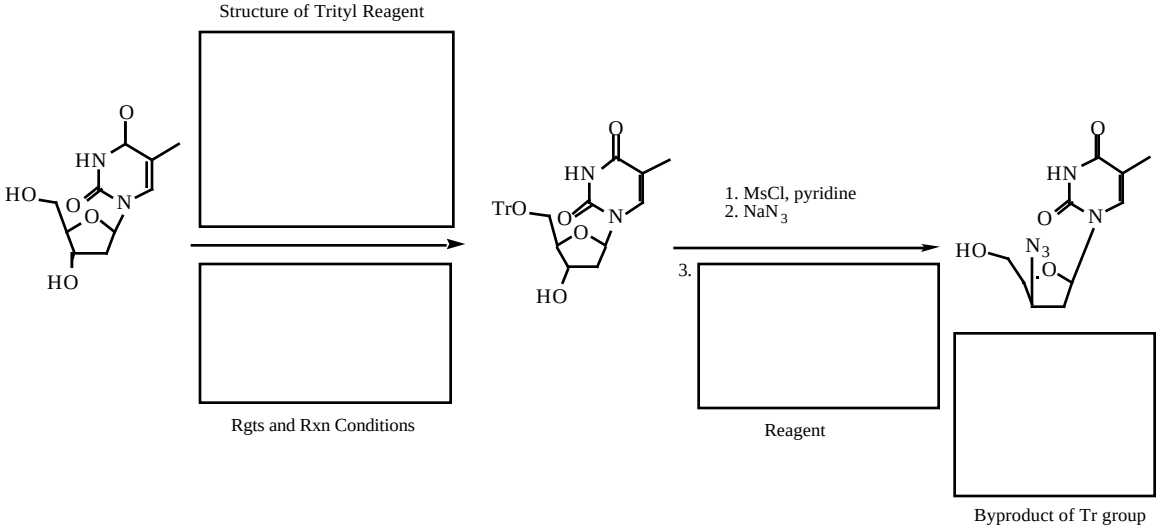
Protecting Group Chemistry

Organic Cumulative Exam, September 1999

The useful book, "Protective Groups in Organic Synthesis" (Greene and Wuts) begins with a statement that clearly summarizes the need for protecting groups in organic chemistry: "When a chemical reaction is to be carried out selectively at one reactive site in a multifunctional compound, other reactive sites must be temporarily blocked". Hundreds of useful blocking groups have been developed over the years. Here we will look at several commonly used protecting groups, along with a couple of new ones. Make sure that you **show the <u>complete structure</u> of the protecting group in your answers**.

1. Trityl group. Please provide the information requested in the boxes.

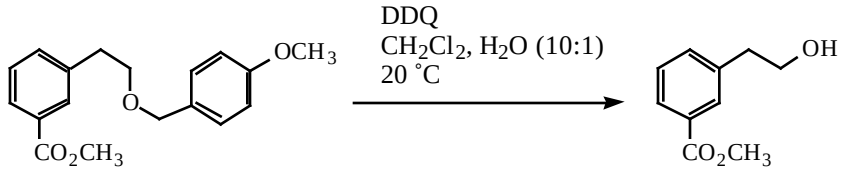


2. Introduction of *p*-methoxy substituents to the trityl group increases the rate of hydrolysis under standard removal conditions (which you gave above).

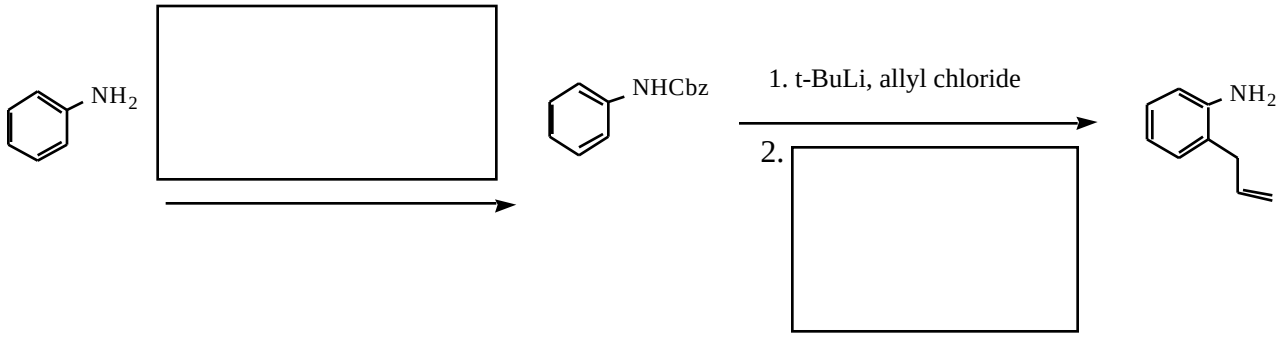
trityl (Tr)	48 h
monomethoxytrityl (MMT)	2 h
dimethoxytrityl (DMT)	15 min
trimethoxytrityl (TMT)	1 min

Please explain the trend in the Table shown above.

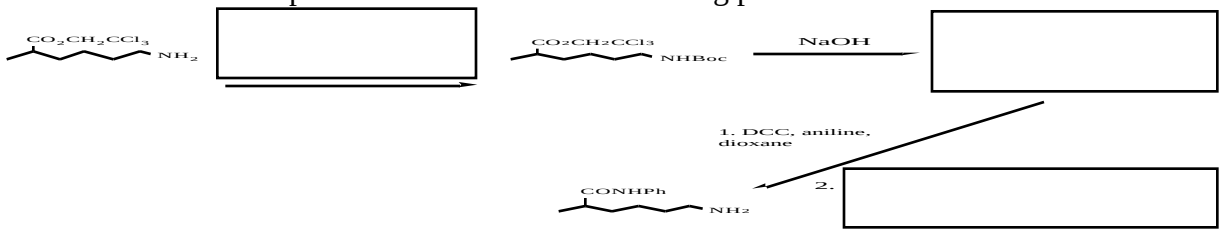
3. Provide a mechanism for removal of the *p*-methoxybenzyl protecting group from an alcohol using DDQ. The structure of the deprotected alcohol is given, be sure to show all products.



4. Cbz or Z protecting group. Provide standard, or common, reagents for the transformations shown.

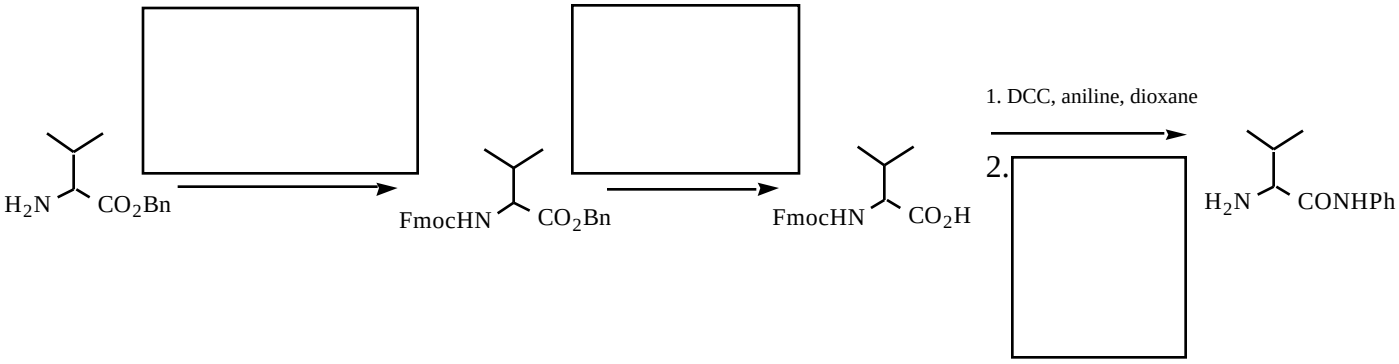


5. Boc and trichloroethyl protecting groups. (a) Provide standard, or common, reagents for the transformations shown and provide a structure for the missing product.



(b) Sometimes when a Boc group is used to protect a highly functionalized molecule, PhSH is added to the deprotection reaction. Suggest a reasonable role for this additive.

6. Fmoc and Bn protecting groups. (a) Provide standard, or common, reagents for the transformations shown. (b) Show the structure of the Bn group. (c) Show the structure of the protecting group-derived species that is initially released during removal of the Fmoc group. Provide a rationalization as to why this is a stable species.

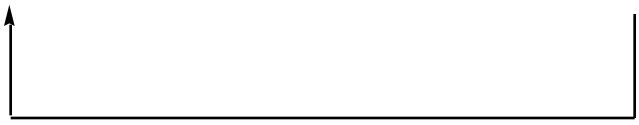


7. Researchers continue to develop new protecting groups to fit specialized needs. The next two questions provide two examples of new protecting group chemistry published this year (1999).

The Scheme below is from Zhang and Matteucci, *Tetrahedron Lett.* **1999**, *40*, 1467-1470.
(a) Provide a mechanism for the formation of **7** from **6**. Show all protecting group-derived byproducts.

(b) How would you remove the protecting group from the 5'-alcohol?

8. The Scheme shown below is from Jobron and Hindsgaul, *JACS* **1999**, *121*, 5835-36. Provide a complete mechanism for deprotection of **6** (conversion of **6** to **5**).



1. $NaOCH_3$
2. Mild oxidation or
65 ˚C