Supplemental Material

Facile synthesis of new *N*-(aminocycloalkylene)amino acid compounds using chiral triflate esters with *N*-Boc-aminopyrrolidines and *N*-Boc-aminopiperidines

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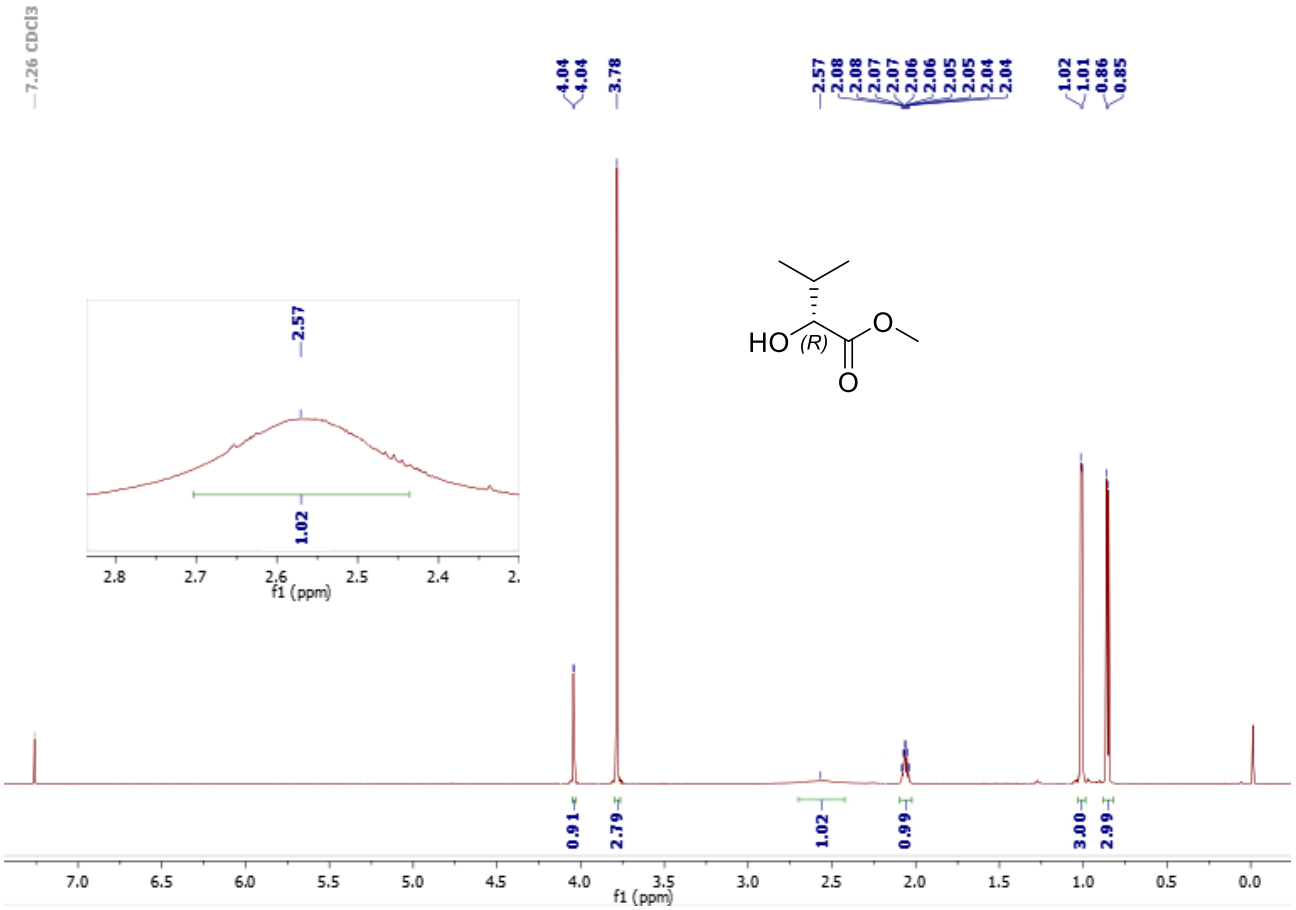

Figure S1. Methyl (2*R*)-2-hydroxy-3-methylbutanoate ((*R*)-1b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

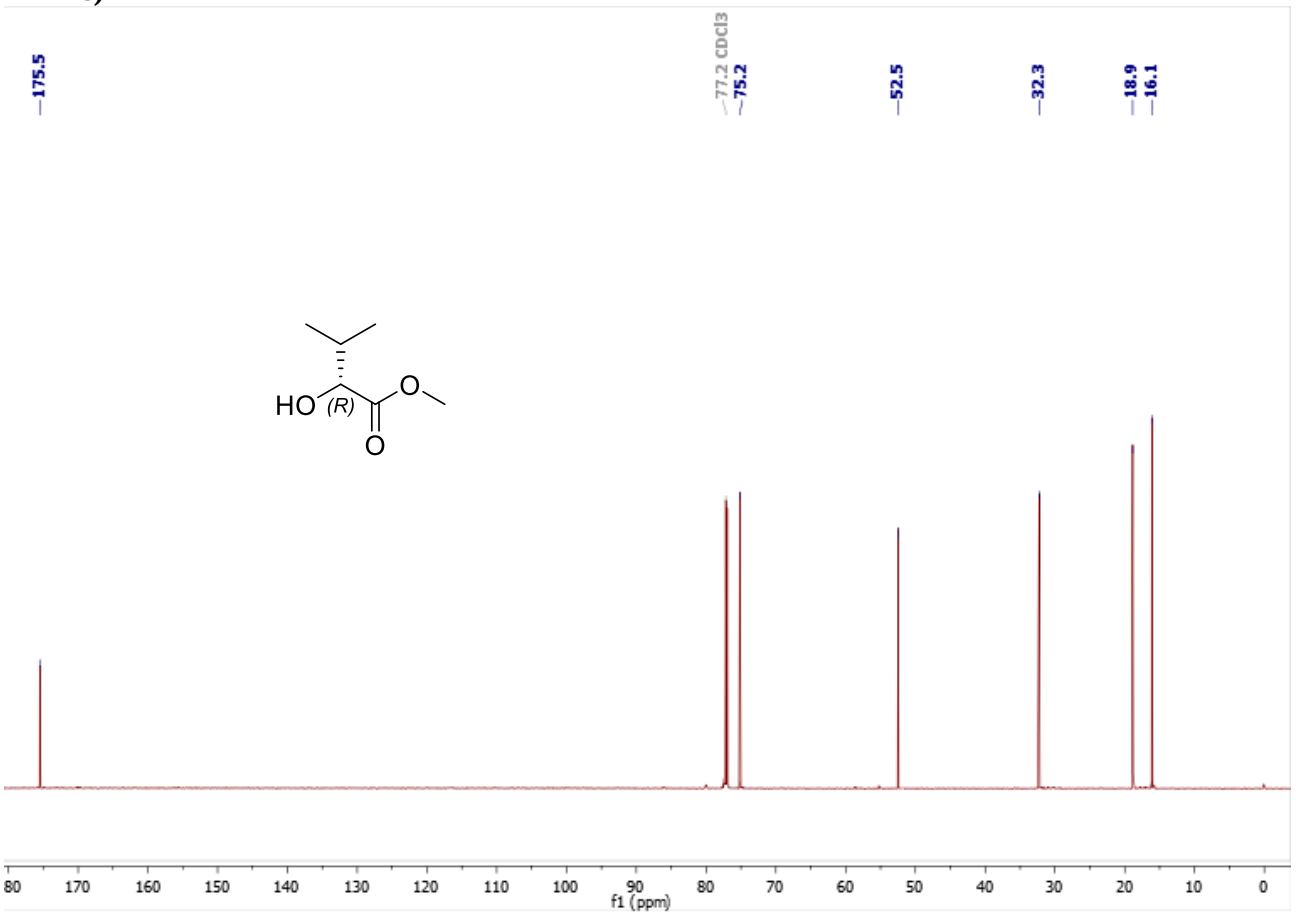

Figure S2. Methyl (2*R*)-2-hydroxy-3-methylbutanoate ((*R*)-1b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

Compound Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\GMP-959.d	Acquisition Date	5/2/2023 7:43:47 PM
Method	DirectInfusion_TuneLow_pos.m	Operator	hplc
Sample Name	GMP-959	Instrument	micrOTOF-Q III 8228888.20448
Comment	AB		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	140.0 Vpp	Set Divert Valve	Waste

#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
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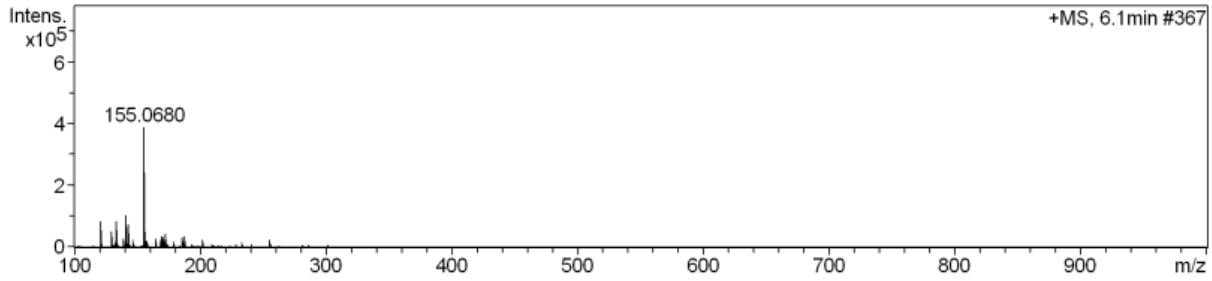
+MS, 6.1min #367



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e⁻ Conf	N-Rule
155.0680	1	C6H12NaO3	155.0679	-0.8	25.6	1	100.00	0.5	even	ok

Figure S3. Methyl (2*R*)-2-hydroxy-3-methylbutanoate ((*R*)-1b). HRMS (ESI-TOF).

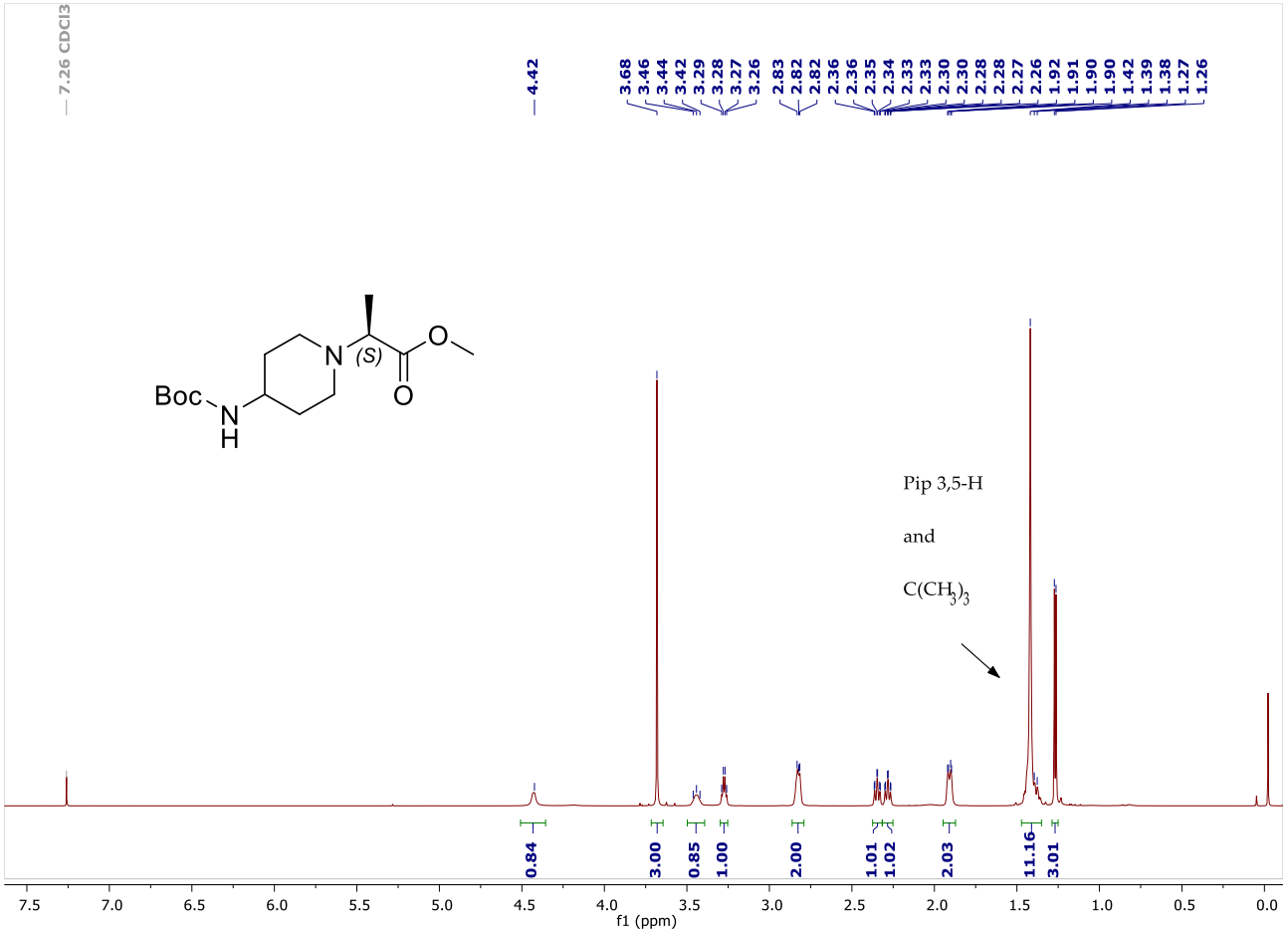


Figure S4. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*S*)-3a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

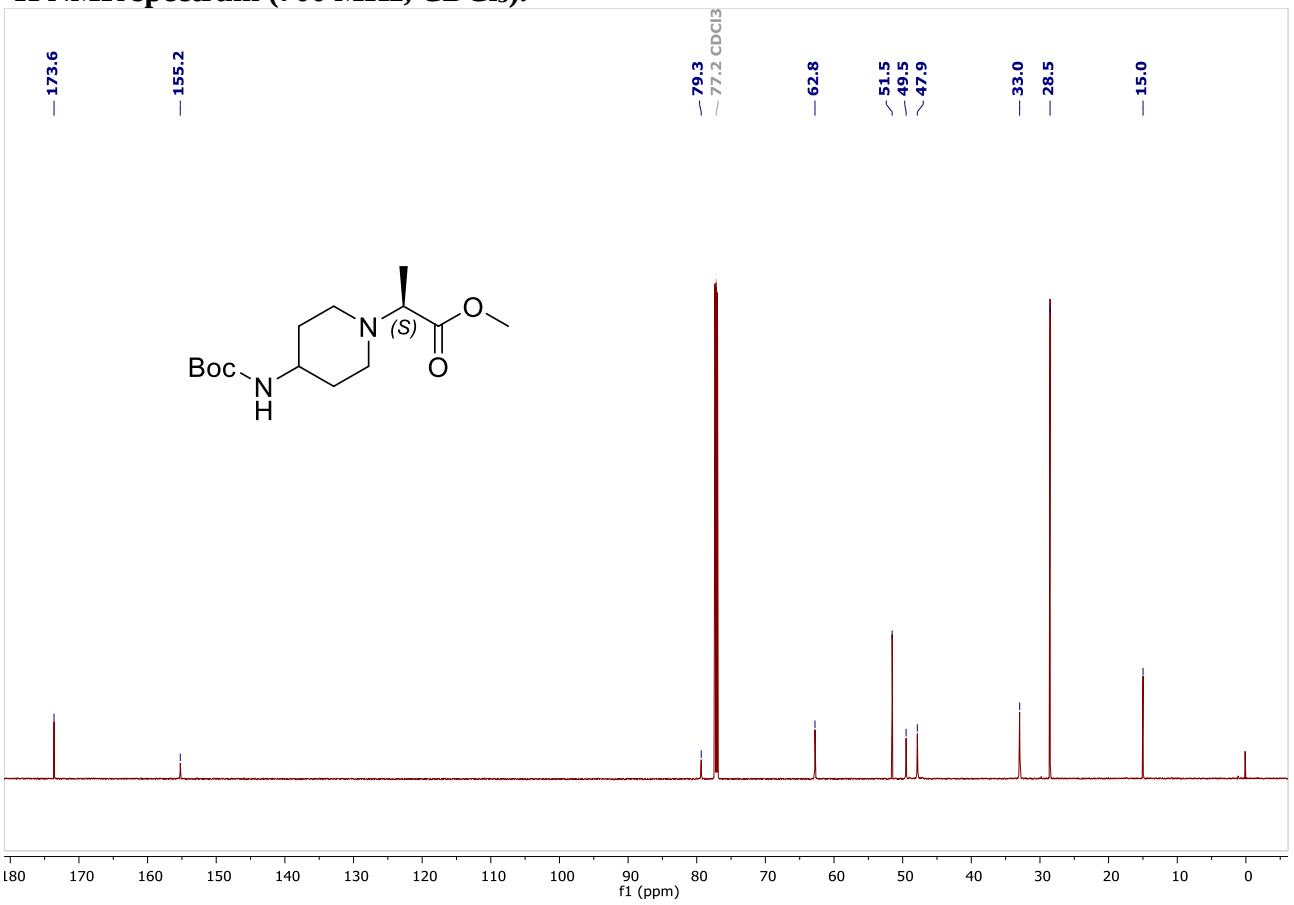


Figure S5. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*S*)-3a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

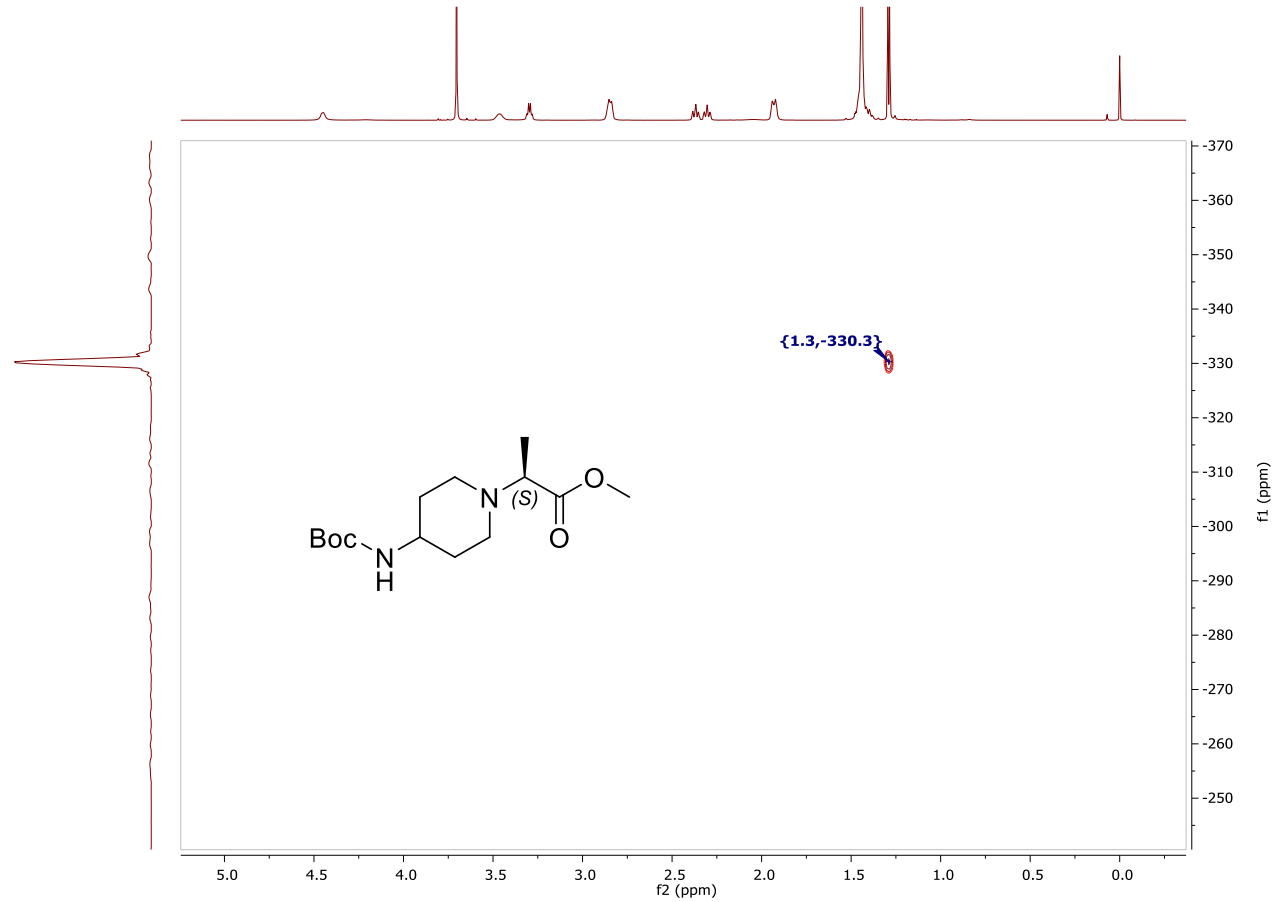


Figure S6. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*S*)-3a). ^{1}H-^{15}N HMBC spectrum (71 MHz, $CDCl_3$).

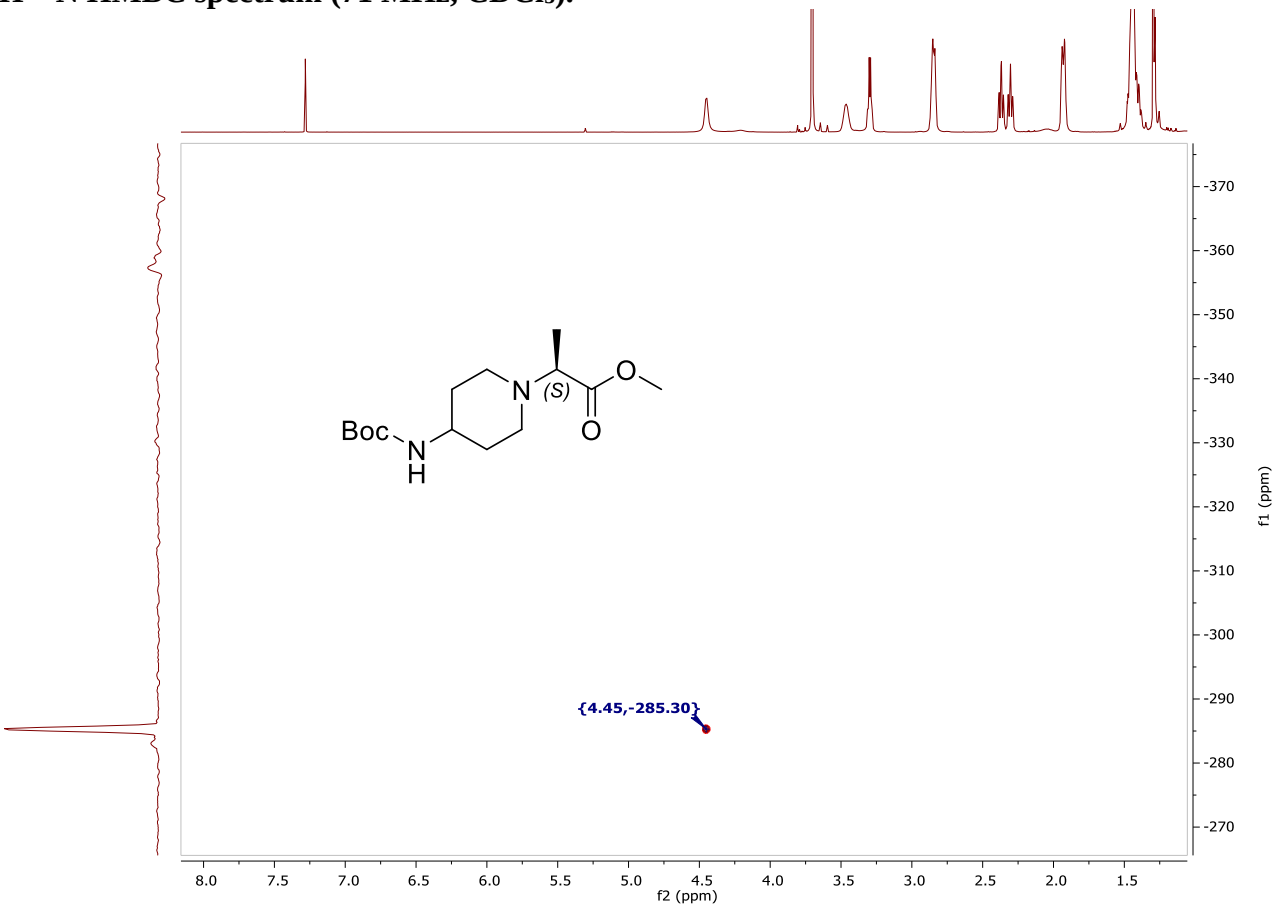


Figure S7. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*S*)-3a). ^{1}H-^{15}N HSQC spectrum (71 MHz, $CDCl_3$).

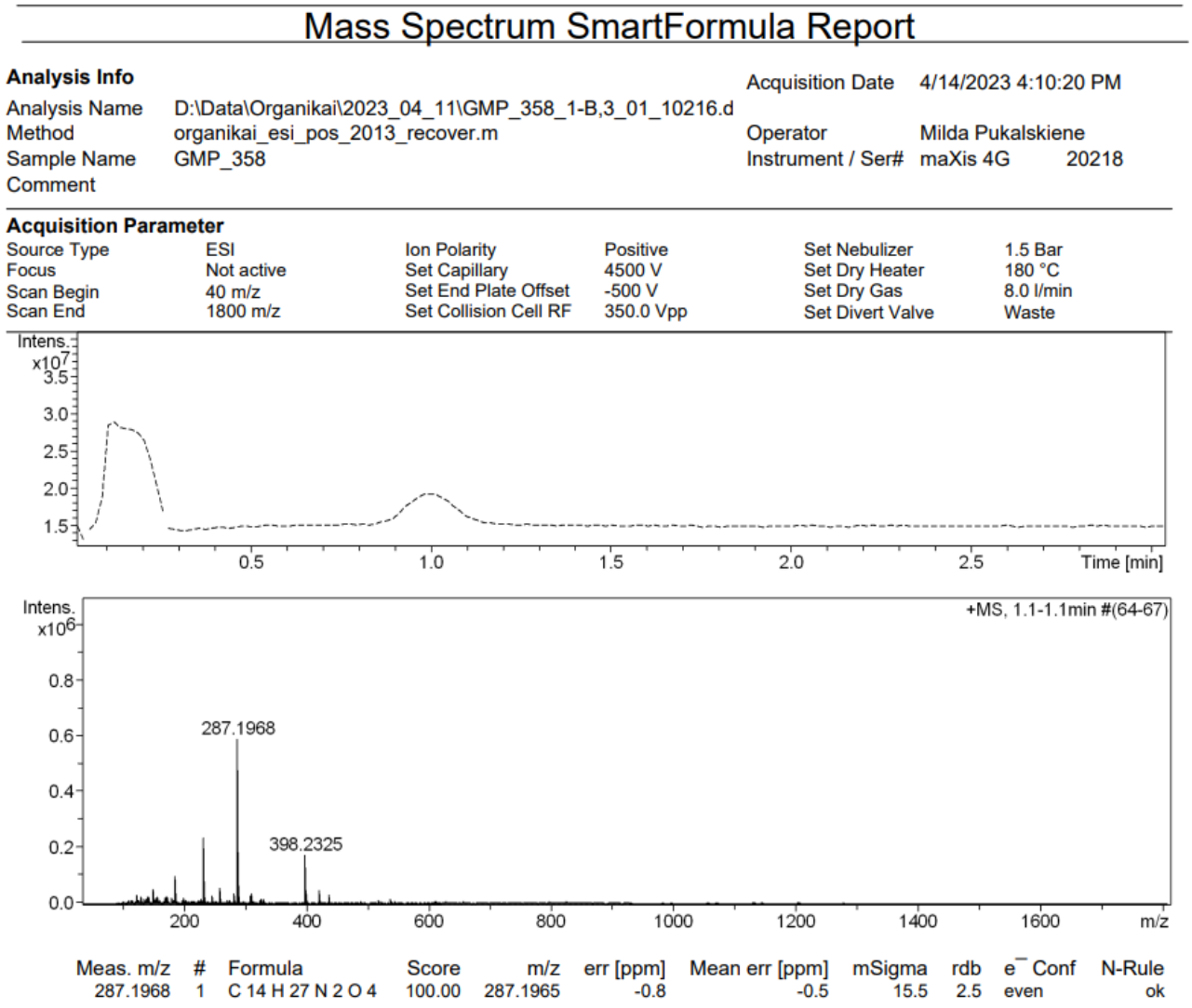


Figure S8. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*S*)-3a). HRMS (ESI-TOF).

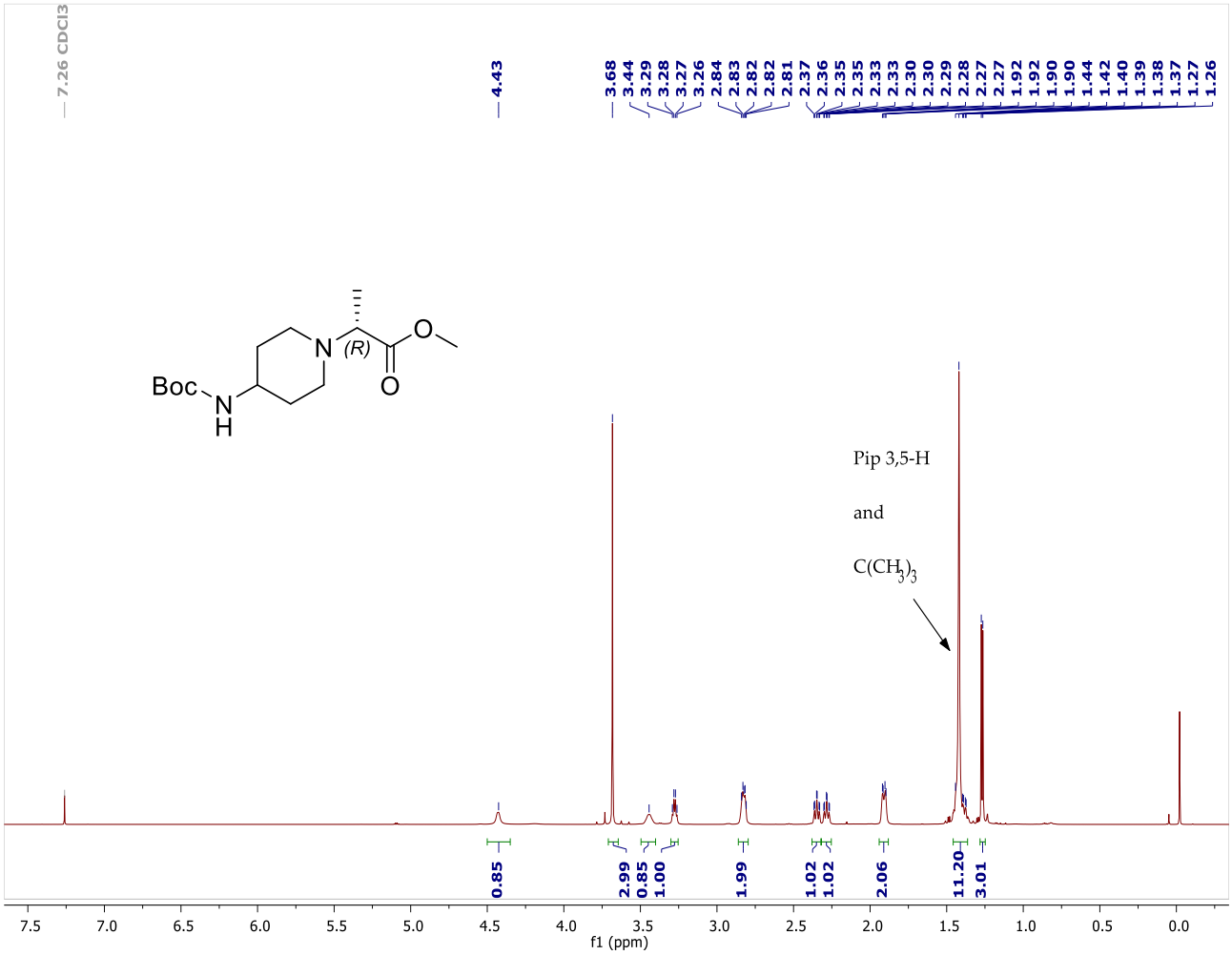


Figure S9. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*R*)-3a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

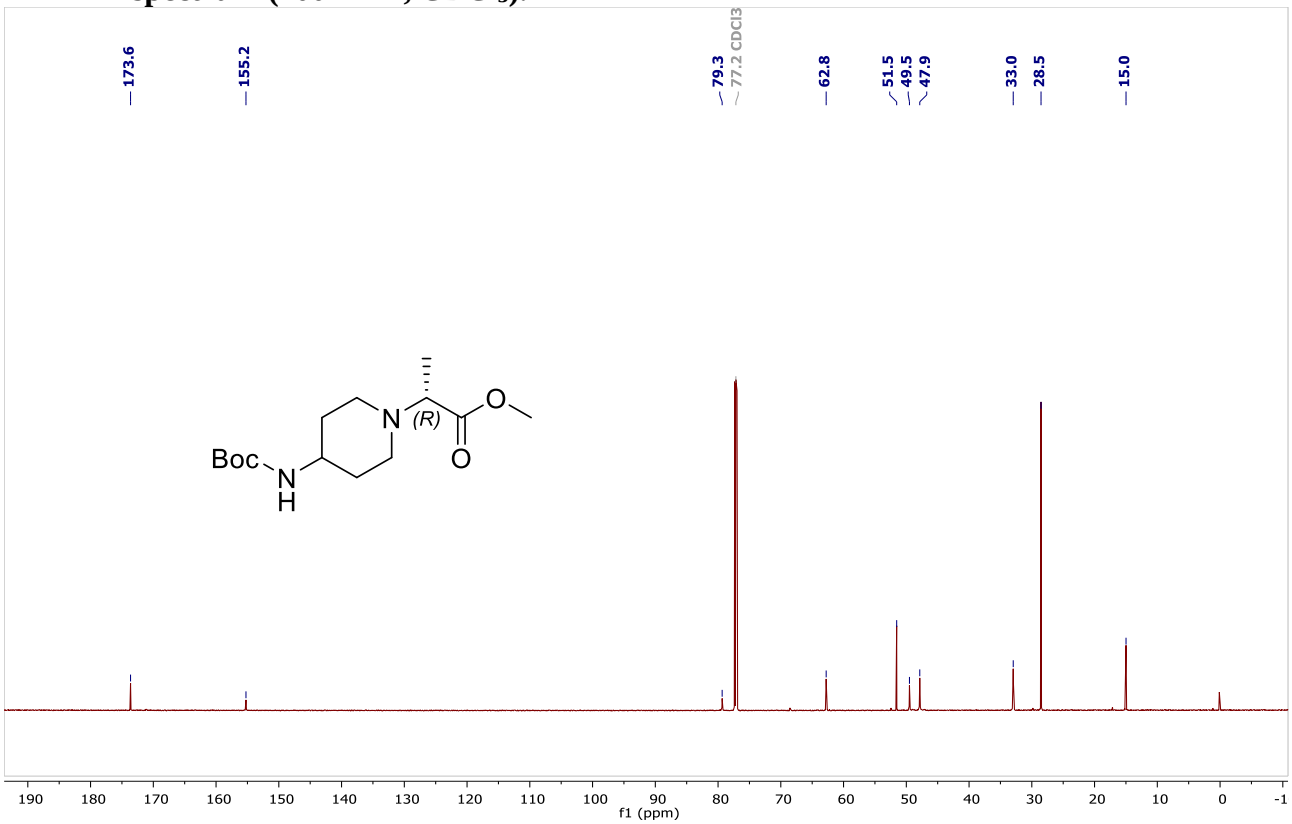


Figure S10. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*R*)-3a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

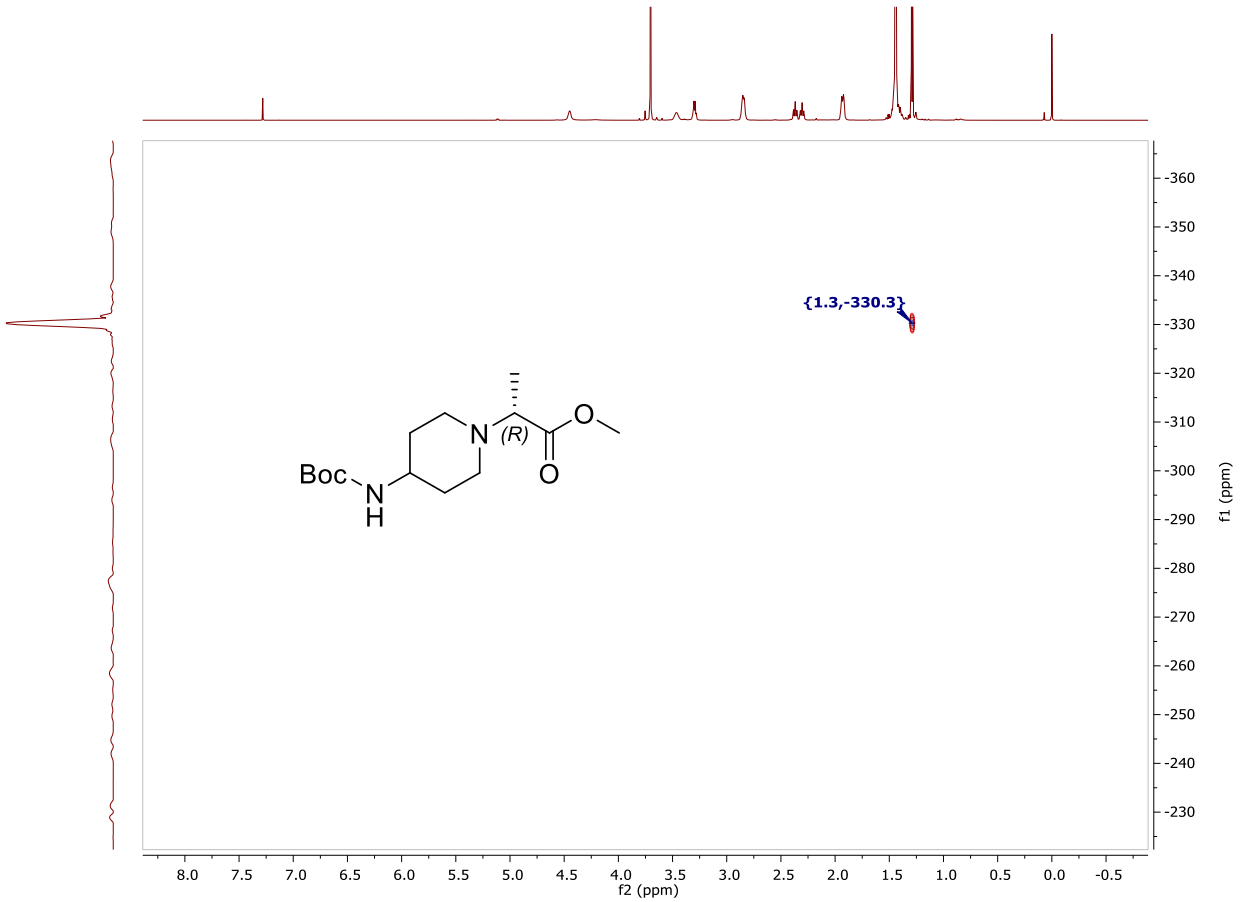


Figure S11. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*R*)-3a). ^{1}H-^{15}N HMBC spectrum (71 MHz, $CDCl_3$).

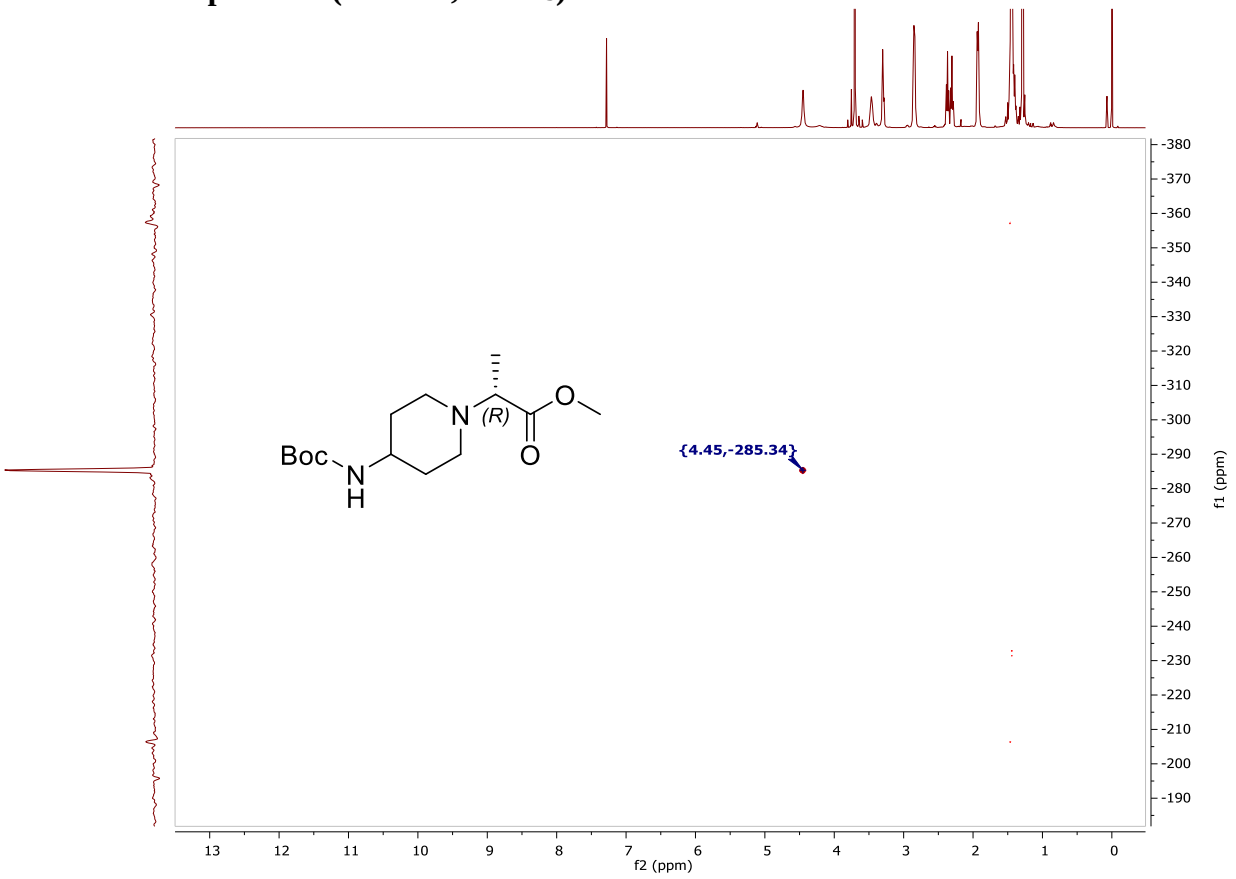


Figure S12. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*R*)-3a). ^{1}H-^{15}N HSQC spectrum (71 MHz, $CDCl_3$).

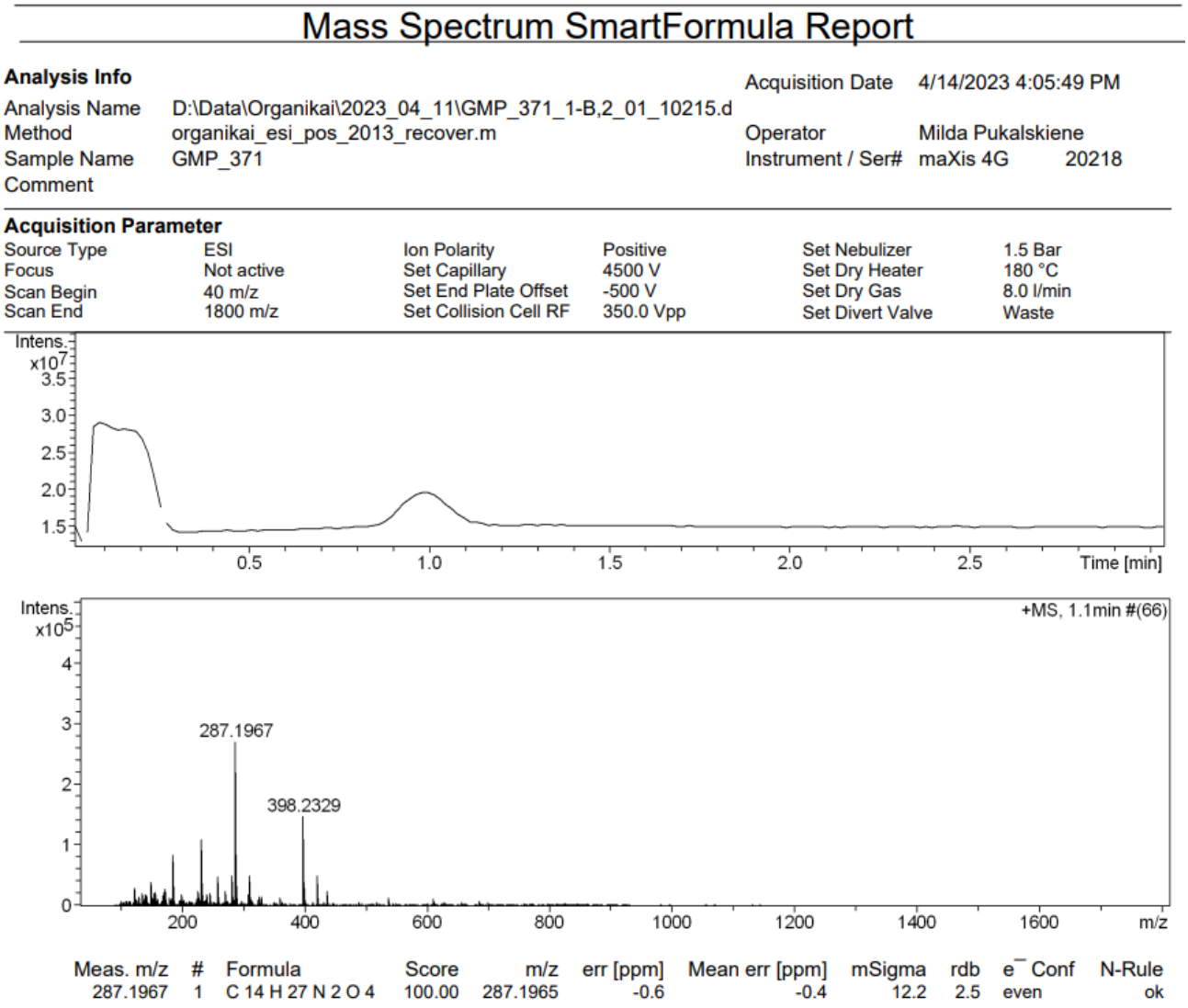


Figure S13. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((*R*)-3a). HRMS (ESI-TOF).

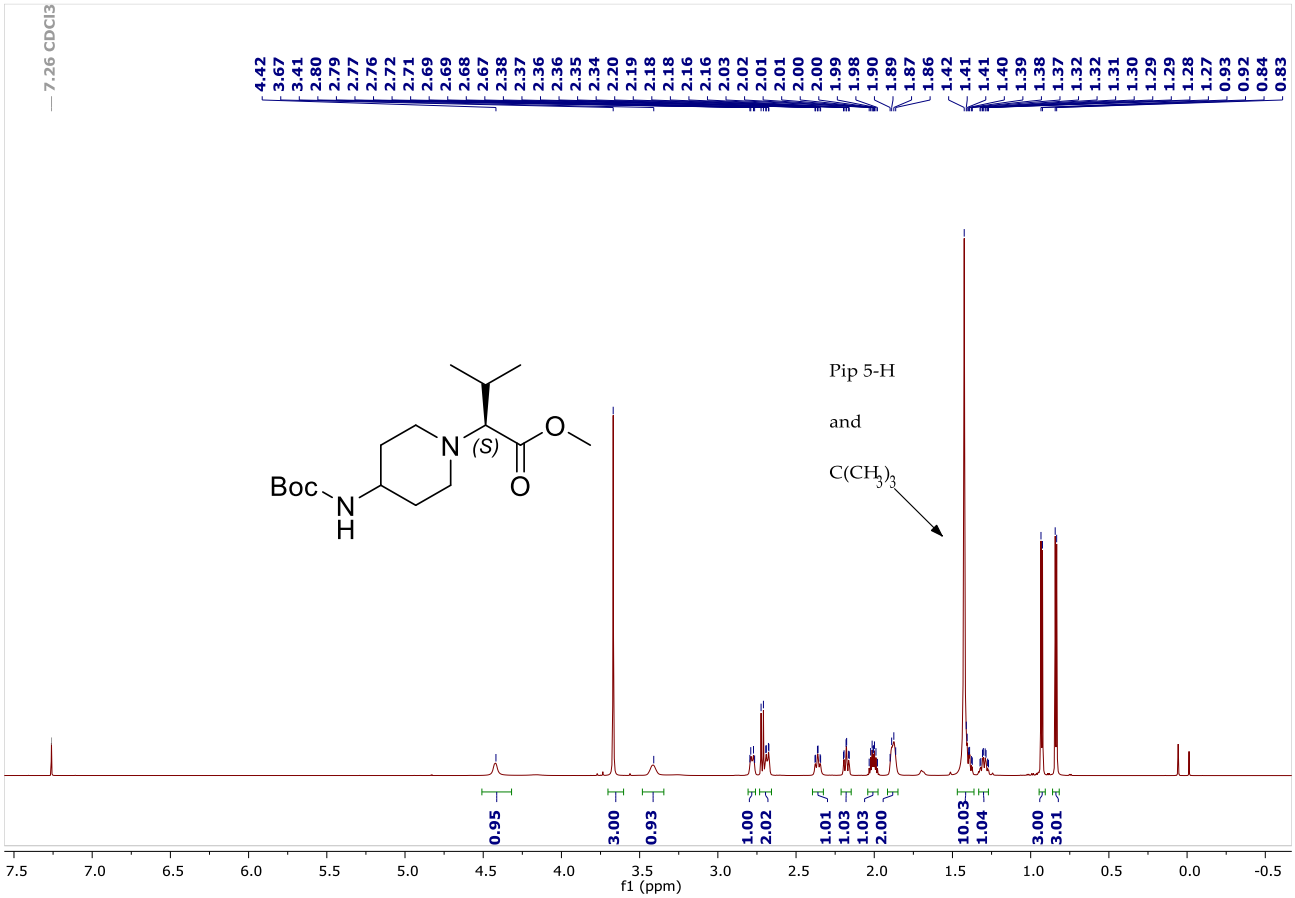


Figure S14. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((*S*)-3b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

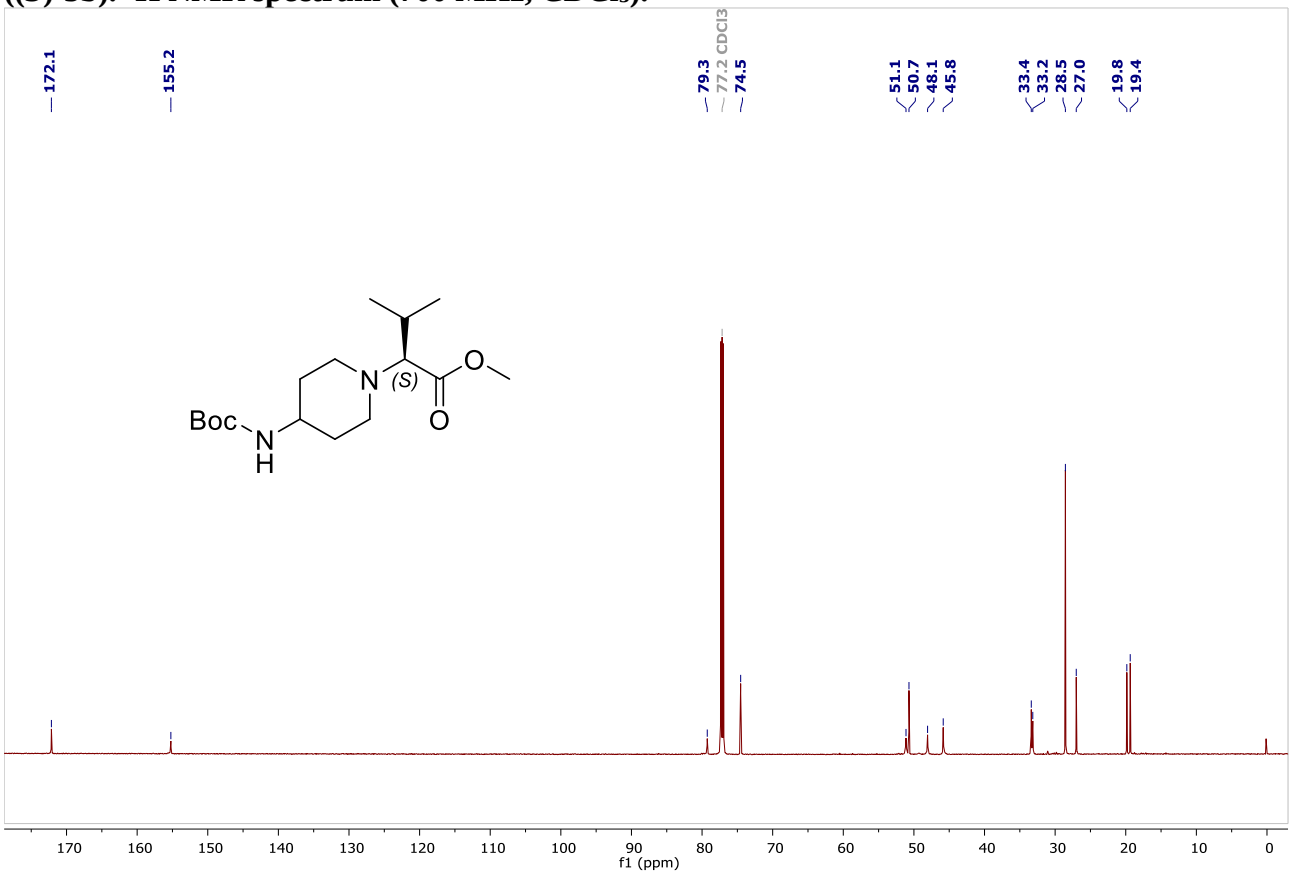


Figure S15. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((*S*)-3b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

Mass Spectrum SmartFormula Report

Analysis Info

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Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_575	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
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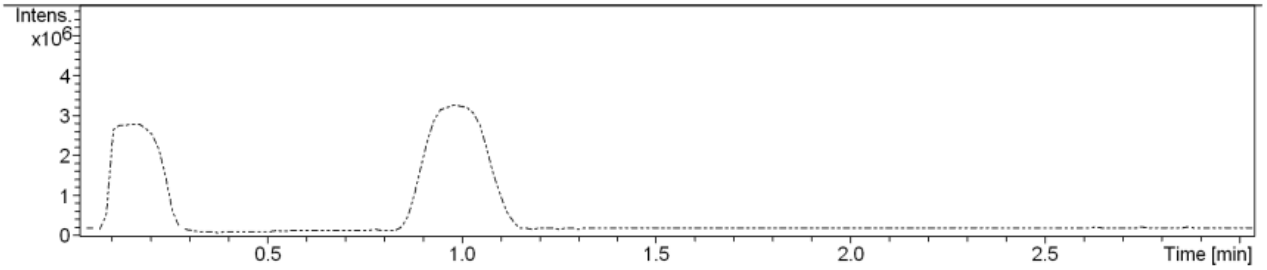
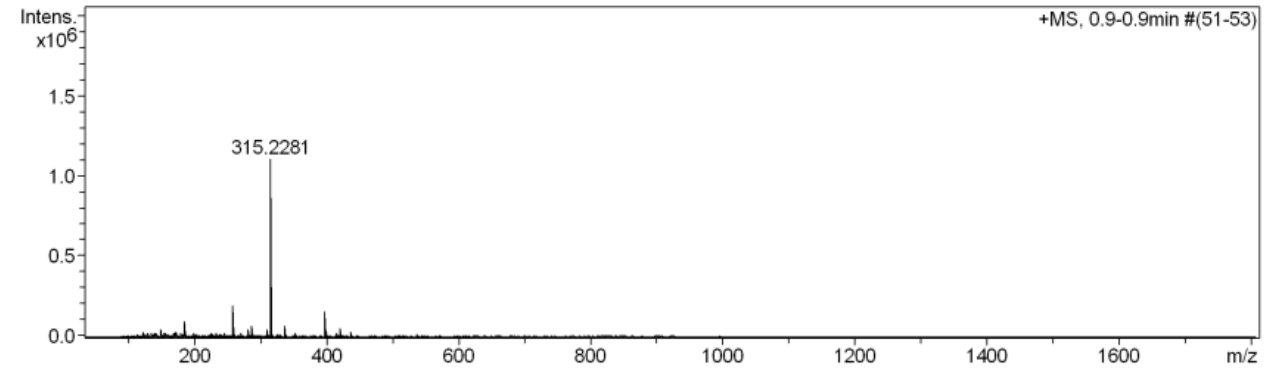
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e¯ Conf	N-Rule
315.2281	1	C 16 H 31 N 2 O 4	100.00	315.2278	-0.9	-0.7	16.9	2.5	even	ok
	2	C 17 H 27 N 6	51.82	315.2292	3.3	3.5	29.2	7.5	even	ok

Figure S16. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((*S*)-3b). HRMS (ESI-TOF).

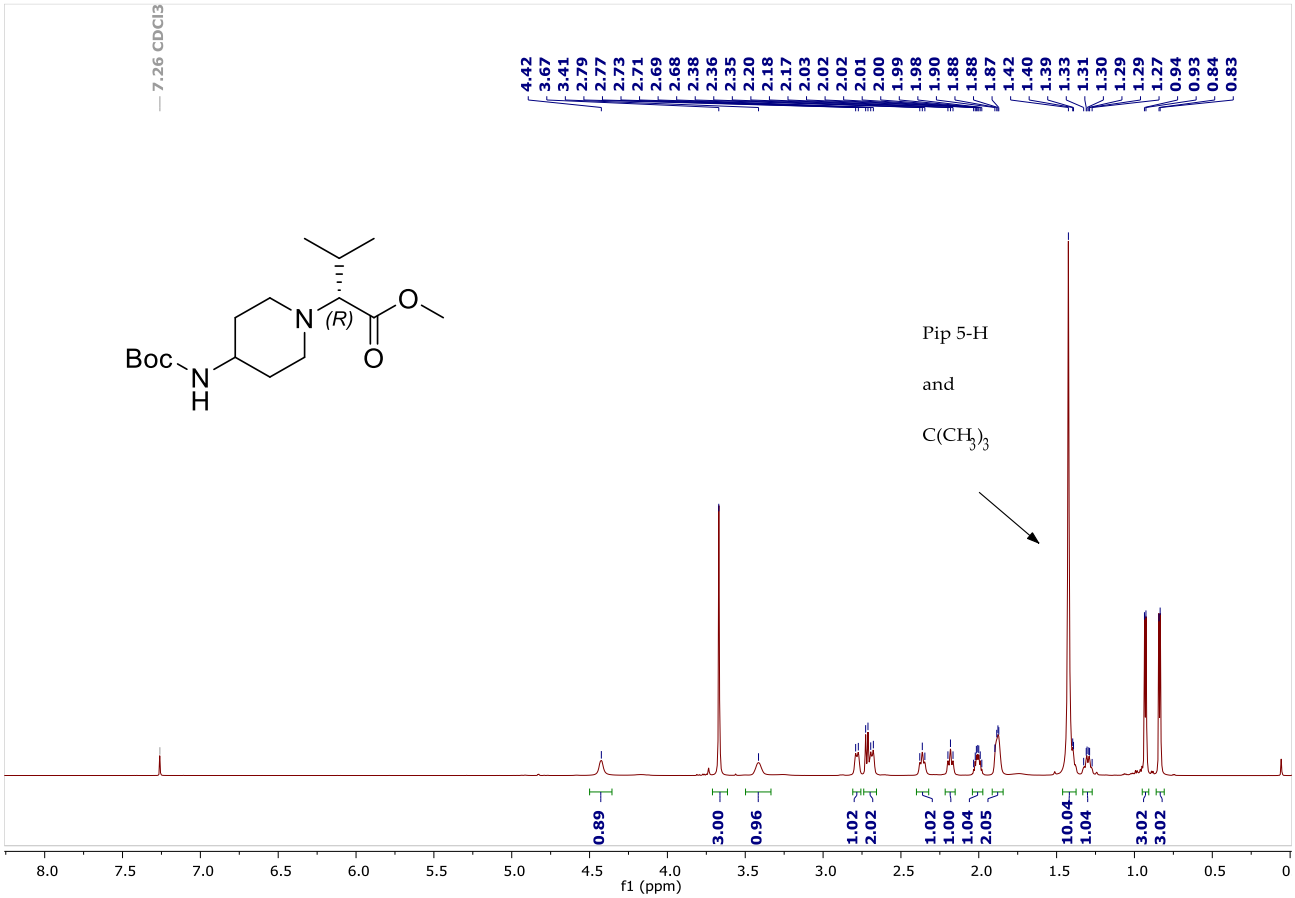


Figure S17. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((*R*)-3b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

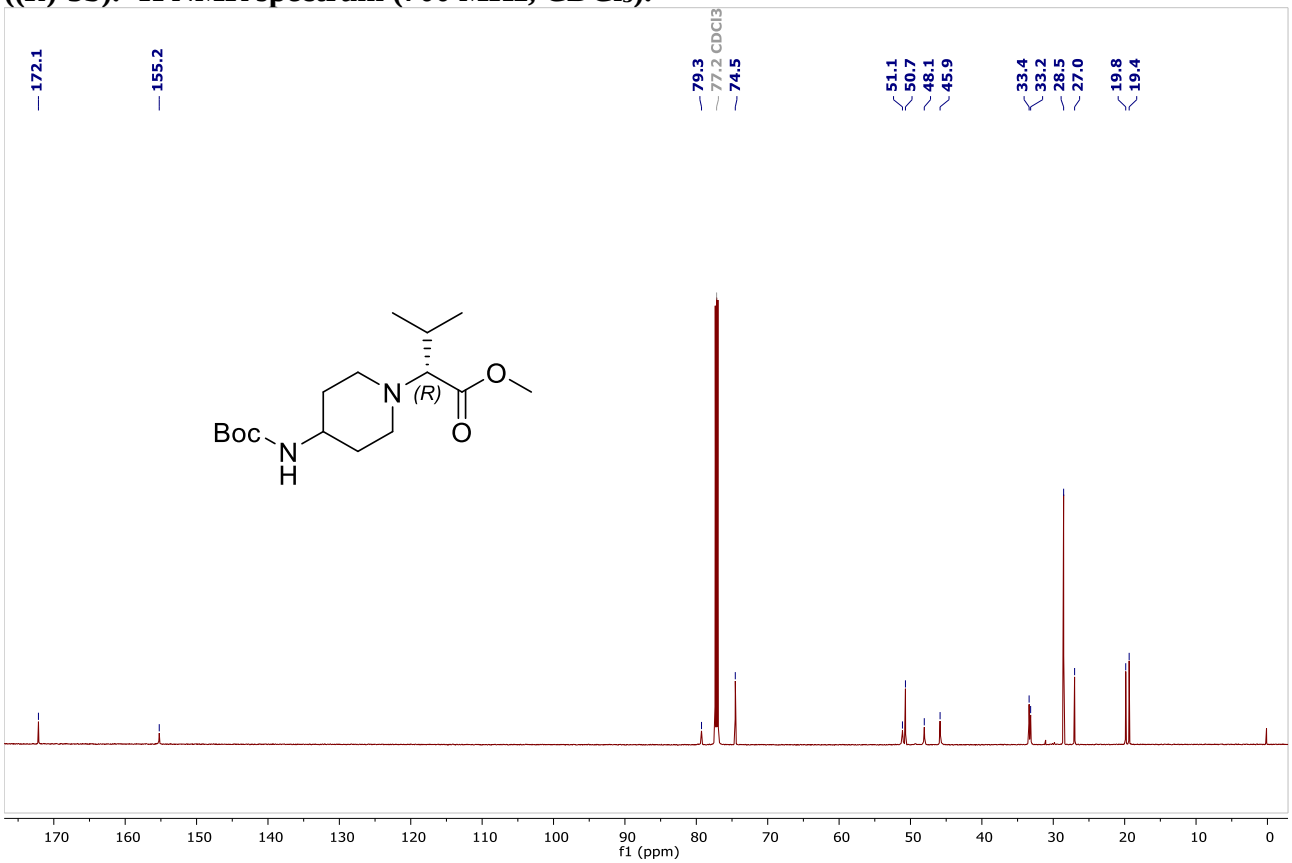


Figure S18. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((*R*)-3b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_571_1-B,4_01_10217.d	Acquisition Date	4/14/2023 4:14:48 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_571	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
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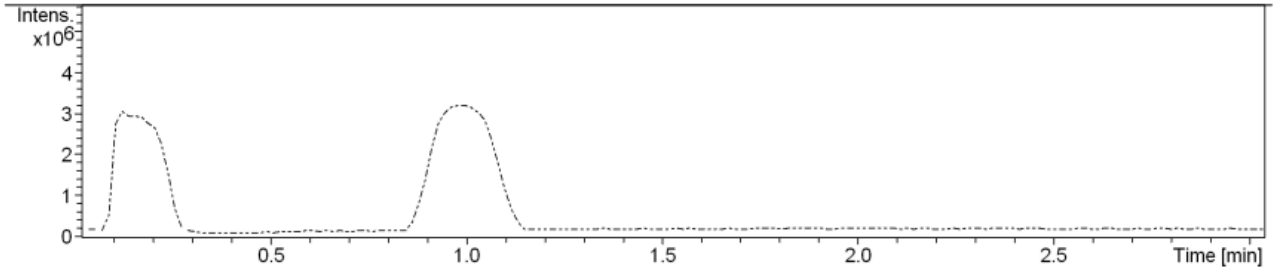
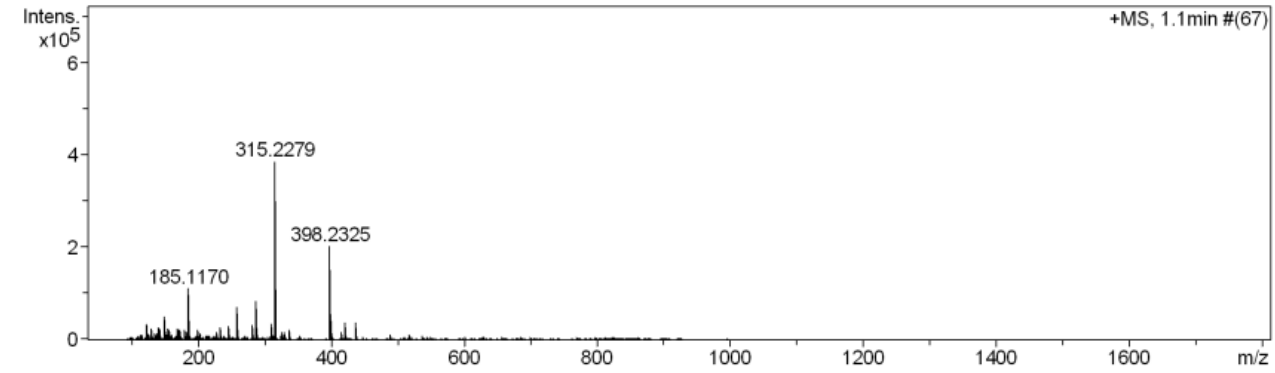
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
315.2279	1	C 16 H 31 N 2 O 4	100.00	315.2278	-0.3	-0.2	18.9	2.5	even	ok
	2	C 17 H 27 N 6	45.53	315.2292	3.9	4.0	27.9	7.5	even	ok

Figure S19. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((*R*)-3b). HRMS (ESI-TOF).

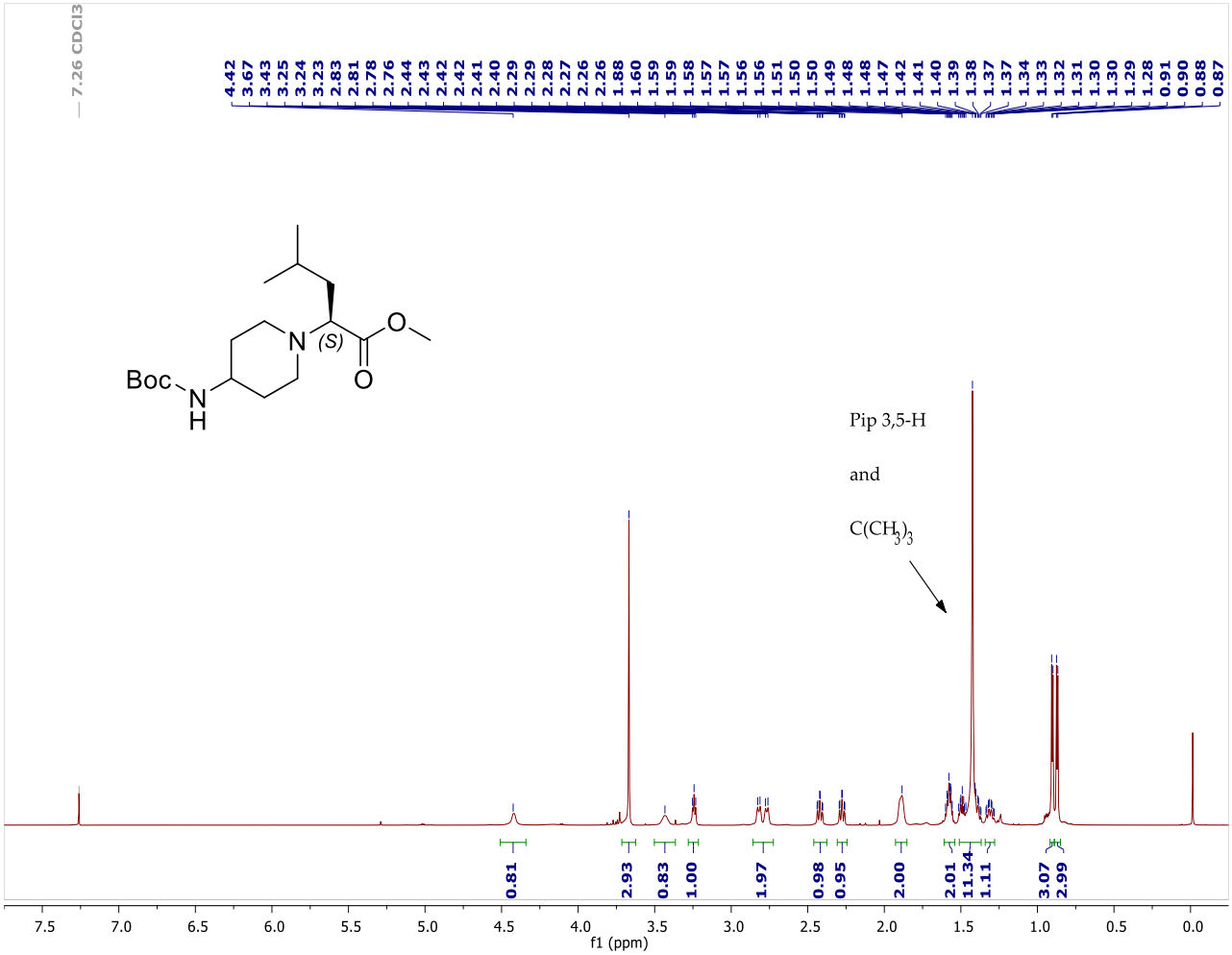


Figure S20. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((*S*)-3c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

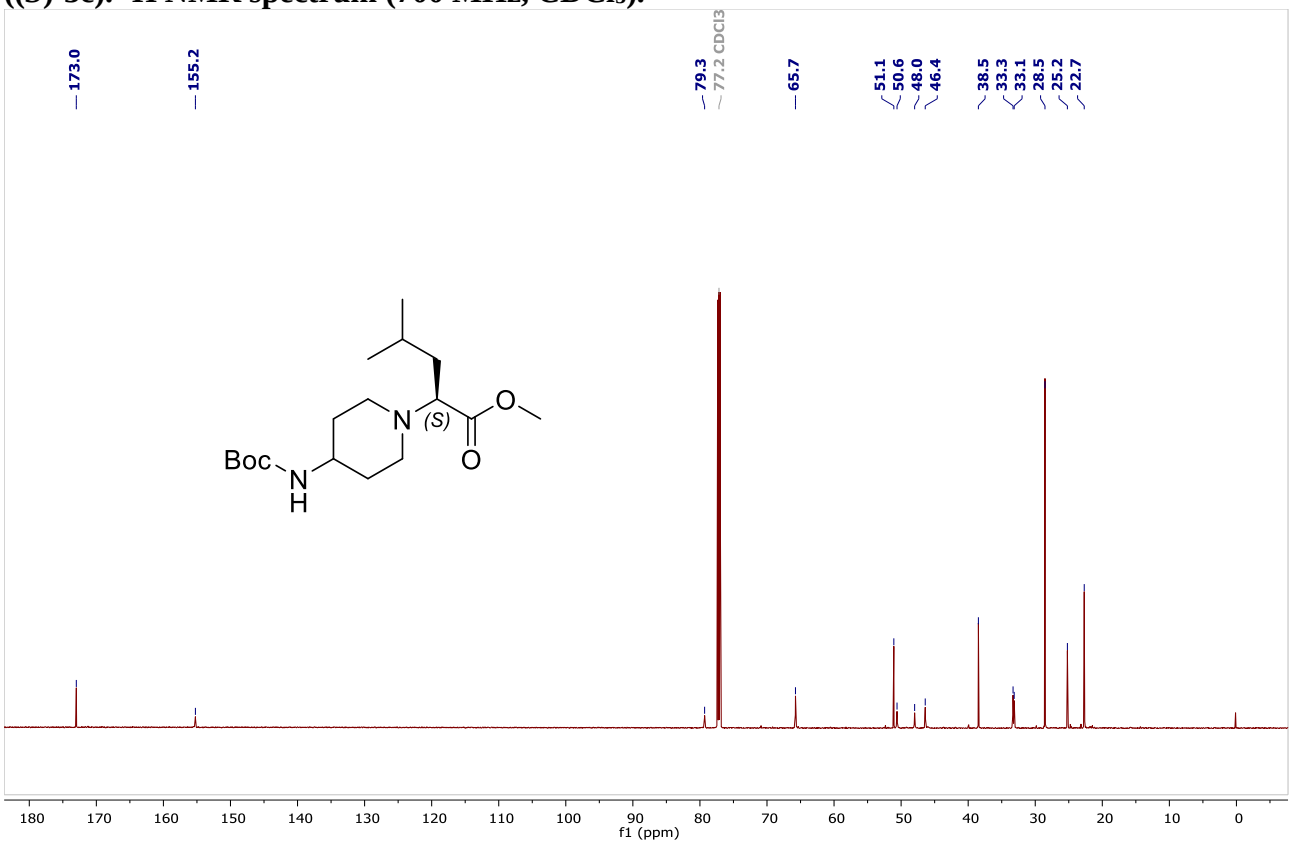


Figure S21. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((*S*)-3c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_602_1-B,7_01_10220.d	Acquisition Date	4/14/2023 4:28:12 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_602	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
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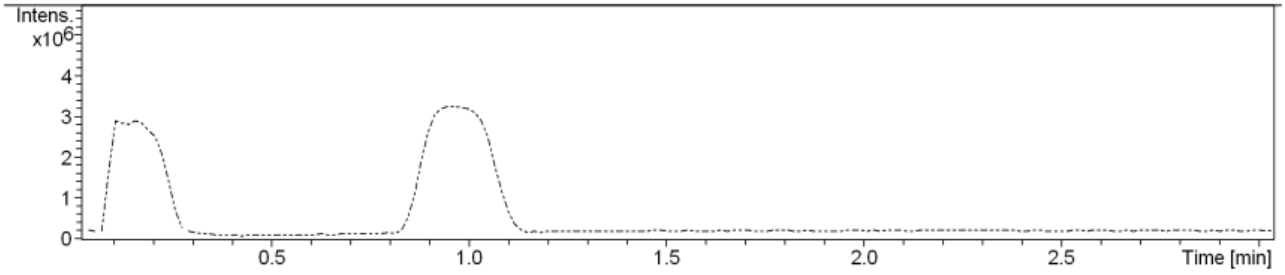
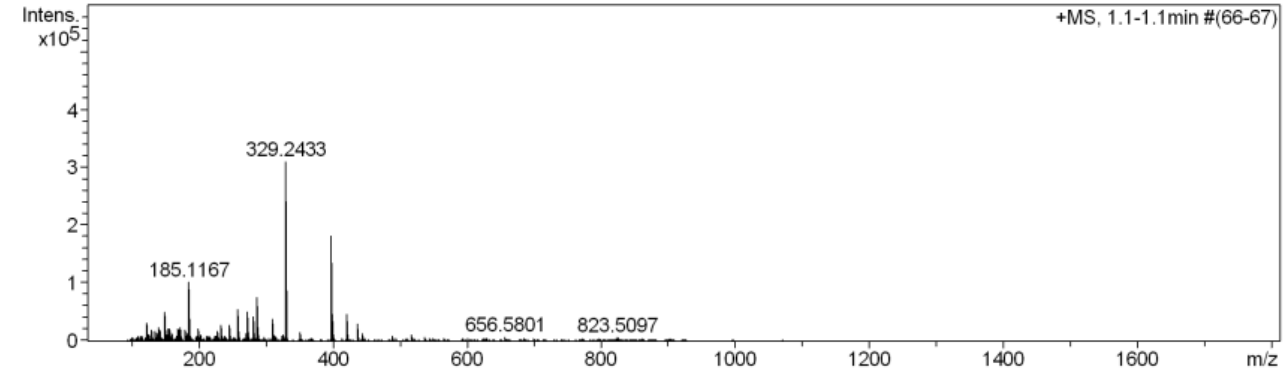
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
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	2	C 18 H 29 N 6	36.31	329.2448	4.7	4.9	29.3	7.5	even	ok

Figure S22. Methyl (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((*S*)-3c). HRMS (ESI-TOF).

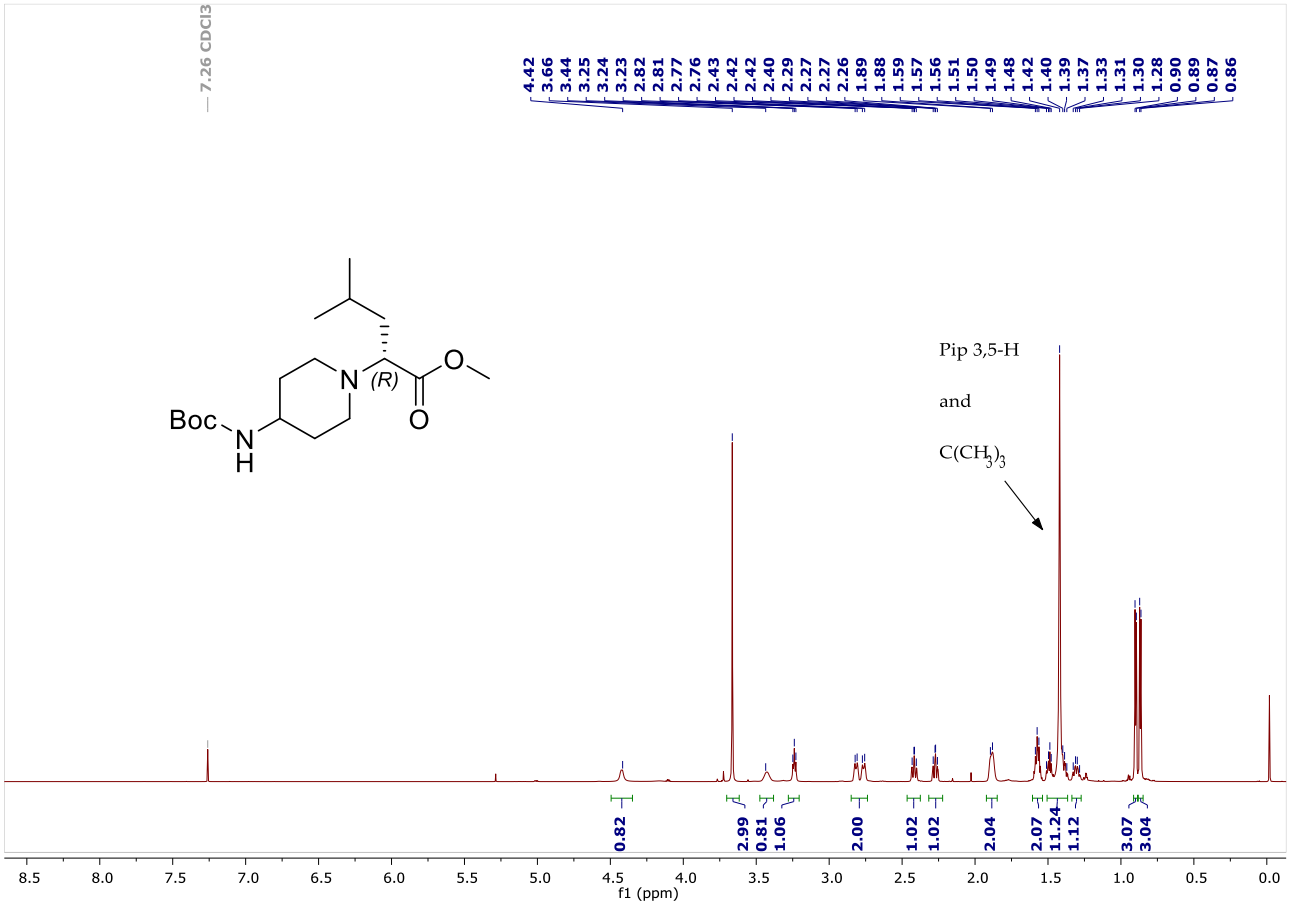


Figure S23. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((*R*)-3c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

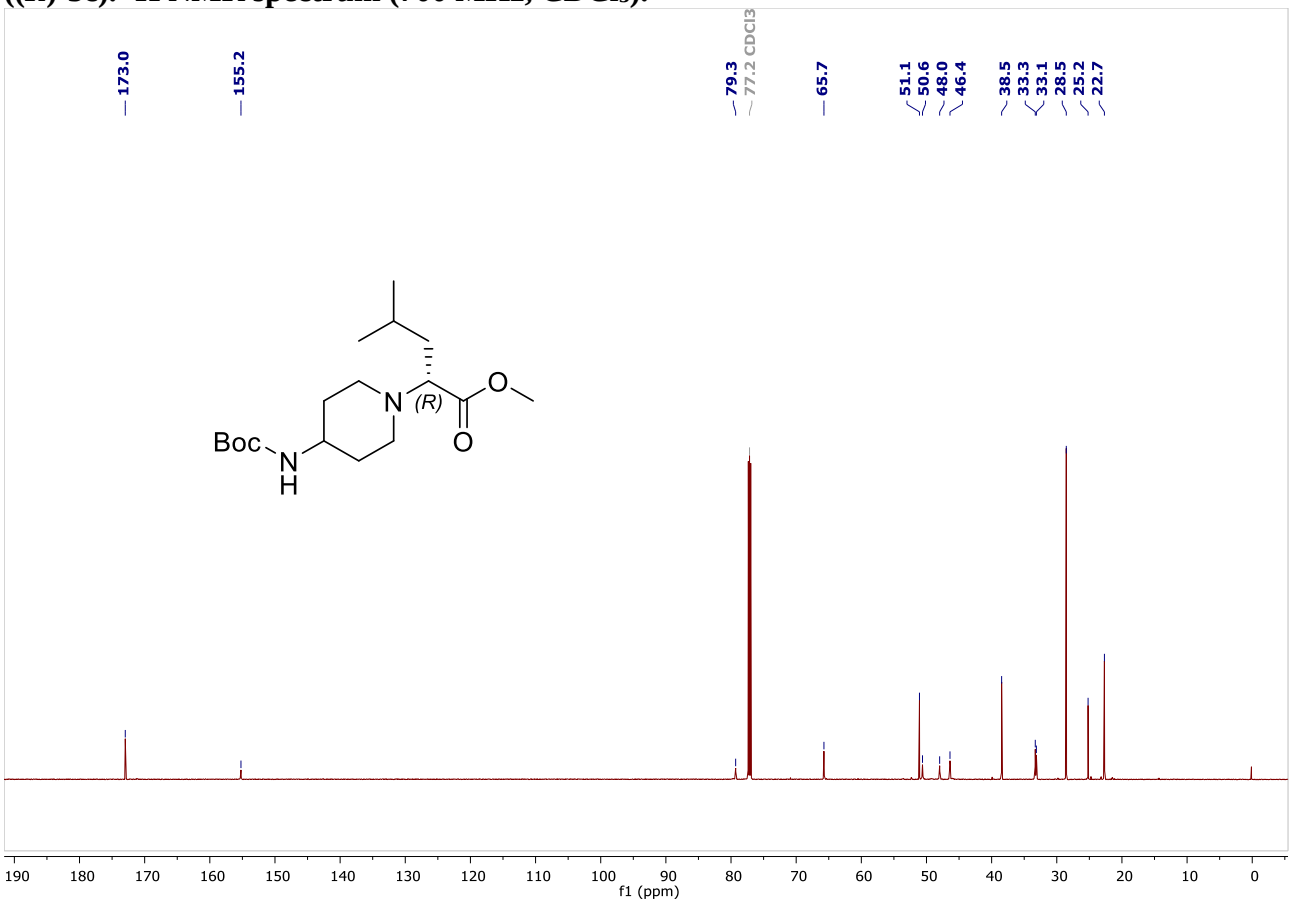


Figure S24. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((*R*)-3c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

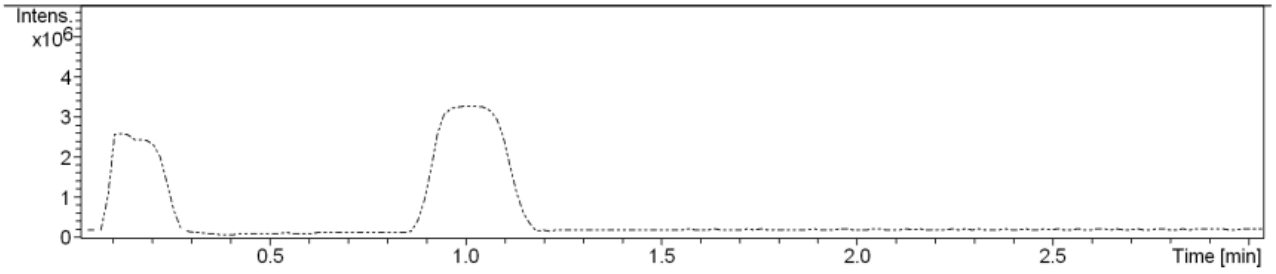
Mass Spectrum SmartFormula Report

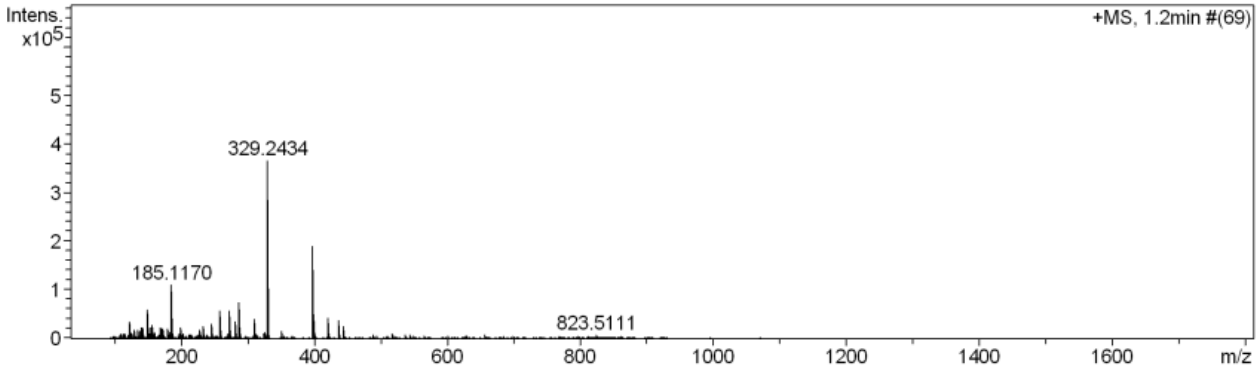
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_610_1-B,6_01_10219.d	Acquisition Date	4/14/2023 4:23:42 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_610	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
329.2434	1	C 17 H 33 N 2 O 4	100.00	329.2435	0.4	0.7	15.1	2.5	even	ok
	2	C 18 H 29 N 6	37.00	329.2448	4.5	4.7	27.8	7.5	even	ok

Figure S25. Methyl (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((*R*)-3c). HRMS (ESI-TOF).

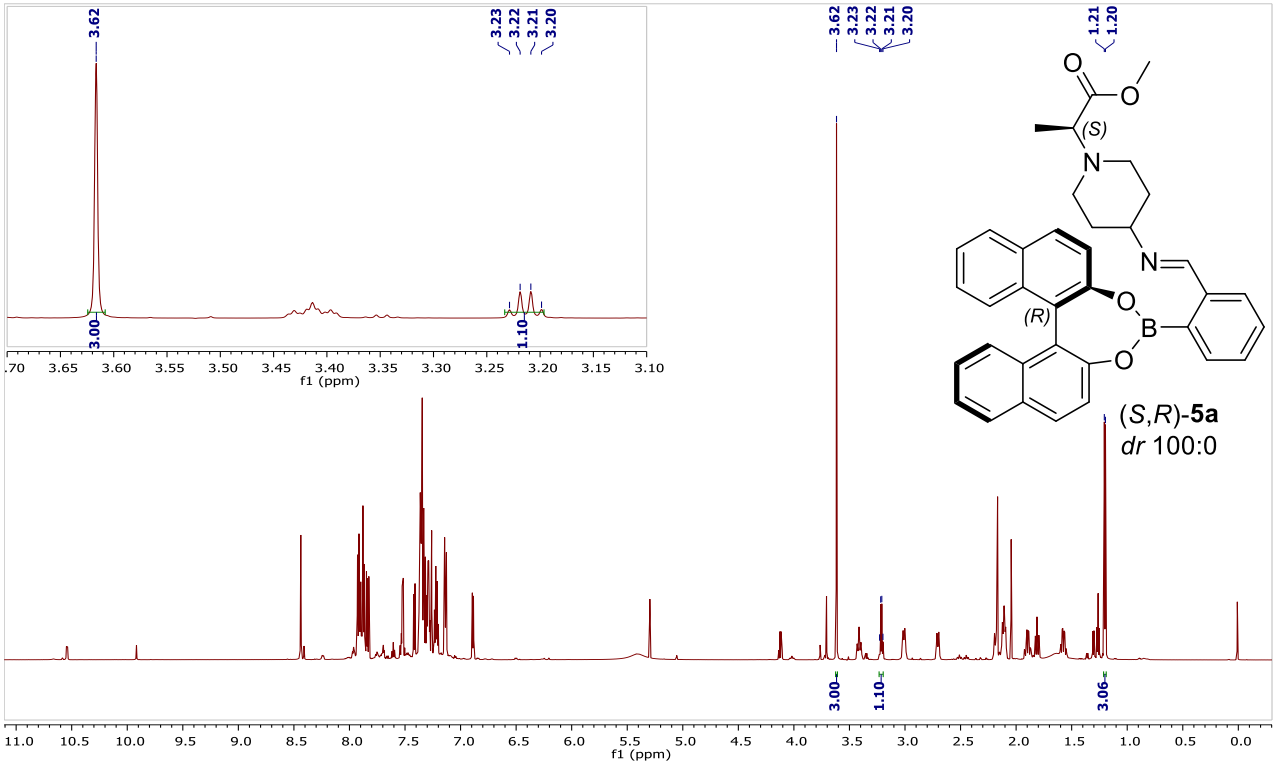


Figure S26. Crude sample from reaction mixture of iminoboronate ester complex ((*S*,*R*)-5a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

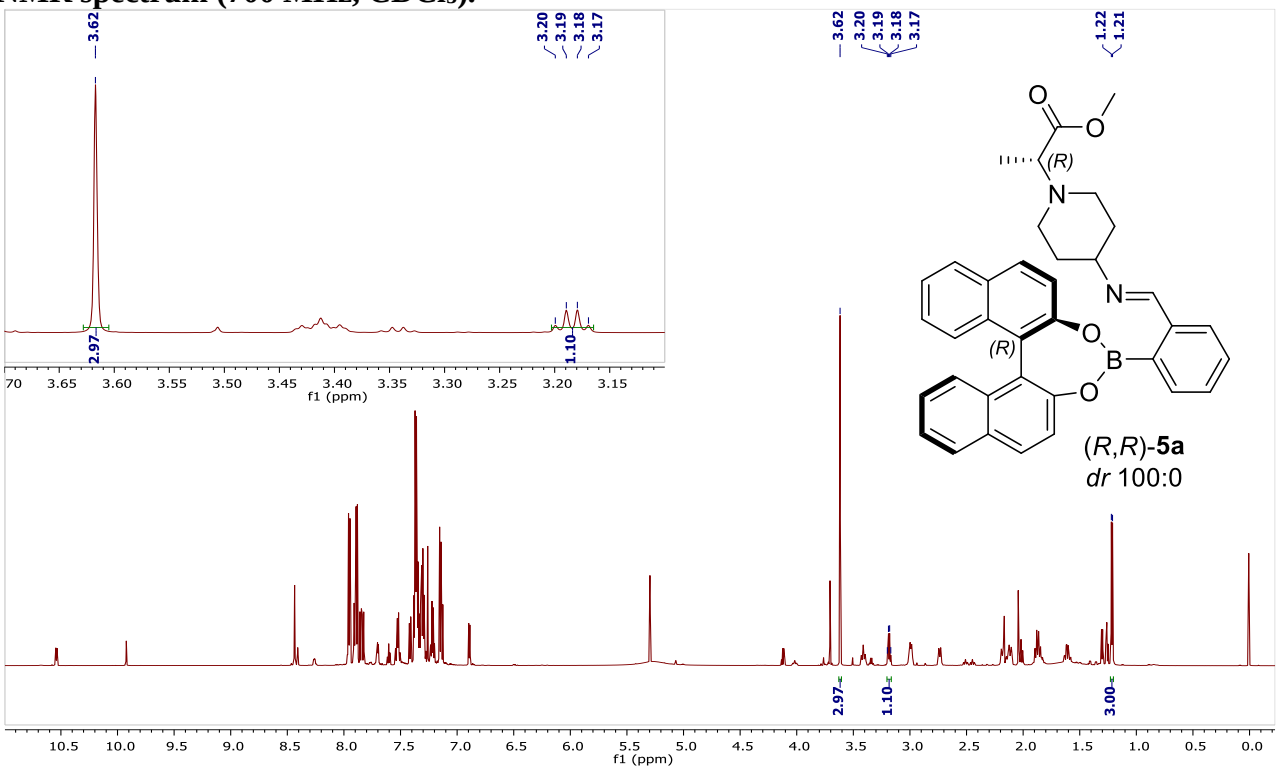


Figure S27. Crude sample from reaction mixture of iminoboronate ester complex ((*R*,*R*)-5a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

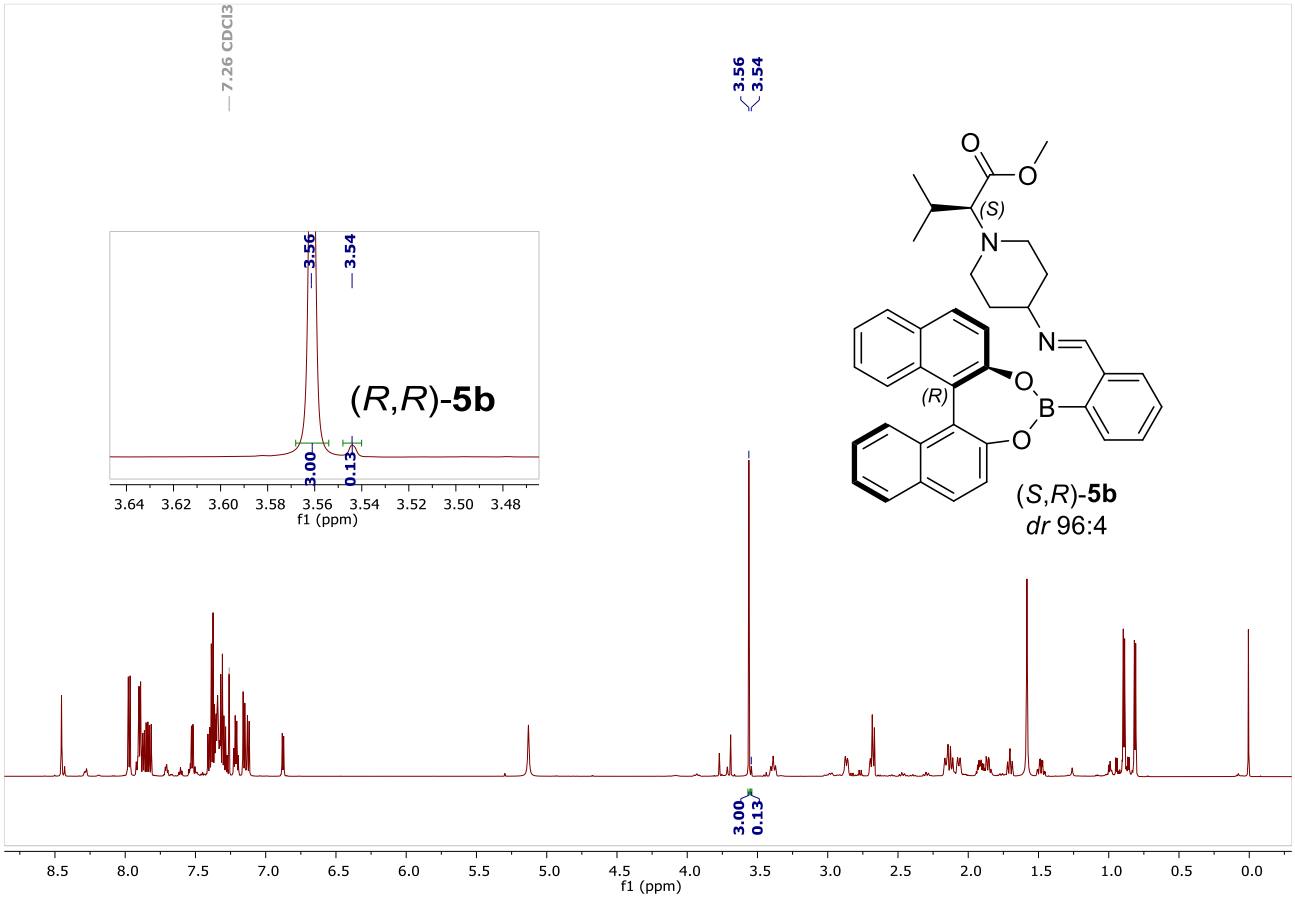


Figure S28. Crude sample from reaction mixture of iminoboronate ester complex ((*S*,*R*)-5b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

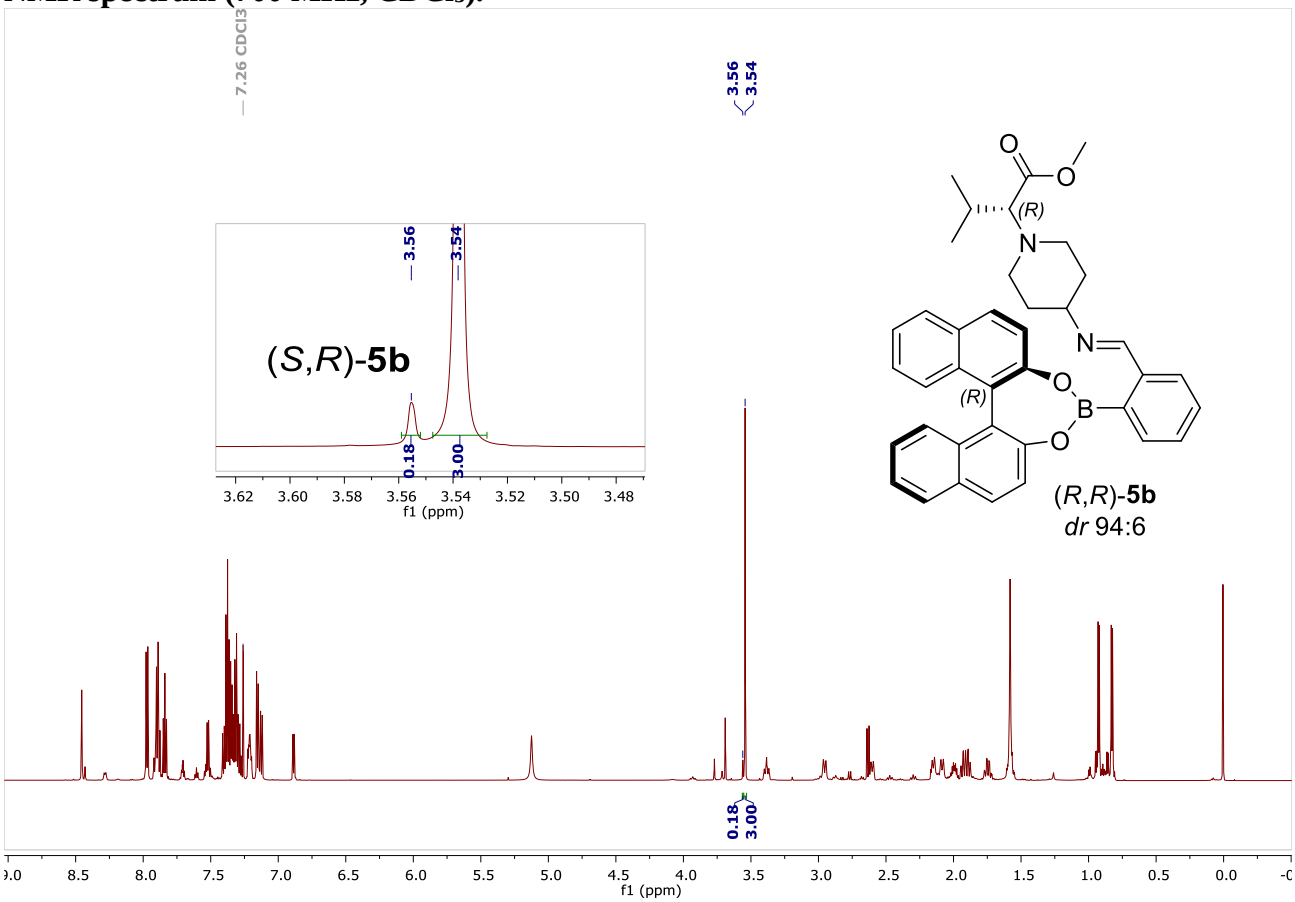


Figure S29. Crude sample from reaction mixture of iminoboronate ester complex ((*R*,*R*)-5b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

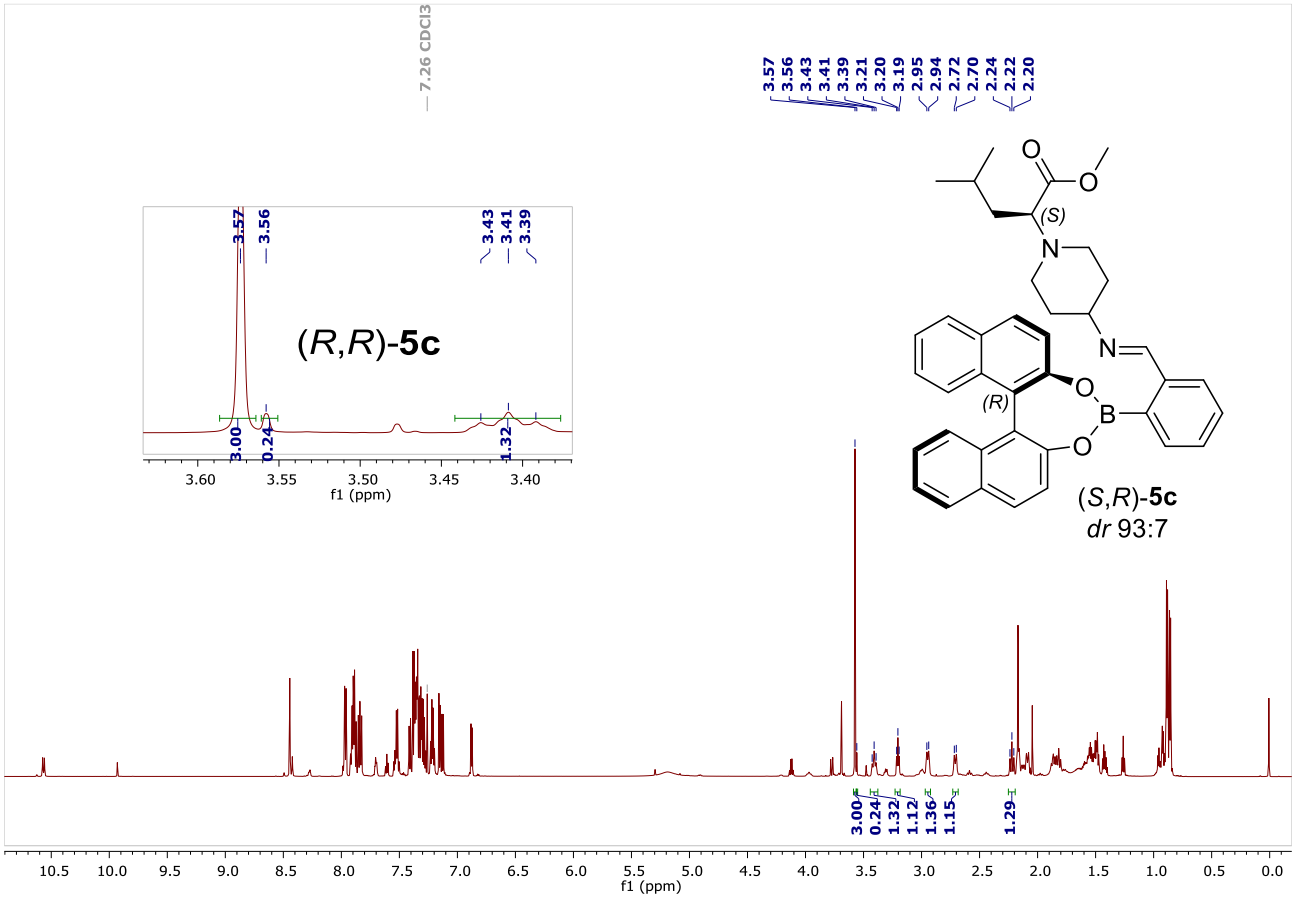


Figure S30. Crude sample from reaction mixture of iminoboronate ester complex ((*S*,*R*)-5c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

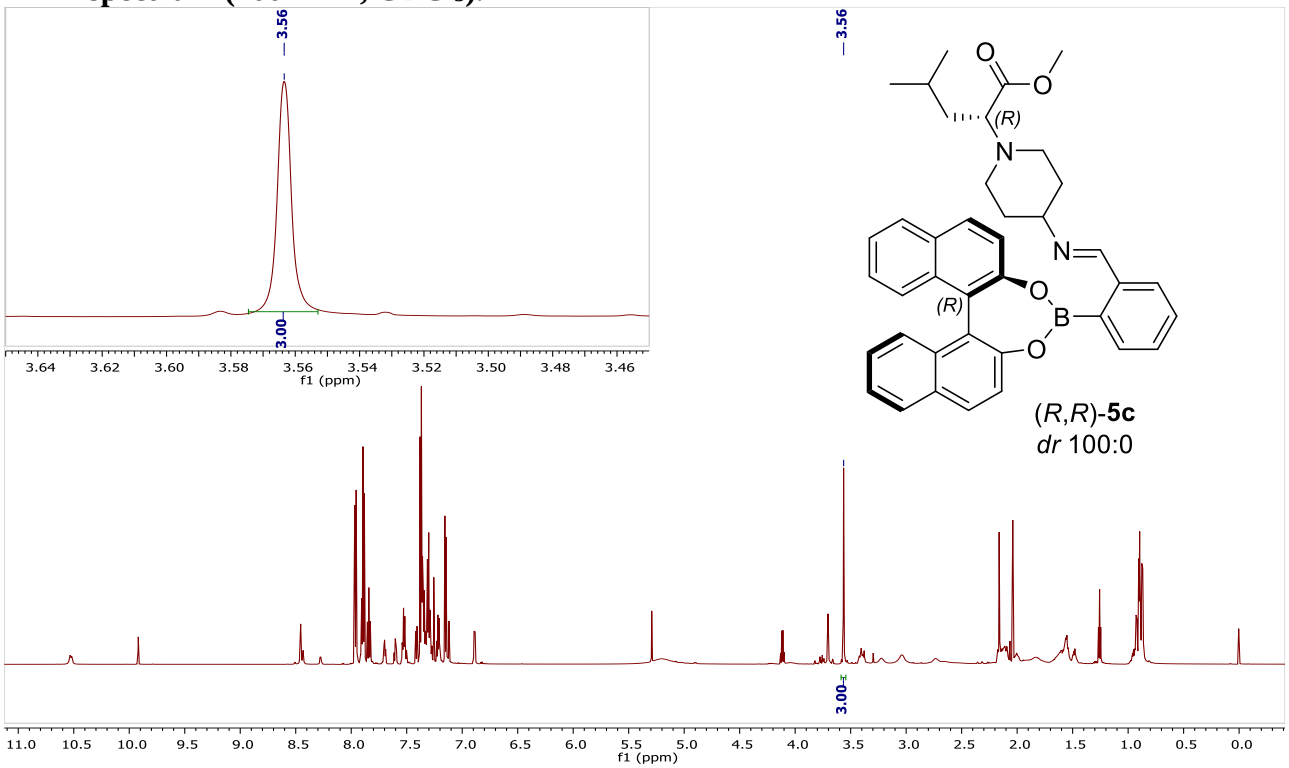


Figure S31. Crude sample from reaction mixture of iminoboronate ester complex ((*R*,*R*)-5c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

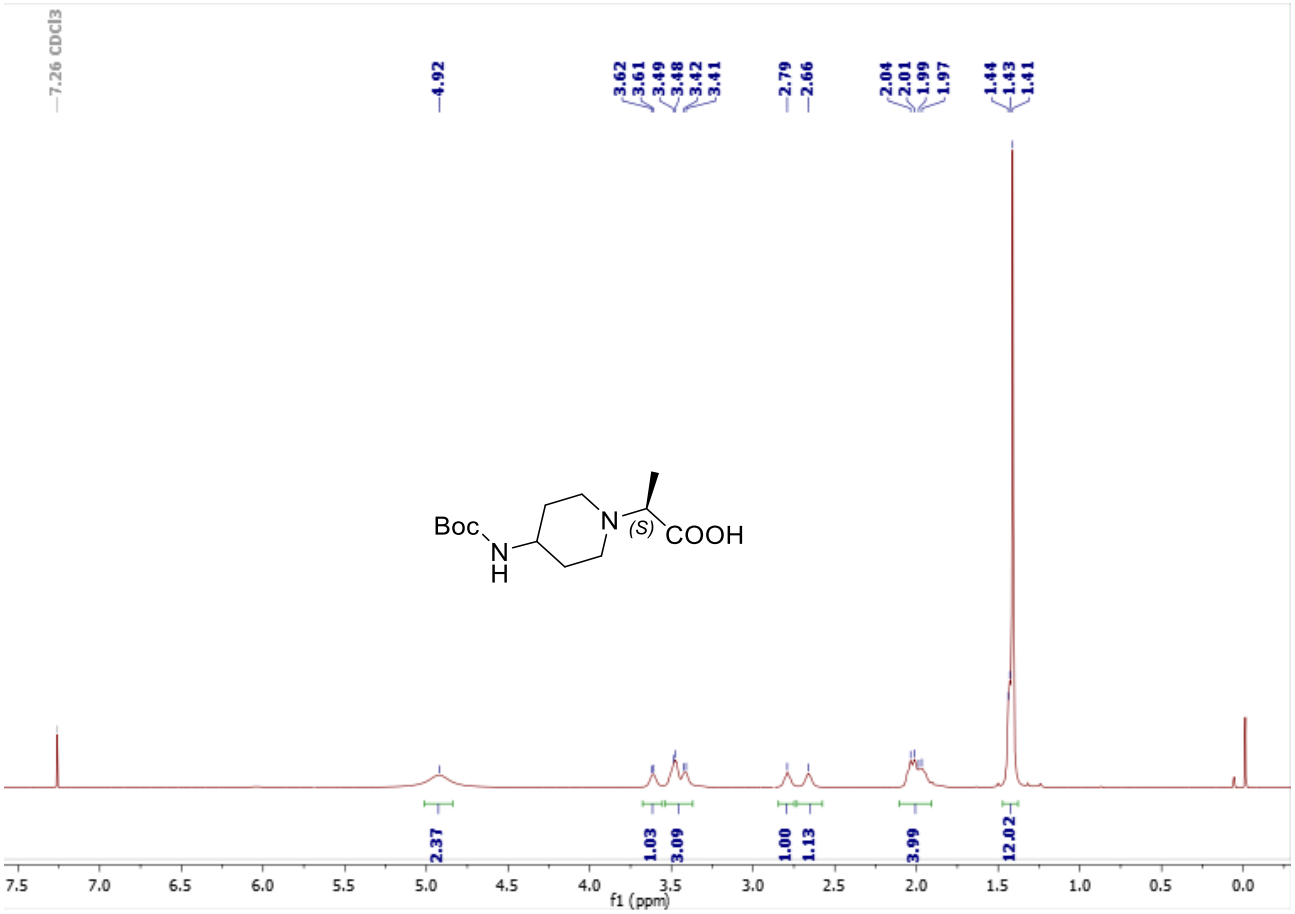


Figure S32. (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoic acid ((*S*)-6). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

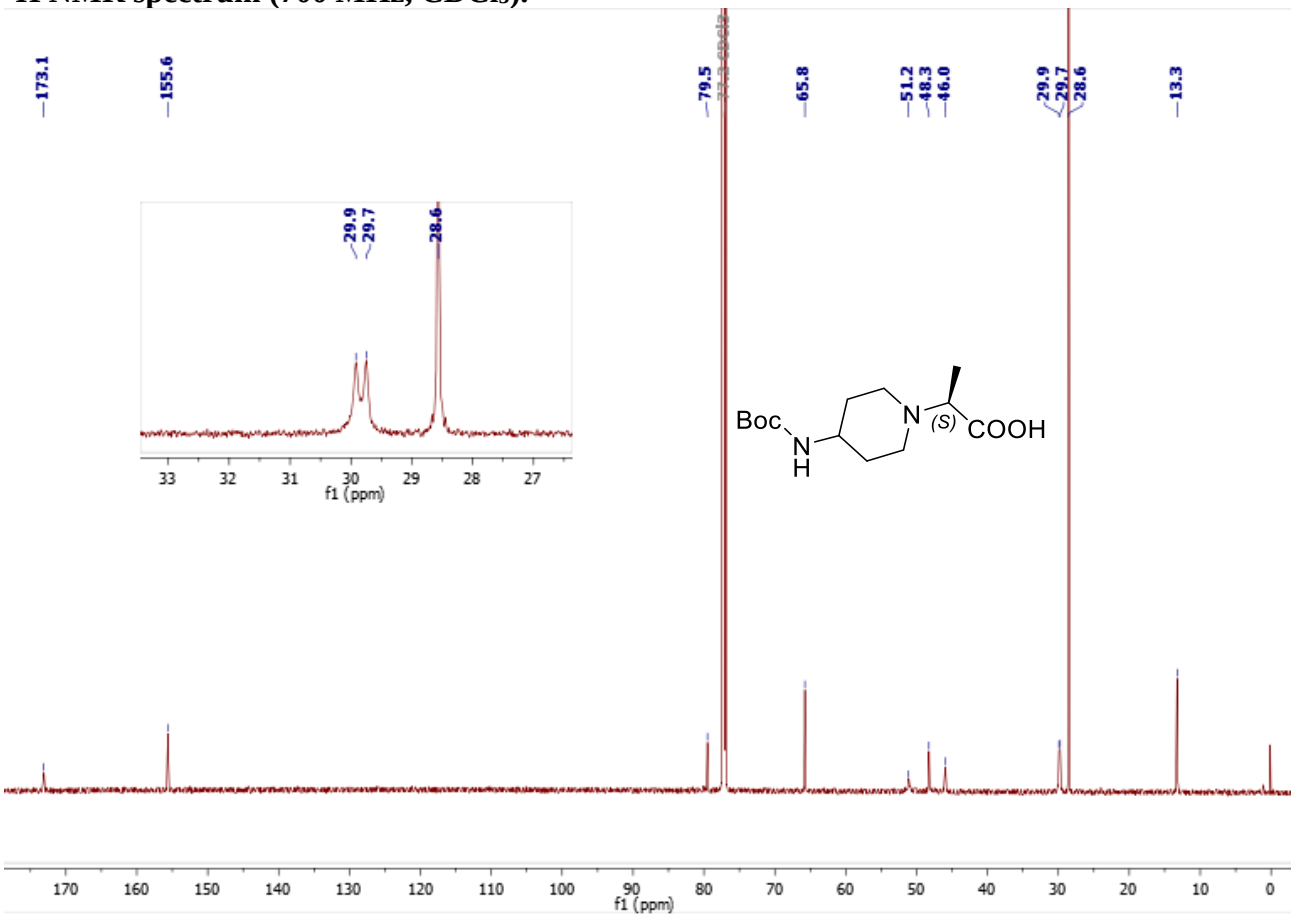


Figure S33. (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoic acid ((*S*)-6). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

Compound Spectrum SmartFormula Report

Analysis Info

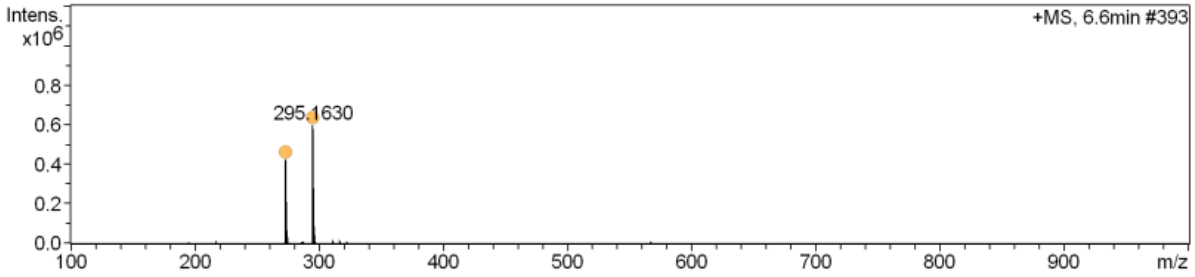
Analysis Name	D:\Data\GMP-1188.d	Acquisition Date	5/2/2023 8:28:21 PM
Method	DirectInfusion_TuneLow_pos.m	Operator	hplc
Sample Name	GMP-1188	Instrument	micrOTOF-Q III 8228888.20448
Comment	AB		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	140.0 Vpp	Set Divert Valve	Waste

#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
n.a.	6.6	n.a.	Single spectrum	n.a.	n.a.	n.a.	295.1630	n.a.

+MS, 6.6min #393



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule
273.1805	1	C13H25N2O4	273.1809	-1.4	6.9	1	100.00	2.5	even	ok
295.1630	1	C13H24N2NaO4	295.1628	-0.6	2.2	1	100.00	2.5	even	ok

Figure S34. (2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoic acid ((*S*)-6). HRMS (ESI-TOF).

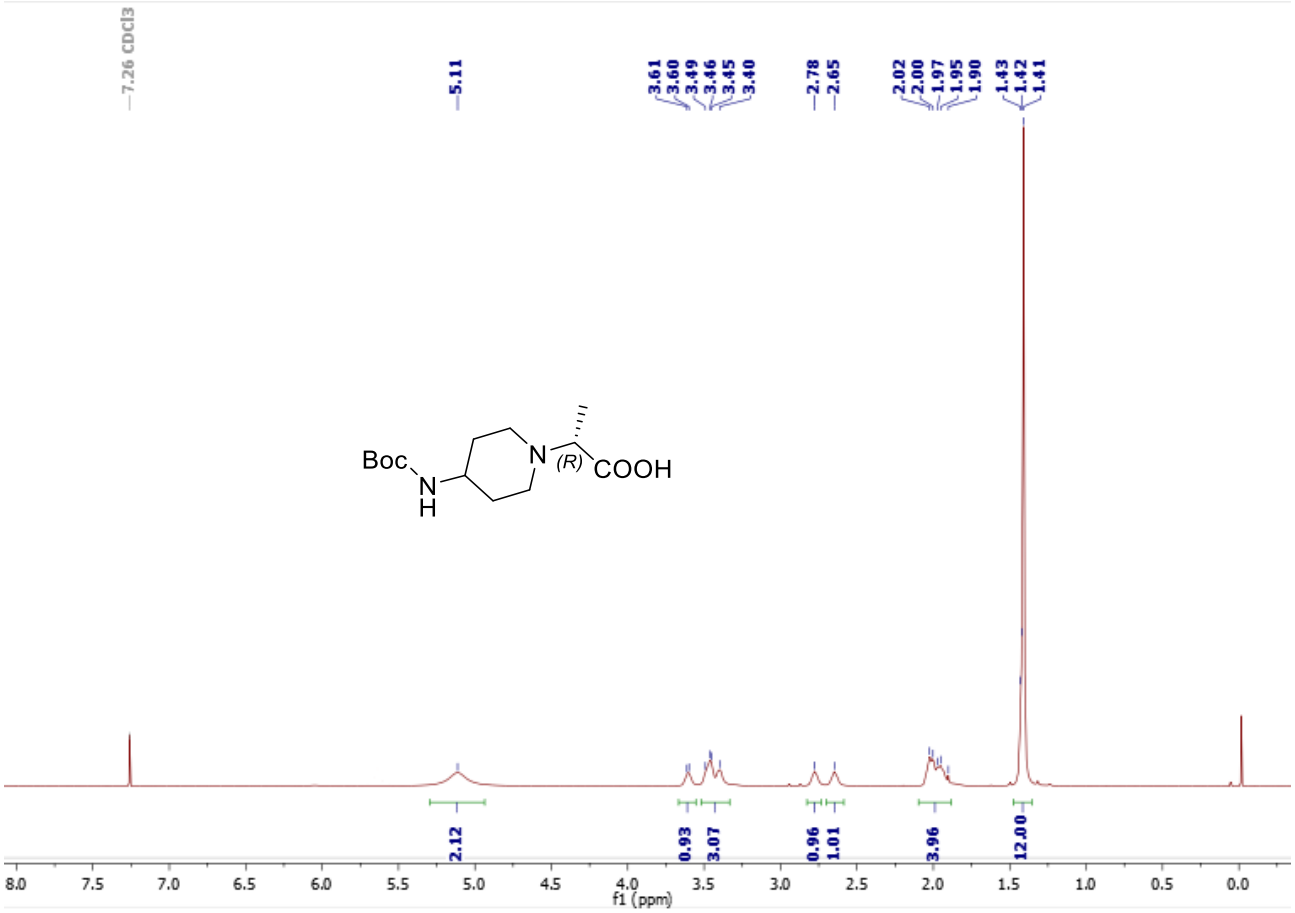


Figure S35. (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoic acid ((*R*)-6). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

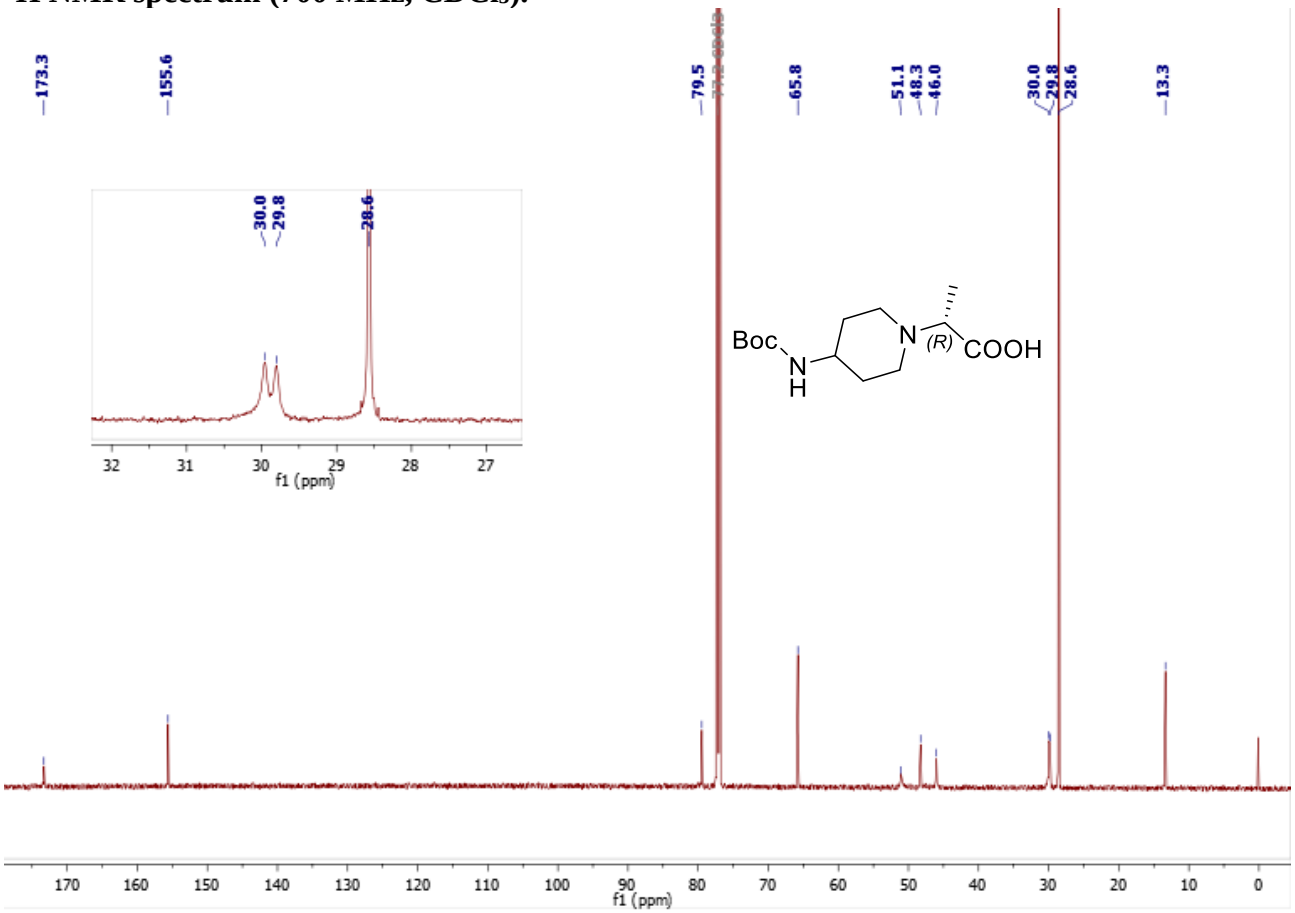


Figure S36. (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoic acid ((*R*)-6). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

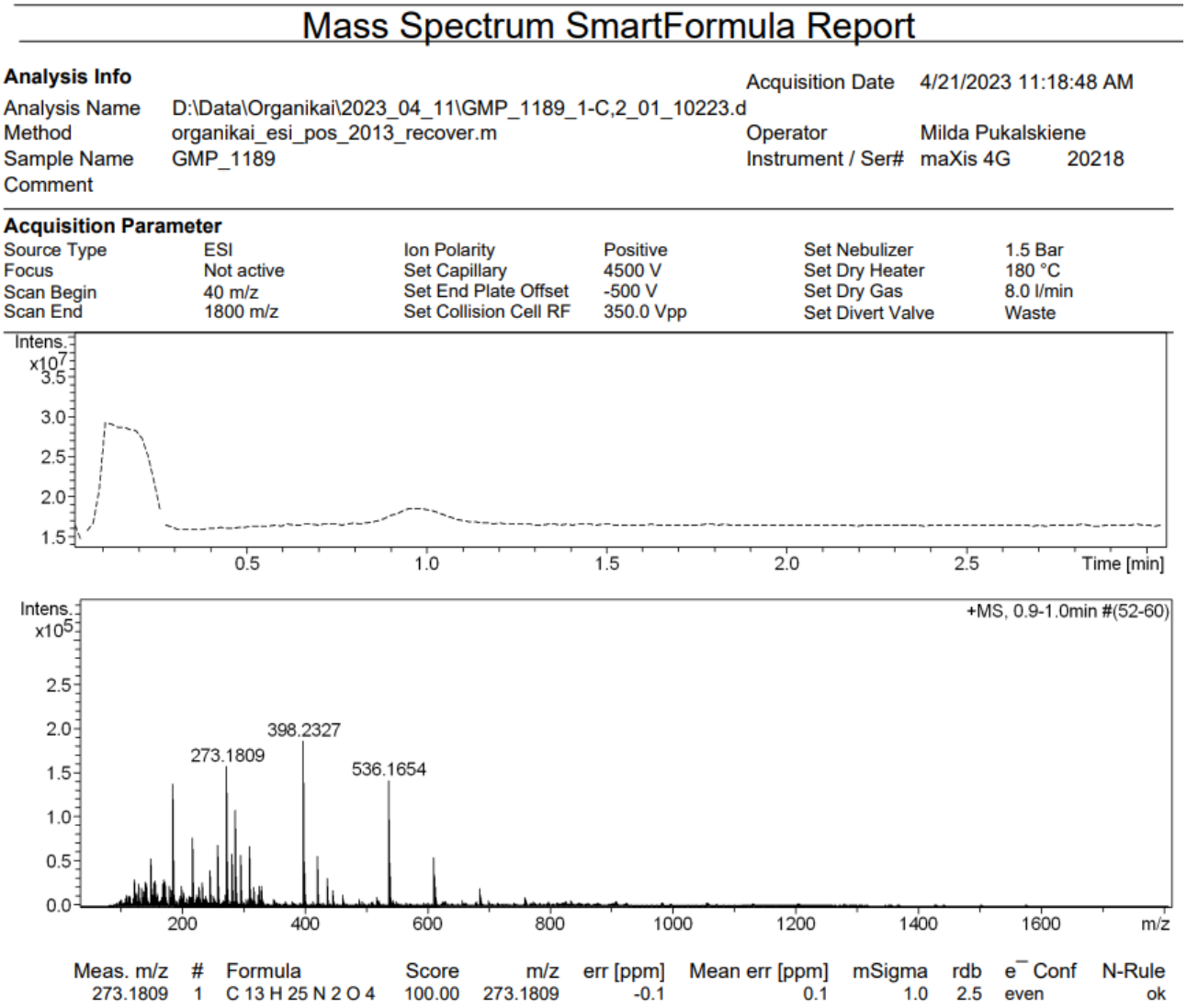


Figure S37. (2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoic acid ((*R*)-6). HRMS (ESI-TOF).

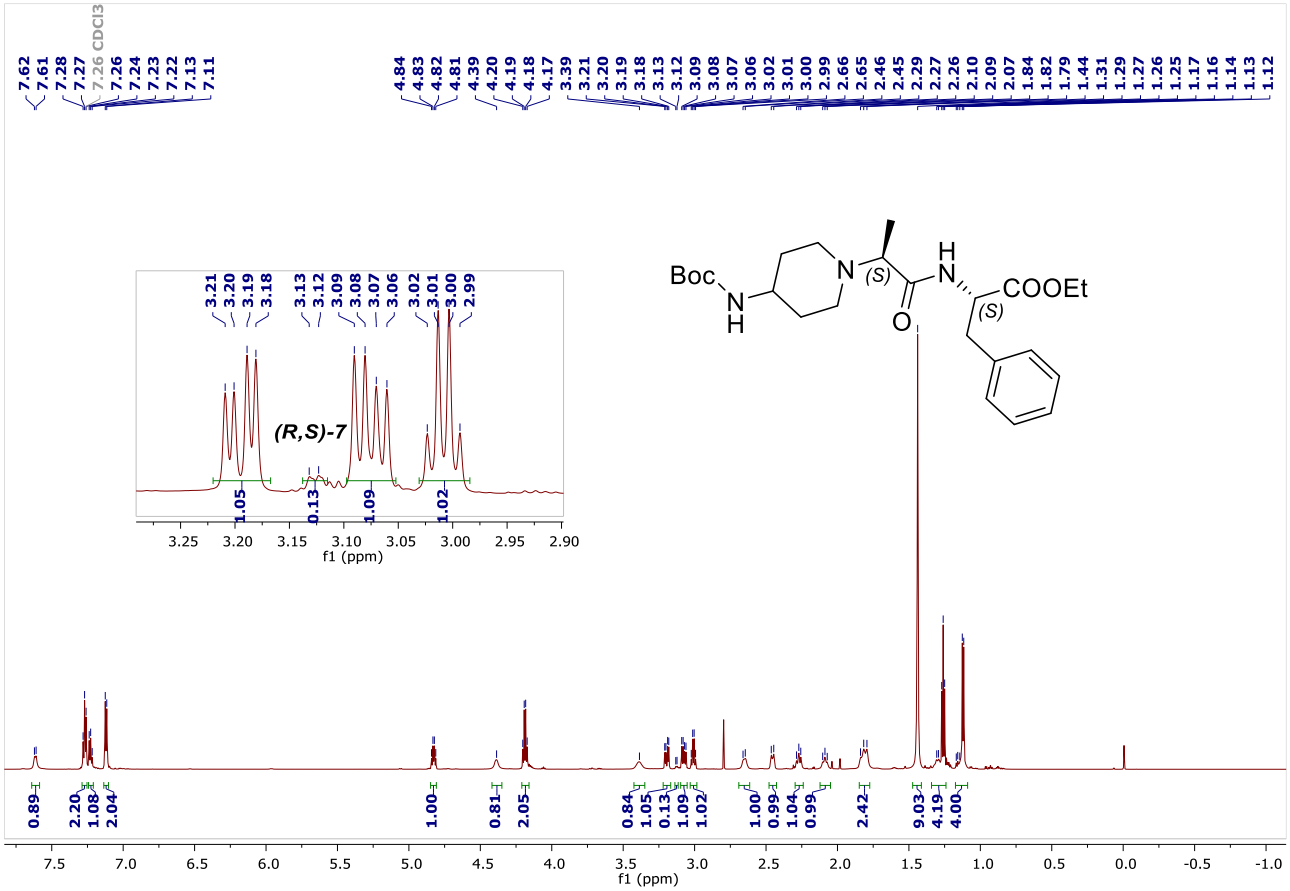


Figure S38. Ethyl *N*-[(2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*S*,*S*)-7). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

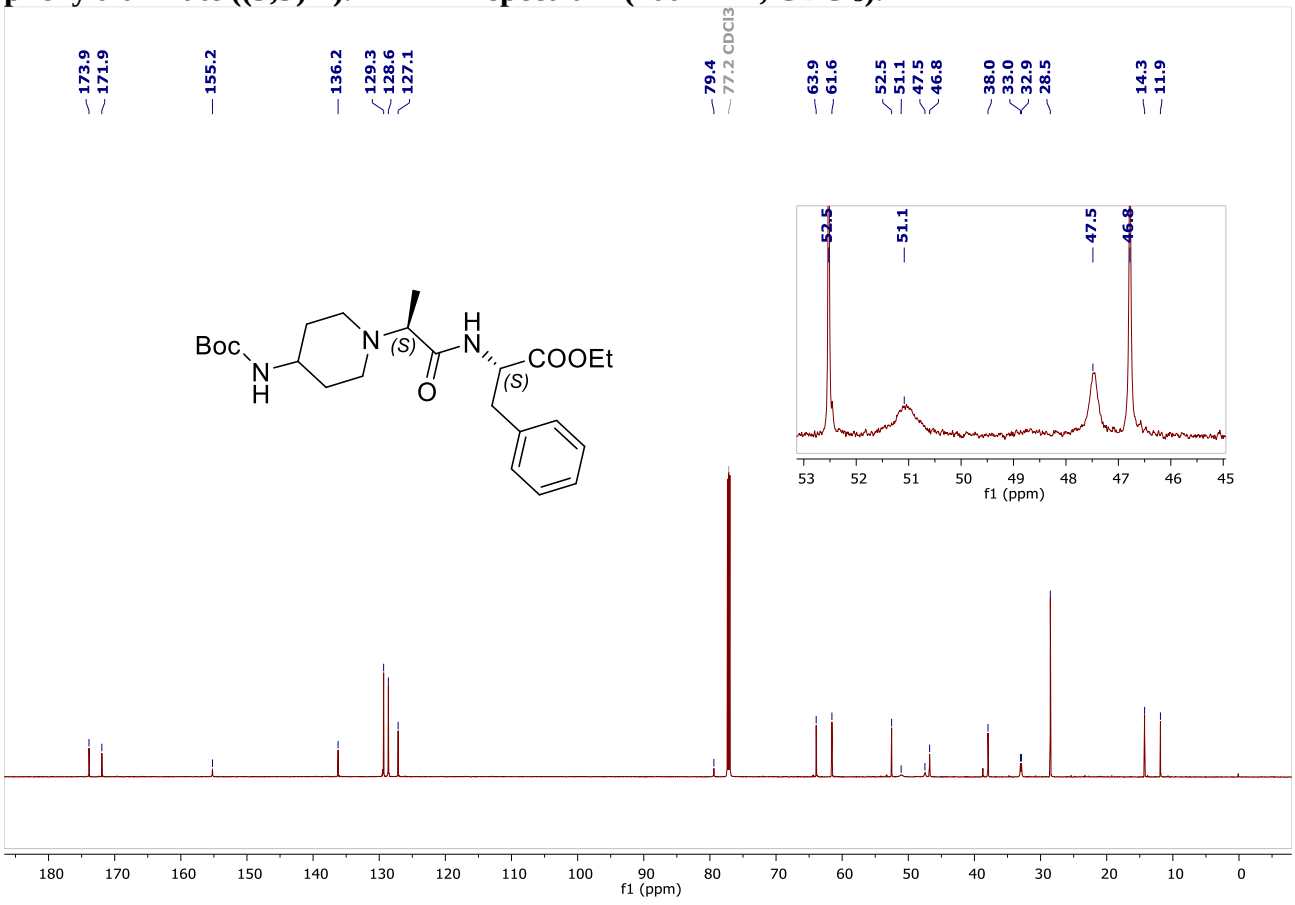


Figure S39. Ethyl *N*-[(2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*S*,*S*)-7). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

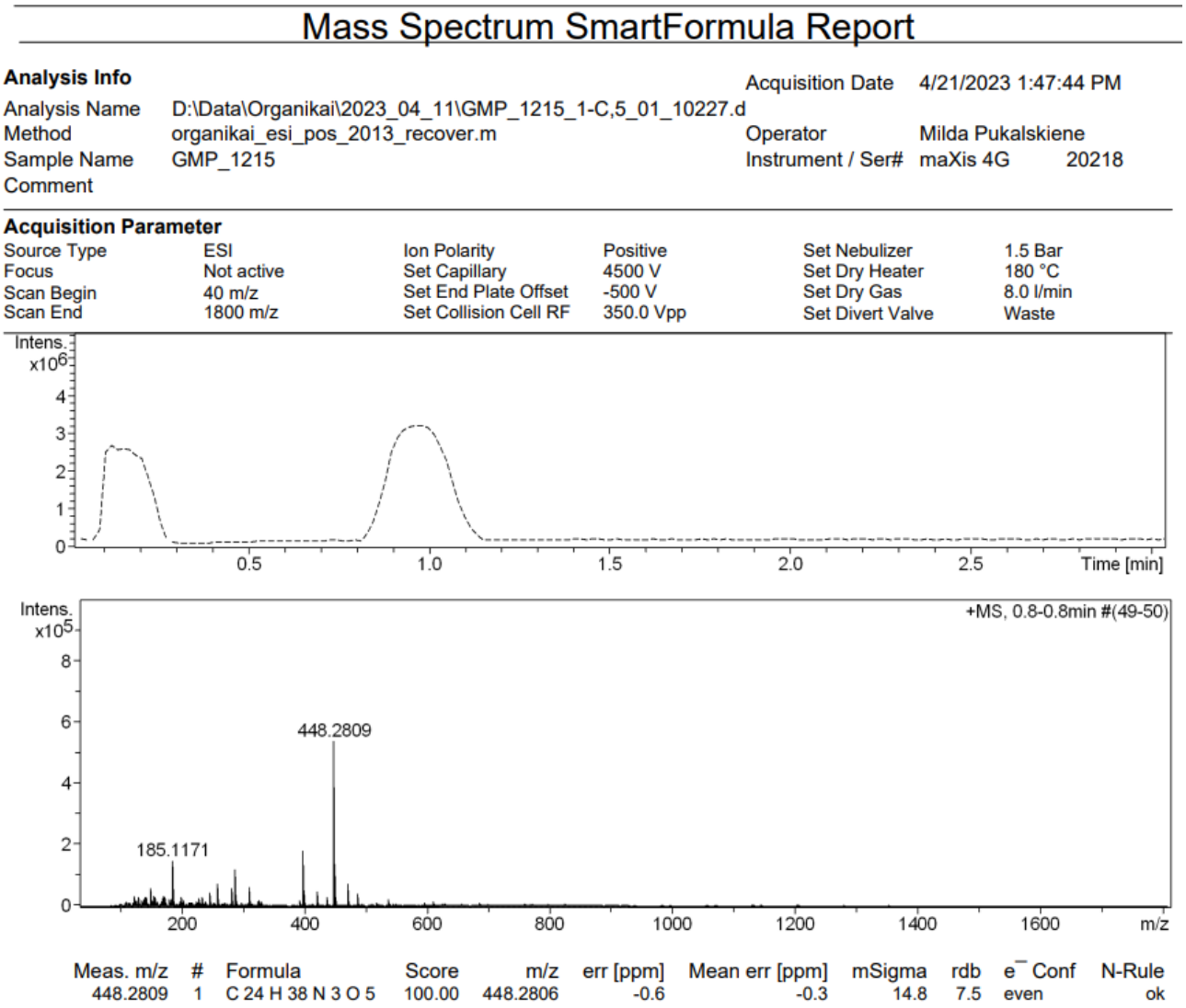


Figure S40. Ethyl *N*-[(2*S*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*S*,*S*)-7). HRMS (ESI-TOF).

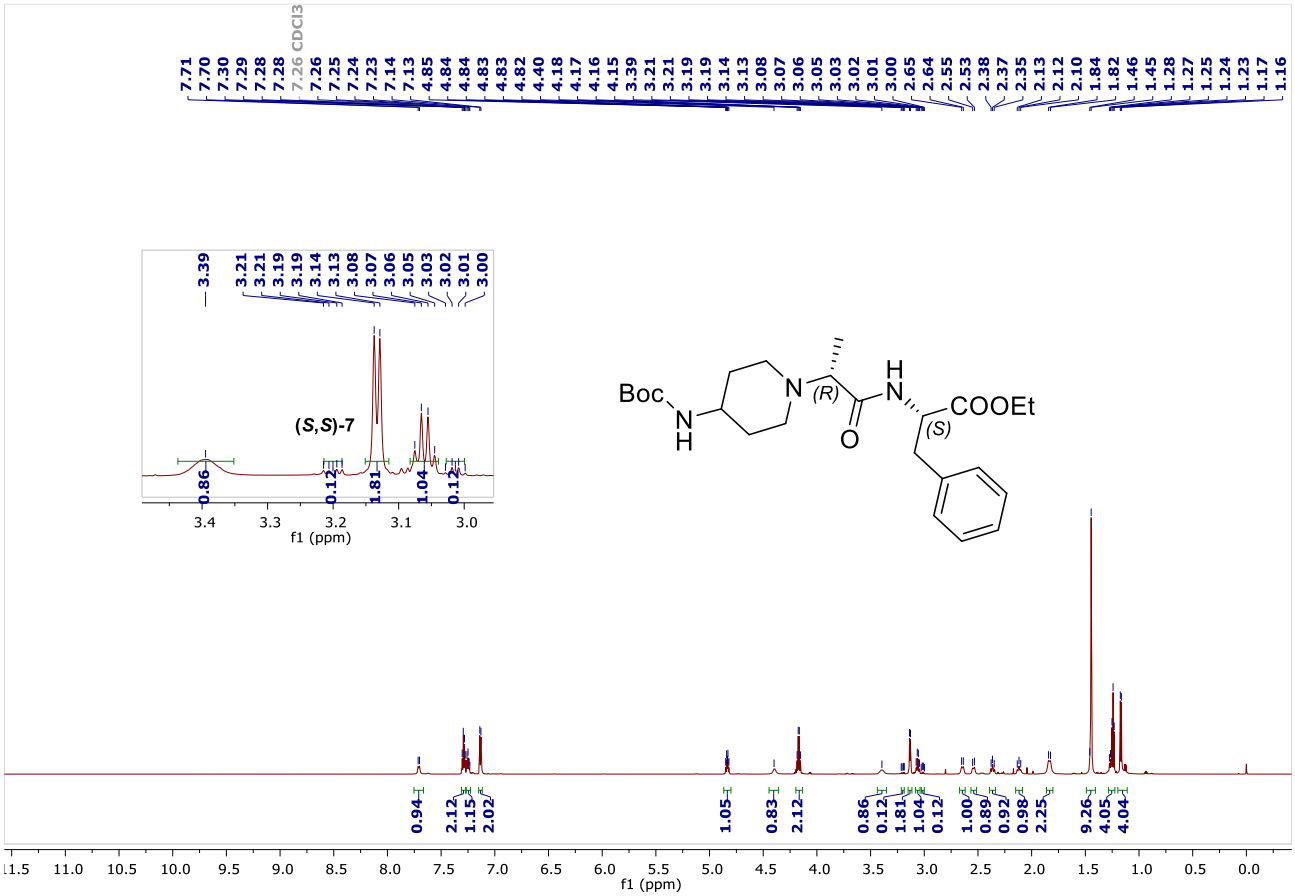


Figure S41. Ethyl *N*-[(2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*R*,*S*)-7). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

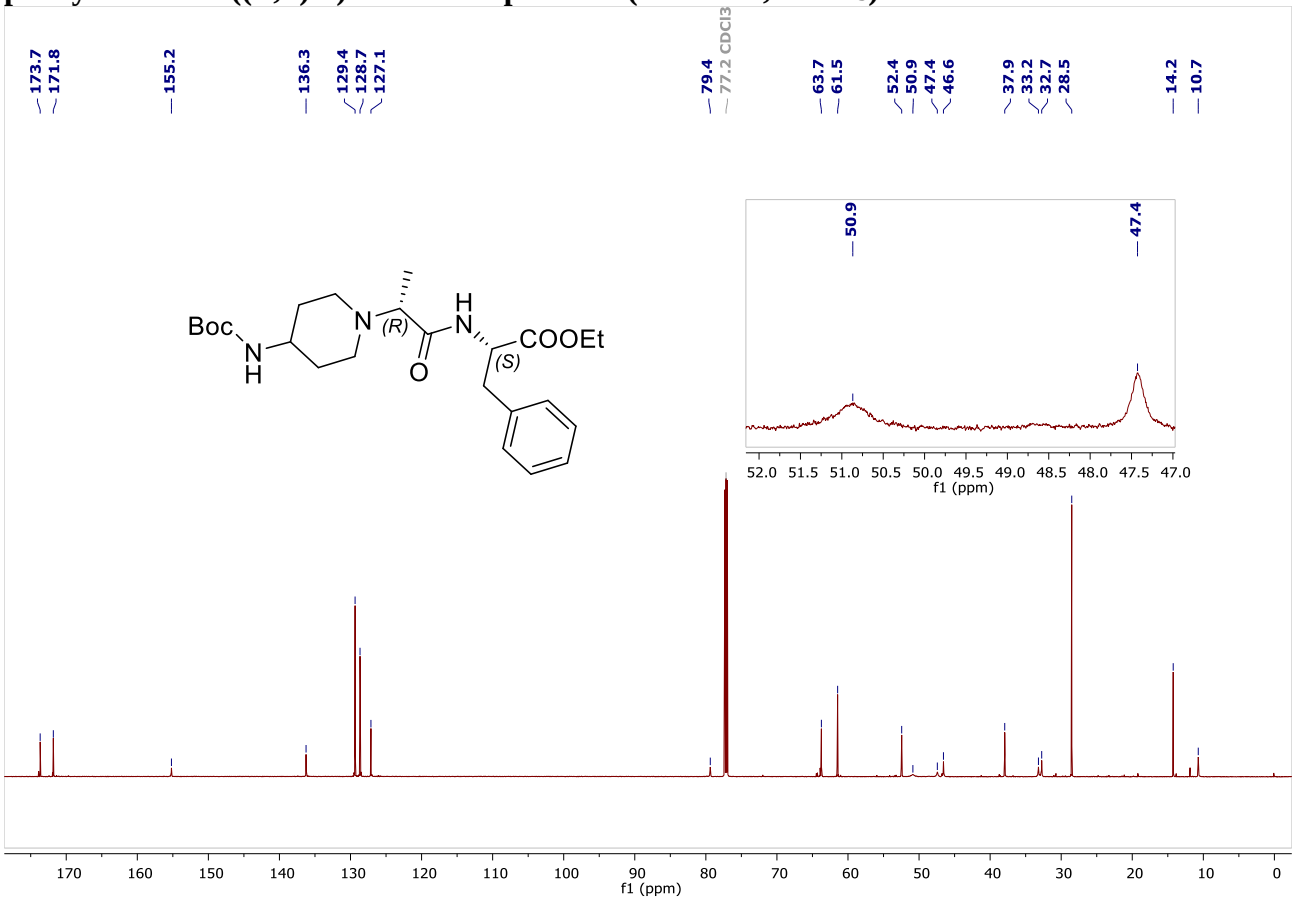


Figure S42. Ethyl *N*-[(2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*R*,*S*)-7). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

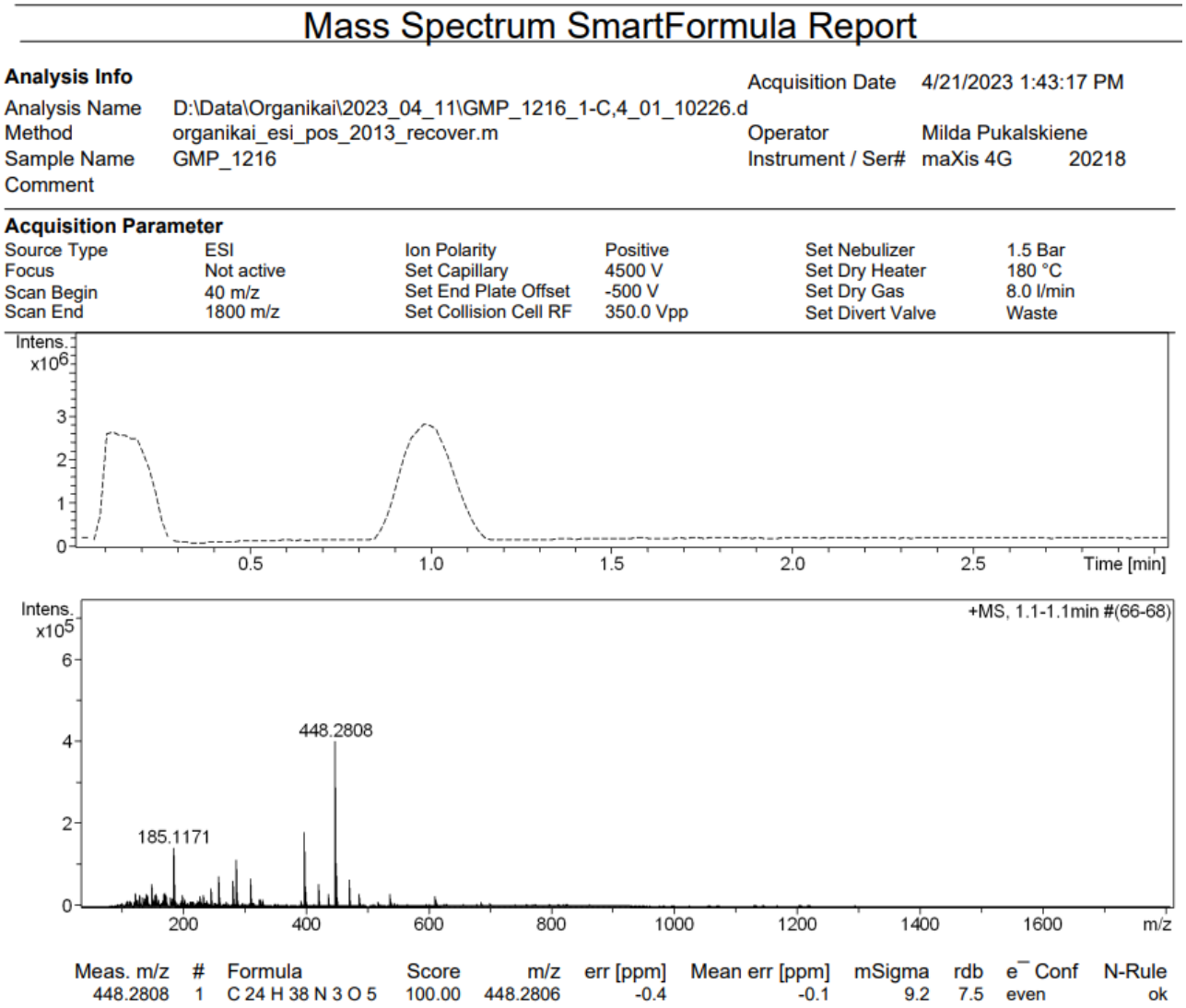


Figure S43. Ethyl *N*-[(2*R*)-2-{4-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*R*,*S*)-7). HRMS (ESI-TOF).

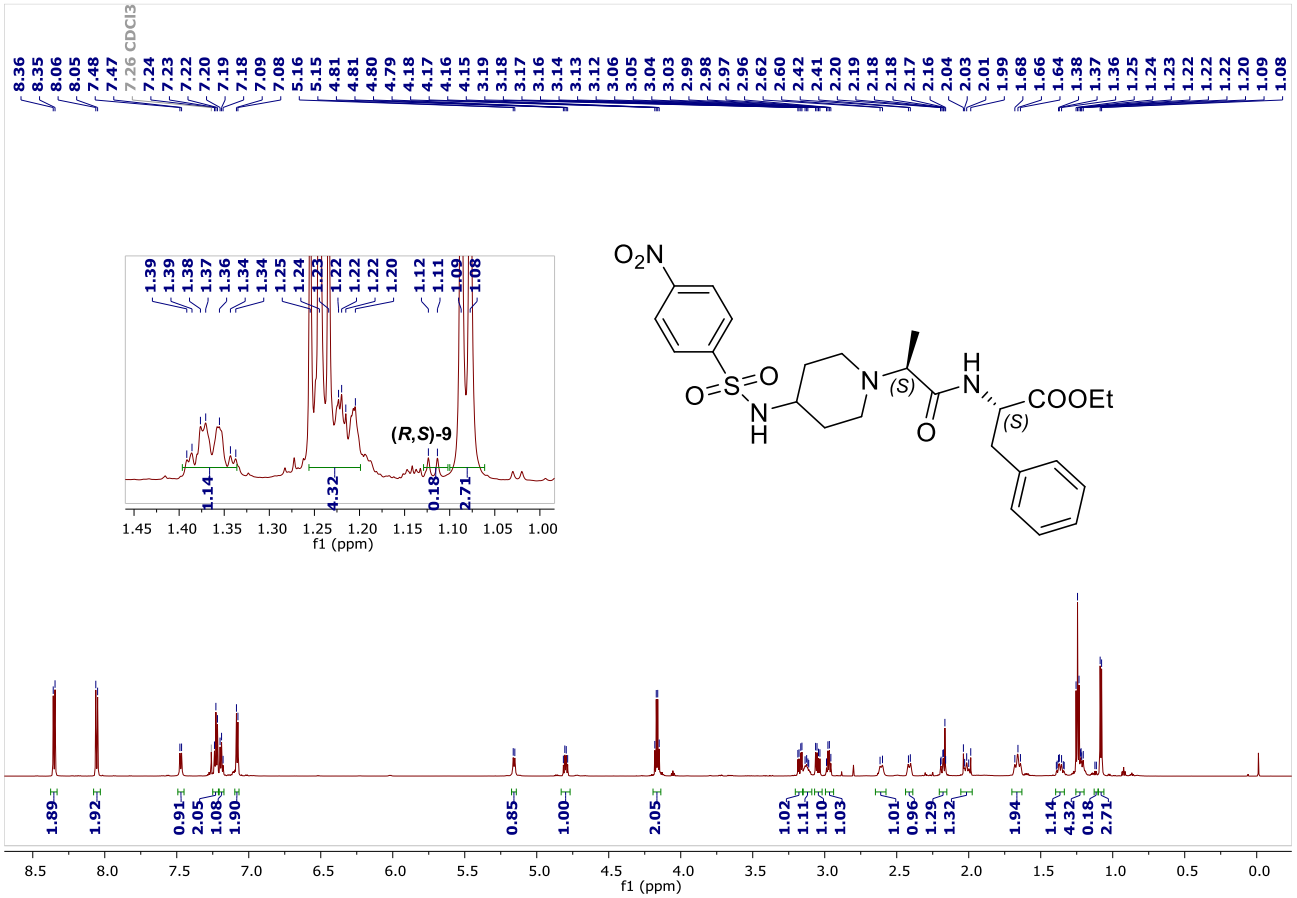


Figure S44. Ethyl *N*-[(2*S*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*S*,*S*)-9). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

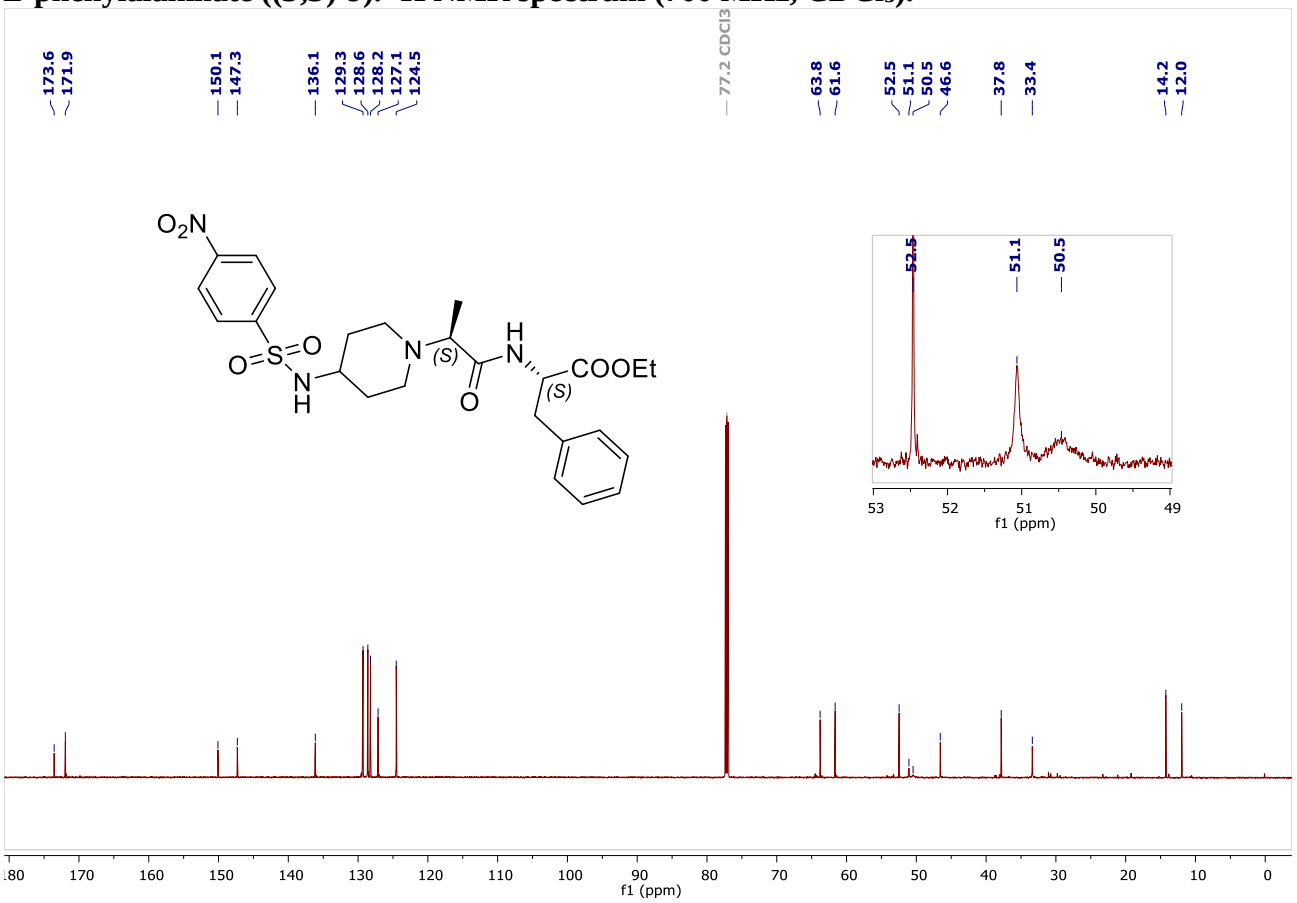


Figure S45. Ethyl *N*-[(2*S*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*S*,*S*)-9). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

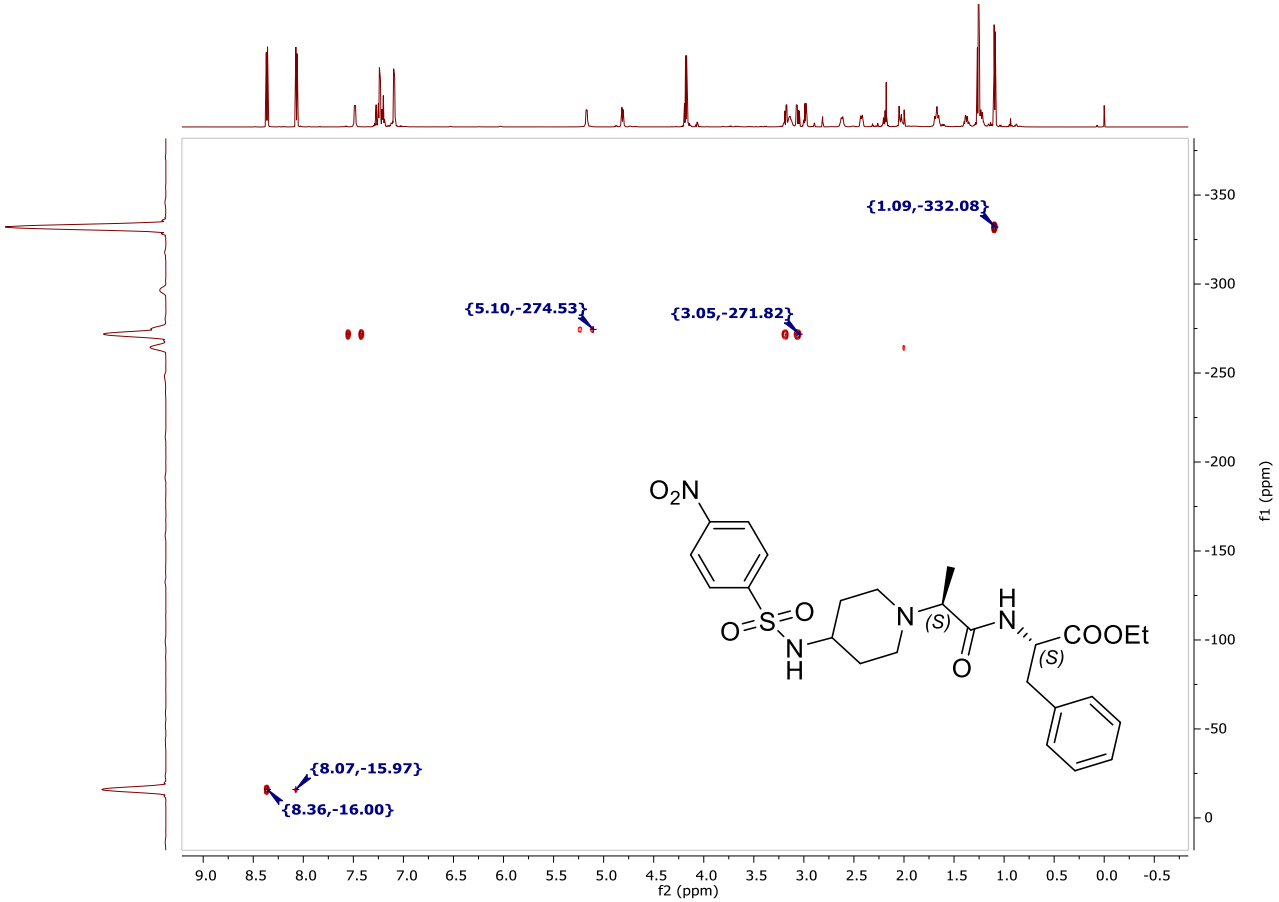


Figure S46. Ethyl *N*-[(2*S*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*S*,*S*)-9). ^{1}H-^{15}N HMBC spectrum (71 MHz, $CDCl_3$).

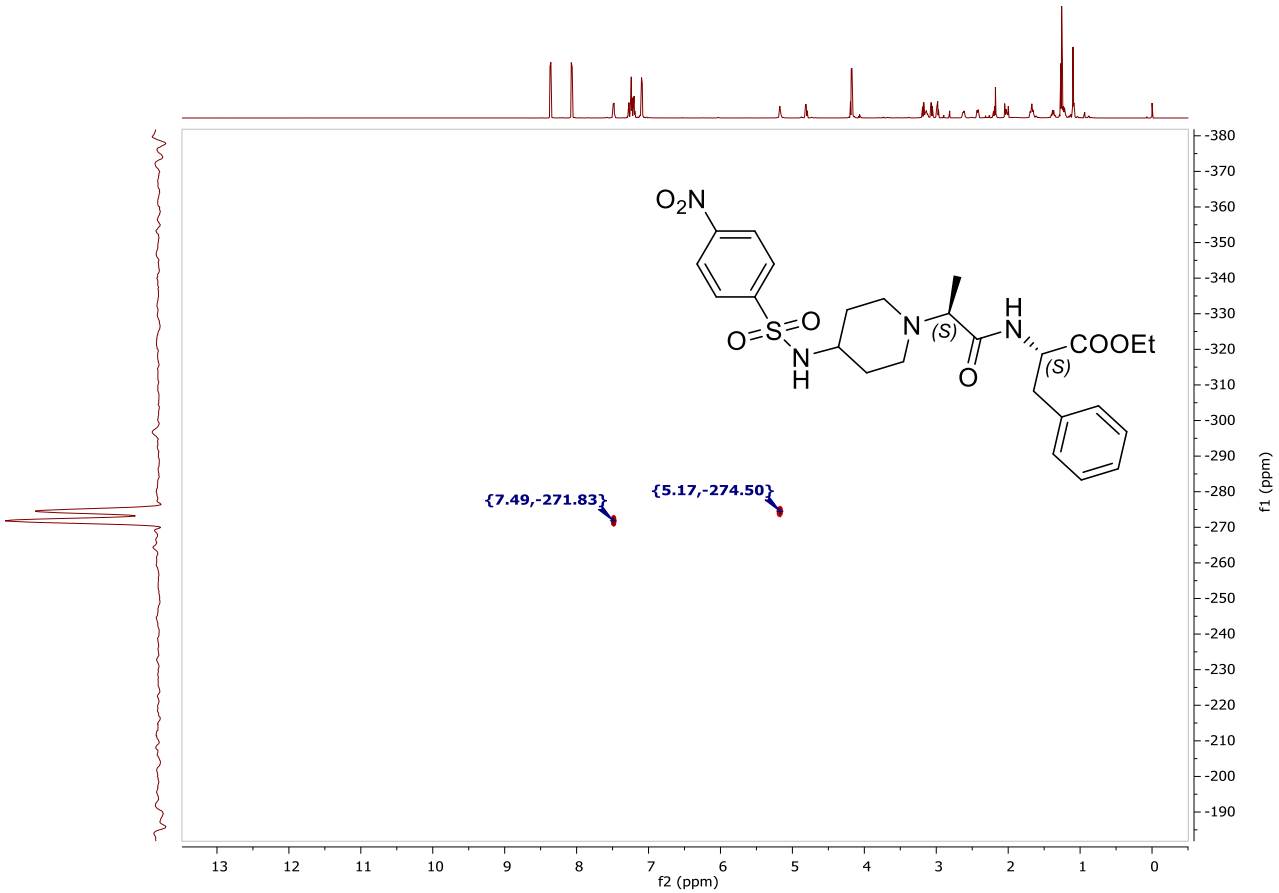


Figure S47. Ethyl *N*-[(2*S*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*S*,*S*)-9). ^{1}H-^{15}N HSQC spectrum (71 MHz, $CDCl_3$).

Mass Spectrum SmartFormula Report

Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_1217_1-C,7_01_10229.d	Acquisition Date	4/21/2023 1:56:42 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_1217	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
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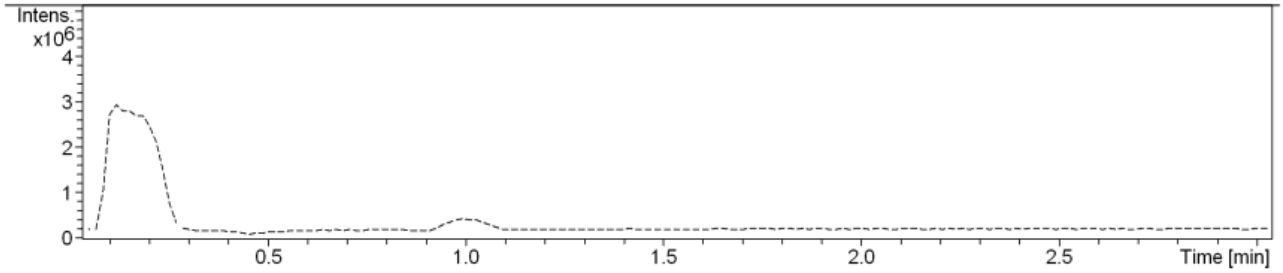
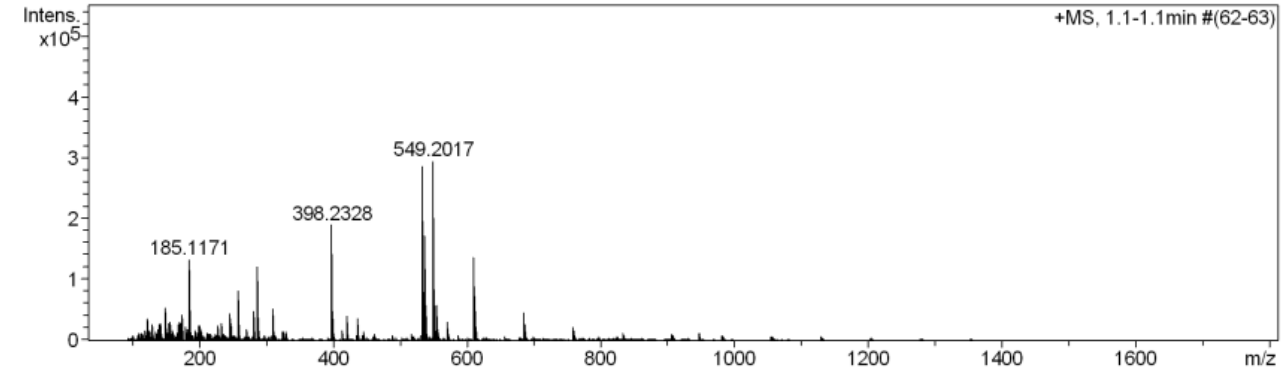
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
533.2068	1	C 24 H 37 O 11 S	49.10	533.2051	-3.1	-3.4	15.3	6.5	even	ok
	2	C 25 H 33 N 4 O 7 S	100.00	533.2064	-0.6	-0.9	17.9	11.5	even	ok
	3	C 20 H 37 O 16	63.13	533.2076	1.6	2.2	27.1	2.5	even	ok
	4	C 33 H 29 N 2 O 5	51.17	533.2071	0.6	1.5	44.9	20.5	even	ok

Figure S48. Ethyl *N*-[(2*S*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*S*,*S*)-9). HRMS (ESI-TOF).

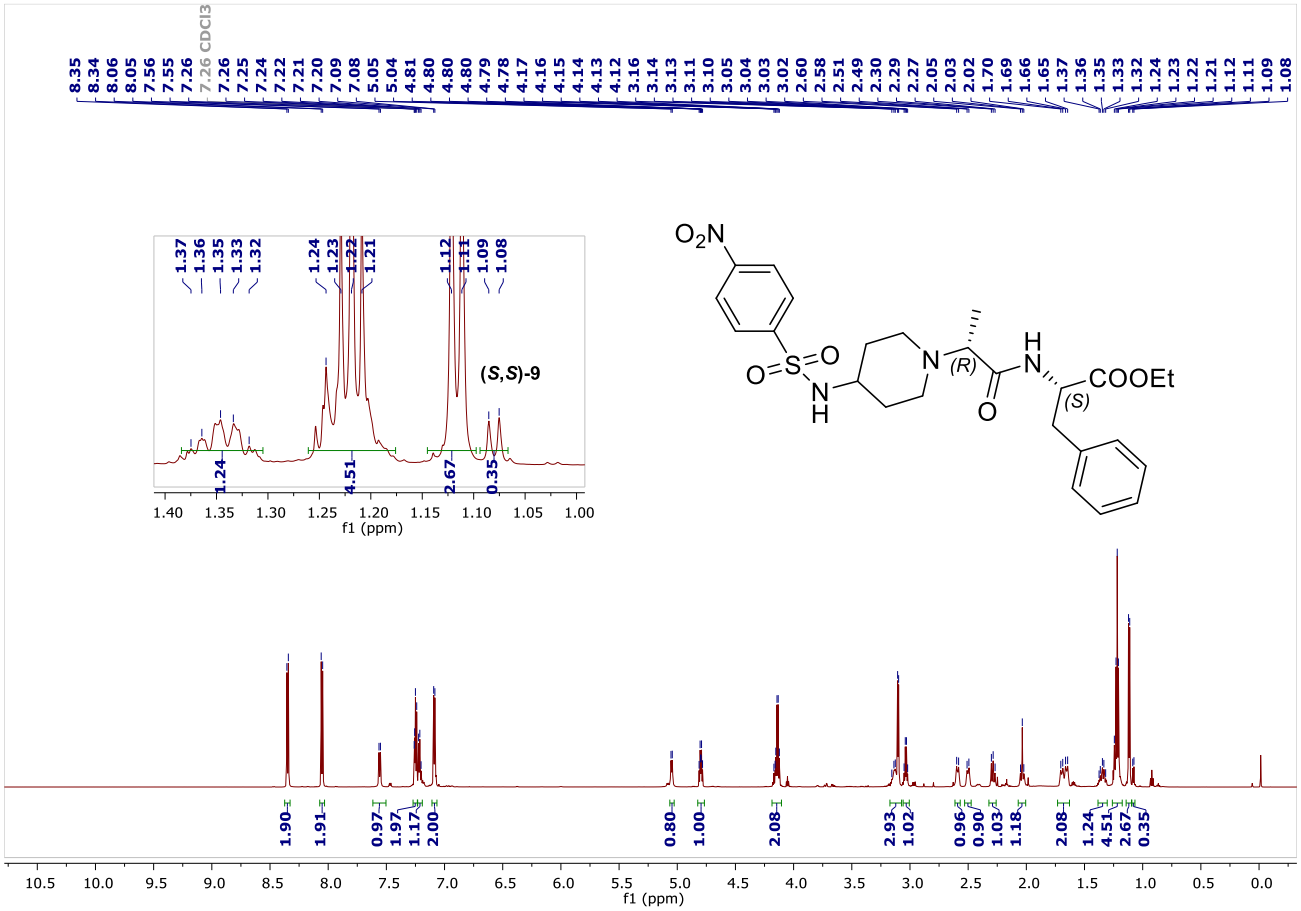


Figure S49. Ethyl *N*-[(2*R*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*R*,*S*)-9). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

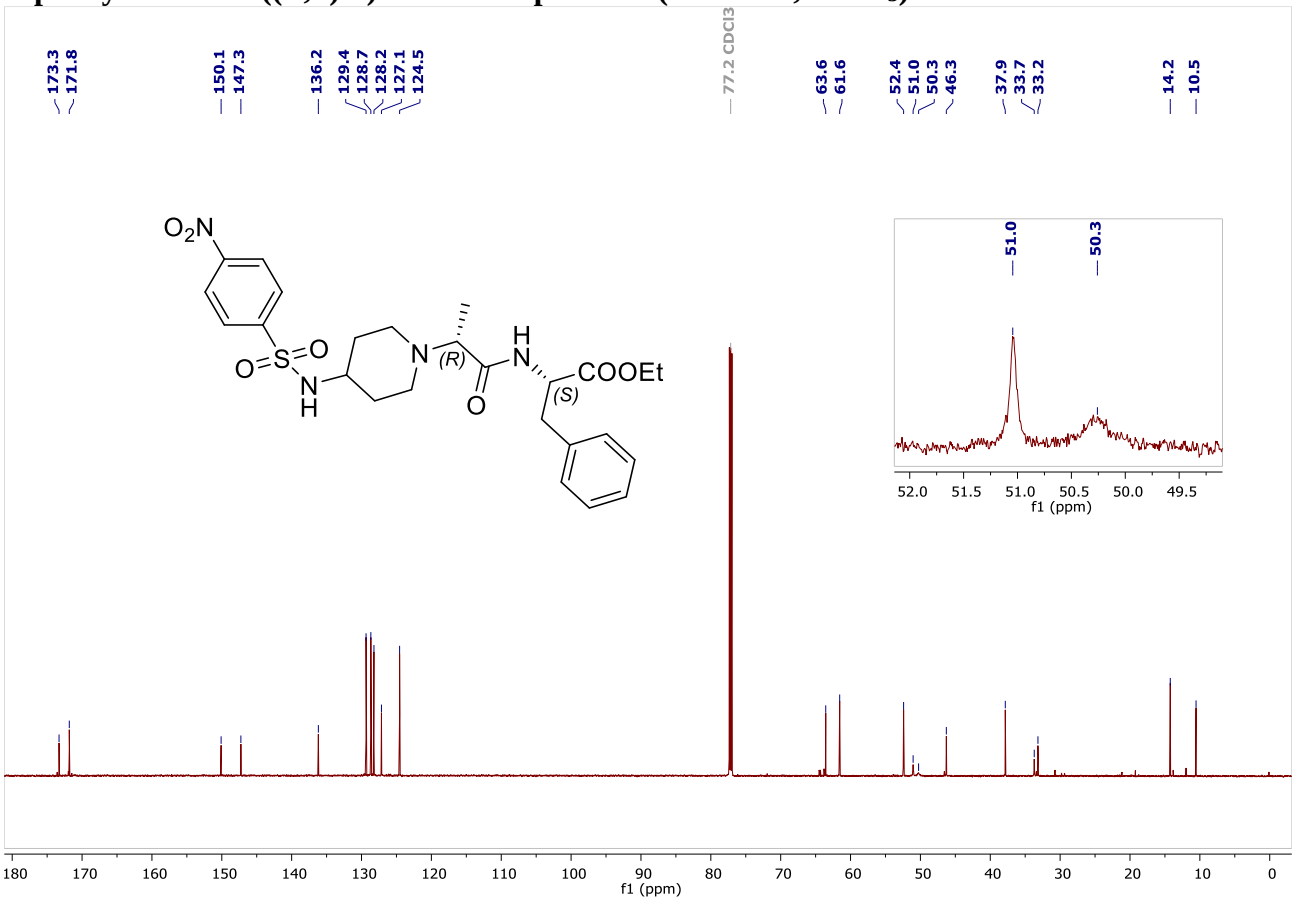


Figure S50. Ethyl *N*-[(2*R*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*R*,*S*)-9). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

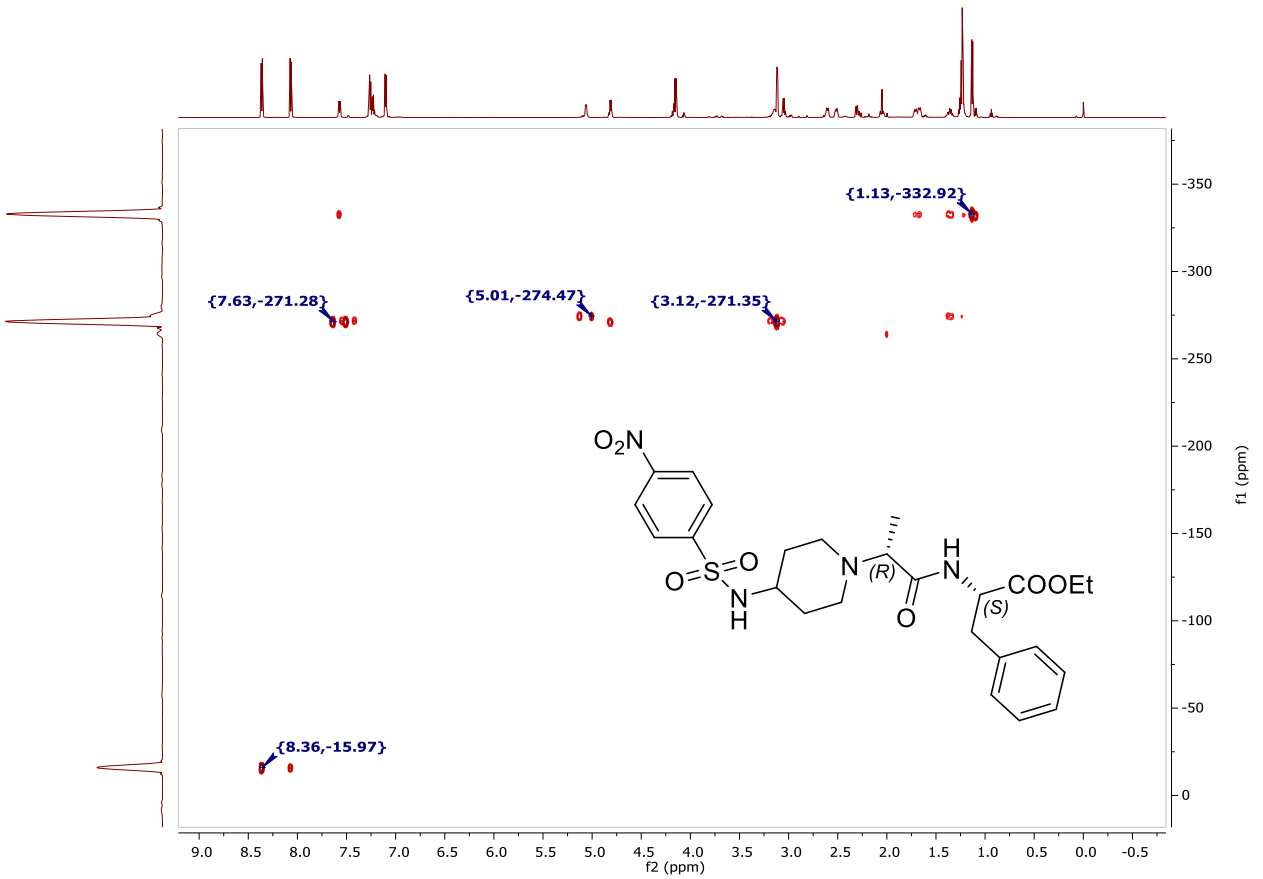


Figure S51. Ethyl *N*-[(2*R*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*R*,*S*)-9). ^{1}H-^{15}N HMBC spectrum (71 MHz, $CDCl_3$).

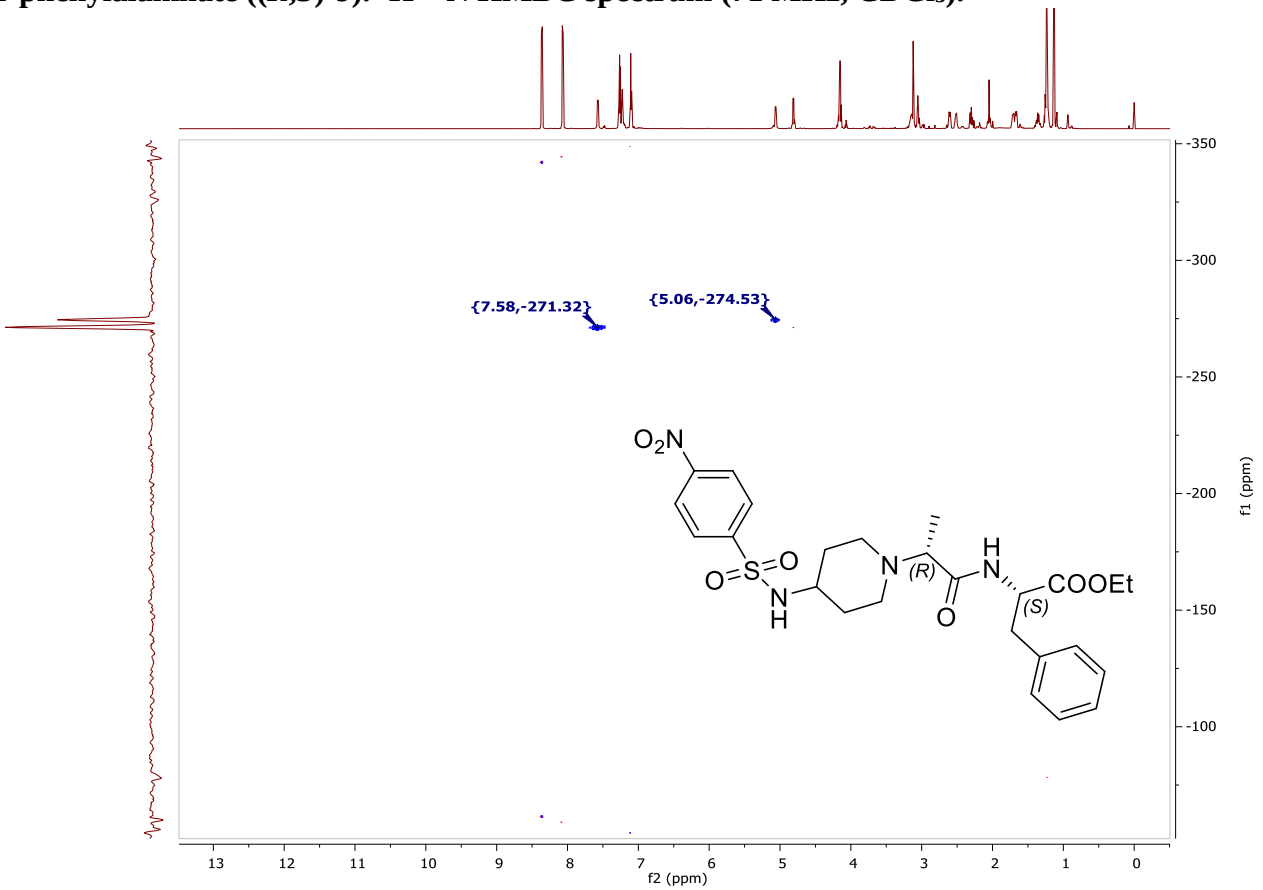


Figure S52. Ethyl *N*-[(2*R*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*R*,*S*)-9). ^{1}H-^{15}N HSQC spectrum (71 MHz, $CDCl_3$).

Mass Spectrum SmartFormula Report

Analysis Info

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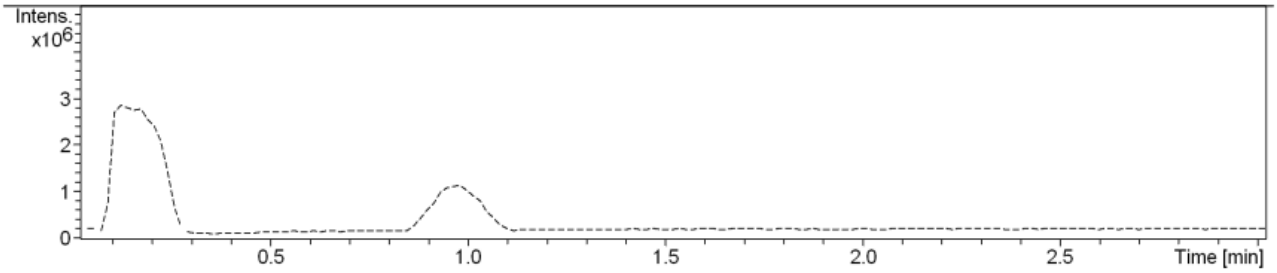
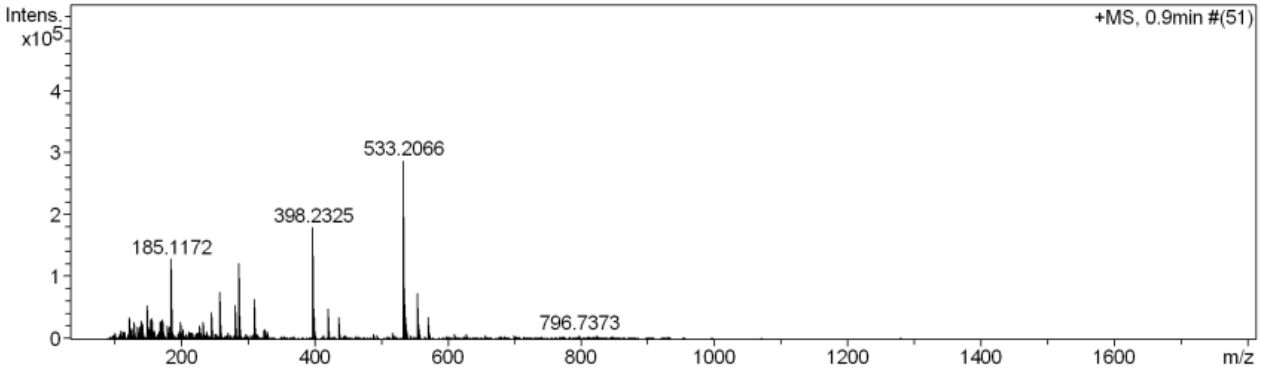
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_1218	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
533.2066	1	C 24 H 37 O 11 S	48.79	533.2051	-2.8	-3.1	17.8	6.5	even	ok
	2	C 25 H 33 N 4 O 7 S	100.00	533.2064	-0.3	-0.6	18.0	11.5	even	ok
	3	C 20 H 37 O 16	50.43	533.2076	1.9	2.4	29.4	2.5	even	ok
	4	C 33 H 29 N 2 O 5	48.33	533.2071	0.9	1.7	41.4	20.5	even	ok

Figure S53. Ethyl *N*-[(2*R*)-2-{4-[(4-nitrobenzene-1-sulfonyl)amino]piperidin-1-yl}propanoyl]-*L*-phenylalaninate ((*R*,*S*)-9). HRMS (ESI-TOF).

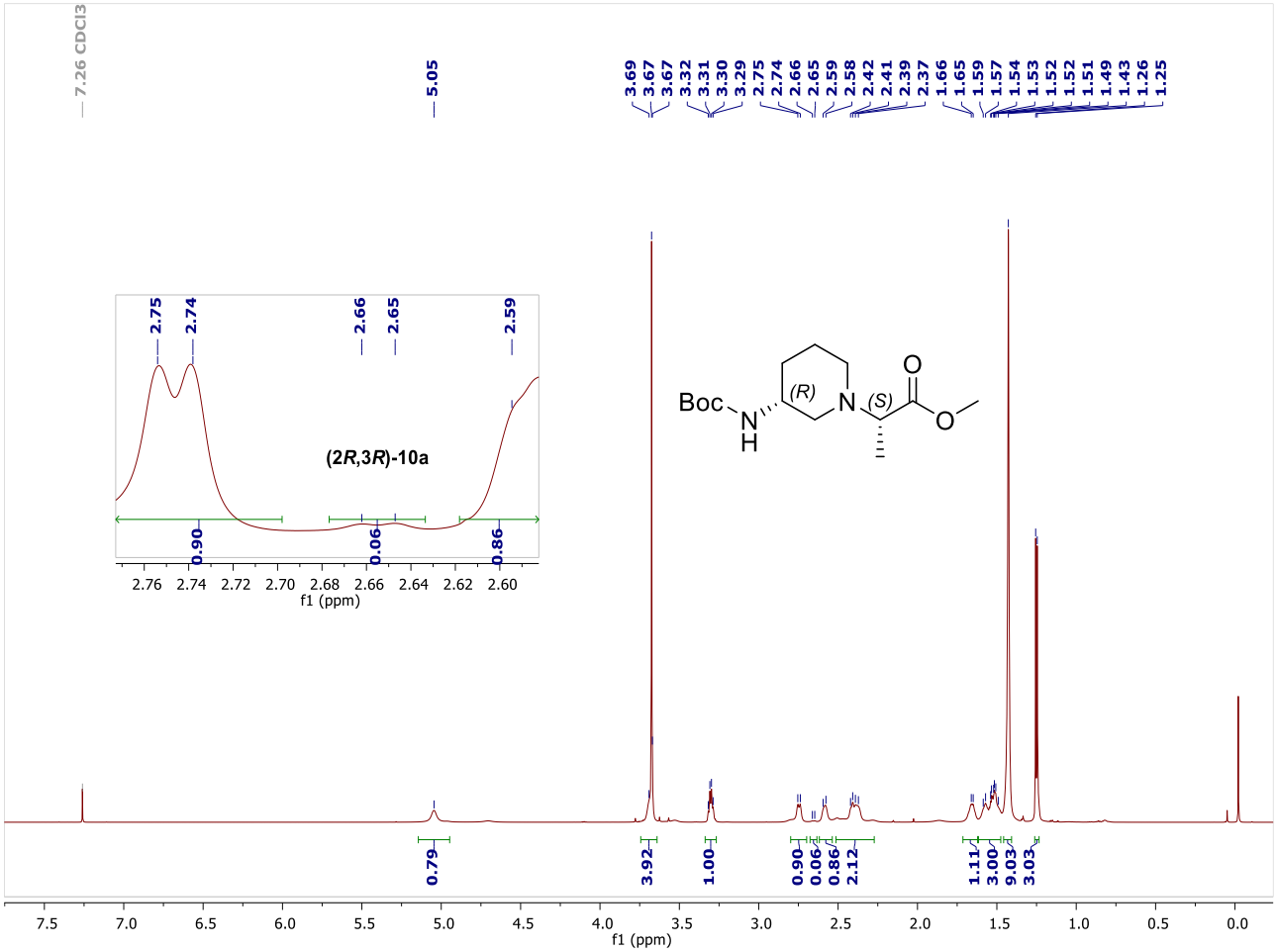


Figure S54. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*R*)-10a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

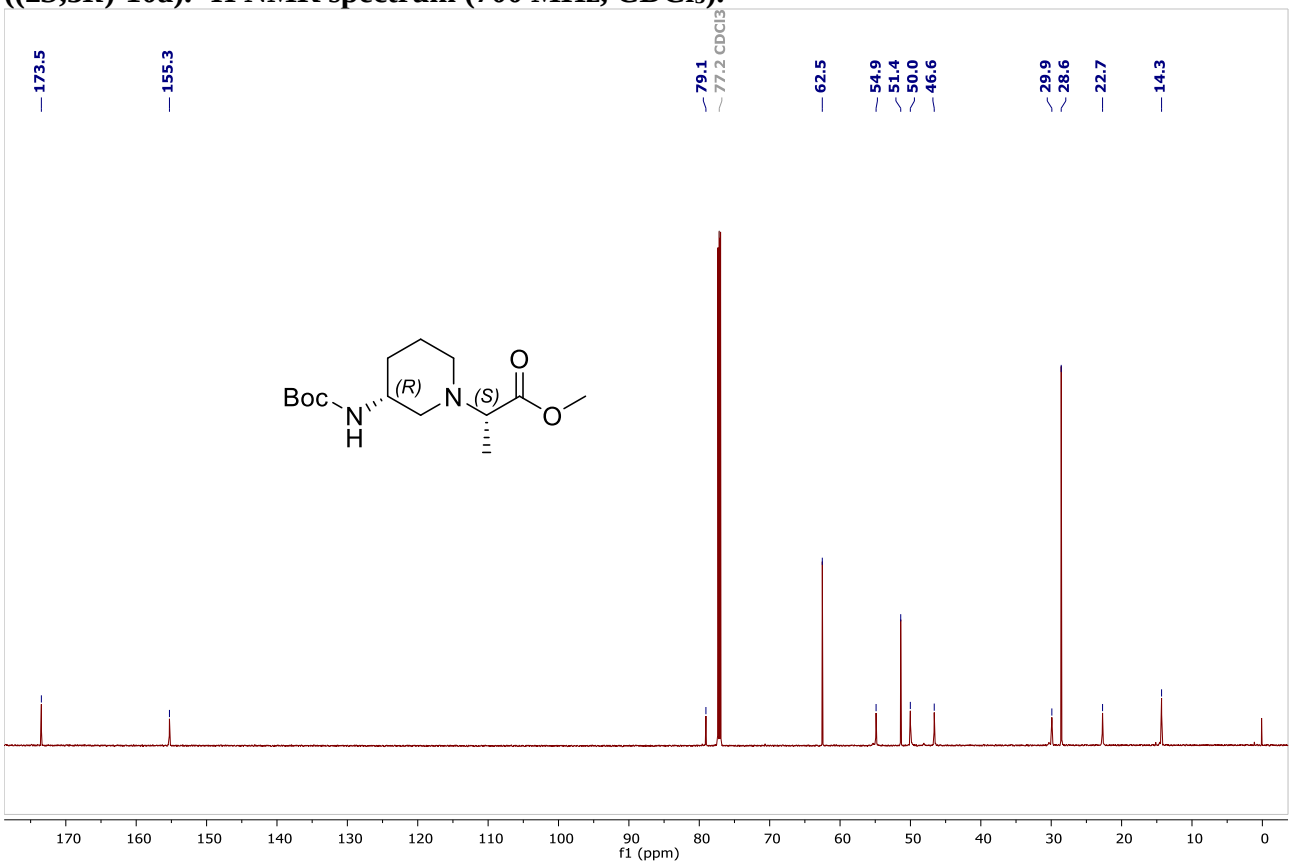


Figure S55. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*R*)-10a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

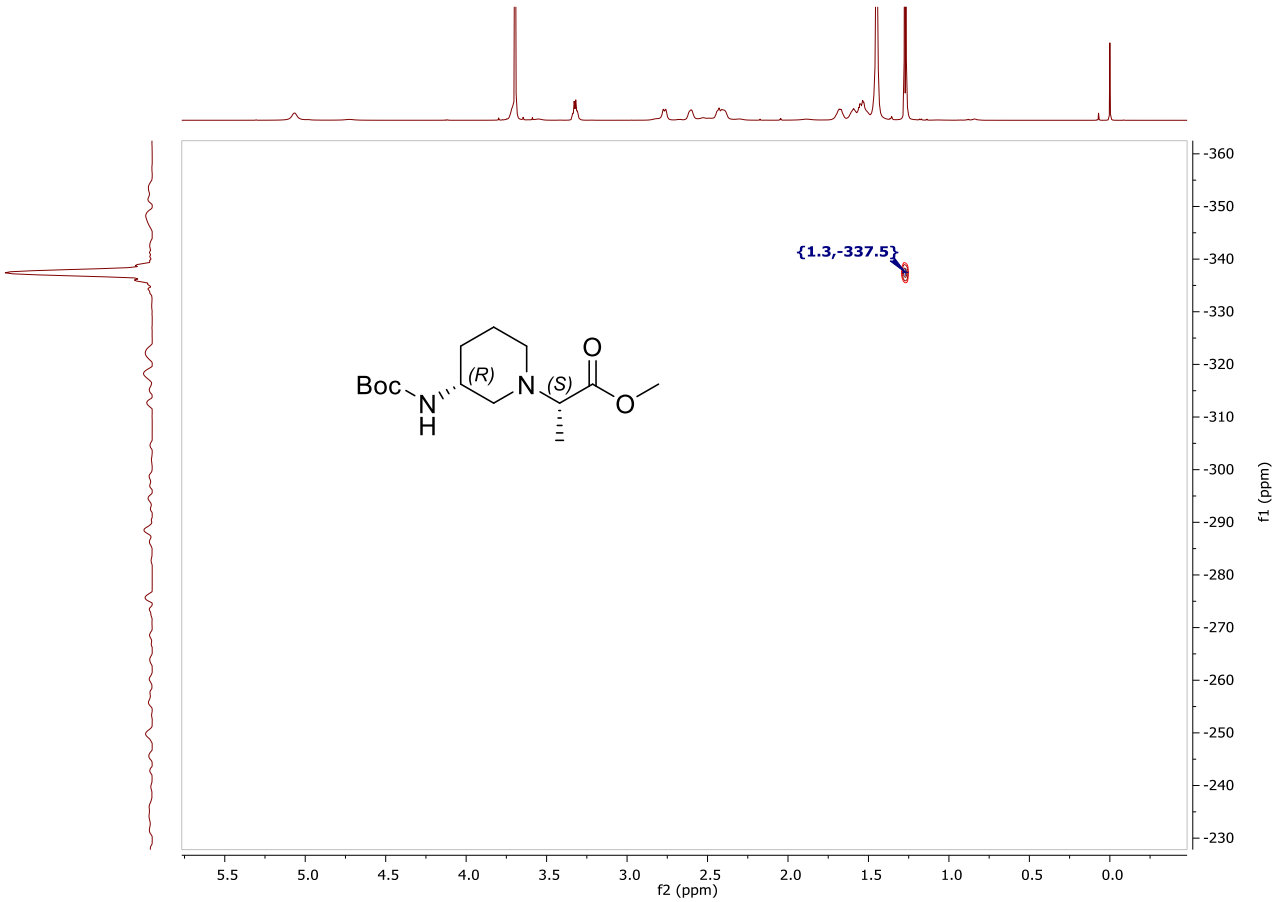


Figure S56. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*R*)-10a). ^{1}H-^{15}N HMBC spectrum (71 MHz, $CDCl_3$).

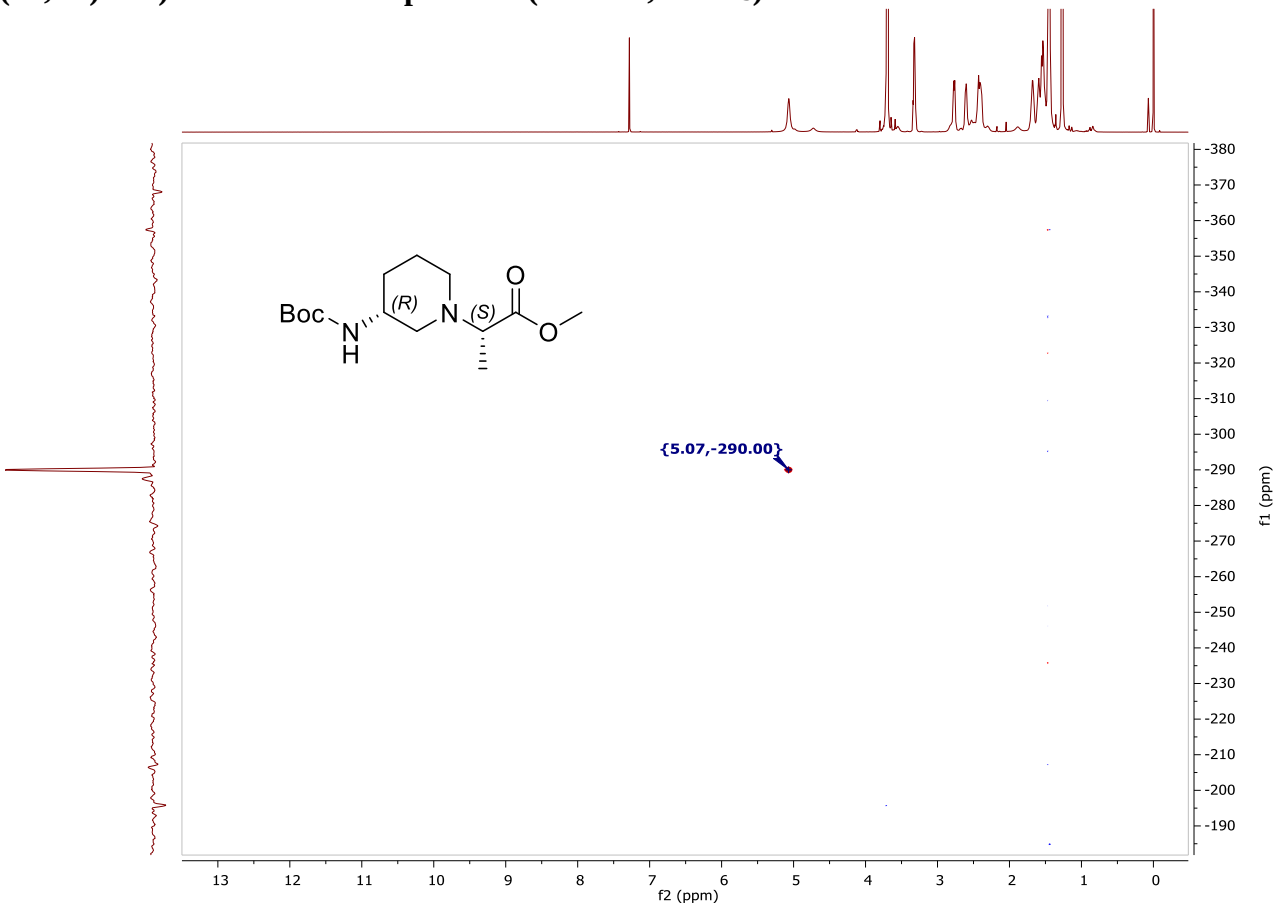


Figure S57. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*R*)-10a). ^{1}H-^{15}N HSQC spectrum (71 MHz, $CDCl_3$).

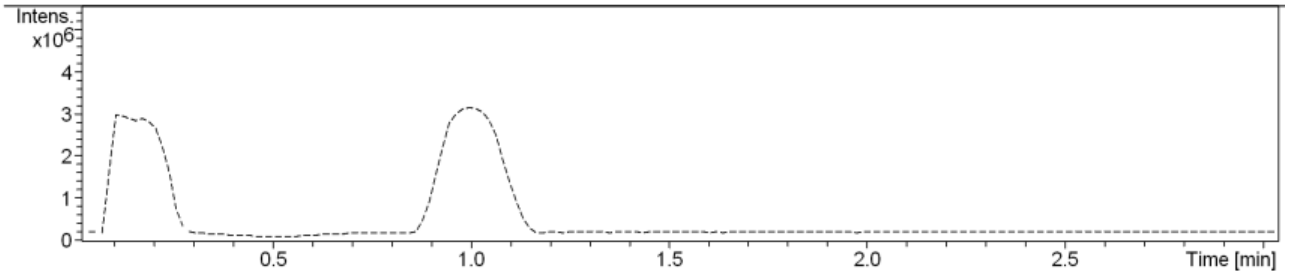
Mass Spectrum SmartFormula Report

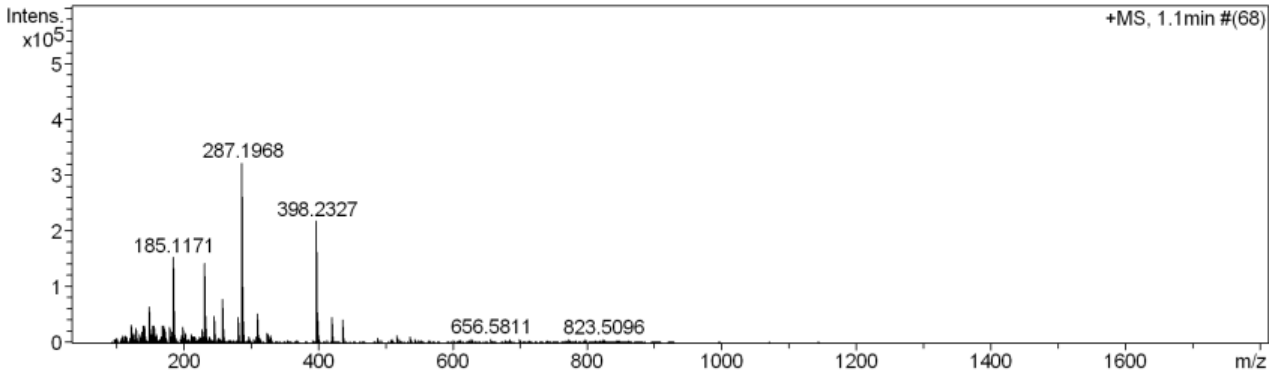
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_367_1-C,8_01_10230.d	Acquisition Date	4/21/2023 2:01:08 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_367	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
287.1968	1	C 14 H 27 N 2 O 4	100.00	287.1965	-0.9	-0.7	13.3	2.5	even	ok

Figure S58. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*R*)-10a). HRMS (ESI-TOF).

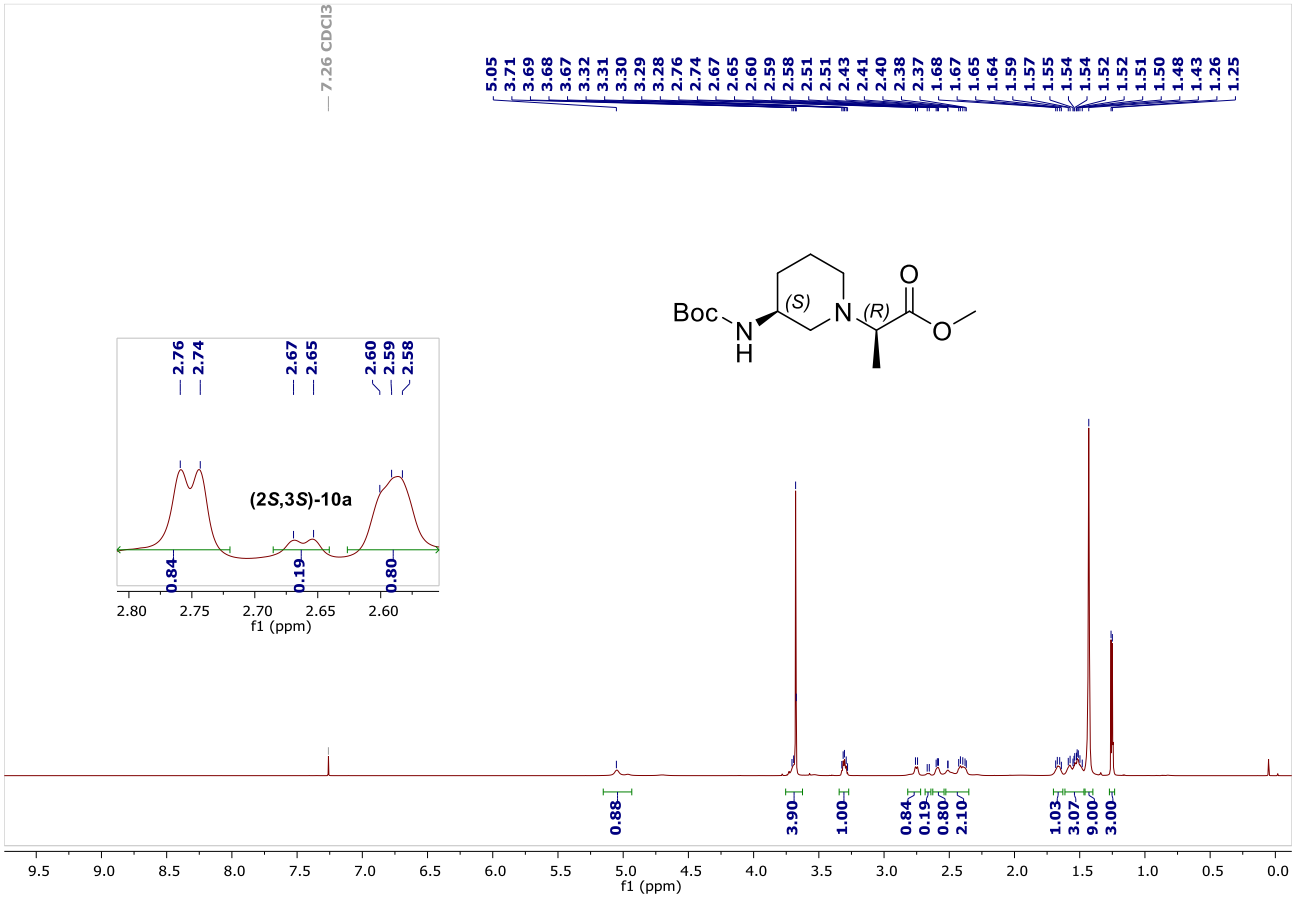


Figure S59. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*R*,3*S*)-10a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

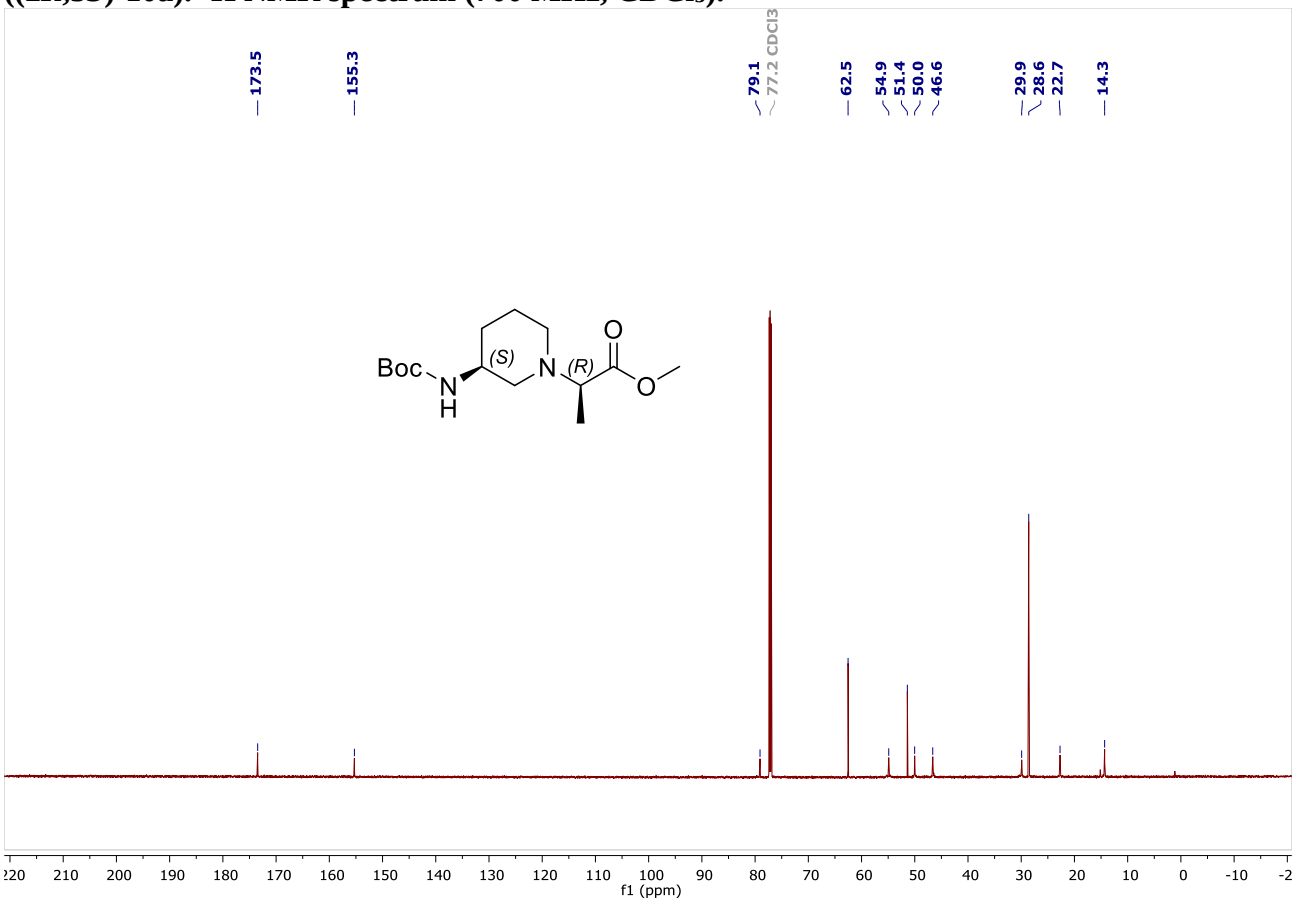


Figure S60. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*R*,3*S*)-10a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

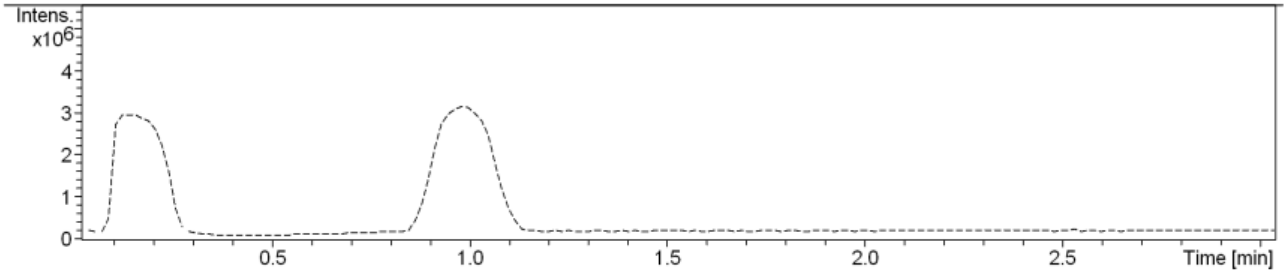
Mass Spectrum SmartFormula Report

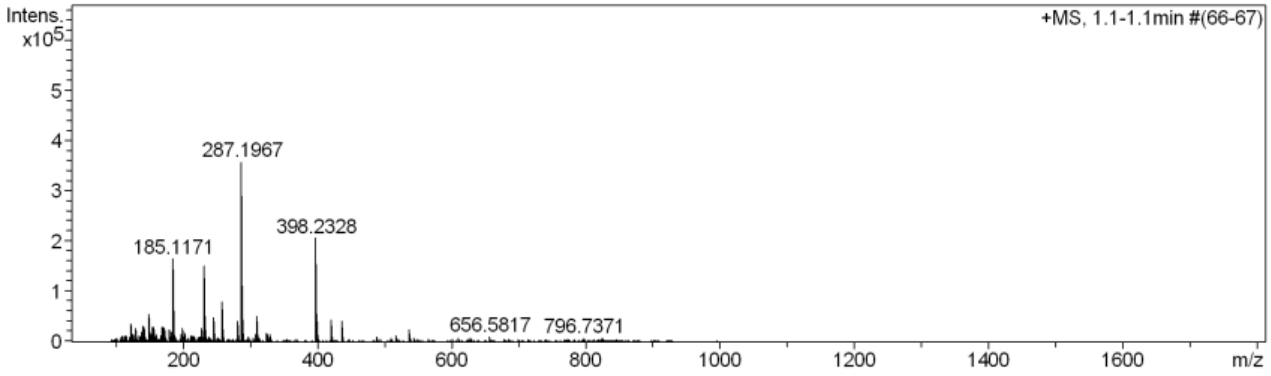
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_462_1-D,3_01_10233.d	Acquisition Date	4/21/2023 2:14:25 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_462	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
287.1967	1	C 14 H 27 N 2 O 4	100.00	287.1965	-0.6	-0.2	1.0	2.5	even	ok

Figure S61. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*R*,3*S*)-10a). HRMS (ESI-TOF).

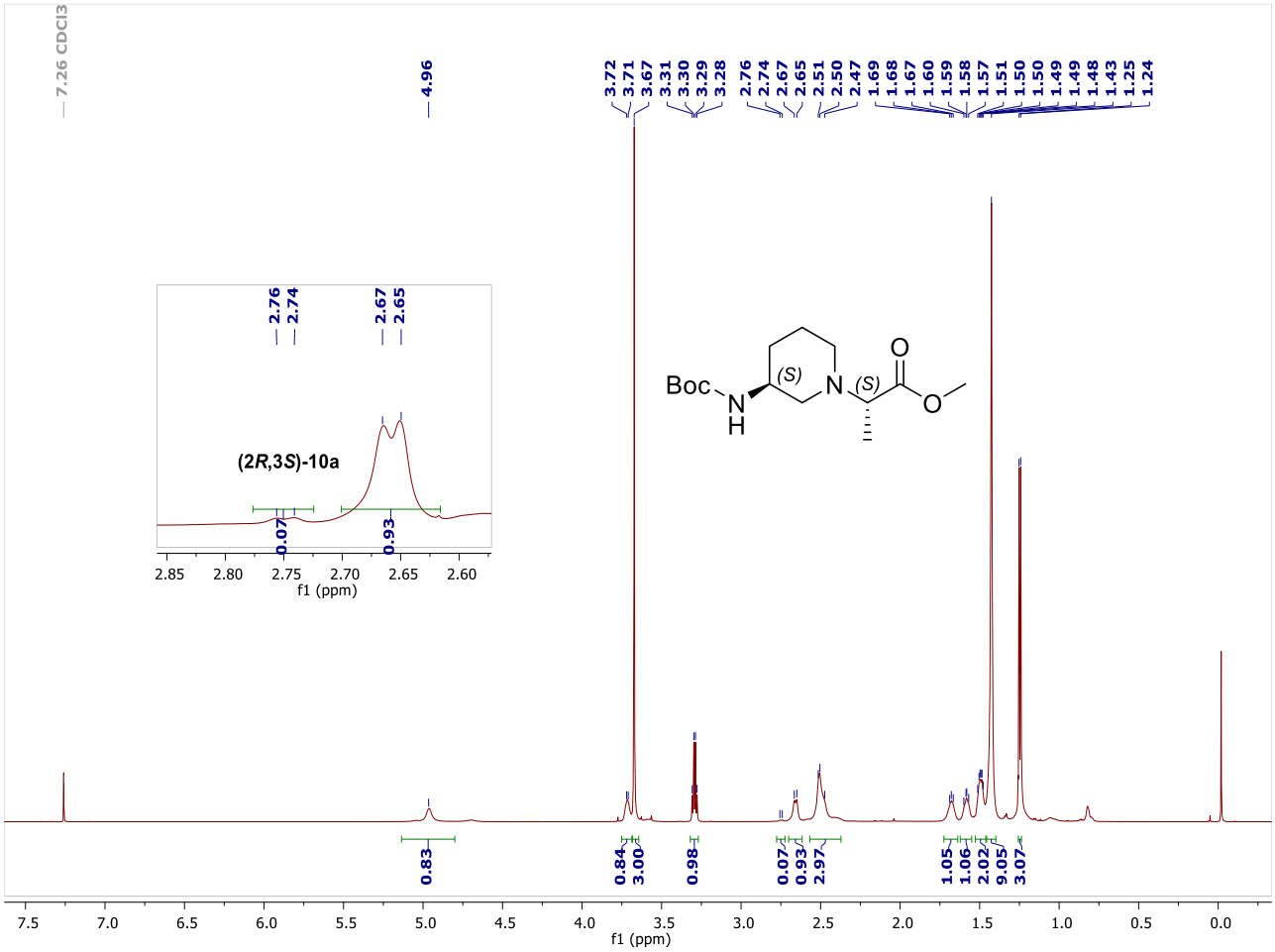


Figure S62. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*S*)-10a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

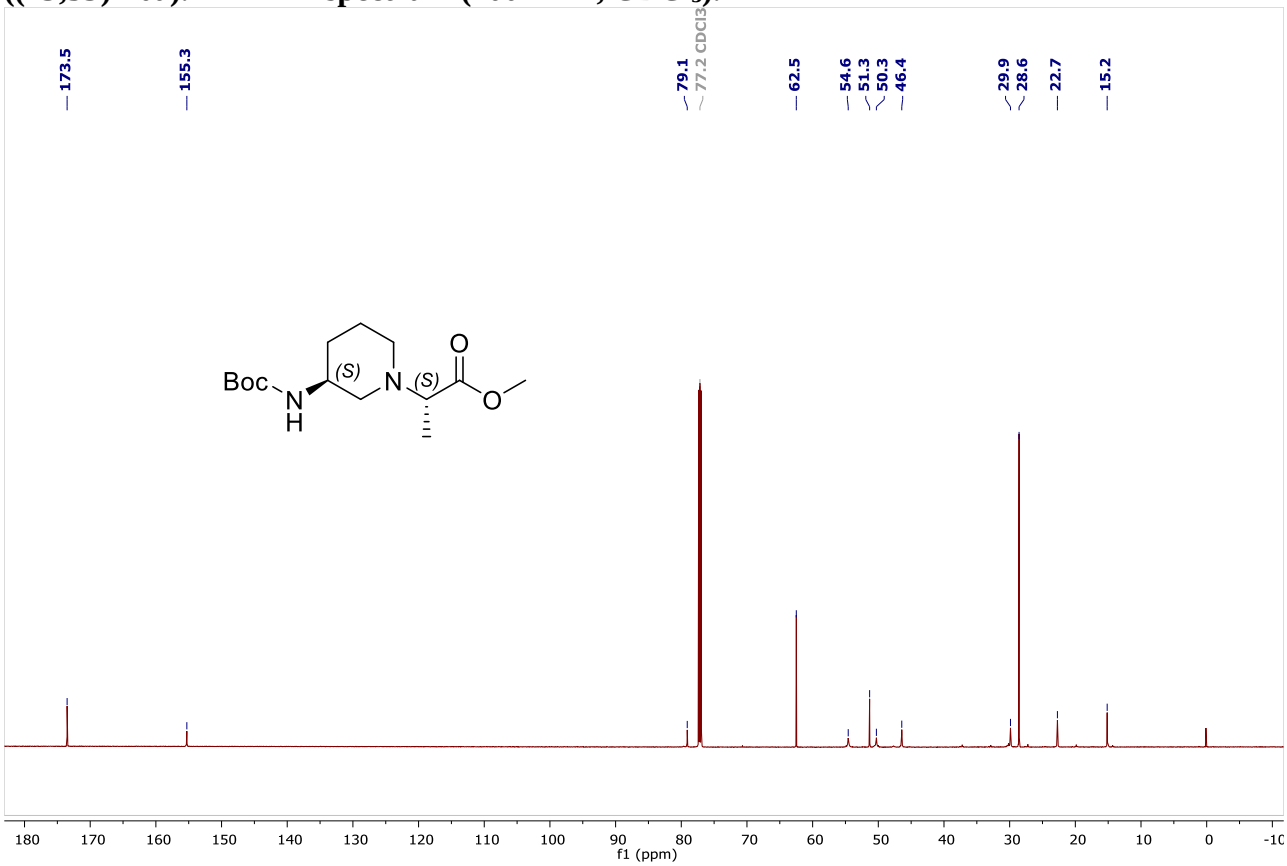


Figure S63. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*S*)-10a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

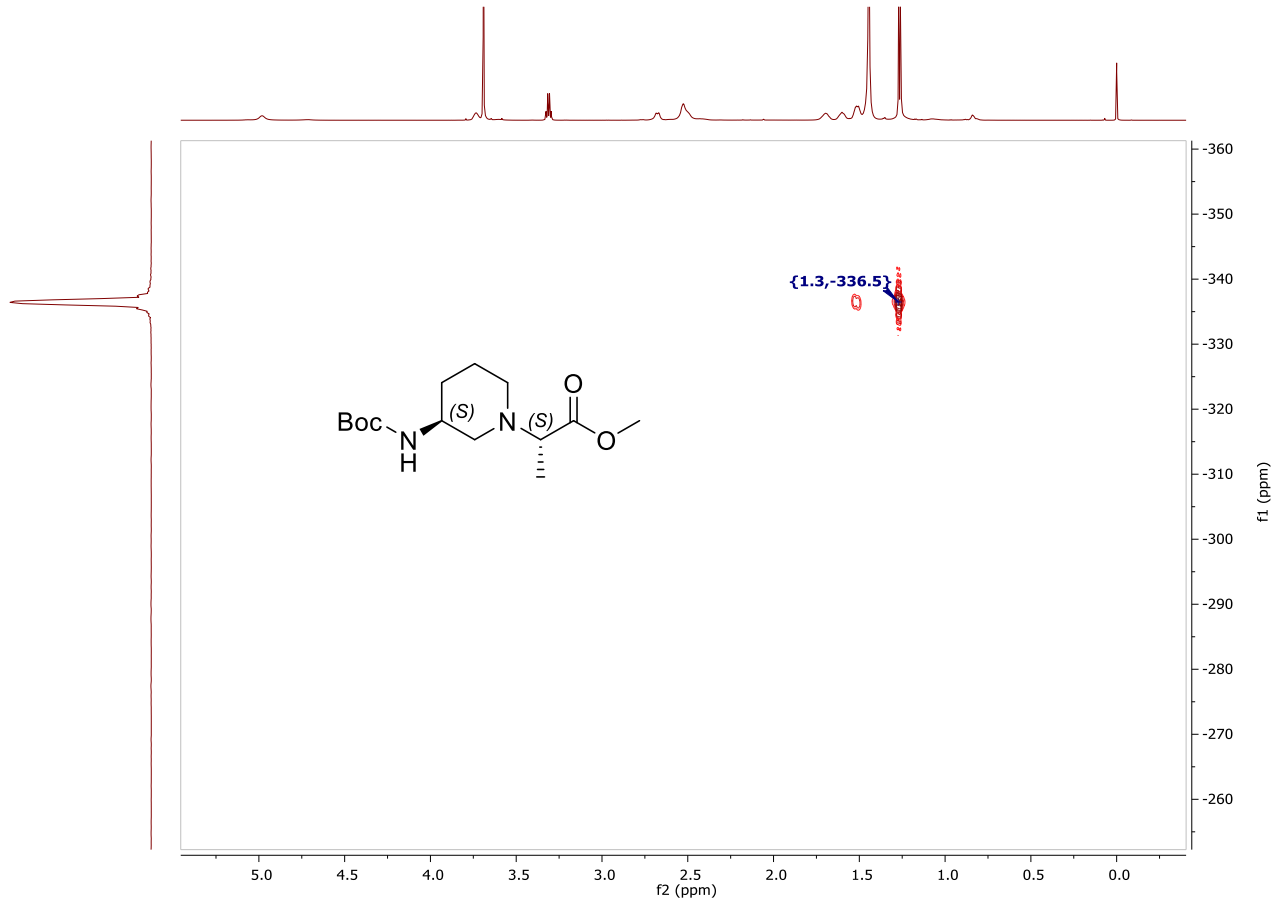


Figure S64. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*S*)-10a). ^{1}H-^{15}N HMBC spectrum (71 MHz, $CDCl_3$).

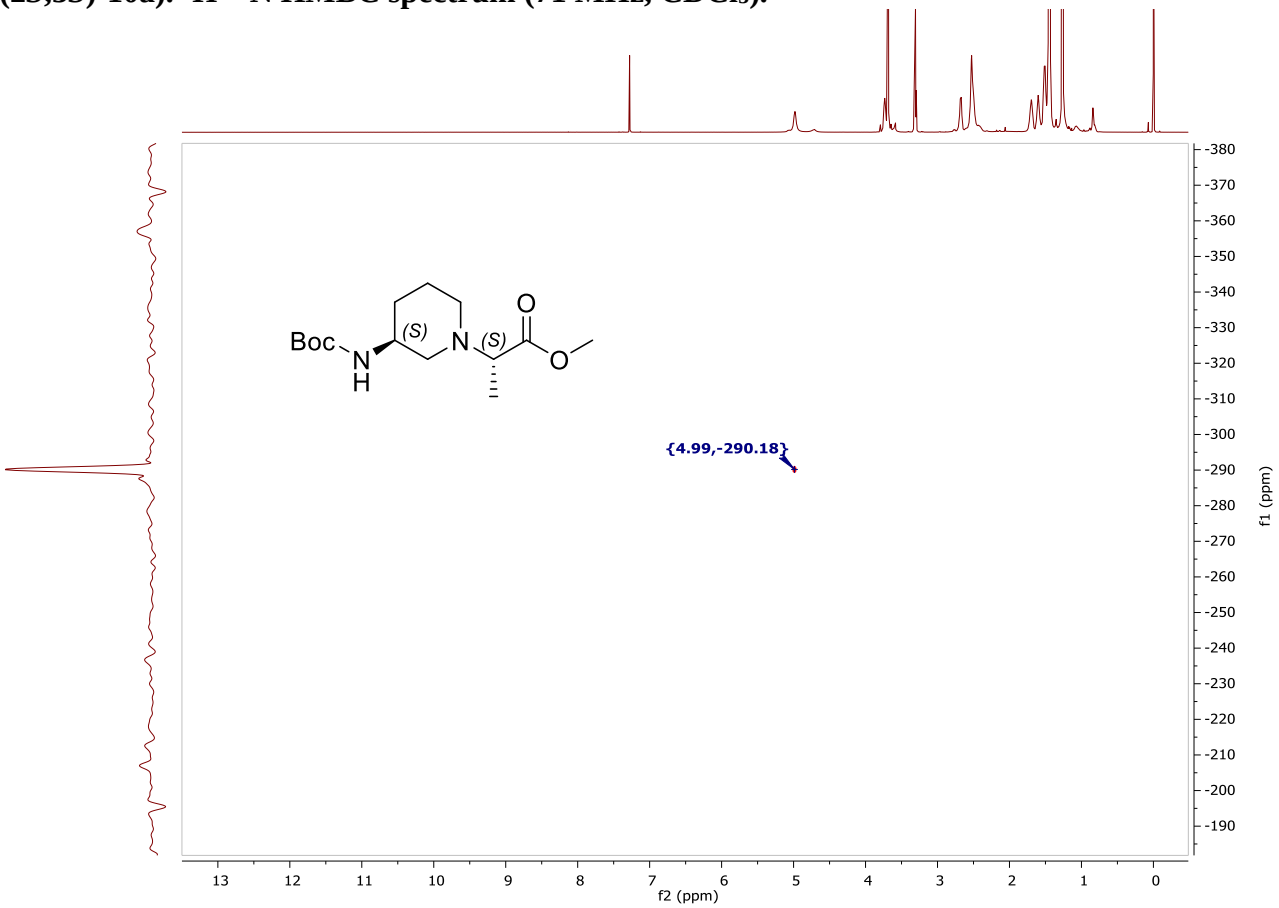


Figure S65. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*S*)-10a). ^{1}H-^{15}N HSQC spectrum (71 MHz, $CDCl_3$).

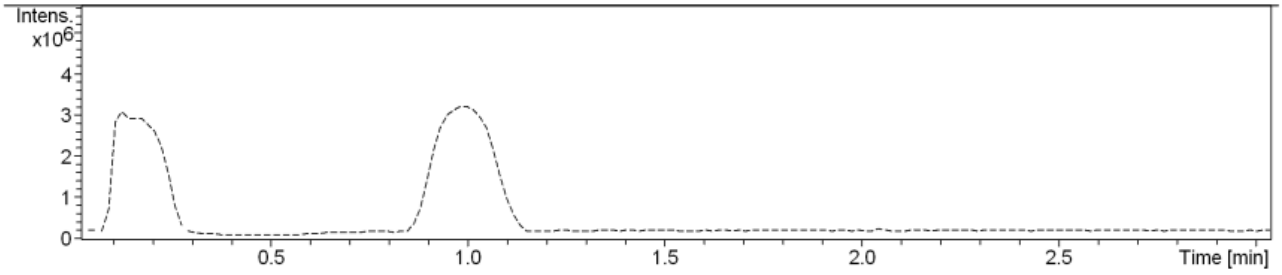
Mass Spectrum SmartFormula Report

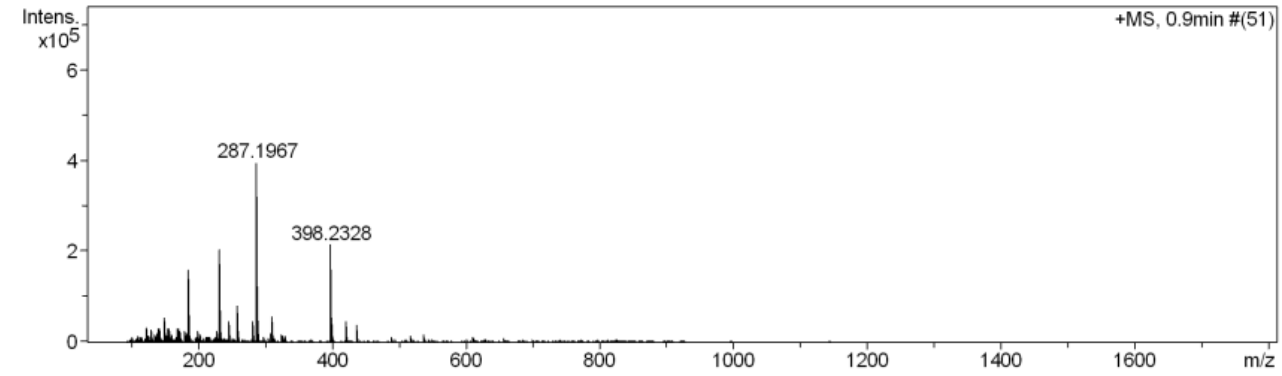
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_372_1-D,2_01_10232.d	Acquisition Date	4/21/2023 2:09:59 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_372	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
287.1967	1	C 14 H 27 N 2 O 4	100.00	287.1965	-0.6	-0.5	13.0	2.5	even	ok

Figure S66. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*S*,3*S*)-10a). HRMS (ESI-TOF).

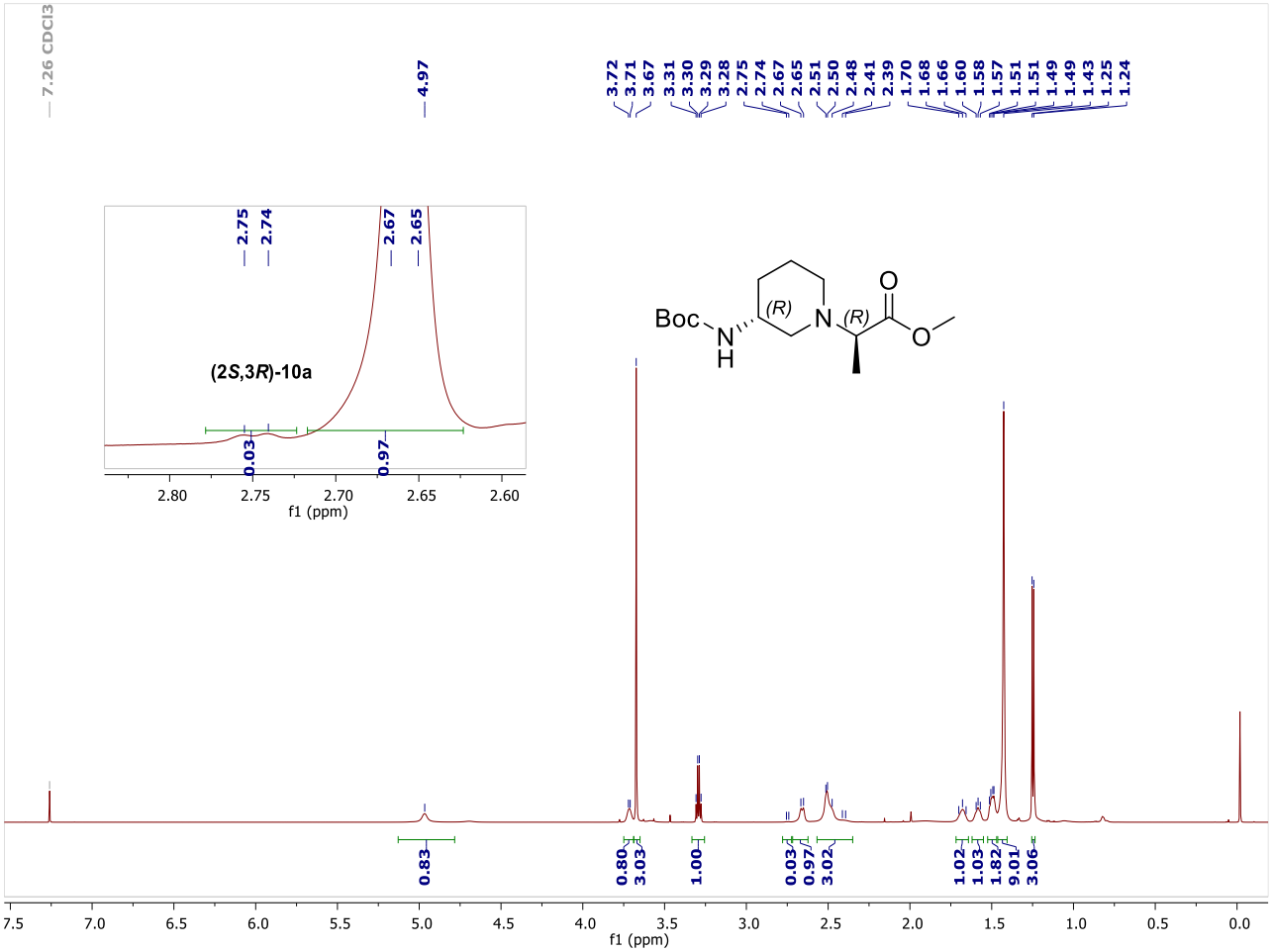


Figure S67. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*R*,3*R*)-10a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

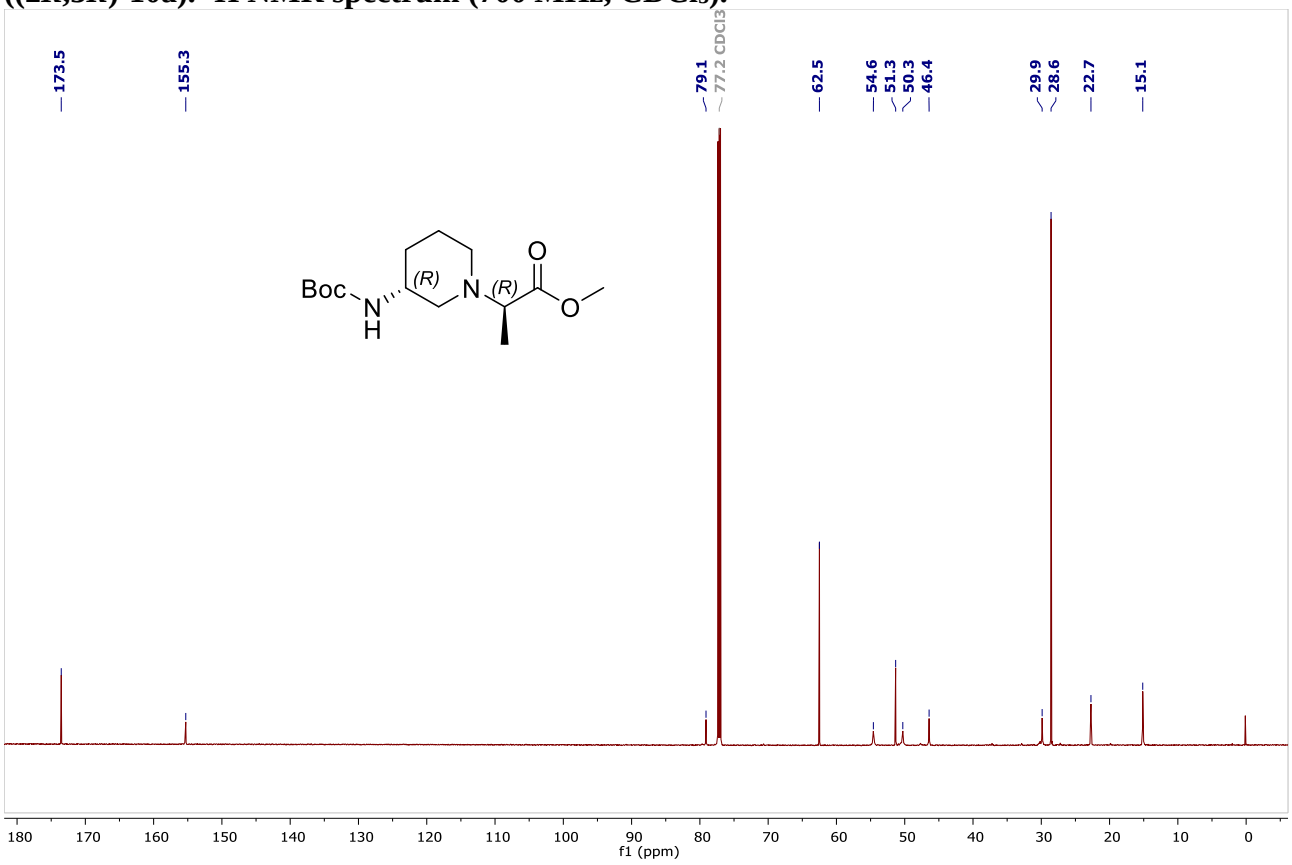


Figure S68. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*R*,3*R*)-10a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

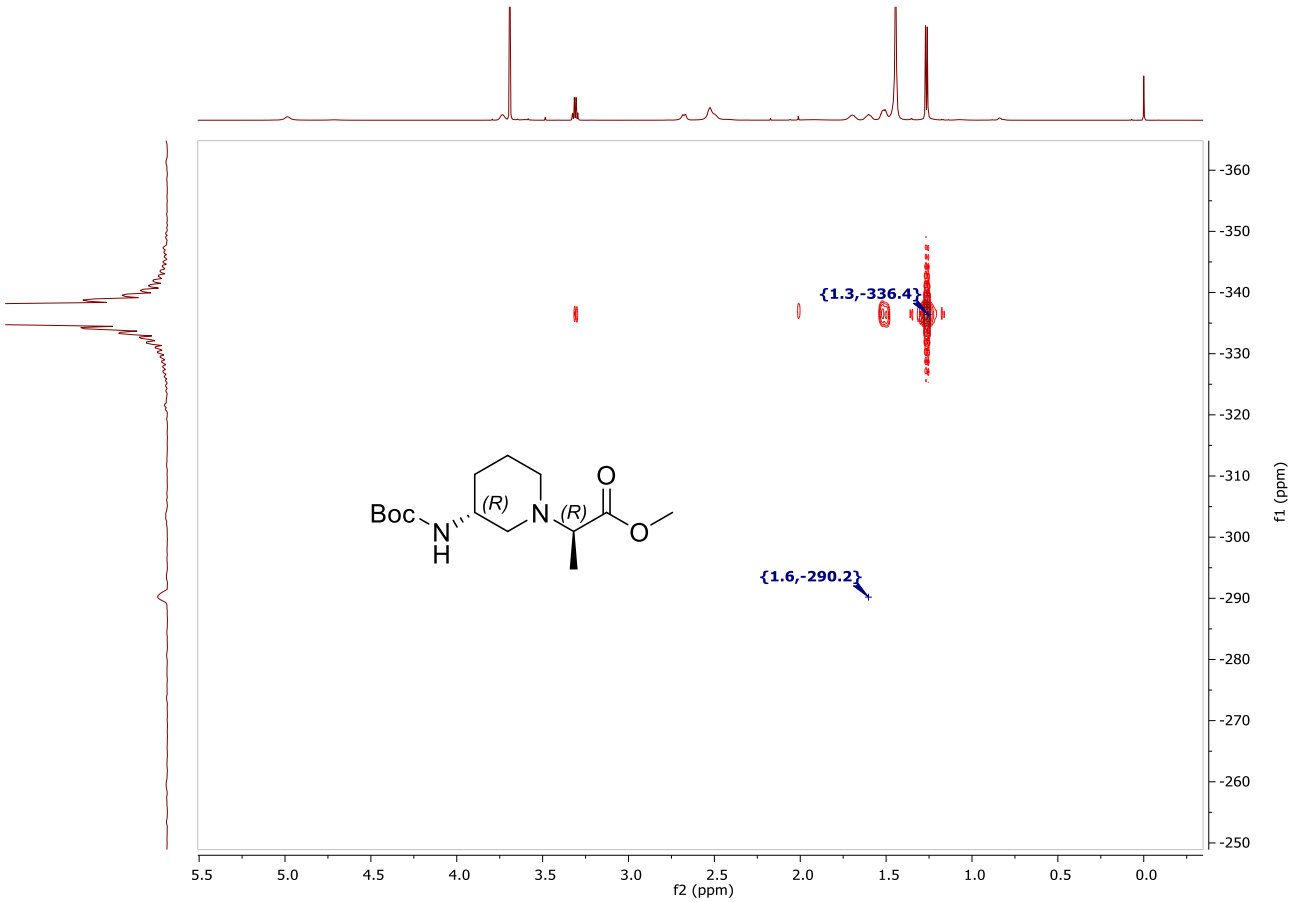


Figure S69. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*R*,3*R*)-10a). ^{1}H-^{15}N HMBC spectrum (71 MHz, $CDCl_3$).

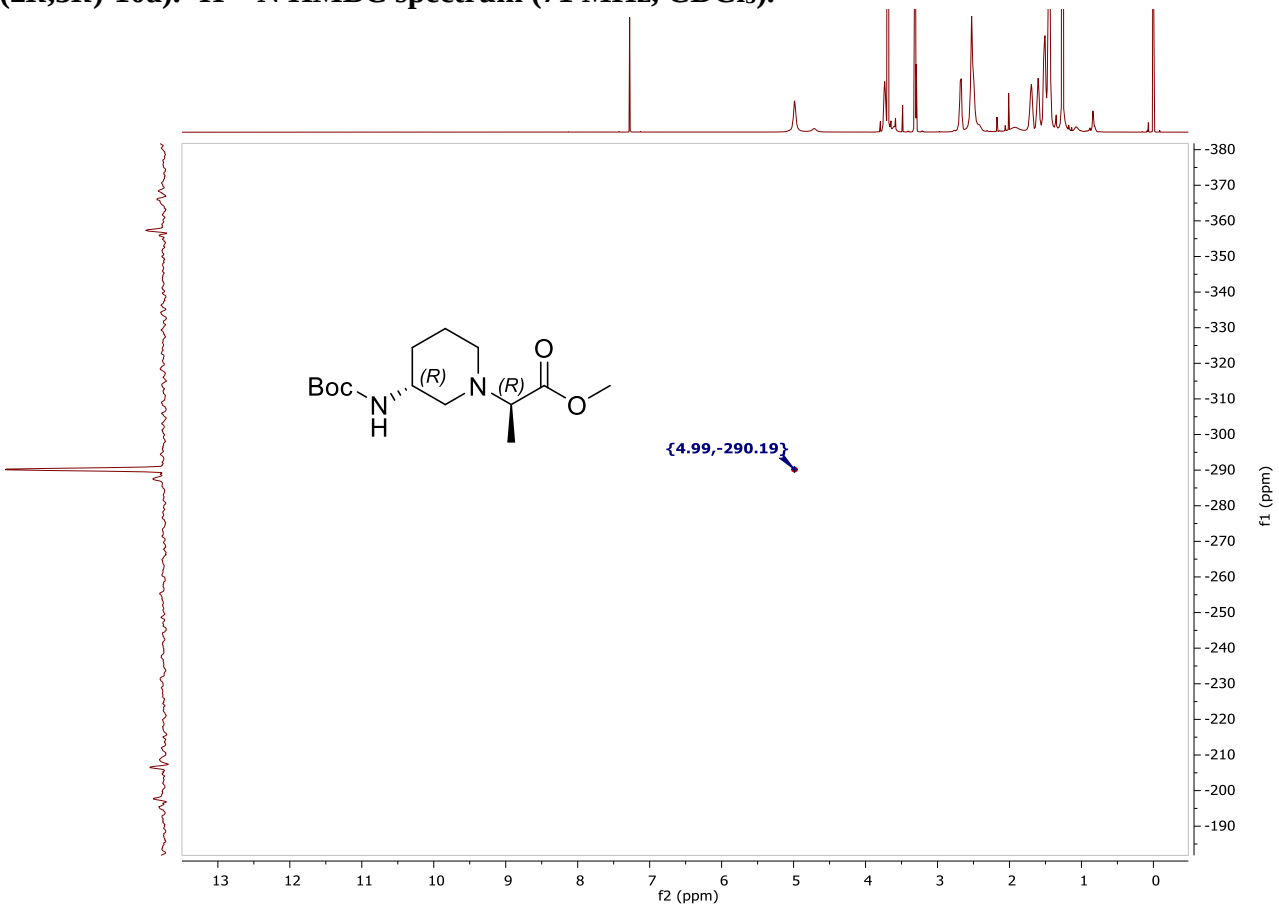


Figure S70. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*R*,3*R*)-10a). ^{1}H-^{15}N HSQC spectrum (71 MHz, $CDCl_3$).

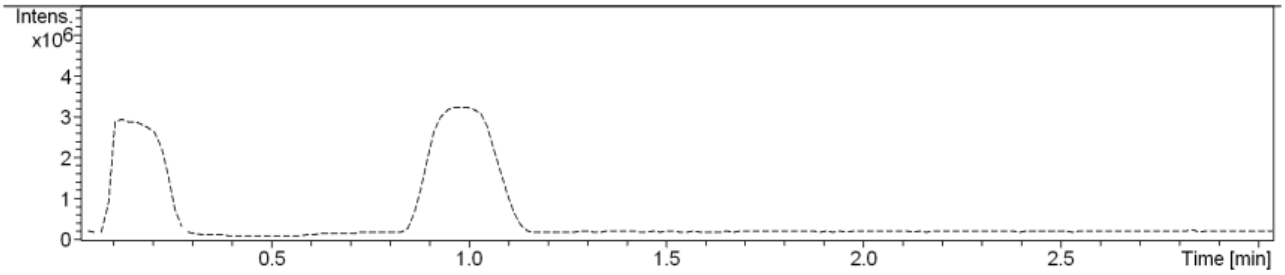
Mass Spectrum SmartFormula Report

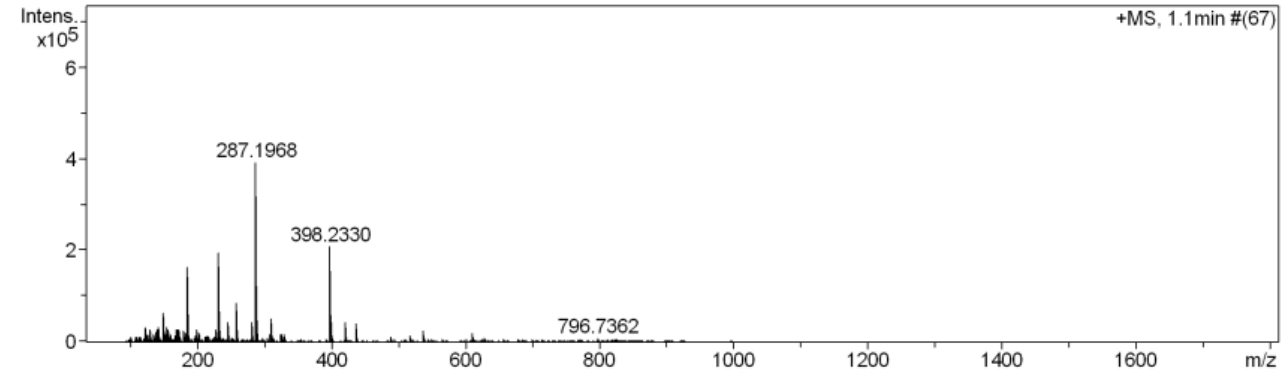
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_379_1-D,1_01_10231.d	Acquisition Date	4/21/2023 2:05:33 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_379	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
287.1968	1	C 14 H 27 N 2 O 4	100.00	287.1965	-1.0	-0.9	13.4	2.5	even	ok

Figure S71. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}propanoate ((2*R*,3*R*)-10a). HRMS (ESI-TOF).

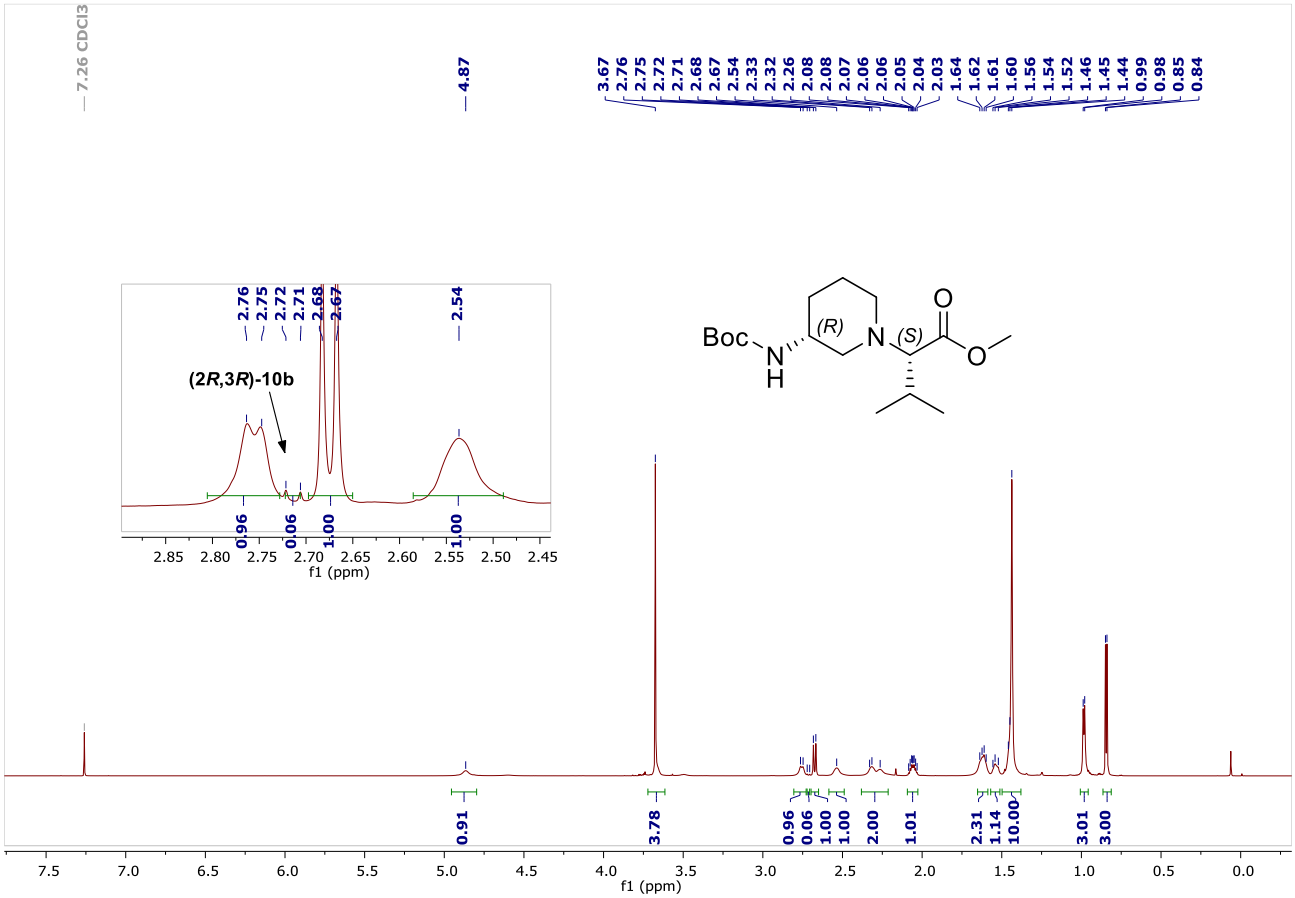


Figure S72. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*S*,3*R*)-10b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

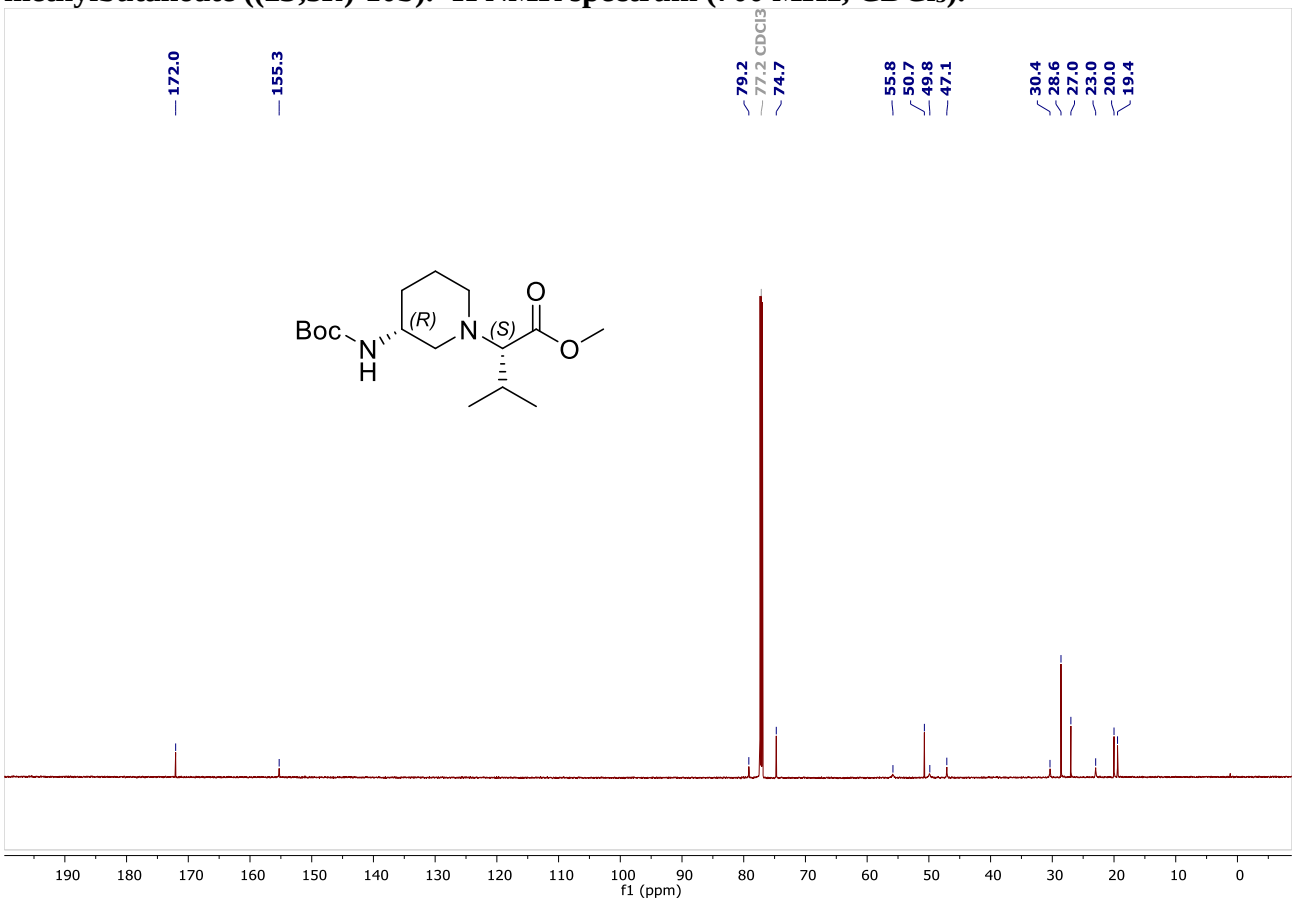


Figure S73. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*S*,3*R*)-10b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

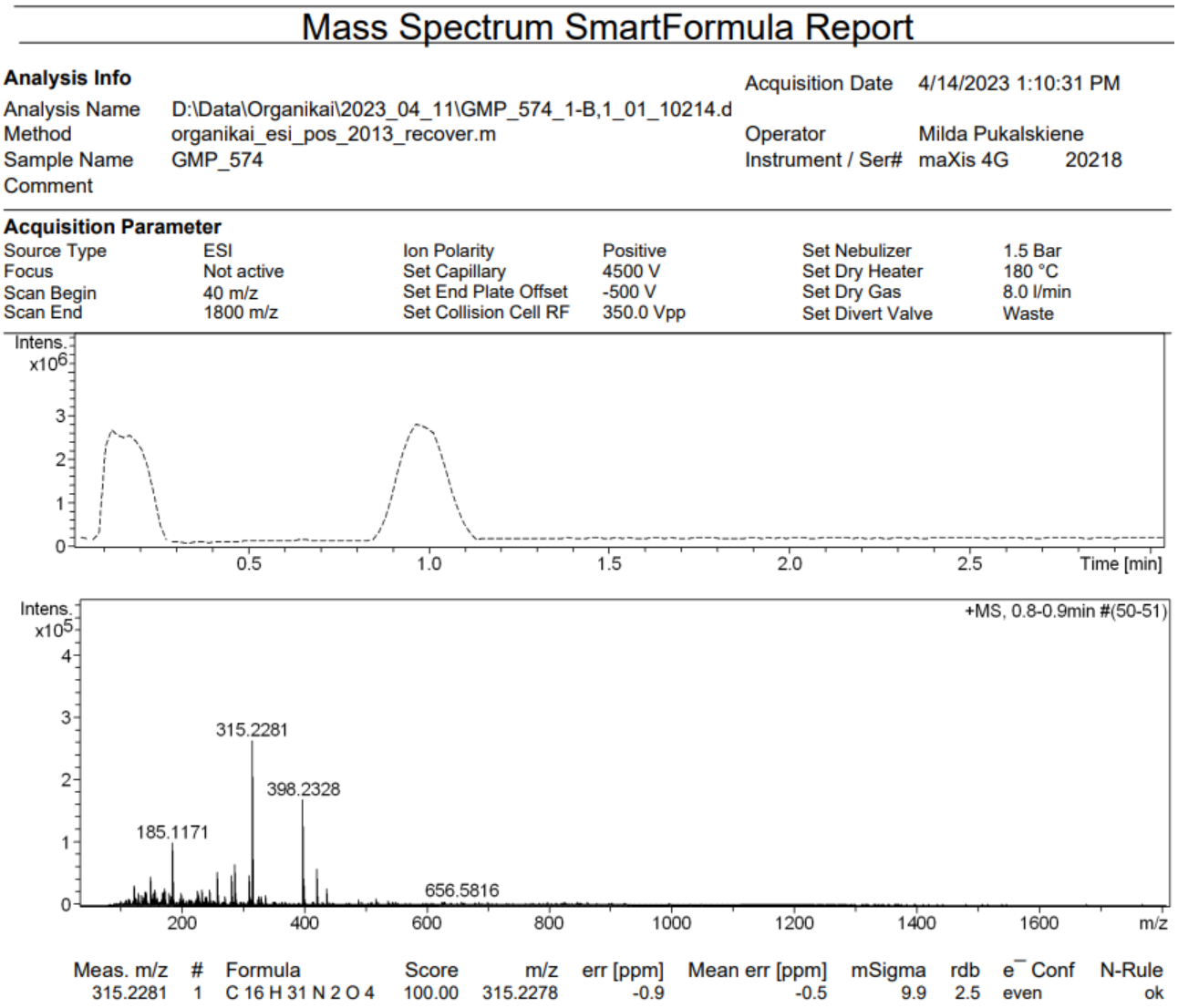


Figure S74. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*S*,3*R*)-10b). HRMS (ESI-TOF).

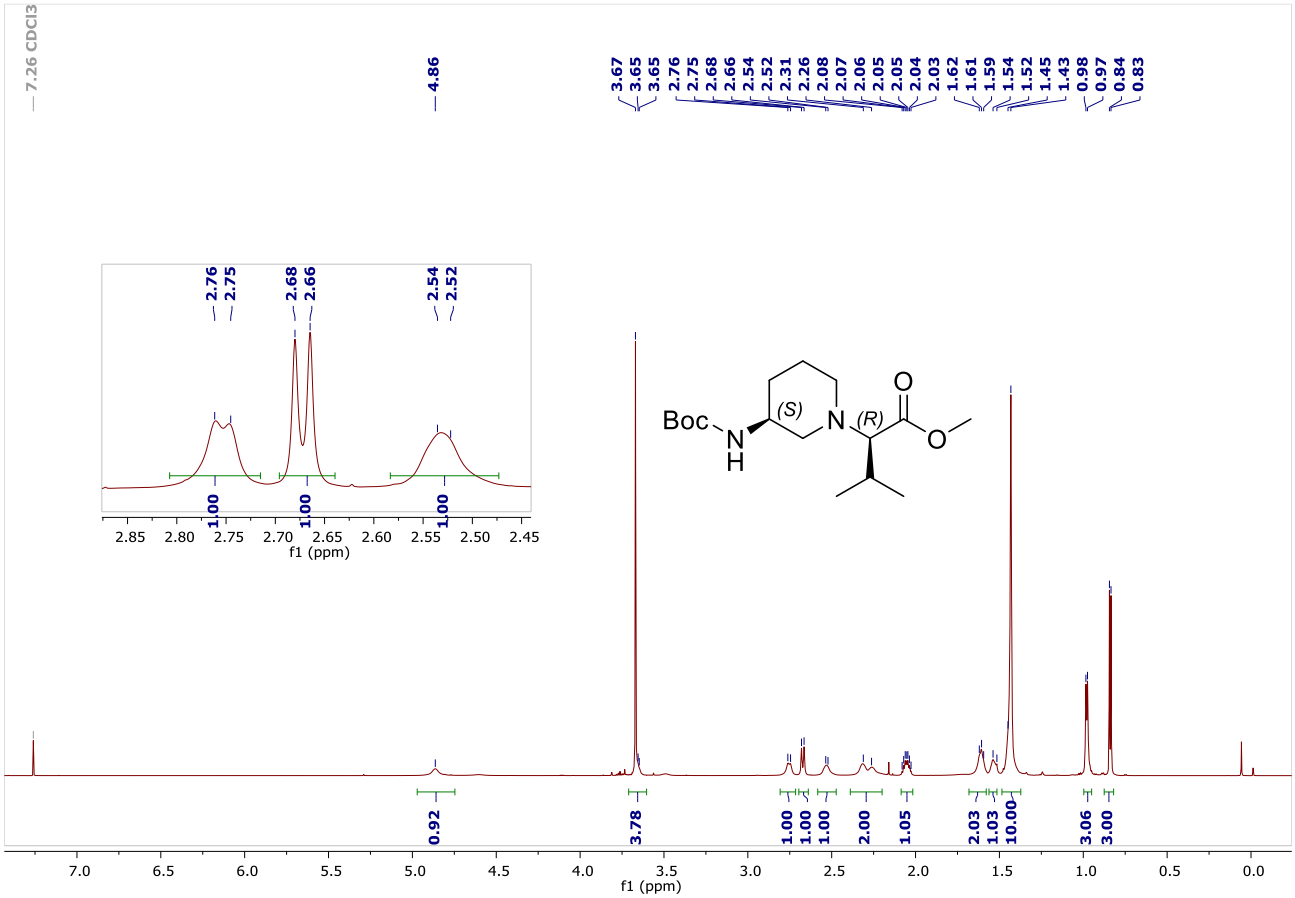


Figure S75. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*R*,3*S*)-10b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

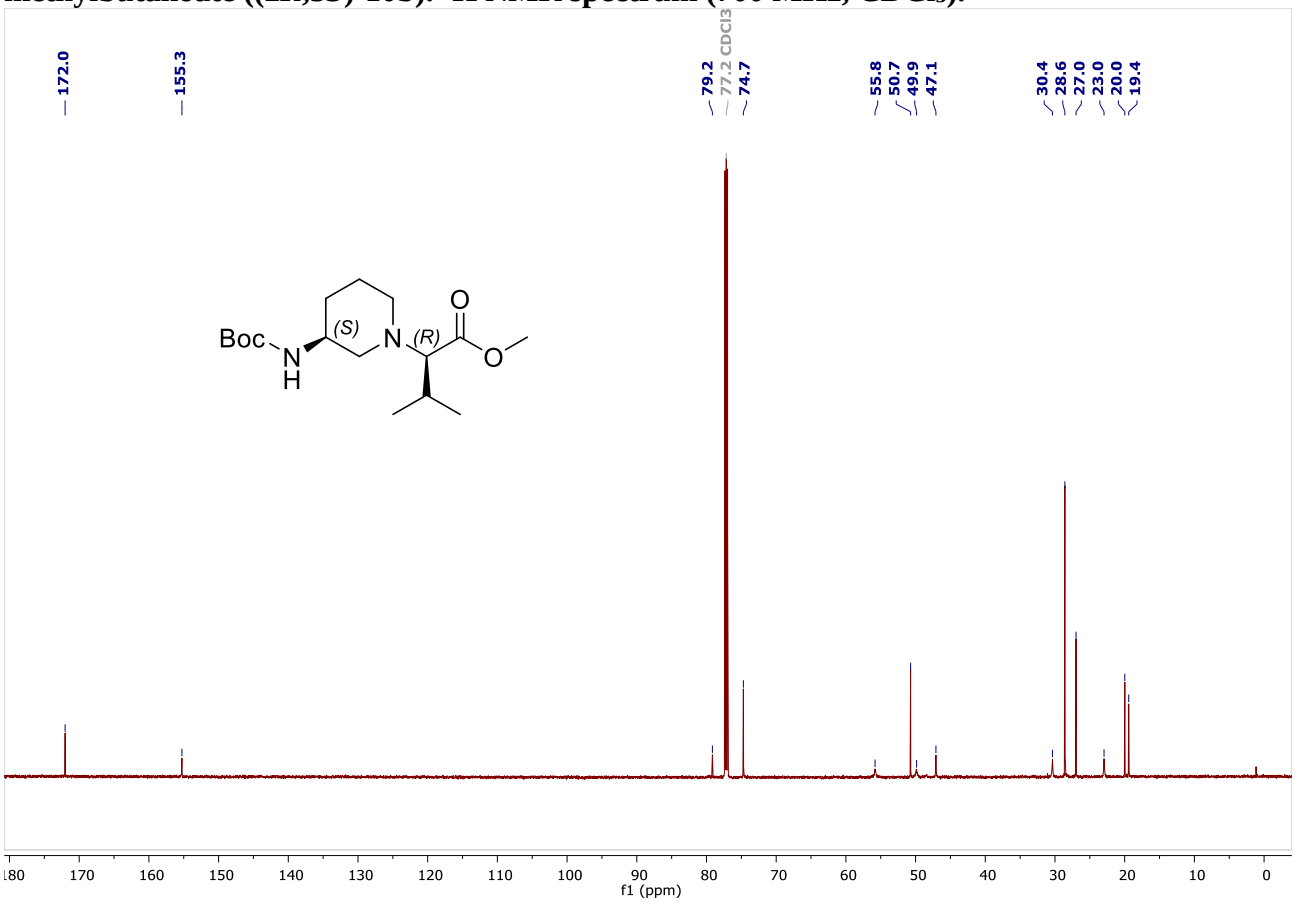


Figure S76. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*R*,3*S*)-10b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

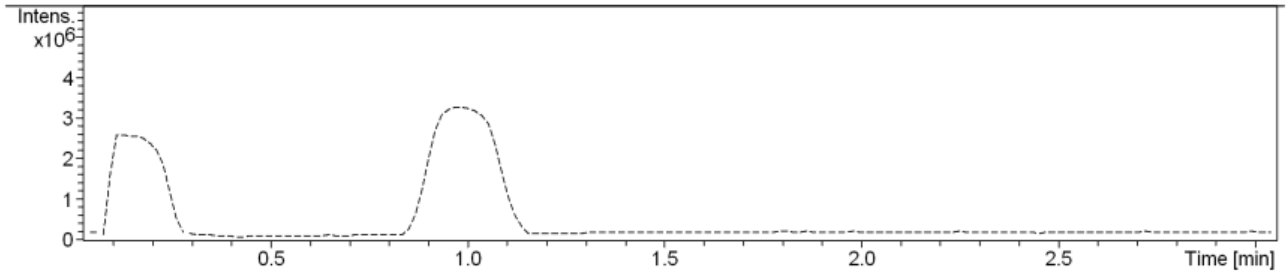
Mass Spectrum SmartFormula Report

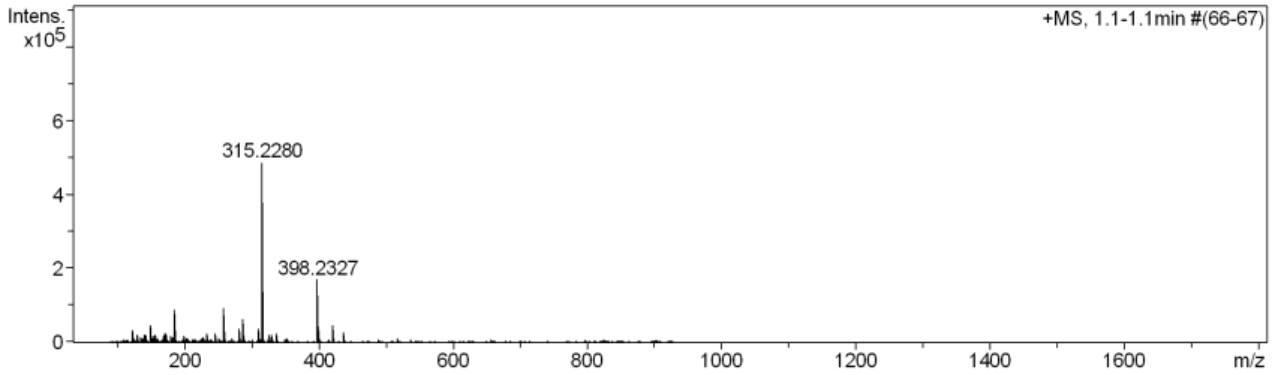
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_564_1-A,6_01_10211.d	Acquisition Date	4/14/2023 12:57:05 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_564	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
315.2280	1	C 16 H 31 N 2 O 4	100.00	315.2278	-0.7	-0.4	14.0	2.5	even	ok

Figure S77. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*R*,3*S*)-10b). HRMS (ESI-TOF).

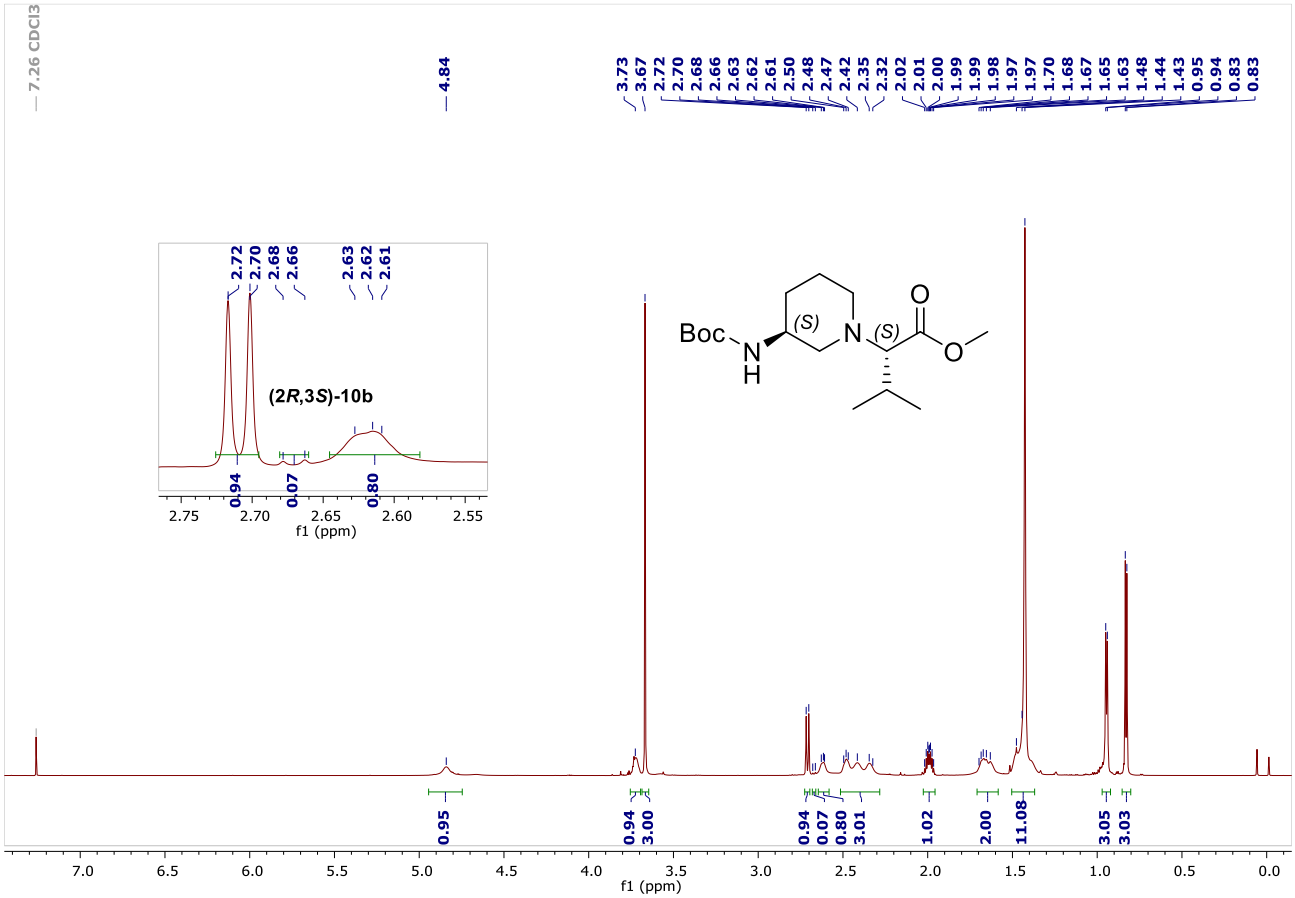


Figure S78. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*S*,3*S*)-10b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

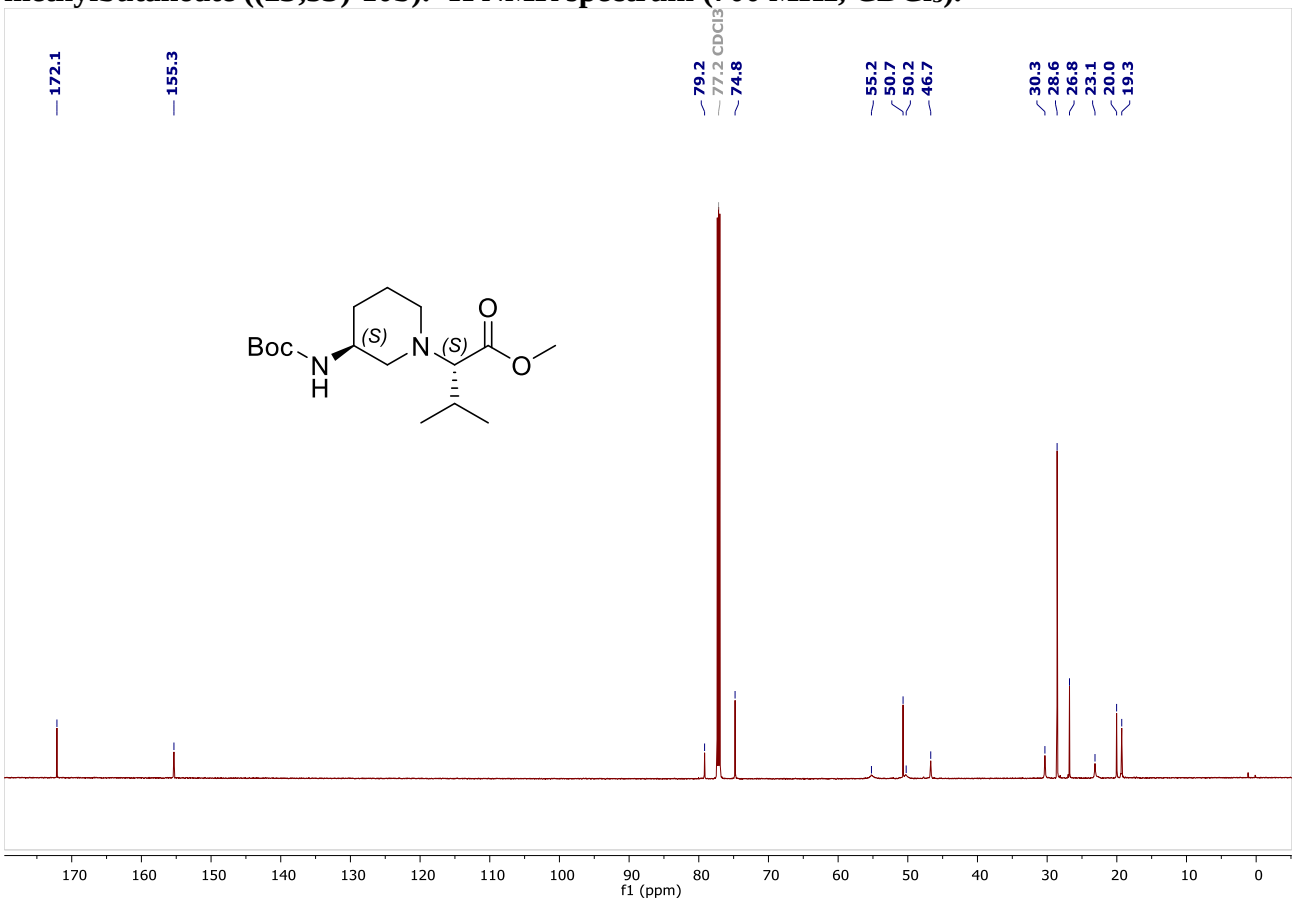


Figure S79. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*S*,3*S*)-10b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

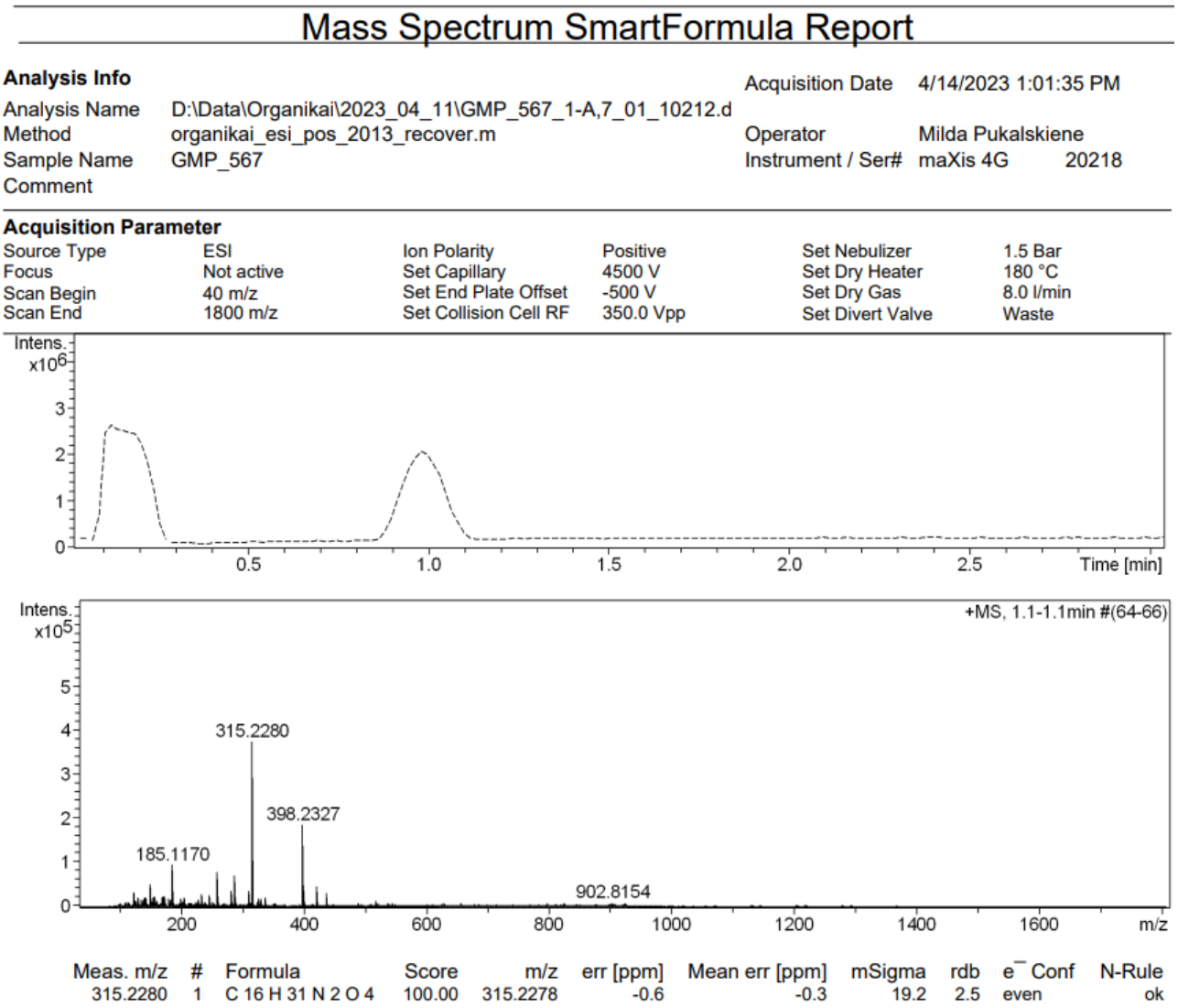


Figure S80. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*S*,3*S*)-10b). HRMS (ESI-TOF).

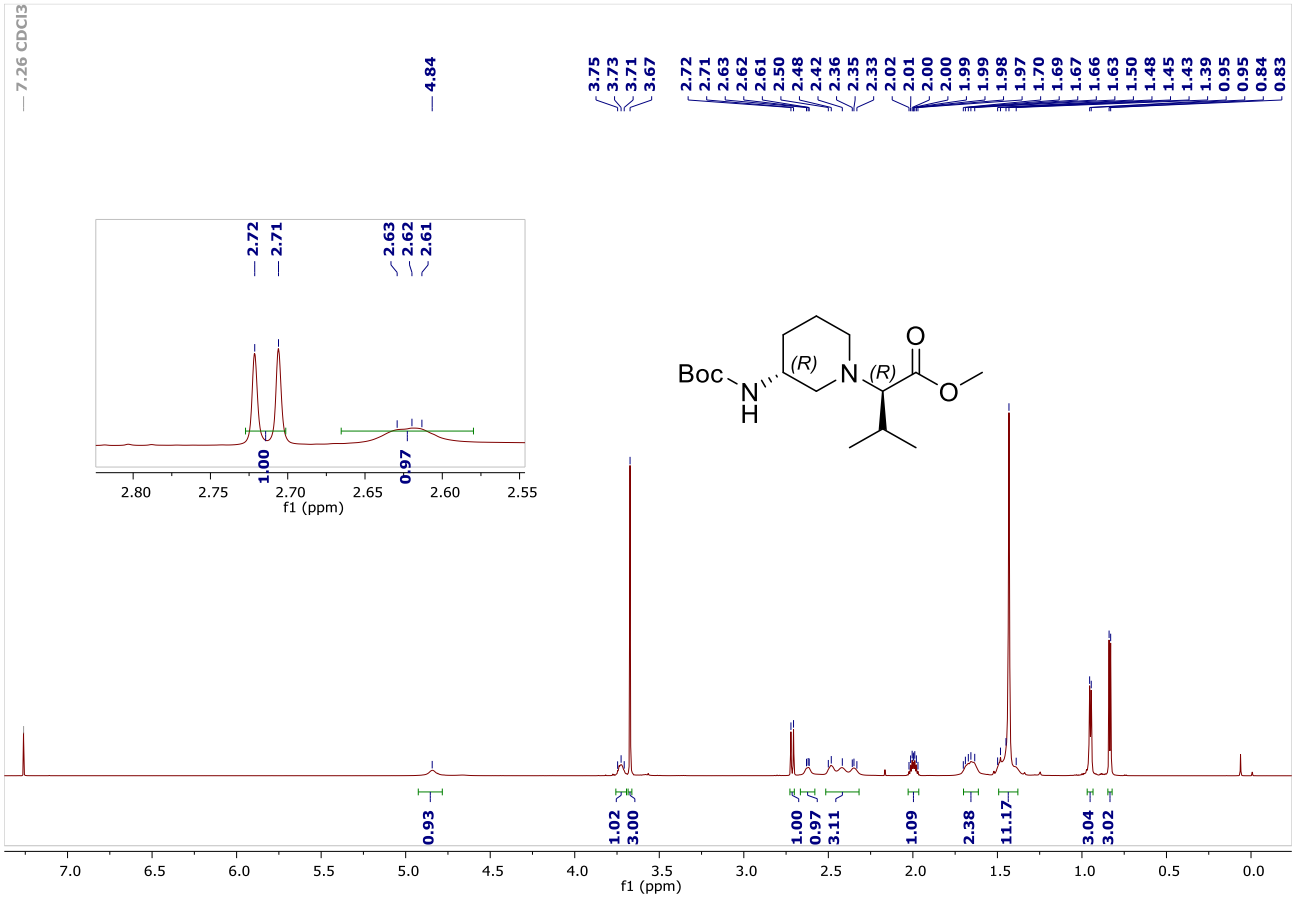


Figure S81. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*R*,3*R*)-10b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

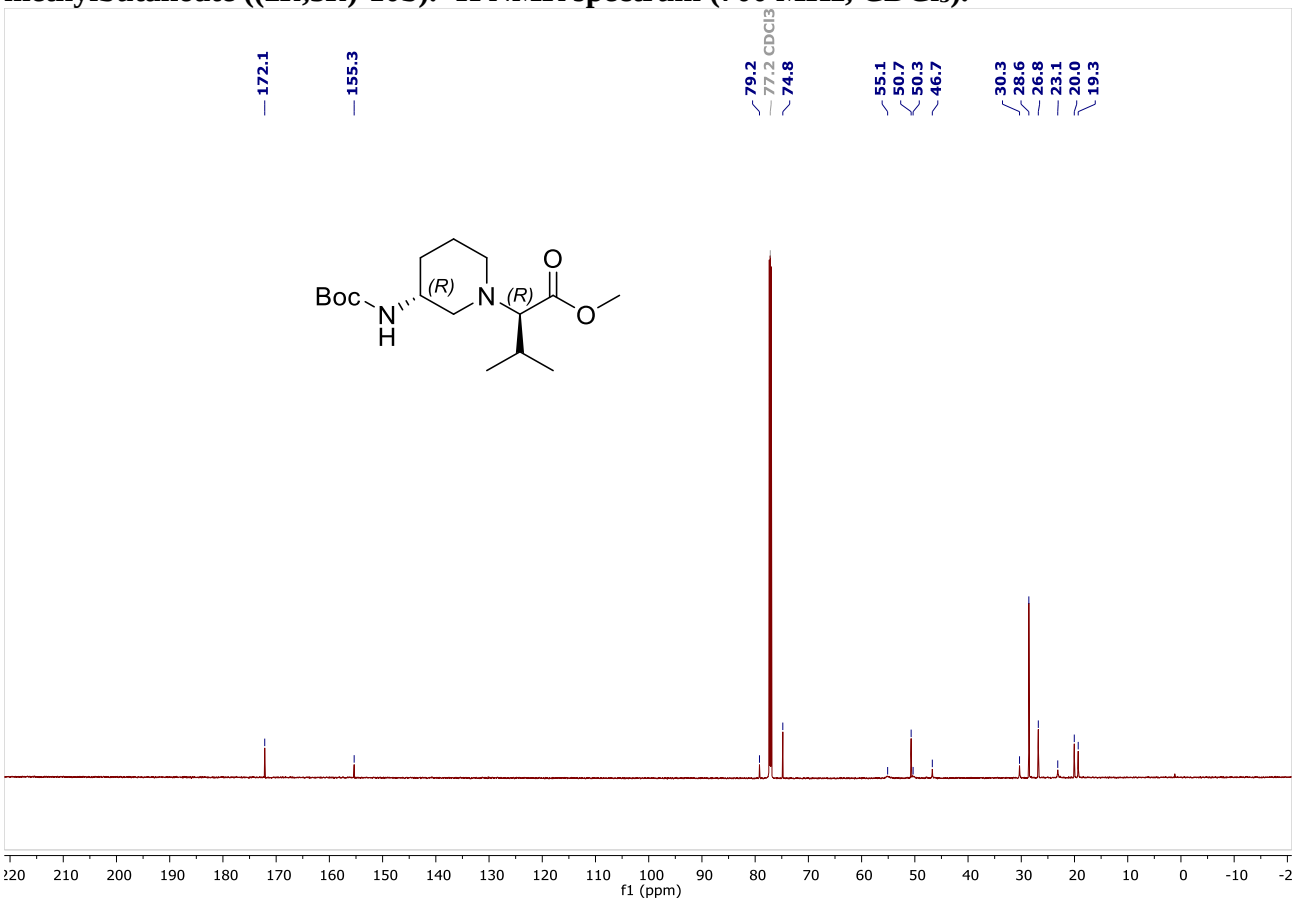


Figure S82. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*R*,3*R*)-10b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

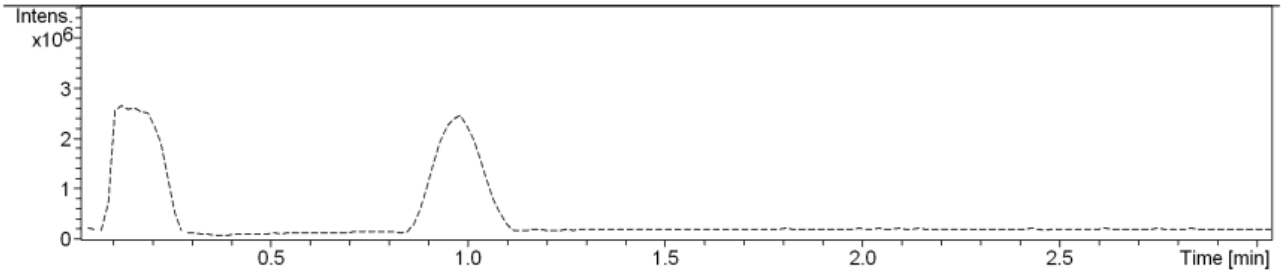
Mass Spectrum SmartFormula Report

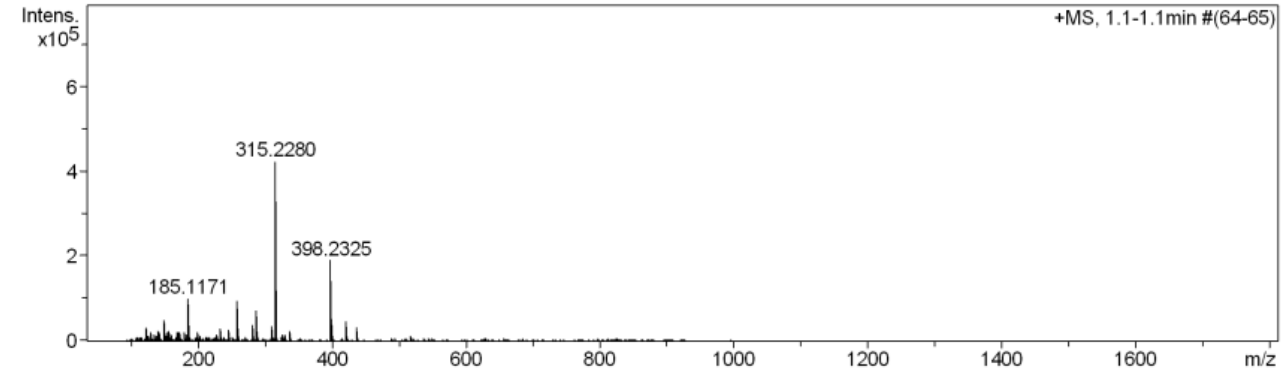
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_570_1-A,8_01_10213.d	Acquisition Date	4/14/2023 1:06:04 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_570	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
315.2280	1	C 16 H 31 N 2 O 4	100.00	315.2278	-0.6	-0.3	11.3	2.5	even	ok

Figure S83. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-3-methylbutanoate ((2*R*,3*R*)-10b). HRMS (ESI-TOF).

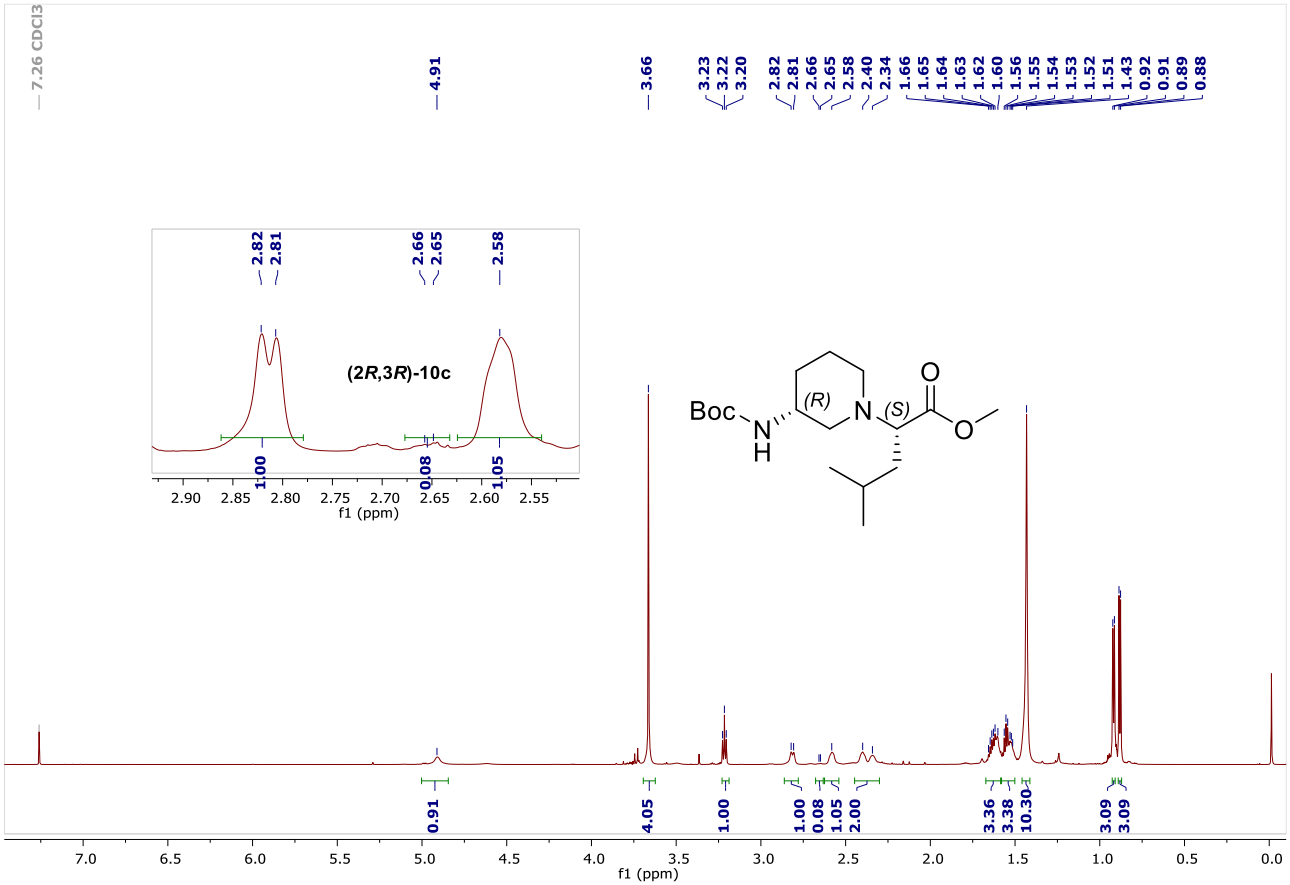


Figure S84. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*S*,3*R*)-10c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

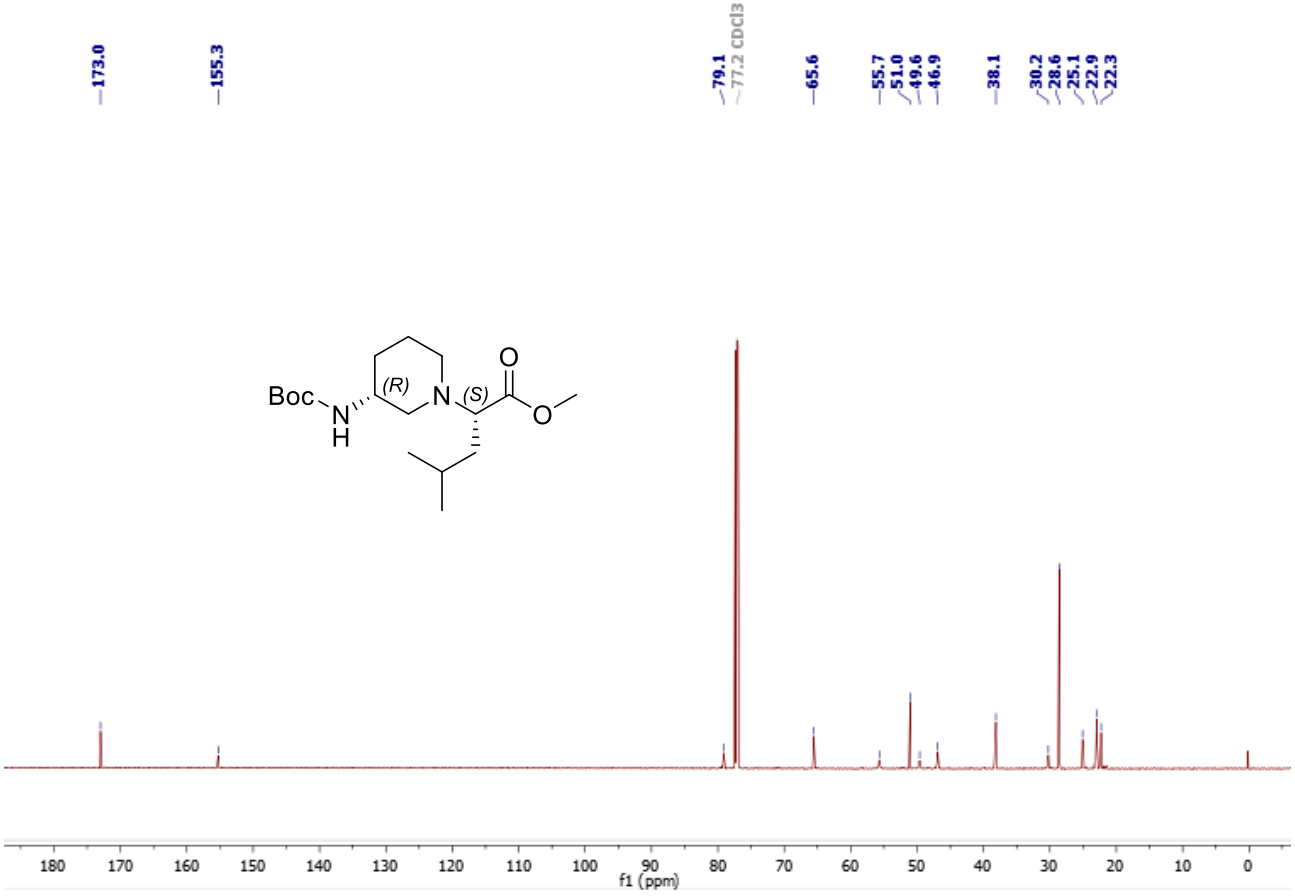


Figure S85. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*S*,3*R*)-10c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

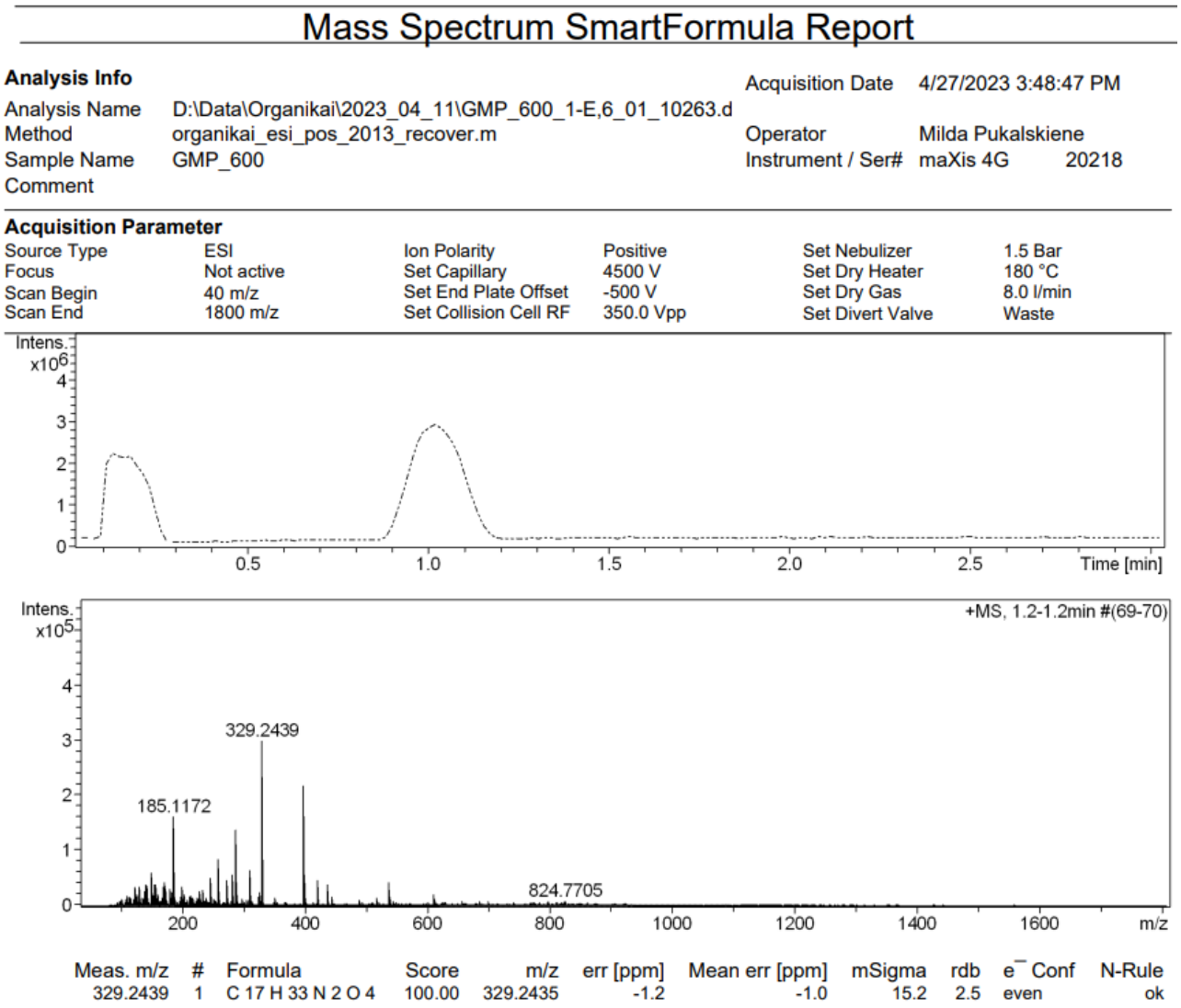


Figure S86. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*S*,3*R*)-10c). HRMS (ESI-TOF).

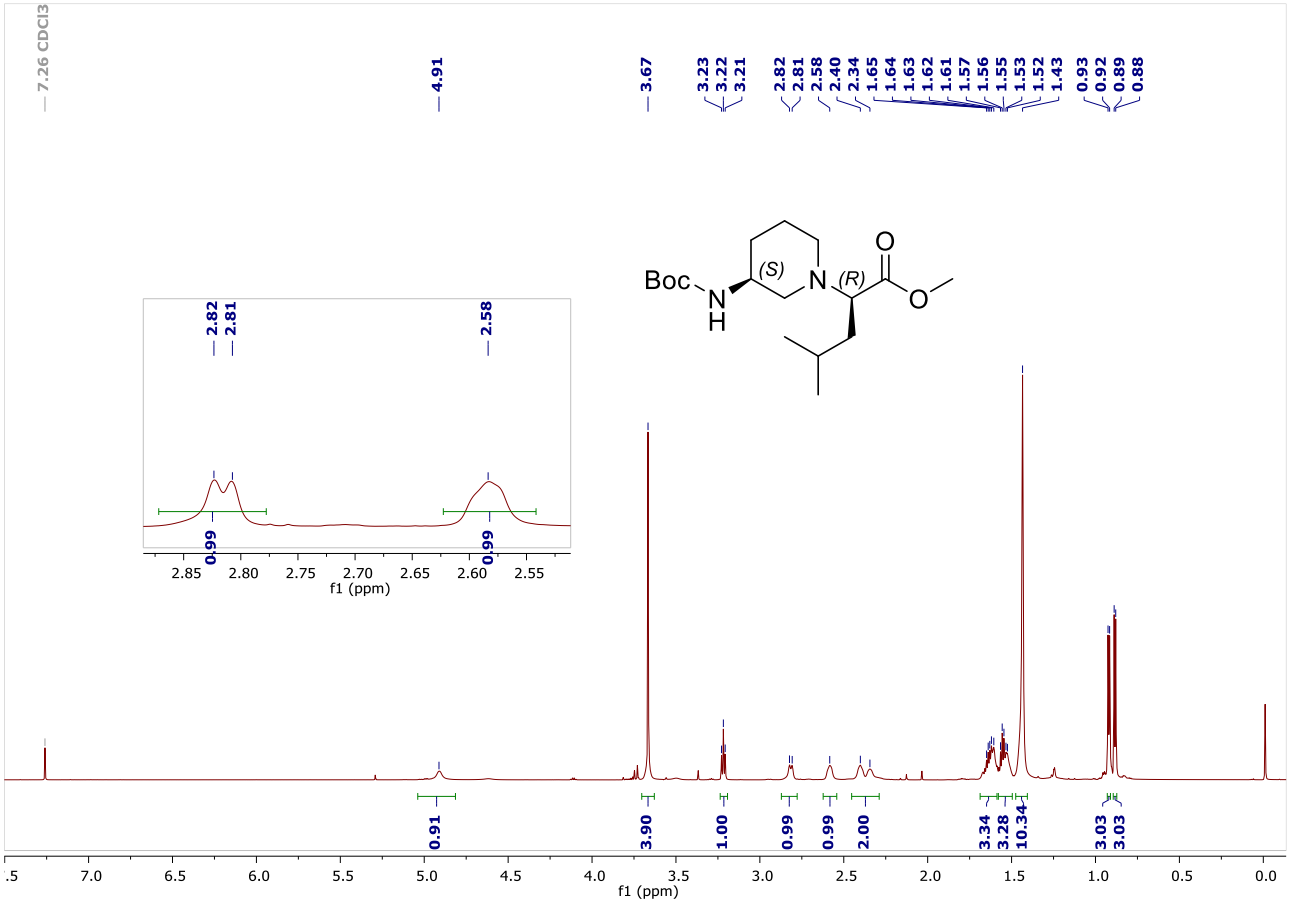


Figure S87. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*R*,3*S*)-10c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

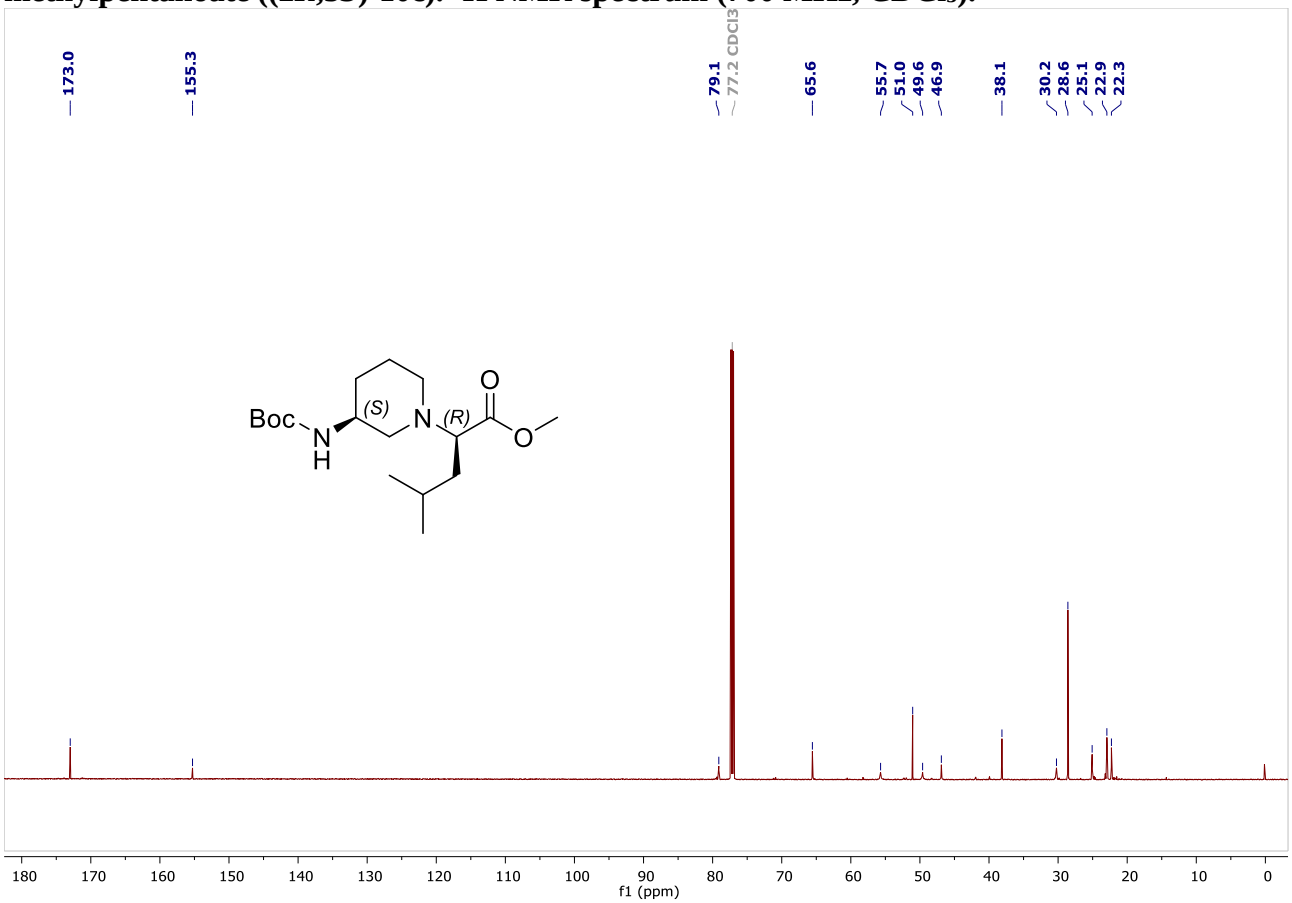


Figure S88. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*R*,3*S*)-10c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

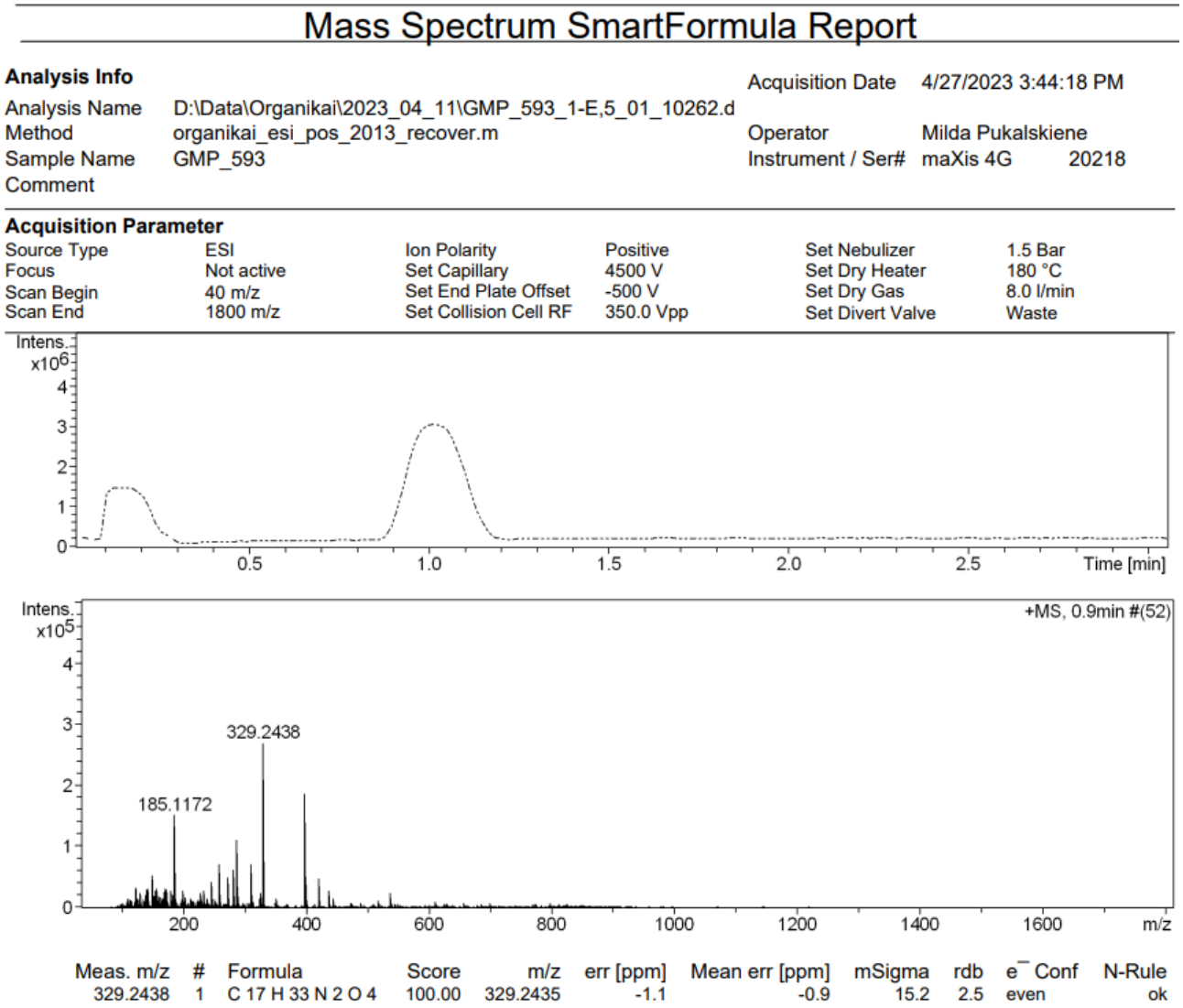


Figure S89. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*R*,3*S*)-10c). HRMS (ESI-TOF).

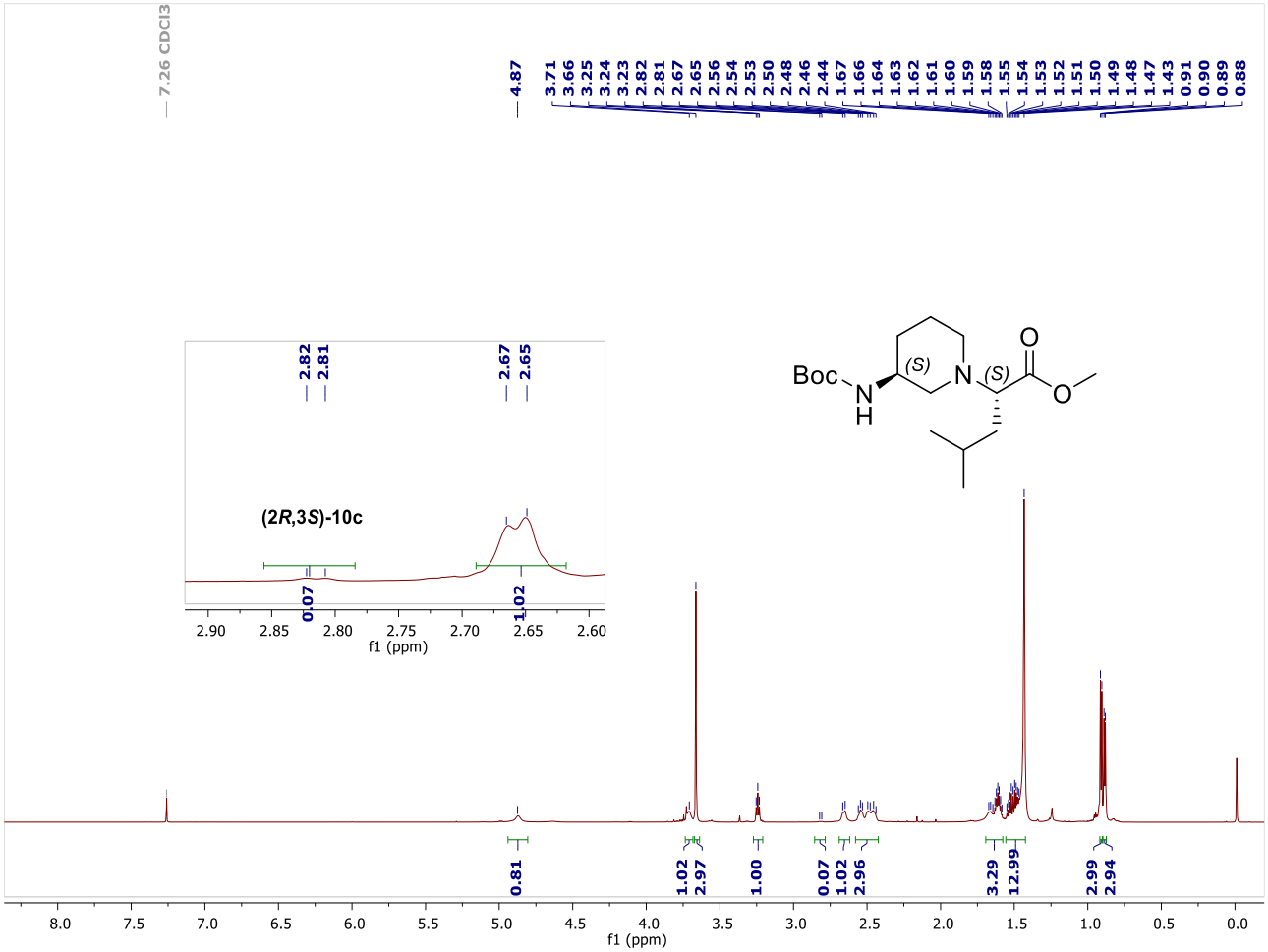


Figure S90. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*S*,3*S*)-10c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

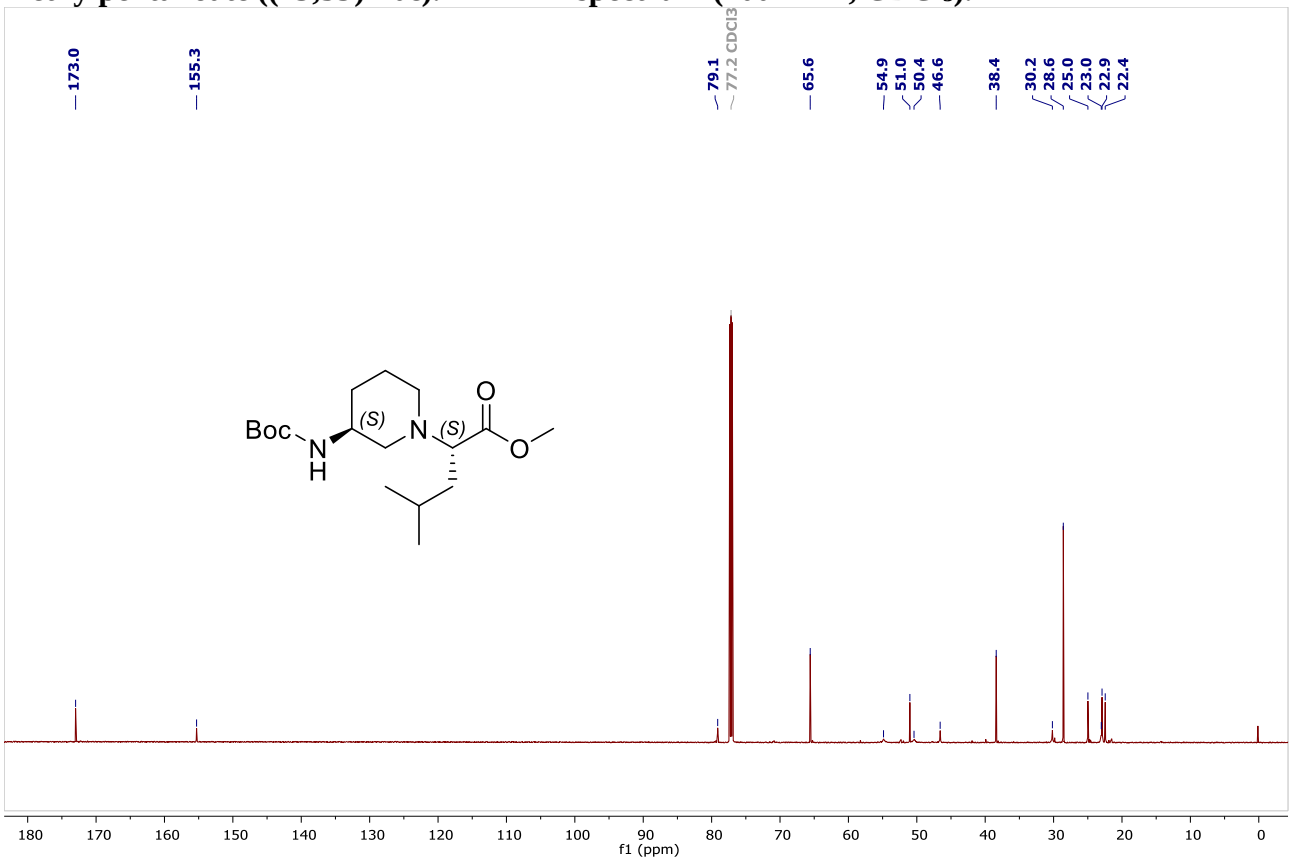


Figure S91. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*S*,3*S*)-10c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

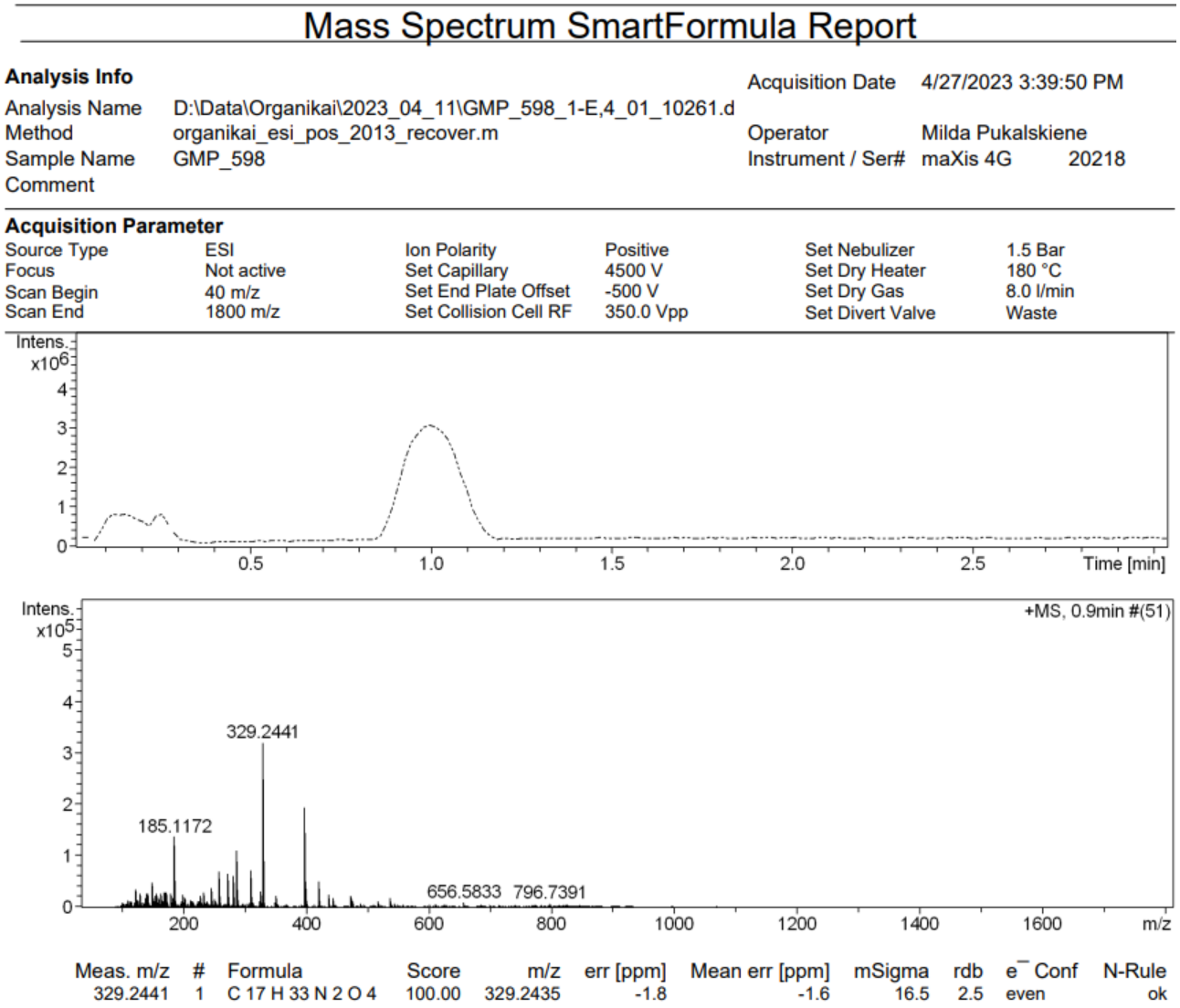


Figure S92. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*S*,3*S*)-10c). HRMS (ESI-TOF).

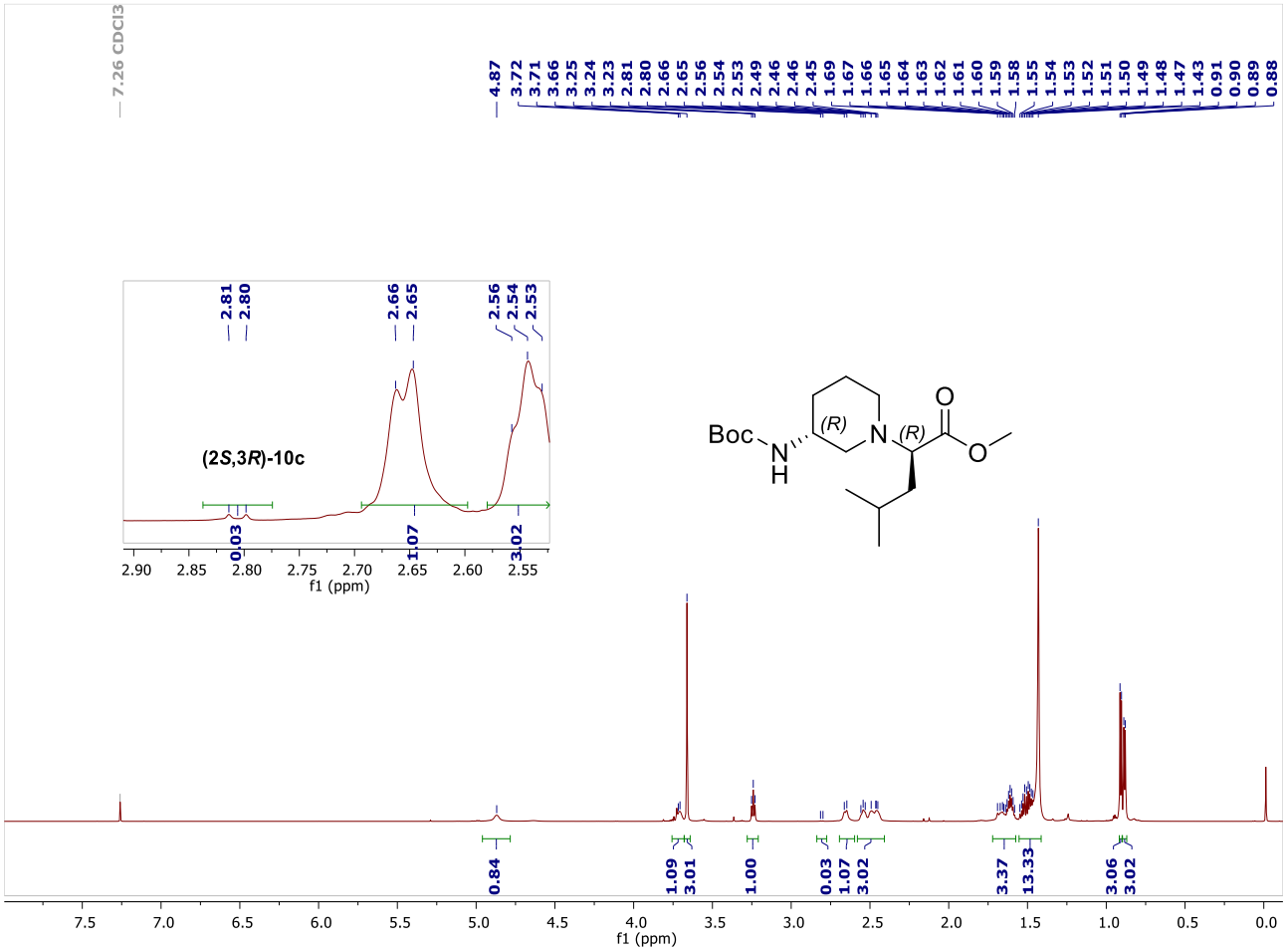


Figure S93. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*R*,3*R*)-10c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

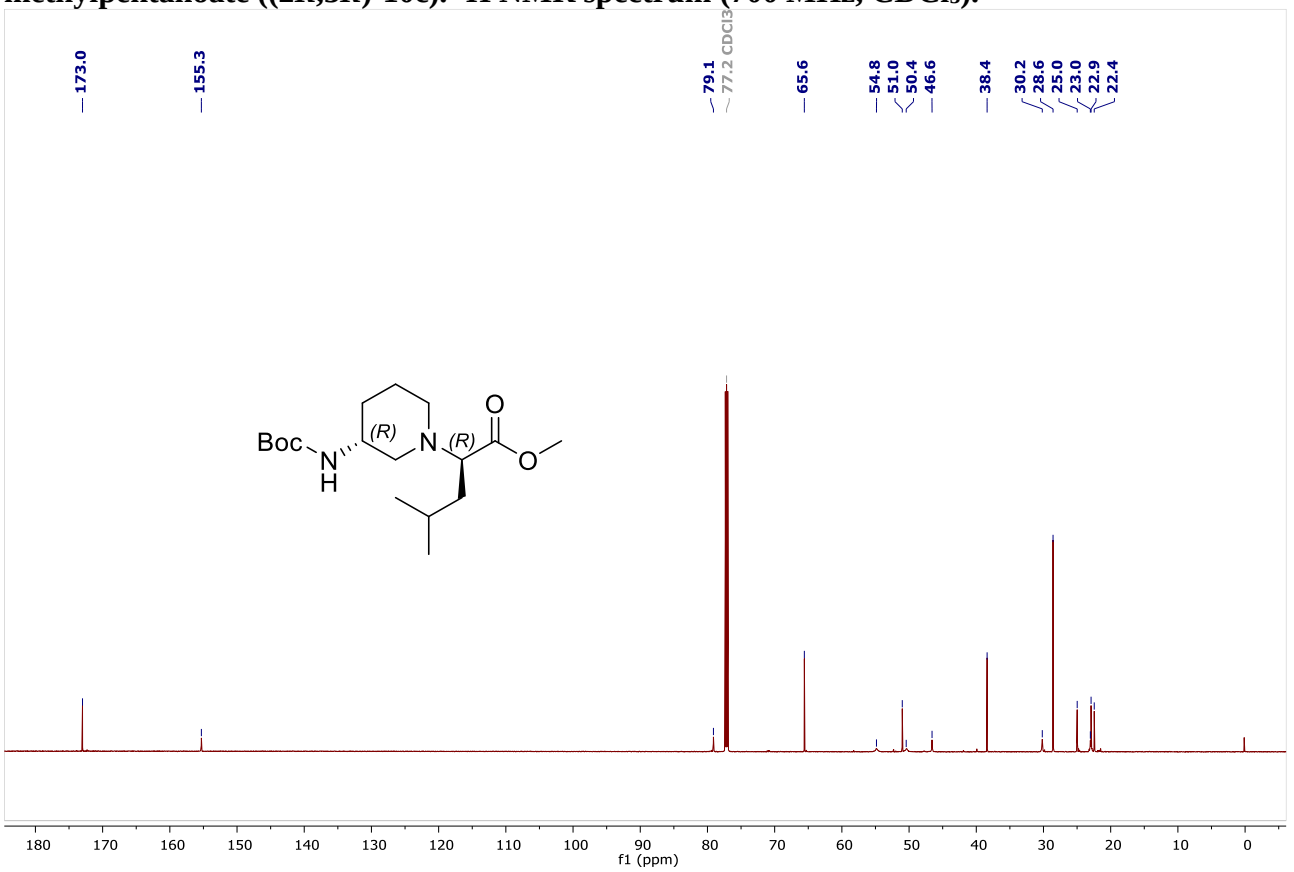


Figure S94. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*R*,3*R*)-10c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

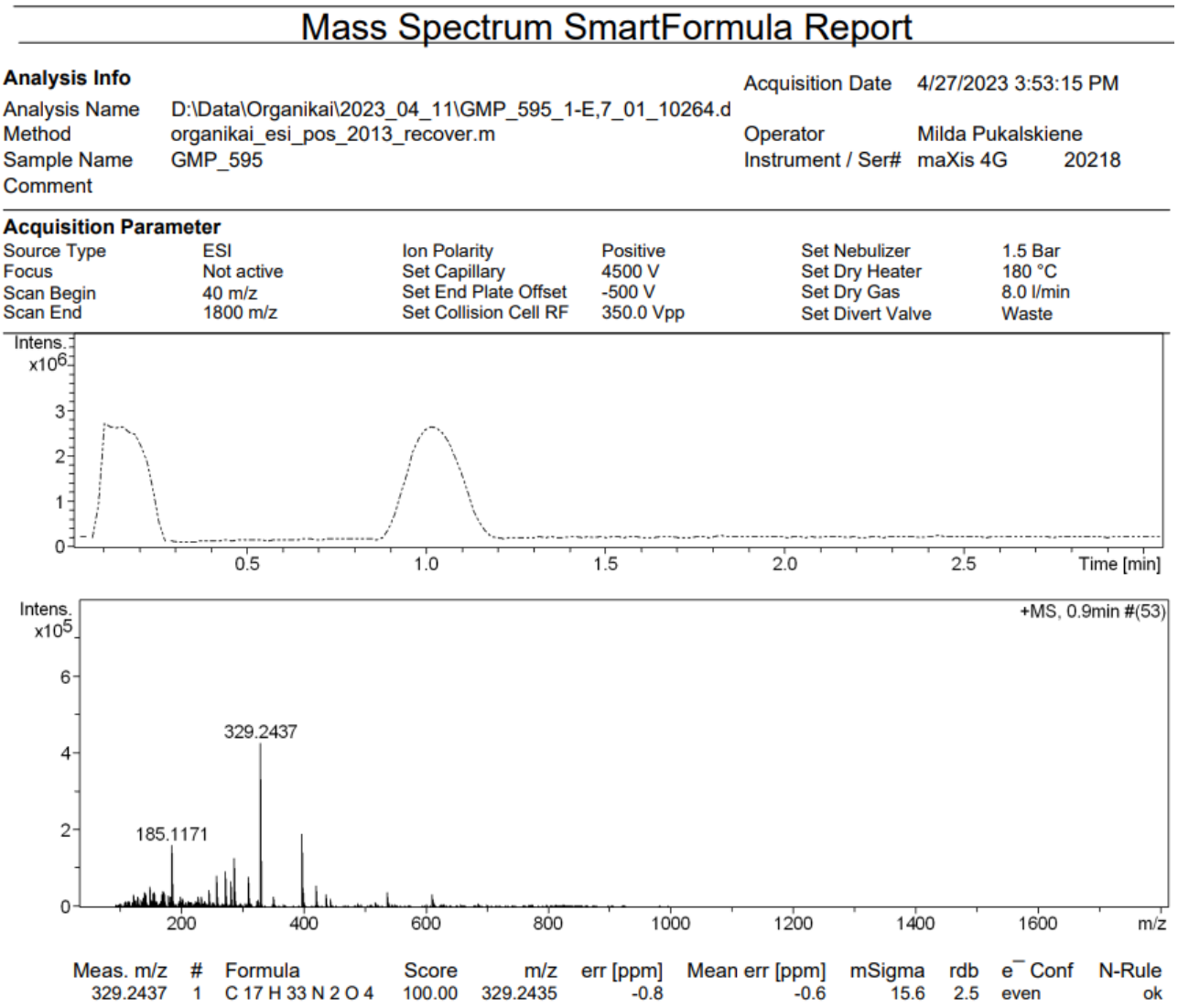


Figure S95. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]piperidin-1-yl}-4-methylpentanoate ((2*R*,3*R*)-10c). HRMS (ESI-TOF).

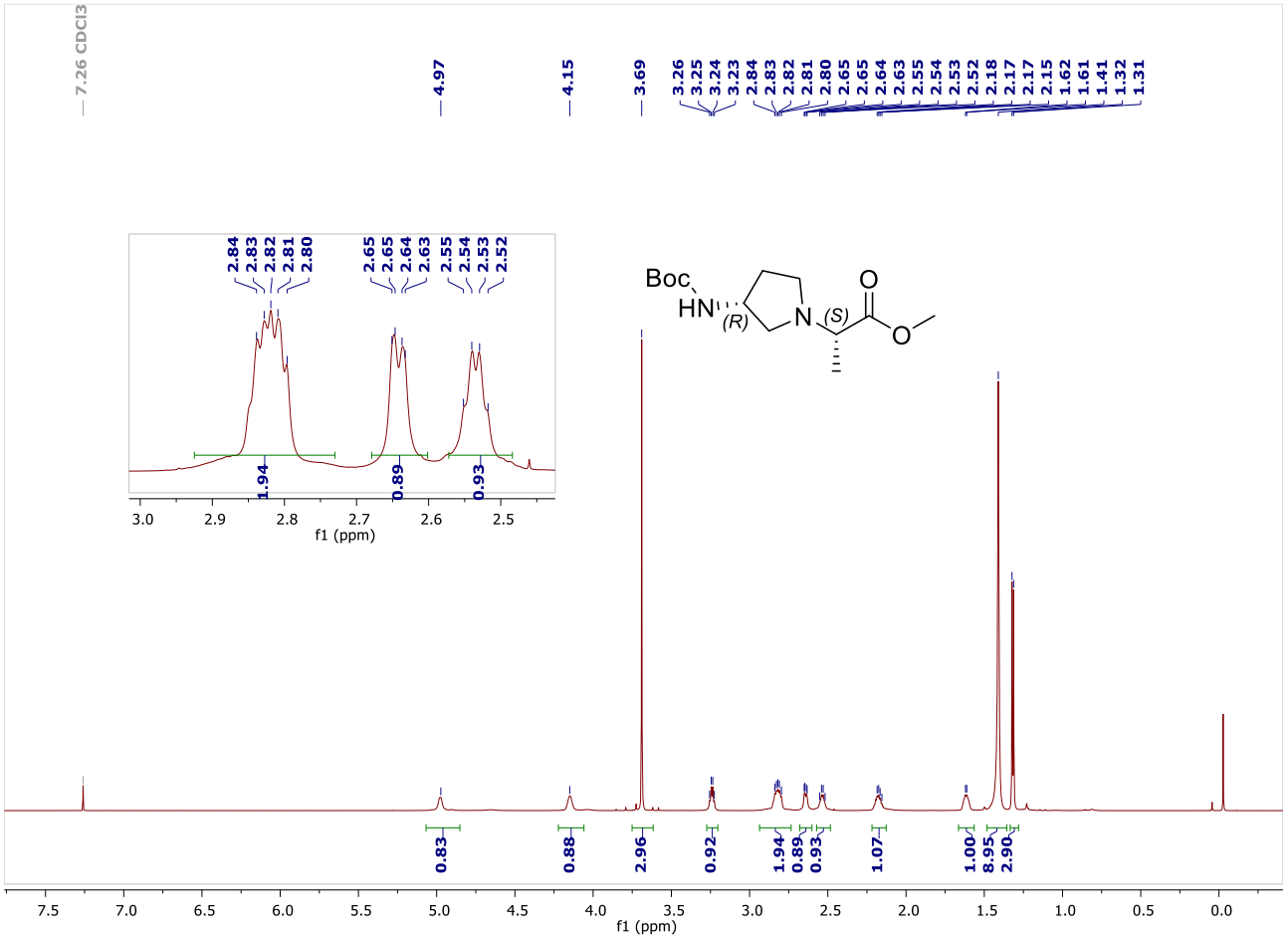


Figure S96. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*S*,3*R*)-11a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

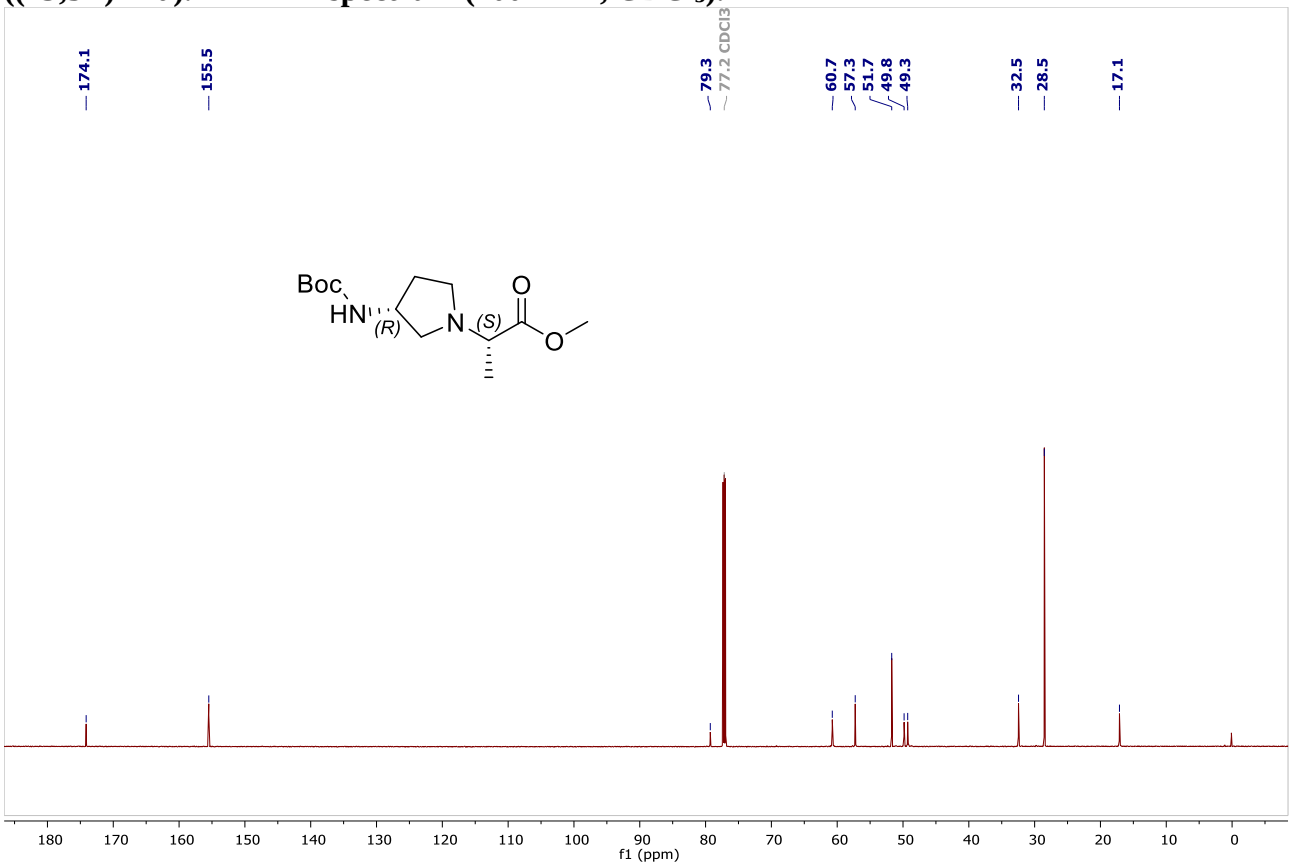


Figure S97. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*S*,3*R*)-11a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

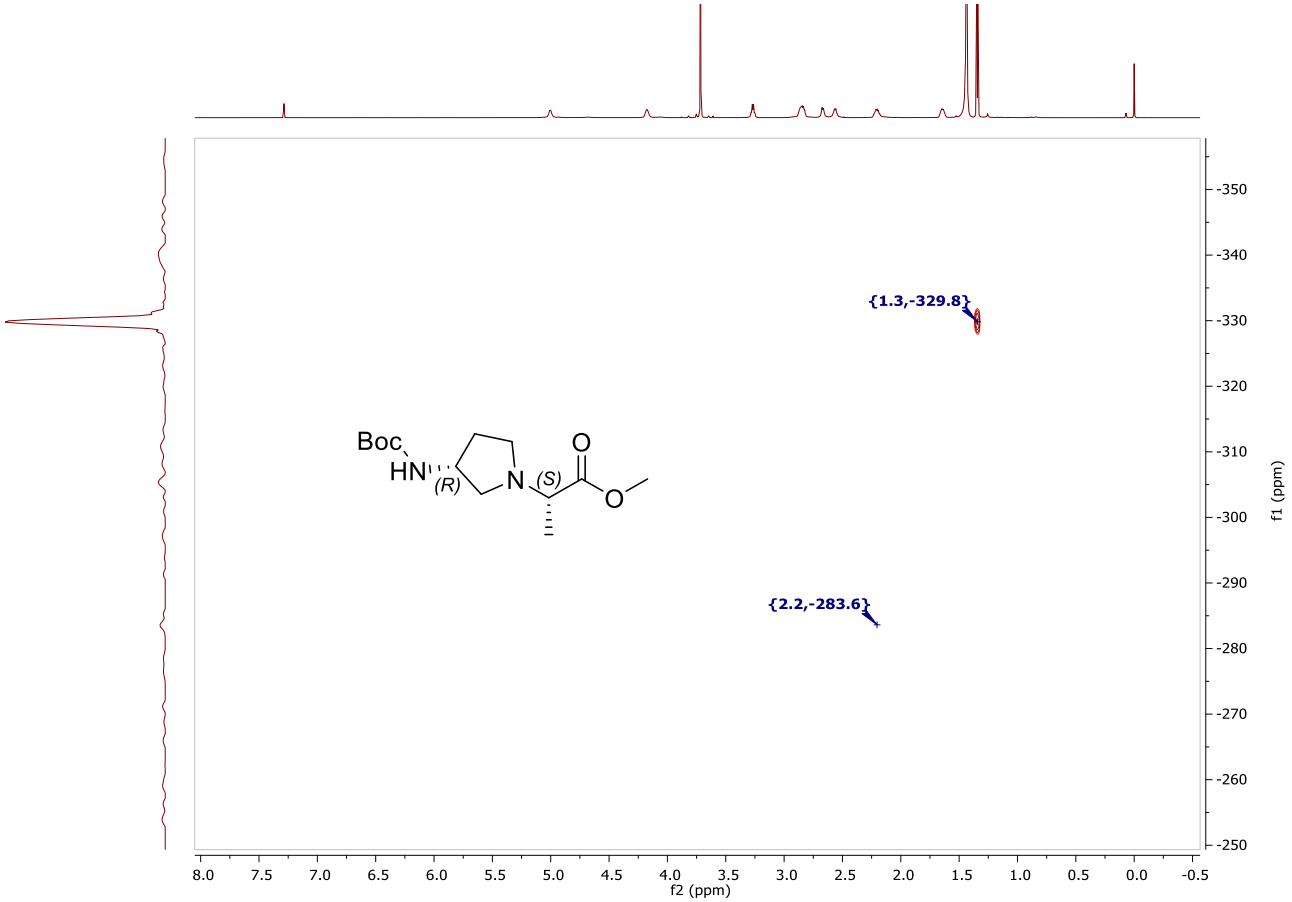


Figure S98. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*S*,3*R*)-11a). ^{1}H-^{15}N HMBC spectrum (71 MHz, $CDCl_3$).

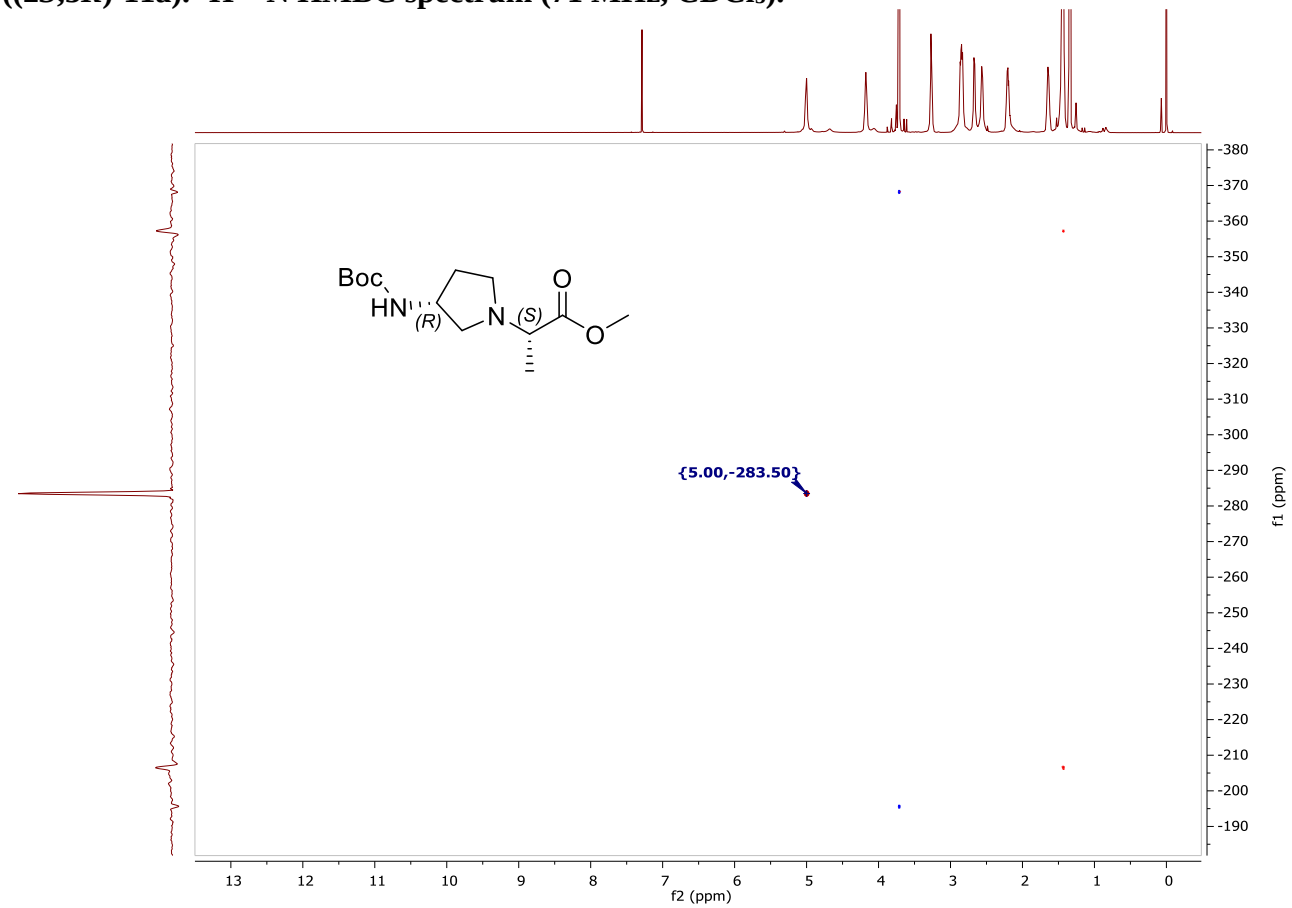


Figure S99. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*S*,3*R*)-11a). ^{1}H-^{15}N HSQC spectrum (71 MHz, $CDCl_3$).

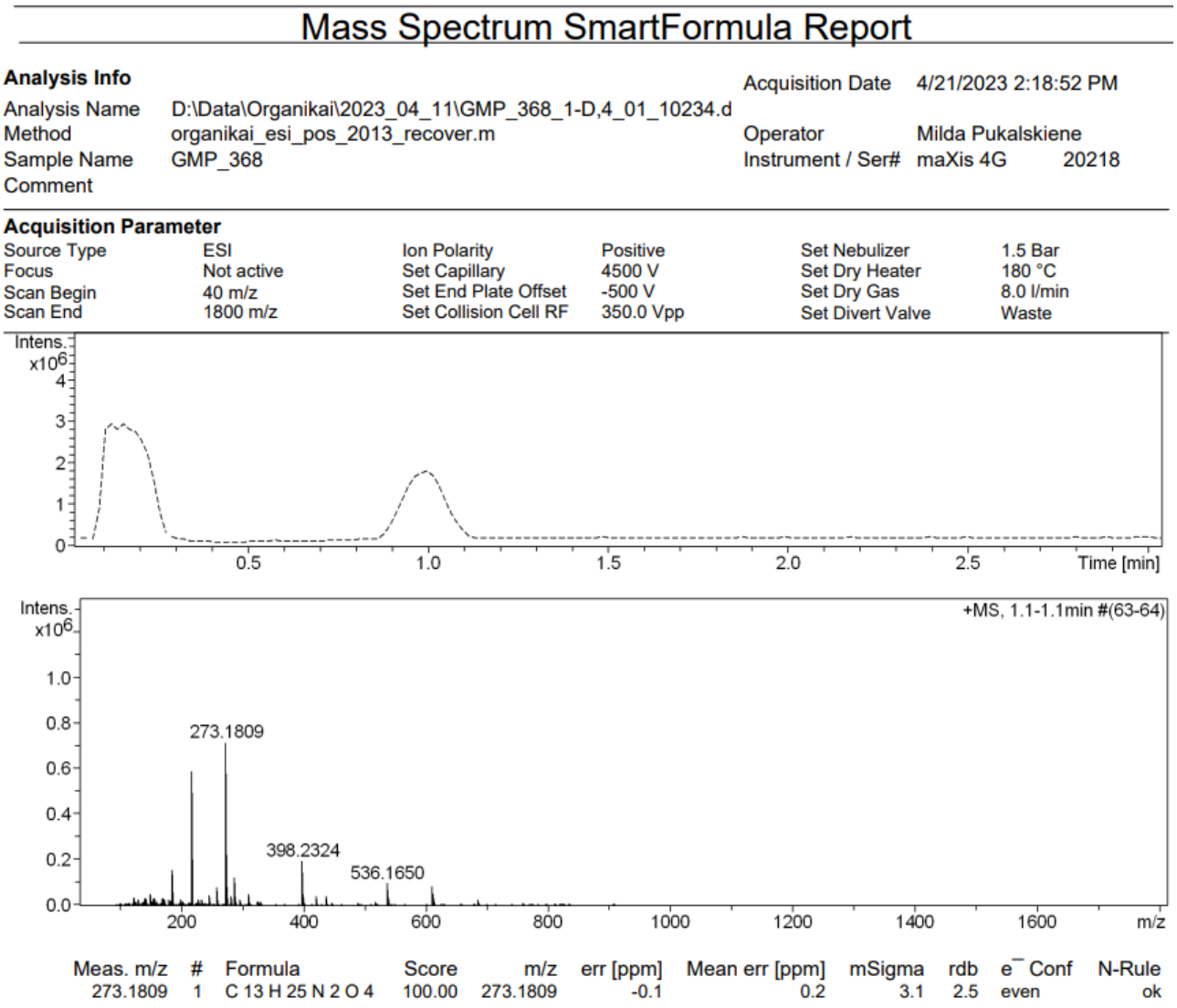


Figure S100. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*S*,3*R*)-11a). HRMS (ESI-TOF).

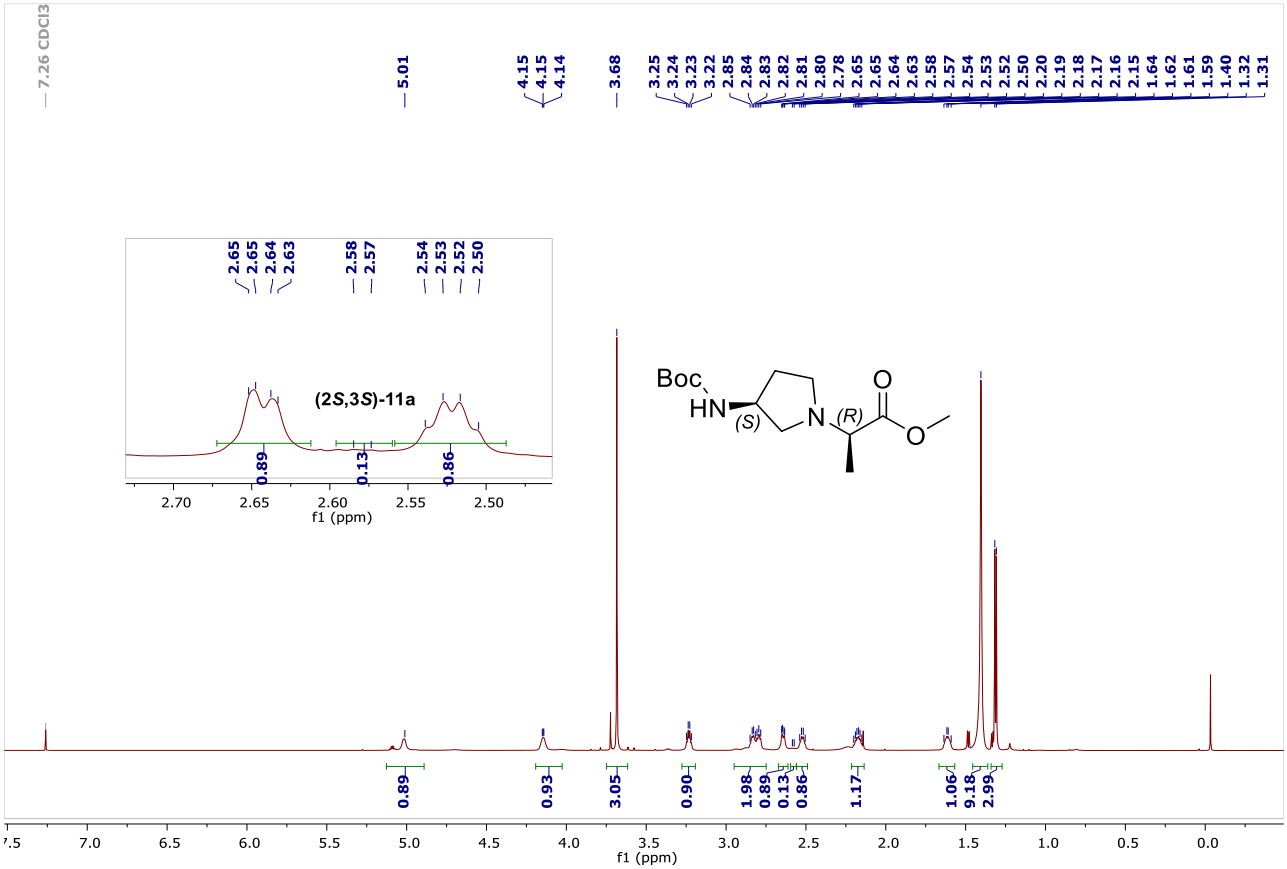


Figure S101. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*R*,3*S*)-11a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

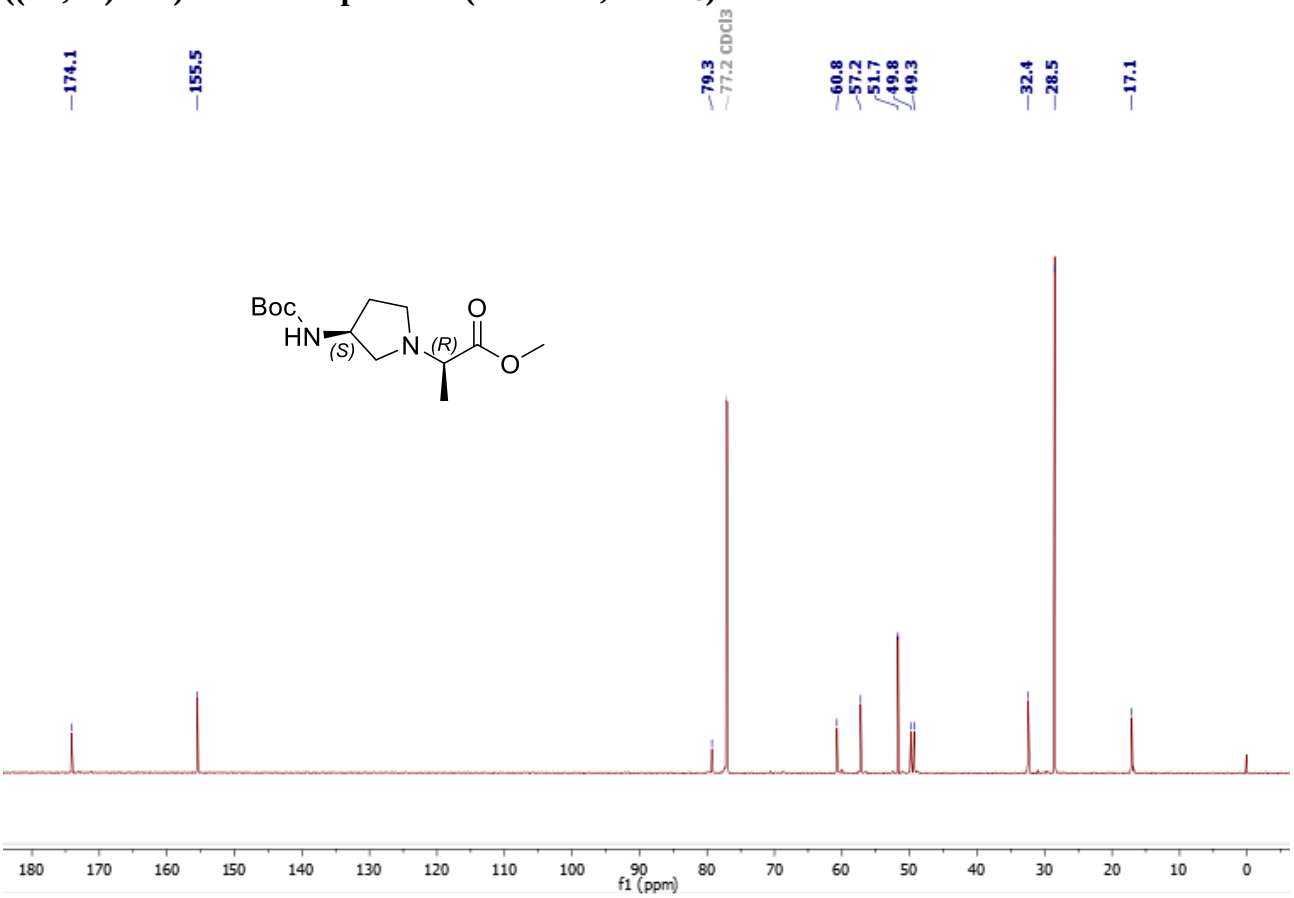


Figure S102. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*R*,3*S*)-11a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

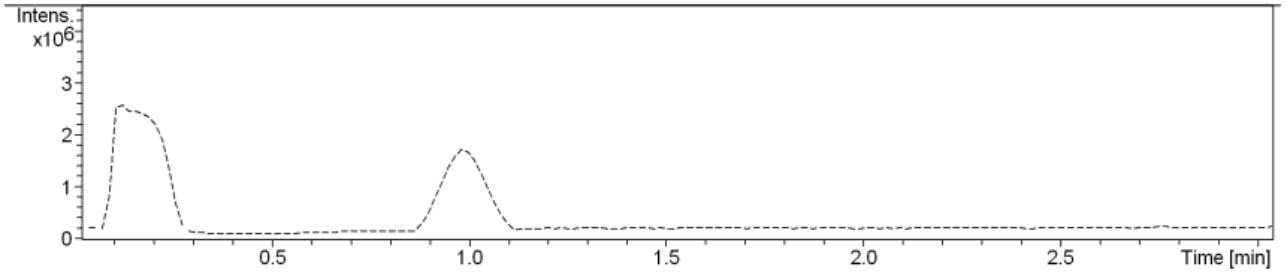
Mass Spectrum SmartFormula Report

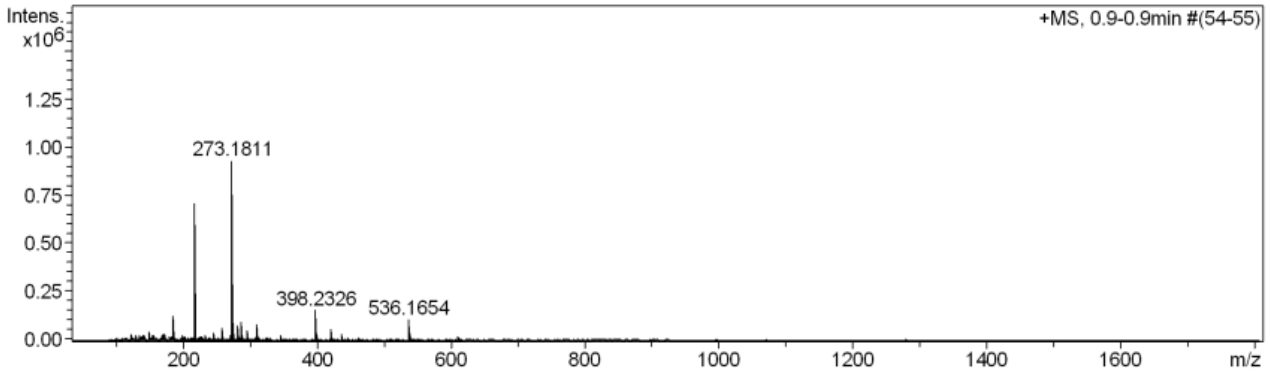
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_482_1-D,7_01_10237.d	Acquisition Date	4/21/2023 2:32:19 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_482	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
273.1811	1	C 13 H 25 N 2 O 4	100.00	273.1809	-0.8	-0.5	18.3	2.5	even	ok

Figure S103. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*R*,3*S*)-11a). HRMS (ESI-TOF).

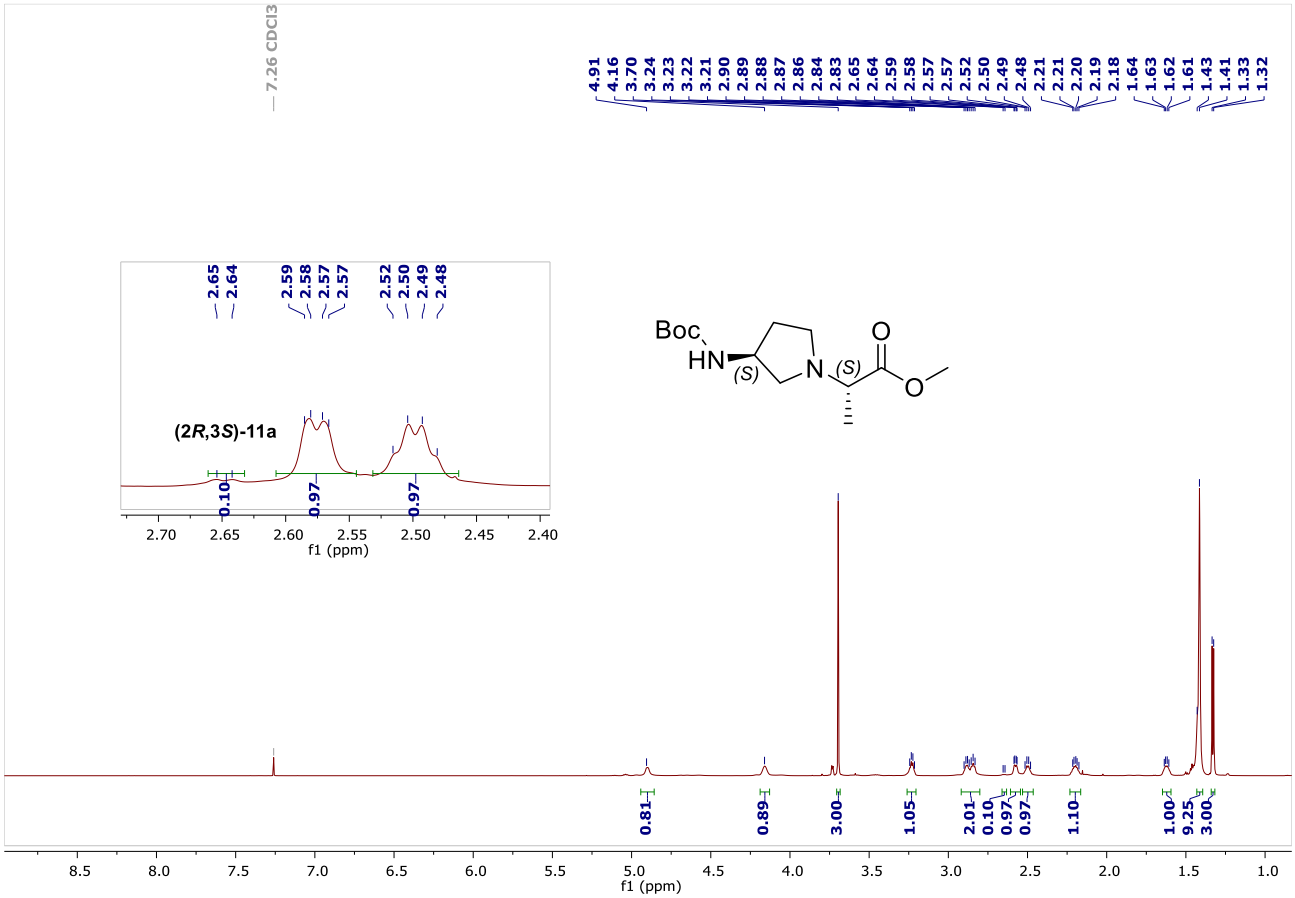


Figure S104. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*S*,3*S*)-11a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

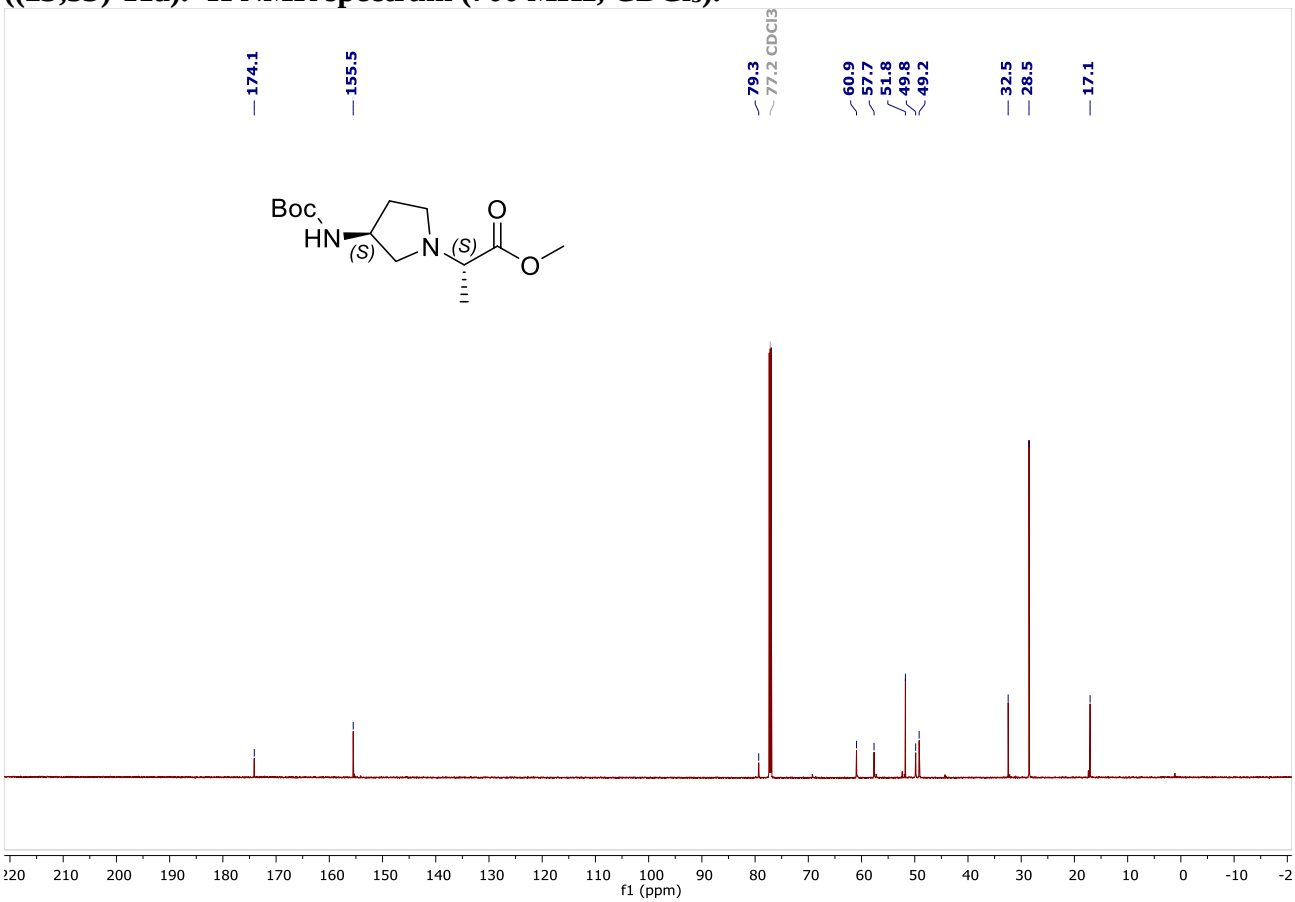


Figure S105. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*S*,3*S*)-11a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

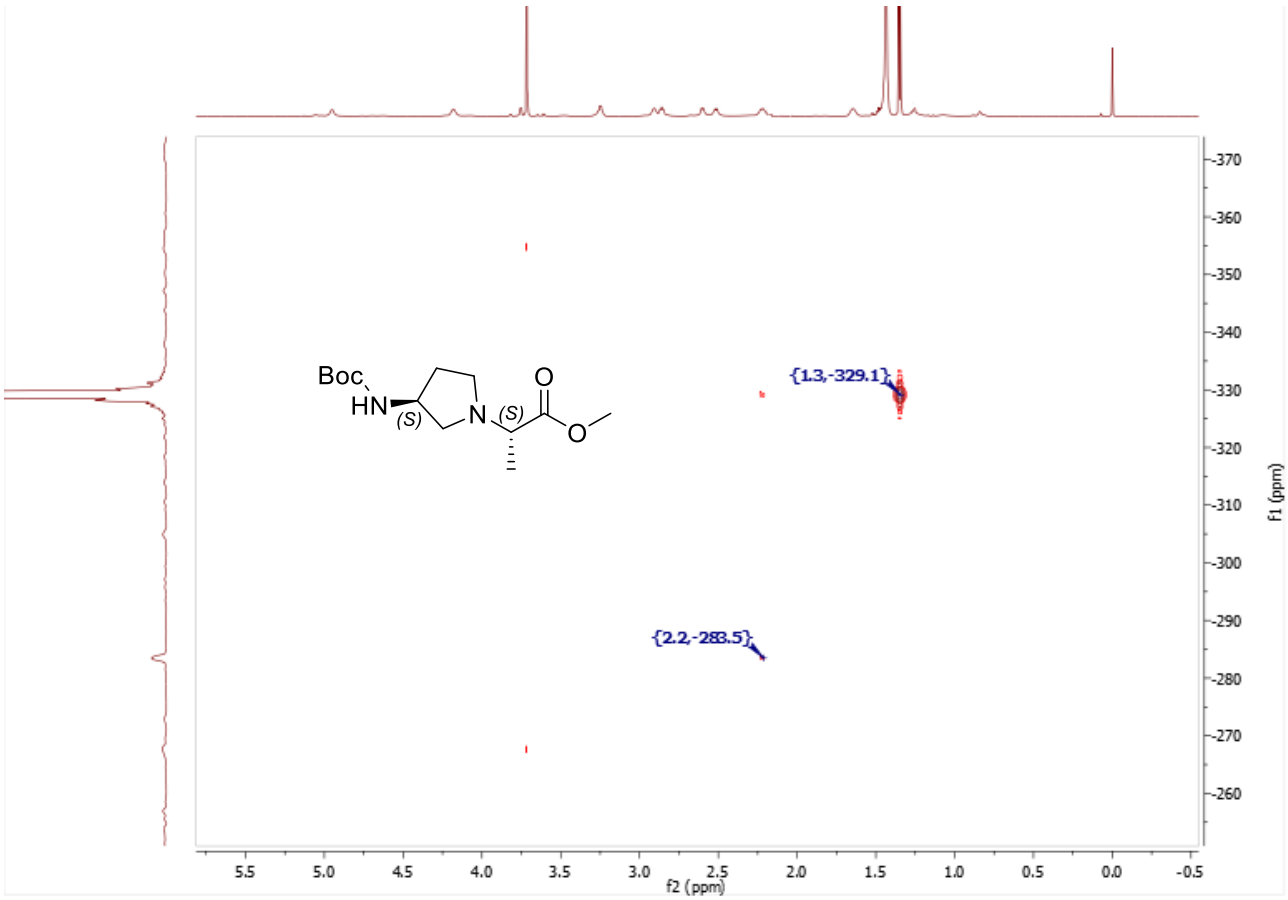


Figure S106. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*S*,3*S*)-11a). ^{1}H-^{15}N HMBC spectrum (71 MHz, $CDCl_3$).

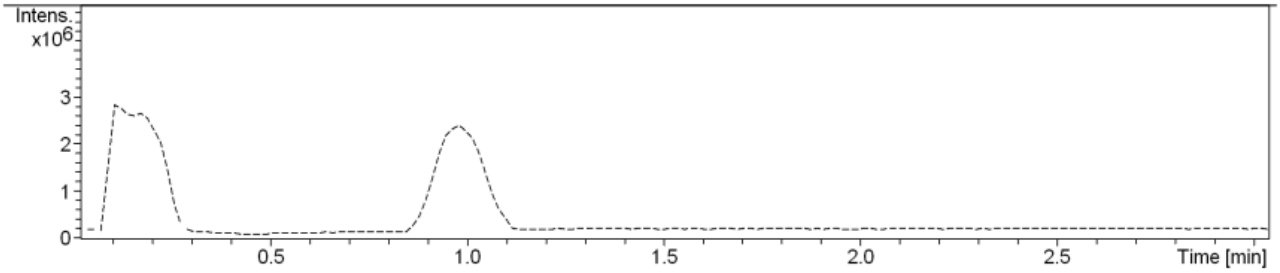
Mass Spectrum SmartFormula Report

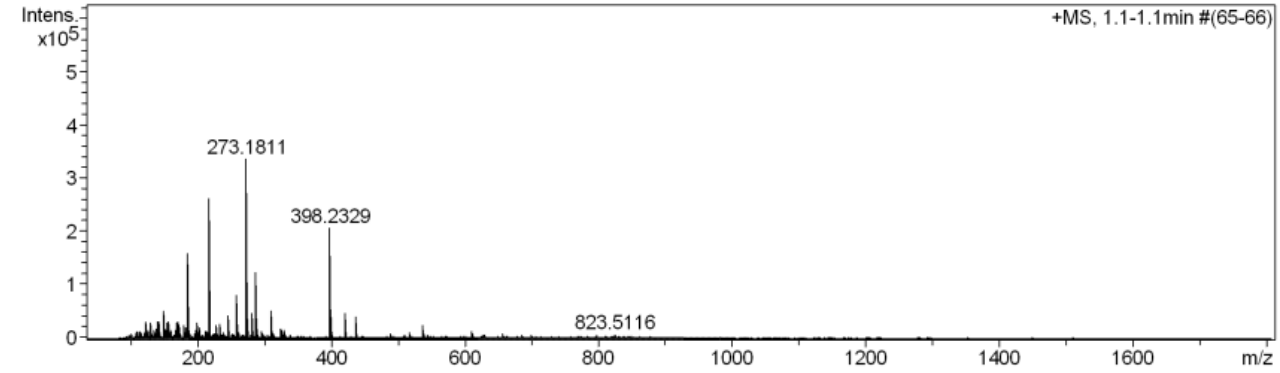
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_373_1-D,6_01_10236.d	Acquisition Date	4/21/2023 2:27:50 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_373	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
273.1811	1	C 13 H 25 N 2 O 4	100.00	273.1809	-0.7	-0.5	8.1	2.5	even	ok

Figure S107. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*S*,3*S*)-11a). HRMS (ESI-TOF).

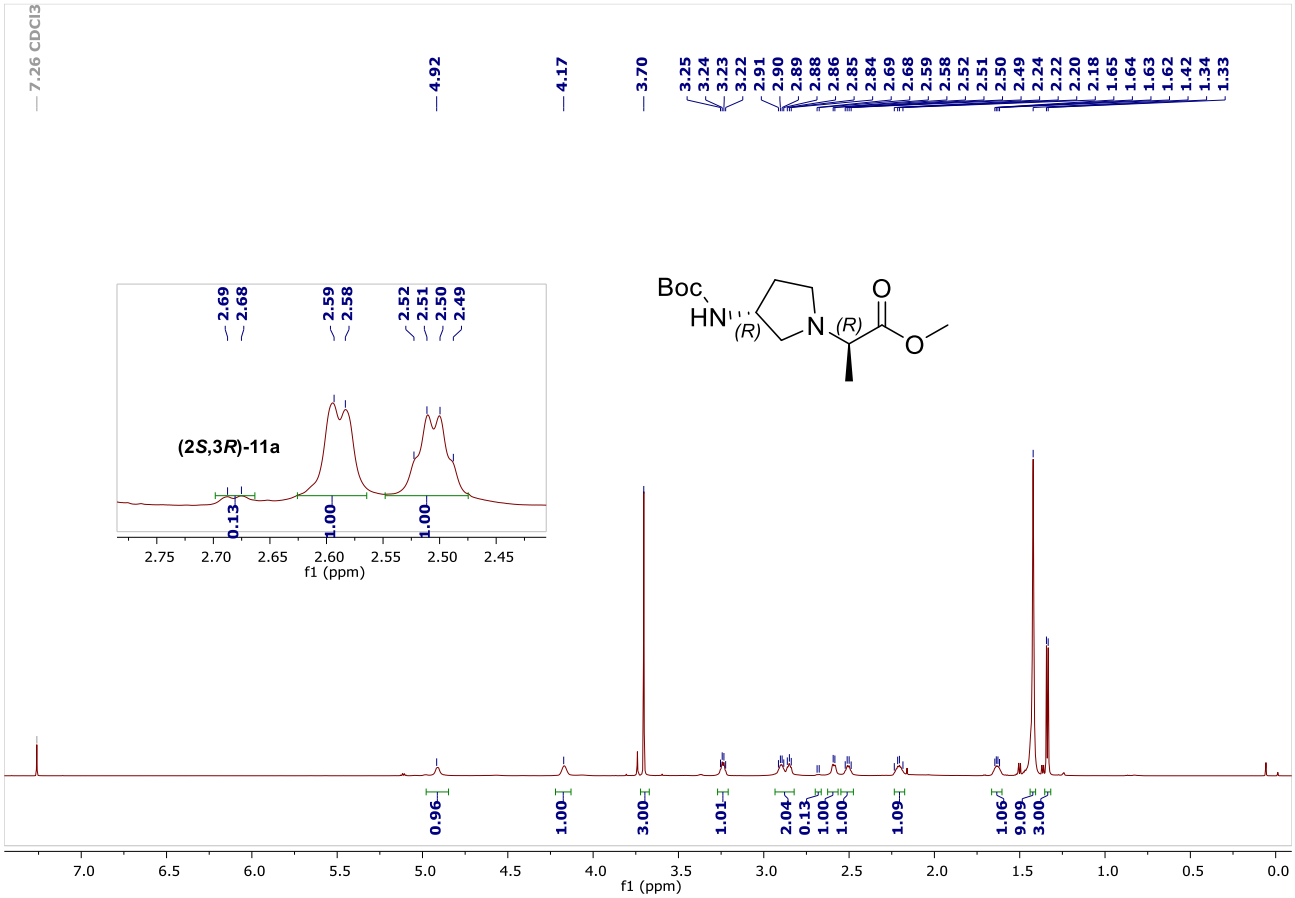


Figure S108. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*R*,3*R*)-11a). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

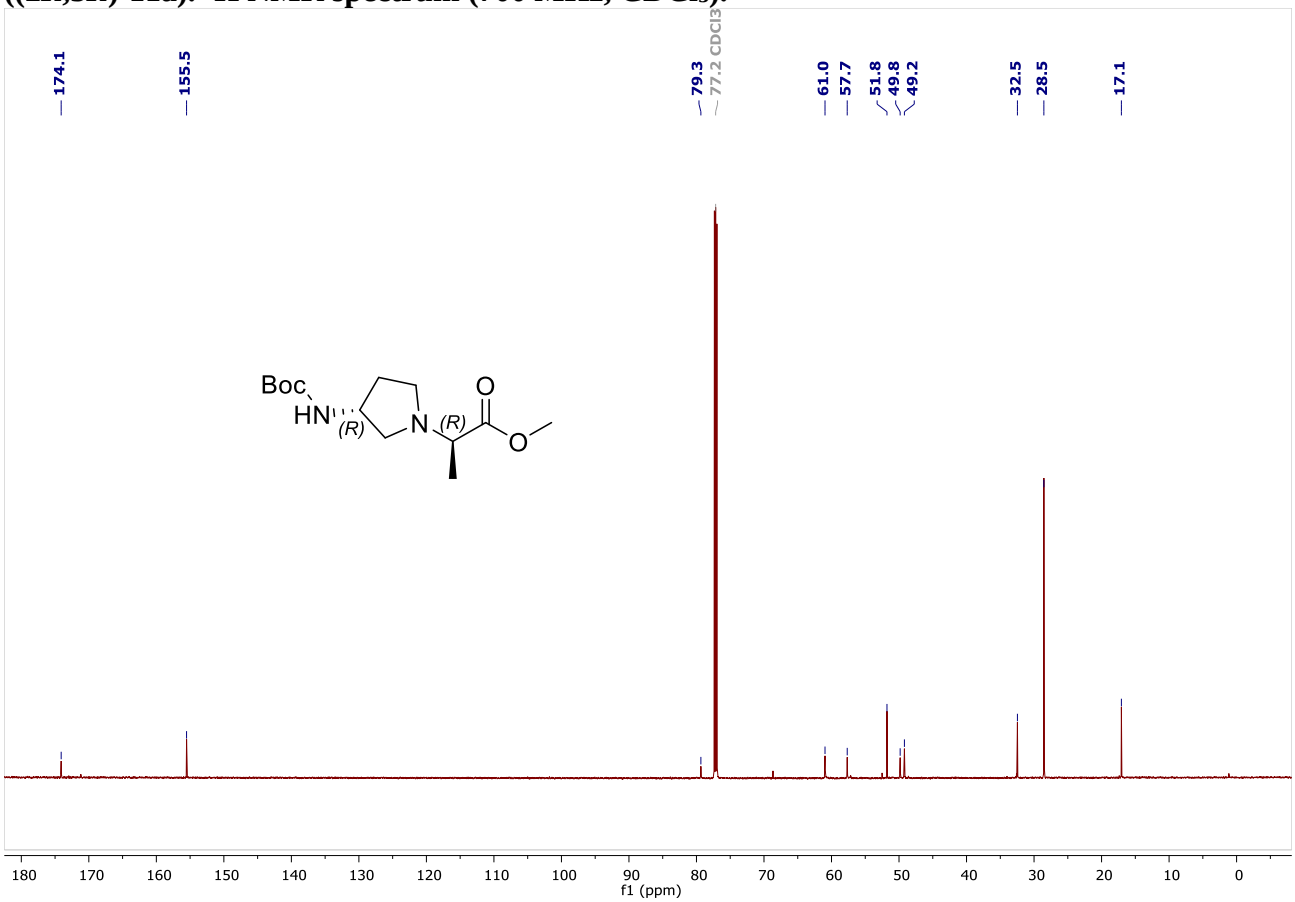


Figure S109. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*R*,3*R*)-11a). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

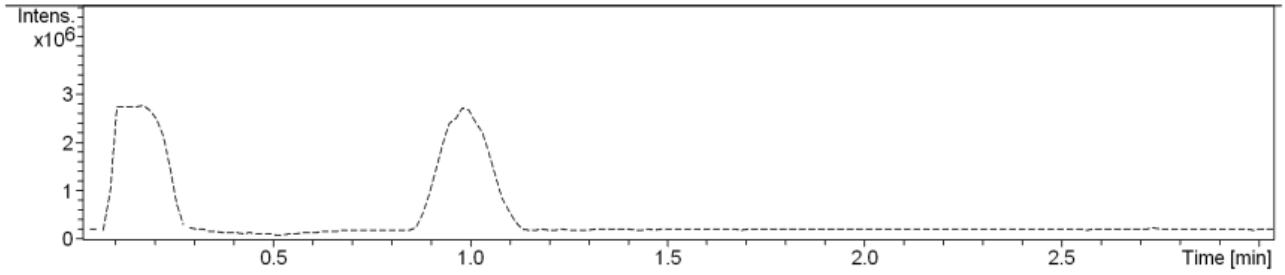
Mass Spectrum SmartFormula Report

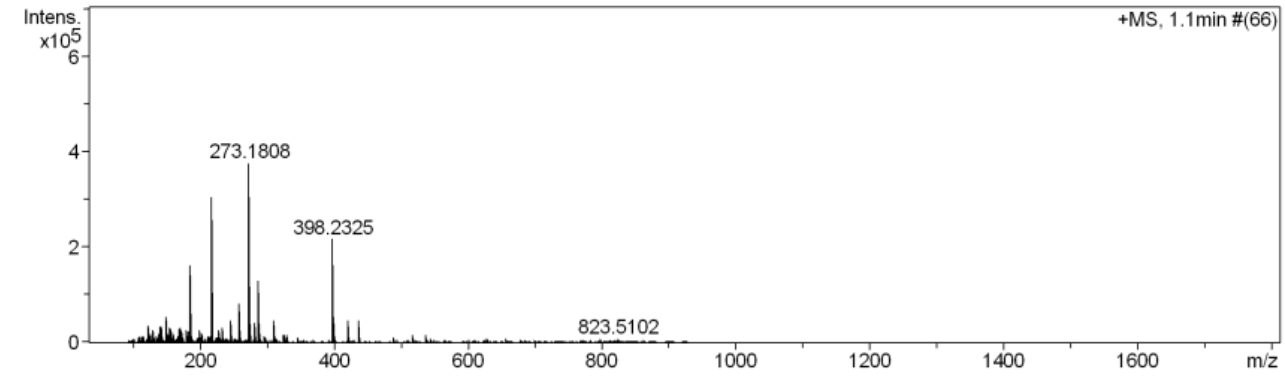
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_476_1-D,5_01_10235.d	Acquisition Date	4/21/2023 2:23:19 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_476	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
273.1808	1	C 13 H 25 N 2 O 4	100.00	273.1809	0.2	0.4	14.7	2.5	even	ok

Figure S110. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}propanoate ((2*R*,3*R*)-11a). HRMS (ESI-TOF).

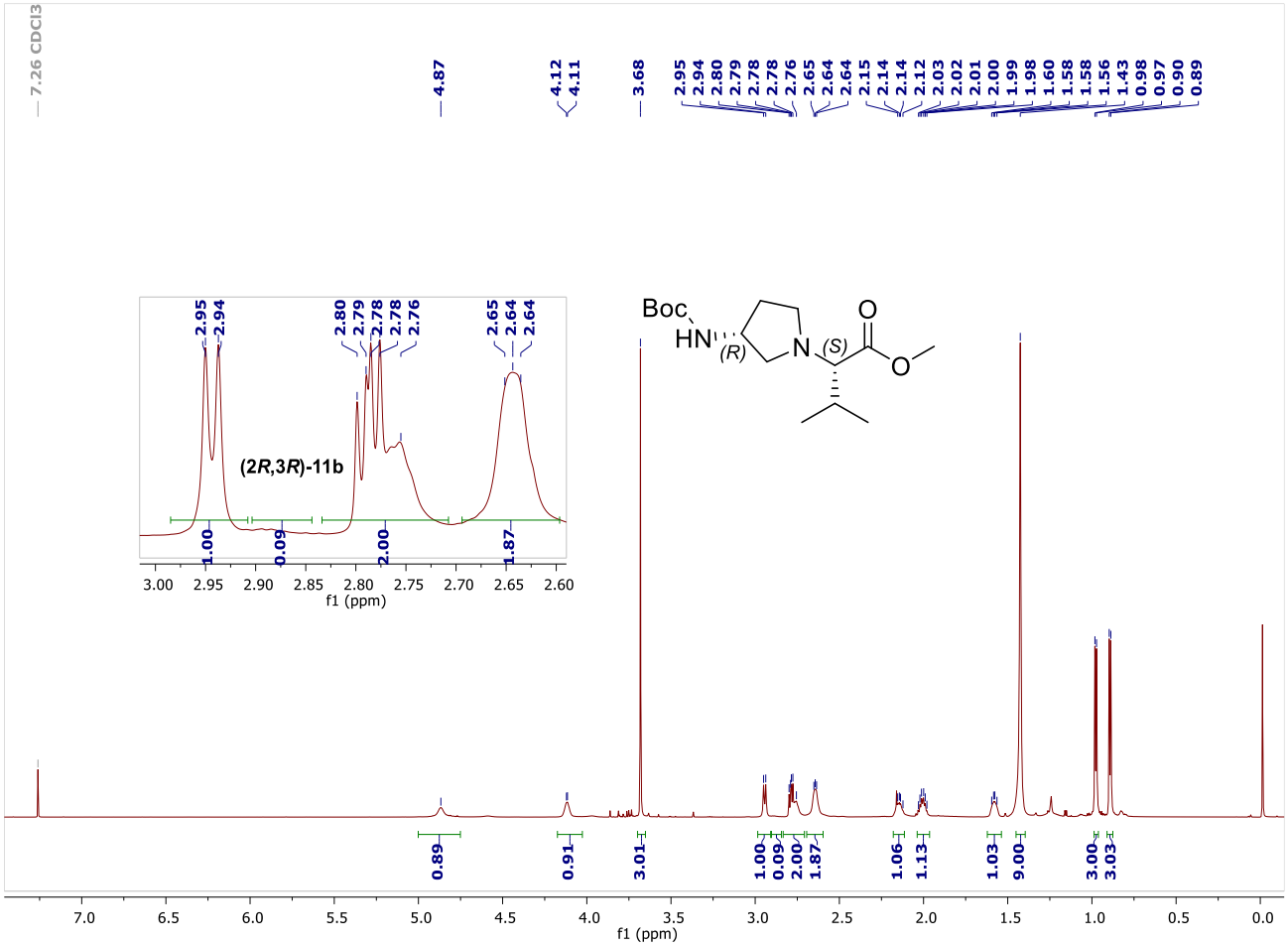


Figure S111. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*S*,3*R*)-11b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

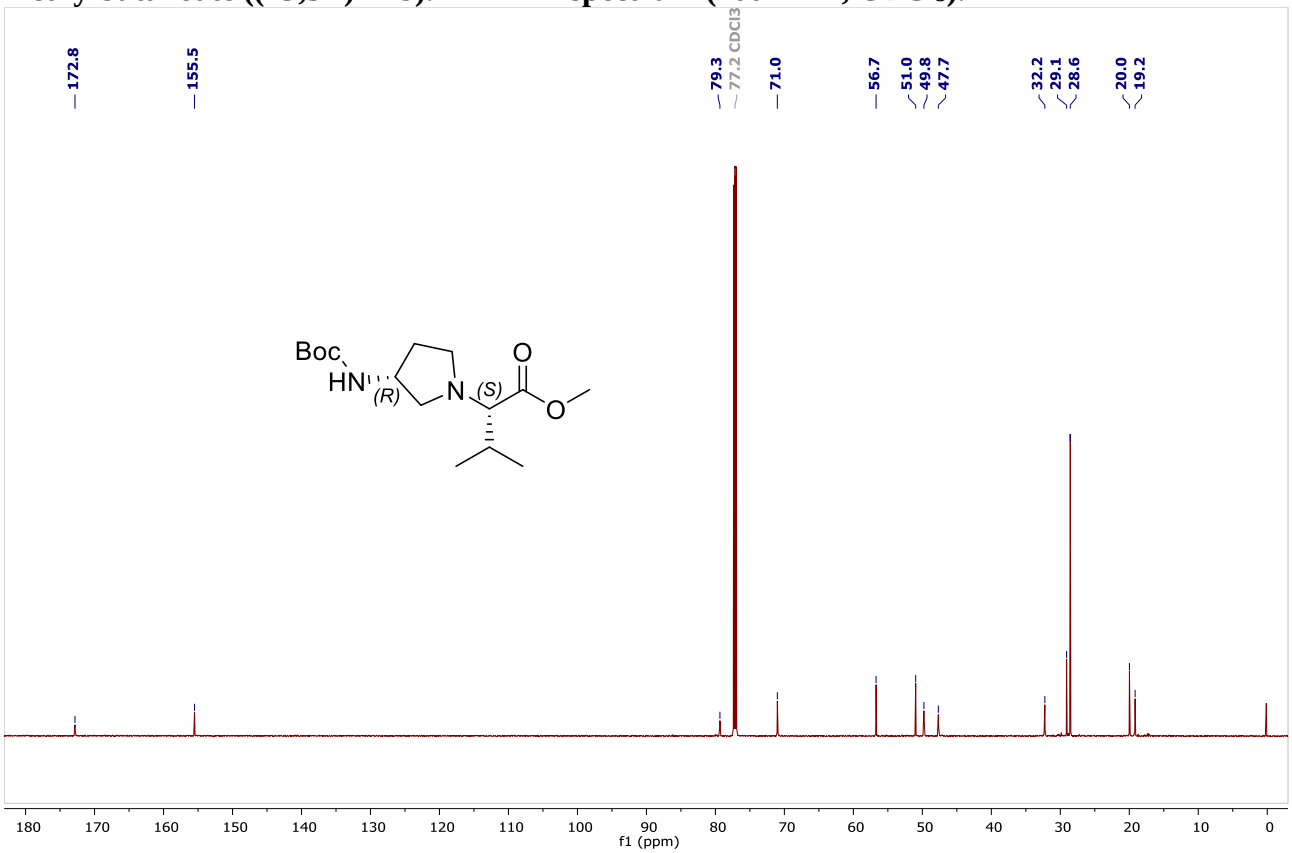


Figure S112. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*S*,3*R*)-11b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

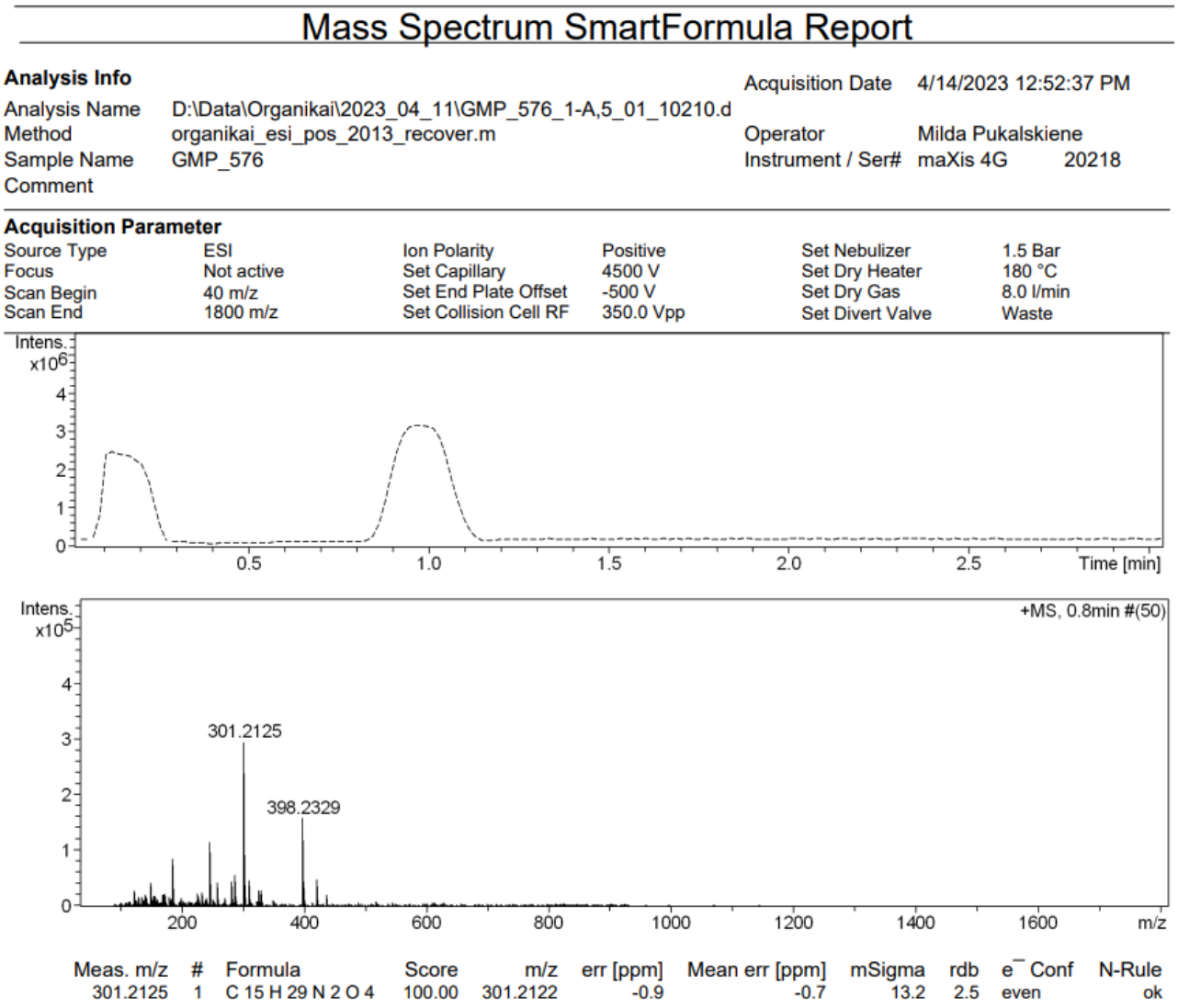


Figure S113. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*S*,3*R*)-11b). HRMS (ESI-TOF).

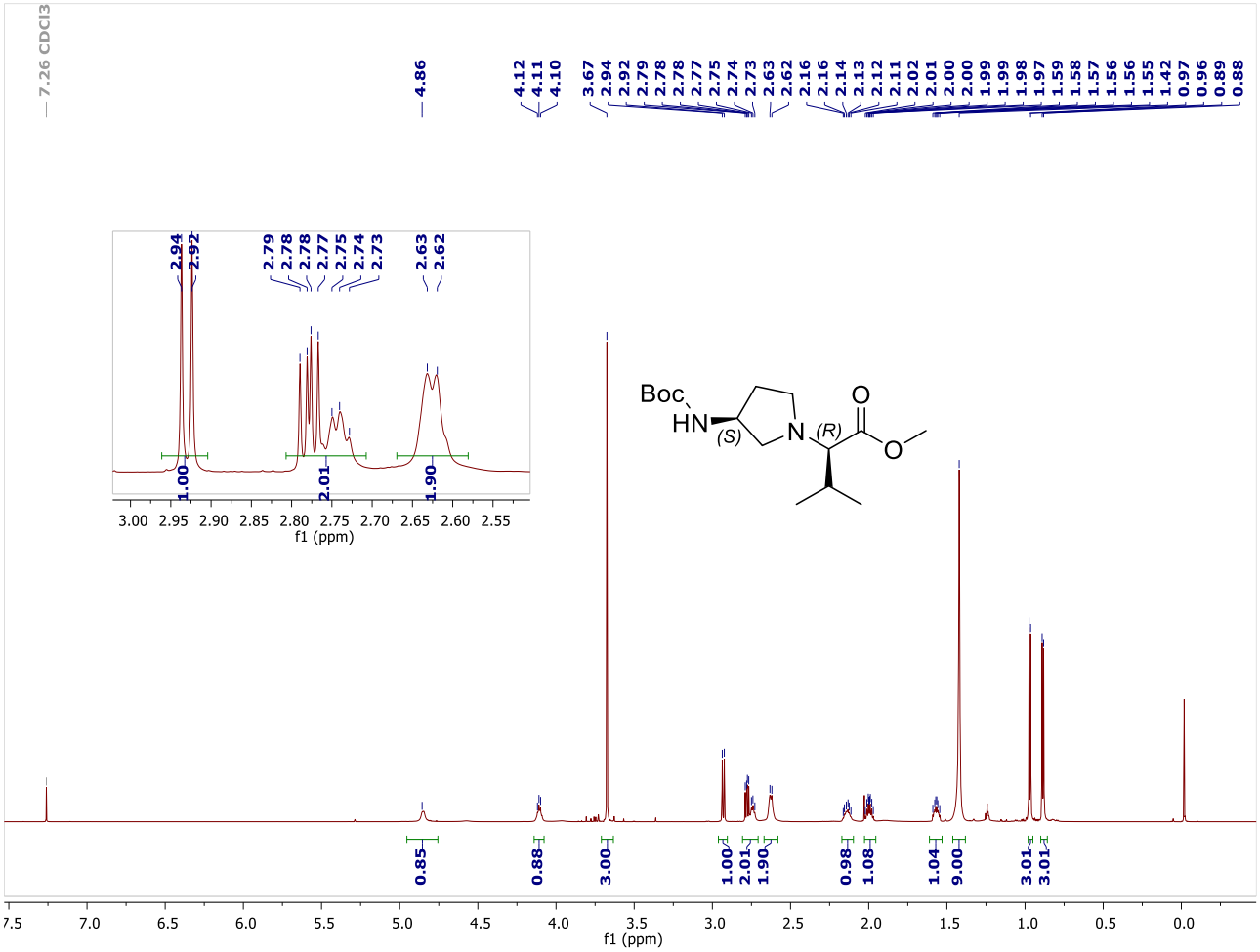


Figure S114. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*R*,3*S*)-11b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

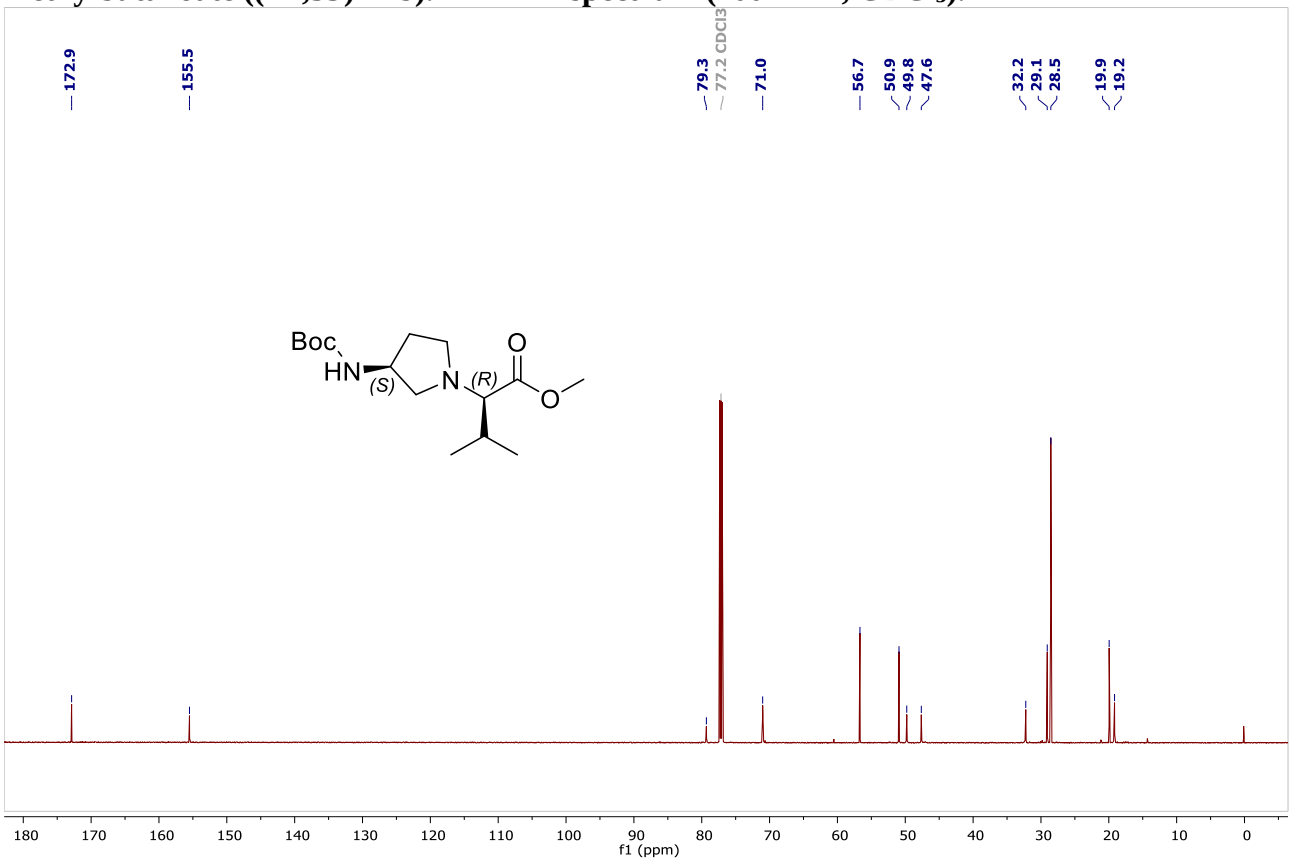


Figure S115. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*R*,3*S*)-11b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

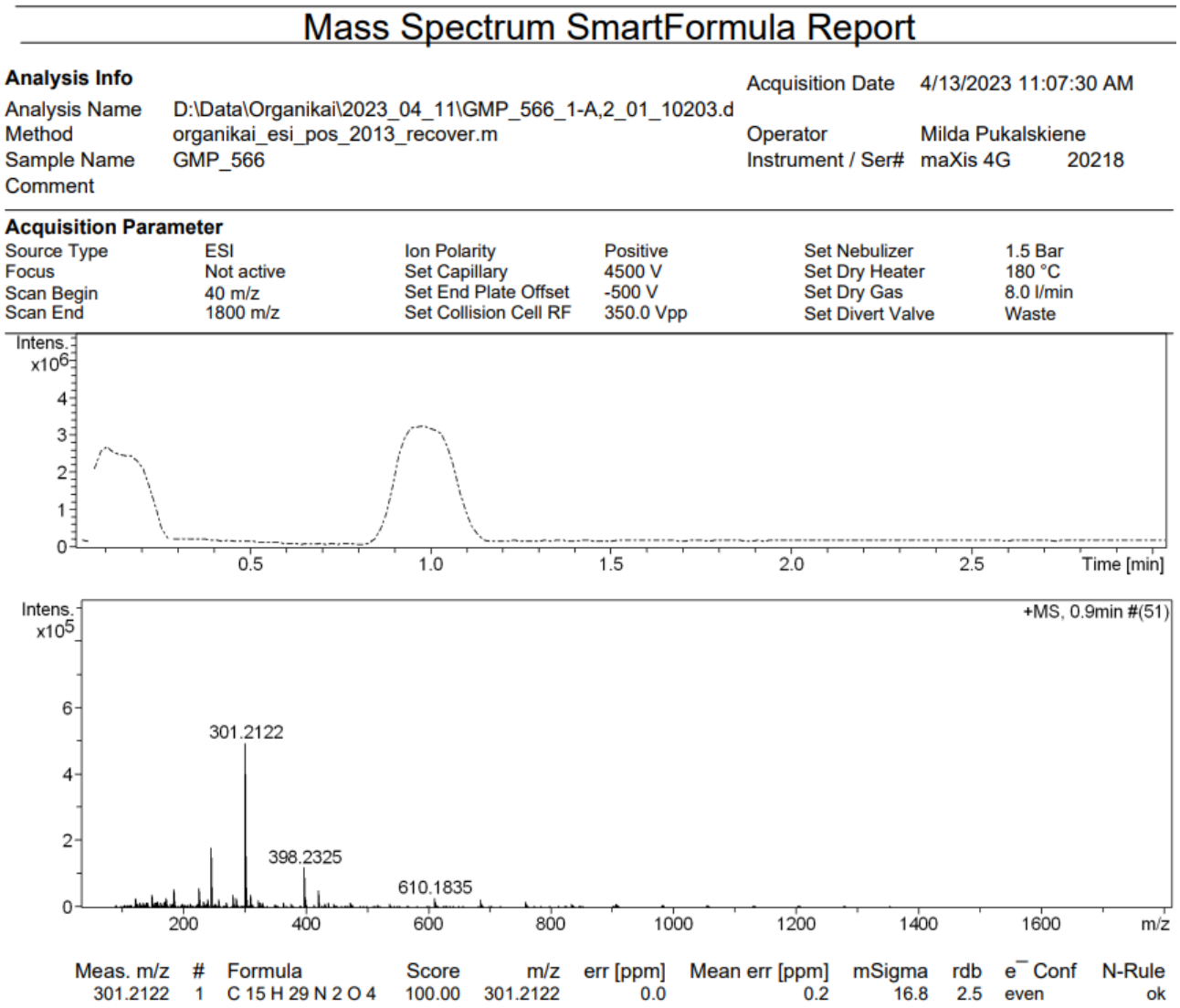


Figure S116. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*R*,3*S*)-11b). HRMS (ESI-TOF).

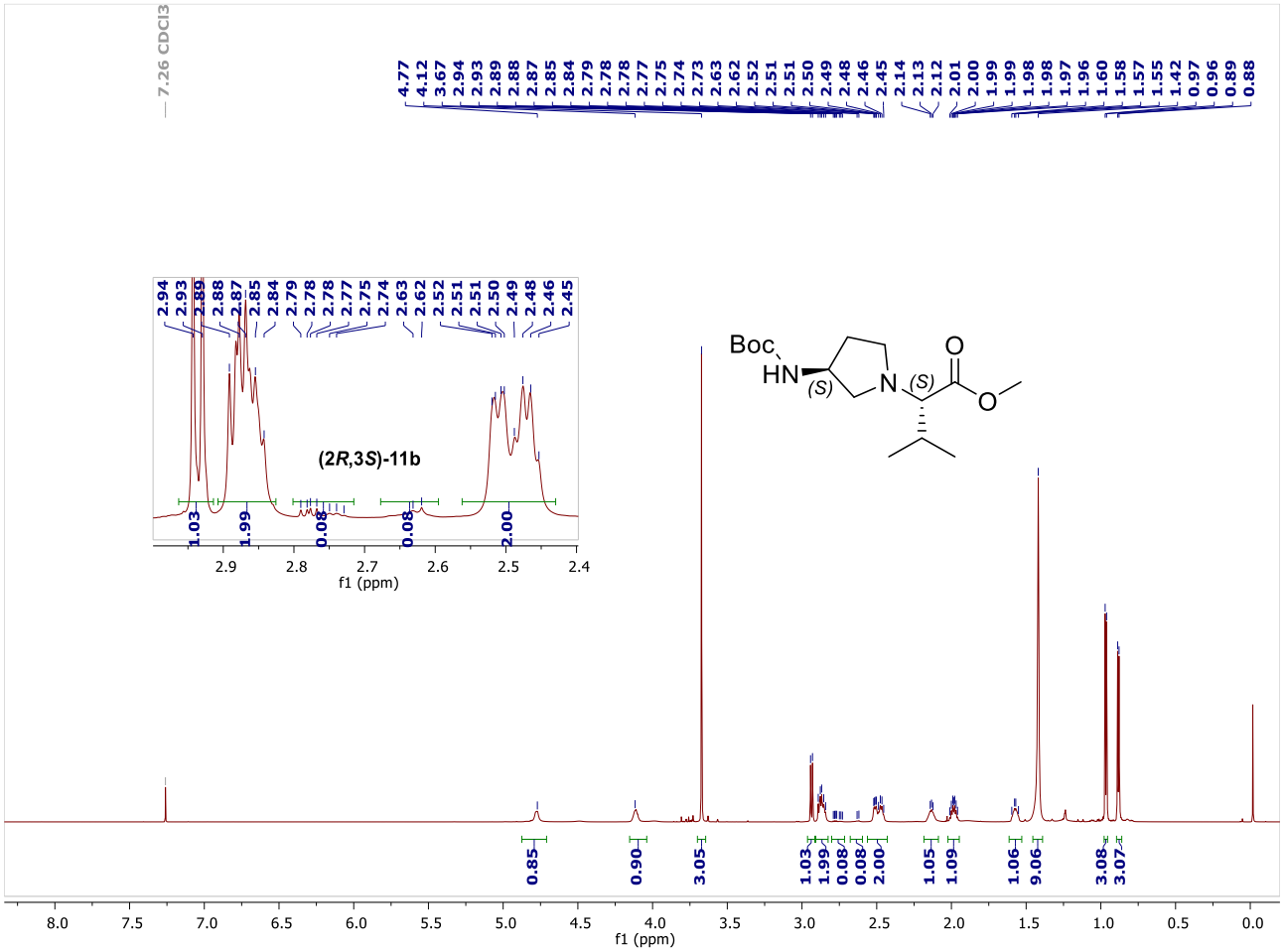


Figure S117. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*S*,3*S*)-11b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

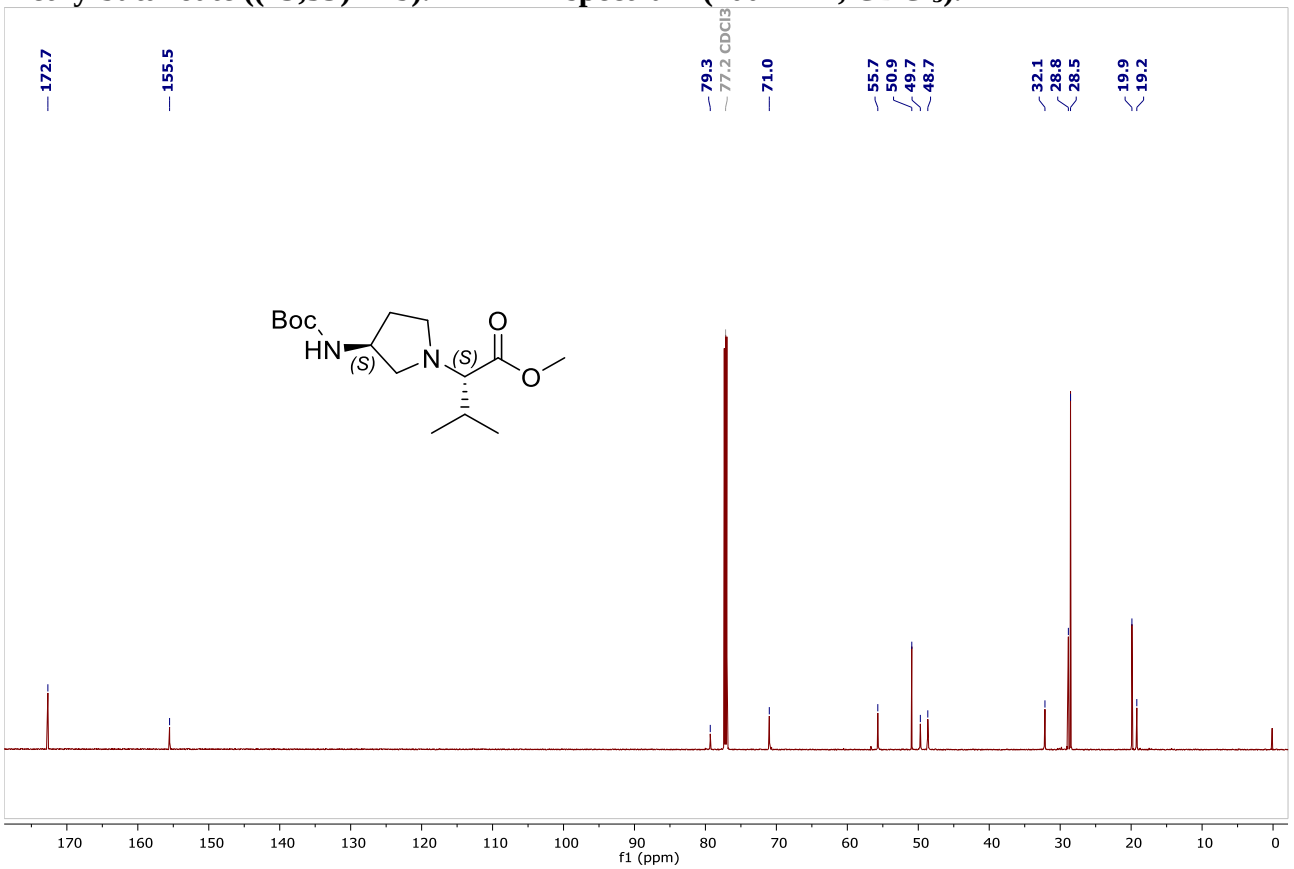


Figure S118. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*S*,3*S*)-11b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

Compound Spectrum SmartFormula Report

Analysis Info

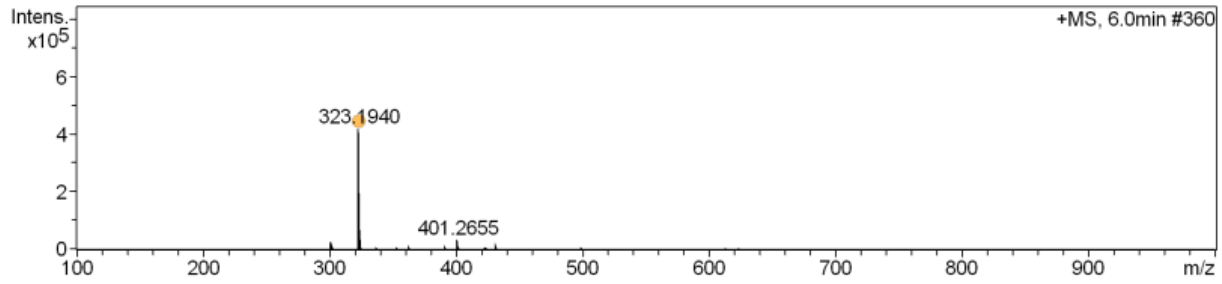
Analysis Name	D:\Data\GMP-569.d	Acquisition Date	5/2/2023 7:57:07 PM
Method	DirectInfusion_TuneLow_pos.m	Operator	hplc
Sample Name	GMP-569	Instrument	micrOTOF-Q III 8228888.20448
Comment	AB		

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.4 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	1000 m/z	Set Collision Cell RF	140.0 Vpp	Set Divert Valve	Waste

#	RT [min]	Area	Int. Type	I	S/N	Chromatogram	Max. m/z	FWHM [min]
n.a.	6.0	n.a.	Single spectrum	n.a.	n.a.	n.a.	323.1940	n.a.

+MS, 6.0min #360



Meas. m/z	#	Ion Formula	m/z	err [ppm]	mSigma	# Sigma	Score	rdb	e¯ Conf	N-Rule
323.1940	1	C15H28N2NaO4	323.1941	-0.5	2.4	1	100.00	2.5	even	ok

Figure S119. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*S*,3*S*)-11b). HRMS (ESI-TOF).

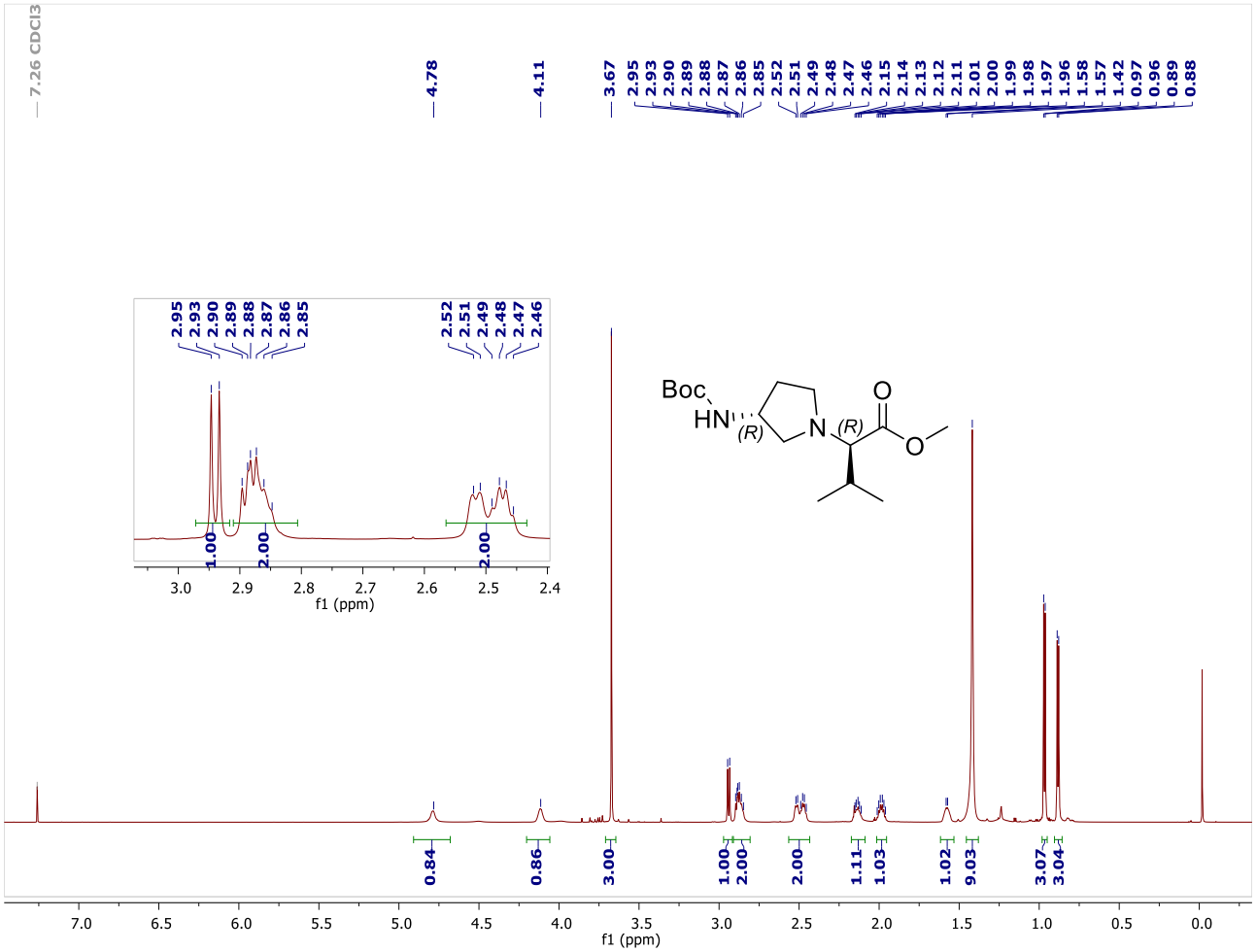


Figure S120. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*R*,3*R*)-11b). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

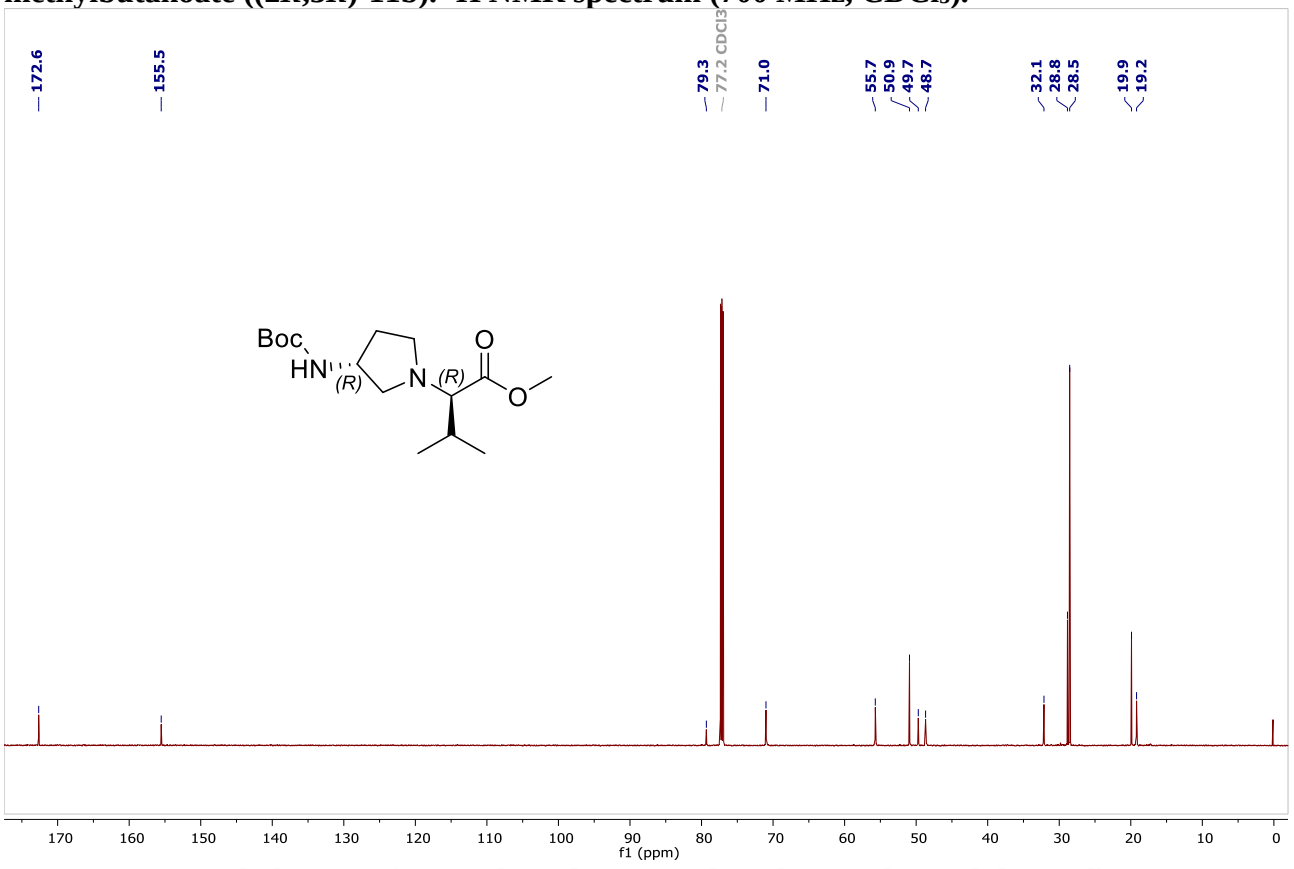


Figure S121. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*R*,3*R*)-11b). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

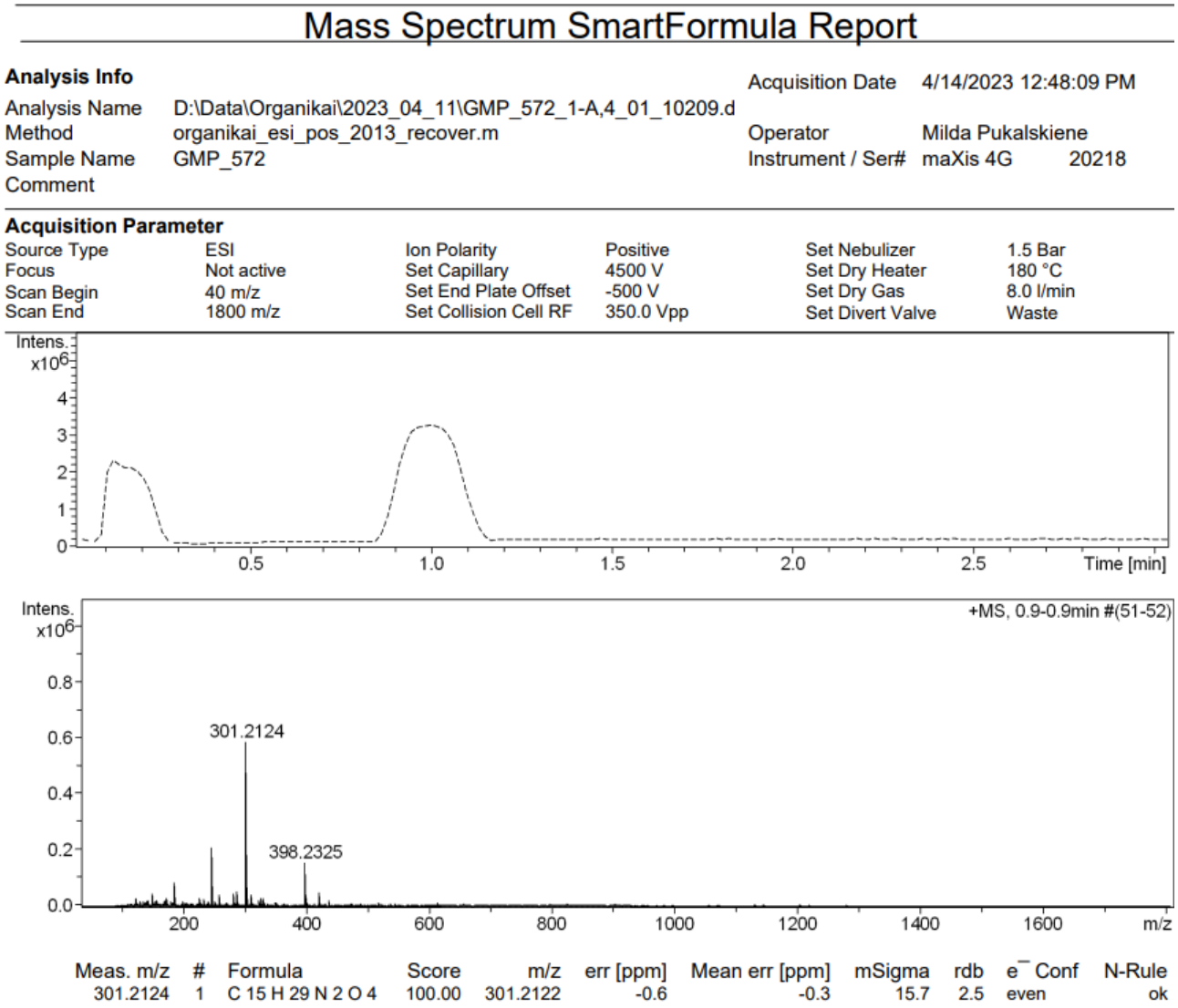


Figure S122. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-3-methylbutanoate ((2*R*,3*R*)-11b). HRMS (ESI-TOF).

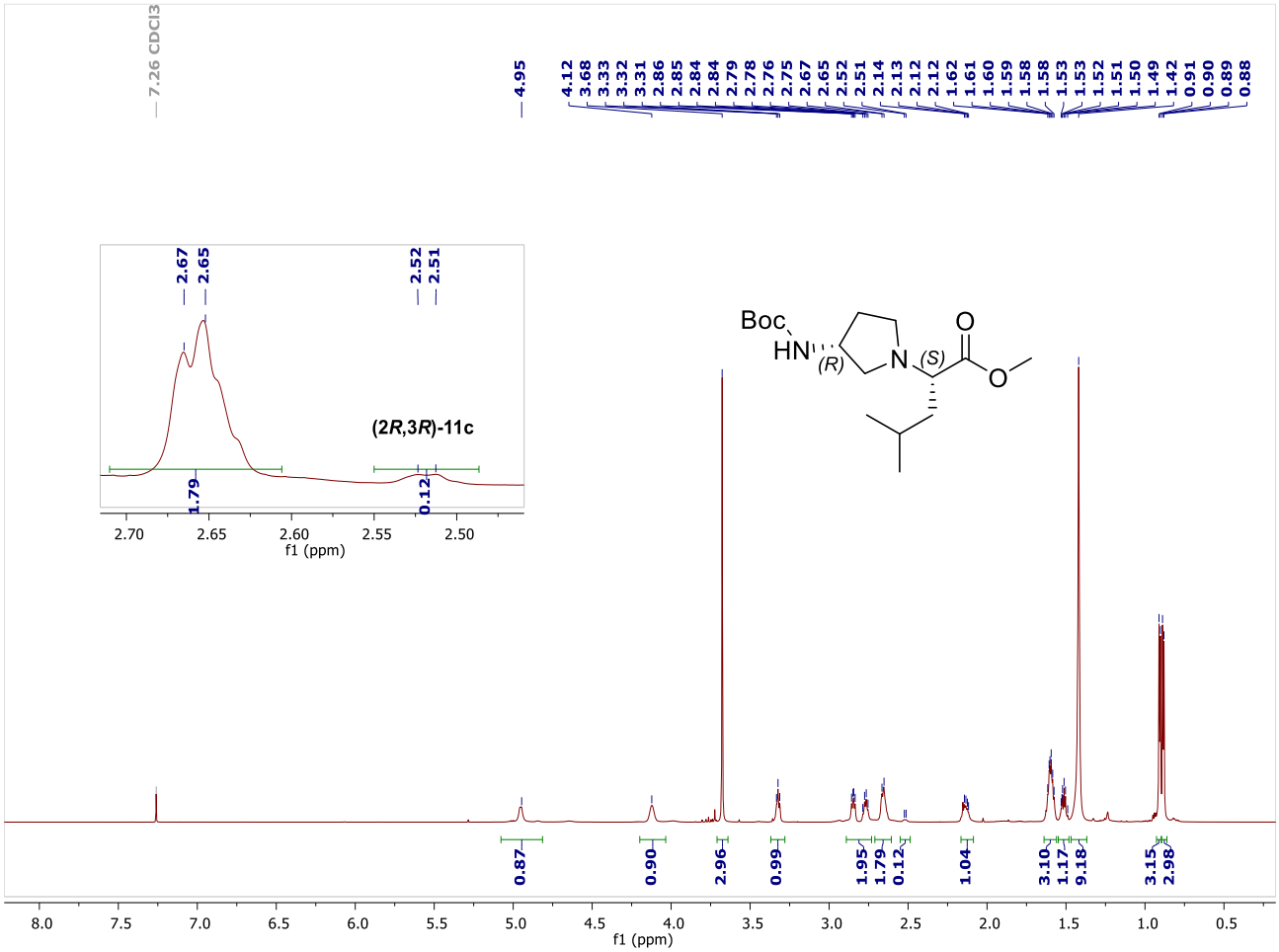


Figure S123. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*S*,3*R*)-11c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

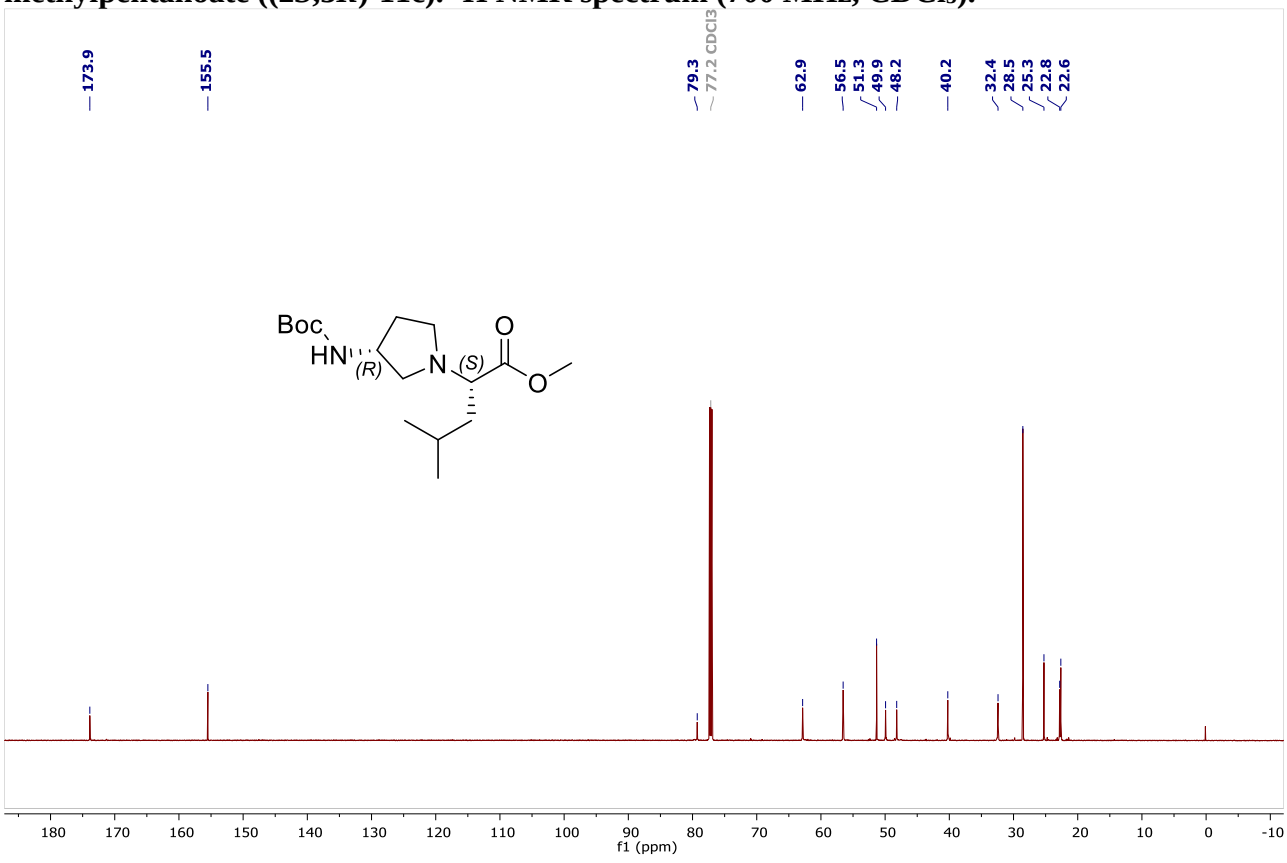


Figure S124. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*S*,3*R*)-11c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

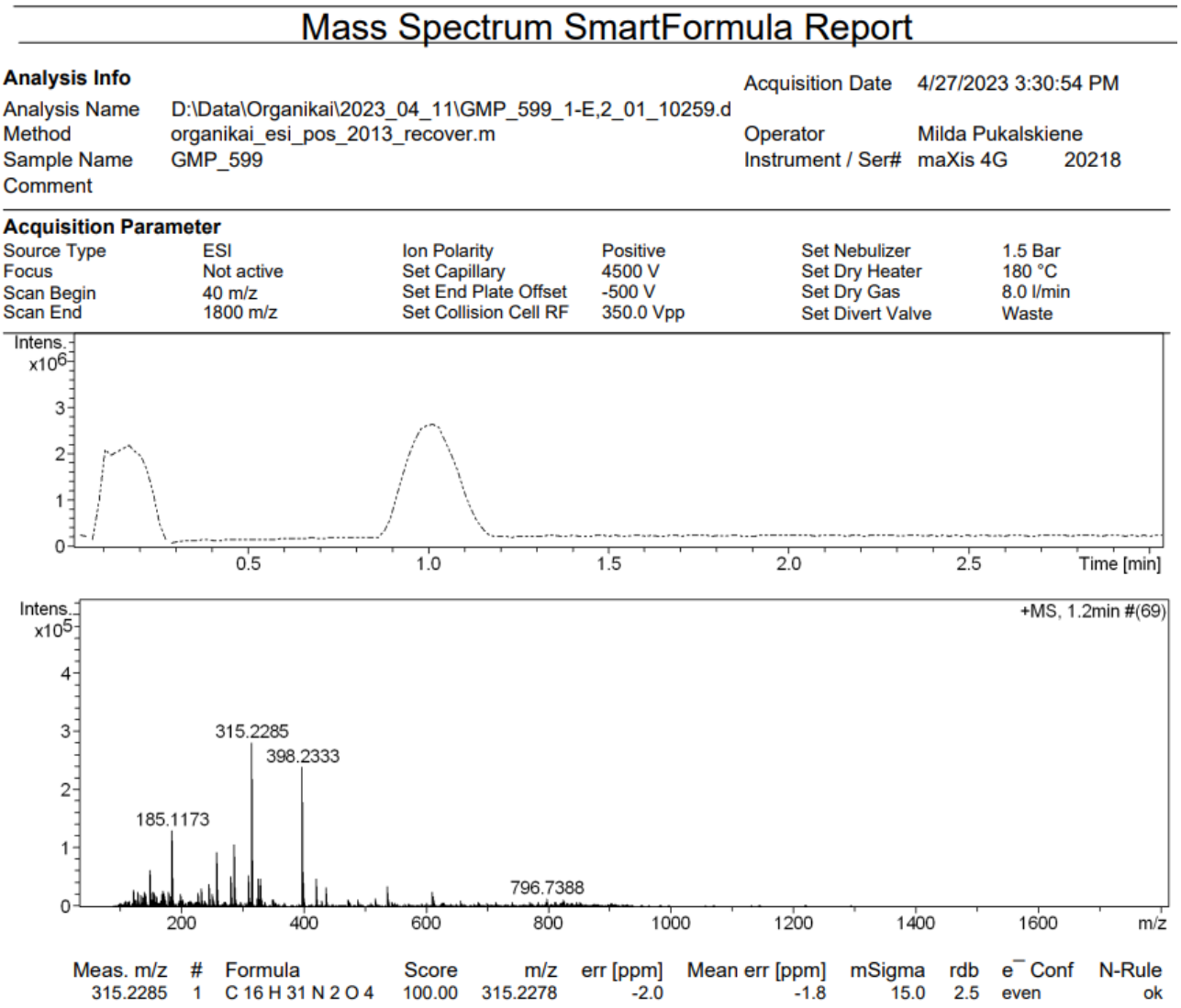


Figure S125. Methyl (2*S*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*S*,3*R*)-11c). HRMS (ESI-TOF).

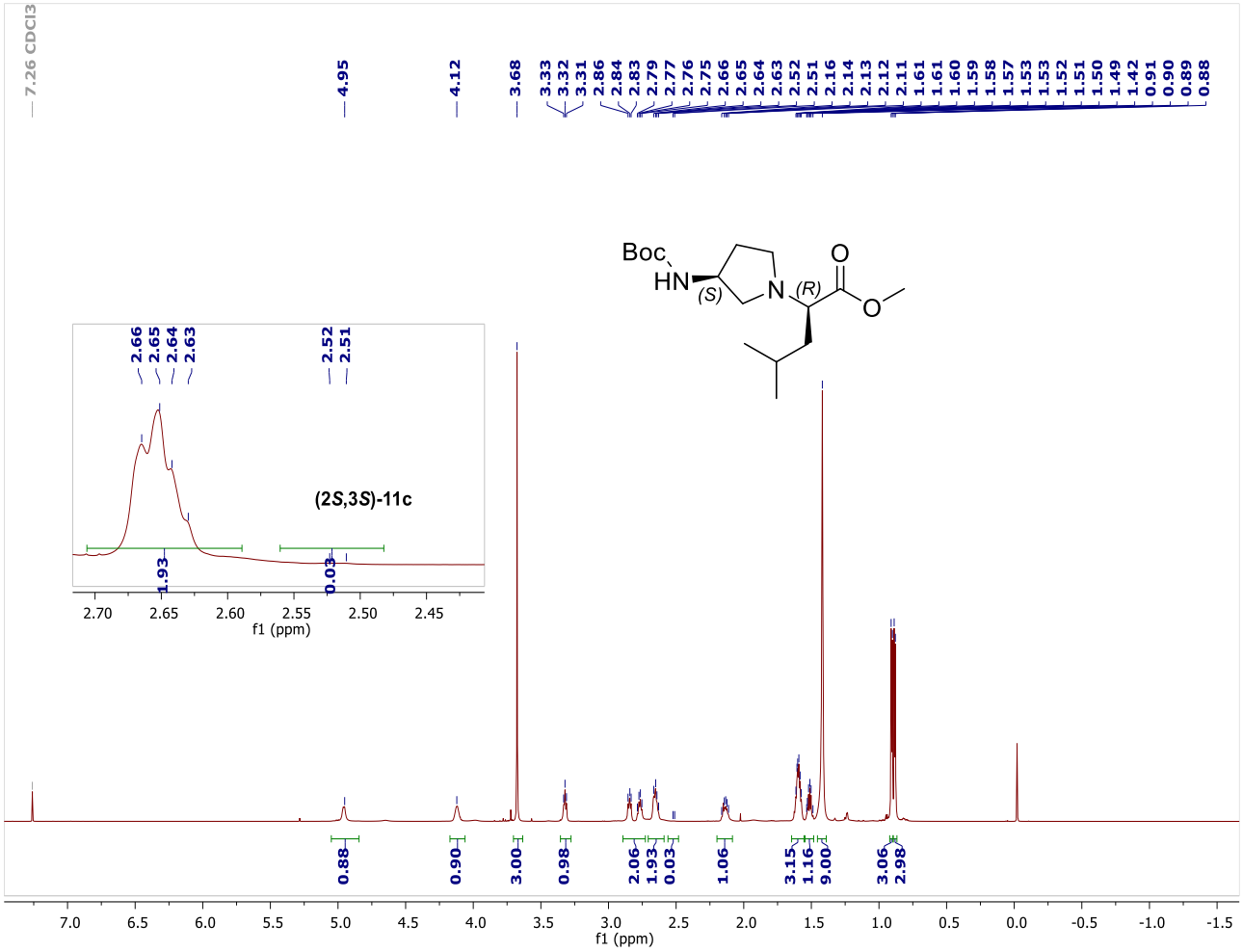


Figure S126. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*R*,3*S*)-11c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

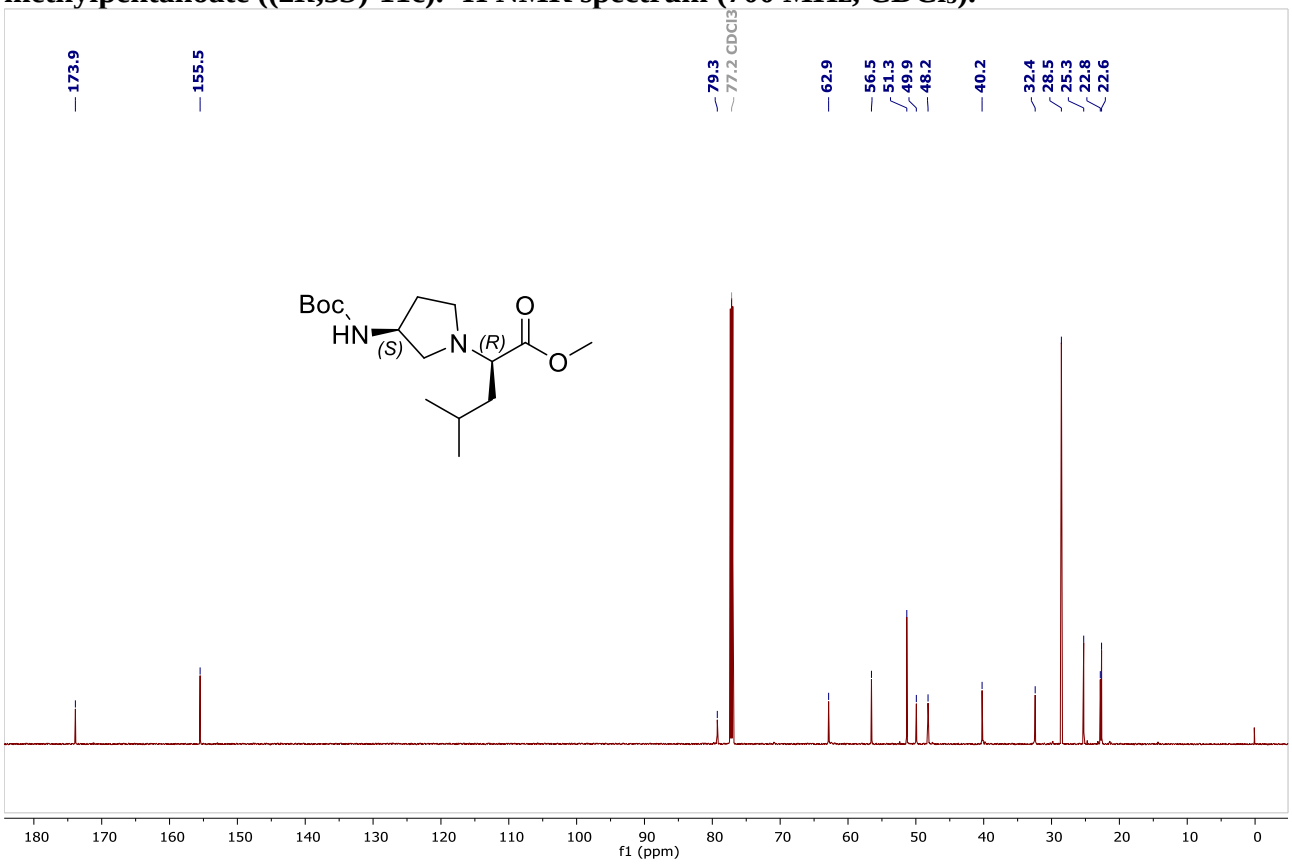


Figure S127. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*R*,3*S*)-11c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

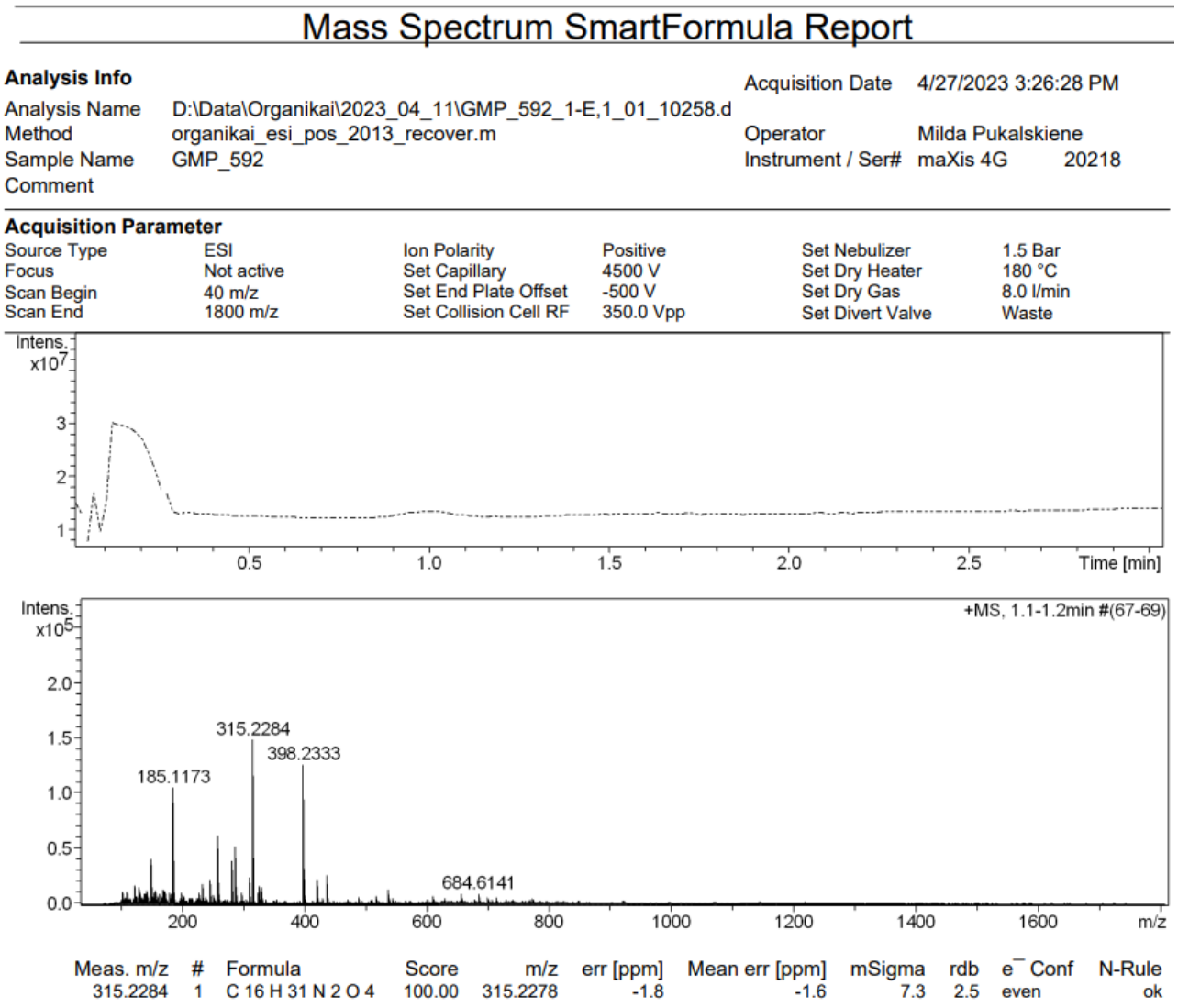


Figure S128. Methyl (2*R*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*R*,3*S*)-11c). HRMS (ESI-TOF).

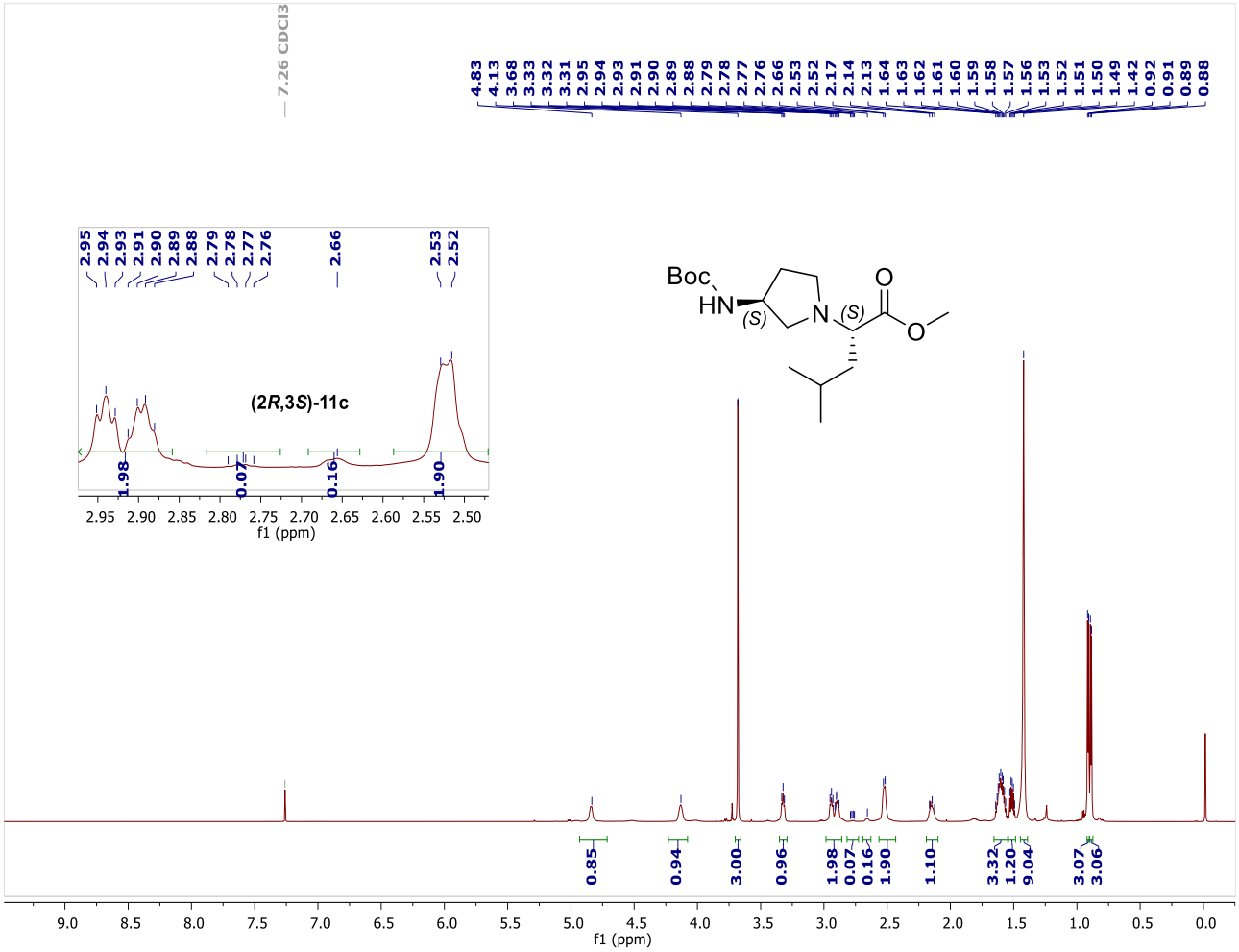


Figure S129. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*S*,3*S*)-11c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

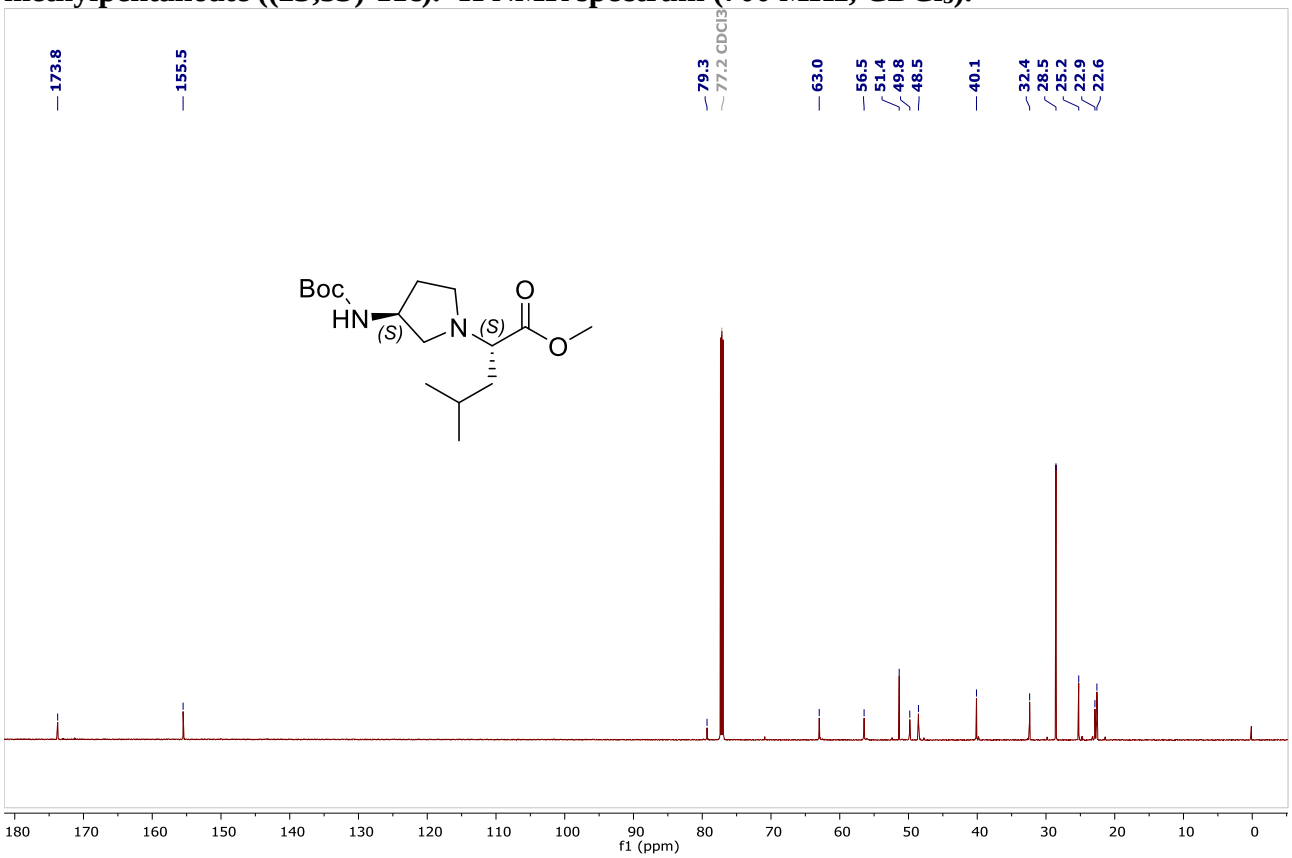


Figure S130. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*S*,3*S*)-11c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

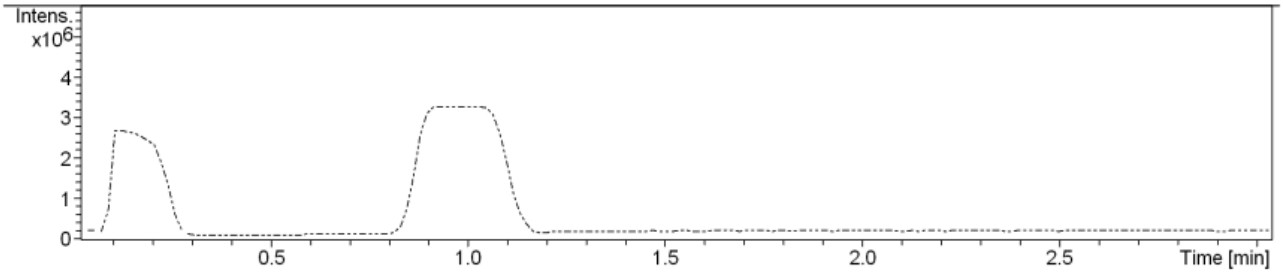
Mass Spectrum SmartFormula Report

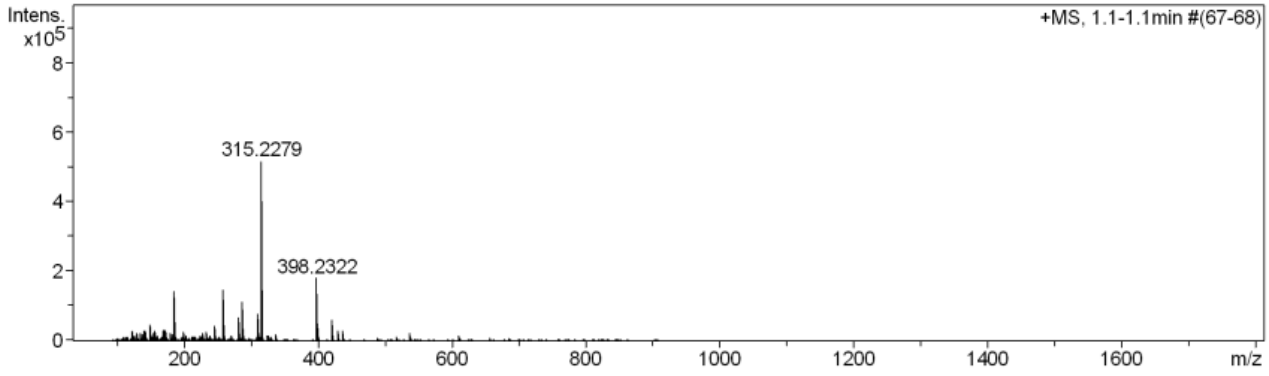
Analysis Info

Analysis Name	D:\Data\Organikai\2023_04_11\GMP_597_1-D,8_01_10238.d	Acquisition Date	4/21/2023 2:36:49 PM
Method	organikai_esi_pos_2013_recover.m	Operator	Milda Pukalskiene
Sample Name	GMP_597	Instrument / Ser#	maXis 4G 20218
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	1.5 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	40 m/z	Set End Plate Offset	-500 V	Set Dry Gas	8.0 l/min
Scan End	1800 m/z	Set Collision Cell RF	350.0 Vpp	Set Divert Valve	Waste





Meas. m/z	#	Formula	Score	m/z	err [ppm]	Mean err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule
315.2279	1	C 16 H 31 N 2 O 4	100.00	315.2278	-0.3	0.1	16.0	2.5	even	ok
	2	C 17 H 27 N 6	41.89	315.2292	4.0	4.3	28.5	7.5	even	ok

Figure S131. Methyl (2*S*)-2-{(3*S*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*S*,3*S*)-11c). HRMS (ESI-TOF).

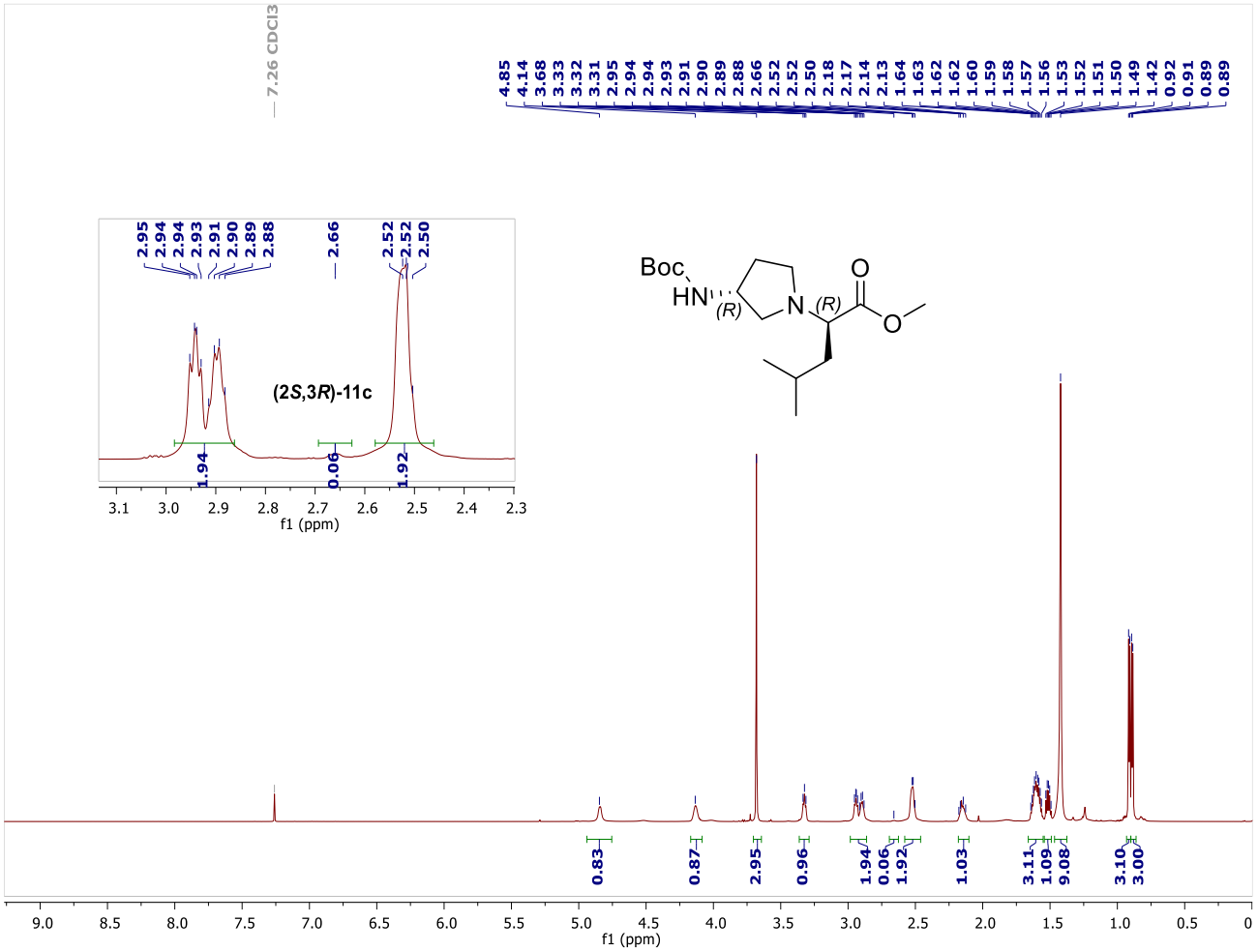


Figure S132. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*R*,3*R*)-11c). ^{1}H NMR spectrum (700 MHz, $CDCl_3$).

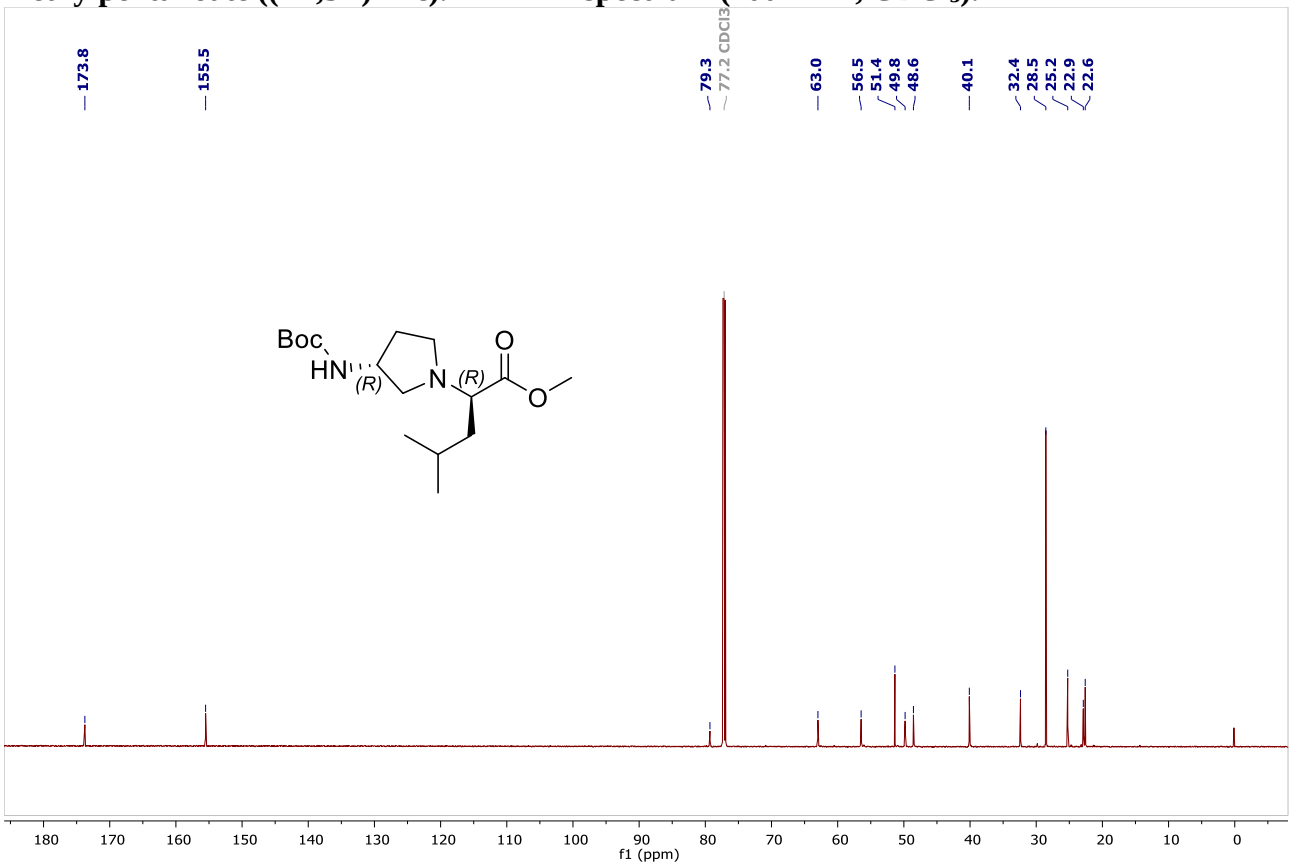


Figure S133. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*R*,3*R*)-11c). ^{13}C NMR spectrum (176 MHz, $CDCl_3$).

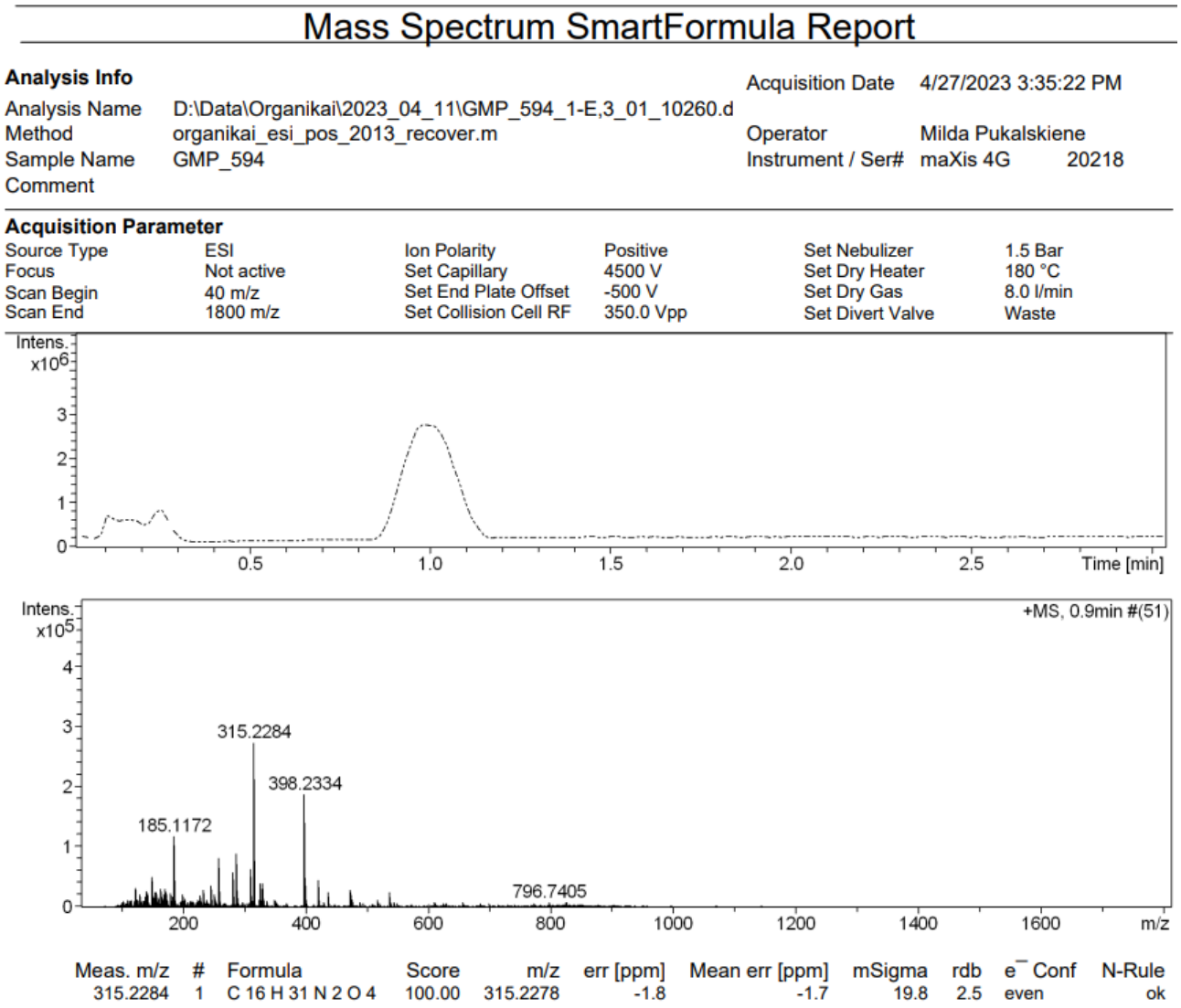


Figure S134. Methyl (2*R*)-2-{(3*R*)-3-[(*tert*-butoxycarbonyl)amino]pyrrolidin-1-yl}-4-methylpentanoate ((2*R*,3*R*)-11c). HRMS (ESI-TOF).

- **X-ray analysis of compound (*S*)-3b:**

Single crystals of $C_{32}H_{60}N_4O_8$ [(***S*)-3b**] were investigated on a Rigaku, XtaLAB Synergy, Dualflex, HyPix diffractometer. The crystal was kept at 150.0(1) K during data collection. Using Olex2 [1], the structure was solved with the ShelXT [2] structure solution program using Intrinsic Phasing and refined with the olex2.refine [3] refinement package using Gauss-Newton minimisation.

Table S1: Experimental parameter and CCDC-2168602.

Sample	**Machine**	**Source**	**Temp.**	**Detector distance**	**Time/ Frame**	**#Frames**	**Frame width**	**CCDC**
			[K]	[mm]	[s]		[°]	
(***S*)-3b**	Rigaku, XtaLAB Synergy, Dualflex, HyPix	μ(Cu Kα) = 0.669mm^{-1}	150	34	1.25	5748	0.50	2168602

Table S2: Sample and crystal data of compound (***S*)-3b**.

Chemical formula	$2(C_{16}H_{30}N_2O_4)$	**Crystal system**	Monoclinic	
Formula weight [g/mol]	628.86	**Space group**	*P2$_1$*	
Temperature [K]	150	**Z**	2	
Measurement method	ϕ and ω scans	**Volume [Å^3]**	1805.08(5)	
Radiation vawelength [Å]	1.54184	**Unit cell dimensions [Å^3] and [°]**	10.0924(2) 12.8242(2) 14.0647(2)	90 97.425(2) 90
Crystal size/ [mm^3]	0.17 × 0.11 × 0.08			
Crystal habit	Block, colourless			
Density (calculated)/ [g/cm^3]	1.1569	**Absorption coefficient [mm^{-1}]**	0.669	
Abs. Correction T$_{min}$	0.859	**Abs. Correction T$_{max}$**	0.961	
Abs. Correction type	multi-scan *CrysAlis PRO* 1.171.40.35a (Rigaku Oxford Diffraction, 2018) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.	**F(000) [e$^-$]**	688	

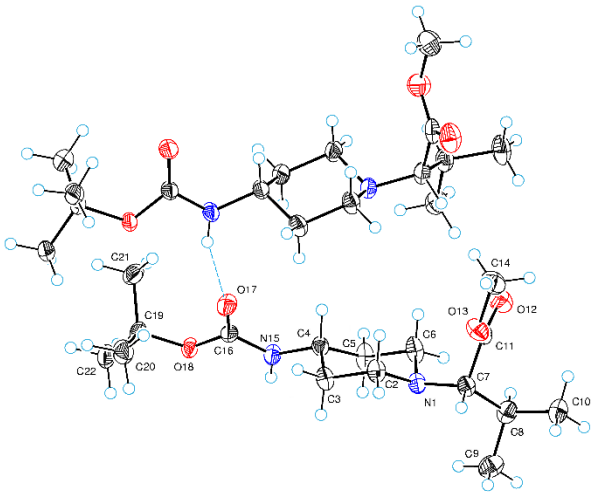


Figure S135. ORTEP view of assymetric unit of crystal (***S***)-**3b**.

Table S3: Data collection and structure refinement of compound (***S***)-**3b**.

Index ranges	$-12 \leq h \leq 12$ $-16 \leq k \leq 13$ $-17 \leq l \leq 17$	**2θ range for data collection [°]**	155.0	
Reflections numbers	37496	**Data / restraints / parameters**	6342/1/417	
Refinement method	Least squares matrix: full	**Final R indices**	All data	R1 = 0.0316; wR2 = 0.0840
Function minimized	$\Sigma w[\lvert Fo \rvert^2 - (1/k)\lvert Fc \rvert^2]$		$I > 2\sigma(I)$	R1 = 0.0309; wR2 = 0.0835
Goodness-of-fit on F_2	1.052	**Weighting scheme**	$w = 1/[\sigma^2(F_o^2) + (0.052P)^2 + 0.1876P]$ where $P = (F_o^2 + 2F_c^2)/3$	
Largest diff. peak and hole [e Å^{-3}]	+0.20 and -0.12	**Flack's *x* parameter**	0.04(9)	

- **X-ray analysis of compound (*R*)-3b:**

Single crystals of $C_{32}H_{60}N_4O_8$ [(***R***)-**3b**] were investigated on a Rigaku, XtaLAB Synergy, Dualflex, HyPix diffractometer. The crystal was kept at 150.0(1) K during data collection. Using Olex2 [1], the structure was solved with the ShelXT [2] structure solution program using Intrinsic Phasing and refined with the olex2.refine [3] refinement package using Gauss-Newton minimisation.

Table S4: Experimental parameter and CCDC-2168596

Sample	**Machine**	**Source**	**Temp.**	**Detector distance**	**Time/ Frame**	**#Frames**	**Frame width**	**CCDC**
			[K]	[mm]	[s]		[°]	
(***R***)-**3b**	Rigaku, XtaLAB Synergy, Dualflex, HyPix	μ(Cu Kα) = 0.669 mm^{-1}	150	34	1.25	5748	0.50	2168596

Table S5: Sample and crystal data of compound (***R***)-**3b**.

Chemical formula	$2(C_{16}H_{30}N_2O_4)$	**Crystal system**	Monoclinic	
Formula weight [g/mol]	628.86	**Space group**	*$P2_1$*	
Temperature [K]	150	**Z**	2	
Measurement method	ϕ and ω scans	**Volume [$Å^3$]**	1802.25(4)	
Radiation vawelength [Å]	1.54184	**Unit cell dimensions [$Å^3$] and [°]**	10.0869(1) 12.8088(2) 14.0693(2)	90 97.4889(12) 90
Crystal size/ [mm^3]	0.18 × 0.11 × 0.08			
Crystal habit	Colourless block			
Density (calculated)/ [g/cm^3]	1.1587	**Absorption coefficient [mm^{-1}]**	0.670	
Abs. Correction T_{min}	0.872	**Abs. Correction T_{max}**	0.960	
Abs. Correction type	multi-scan *CrysAlis PRO* 1.171.40.35a (Rigaku Oxford Diffraction, 2018) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.	**F(000) [e^-]**	688	

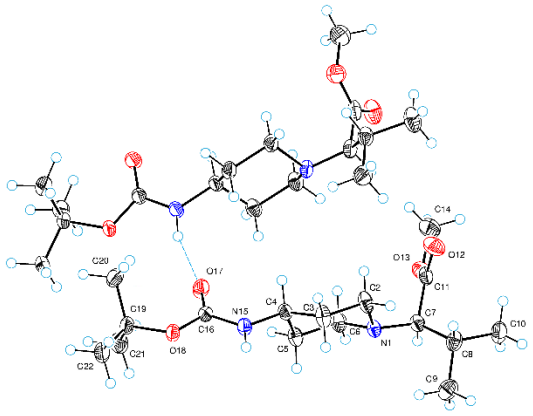


Figure S136. ORTEP view of assymetric unit of crystal (***R***)-**3b**.

Table S6: Data collection and structure refinement of compound (***R***)-**3b**.

Index ranges	$-12 \leq h \leq 9$ $-16 \leq k \leq 16$ $-17 \leq l \leq 17$	**2θ range for data collection [°]**	155.0	
Reflections numbers	22287	**Data / restraints / parameters**	7121/1/417	
Refinement method	Least squares matrix: full	**Final R indices**	All data	R1 = 0.0314; wR2 = 0.0818
Function minimized	$\Sigma w[\lvert Fo \rvert^2 - (1/k)\lvert Fc \rvert^2]$		$I > 2\sigma(I)$	R1 = 0.0306; wR2 = 0.0804
Goodness-of-fit on F2	1.051	**Weighting scheme**	$w = 1/[\sigma^2(F_o^2) + (0.0P)^2 + 0.2072P]$ where $P = (F_o^2 + 2F_c^2)/3$	
Largest diff. peak and hole [e Å^{-3}]	+0.14 and -0.19	**Flack's *x* parameter**	0.06(8)	

- **Examples of unsuccessful HPLC analysis**

Analysis were performed using Shimadzu LC2030C chromatograph with chiral columns and water + 0.1% formic acid / acetonitrile (various gradient conditions).

Table S7. Experimental parameter.

Mobile phase	A – Acetonitrile B – Water + 0.1% formic acid
Temperature	36 °C
Flow rate	1 mL/min
Detection	UV (254, 210 nm); ELSD (Evaporative light scattering detector)
Injection	10 µL
Sample	Dissolved in methanol

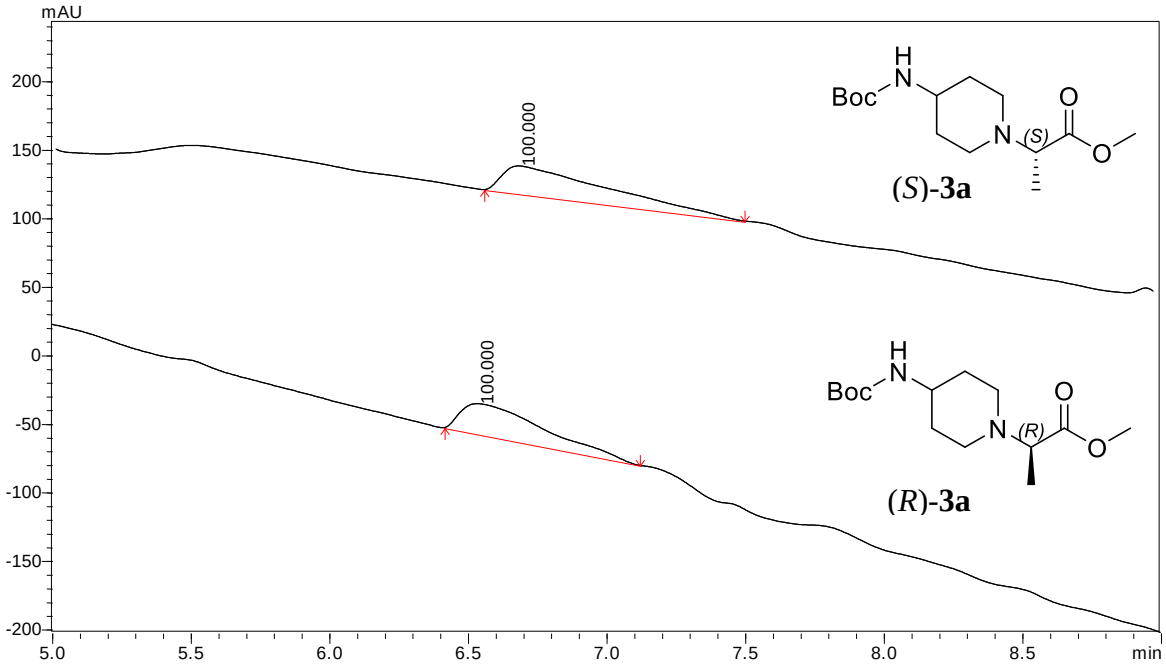


Figure S137. Unsuccessful chiral HPLC analysis of compounds (*S*)-**3a** and (*R*)-**3a**. Separation was carried out on YMC chiral column CHIRAL NEA (R), gradient conditions water + 0.1% formic acid / acetonitrile 90:10 to 20:80 in 15 minutes. UV detector, 210 nm.

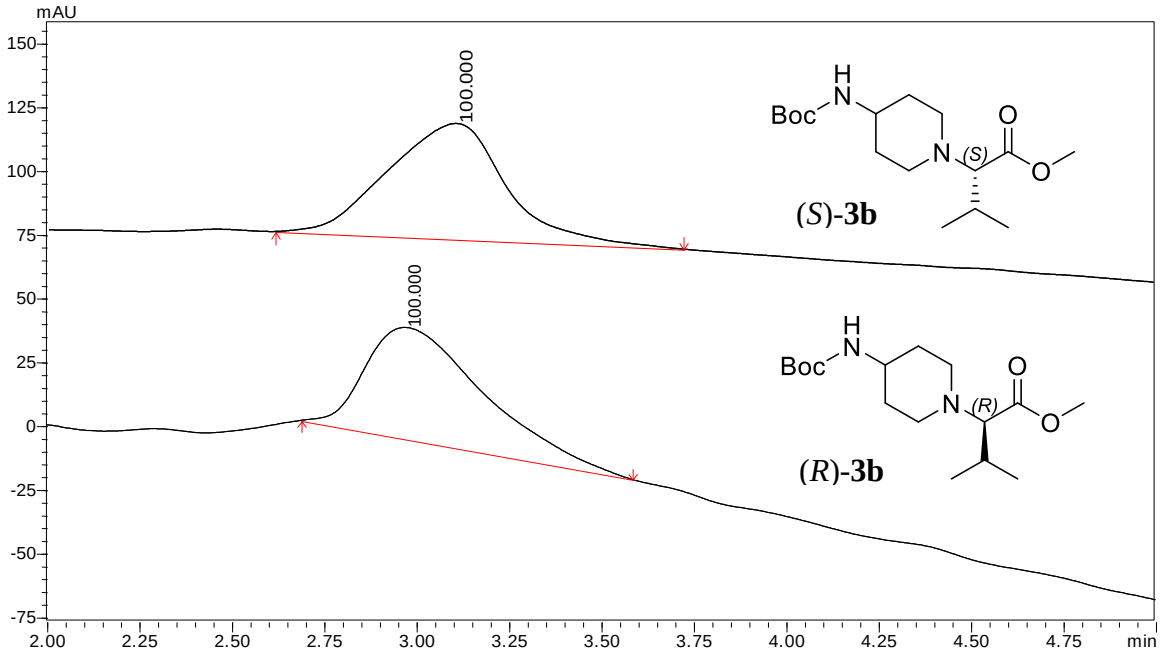


Figure S138. Unsuccessful chiral HPLC analysis of compounds (*S*)-**3b** and (*R*)-**3b**. Separation was carried out on chiral column CHIRAL ART Cellulose-SB, gradient conditions: water + 0.1% formic acid / acetonitrile 90:10 to 60:40 in 12 minutes. UV detector, 210 nm.

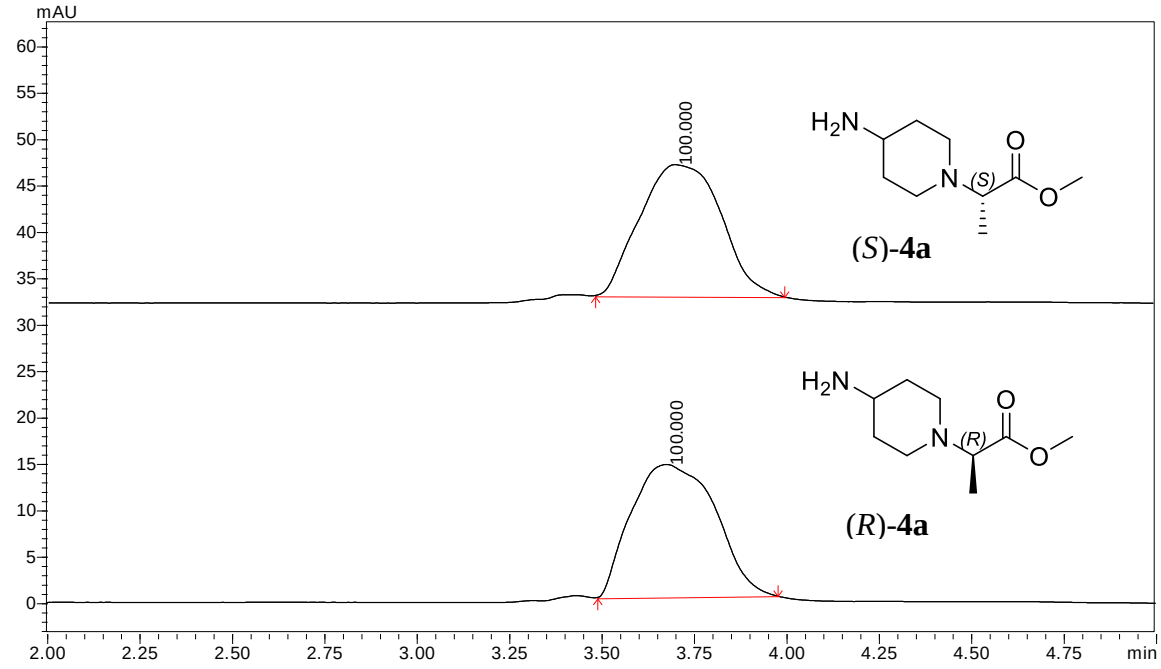


Figure S139. Unsuccessful chiral HPLC analysis of compounds (*S*)-**4a** and (*R*)-**4a**. Separation was carried out on YMC chiral column CHIRAL NEA (R), gradient conditions: water + 0.1% formic acid / acetonitrile 90:10 to 20:80 in 15 minutes. UV detector, 254 nm.

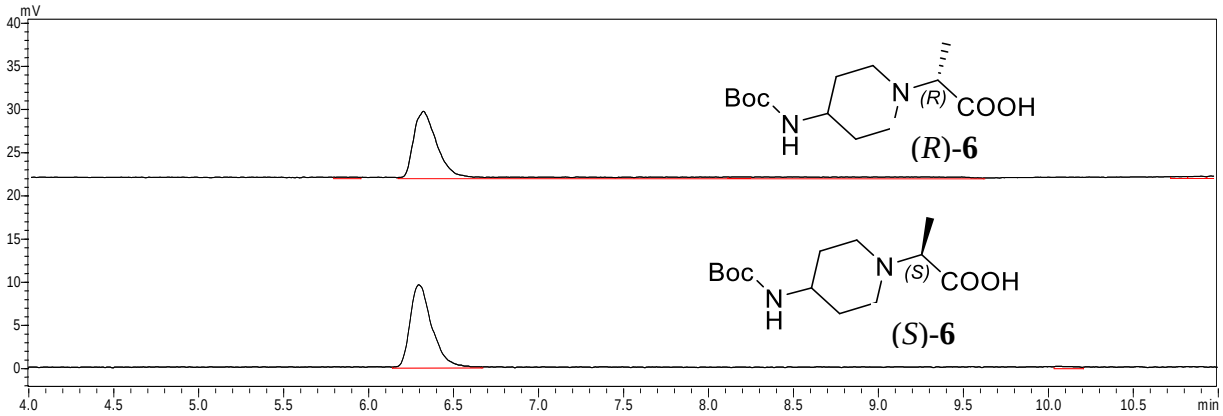


Figure S140. Unsuccessful chiral HPLC analysis of compounds (*S*)-**6** and (*R*)-**6**. Separation was carried out on YMC chiral column CHIRAL NEA (R), gradient conditions water + 0.1% formic acid / acetonitrile 90:10 to 20:80 in 15 minutes. Evaporative light scattering detector.

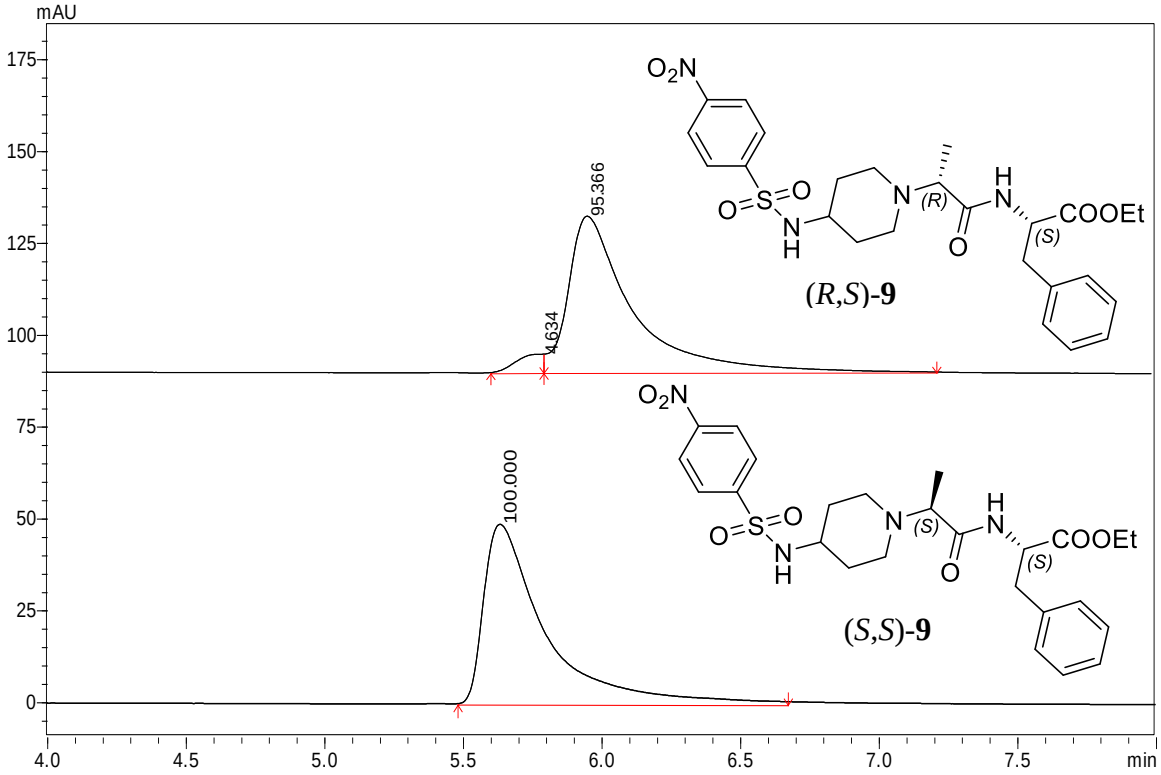


Figure S141. Unsuccessful chiral HPLC analysis of compounds (*S*,*S*)-**9** and (*R*,*S*)-**9**. Separation was carried out on chiral column CHIRAL ART Cellulose-SB, gradient conditions: water + 0.1% formic acid / acetonitrile 85:15 to 60:40 in 10 minutes. UV detector, 254 nm wavelength.

- **References:**

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.
3. Bourhis, L.J., Dolomanov, O.V., Gildea, R.J., Howard, J.A.K., Puschmann, H. (2015). Acta Cryst. A71, 59-75.