

Supporting Information

for

Correction: Mechanochemical enzymatic resolution of *N*-benzylated- β^3 -amino esters

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Experimental section, NMR spectra, chromatograms and X-ray diffraction data

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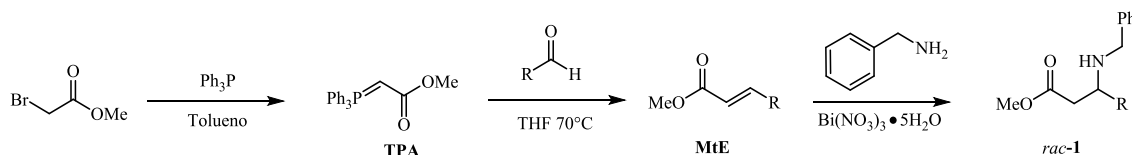
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1) General methods

NMR spectra were recorded on a BRUKER DP300 (300 MHz) and a Jeol Eclipse (400 MHz). High resolution mass spectra were recorded on a HPLC 1100 coupled to a MSD-TOF Agilent series HR-MSTOF model 1969 A. Chromatograms were acquired in a Dionex HPLC Ultimate 3000 with a UV/Visible detector, with diode array, at 210 and 254 nm. HSBM reactions were carry out in a Retsch, Mixer Mill (MM200). *N*-benzylated- β^3 -amino esters were synthesized according to the literature. All reagents for the synthesis were purchased from Sigma-Aldrich. Immobilized CALB was purchased from Novozymes, Novozym 453 (Immobilized on acrylic resine, U/g >100000)

2) General method for the synthesis of *N*-benzylated- β^3 -amino esters.

The substrates *rac*-**1a** to *rac*-**1f** (Table 2 in article) for the enzymatic resolution were synthesized according to previously reported methodologies [1-3], the synthesis for *rac*-**1a** starts from Methyl crotonate. For substrates *rac*-**1g** to *rac*-**1i** we used the methodology describe by Escalante [4].

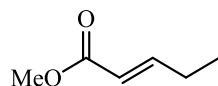


Scheme 1. Route for the synthesis of substrates *rac*-1.

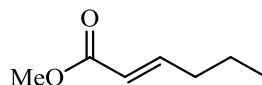
Synthesis of Methyl (triphenylphosphoranyldiene) acetate (**TPA**): Triphenylphosphine (7.86 g, 0.03 mmol) was placed in a round flask equipped with a magnetic bar and was dissolved in Toluene (100 mL), methyl bromoacetate (5.01 g, 0.03 mmol) was added and the reaction was stirred overnight. The reaction product was filtered and the resulting solid was dissolved in water (200 mL), basified till pH 9 using KOH (2M) and phenolphthalein as indicator and was extracted with CH₂Cl₂ (150 mL x 2), the organic fractions were collect, dried with anhydride

sodium sulfate and concentrate to obtain 9.3 g (93% yield) of a white solid (**TPA**). MS-TOF: calculated for $C_{21}H_{20}O_2P$ 335.1156, found 335.1197. 1H NMR ($CDCl_3$, 300MHz): δ = 7.53 (m, 15H), 3.51 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 300MHz): δ 28.7, 30.5, 50.0, 128.8, 128.9, 132.1, 133.0, 133.1. $^{31}P\{^1H\}$ NMR ($CDCl_3$, 300MHz): δ 18.9, 23.1, 30.3.

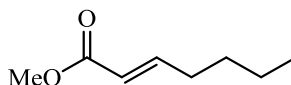
Representative example for the synthesis of Methyl *trans*-2 pentenoate (**MtE-b**): In a round flask equipped with a magnetic bar **TPA** (10.02 g 0.03 mmol) was dissolved in anhydride THF (150 mL), propionaldehyde (1.32 g, 0.03 mmol) was added to the solution and the reaction mixture was refluxed for 4 hrs. The reaction was filtered and evaporated for his purification. The product was purified by flash chromatography on silica gel (Hexanes/Ethyl acetate) to give 5.2 g of a colorless liquid (**M(E)E-b**) (86% yield).



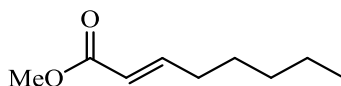
- Methyl *trans*-2 pentenoate (**MtE-b**) [5], from propionaldehyde, colorless liquid, 86% yield. 1H NMR ($CDCl_3$, 300MHz): δ 7.01 (dt, J =6.3 Hz, J_{trans} =15.6 Hz, 1H), 5.80 (d, J =15.6 Hz, 1H), 3.71 (s, 3H), 2.21 (quint, J =6.7 Hz, 2H), 1.05 (t, J =7.2 Hz, 3H), 5.28 (CH_2Cl_2). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 300MHz): δ 12.3, 25.5, 51.5, 120.1, 151.2, 167.4.



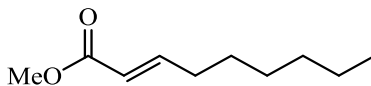
- Methyl *trans*-2 hexenoate (**MtE-c**) [6], from butyraldehyde, colorless liquid, 70% yield. 1H NMR ($CDCl_3$, 300MHz): δ 6.96 (dt, J =6.9 Hz, J_{trans} =15.6 Hz, 1H), 5.81 (d, J =15.6 Hz, 1H), 3.71 (s, 3H), 2.21 (q, J =6.8 Hz, 2H), 1.47 (m, J =7.5 Hz, 2H), 0.92 (t, J =7.3 Hz, 3H), 5.29 (CH_2Cl_2). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 300MHz): δ 13.7, 21.4, 34.6, 51.4, 121.1, 149.8, 167.6.



- Methyl *trans*-2 heptenoate (**MfE-d**) [7], from valeraldehyde, colorless liquid, 83% yield. ^1H NMR (CDCl_3 , 300MHz): δ 6.95 (dt, $J=6.9$ Hz, $J_{\text{trans}}=15.6$ Hz, 1H), 5.79 (d, $J=15.6$ Hz, 1H), 3.69 (s, 3H), 2.17 (q, $J=6.9$ Hz, 2H), 1.35 (m, 2H), 0.88 (t, $J=7.2$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 300MHz): δ 13.7, 22.4, 30.2, 32.3, 51.6, 120.9, 149.7, 167.2.

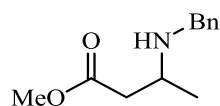


- Methyl *trans*-2 octenoate (**MfE-e**) [8], from hexanal, colorless liquid, 80% yield. ^1H NMR (CDCl_3 , 300MHz): δ 6.82 (dt, $J=7.2$ Hz, $J_{\text{trans}}=15.6$ Hz, 1H), 5.80 (d, $J=15.6$ Hz, 1H), 3.71 (s, 3H), 2.18 (q, $J=7.2$ Hz, 2H), 1.44 (quint, $J=16.5$ Hz, 2H), 1.29 (m, 4H), 0.87 (t, $J=6.3$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 300MHz): δ 41.1, 22.6, 27.8, 31.4, 32.2, 120.8, 150.0, 167.4.

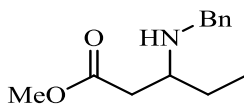


- Methyl *trans*-2 nonenoate (**MfE-f**) [9], from heptanal, colorless liquid, 75% yield. ^1H NMR (CDCl_3 , 300MHz): δ 6.96 (dt, $J=6.9$ Hz, $J_{\text{trans}}=15.6$ Hz, 1H), 5.85 (d, $J=15.9$ Hz, 1H), 3.71 (s, 3H), 2.18 (q, $J=7.2$ Hz, 2H), 1.43 (quint, $J=5.1$ Hz, 2H), 1.27 (m, 4H), 0.87 (t, $J=6.6$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 300MHz): δ 14.2, 22.7, 28.1, 29.0, 31.7, 32.4, 51.6, 120.9, 150.1, 167.5.

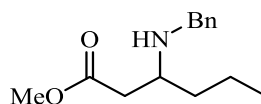
Representative example for the synthesis of Methyl 3-(benzylamino) butanoate (*rac*-**1a**): Bi(NO₃)₃·5H₂O (0.8 g) was added to a round flask containing Methyl crotonate (3.18 mL, 0.03 mmol) equipped with a stir bar, the reaction was stirred by 5 min at 0 °C, after that benzylamine (3.27 mL, 0.03 mmol) was added. The reaction was stirred overnight, filtered, extracted with CH₂Cl₂, dried with anhydride sodium sulfate and concentrated for his purification, obtaining 4 g (63% yield) of an amber liquid, *rac*-**1a**. Compounds *rac*-**1g** to *rac*-**1i** were synthetized as describe in literature [4].



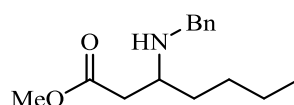
- *rac*-Methyl 3-(benzylamino) butanoate (*rac*-**1a**) [10], from methyl crotonate, amber liquid, 63% yield. MS-TOF: calculated for C₁₂H₁₈N₂O₂ 208.1293, found 208.1331. ¹H NMR (CDCl₃, 300MHz): δ 7.32 (d, *J*=4.2 Hz, 4H), 7.26 (m, 1H), 3.79 (q, *J*=12.3 Hz, 2H), 3.67 (s, 3H), 3.16 (m, *J*=6.3 Hz, 1H), 2.51 (dd, *J*= 6.9, 15.3, 1H), 2.39 (dd, *J*= 6, 15, 1H), 1.83 (br s, 1H), 1.43 (d, *J*=6.3 Hz, 3H). ¹³C{¹H} NMR (CDCl₃, 300MHz): δ 20.58, 41.5, 49.8, 51.3, 51.7, 127.1, 128.3, 128.6, 140.4, 173.0.



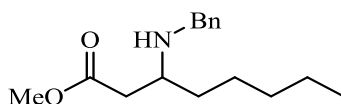
- *rac*-Methyl 3-(benzylamino) pentanoate (*rac*-**1b**) [11], from **MtE-b**, amber liquid, 67% yield. MS-TOF: calculated for C₁₃H₂₀N₂O₂ 222.1449, found 222.1489. ¹H NMR (CDCl₃, 300MHz): δ 7.32 (m, 5H), 3.78 (s, 2H), 3.67 (s, 3H), 2.97 (quint, *J*= 6 Hz, 1H), 2.46 (m, 2H), 1.53 (m, 2H) + (br, 1H), 0.92 (t, *J*= 7.2 Hz, 3H). ¹³C{¹H} NMR (CDCl₃, 300MHz): δ 10.0, 26.9, 38.8, 51.0, 51.6, 55.6, 127.0, 128.3, 128.5, 140.7, 173.2.



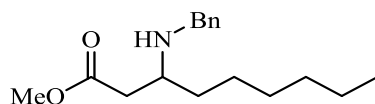
- *rac*-Methyl 3-(benzylamino) hexanoate (*rac*-**1c**) [12], from **MtE-c**, amber liquid, 57% yield. MS-TOF: calculated for C₁₄H₂₂N₂O₂ 236.1606, found 236.1647. ¹H NMR (CDCl₃, 300MHz): δ 7.27 (m, 5H), 3.78 (s, 2H), 3.67 (s, 3H), 3.03 (quint, *J*= 6.3 Hz, 1H), 2.46 (d, *J*= 6.3 Hz, 2H), 1.43 (m, 4H) + (br, 1H), 0.91 (t, *J*= 6.9 Hz, 3H). ¹³C{¹H} NMR (CDCl₃, 300MHz): δ 14.3, 19.1, 36.7, 39.2, 51.1, 51.6, 54.1, 127.0, 128.2, 128.5, 140.7, 173.2.



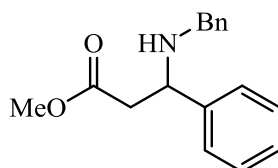
- *rac*-Methyl 3-(benzylamino) heptanoate (*rac*-**1d**), from **MtE-d**, amber liquid, 79% yield. MS-TOF: calculated for C₁₅H₂₄N₂O₂ 250.1762, found 250.1803. ¹H NMR (CDCl₃, 300MHz): δ 7.28 (m, 5H), 3.78 (s, 2H), 3.67 (s, 3H), 3.01 (quint, *J*= 6.3 Hz, 1H), 2.46 (d, *J*= 6.0 Hz, 2H), 1.42 (m, 6H) + (br, 1H), 0.89 (t, *J*= 6.6 Hz, 3H). ¹³C{¹H} NMR (CDCl₃, 300MHz): δ 14.2, 22.9, 28.0, 34.2, 39.2, 51.1, 51.7, 54.4, 127.0, 128.3, 128.5, 140.7, 173.2.



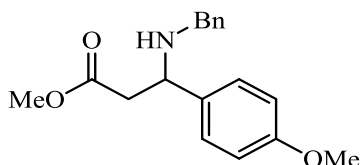
- *rac*-Methyl 3-(benzylamino) octanoate (*rac*-**1e**), from **MtE-e**, amber liquid, 60% yield. MS-TOF: calculated for C₁₆H₂₄N₂O₂ 264.1919, found 264.1956. ¹H NMR (CDCl₃, 300MHz): δ 7.27 (m, 5H), 3.78 (s, 2H), 3.67 (s, 3H), 3.02 (quint, *J*= 6 Hz, 1H), 2.46 (d, *J*= 6 Hz, 2H), 1.46 (m, 8H) + (br, 1H), 0.89 (t, *J*= 6 Hz, 3H). ¹³C{¹H} NMR (CDCl₃, 300MHz): δ 14.1, 22.7, 25.5, 32.0, 34.4, 39.2, 51.1, 51.6, 54.3, 127.0, 128.2, 128.5, 140.7, 173.2.



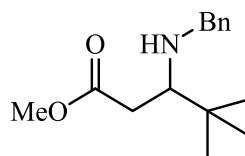
- *rac*-Methyl 3-(benzylamino) nonanoate (*rac*-**1f**), from **MtE-f**, amber liquid, 50% yield. MS-TOF: calculated for C₁₇H₂₈N₂O₂ 278.2075, found 278.1156. ¹H NMR (CDCl₃, 300MHz): δ 7.26 (m, 5H), 3.78 (s, 2H), 3.67 (s, 3H), 3.01 (quint, *J*= 6 Hz, 1H), 2.46 (d, *J*= 6.3 Hz, 2H), 1.46 (m, 10H) + (br, 1H), 0.88 (t, *J*= 5.7 Hz, 3H). ¹³C{¹H} NMR (CDCl₃, 300MHz): δ 14.2, 22.7, 25.8, 29.5, 31.9, 34.5, 39.2, 51.1, 51.6, 54.4, 127.0, 128.3, 128.5, 140.7, 173.2.



- *rac*-Methyl 3-(benzylamino)-3-phenylpropanoate (*rac*-**1g**) [4], amber liquid. MS-TOF: calculated for C₁₇H₂₀N₂O₂ 270.1494, found 270.1501. 79% yield. ¹H NMR (CDCl₃, 400MHz): δ 7.39-7.25 (m, 10H), 4.15 (dd, *J*= 5.2, 8.6 Hz, 1H), 3.71-3.55 (m, 5H), 2.77 (dd, *J*= 8.8, 15.6 Hz, 1H), 2.55 (dd, *J*= 5.2, 15.6 Hz, 1H). ¹³C{¹H} NMR (CDCl₃, 400MHz): δ 42.8, 51.3, 58.8, 65.3, 126.9, 127.1, 127.5, 128.1, 128.3, 128.6, 140.2, 142.4, 172.2.



- *rac*-Methyl 3-(benzylamino)-3-(*p*-methoxy)phenylpropanoate (*rac*-**1h**) [13], amber liquid, 50% yield (0.03 mmol). ¹H NMR (CDCl₃, 300MHz): δ 7.33-7.23 (m, 7H), 6.85 (d, *J*=9 Hz, 2H), 4.06 (q, *J*= 5.4 Hz, 1H), 3.81 (s, 3H), 3.67-3.50 (m, 5H), 2.76-2.57 (m, 2H), 1.97 (br s, 1H). ¹³C{¹H} NMR (CDCl₃, 300MHz): δ 43.1, 51.4, 51.8, 55.4, 58.2, 114.1, 127.0, 128.3, 128.5, 134.6, 140.4, 159.0, 172.6.

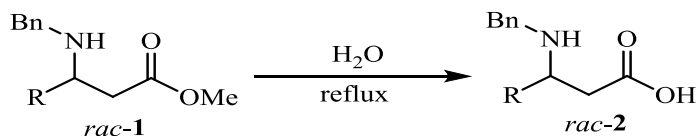


- rac*-Methyl 3-(benzylamino)-4,4-dimethylpentanoate (*rac*-**1i**) [4], amber liquid.

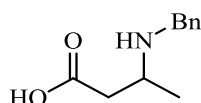
HRMS(ES⁺): calculated for C₁₅H₂₄N₂O₂ 250.3616, found 250.1812. ¹H NMR (CDCl₃, 400MHz): δ 7.32-7.23 (m, 5H), 3.90-3.68 (m, 5H), 2.80 (q, *J*= 4.2 Hz, 1H), 2.57 (dd, *J*=4.2, 14.7 Hz, 1H), 2.29 (dd, *J*= 8.4, 14.7 Hz, 1H), 1.29 (br s, 1H), 0.92 (s, 9H).

¹³C{¹H} NMR (CDCl₃, 100MHz): δ 26.7, 35.6, 37.0, 51.8, 54.3, 64.1, 127.0, 128.4, 141.2, 174.3.

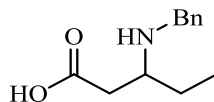
3) General method for the synthesis of *N*-benzylated- β^3 -amino acids



Representative example for the synthesis of *N*-benzylated- β^3 -amino acids⁵: The appropriate *N*-benzylated- β^3 -amino acid methyl ester is placed in a round flask equipped with a stir bar and 10 mL of water, 1 equivalent of NaOH is added when required (substrates **2c** to **2j**), the reaction was refluxed for 4 hrs. The solution was neutralized, the solvent was evaporated under vacuum and the product was washed with CH₂Cl₂, filtered and decanted with MeOH to obtain a white solid.

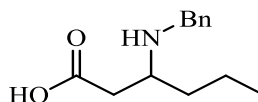


- *rac*-3-(*N*-benzylamino) butanoic acid (*rac*-**2a**) [4], white off solid, 86% yield. mp 170-171 °C (170-171°C [4]). MS-TOF: calculated for C₁₁H₁₅N₂O₂ 194.1136, found 194.1175. ¹H NMR (D₂O, 400MHz): δ 7.42 (s, 5H), 4.18 (q, *J*= 16.8 Hz, 2H), 3.52 (m, *J*= 6.4 Hz, 1H), 3.28 (br s, 1H), 2.59 (dd, *J*=4.8, 13 Hz, 1H), 2.54 (dd, *J*=4.5, 12.8 Hz, 1H), 1.32 (d, *J*= 6.4 Hz, 3H). ¹³C{¹H} NMR (D₂O, 400MHz): δ 15.9, 38.2, 48.1, 51.2, 129.3, 129.6, 130.9, 176.4.

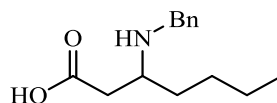


- *rac*-3-(*N*-benzylamino) pentanoic acid (*rac*-**2b**) [14], 89% yield. white solid. mp 167-169°C (169-170°C [14]). MS-TOF: calculated for C₁₁H₁₅N₂O₂ 208.1293, found 208.1331. ¹H NMR (D₂O, 400MHz): δ 7.40 (s, 5H), 4.17 (q, *J*= 9, 1 Hz, 2H), 3.31 (m, 1H), 2.56 (dd, *J*=3.6, 12.9 Hz, 1H), 2.40 (dd, *J*=5.4, 12.7 Hz, 1H), 1.78 (m, 1H), 1.59 (m, 1H),

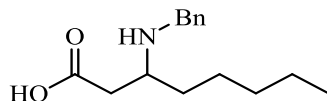
0.88 (t, $J = 7.6\text{ Hz}$, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O , 400MHz): δ 8.8, 23.3, 35.3, 47.9, 56.7, 129.3, 129.5, 131.2, 178.2.



- *rac*-3-(N-benzylamino) hexanoic acid (*rac*-**2c**) [14], 97% yield. white solid. mp 156-159°C (160-162°C [14]). MS-TOF: calculated for $\text{C}_{13}\text{H}_{20}\text{NO}_2$ 222.1449, found 222.1488. ^1H NMR (D_2O , 400MHz): δ 7.40 (s, 5H), 4.18 (q, $J = 10.2\text{ Hz}$, 2H), 3.55 (m, 1H), 2.56 (dd, $J = 3.6, 12.6\text{ Hz}$, 1H), 2.40 (dd, $J = 5.7, 12.6\text{ Hz}$, 1H), 1.70 (m, 1H), 1.55 (m, 1H), 1.30 (m, 2H), 0.83 (t, $J = 5.7\text{ Hz}$, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O , 400MHz): δ 12.9, 18.0, 32.3, 35.9, 47.8, 55.1, 129.3, 129.4, 129.5, 131.4, 178.3.

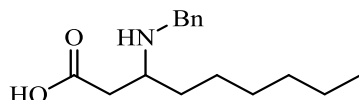


- *rac*-3-(N-benzylamino) heptanoic acid (*rac*-**2d**) [15], 84% yield. white solid. mp 152-155°C. MS-TOF: calculated for $\text{C}_{14}\text{H}_{22}\text{NO}_2$ 236.1606, found 236.1644. ^1H NMR (D_2O , 400MHz): δ 7.26 (s, 5H), 4.0 (t, $J = 10.2\text{ Hz}$, 2H), 3.32 (m, 1H), 2.68 (dd, $J = 4.8, 17.8\text{ Hz}$, 1H), 2.28 (dd, $J = 6.8, 18\text{ Hz}$, 1H), 1.60 (m, 1H), 1.47 (m, 1H), 1.08 (m, 4H), 0.63 (t, $J = 6.4\text{ Hz}$, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O , 400MHz): δ 12.9, 21.4, 26.4, 29.5, 34.0, 48.5, 54.1, 129.1, 129.5, 129.7, 130.3, 137.9.

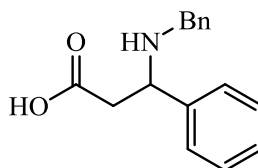


- *rac*-3-(N-benzylamino) octanoic acid (*rac*-**2e**), 80% yield. white solid. mp 150-152°C. MS-TOF: calculated for $\text{C}_{15}\text{H}_{24}\text{NO}_2$ 250.1762, found 250.1803. ^1H NMR (D_2O , 400MHz): δ 7.25 (s, 5H), 4.03 (s, 2H), 3.32 (m, 1H), 2.67 (dd, $J = 4.8, 18\text{ Hz}$, 1H), 2.28 (dd, $J = 6.8,$

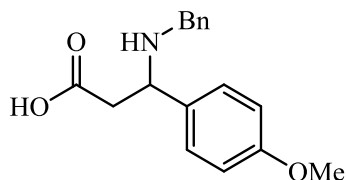
17.6 Hz, 1H), 1.58 (m, 1H), 1.46 (m, 1H), 1.03 (m, 6H), 0.60 (t, J = 6.4 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O , 400MHz): δ 13.0, 21.4, 23.9, 29.7, 30.3, 34.0, 48.5, 54.1, 129.1, 129.5, 129.7, 130.2, 137.9.



- *rac*-3-(N-benzylamino) nonanoic acid (*rac*-**2f**), 83% yield. white solid. mp 151-153°C MS-TOF: calculated for $\text{C}_{16}\text{H}_{26}\text{NO}_2$ 264.1919, found 264.2005. ^1H NMR (D_2O , 400MHz): δ 7.36 (s, 5H), 4.18 (s, 2H), 3.41 (m, 1H), 2.76 (dd, J = 4.8, 17.8 Hz, 1H), 2.67 (dd, J = 6.8, 17.6 Hz, 1H), 1.69 (m, 1H), 1.56 (m, 1H), 1.16 (m, 8H), 0.72 (t, J = 6 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (D_2O , 400MHz): δ 13.2, 21.7, 24.2, 27.8, 29.7, 30.6, 34.1, 48.6, 54.0, 129.2, 129.7, 129.8, 130.3, 174.0.

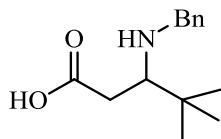


- *rac*-3-(N-benzylamino)-3-phenylpropanoic acid (*rac*-**2g**) [4], 80% yield. white solid. mp 149-151°C (148-151°C [4]). ^1H NMR (CD_3OD , drops NH_4OH , 200MHz): δ 7.42-7.22 (m, 10H), 4.95 (dd, J = 4.4, 10.4, 1H), 3.33 (s, 2H), 2.63 (dd, J = 10.4, 16.8, 1H), 2.48 (dd, J = 4.4, 17.2, 1H), $^{13}\text{C}\{^1\text{H}\}$ NMR ($\text{CD}_3\text{OD}+\text{NH}_4\text{OH}$, 50MHz): δ 45.3, 50.9, 60.3, 126.6, 126.9, 127.3, 128.0, 128.1, 139.3, 142.6, 178.3.



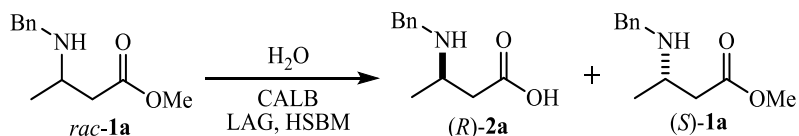
- *rac*-3-(N-benzylamino)-3-(*p*-methoxy)phenylpropanoic acid (*rac*-**2h**), 54% yield. white solid. mp 172-174°C. MS-TOF: calculated for $\text{C}_{16}\text{H}_{25}\text{NO}_2$ 263.1885, found 263.2005. ^1H NMR (CD_3OD , 400MHz): δ 7.26 (d, J = 9.6 Hz, 7H), 7.04 (d, J = 8 Hz, 2H), 4.45 (dd, J =

3.2, 10.2 Hz 1H), 2.76 (dd, J = 4.8, 17.8 Hz, 1H), 4.00 (dd, J = 13.2, 25.2 Hz, 2H), 3.85 (s, 3H), 2.86 (dd, J = 10.8, 16.6 Hz, 1H), 2.65 (dd, J = 3.6, 16.8 Hz, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_3OD , 400MHz): δ 38.5, 48.1, 54.4, 59.3, 14.4, 126.4, 128.9, 128.9, 129.0, 129.1, 131.8, 160.7, 176.0.



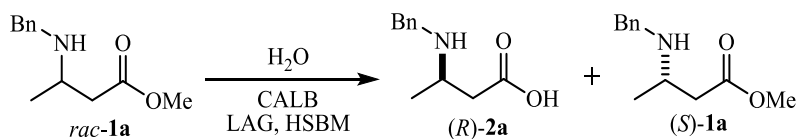
- *rac*-3-(N-benzylamino)-4,4-dimethylpentanoic acid (*rac*-**2i**) [4], 88% yield. white solid. mp 152-153°C (150-153°C [4]). HRMS (ES^+): calculated for $\text{C}_{14}\text{H}_{22}\text{NO}_2$ 236.1651, found 236.1638. ^1H NMR (D_2O) δ 7.27 (s, 5H), 4.28 (m, 1H), 4.04 (m, 1H), 3.14 (m, 1H), 2.69 (m, 1H), 2.53 (m, 1H), 0.75 (m, 9H) $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_3OD , 100MHz): δ 24.6, 32.0, 33.3, 50.6, 62.6, 129.1, 129.8, 130.2, 174.3.

4) General method for the enzymatic resolution using CALB.



Representative example for the enzymatic resolution using CALB and *rac*-**1a**: 82 mg of substrate *rac*-**1a** (0.4 mmol), 3.6 μL of water (0.2 mmol) and 0.2 mL of 2M2B were placed in an Agate jar (12 mm of Diameter) with an Agate ball (6 mm of Diameter, 480mg of weight), 40 mg of enzyme (CALB) were aggregated and the reactor was closed and placed in a Mixer Mill MM200 programed to carry out the reaction at 25 Hz during 30 min. Once the reaction is finished the content was extracted with methanol and transferred to a Falcon tube (50 mL), the solution was centrifuged at 3500 rpm for 5 min twice; the supernatant was collected and concentrated for his purification with silica gel, a mixture of Hexanes and ethyl acetate was used as mobile phase for recovering the raw material and Methanol and CH_2Cl_2 for the purification of the product. Methyl 3-(benzylamino) butanoic acid (*R*)-**2a** was obtain as a white solid (49% yield). In order to avoid contamination by the wear of the stainless-steel reactors we decided to use Agate reactors.

Table S1. Search of the best parameters for the enzymatic hydrolysis resolution under HSBM.



entry ^a	LAG	frequency (Hz)	time (h)	(S)-1a			(R)-2a			<i>c</i> ^f (%)	<i>E</i> ^g
				recovered ^b (%)	<i>ee</i> ^c (%)	$[\alpha]_D^{25d}$	yield ^b (%)	<i>ee</i> ^c (%)	$[\alpha]_D^{25e}$		
1	2M2B	25	0.5	51	99	20.4	49	80	-31.7	55	46
2	2M2B	15	0.5	70	89	22.0	30	77	-33.1	54	23
3	2M2B	15	1	51	99	22.5	49	95	-30.0	51	>200
4	Hexane	15	1	40	97	23.3	60	86	-20.4	53	55
5	AcOEt	15	1	86	69	10.3	13	95	-30.1	42	81
6	DIPE	15	1	76	92	17.3	19	88	-25.6	51	51
7	Toluene	15	1	75	72	12.6	25	93	-29.5	44	60
8	Dioxane	15	1	53	79	16.7	47	95	-30.3	45	94
9	IPA	15	1	80	48	7.4	20	95	-29.8	34	63
10	CH ₃ CN	15	1	65	65	9.8	29	95	-30.0	41	77
11	-	15	1	58	95	16.6	41	92	-28.2	51	89
12	-	25	1	58	93	16.5	42	86	-31.2	52	45
13 ^h	-	15	1	68	74	13.5	31	80	-27.0	48	20
14 ⁱ	2M2B	15	1	-	-	-	92	<i>rac</i>	-	-	-
15 ^j	2M2B	15	1	89	<i>rac</i>	-	-	-	-	-	-

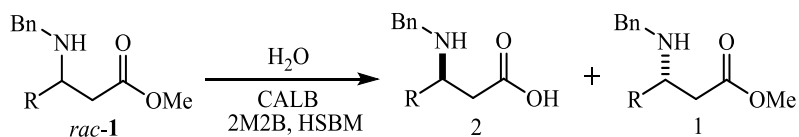
^aReactions were carried out using the general method. ^bDetermined after purification by flash chromatography.

^cDetermined by HPLC with chiral stationary phase. ^dUsing CH₃Cl and *c*=0.33,

^eUsing MeOH and *c*=0.33, ^fCalculated from *c*= *ee*_s/(*ee*_s + *ee*_p). ^g*E*= ln[1-*c*(1+*ee*_p)]/ln[1-*c*(1-*ee*_p)].

^h0.25 equivalents of water were used. ⁱ1 equivalent of water were used. ^jwater-free conditions.

Table S2. Substrate scope for the enzymatic resolution of N-benzylated- β^3 -amino esters.



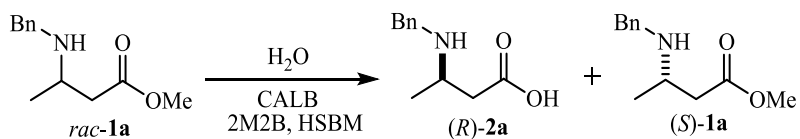
entry ^a	rac-1	R	Substrate-1			2			c ^d (%)	E ^e	a.c. ^f
			recovered ^b (%)	ee ^c (%)	[α] _D ²⁵	yield ^b (%)	ee ^c (%)	[α] _D ²⁵			
1	1b	CH ₃ -(CH ₂)-	51	91	4.5	49	97	-36.5	48	>200	R
2	1c	CH ₃ -(CH ₂) ₂ -	53	84	2.1	43	98	-45.2	46	>200	R
3	1d	CH ₃ -(CH ₂) ₃ -	68	23	2.0	29	94	-35.3	20	40	R
4 ^g	1d	CH ₃ -(CH ₂) ₃ -	66	57	0.2	25	94	-33.3	38	58	R
5 ^h	1d	CH ₃ -(CH ₂) ₃ -	51	30	2.7	41	85	-40.5	26	17	R
6	1e	CH ₃ -(CH ₂) ₄ -	74	16	1.8	24	94	-40.0	15	38	R
7 ^g	1e	CH ₃ -(CH ₂) ₄ -	76	27	0.8	22	82	-30.2	25	13	R
8 ^h	1e	CH ₃ -(CH ₂) ₄ -	82	27	2.7	10	76	-13.0	26	10	R
9	1f	CH ₃ -(CH ₂) ₅ -	79	13	0.8	18	91	-39.7	13	24	R
10 ^g	1f	CH ₃ -(CH ₂) ₅ -	85	21	1.1	11	82	-28.5	20	12	R
11 ^h	1f	CH ₃ -(CH ₂) ₅ -	84	18	0.7	8	83	-28.9	18	13	R
12 ⁱ	1g	Ph	90	18	3.4	10	83	-35.0	18	13	S
13 ^{h, n}	1g	Ph	85	18	3.0	15	68	-44.0	21	6	S
14 ^j	1g	Ph	90	16	3.2	9	37	-18.1	30	3	S
15 ^{h, k}	1g	Ph	80	5	2.5	20	48	-21.0	9	3	S
16	1h	p-MeO-Ph	89	1	-0.5	10	80	-31.7	1	9	S
17	1i	t-Bu	89	4	-0.6	4	94	12.8	4	34	S
18 ⁿ	1i	t-Bu	87	5	-0.7	6	89	16.6	5	18	S

^aReactions were carried out using the general method. ^bDetermined after purification by flash chromatography.

^cDetermined by HPLC with chiral stationary phase. ^dCalculated from $c = ee_s / (ee_s + ee_p)$. ^e $E = \ln[1 - c(1 + ee_p)] / \ln[1 - c(1 - ee_p)]$. **a.c.** Absolute Configuration of product **2**. ^fAssigned by chemical comparison and HPLC with chiral

stationary phase. ^gCarried out with 15 Hz during 1 h. ^hCarried out with 25 Hz during 1 h. ⁱ0.75 equiv. of water were used. ^j1 equiv. of water were used. ^k2 equiv. of enzyme were used.

Table S3. Recycling capacity of immobilized CALB under HSBM conditions.

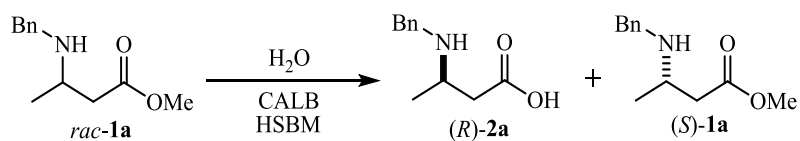


entry ^a	rCALB (cycle)	(S)-1a			(R)-2a			<i>c</i> ^d (%)	<i>E</i> ^e
		recovered ^b (%)	ee ^c (%)	$[\alpha]_D^{25}$	yield ^b (%)	ee ^c (%)	$[\alpha]_D^{25}$		
1	-	51	>99	22.0	49	95	-31.7	51	>200
2	1	65	35	2.8	35	88	-33.3	28	22
3	2	80	6	0.5	20	80	-53.9	7	10
4	3	100	0	0.0	0	0	-	-	-
5 ^f	1	60	67	15.6	38	94	-29.2	42	65
6 ^g	1	62	83	15.9	38	91	-26.8	48	55

^aReactions were carried out using the general method. ^bDetermined after purification by flash chromatography. ^cDetermined by HPLC with chiral stationary phase. ^dCalculated from $c = ee_s / (ee_s + ee_p)$. ^e $E = \ln[1 - c(1 + ee_p)] / \ln[1 - c(1 - ee_p)]$. ^fEnzyme with a pretreatment (Milling for 1h at 15 Hz).

^gPretreatment was carried out using 0.2mL of LAG.

Table S4. Scaling-up for the enzymatic hydrolysis using the substrate *rac*-1a.



entry ^a	substrate equivalents	(S)-1a			(R)-2a			<i>c</i> ^d (%)	<i>E</i> ^e
		recovered ^b (%)	<i>ee</i> ^c (%)	$[\alpha]_D^{25}$	yield ^b (%)	<i>ee</i> ^c (%)	$[\alpha]_D^{25}$		
1	1	51	>99	22.0	49	95	-31.7	51	>200
2	3	52	62	8.0	48	93	-33.0	40	52
3	6	61	53	7.8	38	93	-33.9	36	47
4	9	59	49	7.0	40	94	-33.0	34	53

^aReactions were carried out using the general method but in absence of LAG. ^bDetermined after purification by flash chromatography. ^cDetermined by HPLC with chiral stationary phase.

^dCalculated from $c = ee_s / (ee_s + ee_p)$. ^e $E = \ln[1 - c(1 + ee_p)] / \ln[1 - c(1 - ee_p)]$.

5) ^1H and ^{13}C NMR spectra for TPA, MfE-b to MfE-d, *rac*-1a to *rac*-1j and products 2a to 2j.

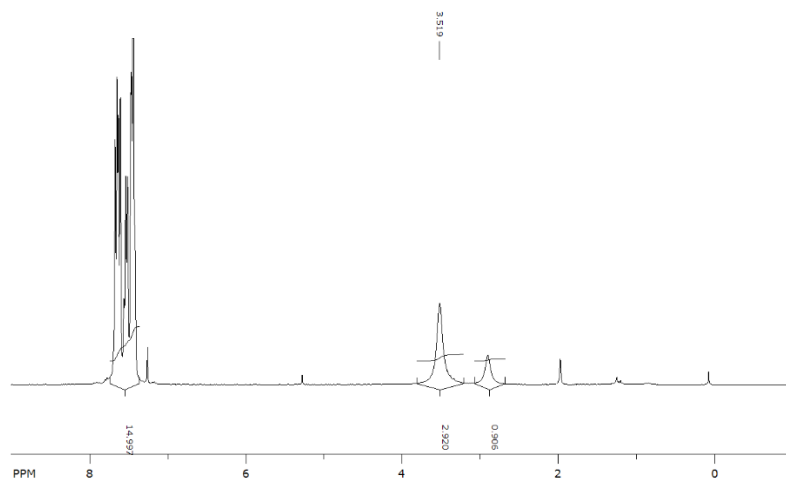
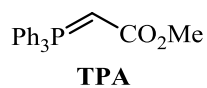


Figure S1. ^1H spectrum (300 MHz, CDCl_3) of TPAc

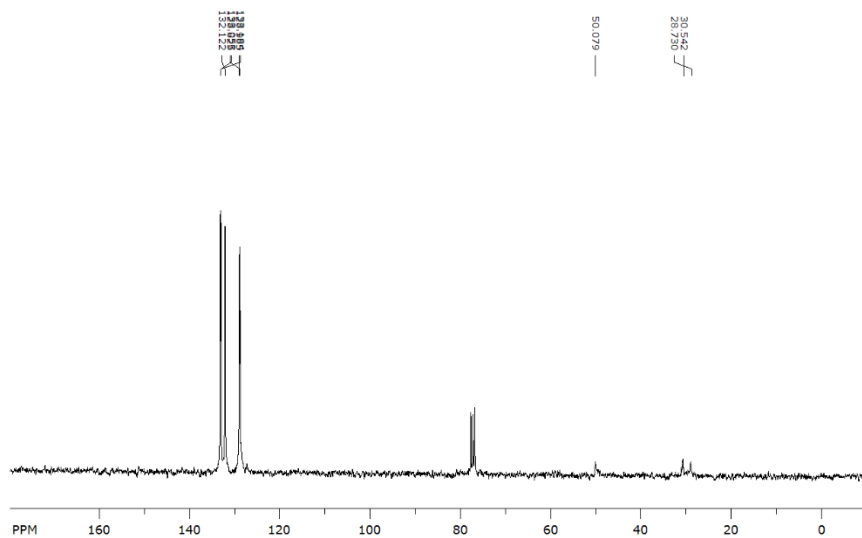


Figure S2. ^{13}C spectrum (75 MHz, CDCl_3) of TPA

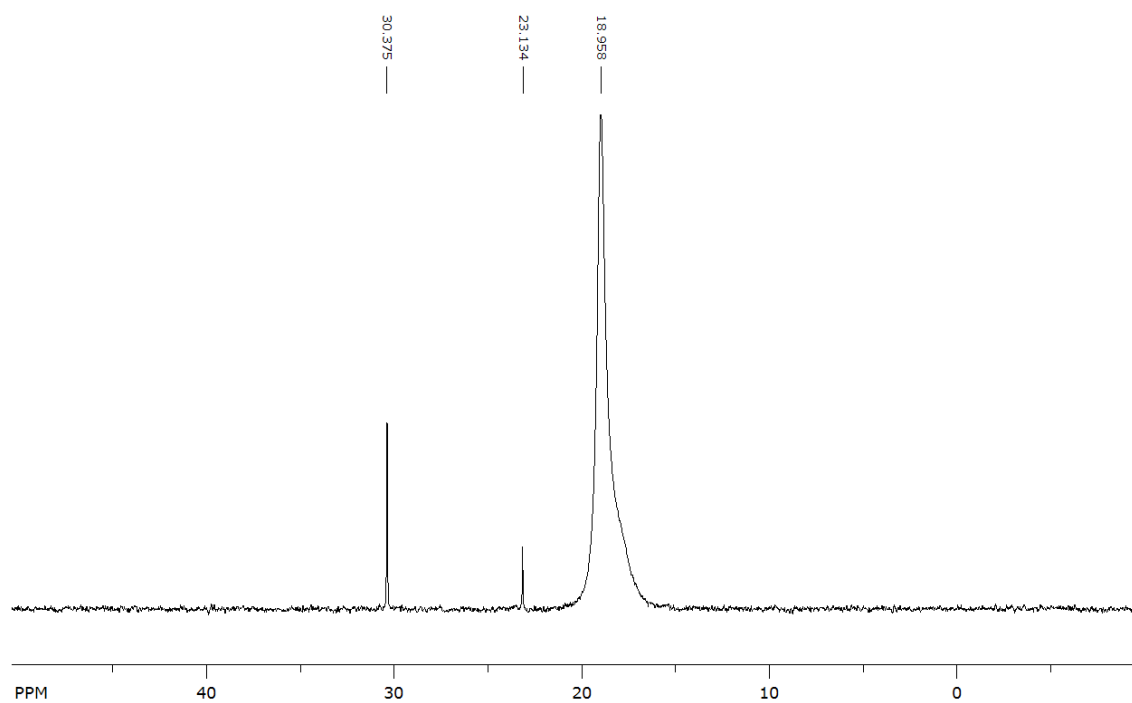


Figure S3. ^{31}P spectrum (120 MHz, CDCl_3) of TPA

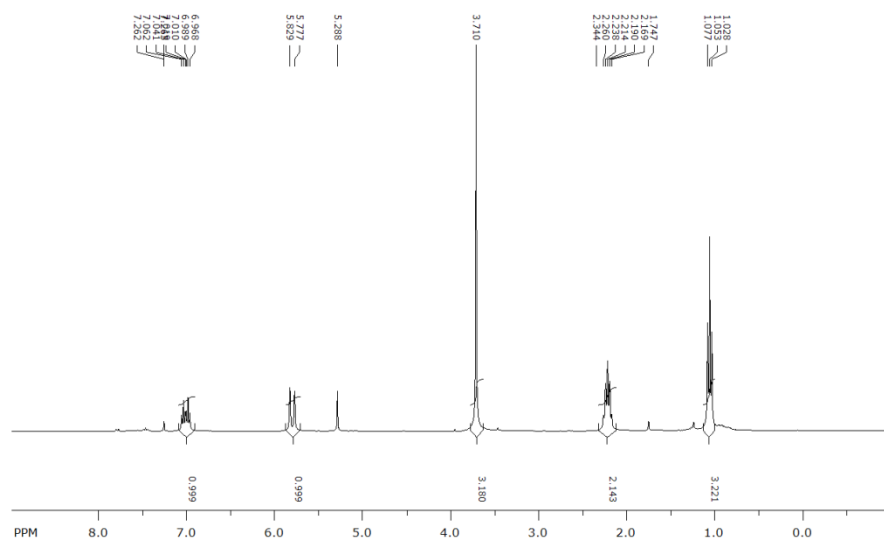
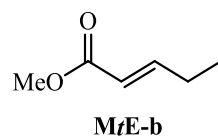


Figure S4. ¹H spectrum (300 MHz, CDCl₃) of MfE-b

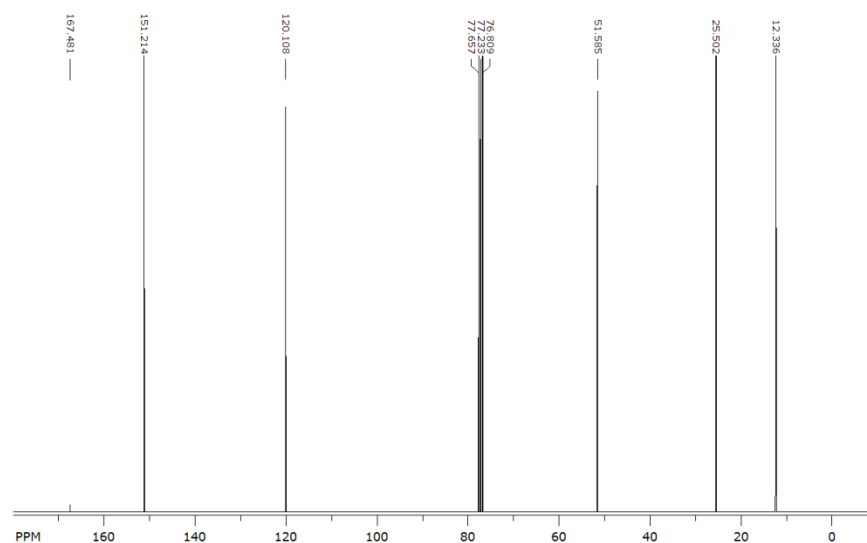


Figure S5. ¹³C spectrum (75 MHz, CDCl₃) of MfE-b

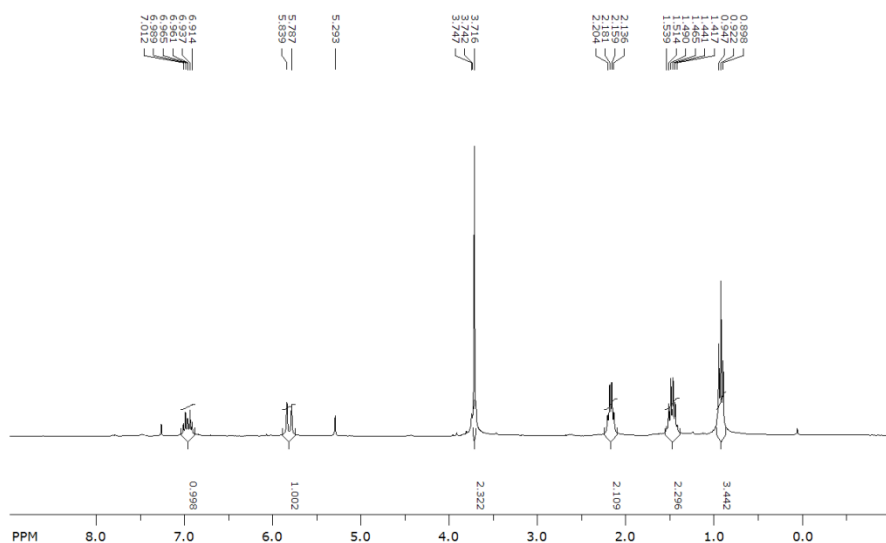
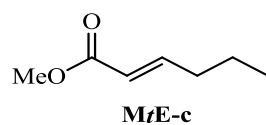


Figure S6. ¹H spectrum (300 MHz, CDCl₃) of MtE-c

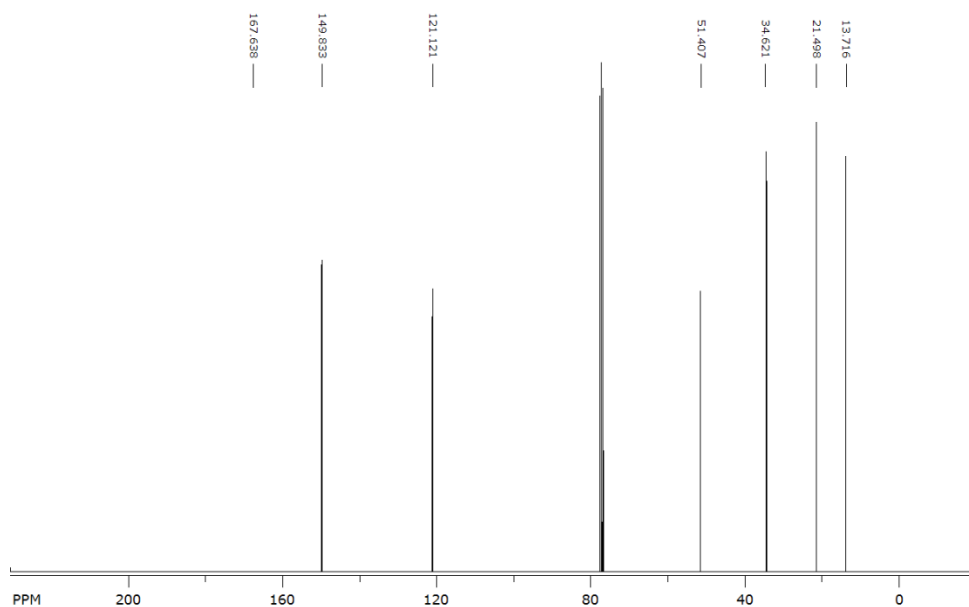


Figure S7. ¹³C spectrum (75 MHz, CDCl₃) of MtE-c

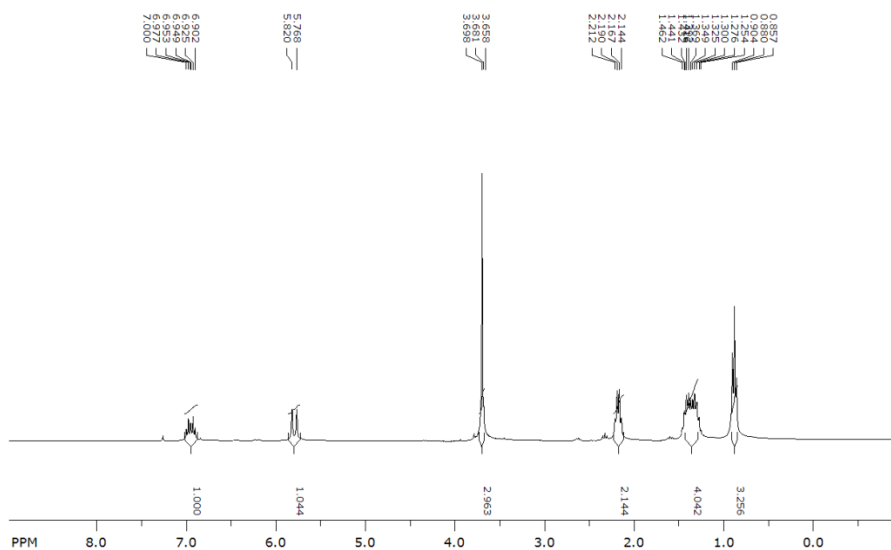
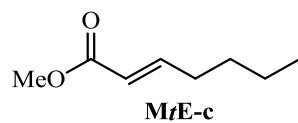


Figure S8. ¹H spectrum (300 MHz, CDCl₃) of MtE-d

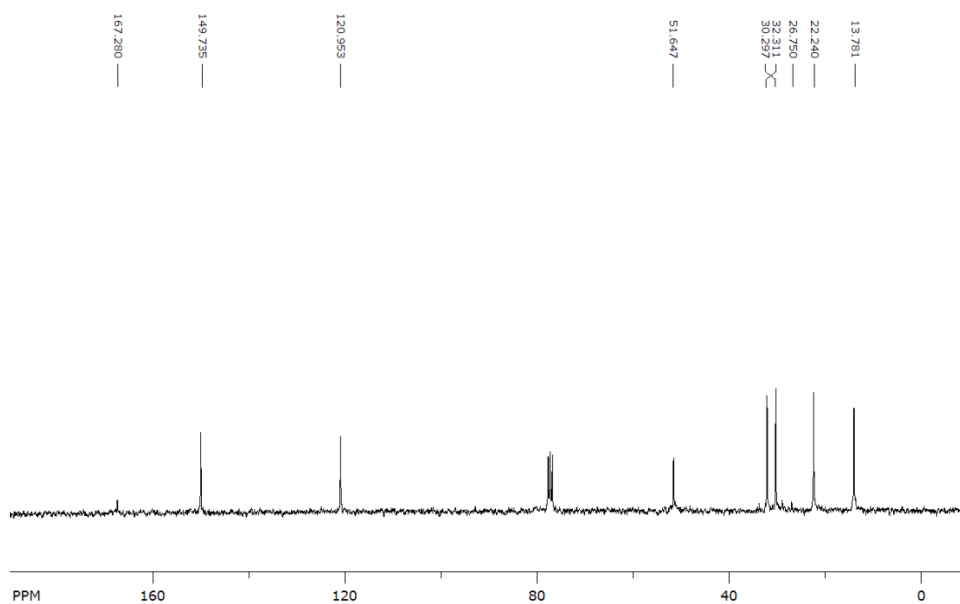


Figure S9. ¹³C spectrum (75 MHz, CDCl₃) of MtE-d

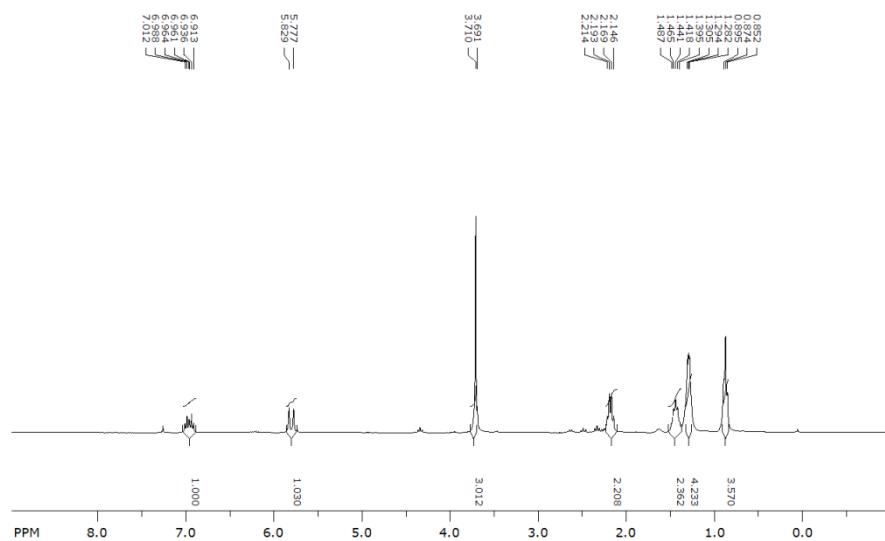
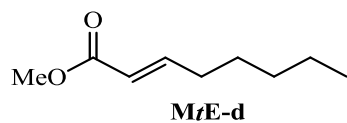


Figure S10. ¹H spectrum (300 MHz, CDCl₃) of MtE-e

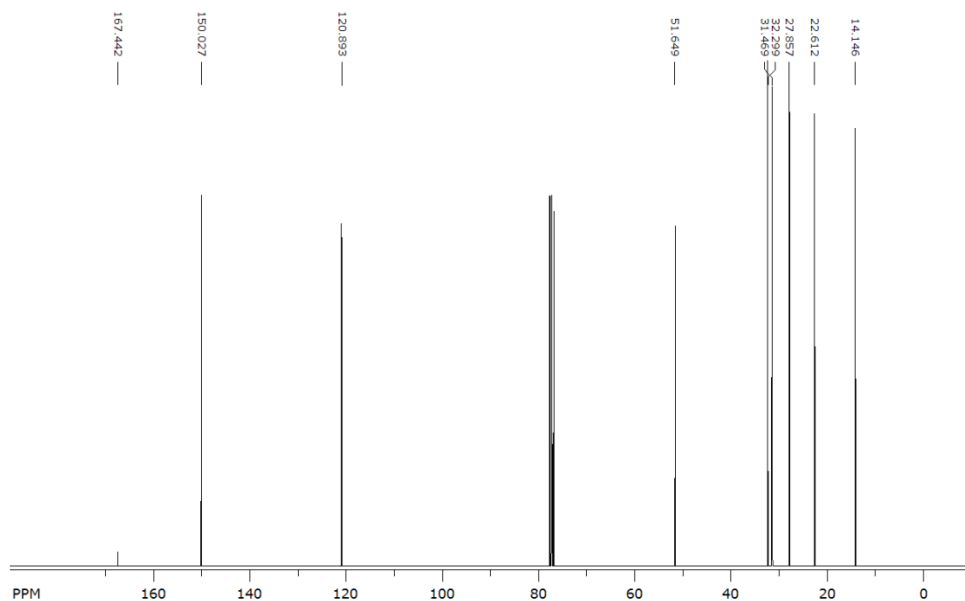
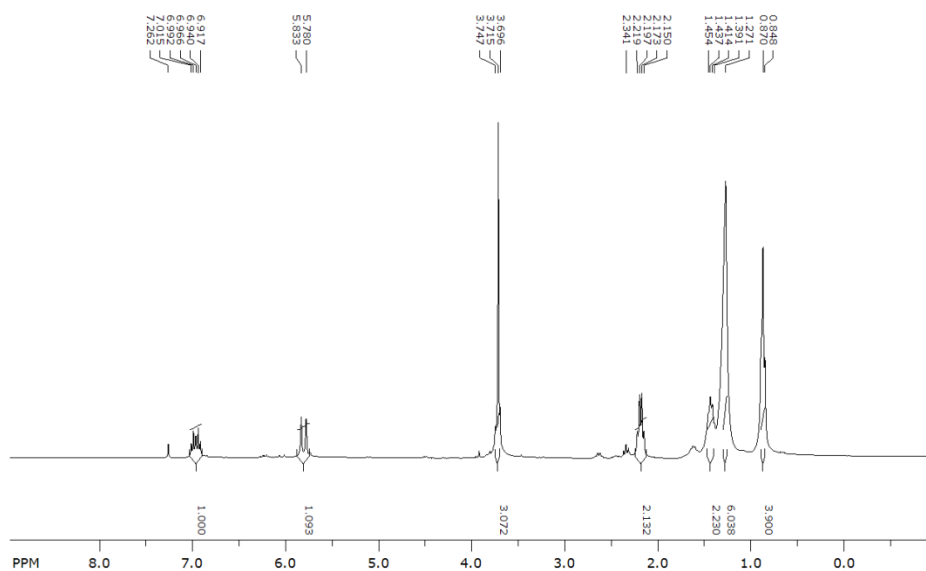


Figure S11. ¹³C spectrum (75 MHz, CDCl₃) of MtE-e



13C NMR spectrum of compound 1. The x-axis is labeled PPM and ranges from 0 to 160. The spectrum shows several sharp peaks. Key peaks are labeled with their chemical shifts: 167.512, 150.163, 120.991, 80.001, 51.618, 22.749, and 14.259. A small inset shows the chemical structure of compound 1, which is a substituted cyclohexane with a carboxylic acid group and a hydroxyl group.

S24

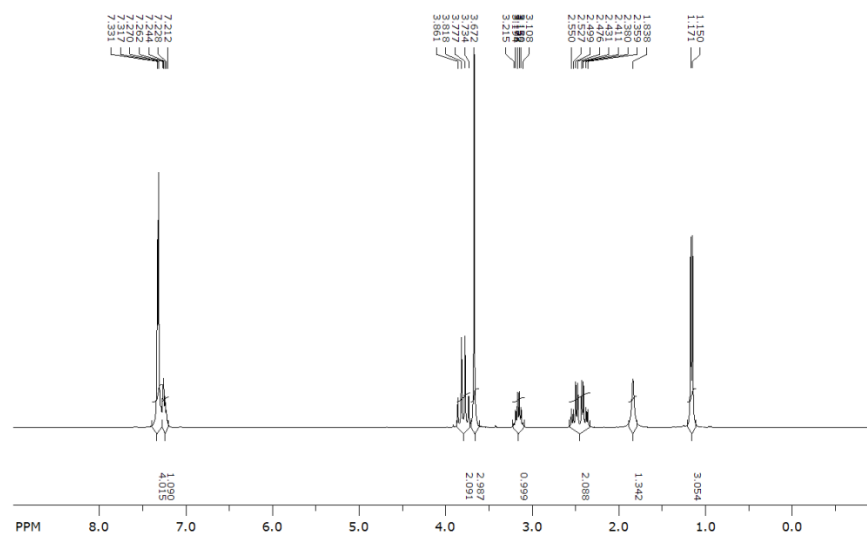
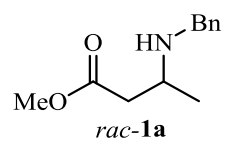


Figure S14. ^1H spectrum (300 MHz, CDCl_3) of *rac-1a*

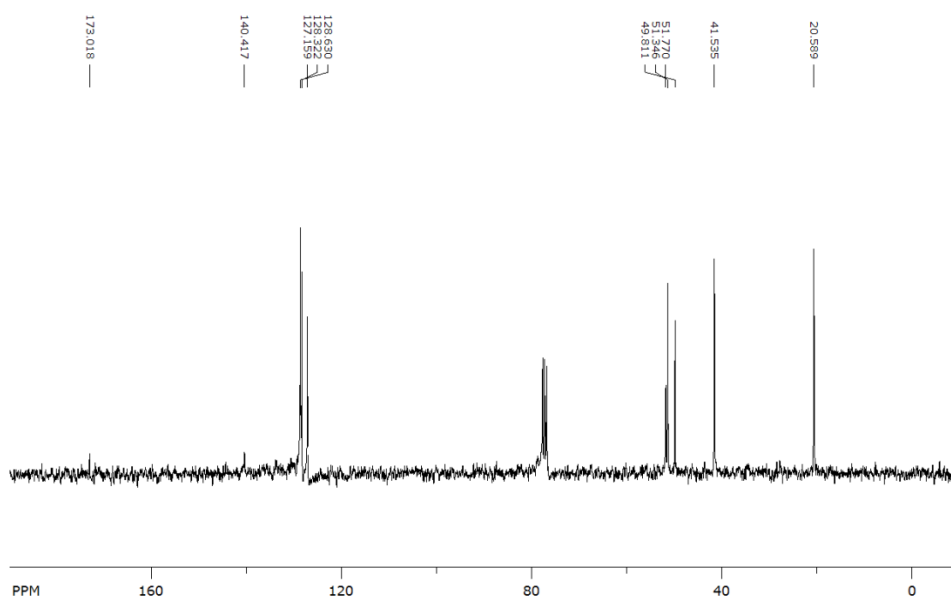


Figure S15. ^{13}C spectrum (75 MHz, CDCl_3) of *rac-1a*

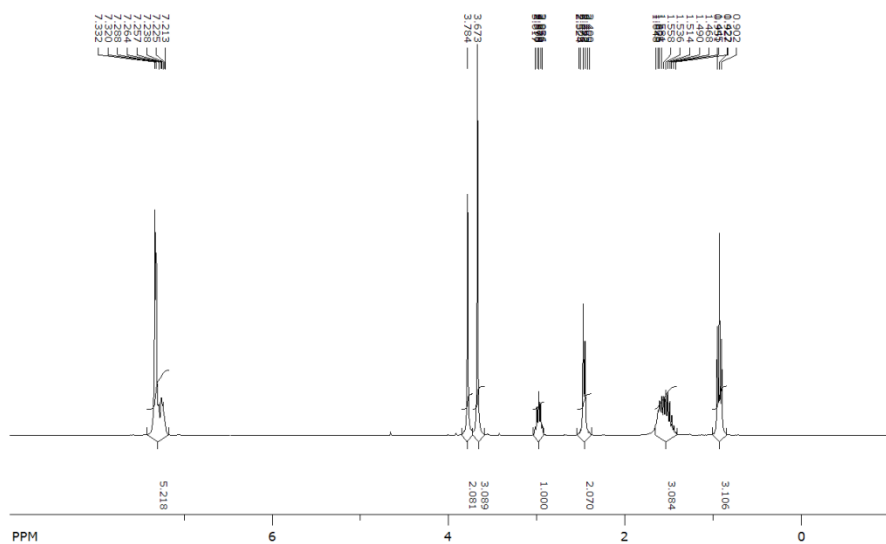
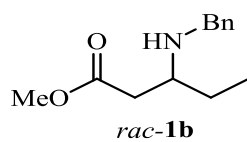


Figure S16. ¹H spectrum (300 MHz, CDCl₃) of *rac-1b*

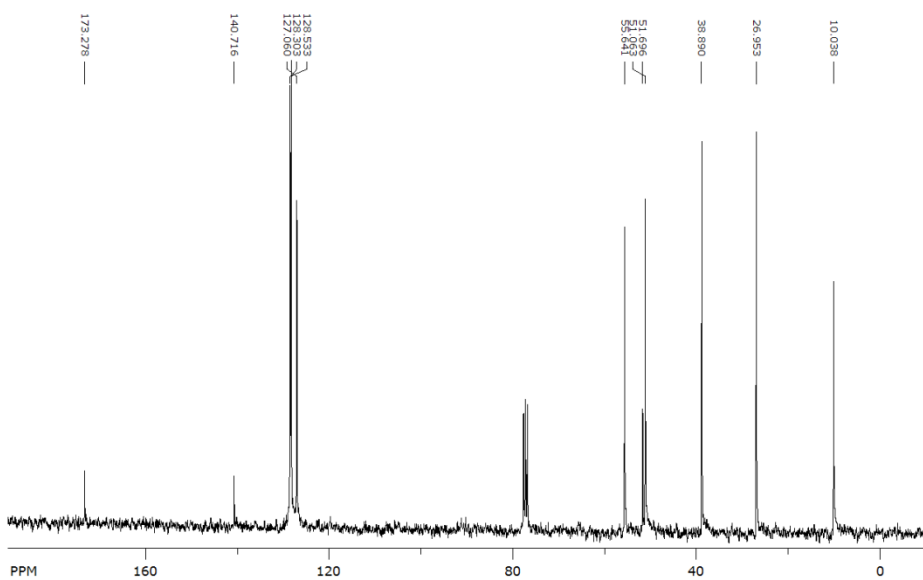
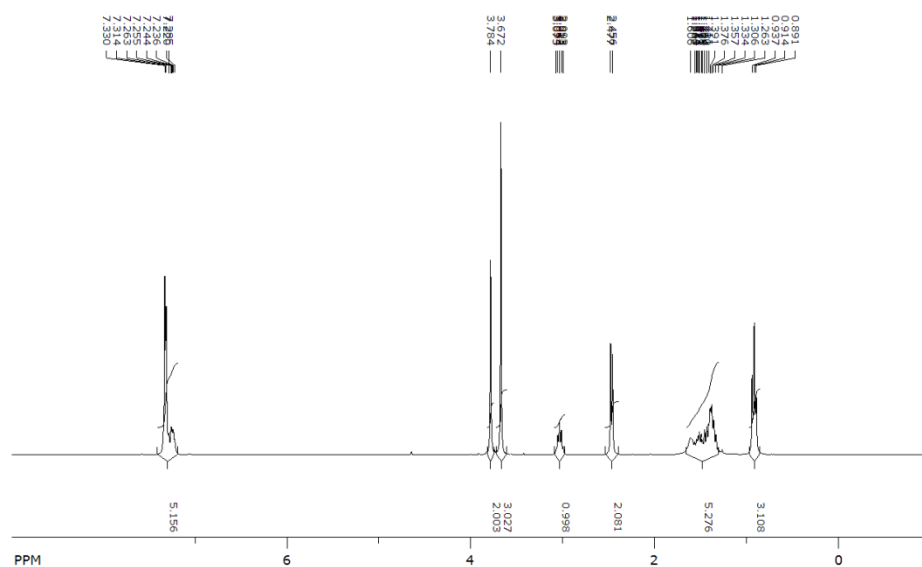


Figure S17. ¹³C spectrum (75 MHz, CDCl₃) of *rac-1b*



13C NMR spectrum (CDCl₃) of compound 1. The x-axis is labeled PPM and ranges from 0 to 180. The spectrum shows several sharp peaks. Key peaks are labeled with their chemical shifts: 179.221, 129.626, 128.295, 127.037, 84.172, 51.651, 39.255, 36.764, 19.101, and 14.318. There is a small peak at 40.719.

S27

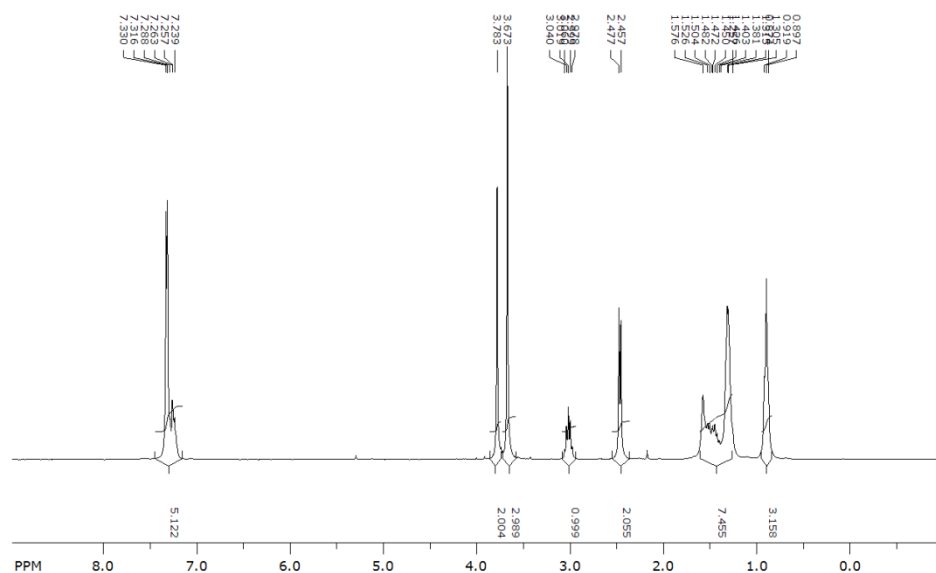
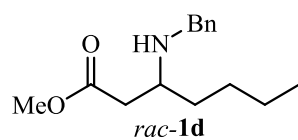


Figure S20. ^1H spectrum (300 MHz, CDCl_3) of *rac*-**1d**

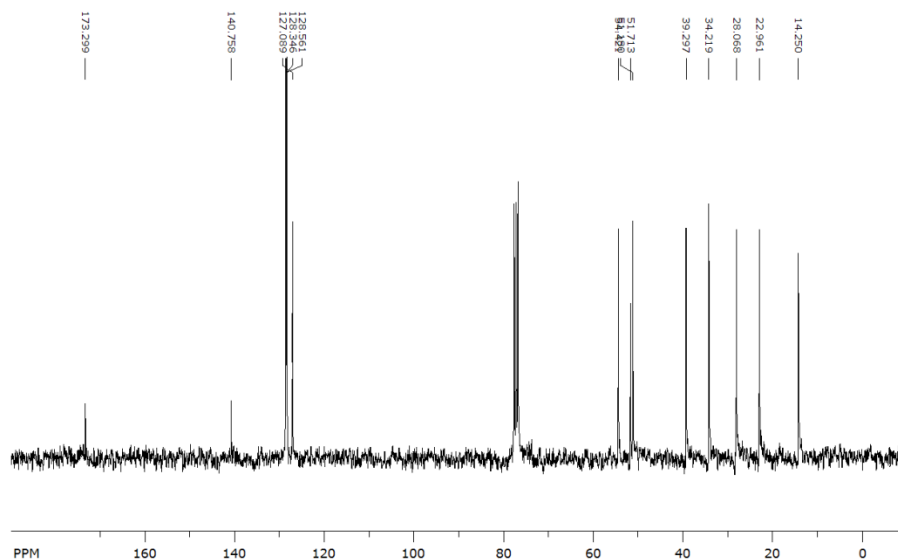
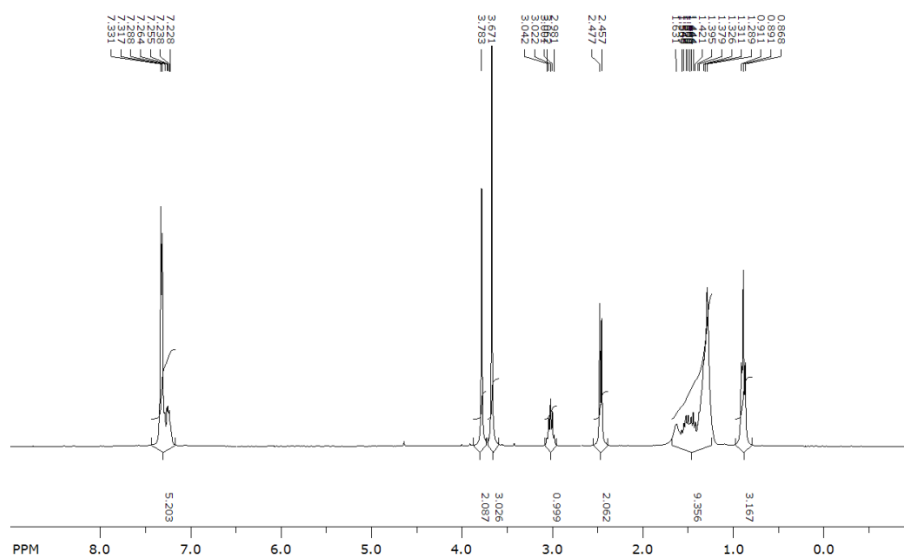


Figure S21. ^{13}C spectrum (75 MHz, CDCl_3) of *rac*-**1d**



13C NMR spectrum (CDCl₃) of compound 10. The x-axis represents chemical shift in PPM, ranging from 0 to 200. The spectrum shows several sharp peaks. Key peaks are labeled with their chemical shift values: 14.276, 22.791, 26.631, 27.540, 29.440, 34.504, 39.275, 51.156, 51.681, 54.402, 72.810, 73.110, 77.658, 120.054, 120.534, 120.534, 140.732, and 173.260. The peak at 77.658 ppm is the solvent peak for CDCl₃.

S29

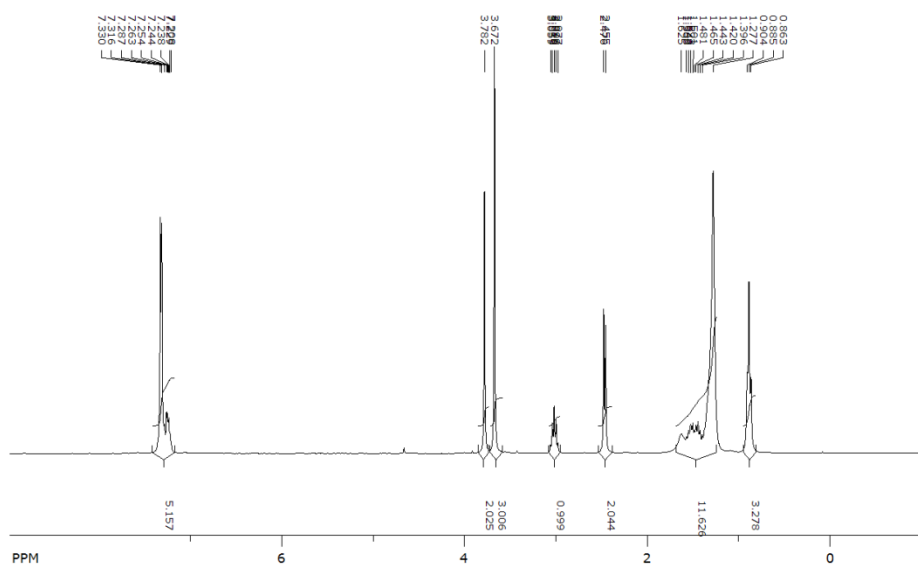
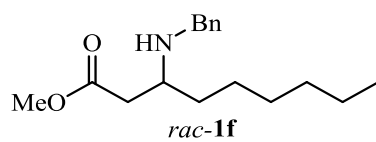


Figure S24. ¹H spectrum (300 MHz, CDCl₃) of *rac-1f*

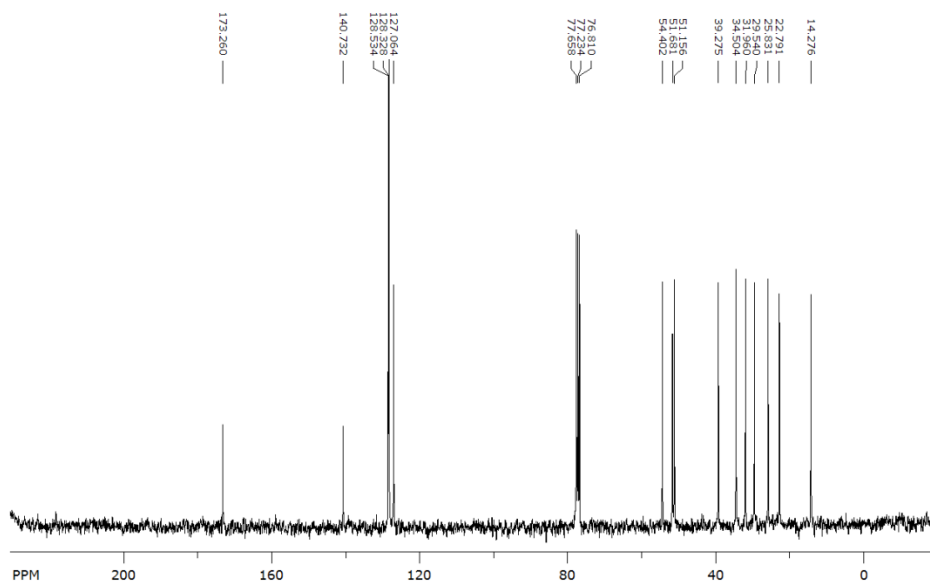


Figure S25. ¹³C spectrum (75 MHz, CDCl₃) of *rac-1f*

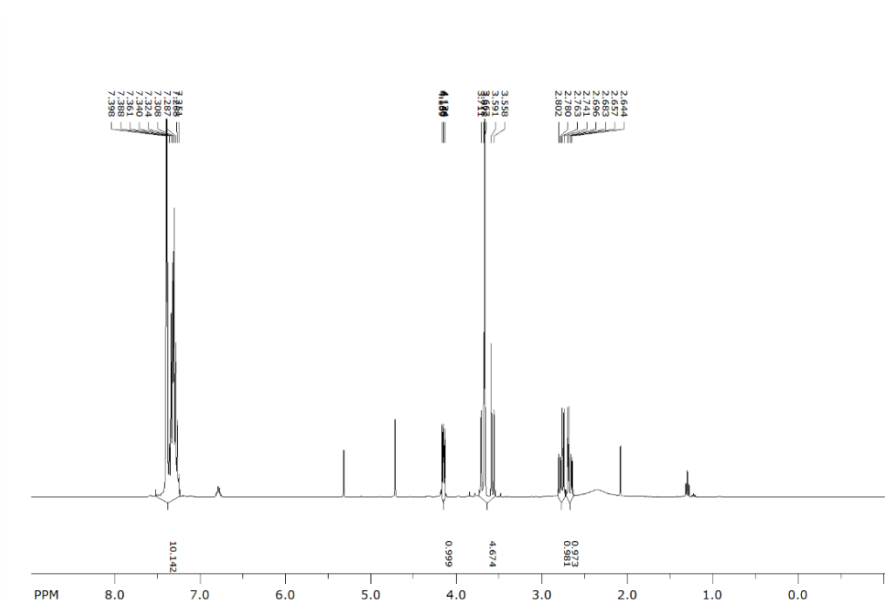
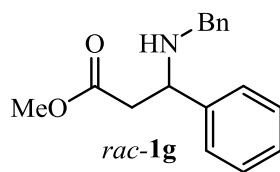


Figure S26. ^1H spectrum (300 MHz, CDCl_3) of *rac*-**1g**.

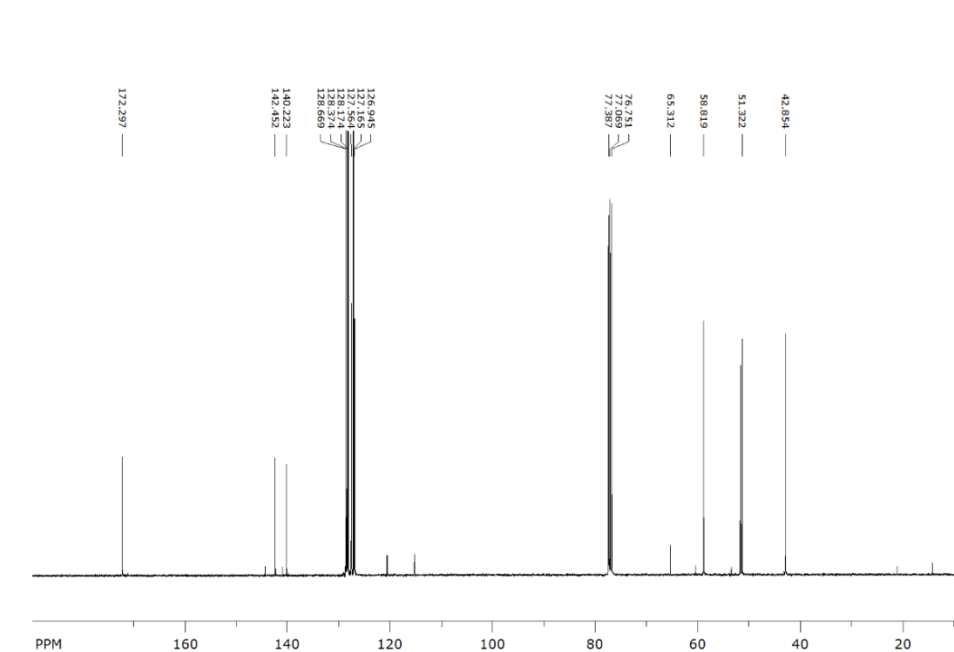
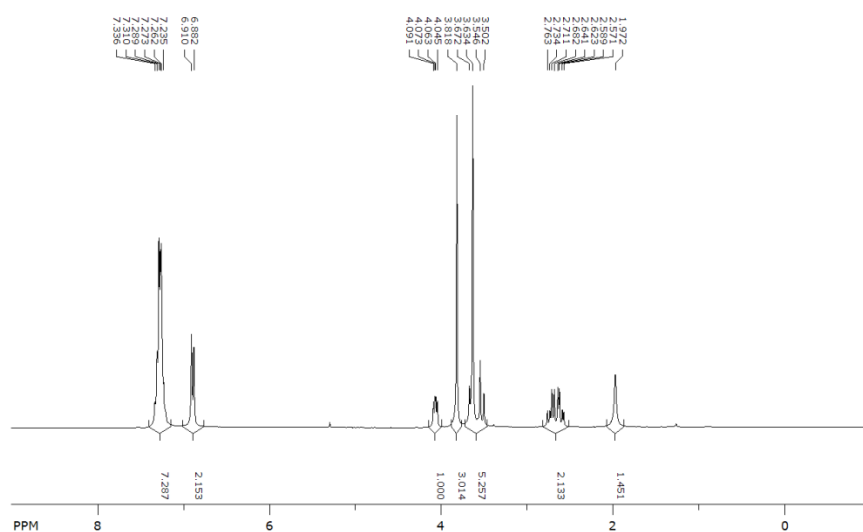
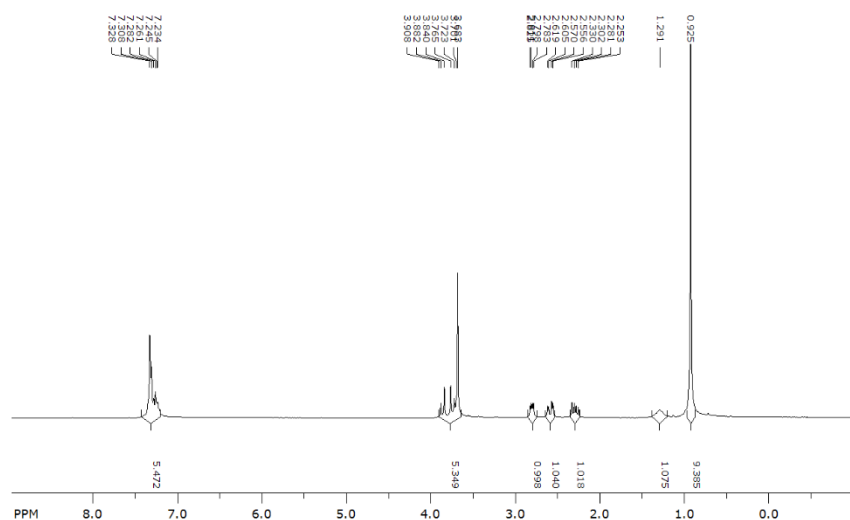


Figure S27. ^{13}C spectrum (75 MHz, CDCl_3) of *rac*-**1g**.



¹³C NMR spectrum (CDCl₃) of compound 1. The x-axis represents chemical shift in PPM, ranging from 0 to 180. The spectrum shows several sharp peaks. Key peaks are labeled with their chemical shift values: 172.601, 159.099, 134.644, 40.456, 128.529, 127.072, 114.139, 59.290, 58.419, 51.830, 43.152, and 34.119. A small peak is also visible at approximately 178 ppm.

S32



13C NMR spectrum of compound 1. The x-axis is labeled 'PPM' and ranges from 0 to 180. The spectrum shows several sharp peaks. Key peaks are labeled with their chemical shifts: 26.799, 37.076, 38.695, 51.844, 54.394, 64.185, 129.449, 129.469, 141.245, and 174.320. The peak at 174.320 is the most intense, followed by the peak at 129.449. The peak at 26.799 is also prominent.

S33

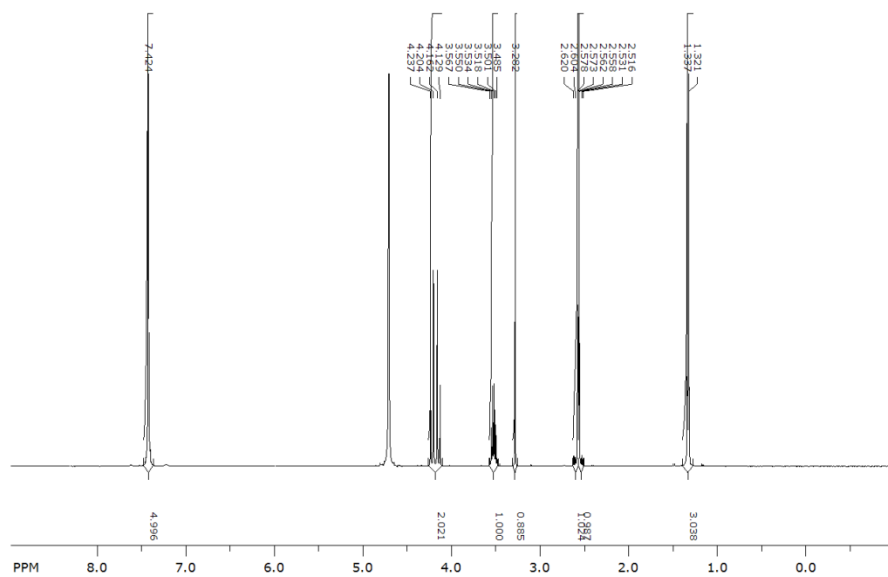
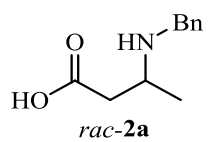


Figure S32. ¹H spectrum (400 MHz, D₂O) of **2a**

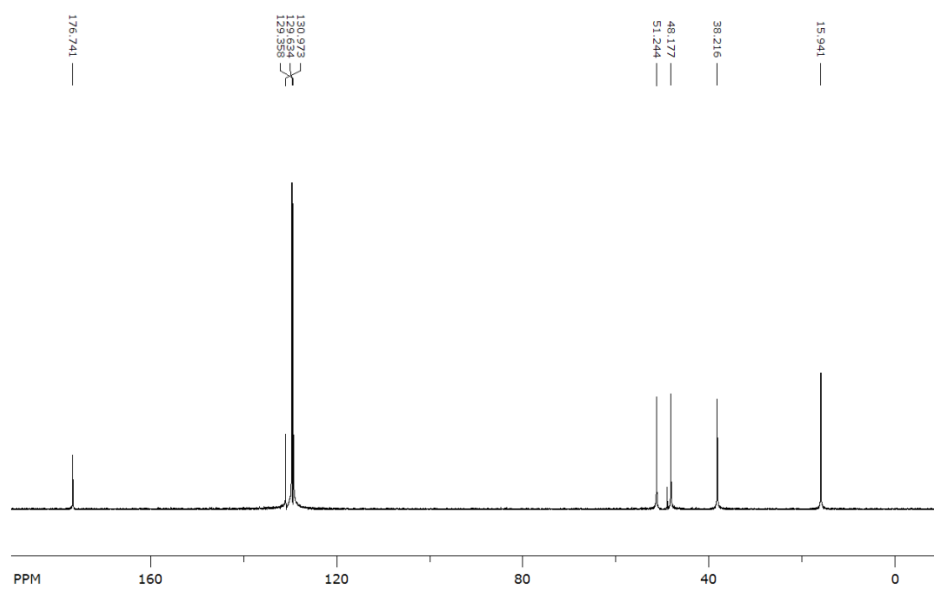


Figure S33. ¹³C spectrum (100 MHz, D₂O) of **2a**

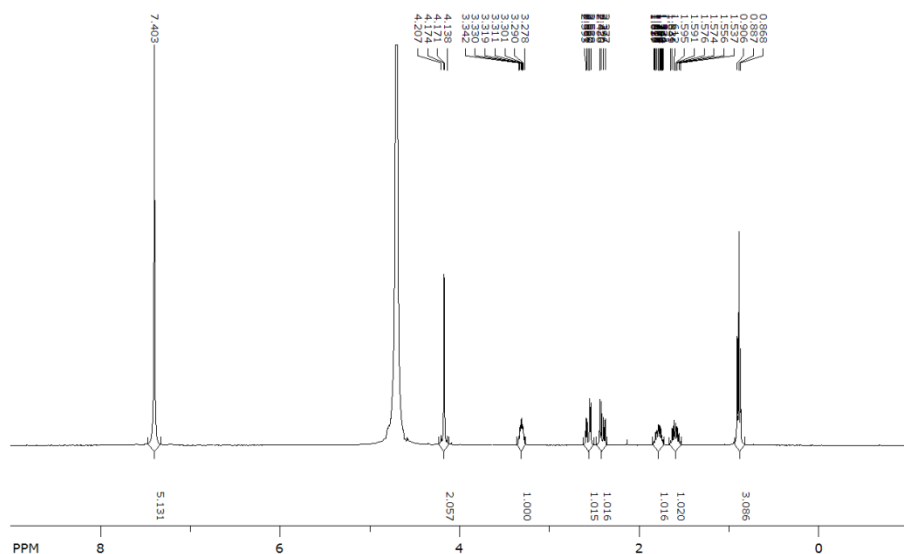
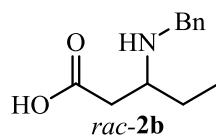


Figure S34. ^{13}C spectrum (400 MHz, D_2O) of **2b**

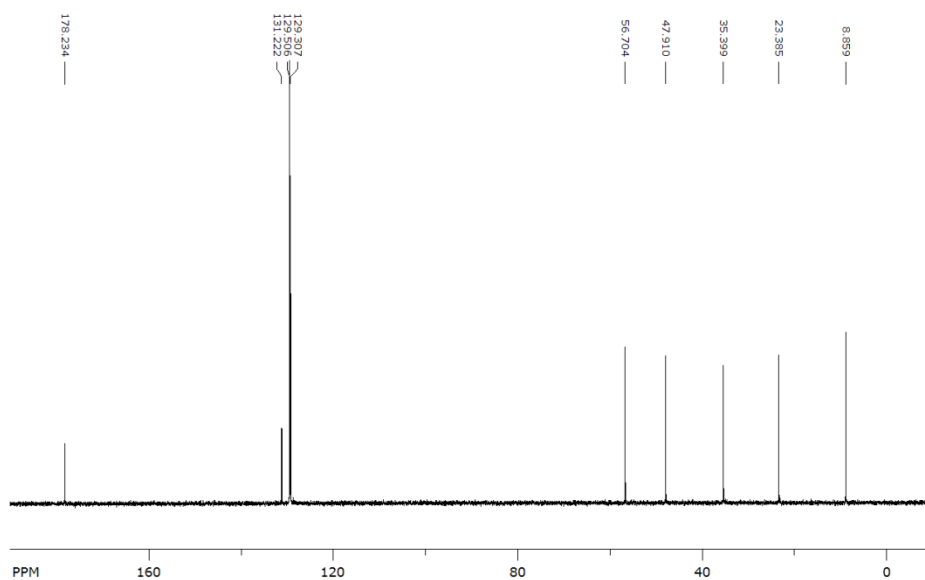


Figure S35. ^{13}C spectrum (100 MHz, D_2O) of **2b**

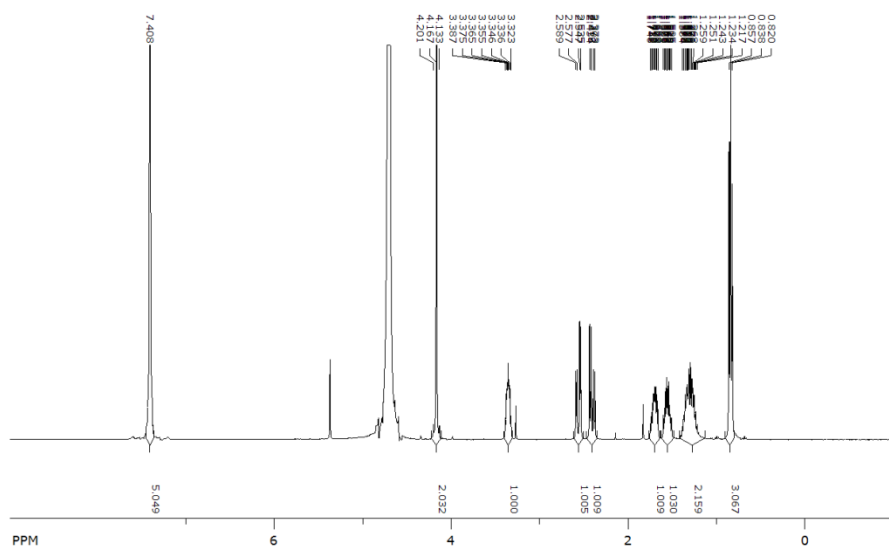
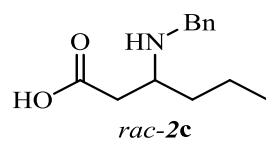


Figure S36. ¹H spectrum (400 MHz, D₂O) of **2c**

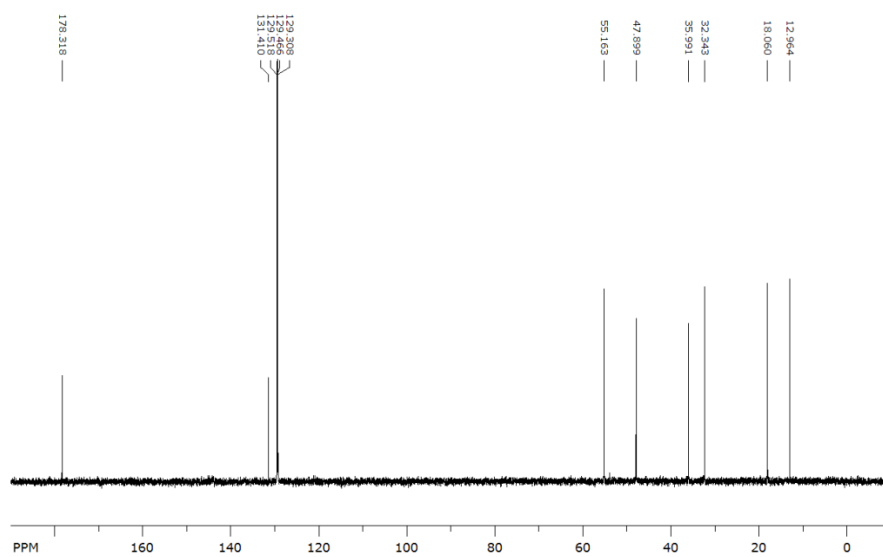


Figure S37. ¹³C spectrum (100 MHz, D₂O) of **2c**

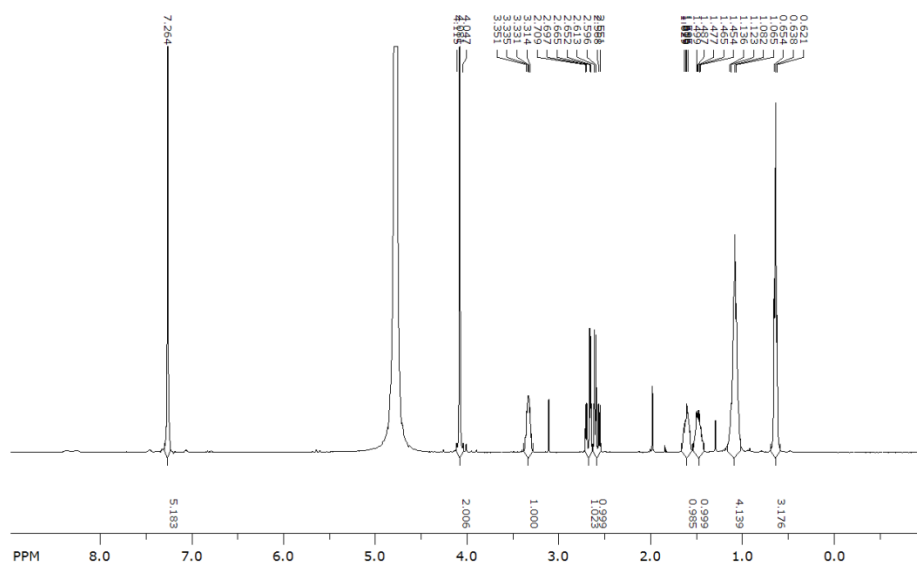
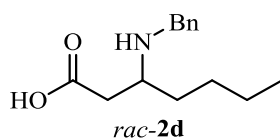


Figure S38. ¹H spectrum (400 MHz, D₂O) of **2d**

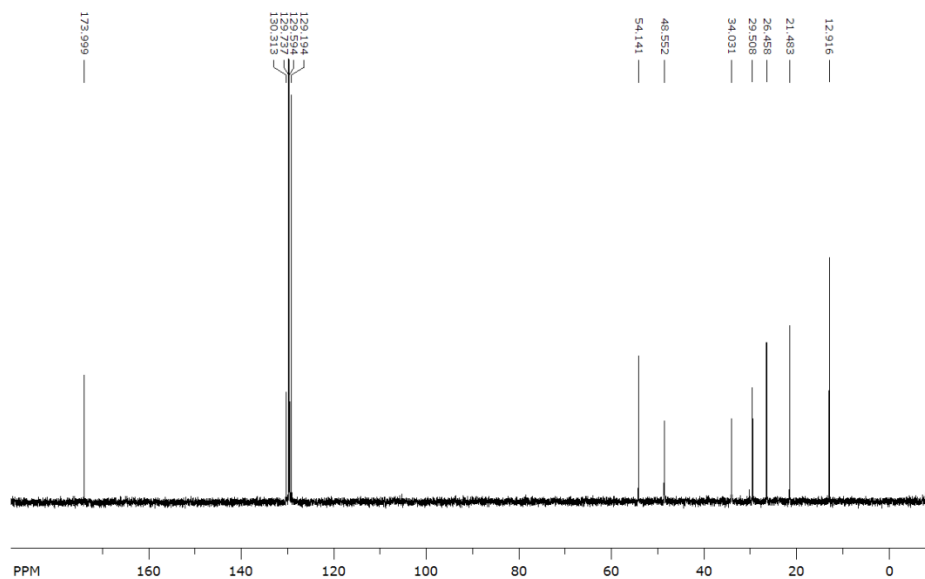


Figure S39. ¹³C spectrum (100 MHz, D₂O) of **2d**

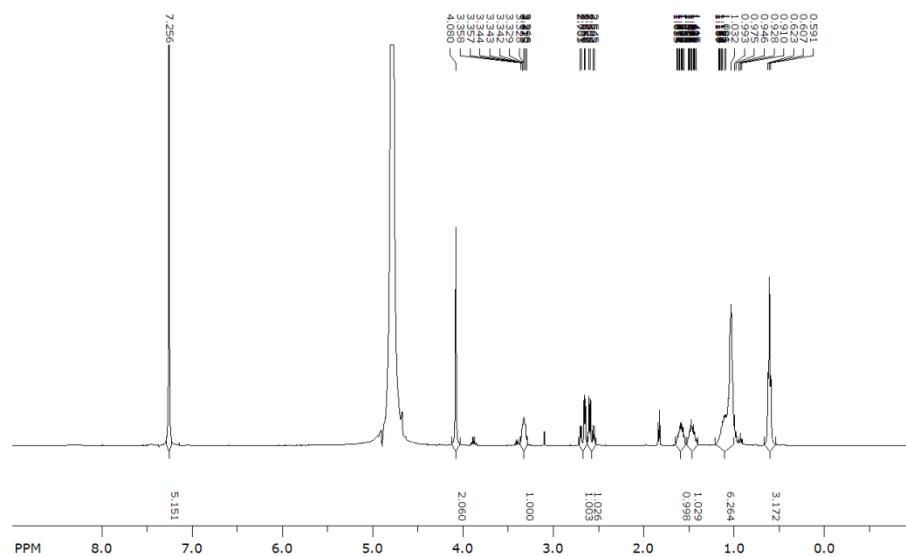
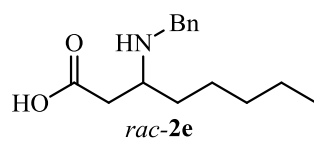


Figure S40. ¹H spectrum (400 MHz, D₂O) of **2e**

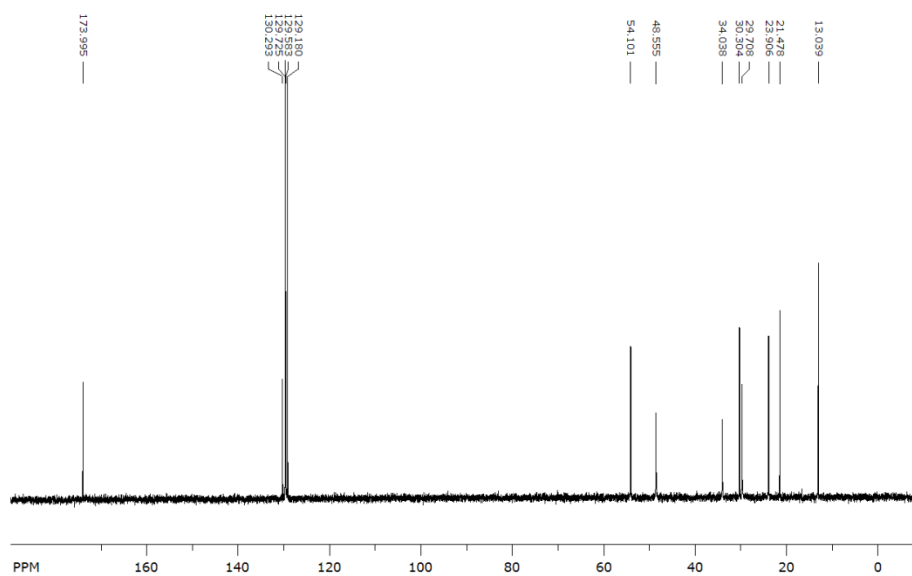


Figure S41. ¹³C spectrum (100 MHz, D₂O) of **2e**

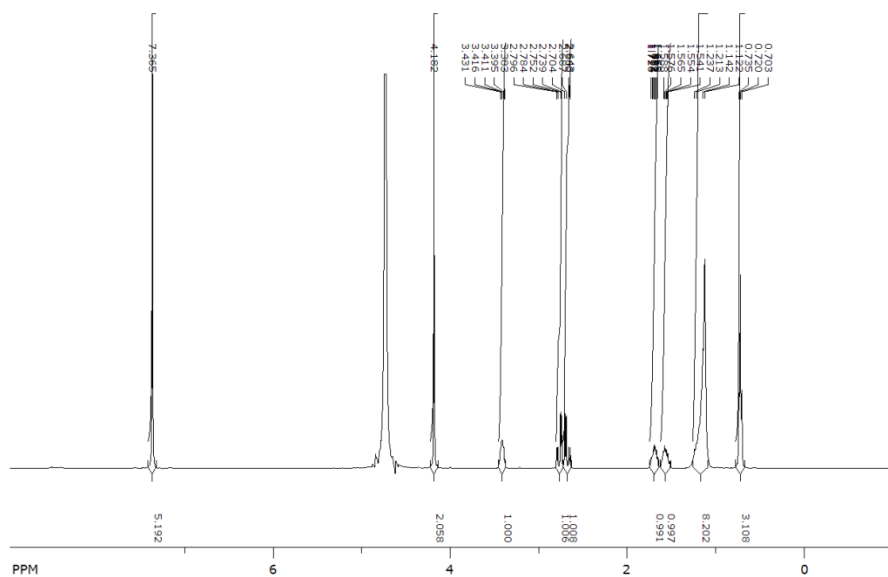
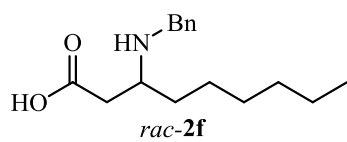


Figure S42. ^1H spectrum (400 MHz, D_2O) of **2f**

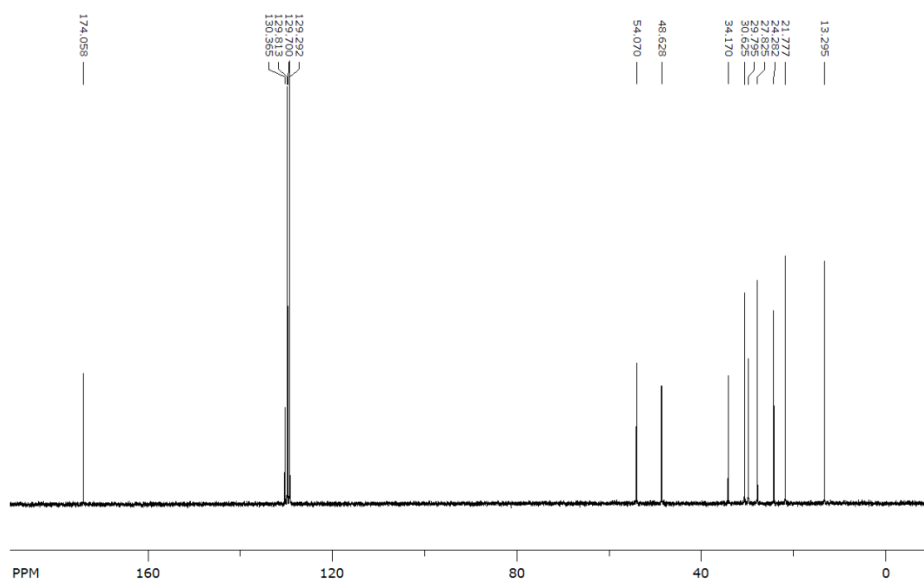


Figure S43. ^{13}C spectrum (100 MHz, D_2O) of **2f**

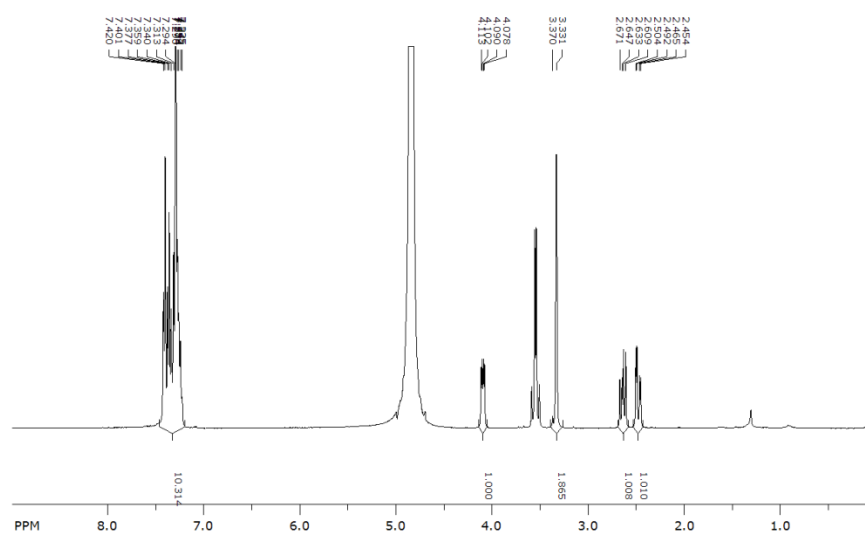
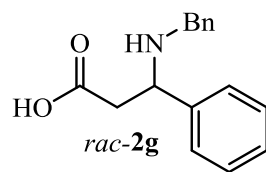


Figure S44. ^1H spectrum (400 MHz, CD_3OD) of **2g**

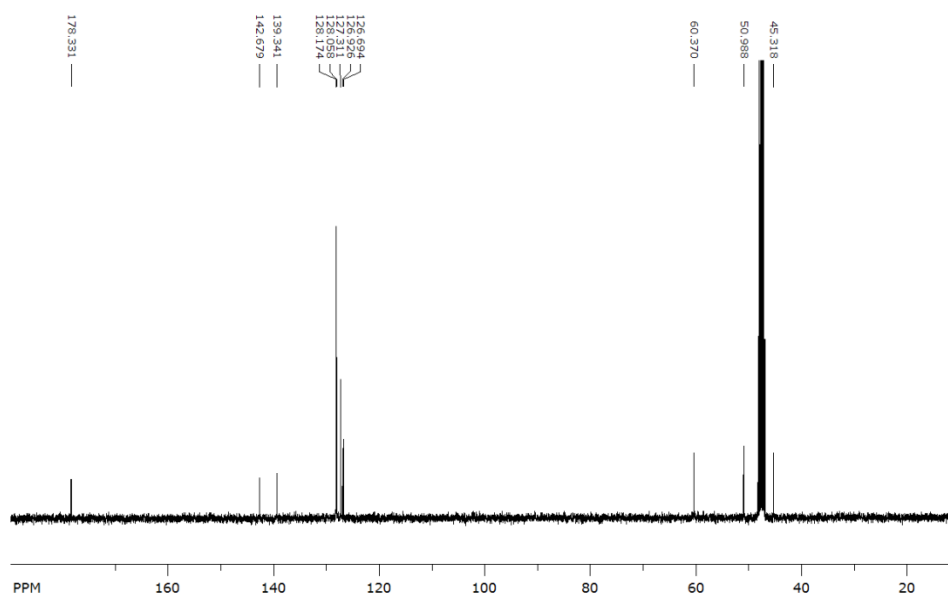


Figure S45. ^{13}C spectrum (100 MHz, CD_3OD) of **2g**

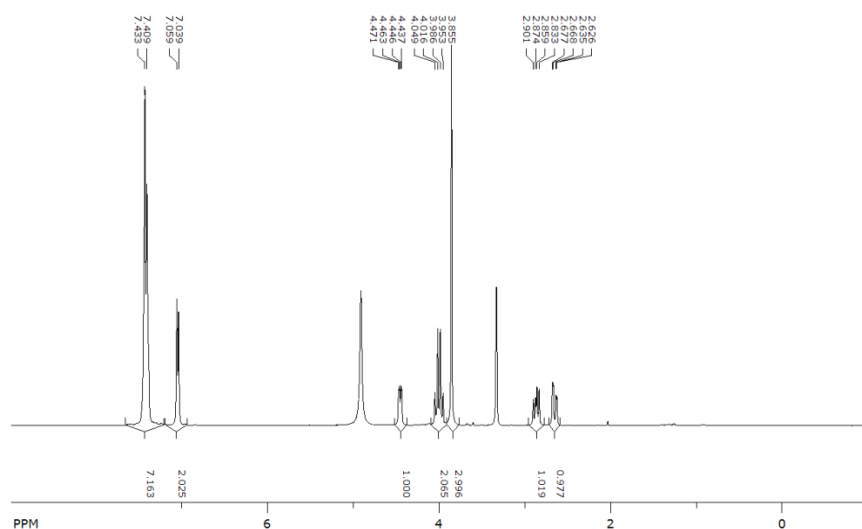
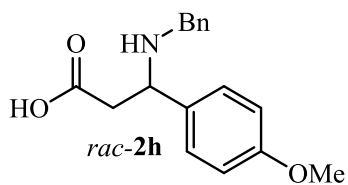


Figure S46. ¹H spectrum (400 MHz, CD₃OD) of *2h*

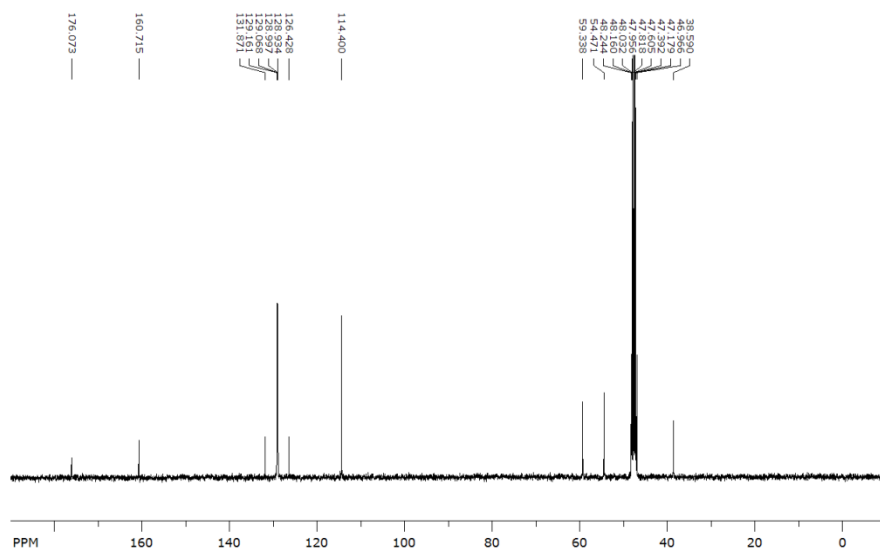


Figure S47. ¹³C spectrum (100 MHz, CD₃OD) of *2h*

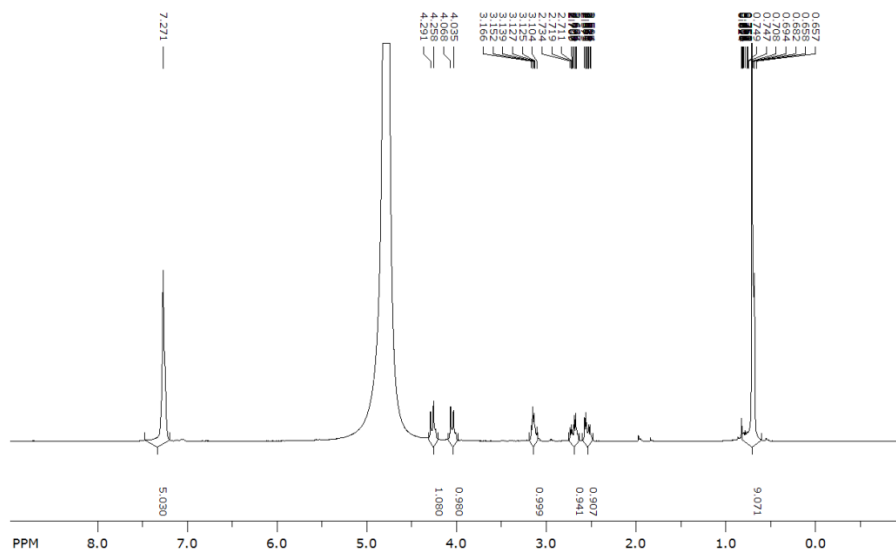
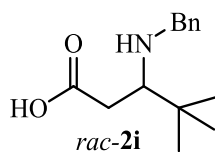


Figure S48. ^1H spectrum (400 MHz, D_2O) of **2i**

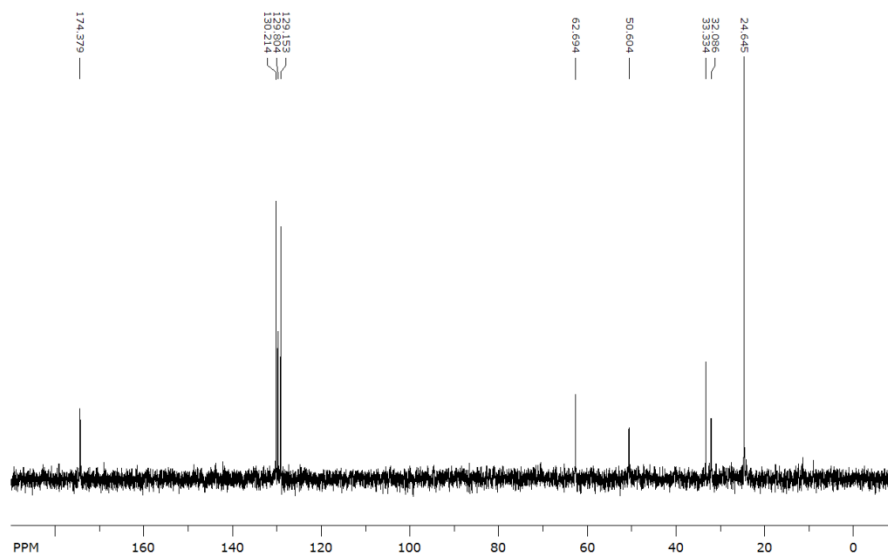
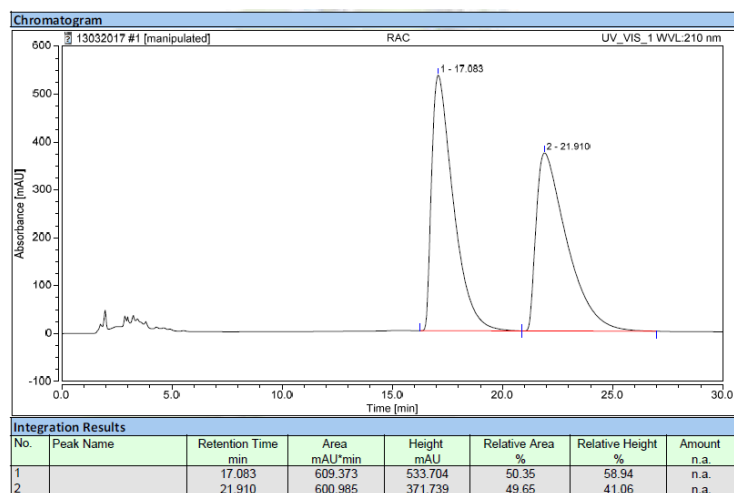
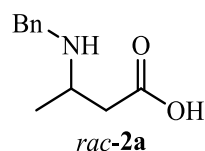
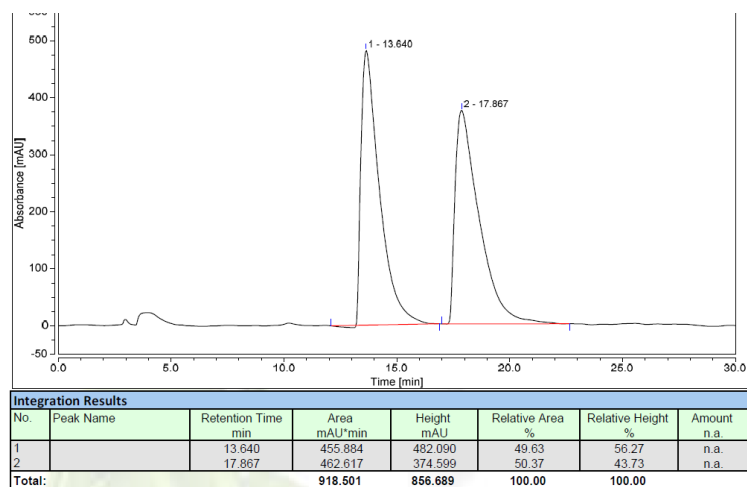
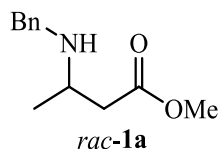


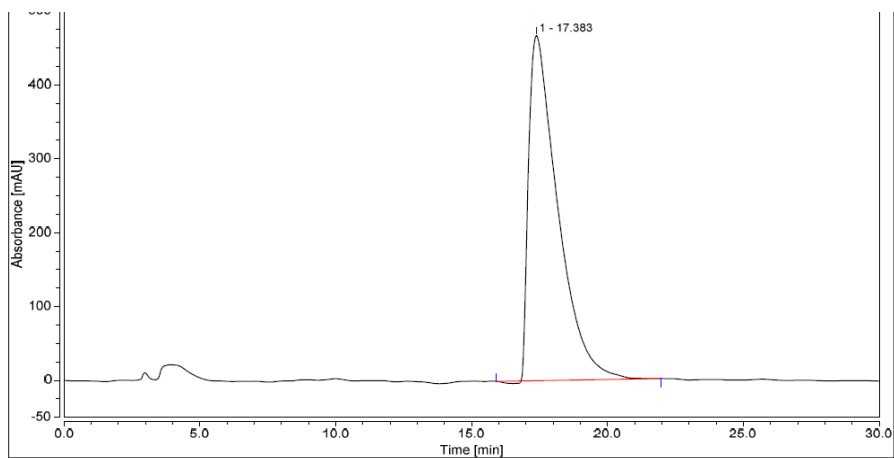
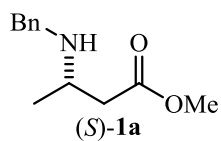
Figure S49. ^{13}C spectrum (100 MHz, D_2O) of **2i**

6) Chromatograms for the determination of enantiomeric excess of raw material and hydrolysis products.

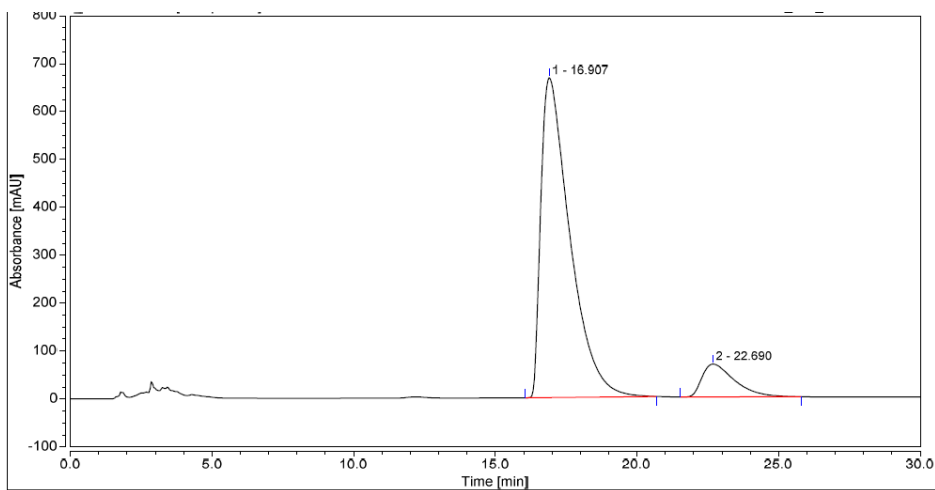
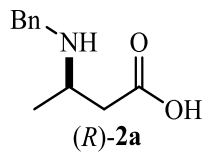
- Chromatograms for the search of best conditions for the enzymatic hydrolysis resolution under HSBM (Table S1).



For entry 1.

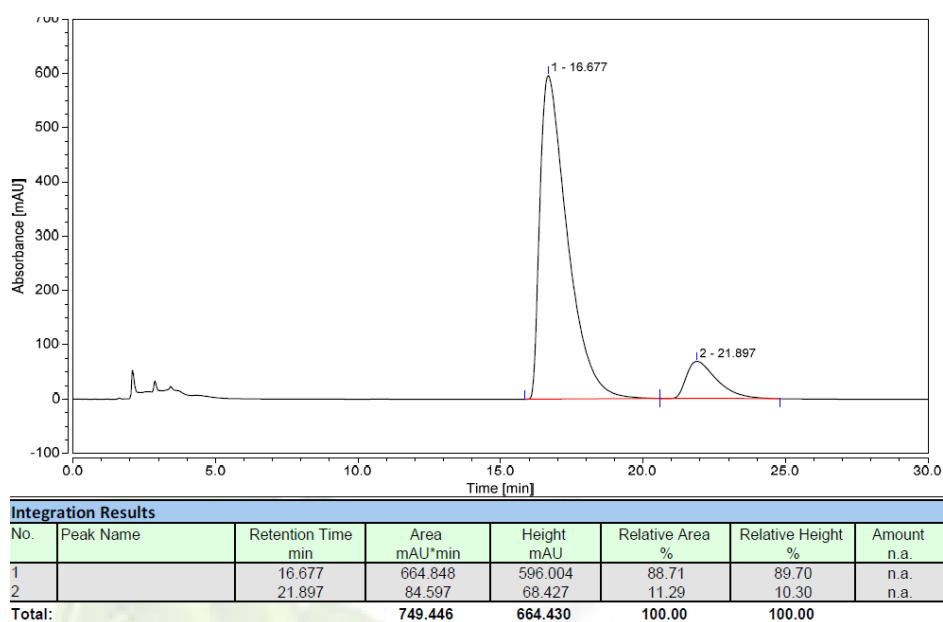
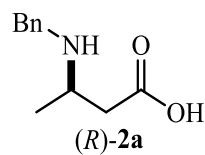
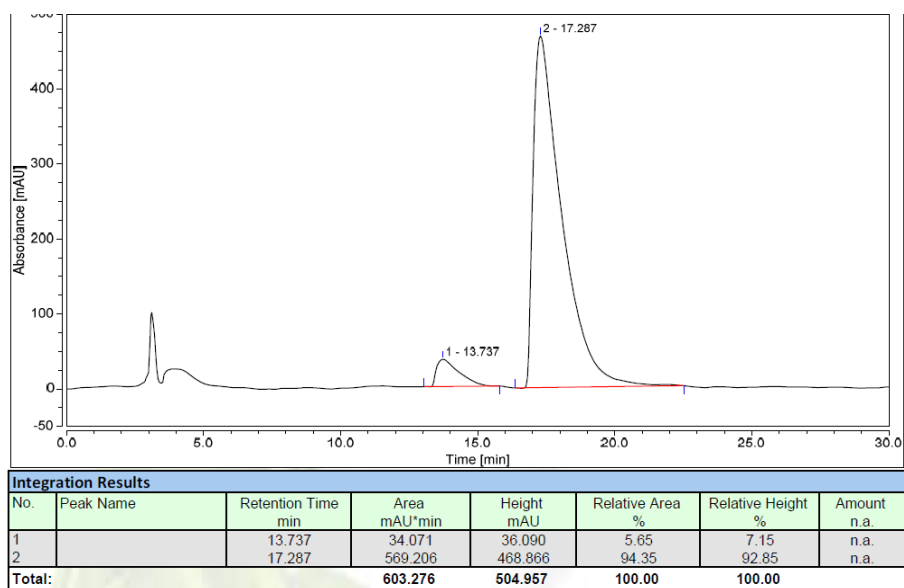
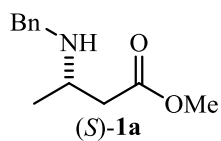


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.383	579.249	467.640	100.00	100.00	n.a.
Total:			579.249	467.640	100.00	100.00	

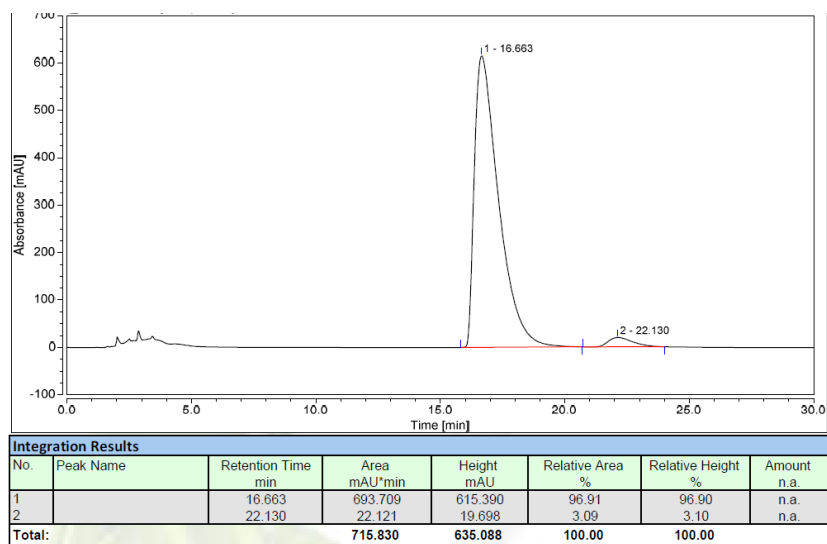
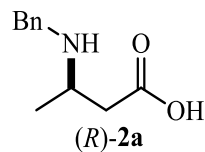
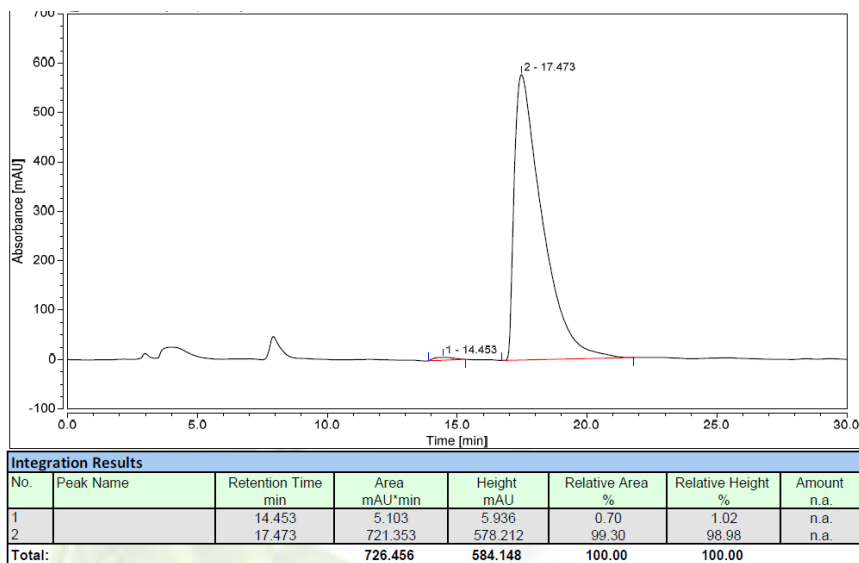
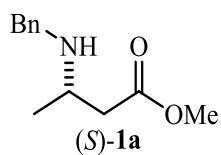


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.907	792.244	668.044	89.68	90.67	n.a.
2		22.690	91.200	68.721	10.32	9.33	n.a.
Total:			883.444	736.764	100.00	100.00	

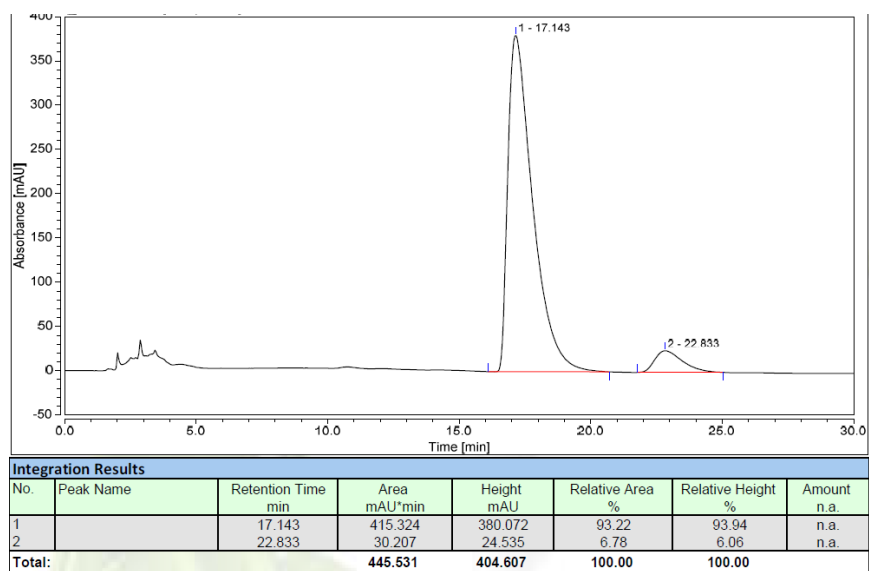
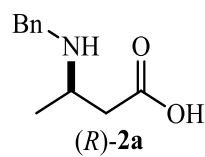
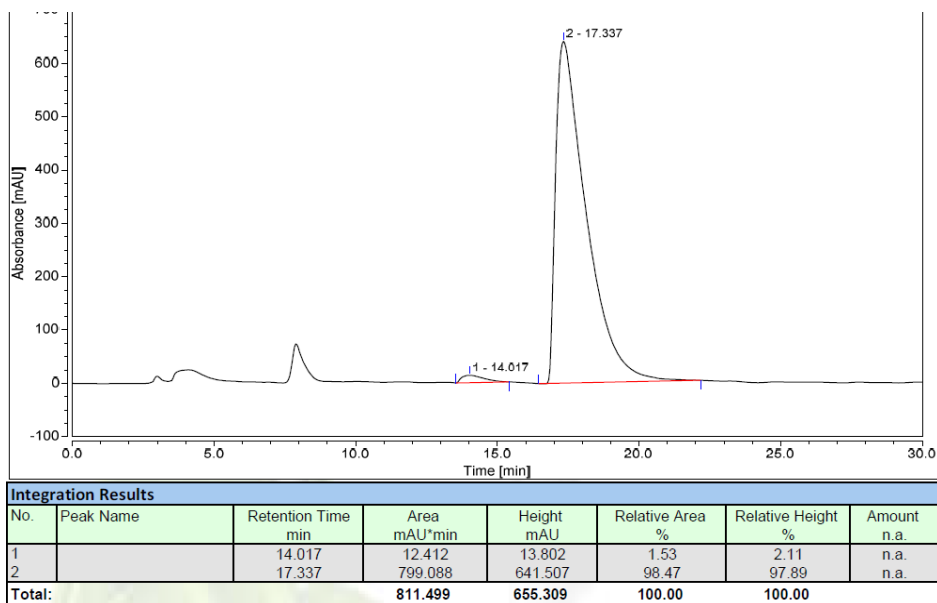
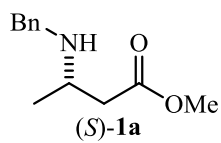
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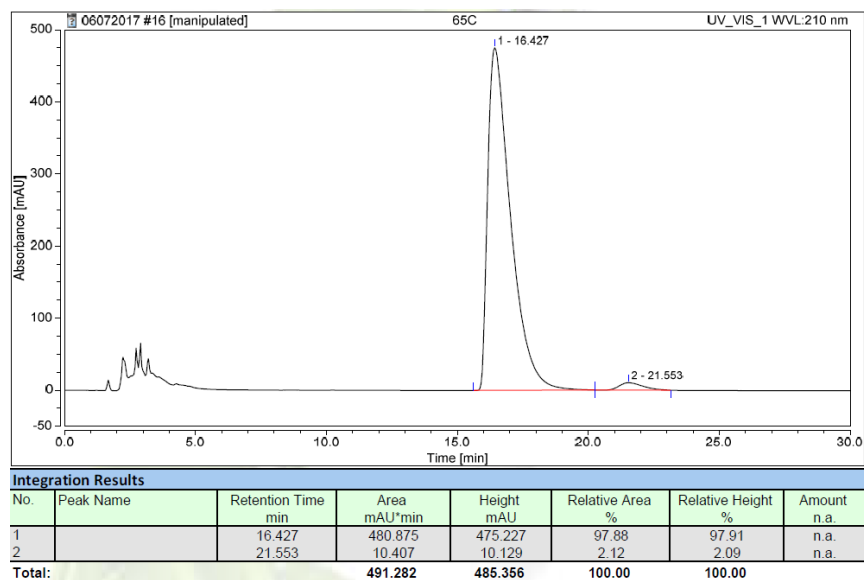
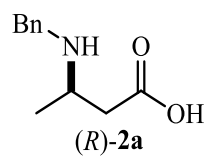
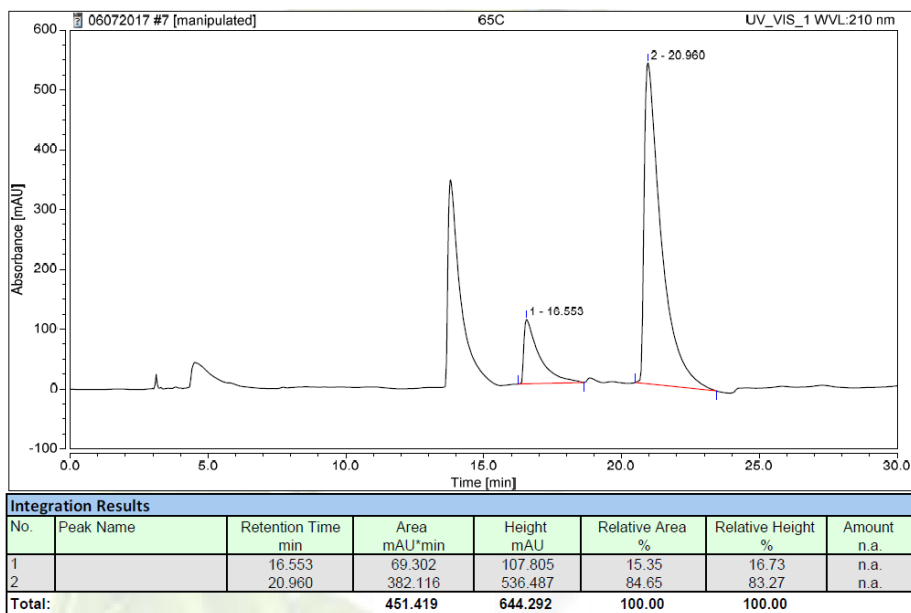
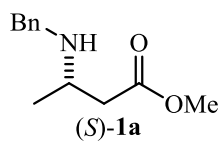
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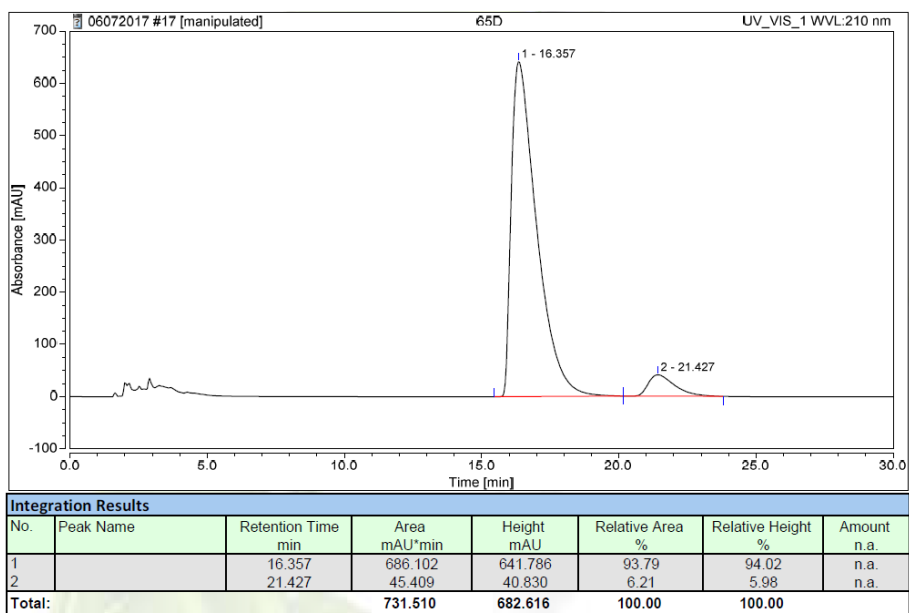
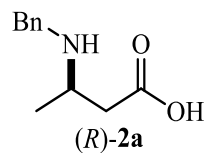
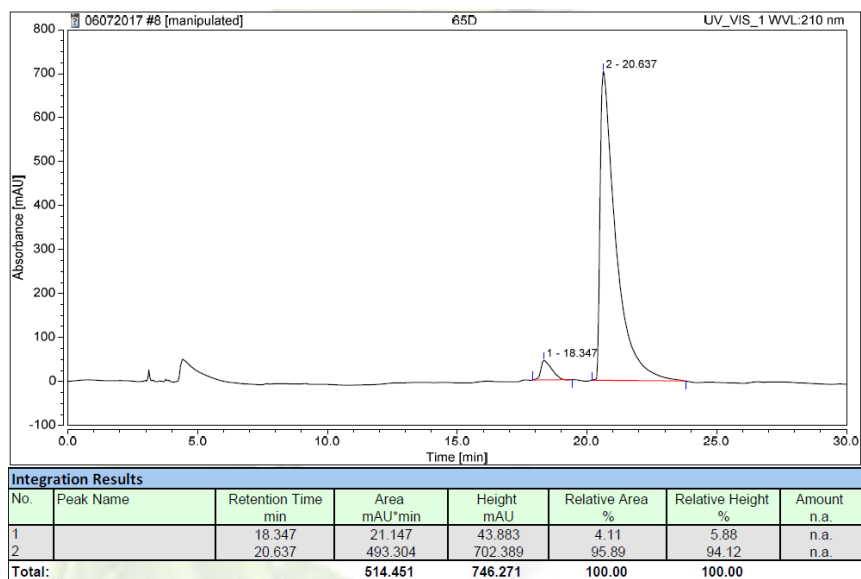
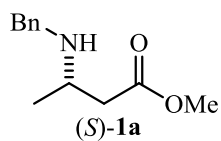
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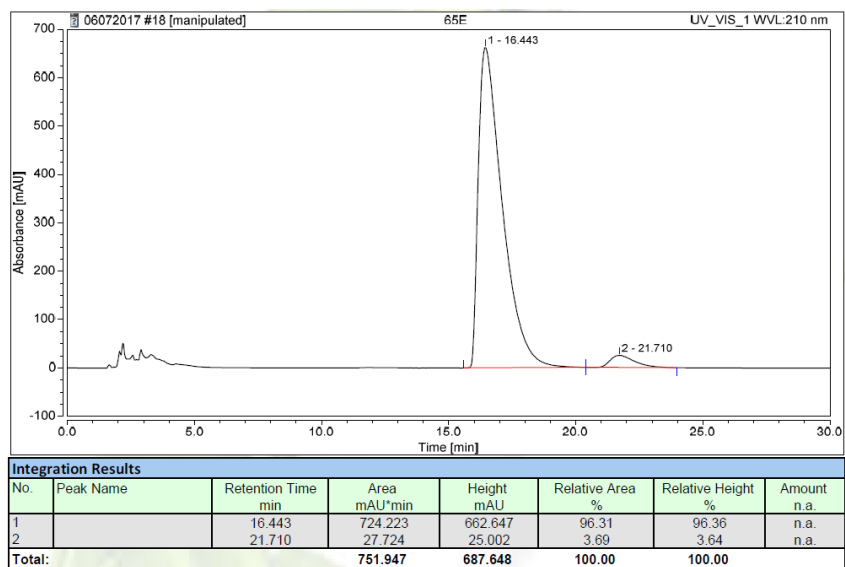
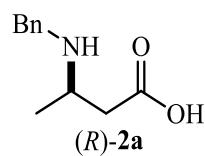
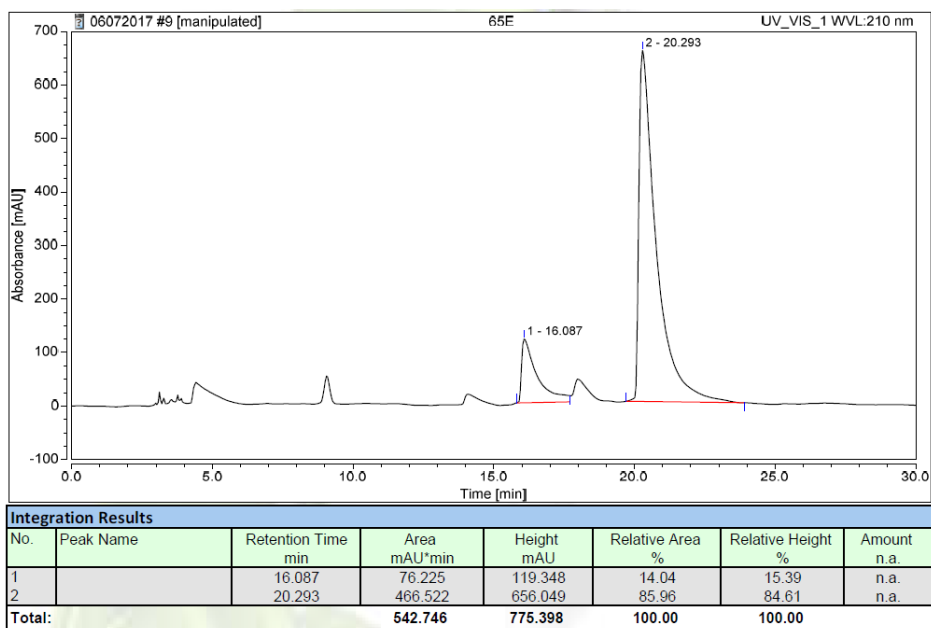
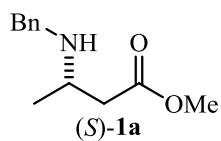
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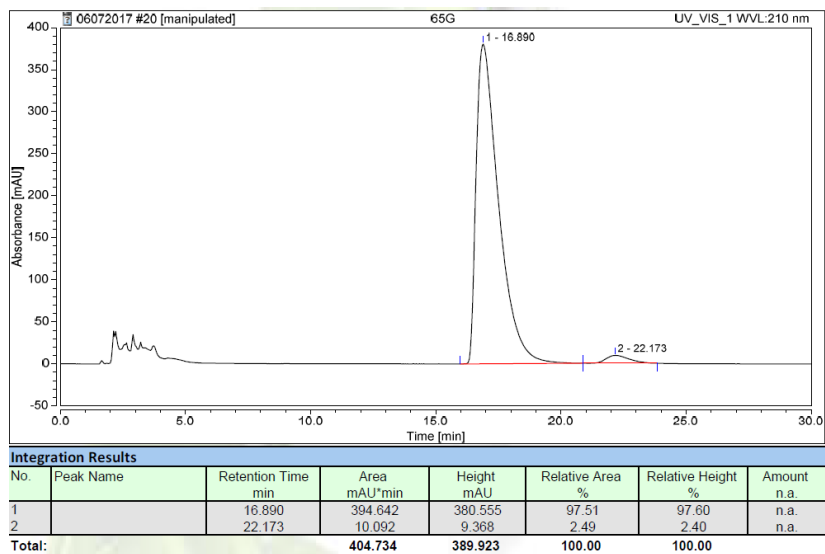
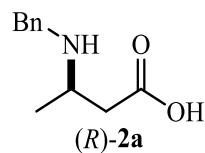
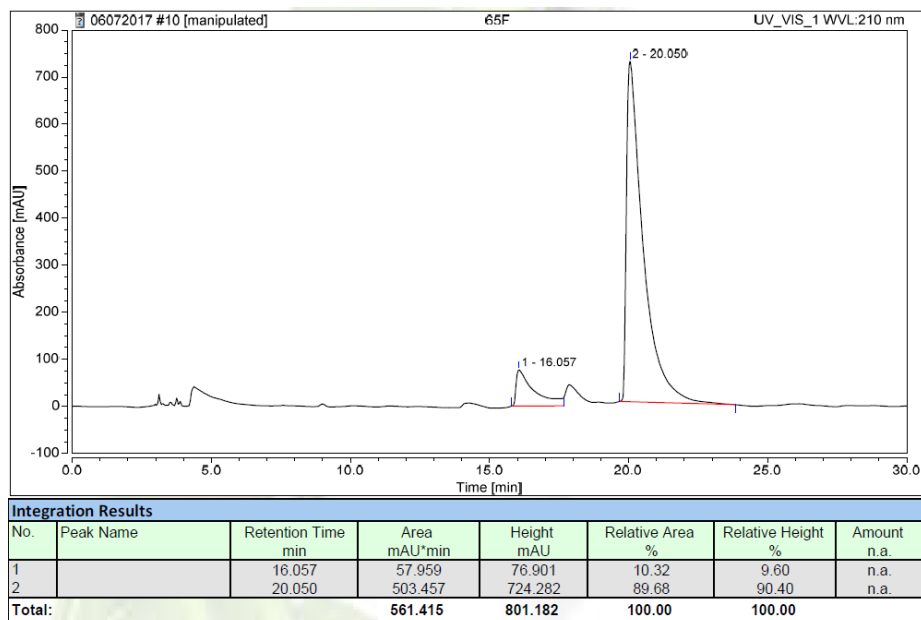
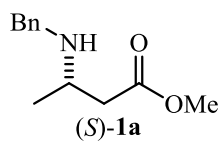
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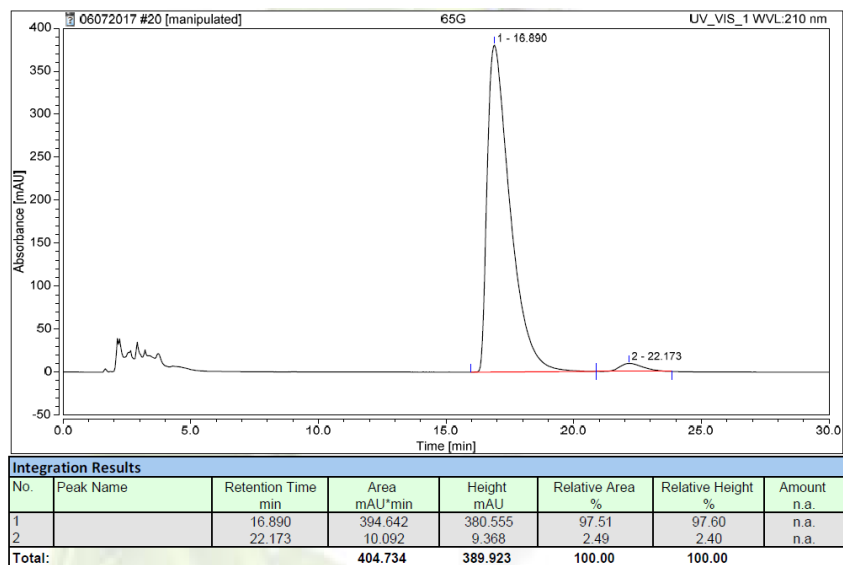
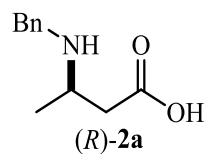
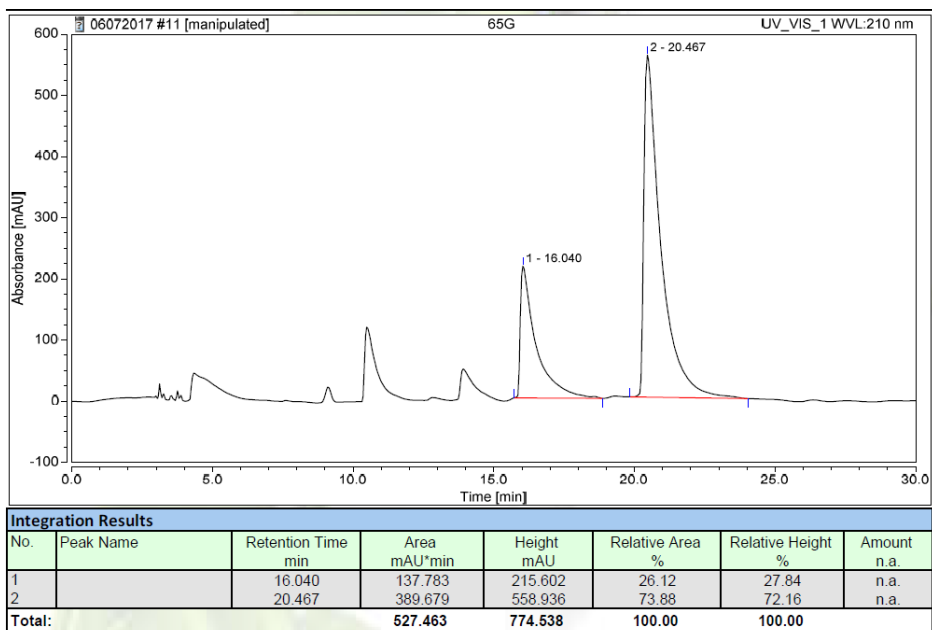
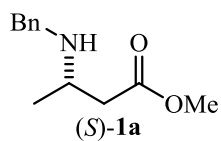
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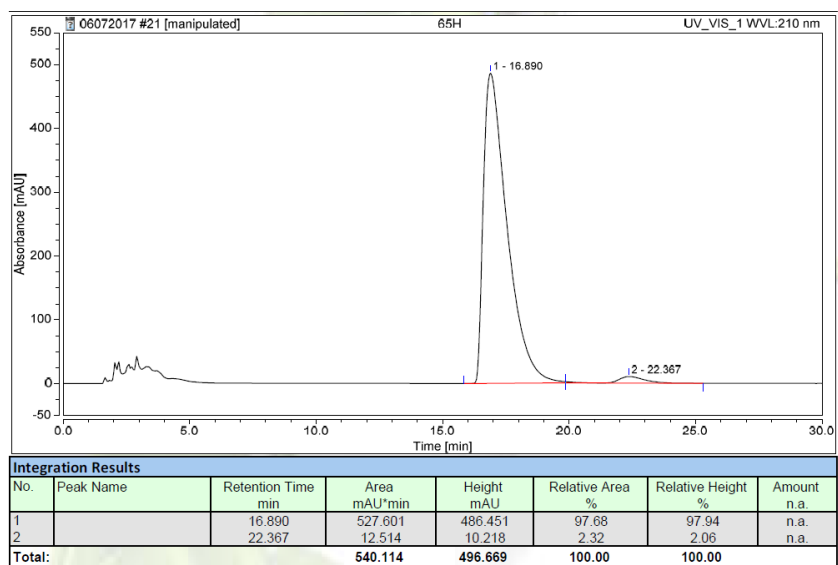
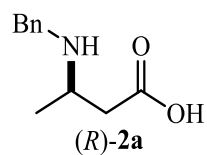
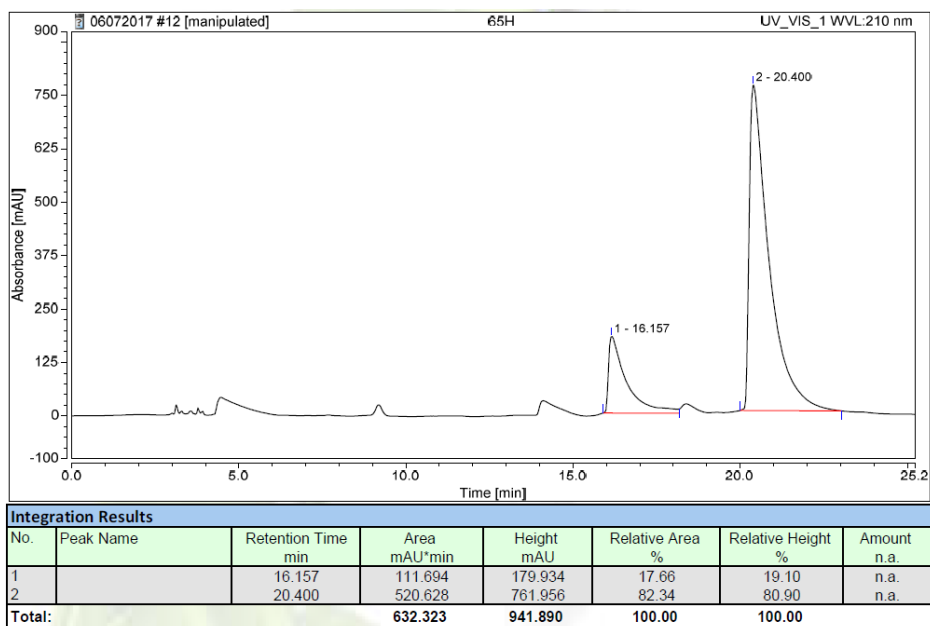
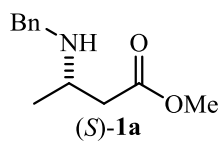
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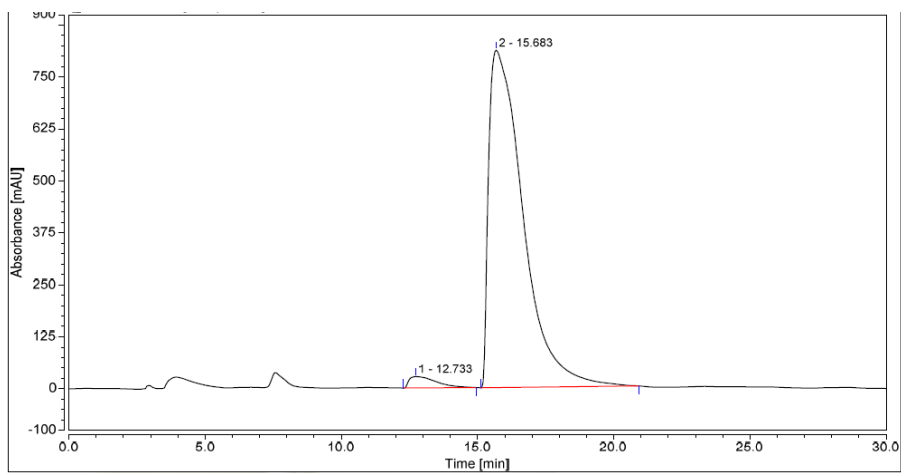
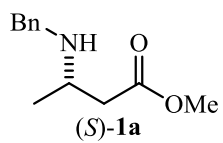
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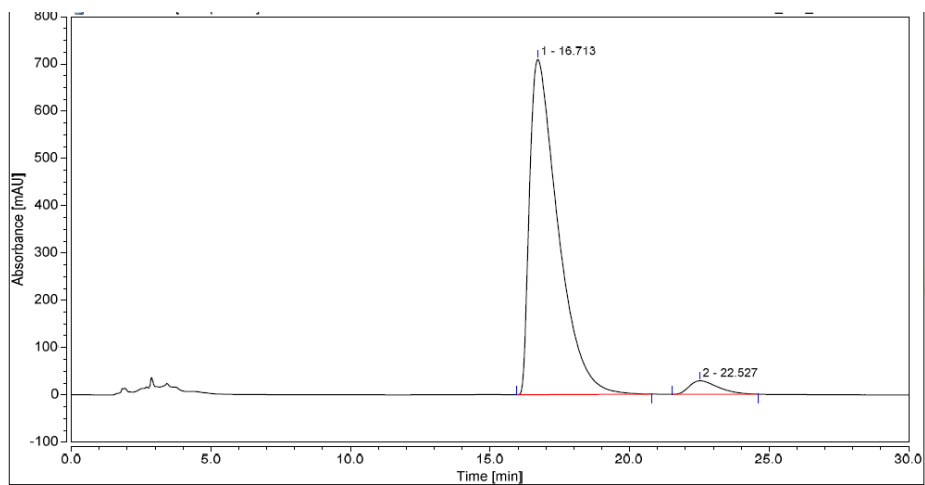
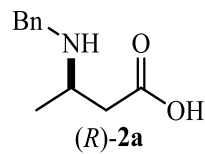
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For entry 11.

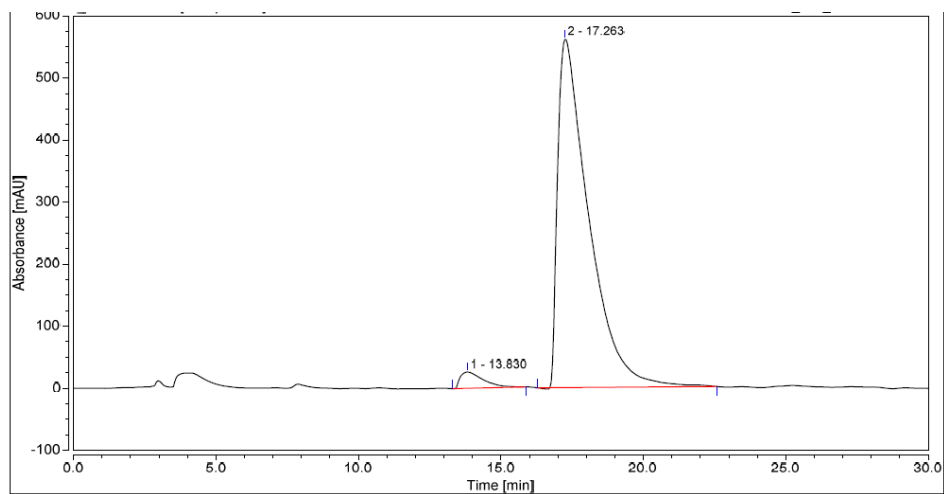
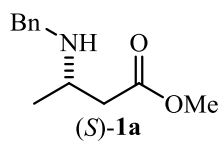


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.733	31.315	27.053	2.57	3.22	n.a.
2		15.683	1185.288	811.859	97.43	96.78	n.a.
Total:			1216.603	838.912	100.00	100.00	

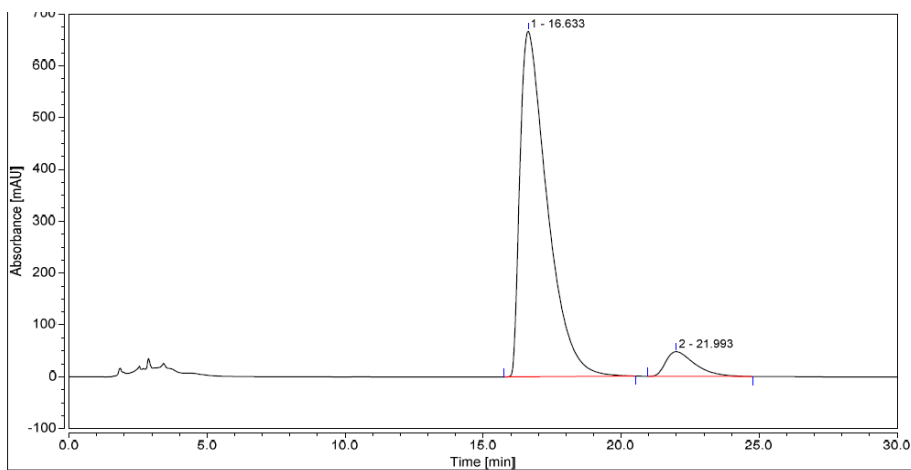
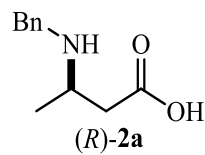


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.713	834.034	710.080	96.02	96.11	n.a.
2		22.527	34.529	28.721	3.98	3.89	n.a.
Total:			868.563	738.800	100.00	100.00	

For entry 12.

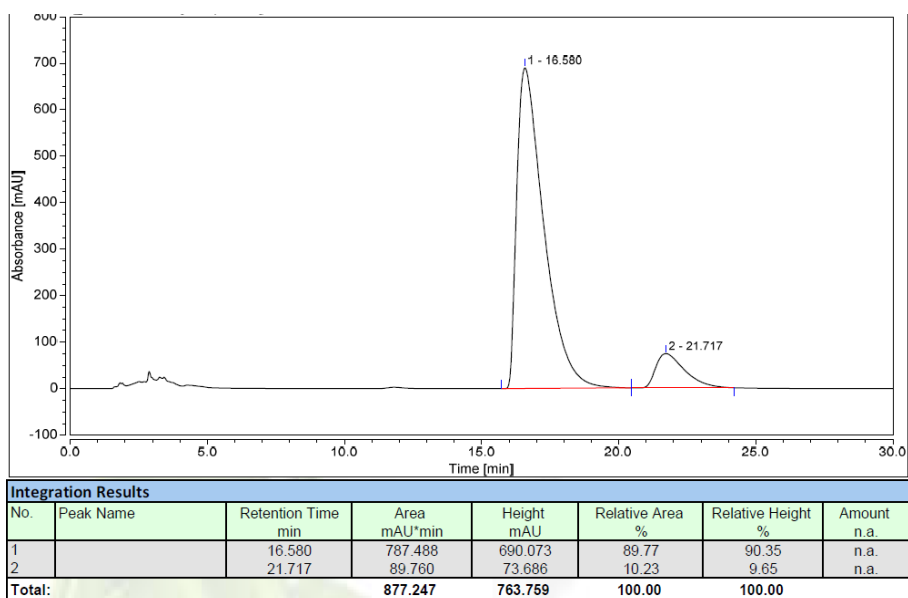
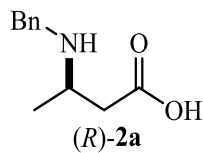
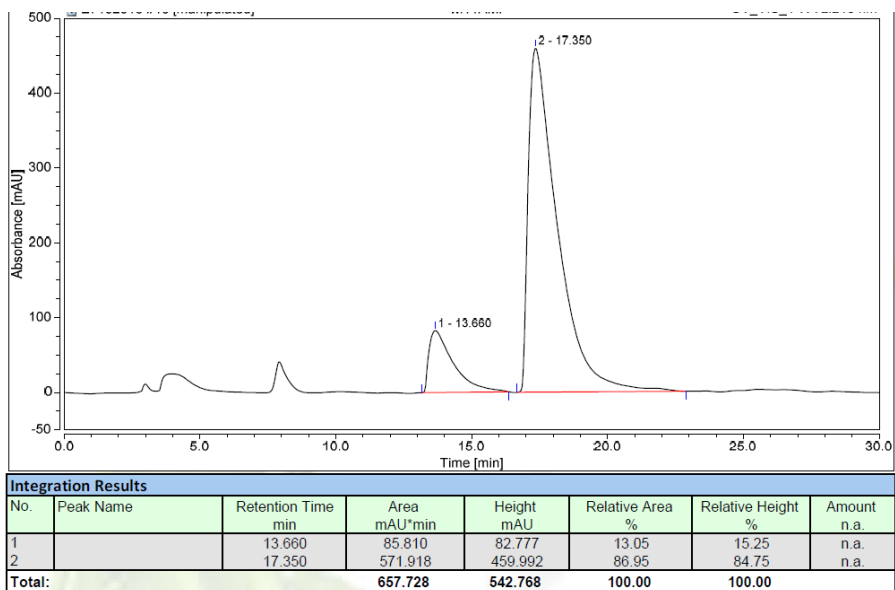
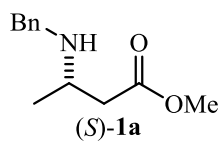


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		13.830	24.251	26.194	3.31	4.46	n.a.
2		17.263	708.473	561.512	96.69	95.54	n.a.
Total:			732.724	587.706	100.00	100.00	

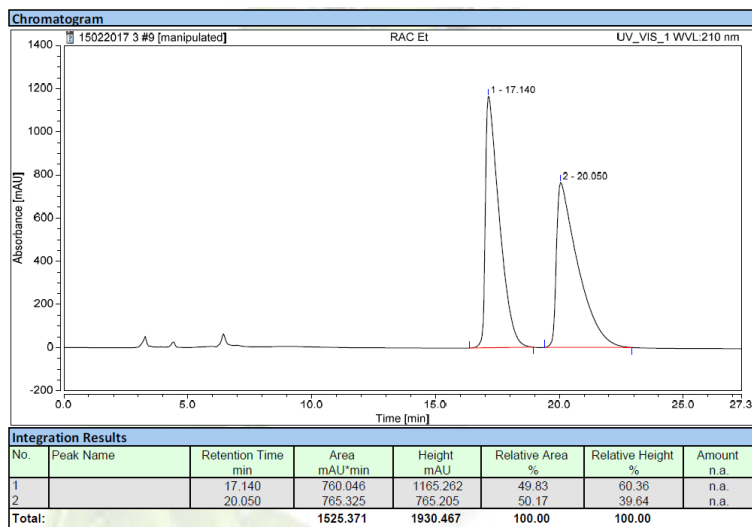
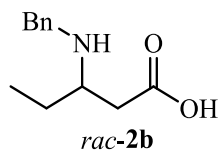
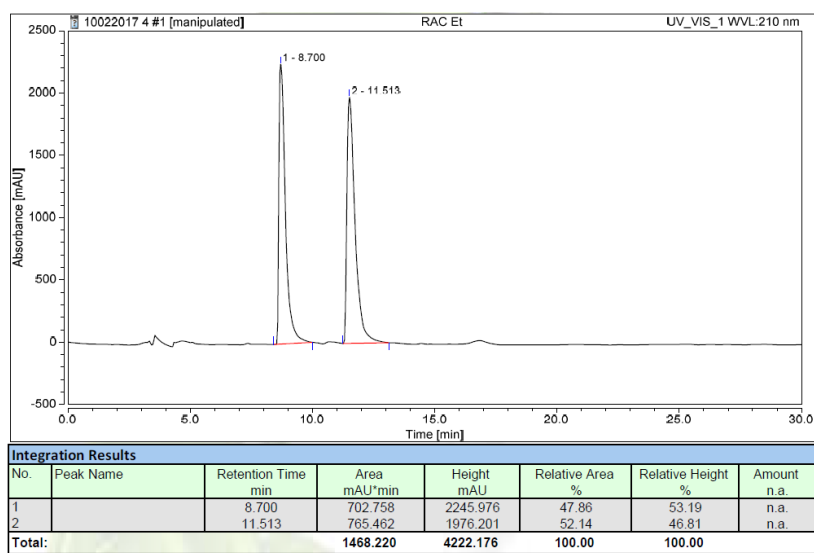
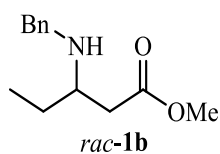


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		16.633	759.988	666.344	92.92	93.34	n.a.
2		21.993	57.872	47.564	7.08	6.66	n.a.
Total:			817.860	713.909	100.00	100.00	

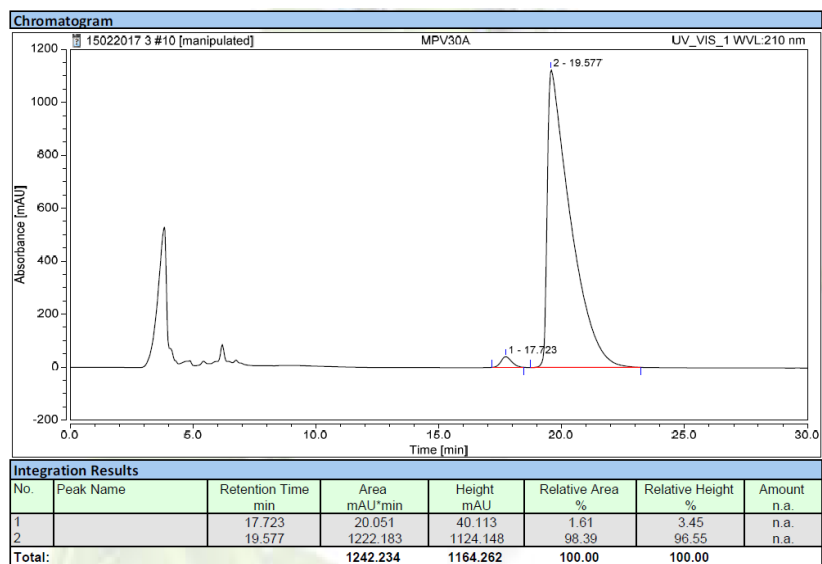
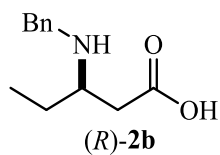
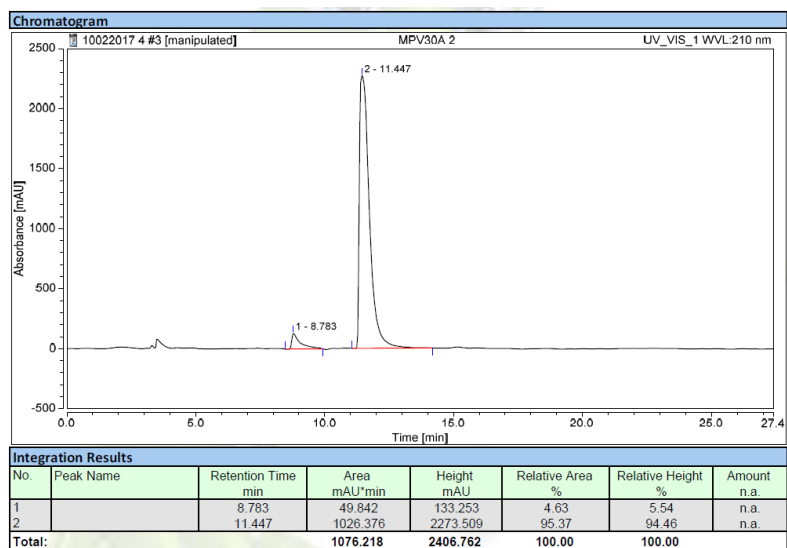
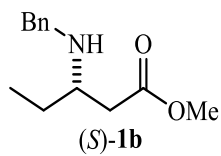
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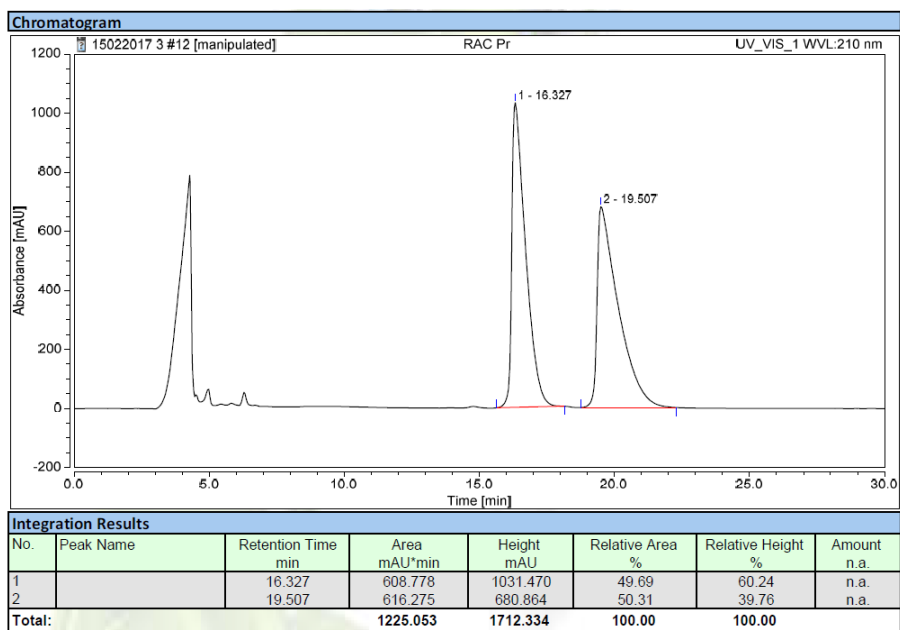
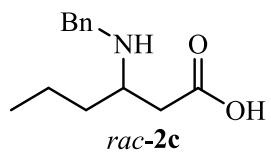
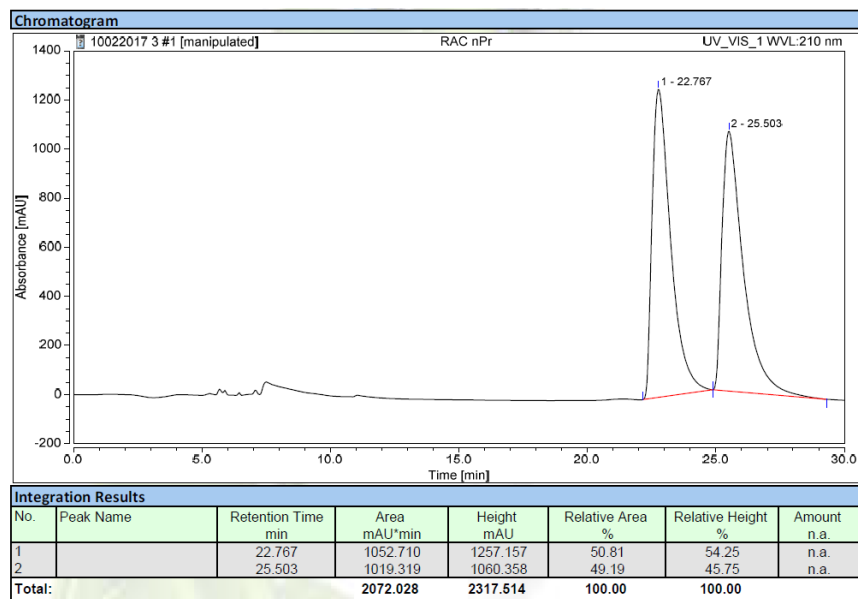
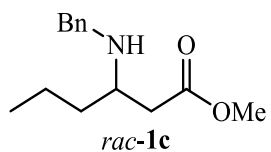


- Chromatograms for substrate scope for the enzymatic resolution of N-benzylated- β^3 -amino acid methyl esters (Table S2)

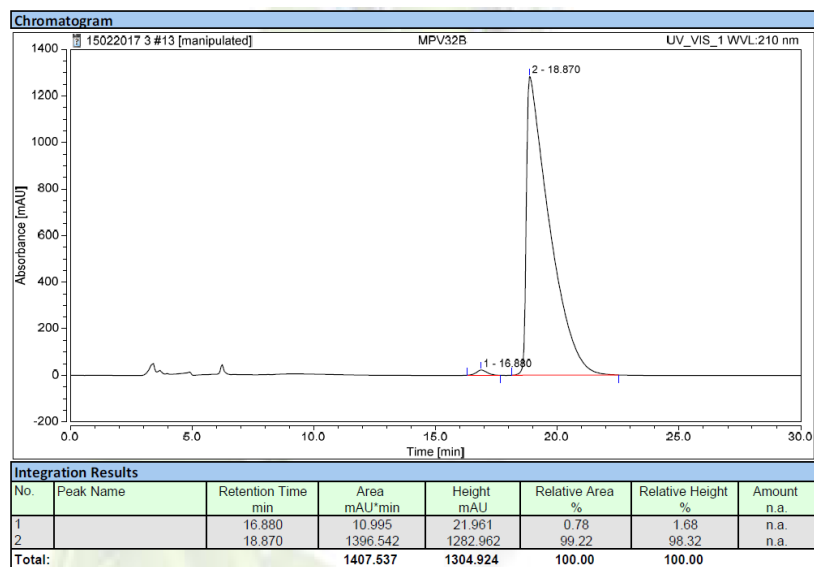
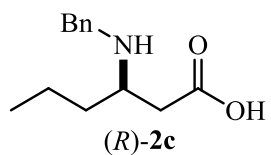
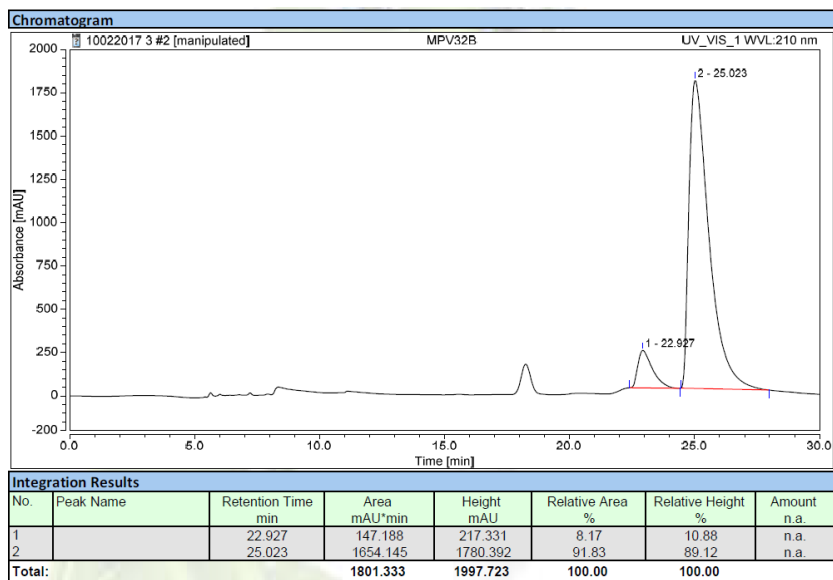
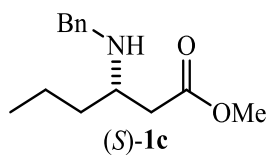


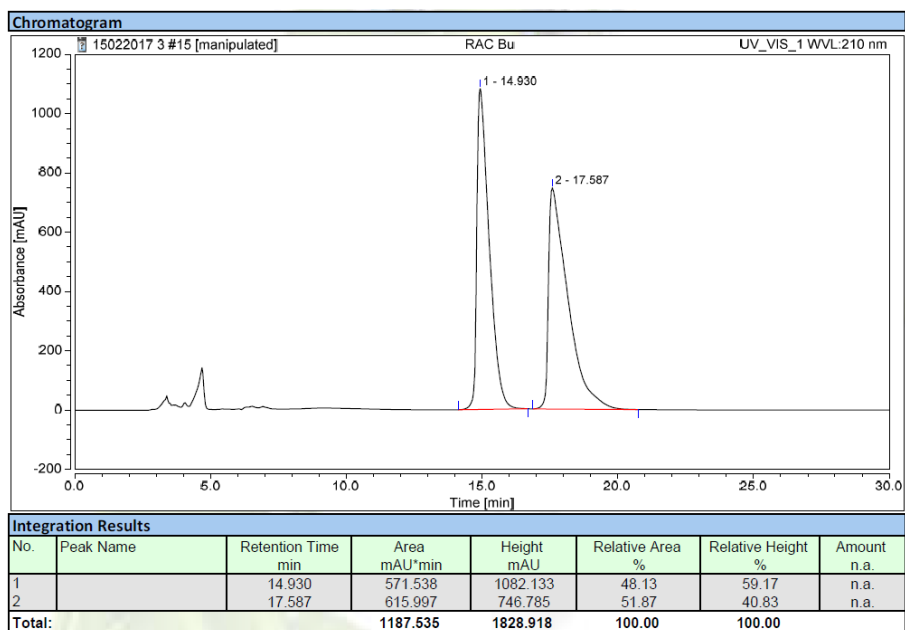
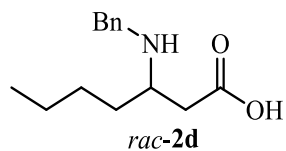
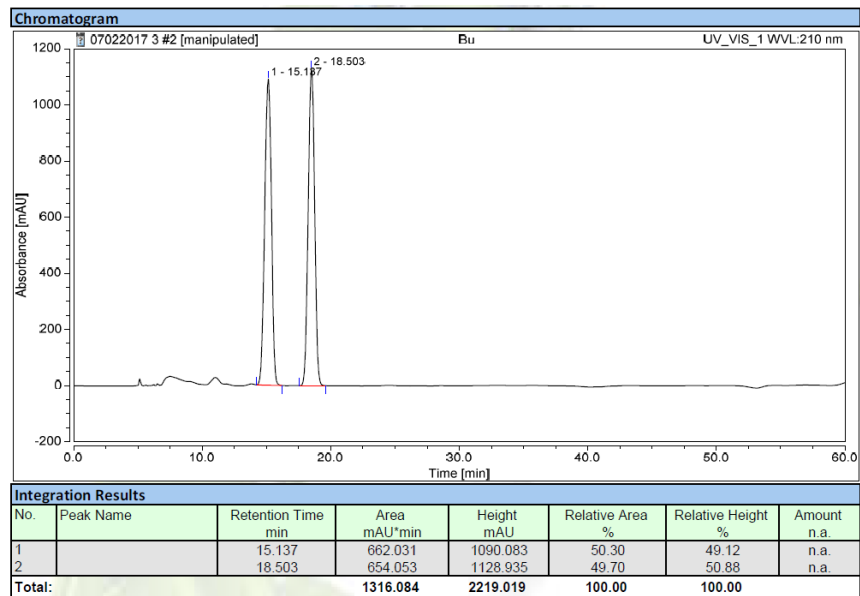
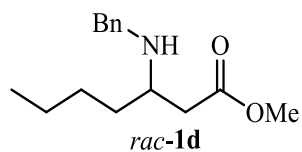
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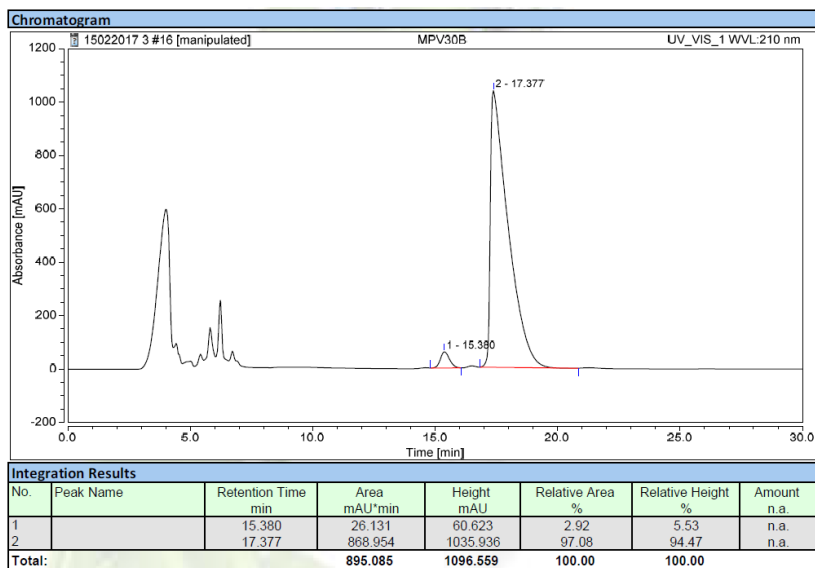
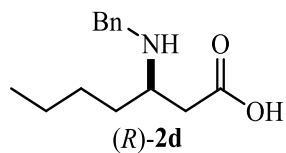
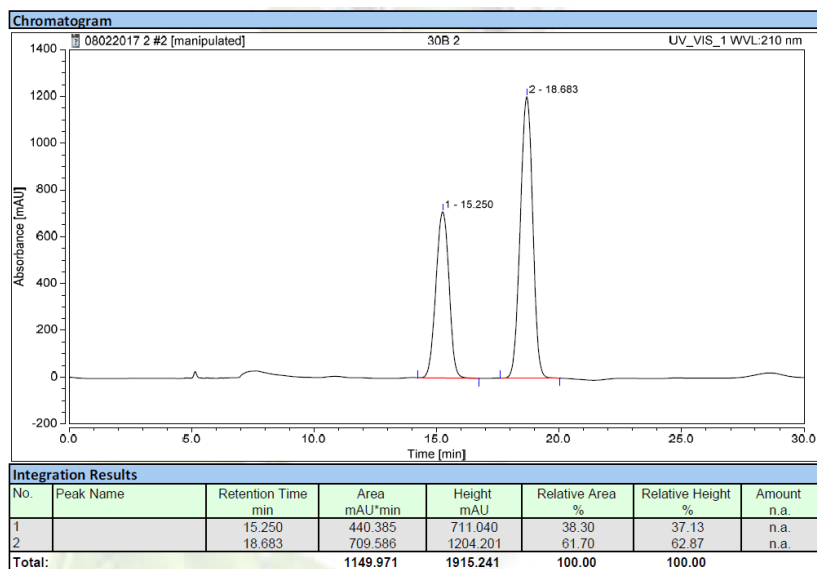
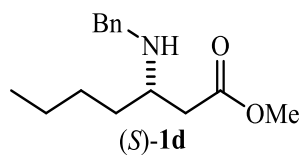


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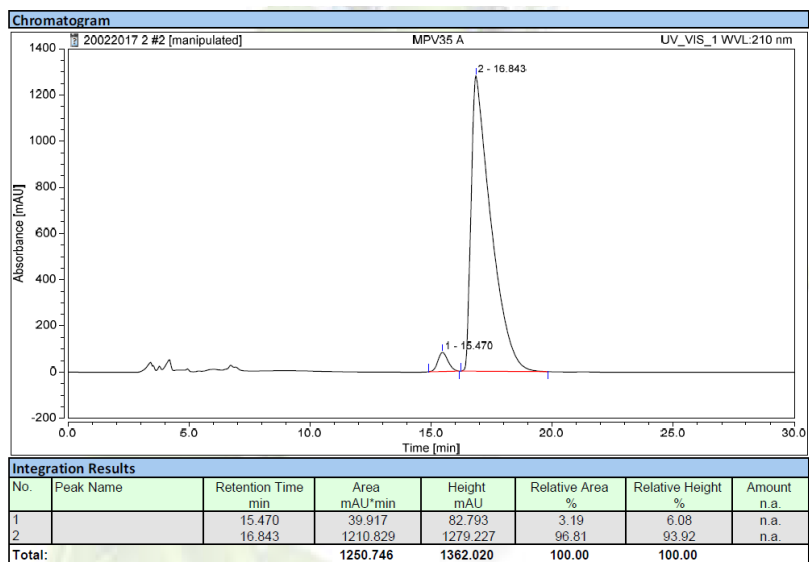
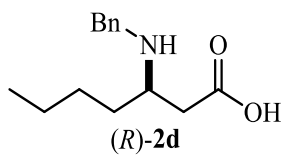
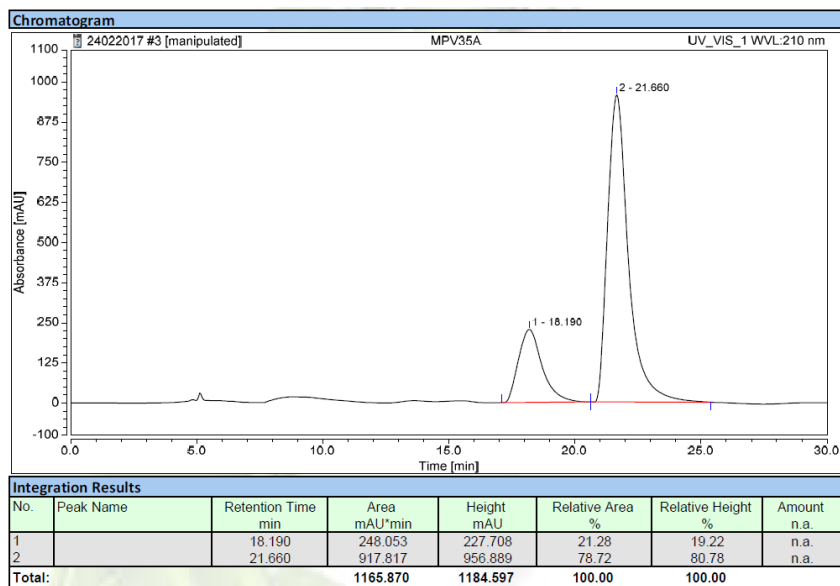
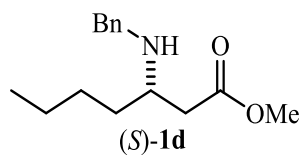




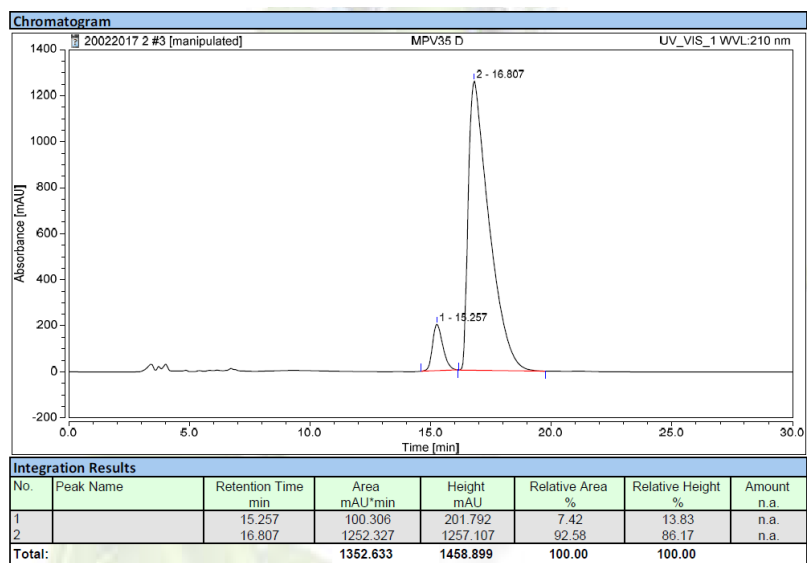
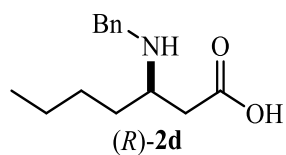
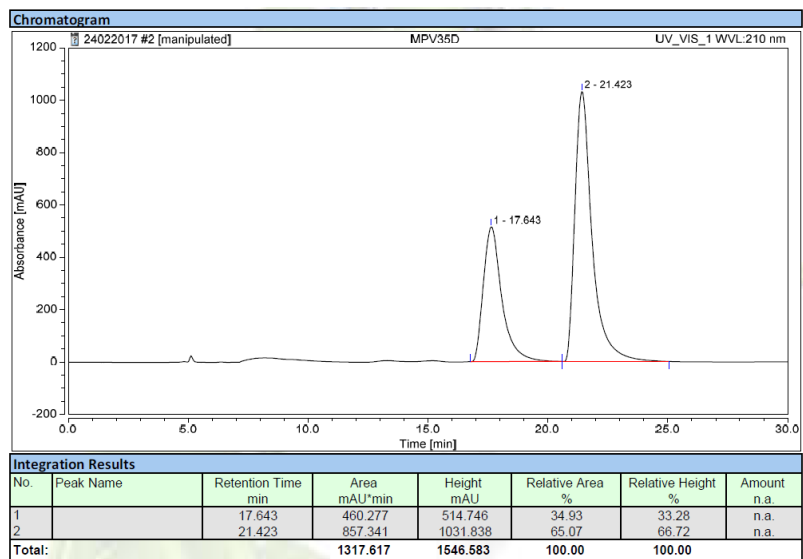
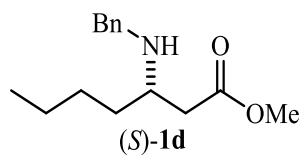
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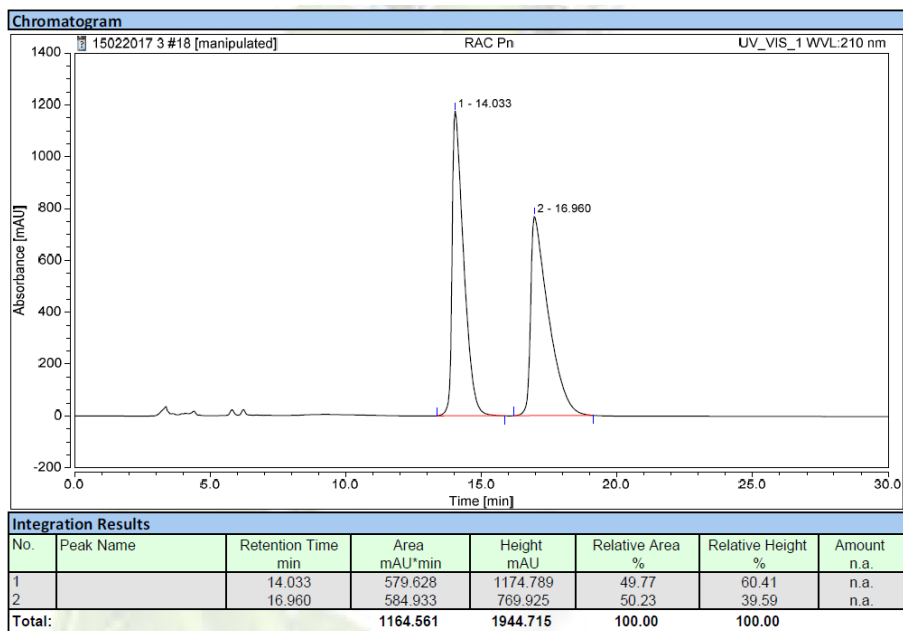
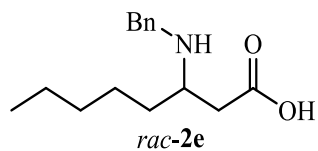
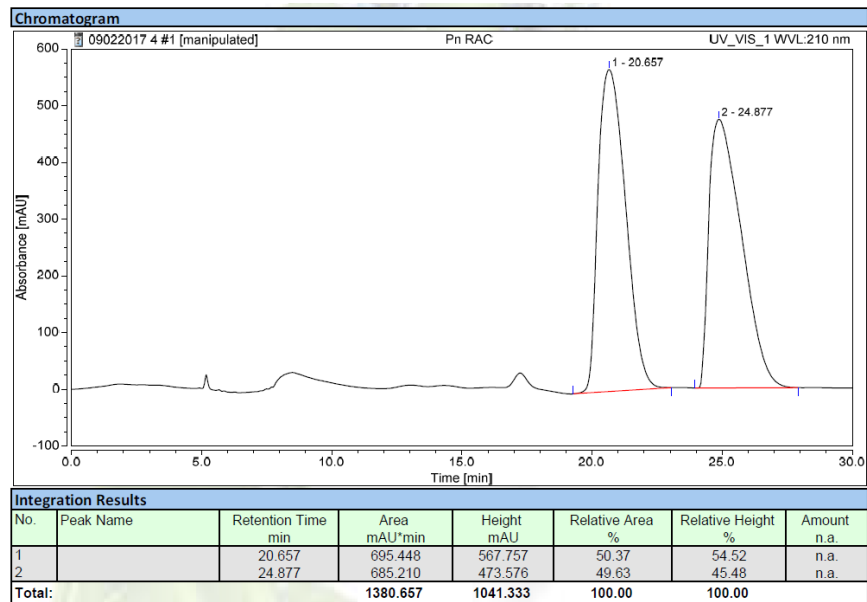
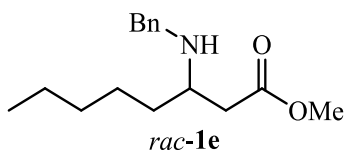


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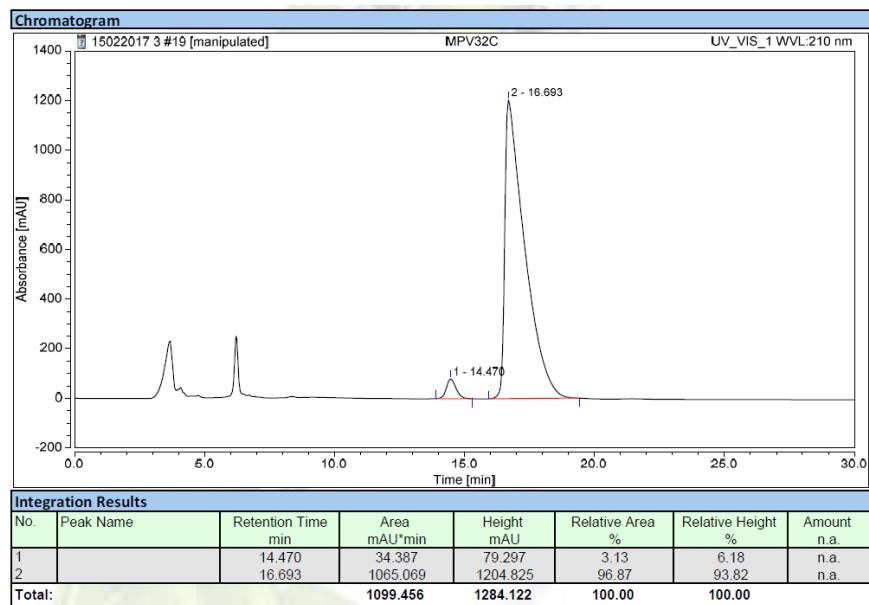
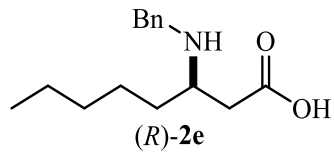
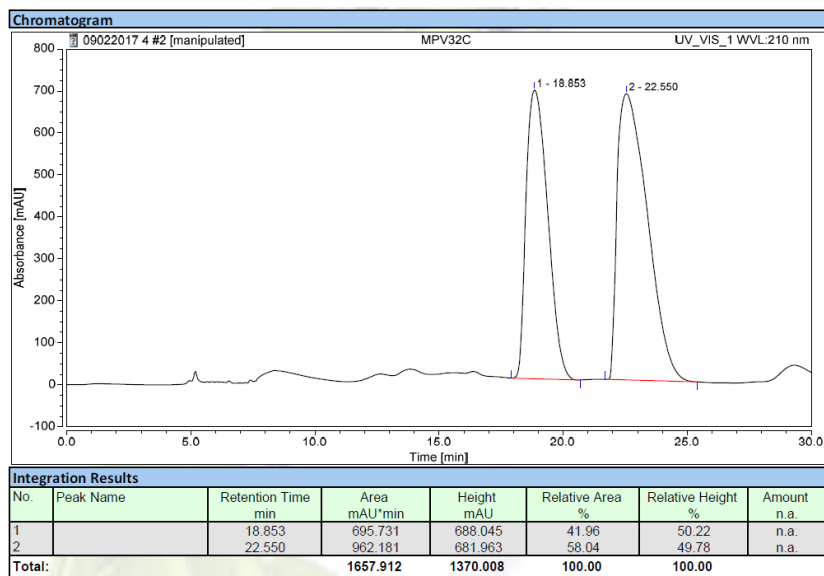
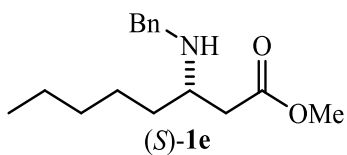


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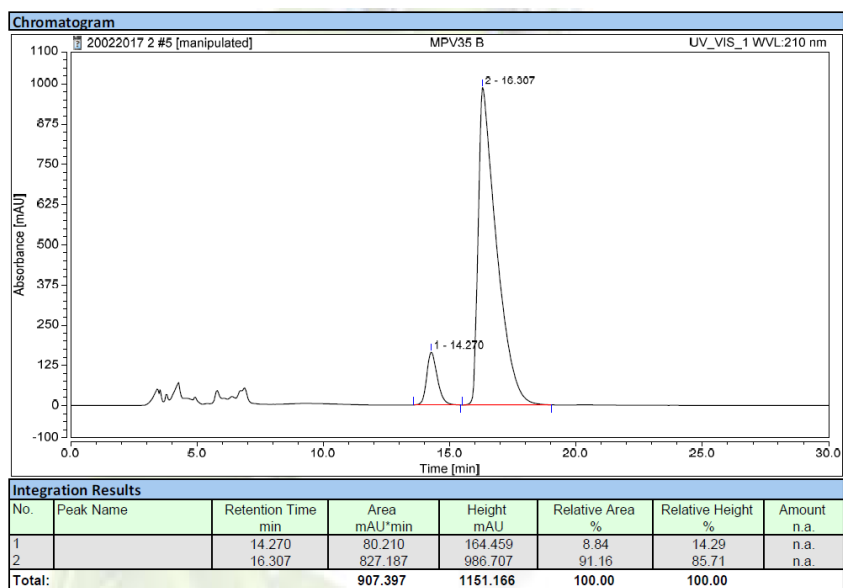
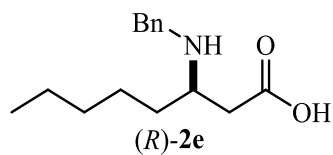
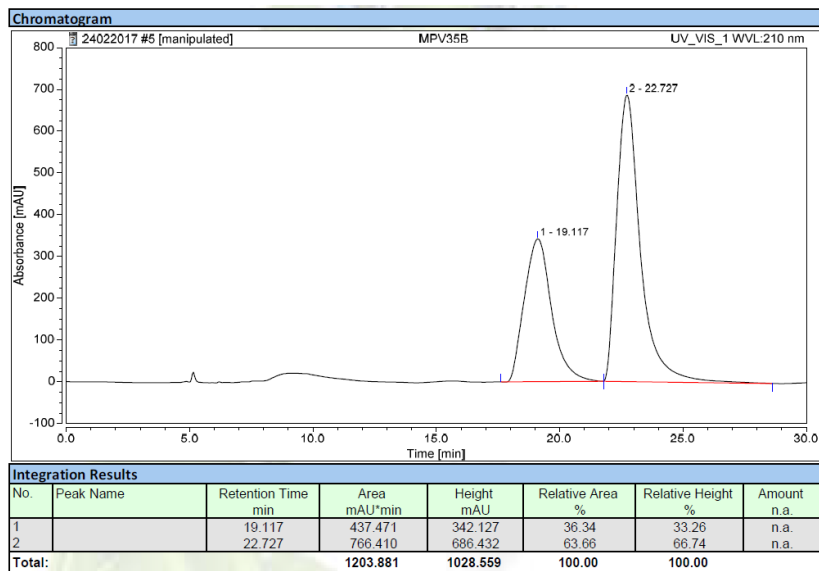
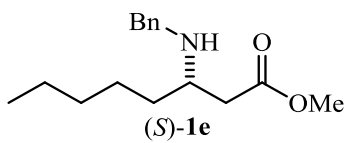




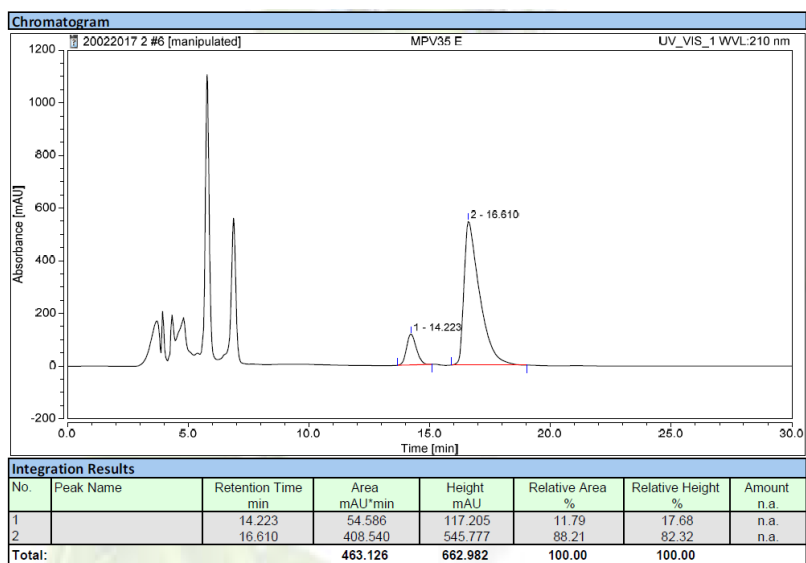
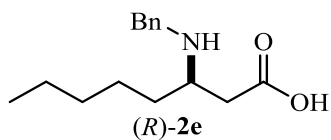
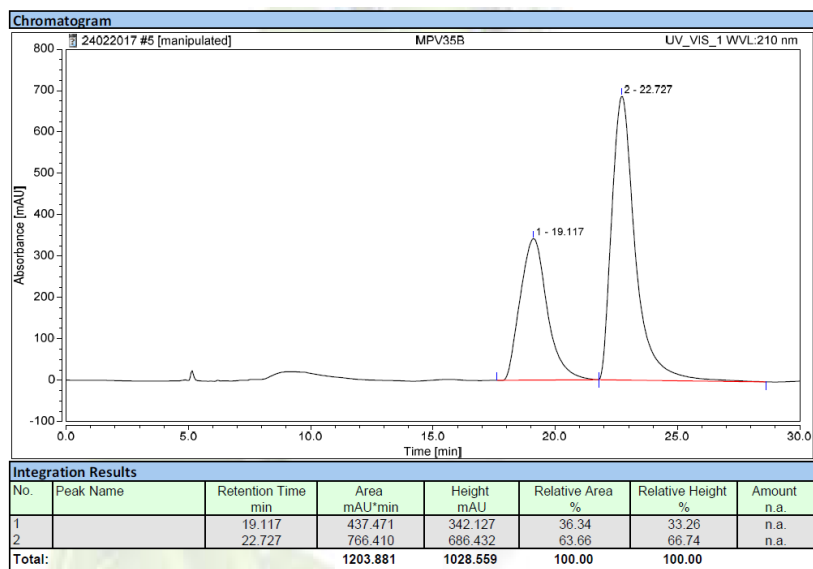
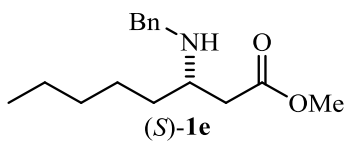
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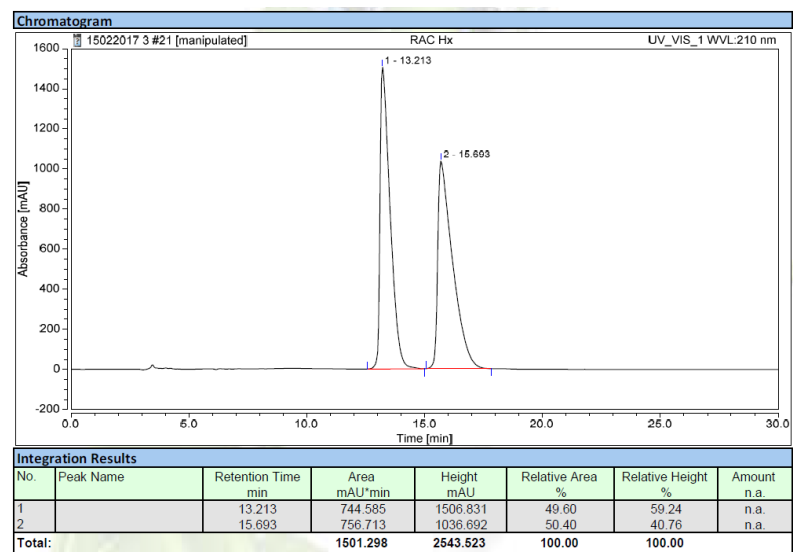
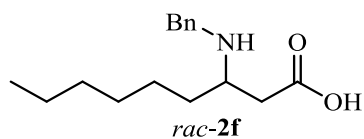
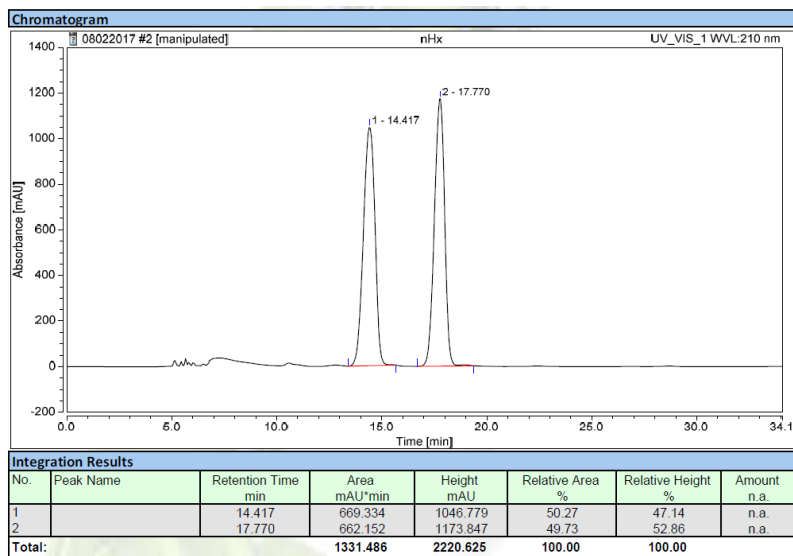
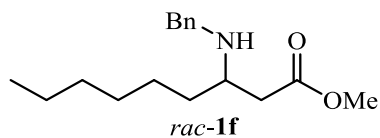


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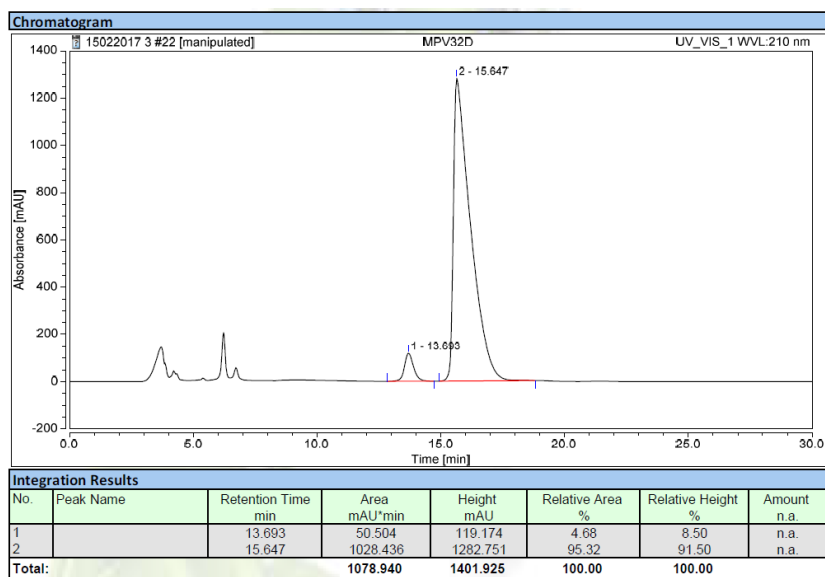
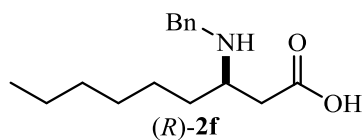
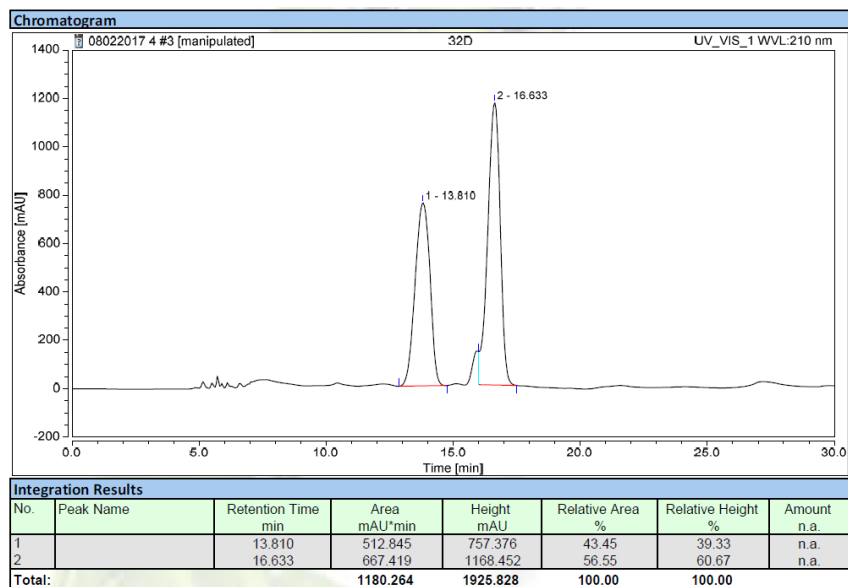
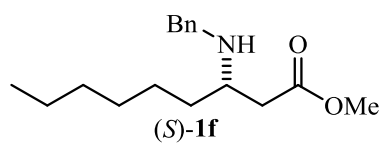


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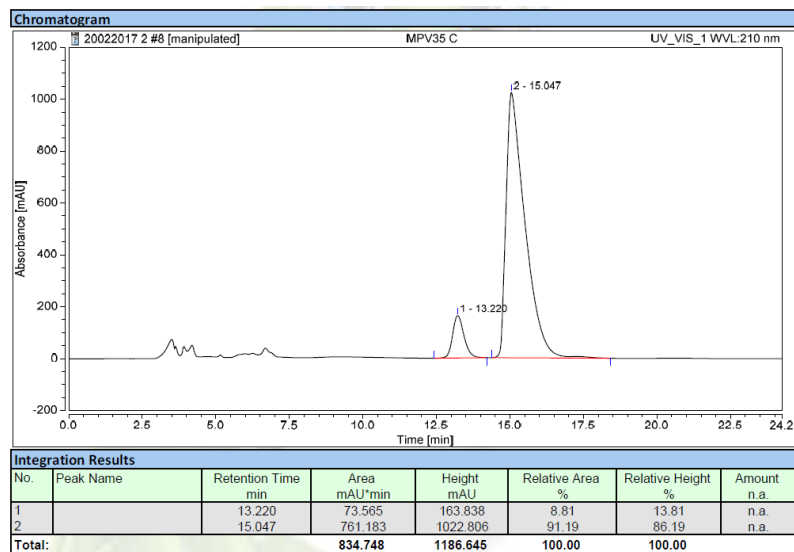
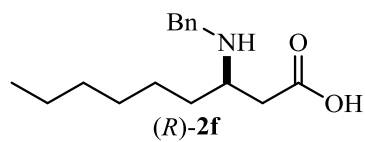
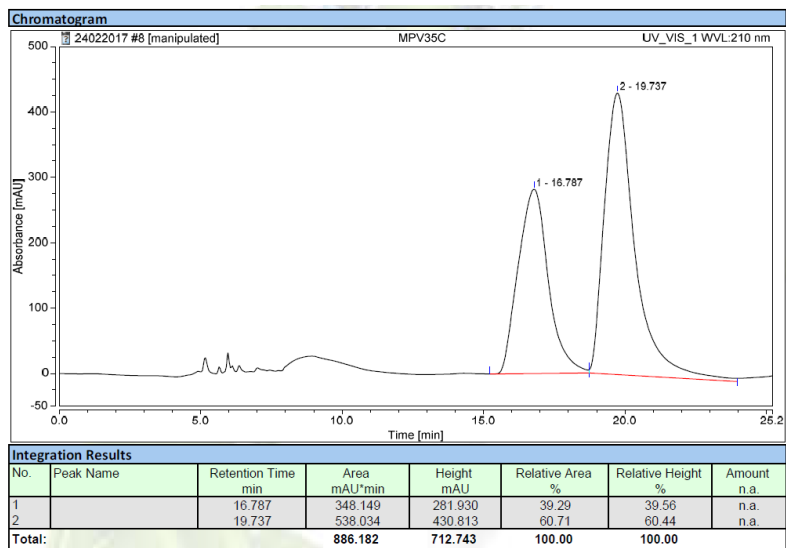
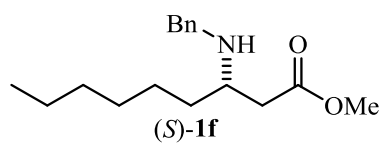




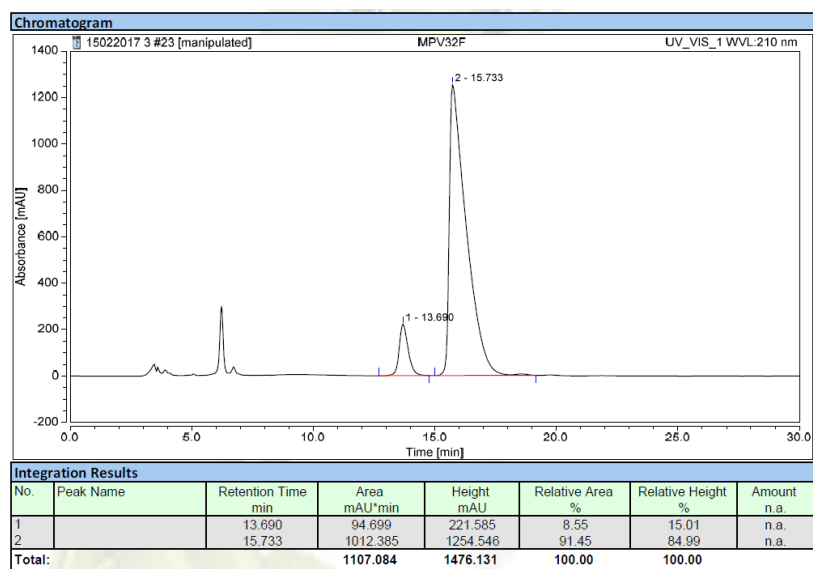
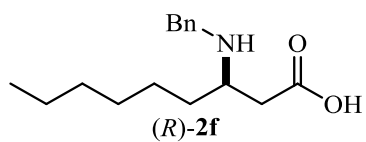
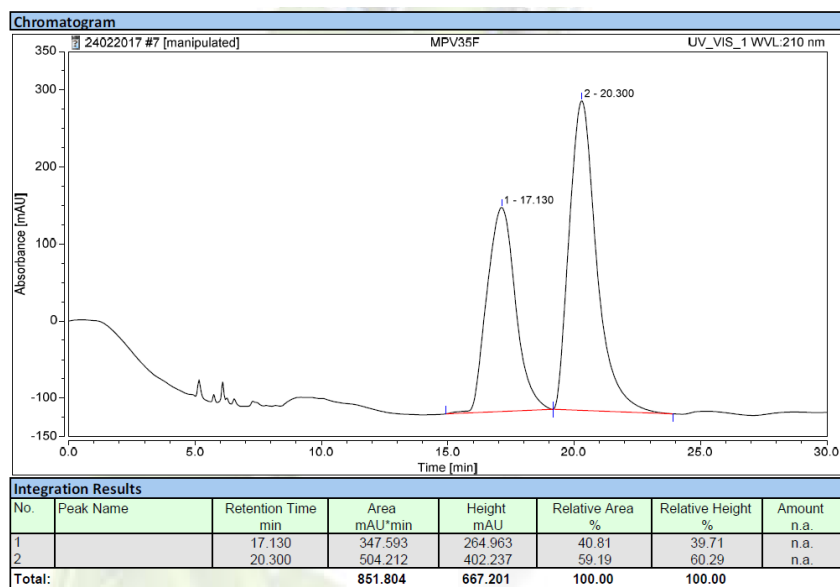
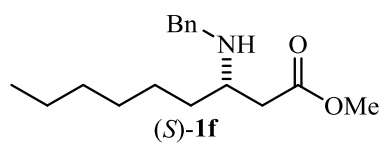
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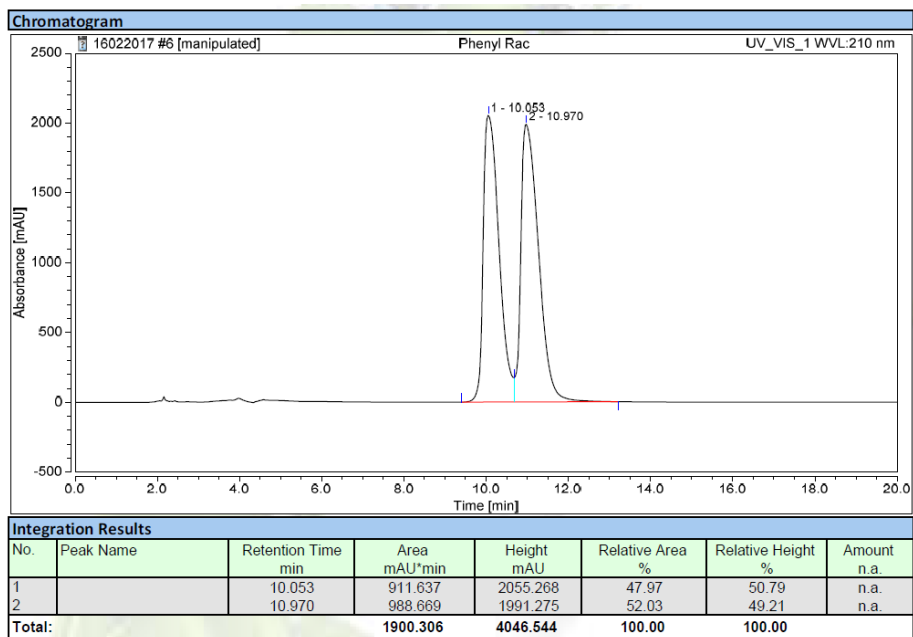
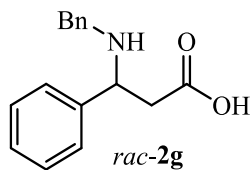
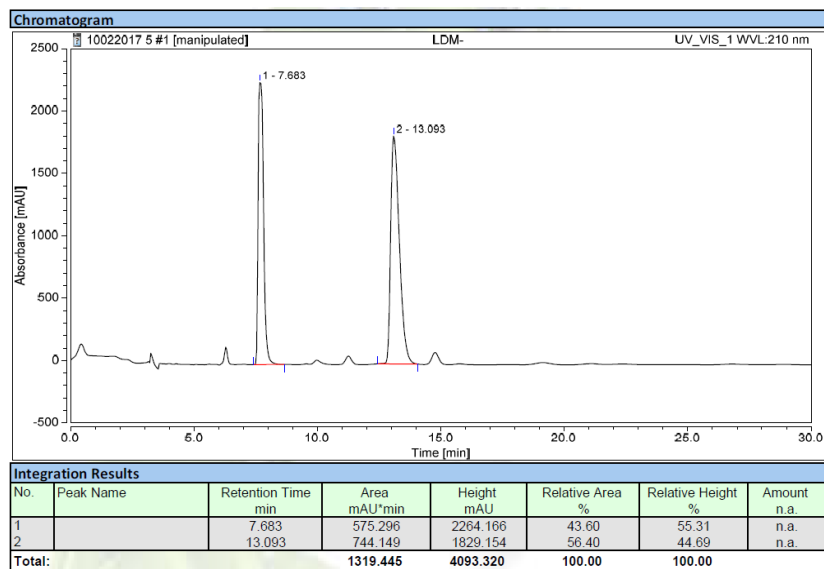
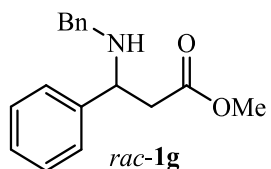


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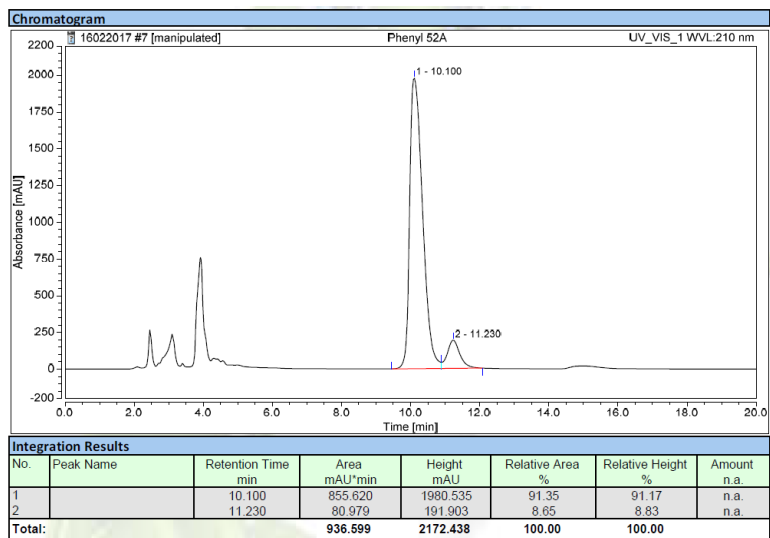
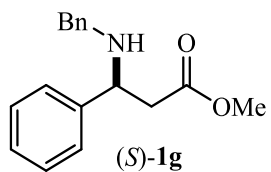
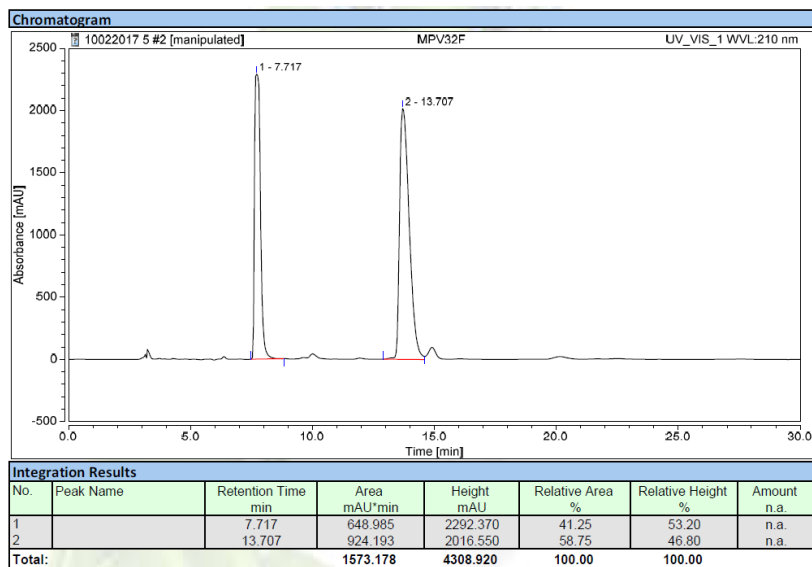
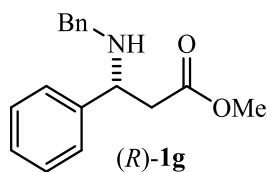


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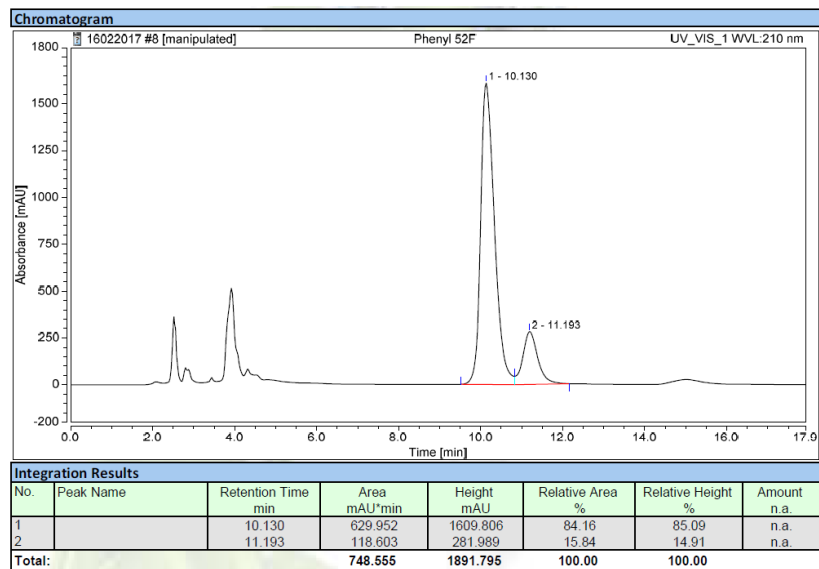
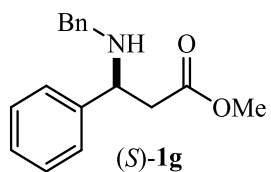
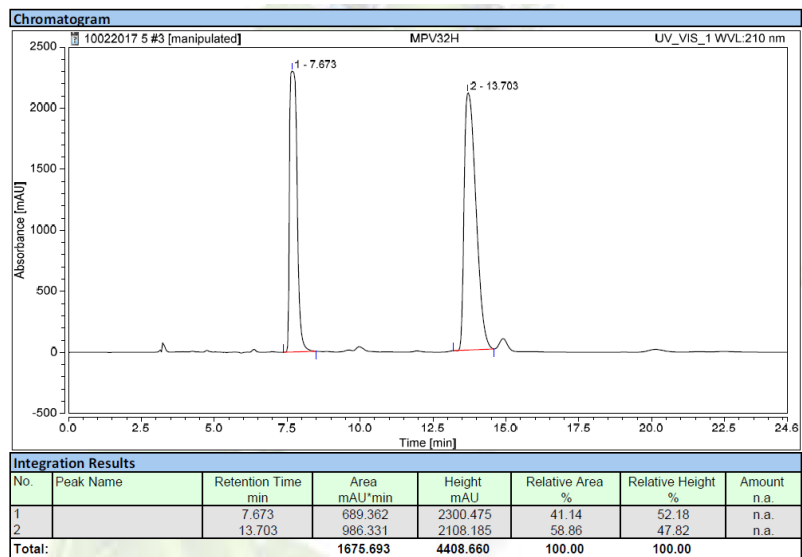
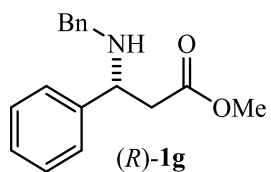




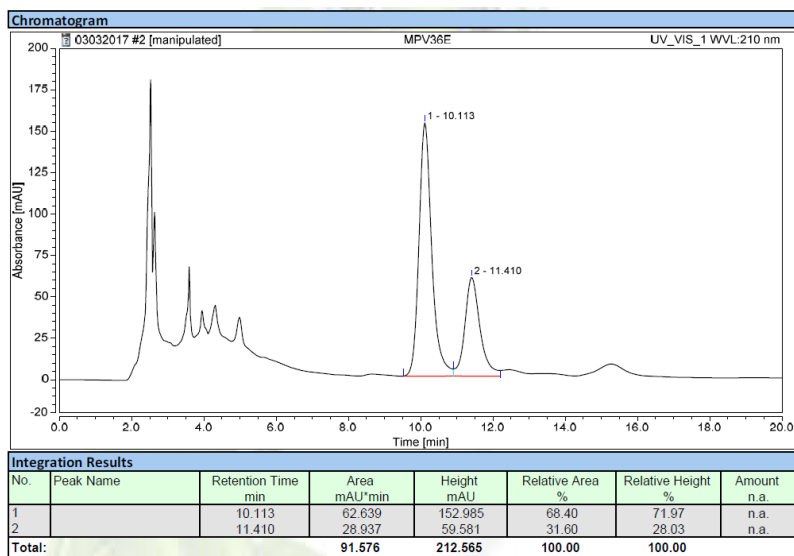
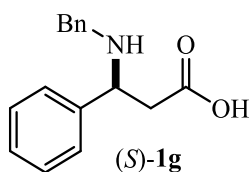
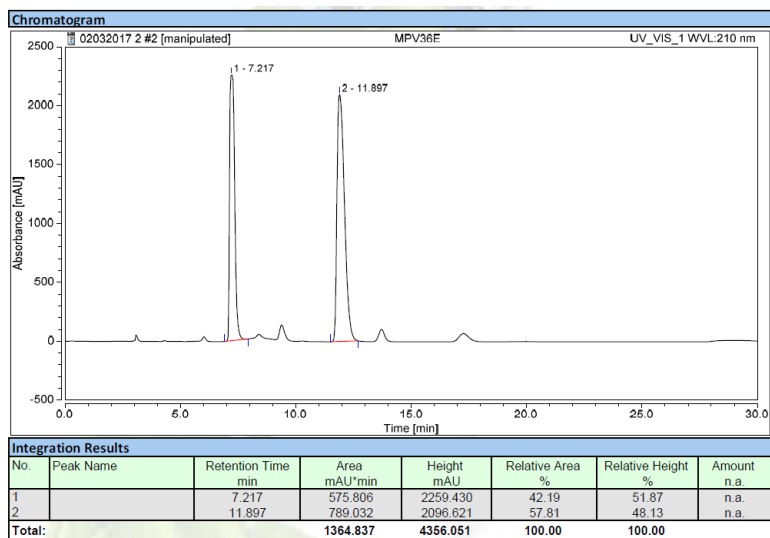
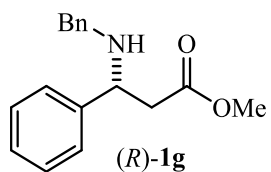
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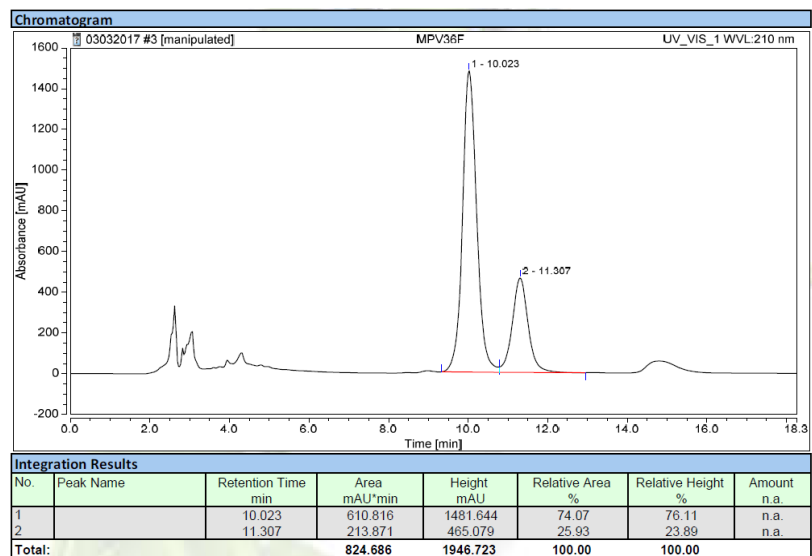
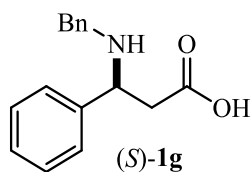
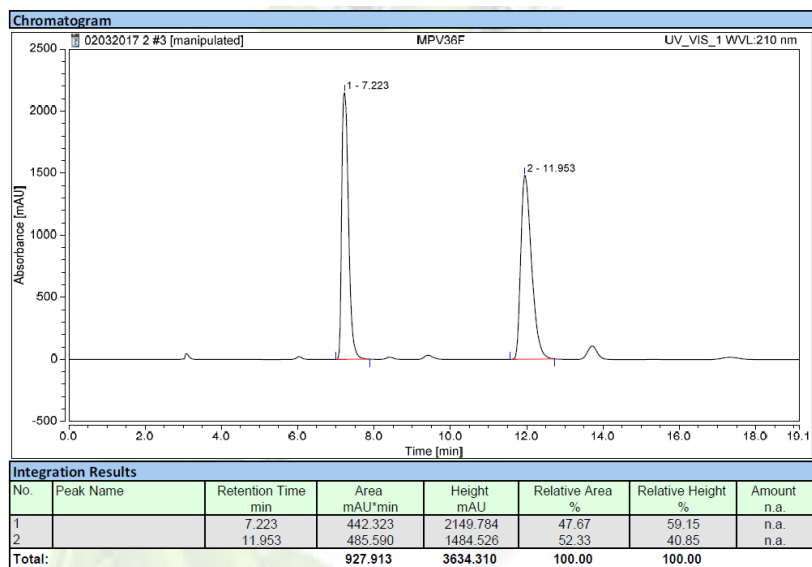
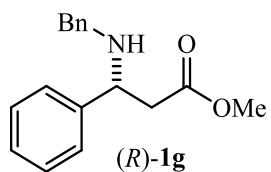
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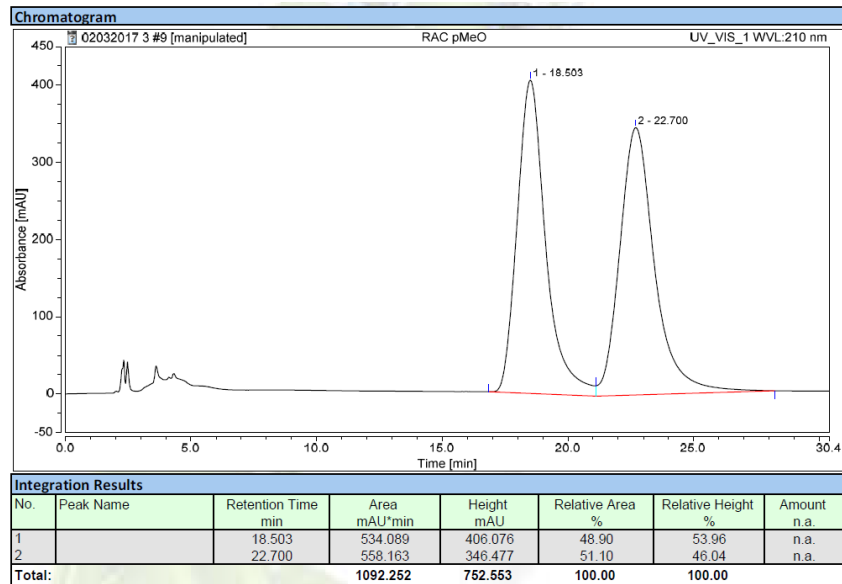
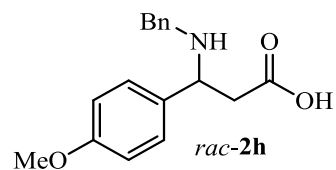
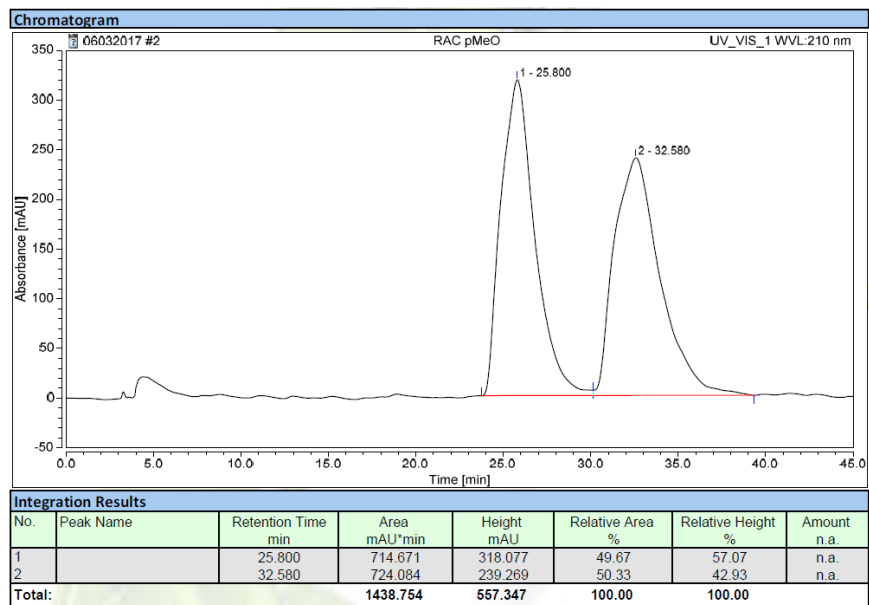
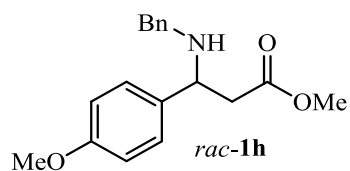


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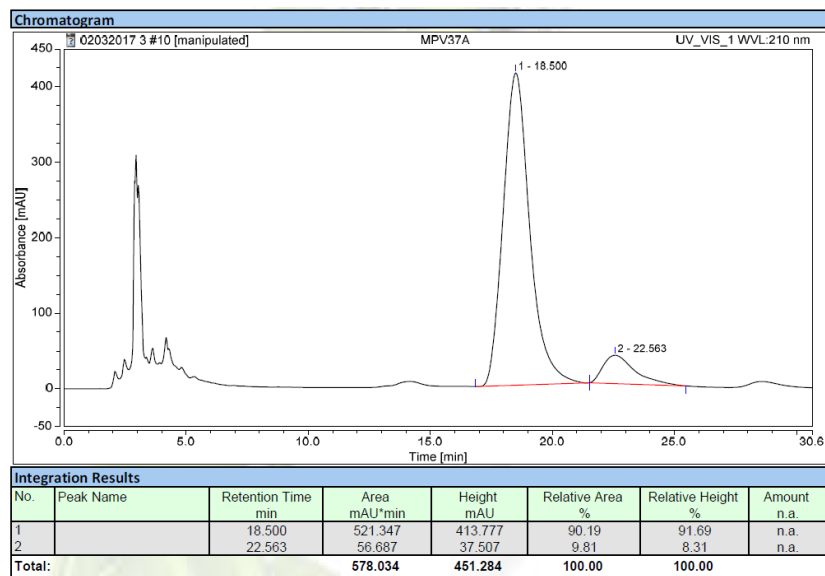
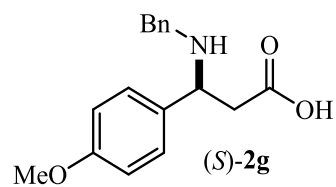
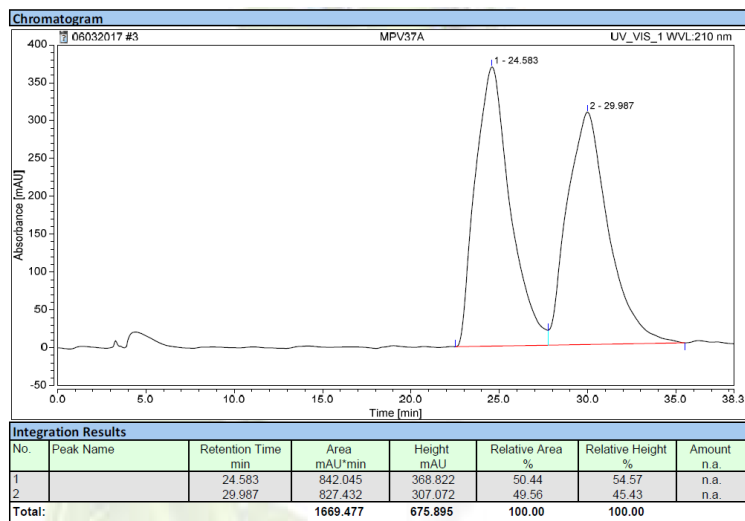
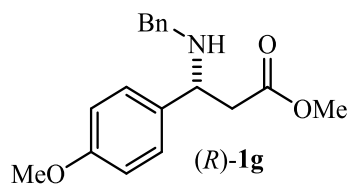


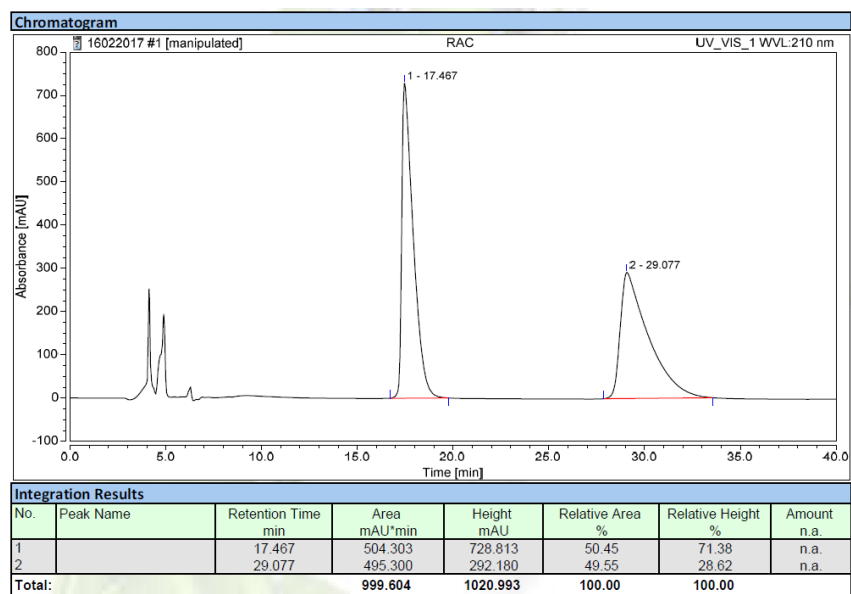
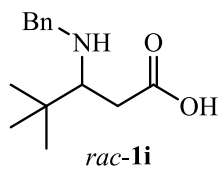
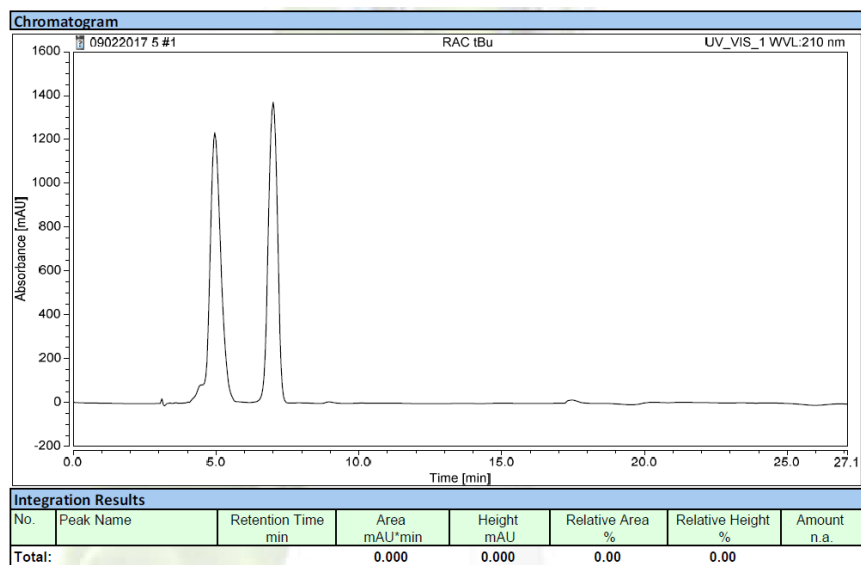
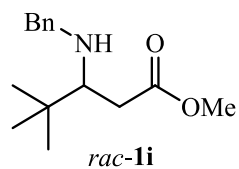
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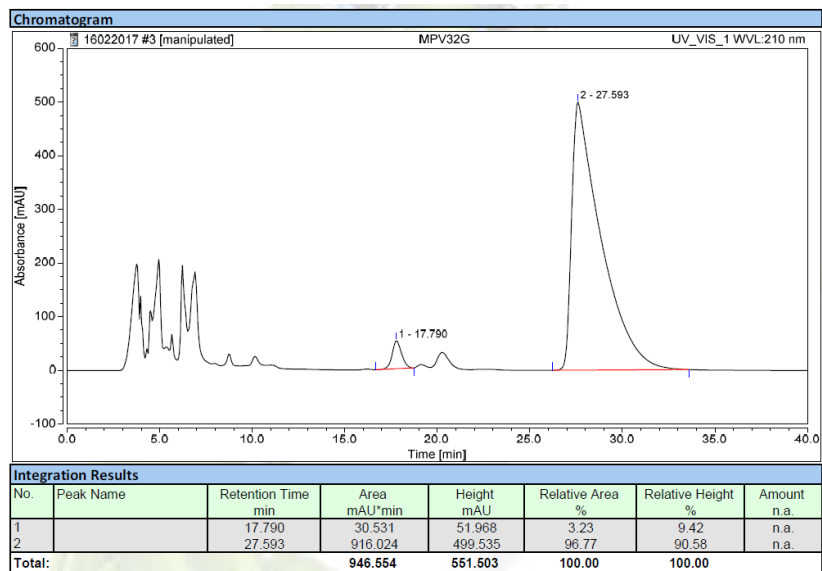
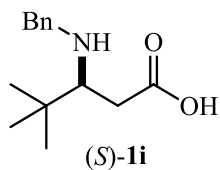
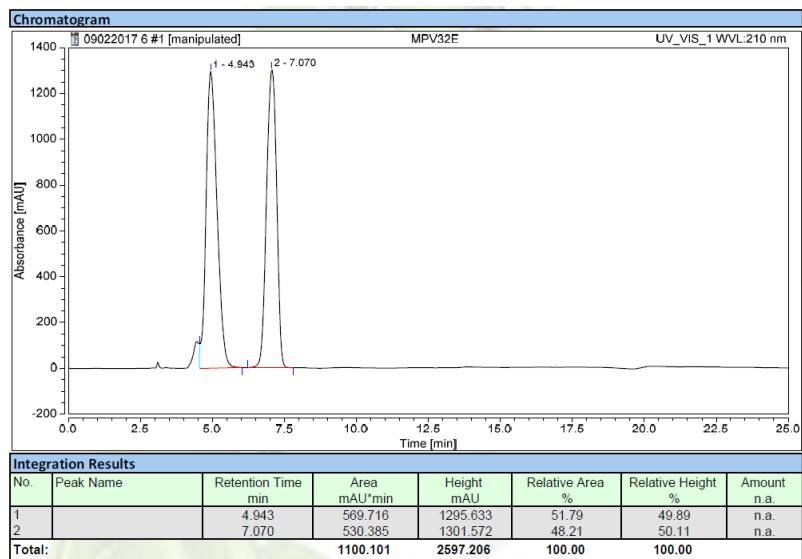
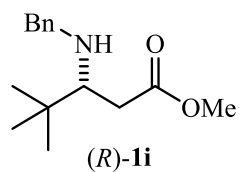


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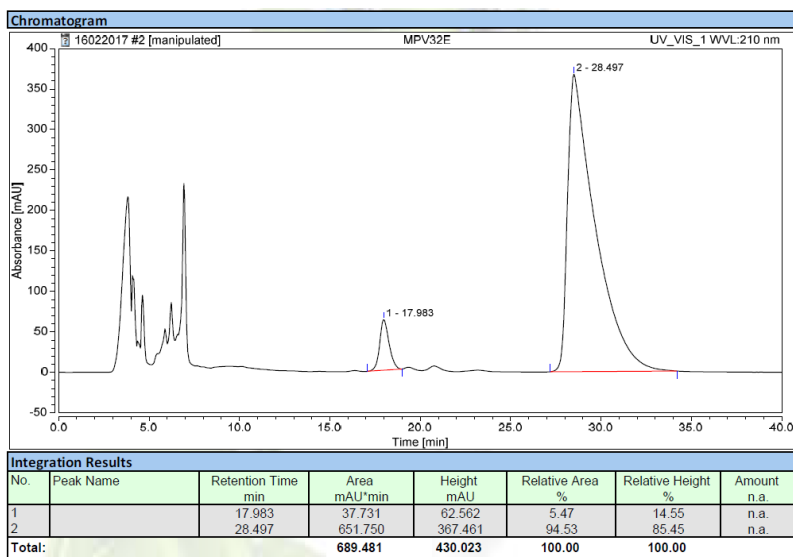
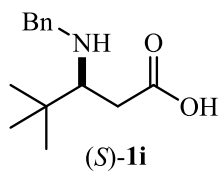
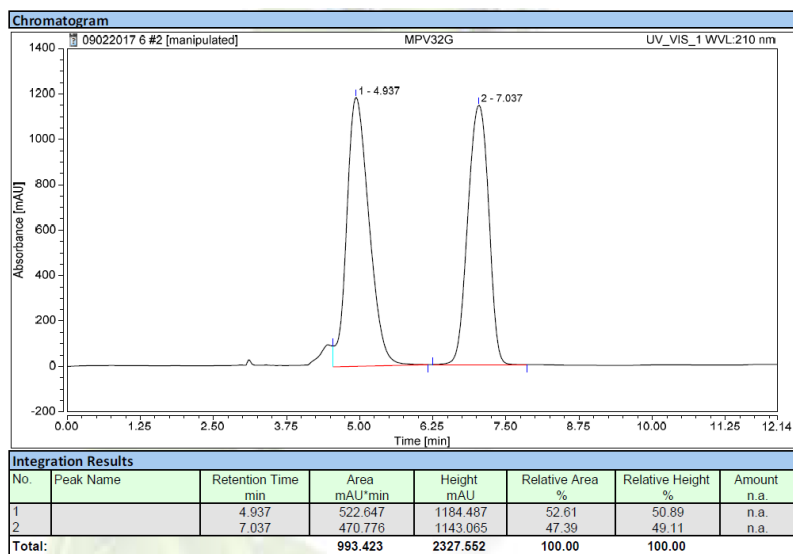
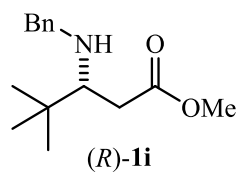




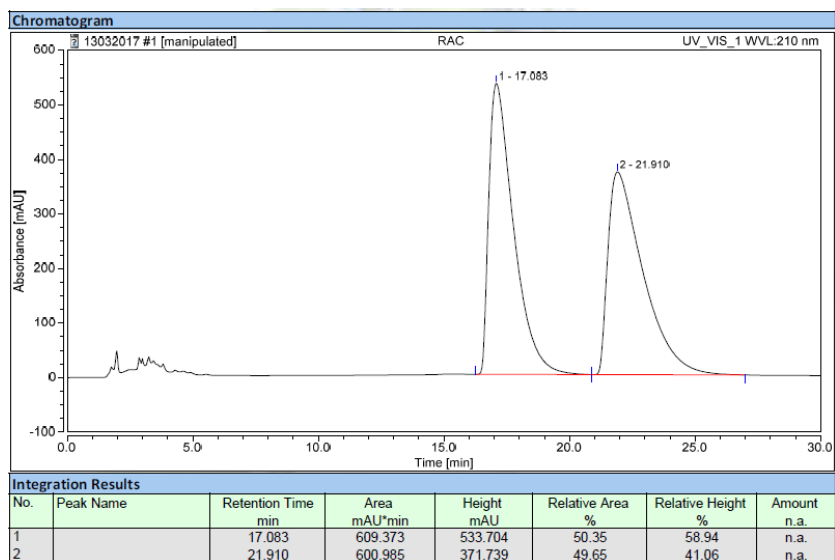
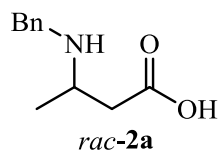
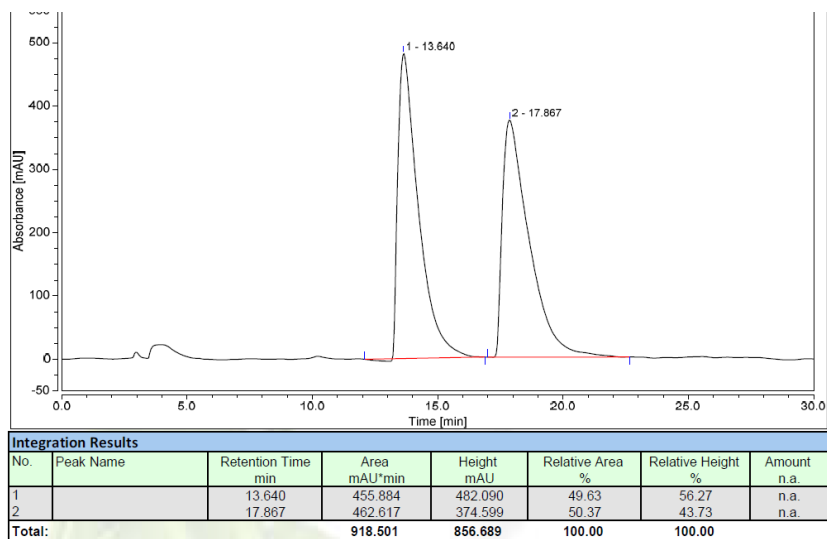
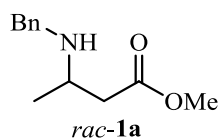
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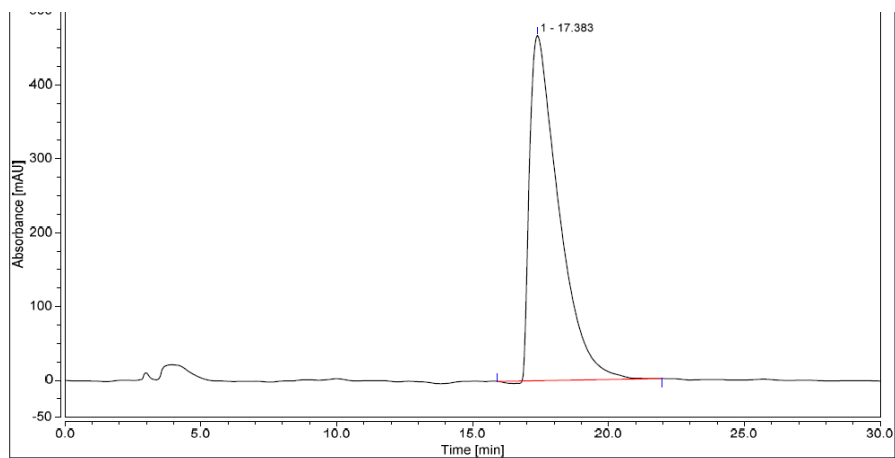
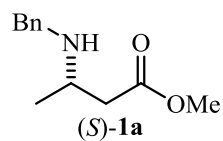
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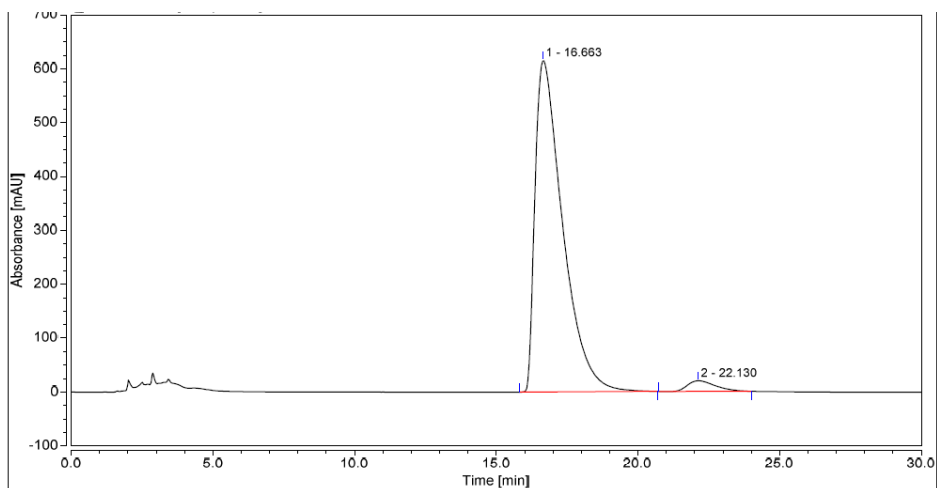
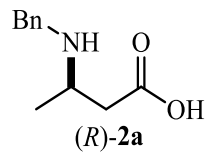
- Chromatograms for the evaluation of recycling capacity of immobilized CALB (Table S3).



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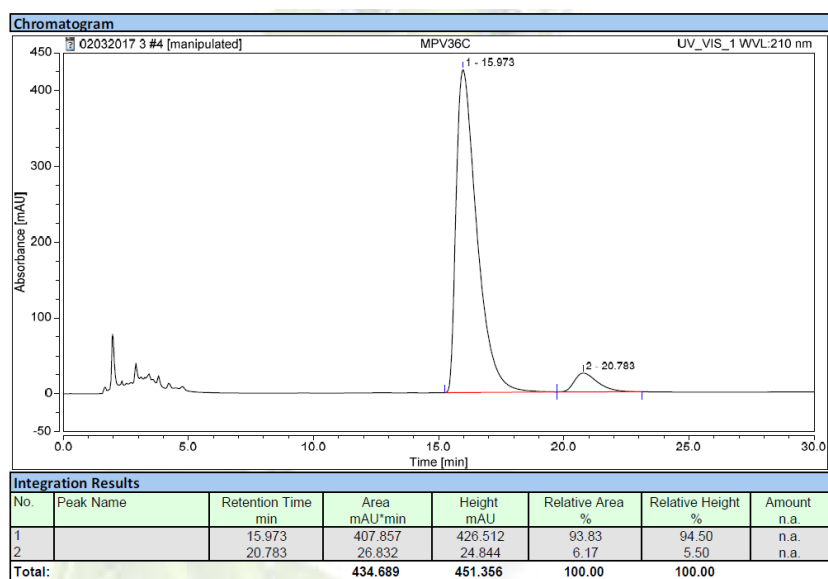
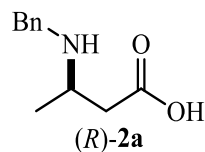
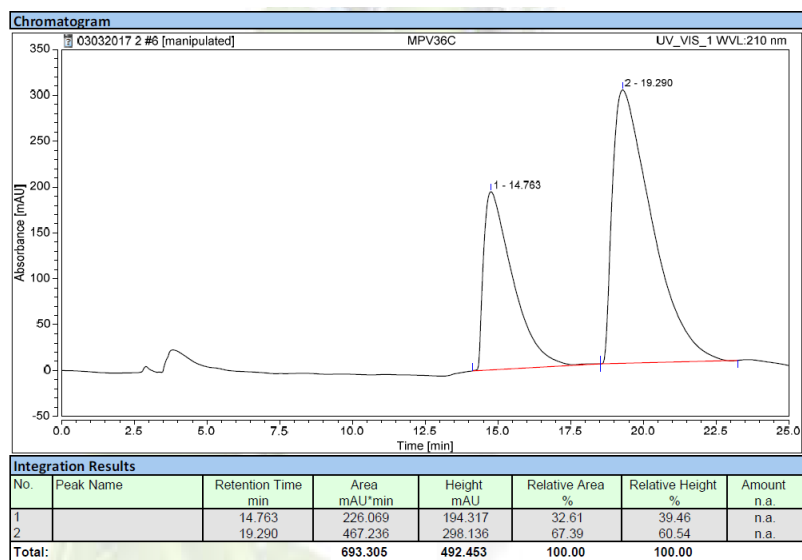
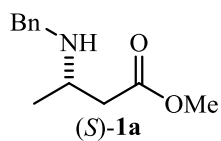


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.383	579.249	467.640	100.00	100.00	n.a.
Total:			579.249	467.640	100.00	100.00	

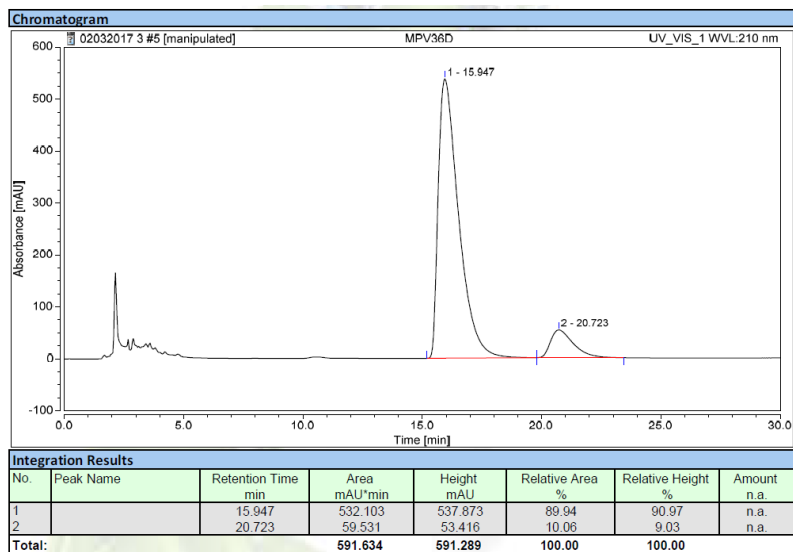
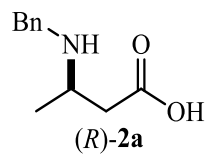
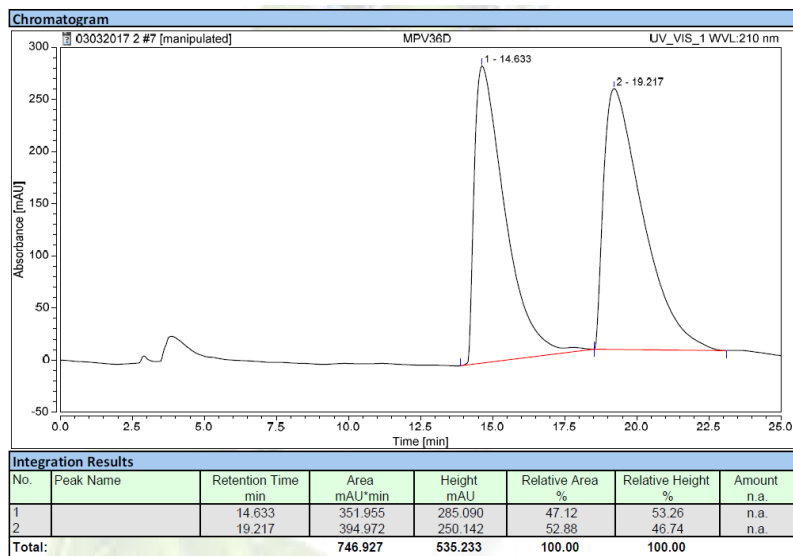
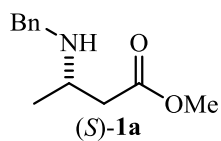


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.663	693.709	615.390	96.91	96.90	n.a.
2		22.130	22.121	19.698	3.09	3.10	n.a.
Total:			715.830	635.088	100.00	100.00	

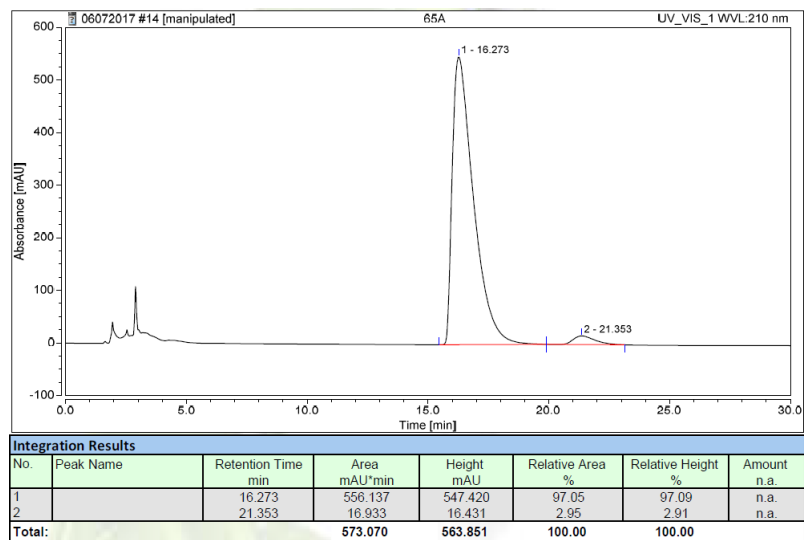
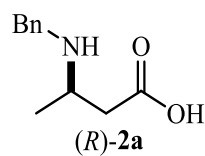
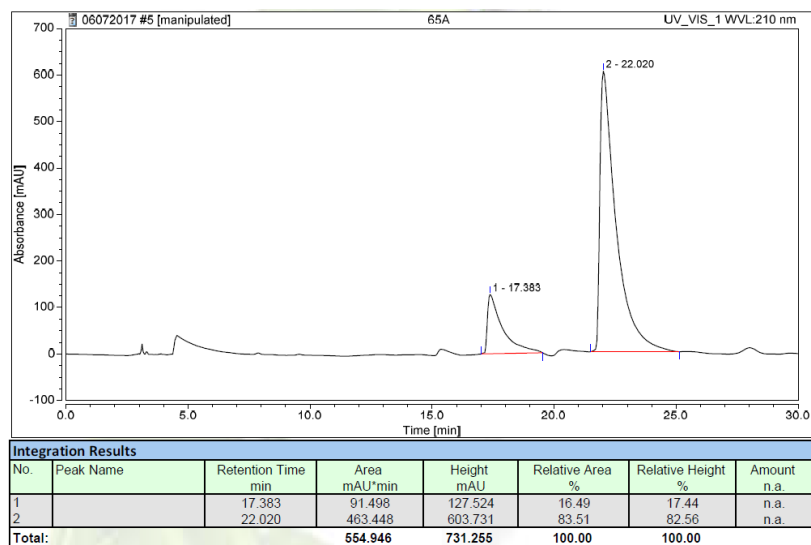
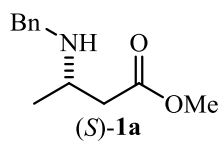
For entry 3.



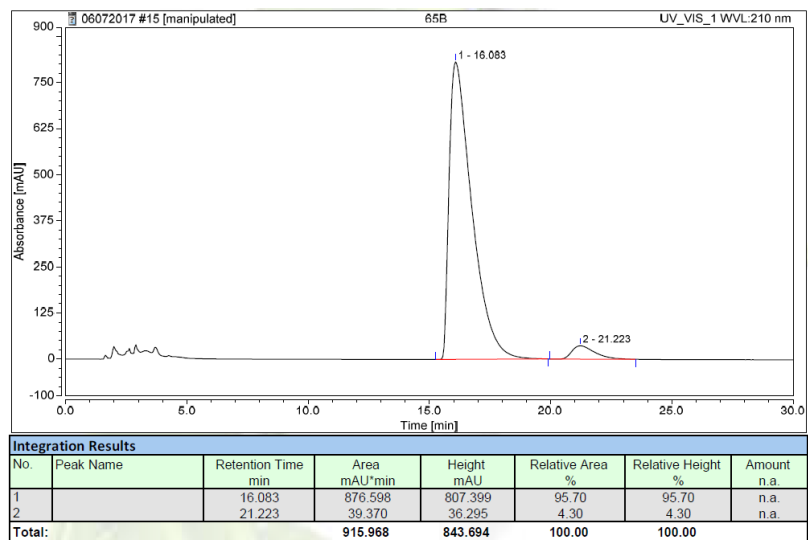
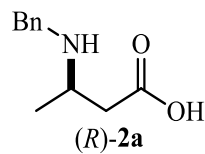
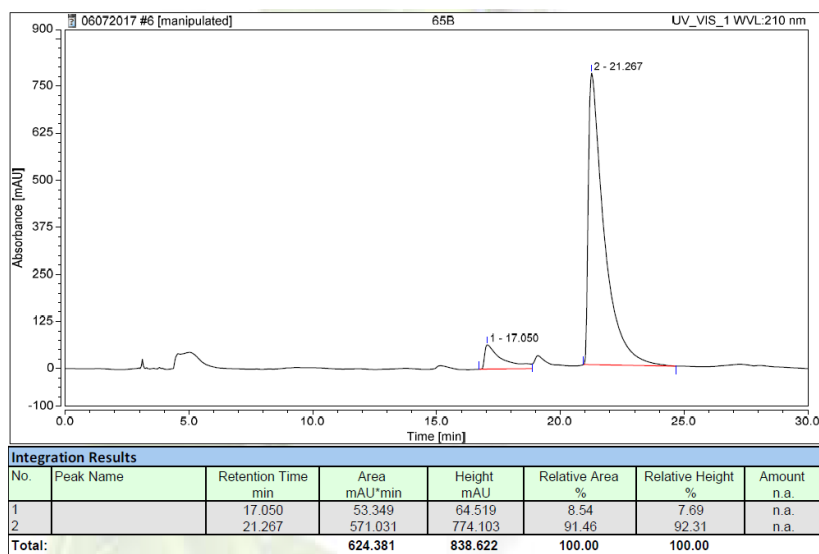
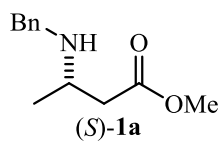
For entry 4.



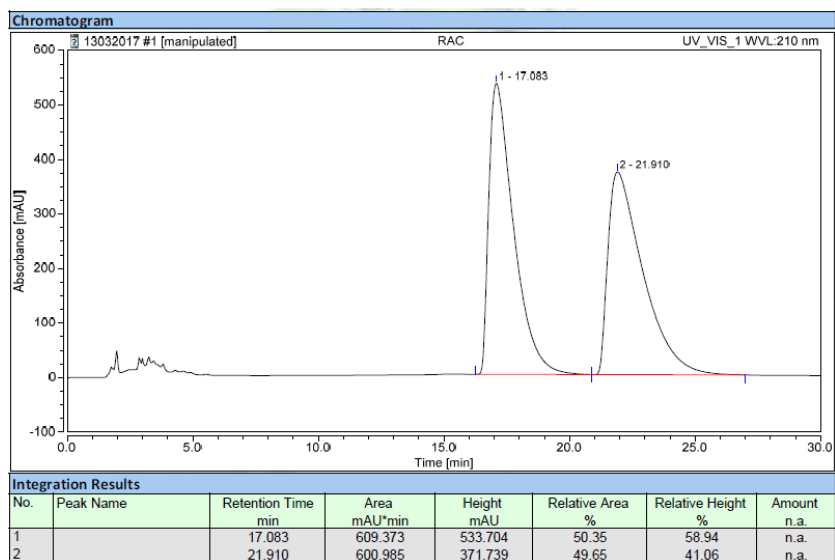
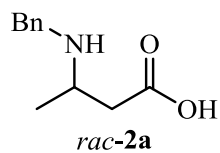
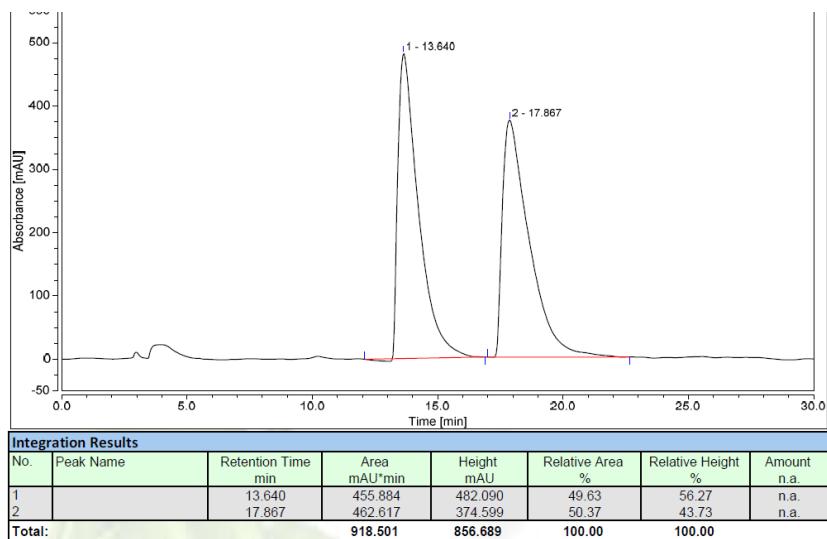
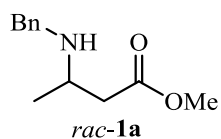
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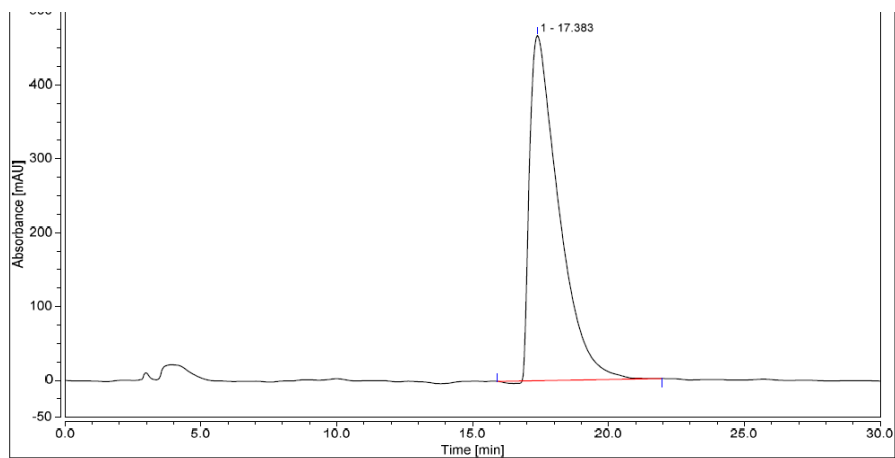
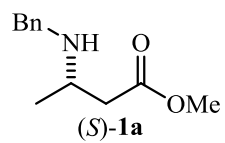
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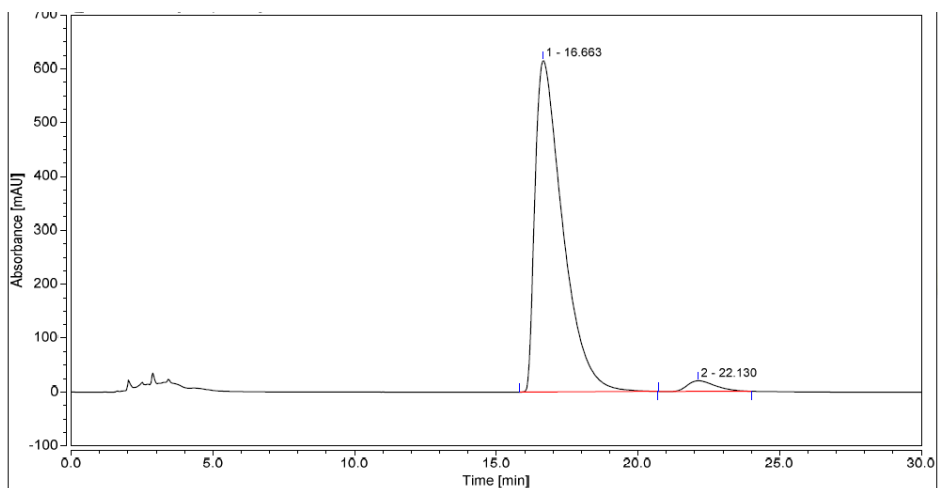
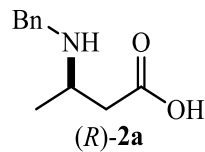
- Chromatograms for scaling-up for the enzymatic hydrolysis using the substrate **1a** (Table S4).



For entry 1.

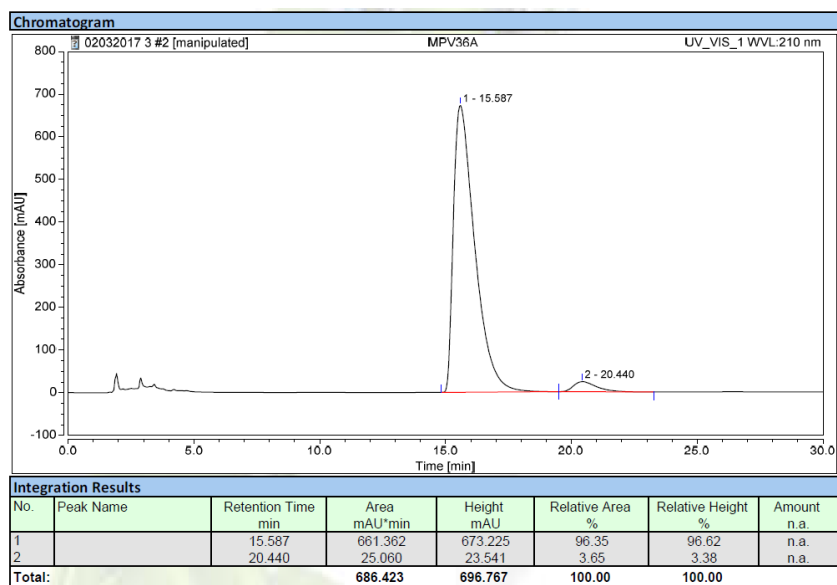
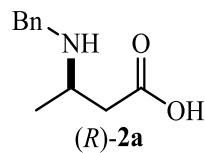
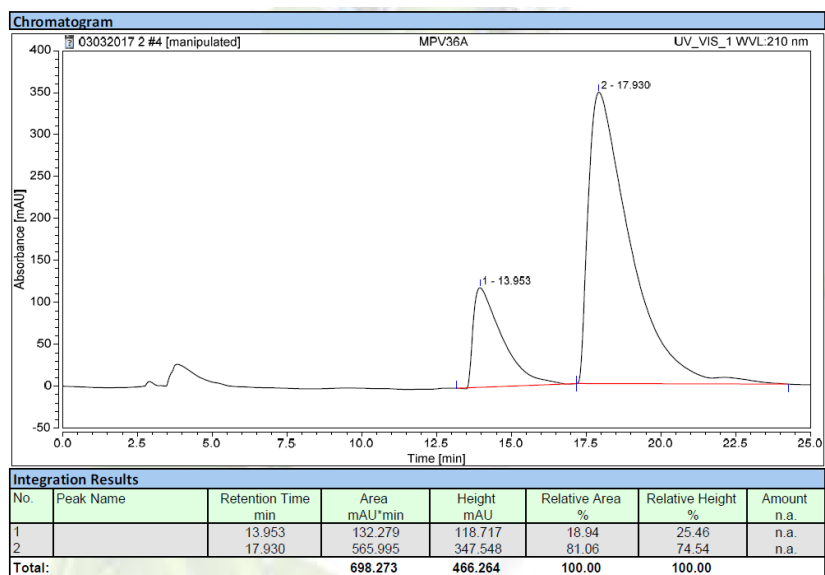
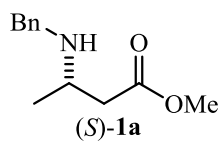


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		17.383	579.249	467.640	100.00	100.00	n.a.
Total:			579.249	467.640	100.00	100.00	

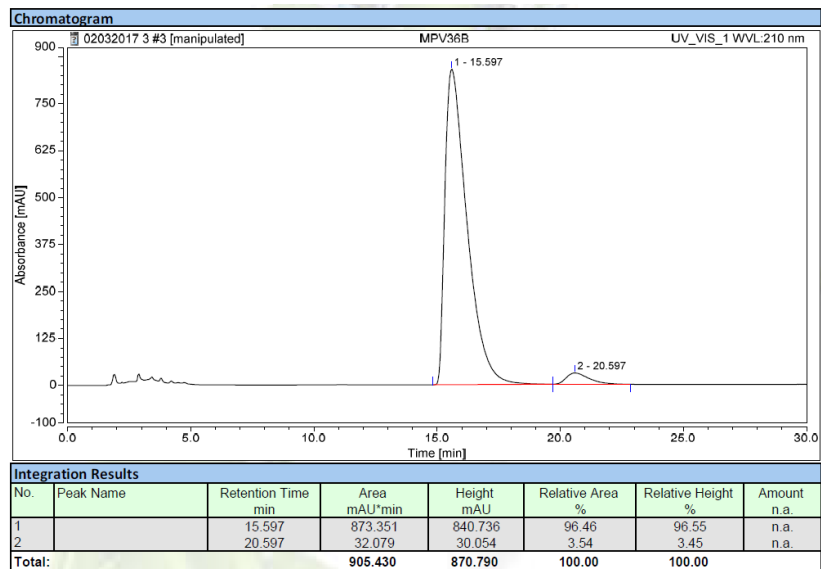
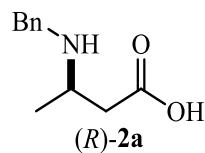
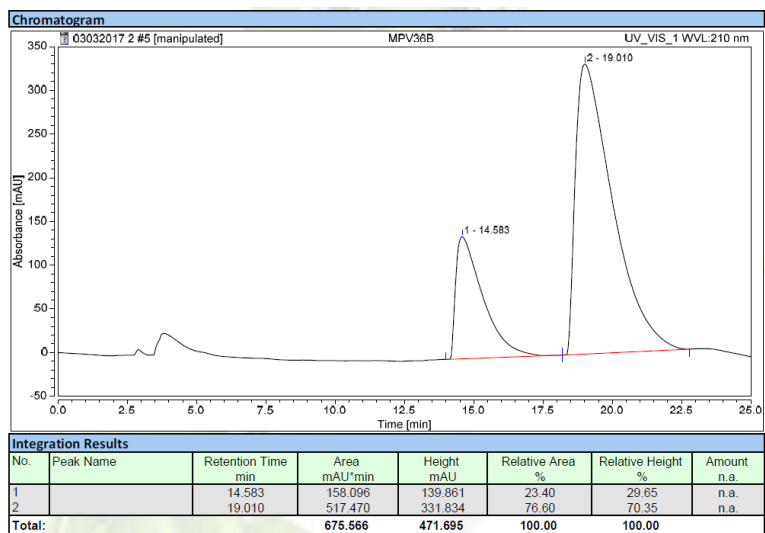
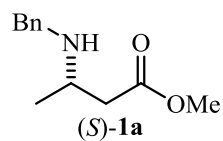


Integration Results							
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		16.663	693.709	615.390	96.91	96.90	n.a.
2		22.130	22.121	19.698	3.09	3.10	n.a.
Total:			715.830	635.088	100.00	100.00	

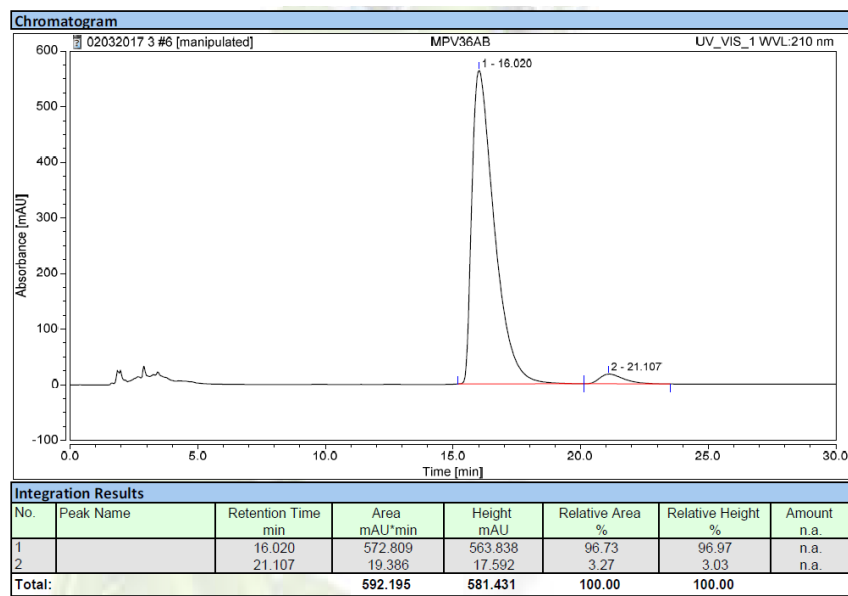
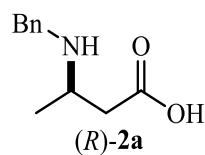
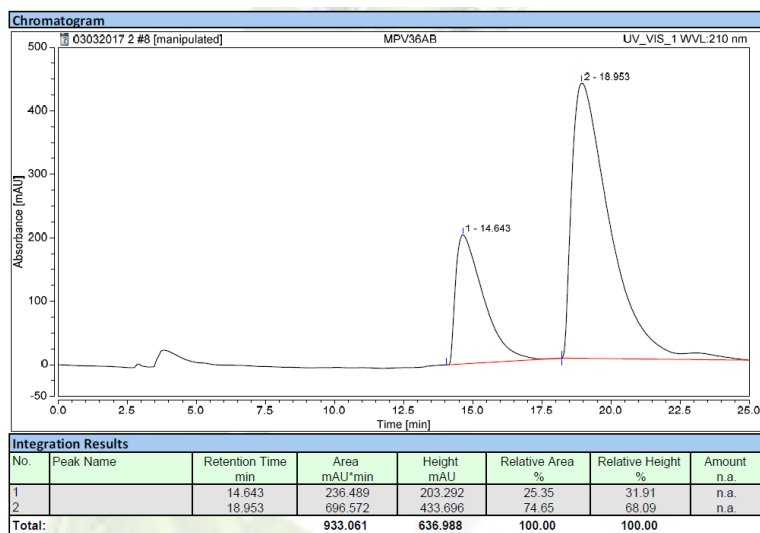
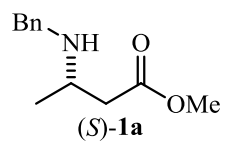
For entry 2.



For entry 3.



For entry 4.



7) HPLC conditions and retention times for the substrates *rac*-1a to *rac*-1j and hydrolysis products 2a to 2j.

Substrates		Products	
Conditions		Conditions	
Column, Eluent, Flow(mL/min), Time(min)		Column, Eluent, Flow(mL/min), Time(min)	
1a	Chiralpack OD , Hex/IPA (99:1), 1, 30	2a	Chirobiotic TAG , MeOH, 1, 30
1b	Chiralpack OD-H , Hex/IPA (98:2), 1, 30	2b	Chirobiotic T , EtOH/H ₂ O (70:30), 0.5, 30
1c	Chiralpack OD-H , Hex/IPA (99:1), 0.6, 30	2c	Chirobiotic T , EtOH/H ₂ O (70:30), 0.5, 30
1d	Chiralpack AD-H , Hex/IPA (99:1), 0.6, 30	2d	Chirobiotic T , EtOH/H ₂ O (70:30), 0.5, 30
1e	Chiralpack AD-H , Hex/IPA (99:1), 0.6, 30	2e	Chirobiotic T , EtOH/H ₂ O (70:30), 0.5, 30
1f	Chiralpack AD-H , Hex/IPA (99:1), 0.6, 30	2f	Chirobiotic T , EtOH/H ₂ O (70:30), 0.5, 30
1g	Chiralpack OD-H , Hex/IPA (95:5), 1, 30	2g	Chirobiotic T , MeOH/H ₂ O (95:5), 0.8, 20
1h	Chiralpack OD , Hex/IPA (99:1), 0.9, 45	2h	Chirobiotic TAG , MeOH, 0.8, 30
1i	Chiralpack AD-H , Hex/IPA (99:1), 1, 15	2i	Chirobiotic T , EtOH/H ₂ O (70:30), 0.5, 40

Substrates			Products		
Retention time (min)			Retention time (min)		
	t_R	t_S		t_R	t_S
1a	13.64	17.86	2a	17.08	21.91
1b	8.70	11.51	2b	17.14	20.50
1c	22.76	25.50	2c	16.31	19.50
1d	15.13	18.50	2d	14.93	17.58
1e	20.65	24.87	2e	14.03	16.96
1f	14.41	17.70	2f	13.21	15.69
1g	13.09	7.68	2g	10.97	10.05
1h	24.58	32.58	2h	7.96	7.13
1i	4.93	7.03	2i	17.46	29.07

8) Determinations of the absolute configuration for the products 2a to 2j.

For the determination of the absolute configuration of all products we used different methodologies. A crystallographic report for product (*R*)-**2a** was obtained and the ORTEP diagram are show below, as well, a CIF report is attached to this archive, the absolute configuration for this product was determined as *R*, furthermore, the specific optical rotation was compared with the reported by Escalante [4] (Table S2, entry 1).

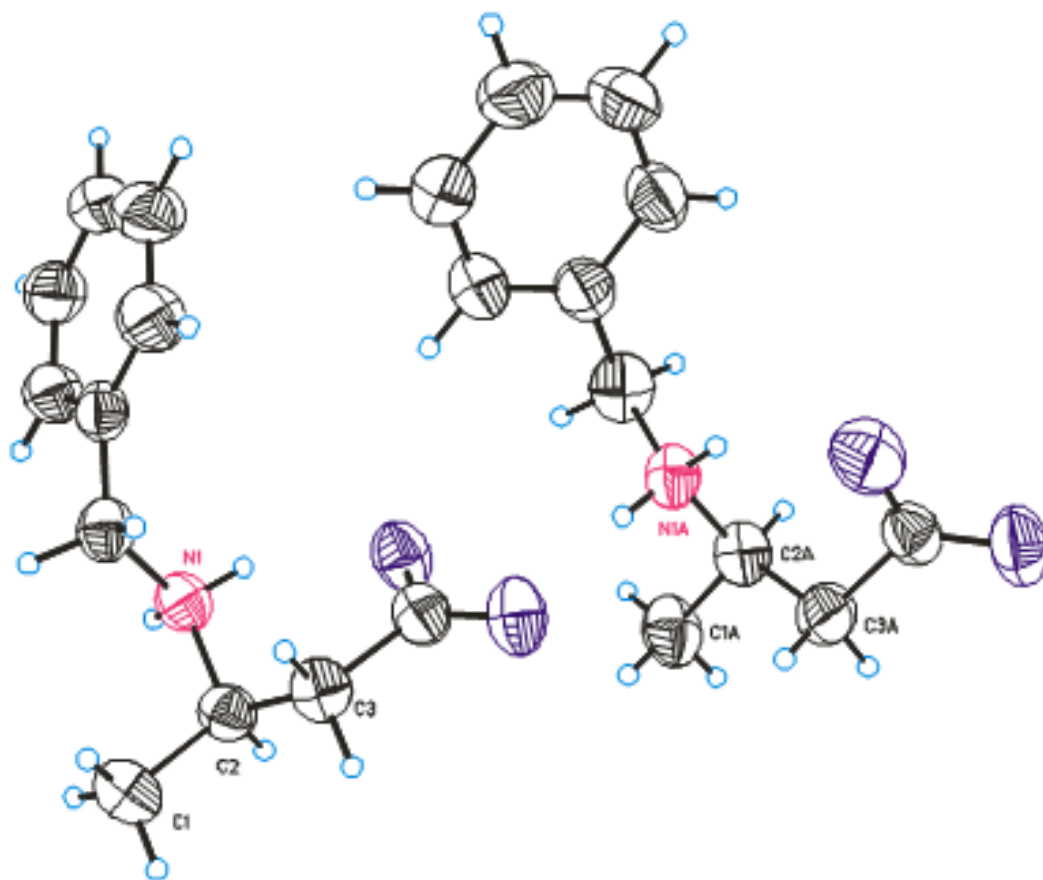
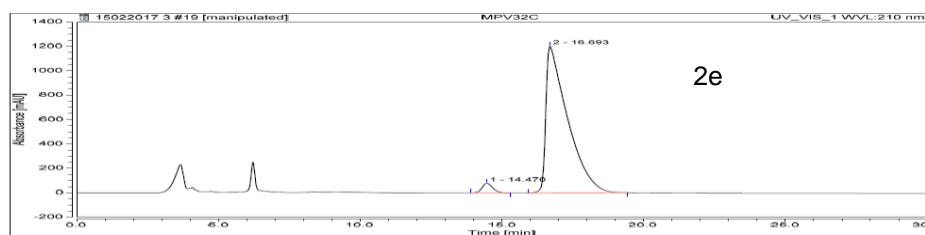
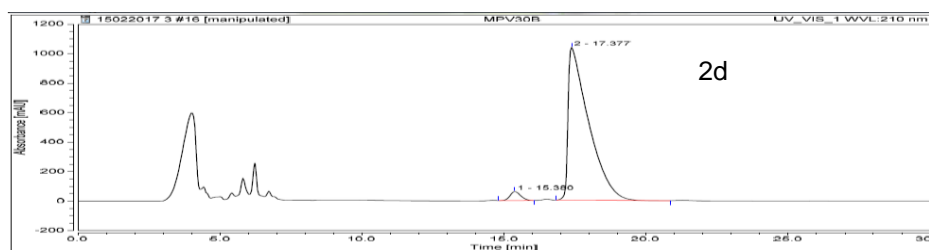
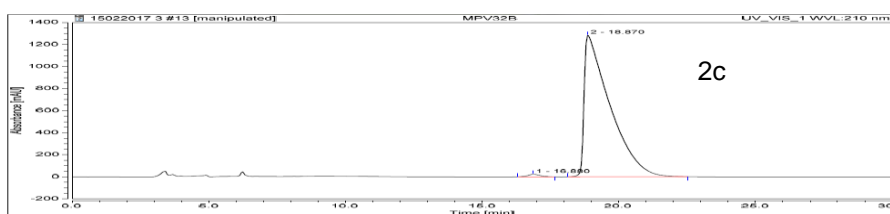
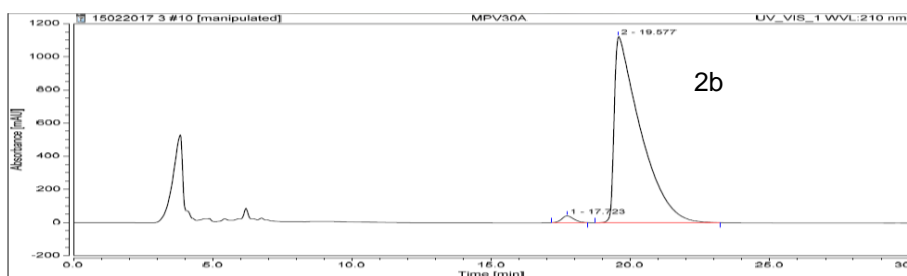
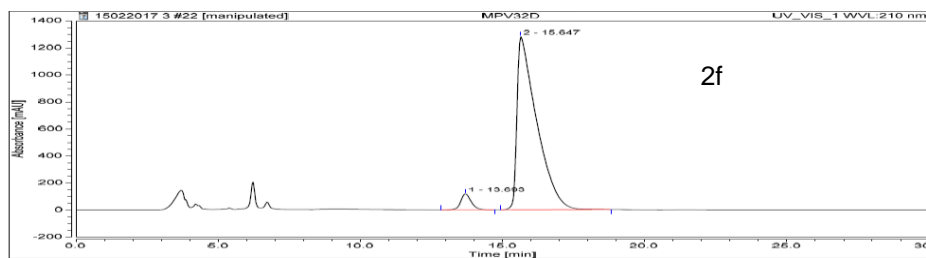


Figure S50. ORTEP diagram for product (*R*)-**2a**.

The absolute configuration of product **2b** was assigned by chemical comparison with the reported data [17], **reference (S)-2b** $[\alpha]_D^{25} = +32.4$ and $ee > 99\%$, **product (R)-2b** $[\alpha]_D^{25} = -36.5$ and $ee = 97\%$, obtaining an *R* configuration. The products **2c** to **2f** were assigned followed an elution sequence general rule already describe [18] using the same column that we used (Chirobiotic T). With the certainty that product **2b** has a well know absolute configuration and that the elution sequence for the majority product is the same for product **2b** to **2f** we assigned the same configuration for all them (*R*).





The absolute configuration for products **2g** and **2i** was assigned by chemical comparison [4], **reference (S)-2g**⁴ $[\alpha]_D^{20} = -51.9$ and $ee > 99\%$, **product (S)-2g** $[\alpha]_D^{25} = -35.0$ and $ee = 83\%$, **reference (S)-2i**⁴ $[\alpha]_D^{20} = +26$ and $ee > 99\%$, **product (S)-2i** $[\alpha]_D^{25} = +12.8$ and $ee = 94\%$, and for product **2h** an elution sequence general rule was used, compare product **2a** and **2h**, obtaining the S configuration for product **2h**.

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