

Supporting Information

Copper-Catalyzed Enantioselective Henry Reaction of β,γ -unsaturated α -ketoesters with nitromethane in Water

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Part I Experimental Section

1.1 General information

^1H NMR and ^{13}C NMR were recorded on a Bruker-400MHz Spectrometer (^1H NMR: 400MHz, ^{13}C NMR: 100MHz) using TMS as internal reference. The chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. HPLC analysis was carried out on an Agilent 1100 series HPLC with a multiple wavelength detector. Chiralpak AS-H columns were purchased from Daicel Chemical Industries, LTD. Optical rotations were measured on a PerKinElmerTM Polarimeter (Model 343). HRMS (ESI) were recorded on a WatersTM Q-TOF Premier. IR spectra were recorded on Thermo Scientific Nicolet iS10. Commercially available compounds were used without further purification. Solvents were purified according to the standard procedures unless otherwise noted. Ligands¹, various β,γ -unsaturated α -ketoesters² were prepared according to literature procedures.

1.2 General procedures of the Henry reaction (3a as an example)

A mixture of Ligand (**L**, 10.7 mg, 0.025 mmol), CuBr_2 (5.5 mg, 0.025 mmol), Cs_2CO_3 (8.1mg, 0.025 mmol), 2- $\text{FC}_6\text{H}_4\text{OH}$ (22.3 μL , 0.25 mmol), Et_4NClO_4 (5.7 mg, 0.025 mmol) and nitromethane **2a** (214.1 μL , 4.0 mmol) in water (1.0 mL) was stirred for 1h at ambient atmosphere. Then resulting mixture was cooled to 0 $^\circ\text{C}$. After 30 min, the β,γ -unsaturated α -ketoester **1a** (54.5 mg, 0.25 mmol) was added slowly and carried out at 0 $^\circ\text{C}$. After reactions were finished (monitored by TLC), and extracted with ethyl acetate (3 $\times$ 3 mL). The organic phase was dried with Na_2SO_4 and evaporated in vacuum. Purification by flash column chromatograph (petroleum ether / ethyl acetate = 20:1) afforded **3a** as a white solid: 90% yield, 62.7 mg, 93% ee.

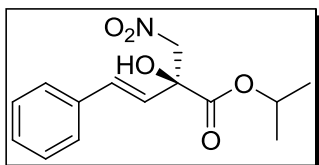
1.3 Procedure for Asymmetric Henry reaction on a gram scale

A mixture of Ligand (**L**, 213.6 mg, 0.5 mmol), CuBr_2 (111.6 mg, 0.5 mmol), Cs_2CO_3 (162.9 mg, 0.5 mmol), 2- $\text{FC}_6\text{H}_4\text{OH}$ (446.2 μL , 5 mmol), Et_4NClO_4 (114.8 mg, 0.5 mmol) and nitromethane **2a** (4.2 mL, 80 mmol) in water (15.0 mL) was stirred for 1h at ambient atmosphere. Then resulting mixture was cooled to 0 $^\circ\text{C}$. After 30 min, the β,γ -unsaturated α -ketoester **1c** (1.24 g, 5 mmol) was added slowly and carried out at 0 $^\circ\text{C}$. After reactions were finished (monitored by TLC), and extracted with ethyl acetate (3 $\times$ 15 mL). The organic phase was dried with Na_2SO_4 and evaporated in vacuum. Purification by flash column

chromatograph (petroleum ether / ethyl acetate = 20:1) afforded **3c** as a white solid: 83% yield, 1.28 g, 94% ee.

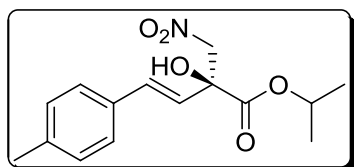
1.4 Experimental data of unsaturated β -nitro- α -hydroxy esters

(*S, E*)-isopropyl 2-hydroxy-2-(nitromethyl)-4-phenylbut-3-enoate (**3a**)



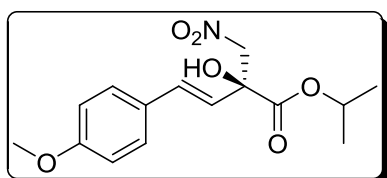
The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a white solid: 90% yield, 62.7 mg; mp = 97-98 °C; $[\alpha]_D^{20} +44.2$ (c = 0.98, CHCl₃, 93% ee); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 90:10, flow rate = 1.0 mL/min, T = 23°C, UV = 230 nm, t_R = 10.85 min (major), t_R = 18.1 min (minor); ¹H NMR (400 MHz, CDCl₃): δ 7.40-7.27 (m, 5H), 7.02 (d, J = 15.6 Hz, 1H), 6.11 (d, J = 15.7 Hz, 1H), 5.26-5.16 (m, 1H), 4.97 (d, J = 13.8 Hz, 1H), 4.57 (d, J = 13.8 Hz, 1H), 4.00 (s, 1H), 1.36-1.34 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 170.9, 135.2, 133.6, 128.77, 128.72, 126.9, 123.5, 79.9, 75.5, 71.9, 21.7, 21.4; IR (film, ν /cm⁻¹): 3846, 3661, 3490, 2987, 2900, 2359, 1933, 1726, 1556, 1450, 1406, 1393, 1287, 1262, 1182, 1073, 978, 905, 865, 751; HRMS (ESI) m/z calcd for C₁₄H₁₇NO₅ [M+Na]⁺ 302.1004, found 302.1010.

(*S, E*)-isopropyl 2-hydroxy-2-(nitromethyl)-4-*p*-tolylbut-3-enoate (**3b**)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow oil: 85% yield, 62.2 mg; $[\alpha]_D^{20} +39.3$ (c = 1.08 CHCl₃, 94% ee); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 23°C, UV = 230 nm, t_R = 5.99 min (major), t_R = 7.94 min (minor); ¹H NMR (400 MHz, CDCl₃): δ 7.27 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 6.98 (d, J = 15.7 Hz, 1H), 6.04 (d, J = 15.7 Hz, 1H), 5.25-5.15 (m, 1H), 4.96 (d, J = 13.8 Hz, 1H), 4.56 (d, J = 13.8 Hz, 1H), 3.94 (s, 1H), 2.34 (s, 3H), 1.35-1.33 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 171.0, 138.7, 133.5, 132.4, 129.4, 126.8, 122.3, 79.9, 75.4, 71.8, 21.7, 21.4, 21.2; IR (film, ν /cm⁻¹): 3846, 3789, 3661, 3489, 2987, 2900, 2360, 1914, 1731, 1692, 1557, 1462, 1408, 1393, 1376, 1287, 1231, 1183, 1151, 1066, 920, 907, 852, 815, 763, 719; HRMS (ESI) m/z calcd for C₁₅H₁₉NO₅ [M+Na]⁺ 316.1161, found 316.1164.

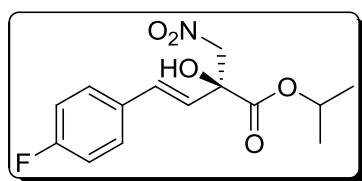
(*S, E*)-isopropyl 2-hydroxy-4-(4-methoxyphenyl)-2-(nitromethyl)but-3-enoate (**3c**)



The title compound was prepared according to the general

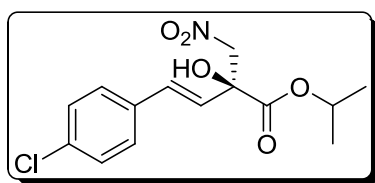
working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a white solid: 88% yield, 68.0 mg; mp = 129-130 °C; $[\alpha]_D^{20} +39.3$ (c = 1.00, CHCl₃, 96% ee); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 23°C, UV = 254 nm, t_R = 10.55 min (major), t_R = 17.65 min (minor); ¹H NMR (400 MHz, CDCl₃): δ 7.31 (d, *J* = 8.6 Hz, 2H), 6.95 (d, *J* = 15.6 Hz, 1H), 6.86(d, *J* = 8.6 Hz, 2H), 5.95 (d, *J* = 15.6 Hz, 1H), 5.25-5.15 (m, 1H), 4.95 (d, *J* = 13.8 Hz, 1H), 4.55 (d, *J* = 13.8 Hz, 1H), 3.95 (s, 1H), 3.81 (s, 3H), 1.35-1.33 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 171.1, 160.0, 133.0, 128.2, 127.9, 121.0, 114.1, 79.9, 75.4, 71.7, 55.3, 21.7, 21.4 ; IR (film, ν/cm⁻¹): 3846, 3829, 3683, 3661, 3497, 2987, 2900, 2360, 1933, 1728, 1606, 1557, 1512, 1410, 1376, 1290, 1231, 1177, 1066, 905, 851, 762, 723, 705; HRMS (ESI) *m/z* calcd for C₁₅H₁₉NO₆ [M+Na]⁺ 332.1110, found 332.1108.

(*S, E*)-isopropyl 4-(4-fluorophenyl)-2-hydroxy-2-(nitromethyl)but-3-enoate (3d)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow oil: 86% yield, 63.8 mg; $[\alpha]_D^{20} +24.5$ (c = 1.13, CHCl₃, 93% ee); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 23°C, UV = 230 nm, t_R = 7.29 min (major), t_R = 10.72 min (minor); ¹H NMR (400 MHz, CDCl₃): δ 7.37-7.33 (m, 2H), 7.05-6.97 (m, 3H), 6.02 (d, *J* = 15.6 Hz, 1H), 5.25-5.16 (m, 1H), 4.96 (d, *J* = 13.8 Hz, 1H), 4.56 (d, *J* = 13.8 Hz, 1H), 3.98 (s, 1H), 1.35-1.34 (m, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 170.9, 164.1, 161.6, 132.5, 131.45, 131.42, 128.6, 128.5, 123.17, 123.15, 115.8, 115.6, 79.8, 75.4, 71.9, 21.7, 21.4; IR (film, ν/cm⁻¹): 3661, 3476, 2987, 2900, 1736, 1599, 1561, 1510, 1406, 1393, 1380, 1250, 1241, 1230, 1065, 1056, 1027, 891, 879, 823; HRMS (ESI) *m/z* calcd for C₁₄H₁₆FNO₅ [M+Na]⁺ 320.0910, found 320.0909.

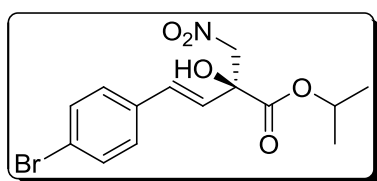
(*S, E*)-isopropyl 4-(4-chlorophenyl)-2-hydroxy-2-(nitromethyl)but-3-enoate (3e)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow oil: 87% yield, 68.0 mg; $[\alpha]_D^{20} +40.2$ (c = 1.02, CHCl₃, 92% ee); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 23°C, UV = 230 nm, t_R

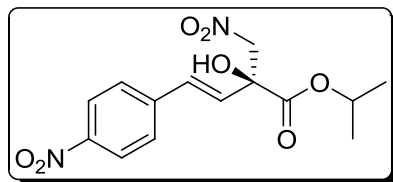
= 7.59 min (major), t_R = 11.03 min (minor); ^1H NMR (400 MHz, CDCl_3): δ 7.31 (s, 4H), 6.98 (d, J = 15.6 Hz, 1H), 6.08 (d, J = 15.6 Hz, 1H), 5.25-5.16 (m, 1H), 4.96 (d, J = 13.8 Hz, 1H), 4.55 (d, J = 13.8 Hz, 1H), 3.98 (s, 1H), 1.35-1.33 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.8, 134.4, 133.7, 132.5, 128.9, 128.1, 124.0, 79.8, 75.4, 72.0, 21.7, 21.4; IR (film, ν/cm^{-1}): 3846, 3661, 3484, 2987, 2900, 2359, 1914, 1733, 1557, 1492, 1405, 1393, 1375, 1283, 1256, 1231, 1181, 1149, 1066, 976, 944, 869, 848, 760, 721; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{16}\text{ClNO}_5$ $[\text{M}+\text{Na}]^+$ 336.0615, found 336.0616.

(*S, E*)-isopropyl 4-(4-bromophenyl)-2-hydroxy-2-(nitromethyl)but-3-enoate (3f)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow solid: 85% yield, 75.8 mg; mp = 97-98 °C; $[\alpha]_D^{20}$ +37.0 (c = 1.24, CHCl_3 , 91% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 90:10, flow rate = 1.0 mL/min, T = 23°C, UV = 240 nm, t_R = 15.98 min (major), t_R = 28.50 min (minor); ^1H NMR (400 MHz, CDCl_3): δ 7.46 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 6.96 (d, J = 15.6 Hz, 1H), 6.09 (d, J = 15.6 Hz, 1H), 5.25-5.16 (m, 1H), 4.95 (d, J = 13.8 Hz, 1H), 4.55 (d, J = 13.8 Hz, 1H), 4.00 (s, 1H), 1.35-1.33 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.7, 134.1, 132.5, 131.9, 128.4, 124.2, 122.6, 79.7, 75.4, 72.0, 21.6, 21.4; IR (film, ν/cm^{-1}): 3846, 3829, 3683, 3661, 3487, 2359, 1914, 1732, 1586, 1556, 1488, 1451, 1406, 1393, 1374, 1283, 1231, 1182, 1149, 1073, 1009, 944, 906, 867, 815, 790, 719; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{16}\text{BrNO}_5$ $[\text{M}+\text{Na}]^+$ 380.0110, found 380.0111.

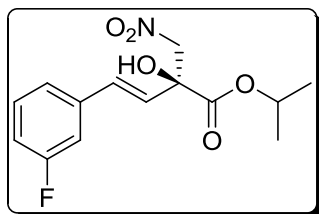
(*S, E*)-isopropyl 2-hydroxy-2-(nitromethyl)-4-(4-nitrophenyl)but-3-enoate (3g)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 6:1) to give the product as a light yellow oil: 80% yield, 64.8 mg; $[\alpha]_D^{20}$ +32.1 (c = 1.10, CHCl_3 , 83% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 23°C, UV = 240 nm, t_R = 25.76 min (major), t_R = 36.63 min (minor); ^1H NMR (400 MHz, CDCl_3): δ 8.19 (d, J = 8.6 Hz, 2H), 7.52 (d, J = 8.7 Hz, 2H), 7.11 (d, J = 15.6 Hz, 1H), 6.29 (d, J = 15.6 Hz, 1H), 5.26-5.17 (m, 1H), 4.99 (d, J = 13.8 Hz, 1H), 4.58 (d, J = 13.8 Hz, 1H), 4.08 (s, 1H), 1.35-1.34 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 170.3, 147.6, 141.5, 131.7, 128.1, 127.6, 124.1, 79.6, 75.5, 72.4, 21.6, 21.4; IR (film, ν/cm^{-1}): 3661, 3474, 2987,

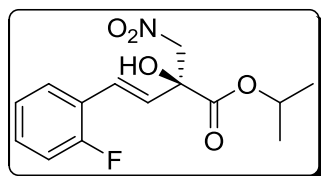
2900, 1735, 1597, 1560, 1518, 1452, 1407, 1393, 1378, 1291, 1259, 1101, 1075, 1066, 1056, 1027, 891, 879, 760; HRMS (ESI) m/z calcd for $C_{14}H_{16}N_2O_7$ $[M+Na]^+$ 347.0855, found 347.0865.

(S, E)-isopropyl 4-(3-fluorophenyl)-2-hydroxy-2-(nitromethyl)but-3-enoate (3h)



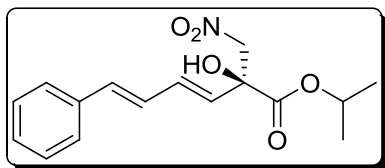
The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow oil: 88% yield, 65.3 mg; $[\alpha]_D^{20} +34.7$ ($c = 0.90$, $CHCl_3$, 90% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, $T = 23^\circ C$, UV = 230 nm, $t_R = 6.49$ min (major), $t_R = 8.43$ min (minor); 1H NMR (400 MHz, $CDCl_3$): δ 7.33-7.27 (m, 1H), 7.14 (d, $J = 7.7$ Hz, 1H), 7.08 (d, $J = 9.9$ Hz, 1H), 7.02-6.98 (m, 2H), 6.11 (d, $J = 15.6$ Hz, 1H), 5.26-5.16 (m, 1H), 4.96 (d, $J = 13.8$ Hz, 1H), 4.56 (d, $J = 13.8$ Hz, 1H), 4.01 (s, 1H), 1.36-1.34 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 164.2, 161.8, 137.5, 137.4, 132.67, 132.65, 130.3, 130.2, 124.8, 123.04, 123.02, 115.6, 115.4, 113.4, 113.2, 79.7, 75.4, 72.1, 21.6, 21.4; IR (film, ν/cm^{-1}): 3675, 2968, 2900, 1735, 1584, 1560, 1449, 1406, 1393, 1378, 1263, 1066, 1056, 879, 819, 762; HRMS (ESI) m/z calcd for $C_{14}H_{16}FNO_5$ $[M+Na]^+$ 320.0910, found 320.0910.

(S, E)-isopropyl 4-(2-fluorophenyl)-2-hydroxy-2-(nitromethyl)but-3-enoate (3i)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow solid: 85% yield, 63.1 mg; mp = 72-73 $^\circ C$; $[\alpha]_D^{20} +38.5$ ($c = 1.20$, $CHCl_3$, 90% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, $T = 23^\circ C$, UV = 230 nm, $t_R = 6.81$ min (major), $t_R = 10.04$ min (minor); 1H NMR (400 MHz, $CDCl_3$): δ 7.38 (t, $J = 7.6$ Hz, 1H), 7.29-7.24 (m, 1H), 7.14-7.10 (m, 2H), 7.08-7.03 (m, 1H), 6.24 (d, $J = 15.9$ Hz, 1H), 5.26-5.17 (m, 1H), 4.98 (d, $J = 13.8$ Hz, 1H), 4.57 (d, $J = 13.8$ Hz, 1H), 3.99 (s, 1H), 1.36-1.33 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 161.8, 159.3, 130.0, 129.9, 128.55, 128.51, 126.77, 126.75, 126.48, 126.42, 124.3, 124.2, 123.1, 123.0, 116.1, 115.9, 79.7, 75.5, 71.9, 21.6, 21.4; IR (film, ν/cm^{-1}): 3789, 3661, 3489, 2987, 2900, 2359, 1919, 1725, 1655, 1609, 1556, 1487, 1458, 1414, 1393, 1375, 1284, 1262, 1228, 1184, 1150, 1077, 946, 905, 858, 811, 777, 756, 708; HRMS (ESI) m/z calcd for $C_{14}H_{16}FNO_5$ $[M+Na]^+$ 320.0910, found 320.0907.

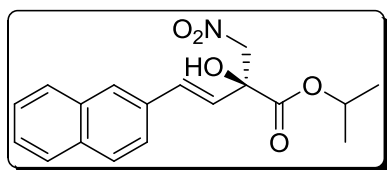
(S, 3E, 5E)-isopropyl 2-hydroxy-2-(nitromethyl)-6-phenylhexa-3,5-dienoate (3j)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 30:1) to give the product as a light yellow oil: 75% yield, 57.2 mg;

$[\alpha]_D^{20} +88.7$ ($c = 1.03$, CHCl_3 , 94% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, $T = 23^\circ\text{C}$, UV = 254 nm, $t_R = 7.38$ min (major), $t_R = 9.40$ min (minor); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 7.49 (d, $J = 7.6$ Hz, 2H), 7.34 (t, $J = 7.3$ Hz, 2H), 7.25 (t, $J = 7.4$ Hz, 1H), 6.98-6.92 (m, 1H), 6.82-6.71 (m, 2H), 5.95 (d, $J = 15.0$ Hz, 1H), 5.23-5.19 (m, 2H), 5.14-5.07 (m, 1H), 4.61 (d, $J = 13.3$ Hz, 1H), 1.31-1.28 (m, 6H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 170.5, 136.9, 134.6, 132.8, 129.4, 128.6, 127.9, 127.3, 126.5, 80.4, 75.8, 70.2, 20.9, 20.7; IR (film, v/cm^{-1}): 3661, 3476, 2981, 2900, 1735, 1560, 1449, 1406, 1393, 1379, 1229, 1066, 1056, 891, 759, 692; HRMS (ESI) m/z calcd for $\text{C}_{16}\text{H}_{19}\text{NO}_5$ $[\text{M}+\text{Na}]^+$ 328.1161, found 328.1166.

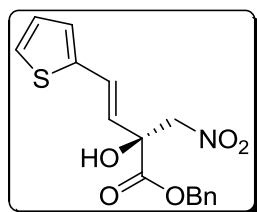
(S, E)-isopropyl 2-hydroxy-4-(naphthalen-2-yl)-2-(nitromethyl)but-3-enoate (3k)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow solid: 91% yield, 74.8 mg;

mp = 111-112 $^\circ\text{C}$; $[\alpha]_D^{20} +60.0$ ($c = 0.98$, CHCl_3 , 90% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 90:10, flow rate = 1.0 mL/min, $T = 23^\circ\text{C}$, UV = 215 nm, $t_R = 14.30$ min (major), $t_R = 19.31$ min (minor); ^1H NMR (400 MHz, CDCl_3): δ 7.82-7.77 (m, 4H), 7.56 (d, $J = 8.5$ Hz, 1H), 7.51-7.46 (m, 2H), 7.19 (d, $J = 15.6$ Hz, 1H), 6.23 (d, $J = 15.6$ Hz, 1H), 5.28-5.19 (m, 1H), 5.02 (d, $J = 13.8$ Hz, 1H), 4.61 (d, $J = 13.8$ Hz, 1H), 4.06 (s, 1H), 1.38-1.36 (m, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.0, 133.7, 133.43, 133.41, 132.6, 128.4, 128.1, 127.7, 127.6, 126.58, 126.52, 123.7, 123.3, 79.9, 75.6, 71.9, 21.7, 21.4; IR (film, v/cm^{-1}): 3846, 3810, 3661, 3490, 2987, 2900, 2360, 1932, 1719, 1573, 1452, 1406, 1393, 1377, 1274, 1250, 1220, 1178, 1152, 1066, 978, 923, 905, 841, 826, 756, 744; HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_5$ $[\text{M}+\text{Na}]^+$ 352.1161, found 352.1160.

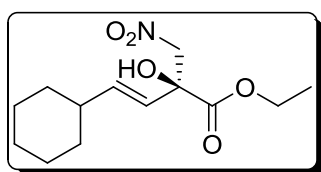
(S, E)-benzyl 2-hydroxy-2-(nitromethyl)-4-(thiophen-2-yl)but-3-enoate (3l)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow oil: 79% yield, 65.7 mg; $[\alpha]_D^{20} +51.4$ ($c = 0.70$, CHCl_3 , 91% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0

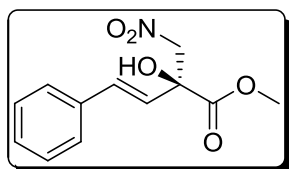
mL/min, T = 23°C, UV = 254 nm, t_R = 16.44 min (major), t_R = 23.76 min (minor); ^1H NMR (400 MHz, CDCl_3): δ 7.39-7.36 (m, 5H), 7.23 (d, J = 5.0 Hz, 1H), 7.12 (d, J = 15.4 Hz, 1H), 7.01 (d, J = 3.0 Hz, 1H), 6.99-6.97 (m, 1H), 5.91 (d, J = 15.4 Hz, 1H), 5.32 (s, 2H), 4.95 (d, J = 13.9 Hz, 1H), 4.55 (d, J = 13.9 Hz, 1H), 3.97 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3): δ 171.2, 139.9, 134.3, 128.9, 128.8, 128.6, 127.9, 127.6, 127.1, 125.9, 122.0, 79.7, 75.4, 69.2; IR (film, v/cm^{-1}): 3845, 3661, 3516, 2987, 2900, 2359, 1926, 1734, 1553, 1491, 1454, 1406, 1386, 1260, 1241, 1206, 1102, 1065, 1027, 951, 937, 908, 859, 823, 728, 694; HRMS (ESI) m/z calcd for $\text{C}_{16}\text{H}_{15}\text{NO}_5\text{S}$ $[\text{M}+\text{Na}]^+$ 356.0569, found 356.0567.

(S, E)-ethyl 4-cyclohexyl-2-hydroxy-2-(nitromethyl)but-3-enoate (3m)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 30:1) to give the product as a light yellow solid: 78% yield, 52.8 mg; mp = 75-76 °C; $[\alpha]_D^{20}$ +41.3 (c = 0.67, CHCl_3 , 93% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 23°C, UV = 230 nm, t_R = 5.14 min (major), t_R = 6.12 min (minor); ^1H NMR (400 MHz, CDCl_3): δ 6.07 (dd, J = 15.4 Hz, 6.8 Hz, 1H), 5.36 (dd, J = 15.4 Hz, 1.3 Hz, 1H), 4.87 (d, J = 13.8 Hz, 1H), 4.47 (d, J = 13.8 Hz, 1H), 4.37-4.33 (m, 2H), 3.77 (s, 1H), 2.03-1.96 (m, 1H), 1.74-1.63 (m, 5H), 1.33 (t, J = 7.1 Hz, 3H), 1.27-1.06 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3): δ 172.0, 141.2, 122.1, 80.1, 75.1, 63.2, 40.2, 32.4, 25.9, 25.8, 14.0; IR (film, v/cm^{-1}): 3846, 3810, 3661, 3485, 2987, 2900, 2359, 1933, 1731, 1692, 1659, 1563, 1512, 1462, 1406, 1393, 1382, 1265, 1221, 1159, 1133, 1065, 981, 891, 865, 793, 777, 691; HRMS (ESI) m/z calcd for $\text{C}_{13}\text{H}_{21}\text{NO}_5$ $[\text{M}+\text{Na}]^+$ 294.1317, found 294.1324.

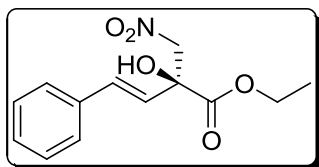
(S, E)-methyl 2-hydroxy-2-(nitromethyl)-4-phenylbut-3-enoate (3n)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow oil: 89% yield, 55.8 mg; $[\alpha]_D^{20}$ +31.5 (c = 0.63, CHCl_3 , 92% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 90:10, flow rate = 1.0 mL/min, T = 23°C, UV = 230 nm, t_R = 17.42 min (major), t_R = 19.50 min (minor); ^1H NMR (400 MHz, CDCl_3): δ 7.40-7.29 (m, 5H), 7.02 (d, J = 15.6 Hz, 1H), 6.11 (d, J = 15.7 Hz, 1H), 4.98 (d, J = 13.9 Hz, 1H), 4.58 (d, J = 13.8 Hz, 1H), 3.97 (s, 1H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3): δ 172.0, 135.0, 133.8, 128.8, 128.7, 127.0, 123.0, 79.9, 75.6, 54.1; IR (film, v/cm^{-1}): 3661, 2970, 2900, 2359, 1753, 1561,

1451, 1406, 1393, 1381, 1260, 1229, 1065, 1056, 891, 879, 810, 761; HRMS (ESI) m/z calcd for $C_{12}H_{13}NO_5$ $[M+Na]^+$ 274.0691, found 274.0690.

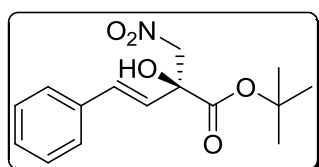
(S, E)-ethyl 2-hydroxy-2-(nitromethyl)-4-phenylbut-3-enoate (3o)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow oil: 87% yield, 57.6 mg; $[\alpha]_D^{20} +42.8$ ($c = 0.79$, $CHCl_3$, 93% *ee*); HPLC:

Daicel Chiralpak AS-H, hexane: 2-propanol = 90:10, flow rate = 1.0 mL/min, $T = 23^\circ C$, UV = 230 nm, $t_R = 12.77$ min (major), $t_R = 16.77$ min (minor); 1H NMR (400 MHz, $CDCl_3$): δ 7.40-7.27 (m, 5H), 7.02 (d, $J = 15.7$ Hz, 1H), 6.11 (d, $J = 15.7$ Hz, 1H), 4.99 (d, $J = 13.8$ Hz, 1H), 4.58 (d, $J = 13.8$ Hz, 1H), 4.42-4.35 (m, 2H), 3.99 (s, 1H), 1.36 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.5, 135.1, 133.7, 128.78, 128.76, 126.9, 123.3, 79.9, 75.5, 63.6, 14.0; IR (film, ν/cm^{-1}): 3661, 2987, 2900, 1741, 1561, 1450, 1406, 1393, 1380, 1250, 1228, 1065, 1056, 1027, 891, 761; HRMS (ESI) m/z calcd for $C_{13}H_{15}NO_5$ $[M+Na]^+$ 288.0848, found 288.0851.

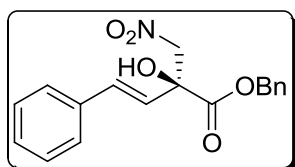
(S, E)-tert-butyl 2-hydroxy-2-(nitromethyl)-4-phenylbut-3-enoate (3p)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow oil: 87% yield, 63.7 mg; $[\alpha]_D^{20} +30.2$ ($c = 0.38$,

$CHCl_3$, 91% *ee*); HPLC: Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, $T = 23^\circ C$, UV = 230 nm, $t_R = 5.60$ min (major), $t_R = 7.60$ min (minor); 1H NMR (400 MHz, $CDCl_3$): δ 7.39-7.29 (m, 5H), 7.01(d, $J = 15.7$ Hz, 1H), 6.09 (d, $J = 15.6$ Hz, 1H), 4.92 (d, $J = 13.7$ Hz, 1H), 4.54 (d, $J = 13.7$ Hz, 1H), 3.98 (s, 1H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 135.3, 133.4, 128.7, 128.6, 126.9, 123.9, 85.0, 80.0, 75.5, 27.8; IR (film, ν/cm^{-1}): 3846, 3661, 3487, 2987, 2900, 2359, 1933, 1724, 1556, 1491, 1449, 1394, 1379, 1290, 1241, 1134, 1066, 977, 879, 869, 791, 755, 715, 694; HRMS (ESI) m/z calcd for $C_{15}H_{19}NO_5$ $[M+Na]^+$ 316.1161, found 316.1162.

(S, E)-benzyl 2-hydroxy-2-(nitromethyl)-4-phenylbut-3-enoate (3q)



The title compound was prepared according to the general working procedure and purified by flash column chromatography (petroleum ether / ethyl acetate = 20:1) to give the product as a light yellow oil: 85% yield, 69.5 mg; $[\alpha]_D^{20} +62.2$ ($c = 0.79$, $CHCl_3$, 91% *ee*); HPLC:

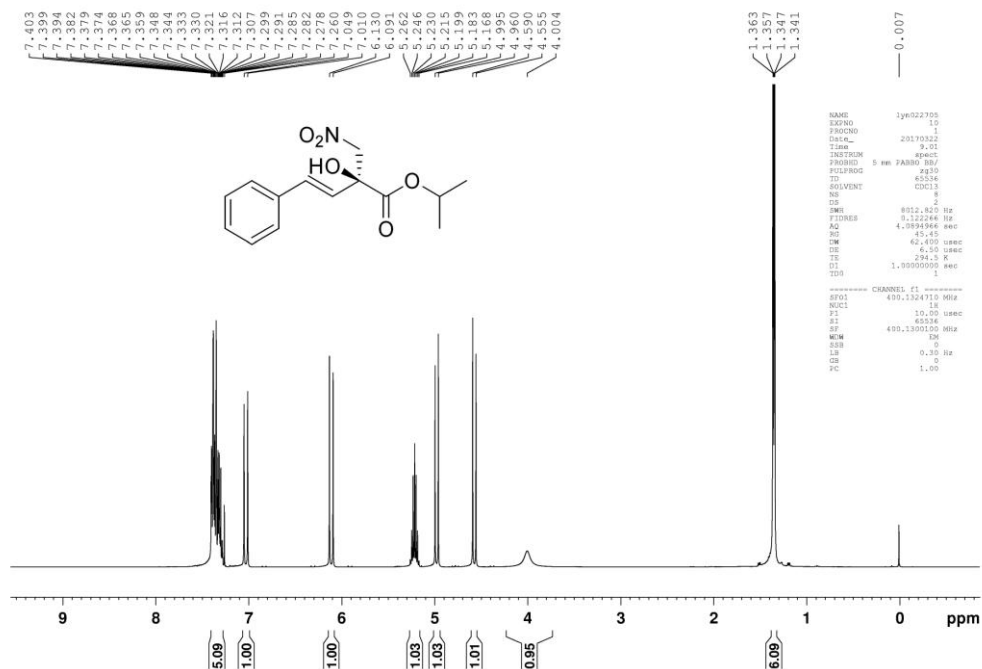
Daicel Chiralpak AS-H, hexane: 2-propanol = 80:20, flow rate = 1.0 mL/min, T = 23°C, UV = 230 nm, t_R = 12.92 min (major), t_R = 19.56 min (minor); ^1H NMR (400 MHz, $(\text{CD}_3)_2\text{CO}$): δ 7.49-7.43 (m, 4H), 7.40-7.27 (m, 6H), 6.98 (d, J = 15.8 Hz, 1H), 6.42 (d, J = 15.8 Hz, 1H), 5.52 (d, J = 1.2 Hz, 1H), 5.38-5.28 (m, 3H), 4.71 (d, J = 13.6 Hz, 1H); ^{13}C NMR (100 MHz, $(\text{CD}_3)_2\text{CO}$): δ 171.0, 135.8, 135.6, 132.4, 128.6, 128.4, 128.36, 128.30, 128.2, 126.8, 125.7, 80.5, 76.2, 67.7; IR (film, v/cm^{-1}): 3661, 2970, 2900, 2360, 1740, 1556, 1450, 1406, 1393, 1380, 1258, 1227, 1066, 1056, 1027, 891, 802, 760, 696; HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{17}\text{NO}_5$ $[\text{M}+\text{Na}]^+$ 350.1004, found 350.1013.

References:

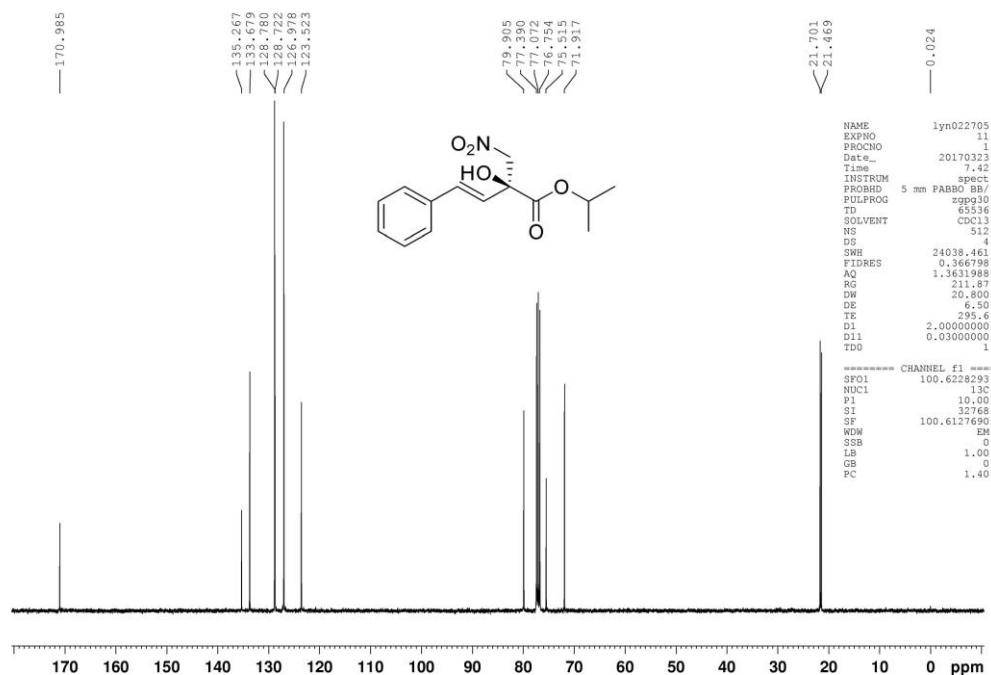
- (1) (a) Guo, F.; Lai, G.; Xiong, S.; Wang, S.; Wang, Z. *Chem. -Eur. J.* **2010**, *16*, 6438-6441; (b) Zhang, S.; Xu, K.; Guo, F.; Hu, Y.; Zha, Z.; Wang, Z. *Chem. -Eur. J.* **2014**, *20*, 979-982.
- (2) (a) Evans, D.; Johnson, J.; Olhava, E. *J. Am. Chem. Soc.* **2000**, *122*, 1635-1649; (b) Takashi, S.; Kubota, A.; Nakata, T. *Angew. Chem. Int. Ed.* **2002**, *41*, 4751-4754; (c) Srivastava, B.; Joharapurkar, A.; Raval, S. *et al. J. Med. Chem.* **2007**, *50*, 5951-5966; (d) Gremaud, L.; Alexakis, A. *Angew. Chem. Int. Ed.* **2012**, *51*, 794-797.

Part II ^1H NMR & ^{13}C NMR

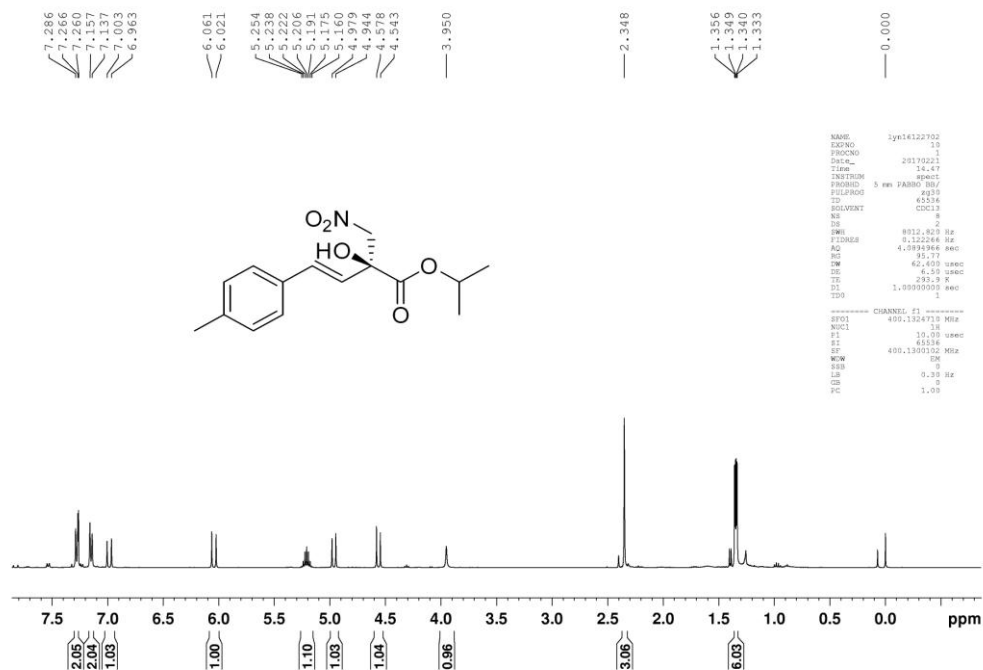
^1H NMR of **3a**



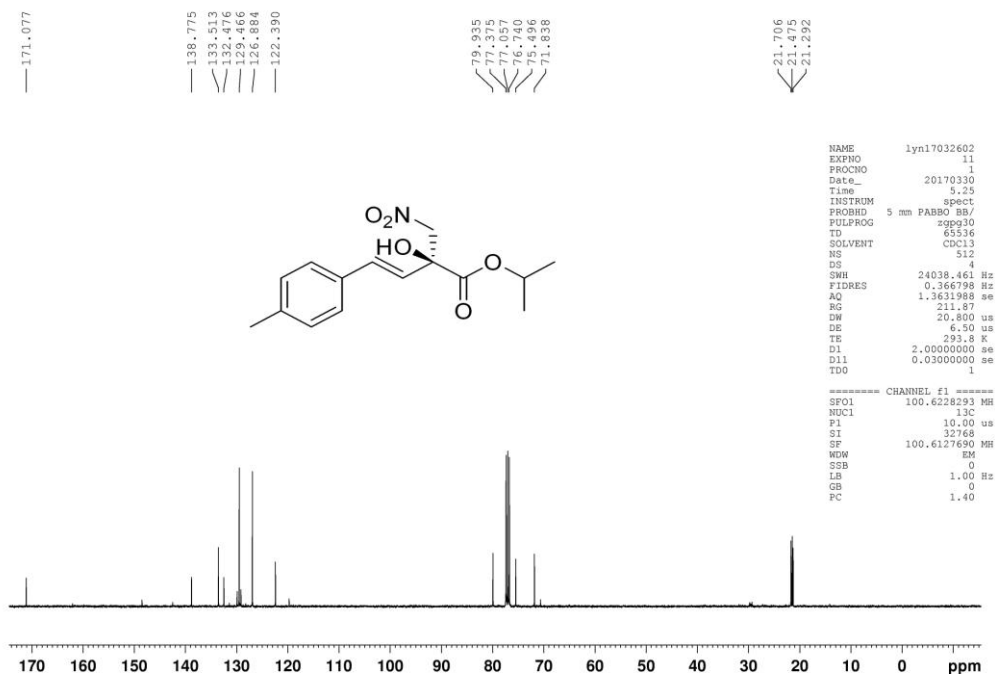
^{13}C NMR of **3a**



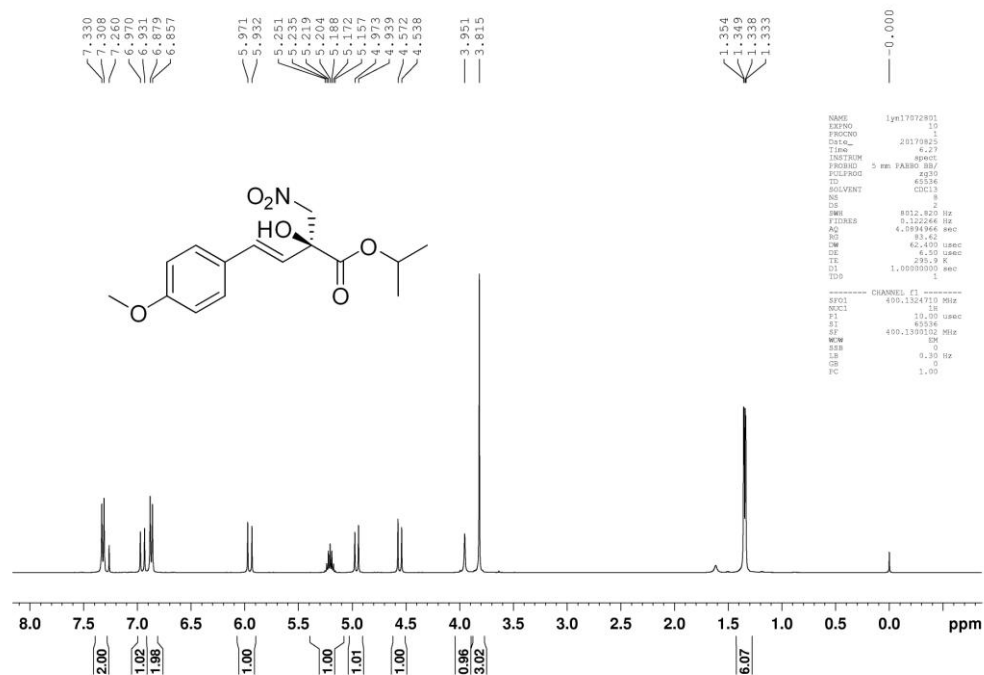
¹H NMR of **3b**



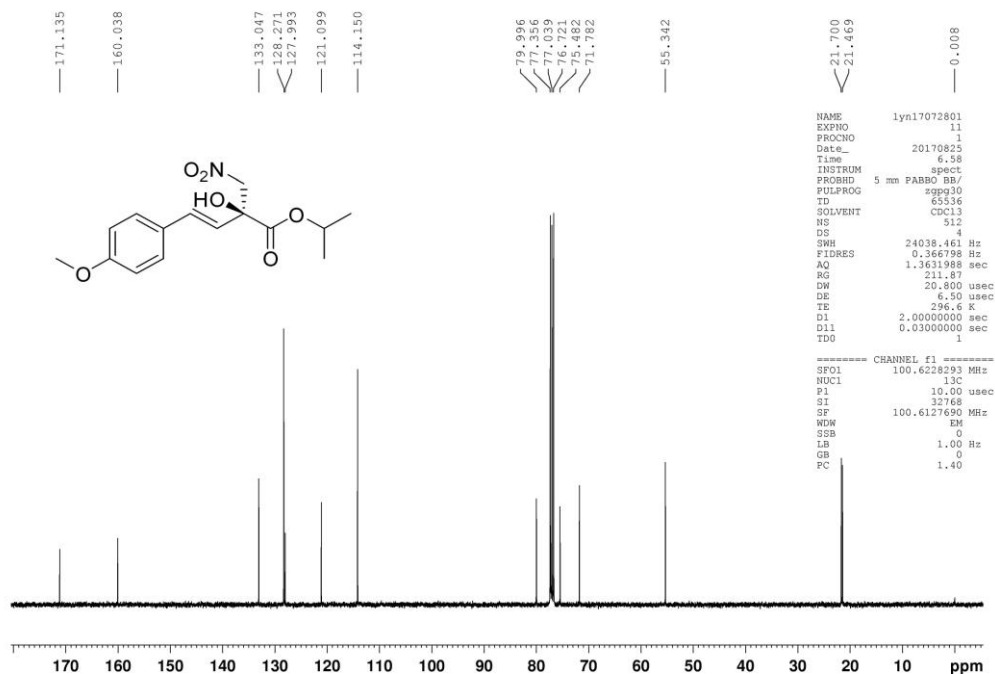
¹³C NMR of **3b**



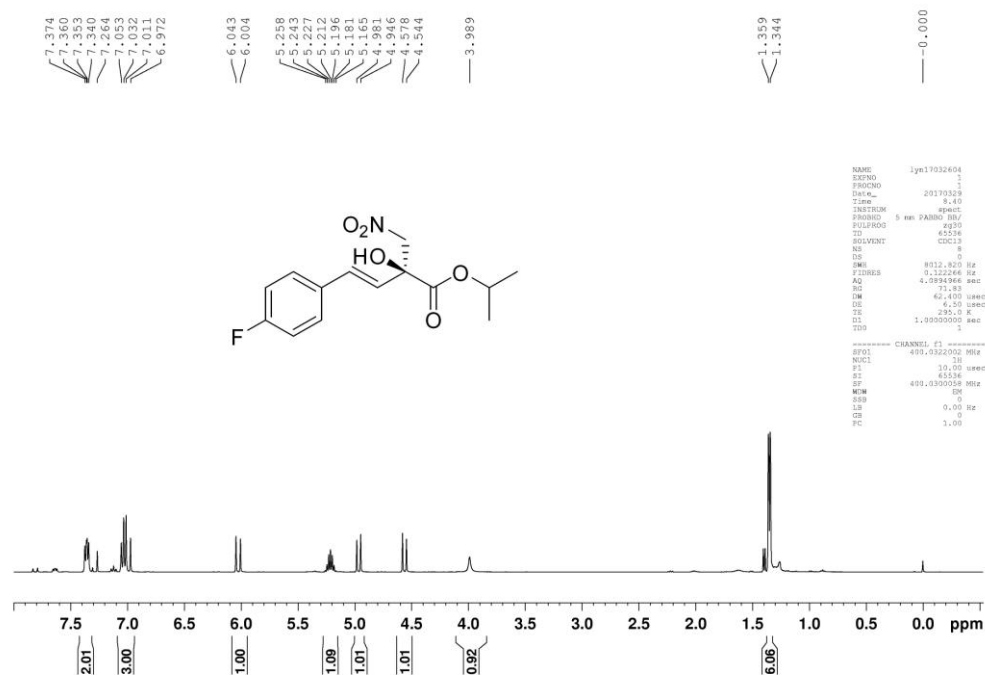
¹H NMR of **3c**



¹³C NMR of **3c**



¹H NMR of **3d**

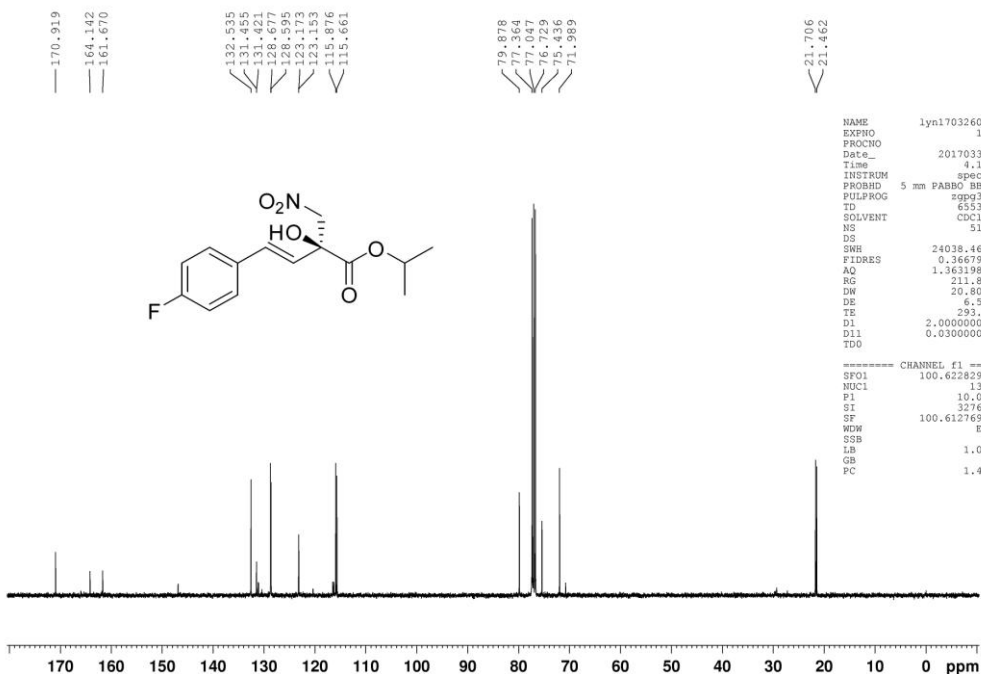


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¹³C NMR of **3d**

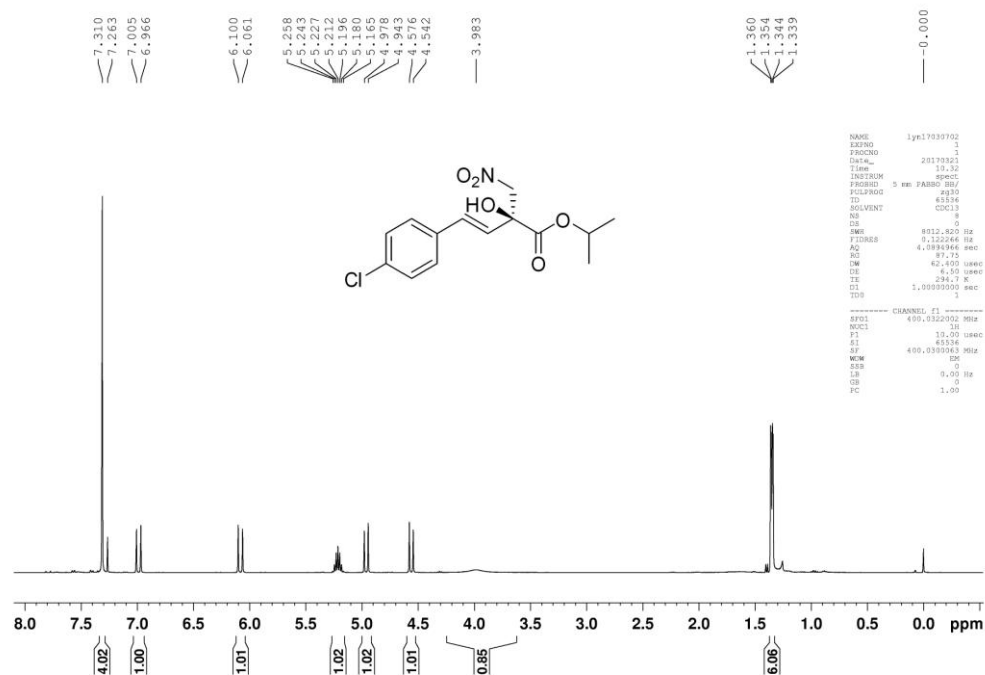


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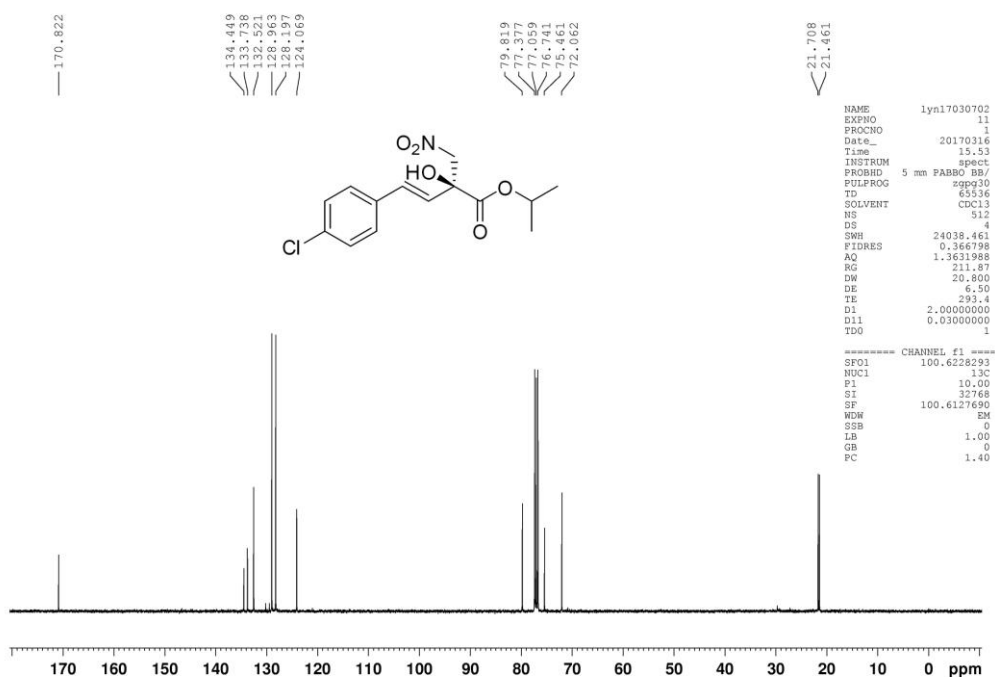
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FIDRES      0.366798
AQ          1.3631988
RG          211.87
DW          20.800
DE          6.50
TE          293.6
D1          2.0000000
D11         0.0300000
TD0         1

===== CHANNEL f1 =====
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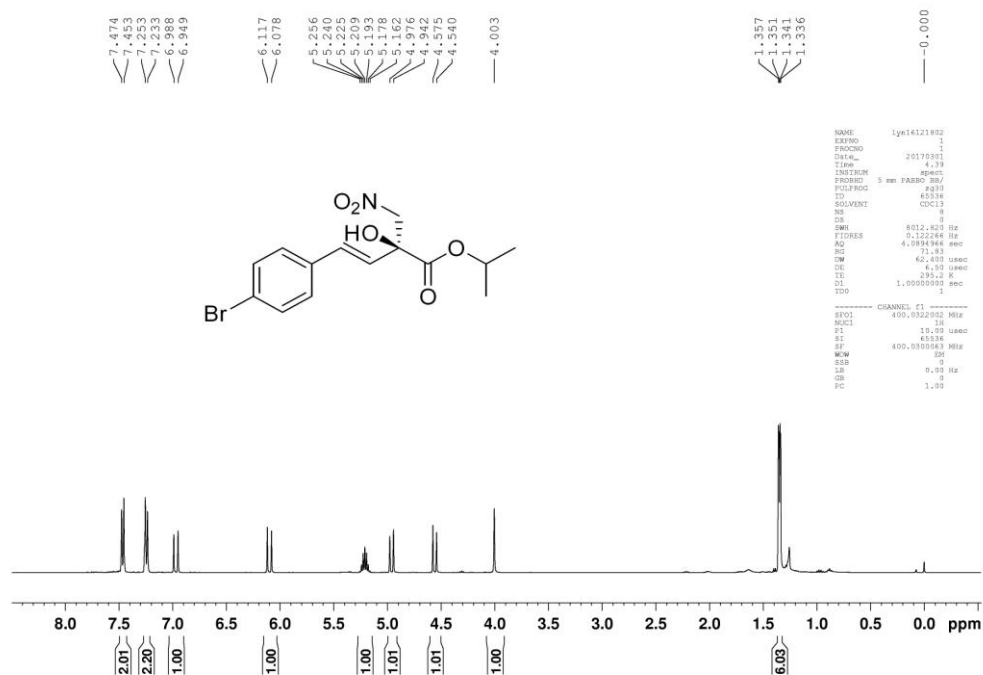
¹H NMR of 3e



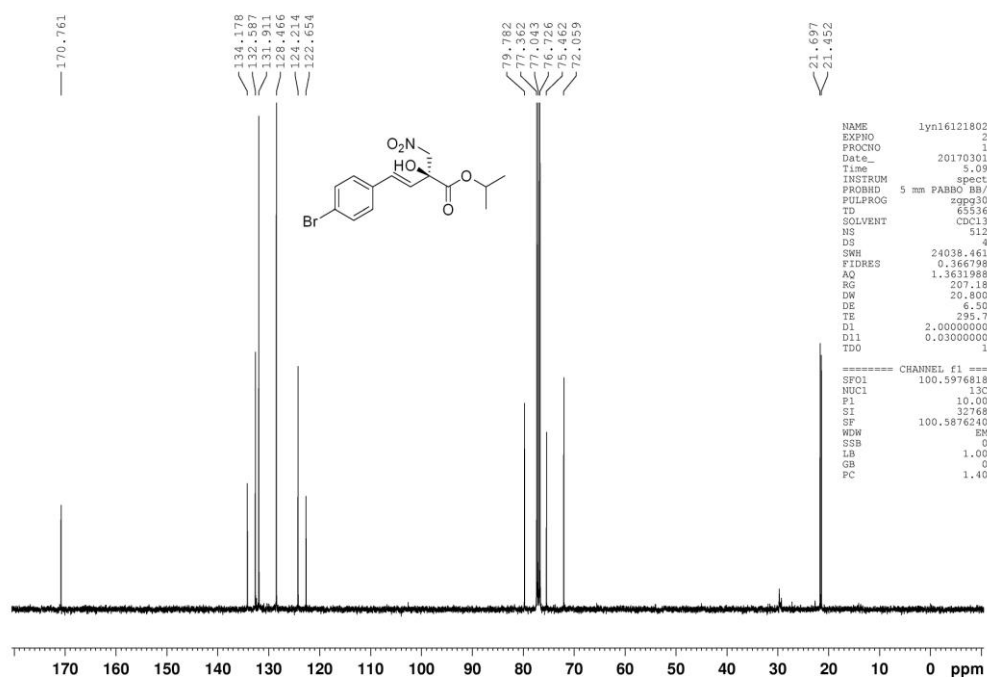
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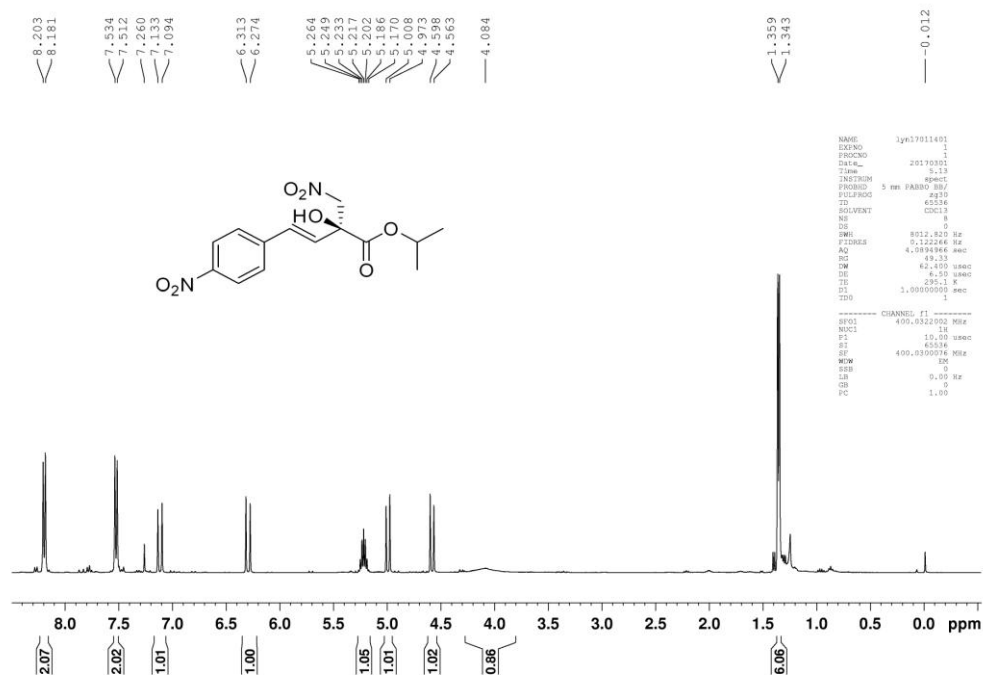
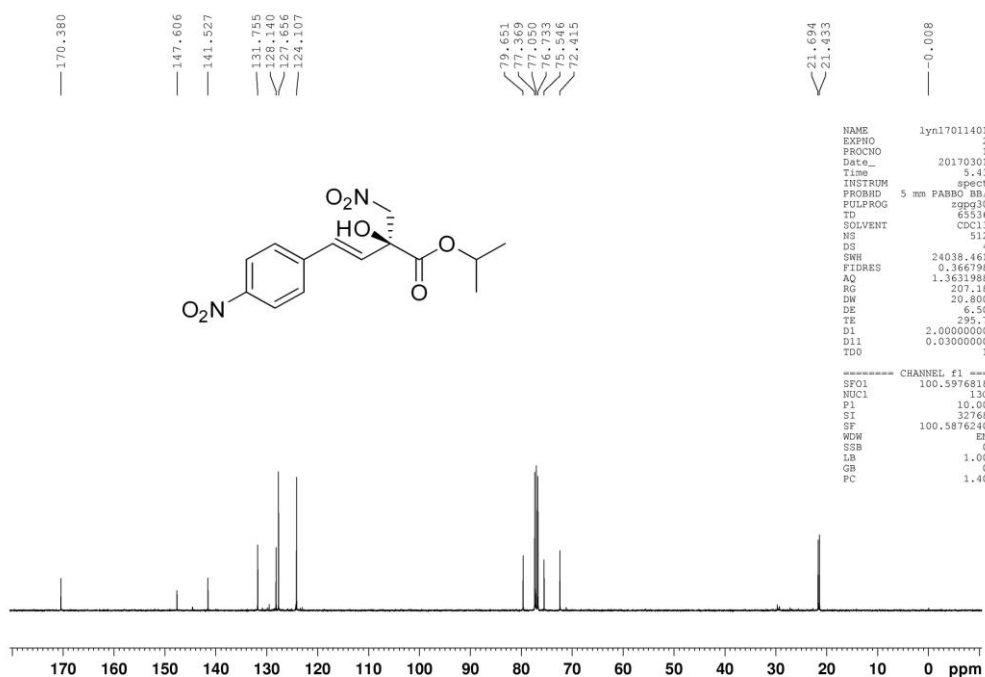


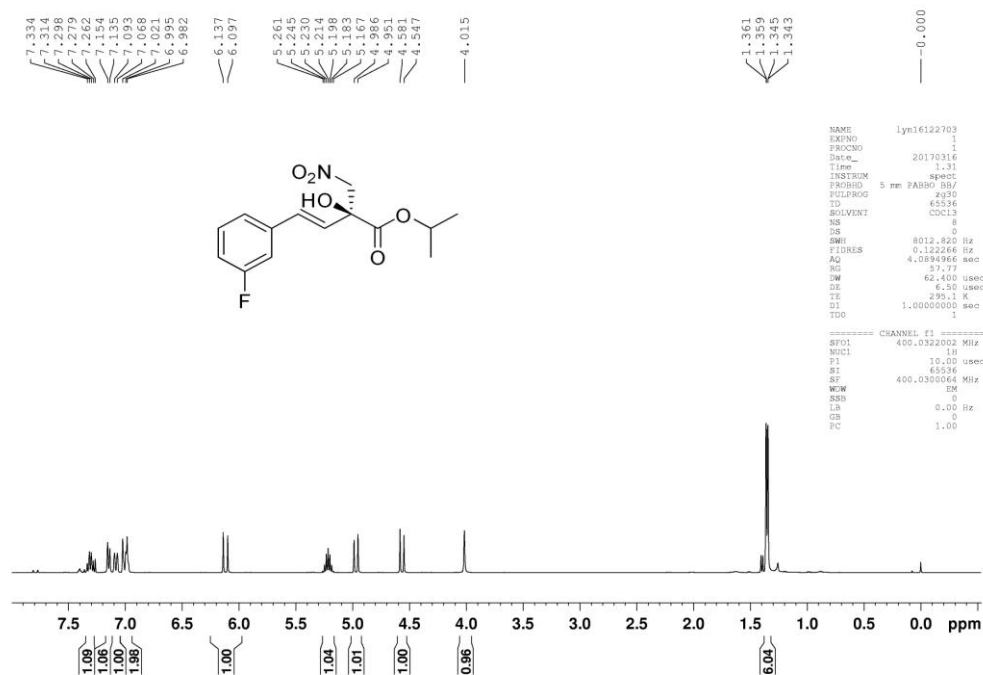
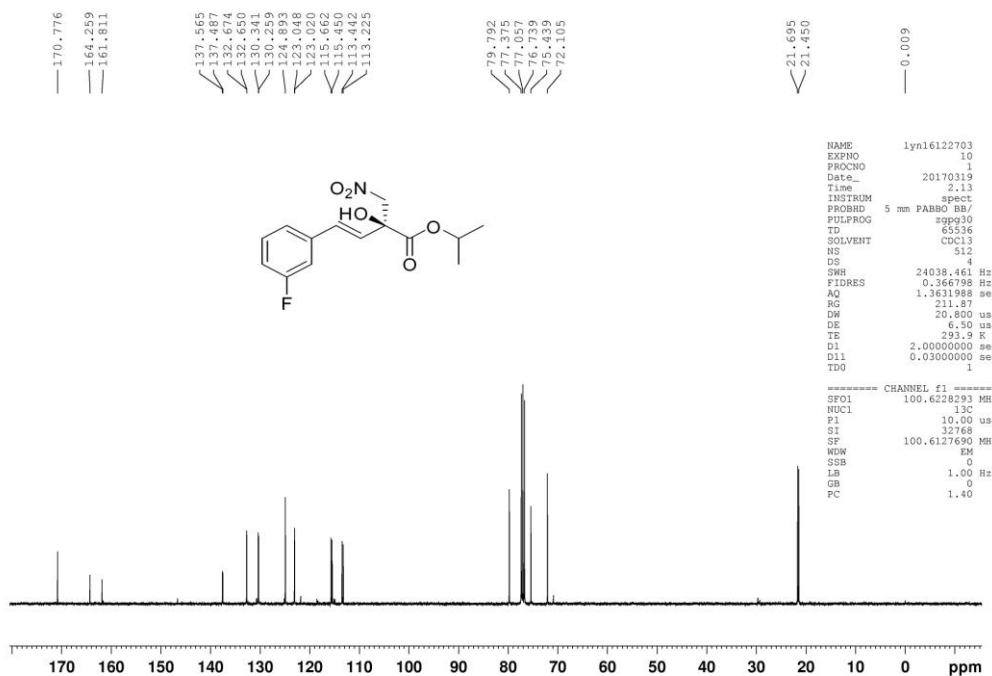
¹H NMR of **3f**

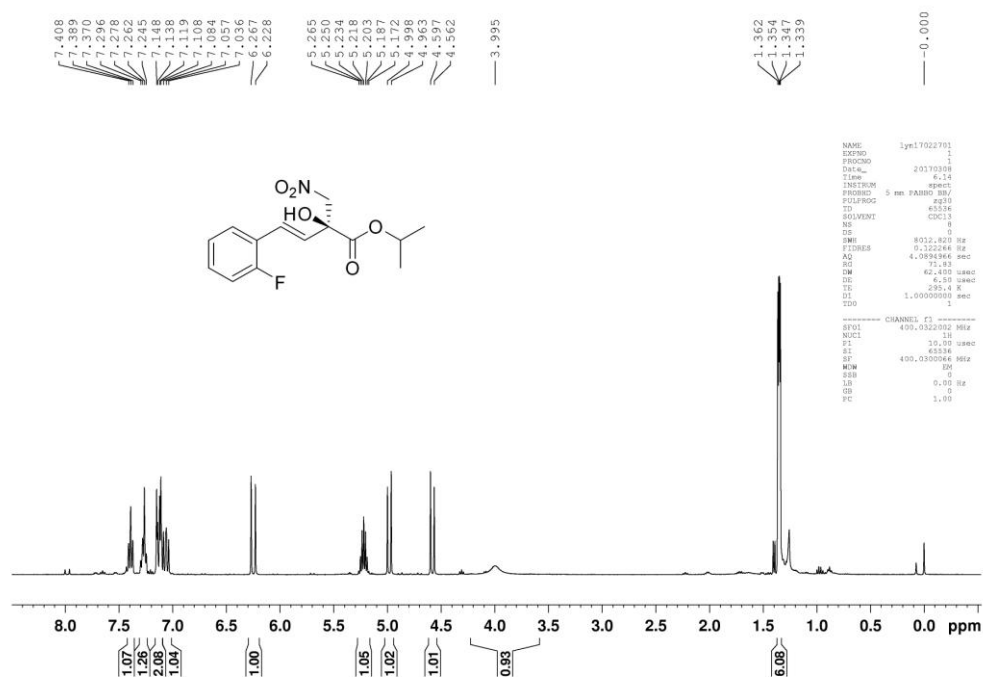
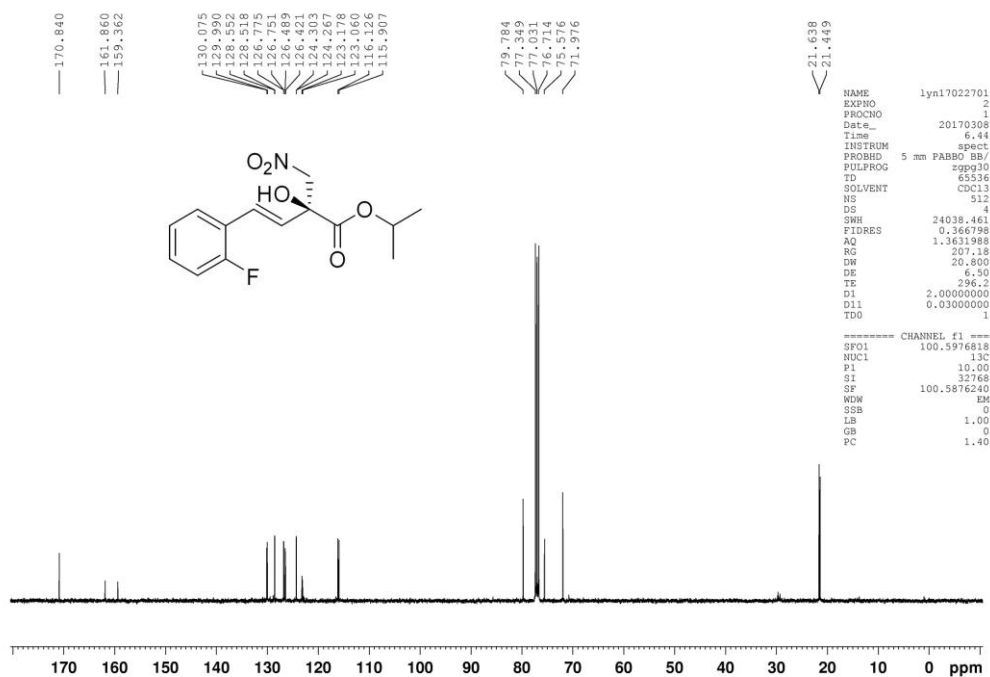


¹³C NMR of **3f**

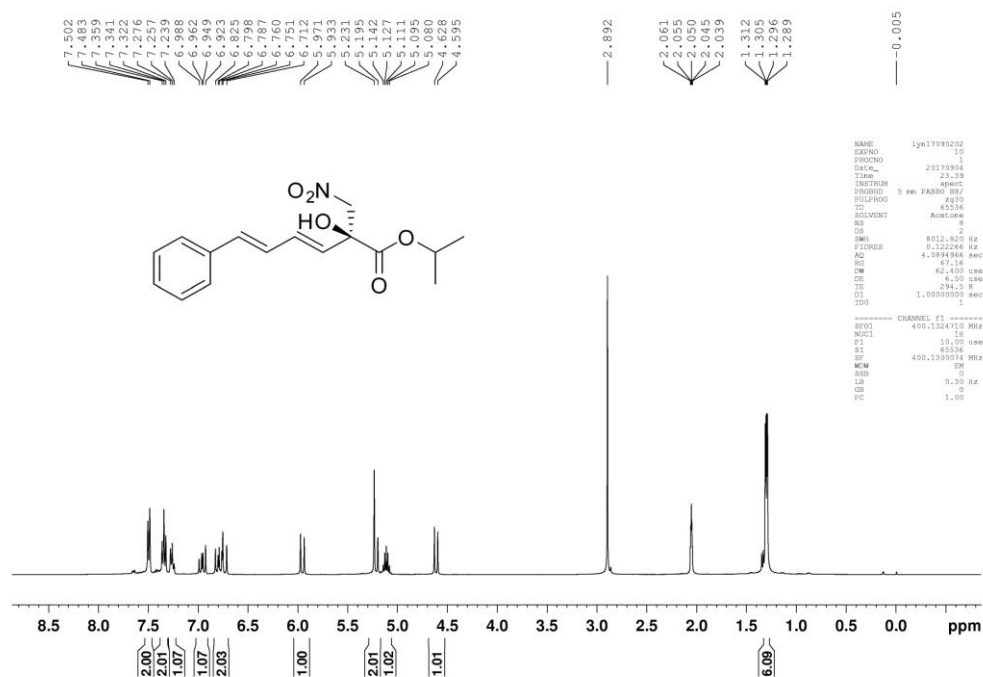


¹H NMR of **3g** ^{13}C NMR of **3g**

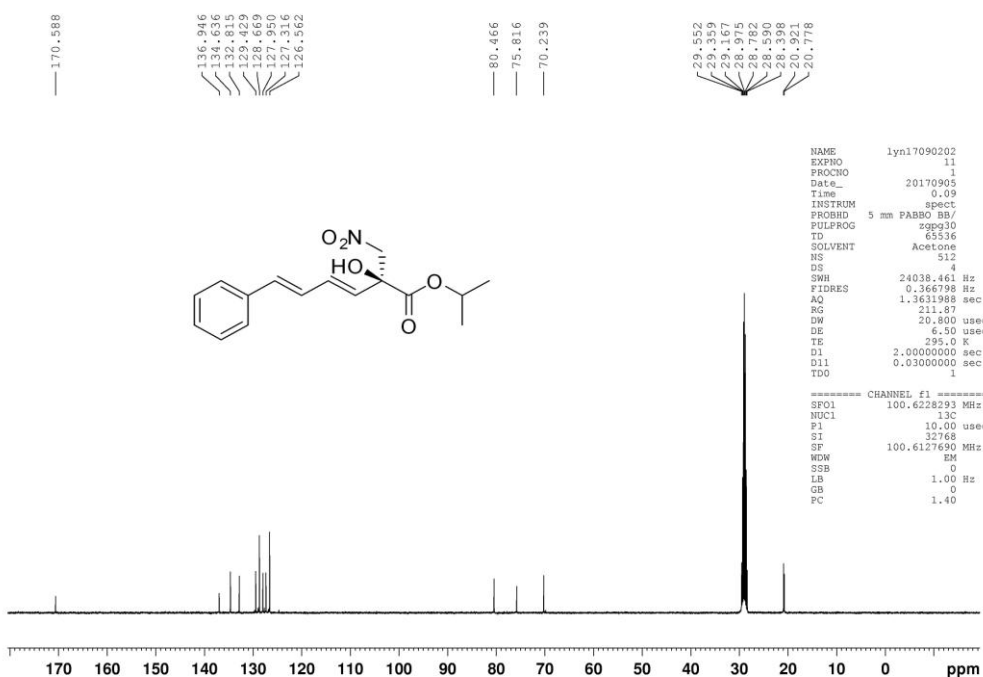
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¹H NMR of **3i** ^{13}C NMR of **3i**

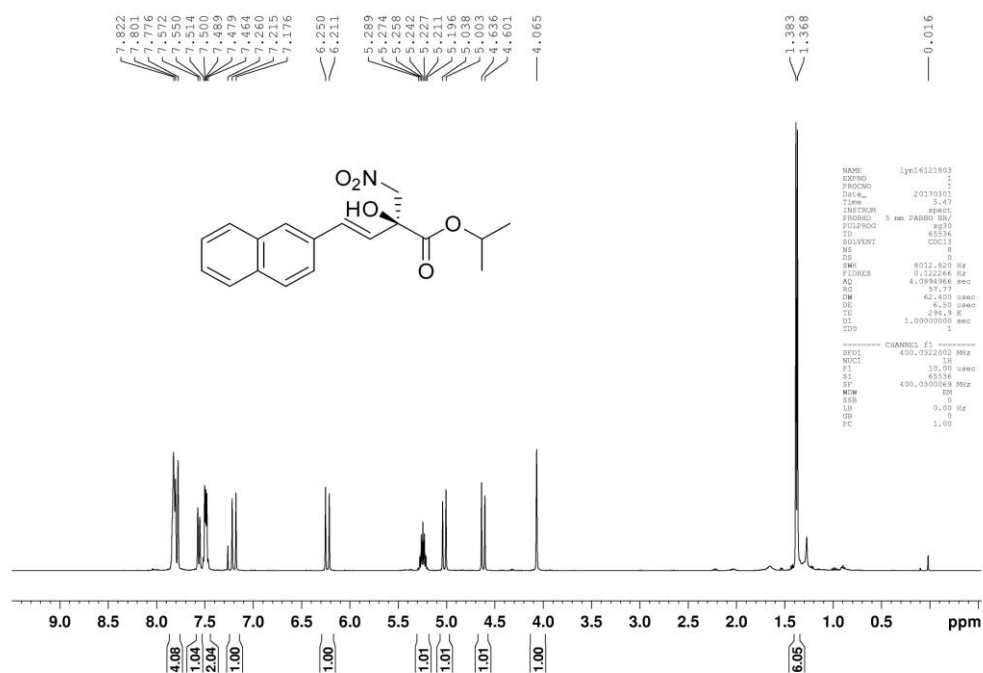
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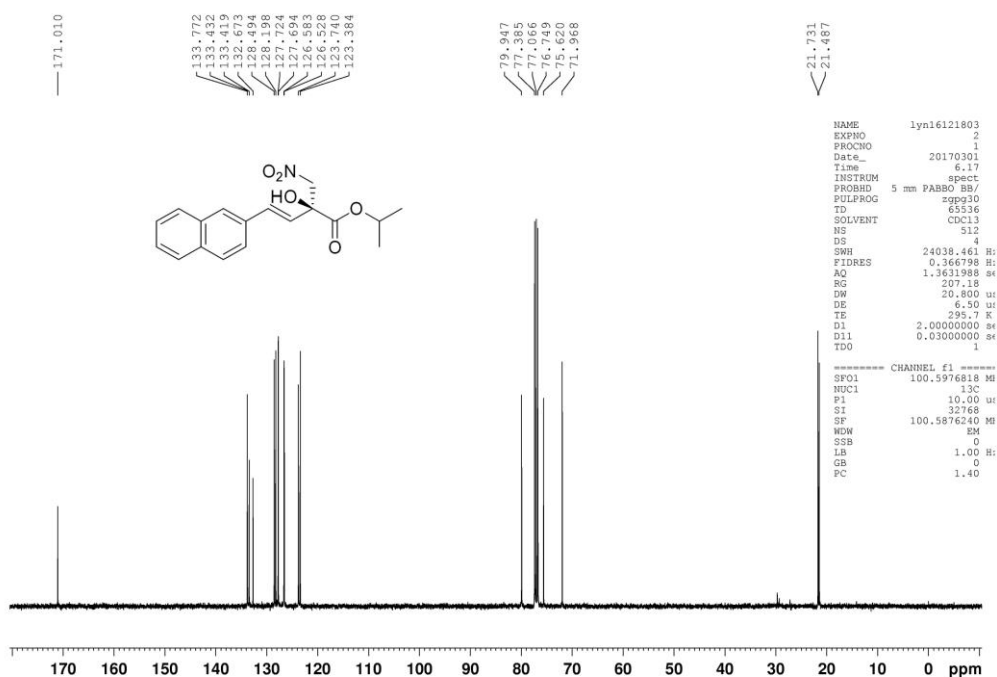
¹³C NMR of **3j**



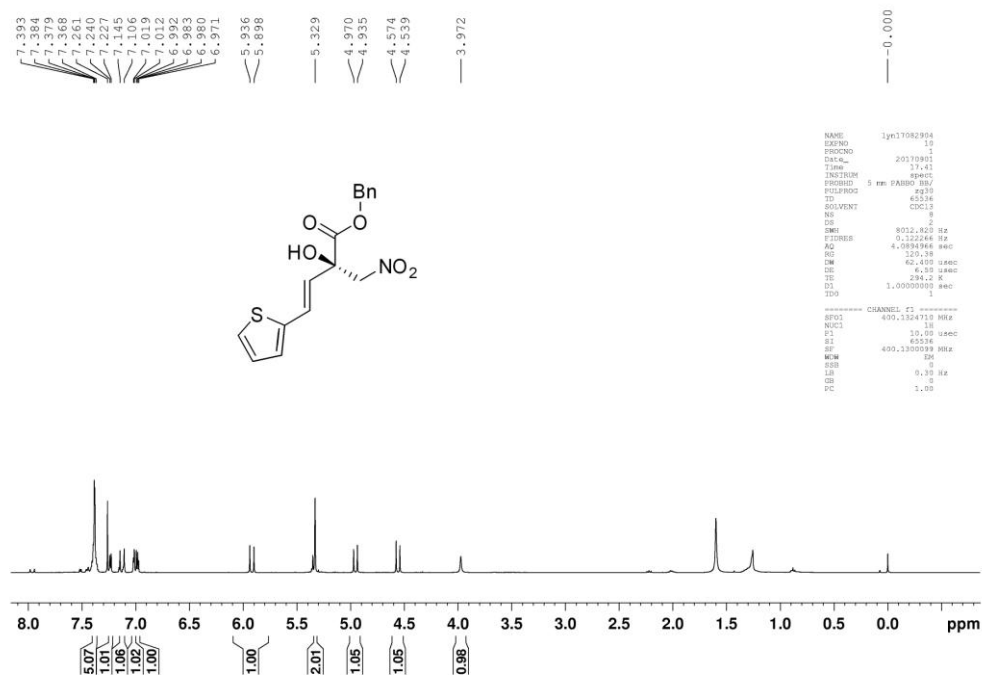
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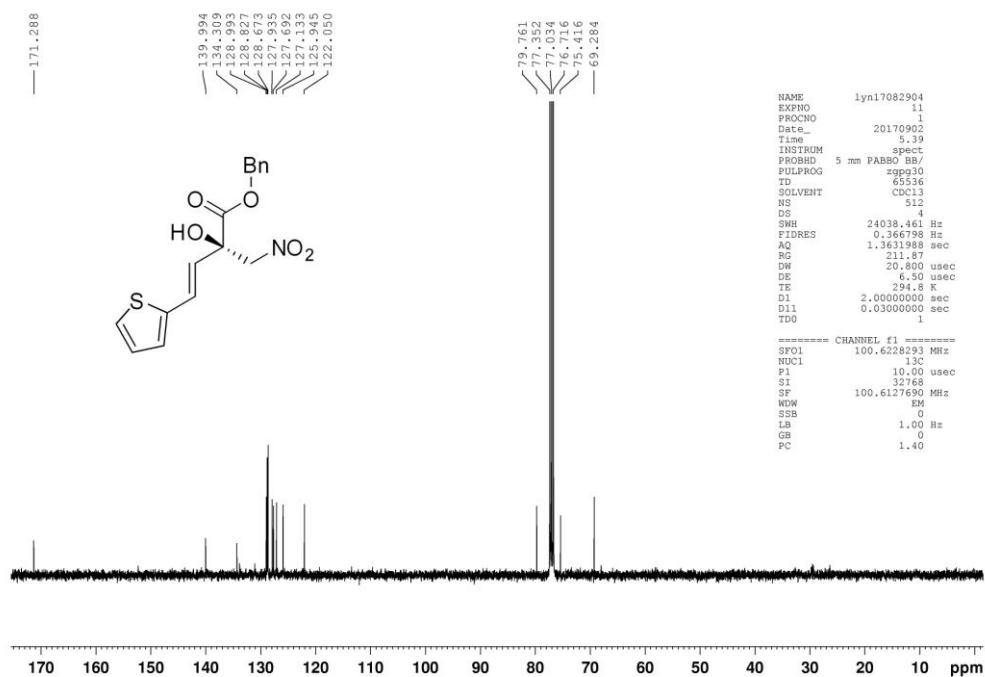
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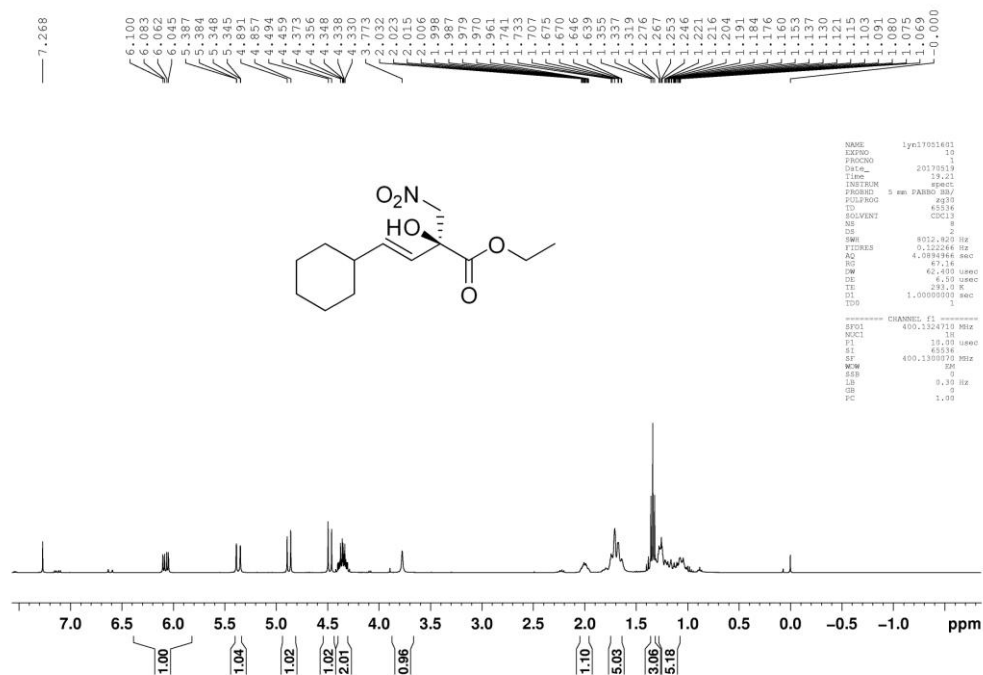
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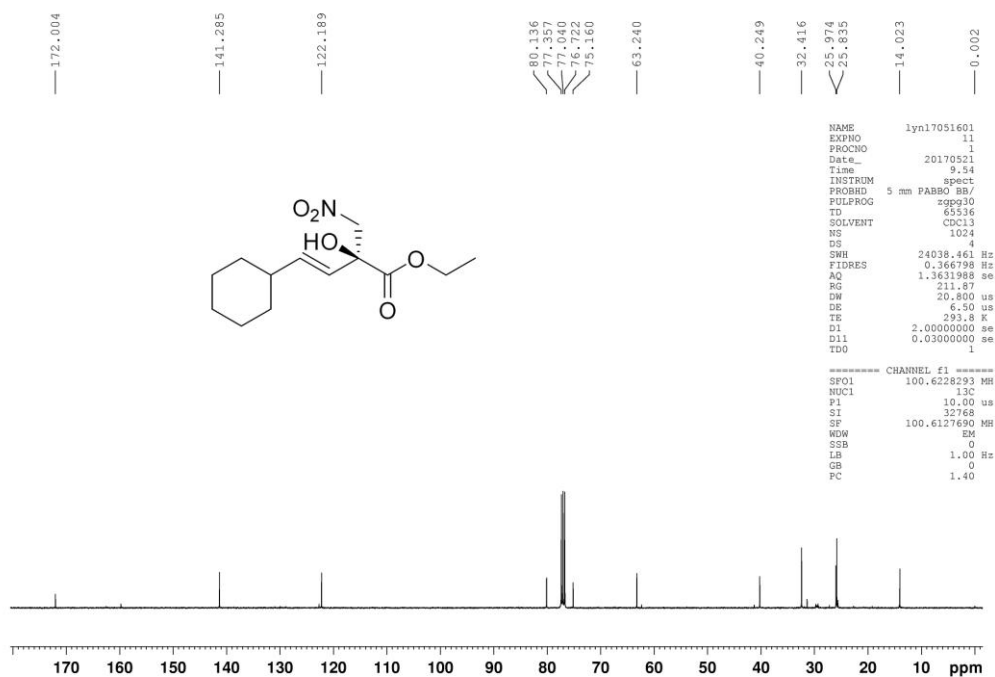
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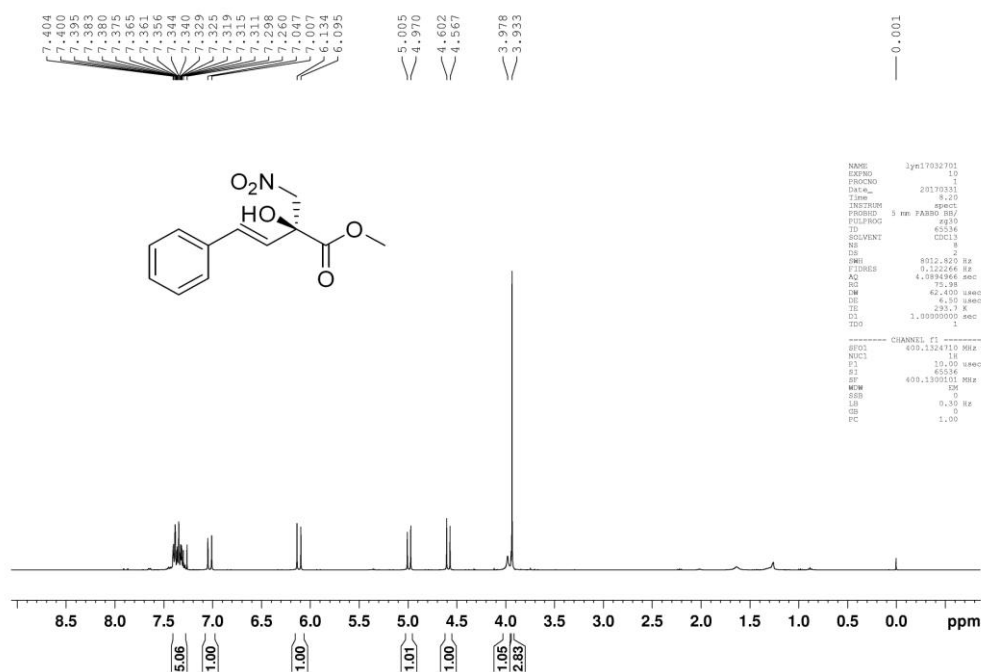
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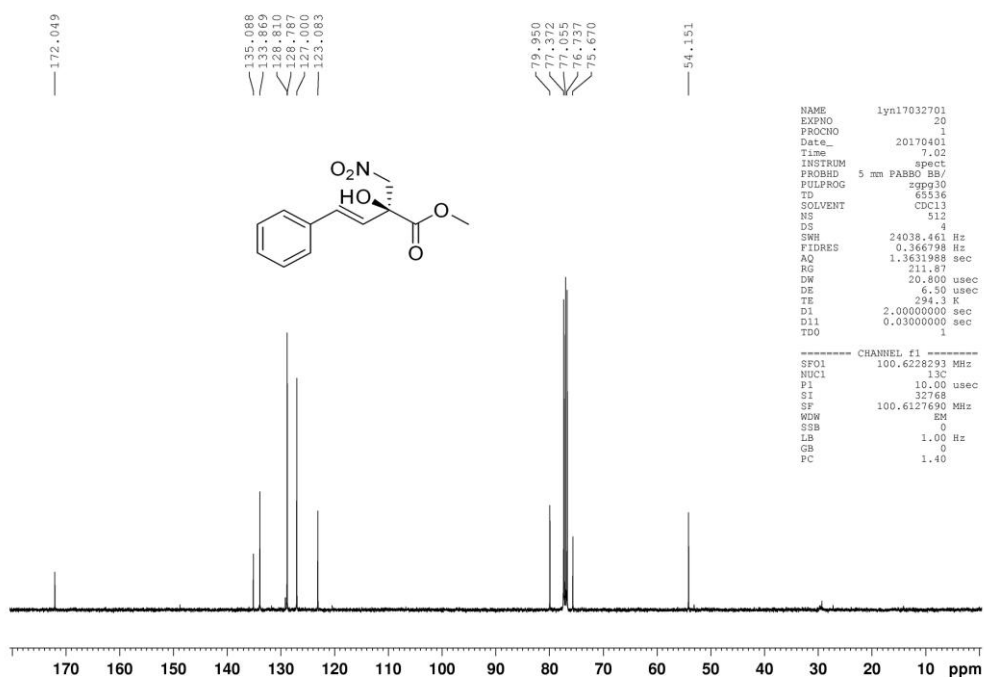
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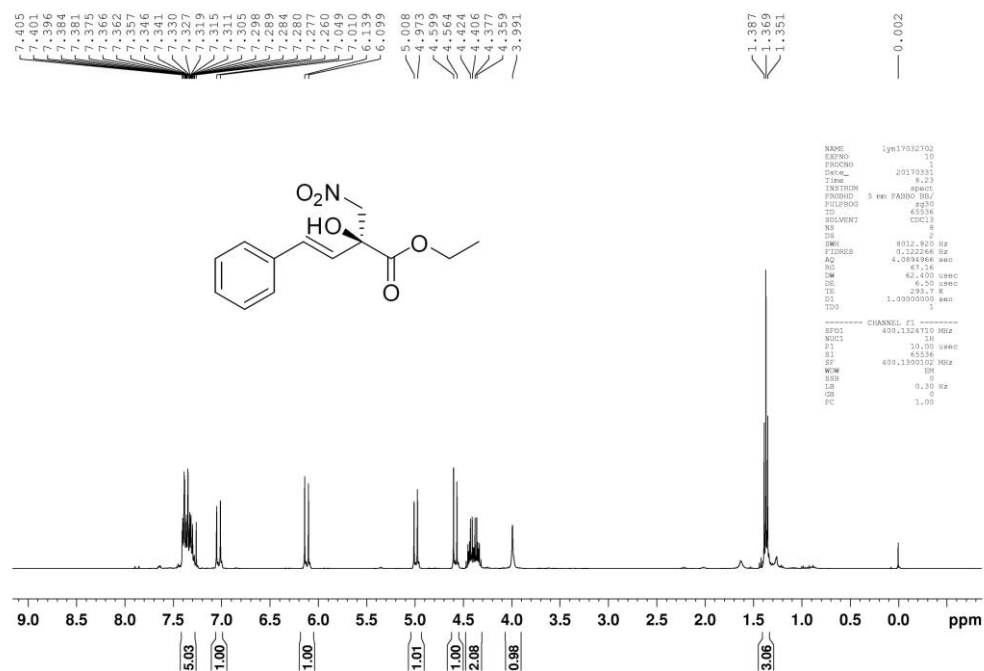
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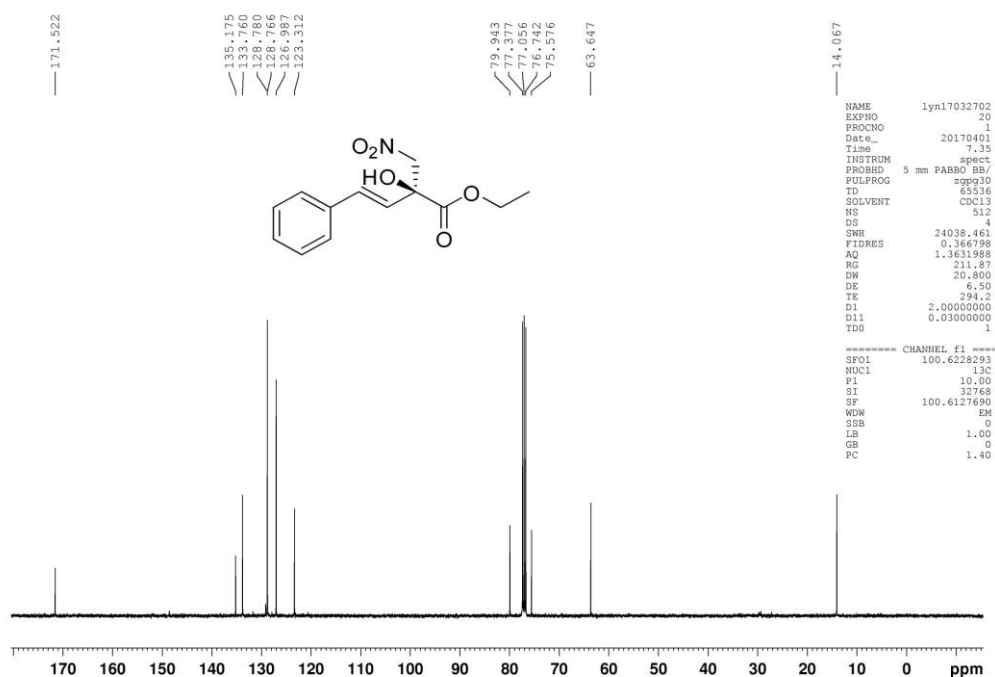
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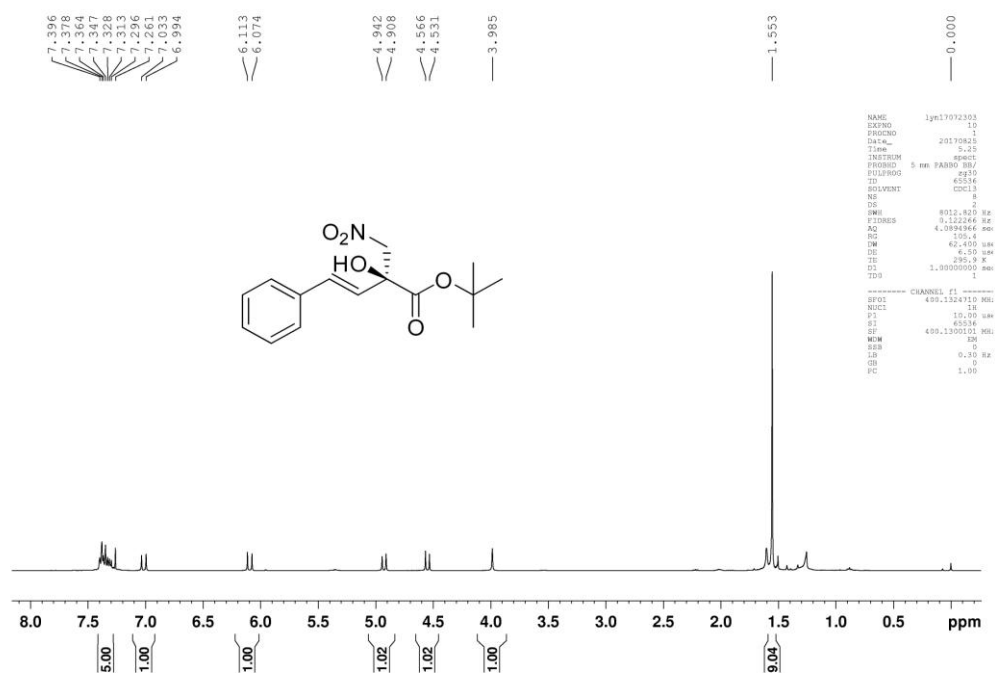
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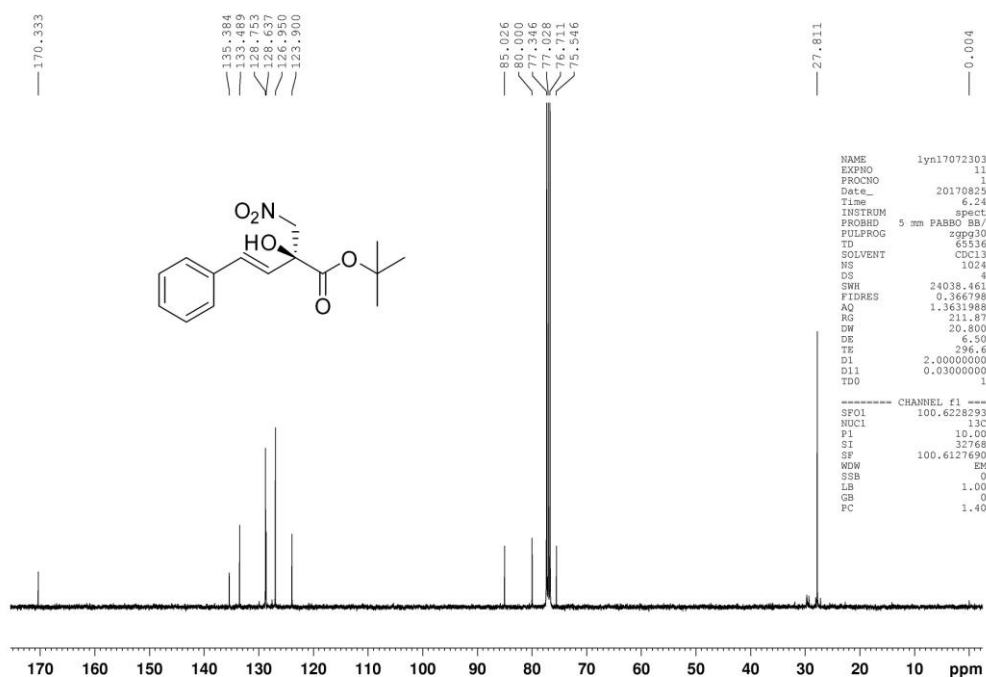
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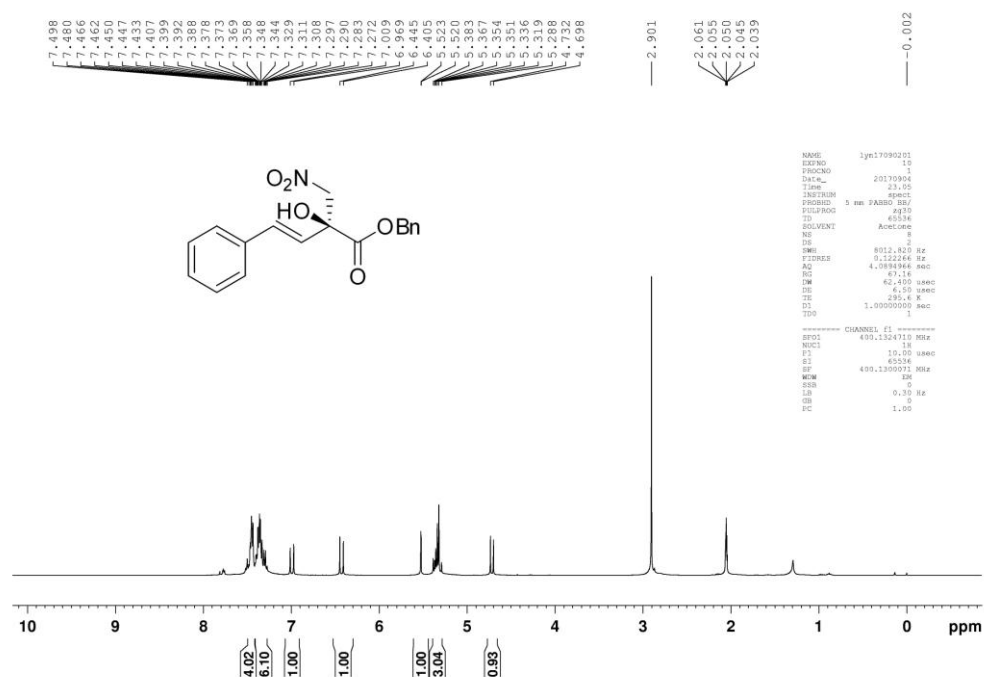
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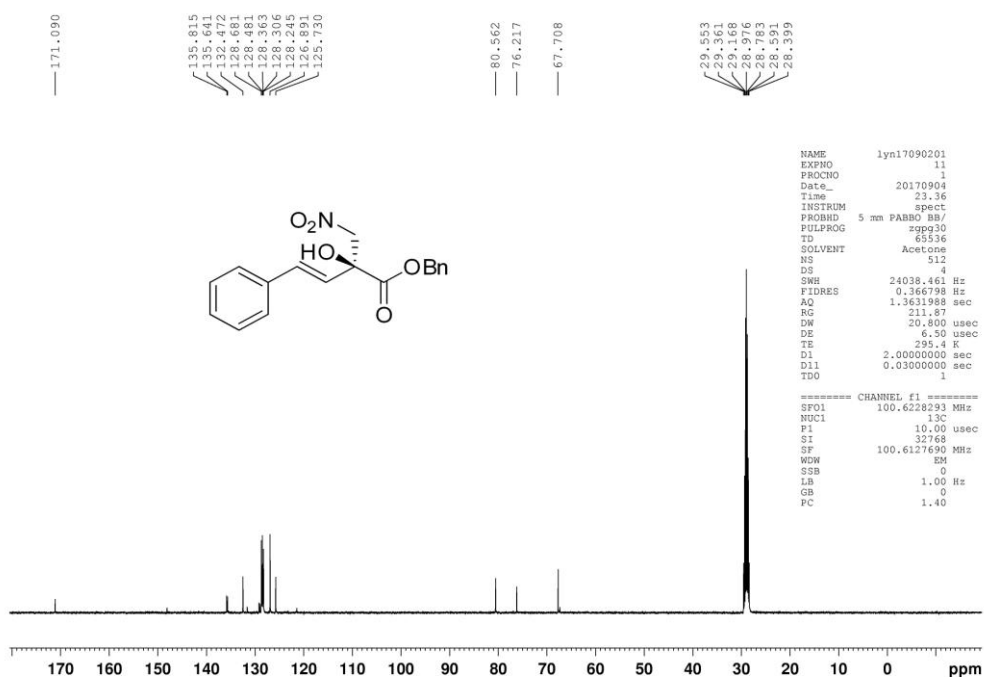
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¹H NMR of **3q**



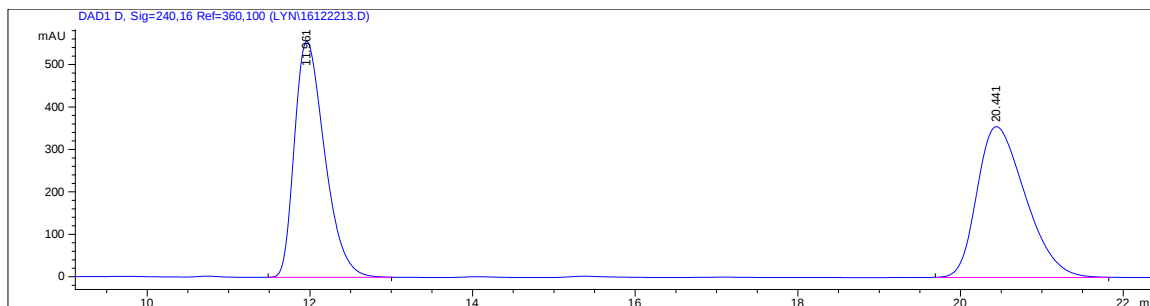
¹³C NMR of **3q**



Part III HPLC data

3a

Racemic sample



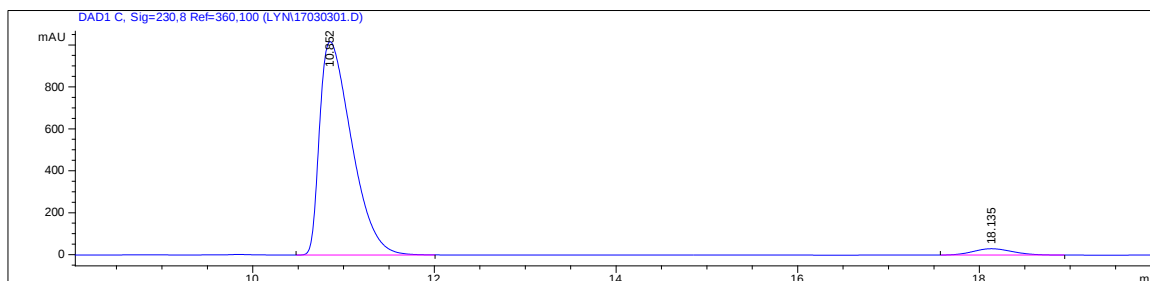
Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.961	BB	0.3999	1.42862e4	555.73553	49.3835
2	20.441	BB	0.6389	1.46429e4	355.24042	50.6165

Totals : 2.89290e4 910.97595

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

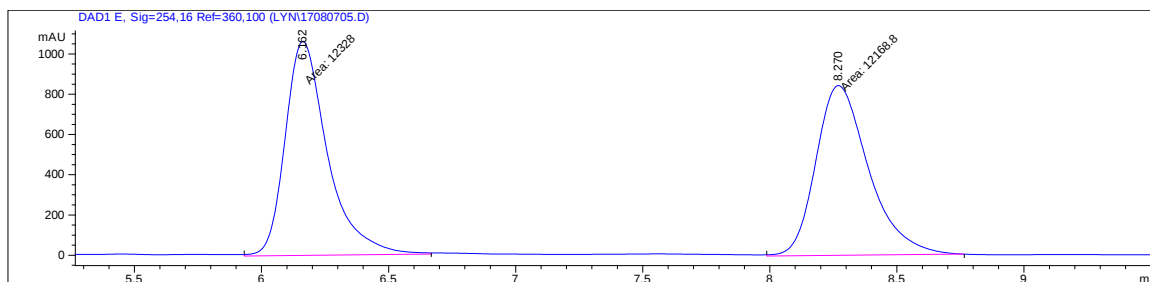
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.852	PB	0.3783	2.47968e4	1017.40411	96.4327
2	18.135	BB	0.4752	917.30963	30.12799	3.5673

Totals : 2.57141e4 1047.53210

Results obtained with enhanced integrator!

3b

Racemic sample



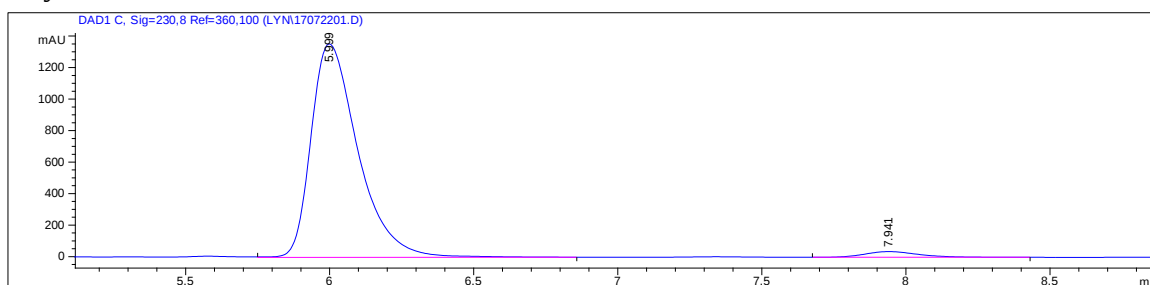
Signal 5: DAD1 E, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.162	MM	0.1930	1.23280e4	1064.77307	50.3249
2	8.270	MM	0.2404	1.21688e4	843.62543	49.6751

Totals : 2.44969e4 1908.39850

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

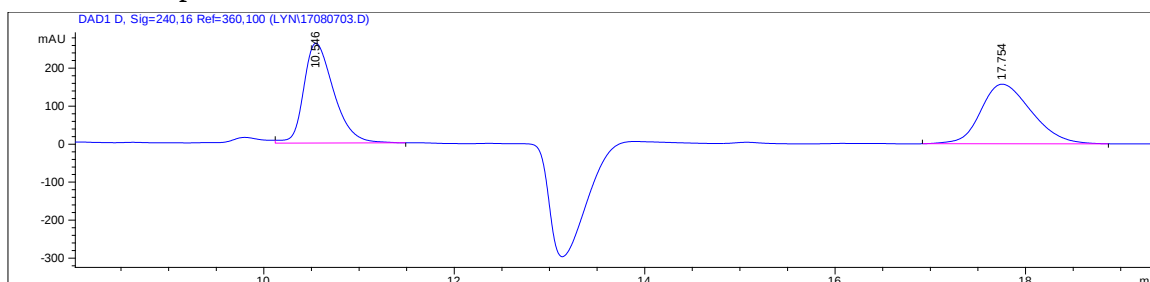
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.999	VB	0.1721	1.53418e4	1355.40796	97.0401
2	7.941	VB	0.1984	467.95236	35.81178	2.9599

Totals : 1.58098e4 1391.21974

Results obtained with enhanced integrator!

3c

Racemic sample



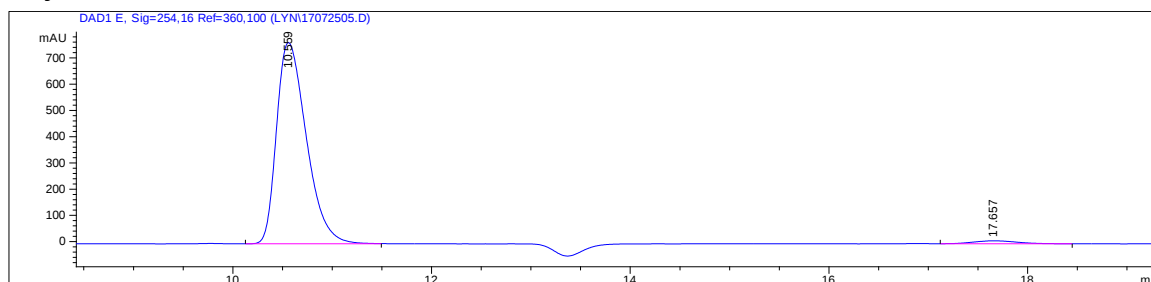
Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.546	VP	0.3349	5741.29688	262.75153	49.6465
2	17.754	BB	0.5747	5823.05469	157.00262	50.3535

Totals : 1.15644e4 419.75415

Results obtained with enhanced integrator!

Asymmetric version:



Signal 5: DAD1 E, Sig=254,16 Ref=360,100

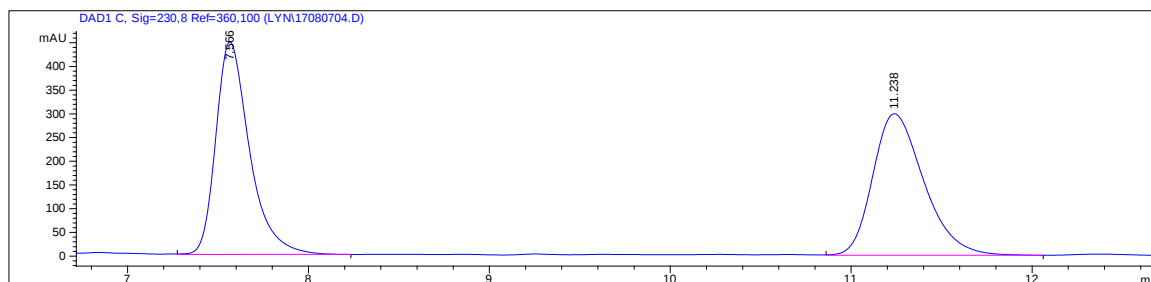
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.559	VB	0.3245	1.59330e4	766.52325	97.9494
2	17.657	PP	0.4432	333.56708	11.14487	2.0506

Totals : 1.62666e4 777.66812

Results obtained with enhanced integrator!

3d

Racemic sample



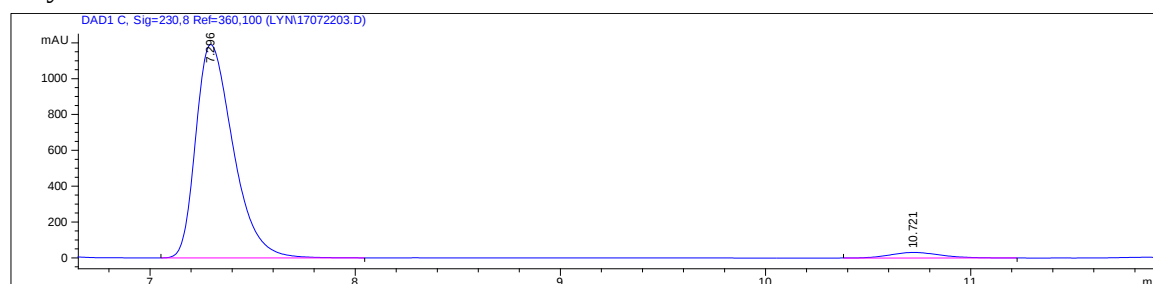
Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.566	BP	0.1971	5809.56299	448.56821	49.8619
2	11.238	BB	0.3025	5841.73828	298.27707	50.1381

Totals : 1.16513e4 746.84528

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

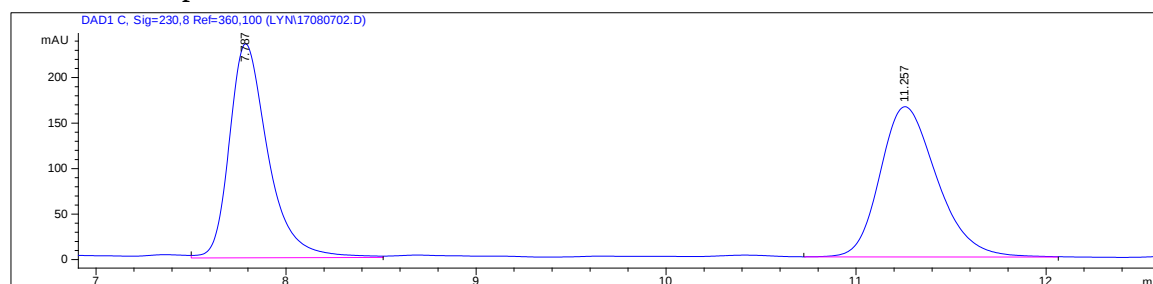
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.296	BB	0.1953	1.50431e4	1191.23328	96.5926
2	10.721	BB	0.2623	530.66431	30.91457	3.4074

Totals : 1.55738e4 1222.14785

Results obtained with enhanced integrator!

3e

Racemic sample



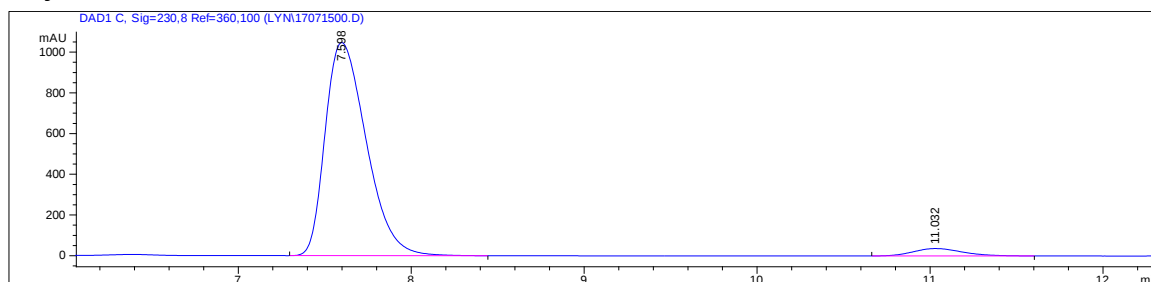
Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.787	VB	0.2128	3321.40527	235.09663	49.1567
2	11.257	VB	0.3208	3435.36499	165.09038	50.8433

Totals : 6756.77026 400.18701

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

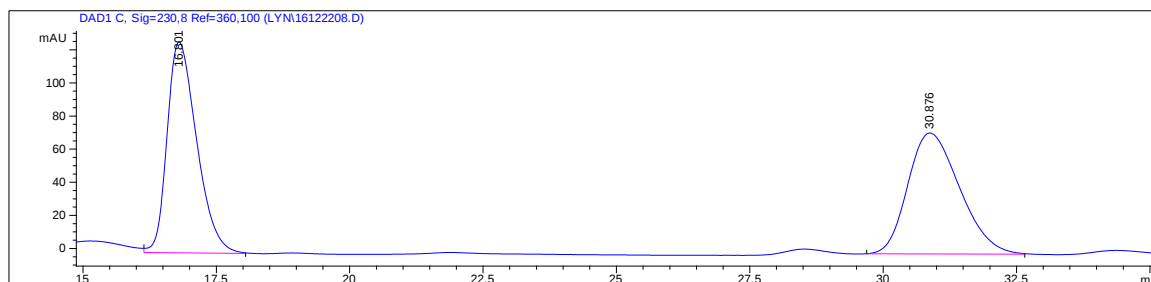
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.598	PB	0.2605	1.72734e4	1046.91248	95.9756
2	11.032	BB	0.3078	724.30499	36.44996	4.0244

Totals : 1.79977e4 1083.36243

Results obtained with enhanced integrator!

3f

Racemic sample



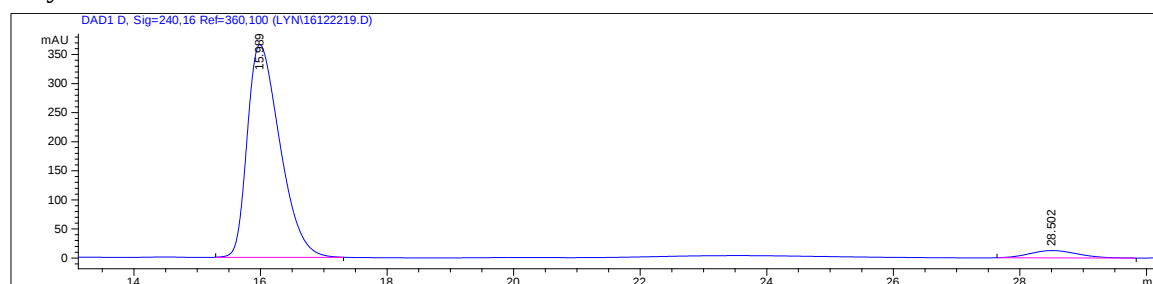
Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.801	VB	0.5950	4901.83496	127.35957	49.8823
2	30.876	BB	1.0469	4924.97314	73.01880	50.1177

Totals : 9826.80811 200.37836

Results obtained with enhanced integrator!

Asymmetric version:



Signal 4: DAD1 D, Sig=240,16 Ref=360,100

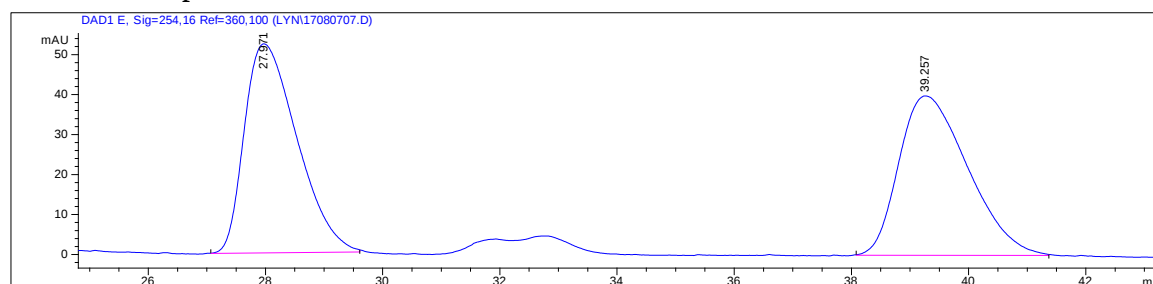
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.989	BB	0.5551	1.30857e4	366.05524	95.2186
2	28.502	BP	0.7681	657.09534	12.56467	4.7814

Totals : 1.37428e4 378.61991

Results obtained with enhanced integrator!

3g

Racemic sample



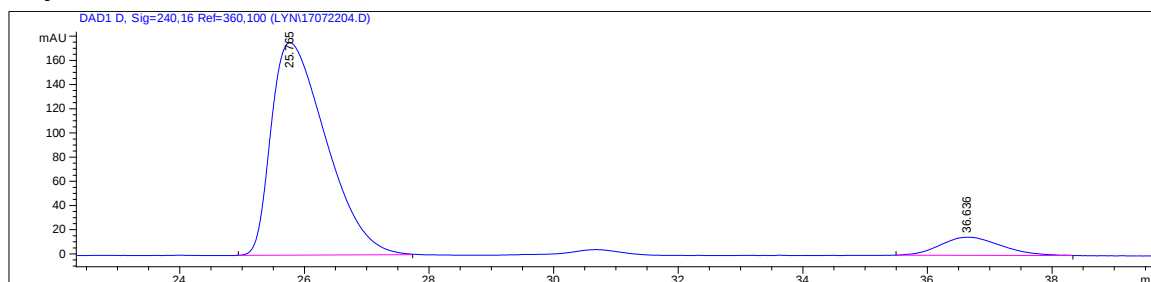
Signal 5: DAD1 E, Sig=254,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.971	BB	0.9442	3264.08862	52.29478	50.0967
2	39.257	BB	1.1078	3251.48120	39.85315	49.9033

Totals : 6515.56982 92.14792

Results obtained with enhanced integrator!

Asymmetric version:



Signal 4: DAD1 D, Sig=240,16 Ref=360,100

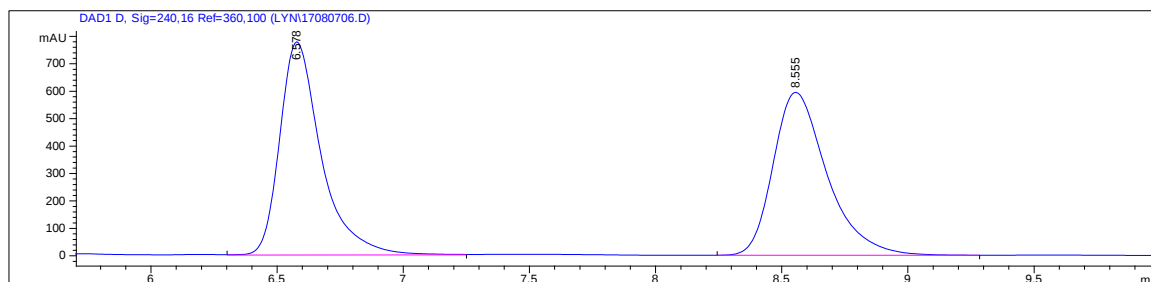
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.765	BB	0.9526	1.07350e4	175.75618	91.2881
2	36.636	BB	0.8237	1024.47278	14.98371	8.7119

Totals : 1.17595e4 190.73989

Results obtained with enhanced integrator!

3h

Racemic sample



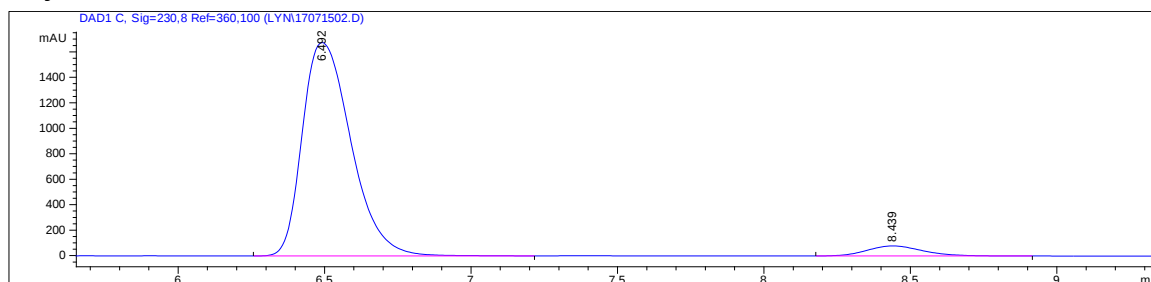
Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.578	VB	0.1714	8881.33008	776.79193	50.2192
2	8.555	PP	0.2250	8803.81250	593.66498	49.7808

Totals : 1.76851e4 1370.45691

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

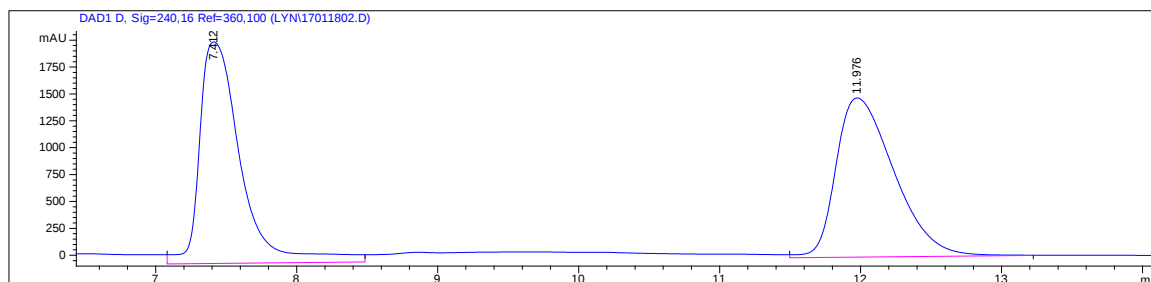
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.492	PB	0.1806	1.93367e4	1675.53381	94.8641
2	8.439	BB	0.2041	1046.87793	79.25505	5.1359

Totals : 2.03836e4 1754.78886

Results obtained with enhanced integrator!

3i

Racemic sample



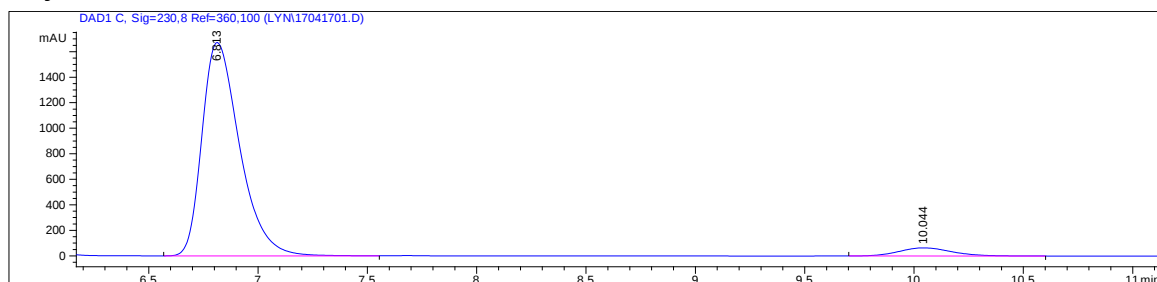
Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.412	VB	0.3109	4.18274e4	2059.98730	49.6601
2	11.976	VB	0.4462	4.23999e4	1479.95508	50.3399

Totals : 8.42273e4 3539.94238

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

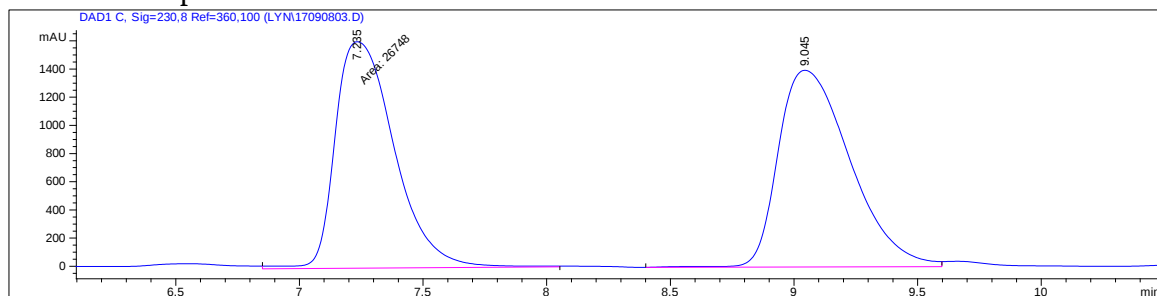
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.813	BB	0.1837	2.00181e4	1671.91394	94.9201
2	10.044	BB	0.2596	1071.30981	63.91401	5.0799

Totals : 2.10894e4 1735.82795

Results obtained with enhanced integrator!

3j

Racemic sample



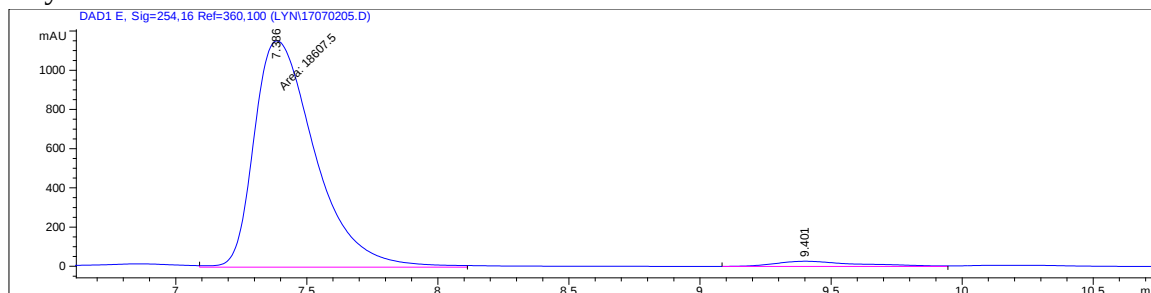
Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.235	MM	0.2773	2.67480e4	1607.74182	48.6239
2	9.045	PV	0.3182	2.82620e4	1396.23047	51.3761

Totals : 5.50101e4 3003.97229

Results obtained with enhanced integrator!

Asymmetric version:



Signal 5: DAD1 E, Sig=254,16 Ref=360,100

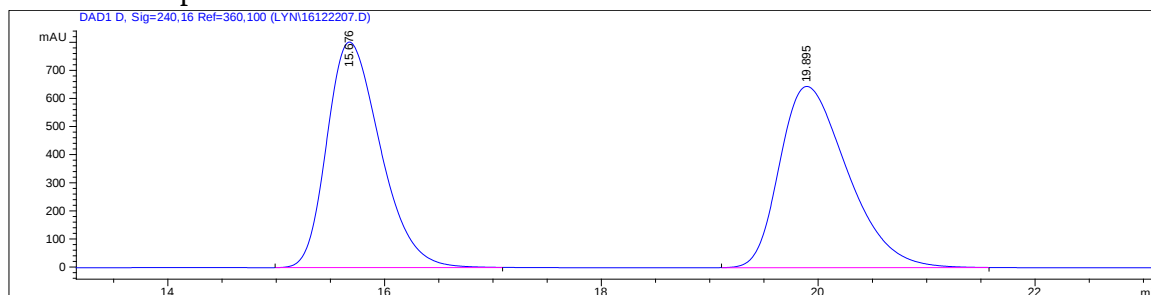
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.386	MM	0.2685	1.86075e4	1154.83118	96.9292
2	9.401	BV	0.3190	589.50812	26.55872	3.0708

Totals : 1.91971e4 1181.38989

Results obtained with enhanced integrator!

3k

Racemic sample



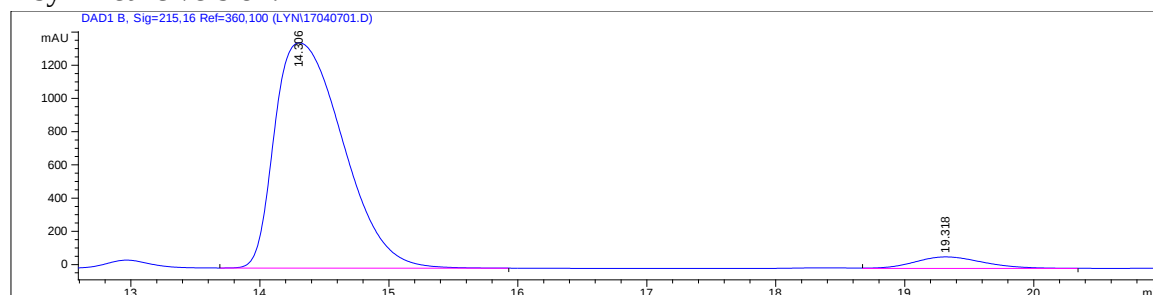
Signal 4: DAD1 D, Sig=240,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.676	BB	0.5311	2.74766e4	803.23126	49.4926
2	19.895	BB	0.6748	2.80400e4	645.47369	50.5074

Totals : 5.55166e4 1448.70496

Results obtained with enhanced integrator!

Asymmetric version:



Signal 2: DAD1 B, Sig=215,16 Ref=360,100

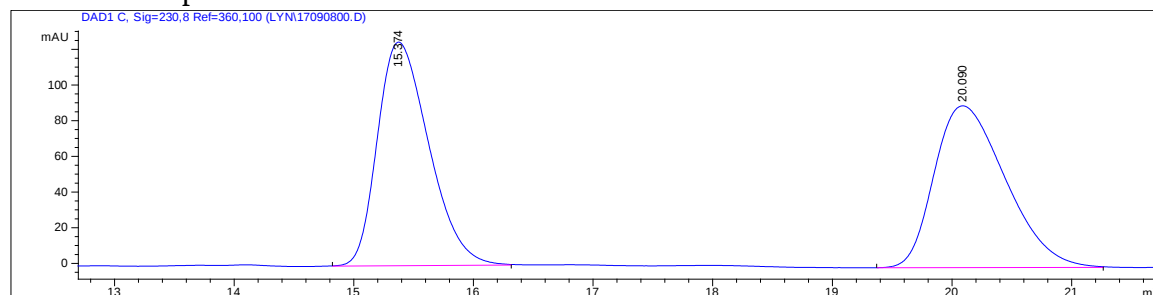
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.306	BB	0.5873	4.99496e4	1357.40723	95.1464
2	19.318	VB	0.5713	2548.04248	69.24368	4.8536

Totals : 5.24976e4 1426.65091

Results obtained with enhanced integrator!

31

Racemic sample



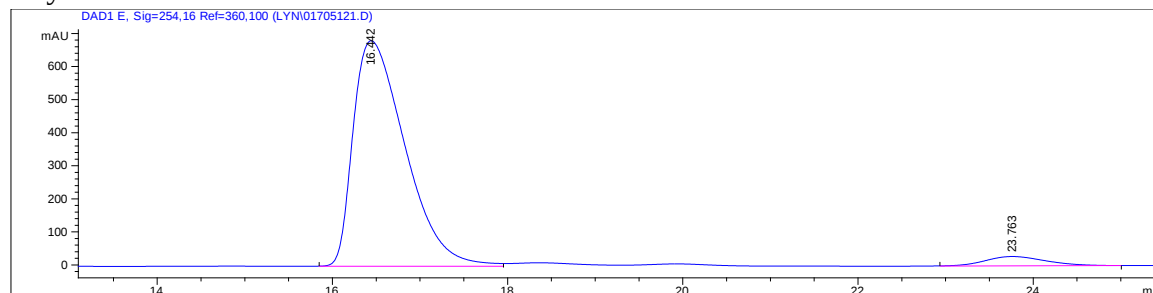
Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.374	BB	0.4675	3734.75464	125.38595	49.9051
2	20.090	PB	0.6462	3748.95972	90.69732	50.0949

Totals : 7483.71436 216.08327

Results obtained with enhanced integrator!

Asymmetric version:



Signal 5: DAD1 E, Sig=254,16 Ref=360,100

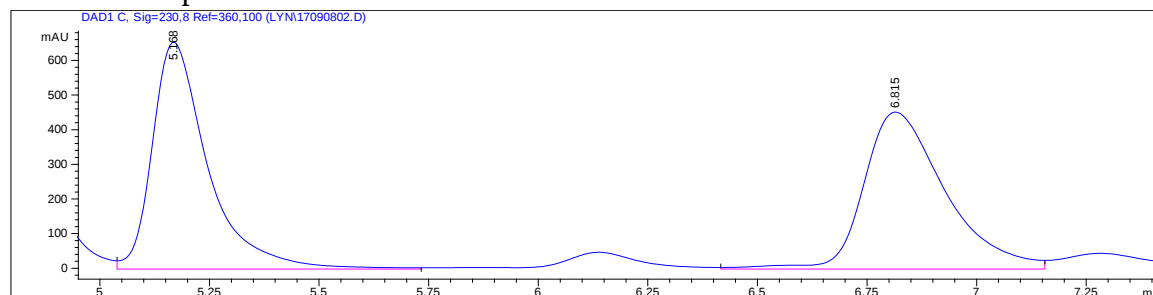
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.442	BB	0.6481	2.80644e4	681.96704	95.4086
2	23.763	BB	0.7121	1350.54639	28.23408	4.5914

Totals : 2.94149e4 710.20112

Results obtained with enhanced integrator!

3m

Racemic sample



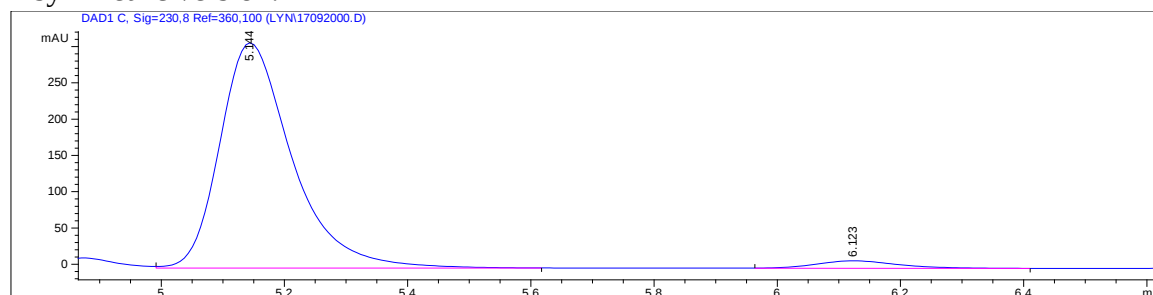
Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.168	VB	0.1307	5773.44434	655.70636	49.6534
2	6.815	VV	0.1967	5854.04395	453.24619	50.3466

Totals : 1.16275e4 1108.95255

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

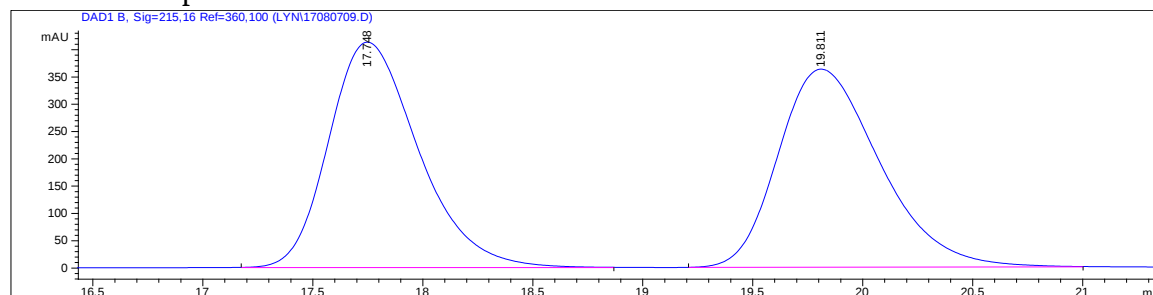
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.144	VB	0.1252	2534.30200	310.53177	96.4520
2	6.123	BP	0.1381	93.22485	10.24622	3.5480

Totals : 2627.52685 320.77799

Results obtained with enhanced integrator!

3n

Racemic sample



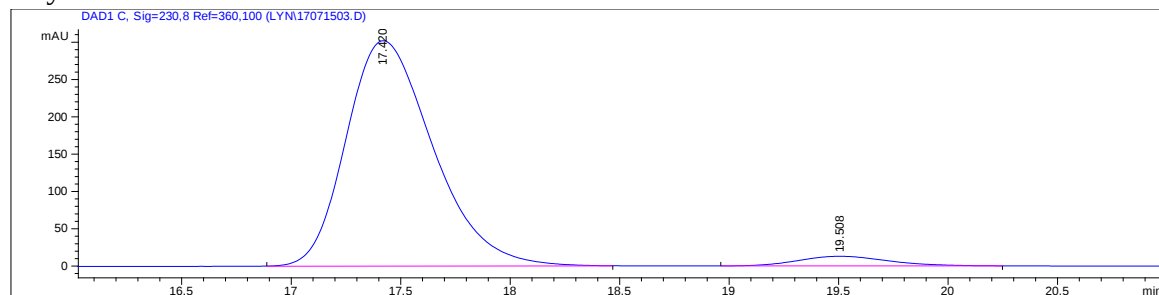
Signal 2: DAD1 B, Sig=215,16 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.748	BB	0.4410	1.17207e4	413.06918	50.0927
2	19.811	BB	0.4975	1.16773e4	362.83316	49.9073

Totals : 2.33980e4 775.90234

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

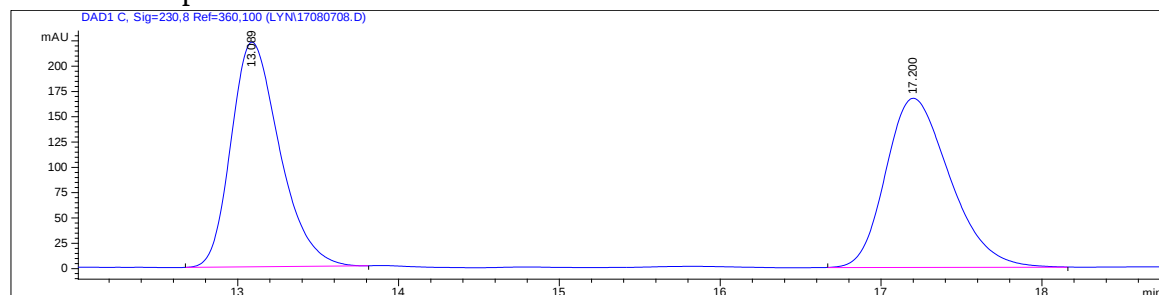
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.420	BB	0.4261	8337.65918	302.01251	95.7612
2	19.508	BB	0.4432	369.06131	12.92299	4.2388

Totals : 8706.72049 314.93550

Results obtained with enhanced integrator!

30

Racemic sample



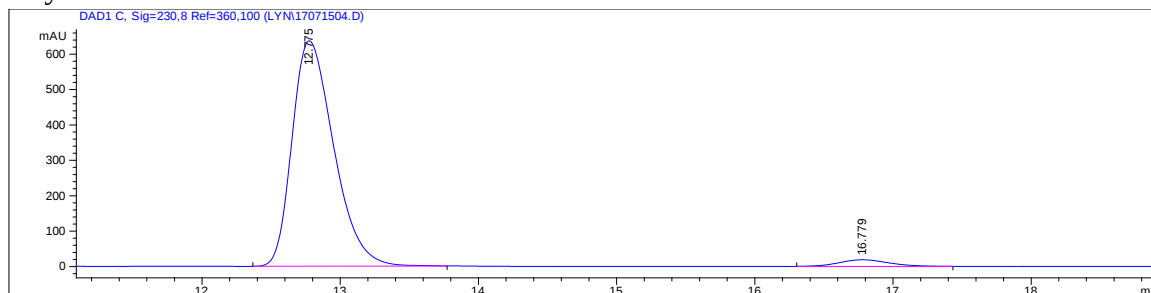
Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.089	PB	0.3219	4641.43848	222.02718	50.0254
2	17.200	BB	0.4276	4636.73242	167.15999	49.9746

Totals : 9278.17090 389.18716

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

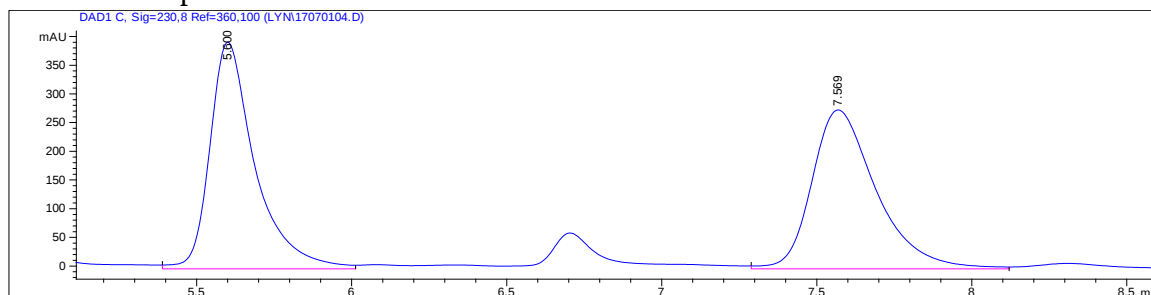
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.775	PB	0.3242	1.33368e4	637.10474	96.5413
2	16.779	BB	0.3924	477.80997	18.80712	3.4587

Totals : 1.38146e4 655.91186

Results obtained with enhanced integrator!

3p

Racemic sample



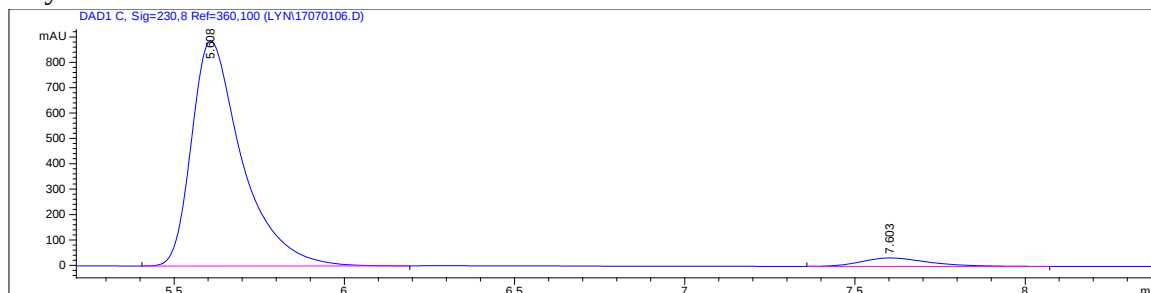
Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.600	BV	0.1499	3994.93115	395.28979	49.9606
2	7.569	VV	0.2186	4001.23877	276.82849	50.0394

Totals : 7996.16992 672.11829

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

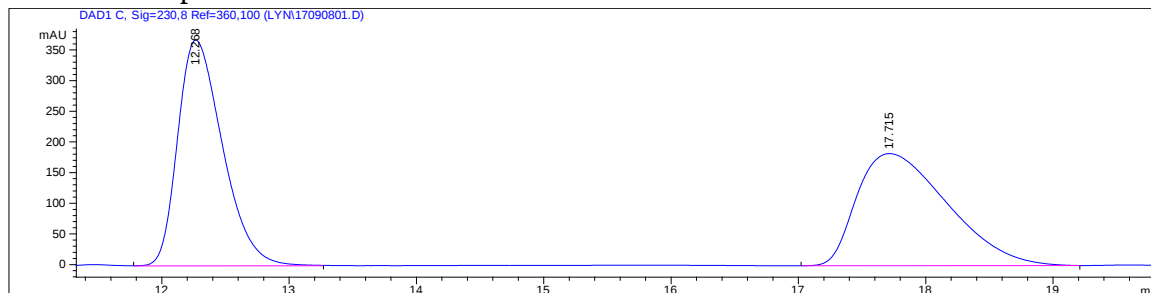
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.608	PP	0.1537	9109.98535	887.85645	95.2387
2	7.603	BB	0.2081	455.43826	33.19786	4.7613

Totals : 9565.42361 921.05431

Results obtained with enhanced integrator!

3q

Racemic sample



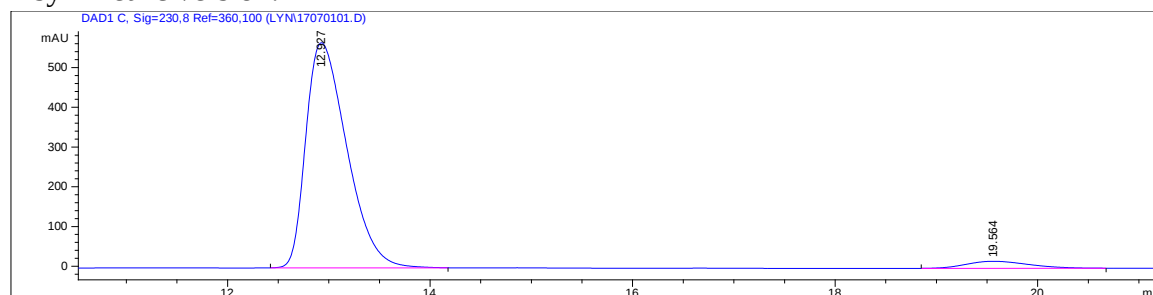
Signal 3: DAD1 C, Sig=230,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.268	VB	0.3792	9001.83398	368.26566	49.9305
2	17.715	PP	0.7782	9026.89453	182.76022	50.0695

Totals : 1.80287e4 551.02588

Results obtained with enhanced integrator!

Asymmetric version:



Signal 3: DAD1 C, Sig=230,8 Ref=360,100

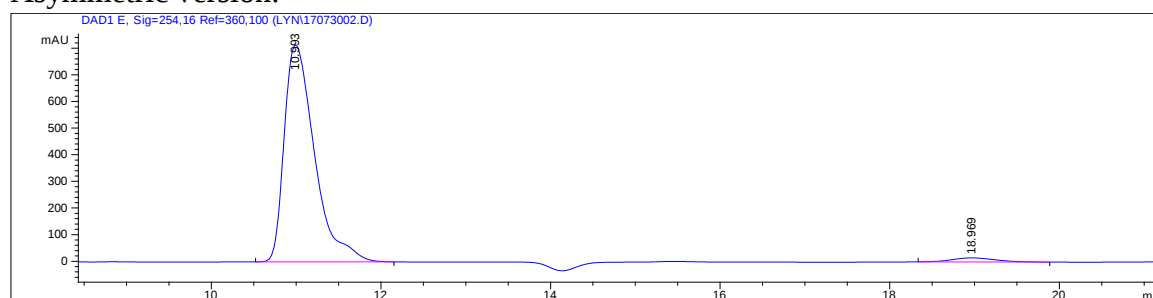
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.927	BB	0.4377	1.59211e4	566.87927	95.4647
2	19.564	BB	0.6489	756.37299	17.68719	4.5353

Totals : 1.66775e4 584.56646

Results obtained with enhanced integrator!

3c (on a gram scale)

Asymmetric version:



Signal 5: DAD1 E, Sig=254,16 Ref=360,100

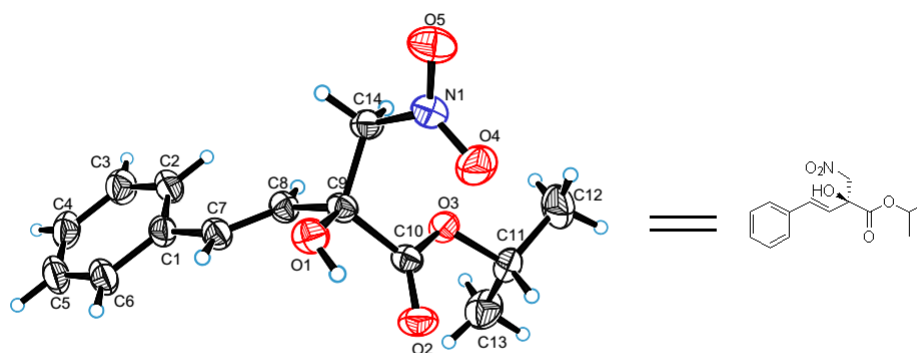
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.993	BB	0.3841	2.02436e4	814.06519	97.3993
2	18.969	BB	0.5447	540.52527	15.27977	2.6007

Totals : 2.07841e4 829.34496

Results obtained with enhanced integrator!

Part IV Crystal data

A single crystal for X-ray analysis of **3a** was obtained by recrystallation from CH₂Cl₂/petroleum ether



CCDC-1561759

Table 1 Crystal data and structure refinement for 3a.

Empirical formula	C ₁₄ H ₁₇ NO ₅
Formula weight	279.28
Temperature/K	292(2)
Crystal system	monoclinic
Space group	P2 ₁
a/Å	8.29130(10)

b/Å	5.80120(10)
c/Å	15.8364(2)
α /°	90
β /°	103.8130(10)
γ /°	90
Volume/Å ³	739.694(18)
Z	2
$\rho_{\text{calc}}/\text{cm}^3$	1.254
μ/mm^{-1}	0.801
F(000)	296.0
Crystal size/mm ³	0.280 × 0.250 × 0.210
Radiation	CuK α (λ = 1.54184)
2 Θ range for data collection/°	10.988 to 142.508
Index ranges	-10 ≤ h ≤ 10, -6 ≤ k ≤ 6, -14 ≤ l ≤ 19
Reflections collected	10235
Independent reflections	2692 [R_{int} = 0.0165, R_{sigma} = 0.0133]
Data/restraints/parameters	2692/1/185
Goodness-of-fit on F^2	1.039
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0287, wR_2 = 0.0793
Final R indexes [all data]	R_1 = 0.0288, wR_2 = 0.0795
Largest diff. peak/hole / e Å ⁻³	0.14/-0.10
Flack parameter	0.06(7)

Table 2 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3a. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij} tensor.

Atom	x	y	z	U(eq)
O3	4825.7(14)	4913(2)	1669.8(7)	50.6(3)
O1	8961.8(14)	3055(2)	2581.0(8)	55.6(3)
O2	6106.6(18)	1559(3)	1553.1(10)	65.8(4)
N1	8442.6(19)	7210(3)	1542.4(10)	53.0(4)
O4	7890(2)	5913(3)	944.8(9)	80.3(5)
O5	9383(2)	8798(3)	1506.2(12)	75.5(5)
C10	6073(2)	3440(3)	1855.5(11)	45.8(4)
C9	7541.5(19)	4410(3)	2549.9(10)	45.4(4)
C14	7933(2)	6906(3)	2377.6(11)	48.7(4)
C8	7078(2)	4399(3)	3419.7(11)	49.9(4)
C11	3387(2)	4291(4)	958.2(11)	54.2(5)
C1	7483(2)	3114(4)	4958.2(11)	53.8(4)

C7	7826 (2)	3124 (4)	4086.8 (12)	53.8 (4)
C4	6891 (3)	2937 (5)	6616.5 (13)	75.0 (7)
C2	6623 (3)	4864 (4)	5253.9 (13)	66.8 (5)
C6	8036 (2)	1272 (4)	5513.1 (14)	66.5 (6)
C3	6332 (3)	4786 (5)	6077.8 (14)	76.3 (6)
C5	7741 (3)	1197 (5)	6334.2 (14)	75.9 (7)
C13	2143 (3)	3048 (7)	1327.7 (19)	90.1 (8)
C12	2755 (4)	6556 (6)	537.1 (18)	94.4 (9)

Table 3 Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3a. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\dots]$.

Atom	U ₁₁	U ₂₂	U ₃₃	U ₂₃	U ₁₃	U ₁₂
O3	46.7 (6)	49.6 (7)	52.2 (6)	-5.4 (5)	5.3 (4)	7.9 (5)
O1	45.4 (6)	51.3 (8)	68.4 (7)	-1.9 (6)	10.2 (5)	8.8 (5)
O2	64.9 (8)	41.4 (8)	84.7 (9)	-9.5 (7)	5.2 (6)	3.9 (6)
N1	56.3 (8)	45.1 (9)	60.0 (8)	3.0 (6)	18.8 (6)	1.2 (7)
O4	108.4 (12)	78.7 (12)	58.9 (8)	-11.9 (8)	29.9 (8)	-21.3 (10)
O5	77.0 (9)	62.3 (10)	97.5 (11)	3.2 (8)	41.2 (8)	-15.0 (8)
C10	47.3 (8)	37.8 (9)	52.3 (8)	2.4 (7)	11.7 (6)	2.2 (7)
C9	43.7 (7)	39.2 (9)	52.8 (8)	3.1 (7)	10.6 (6)	5.1 (7)
C14	54.8 (8)	41.3 (10)	50.6 (8)	-1.7 (7)	13.4 (7)	-2.6 (7)
C8	45.9 (7)	51.3 (11)	51.7 (8)	5.5 (8)	9.8 (6)	3.2 (7)
C11	48.3 (8)	66.7 (13)	44.6 (8)	-8.5 (8)	5.2 (6)	6.2 (8)
C1	47.2 (8)	56.4 (12)	52.2 (8)	9.5 (9)	0.9 (6)	-2.8 (8)
C7	50.2 (8)	50.7 (11)	58.2 (9)	8.2 (8)	8.6 (7)	2.6 (8)
C4	72.8 (12)	99.0 (19)	47.7 (9)	12.7 (11)	3.6 (8)	-13.8 (14)
C2	82.7 (13)	60.3 (13)	54.2 (9)	11.5 (10)	9.7 (9)	7.8 (11)
C6	60.3 (11)	67.2 (15)	65.6 (11)	19.9 (10)	2.3 (9)	9.2 (10)
C3	88.1 (14)	80.8 (17)	59.0 (11)	1.5 (12)	15.6 (10)	5.0 (14)
C5	72.9 (13)	83.9 (18)	61.8 (11)	29.6 (12)	-2 (1)	1.2 (12)
C13	68.3 (13)	109 (2)	89.3 (15)	-3.7 (16)	11.2 (11)	-25.3 (15)
C12	87.6 (16)	104 (2)	77.7 (15)	22.3 (15)	-7.1 (12)	16.8 (17)

Table 4 Bond Lengths for 3a.

Atom Atom	Length/\AA	Atom Atom	Length/\AA
O3 C10	1.319 (2)	C8 C7	1.317 (2)
O3 C11	1.4768 (19)	C11 C13	1.488 (3)

O1	C9	1.407 (2)	C11	C12	1.509 (4)
O2	C10	1.195 (2)	C1	C2	1.385 (3)
N1	O4	1.210 (2)	C1	C6	1.390 (3)
N1	O5	1.217 (2)	C1	C7	1.474 (3)
N1	C14	1.492 (2)	C4	C5	1.366 (4)
C10	C9	1.539 (2)	C4	C3	1.380 (4)
C9	C8	1.516 (2)	C2	C3	1.383 (3)
C9	C14	1.522 (3)	C6	C5	1.380 (3)

Table 5 Bond Angles for 3a.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C10	O3	C11	117.34 (14)	C7	C8	C9	123.93 (16)
O4	N1	O5	124.11 (17)	O3	C11	C13	109.13 (16)
O4	N1	C14	119.03 (16)	O3	C11	C12	104.86 (19)
O5	N1	C14	116.85 (16)	C13	C11	C12	113.3 (2)
O2	C10	O3	126.47 (17)	C2	C1	C6	117.94 (18)
O2	C10	C9	122.00 (16)	C2	C1	C7	122.95 (17)
O3	C10	C9	111.52 (14)	C6	C1	C7	119.11 (19)
O1	C9	C8	110.95 (13)	C8	C7	C1	126.43 (18)
O1	C9	C14	108.96 (14)	C5	C4	C3	119.7 (2)
C8	C9	C14	106.14 (14)	C3	C2	C1	121.0 (2)
O1	C9	C10	109.49 (14)	C5	C6	C1	120.9 (2)
C8	C9	C10	108.58 (13)	C4	C3	C2	120.0 (2)
C14	C9	C10	112.69 (13)	C4	C5	C6	120.4 (2)
N1	C14	C9	112.90 (14)				

Table 6 Hydrogen Bonds for 3a.

D	H	A	d(D-H)/Å	d(H-A)/Å	d(D-A)/Å	D-H-A/°
O1	H1	O2	0.82	2.21	2.6772 (18)	116.3
O1	H1	O5 ¹	0.82	2.32	3.066 (2)	152.3

¹+X,-1+Y,+Z

Table 7 Torsion Angles for 3a.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C11	O3	C10	O2	-6.4 (3)	C10	C9	C8	C7	114.8 (2)

C11O3 C10C9	174.85 (14)	C10O3C11C13	91.9 (2)
O2 C10C9 O1	14.9 (2)	C10O3C11C12	-146.41 (19)
O3 C10C9 O1	-166.34 (14)	C9 C8C7 C1	177.09 (17)
O2 C10C9 C8	-106.39 (19)	C2 C1C7 C8	-17.1 (3)
O3 C10C9 C8	72.38 (17)	C6 C1C7 C8	162.7 (2)
O2 C10C9 C14	136.32 (18)	C6 C1C2 C3	0.4 (3)
O3 C10C9 C14	-44.91 (18)	C7 C1C2 C3	-179.8 (2)
O4 N1 C14C9	30.1 (2)	C2 C1C6 C5	-0.2 (3)
O5 N1 C14C9	-150.99 (16)	C7 C1C6 C5	180.0 (2)
O1 C9 C14N1	59.58 (18)	C5 C4C3 C2	0.5 (4)
C8 C9 C14N1	179.12 (13)	C1 C2C3 C4	-0.6 (4)
C10C9 C14N1	-62.15 (18)	C3 C4C5 C6	-0.3 (4)
O1 C9 C8 C7	-5.5 (3)	C1 C6C5 C4	0.2 (3)
C14C9 C8 C7	-123.8 (2)		

Table 8 Hydrogen Atom Coordinates ($\text{\AA} \times 10^4$) and Isotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for 3a.

Atom	x	y	z	U(eq)
H1	8758	2093	2190	83
H14A	6960	7845	2365	58
H14B	8819	7451	2852	58
H8	6214	5350	3486	60
H11	3750	3303	537	65
H7	8652	2132	3999	65
H4	6689	2876	7169	90
H2	6234	6109	4893	80
H6	8613	73	5328	80
H3	5761	5981	6269	92
H5	8123	-46	6698	91
H13A	2650	1713	1639	135
H13B	1227	2580	865	135
H13C	1749	4051	1717	135
H12A	2378	7503	948	142
H12B	1851	6275	43	142
H12C	3635	7331	352	142