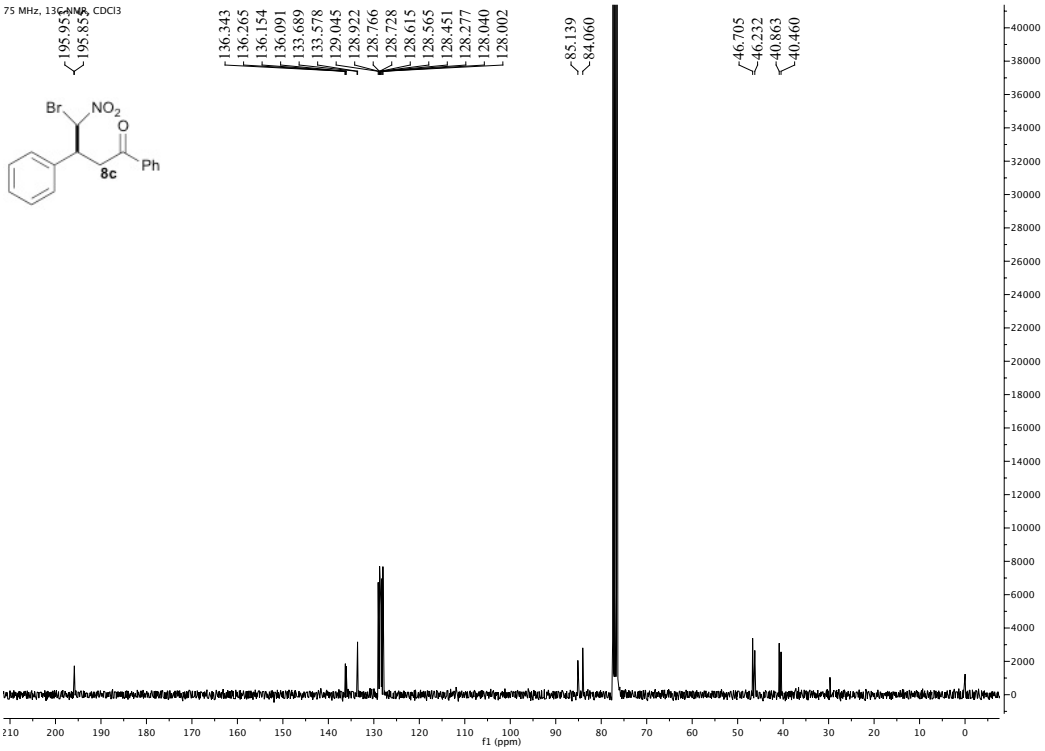


(3*S*)-4-Bromo-4-nitro-1,3-diphenylbutan-1-one **8c**

^{1}H NMR 500 MHz

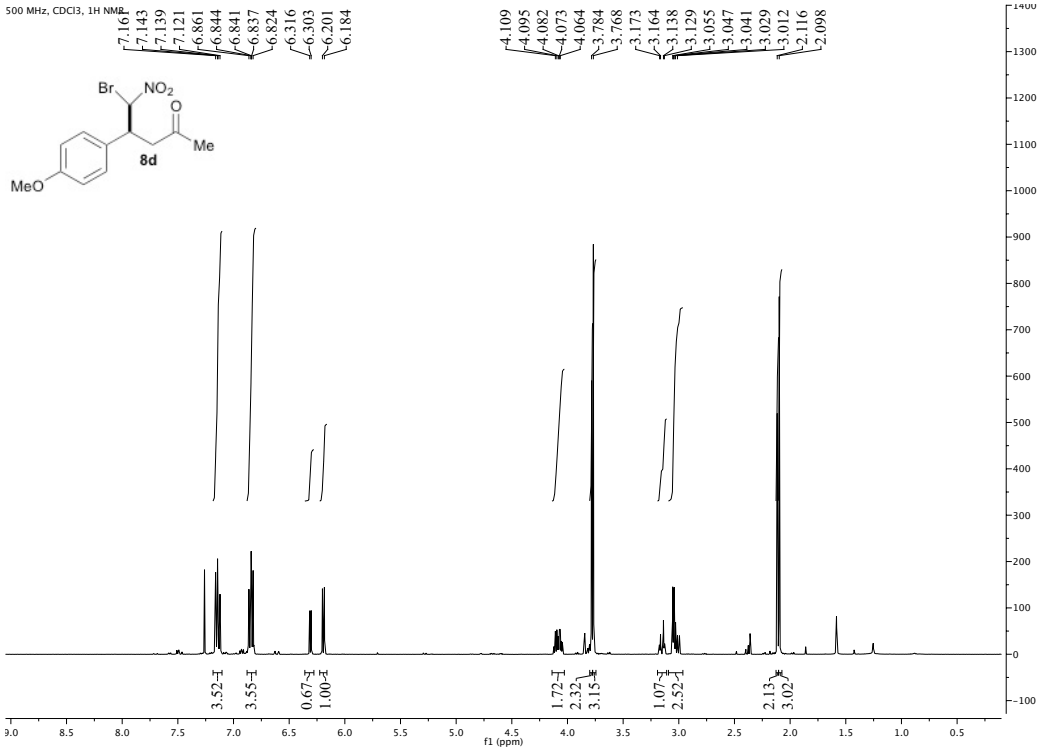


^{13}C NMR 126 MHz

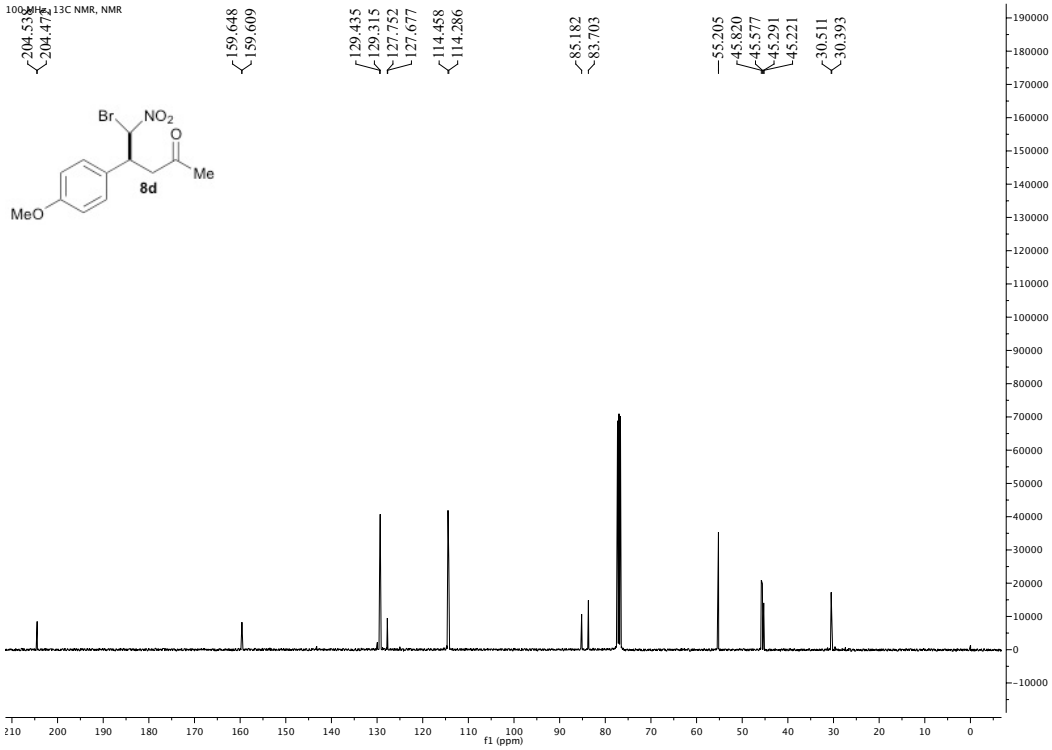


(4*S*)-5-Bromo-4-(4-methoxyphenyl)-5-nitropentan-2-one **8d**

^{1}H NMR 500 MHz

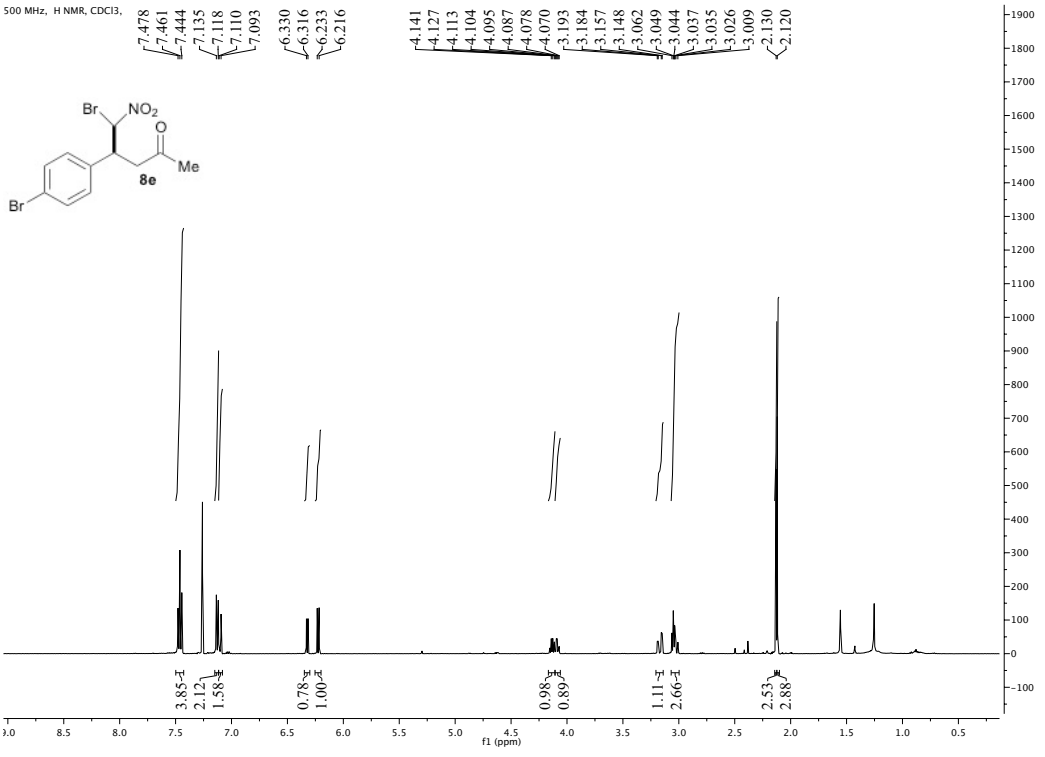


^{13}C NMR 126 MHz

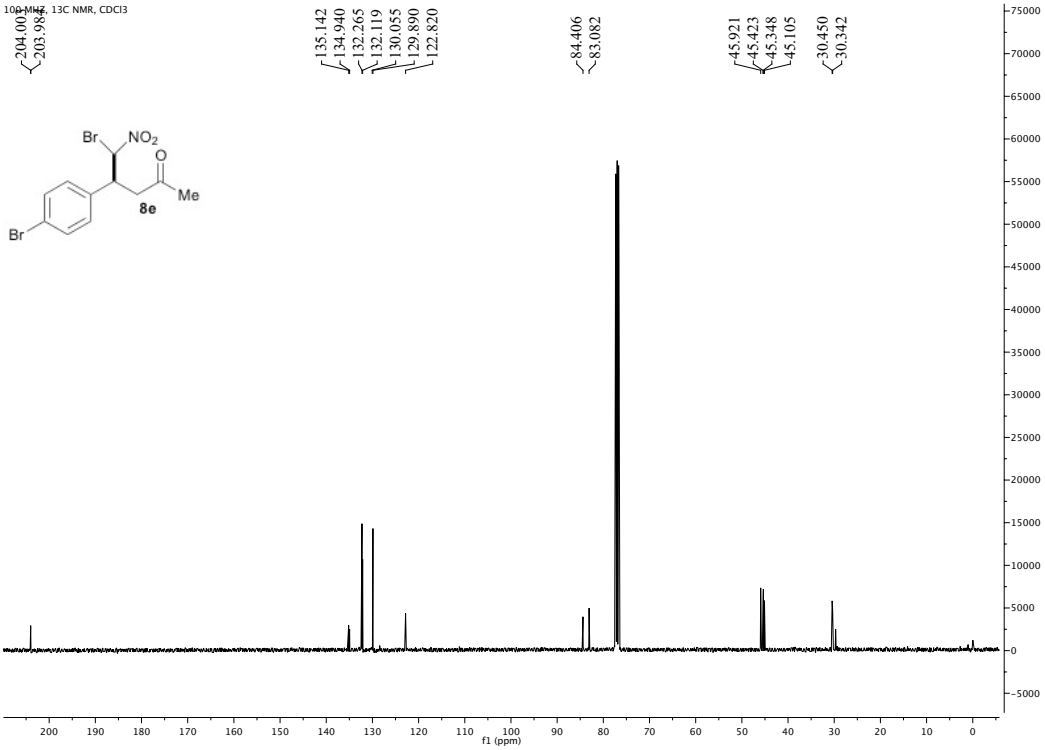


(4*S*)-5-Bromo-4-(4-bromophenyl)-5-nitropentan-2-one **8e**

^{1}H NMR 500 MHz

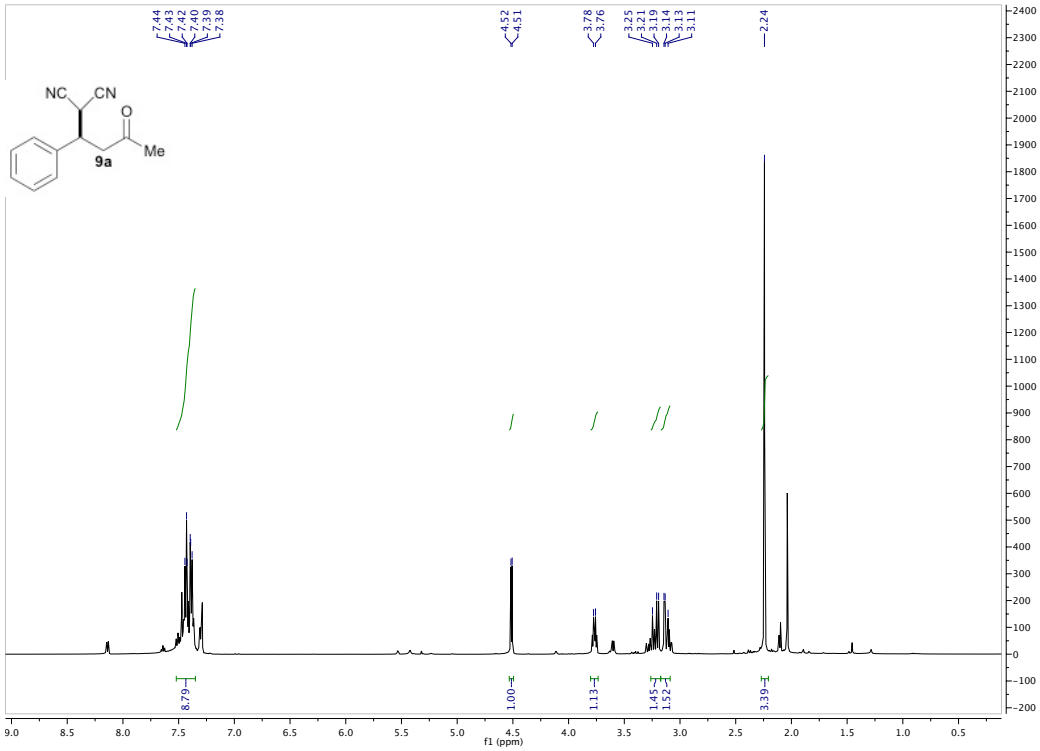


^{13}C NMR 126 MHz

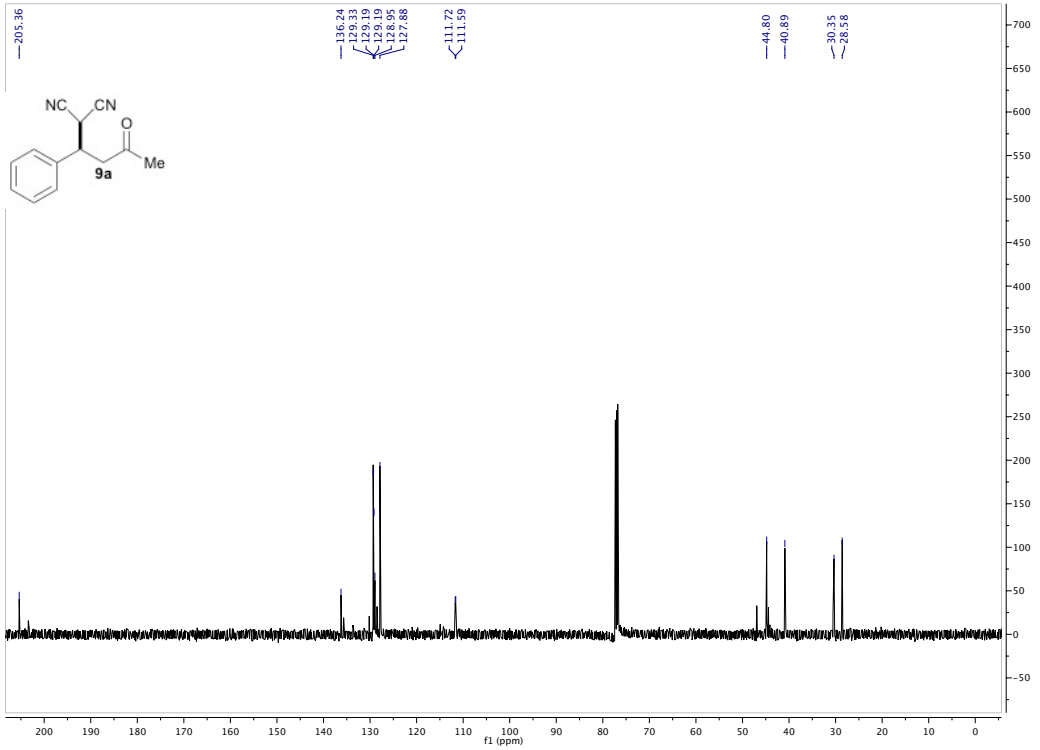


(*R*)-2-(3-Oxo-1-phenylbutyl)malononitrile **9a**

^{1}H NMR 500 MHz

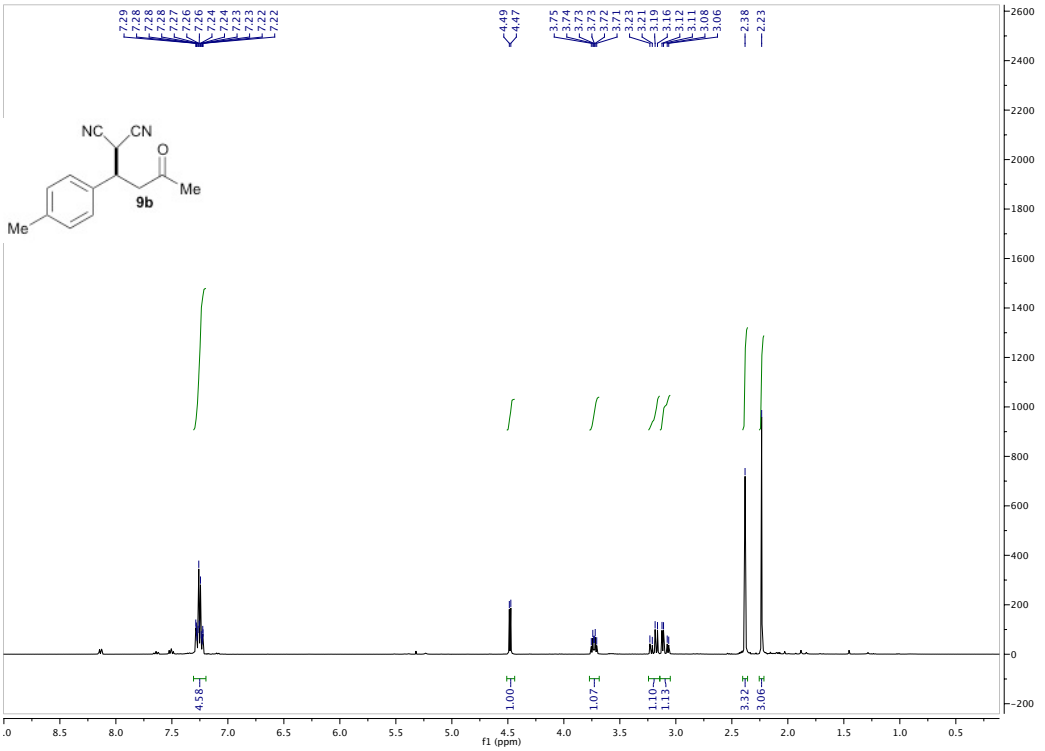


^{13}C NMR 126 MHz

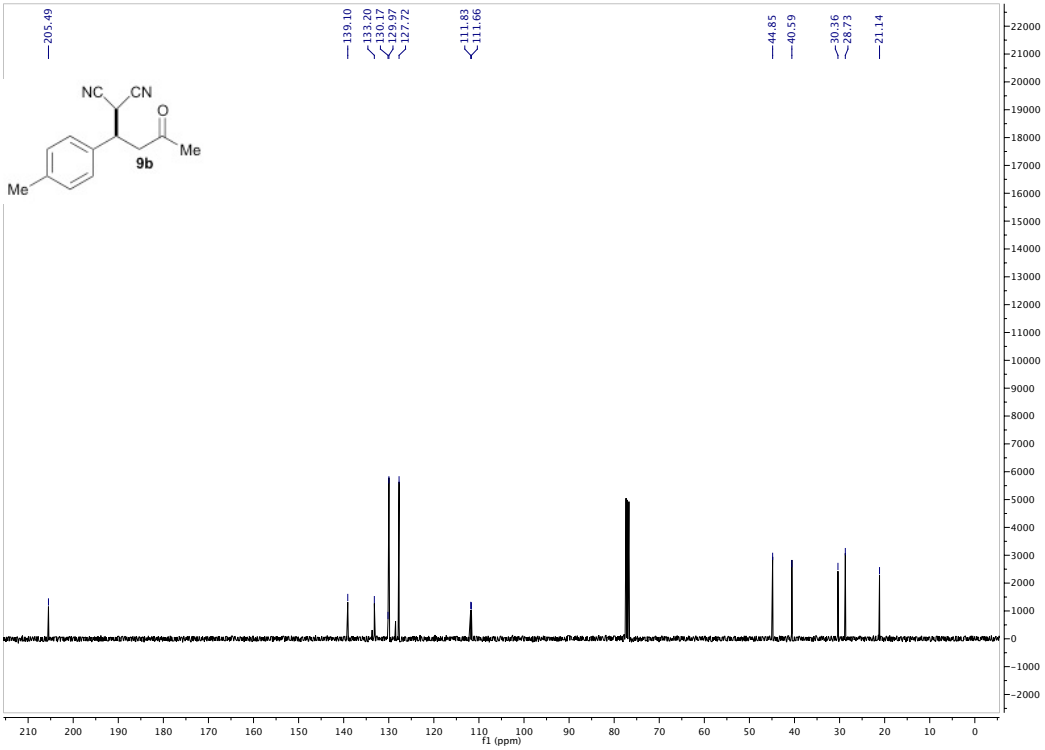


(*R*)-2-(3-Oxo-1-(*p*-tolyl)butyl)malononitrile **9b**

^{1}H NMR 400 MHz

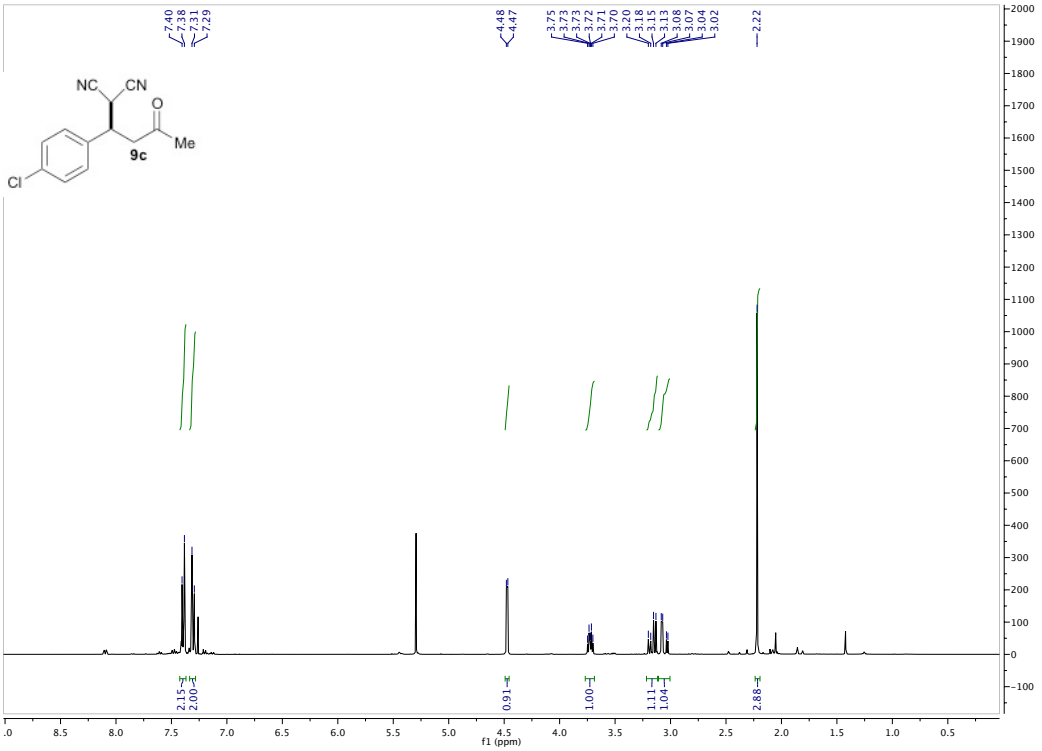


^{13}C NMR 101 MHz

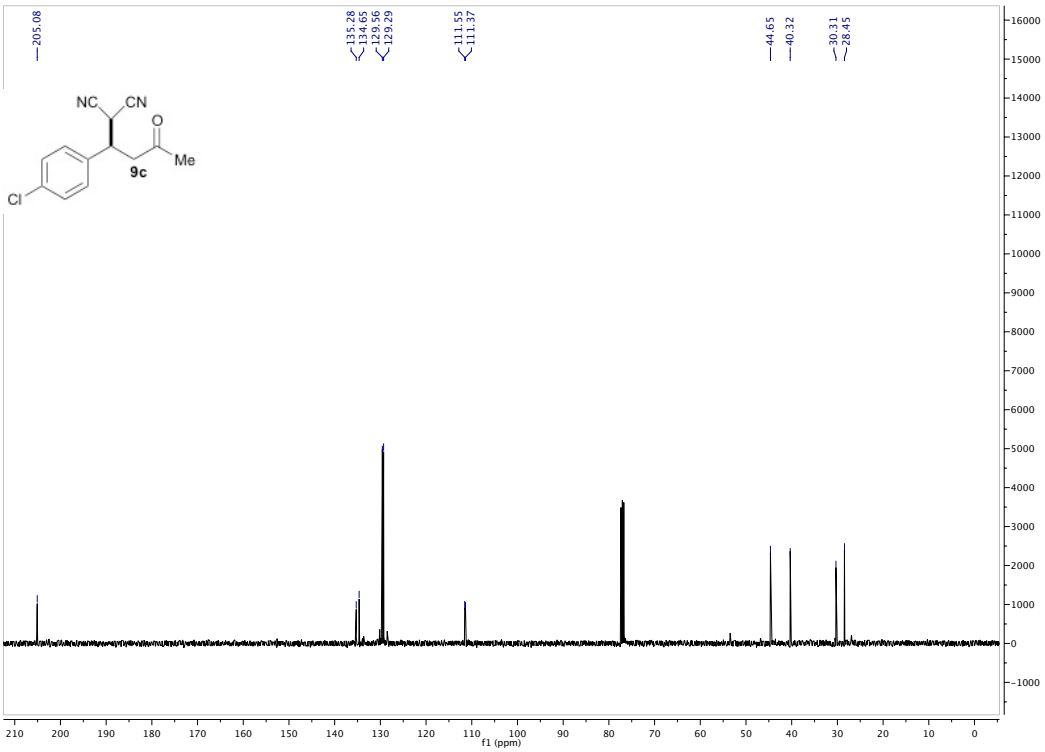


(*R*)-2-(1-(4-Chlorophenyl)-3-oxobutyl)malononitrile **9c**

^{1}H NMR 400 MHz

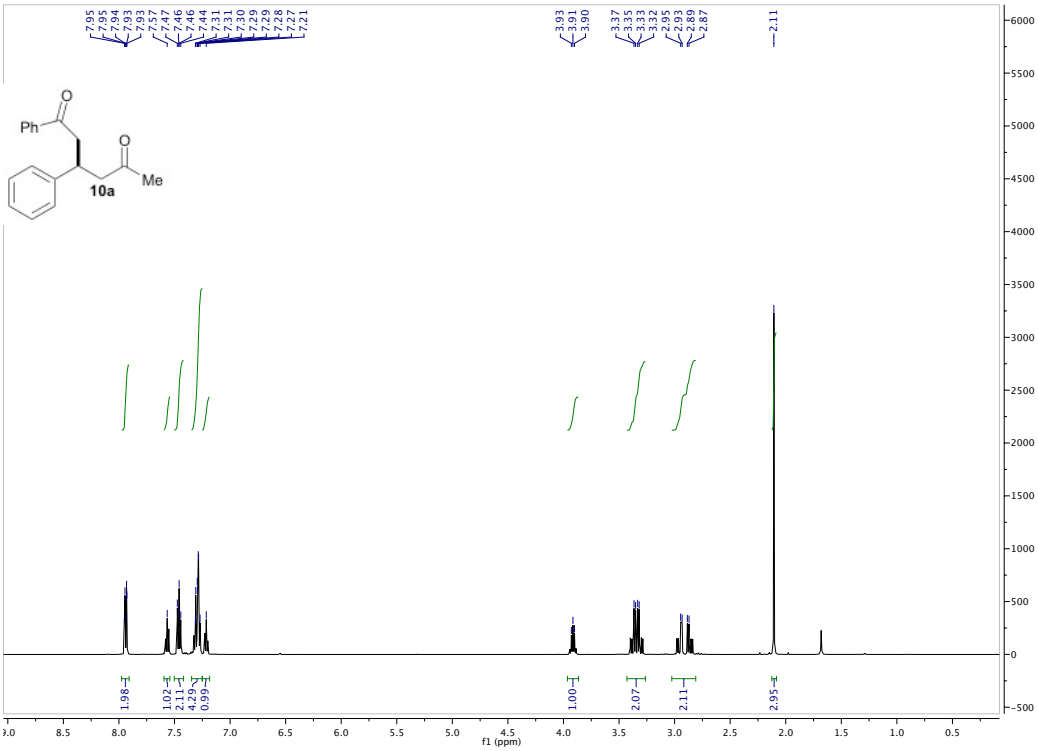


^{13}C NMR 101 MHz

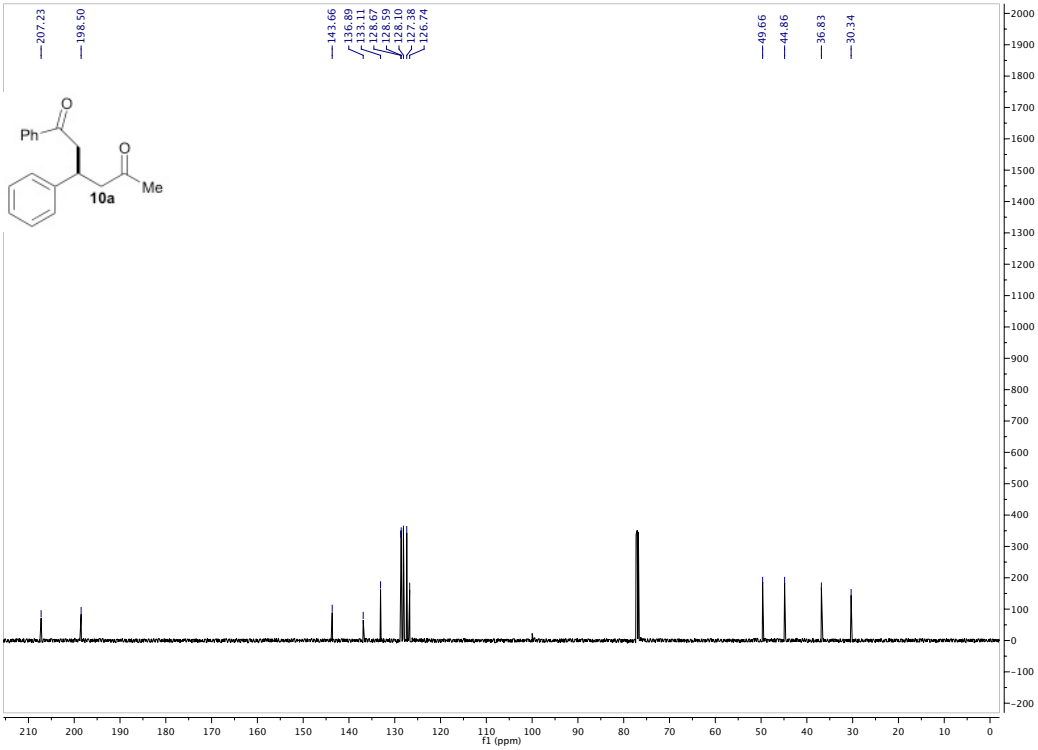


(*S*)-4,5-Diphenylpentan-2-one **10a**

^{1}H NMR 500 MHz

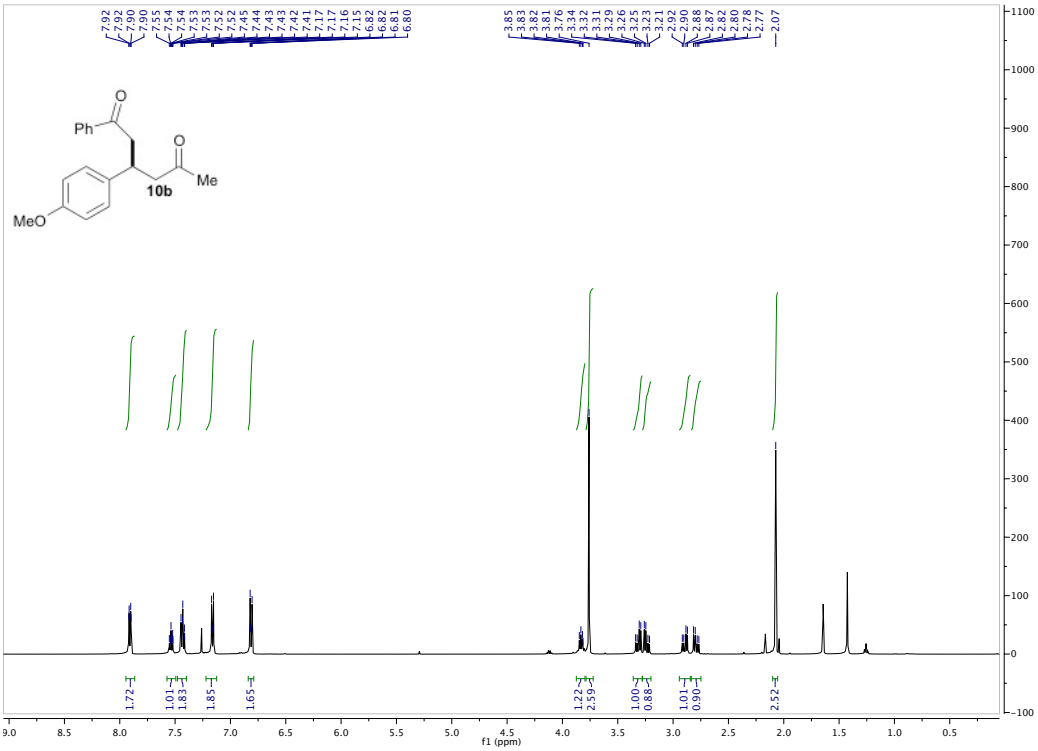


^{13}C RMN 126 MHz

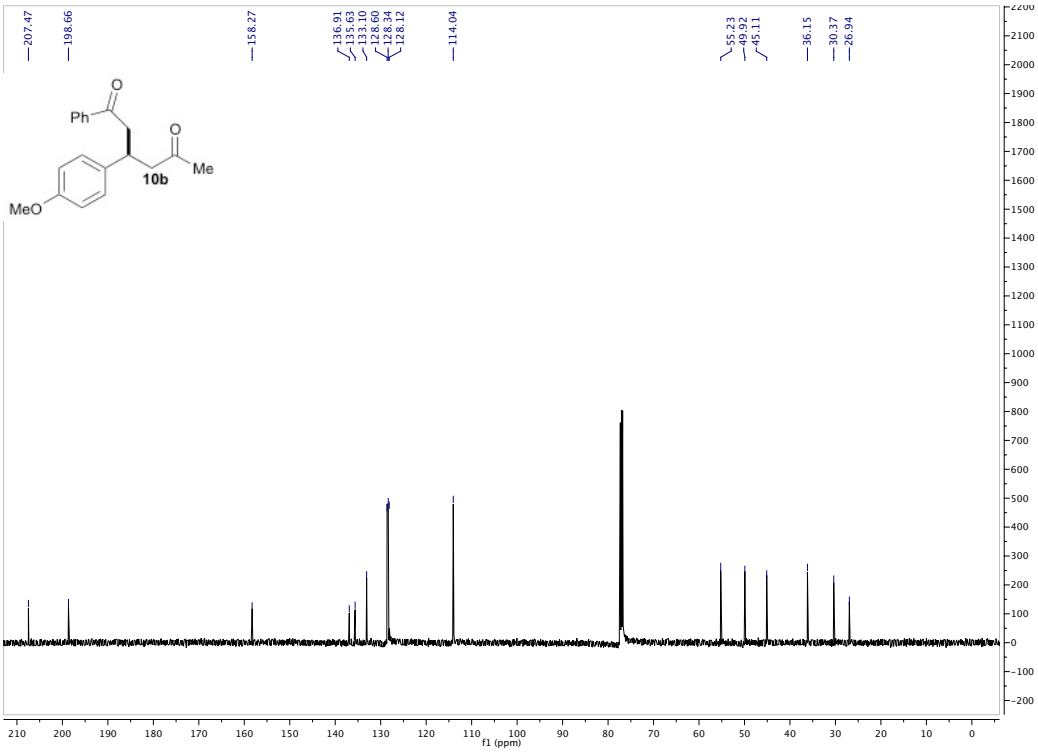


(*S*)-4-(4-Methoxyphenyl)-5-phenylpentan-2-one **10b**

^{1}H NMR 500 MHz

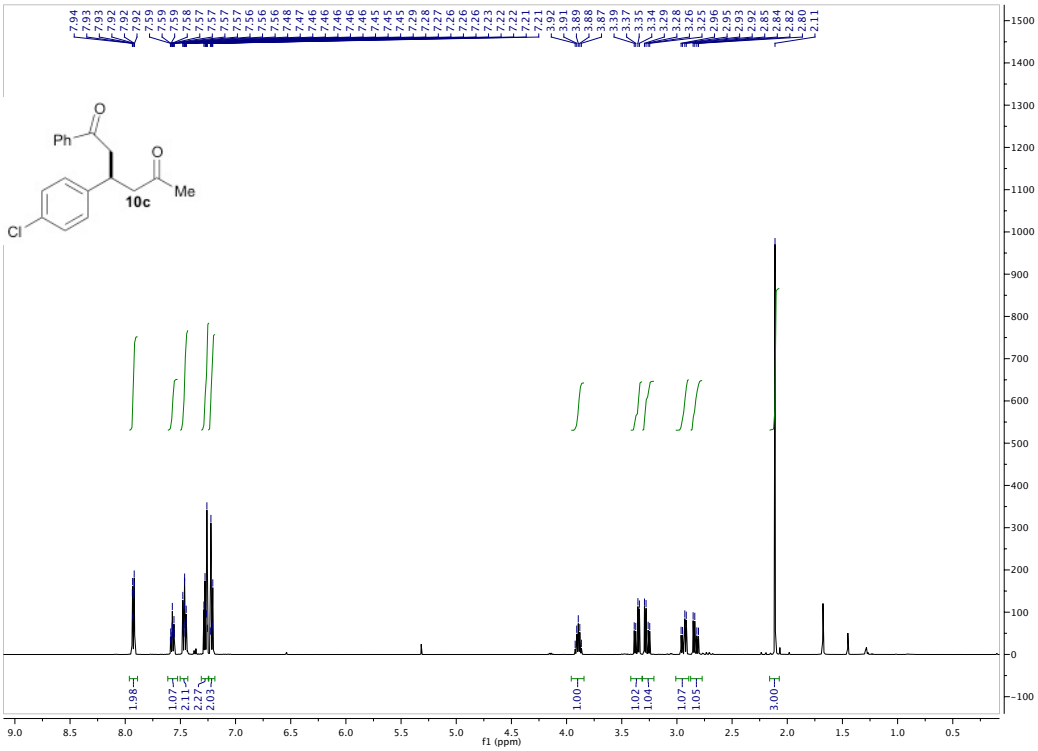


^{13}C NMR 126 MHz

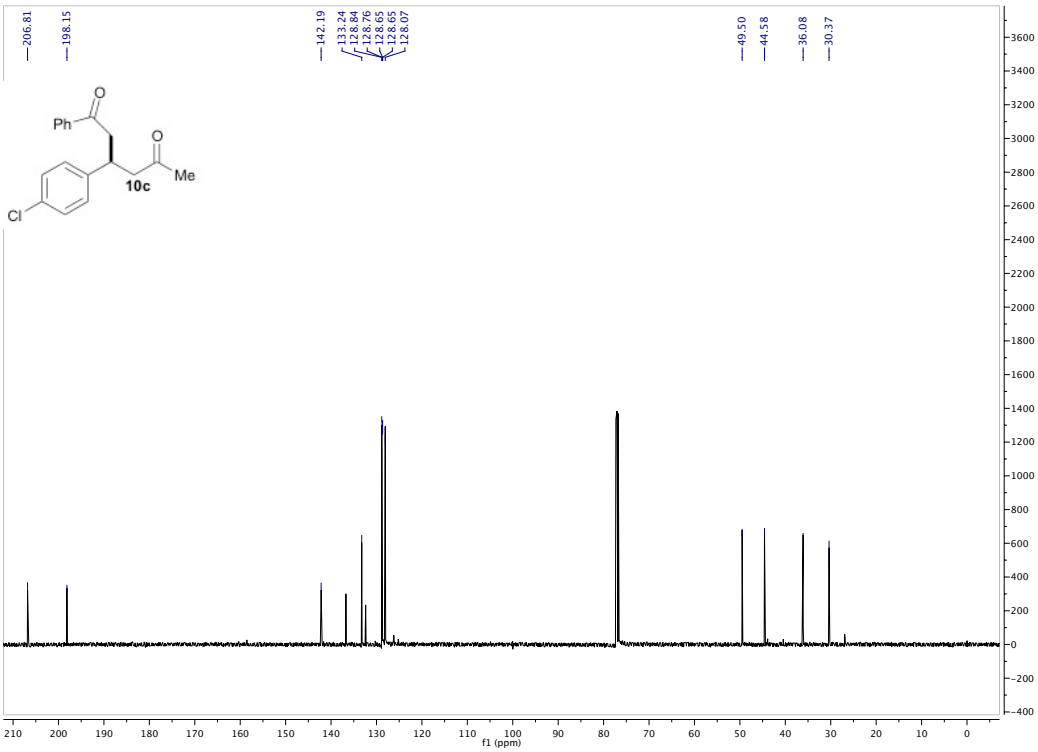


(*S*)-4-(4-Chlorophenyl)-5-phenylpentan-2-one **10c**

^{1}H NMR 500 MHz

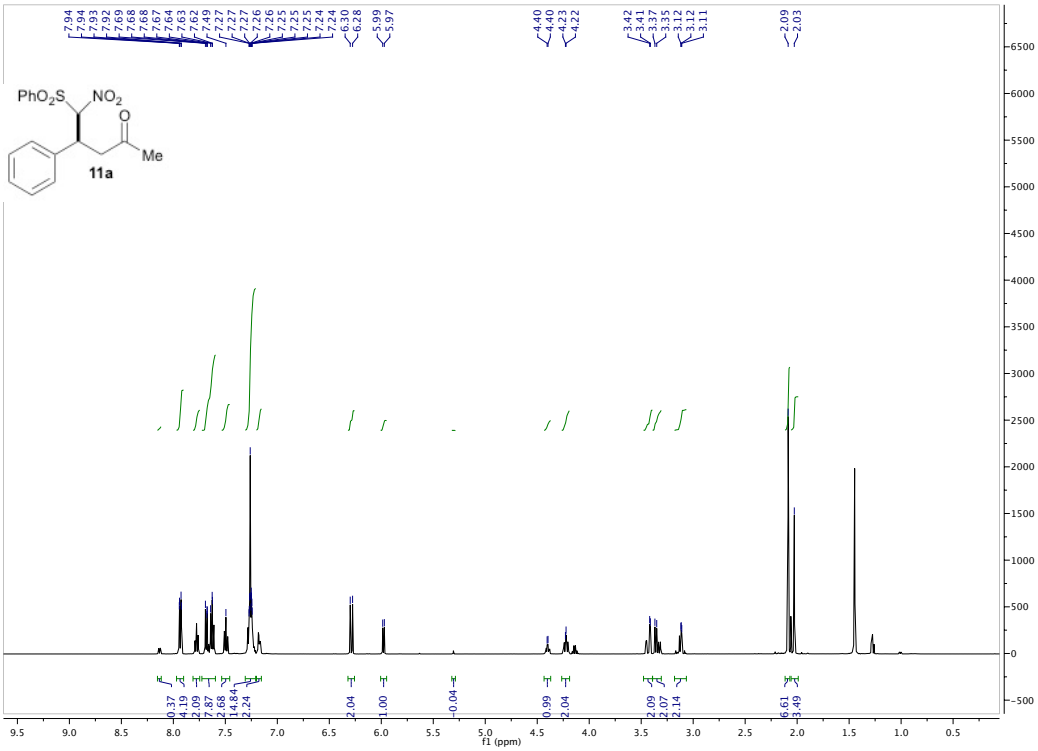


^{13}C NMR 126 MHz

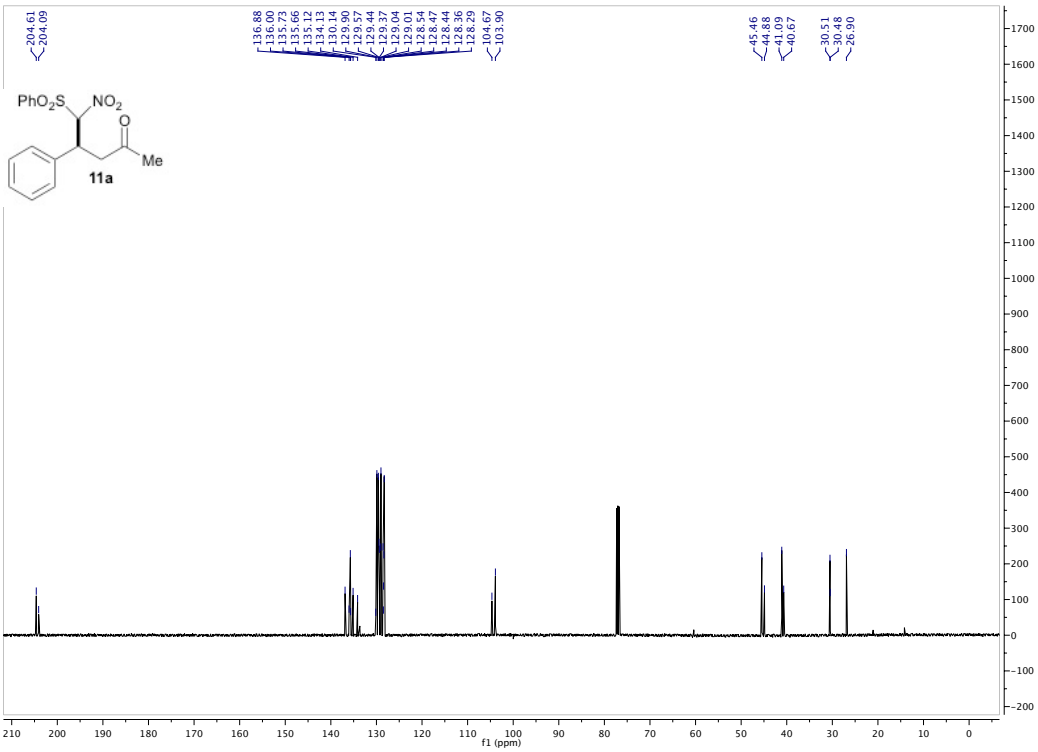


(4*S*)-5-Nitro-4-phenyl-5-(phenylsulfonyl)pentan-2-one **11a**

^{1}H NMR 500 MHz

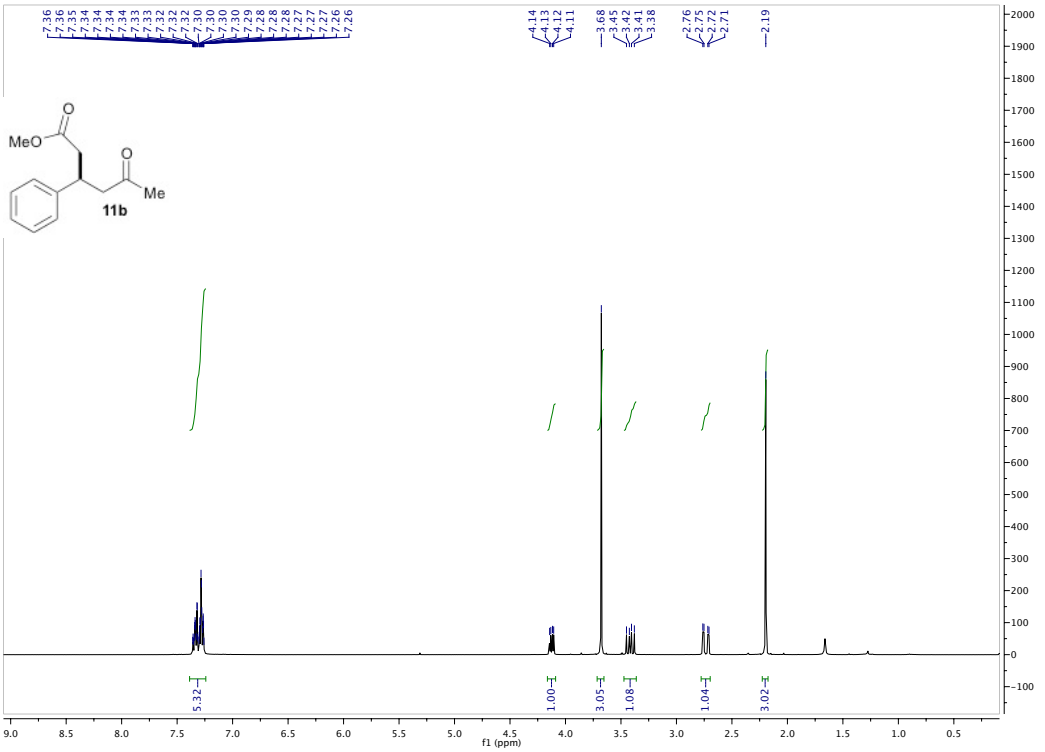


^{13}C NMR 126 MHz

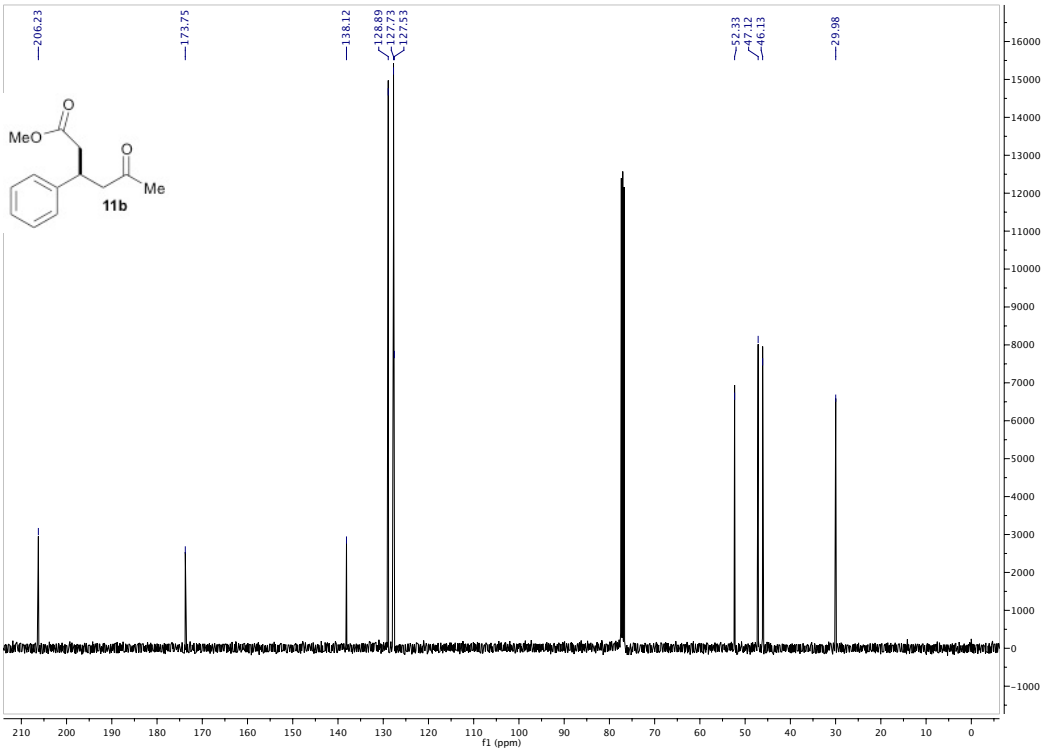


(*R*)-Methyl 5-oxo-3-phenylhexanoate **11b**

^{1}H NMR 400 MHz

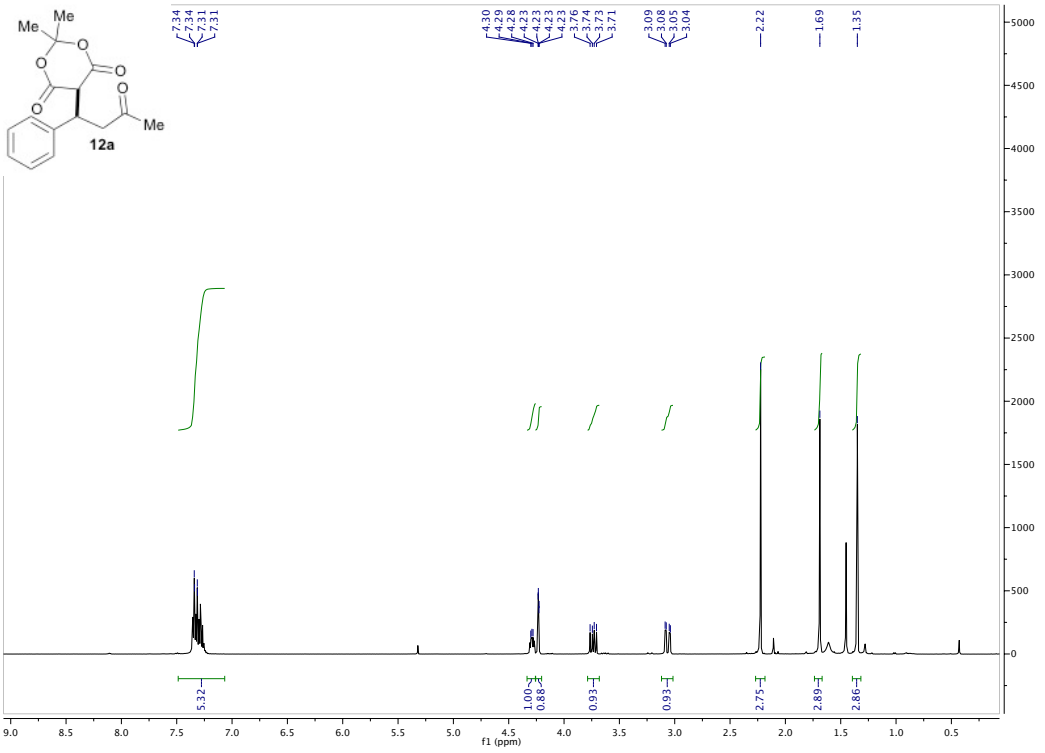


^{13}C NMR 126 MHz

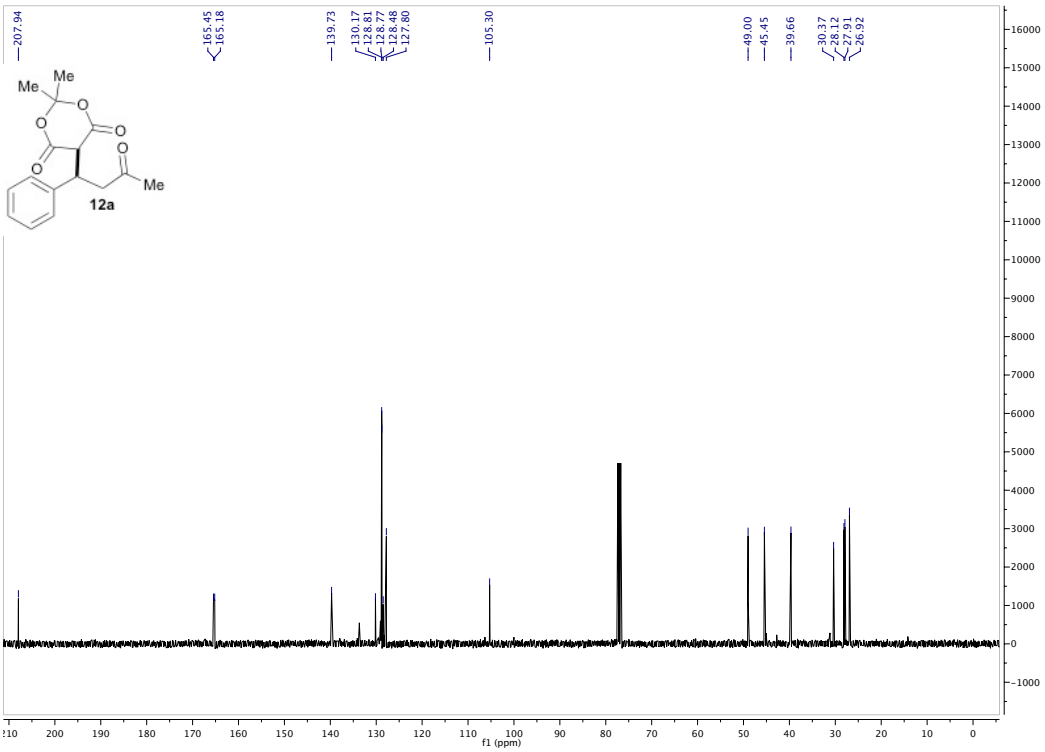


(*R*)-2,2-Dimethyl-5-(3-oxo-1-phenylbutyl)-1,3-dioxane-4,6-dione **12a**

^{1}H NMR 500 MHz

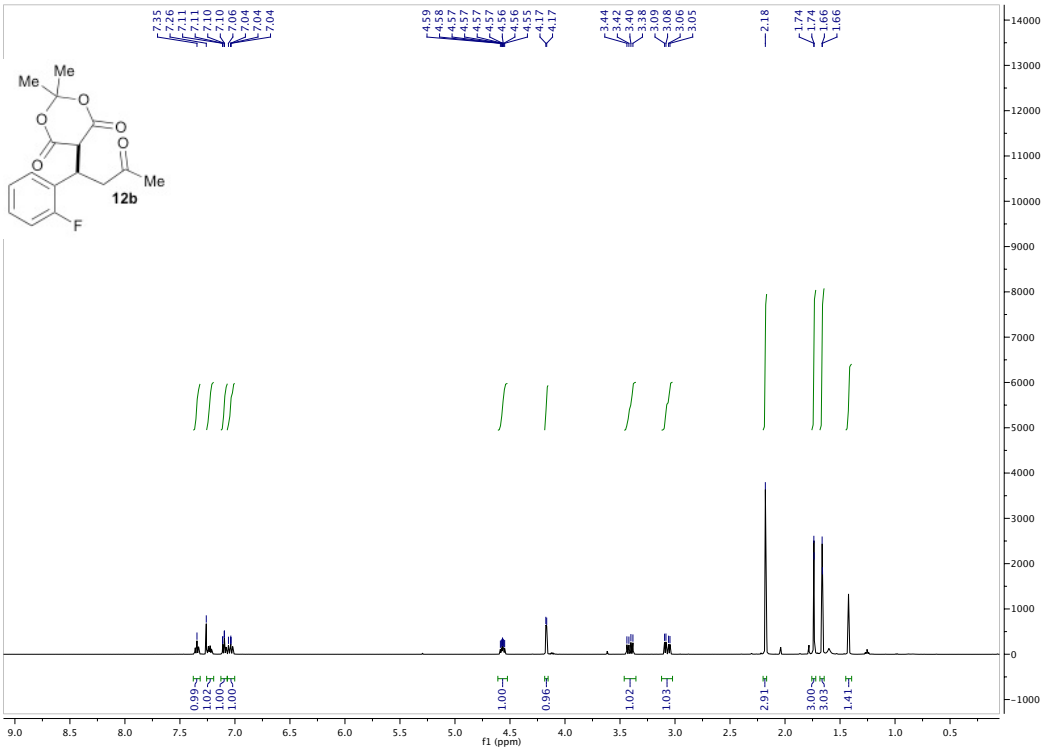


^{13}C NMR 126 MHz

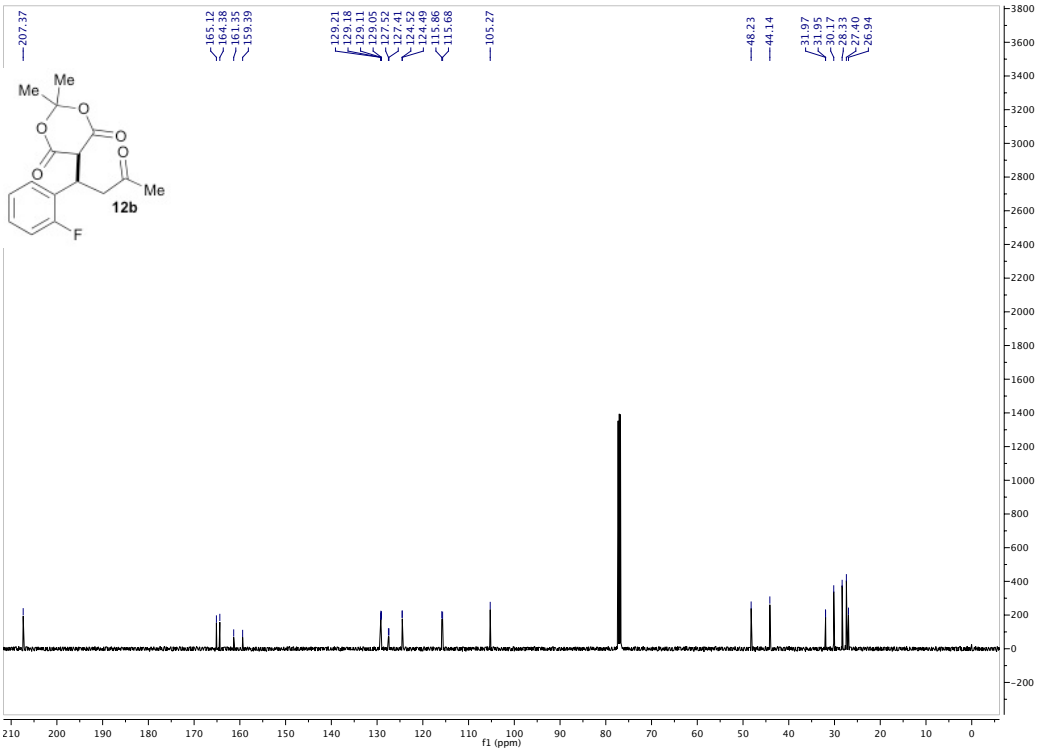


(*R*)-5-(1-(2-Fluorophenyl)-3-oxobutyl)-2,2-dimethyl-1,3-dioxane-4,6-dione **12b**

^{1}H NMR 500 MHz

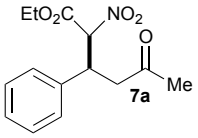


^{13}C NMR 126 MHz

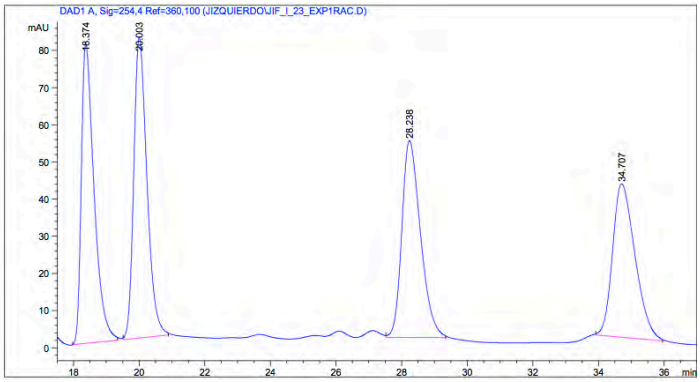


10. CHROMATOGRAMS

(3*S*)-Ethyl 2-nitro-5-oxo-3-phenylhexanoate **7a** (Chiralpak IC, λ = 254 nm, 20% iPrOH/hexane, flow rate = 0.5 mL/min)



RACEMIC



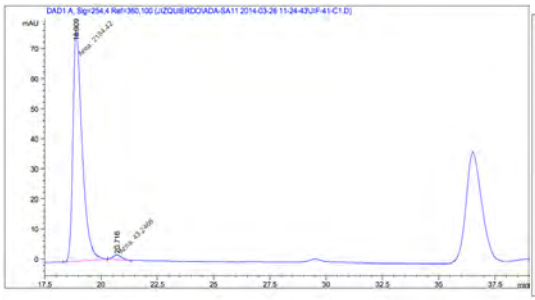
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.374	BB	0.4041	2171.63428	80.67200	25.6104
2	20.003	BB	0.4271	2257.39355	81.01295	26.6218
3	28.238	VB	0.5956	2086.79517	52.97257	24.6099
4	34.707	BB	0.7280	1963.66479	41.35075	23.1578

ENANTIOPURE

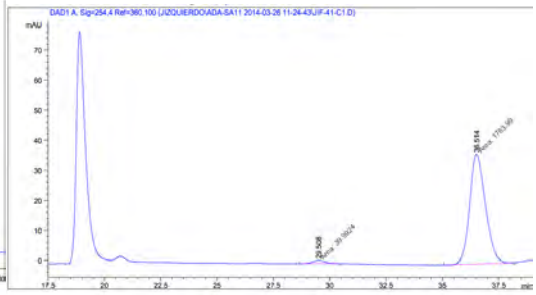


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.909	MM	0.4737	2184.42407	76.86483	98.0587
2	20.716	MM	0.4373	43.24679	1.64823	1.9413



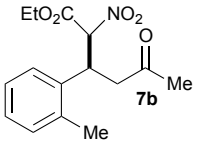
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

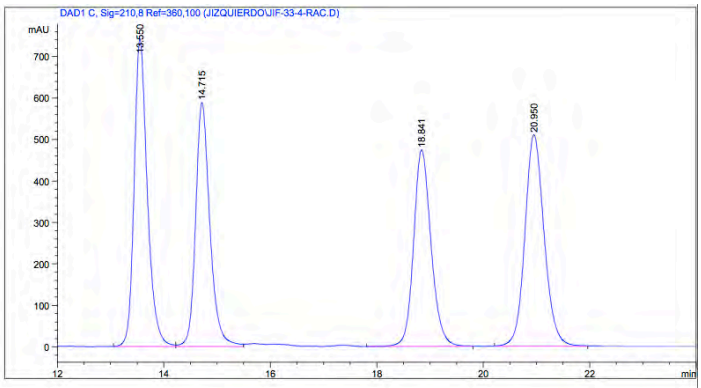
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.508	MM	0.6293	39.99242	1.05924	2.1926
2	36.514	MM	0.8118	1783.98621	36.62444	97.8074

(3*S*)-Ethyl 2-nitro-5-oxo-3-(*o*-tolyl)hexanoate **7b** (Chiralpak AD-H, λ = 210 nm, 10% *i*PrOH/hexane, flow rate = 0.5 mL/min)



7b

RACEMIC



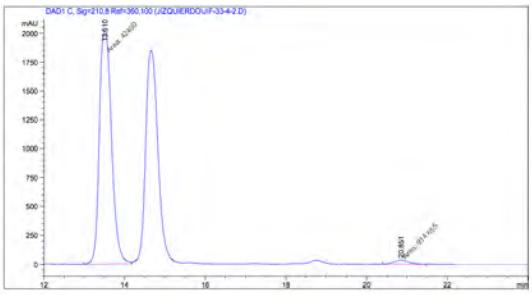
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.550	BV	0.2606	1.27462e4	741.48663	26.9336
2	14.715	VV	0.2807	1.09411e4	588.93243	23.1194
3	18.841	VB	0.3497	1.07960e4	474.08328	22.8126
4	20.950	BB	0.3857	1.28412e4	510.12399	27.1344

ENANTIOPURE



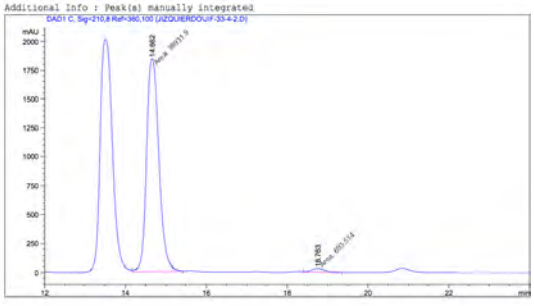
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.510	MF	0.3506	4.24000e4	2015.60999	97.8883
2	20.851	MM	0.4093	914.65509	37.24790	2.1117
Totals :				4.33146e4	2052.85788	

Additional Info : Peak(s) manually integrated



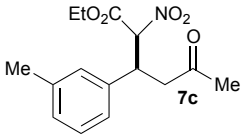
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

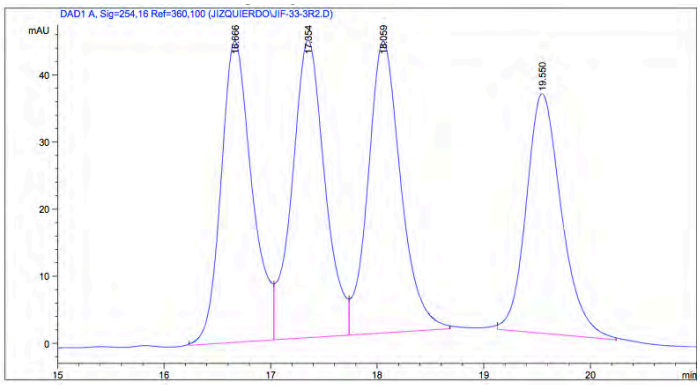
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.662	PM	0.3526	3.89319e4	1840.36865	98.2498
2	18.763	MM	0.3548	693.51367	32.58001	1.7502
Totals :				3.96254e4	1872.94866	

(3*S*)-Ethyl 2-nitro-5-oxo-3-(*m*-tolyl)hexanoate **7c** (Chiralpak AD-H, λ = 254 nm, 10% *i*PrOH/hexane, flow rate = 0.5 mL/min);



7c

RACEMIC



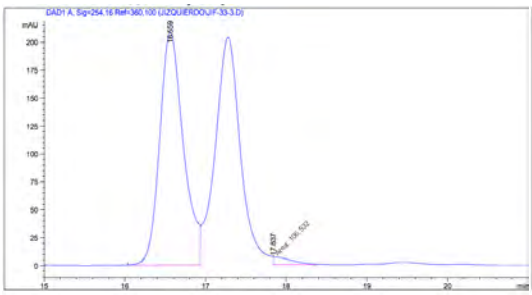
Area Percent Report

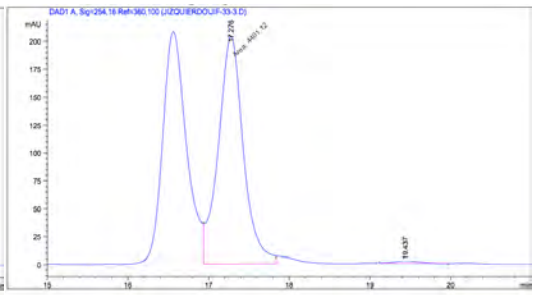
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.666	BV	0.3052	905.82861	44.92704	25.1346
2	17.354	VV	0.3222	951.85931	44.39337	26.4119
3	18.059	VB	0.3229	928.21014	43.51426	25.7557
4	19.550	BB	0.3489	818.00861	35.75694	22.6978

ENANTIOPURE





Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.559	BV	0.3085	4261.75000	208.50426	97.5612
2	17.837	PM	0.2497	106.53231	7.11087	2.4388
Totals :				4368.28231	215.61512	

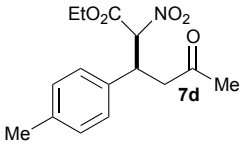
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

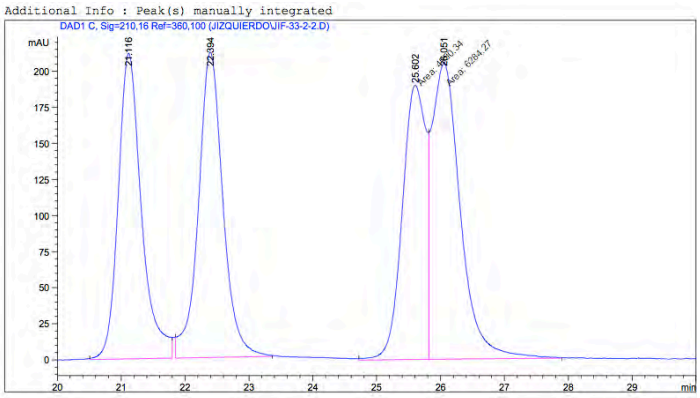
Signal 1: DAD1 A, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.276	MF	0.3599	4401.12012	203.82858	99.0496
2	19.437	BB	0.3221	42.23022	2.01838	0.9504
Totals :				4443.35034	205.84696	

(3*S*)-Ethyl 2-nitro-5-oxo-3-(*p*-tolyl)hexanoate **7d** (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 0.5 mL/min)



RACEMIC



Additional Info : Peak(s) manually integrated

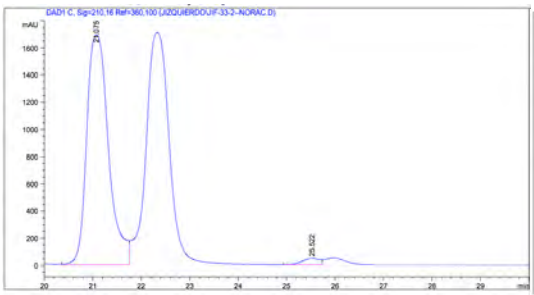
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.116	BB	0.3811	5349.31006	211.51764	24.0671
2	22.394	BB	0.3992	5642.69043	211.53822	25.3871
3	25.602	MF	0.4344	4950.34180	189.93803	22.2721
4	26.051	FM	0.5116	6284.27490	204.72252	28.2736

ENANTIOPURE

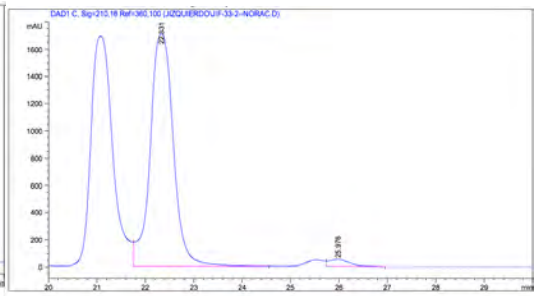


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.075	BV	0.4859	5.28362e4	1693.92139	97.7186
2	25.522	VV	0.3810	1233.53247	49.12109	2.2814
Totals :				5.40698e4	1743.04248	



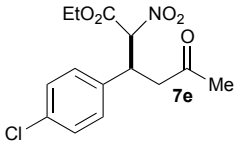
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,16 Ref=360,100

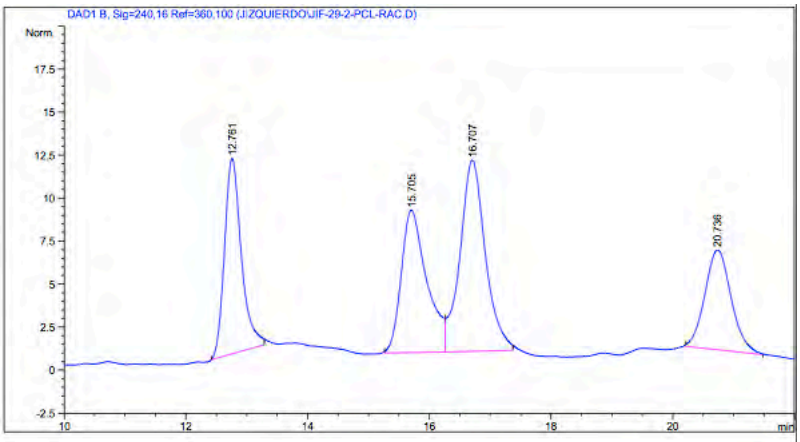
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.331	VB	0.5173	5.68087e4	1711.20154	97.3384
2	25.976	VB	0.4374	1553.33484	53.07544	2.6616
Totals :				5.83620e4	1764.27698	

(3*S*)-Ethyl 3-(4-cyanophenyl)-2-nitro-5-oxohexanoate **7e** (Chiralpak IC, λ = 210 nm, 7% CH_2Cl_2 / 3% *i*PrOH/hexane, flow rate = 1 mL/min)



7e

RACEMIC



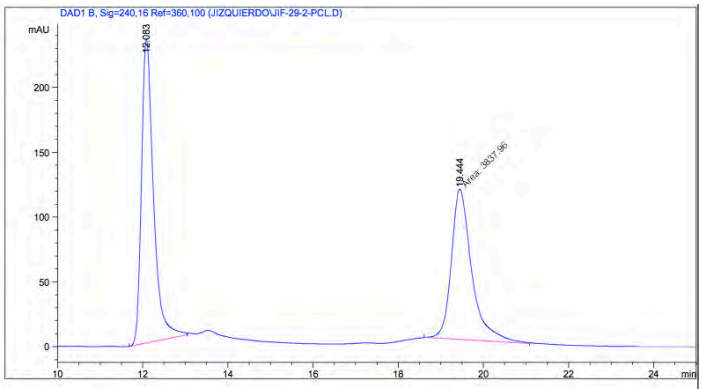
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.761	BB	0.2898	217.71848	11.34818	22.8212
2	15.705	BV	0.4194	240.63585	8.27131	25.2234
3	16.707	VB	0.4341	321.81717	11.10609	33.7329
4	20.736	BB	0.4438	173.84546	5.79881	18.2225

ENANTIOPURE



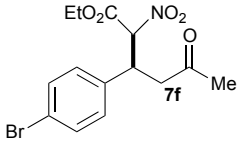
Area Percent Report

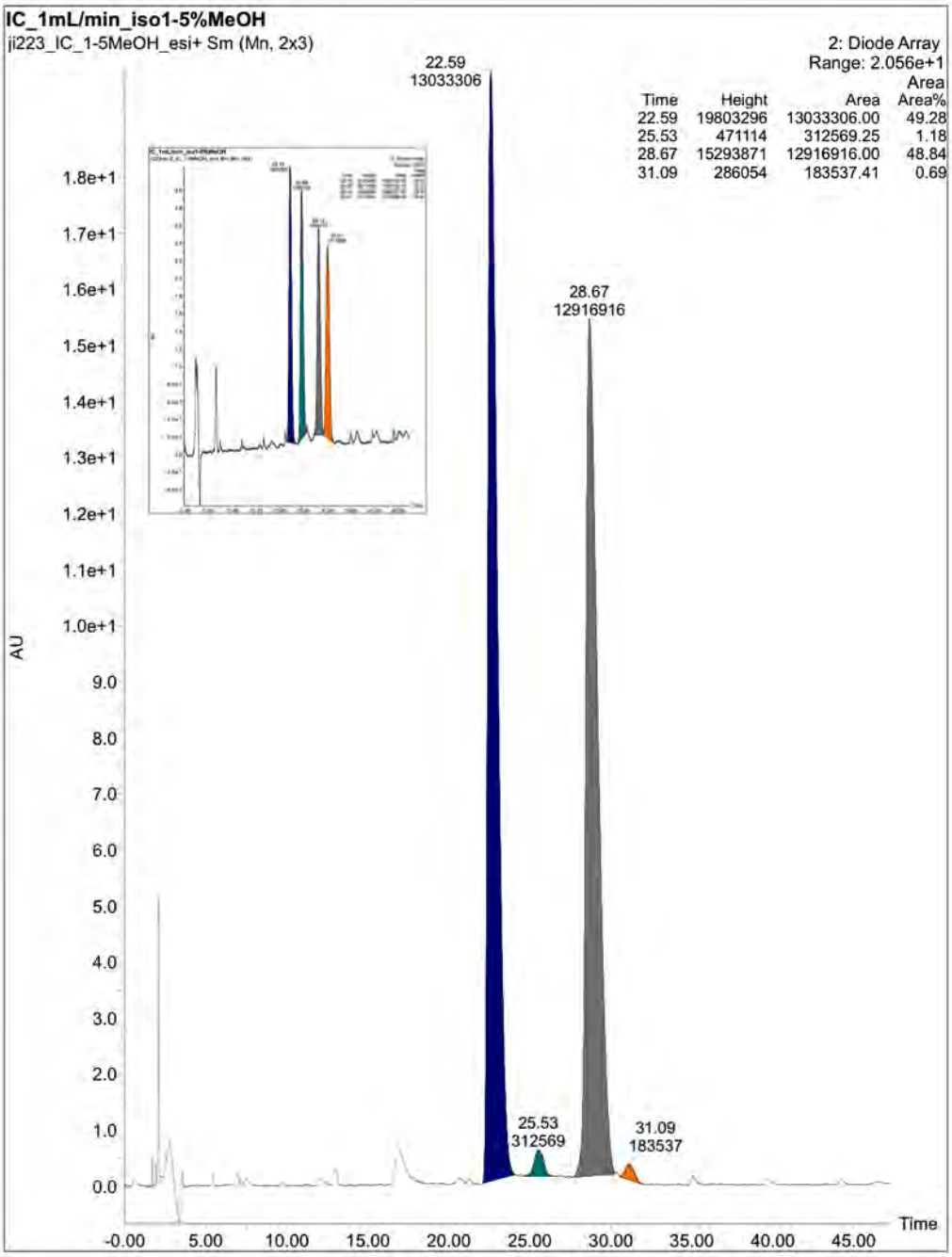
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=240,16 Ref=360,100

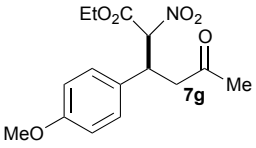
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.083	BB	0.2940	4580.30811	234.35692	54.4092
2	19.444	MM	0.5523	3837.95508	115.81141	45.5908

(3*S*)-Ethyl 3-(4-bromophenyl)-2-nitro-5-oxohexanoate **7f** (UPC^2, Chiralpak IC, gradient: 1-5% MeOH/CO_2, flow rate = 1 mL/min)

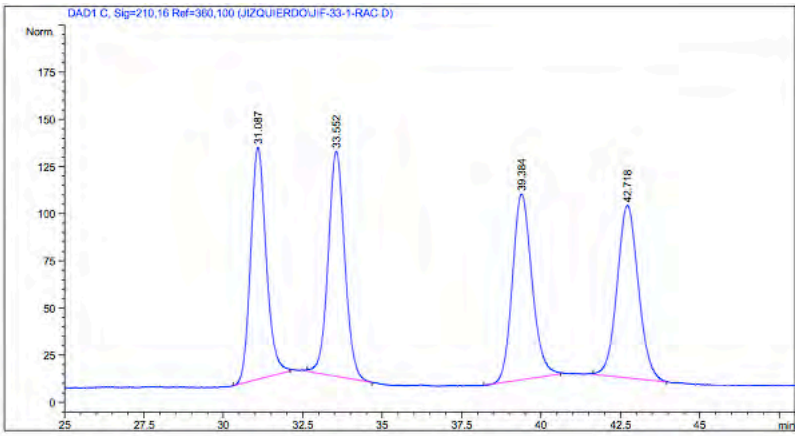




(3*S*)-Ethyl 3-(4-methoxyphenyl)-2-nitro-5-oxohexanoate **7g** (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 0.5 mL/min)



RACEMIC



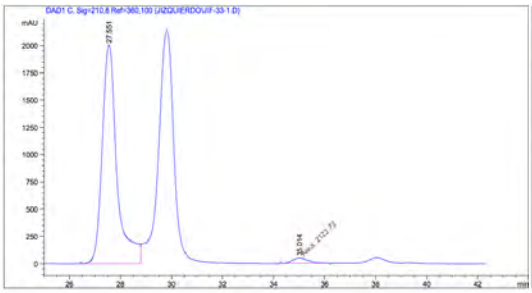
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.087	BB	0.5240	4178.16895	123.10957	24.6253
2	33.552	BB	0.5492	4306.29736	119.26624	25.3804
3	39.384	BB	0.6424	4222.72217	98.45852	24.8879
4	42.718	BB	0.6528	4259.80078	91.56023	25.1064

ENANTIOPURE

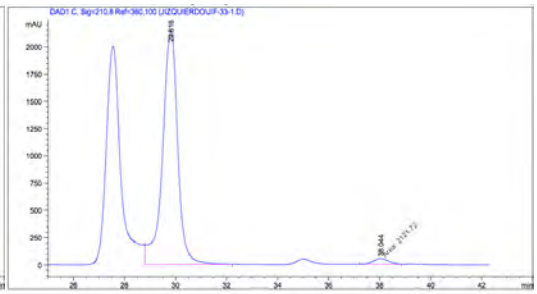


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.551	BV	0.5981	8.01190e4	2005.23499	97.4189
2	35.014	MM	0.6995	2122.72119	50.57514	2.5811
Totals :				8.22417e4	2055.81012	



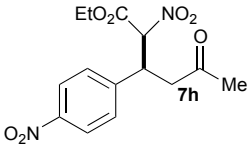
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

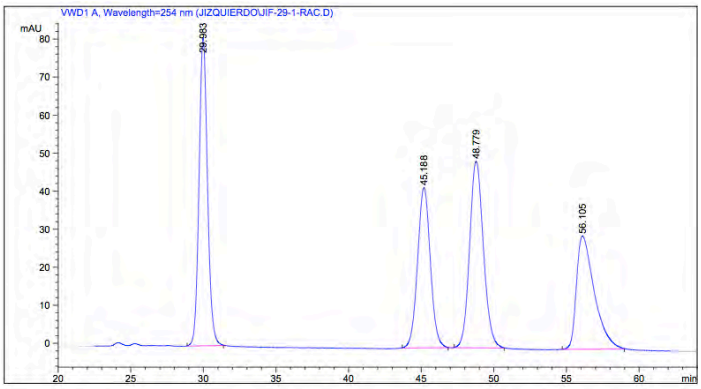
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.816	VB	0.6339	8.90106e4	2137.08008	97.6718
2	38.044	MM	0.6041	2121.72046	51.68868	2.3282
Totals :				9.11323e4	2188.76876	

(3*S*)-Ethyl 2-nitro-3-(4-nitrophenyl)-5-oxohexanoate **7h** (Chiralpak AD-H, λ = 210 nm, 10% *i*PrOH/hexane, flow rate = 1 mL/min)



RACEMIC



Area Percent Report

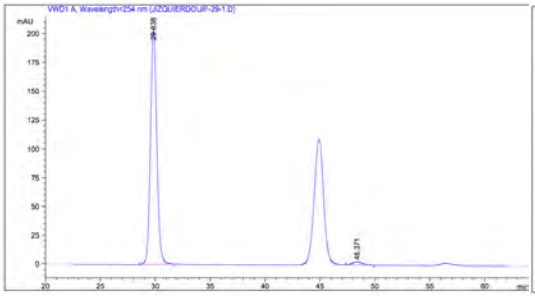
Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	29.983	BB	0.6221	3282.43140	80.85554	28.1951
2	45.188	BB	0.9333	2572.53857	42.15367	22.0973
3	48.779	BB	0.9836	3246.88159	49.03739	27.8898
4	56.105	BB	1.1792	2539.99341	29.80201	21.8178

Totals : 1.16418e4 201.84860

ENANTIOPURE



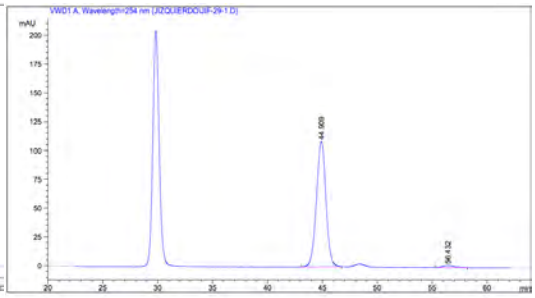
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	29.936	BB	0.6144	8189.63086	204.43005	97.9533
2	48.371	BB	0.7366	171.11870	2.79863	2.0467

Totals : 8360.74956 207.22868



Area Percent Report

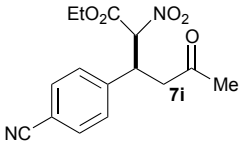
Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	44.909	BB	0.9235	6570.83740	109.17053	97.8451
2	56.432	BB	0.9059	144.71246	1.89100	2.1549

Totals : 6715.54987 111.06153

(3*S*)-Ethyl 3-(4-cyanophenyl)-2-nitro-5-oxohexanoate **7i** (Chiralpak AD-H, λ = 210 nm, 20% *i*PrOH/hexane, flow rate = 1 mL/min)



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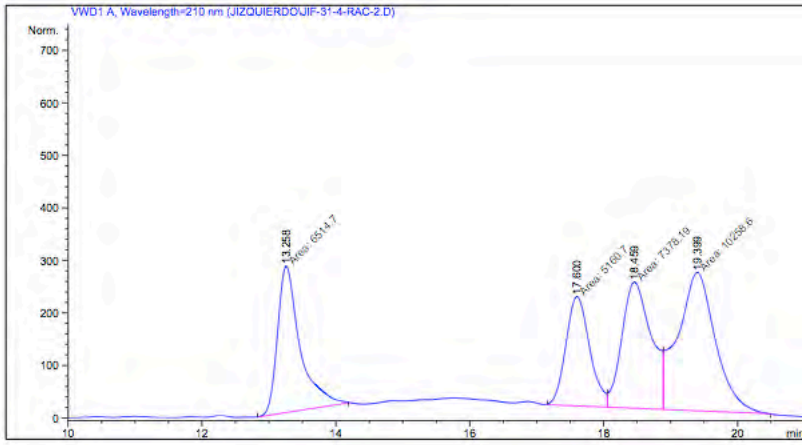


Area Percent Report

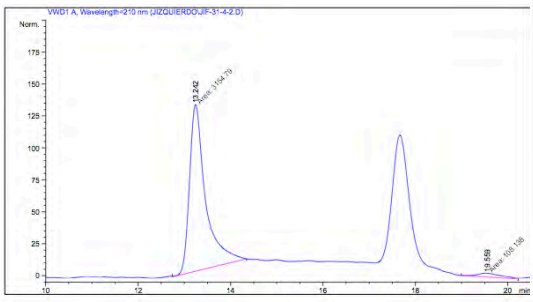
Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.258	MM	0.3895	6514.70313	278.74213	22.2253
2	17.600	MF	0.4133	5160.70361	208.11310	17.6060
3	18.459	MF	0.5119	7378.19385	240.22214	25.1711
4	19.399	FM	0.6493	1.02586e4	263.32901	34.9976

Totals : 2.93122e4 990.40637

ENANTIOPURE



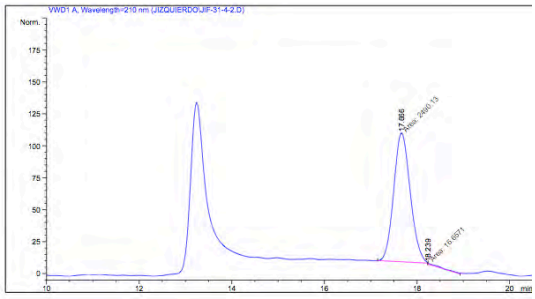
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.242	MM	0.4036	3154.78979	130.27946	96.6859
2	19.559	MM	0.6044	108.13799	2.98176	3.3141

Totals : 3262.92778 133.26123



Area Percent Report

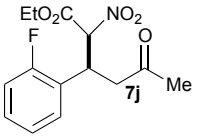
Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

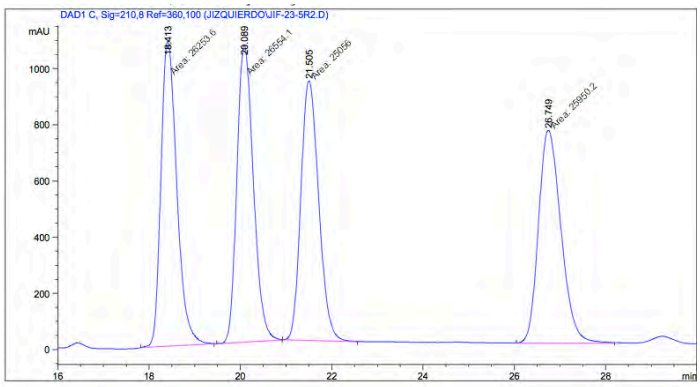
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	17.666	MM	0.4123	2490.12695	100.66517	99.3355
2	18.239	MM	0.2422	16.65714	8.82095e-1	0.6645

Totals : 2506.78409 101.54726

(3*S*)-Ethyl 3-(2-fluorophenyl)-2-nitro-5-oxohexanoate **7j** (Chiralpak AS-H, λ = 210 nm, 20% *i*PrOH/hexane, flow rate = 0.5 mL/min)



RACEMIC



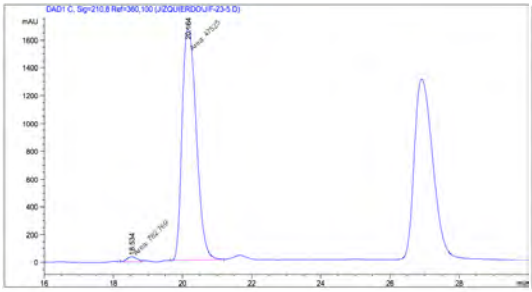
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.413	MM	0.4026	2.62536e4	1086.90369	25.2891
2	20.089	MM	0.4177	2.65541e4	1059.42859	25.5786
3	21.505	MM	0.4521	2.50560e4	923.59296	24.1355
4	26.749	MM	0.5711	2.59502e4	757.25354	24.9969

ENANTIOPURE

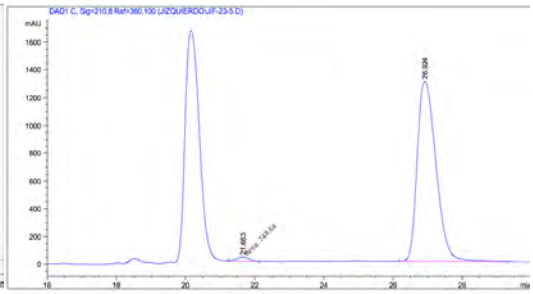


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.534	MF	0.3385	782.76917	38.53647	1.6204
2	20.164	MM	0.4762	4.75250e4	1663.33313	98.3796



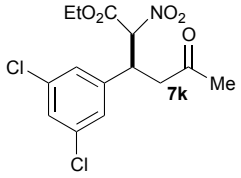
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

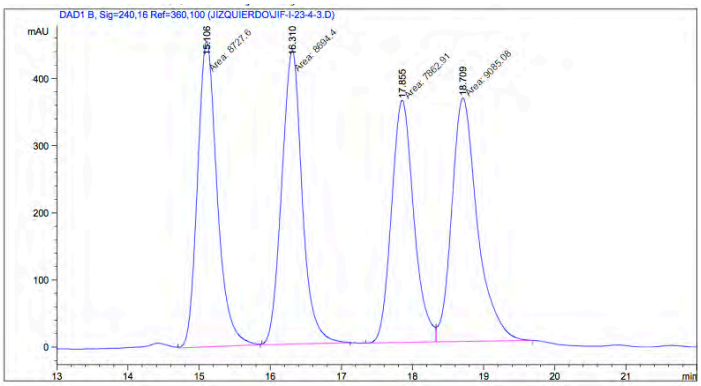
Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.663	MM	0.3996	748.63959	31.22291	1.5106
2	26.924	BB	0.5906	4.88096e4	1298.83606	98.4894

(3*S*)-Ethyl 3-(3,5-dichlorophenyl)-2-nitro-5-oxohexanoate **7k** (Chiralpak IA, λ = 240 nm, 5% *i*PrOH/hexane, flow rate = 0.5 mL/min)



RACEMIC

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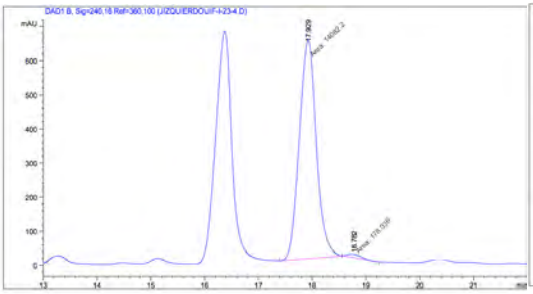
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=240,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.106 MM    0.3196 8727.60059  455.13651  25.3931
   2  16.310 MM    0.3317 8694.40430  436.82132  25.2965
   3  17.855 MF    0.3638 7862.91016  360.22479  22.8772
   4  18.709 FM    0.4180 9085.08301  362.28552  26.4332
```

ENANTIOPURE

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================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=240,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  17.929 MM    0.3666 1.40822e4  640.26971  98.7515
   2  18.782 MM    0.2733  178.03580  10.85725   1.2485
```

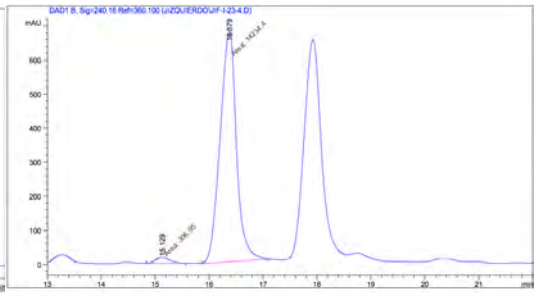


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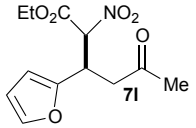
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=240,16 Ref=360,100

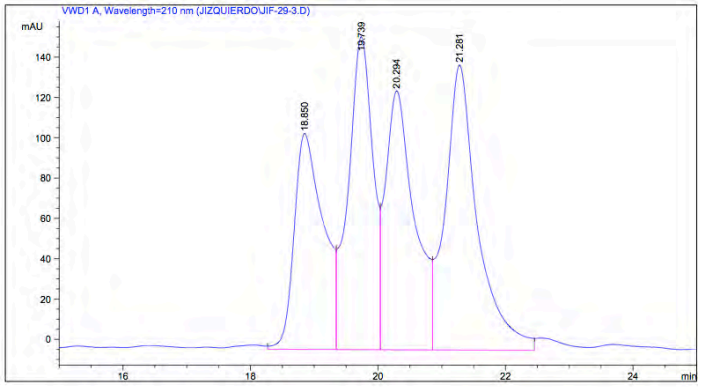
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.129 MM    0.3045  306.95007  16.80132   2.1109
   2  16.379 MM    0.3491 1.42344e4  679.66559  97.8891
```

(3*R*)-Ethyl 3-(furan-2-yl)-2-nitro-5-oxohexanoate **7l** (Chiralpak AD-H, λ = 210 nm, 10% *i*PrOH/hexane, flow rate = 0.5 mL/min)



7l

RACEMIC

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================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=210 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  18.850 VV    0.4517 3396.47095  107.05022  20.4733
   2  19.739 VV    0.3936 4168.97266  155.15582  25.1298
   3  20.294 VV    0.4465 4050.24731  128.43228  24.4142
   4  21.281 VV    0.4979 4974.04688  141.35350  29.9827

Totals :                  1.65897e4   531.99183
```
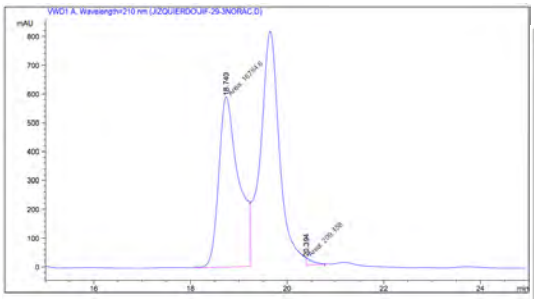

ENANTIOPURE



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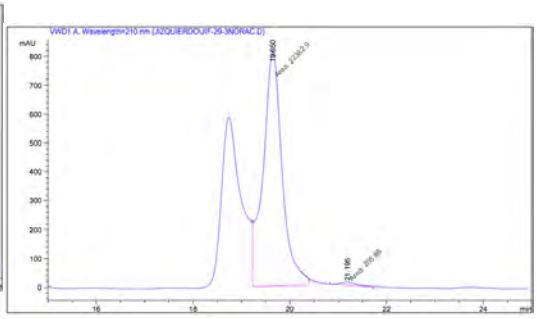
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=210 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  18.740 MF    0.4744 1.67846e4  589.70984  98.7692
   2  20.394 FM    0.1532  209.15773   22.75525   1.2308

Totals :                  1.69938e4   612.46509
```



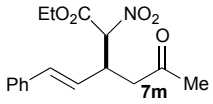
```
================================================================================
                          Area Percent Report
================================================================================

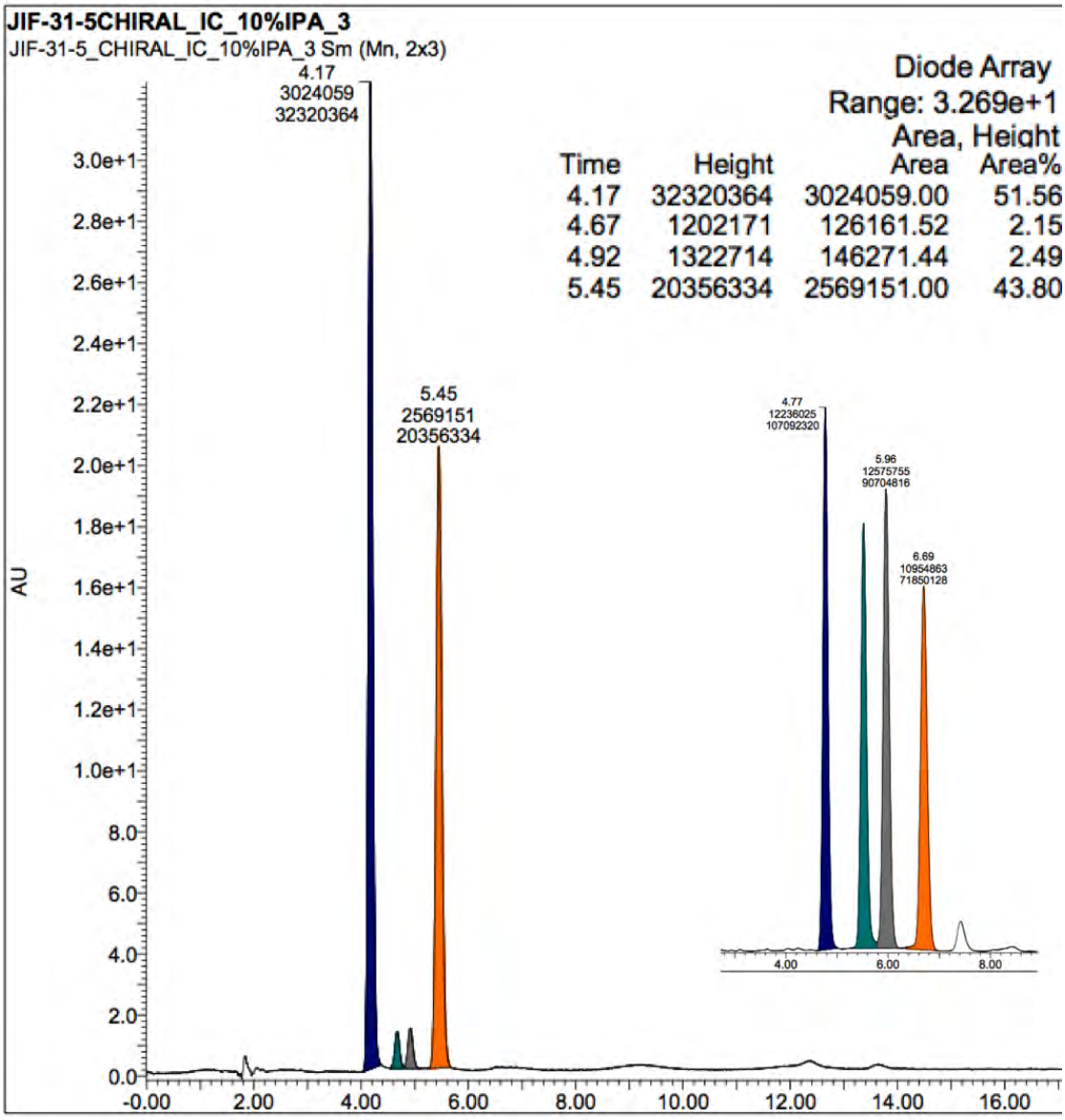
Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=210 nm

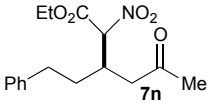
Peak RetTime Type  Width     Area      Height     Area
  #   [min]       [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  19.650 FM    0.4567 2.23829e4  813.30212  99.0886
   2  21.193 MM    0.3507  205.87982   9.78552   0.9114
```

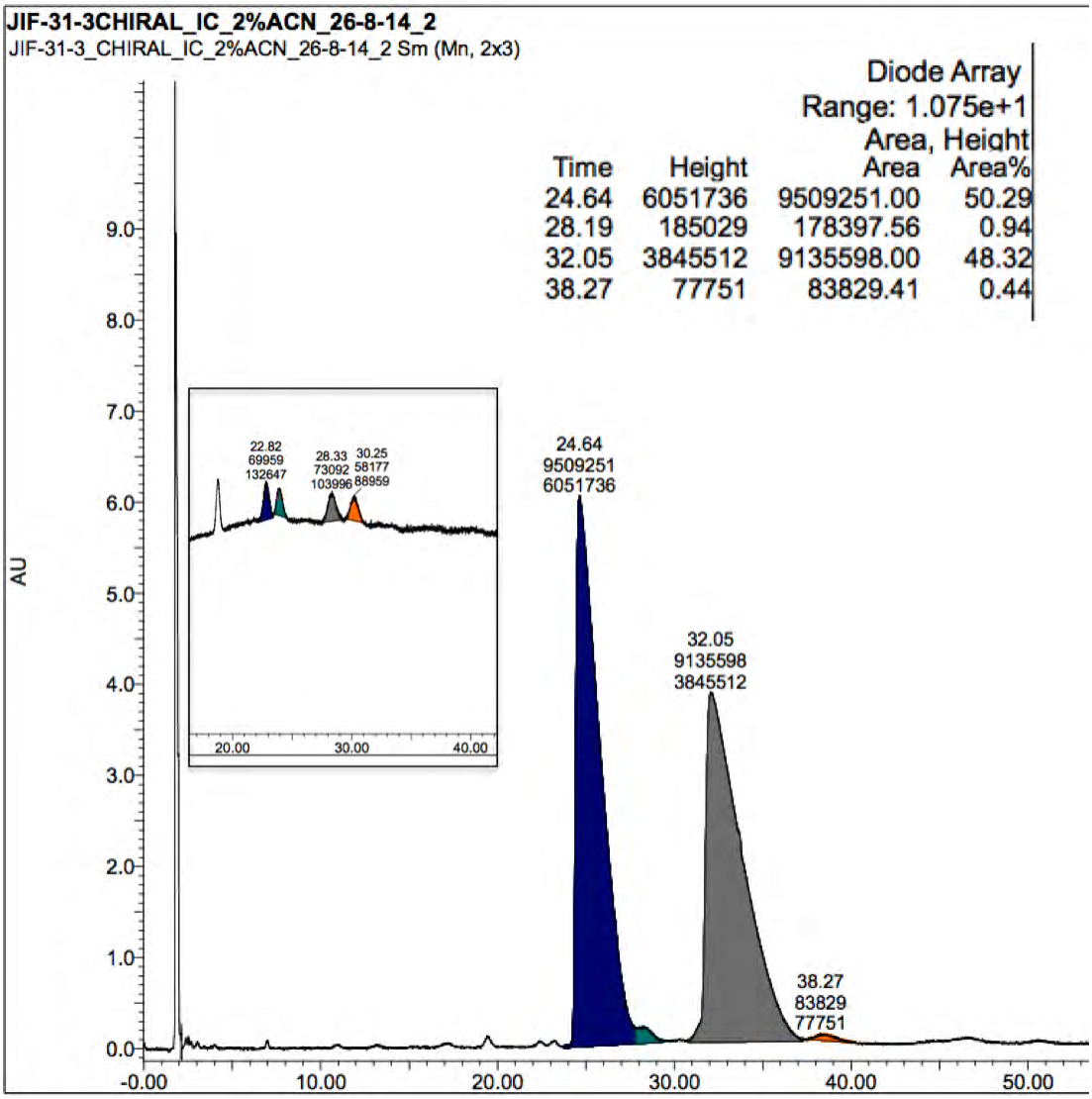
(3*S*)-Ethyl 2-nitro-5-oxo-3-((*E*)-styryl)hexanoate **7m** (UPC^2, Chiralpak IC, 10% *i*PrOH/CO_2, flow rate = 1 mL/min



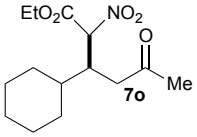


(3*R*)-Ethyl 2-nitro-5-oxo-3-phenethylhexanoate **7n** (UPC^2, Chiralpak IC, 2% acetonitrile/CO_2, flow rate = 1 mL/min)

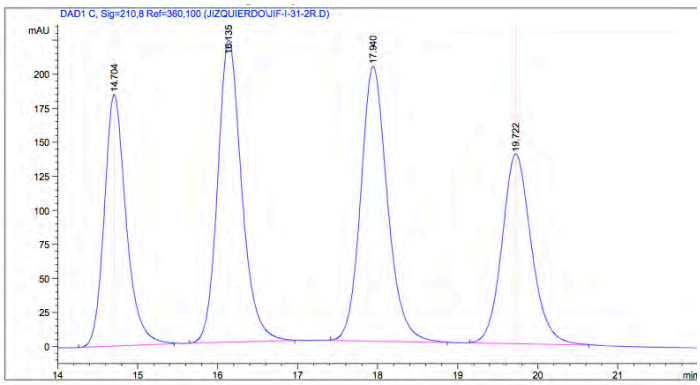




(3*S*)-Ethyl 3-cyclohexyl-2-nitro-5-oxohexanoate **7o** (Chiralpak IC, λ = 210 nm, 20% *i*PrOH/hexane, flow rate = 0.5 mL/min)



RACEMIC



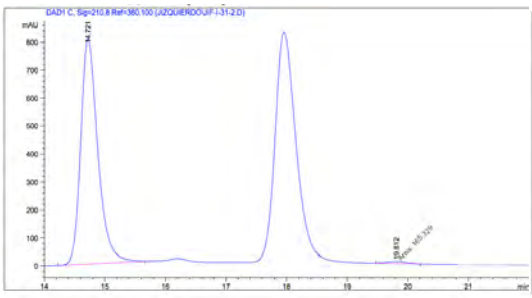
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.704	BB	0.2871	3501.90967	184.81003	21.3990
2	16.135	BB	0.3150	4626.21484	222.13167	28.2692
3	17.940	BB	0.3524	4683.79980	202.05054	28.6211
4	19.722	BB	0.3873	3552.93628	139.44682	21.7108

ENANTIOPURE

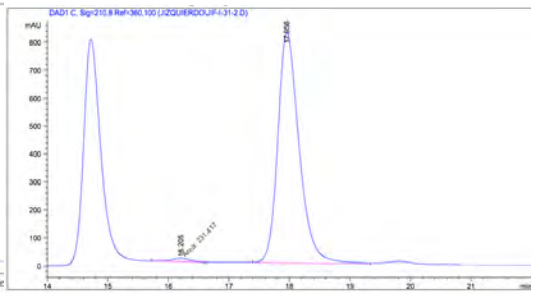


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.721	BB	0.2980	1.58773e4	805.41248	98.9694
2	19.812	MM	0.3664	165.32877	7.52011	1.0306



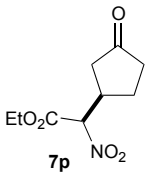
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

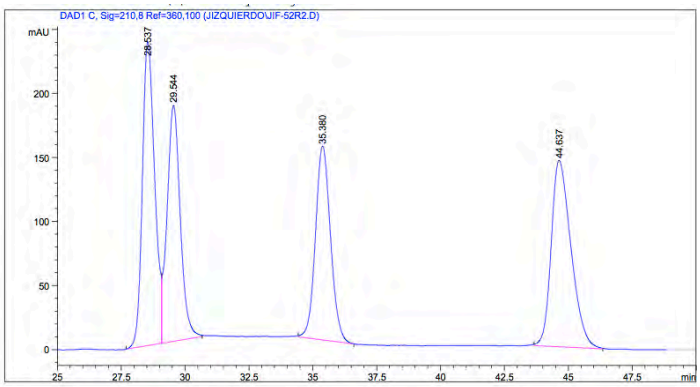
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.205	MM	0.3359	231.41742	11.48246	1.1359
2	17.956	BB	0.3688	2.01425e4	825.22363	98.8641

(*S*)-Ethyl 2-nitro-2-((*R*)-3-oxocyclopentyl)acetate **7p** (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 1 mL/min)



7p

RACEMIC



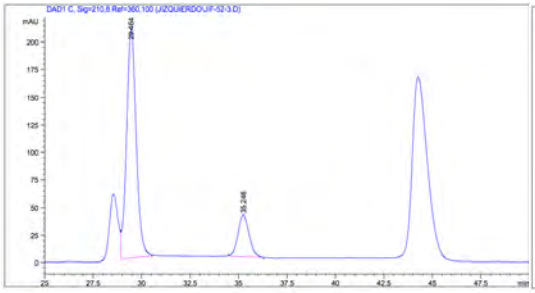
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.537	BV	0.5121	7932.61914	237.21954	27.7531
2	29.544	VB	0.5436	6629.78223	184.35327	23.1950
3	35.380	BB	0.6255	6199.90381	151.47986	21.6910
4	44.637	BB	0.8274	7820.52588	145.42261	27.3609

ENANTIOPURE



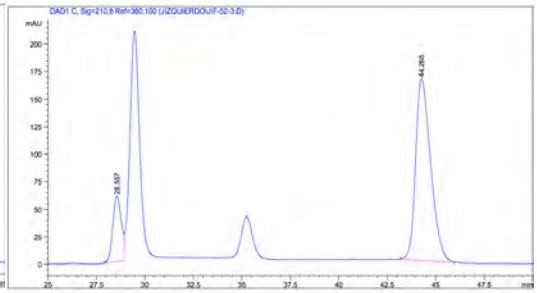
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.464	VB	0.5299	7195.12354	207.82649	82.6196
2	35.246	BB	0.6161	1513.61816	37.88859	17.3804

Totals : 8708.74170 245.71508



Area Percent Report

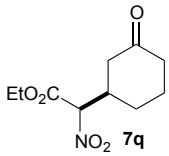
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.557	BV	0.4677	1820.65076	59.72144	16.9165
2	44.265	BB	0.8240	8941.91992	165.60356	83.0835

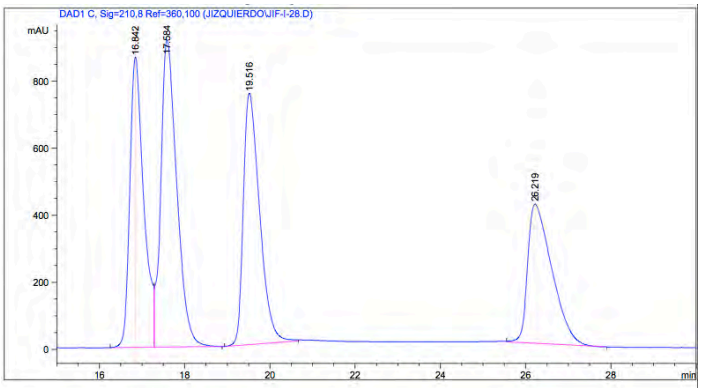
Totals : 1.07626e4 225.32500

(*S*)-Ethyl 2-nitro-2-((*R*)-3-oxocyclohexyl)acetate **7q** (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 0.5 mL/min)



7q

RACEMIC



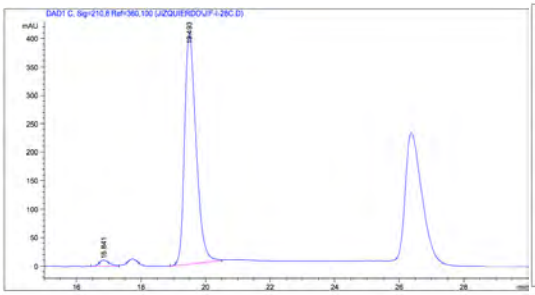
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.842	BV	0.3401	1.96074e4	866.05054	24.6239
2	17.584	VB	0.3916	2.38311e4	915.80804	29.9282
3	19.516	BB	0.4051	1.98541e4	749.28387	24.9337
4	26.219	BB	0.5928	1.63350e4	415.40750	20.5142

ENANTIOPURE

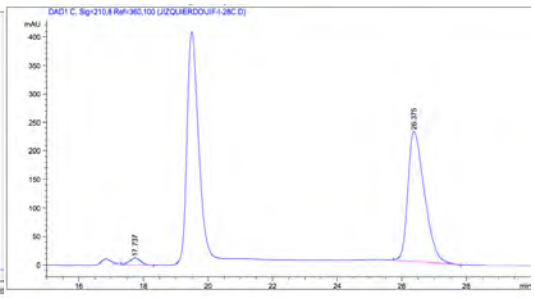


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.841	BV	0.3398	234.62215	10.22017	2.2749
2	19.493	BB	0.3818	1.00791e4	405.76328	97.7251



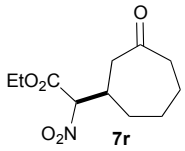
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 C, Sig=210,8 Ref=360,100

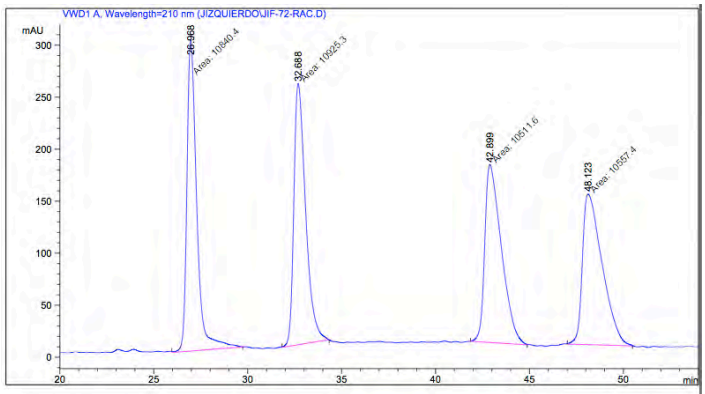
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.737	VB	0.3561	291.86995	12.42209	3.4511
2	26.375	BB	0.5472	8164.93213	228.31992	96.5489

(*S*)-Ethyl 2-nitro-2-((*R*)-3-oxocycloheptyl)acetate **7r** (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 1 mL/min)



7r

RACEMIC



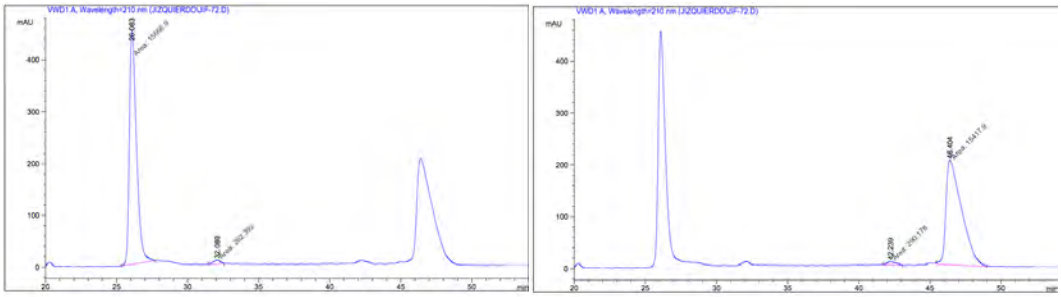
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	26.968	MM	0.6048	1.08404e4	298.74866	25.3075
2	32.688	MM	0.7257	1.09253e4	250.90021	25.5057
3	42.899	MM	1.0243	1.05116e4	171.03339	24.5399
4	48.123	MM	1.2162	1.05574e4	144.67682	24.6469

ENANTIOPURE



Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	26.083	MM	0.5770	1.56669e4	452.52768	98.3528
2	32.089	MM	0.5978	262.39230	7.31503	1.6472

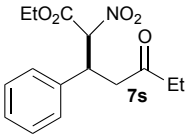
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

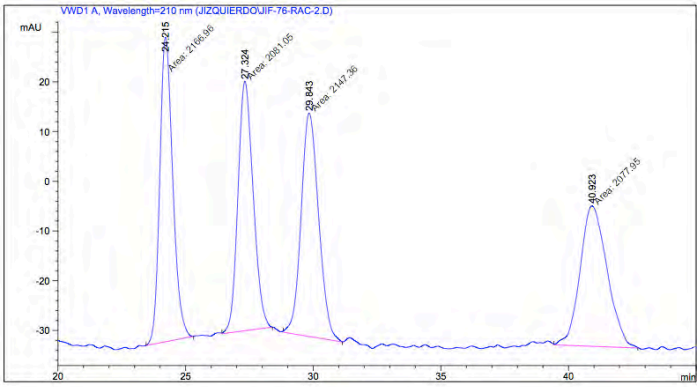
Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	42.239	MM	0.7799	290.17789	6.20081	1.8473
2	46.404	MM	1.2743	1.54179e4	201.65891	98.1527

(3*S*)-Ethyl 2-nitro-5-oxo-3-phenylheptanoate **7s** (Chiralpak AD-H, λ = 210 nm, 5% *i*PrOH/hexane, flow rate = 1 mL/min)



RACEMIC



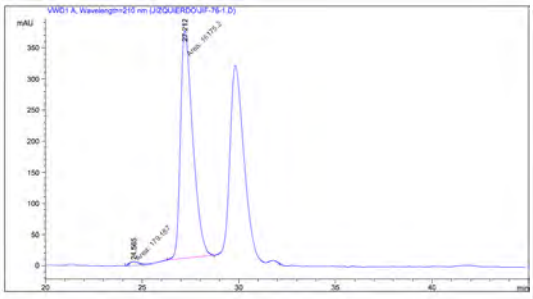
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	24.215	MM	0.5894	2166.95996	61.27668	25.5739
2	27.324	MM	0.6911	2081.05005	50.18790	24.5600
3	29.843	MM	0.7964	2147.36133	44.93977	25.3426
4	40.923	MM	1.2273	2077.95117	28.21794	24.5235

ENANTIOPURE

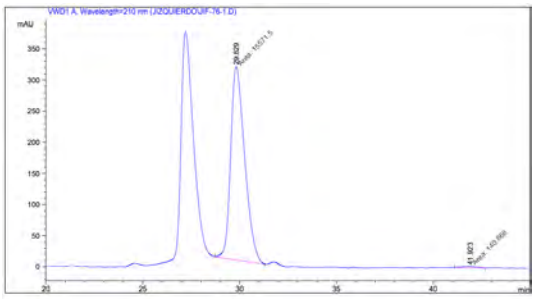


Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	24.565	MM	0.5638	179.18713	5.29671	1.0957
2	27.212	MM	0.7366	1.61752e4	365.96603	98.9043



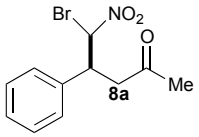
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

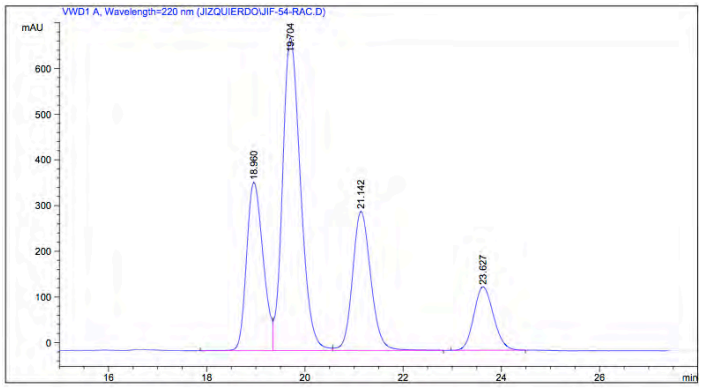
Signal 1: VWD1 A, Wavelength=210 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	29.829	MM	0.9386	1.55715e4	309.75572	99.1035
2	41.923	MM	0.9386	140.86797	2.50142	0.8965

(4*S*)-5-Bromo-5-nitro-4-phenylpentan-2-one **8a** (Chiralpak AS-H, λ = 220 nm, 25% *i*PrOH/hexane, flow rate = 0.5 mL/min)



SCALEMIC

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=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]     %
----|-------|----|-------|----------|----------|--------|
   1  18.960 VV     0.3640 8588.42676  367.95081  22.7709
   2  19.704 VV     0.3927 1.73942e4   684.23242  46.1183
   3  21.142 VB     0.3996 7872.77539  304.10281  20.8735
   4  23.627 BB     0.4292 3861.16992  138.88689  10.2373

Totals :                  3.77166e4  1495.17293
```
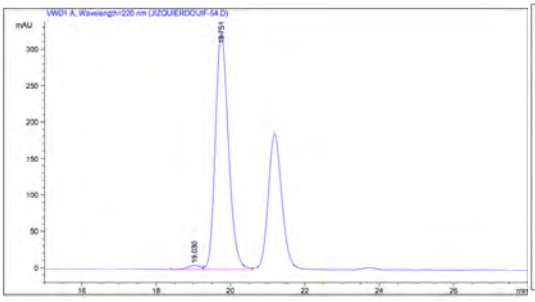

ENANTIOPURE

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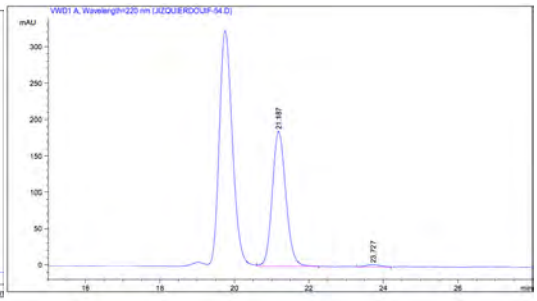
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]     %
----|-------|----|-------|----------|----------|--------|
   1  19.030 VV     0.3660  133.07436    5.87077   1.6473
   2  19.751 VV     0.3790 7945.14111  324.32907  98.3527

Totals :                  8078.21547  330.19985
```

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=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier:                  :      1.0000
Dilution:                    :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=220 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]     %
----|-------|----|-------|----------|----------|--------|
   1  21.187 VB     0.3941 4721.82666  185.73970  98.2536
   2  23.727 VV     0.3903   83.92540    3.12656   1.7464

Totals :                  4805.75206  188.86626
```
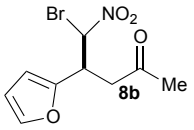
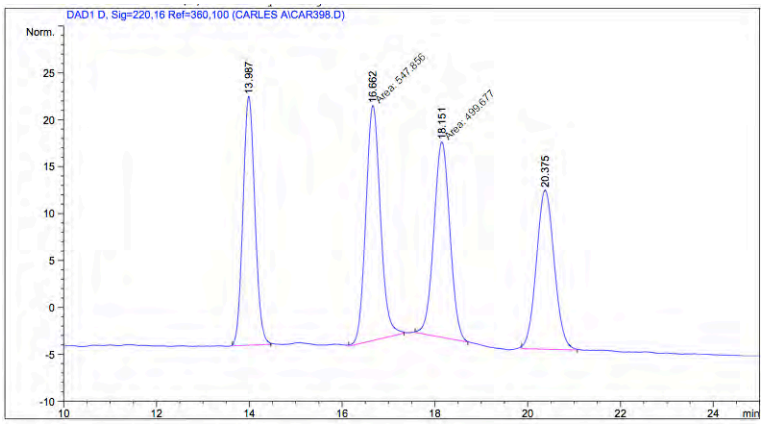

(4*S*)-5-Bromo-4-(furan-2-yl)-5-nitropentan-2-one **8b** (Chiralpak AS-H, λ = 220 nm,10% *i*PrOH/hexane, flow rate = 1.0 mL/min)



RACEMIC



Area Percent Report

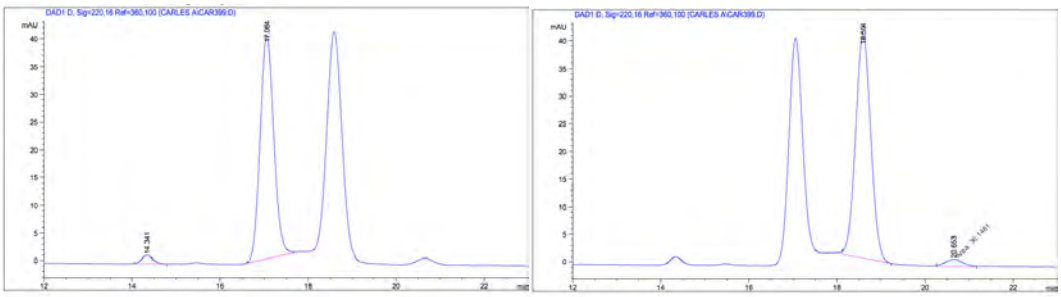
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.987	BB	0.2780	472.64105	26.51187	23.9312
2	16.662	MM	0.3644	547.85620	25.05857	27.7396
3	18.151	MM	0.3998	499.67728	20.82811	25.3001
4	20.375	BB	0.4152	454.82391	16.94036	23.0291

Totals : 1974.99844 89.33891

ENANTIOPURE



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.341	BB	0.2744	27.92675	1.57840	3.1132
2	17.064	BB	0.3384	869.11523	40.16778	96.8868

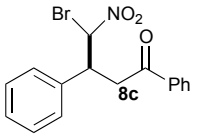
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

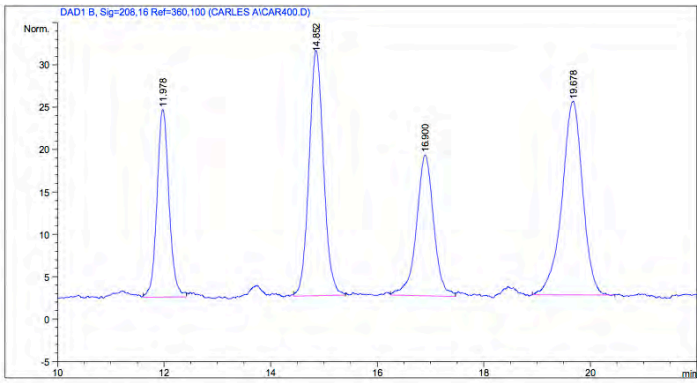
Signal 1: DAD1 D, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.594	BB	0.3731	969.80676	40.54053	96.4066
2	20.653	MM	0.4590	36.14808	1.31266	3.5934

(3*S*)-4-Bromo-4-nitro-1,3-diphenylbutan-1-one **8c** (Chiralpak AD-H, λ = 208 nm,10% *i*PrOH/hexane, flow rate = 1.0 mL/min)



RACEMIC



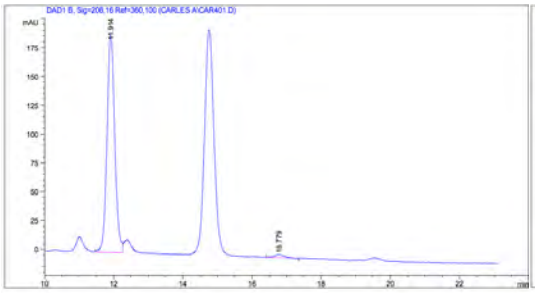
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=208,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.978	BB	0.2385	346.34647	22.14342	18.3694
2	14.852	BB	0.2885	547.16479	28.94455	29.0203
3	16.900	VB	0.3181	374.00189	16.64849	19.8362

ENANTIOPURE

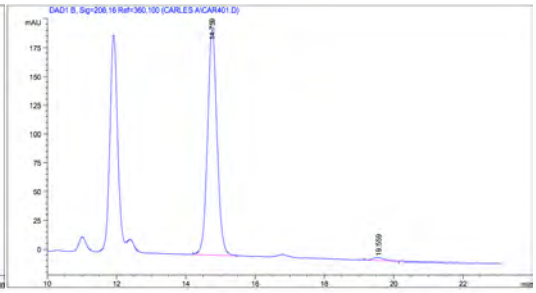


Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=208,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.914	BV	0.2379	2942.42676	188.70132	98.2111
2	16.779	BB	0.2615	53.59450	2.61106	1.7889



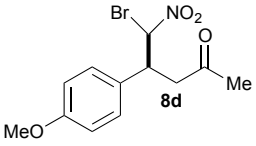
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=208,16 Ref=360,100

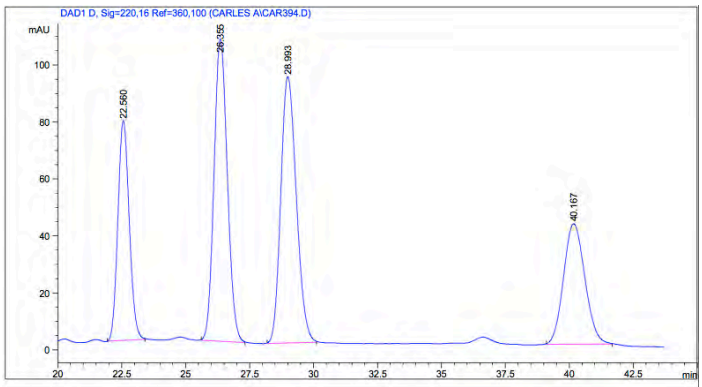
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.759	BB	0.2931	3739.84326	195.56923	98.4929
2	19.559	BB	0.2939	57.22478	2.47381	1.5071

(4*S*)-5-Bromo-4-(4-methoxyphenyl)-5-nitropentan-2-one **8d** (Chiralpak AS-H, λ = 220 nm,10% *i*PrOH/hexane, flow rate = 1.0 mL/min)



8d

RACEMIC



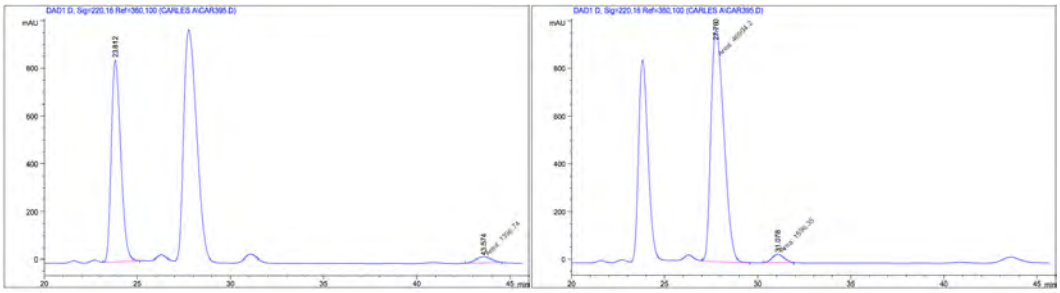
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.560	BB	0.4794	2376.41040	77.14242	18.8254
2	26.355	BB	0.5638	3839.66187	106.20187	30.4170
3	28.993	BB	0.6592	3954.14941	93.53188	31.3239

ENANTIOPURE



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=220,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.812	VB	0.5481	2.97121e4	845.18182	95.5102
2	43.574	MM	0.9967	1396.73889	23.35705	4.4898

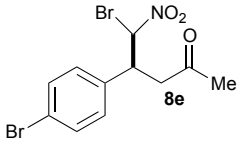
Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 D, Sig=220,16 Ref=360,100

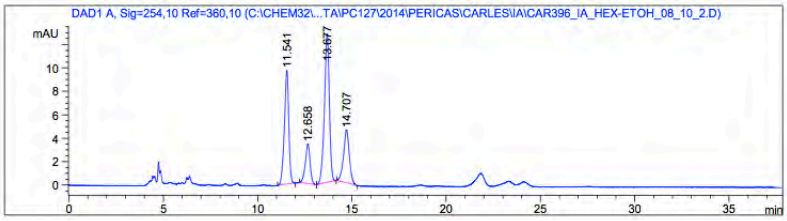
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.760	MM	0.8056	4.69042e4	970.34222	96.7086
2	31.078	MM	0.7344	1596.34900	36.22983	3.2914

(4*S*)-5-Bromo-4-(4-bromophenyl)-5-nitropentan-2-one **8e** (Chiralpak IA, λ = 254 nm,10% *i*PrOH/hexane, flow rate = 0.8 mL/min)



8e

SCALEMIC

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================================================================================
                          Area Percent Report
================================================================================

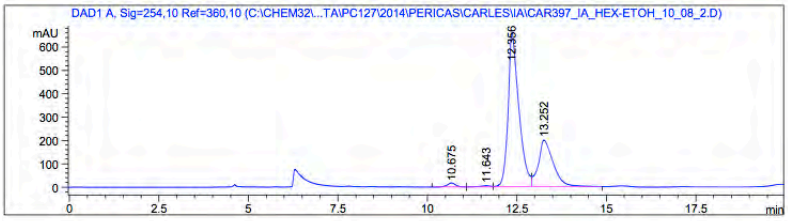
Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,10 Ref=360,10

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.541 BB    0.2388  157.65172    9.74156  28.9181
   2  12.658 BV    0.2572   59.89429    3.40513  10.9864
   3  13.677 VB    0.2699  231.24292   12.73265  42.4170
   4  14.707 BB    0.3131   96.37669    4.51303  17.6784

Totals :                   545.16563   30.39237
```

ENANTIOPURE

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================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,10 Ref=360,10

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  10.675 VV    0.2487  282.76035   17.11739   1.4138
   2  11.643 VV    0.2981  107.56919    5.22698   0.5378
   3  12.356 VV    0.2993 1.38423e4   658.45685  69.2105
   4  13.252 VB    0.4226 5767.64307  199.88028  28.8379

Totals :               2.00002e4   880.68150
```
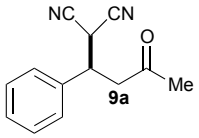
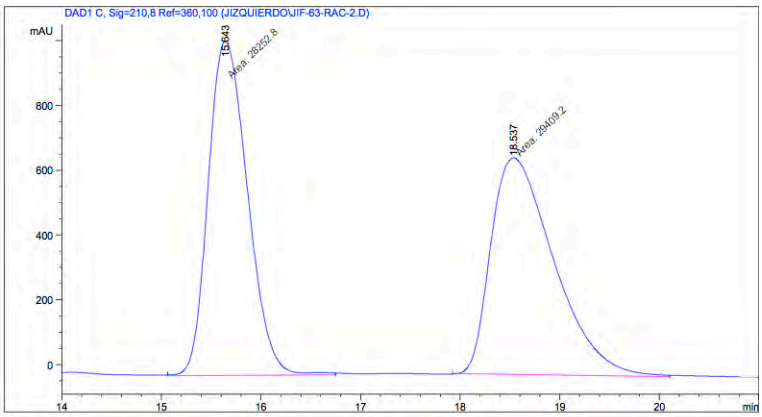

(*R*)-2-(3-Oxo-1-phenylbutyl)malononitrile **9a** (Chiralpak AS-H, λ = 210 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min)

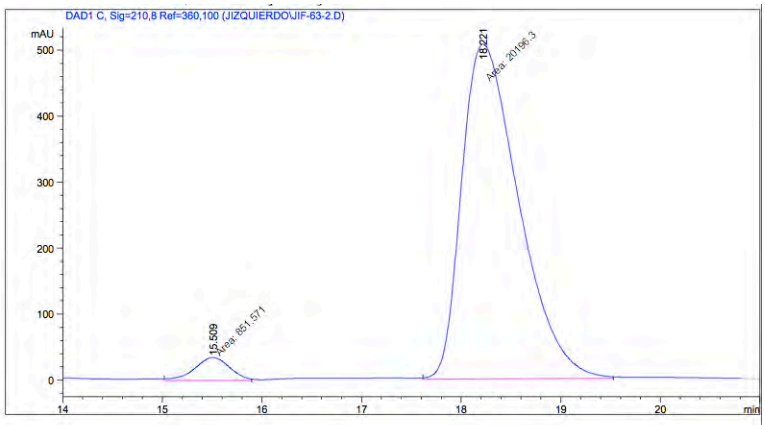


RACEMIC



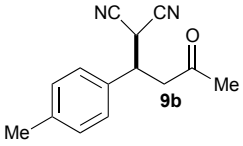

```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.643 MM    0.4568 2.82528e4  1030.76794  48.9973
   2  18.537 MM    0.7334 2.94092e4   668.33179  51.0027

Totals :                  5.76619e4  1699.09973
```

ENANTIOPURE



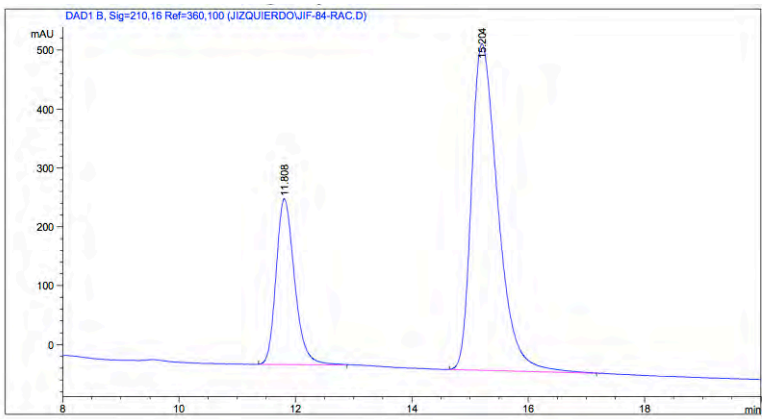

```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.509 MM    0.4087  851.57104   34.72826   4.0459
   2  18.221 MM    0.6634 2.01963e4   507.37869  95.9541

Totals :                  2.10479e4   542.10695
```

(*R*)-2-(3-Oxo-1-(*p*-tolyl)butyl)malononitrile **9b** (Chiralcel OD-H, λ = 210 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min)



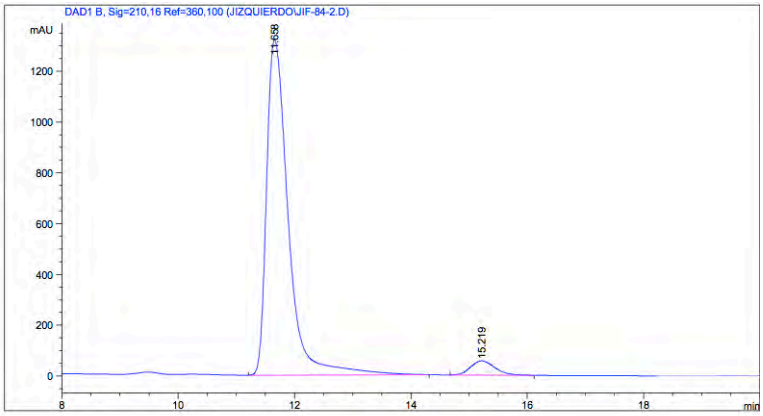
9b

SCALEMIC



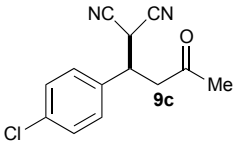

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=210,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.808 BB    0.3407 6187.54297  281.20145  26.1458
   2  15.204 BB    0.4796 1.74780e4   554.72552  73.8542
```

ENANTIOPURE



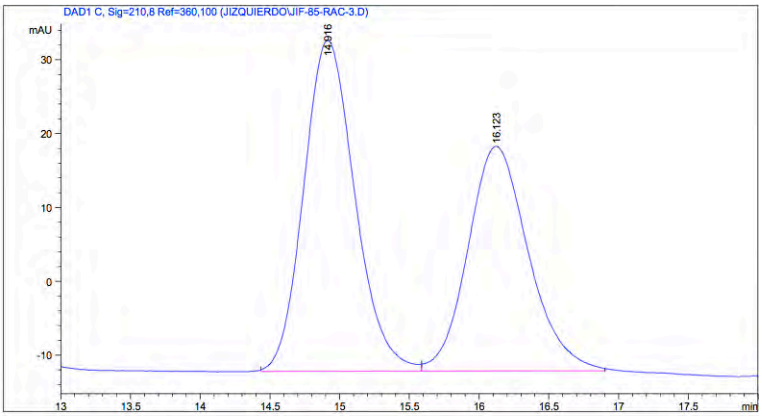

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=210,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  11.658 BB    0.3966 3.42395e4  1320.30383  95.4668
   2  15.219 BB    0.4411 1625.83521   56.26775   4.5332
```

(*R*)-2-(1-(4-Chlorophenyl)-3-oxobutyl)malononitrile **9c** (Chiralpak AS-H, λ = 210 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min)



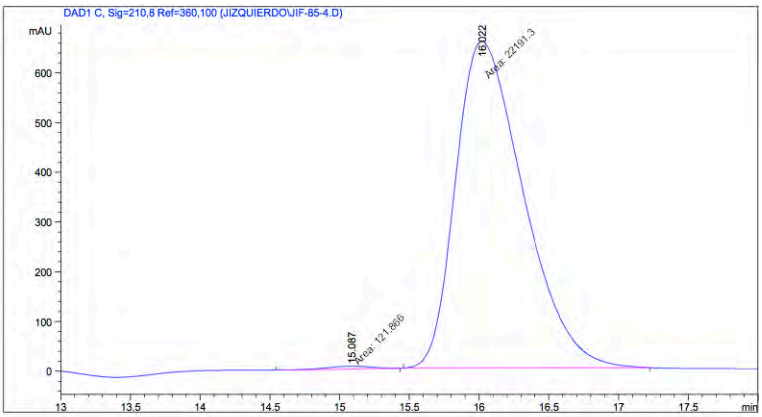
9c

SCALEMIC



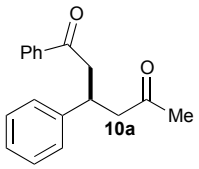

```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.916 BB    0.3975 1142.88953   44.82282  55.5136
   2  16.123 BB    0.4593  915.86646   30.41685  44.4864

Totals :                  2058.75598   75.23967
```

ENANTIOPURE

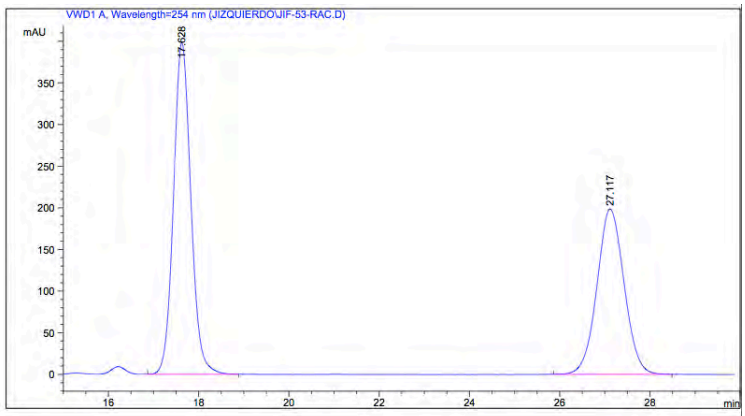



```
================================================================================
                          Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=210,8 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.087 MM    0.3683  121.86587    5.51521   0.5462
   2  16.022 MM    0.5631 2.21913e4   656.77533  99.4538

Totals :               2.23132e4   662.29054
```

(*S*)-4,5-Diphenylpentan-2-one **10a** (Chiralpak IC, λ = 254 nm, 20% *i*PrOH/hexane, flow rate = 1 mL/min)



SCALEMIC



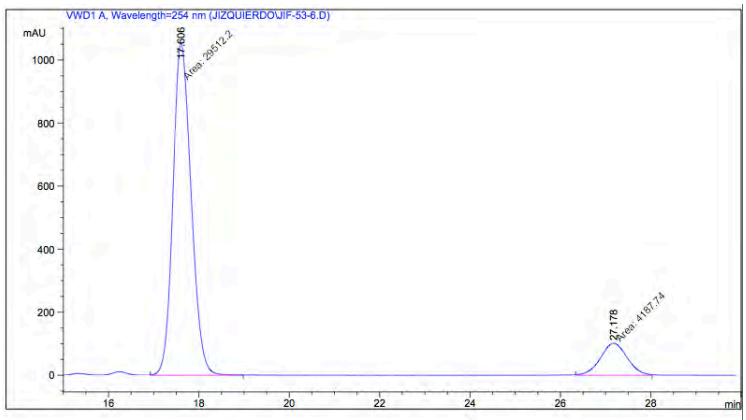
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	17.628	BB	0.4122	1.06453e4	398.40591	56.1762
2	27.117	BB	0.6478	8304.49121	198.67223	43.8238

ENANTIOPURE



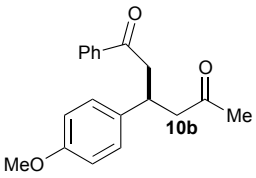
Area Percent Report

Sorted By : Signal
Multiplier: : 1.0000
Dilution: : 1.0000
Use Multiplier & Dilution Factor with ISTDs

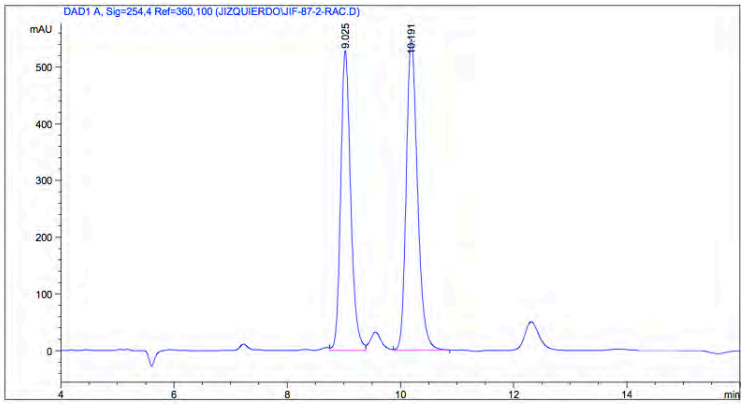
Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	17.606	MM	0.4671	2.95122e4	1052.99036	87.5734
2	27.178	MM	0.6866	4187.74268	101.65700	12.4266

(*S*)-4-(4-Methoxyphenyl)-5-phenylpentan-2-one **10b** (Chiralpak IA, λ = 254 nm, 20% *i*PrOH/hexane, flow rate = 1 mL/min)



RACEMIC



Area Percent Report

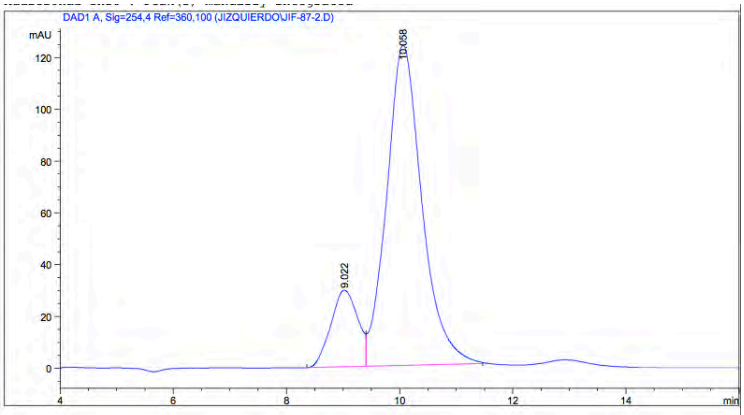
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.025	VV	0.1869	6472.00928	528.46320	46.0461
2	10.191	VB	0.2113	7583.49170	548.38831	53.9539

Totals : 1.40555e4 1076.85150

ENANTIOPURE



Area Percent Report

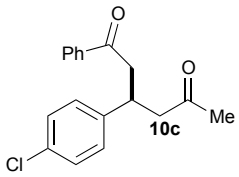
Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.022	BV	0.5065	981.03845	29.61004	15.4565
2	10.058	VB	0.6420	5366.06445	123.72800	84.5435

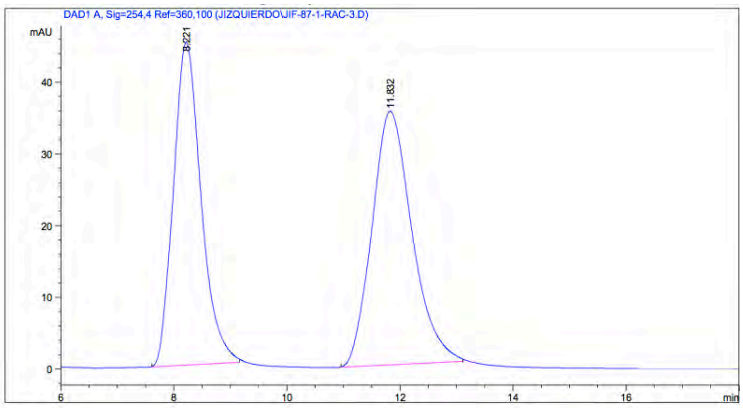
Totals : 6347.10291 153.33804

(*S*)-4-(4-Chlorophenyl)-5-phenylpentan-2-one **10c** (Chiralpak IA, λ = 254 nm, 20% *i*PrOH/hexane, flow rate = 1 mL/min)



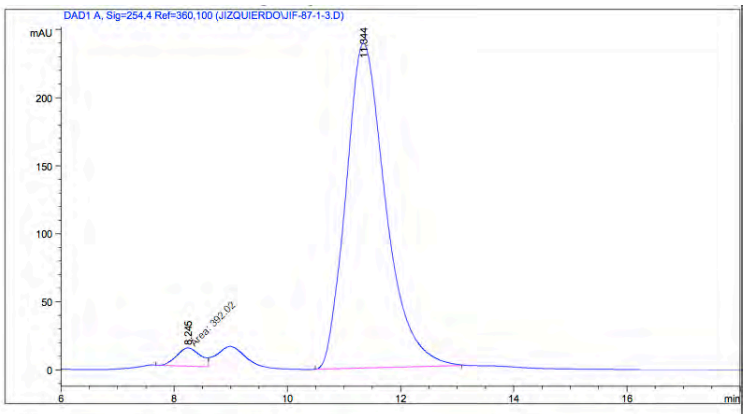
10c

RACEMIC



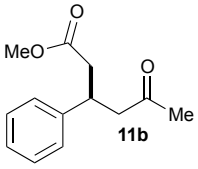

```
================================================================
                    Area Percent Report
================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|-------|
   1   8.221 BB    0.5081 1528.38696   45.02037  46.7768
   2  11.832 BB    0.7360 1739.01624   35.34796  53.2232

Totals :                  3267.40320   80.36833
```

ENANTIOPURE



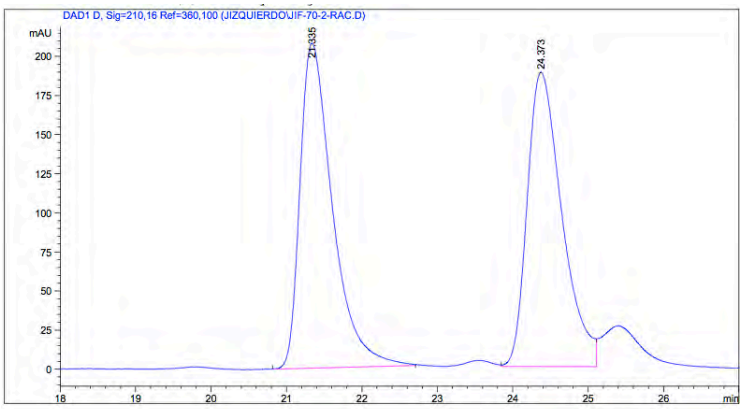

```
================================================================
                    Area Percent Report
================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|-------|
   1   8.245 MF    0.4903  392.01993   13.32652   3.2540
   2  11.344 BB    0.7317 1.16551e4   238.67497  96.7460

Totals :                  1.20472e4   252.00150
```

(*R*)-Methyl 5-oxo-3-phenylhexanoate **11b** (Chiralcel OD-H, λ = 210 nm, 7% *i*PrOH/hexane, flow rate = 0.5 mL/min)



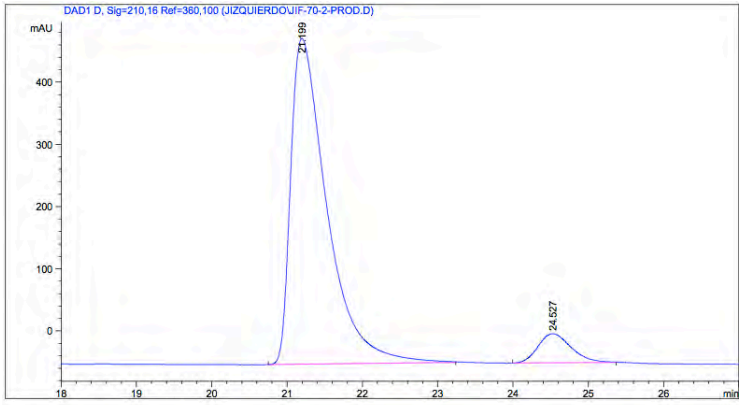
11b

RACEMIC



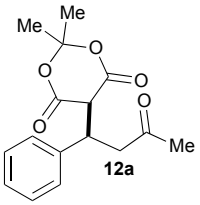

```
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=210,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  21.335 BB    0.4506 6209.64063  207.82367  50.8054
   2  24.373 VV    0.4866 6012.76709  188.25633  49.1946

Totals :                  1.22224e4   396.08000
```

ENANTIOPURE



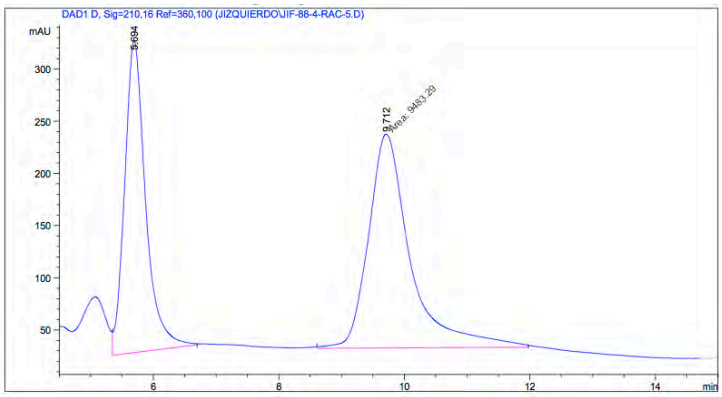

```
=====================================================================
                    Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=210,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  21.199 BB    0.4968 1.74626e4  523.98462  92.4376
   2  24.527 BB    0.4589 1428.63635  46.70597   7.5624

Totals :                  1.88913e4   570.69059
```

(*R*)-2,2-Dimethyl-5-(3-oxo-1-phenylbutyl)-1,3-dioxane-4,6-dione **12a** (Chiralpak IA, λ = 210 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min)



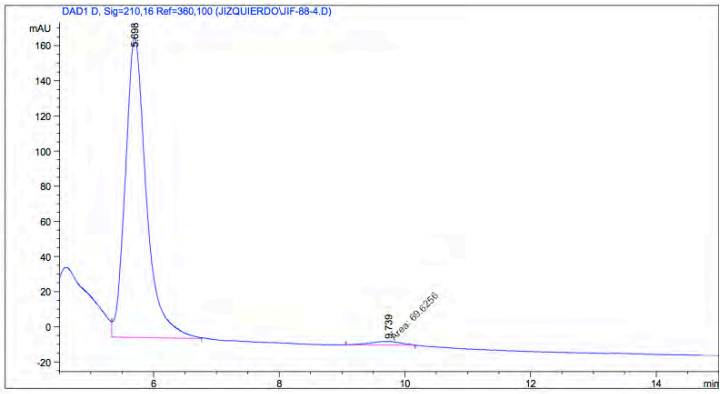
12a

SCALEMIC



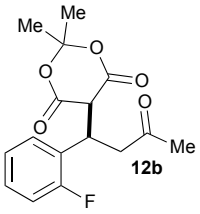

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=210,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.694 VB    0.3452 6939.88232  298.49683  42.2566
   2   9.712 MM    0.7713 9483.29199  204.91403  57.7434

Totals :                  1.64232e4   503.41086
```

ENANTIOPURE



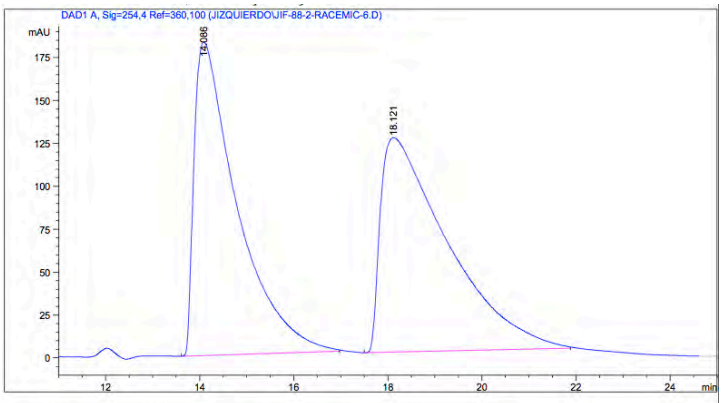

```
=====================================================================
                      Area Percent Report
=====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 D, Sig=210,16 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   5.698 VB    0.3445 3948.58398  170.28409  98.2672
   2   9.739 MM    0.5587   69.62556    2.07687   1.7328

Totals :                  4018.20954  172.36096
```

(*R*)-5-(1-(2-Fluorophenyl)-3-oxobutyl)-2,2-dimethyl-1,3-dioxane-4,6-dione **12b** (Chiralpak IC, λ = 254 nm, 30% *i*PrOH/hexane, flow rate = 1 mL/min)



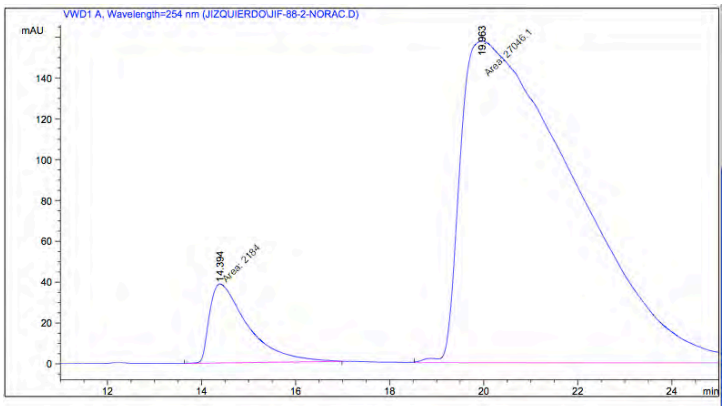
12b

SCALEMIC




```
================================================================================
                              Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  14.086 BB    0.9052 1.15756e4   182.68597  48.3326
   2  18.121 BB    1.3554 1.23743e4   124.94679  51.6674

Totals :                  2.39498e4   307.63277
```

ENANTIOPURE




```
================================================================================
                              Area Percent Report
================================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   mAU   *s    [mAU   ]     %
----|-------|----|-------|----------|----------|--------|
   1  14.394 MM    0.9409 2184.00171   38.68470   7.4718
   2  19.963 MM    2.8617 2.70461e4   157.51747  92.5282

Totals :                  2.92301e4   196.20218
```

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