

Supporting Information

A Dienamine-Mediated Deconjugative Addition/Cyclization Cascade of γ,γ -Disubstituted Enals with Carboxylic-Activated Enones: A Rapid Access to Highly Functionalized γ -Lactones

Wei Jiang,^{a,c} Jia Zhou,^c Ai-Jun Ma,^a Dongli Li,^a Yan-Yan Ma,^a Deng-Gao Zhao,^a Si-Hua Hou,^c Jun-Bing Lin,^{*,b,c} and Shu-Yu Zhang^{*,a,c}

^a School of Biotechnology and Health Sciences, International Healthcare Innovation Institute, Wuyi University, Jiangmen, 529020, China.

^b Shaanxi Key Laboratory of Chemical Reaction Engineering, College of Chemistry and Chemical Engineering, Yan'an University, Yan'an 716000, China.

^c Shanghai Key Laboratory for Molecular Engineering of Chiral Drugs, School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, Shanghai, 200240, China

Contents

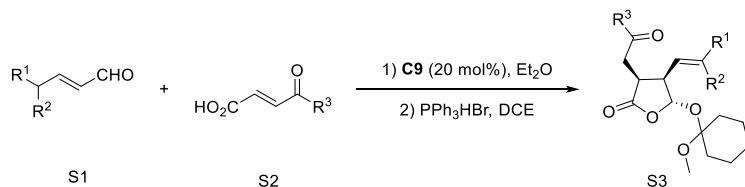
1 General Information.....	1
2 General Procedure for the Synthesis of γ -Lactones S3.....	1
3 Synthetical Transformations	1
4 X-ray Crystallographic Data of Product 3m	2
5 Characterization Data for the Products	4
6 References.....	18
7 ^1H NMR and ^{13}C NMR Spectra	19
8 HPLC and UPC Trace.....	47

1 General Information

All ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AVANCE III HD 400, 500 and 600 instruments and calibrated using residual solvent peaks as internal reference. Enantiomeric excesses were measured on Agilent HPLC and Waters UPC. High resolution ESI mass experiments were operated on a SolariX 7.0T FT ICRMS. Optical rotations were measured on a Rudolph Research Analytical (Autopol VI).

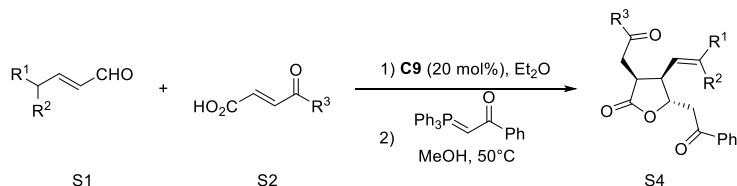
All chemicals and materials in the experiments were purchased from commercial suppliers and used as received unless otherwise noted. Flash Column chromatography was performed using 200-300 mesh silica gel, SiO_2 . The α, β -unsaturated aldehydes^[1], 4-oxa- α, β -unsaturated carboxylic acids^[2,3] and 1-methoxycyclohex-1-ene^[4] were prepared according to known procedures.

2 General Procedure for the Synthesis of γ -Lactones S3



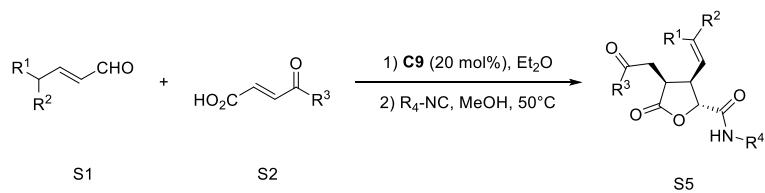
A reaction mixture of 4-oxa- α, β -unsaturated carboxylic acids **S2** (1 mmol, 1.0 eq.), α, β -unsaturated aldehydes **S1** (2 mmol, 2.0 eq.) and diphenylprolinol silyl ether **C9** (0.2 mmol, 0.2 eq.) in 5 ml Et₂O stirred at 25°C for 24-72 h until completion of the reaction (monitored by TLC). The reaction mixture was concentrated in vacuo and the resulting residue was treated with PPh₃HBr (0.1 mmol, 0.1 eq.), 1-methoxycyclohex-1-ene (10 mmol, 10 eq.) and 10 ml DCE. After stirred at 25°C for 6-12 h until completion of the reaction (monitored by TLC), The reaction mixture was concentrated in vacuo and purified by flash column chromatography to give the desired product **S3**.

3 Synthetical Transformations



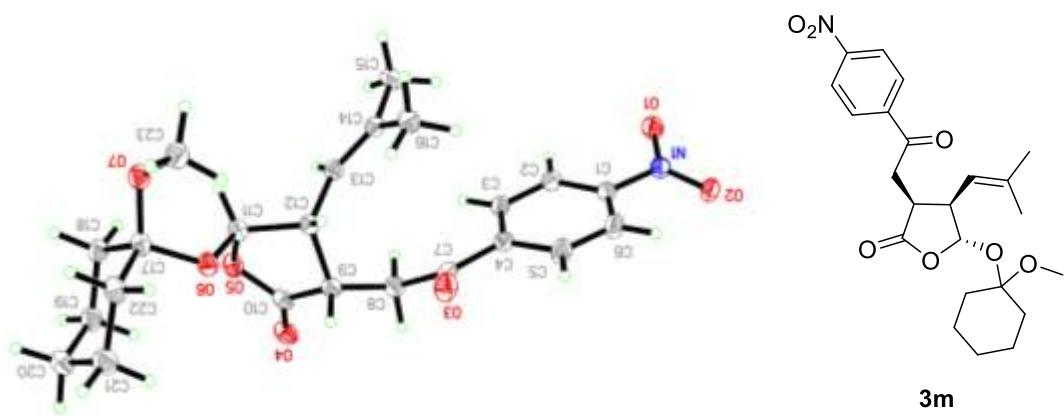
A reaction mixture of 4-oxa- α, β -unsaturated carboxylic acids **S2** (1 mmol, 1.0 eq.), α, β -unsaturated aldehydes **S1** (2 mmol, 2.0 eq.) and diphenylprolinol silyl ether **C9** (0.2

mmol, 0.2 eq.) in 5 ml Et₂O stirred at 25°C for 24-72 h until completion of the reaction (monitored by TLC). The reaction mixture was concentrated in vacuo and the resulting residue was treated with (benzoylmethylene)triphenylphosphorane (3 mmol, 3.0 eq.) and 10 ml MeOH. After stirred at 50°C for 6-12 h until completion of the reaction (monitored by TLC), The reaction mixture was concentrated in vacuo and purified by flash column chromatography to give the desired product **S4**.



A reaction mixture of 4-oxa- α , β -unsaturated carboxylic acids **S2** (1 mmol, 1.0 eq.), α , β -unsaturated aldehydes **S1** (2 mmol, 2.0 eq.) and diphenylprolinol silyl ether **C9** (0.2 mmol, 0.2 eq.) in 5 ml Et₂O stirred at 25°C for 24-72 h until completion of the reaction (monitored by TLC). The reaction mixture was concentrated in vacuo and the resulting residue was treated with isonitrile (2.4 mmol, 2.4 eq.) and 10 ml MeOH. After stirred at 50°C for 6-12 h until completion of the reaction (monitored by TLC), The reaction mixture was concentrated in vacuo and purified by flash column chromatography to give the desired product **S5**.

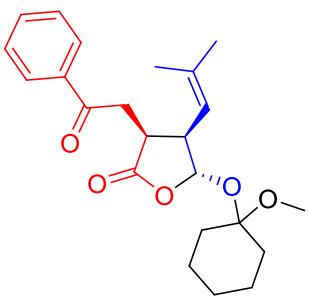
4 X-ray Crystallographic Data of Product 3m



X-Ray of 3m (CCDC:1936160)

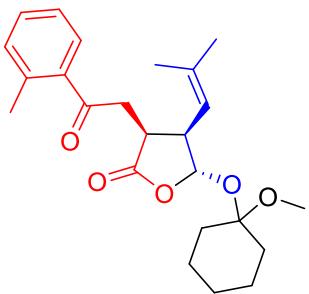
Identification code	ta_a
Empirical formula	C23 H29 N O7
Formula weight	431.47
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 7.0322(5) Å alpha = 90 deg. b = 15.7295(11) Å beta = 90 deg. c = 20.0907(14) Å gamma = 90 deg.
Volume	2222.3(3) Å^3
Z, Calculated density	4, 1.290 Mg/m^3
Absorption coefficient	0.790 mm^-1
F(000)	920
Crystal size	0.200 x 0.200 x 0.180 mm
Theta range for data collection	3.569 to 68.335 deg.
Limiting indices	-8<=h<=8, -18<=k<=18, -24<=l<=24
Reflections collected / unique	17072 / 4066 [R(int) = 0.0509]
Completeness to theta	= 67.679 99.9 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4066 / 0 / 283
Goodness-of-fit on F^2	1.022
Final R indices [I>2sigma(I)]	R1 = 0.0359, wR2 = 0.0939
R indices (all data)	R1 = 0.0376, wR2 = 0.0961
Absolute structure parameter	0.09(7)
Extinction coefficient	n/a
Largest diff. peak and hole	0.233 and -0.232 e.Å^-3

5 Characterization Data for the Products



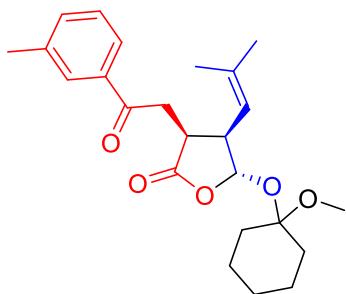
3a:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-oxo-2-phenylethyl)dihydrofuran-2(3H)-one

colourless oil; 225 mg; 58% yield; 99% ee; $[\alpha]_{D20} = 7.33$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, Acetone-d₆) δ 8.09 - 7.95 (m, 2H), 7.69 - 7.60 (m, 1H), 7.59 - 7.47 (m, 2H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.02 - 4.92 (m, 1H), 3.71 - 3.57 (m, 1H), 3.51 - 3.41 (m, 1H), 3.35 - 3.26 (m, 2H), 3.20 (s, 3H), 1.82 - 1.31 (m, 16H). ¹³C NMR (100 MHz, Acetone-d₆) δ 198.2, 178.1, 138.2, 137.6, 134.0, 129.5, 128.7, 120.0, 103.1, 100.2, 48.3, 45.8, 38.9, 35.9, 35.6, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₃H₃₀O₅ [M+H]⁺: 387.21660, Found 387.21657. HPLC analysis: Chiraldak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, *t*_{major} = 11.8 min, *t*_{minor} = 14.4 min

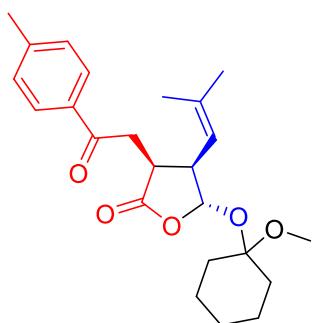


3b:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-oxo-2-(o-tolyl)ethyl)dihydrofuran-2(3H)-one

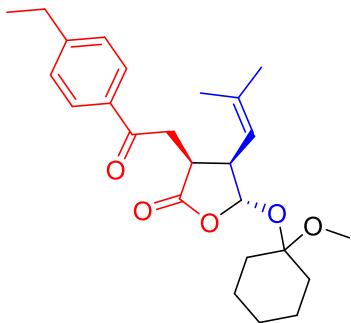
colourless oil; 228 mg; 57% yield; 96% ee; $[\alpha]_{D20} = -15.33$ (*c* 0.3, CHCl₃); ¹H NMR (500 MHz, Acetone-d₆) δ 7.75 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.46 - 7.39 (m, 1H), 7.37 - 7.24 (m, 2H), 5.51 (d, *J* = 1.0 Hz, 1H), 5.03 - 4.97 (m, 1H), 3.66 - 3.57 (m, 1H), 3.53 - 3.45 (m, 1H), 3.26 (dd, *J* = 18.5, 4.0 Hz, 1H), 3.22 - 3.13 (m, 4H), 2.44 (s, 3H), 1.80 - 1.35 (m, 16H). ¹³C NMR (125 MHz, Acetone-d₆) δ 202.0, 178.1, 138.6, 138.4, 138.2, 132.6, 132.2, 129.4, 126.7, 120.0, 103.2, 100.3, 48.3, 45.8, 38.8, 38.5, 35.9, 33.6, 25.9, 25.8, 23.5, 23.4, 21.1, 18.1. HRMS: calculated for C₂₄H₃₂O₅ [M+H]⁺: 401.23225, Found 401.23220. HPLC analysis: Chiraldak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, *t*_{major} = 10.8min, *t*_{minor} = 13.0 min



3c:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-oxo-2-(m-tolyl)ethyl)dihydrofuran-2(3H)-one
colourless oil; 272 mg; 68% yield; 98% ee; $[\alpha]_{D20} = 3.33$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 7.96 - 7.66 (m, 2H), 7.59 - 7.30 (m, 2H), 5.51 (d, *J* = 1.2 Hz, 1H), 5.01 - 4.91 (m, 1H), 3.71 - 3.57 (m, 1H), 3.52 - 3.39 (m, 1H), 3.35 - 3.24 (m, 2H), 3.20 (s, 3H), 2.41 (s, 3H), 1.82 - 1.31 (m, 16H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 198.3, 178.1, 139.3, 138.3, 137.7, 134.7, 129.4, 129.2, 125.9, 120.0, 103.2, 100.2, 48.3, 45.8, 38.9, 35.9, 35.7, 33.6, 25.8, 25.8, 23.5, 23.4, 21.3, 18.0. HRMS: calculated for C₂₄H₃₂O₅ [M+H]⁺: 401.23225, Found 401.23221. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 11.6 min, *t*_{minor} = 13.5 min

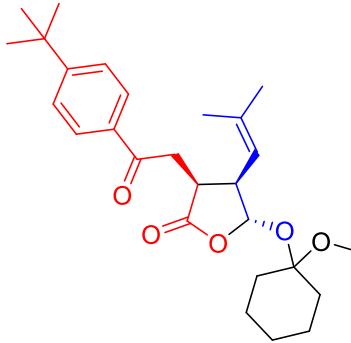


3d:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-oxo-2-(p-tolyl)ethyl)dihydrofuran-2(3H)-one
colourless oil; 304 mg; 76% yield; 98% ee; $[\alpha]_{D20} = -0.67$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 8.10 - 7.74 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 5.51 (d, *J* = 1.2 Hz, 1H), 4.95 (dt, *J* = 10.9, 1.5 Hz, 1H), 3.71 - 3.55 (m, 1H), 3.51 - 3.39 (m, 1H), 3.31 - 3.22 (m, 2H), 3.20 (s, 3H), 2.41 (s, 3H), 1.81 - 1.28 (m, 16H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 197.7, 178.2, 144.8, 138.2, 135.2, 130.1, 128.8, 120.0, 103.1, 100.2, 48.3, 45.8, 38.9, 35.9, 35.5, 33.6, 25.8, 25.8, 23.5, 23.4, 21.5, 18.0. HRMS: calculated for C₂₄H₃₂O₅ [M+H]⁺: 401.23225, Found 401.23219. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 13.4 min, *t*_{minor} = 14.9 min



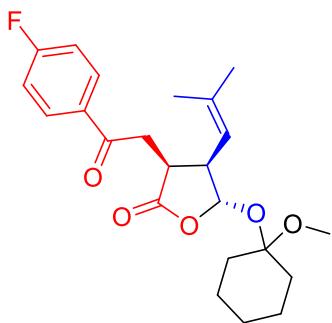
3e:(3S,4R,5R)-3-(2-(4-ethylphenyl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 323 mg; 78% yield; 99% ee; $[\alpha]_{D20} = -4.57$ (*c* 0.35, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 8.12 - 7.73 (m, 2H), 7.56 - 7.13 (m, 2H), 5.51 (d, *J* = 1.2 Hz, 1H), 5.01 - 4.91 (m, 1H), 3.67 - 3.59 (m, 1H), 3.50 - 3.40 (m, 1H), 3.36 - 3.24 (m, 2H), 3.20 (s, 3H), 2.72 (q, *J* = 7.6 Hz, 2H), 1.82 - 1.30 (m, 16H), 1.24 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 197.7, 178.2, 150.9, 138.2, 135.4, 129.0, 128.9, 120.0, 103.1, 100.2, 48.3, 45.8, 38.9, 35.9, 35.5, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0, 15.6. HRMS: calculated for C₂₅H₃₄O₅ [M+H]⁺: 415.24790, Found 415.24795. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 12.4 min, *t*_{minor} = 14.2 min



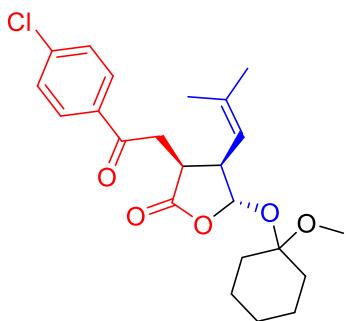
3f:(3S,4R,5R)-3-(2-(4-(tert-butyl)phenyl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 327 mg; 74% yield; 99% ee; $[\alpha]_{D20} = -4.00$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 8.07 - 7.77 (m, 2H), 7.66 - 7.50 (m, 2H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.02 - 4.89 (m, 1H), 3.68 - 3.57 (m, 1H), 3.50 - 3.42 (m, 1H), 3.28 (d, *J* = 6.8 Hz, 2H), 3.20 (s, 3H), 1.80 - 1.30 (m, 25H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 197.7, 178.2, 157.6, 138.3, 135.2, 128.7, 126.4, 120.0, 103.1, 100.2, 48.3, 45.8, 38.9, 35.9, 35.6, 35.5, 33.6, 31.3, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₇H₃₈O₅ [M+H]⁺: 443.27920, Found 443.27902. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 11.1 min, *t*_{minor} = 13.4 min



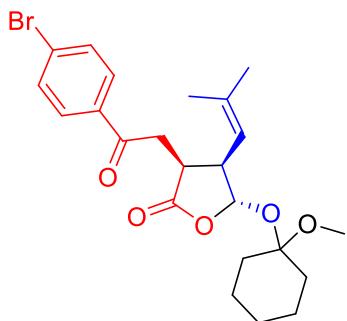
3g:(3S,4R,5R)-3-(2-(4-fluorophenyl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 302 mg; 75% yield; 99% ee; $[\alpha]_{D20} = 7.65$ (*c* 0.34, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 8.19 - 7.96 (m, 2H), 7.48 - 7.07 (m, 2H), 5.51 (d, *J* = 0.8 Hz, 1H), 5.04 - 4.89 (m, 1H), 3.71 - 3.58 (m, 1H), 3.51 - 3.40 (m, 1H), 3.37 - 3.26 (m, 2H), 3.20 (s, 3H), 1.81 - 1.32 (m, 16H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 196.8, 178.1, 166.6 (d, *J* = 253.3 Hz), 138.3, 134.3 (d, *J* = 3.0 Hz), 131.7 (d, *J* = 9.4 Hz), 120.0, 116.4 (d, *J* = 21.9 Hz), 103.2, 100.2, 48.3, 45.8, 38.9, 35.9, 35.6, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₃H₂₉FO₅ [M+H]⁺: 405.20718, Found 405.20724. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 11.1 min, *t*_{minor} = 12.7 min



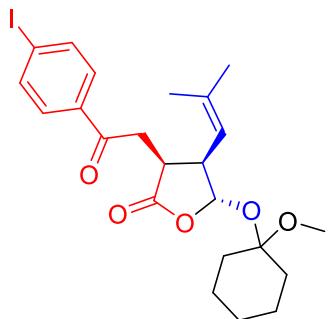
3h:(3S,4R,5R)-3-(2-(4-chlorophenyl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 340 mg; 81% yield; 99% ee; $[\alpha]_{D20} = -3.89$ (*c* 0.36, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 8.10 - 7.94 (m, 2H), 7.68 - 7.40 (m, 2H), 5.51 (d, *J* = 1.2 Hz, 1H), 5.05 - 4.91 (m, 1H), 3.71 - 3.57 (m, 1H), 3.53 - 3.41 (m, 1H), 3.31 (d, *J* = 6.8 Hz, 2H), 3.20 (s, 3H), 1.82 - 1.31 (m, 16H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 197.3, 178.0, 139.8, 138.3, 136.2, 130.5, 129.7, 120.0, 103.2, 100.2, 48.3, 45.8, 38.9, 35.9, 35.6, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₃H₂₉ClO₅ [M+H]⁺: 421.17763, Found 421.17749. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 11.1 min, *t*_{minor} = 13.3 min



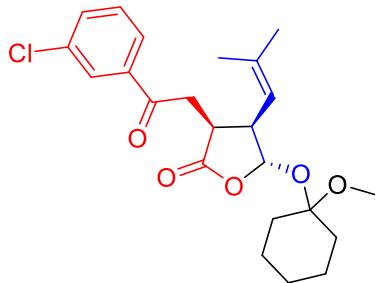
3i:(3S,4R,5R)-3-(2-(4-bromophenyl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 392 mg; 84% yield; 99% ee; $[\alpha]_{D20} = -4.50$ (*c* 0.4, CHCl₃); ¹H NMR (500 MHz, Acetone-*d*₆) δ 8.02 - 7.88 (m, 2H), 7.81 - 7.67 (m, 2H), 5.51 (d, *J* = 1.5 Hz, 1H), 5.02 - 4.89 (m, 1H), 3.69 - 3.59 (m, 1H), 3.51 - 3.41 (m, 1H), 3.30 (d, *J* = 6.5 Hz, 2H), 3.20 (s, 3H), 1.80 - 1.33 (m, 16H). ¹³C NMR (125 MHz, Acetone-*d*₆) δ 197.5, 178.0, 138.3, 136.6, 132.7, 130.6, 128.5, 120.0, 103.2, 100.2, 48.3, 45.8, 38.9, 35.9, 35.6, 33.6, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₃H₂₉BrO₅ [M+H]⁺: 465.12711, Found 465.12684. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 11.7 min, *t*_{minor} = 14.3 min



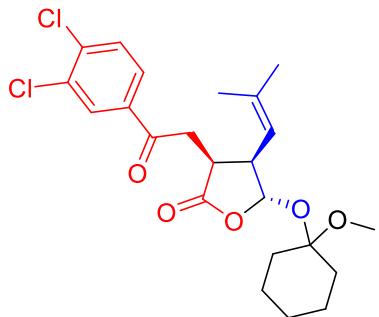
3j:(3S,4R,5R)-3-(2-(4-iodophenyl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

white solid; 388 mg; 76% yield; 99% ee; $[\alpha]_{D20} = 11.33$ (*c* 0.3, CHCl₃); ¹H NMR (500 MHz, Acetone-*d*₆) δ 8.07 - 7.86 (m, 2H), 7.82 - 7.69 (m, 2H), 5.51 (d, *J* = 1.5 Hz, 1H), 5.01 - 4.89 (m, 1H), 3.69 - 3.58 (m, 1H), 3.49 - 3.41 (m, 1H), 3.29 (d, *J* = 7.0 Hz, 2H), 3.19 (s, 3H), 1.79 - 1.33 (m, 16H). ¹³C NMR (125 MHz, Acetone-*d*₆) δ 197.8, 178.0, 138.8, 138.3, 137.0, 130.4, 119.9, 103.1, 101.4, 100.2, 48.3, 45.7, 38.9, 35.9, 35.5, 33.6, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₃H₂₉IO₅ [M+H]⁺: 513.11324, Found 513.11306. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 12.7 min, *t*_{minor} = 16.0 min



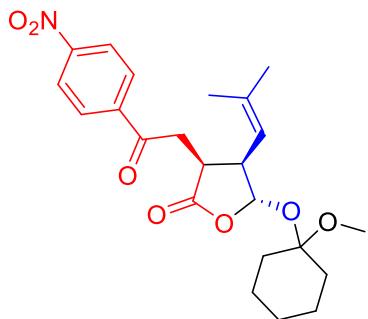
3k:(3S,4R,5R)-3-(2-(3-chlorophenyl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 313 mg; 75% yield; 98% ee; $[\alpha]_{D20} = 10.67$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 8.01 - 7.93 (m, 2H), 7.78 - 7.62 (m, 1H), 7.57 (t, *J* = 8.0 Hz, 1H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.02 - 4.93 (m, 1H), 3.71 - 3.58 (m, 1H), 3.53 - 3.41 (m, 1H), 3.38 - 3.29 (m, 2H), 3.20 (s, 3H), 1.80 - 1.32 (m, 16H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 197.3, 177.9, 139.4, 138.4, 135.3, 133.8, 131.4, 128.5, 127.3, 120.0, 103.2, 100.3, 48.3, 45.8, 38.9, 35.9, 35.8, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₃H₂₉ClO₅ [M+H]⁺: 421.17763, Found 421.17751. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 10.8 min, *t*_{minor} = 13.9 min



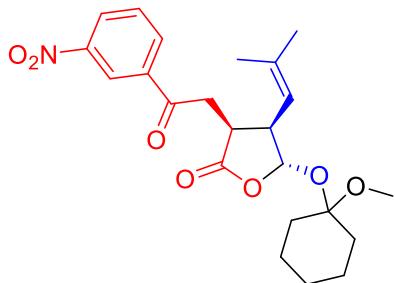
3l:(3S,4R,5R)-3-(2-(3,4-dichlorophenyl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 304 mg; 67% yield; 99% ee; $[\alpha]_{D20} = 2.67$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 8.15 (d, *J* = 2.0 Hz, 1H), 8.01 - 7.94 (m, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 5.51 (d, *J* = 1.2 Hz, 1H), 5.05 - 4.90 (m, 1H), 3.71 - 3.58 (m, 1H), 3.51 - 3.41 (m, 1H), 3.34 (d, *J* = 6.8 Hz, 2H), 3.20 (s, 3H), 1.81 - 1.28 (m, 16H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 196.6, 177.9, 138.4, 137.7, 137.6, 133.4, 131.9, 130.7, 128.6, 120.0, 103.2, 100.3, 48.3, 45.8, 39.0, 35.9, 35.8, 33.6, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₃H₂₈Cl₂O₅ [M+H]⁺: 455.13866, Found 455.13844. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 11.4 min, *t*_{minor} = 14.1 min



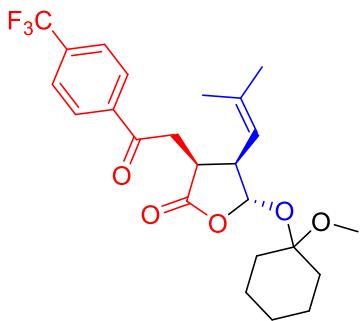
3m:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-(4-nitrophenyl)-2-oxoethyl)dihydrofuran-2(3H)-one

white solid; 224 mg; 52% yield; 99% ee; $[\alpha]_{D20} = -1.33$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, Acetone-d₆) δ 8.45 - 8.32 (m, 2H), 8.31 - 8.23 (m, 2H), 5.52 (d, *J* = 1.2 Hz, 1H), 5.07 - 4.89 (m, 1H), 3.74 - 3.61 (m, 1H), 3.54 - 3.44 (m, 1H), 3.44 - 3.35 (m, 2H), 3.20 (s, 3H), 1.79 - 1.35 (m, 16H). ¹³C NMR (100 MHz, Acetone-d₆) δ 197.6, 177.9, 151.4, 142.1, 138.5, 130.1, 124.7, 119.9, 103.2, 100.3, 48.3, 45.8, 39.0, 36.2, 35.9, 33.6, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₃H₂₉NO₇ [M+NH₄]⁺: 449.22823, Found 449.22798. HPLC analysis: Chiralpak ID, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 15.9 min, *t*_{minor} = 12.9 min



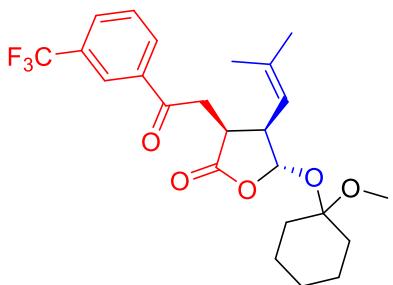
3n:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-(3-nitrophenyl)-2-oxoethyl)dihydrofuran-2(3H)-one

colourless oil; 245 mg; 57% yield; 98% ee; $[\alpha]_{D20} = 8.00$ (*c* 0.4, CHCl₃); ¹H NMR (400 MHz, Acetone-d₆) δ 8.75 (t, *J* = 2.0 Hz, 1H), 8.59 - 8.28 (m, 2H), 7.88 (t, *J* = 8.0 Hz, 1H), 5.53 (d, *J* = 1.2 Hz, 1H), 5.10 - 4.90 (m, 1H), 3.75 - 3.63 (m, 1H), 3.56 - 3.39 (m, 3H), 3.20 (s, 3H), 1.83 - 1.31 (m, 16H). ¹³C NMR (100 MHz, Acetone-d₆) δ 196.9, 177.9, 149.5, 138.8, 138.5, 134.7, 131.3, 128.2, 123.2, 120.0, 103.2, 100.3, 48.3, 45.8, 39.0, 36.0, 35.9, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₃H₂₉NO₇ [M+H]⁺: 432.20168, Found 432.20143. HPLC analysis: Chiralpak ID, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 17.9 min, *t*_{minor} = 14.2 min



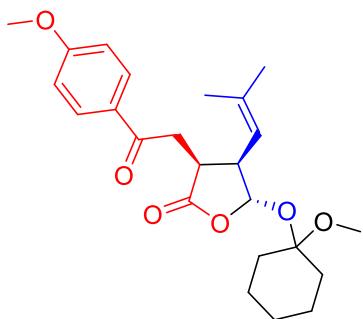
3o:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)dihydrofuran-2(3H)-one

white solid; 254 mg; 56% yield; 99% ee; $[\alpha]_{D20} = 29.00$ (*c* 0.2, CHCl₃); ¹H NMR (500 MHz, Acetone-*d*₆) δ 8.22 (d, *J* = 8.0 Hz, 2H), 7.89 (d, *J* = 8.5 Hz, 2H), 5.52 (d, *J* = 1.0 Hz, 1H), 5.04 - 4.91 (m, 1H), 3.71 - 3.62 (m, 1H), 3.52 - 3.44 (m, 1H), 3.44 - 3.32 (m, 2H), 3.20 (s, 3H), 1.81 - 1.33 (m, 16H). ¹³C NMR (125 MHz, Acetone-*d*₆) δ 197.8, 177.9, 140.6, 138.4, 134.5 (q, *J* = 32.5 Hz), 129.5, 126.5 (q, *J* = 3.9 Hz), 124.8 (q, *J* = 270.1 Hz), 119.9, 103.2, 100.2, 48.3, 45.8, 38.9, 36.0, 35.9, 33.6, 25.8, 25.8, 23.5, 23.4, 17.9. HRMS: calculated for C₂₄H₂₉F₃O₅ [M+H]⁺: 455.20399, Found 455.20402. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 8.0 min, *t*_{minor} = 9.4 min



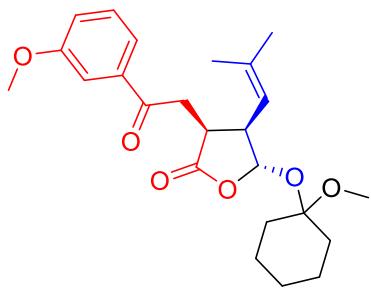
3p:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-oxo-2-(3-(trifluoromethyl)phenyl)ethyl)dihydrofuran-2(3H)-one

colourless oil; 278 mg; 61% yield; 99% ee; $[\alpha]_{D20} = 8.00$ (*c* 0.4, CHCl₃); ¹H NMR (500 MHz, Acetone-*d*₆) δ 8.38 - 8.24 (m, 2H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.81 (t, *J* = 7.8 Hz, 1H), 5.52 (d, *J* = 1.0 Hz, 1H), 5.05 - 4.93 (m, 1H), 3.72 - 3.62 (m, 1H), 3.52 - 3.44 (m, 1H), 3.44 - 3.33 (m, 2H), 3.20 (s, 3H), 1.78 - 1.34 (m, 16H). ¹³C NMR (125 MHz, Acetone-*d*₆) δ 197.5, 177.9, 138.4, 138.3, 132.5, 131.4 (q, *J* = 22.3 Hz), 130.8, 130.4 (q, *J* = 3.6 Hz), 125.2 (q, *J* = 3.9 Hz), 124.9 (q, *J* = 270.1 Hz), 120.0, 103.2, 100.3, 48.3, 45.7, 39.0, 35.9, 35.8, 33.6, 25.8, 25.7, 23.5, 23.4, 18.0. HRMS: calculated for C₂₄H₂₉F₃O₅ [M+H]⁺: 455.20399, Found 455.20382. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 ml/min, λ = 254 nm, *t*_{major} = 7.9 min, *t*_{minor} = 9.9 min



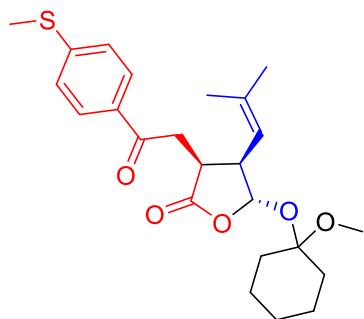
3q:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-3-(2-(4-methoxyphenyl)-2-oxoethyl)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 335 mg; 80% yield; 98% ee; $[\alpha]_{D20} = -9.33$ (*c* 0.3, CHCl₃); ¹H NMR (500 MHz, Acetone-d₆) δ 8.10 - 7.85 (m, 2H), 7.13 - 6.93 (m, 2H), 5.51 (d, *J* = 1.5 Hz, 1H), 4.99 - 4.89 (m, 1H), 3.89 (s, 3H), 3.67 - 3.57 (m, 1H), 3.48 - 3.39 (m, 1H), 3.28 - 3.21 (m, 2H), 3.19 (s, 3H) 1.76 - 1.35 (m, 16H). ¹³C NMR (125 MHz, Acetone-d₆) δ 196.5, 178.2, 164.6, 138.2, 131.0, 130.6, 120.0, 114.6, 103.1, 100.2, 55.9, 48.3, 45.8, 38.9, 35.9, 35.2, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. $[\alpha]_{D20} = -9.33$, (*c* 0.3, CHCl₃); HRMS: calculated for C₂₄H₃₂O₆ [M+H]⁺: 417.22717, Found 417.22706. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 12.6 min, t_{minor} = 14.4 min



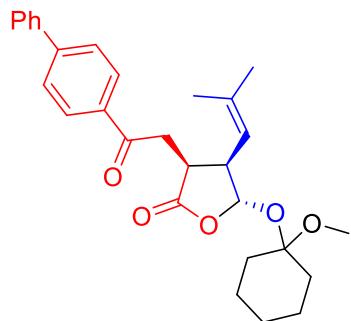
3r:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-3-(2-(3-methoxyphenyl)-2-oxoethyl)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 340 mg; 82% yield; 99% ee; $[\alpha]_{D20} = 12.00$ (*c* 0.3, CHCl₃); ¹H NMR (500 MHz, Acetone-*d*₆) δ 7.62 - 7.57 (m, 1H), 7.52 - 7.48 (m, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.22 - 7.18 (m, 1H), 5.52 (d, *J* = 1.5 Hz, 1H), 5.01 - 4.92 (m, 1H), 3.87 (s, 3H), 3.68 - 3.59 (m, 1H), 3.50 - 3.41 (m, 1H), 3.36 - 3.25 (m, 2H), 3.20 (s, 3H), 1.81 - 1.32 (m, 16H). ¹³C NMR (125 MHz, Acetone-*d*₆) δ 198.1, 178.1, 160.9, 139.0, 138.3, 130.6, 121.2, 120.0, 120.0, 113.3, 103.1, 100.3, 55.8, 48.3, 45.8, 38.9, 35.9, 35.8, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₄H₃₂O₆ [M+H]⁺: 417.22717, Found 417.22707. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 9.7 min, t_{minor} = 12.0 min



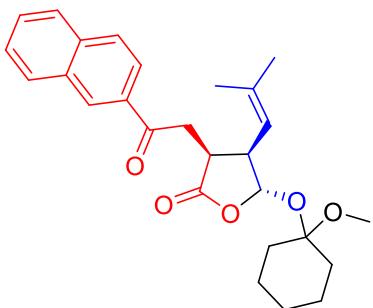
3s:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-(4-(methylthio)phenyl)-2-oxoethyl)dihydrofuran-2(3H)-one

colourless oil; 295 mg; 68% yield; 99% ee; $[\alpha]_{D20} = -23.50$ (*c* 0.4, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 8.14 - 7.79 (m, 2H), 7.50 - 7.27 (m, 2H), 5.51 (d, *J* = 1.2 Hz, 1H), 4.99 - 4.91 (m, 1H), 3.69 - 3.57 (m, 1H), 3.50 - 3.39 (m, 1H), 3.33 - 3.22 (m, 2H), 3.19 (s, 3H), 2.57 (s, 3H), 1.81 - 1.32 (m, 16H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 197.1, 178.1, 147.1, 138.3, 133.8, 129.2, 125.7, 120.0, 103.1, 100.2, 48.3, 45.8, 38.9, 35.9, 35.3, 33.6, 25.8, 23.5, 23.4, 18.0, 14.5. HRMS: calculated for C₂₄H₃₂O₅S [M+H]⁺: 433.20432, Found 433.20416. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 12.3 min, t_{minor} = 15.1 min



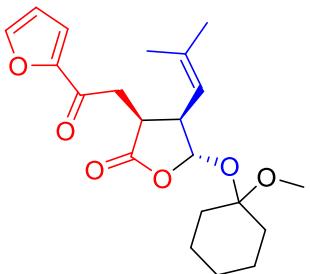
3t:(3S,4R,5R)-3-(2-([1,1'-biphenyl]-4-yl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

colourless oil; 305 mg; 66% yield; 99% ee; $[\alpha]_{D20} = -17.00$ (*c* 0.2, CHCl₃); ¹H NMR (500 MHz, Acetone-*d*₆) δ 8.23 - 7.96 (m, 2H), 7.91 - 7.78 (m, 2H), 7.77 - 7.71 (m, 2H), 7.54 - 7.48 (m, 2H), 7.48 - 7.39 (m, 1H), 5.53 (d, *J* = 1.0 Hz, 1H), 5.03 - 4.93 (m, 1H), 3.71 - 3.63 (m, 1H), 3.52 - 3.45 (m, 1H), 3.38 - 3.27 (m, 2H), 3.21 (s, 3H), 1.83 - 1.32 (m, 16H). ¹³C NMR (125 MHz, Acetone-*d*₆) δ 197.8, 178.2, 146.4, 140.5, 138.3, 136.4, 129.9, 129.5, 129.2, 128.0, 127.9, 120.0, 103.2, 100.3, 48.3, 45.8, 38.9, 35.9, 35.7, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₉H₃₄O₅ [M+H]⁺: 463.24790, Found 463.24761. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 10.5 min, t_{minor} = 14.3 min



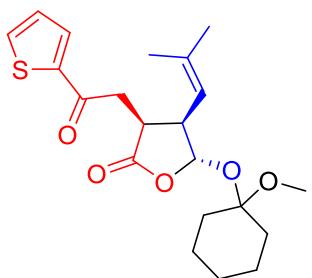
3u:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-(naphthalen-2-yl)-2-oxoethyl)dihydrofuran-2(3H)-one

white solid; 314 mg; 72% yield; 99% ee; $[\alpha]_{D20} = -17.00$ (*c* 0.2, CHCl₃); ¹H NMR (500 MHz, Acetone-*d*₆) δ 8.69 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 8.06 - 7.97 (m, 3H), 7.70 - 7.59 (m, 2H), 5.54 (d, *J* = 1.0 Hz, 1H), 5.05 - 4.95 (m, 1H), 3.75 - 3.65 (m, 1H), 3.54 - 3.41 (m, 3H), 3.21 (s, 3H), 1.81 - 1.34 (m, 16H). ¹³C NMR (125 MHz, Acetone-*d*₆) δ 198.2, 178.2, 138.4, 136.5, 135.0, 133.6, 130.7, 130.5, 129.5, 129.2, 128.6, 127.7, 124.3, 120.0, 103.2, 100.3, 48.3, 45.8, 39.0, 35.9, 35.7, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₇H₃₂O₅ [M+H]⁺: 437.23225, Found 437.23213. HPLC analysis: Chiraldak IC, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 9.6 min, t_{minor} = 12.2 min



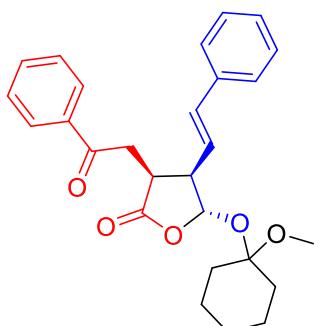
3v:(3S,4R,5R)-3-(2-(furan-2-yl)-2-oxoethyl)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)dihydrofuran-2(3H)-one

yellow oil; 241 mg; 64% yield; 99% ee; $[\alpha]_{D20} = 19.33$ (*c* 0.3, CHCl₃); ¹H NMR (500 MHz, Acetone-*d*₆) δ 7.84 (d, *J* = 1.8 Hz, 1H), 7.37 (d, *J* = 3.6 Hz, 1H), 6.70 - 6.65 (m, 1H), 5.50 (d, *J* = 1.0 Hz, 1H), 5.02 - 4.91 (m, 1H), 3.67 - 3.55 (m, 1H), 3.47 - 3.36 (m, 1H), 3.19 (s, 3H), 3.15 - 3.08 (m, 2H), 1.78 - 1.34 (m, 16H). ¹³C NMR (125 MHz, Acetone-*d*₆) δ 186.7, 177.9, 153.3, 148.0, 138.4, 119.8, 118.2, 113.1, 103.2, 100.2, 48.3, 45.7, 38.4, 35.9, 35.2, 33.6, 25.8, 23.5, 23.4, 17.9. HRMS: calculated for C₂₁H₂₈O₆ [M+H]⁺: 377.19587, Found 377.19584. HPLC analysis: Chiraldak IC, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 12.6 min, t_{minor} = 14.1 min



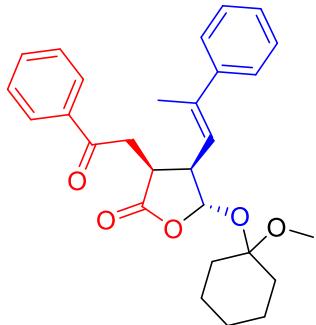
3w:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-4-(2-methylprop-1-en-1-yl)-3-(2-oxo-2-(thiophen-2-yl)ethyl)dihydrofuran-2(3H)-one

yellow oil; 265 mg; 68% yield; 98% ee; $[\alpha]_{D20} = 7.33$ (*c* 0.3, CHCl₃); ¹H NMR (400 MHz, Acetone-*d*₆) δ 8.27 - 7.60 (m, 2H), 7.31 - 7.17 (m, 1H), 5.51 (d, *J* = 1.2 Hz, 1H), 5.05 - 4.90 (m, 1H), 3.70 - 3.55 (m, 1H), 3.49 - 3.35 (m, 1H), 3.34 - 3.12 (m, 5H), 1.79 - 1.33 (m, 16H). ¹³C NMR (100 MHz, Acetone-*d*₆) δ 191.2, 177.9, 144.7, 138.5, 135.0, 133.6, 129.3, 119.9, 103.2, 100.2, 48.3, 45.8, 38.9, 36.0, 35.9, 33.6, 25.8, 25.8, 23.5, 23.4, 18.0. HRMS: calculated for C₂₁H₂₈O₅S [M+H]⁺: 393.17302, Found 393.17303. HPLC analysis: Chiraldak IC, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 10.3 min, t_{minor} = 12.2 min



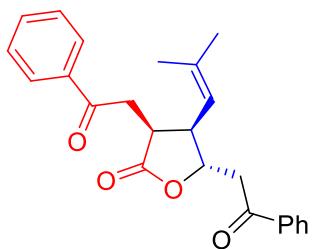
3x:(3S,4R,5R)-5-((1-methoxycyclohexyl)oxy)-3-(2-oxo-2-phenylethyl)-4-((E)-styryl)dihydrofuran-2(3H)-one

yellow oil; 122 mg; 28% yield; 99% ee; $[\alpha]_{D20} = 63.30$ (*c* 0.1, CHCl₃); ¹H NMR (600 MHz, Acetone-*d*₆) δ 8.03 - 7.95 (m, 2H), 7.59 - 7.53 (m, 1H), 7.50 - 7.42 (m, 2H), 7.37 - 7.32 (m, 2H), 7.28 - 7.22 (m, 2H), 7.21 - 7.15 (m, 1H), 6.53 (d, *J* = 15.6 Hz, 1H), 6.19 - 6.12 (m, 1H), 5.75 (s, 1H), 3.75 - 3.68 (m, 1H), 3.50 - 3.43 (m, 2H), 3.41 - 3.31 (m, 1H), 3.22 (s, 3H), 1.83 - 1.32 (m, 10H). ¹³C NMR (150 MHz, Acetone-*d*₆) δ 198.0, 177.8, 137.5, 137.4, 135.4, 134.0, 129.5, 129.3, 128.7, 128.6, 127.3, 125.0, 103.3, 99.6, 50.8, 48.4, 39.2, 35.9, 35.9, 33.6, 25.8, 23.5, 23.4. HRMS: calculated for C₂₇H₃₀O₅ [M+H]⁺: 435.21660, Found 435.21643. HPLC analysis: Chiraldak IC, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 7.9 min, t_{minor} = 9.3 min



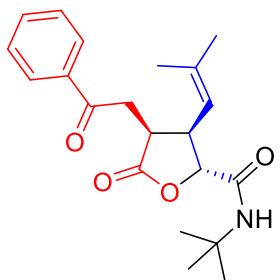
3y:(3*S*,4*R*,5*R*)-5-((1-methoxycyclohexyl)oxy)-3-(2-oxo-2-phenylethyl)-4-((*E*)-2-phenylprop-1-en-1-yl)dihydrofuran-2(3*H*)-one

yellow oil; 210 mg; 47% yield; 99% ee; $[\alpha]_{D20} = 63.00$ (*c* 0.2, CHCl₃); ¹H NMR (600 MHz, Acetone-*d*₆) δ 8.03 - 7.98 (m, 2H), 7.63 - 7.57 (m, 1H), 7.50 - 7.45 (m, 2H), 7.29 - 7.25 (m, 2H), 7.25 - 7.17 (m, 3H), 5.71 (d, *J* = 1.2 Hz, 1H), 5.59 - 5.54 (m, 1H), 3.81 - 3.74 (m, 1H), 3.74 - 3.67 (m, 1H), 3.49 - 3.37 (m, 2H), 3.23 (s, 3H), 1.97 (d, *J* = 1.8 Hz, 3H), 1.89 - 1.23 (m, 10H). ¹³C NMR (150 MHz, Acetone-*d*₆) δ 198.3, 177.9, 143.6, 141.1, 137.5, 134.1, 129.5, 129.0, 128.8, 128.1, 126.6, 123.0, 103.3, 100.1, 48.4, 46.4, 39.2, 36.0, 35.9, 33.7, 25.8, 23.5, 23.4, 16.4. HRMS: calculated for C₂₈H₃₂O₅ [M+H]⁺: 449.23225, Found 449.23201. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 8.4 min, t_{minor} = 10.5 min



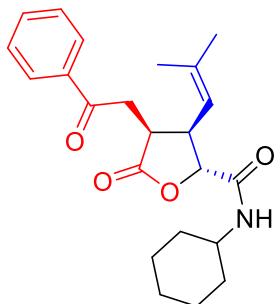
5:2,2'-(2*S*,3*R*,4*S*)-3-(2-methylprop-1-en-1-yl)-5-oxotetrahydrofuran-2,4-diylbis(1-phenylethan-1-one)

white solid; 274 mg; 73% yield; 2:1 dr; 95% ee; $[\alpha]_{D20} = 56.44$ (*c* 0.3, CHCl₃); ¹H NMR (600 MHz, Acetone-*d*₆) δ 8.11 - 8.04 (m, 1H), 8.03 - 7.95 (m, 5H), 7.69 - 7.59 (m, 3H), 7.58 - 7.47 (m, 6H), 5.29 - 5.21 (m, 1H), 5.12 - 5.05 (m, 0.5H), 4.99 (d, *J* = 11.4 Hz, 1H), 4.89 - 4.83 (m, 0.5H), 3.85 - 3.77 (m, 1H), 3.74 - 3.63 (m, 2H), 3.60 - 3.53 (m, 0.5H), 3.53 - 3.36 (m, 3H), 3.33 - 3.18 (m, 2.5H), 1.53 (d, *J* = 1.2 Hz, 1.5H), 1.48 (d, *J* = 1.2 Hz, 1.5H), 1.46 (d, *J* = 1.2 Hz, 3H), 1.28 (d, *J* = 1.2 Hz, 3H). ¹³C NMR (150 MHz, Acetone-*d*₆) δ 198.2, 198.2, 197.4, 197.3, 178.5, 177.9, 139.2, 137.9, 137.82, 137.8, 137.7, 137.3, 134.1, 134.0, 134.0, 134.0, 129.5, 129.5, 129.5, 129.0, 128.7, 128.7, 128.7, 122.1, 118.3, 81.4, 79.0, 43.1, 42.8, 42.2, 41.9, 39.8, 39.3, 36.0, 35.7, 25.9, 25.8, 18.0, 17.6. HRMS: calculated for C₂₄H₂₄O₄ [M+H]⁺: 377.17474, Found 377.17463. UPC analysis: Acquity UPC² TrefoilTM Cel2, 2.5 μm, CO₂/MeOH = 90/10, flow rate 2.0 ml/min, λ = 240 nm, t_{major} = 8.0 min, t_{minor} = 7.5 min and t_{major} = 6.5 min, t_{minor} = 5.3 min



6:(2R,3R,4S)-N-(tert-butyl)-3-(2-methylprop-1-en-1-yl)-5-oxo-4-(2-oxo-2-phenylethyl)tetrahydrofuran-2-carboxamide

colourless oil; 243 mg; 68% yield; 5:1 dr; 98% ee; $[\alpha]_{D20} = 15.78$ (*c* 0.3, CHCl₃); ¹H NMR (600 MHz, Acetone-*d*₆) δ 8.03 - 7.94 (m, 2H), 7.69 - 7.60 (m, 1H), 7.57 - 7.48 (m, 2H), 7.12 (s, 1H), 5.01 - 4.99 (m, 1H), 4.51 (d, *J* = 2.4 Hz, 1H), 3.72 - 3.65 (m, 1H), 3.65 - 3.58 (m, 1H), 3.38 - 3.30 (m, 1H), 3.29 - 3.21 (m, 1H), 1.53 (d, *J* = 1.8 Hz, 3H), 1.46 (d, *J* = 1.8 Hz, 3H), 1.39 (s, 9H). ¹³C NMR (150 MHz, Acetone-*d*₆) δ 198.1, 178.4, 169.1, 137.6, 137.2, 134.0, 129.5, 128.7, 121.8, 82.4, 51.8, 42.3, 38.9, 36.0, 28.7, 25.7, 17.9. HRMS: calculated for C₂₁H₂₇NO₄ [M+H]⁺: 358.20128, Found 358.20147. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 60/40, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 11.7 min, t_{minor} = 15.5 min



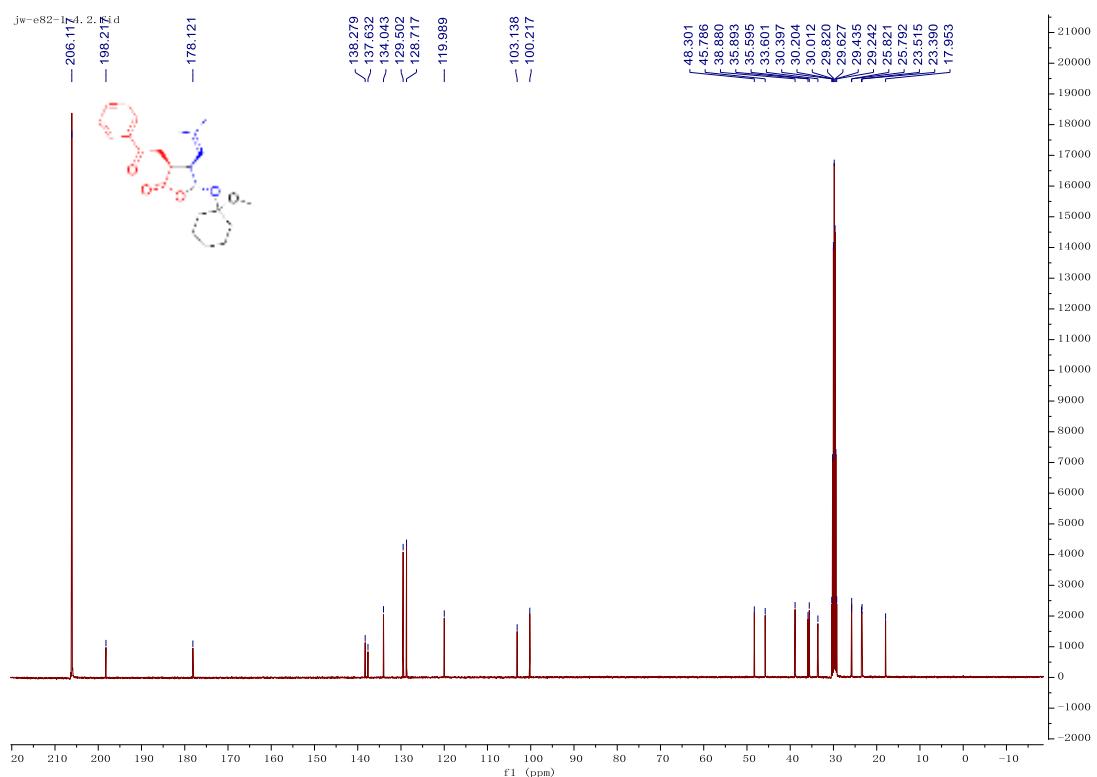
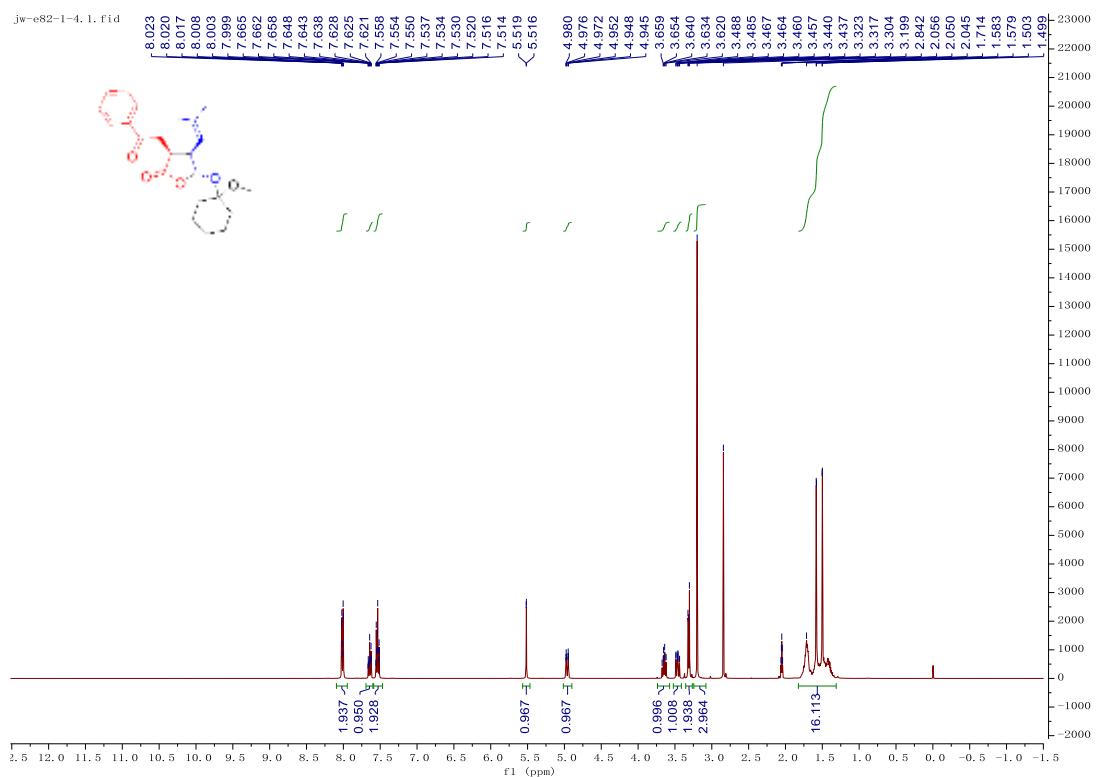
7:(2R,3R,4S)-N-cyclohexyl-3-(2-methylprop-1-en-1-yl)-5-oxo-4-(2-oxo-2-phenylethyl)tetrahydrofuran-2-carboxamide

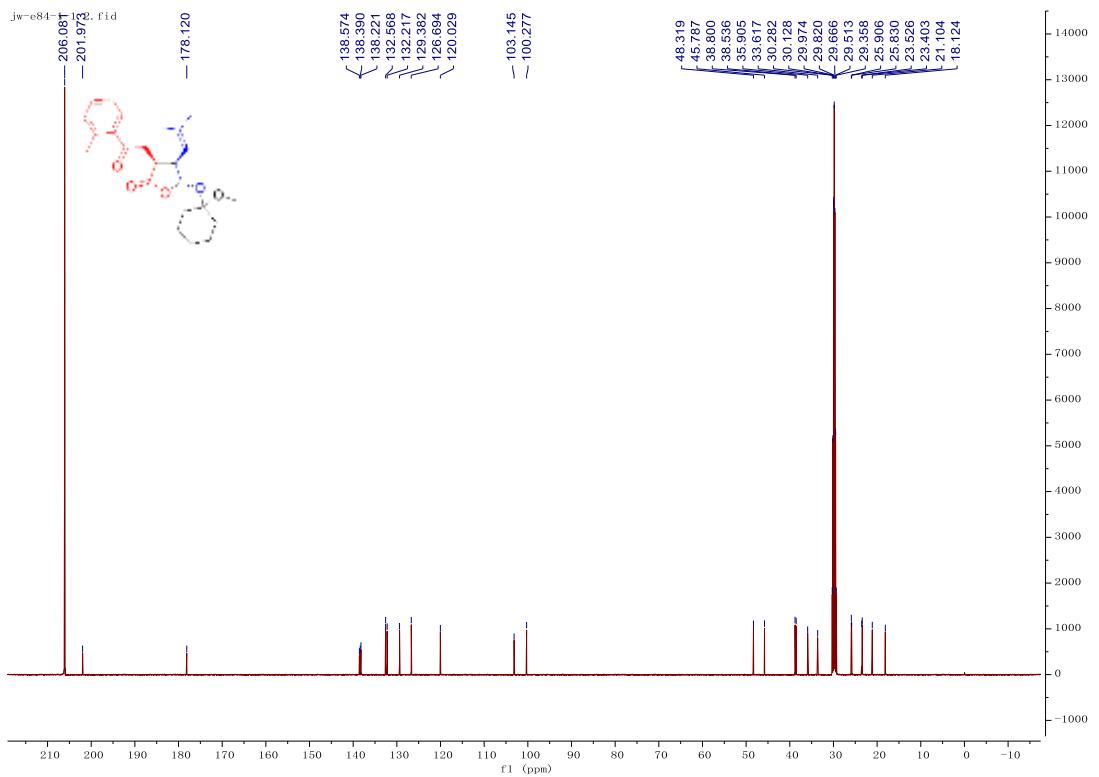
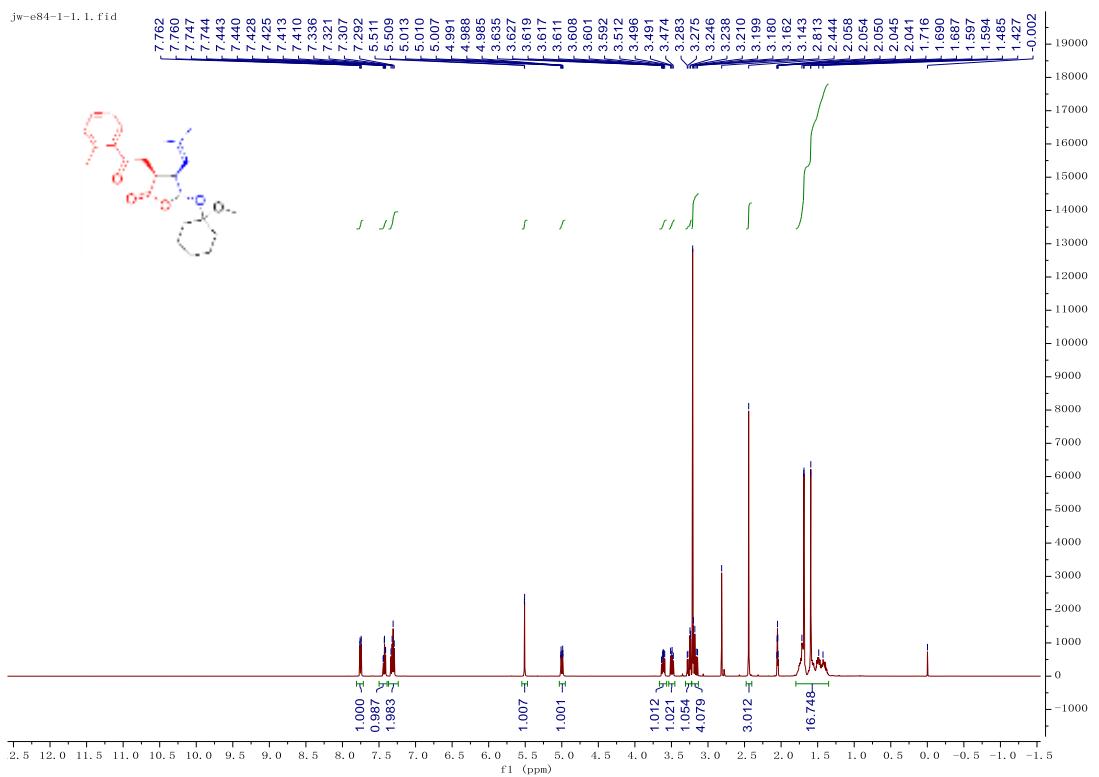
colourless oil; 272 mg; 71% yield; 5:1 dr; 99% ee; $[\alpha]_{D20} = 4.22$ (*c* 0.3, CHCl₃); ¹H NMR (600 MHz, Acetone-*d*₆) δ 8.02 - 7.95 (m, 2H), 7.66 - 7.60 (m, 1H), 7.56 - 7.48 (m, 2H), 7.41 (d, *J* = 7.8 Hz, 1H), 5.11 - 5.02 (m, 1H), 4.55 (d, *J* = 2.4 Hz, 1H), 3.76 (m, 1H), 3.72 - 3.66 (m, 1H), 3.62 - 3.55 (m, 1H), 3.38 - 3.30 (m, 1H), 3.29 - 3.22 (m, 1H), 1.94 - 1.83 (m, 2H), 1.78 - 1.68 (m, 2H), 1.66 - 1.57 (m, 1H), 1.53 (d, *J* = 1.2 Hz, 3H), 1.46 (d, *J* = 1.2 Hz, 3H), 1.40 - 1.27 (m, 4H), 1.22 - 1.13 (m, 1H). ¹³C NMR (150 MHz, Acetone-*d*₆) δ 198.1, 178.3, 168.7, 137.6, 137.4, 134.0, 129.5, 128.7, 121.8, 82.4, 49.1, 42.4, 38.9, 35.9, 33.4, 33.2, 26.2, 25.7, 25.7, 17.9. HRMS: calculated for C₂₃H₂₉NO₄ [M+H]⁺: 384.21693, Found 384.21690. HPLC analysis: Chiralpak IC, *n*-hexane/*i*-PrOH = 60/40, flow rate 1.0 ml/min, λ = 254 nm, t_{major} = 16.0 min, t_{minor} = 35.2 min

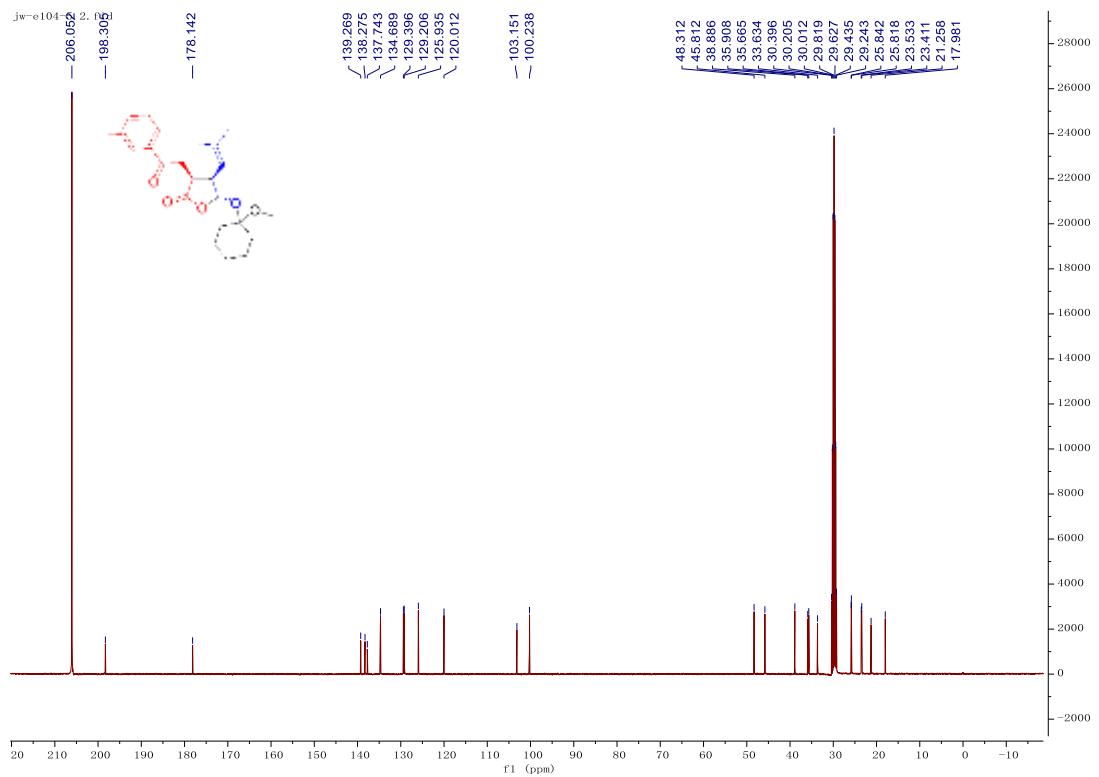
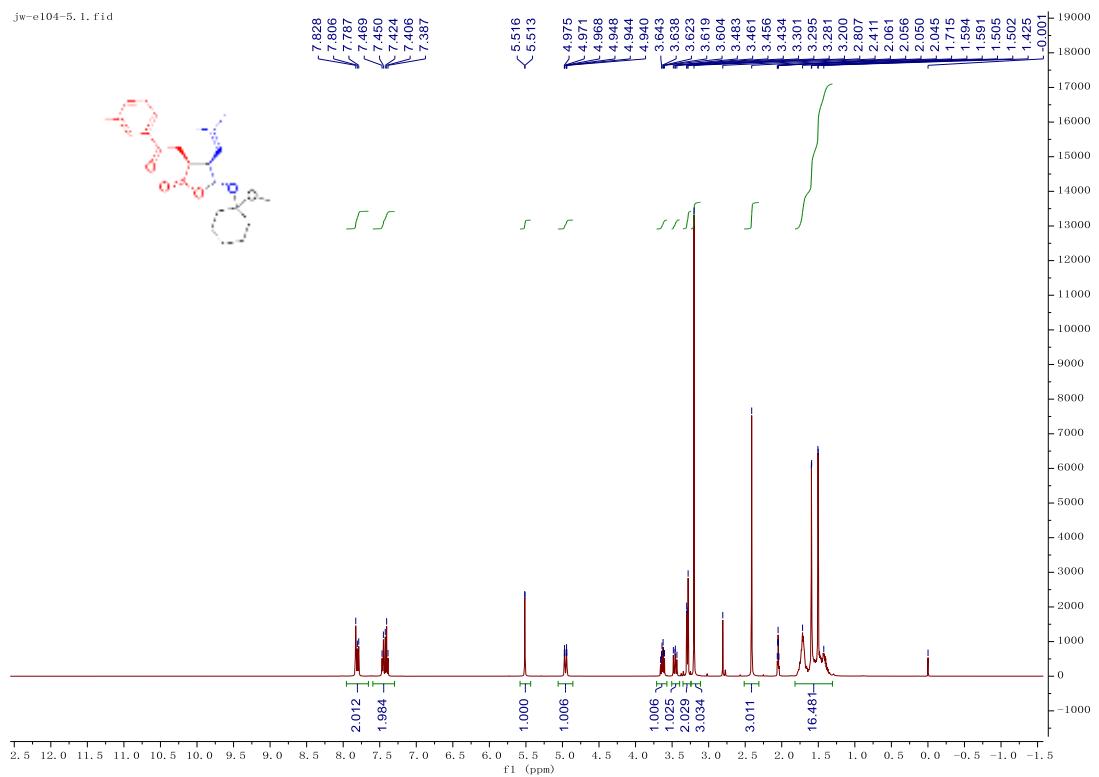
6 References

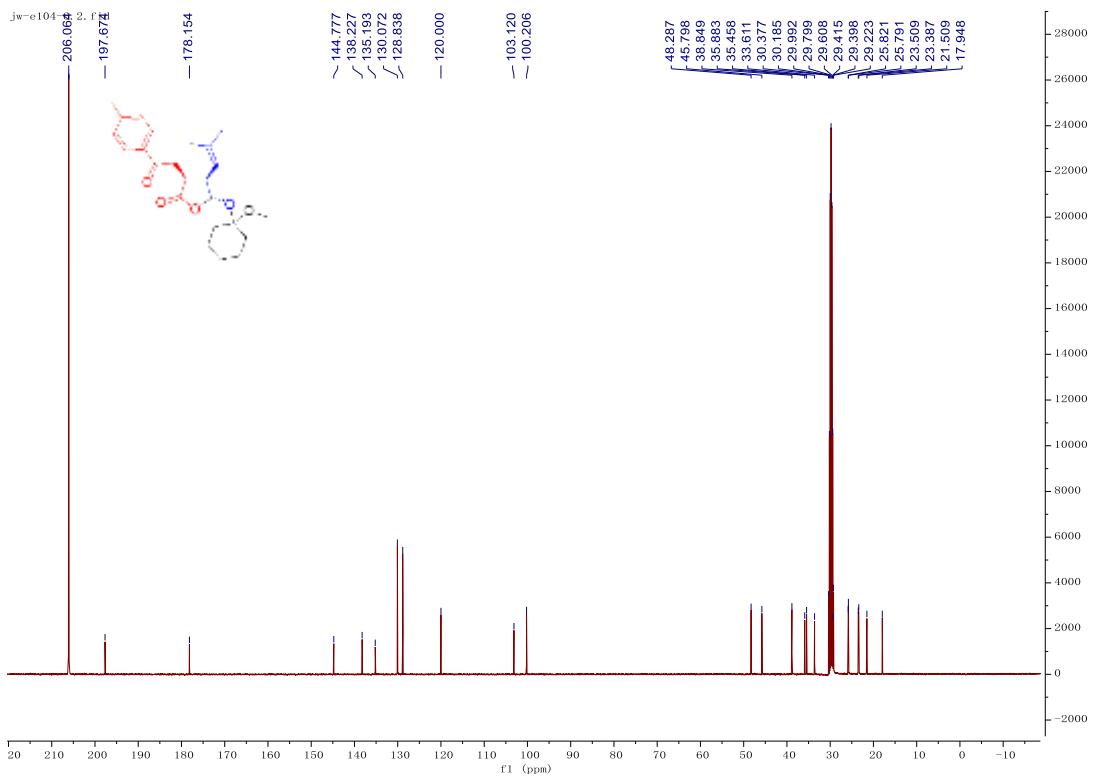
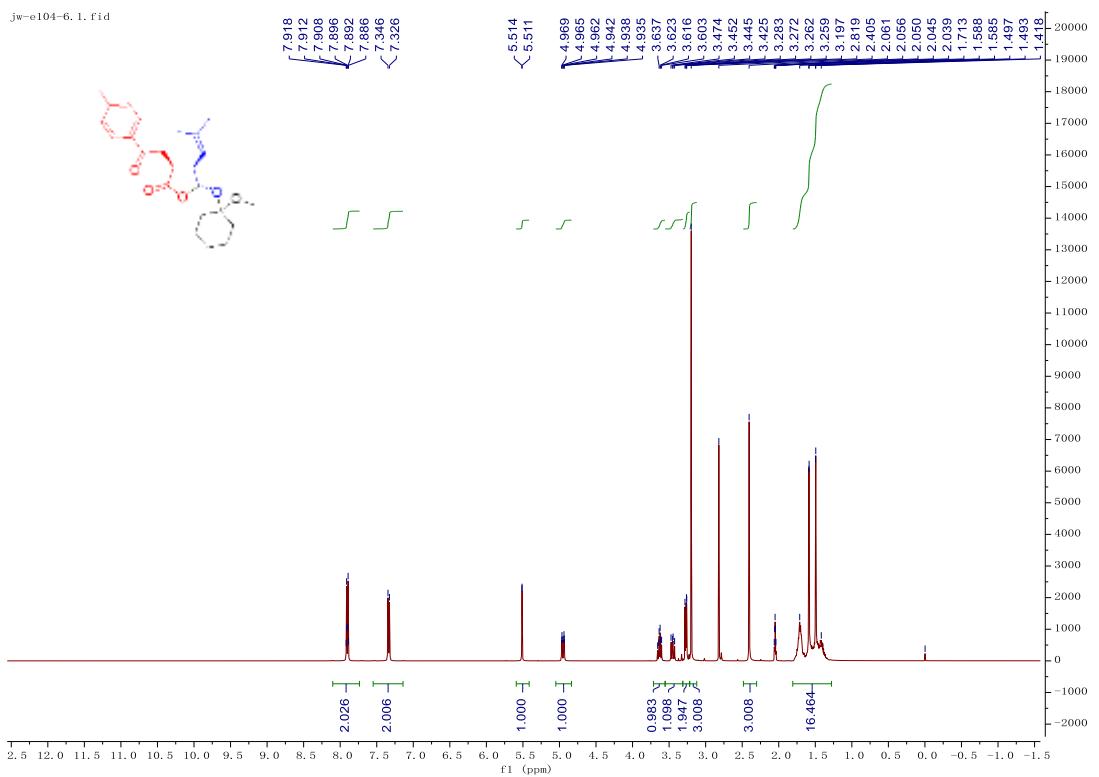
1. Juliette Sabbatani and Nuno Maulide, *Angew. Chem. Int. Ed.*, **2016**, *55*, 6780–6783
2. S. Zhao, J.-B. Lin, Y.-Y. Zhao, Y.-M. Liang, P.-F. Xu, *Org Lett.*, **2014**, *16*, 1802-1805
3. Wei-Wei Zhao and Yan-Kai Liu, *Org. Chem. Front.*, **2017**, *4*, 2358-2363
4. Kozo Shishido, Kou Hiroya, Yutaka Ueno and Keiichiro Fukumoto, *J. Chem. Soc. Perkin Trans. I* **1986**, 829-836

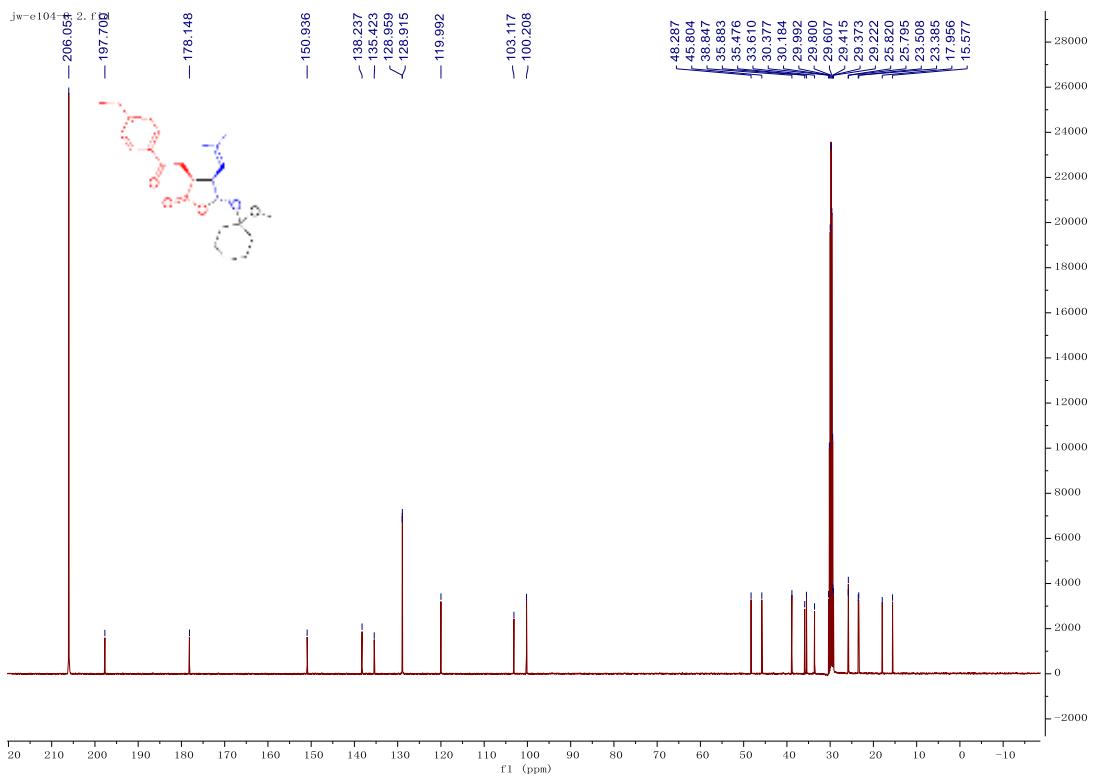
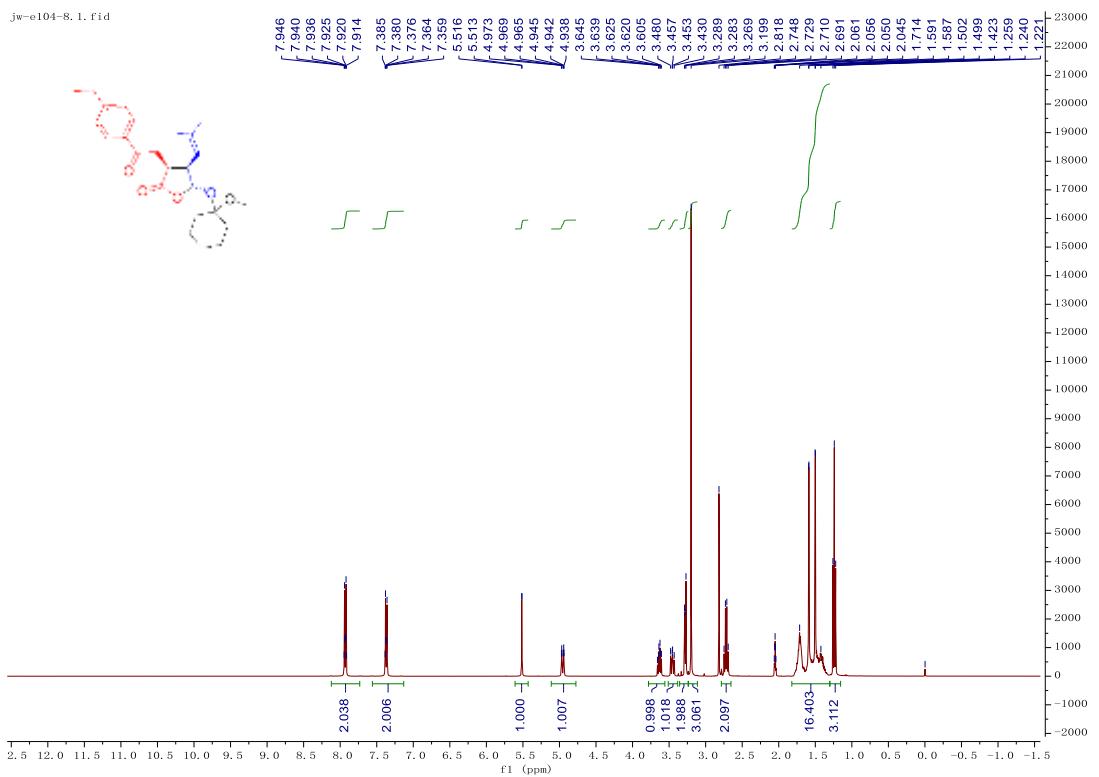
7 ^1H NMR and ^{13}C NMR Spectra

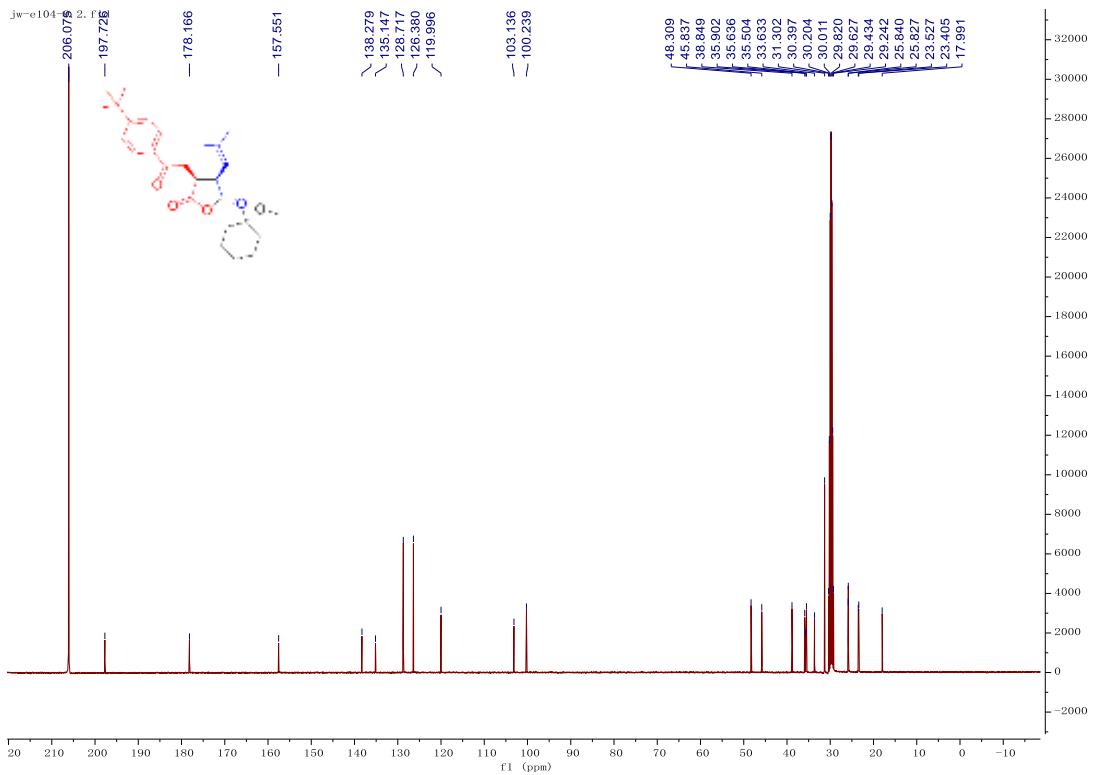
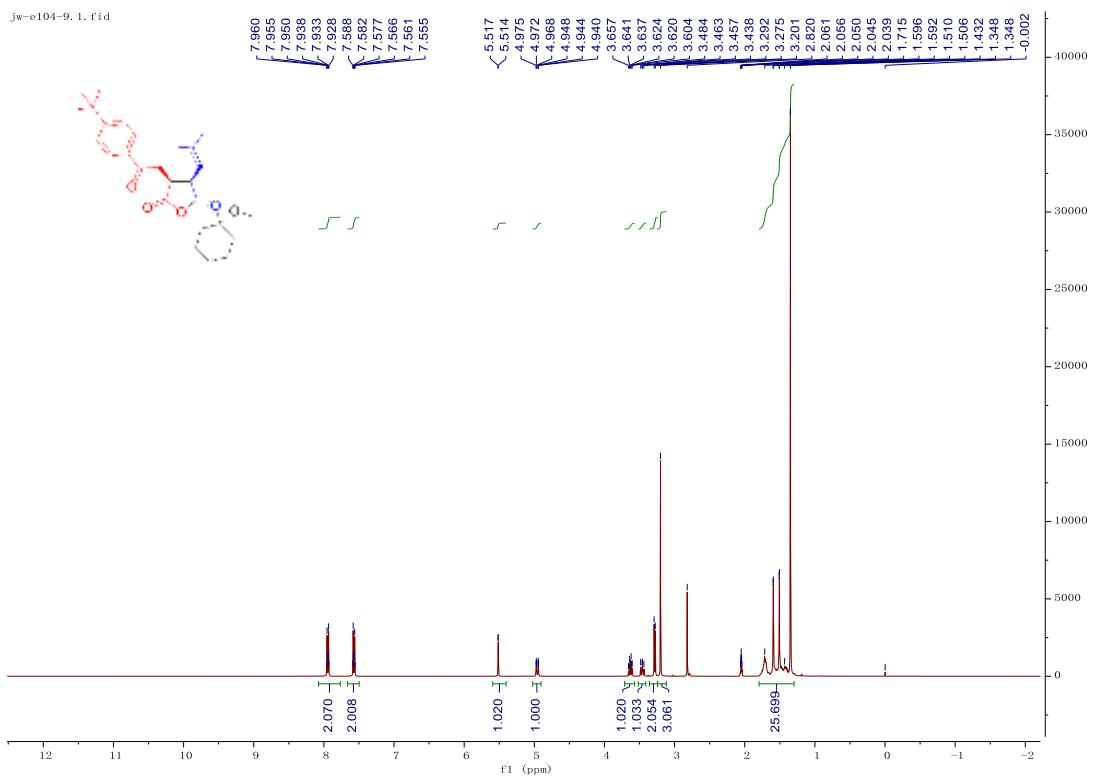


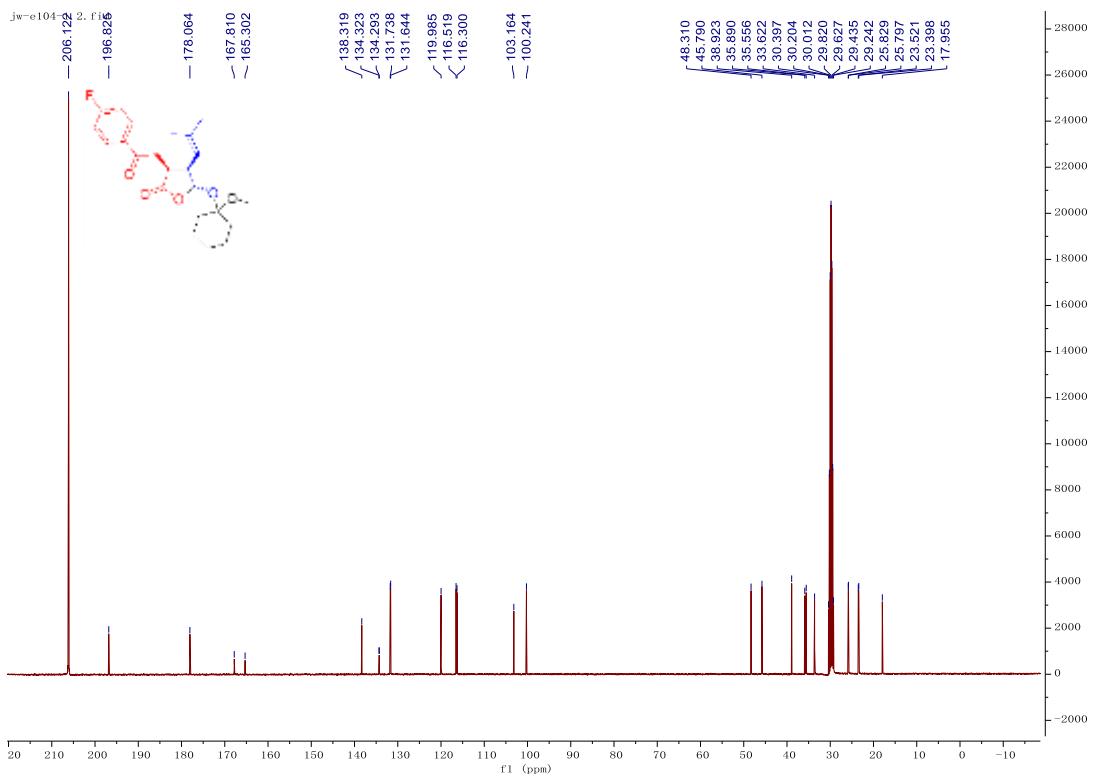
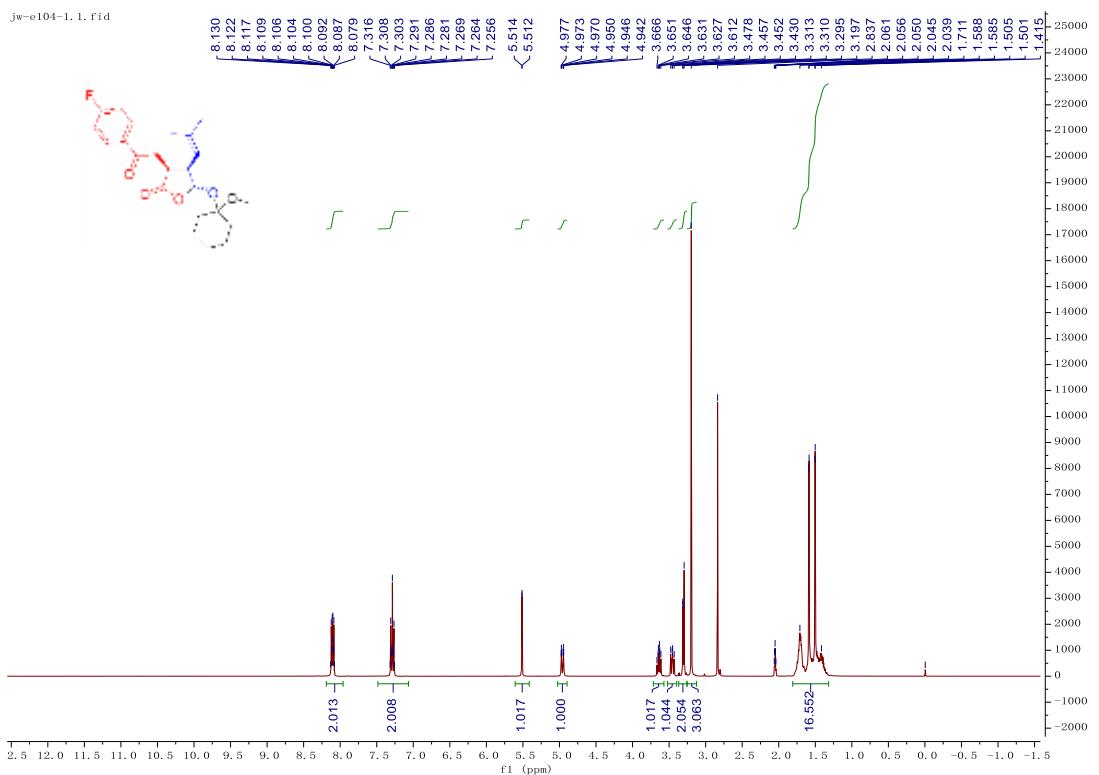


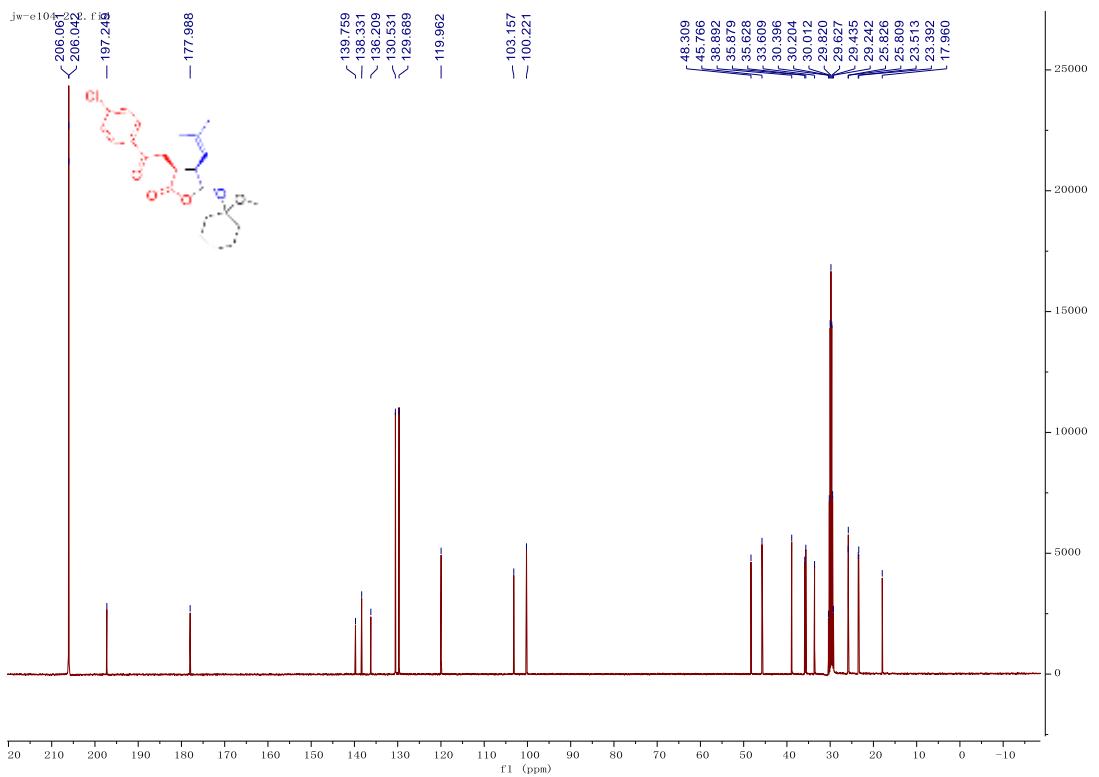
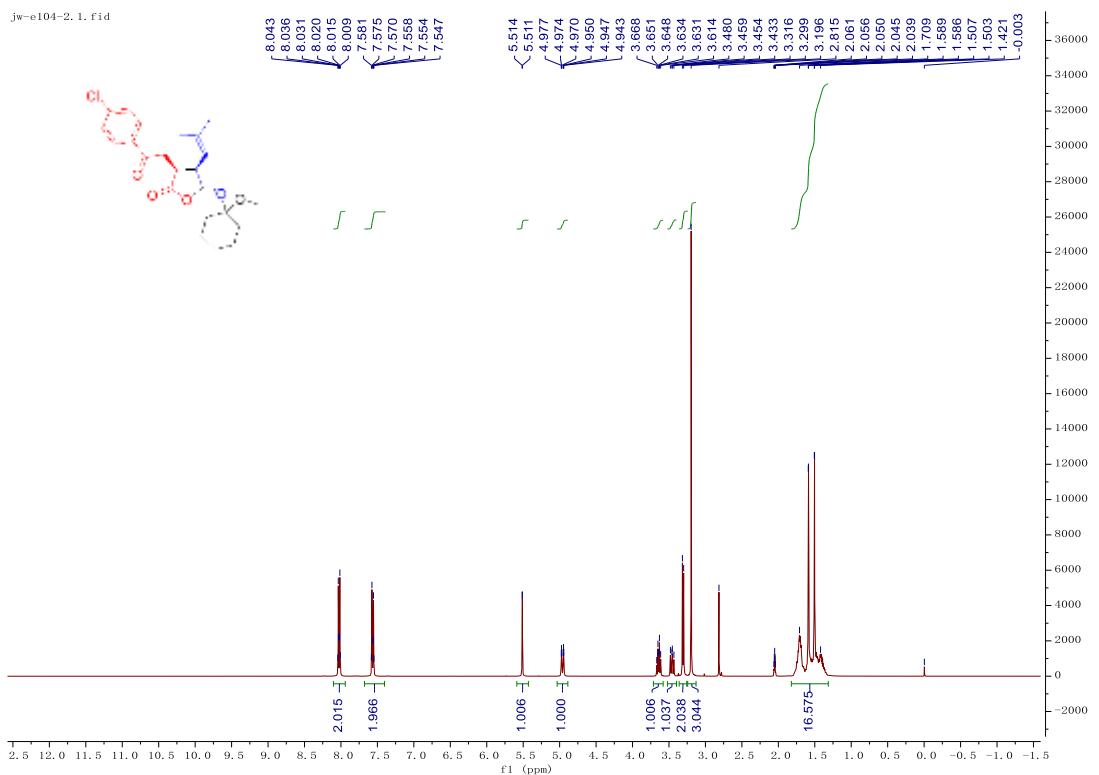


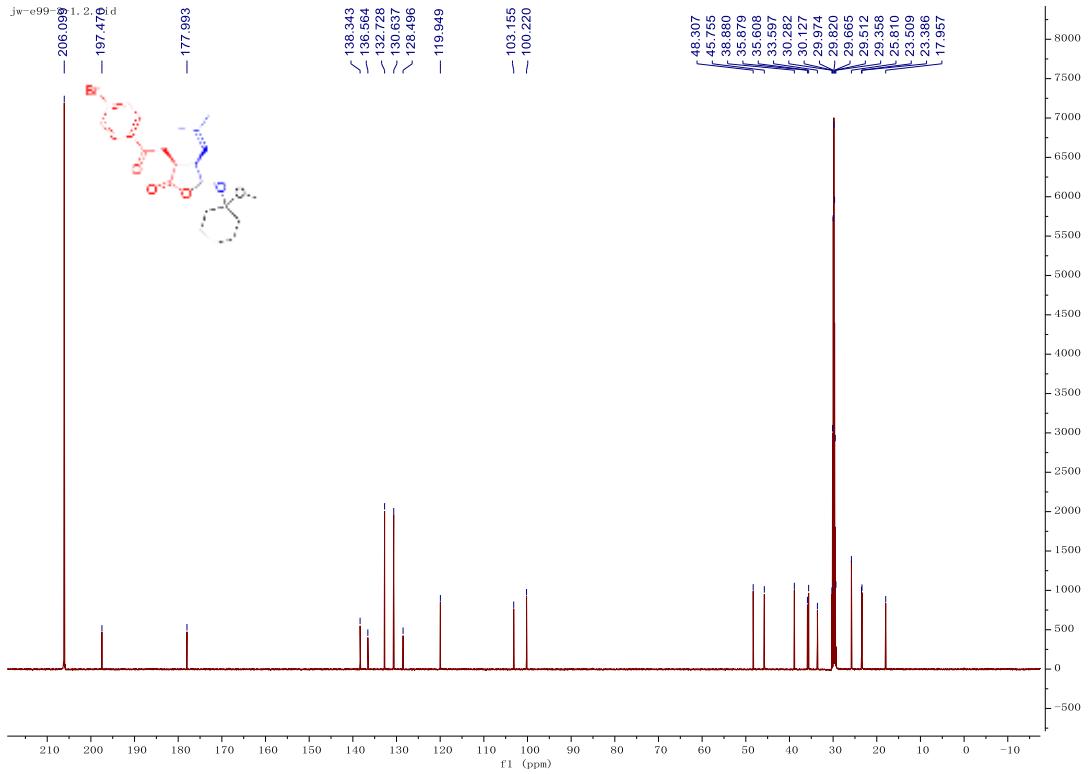
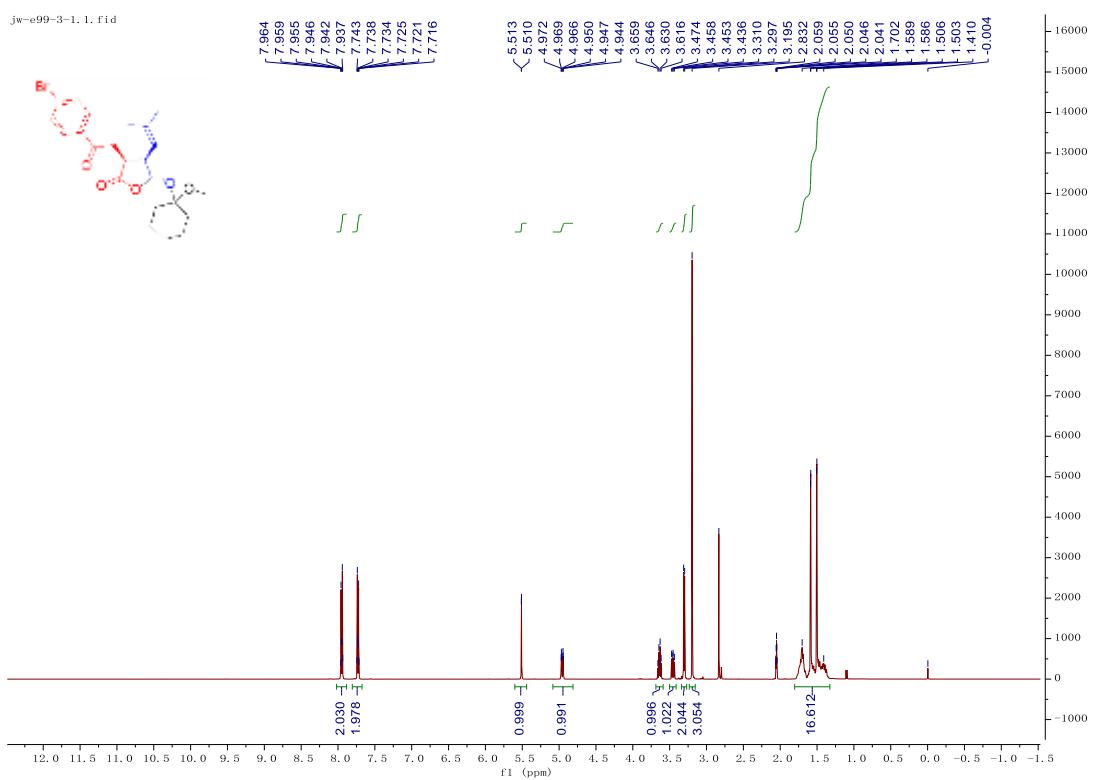


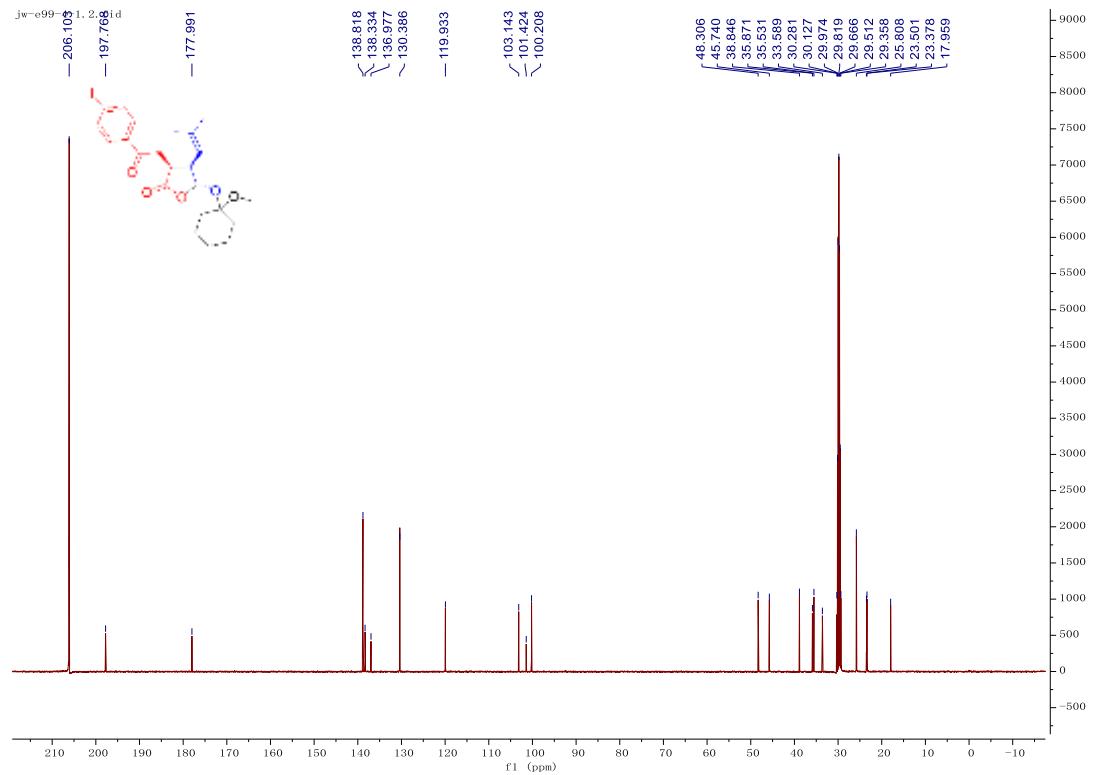
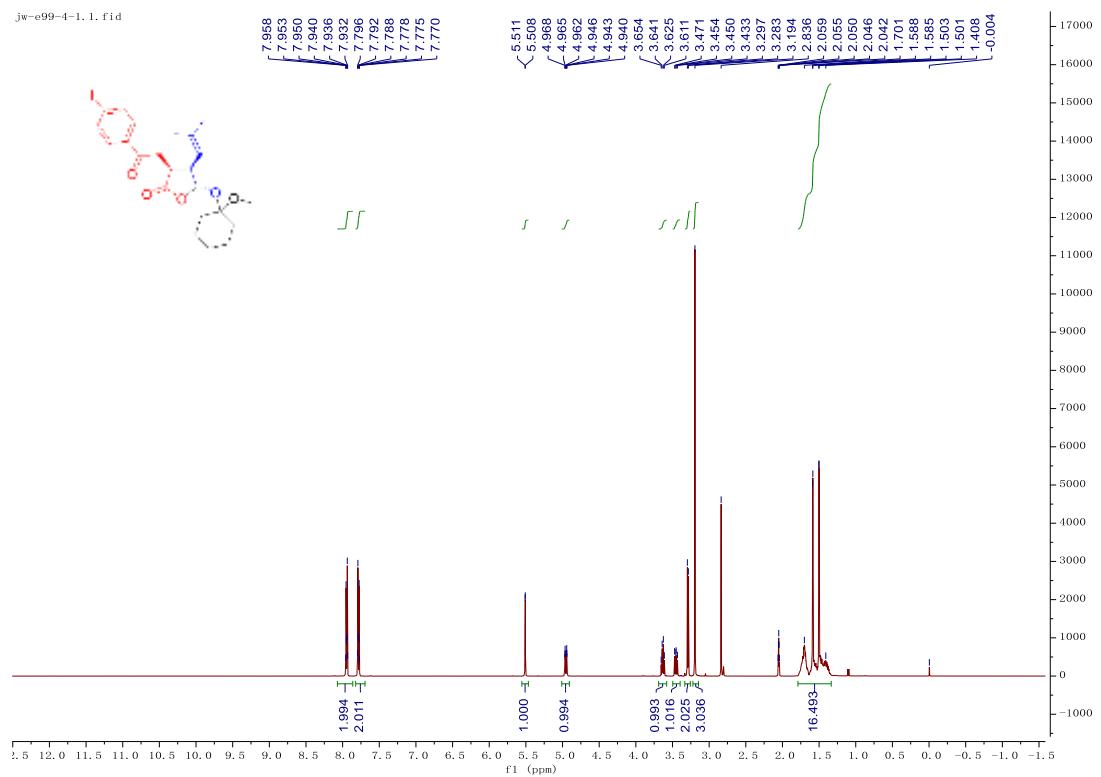


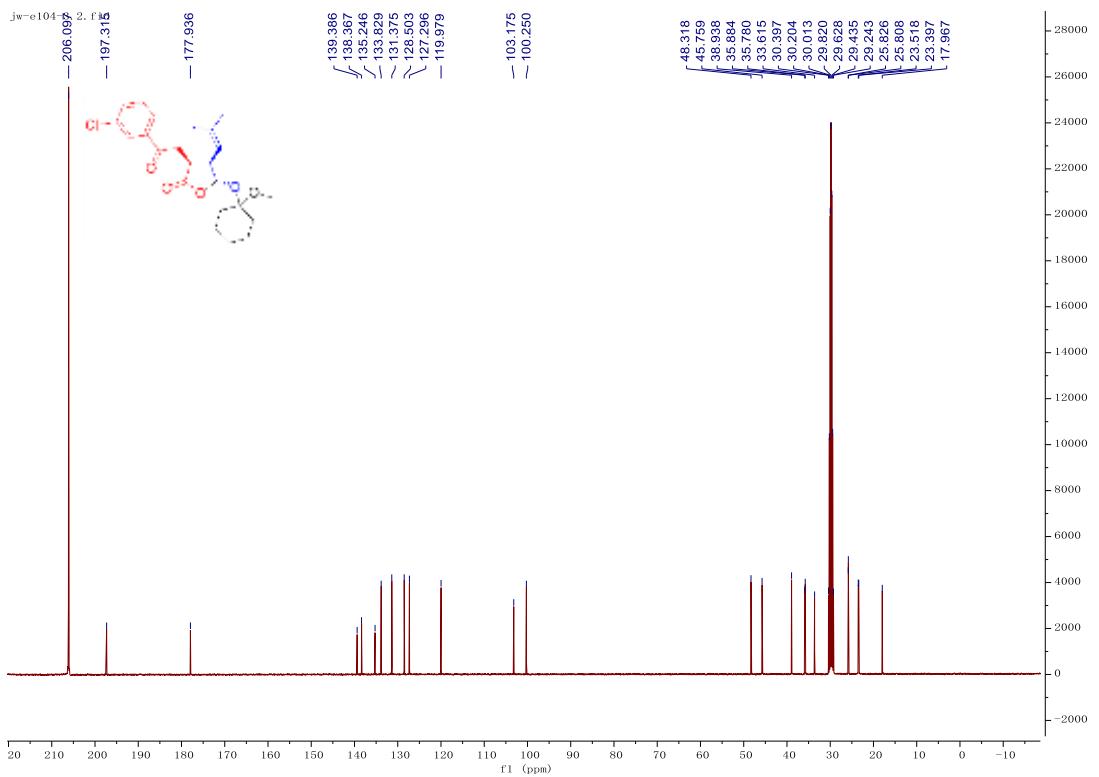
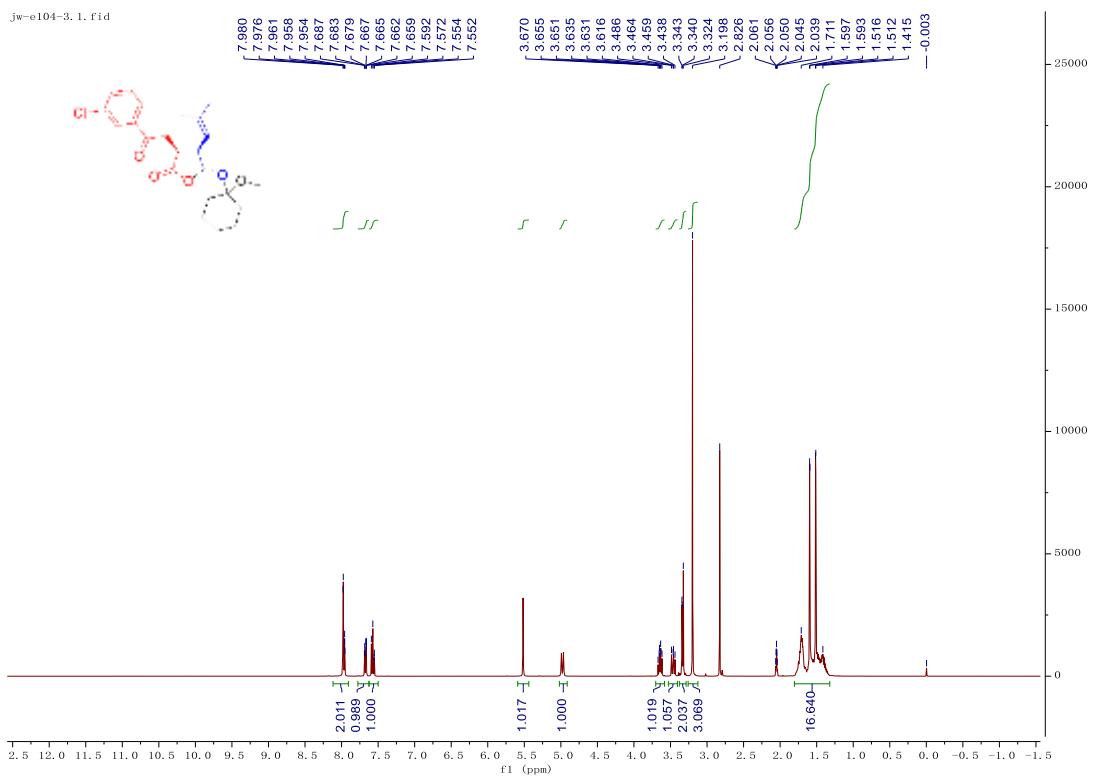


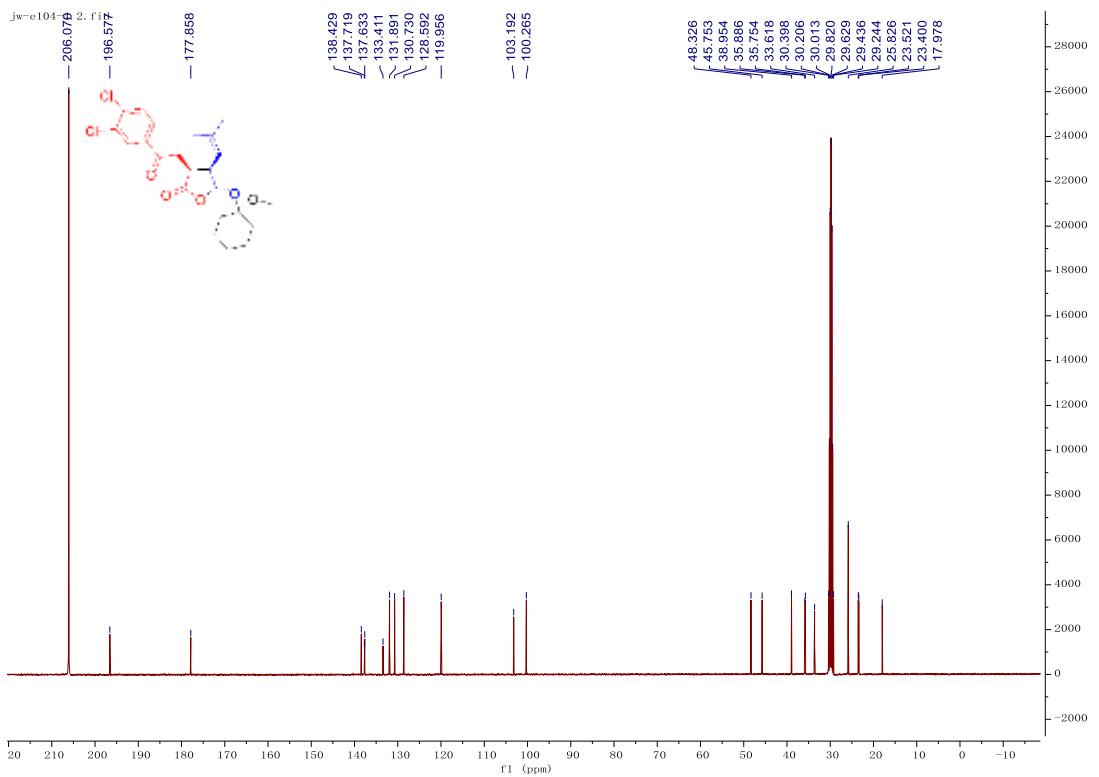
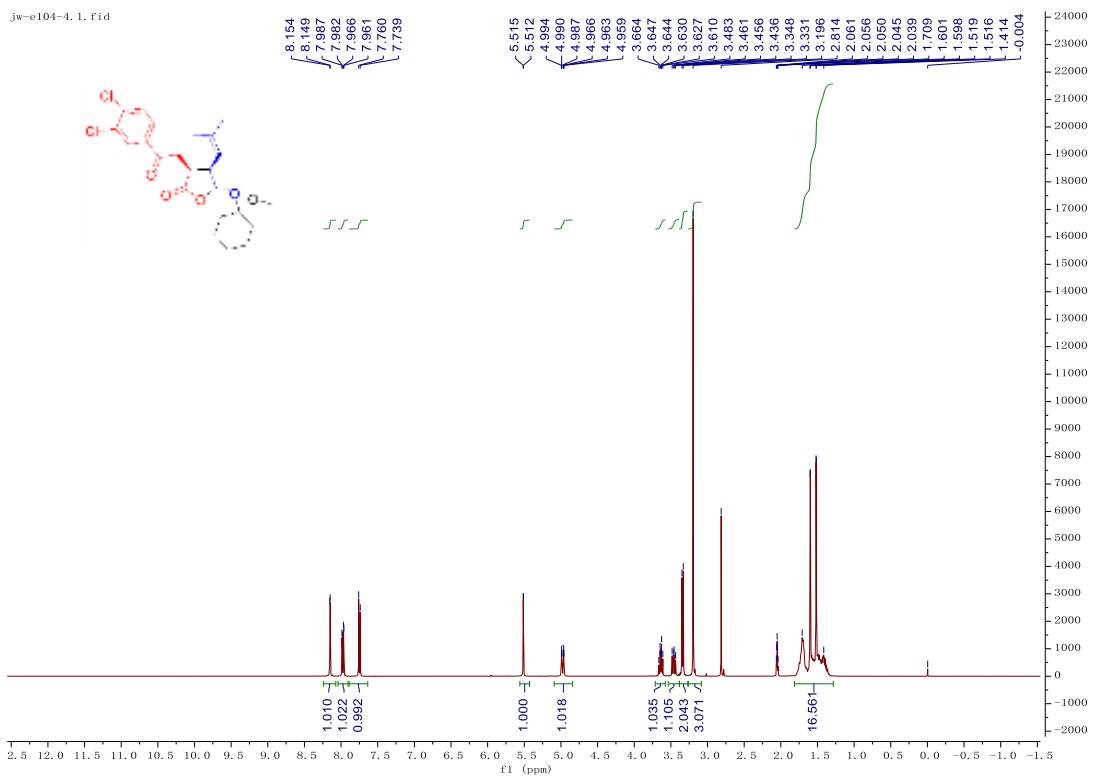


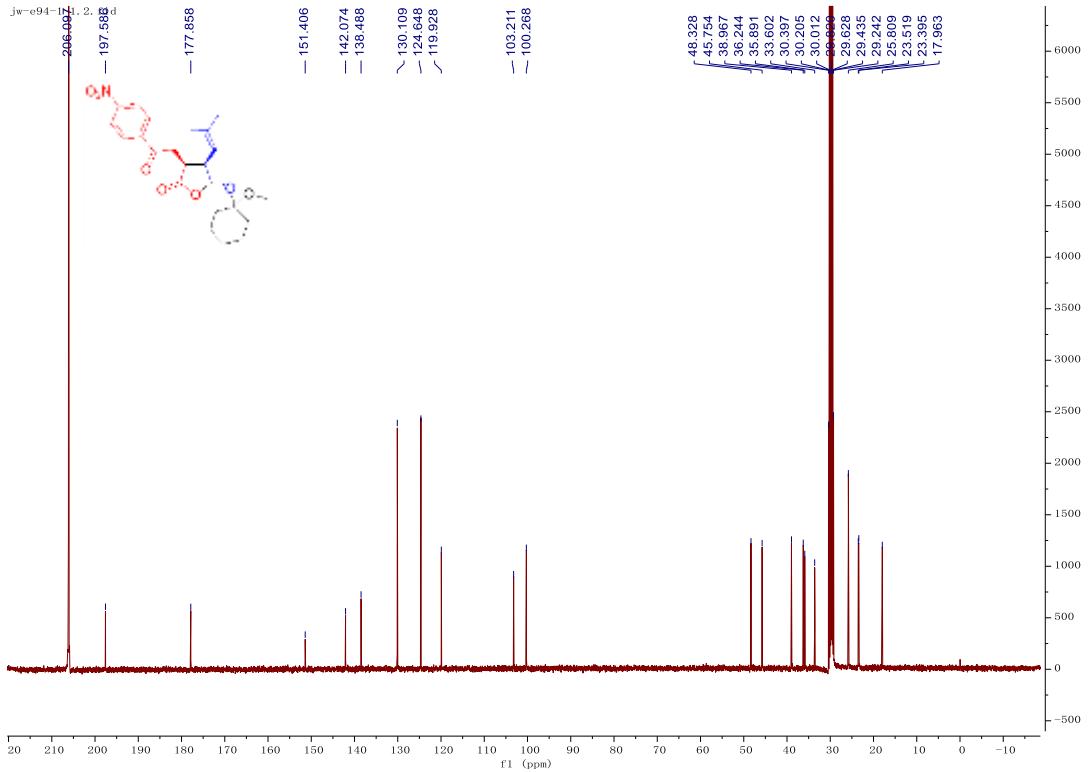
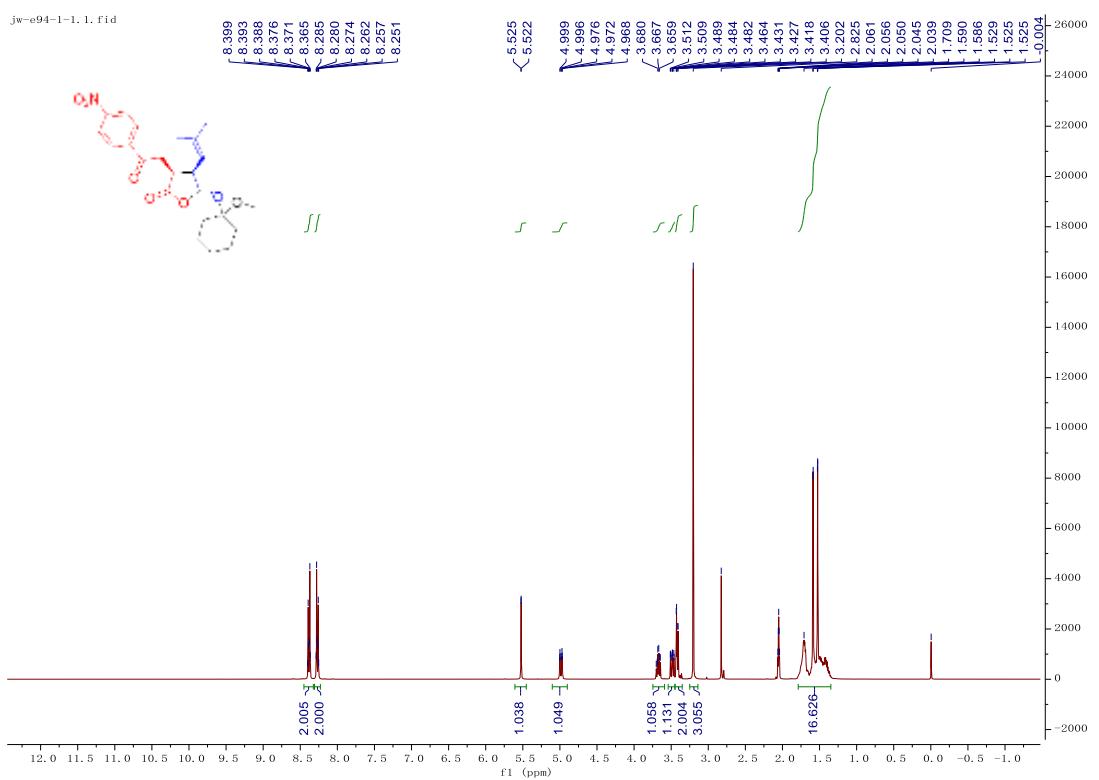


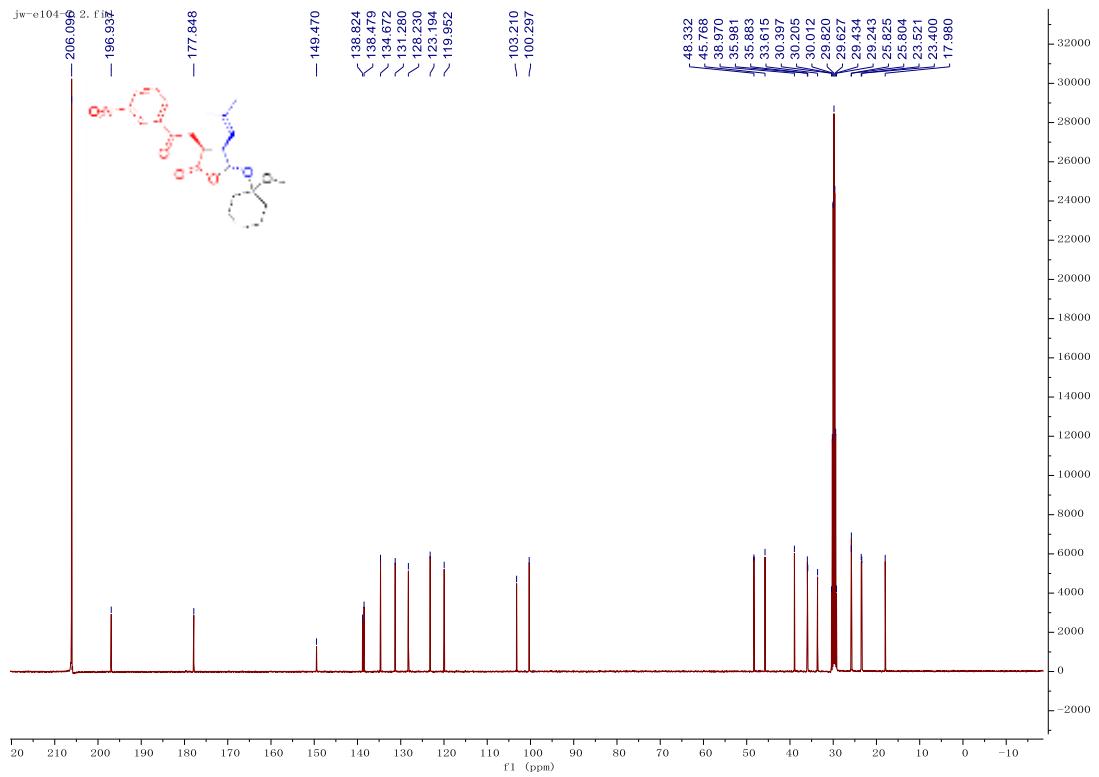
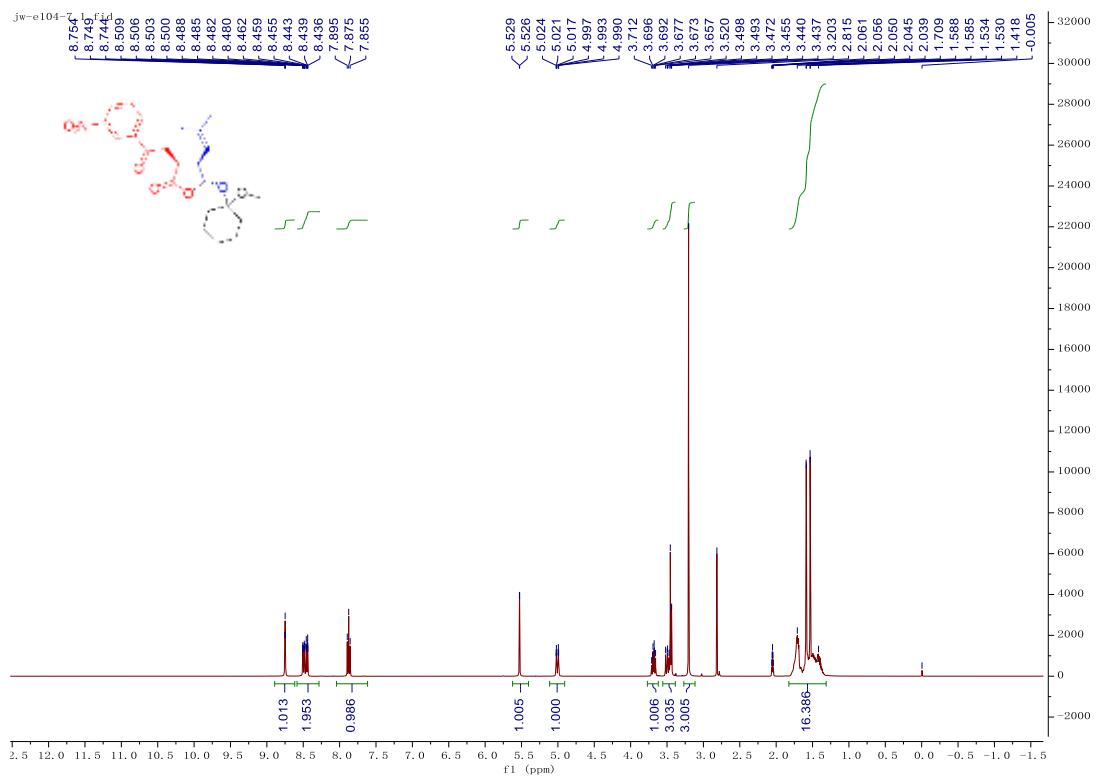


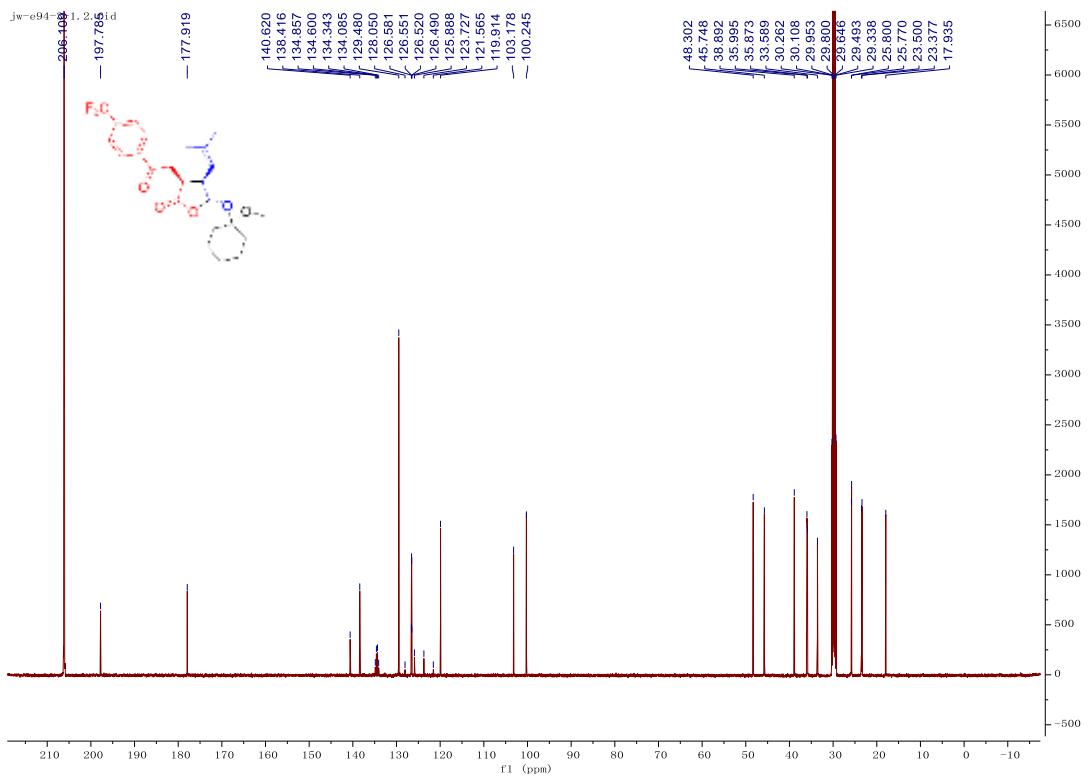
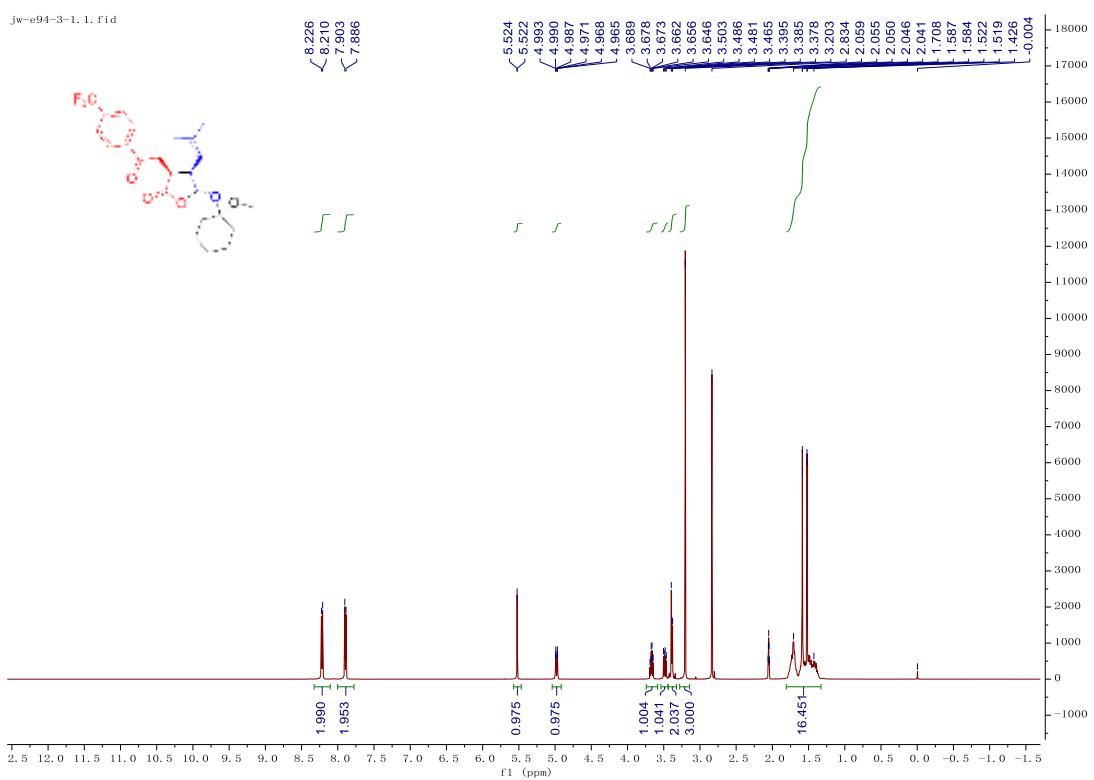


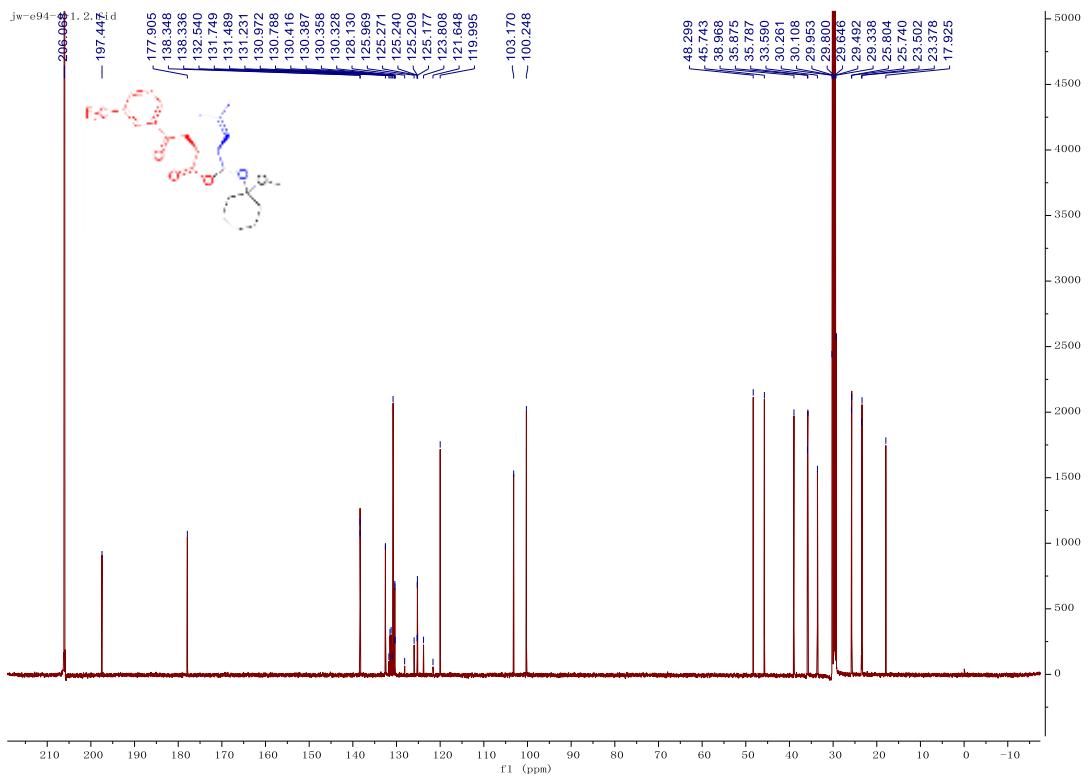
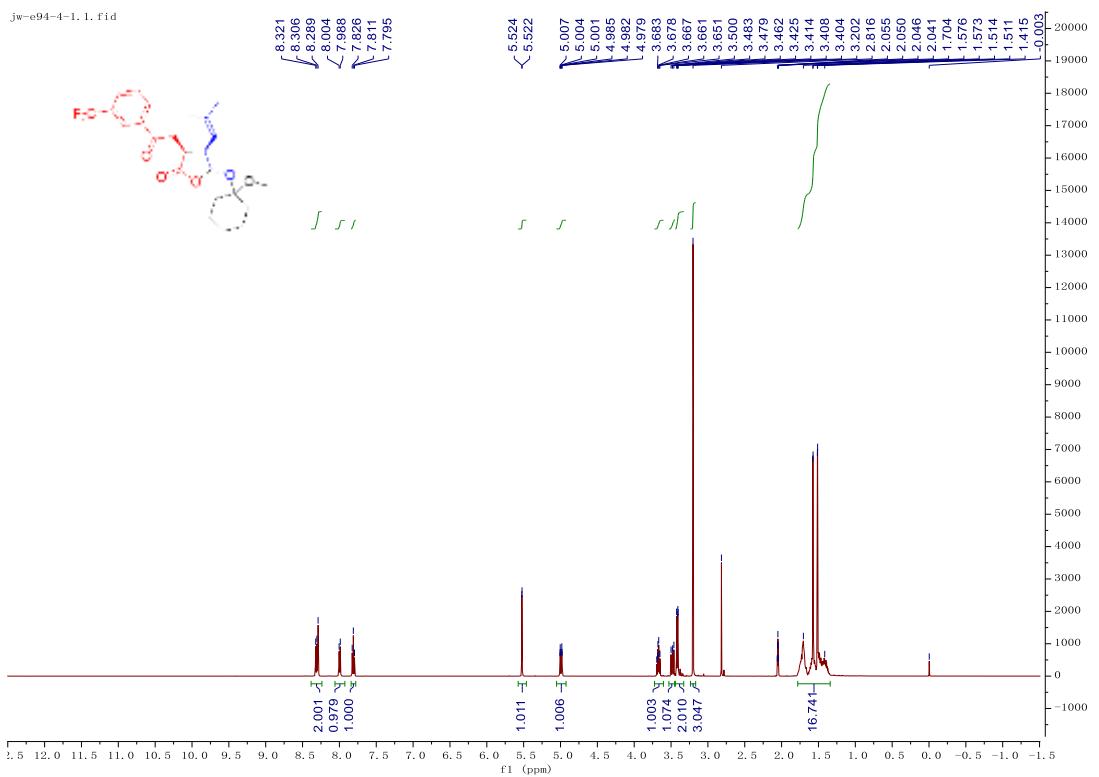


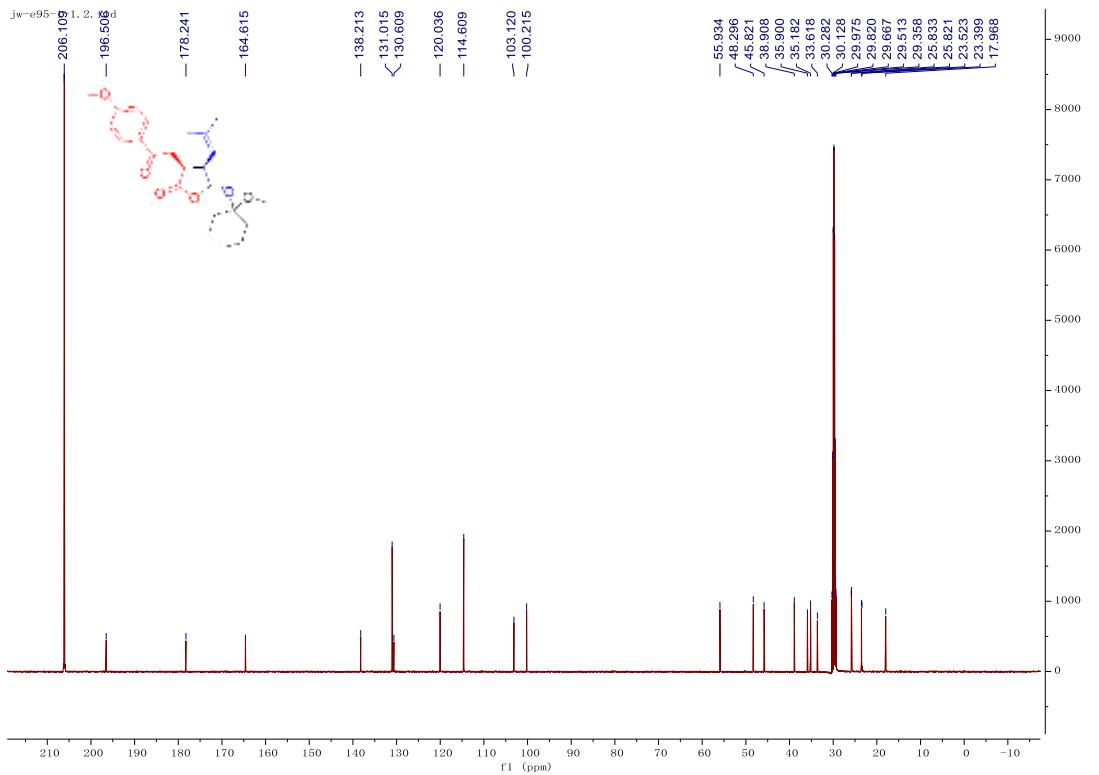
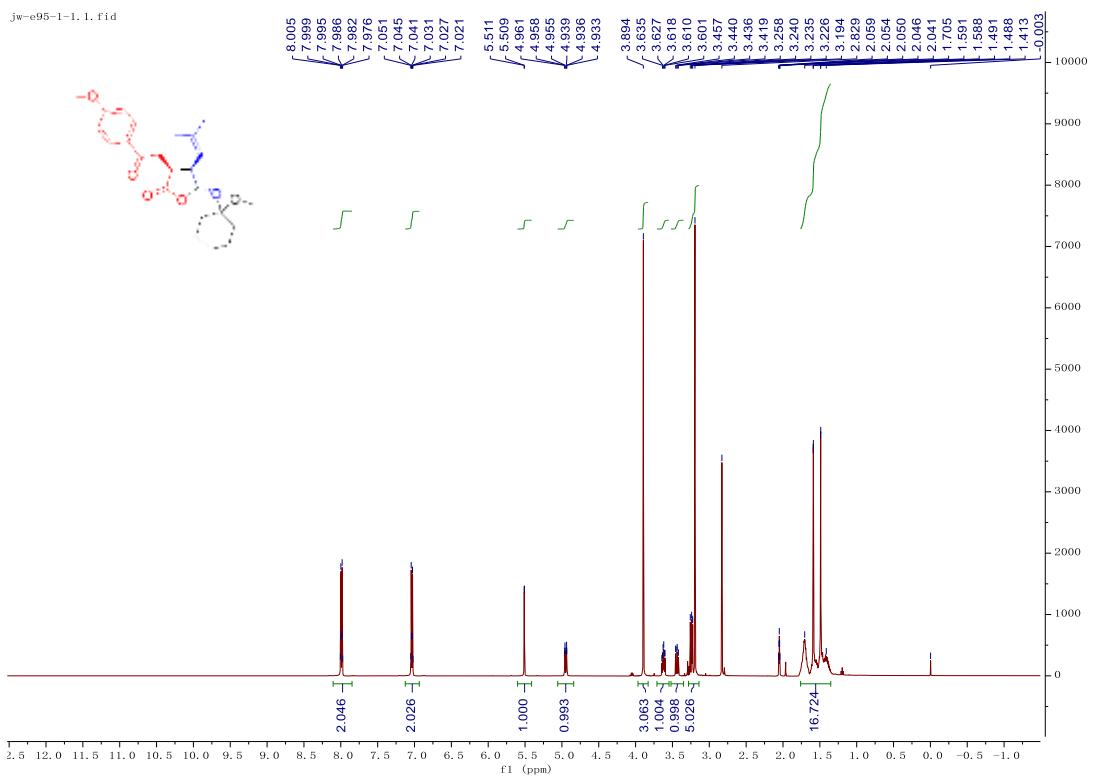


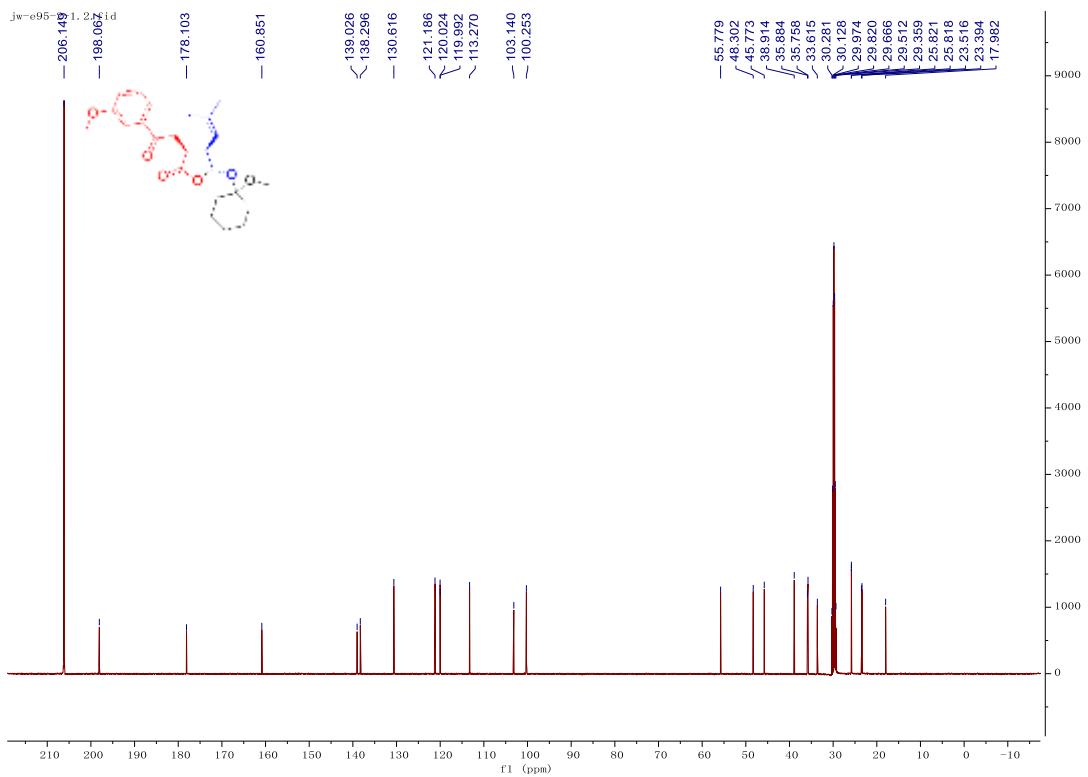
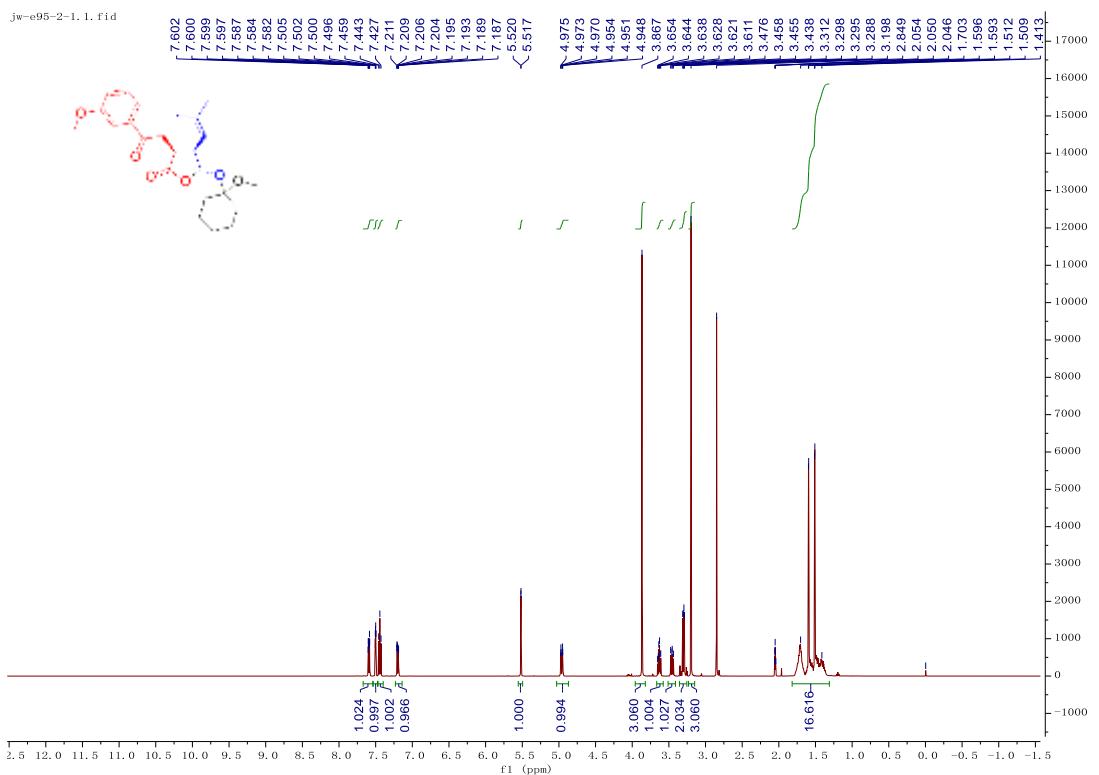


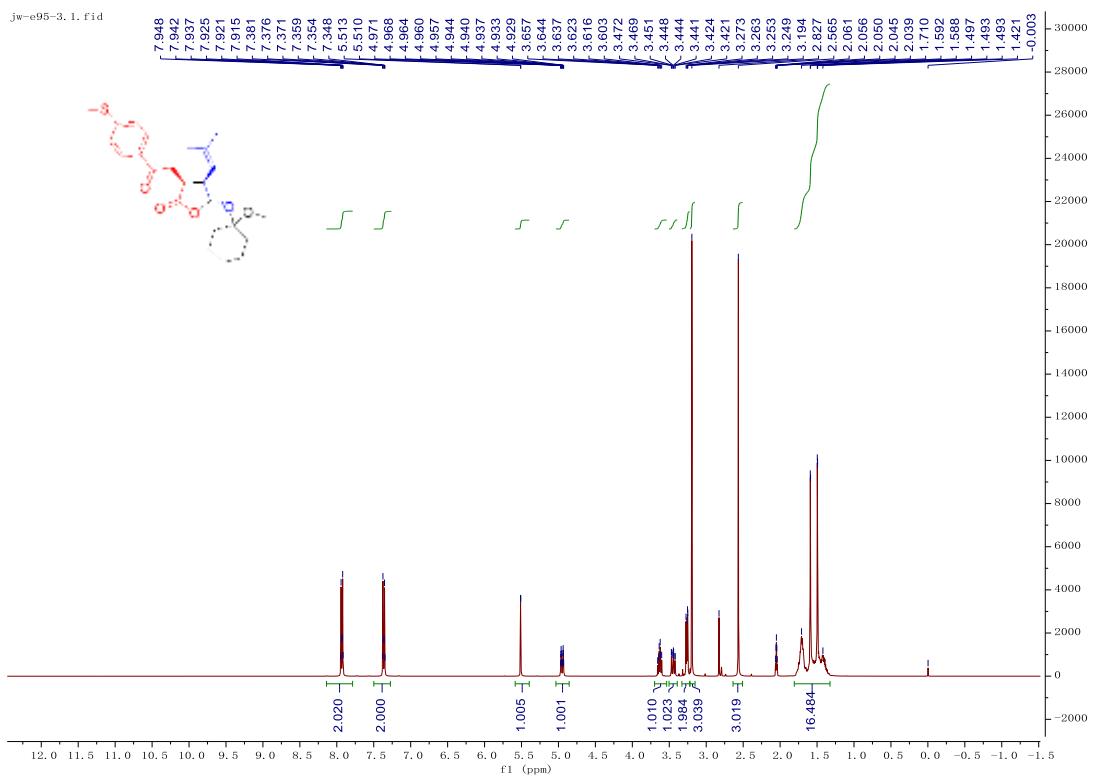


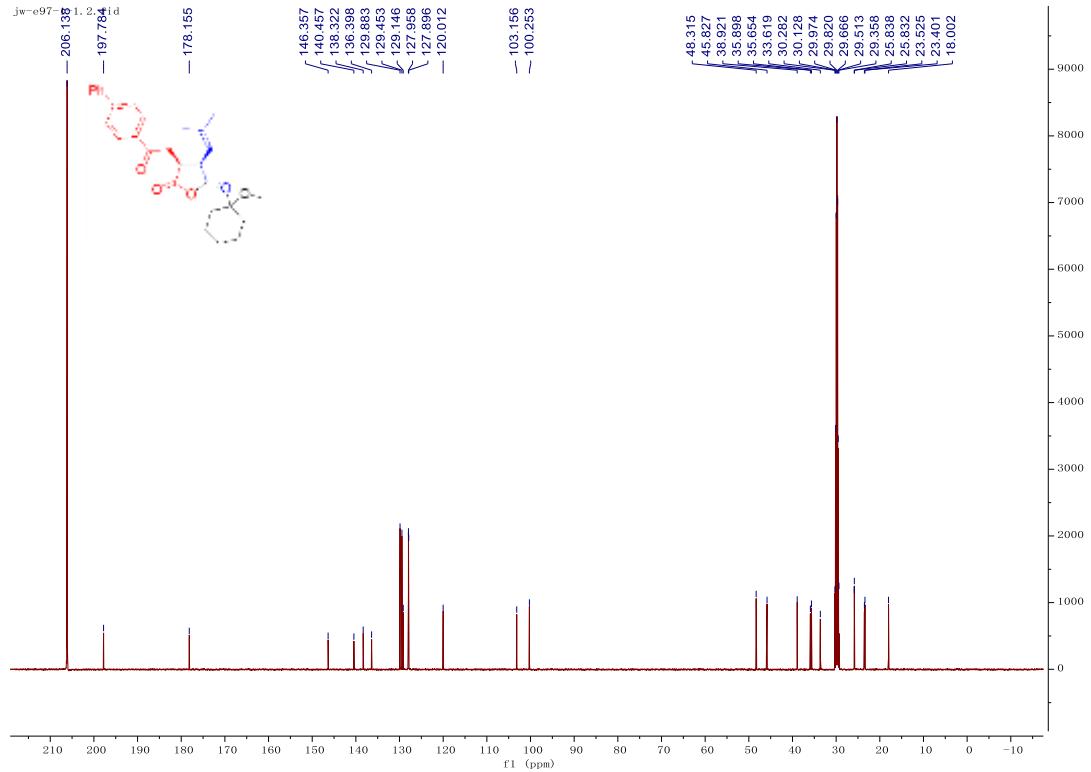
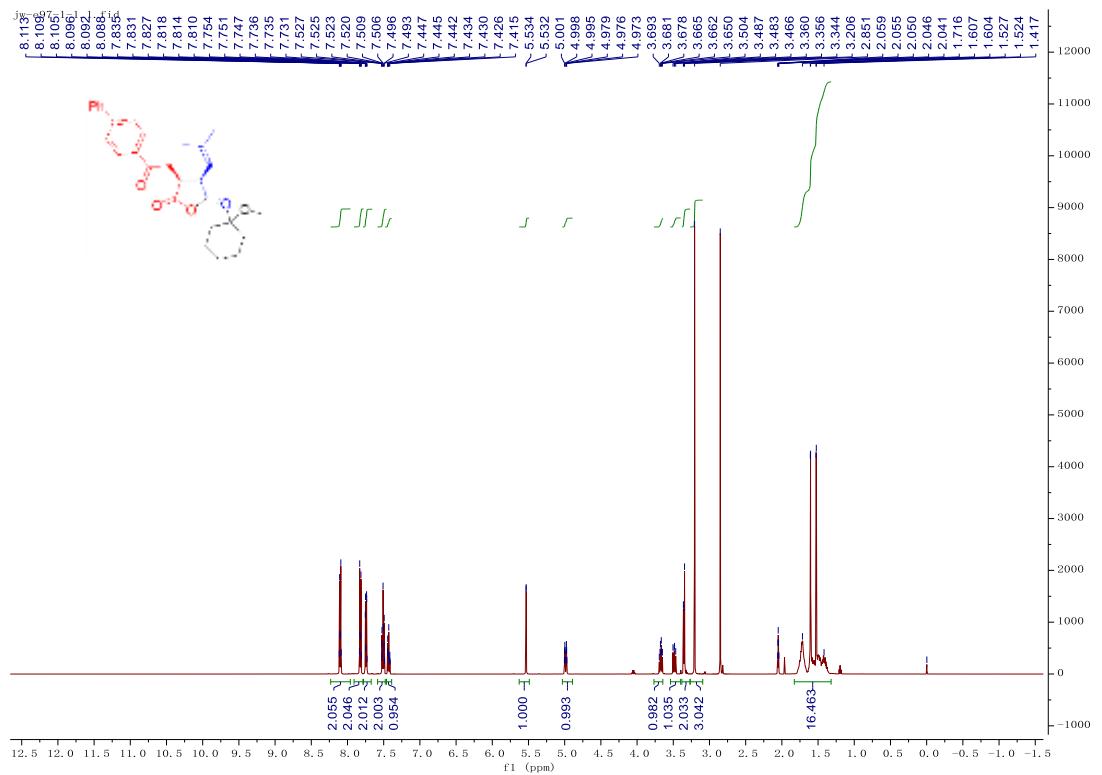


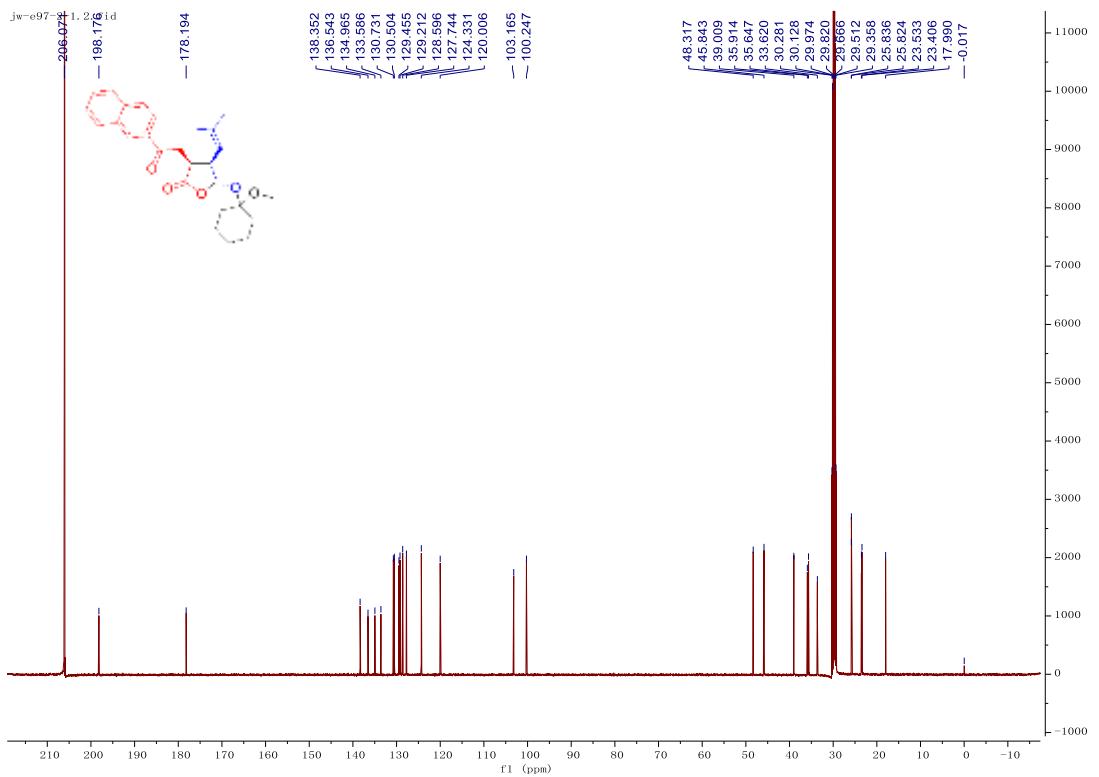
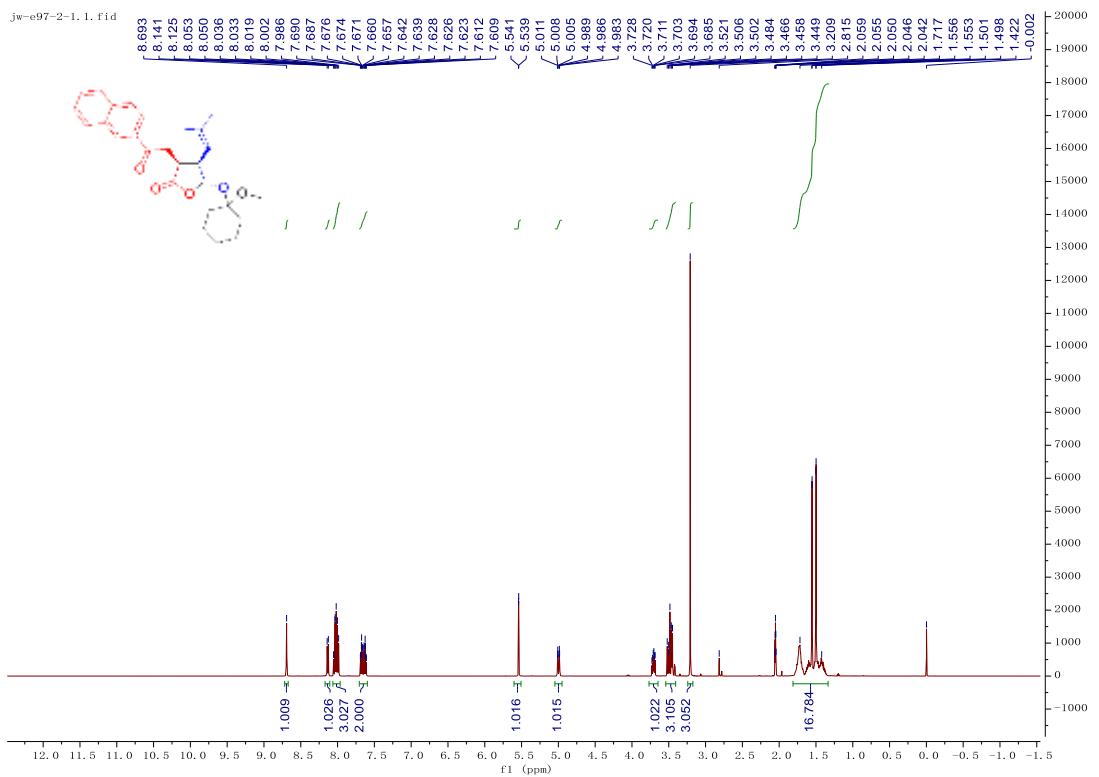


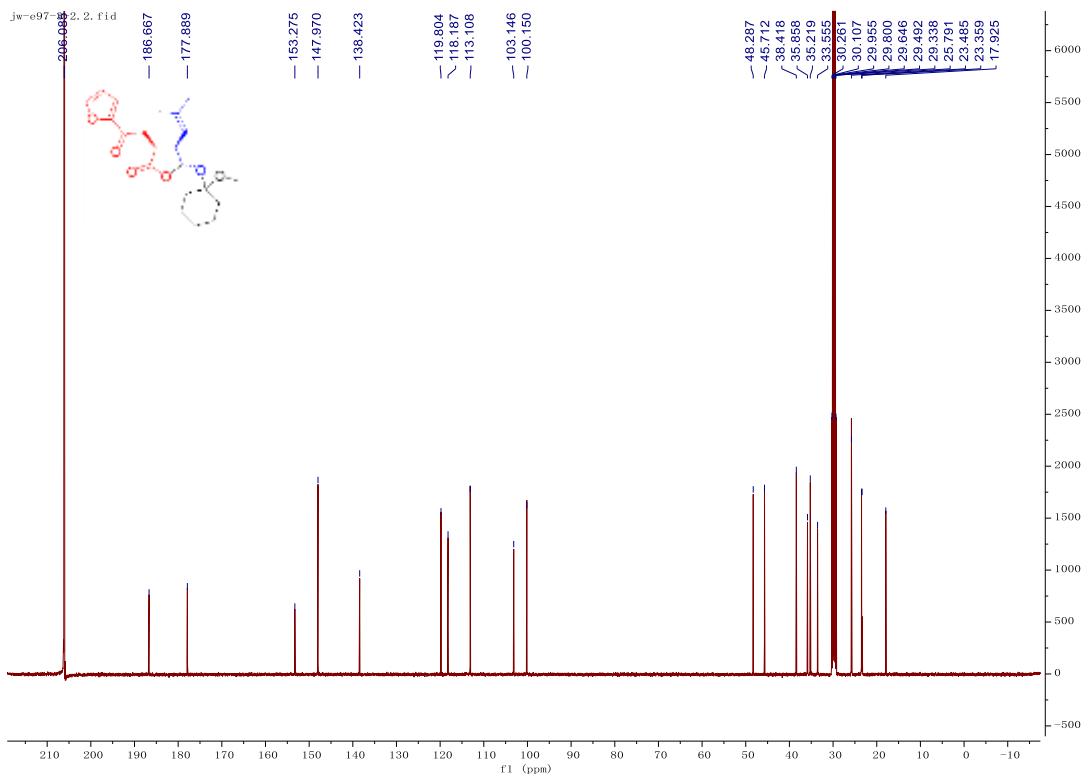
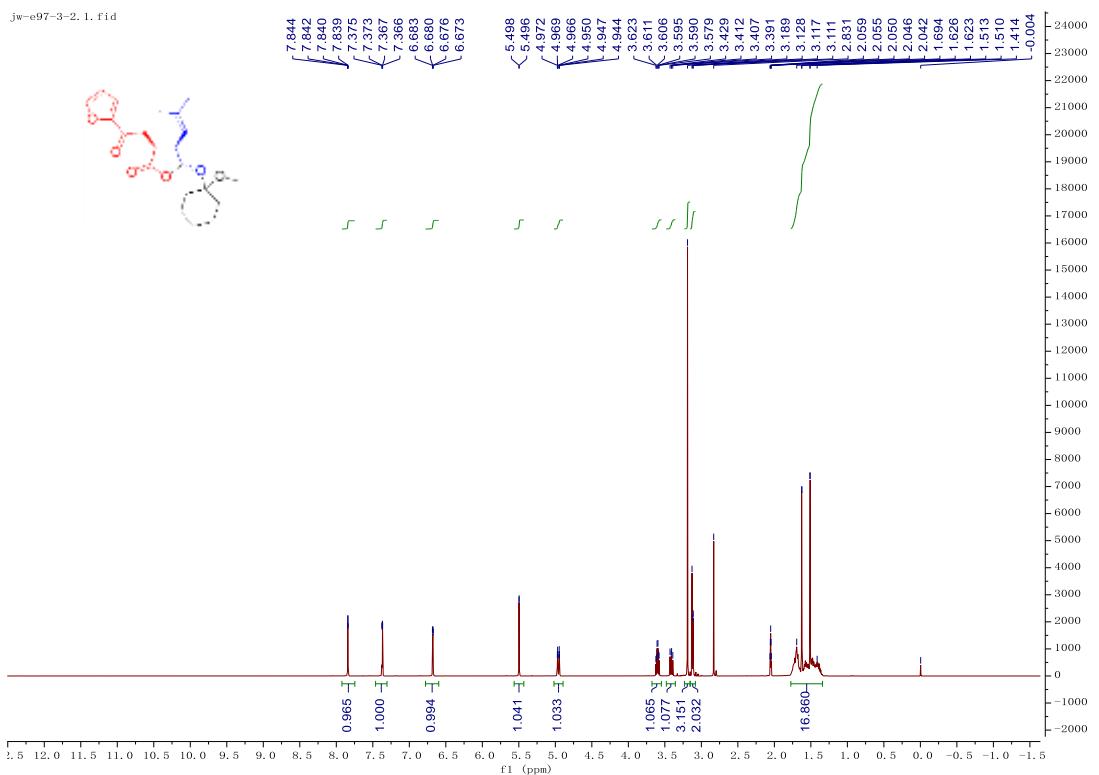


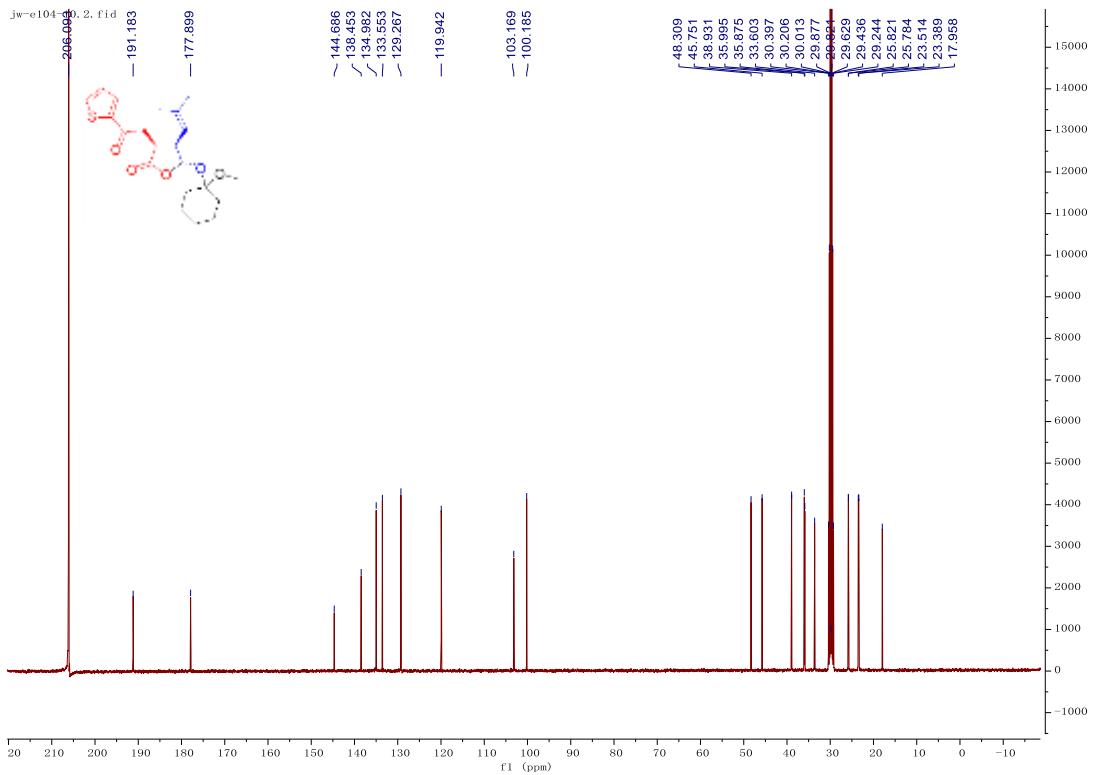
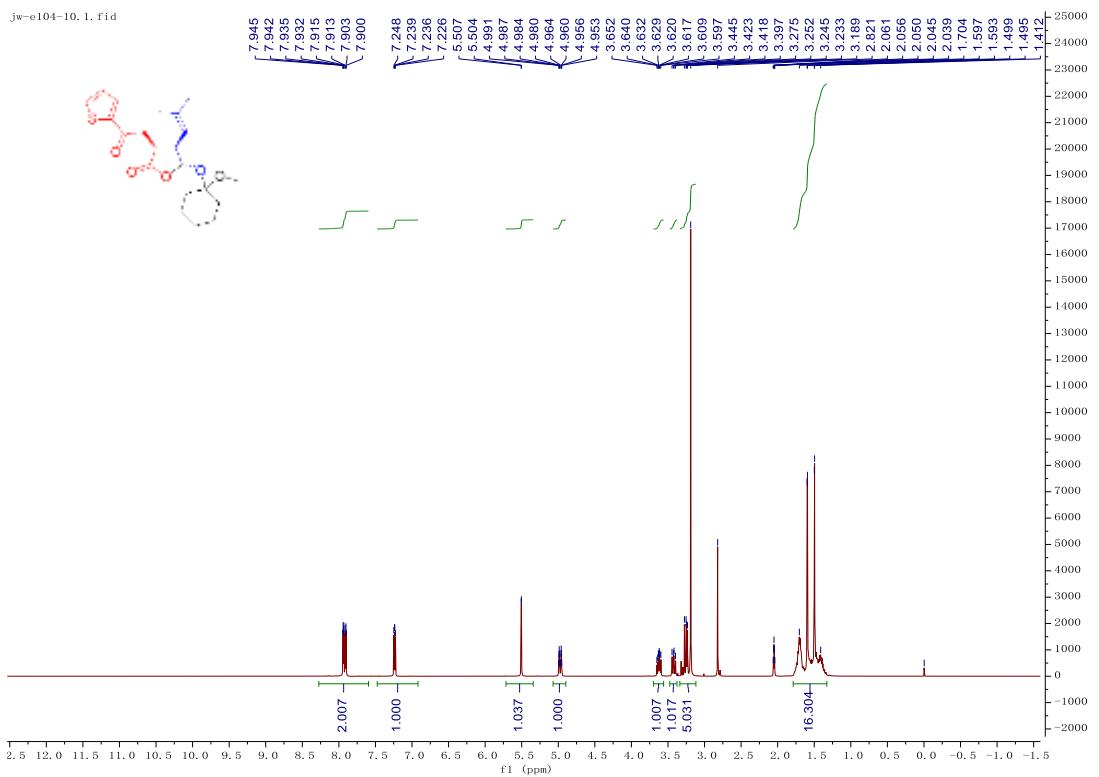


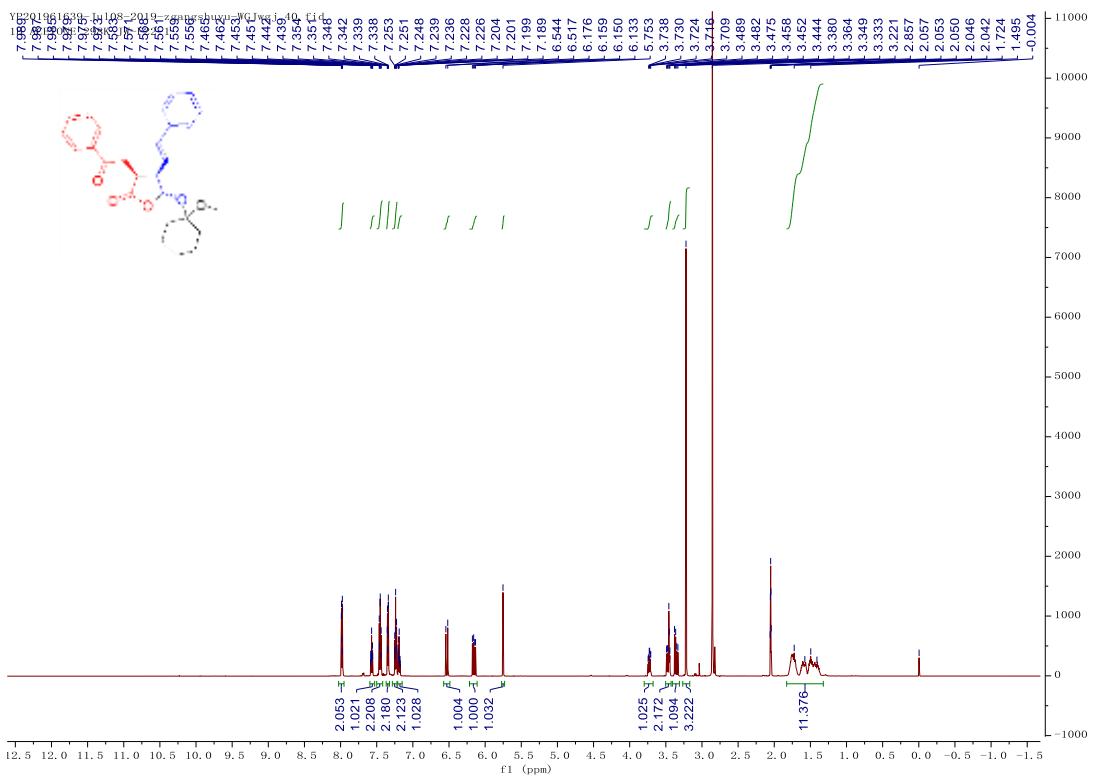


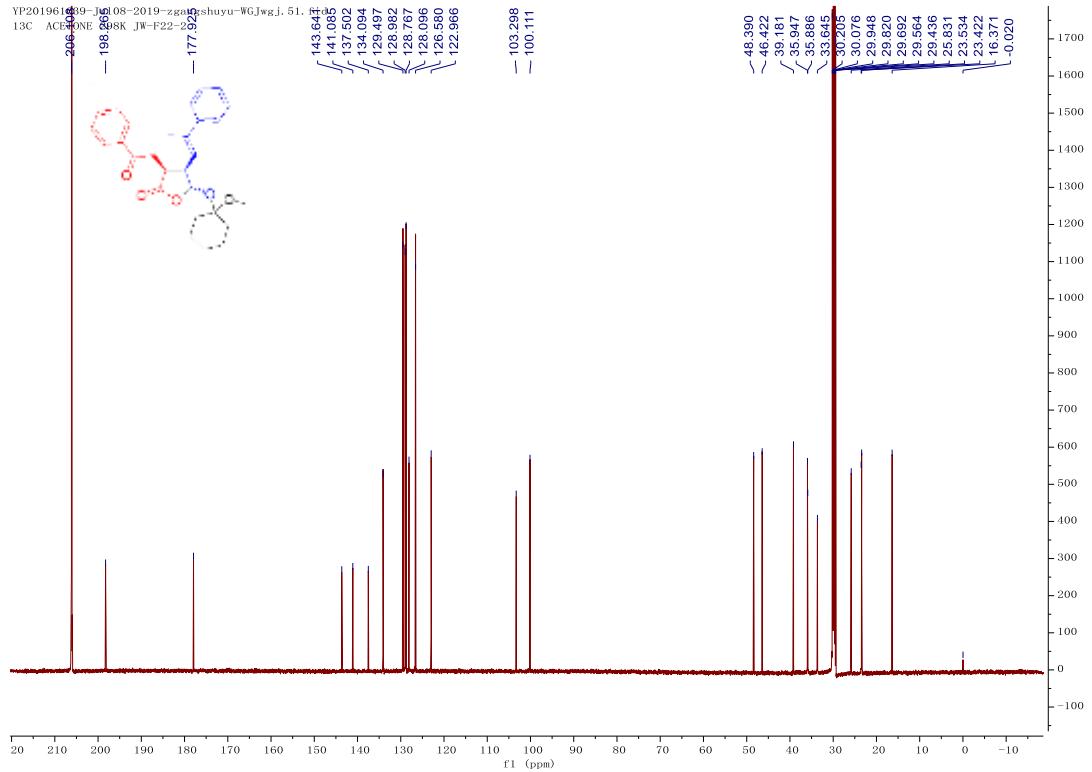
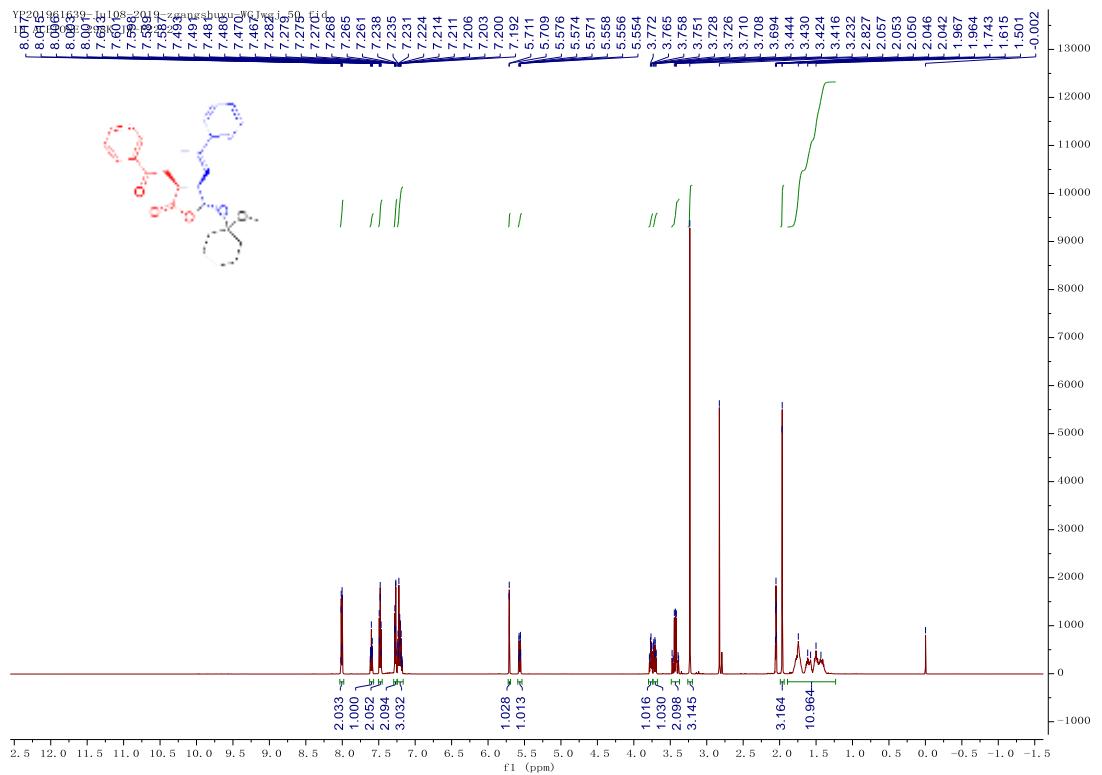


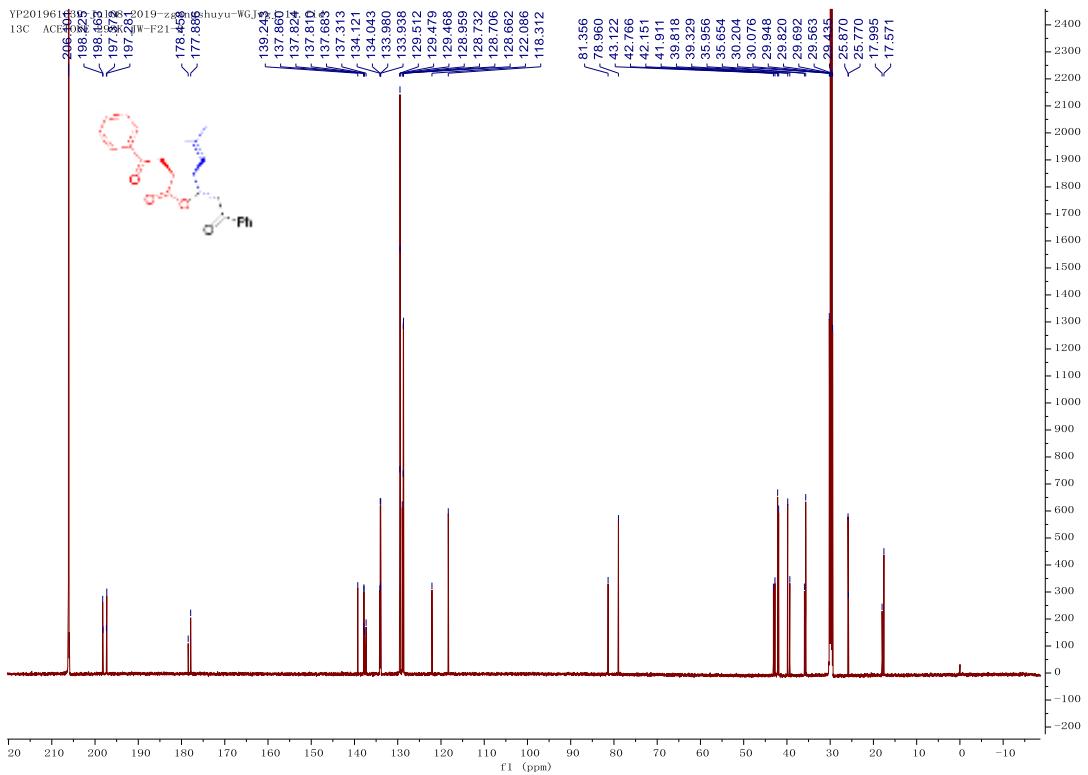
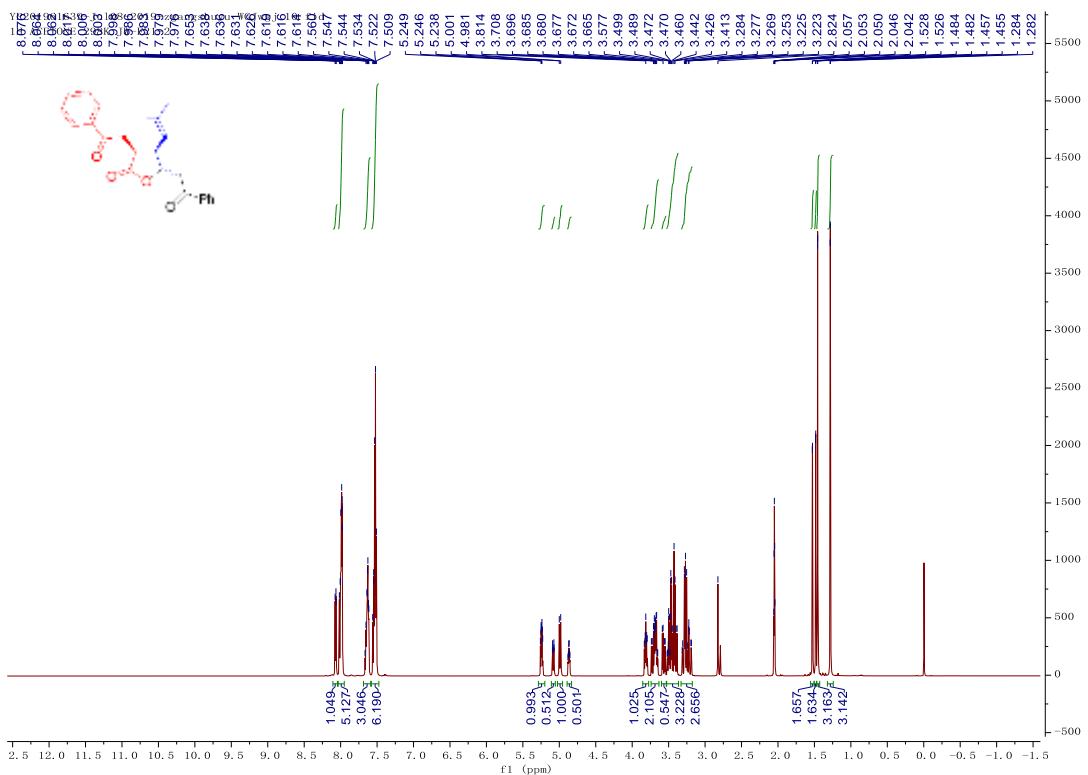


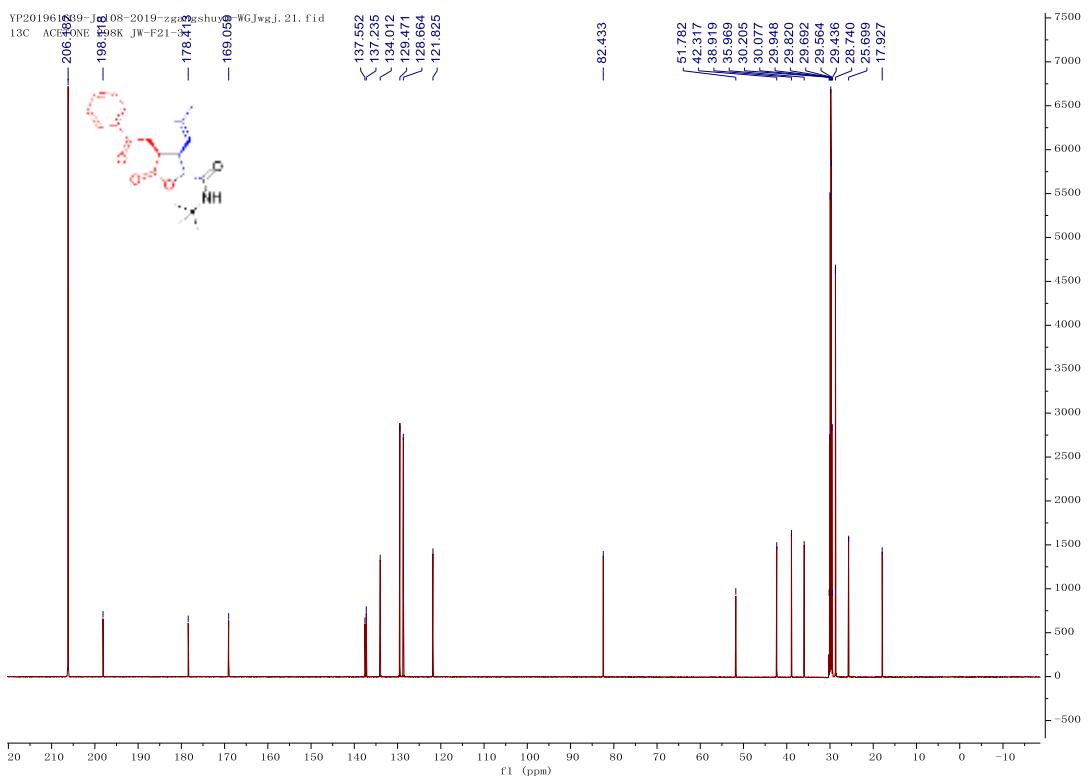
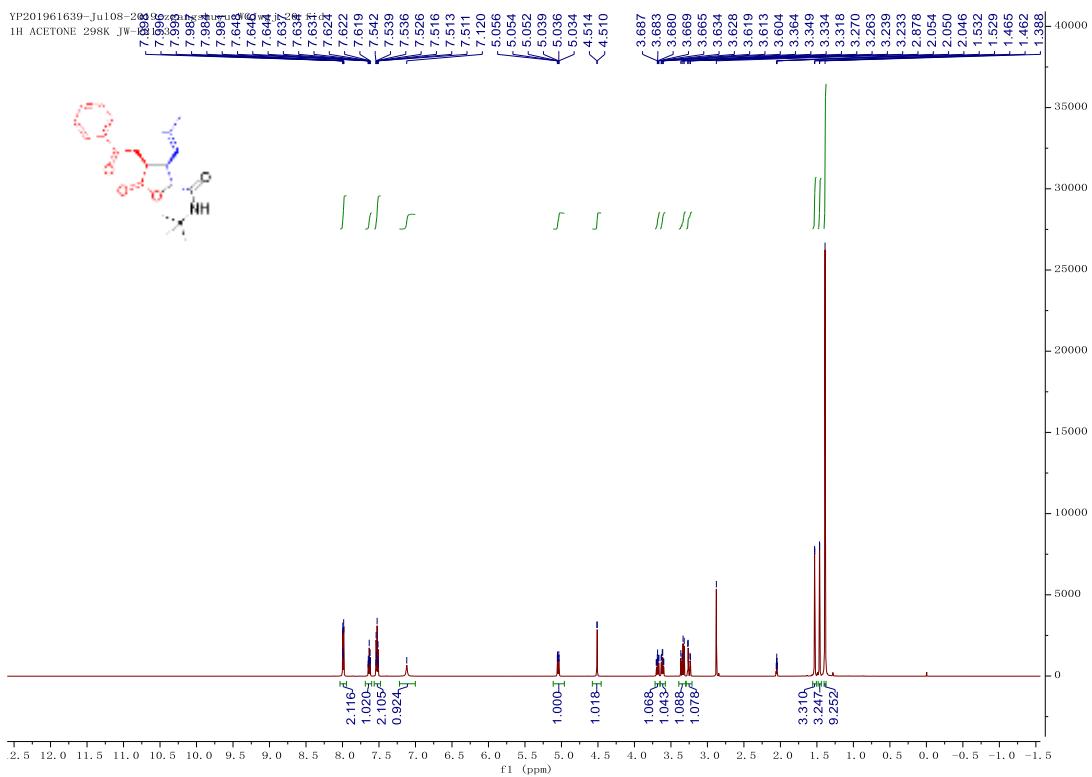


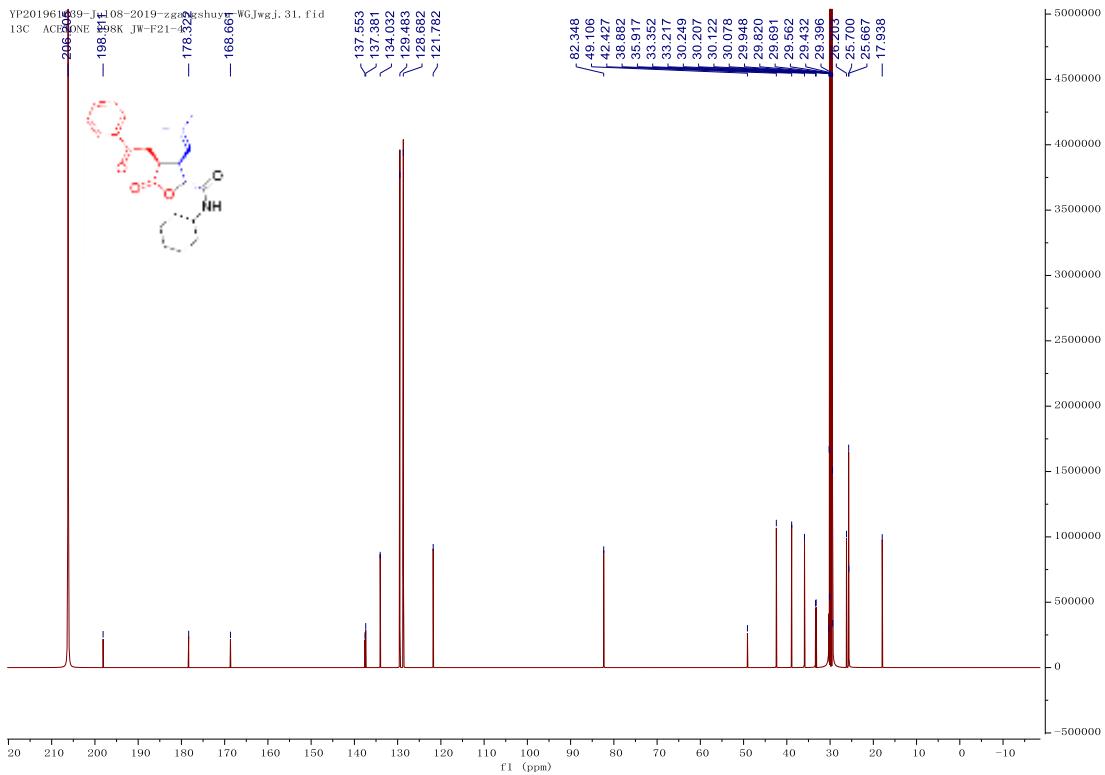
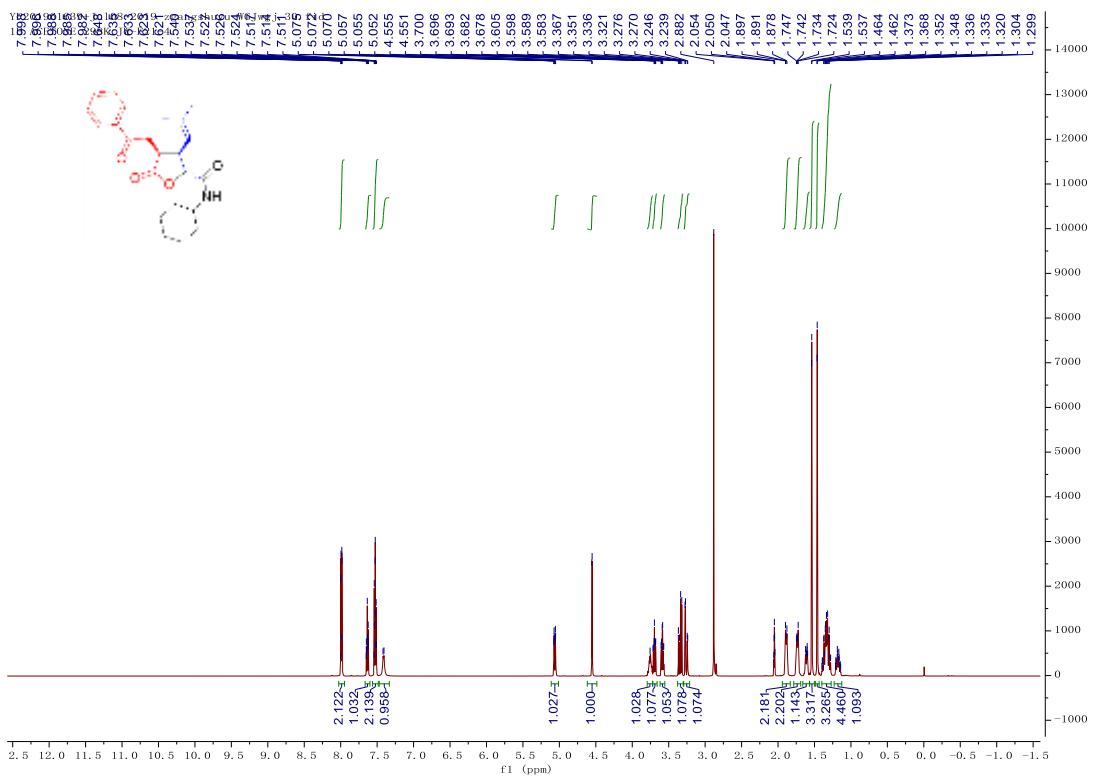




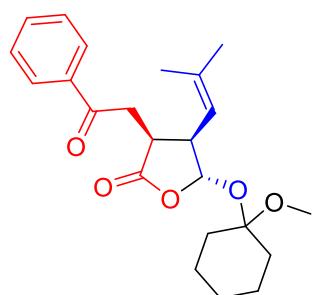




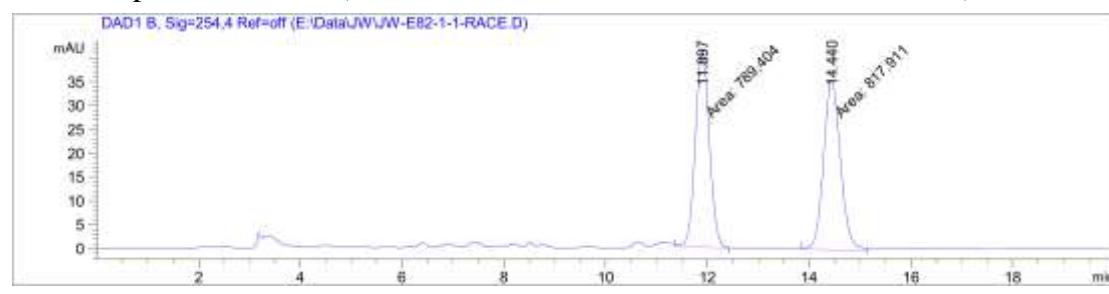




8 HPLC and UPC Trace

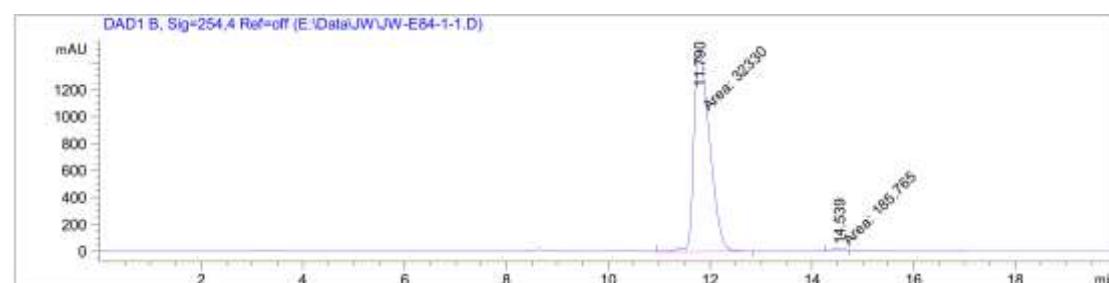


3a: Chiralpak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



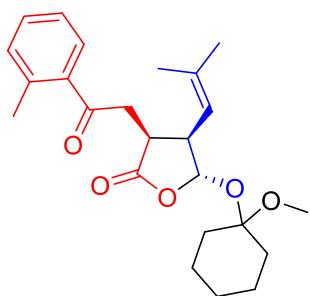
Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	11.897	MM	0.3183	789.40442	41.33144	49.1132
2	14.440	MM	0.3846	817.91071	35.44087	50.8868

Totals : 1607.31512 76.77231

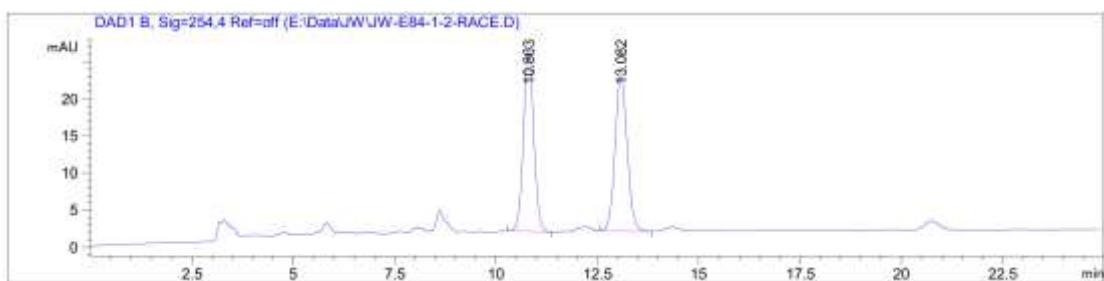


Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	11.790	MM	0.3622	3.23300e4	1487.55579	99.4287
2	14.539	MM	0.2510	185.76512	12.33290	0.5713

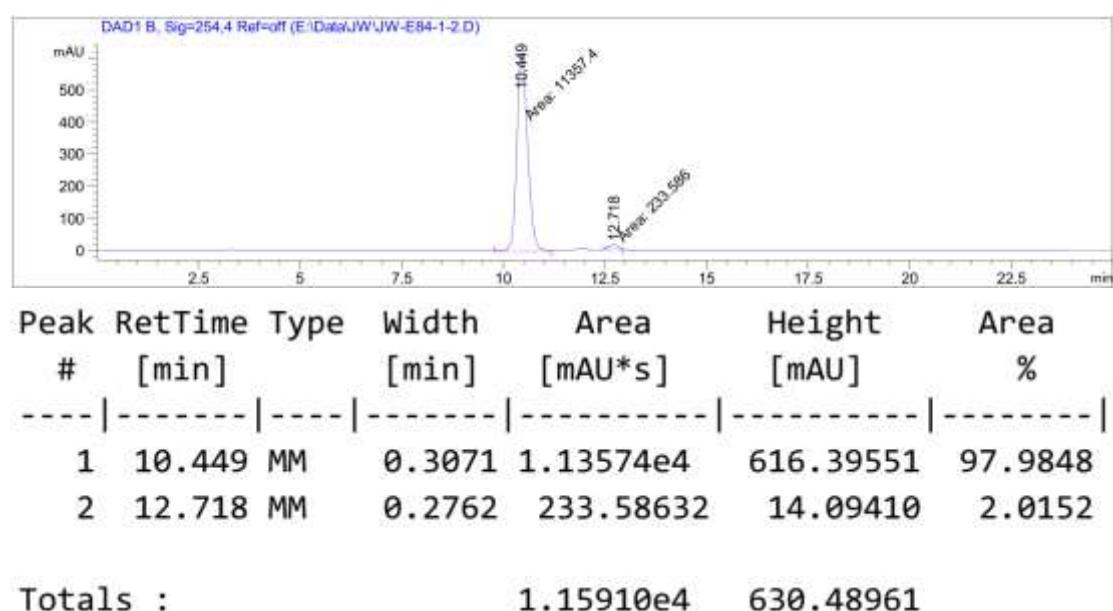
Totals : 3.25158e4 1499.88869



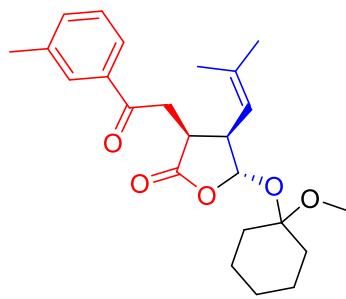
3b: Chiraldak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



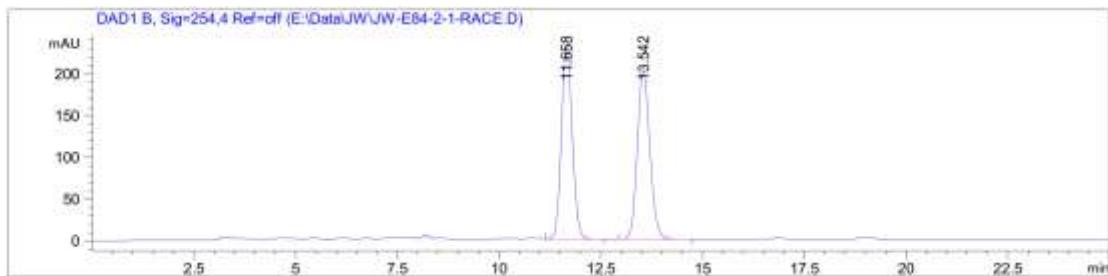
Peak Totals :	869.54718	45.65624
---------------	-----------	----------



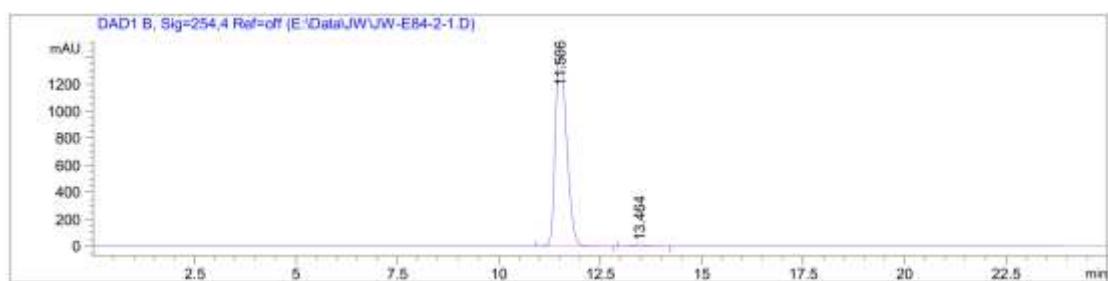
Peak Totals :	1.15910e4	630.48961
---------------	-----------	-----------



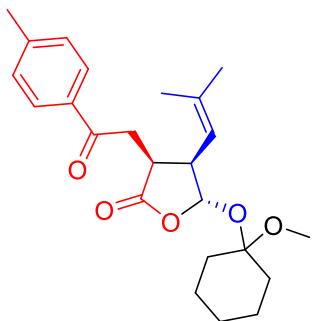
3c: Chiraldex IC Column (*n*-hexane/*i*-PrOH = 90/10, 1.0 ml/min, λ = 254 nm)



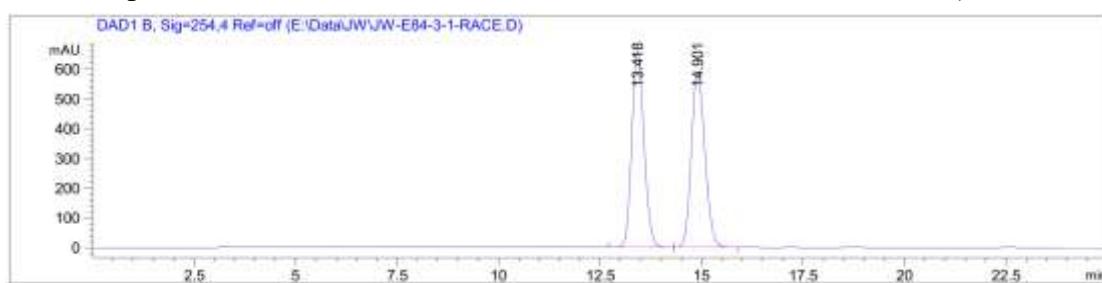
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.658	BB	0.2864	4299.24219	231.75517	49.9366
2	13.542	BB	0.3338	4310.15088	201.26230	50.0634
Totals :				8609.39307	433.01747	



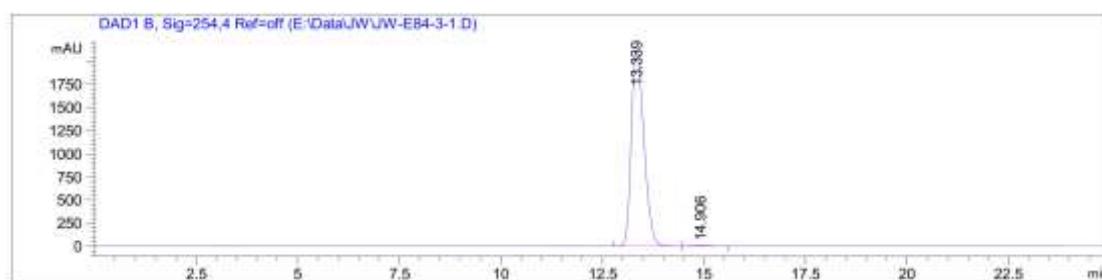
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.506	BB	0.2960	2.76020e4	1450.67505	99.1542
2	13.464	BB	0.3276	235.45113	11.18593	0.8458
Totals :				2.7837E+04	1461.86098	



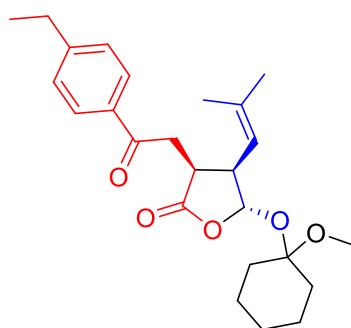
3d: Chiraldak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



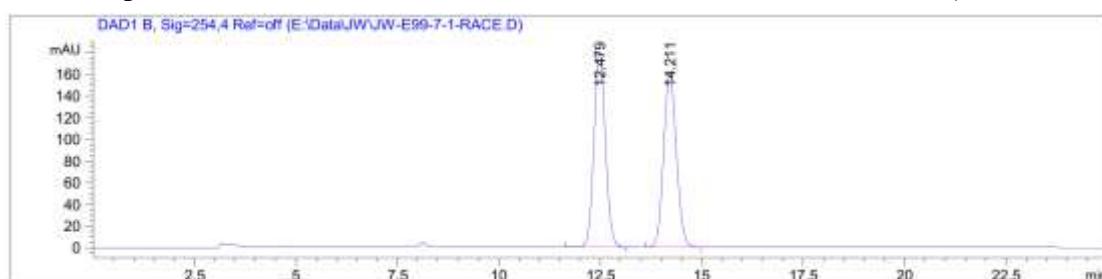
Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
<hr/>						
Totals :				2.74645e4	1248.94318	



Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
<hr/>						
Totals :				4.60801e4	2136.35586	

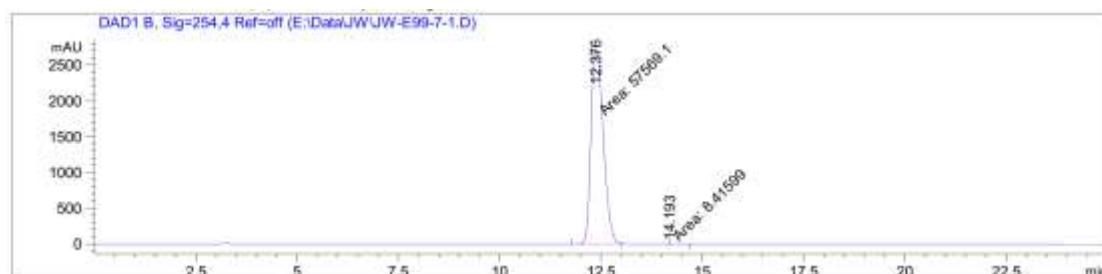


3e: Chiralpak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



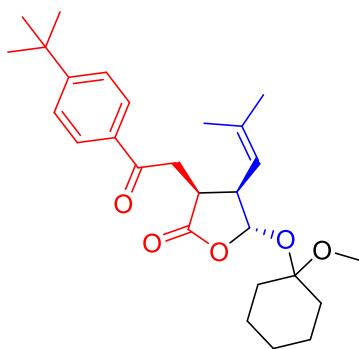
Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	12.479	BB	0.3035	3518.38867	180.40329	50.0917
2	14.211	BB	0.3396	3505.50854	159.99940	49.9083

Totals : 7023.89722 340.40269

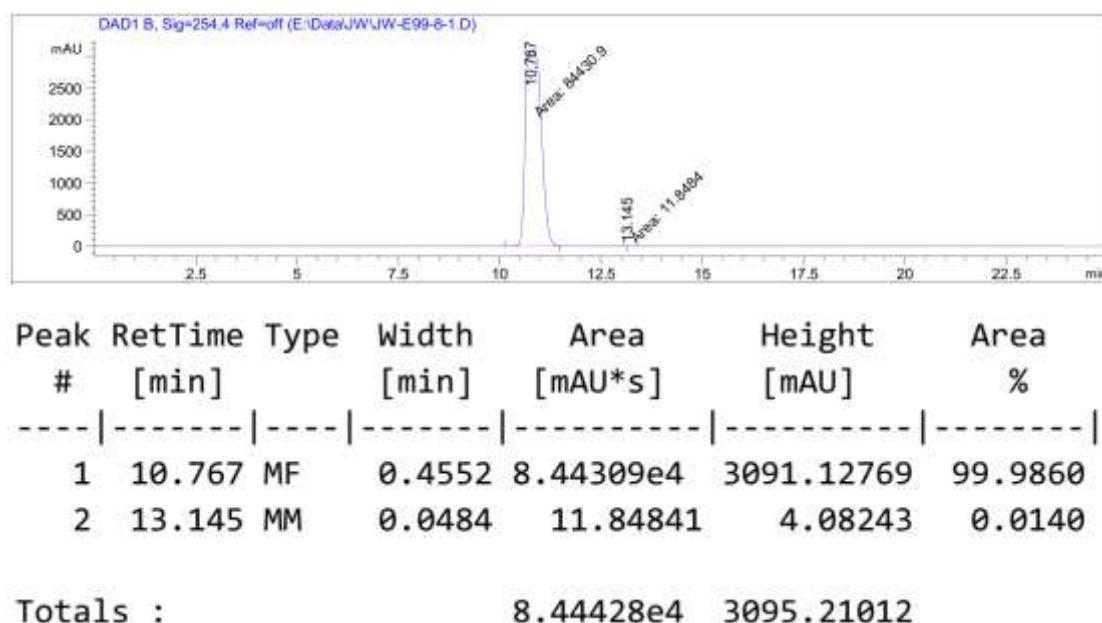
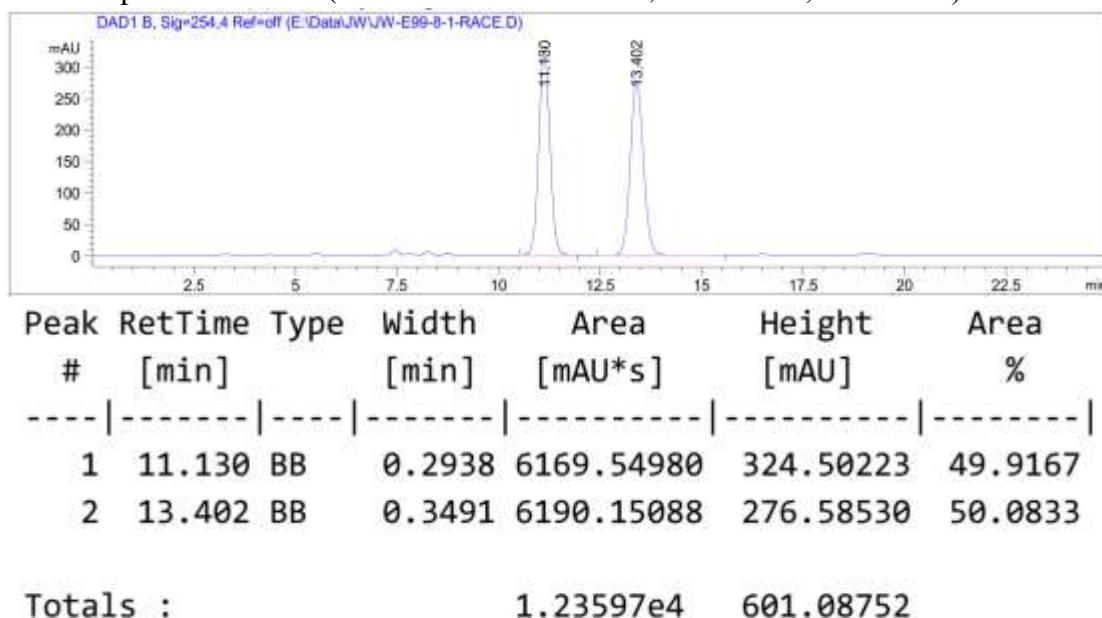


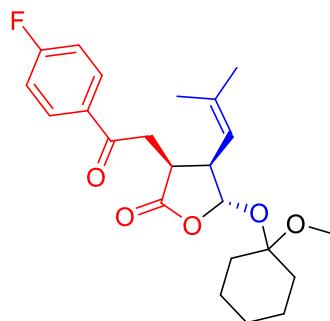
Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	12.376	MF	0.3522	5.75691e4	2724.35913	99.9854
2	14.193	MF	0.2980	8.41599	4.70726e-1	0.0146

Totals : 5.75776e4 2724.82986

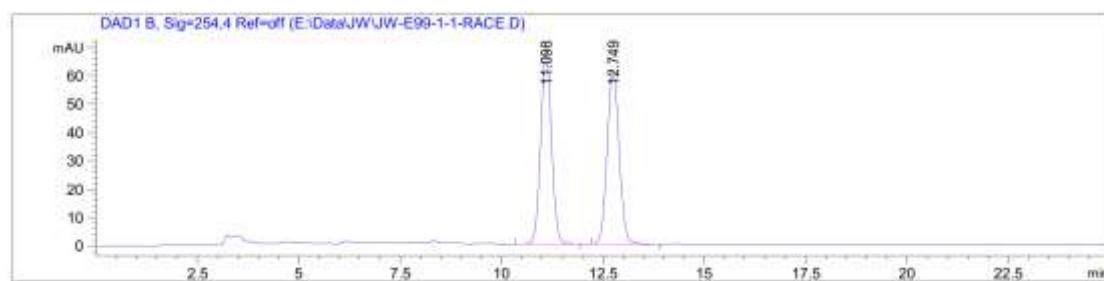


3f: Chiralpak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)

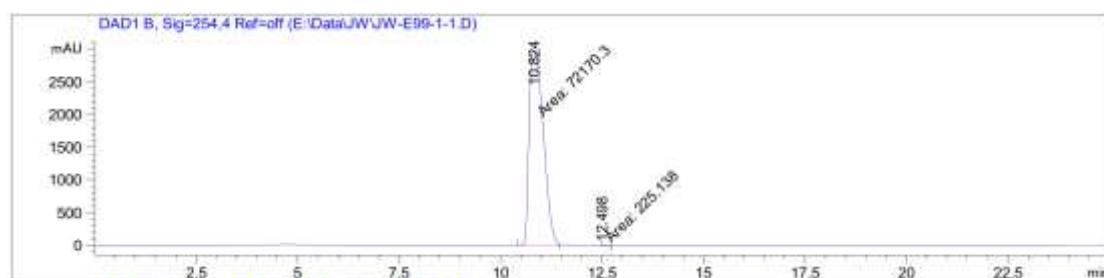




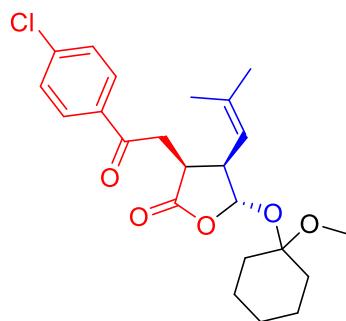
3g: Chiraldak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



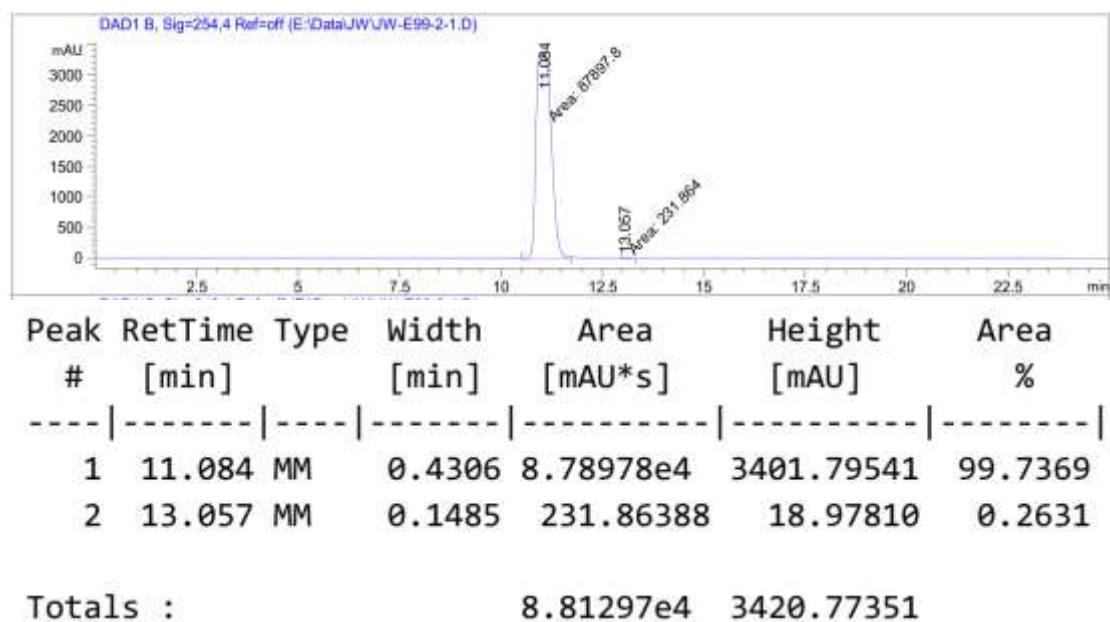
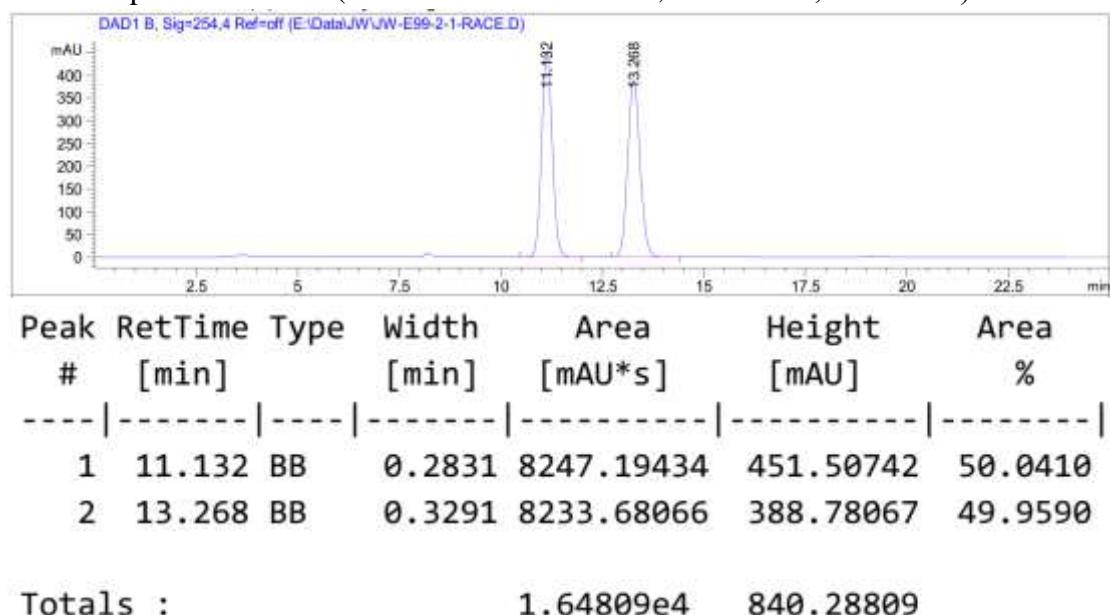
Totals :		2530.92163	129.72839
----------	--	------------	-----------

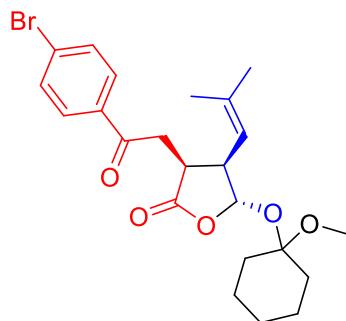


Totals :		7.23954e4	2996.55022
----------	--	-----------	------------

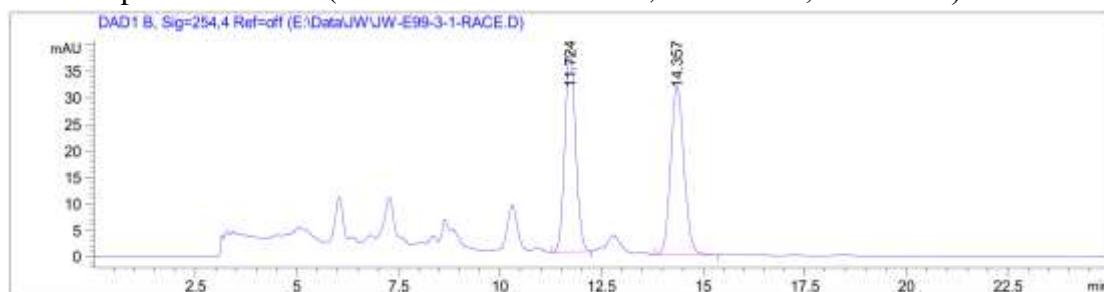


3h: Chiraldak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



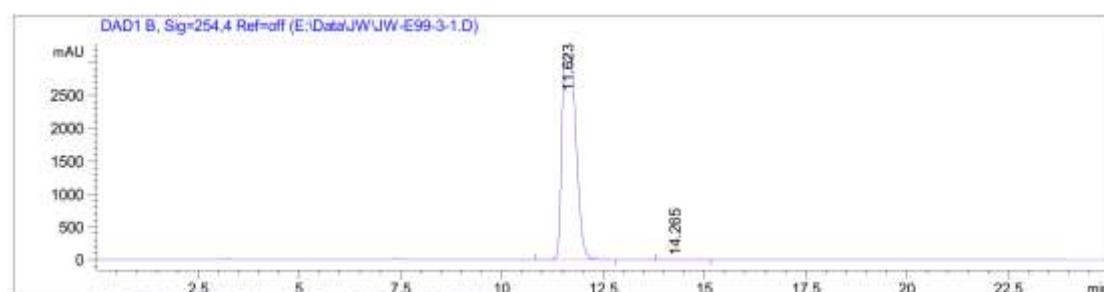


3i: Chiralpak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



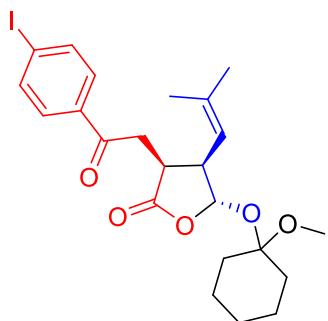
Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	11.724	BB	0.2857	704.49622	38.10728	49.1746
2	14.357	BB	0.3514	728.14734	32.00572	50.8254

Totals : 1432.64355 70.11300

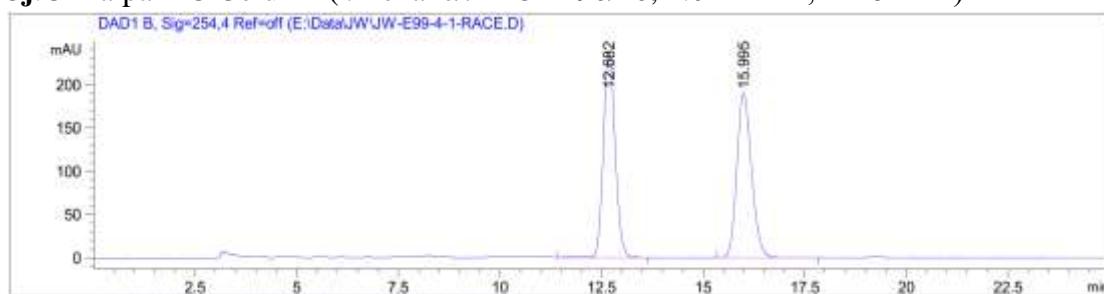


Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	11.623	BB	0.3839	7.52251e4	3135.63940	99.9473
2	14.265	BB	0.3680	39.67209	1.55320	0.0527

Totals : 7.52648e4 3137.19260

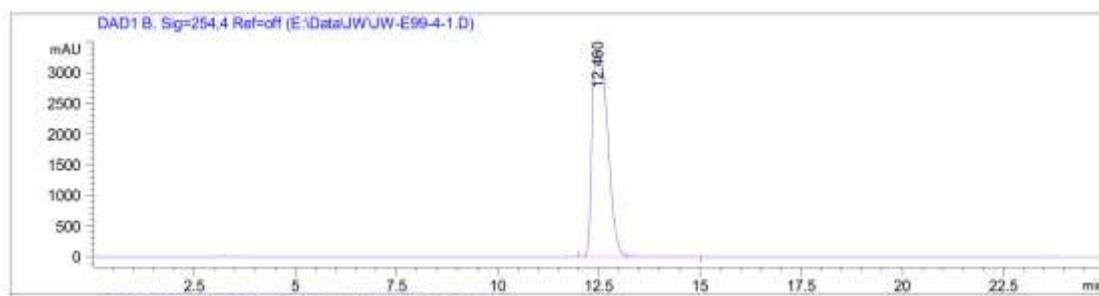


3j: Chiralpak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



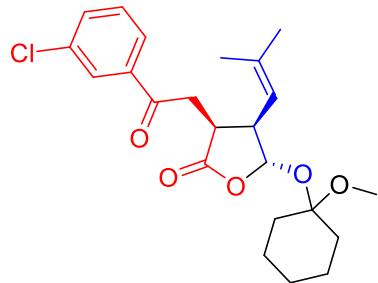
Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	12.682	BB	0.3103	4763.28174	237.21007	50.0259
2	15.995	BB	0.3890	4758.34814	189.48361	49.9741

Totals : 9521.62988 426.69368

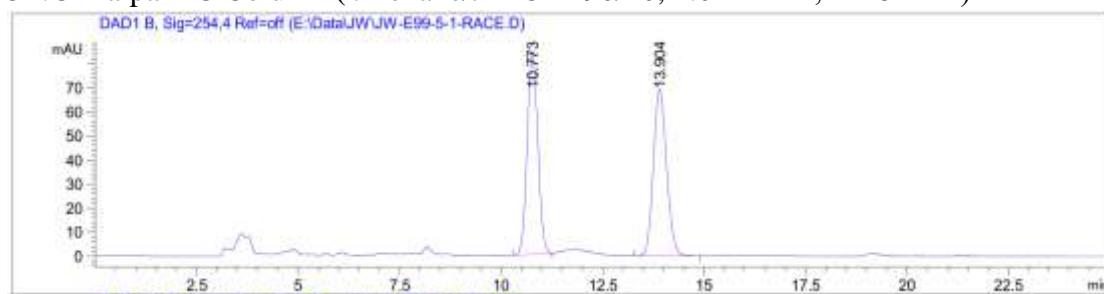


Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	12.460	BB	0.4333	8.99283e4	3348.38623	100.0000

Totals : 8.99283e4 3348.38623

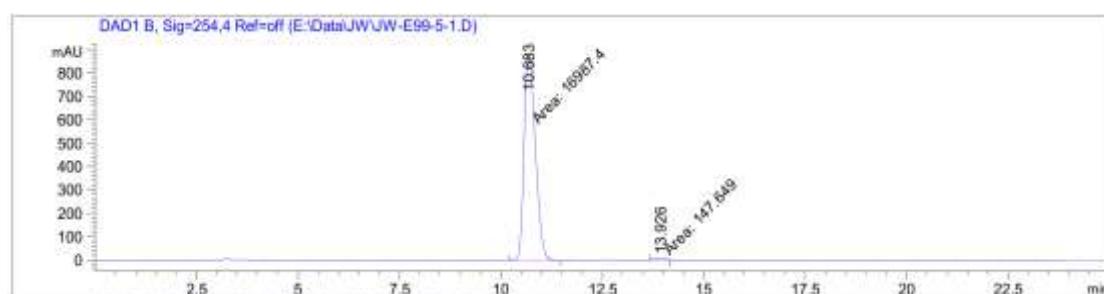


3k: Chiralpak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



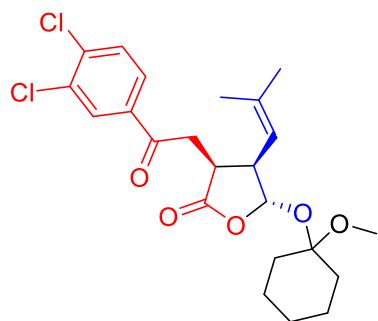
Peak RetTime Type		Width	Area	Height	Area
#	[min]	[min]	[mAU*s]	[mAU]	%
1	10.773	BB	0.2844	1538.17688	84.50094
2	13.904	BB	0.3527	1567.07178	69.06185

Totals : 3105.24866 153.56279

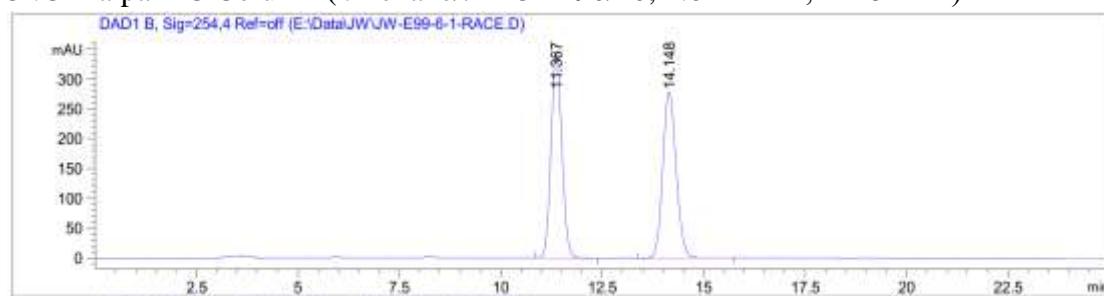


Peak RetTime Type		Width	Area	Height	Area	
#	[min]		[min]	[mAU*s]	[mAU]	%
1	10.683	FM	0.3212	1.69874e4	881.43640	99.1383
2	13.926	MF	0.3344	147.64891	7.35906	0.8617

Totals : 1.71350e4 888.79546

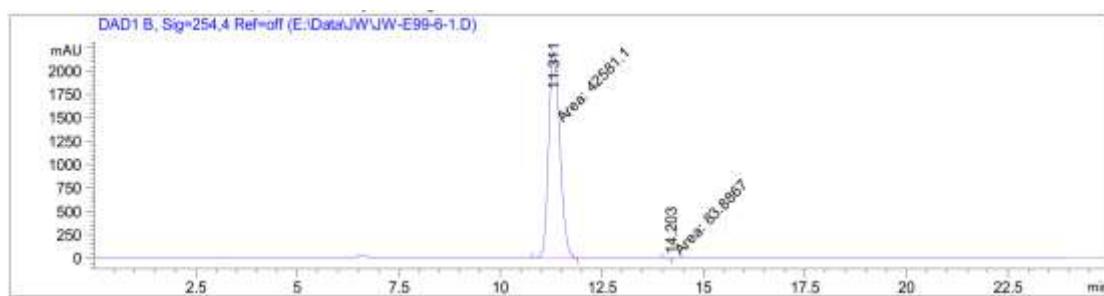


3l: Chiralpak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



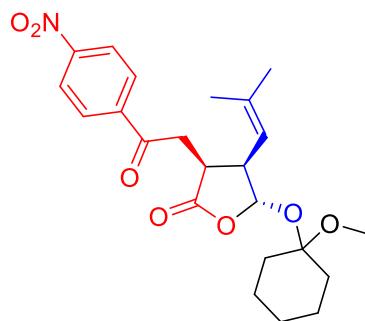
Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	11.367	BB	0.2872	6365.09424	345.07767	50.0226
2	14.148	BB	0.3551	6359.33447	277.72601	49.9774

Totals : 1.27244e4 622.80368

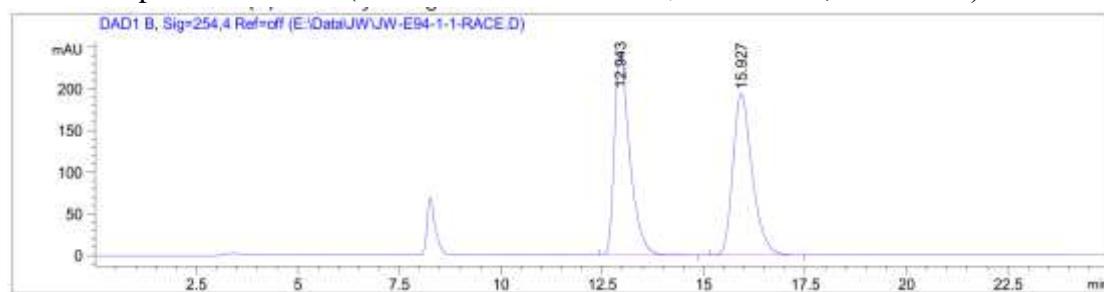


Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	11.311	MF	0.3225	4.25811e4	2200.81909	99.8034
2	14.203	MM	0.1318	83.88667	10.60449	0.1966

Totals : 4.26650e4 2211.42358



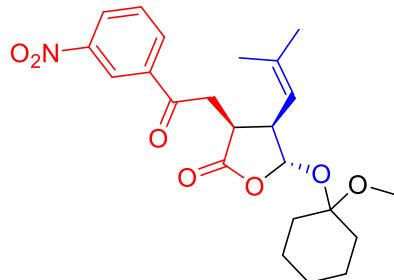
3m: Chiralpak ID Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)



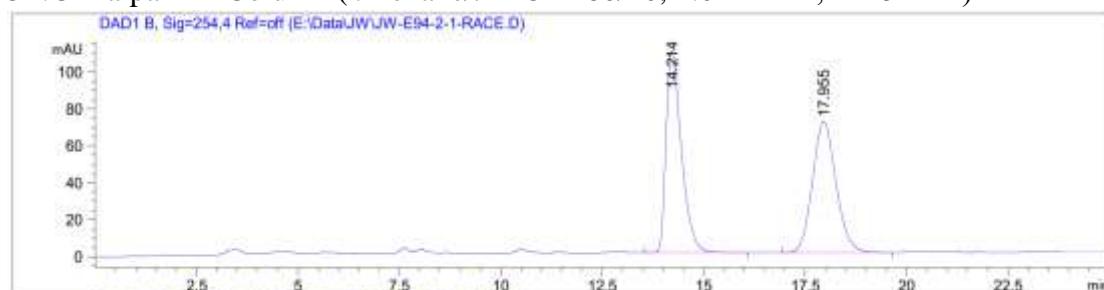
Totals : 1.27638e4 437.45627



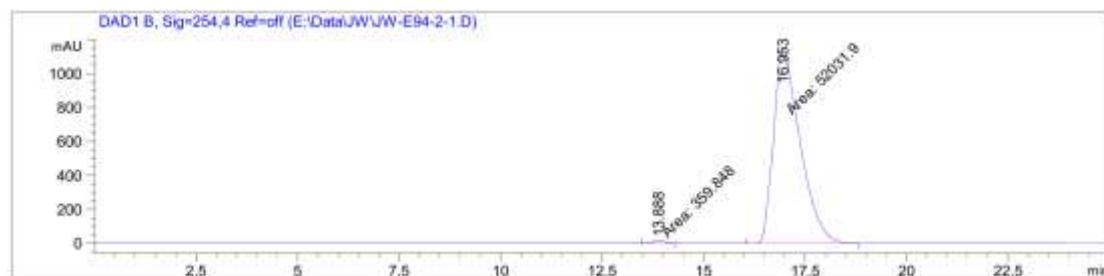
Totals : 1.28553e4 388.03000



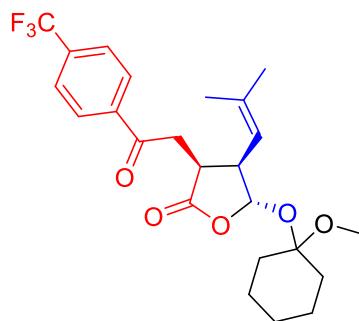
3n: Chiralpak ID Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)



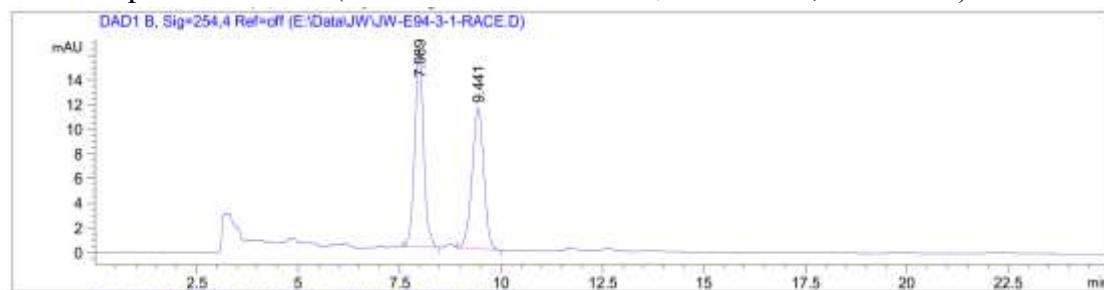
Totals : 5709.93994 180.00375



Totals : 5.23918e4 1164.51672

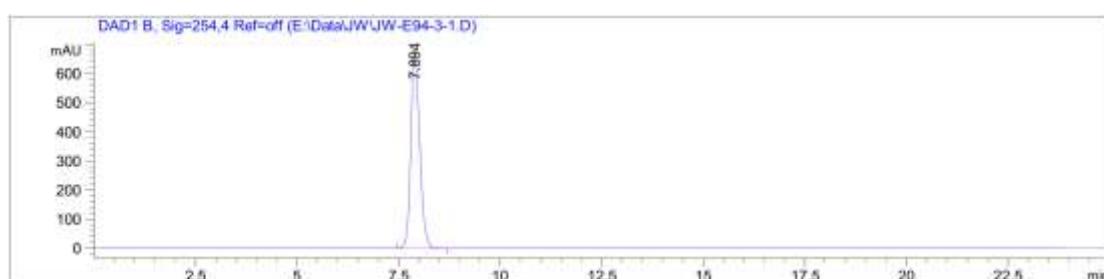


3o: Chiraldak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	7.989	BB	0.2306	243.11800	16.06452	51.5596
2	9.441	BB	0.3060	228.41016	11.48444	48.4404

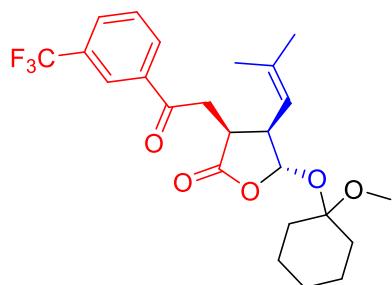
Totals : 471.52815 27.54897



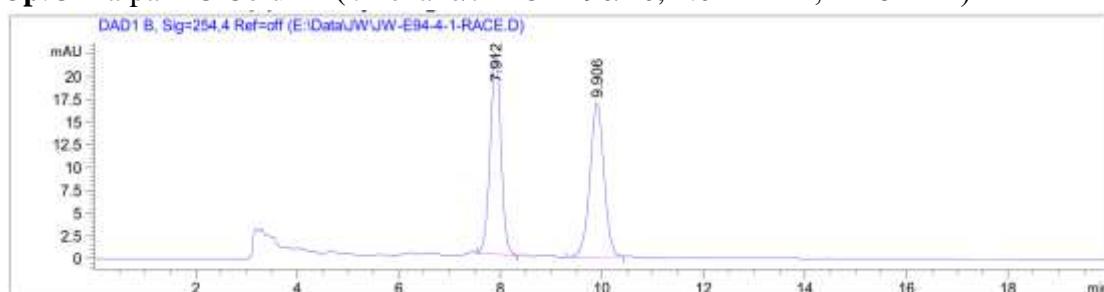
Signal 1: DAD1 B, Sig=254,4 Ref=off

Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	7.894	BB	0.2338	1.02558e4	672.95502	100.0000

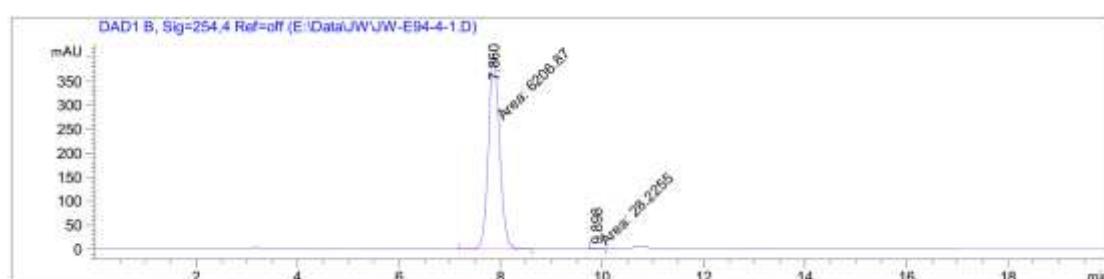
Totals : 1.02558e4 672.95502



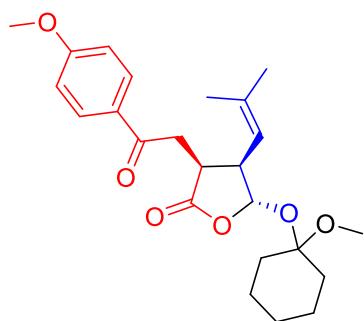
3p: Chiralpak IC Column (*n*-hexane/*i*-PrOH=90/10, 1.0 ml/min, λ =254 nm)



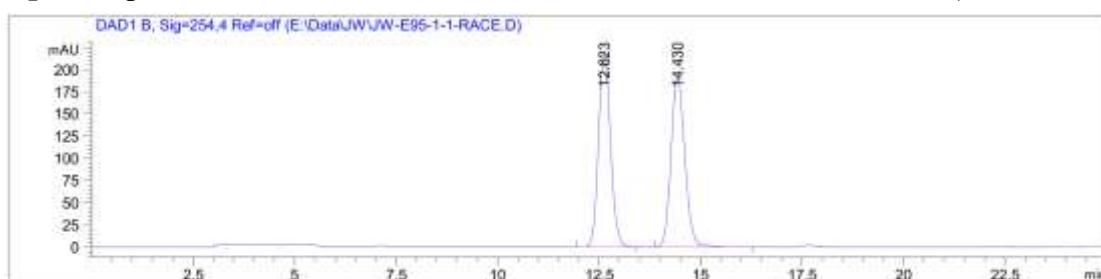
Totals : 649.84326 39.07432



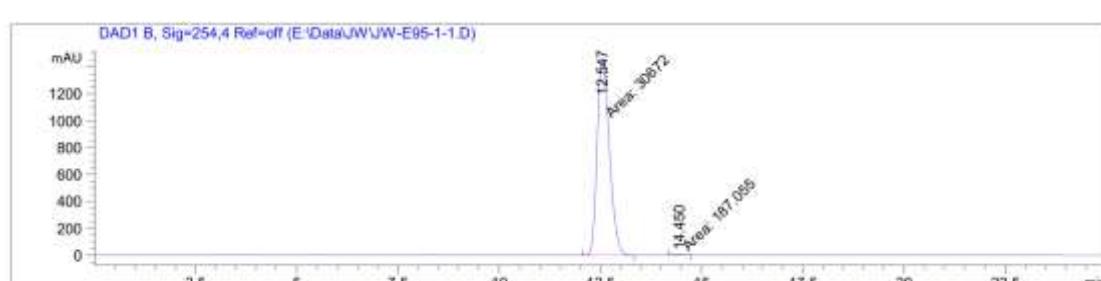
Totals : 6235.09317 410.05848



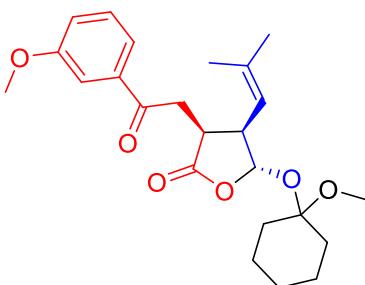
3q: Chiraldak IC Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)



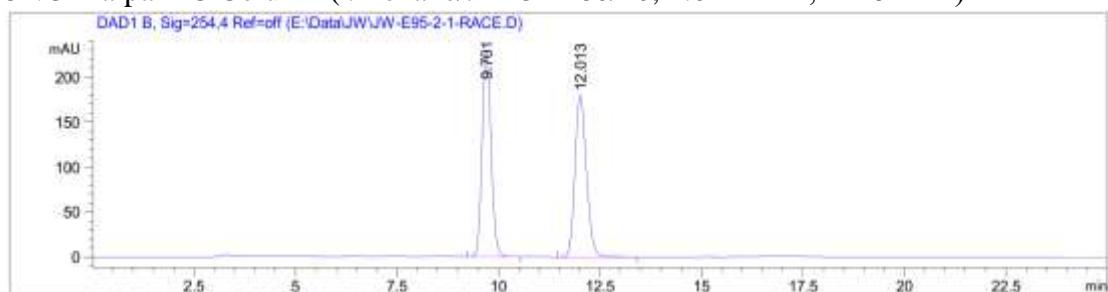
Totals : 9006.10840 410.60951



Totals : 3.08591e4 1463.12585

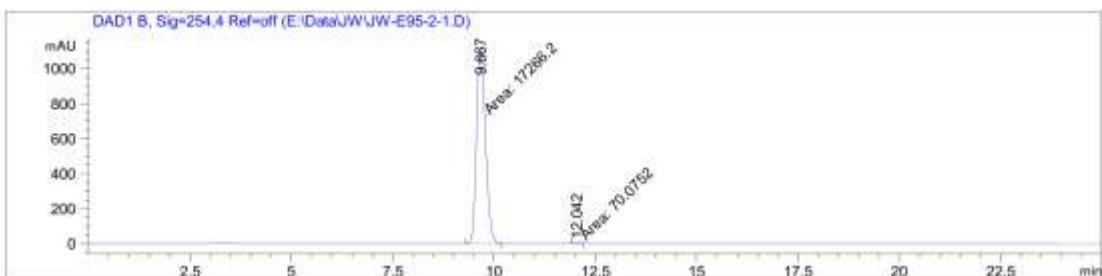


3r: Chiralpak IC Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)



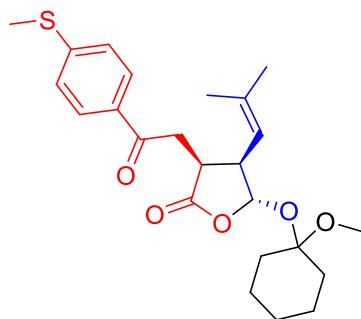
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.701	BB	0.2385	3502.60767	228.86508	49.9747
2	12.013	BB	0.3018	3506.15137	179.60115	50.0253

Totals : 7008.75903 408.46623

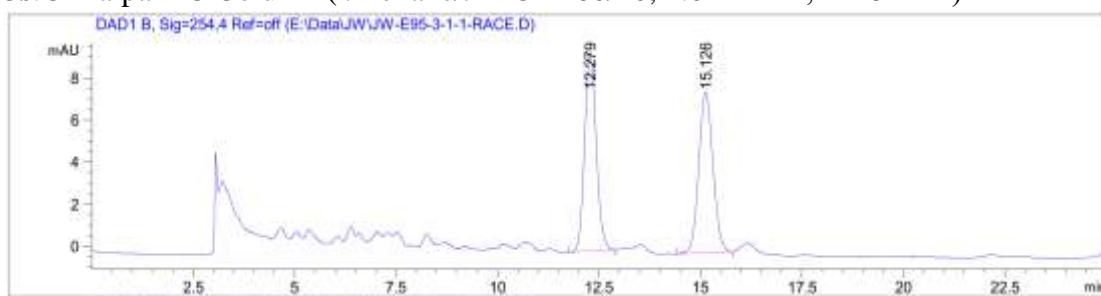


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.667	FM	0.2570	1.72662e4	1119.67480	99.5958
2	12.042	MF	0.2270	70.07519	5.14586	0.4042

Totals : 1.73362e4 1124.82067

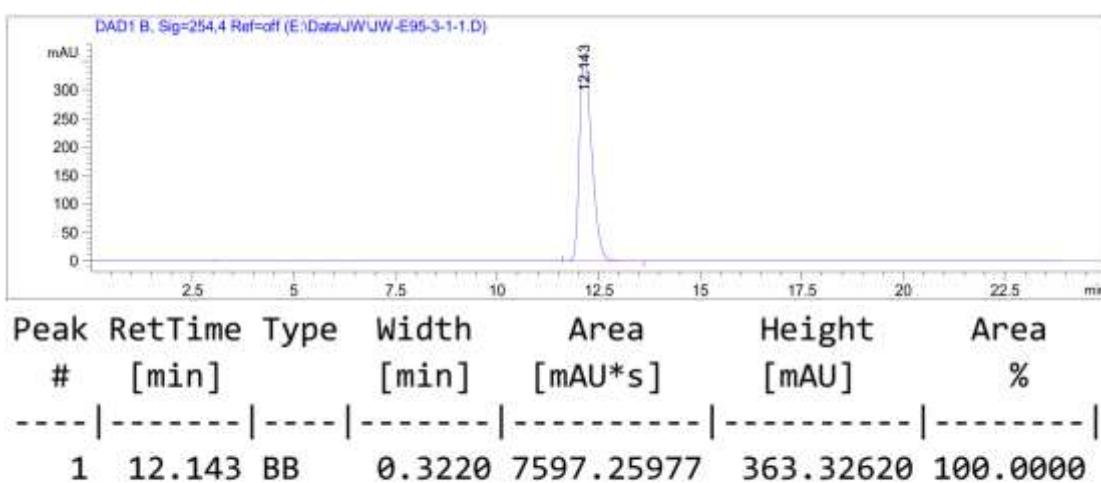


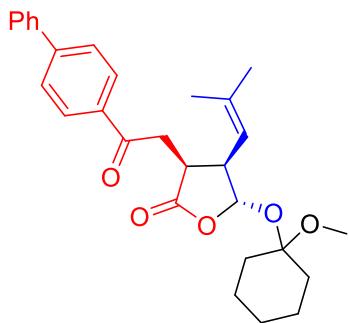
3s: Chiralpak IC Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)



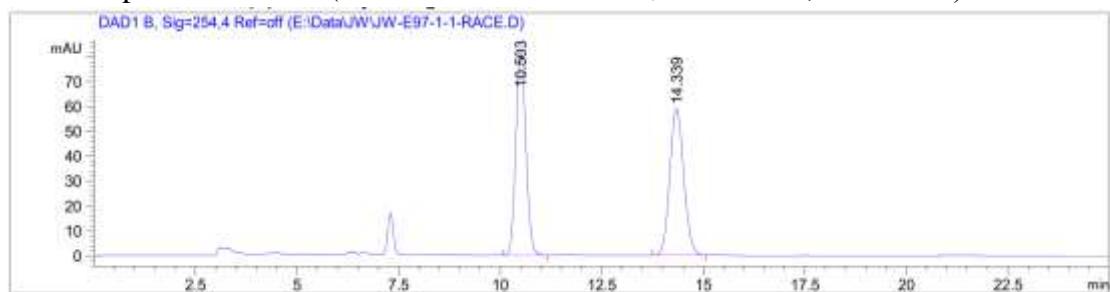
Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	
1	12.279	BB	0.3052	187.51254	9.46132	50.3367
2	15.126	BB	0.3790	185.00409	7.62806	49.6633

Totals : 372.51663 17.08939

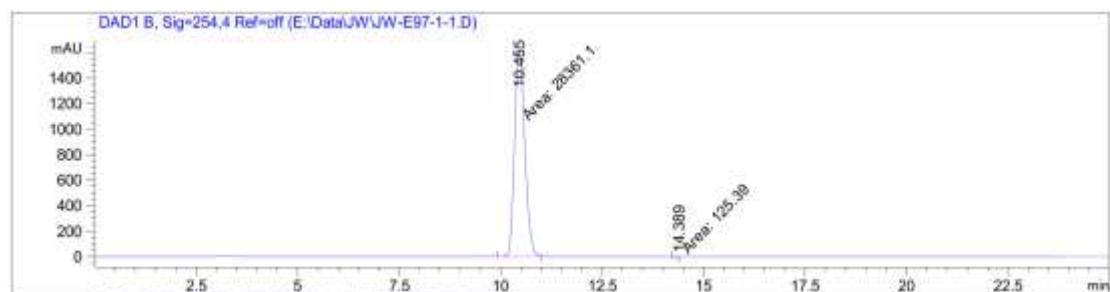




3t: Chiralpak IC Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)

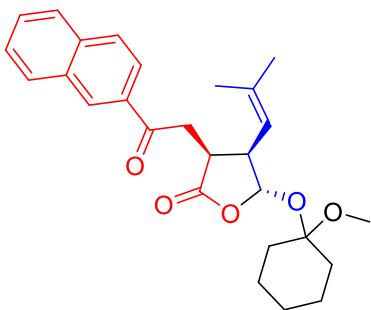


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.503	BB	0.2683	1418.22461	82.58879	50.1363
2	14.339	BB	0.3702	1410.51550	59.14673	49.8637
Totals :				2828.74011	141.73552	

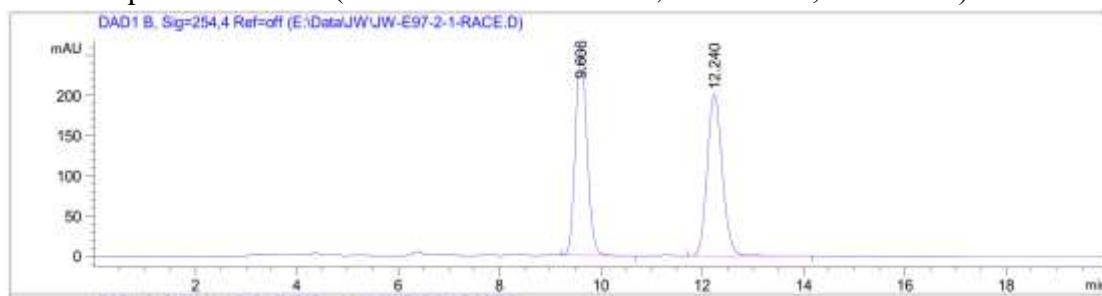


Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	10.455	MF	0.2920	2.83611e4	1618.54102	99.5598
2	14.389	MM	0.1691	125.39048	12.35615	0.4402

Totals : 2.84864e4 1630.89717

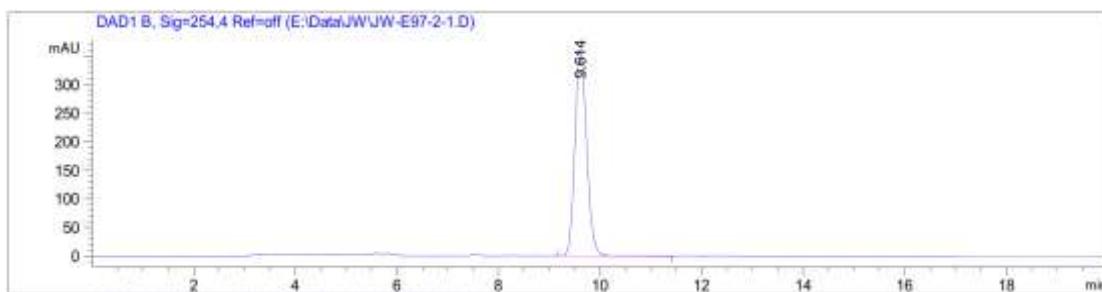


3u: Chiralpak IC Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)



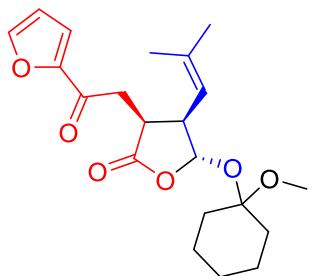
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.606	BB	0.2458	4069.45166	255.53871	49.4333
2	12.240	BB	0.3211	4162.75830	201.47086	50.5667

Totals : 8232.20996 457.00957

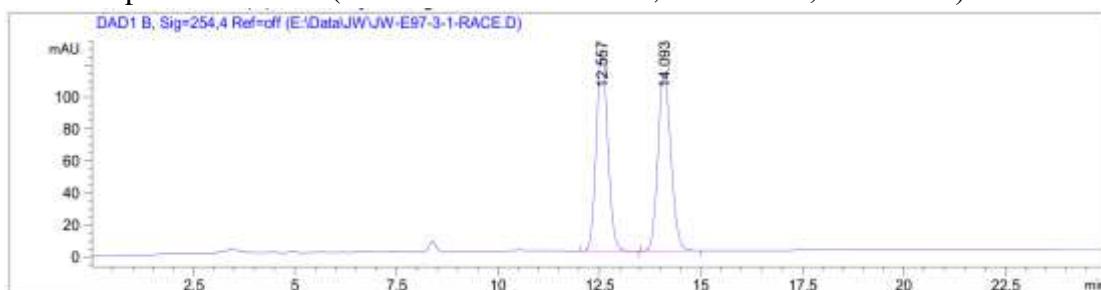


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.614	BB	0.2499	5799.76611	360.19412	100.0000

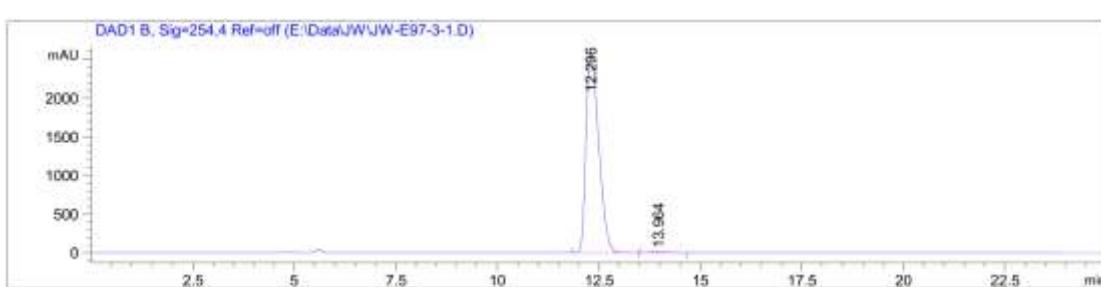
Totals : 5799.76611 360.19412



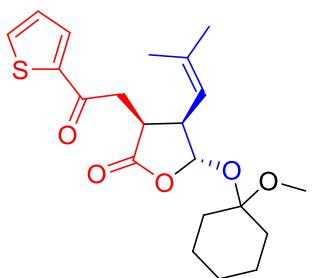
3v: Chiralpak IC Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)



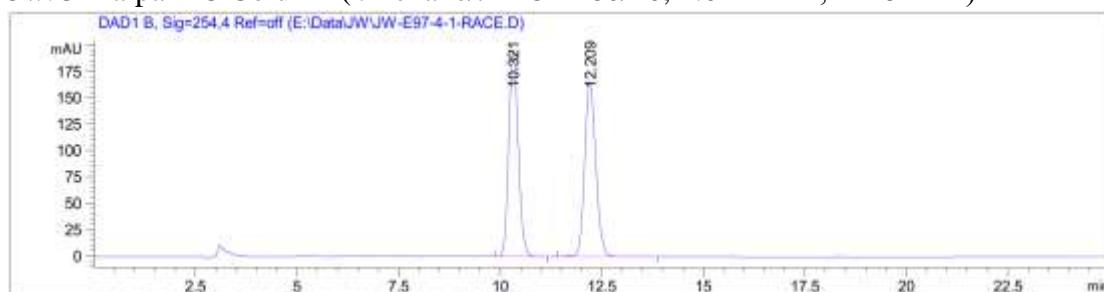
Totals : 4927.21973 235.95654



Totals : 5.61514e4 2545.16986

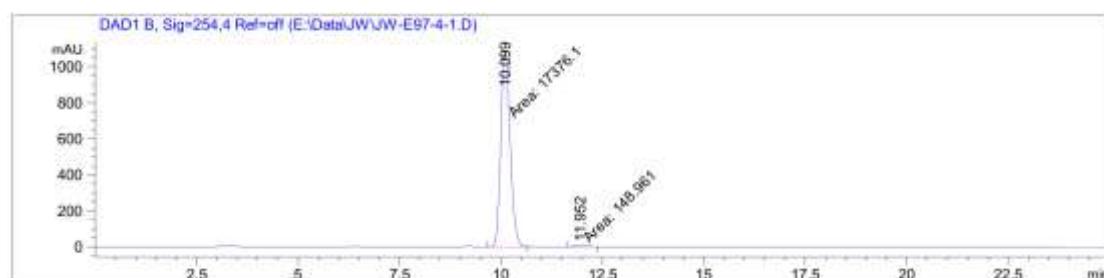


3w: Chiralpak IC Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)



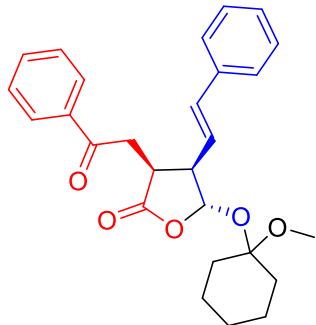
Peak RetTime		Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	10.321	BB	0.2515	3178.94360	195.68979	49.8778
2	12.209	BB	0.2965	3194.52100	166.00899	50.1222

Totals : 6373.46460 361.69878

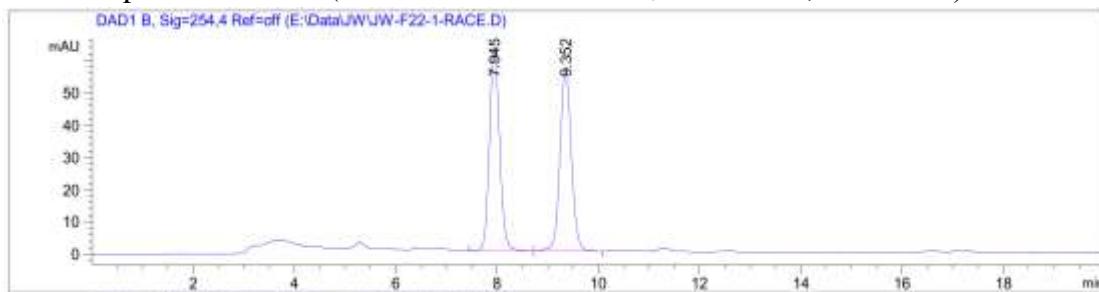


Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	10.099	MF	0.2664	1.73761e4	1087.14819	99.1500
2	11.952	MF	0.3102	148.96147	8.00249	0.8500

Totals : 1.75251e4 1095.15069

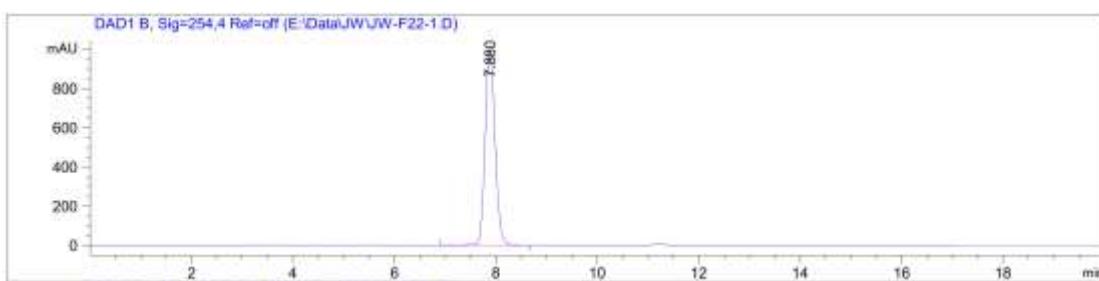


3x: Chiraldak IC Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)



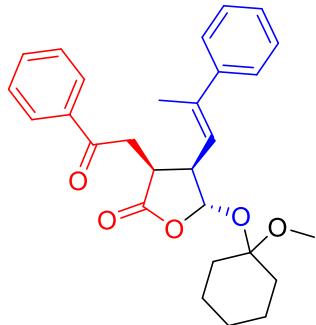
Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	7.945	BB	0.2143	871.77960	62.66162	49.6739
2	9.352	BB	0.2396	883.22638	56.73471	50.3261

Totals : 1755.00598 119.39633

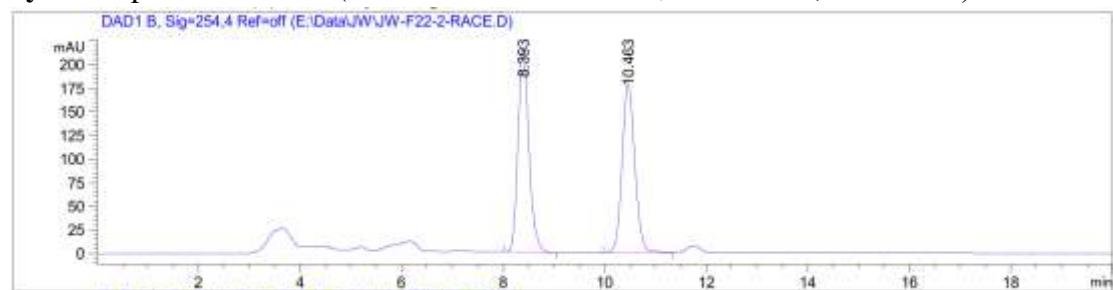


Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	7.880	VB R	0.2103	1.35647e4	995.50220	100.0000

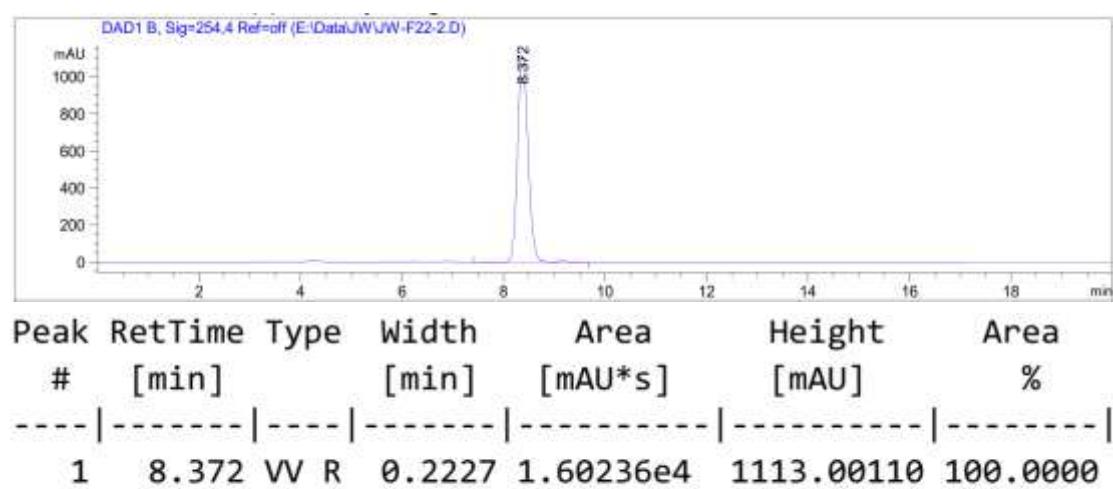
Totals : 1.35647e4 995.50220

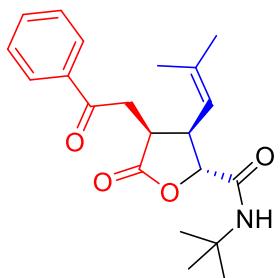


3y: Chiraldak IC Column (*n*-hexane/*i*-PrOH=80/20, 1.0 ml/min, λ =254 nm)

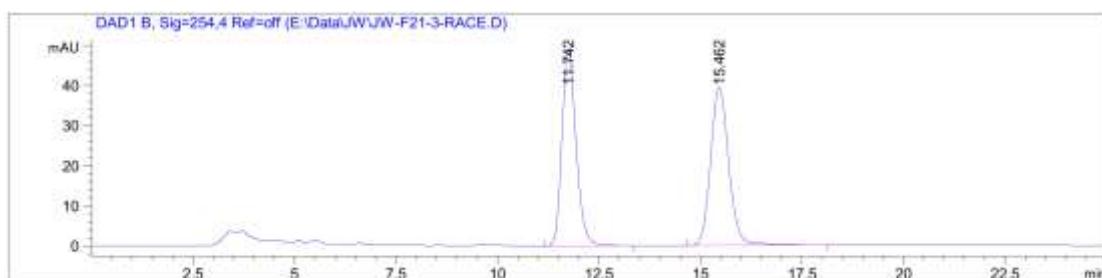


Totals : 6342.78882 393.33859



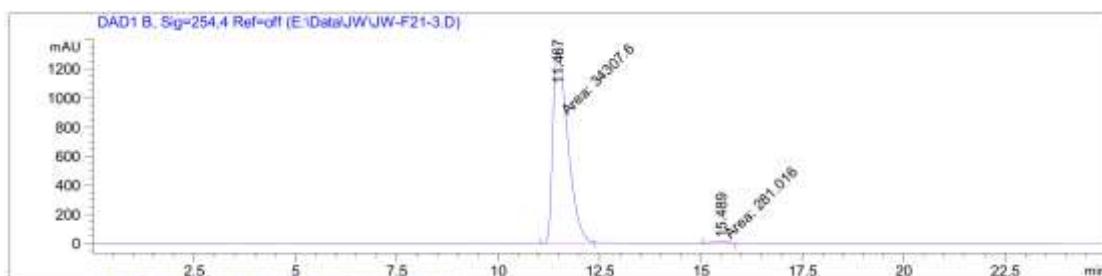


6:Chiraldak IC Column (*n*-hexane/*i*-PrOH=60/40, 1.0 ml/min, λ =254 nm)



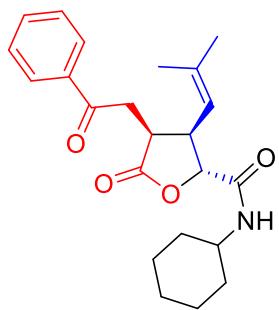
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.742	BB	0.3730	1189.94641	49.06217	49.1242
2	15.462	BB	0.4805	1232.37451	39.44189	50.8758

Totals : 2422.32092 88.50406

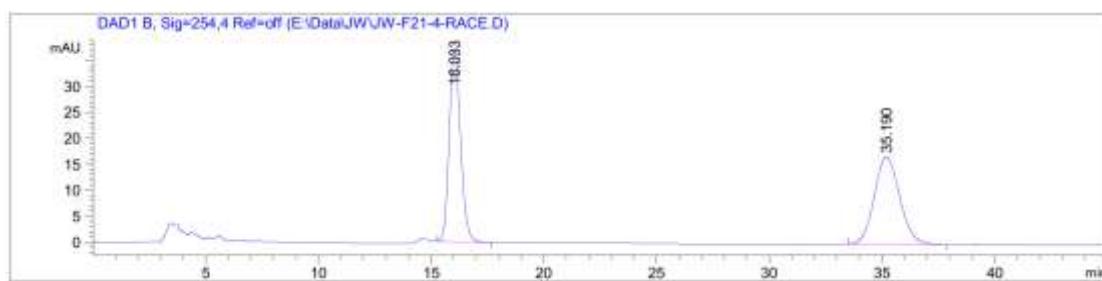


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.467	MF	0.4269	3.43076e4	1339.27563	99.1875
2	15.489	MF	0.4606	281.01611	10.16738	0.8125

Totals : 3.45886e4 1349.44301

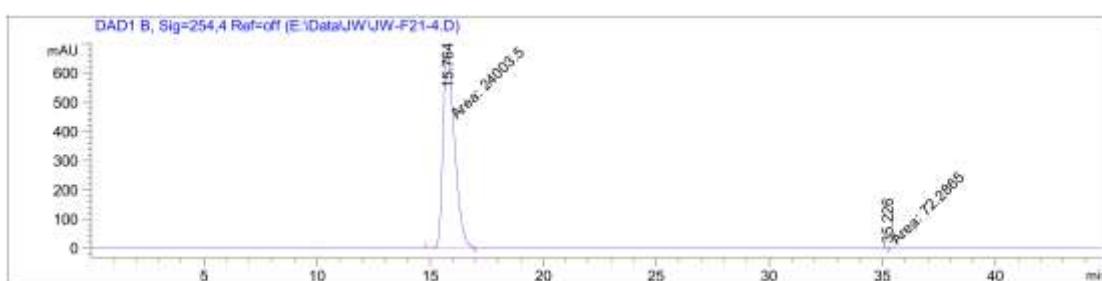


7:Chiraldak IC Column (*n*-hexane/*i*-PrOH=60/40, 1.0 ml/min, $\lambda=254$ nm)



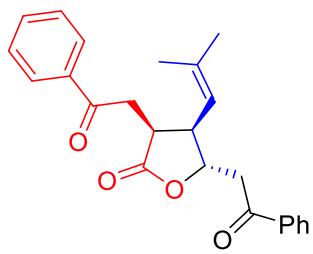
Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	16.033	BB	0.5389	1292.24817	37.04837	49.7602
2	35.190	BB	1.1075	1304.70483	16.80935	50.2398

Totals : 2596.95300 53.85772



Peak	RetTime	Type	Width	Area	Height	Area %
#	[min]		[min]	[mAU*s]	[mAU]	%
1	15.764	MF	0.5956	2.40035e4	671.73999	99.6998
2	35.226	FM	0.2034	72.28654	5.92425	0.3002

Totals : 2.40758e4 677.66424



5: Acquity UPC² TrefoilTM Cel2, 2.5 μ m Column (CO₂/MeOH= 90/10, 2.0 ml/min, λ =240 nm)

