

# **(S)-Pramipexole and Its Enantiomer, Dexpramipexole: A New Chemoenzymatic Synthesis and Crystallographic Investigation of Key Enantiomeric Intermediates**

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## **SUPPLEMENTARY MATERIALS**

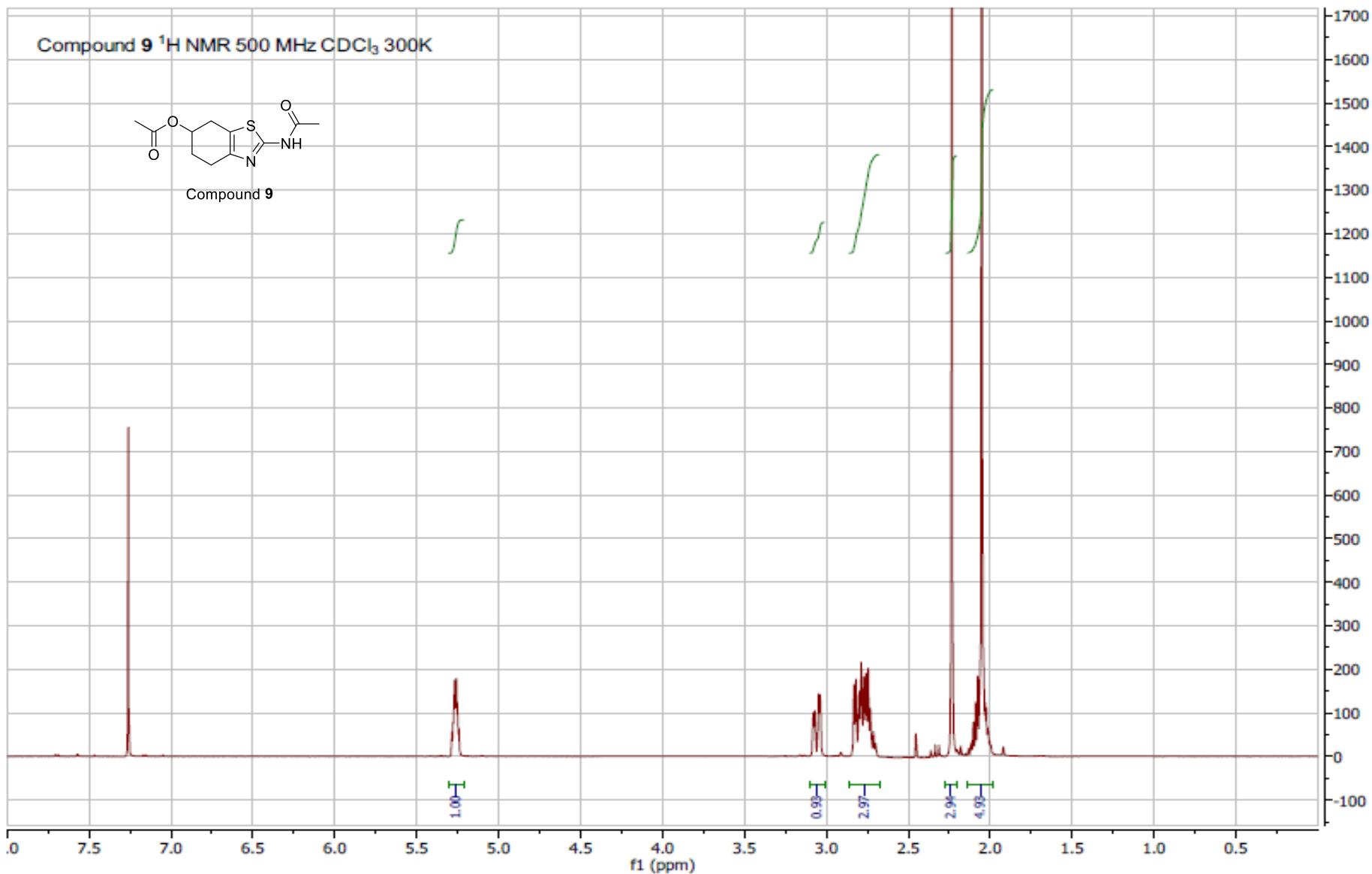


Figure S1.  $^1\text{H}$  NMR of compound 9

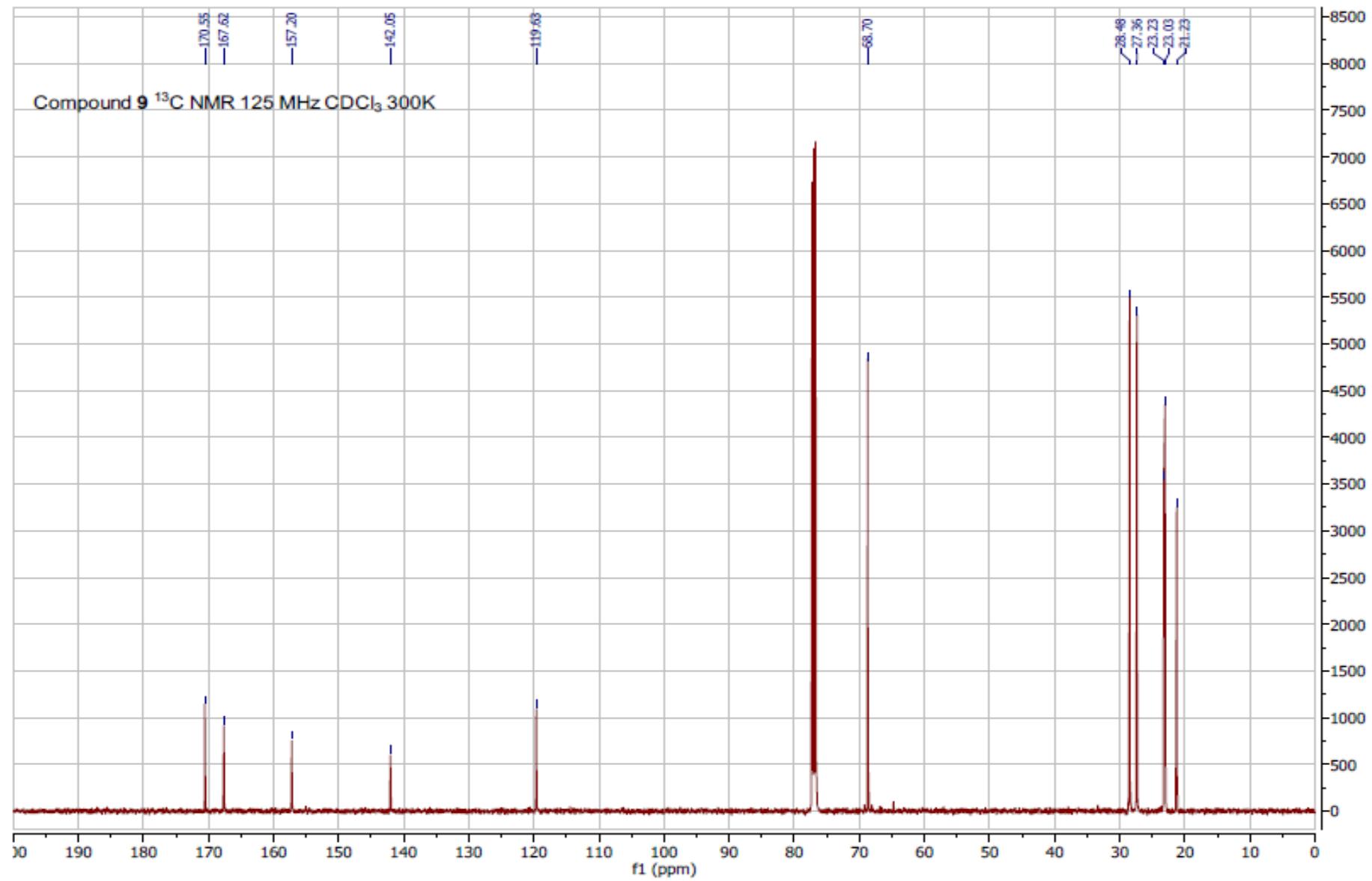


Figure S2.  $^{13}\text{C}$  NMR of compound 9

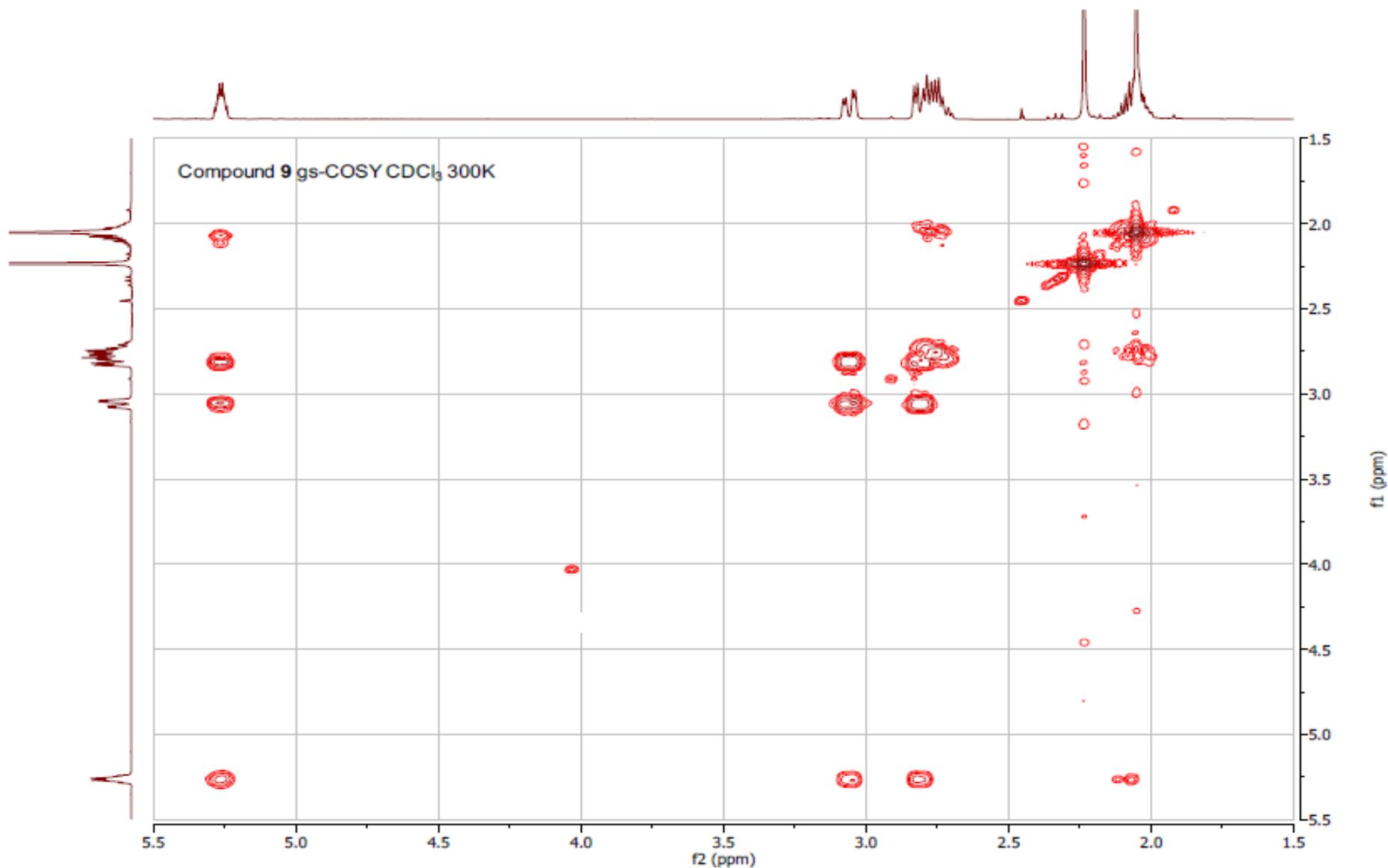


Figure S3. COSY of compound 9

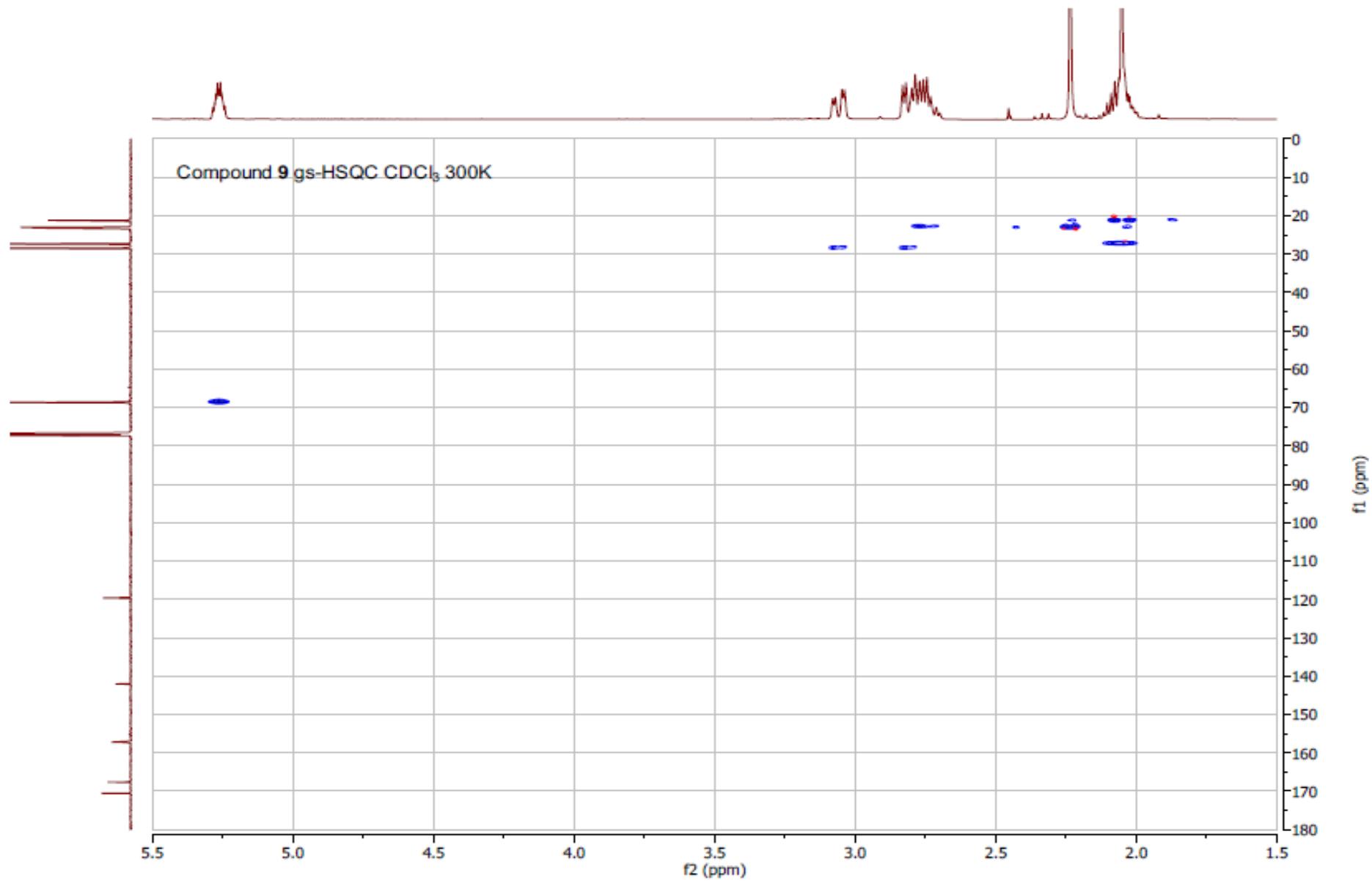


Figure S4. HSQC of compound 9

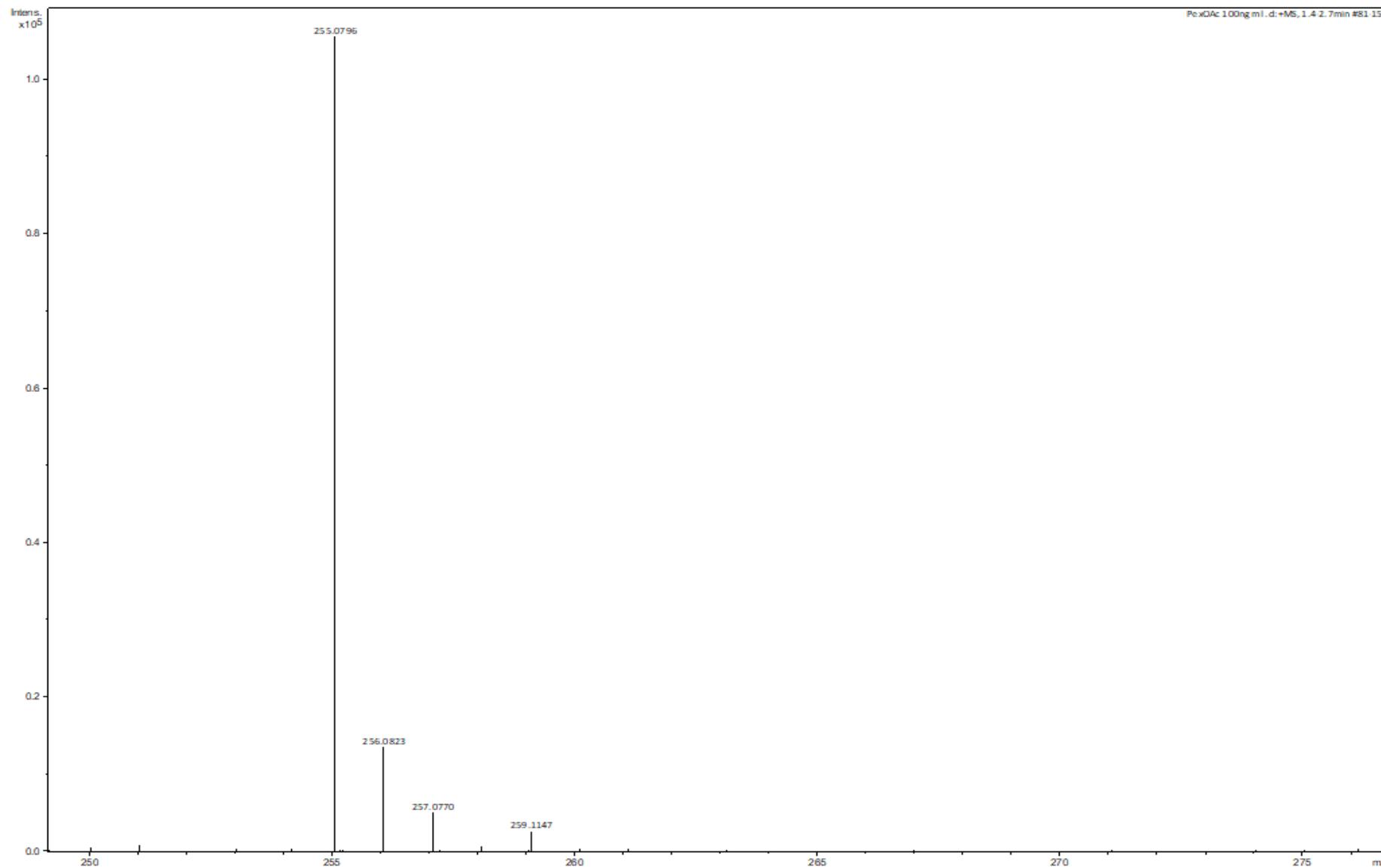
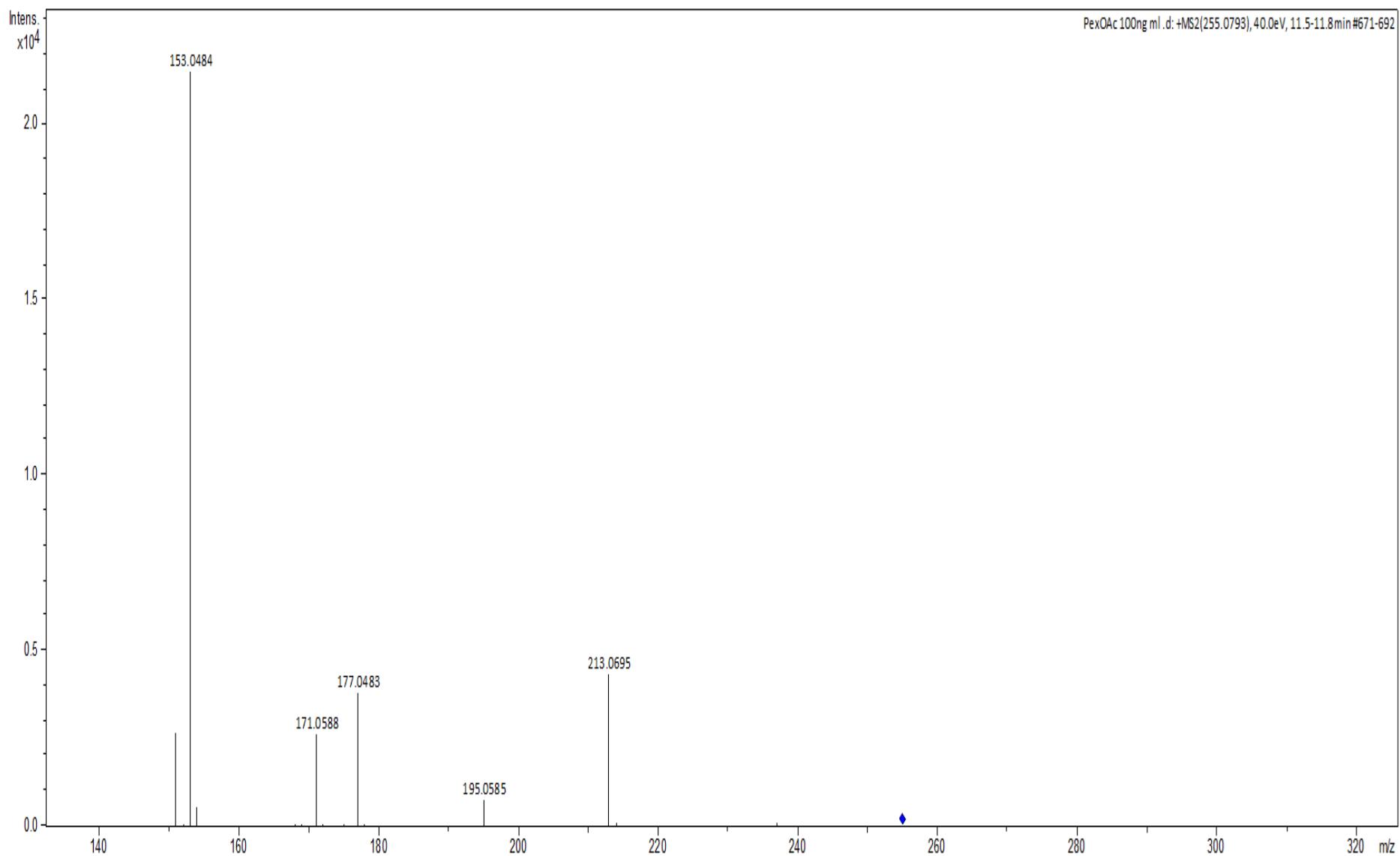
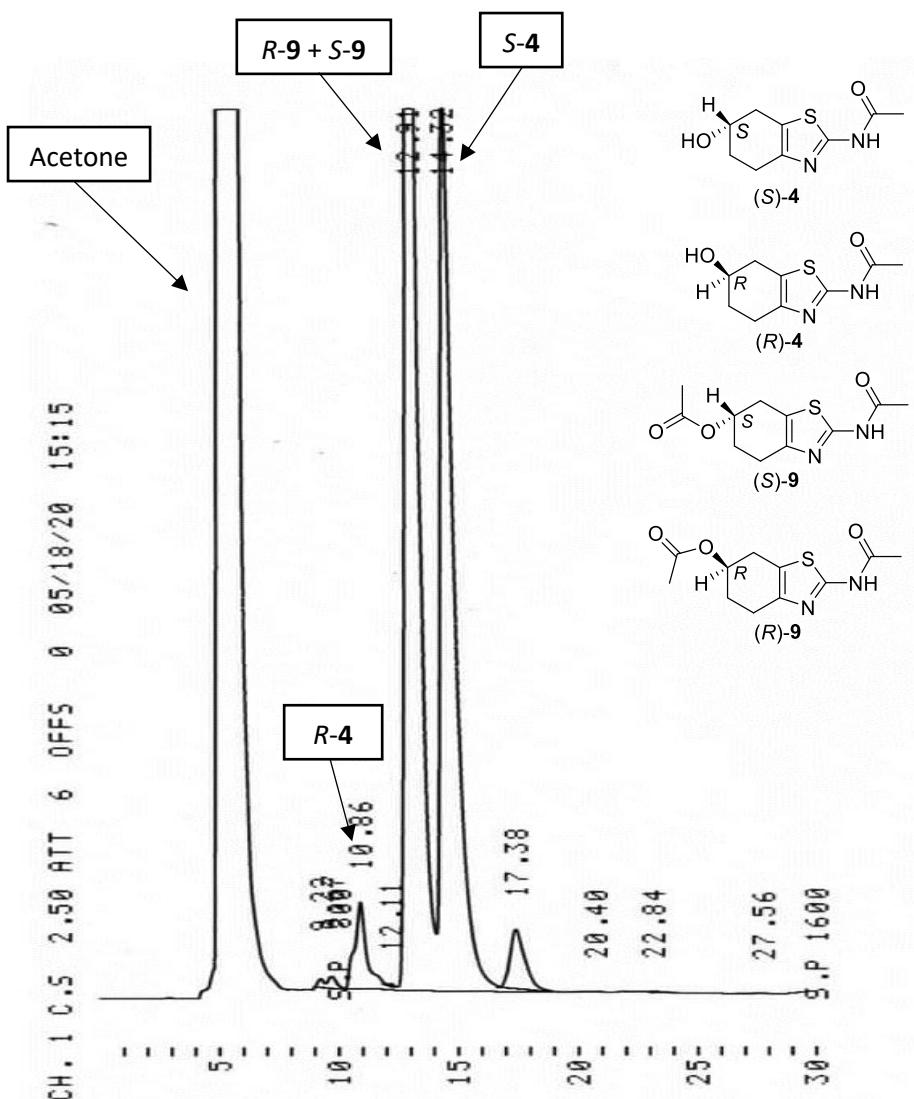


Figure S5. HRMS of compound 9



**Figure S6.** MS-MS of compound 9



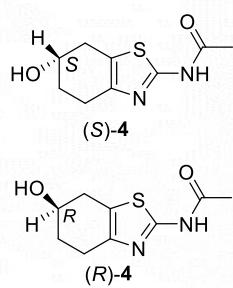
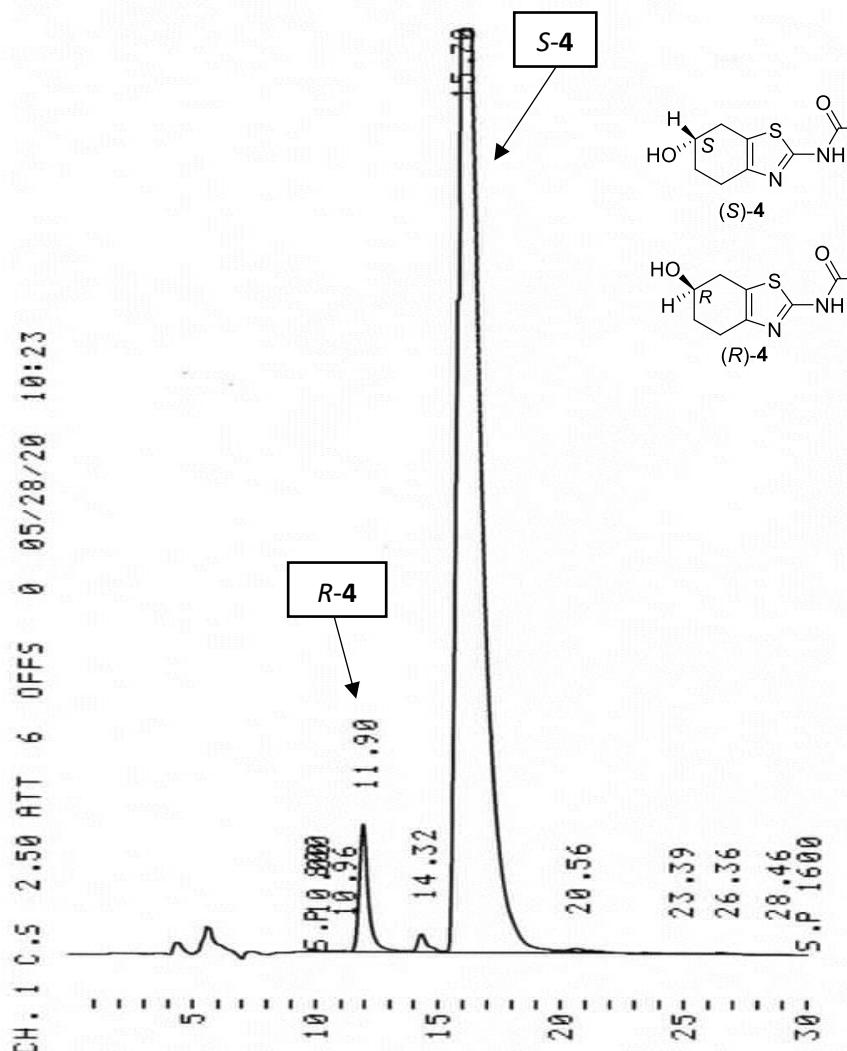
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1	9.22	8526	0.121	BV
2	9.67	18975	0.268	VB
3	10.86	231797	3.278	BV
4	12.11	17998	0.025	TBB
5	12.91	4002316	56.608	UV
6	14.32	2614438	36.978	UV
7	17.38	179840	2.544	TBB
8	20.40	4265	0.060	BB
9	22.84	5004	0.071	BB
10	27.56	3330	0.047	BB
TOTAL		7070289	100.000	
PEAK REJ :		0		
RAW DATA STORAGE NO.		1		

**Figure S7.** Lipase-catalyzed synthesis of enantioenriched (*S*)-*N*-(6-hydroxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)acetamide [(*S*)-4]. HPLC analysis of the crude reaction mixture



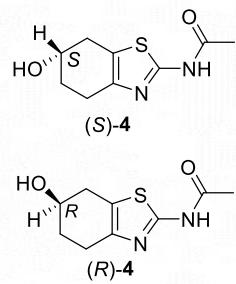
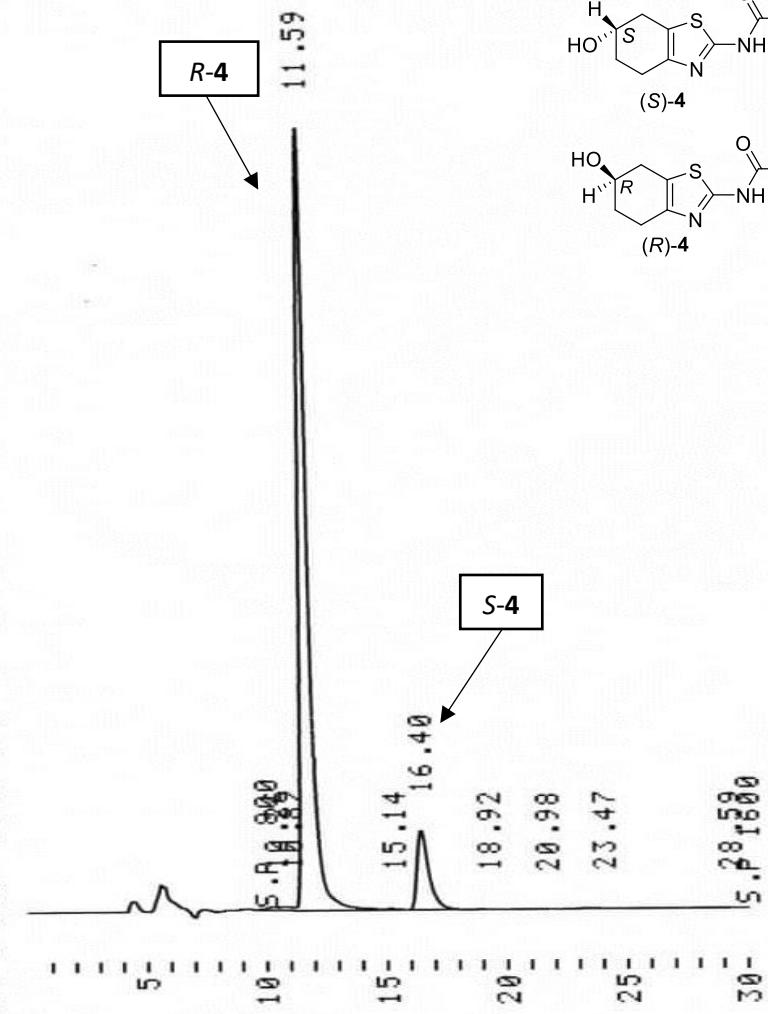
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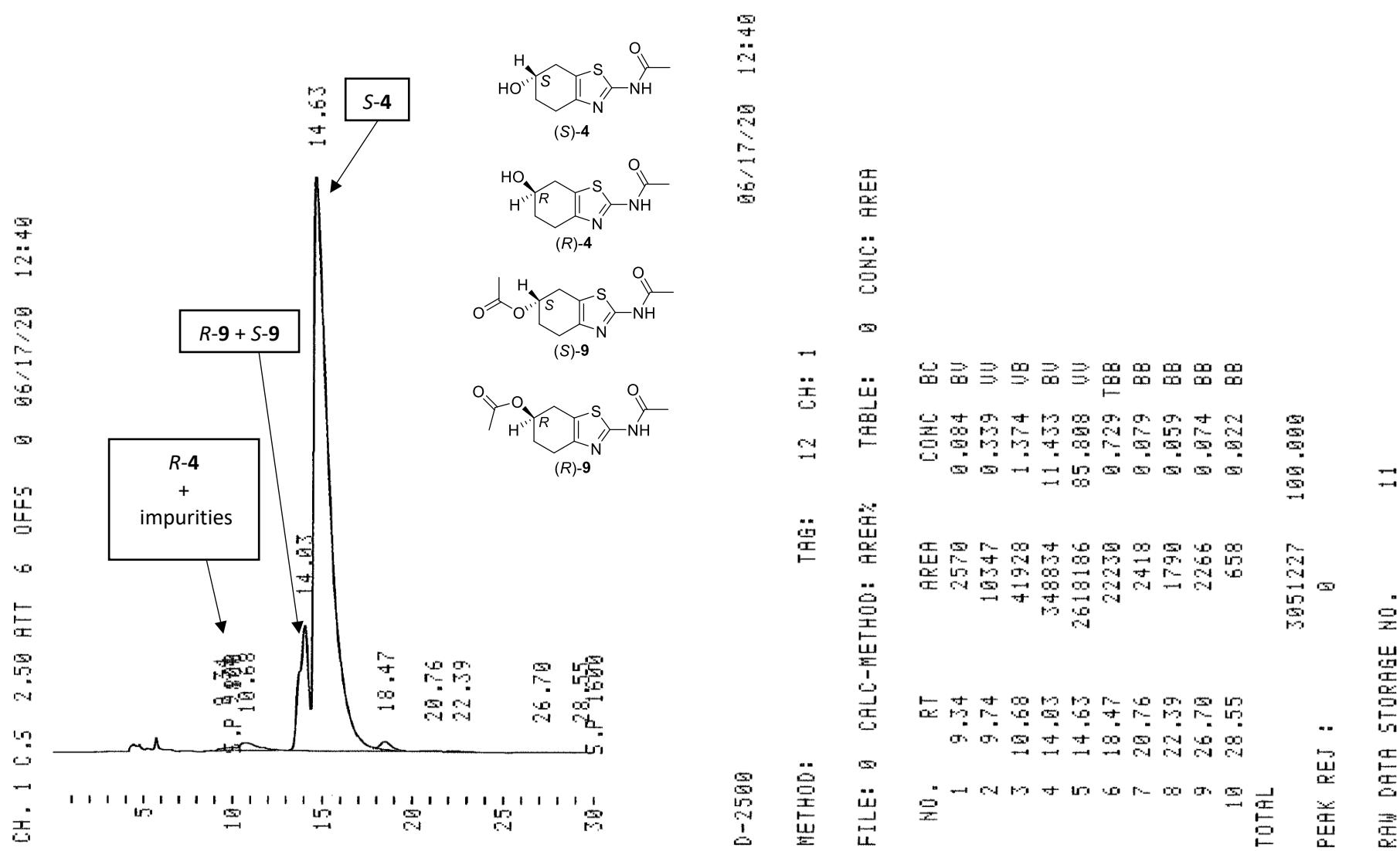
NO.	RT	AREA	CONC	BC
1	10.00	3153	0.063	BU
2	10.96	4120	0.082	UU
3	11.90	234928	4.670	UU
4	14.32	35460	0.705	UU
5	15.70	4726830	93.965	UU
6	20.56	10358	0.206	TBB
7	23.39	5828	0.116	BU
8	26.36	6182	0.123	UB
9	28.46	3571	0.071	B
TOTAL		5030430	100.000	
PEAK REJ :		0		

RAW DATA STORAGE NO. 5

CH. 1 C.5 2.50 ATT 6 OFFS 0 05/28/20 13:36

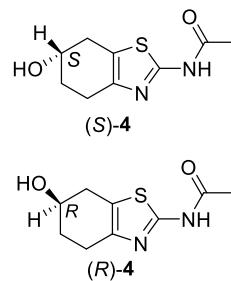
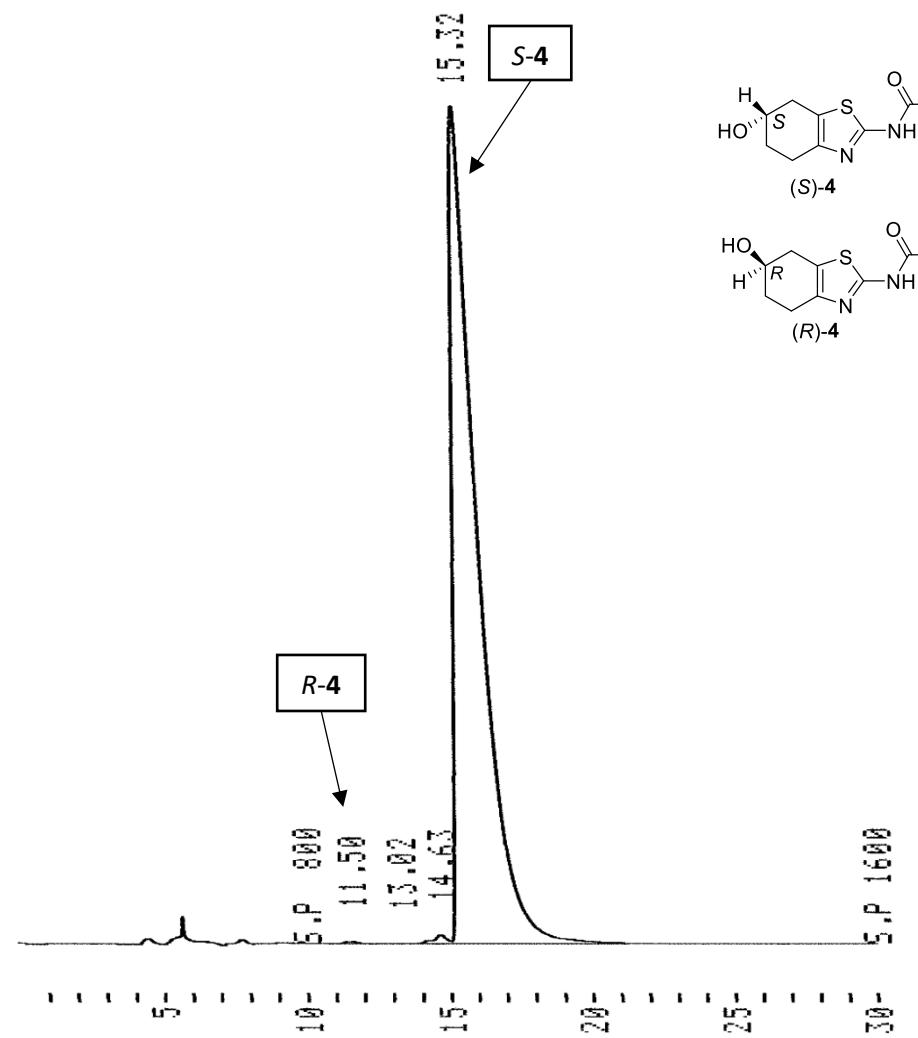


D-2500					
05/28/20 13:36					
METHOD: TAG: 9 CH: 1					
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NO.	RT	AREA	CONC	BC	
1	10.26	5.665	0.396	BU	
2	10.82	6.288	0.439	UU	
3	11.59	123.0278	85.925	UU	
4	15.14	1.670	0.117	TBB	
5	16.40	173.0103	12.090	BU	
6	18.92	1.719	0.120	TBB	
7	20.98	1.852	0.129	BB	
8	23.47	9.571	0.668	BB	
9	28.59	1.666	0.116	BB	
TOTAL		1431.812	100.000		
PEAK REJ:		0			
RAW DATA STORAGE NO.		7			



**Figure S10.** Lipase-catalyzed synthesis of enantiopure (S)-N-(6-hydroxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)acetamide [(S)-4]. HPLC analysis of the crude reaction mixture

CH. 1 C.5 2.50 ATT 6 OFFS 0 06/22/20 14:33



06/22/20 14:33

METHOD: TAG: 7 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

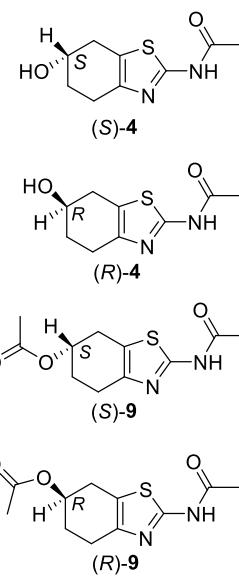
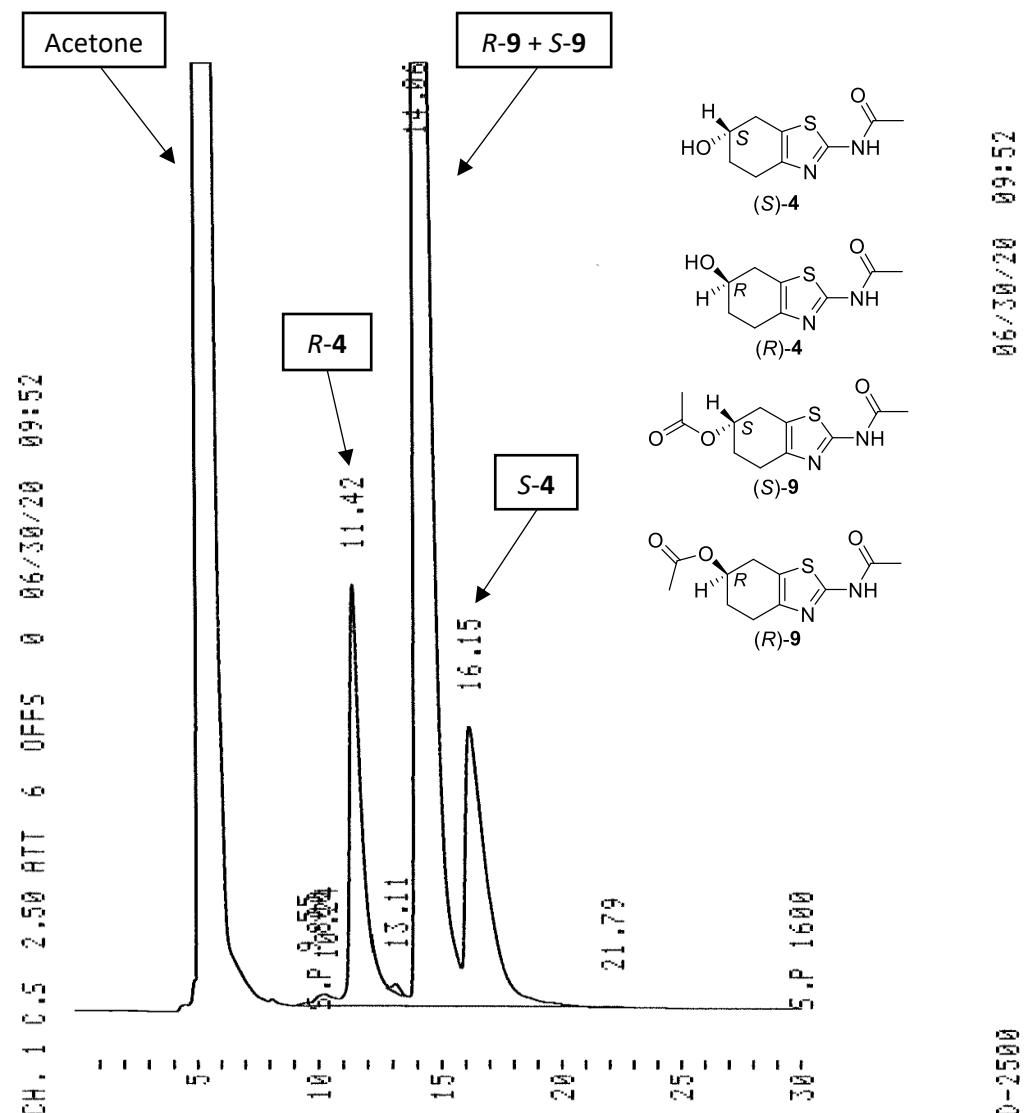
NO.	RT	AREA	CONC	BC
1	11.50	5140	0.142	BB
2	13.02	828	0.023	BB
3	14.63	19552	0.541	BU
4	15.32	3591333	99.294	VB

TOTAL

3616853 100.000

PEAK REJ : 0

**Figure S11.** Lipase-catalyzed synthesis of enantiopure (S)-N-(6-hydroxy-4,5,6,7-tetrahydrobenzo[d]thiazol-2-yl)acetamide [(S)-4]. HPLC analysis of the purified (S)-4



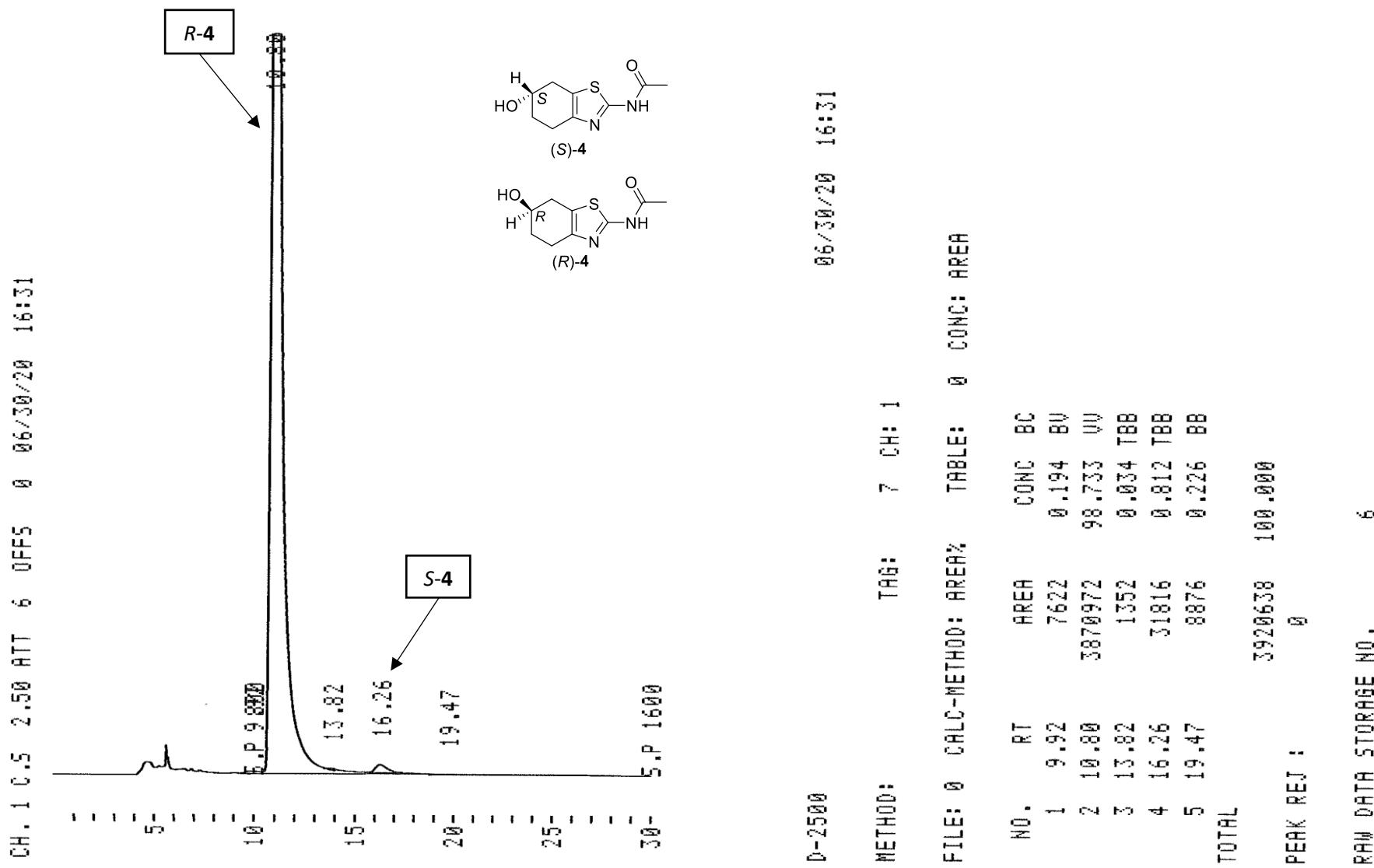
METHOD: TAG: 3 CH: 1

FILE: 0 CALC-METHOD: AREA%

TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	9.55	4313	0.044	BV
2	10.24	38525	0.389	VU
3	11.42	1032540	10.427	VU
4	13.11	8381	0.085	TBB
5	14.06	7664037	77.398	VU
6	16.15	1151424	11.628	VU
7	21.79	2896	0.029	BB
TOTAL		9902116	100.000	
PERK REJ :	0			
RAW DATA STORAGE NO.	2			

**Figure S12.** Lipase-catalyzed synthesis of enantiopure (*R*)-2-Acetamido-4,5,6,7-tetrahydrobenzo[d]thiazol-6-yl acetate [(*R*)-9]. HPLC analysis of the crude reaction mixture



**Figure S13.** Lipase-catalyzed synthesis of enantiopure (*R*)-2-Acetamido-4,5,6,7-tetrahydrobenzo[d]thiazol-6-yl acetate [(*R*)-9]. HPLC analysis of the purified and hydrolyzed (*R*)-9