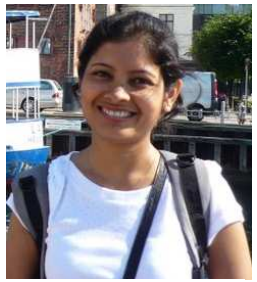

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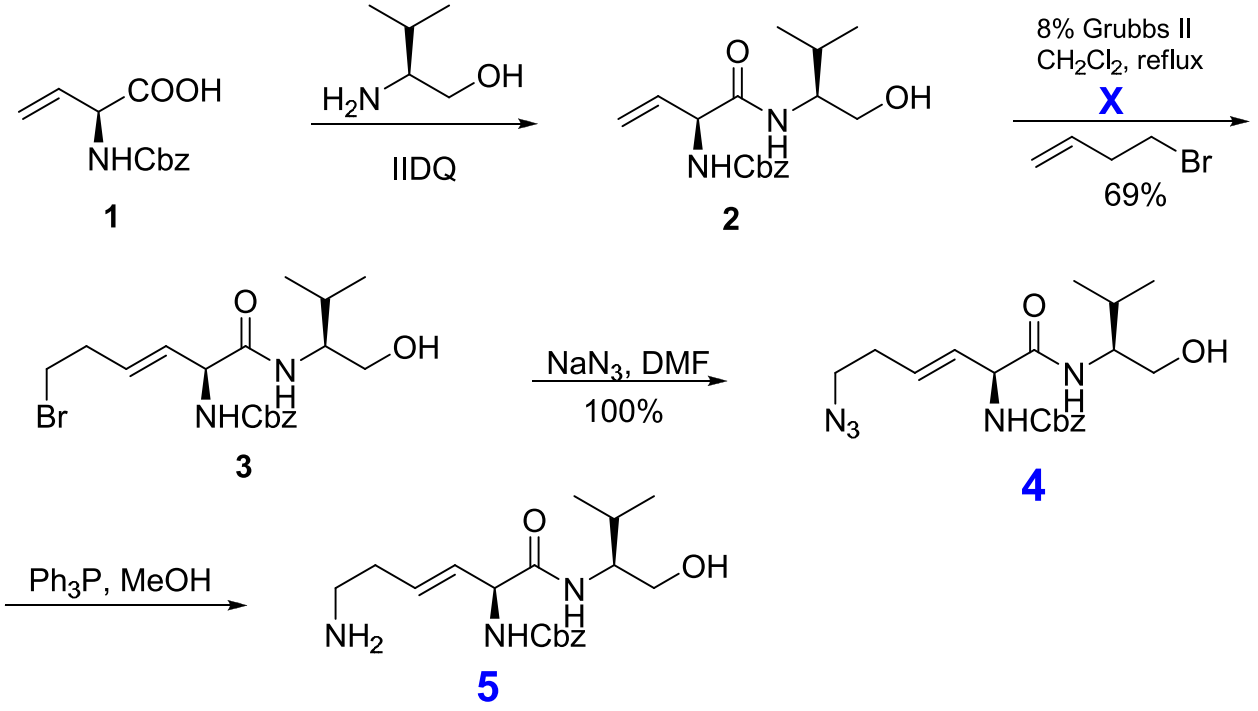
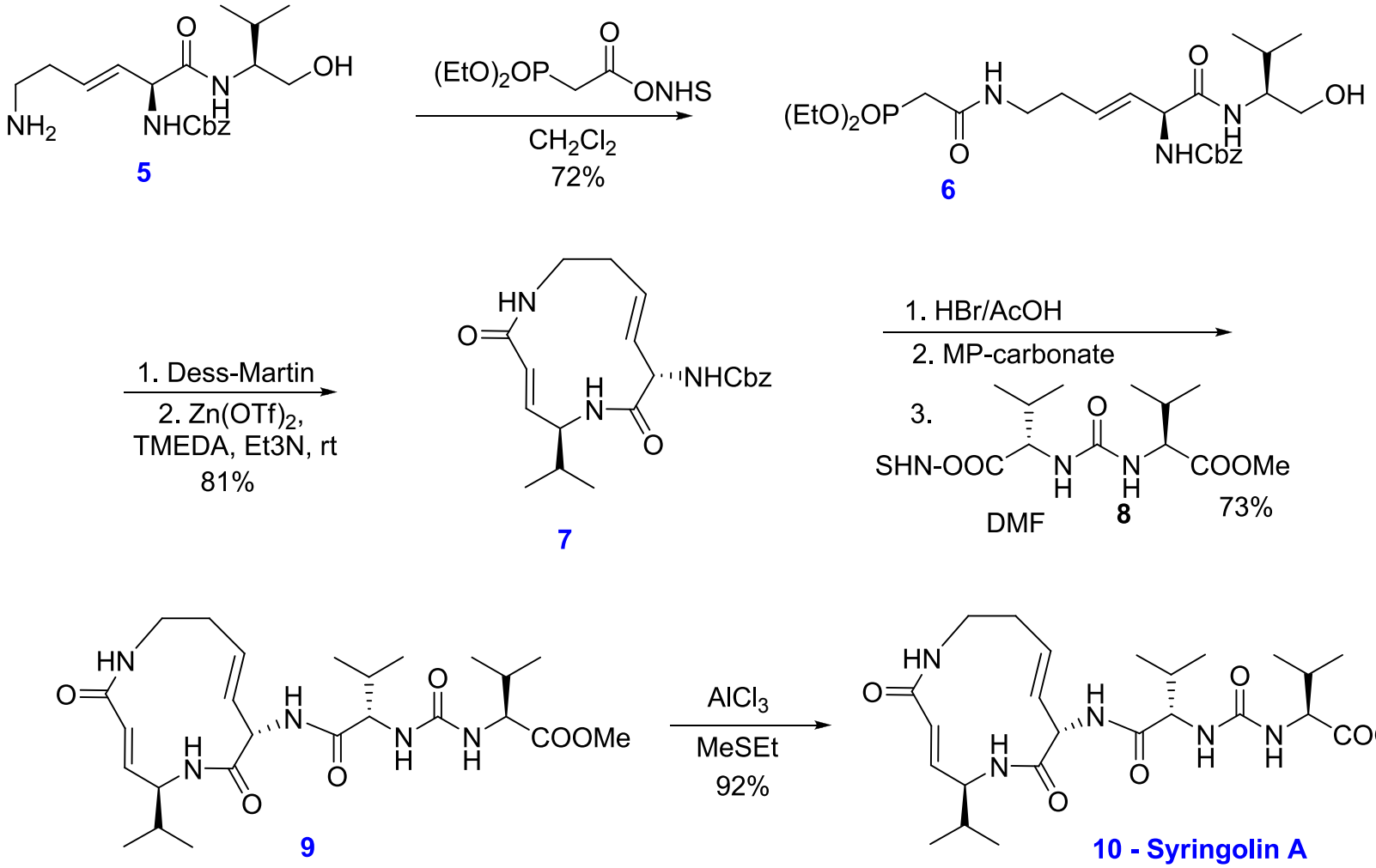
Synthesis of Proteasome Inhibitor (Syringolin A).

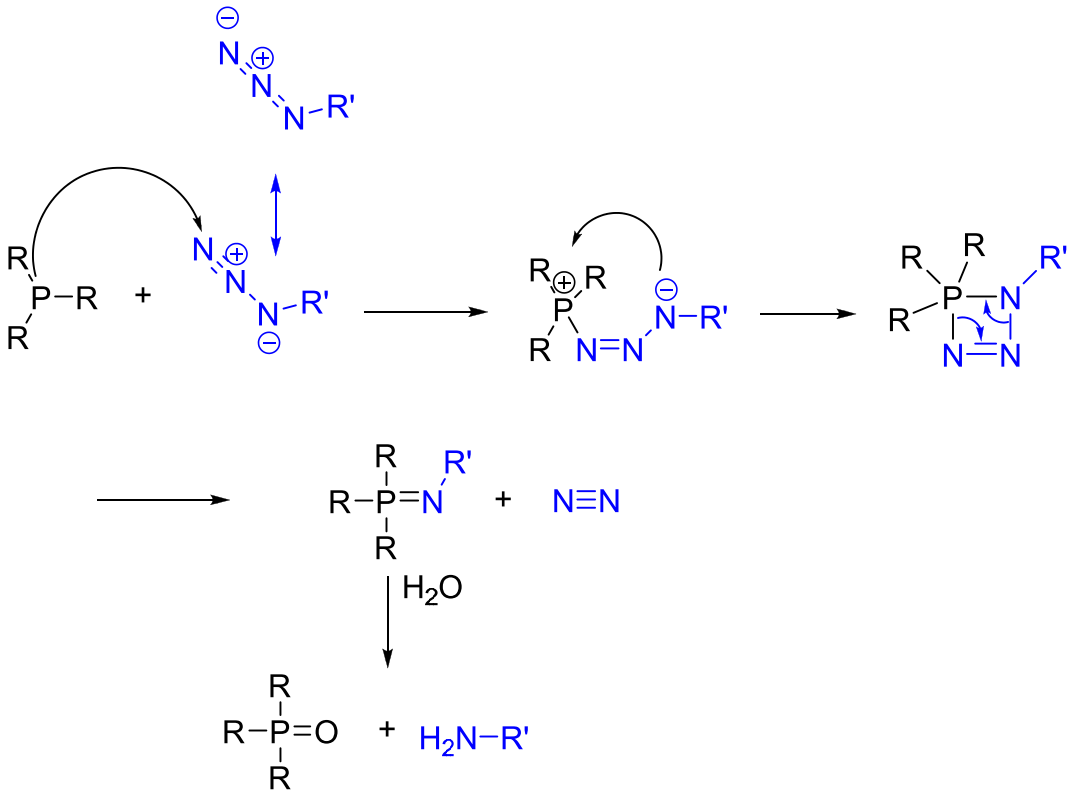
In 2008, two macrolactams, syringolin A and B were shown to affect plant-pathogen interactions and to act as virulence factors via inhibition of the proteasome. Given below is the total synthesis of proteasome inhibitor, syringolin A.



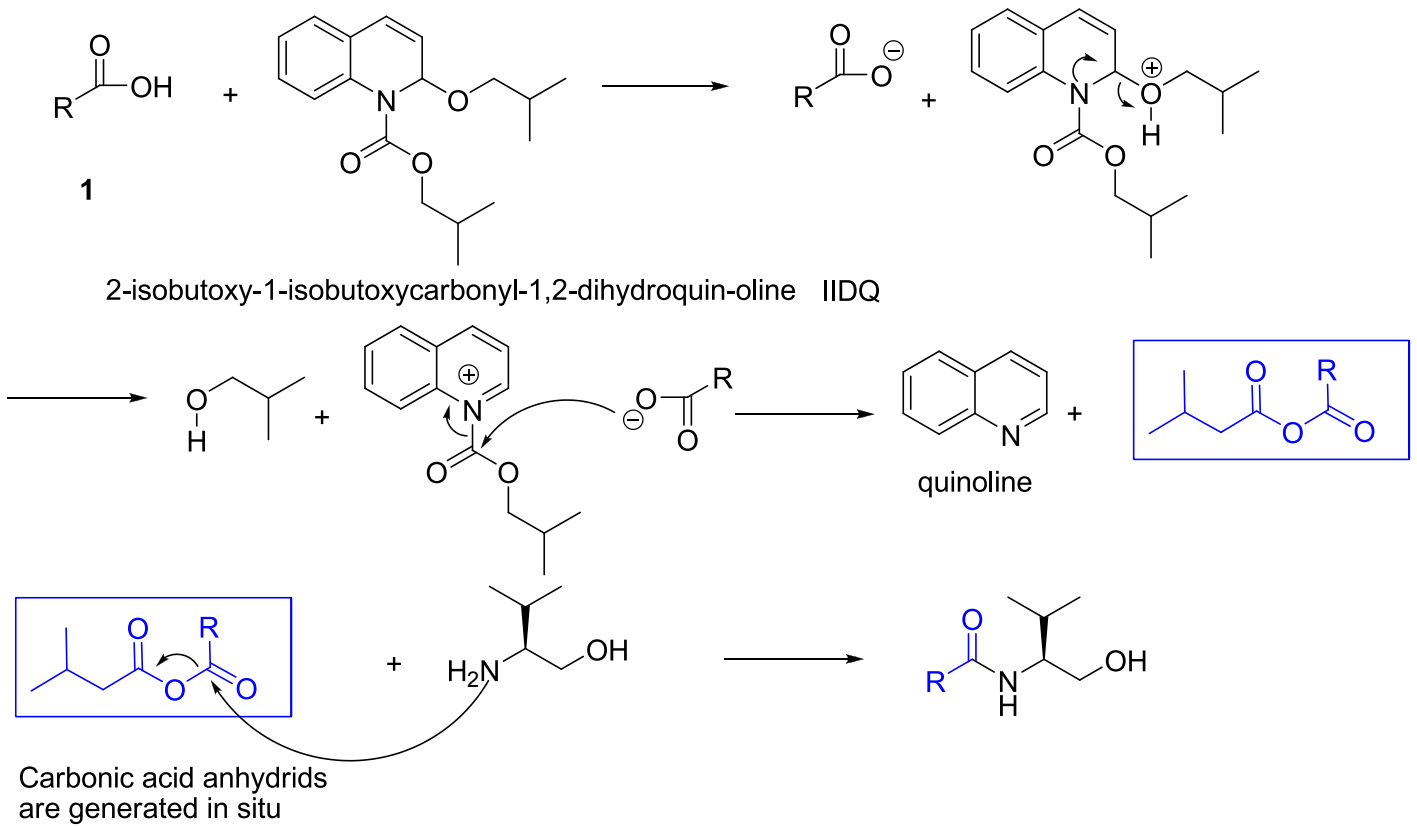
**IIDQ = 2-isobutoxy-1-isobutoxycarbonyl-1,2-dihydroquin-oline (IIDQ).


NH2
NHCbz
OH
5
(EtO)2OP
ONHS
CH2Cl2
72%
6
1. Dess-Martin
2. Zn(OTf)2,
TMEDA, Et3N, rt
81%
HN
NHCbz
7
1. HBr/AcOH
2. MP-carbonate
3.
SHN-OOC
COOMe
DMF
8
73%
9
AlCl3
MeSEt
92%
COOH
10 - Syringolin A

2. Staudinger reduction



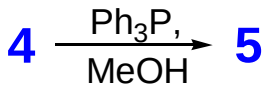
3. Mechanism of coupling with IIDQ



An advantage of using EEDQ or IIDQ for the generation of mixed carbonic anhydrides is that the activated carboxyl component can undergo aminolysis immediately so that there is less likelihood of troublesome side reactions intervening. As might be expected, IIDQ leads to less acylation at the wrong carbonyl group than does EEDQ. The by-products of the reaction are carbon dioxide, quinoline **40**, and ethanol or isobutanol, so that coupling is clean and workup straightforward.

Questions:

1. Find out X and the structures 4-10.
2. Identify the Name reaction for the step and also give the mechanism:



3. Show the synthesis of compound 8.
4. Give the mechanism of coupling with IIDQ

Pour toute erreur veuillez me contacter sur mon adresse e.mail : abdallah.hamze@u-psud.fr