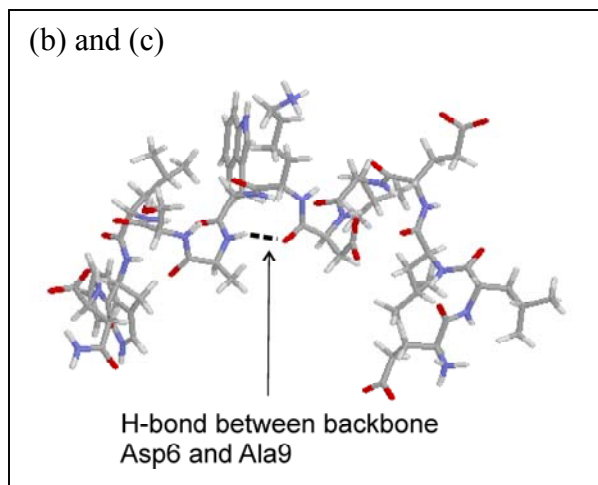


Key to HW #1, Spring 2006, CHEM 519

1. A --> (c); B --> (e); C --> (d); D --> (a); E --> (b)

2. (a) From Tonlolo & Benedetti, *TiBS* 1991, 16, 350-3.

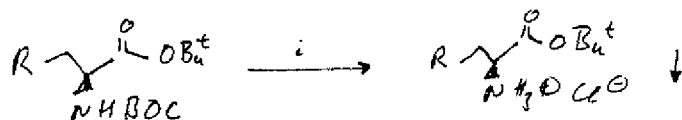
ϕ : -57°; ψ : -30°; backbone H-bonding:
i -> *i*+3; residue per turn: 3.24



3.

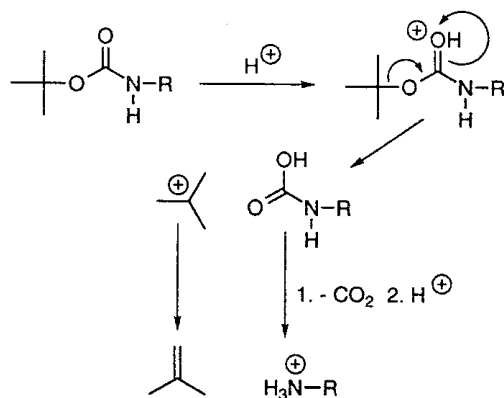
H. Rapoport et al., JOC (1994) 59, 3216.

5x (1M) HCl in dry EtOAc, 5 hrs. (= *i*)



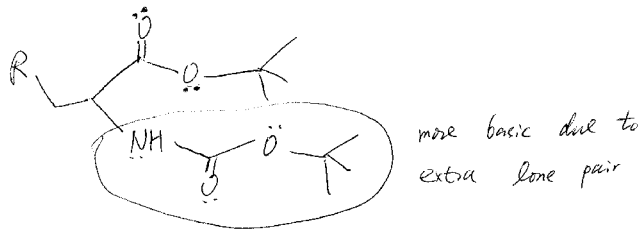
The question is why the N-Boc group is selectively removed while keeping the tBu on the ester intact. The key points are:

- The mechanism for N-Boc removal in dry HCl (non-nucleophilic solvent):



SCHEME 2.1 Acidolytic removal of the Boc group.

- Compare the Boc protected amide and the tBu protected ester, the amide is more basic, thus is selectively deprotected.



- Product hydrochloride ppt., favors the removal of N-Boc.

4. (a) See Table

	Pka	net charge		
		pH 7	pH 8	pH 9
Terminal amino	8	1	0.5	0
H	6	0	0	0
Y	10.9	0	0	0
G				
R	12.5	1	1	1
P				
C	8.3	0	0	-1
Terminal carboxyl	3.1	-1	-1	-1
Total Charge		1	0.5	-1

(b) Estimated pI between 8 and 9.

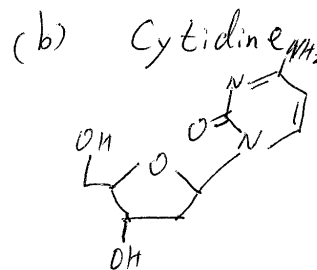
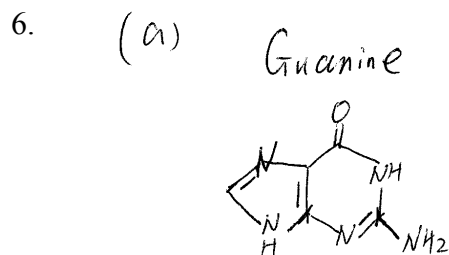
5. The peptide sequence is AVRYSR

(a) N-terminal is A;

(b) No Carboxypeptidase digestion --> C terminal is R

(c) Trypsin digest (carboxyl side of R)--> two fragment A?R and ??R --> one of the fragment is AVR

(d) Chymotrypsin digest (carboxyl side of Y) --> C terminal side SR --> the other fragment is YSR



7. (a) Yes. C⁶ amino of A.

(b) No.

(c) Any amino acid side chain with H-bond donor, as the minor groove of the A/T pair has two H-bond acceptor (C2 carbonyl of T and N3 of A).

8. Duplex 1 is thermodynamically more stable and has a higher Tm.

- There are two major factors dictating duplex stability: (1) H-bonding; and (2) base stacking.
- Duplex 1 and 2 have the same total # of A/T and G/C pairs, thus the same # of H-bonds.
- The difference is in stacking, which is related to the nearest-neighbor pattern. Duplex 1 has consecutive G/C pairs (GG/CC), which stacks better than the GT/CA pairs.
- This leads to a more negative ΔG_{37}^0 for duplex 1, and therefore higher Tm.
- While a detailed calculation of ΔG_{37}^0 is not necessary, the ΔG_{37}^0 calculations confirm the previous statements.

Duplex 1:

5' AACGGGTTT 3'
3' TTGCCAAA 5'

NN pairs	ΔG_{37}^0	total #
5' AA TT	-1.02	4
5' AC TG	-1.43	2
5' CG GC	-2.09	1
5' GG CC	-1.77	2

$\Delta G_{37}^0(NN) = -12.57 \text{ kcal/mol.}$

$\Delta G_{37}^0(\text{duplex 1}) = \Delta G_{37}^0(NN) + \Delta G^0(\text{ini. } \overset{G-C}{\cancel{\text{TTT}}})$
 ~~$+ \Delta G_{37}^0(\text{TTT})$~~
 $= -12.57 + 1.82$
 $\Delta G_{37}^0(\text{duplex 1}) = -10.75 \text{ kcal/mol.}$

Duplex 2:

5' AACCTGTGTG T 3'
3' TTGACACACA 5'

NN pairs	ΔG_{37}^0	total #
5' AA TT	-1.02	1
5' AC TG	-1.43	1
5' CT GA	-1.16	1
5' TG AC	-1.38	3
5' GT CA	-1.43	3

$\Delta G_{37}^0(NN) = -12.04$

$\Delta G_{37}^0(\text{duplex 2}) = -10.22 \text{ kcal/mol.}$

Notes: (1) No symmetry correction as the sequences are none-self-complementary; (2) The initiation penalty is 1.82 kcal/mol as each sequence has at least one G/C pair; and (3) penalty of 5' terminal T.A pair does not apply.

9. (a) Primers shown in red

1 10 20 910 920 930

5' GCA, ATG, GTA, CGG, TAC, TTC, CAT, TGTC-----TAT, GTT, GGG, GAT, TAA, ACC, CTG, ATT, GAG 3'
CCC, CTA, CTT, TGG, GAC, TAA, CTC 5'

5' GCA, ATG, GTA, CGG, TAC, TTC, C

3' CGT, TAC, CAT, GCC, ATG, AAG, GTA, ACAG-----ATA, CAA, CCC, CTA, CTT, TGG, GAC, TAA, CTC 5'

(b)

$$N = N_0 (1 + \gamma)^x$$

$$N = 1 \times 10^9$$

$$N_0 = 1,$$

$$\gamma = 0.9.$$

$$(1 + \gamma)^x = N_0 / N$$

~~⊗~~

$$x \log_{10}(1 + \gamma) = \log_{10}(N_0 / N)$$

$$x = \frac{\log_{10}(N_0 / N)}{\log_{10}(1 + \gamma)} = \frac{\log_{10}(1 \times 10^9)}{\log_{10}(1.9)}$$

$$x = \frac{9}{0.2787} = 32.3 \approx 33$$

need 33 cycles.