

Enantioselective Synthesis of (Thiolan-2-yl)diphenylmethanol and Its Application in Asymmetric, Catalytic Sulfur Ylide-Mediated Epoxidation

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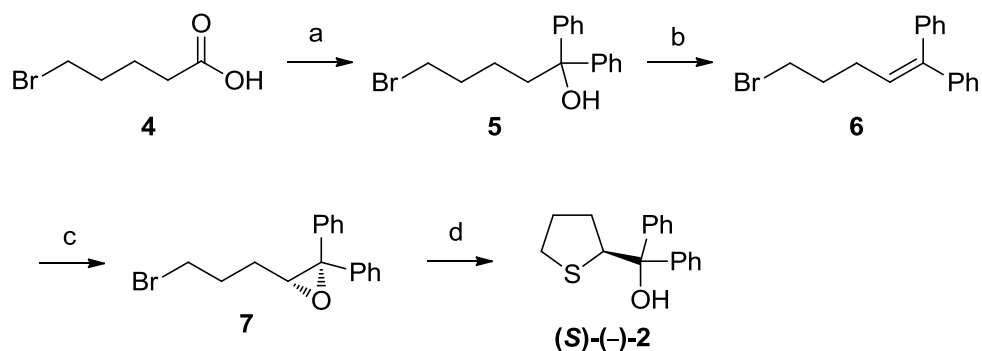
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Scheme 1. Synthesis of ((S)-(-)-thiolan-2-yl)diphenylmethanol (**2**)



Reagents and conditions: a) (i) SOCl₂, DMF(cat.), CH₂Cl₂, reflux; (ii) PhMgBr, THF, 68% in two steps. b) PTSA(cat.) toluene, 70°C, 82%. c) Shi epoxidation, 96%, 96% ee. d) Na₂S·9H₂O, EtOH, sonication, 86%, > 99% ee after one recrystallization.

X-ray crystallographic data of (S)-2

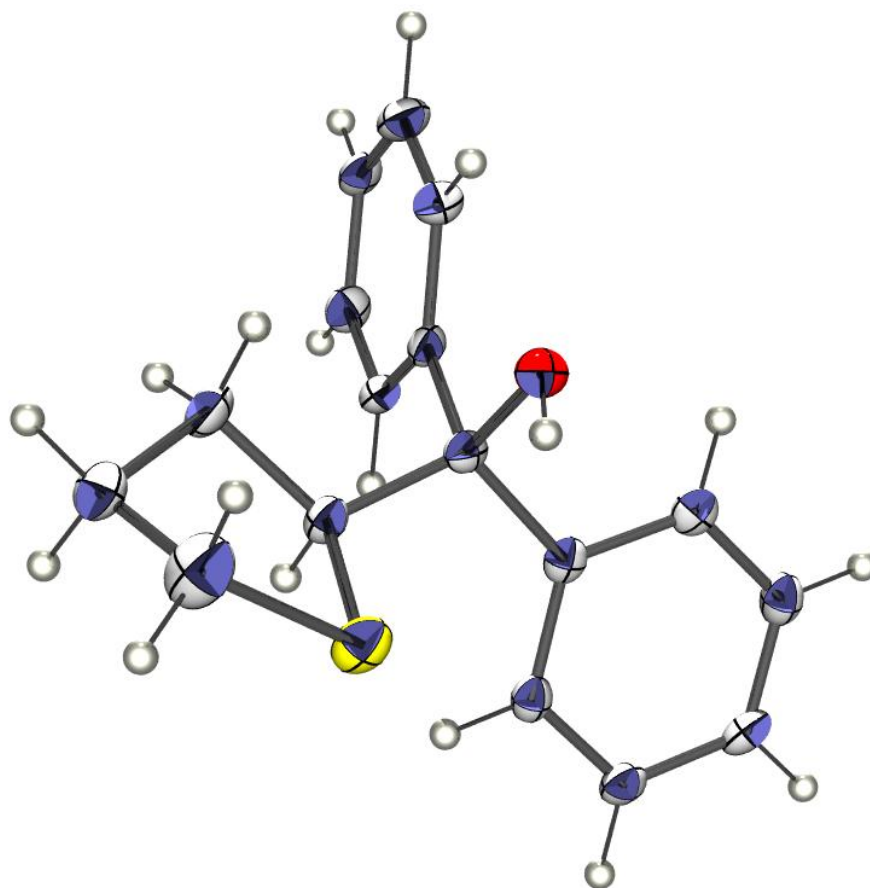


Table 1. Crystal data and structure refinement for (S)-2

Identification code	shelxl	
Empirical formula	C ₁₇ H ₁₈ O S	
Formula weight	270.37	
Temperature	100.0(1) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 21.2731(16) Å	$\alpha = 90^\circ$.
	b = 5.6491(5) Å	$\beta = 98.130(2)^\circ$.
	c = 12.1122(8) Å	$\gamma = 90^\circ$.
Volume	1440.94(19) Å ³	
Z	4	
Density (calculated)	1.246 Mg/m ³	
Absorption coefficient	0.214 mm ⁻¹	
F(000)	576	
Crystal size	0.14 x 0.14 x 0.12 mm ³	
Theta range for data collection	1.93 to 26.36°.	
Index ranges	-26 ≤ h ≤ 26, -6 ≤ k ≤ 7, -15 ≤ l ≤ 10	
Reflections collected	5749	
Independent reflections	2713 [R(int) = 0.0456]	
Completeness to theta = 25.00°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7454 and 0.6515	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2713 / 1 / 177	
Goodness-of-fit on F ²	1.019	
Final R indices [I > 2σ(I)]	R1 = 0.0461, wR2 = 0.0851	
R indices (all data)	R1 = 0.0684, wR2 = 0.0942	
Absolute structure parameter	-0.06(10)	
Extinction coefficient	0.0089(10)	
Largest diff. peak and hole	0.264 and -0.250 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for (S)-2. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S	707(1)	3053(2)	8843(1)	27(1)
O	1188(1)	7239(4)	7596(2)	23(1)
C(1)	1416(1)	4974(6)	7287(2)	18(1)
C(2)	919(1)	3058(7)	7413(2)	20(1)
C(3)	292(1)	3346(7)	6646(2)	26(1)
C(4)	-212(1)	2045(6)	7177(2)	31(1)
C(5)	-146(1)	2919(9)	8377(2)	38(1)
C(6)	1504(1)	5150(6)	6060(2)	18(1)
C(7)	1821(1)	3323(6)	5587(2)	20(1)
C(8)	1914(1)	3404(6)	4476(2)	24(1)
C(9)	1689(1)	5343(6)	3820(2)	23(1)
C(10)	1374(1)	7126(6)	4277(2)	27(1)
C(11)	1277(1)	7050(6)	5396(2)	23(1)
C(12)	2063(1)	4462(6)	7984(2)	18(1)
C(13)	2214(1)	2377(6)	8564(2)	19(1)
C(14)	2819(1)	2012(6)	9154(2)	22(1)
C(15)	3280(1)	3750(6)	9158(2)	23(1)
C(16)	3136(1)	5842(6)	8586(2)	24(1)
C(17)	2534(1)	6212(6)	8009(2)	21(1)

Table 3. Bond lengths [Å] and angles [°] for (S)-2.

S-C(5)	1.824(3)
S-C(2)	1.851(2)
O-C(1)	1.436(3)
O-H(1)	0.85(3)
C(1)-C(6)	1.527(4)
C(1)-C(2)	1.534(4)
C(1)-C(12)	1.537(4)
C(2)-C(3)	1.524(3)
C(2)-H(2)	0.9800
C(3)-C(4)	1.516(4)
C(3)-H(3A)	0.9700
C(3)-H(3B)	0.9700
C(4)-C(5)	1.523(4)
C(4)-H(4A)	0.9700
C(4)-H(4B)	0.9700
C(5)-H(5A)	0.9700
C(5)-H(5B)	0.9700
C(6)-C(11)	1.386(4)
C(6)-C(7)	1.399(4)
C(7)-C(8)	1.389(3)
C(7)-H(7)	0.9300
C(8)-C(9)	1.398(4)
C(8)-H(8)	0.9300
C(9)-C(10)	1.369(4)
C(9)-H(9)	0.9300
C(10)-C(11)	1.401(4)
C(10)-H(10)	0.9300
C(11)-H(11)	0.9300
C(12)-C(13)	1.386(4)
C(12)-C(17)	1.406(4)
C(13)-C(14)	1.397(3)
C(13)-H(13)	0.9300
C(14)-C(15)	1.387(4)
C(14)-H(14)	0.9300
C(15)-C(16)	1.382(4)
C(15)-H(15)	0.9300

C(16)-C(17)	1.385(4)
C(16)-H(16)	0.9300
C(17)-H(17)	0.9300
C(5)-S-C(2)	94.29(12)
C(1)-O-H(1)	103(2)
O-C(1)-C(6)	106.7(2)
O-C(1)-C(2)	109.9(2)
C(6)-C(1)-C(2)	108.9(2)
O-C(1)-C(12)	109.4(2)
C(6)-C(1)-C(12)	108.8(2)
C(2)-C(1)-C(12)	112.8(2)
C(3)-C(2)-C(1)	114.8(3)
C(3)-C(2)-S	105.16(17)
C(1)-C(2)-S	110.89(19)
C(3)-C(2)-H(2)	108.6
C(1)-C(2)-H(2)	108.6
S-C(2)-H(2)	108.6
C(4)-C(3)-C(2)	107.5(2)
C(4)-C(3)-H(3A)	110.2
C(2)-C(3)-H(3A)	110.2
C(4)-C(3)-H(3B)	110.2
C(2)-C(3)-H(3B)	110.2
H(3A)-C(3)-H(3B)	108.5
C(3)-C(4)-C(5)	105.8(3)
C(3)-C(4)-H(4A)	110.6
C(5)-C(4)-H(4A)	110.6
C(3)-C(4)-H(4B)	110.6
C(5)-C(4)-H(4B)	110.6
H(4A)-C(4)-H(4B)	108.7
C(4)-C(5)-S	105.2(2)
C(4)-C(5)-H(5A)	110.7
S-C(5)-H(5A)	110.7
C(4)-C(5)-H(5B)	110.7
S-C(5)-H(5B)	110.7
H(5A)-C(5)-H(5B)	108.8
C(11)-C(6)-C(7)	118.9(3)
C(11)-C(6)-C(1)	122.3(3)

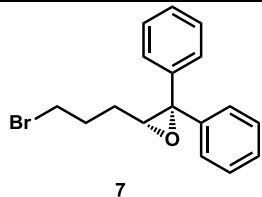
C(7)-C(6)-C(1)	118.9(3)
C(8)-C(7)-C(6)	121.1(3)
C(8)-C(7)-H(7)	119.5
C(6)-C(7)-H(7)	119.5
C(7)-C(8)-C(9)	119.4(3)
C(7)-C(8)-H(8)	120.3
C(9)-C(8)-H(8)	120.3
C(10)-C(9)-C(8)	119.7(3)
C(10)-C(9)-H(9)	120.1
C(8)-C(9)-H(9)	120.1
C(9)-C(10)-C(11)	121.1(3)
C(9)-C(10)-H(10)	119.5
C(11)-C(10)-H(10)	119.5
C(6)-C(11)-C(10)	119.8(3)
C(6)-C(11)-H(11)	120.1
C(10)-C(11)-H(11)	120.1
C(13)-C(12)-C(17)	118.2(3)
C(13)-C(12)-C(1)	124.3(3)
C(17)-C(12)-C(1)	117.4(3)
C(12)-C(13)-C(14)	121.0(3)
C(12)-C(13)-H(13)	119.5
C(14)-C(13)-H(13)	119.5
C(15)-C(14)-C(13)	119.8(3)
C(15)-C(14)-H(14)	120.1
C(13)-C(14)-H(14)	120.1
C(16)-C(15)-C(14)	119.8(3)
C(16)-C(15)-H(15)	120.1
C(14)-C(15)-H(15)	120.1
C(15)-C(16)-C(17)	120.3(3)
C(15)-C(16)-H(16)	119.8
C(17)-C(16)-H(16)	119.8
C(16)-C(17)-C(12)	120.7(3)
C(16)-C(17)-H(17)	119.6
C(12)-C(17)-H(17)	119.6

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for (S)-2. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S	24(1)	40(1)	19(1)	2(1)	5(1)	-2(1)
O	27(1)	21(1)	20(1)	-1(1)	5(1)	3(1)
C(1)	22(2)	16(2)	14(1)	-3(1)	1(1)	3(2)
C(2)	19(1)	24(2)	16(1)	-1(2)	1(1)	-1(2)
C(3)	22(2)	30(2)	23(2)	-2(2)	-6(1)	1(2)
C(4)	20(2)	35(2)	35(2)	5(2)	-3(1)	-2(2)
C(5)	26(2)	55(3)	33(2)	0(2)	7(1)	-1(2)
C(6)	18(2)	19(2)	14(1)	-2(1)	-1(1)	-1(1)
C(7)	22(1)	20(2)	16(1)	1(2)	-2(1)	0(2)
C(8)	27(2)	26(2)	18(1)	-4(2)	3(1)	1(2)
C(9)	24(2)	30(2)	13(2)	2(2)	1(1)	-4(2)
C(10)	28(2)	32(2)	20(2)	6(2)	-1(1)	2(2)
C(11)	22(2)	24(2)	23(2)	2(2)	2(1)	3(2)
C(12)	19(2)	24(2)	13(1)	-2(1)	5(1)	-2(2)
C(13)	18(2)	23(2)	17(1)	-2(1)	3(1)	-3(1)
C(14)	27(2)	24(2)	14(1)	0(1)	1(1)	1(2)
C(15)	21(2)	33(2)	14(1)	0(1)	-1(1)	3(2)
C(16)	20(2)	29(2)	22(2)	-2(2)	4(1)	-5(2)
C(17)	24(2)	25(2)	14(1)	-3(1)	5(1)	1(2)

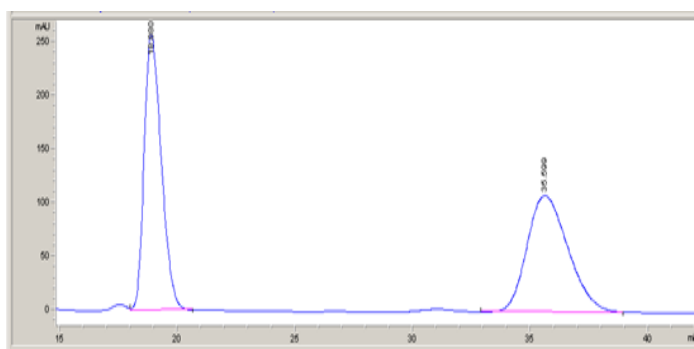
HPLC analysis



HPLC condition: Chiralcel-OJ column, 20% *i*-PrOH/hexanes, 220 nm, 18.9 min (enantiomer), 35.6 min (major)

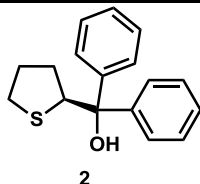
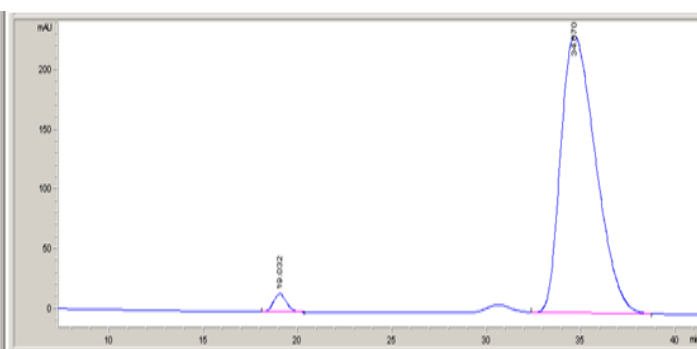
racemic 7

#	Time	Area	Height	Width	Area%
1	18.88	13078.9	257	0.7918	49.801
2	35.599	13183.5	108.7	1.8452	50.199



(*R*)-7 with 96% ee

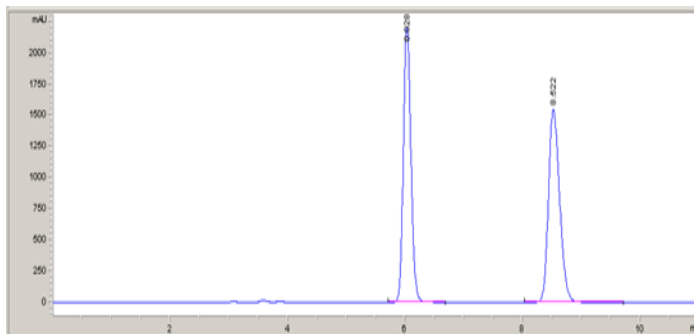
#	Time	Area	Height	Width	Area%
1	19.032	713.7	15	0.7334	2.318
2	34.67	30077.1	232.7	2.0139	97.682



HPLC condition: Chiralpak-AD column, 5% *i*-PrOH/hexanes, 220 nm, 6.0 min (enantiomer), 8.5 min (major)

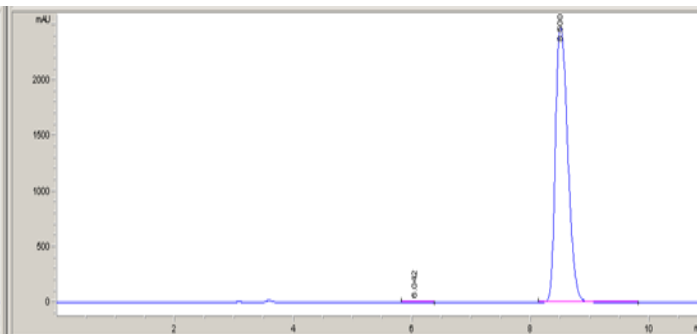
racemic 2

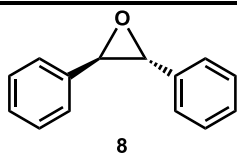
#	Time	Area	Height	Width	Area%
1	6.028	19881.4	2203.1	0.1413	49.338
2	8.522	20414.9	1545.8	0.2041	50.662



(*S*)-2 with >99% ee

#	Time	Area	Height	Width	Area%
1	6.042	20.4	1.8	0.165	0.057
2	8.5	35953.1	2476.2	0.2274	99.943

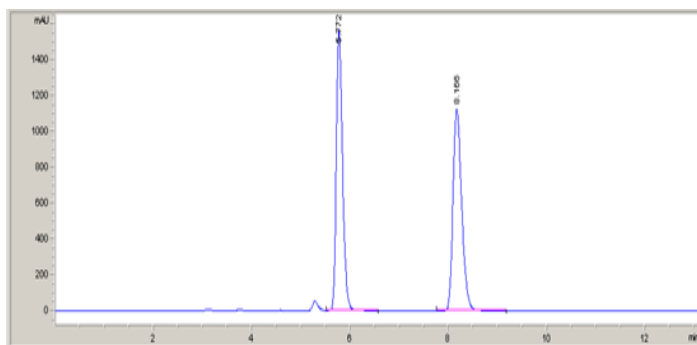




HPLC condition: Chiralcel-OD column, 5% *i*-PrOH/hexanes, 228 nm, 5.8 min (enantiomer), 8.0 min (major)

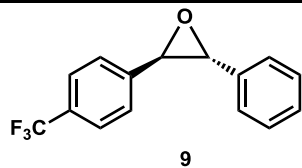
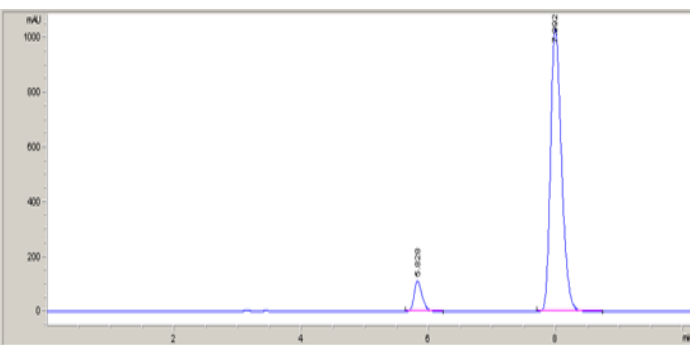
racemic **8**

#	Time	Area	Height	Width	Area%
1	5.772	13896.8	1577.3	0.1348	49.967
2	8.166	13915	1129.9	0.1877	50.033



(*R,R*)-**8** with 86% ee

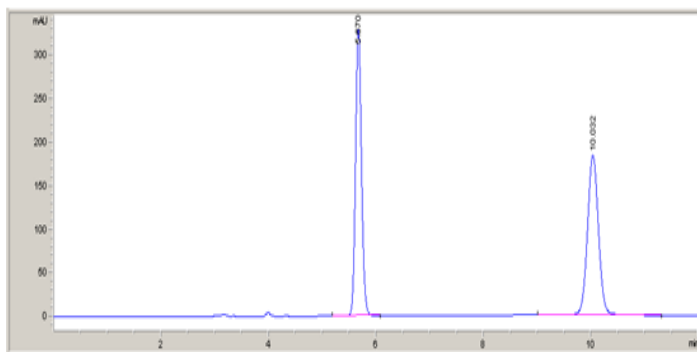
#	Time	Area	Height	Width	Area%
1	5.828	971.8	111.7	0.1335	7.248
2	7.992	12435.1	1035.3	0.1841	92.752



HPLC condition: Chiralpak-AD column, 5% *i*-PrOH/hexanes, 231 nm, 5.6 min (major), 10.3 min (enantiomer)

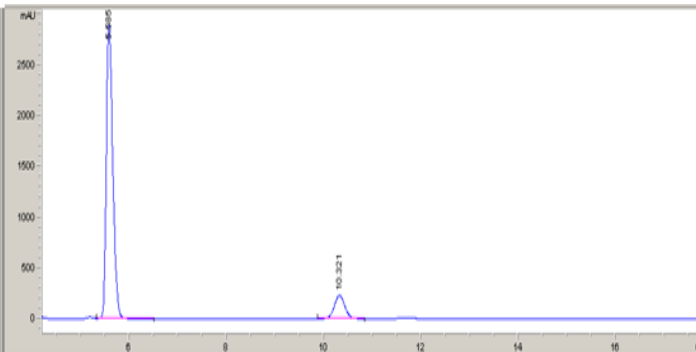
racemic **9**

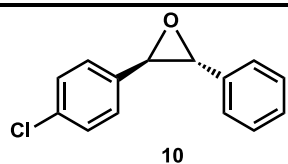
#	Time	Area	Height	Width	Area%
1	5.67	2526.9	328.9	0.1176	48.885
2	10.032	2642.2	183.6	0.2219	51.115



(*R,R*)-**9** with 78% ee

#	Time	Area	Height	Width	Area%
1	5.585	26902.5	2897.1	0.1423	88.883
2	10.321	3364.7	227.5	0.2285	11.117

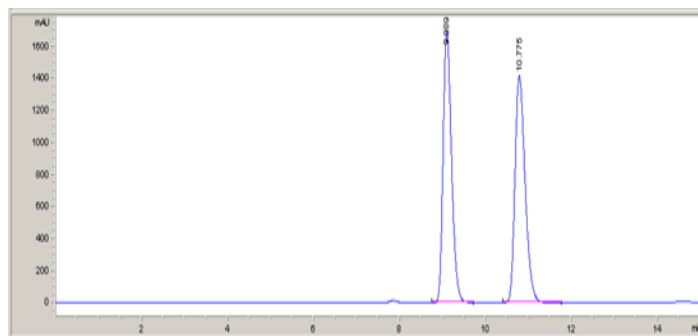




HPLC condition: Chiralcel-OD column, 1% *i*-PrOH/hexanes, 234 nm, 9.0 min (enantiomer), 10.4 min (major)

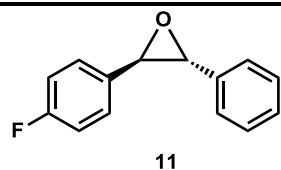
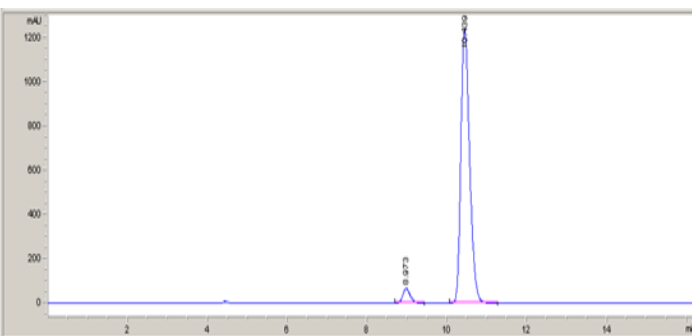
racemic 10

#	Time	Area	Height	Width	Area%
1	9.089	23017.4	1698.3	0.2101	49.907
2	10.775	23103.2	1416.5	0.2523	50.093



(*R,R*)-10 with 92% ee

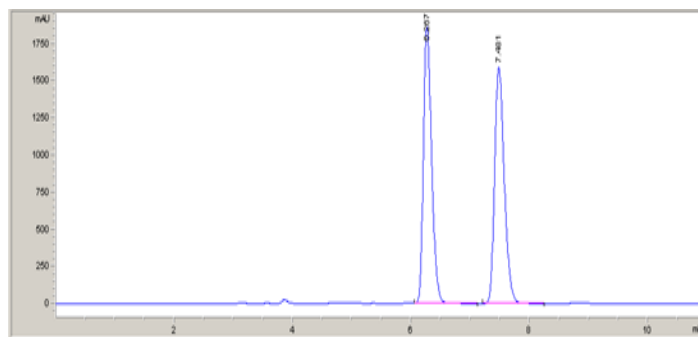
#	Time	Area	Height	Width	Area%
1	8.973	831.6	65.7	0.1936	4.223
2	10.439	18857.7	1239	0.2356	95.777



HPLC condition: Chiralcel-OD column, 5% *i*-PrOH/hexanes, 220 nm, 6.4 min (enantiomer), 7.8 min (major)

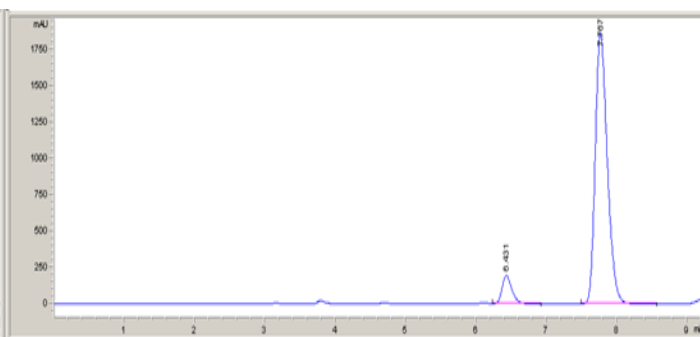
racemic 11

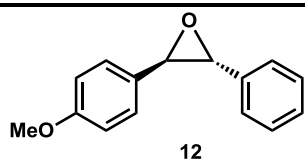
#	Time	Area	Height	Width	Area%
1	6.267	17929.8	1859.1	0.1465	49.878
2	7.481	18017.7	1591.6	0.1741	50.122



(*R,R*)-11 with 84% ee

#	时间	峰面积	峰高	峰宽	对映因子	Area%
1	6.431	1862.5	193.8	0.1481	0.735	7.765
2	7.767	22124.5	1864.5	0.1824	0.715	92.235

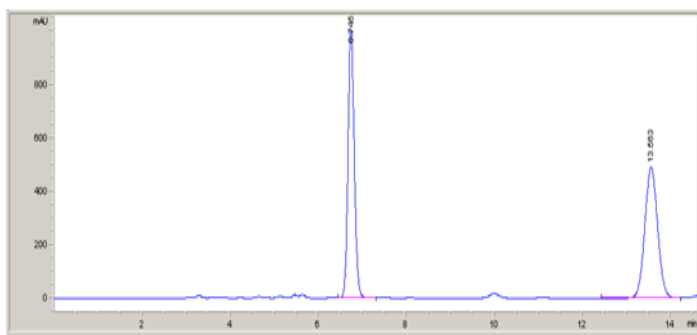




HPLC condition: Chiralpak-AD column, 15% *i*-PrOH/hexanes, 234 nm, 6.8 min (major), 13.8 min (enantiomer)

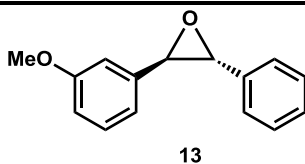
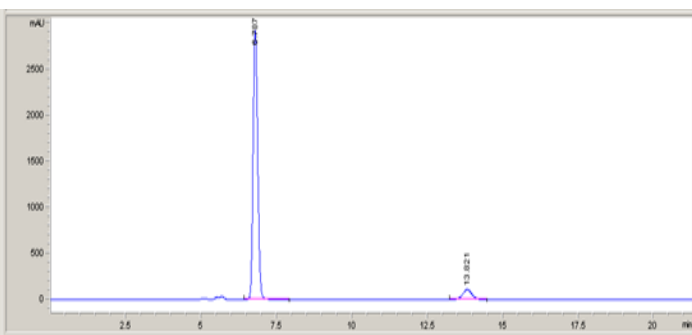
racemic 12

#	Time	Area	Height	Width	Area%
1	6.745	9909.7	1006.4	0.1509	50.104
2	13.563	9868.5	490	0.313	49.896



(*R,R*)-12 with 87% ee

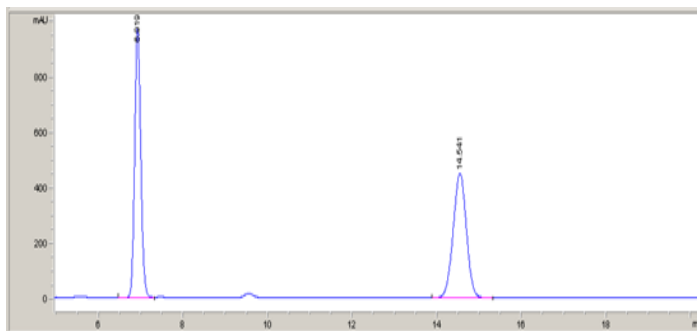
#	Time	Area	Height	Width	Area%
1	6.787	31011	2910	0.1683	93.418
2	13.821	2185	105.8	0.3209	6.582



HPLC condition: Chiralpak-AD column, 10% *i*-PrOH/hexanes, 220 nm, 6.9 min (major), 14.4 min (enantiomer)

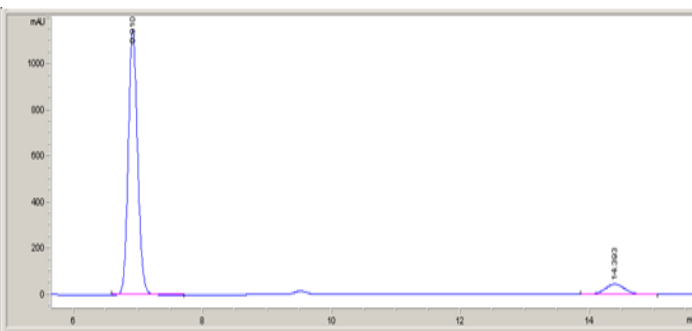
racemic 13

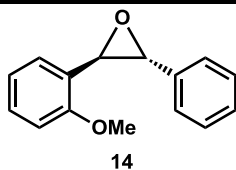
#	Time	Area	Height	Width	Area%
1	6.919	9876.9	974	0.1563	50.462
2	14.541	9696.1	446.7	0.3373	49.538



(*R,R*)-13 with 85% ee

#	Time	Area	Height	Width	Area%
1	6.91	11510.8	1149.5	0.1548	92.369
2	14.393	951	44.4	0.334	7.631

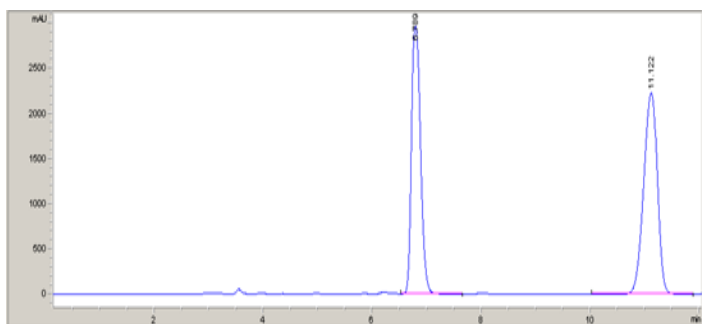




HPLC condition: Chiralpak-AD column, 5% *i*-PrOH/hexanes, 234 nm, 6.8 min (major), 11.0 min (enantiomer)

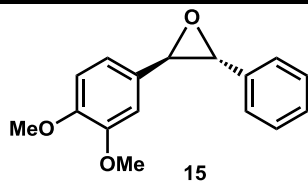
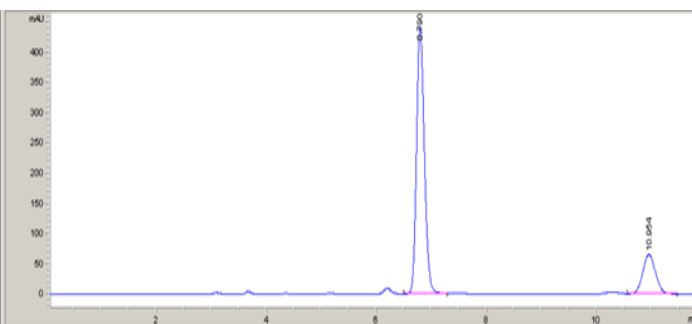
racemic 14

#	Time	Area	Height	Width	Area%
1	6.789	34451.7	2960.4	0.1838	47.397
2	11.122	38235.1	2224.4	0.2705	52.603



(*R,R*)-14 with 62% ee

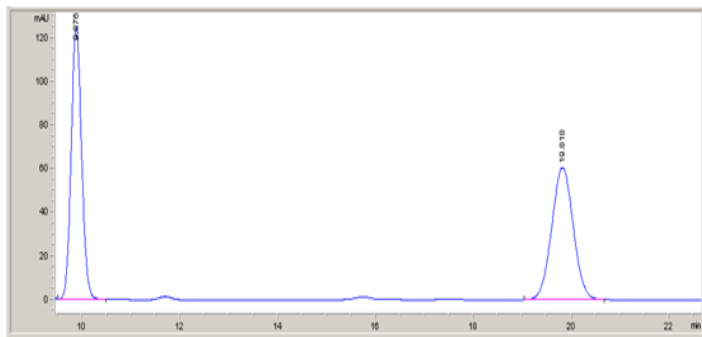
#	Time	Area	Height	Width	Area%
1	6.79	4435.8	442.2	0.155	81.020
2	10.954	1039.1	65.2	0.248	18.980



HPLC condition: Chiralpak-AD column, 10% *i*-PrOH/hexanes, 231 nm, 9.9 min (major), 20.0 min (enantiomer)

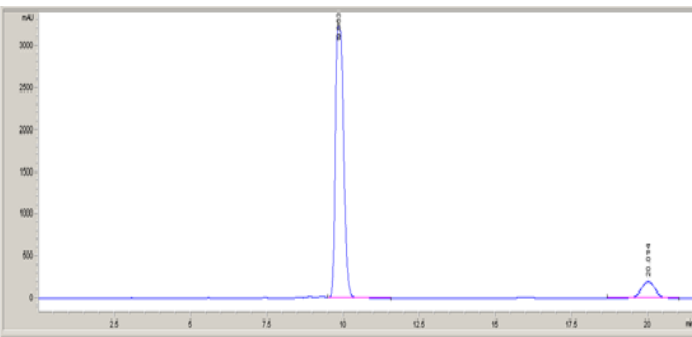
racemic 15

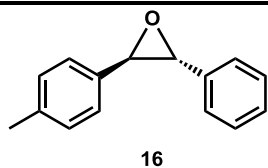
#	Time	Area	Height	Width	Area%
1	9.876	1854.4	125.1	0.2309	49.987
2	19.818	1855.4	60.6	0.4771	50.013



(*R,R*)-15 with 82% ee

#	Time	Area	Height	Width	Area%
1	9.863	60520.4	3233	0.2944	90.672
2	20.014	6226	199.4	0.4862	9.328

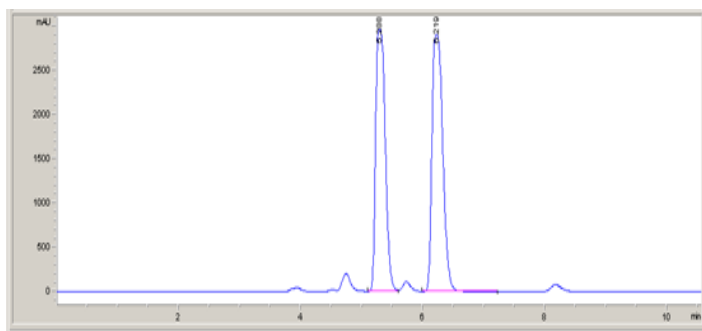




HPLC condition: Chiralcel-OD column, 5% *i*-PrOH/hexanes, 231 nm, 5.4 min (enantiomer), 6.4 min (major)

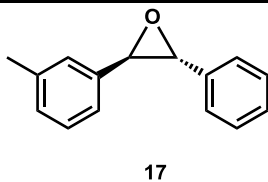
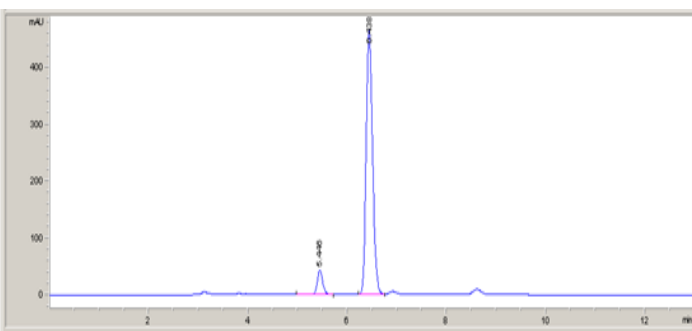
racemic 16

#	Time	Area	Height	Width	Area%
1	5.288	32572	2962.6	0.1743	47.827
2	6.219	35531.5	2908.4	0.1945	52.173



(*R,R*)-16 with 87% ee

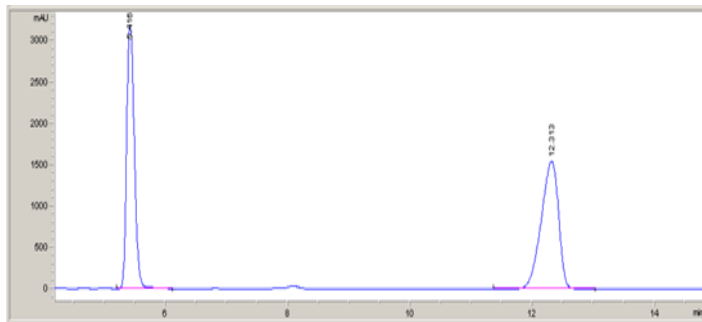
#	Time	Area	Height	Width	Area%
1	5.446	344.1	43.2	0.1209	7.573
2	6.438	4199.9	466	0.1391	92.427



HPLC condition: Chiralpak-AD column, 5% *i*-PrOH/hexanes, 231 nm, 5.4 min (major), 12.3 min (enantiomer)

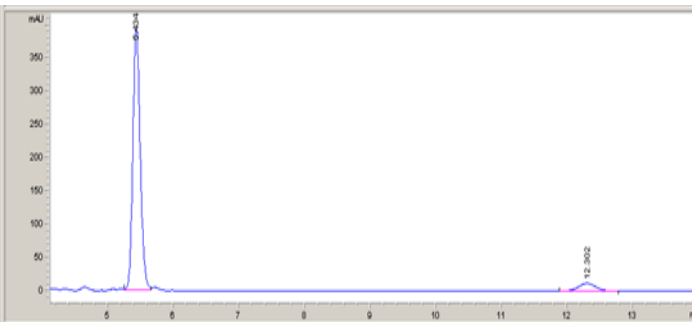
racemic 17

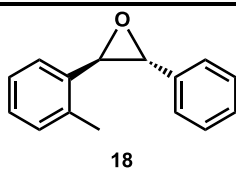
#	Time	Area	Height	Width	Area%
1	5.416	28108.9	3183.6	0.137	48.013
2	12.313	30435.1	1542.1	0.3103	51.987



(*R,R*)-17 with 87% ee

#	Time	Area	Height	Width	Area%
1	5.434	3103.2	396.8	0.1212	93.715
2	12.302	208.1	11.6	0.2779	6.285

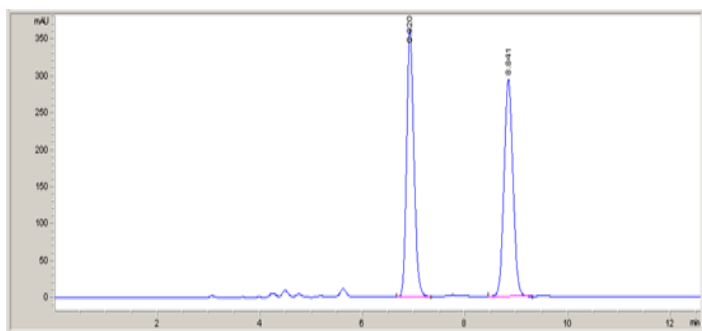




HPLC condition: Chiralpak-AD column, 1% *i*-PrOH/hexanes, 228 nm, 6.9 min (major), 8.9 min (enantiomer)

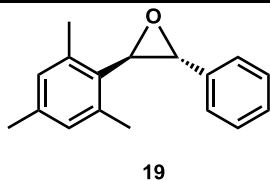
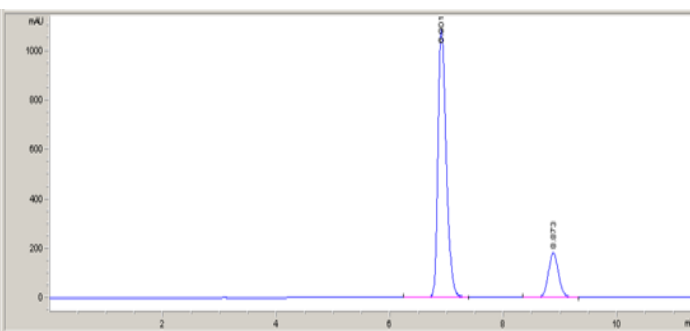
racemic 18

#	Time	Area	Height	Width	Area%
1	6.92	3577	362.7	0.1511	50.054
2	8.841	3569.3	294.5	0.1894	49.946



(*R,R*)-18 with 66% ee

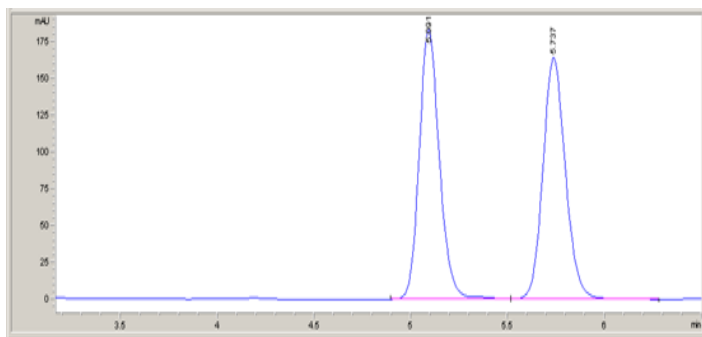
#	Time	Area	Height	Width	Area%
1	6.901	11060.4	1084.7	0.155	83.231
2	8.873	2228.4	180	0.1904	16.769



HPLC condition: Chiralpak-AD column, 2% *i*-PrOH/hexanes, 228 nm, 5.2 min (major), 5.9 min (enantiomer)

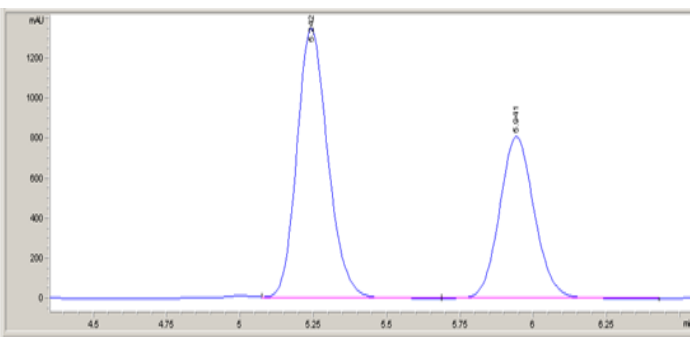
racemic 19

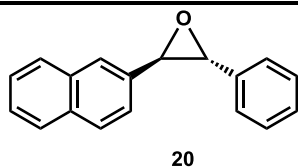
#	Time	Area	Height	Width	Area%
1	5.091	1330.5	183.6	0.1106	50.128
2	5.737	1323.7	163.9	0.1242	49.872



(*R,R*)-19 with 20% ee

#	Time	Area	Height	Width	Area%
1	5.242	9958.8	1351	0.114	59.941
2	5.941	6655.6	808.7	0.126	40.059

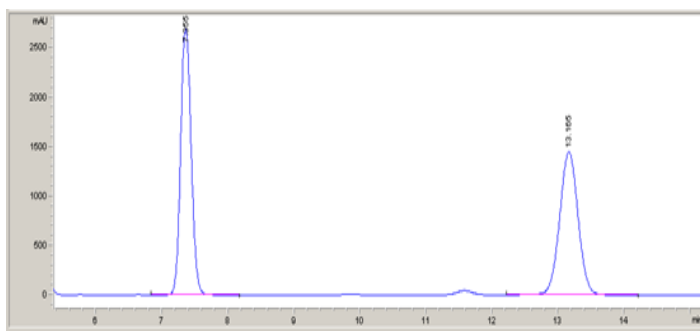




HPLC condition: Chiralpak-AD column, 10% *i*-PrOH/hexanes, 231 nm, 7.2 min (major), 12.9 min (enantiomer)

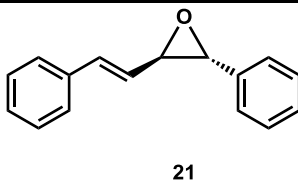
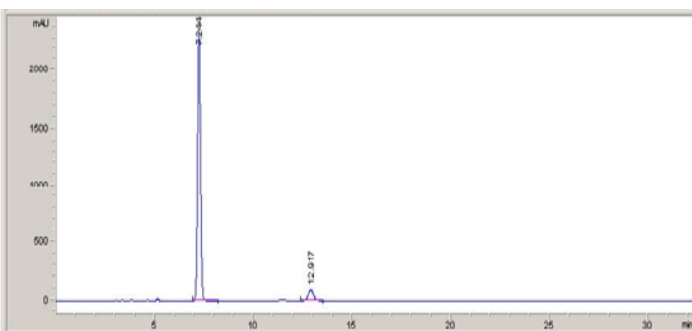
racemic 20

#	Time	Area	Height	Width	Area%
1	7.355	29966.7	2690.5	0.1739	51.554
2	13.165	28159.9	1447.4	0.303	48.446



(*R,R*)-20 with 87% ee

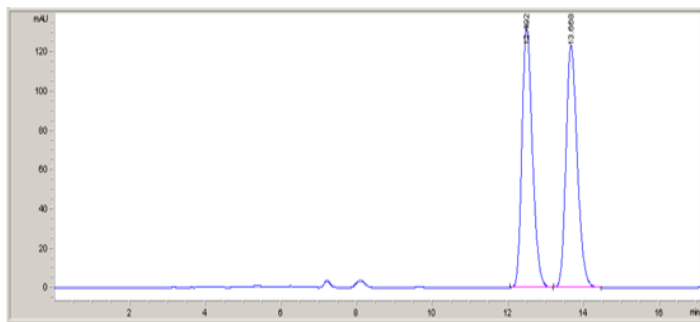
#	Time	Area	Height	Width	Area%
1	7.244	23975.3	2356.6	0.1587	93.571
2	12.917	1647.3	89	0.2879	6.429



HPLC condition: Chiralcel-OD column, 1% *i*-PrOH/hexanes, 220 nm, 12.5 min (enantiomer), 13.7 min (major)

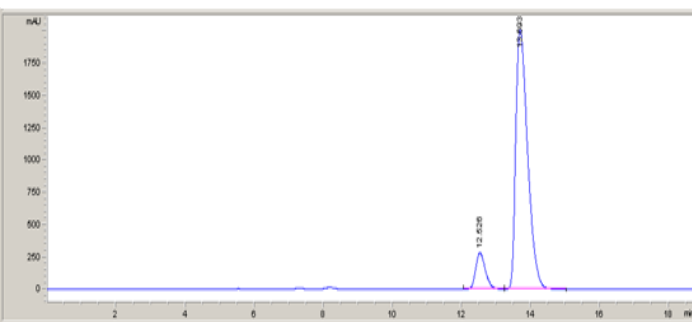
racemic 21

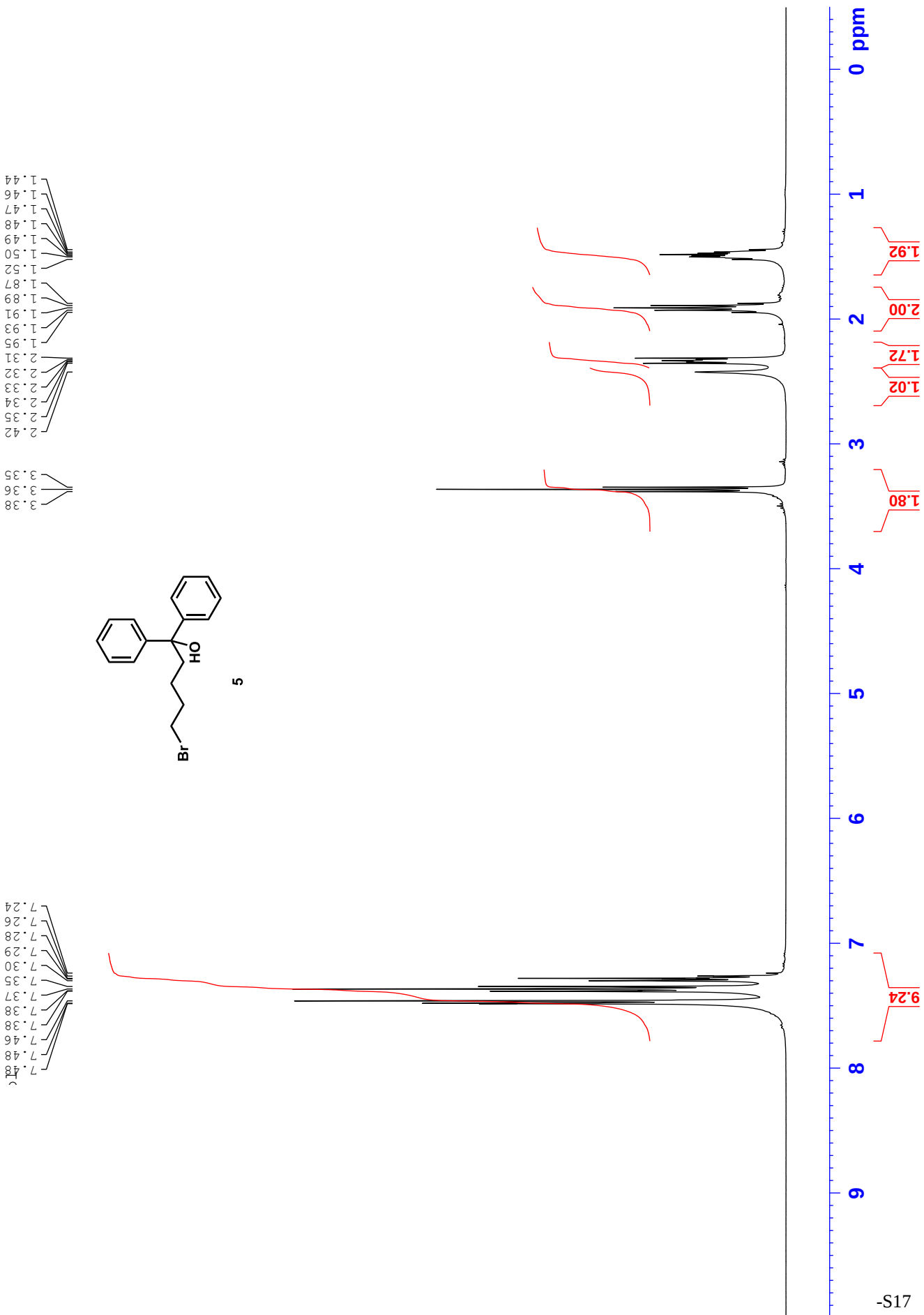
#	Time	Area	Height	Width	Area%
1	12.492	2551.4	133	0.2959	49.927
2	13.668	2558.9	123.4	0.3199	50.073

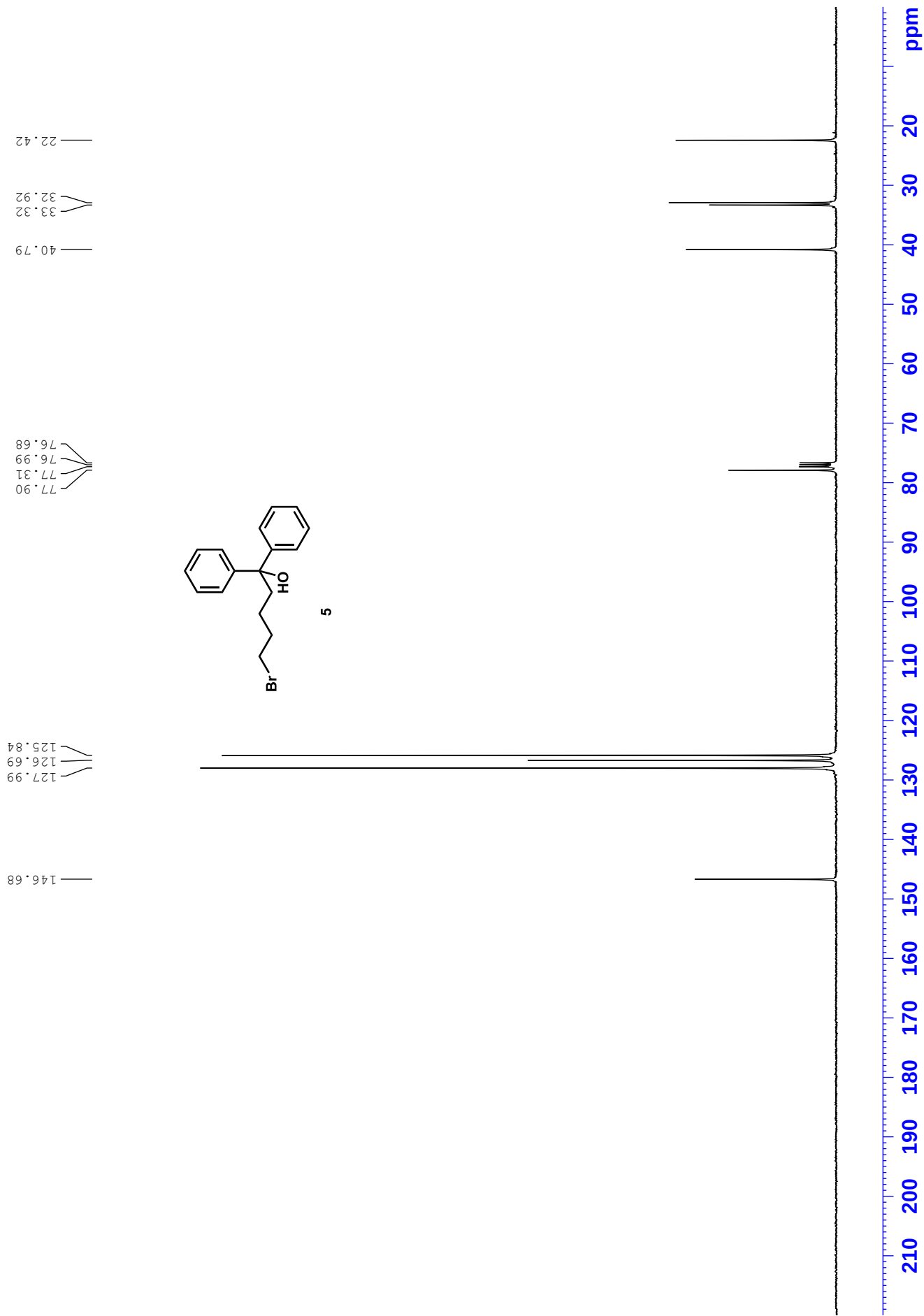


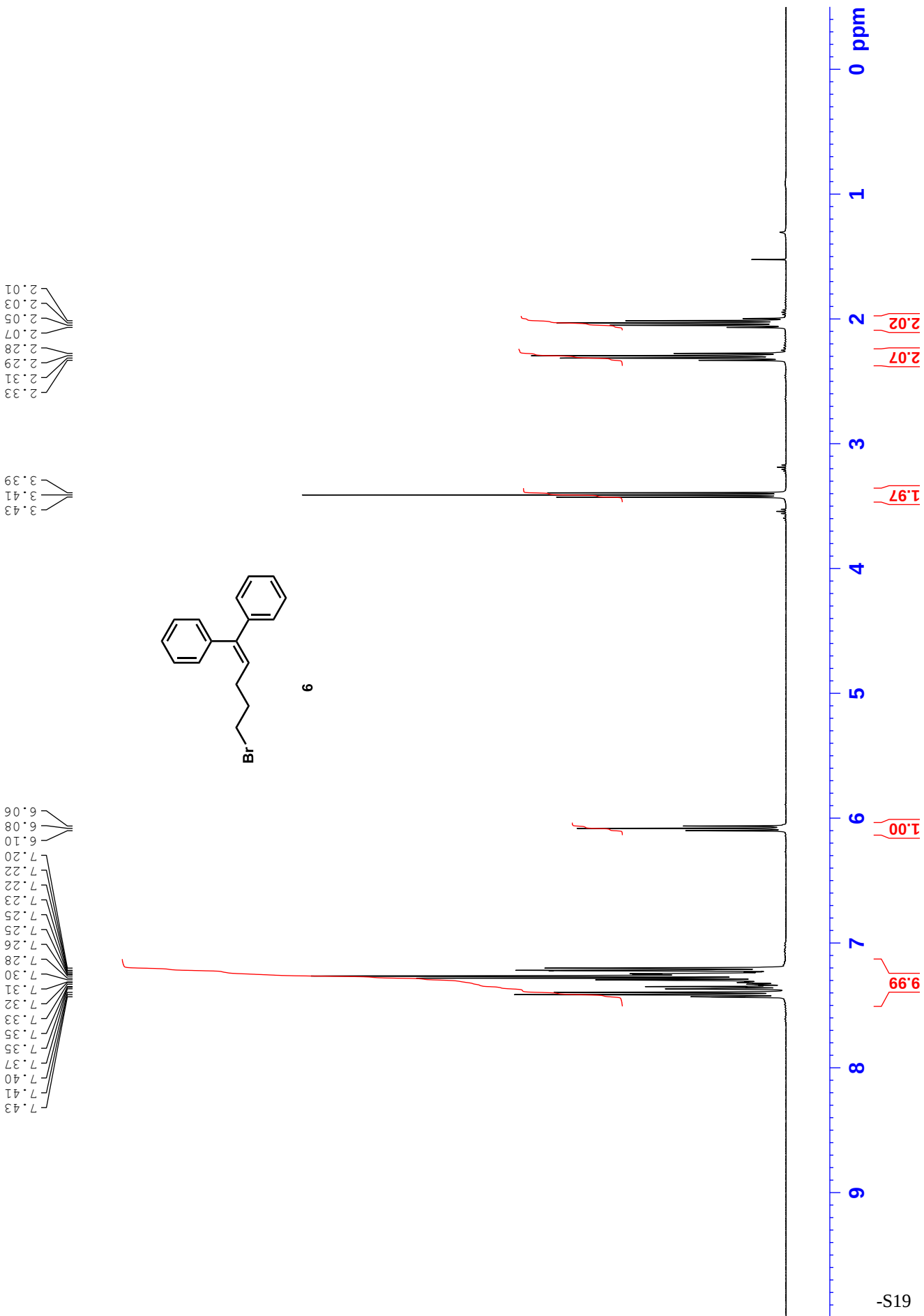
(*R,R*)-21 with 79% ee

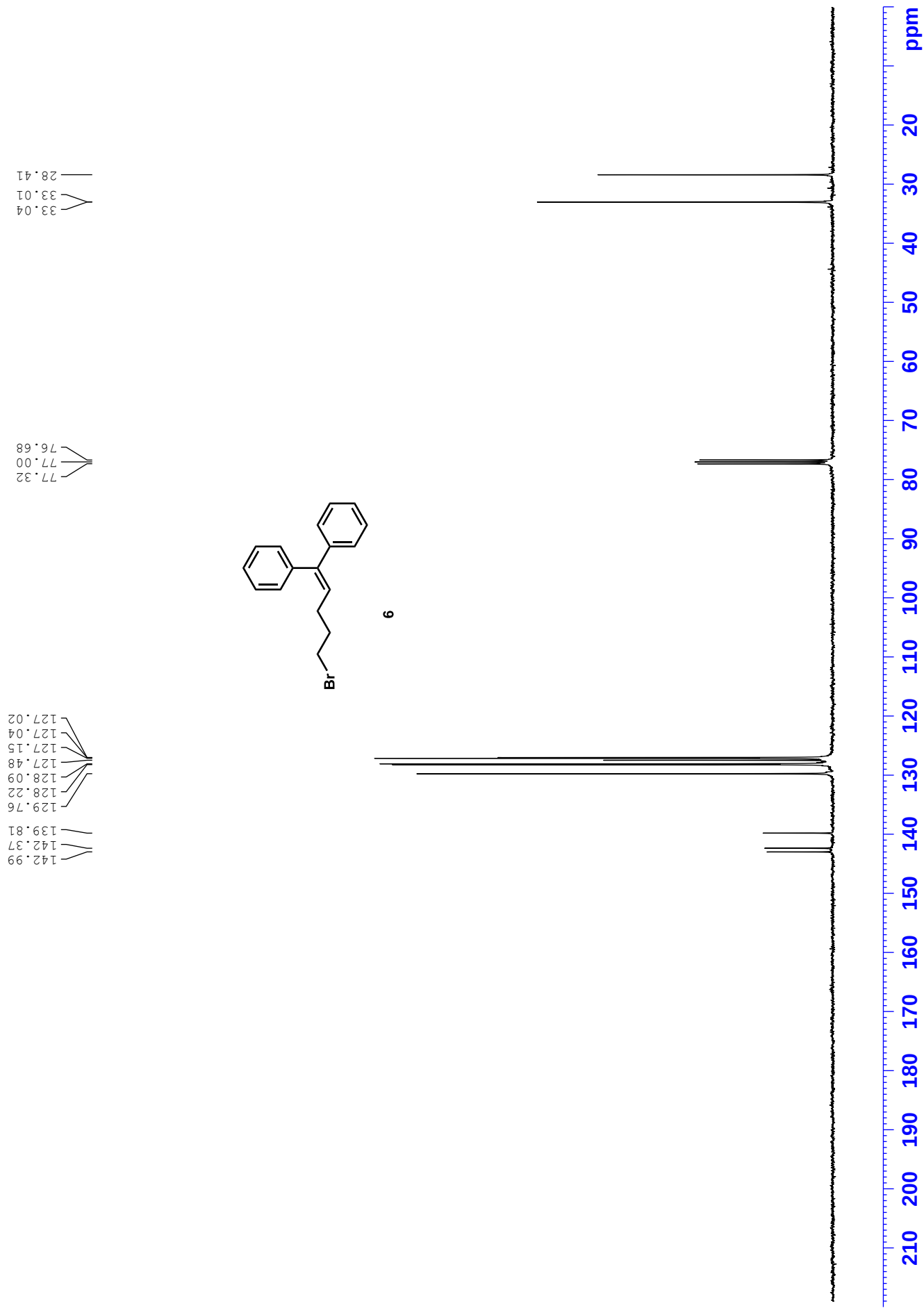
#	Time	Area	Height	Width	Area%
1	12.526	5409.8	282	0.2958	10.135
2	13.693	47967.2	2014.1	0.3679	89.865

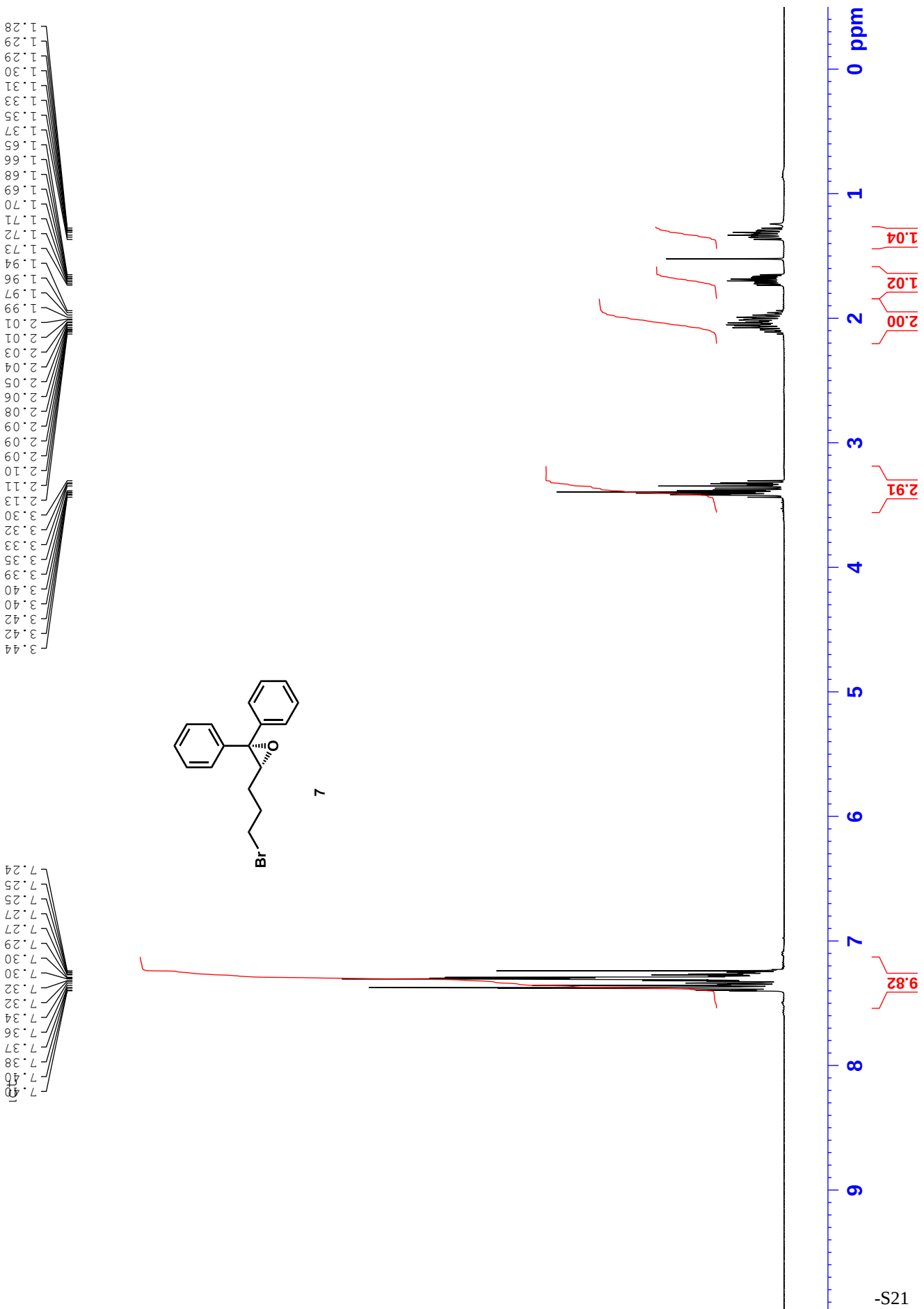




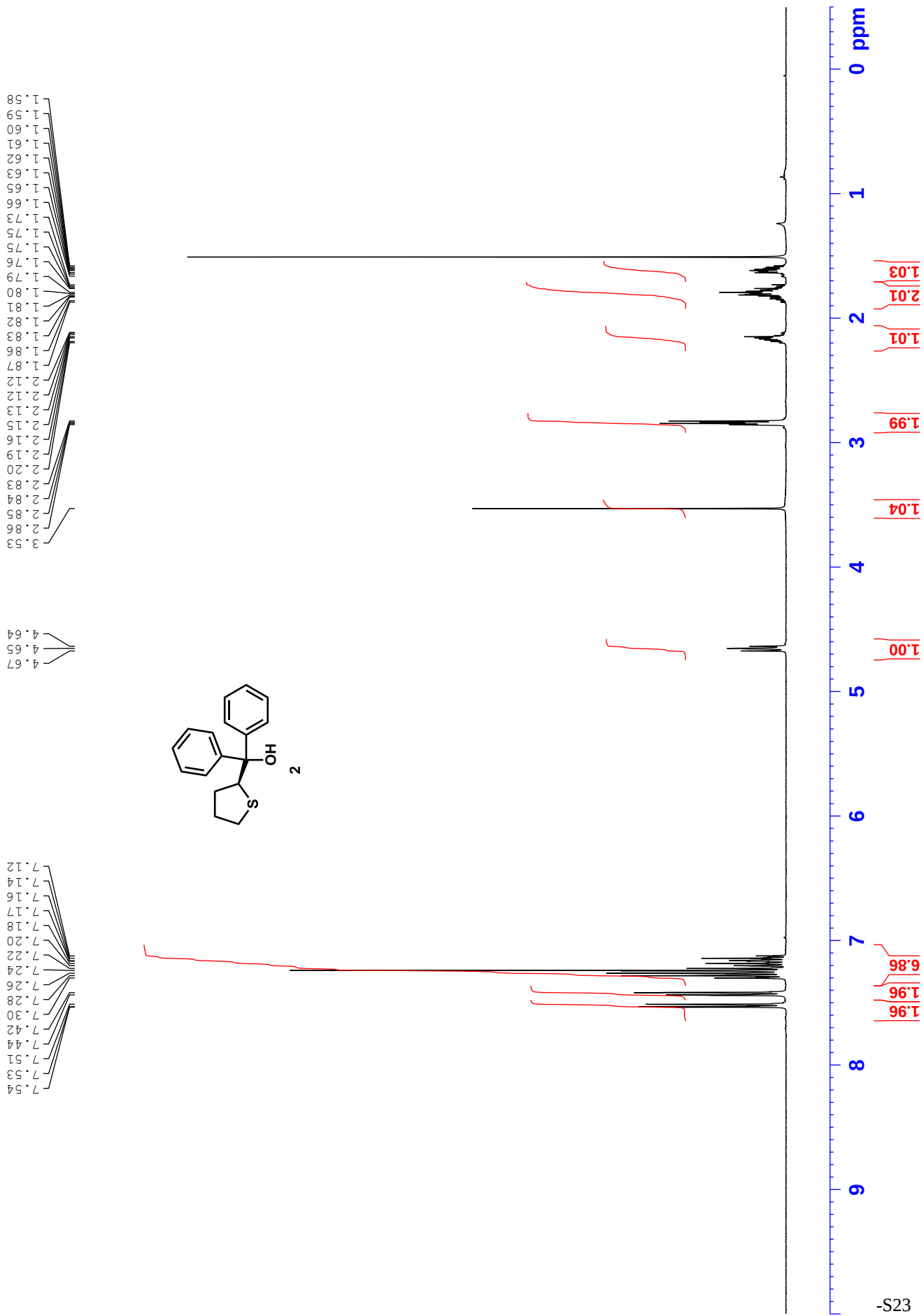


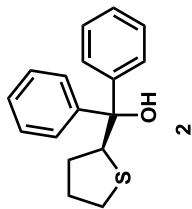
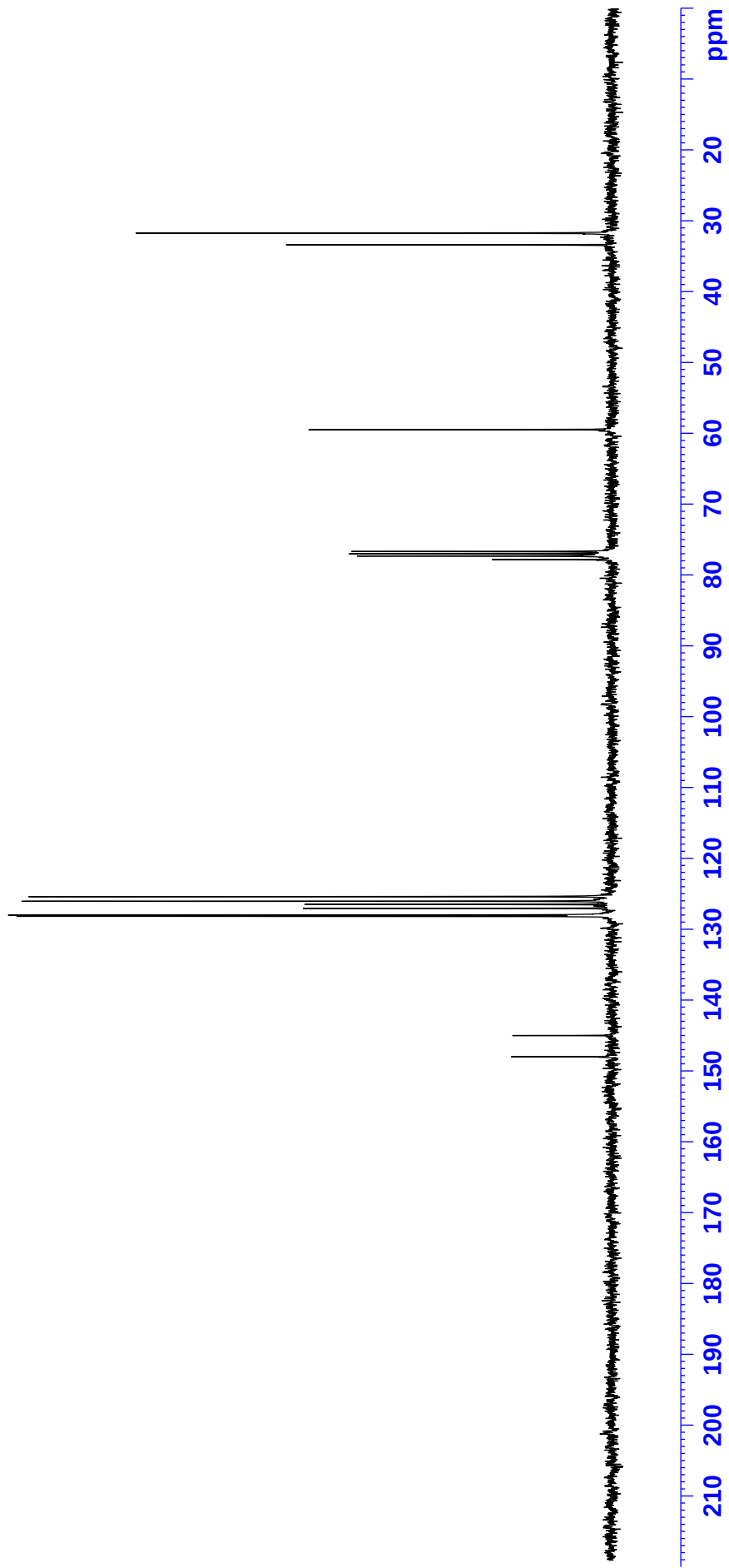












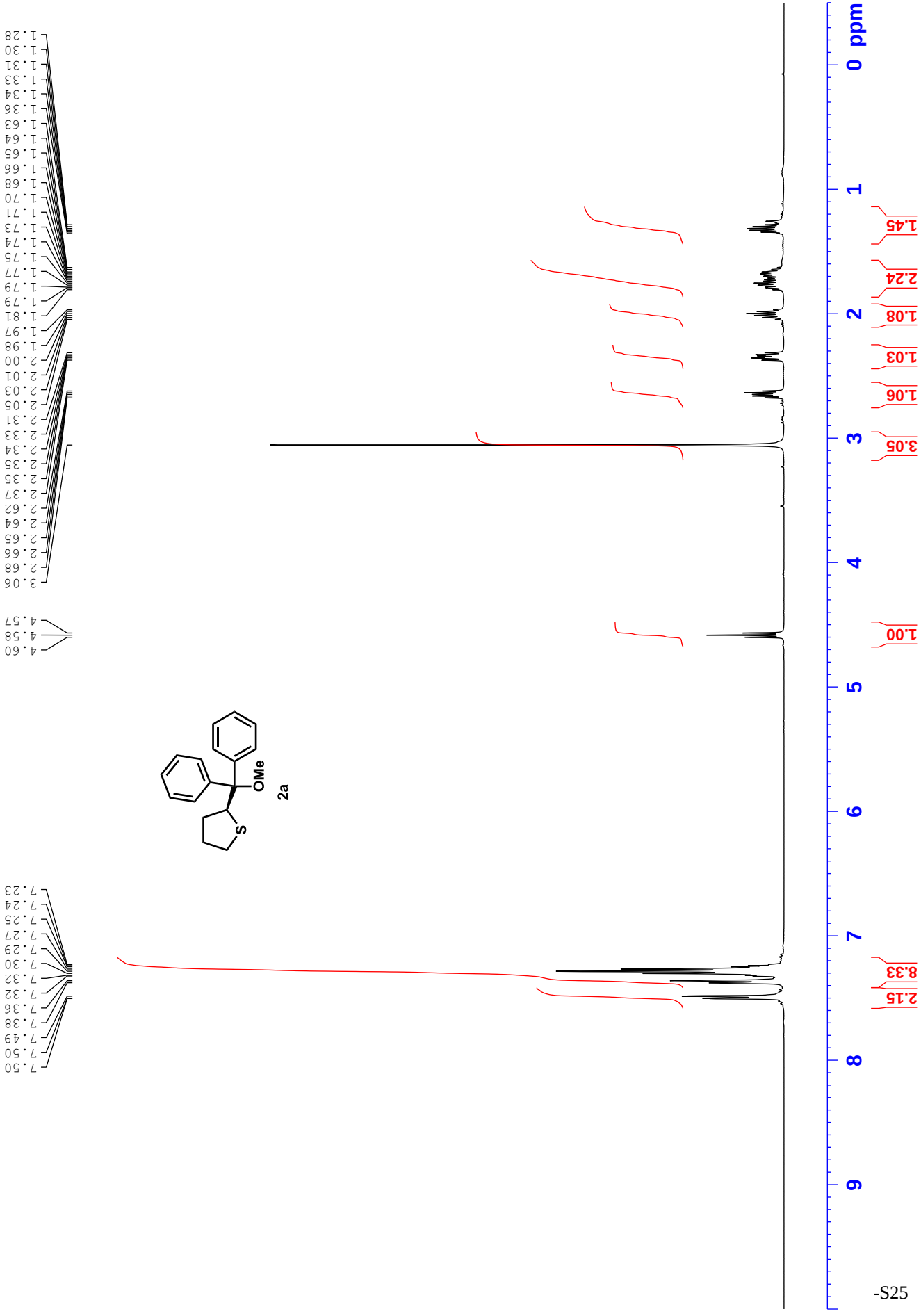
33.41
31.75

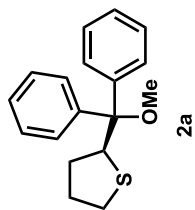
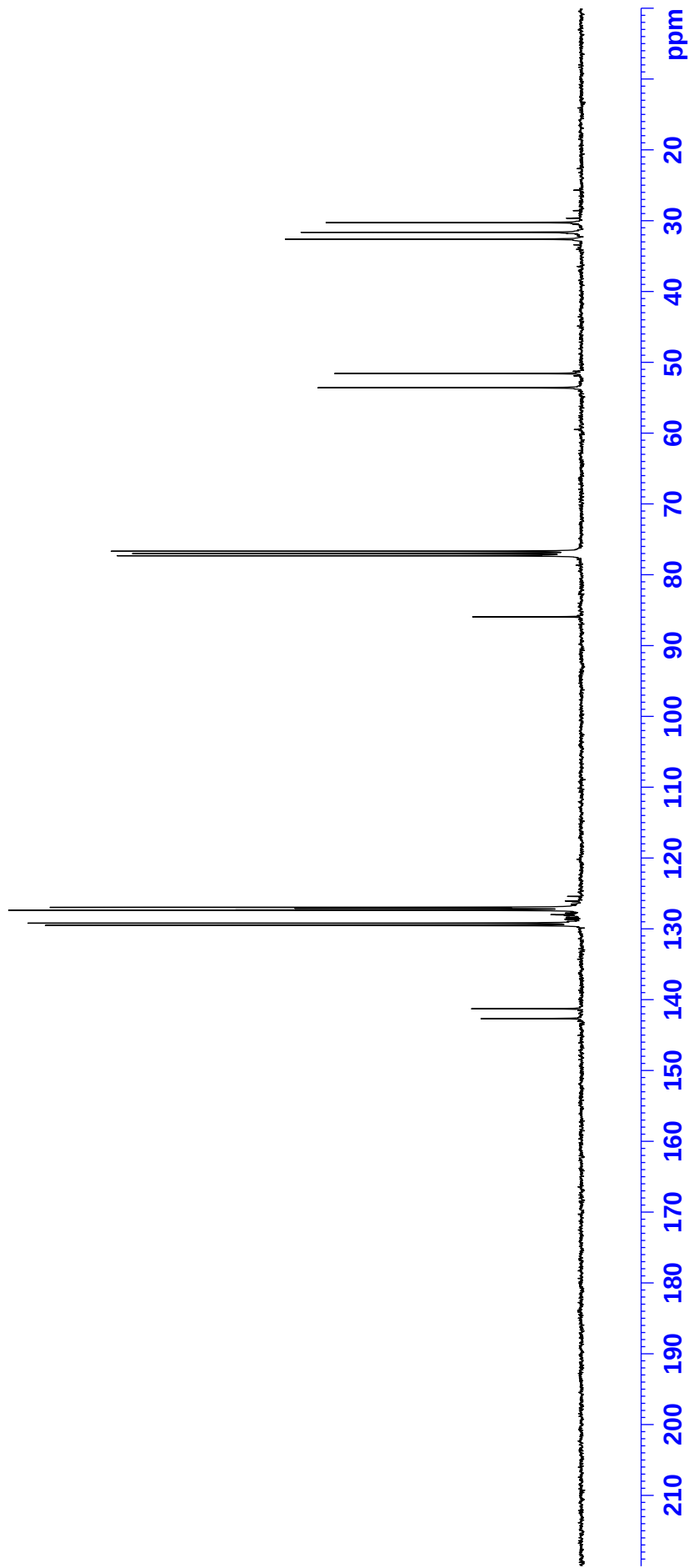
59.47

77.83
77.32
77.00
76.68

128.18
128.00
127.06
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126.05
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147.99
145.00





32.61
31.64
30.26

53.59
51.58

77.31
76.99
76.68

85.94

129.52
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127.09
126.96

142.67
141.28

