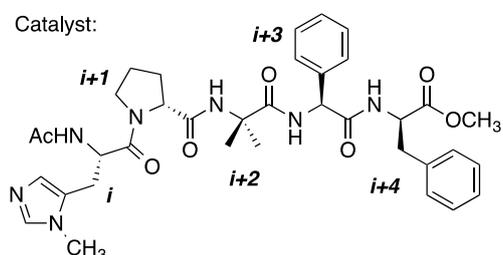
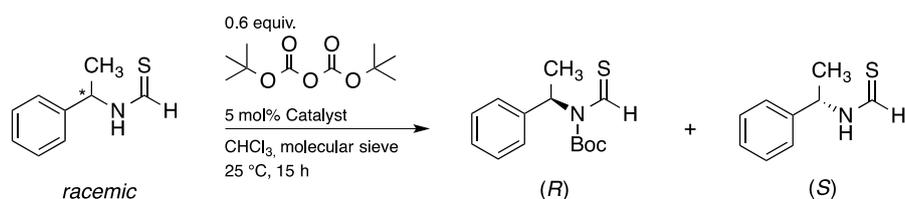
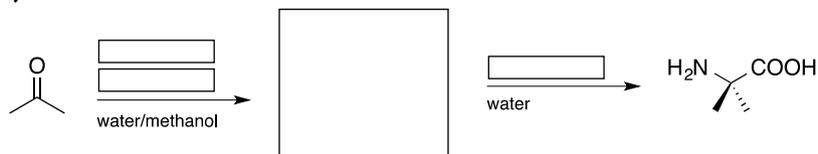


## Problem Set 12

1. In 2010, Prof. Scott Miller and his co-workers reported a peptide-catalyzed kinetic resolution of thioformamides. Towards this goal, the group developed a tetrapeptide that performs a selective Boc-protection of the (*R*)-enantiomer while the (*S*)-enantiomer does not react (see scheme below).



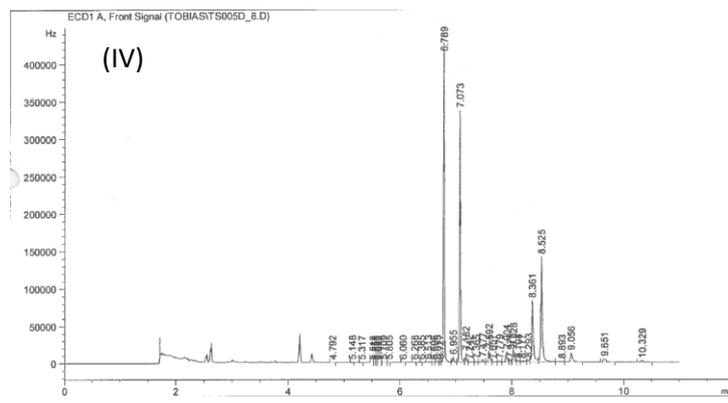
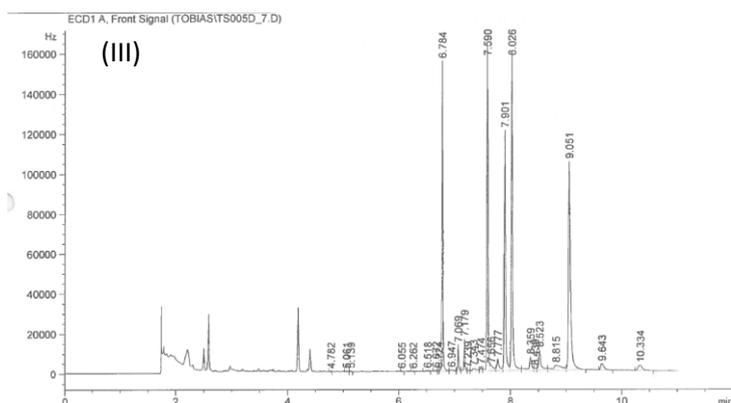
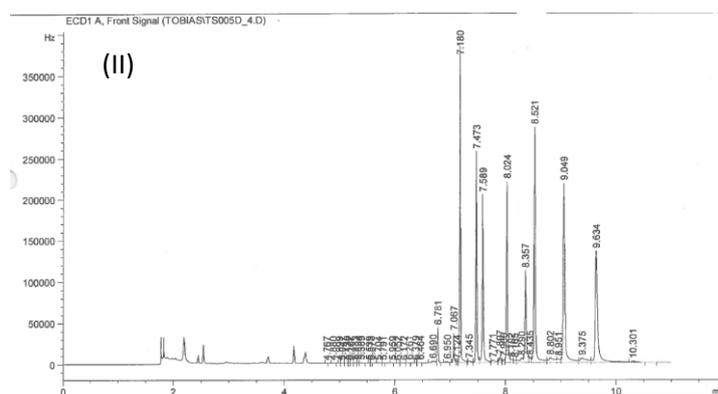
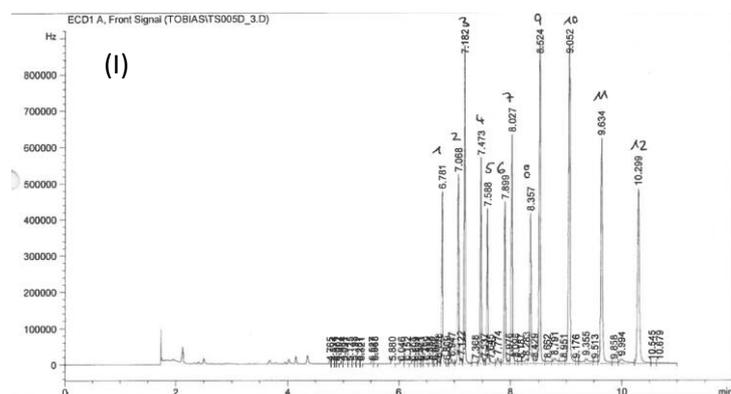
- a) Explain the role of the amino acids in the following positions for the structure and the reactivity of the catalyst: **(6 points)**
- (I) *i*  
 (II) *i+1* and *i+2*  
 (III) *i+3* and *i+4*
- b) Propose a mechanism for the kinetic resolution based on your reasoning in a). **(6 points)**
- c) What is the name and the three letter code of the amino acid in position *i+2*? **(2 points)**
- d) The amino acid in position *i+2* can be synthesized from acetone in two steps. Fill in the missing structures into the following reaction scheme and provide the name of the reaction. **(5 points)**



reaction name:

2. Split-and-mix libraries can be used to identify e.g. catalysts, enzyme inhibitors or selective supramolecular binders. After performing an appropriate assay, you have isolated three beads as “hits” from a tripeptide library Ac-AA<sub>3</sub>-AA<sub>2</sub>-AA<sub>1</sub>-resin that had been encoded using electrophoretic tag molecules as introduced by Prof. W. Clark Still (PNAS 1993, 90, 10922).

Gas chromatograms of all of the “tags” (I) and the “tags” recorded for each of the three beads (II–IV) are shown below together with the encoding scheme of the library. Which peptides are on the three “hits”?



AA3	AA2	AA1	Tag Code
T1-T4	T5-T8	T9-T12	
Gly	Gly	Gly	0001
L-Pro	D-Pro	L-Pro	0010
D-Pro	L-Pro	D-Pro	0011
L-Ala	D-Ala	L-Ala	0100
D-Val	L-Val	D-Val	0101
L-Ser	D-Ser	L-Ser	0110
D-Thr	L-Thr	D-Thr	0111
L-Asp	D-Asp	L-Asp	1000
D-Glu	L-Glu	D-Glu	1001
L-Asn	D-Asn	L-Asn	1010
D-Gln	L-Gln	D-Gln	1011
L-His	D-His	L-His	1100
D-Arg	L-Arg	D-Arg	1101
L-Phe	D-Phe	L-Phe	1110
D-Tyr	L-Tyr	D-Tyr	1111