Molecules Of Life

15-06-2016

14:00

time: 3 hours

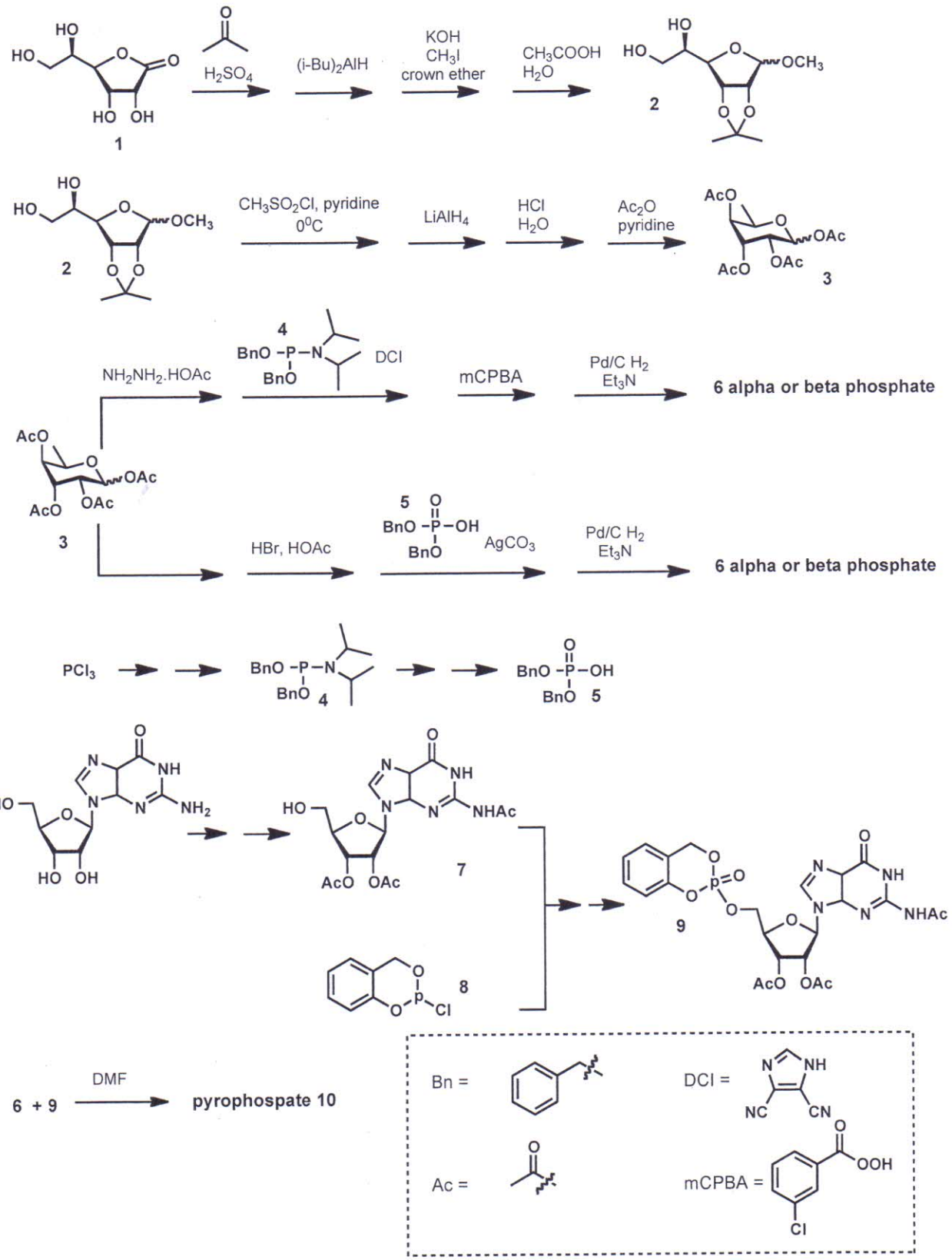
Each answer sheet must be provided with your name and student number

Each answer must be provided with the number of the corresponding question

(The maximum points for every question is indicated)

Question 1. (40 points)

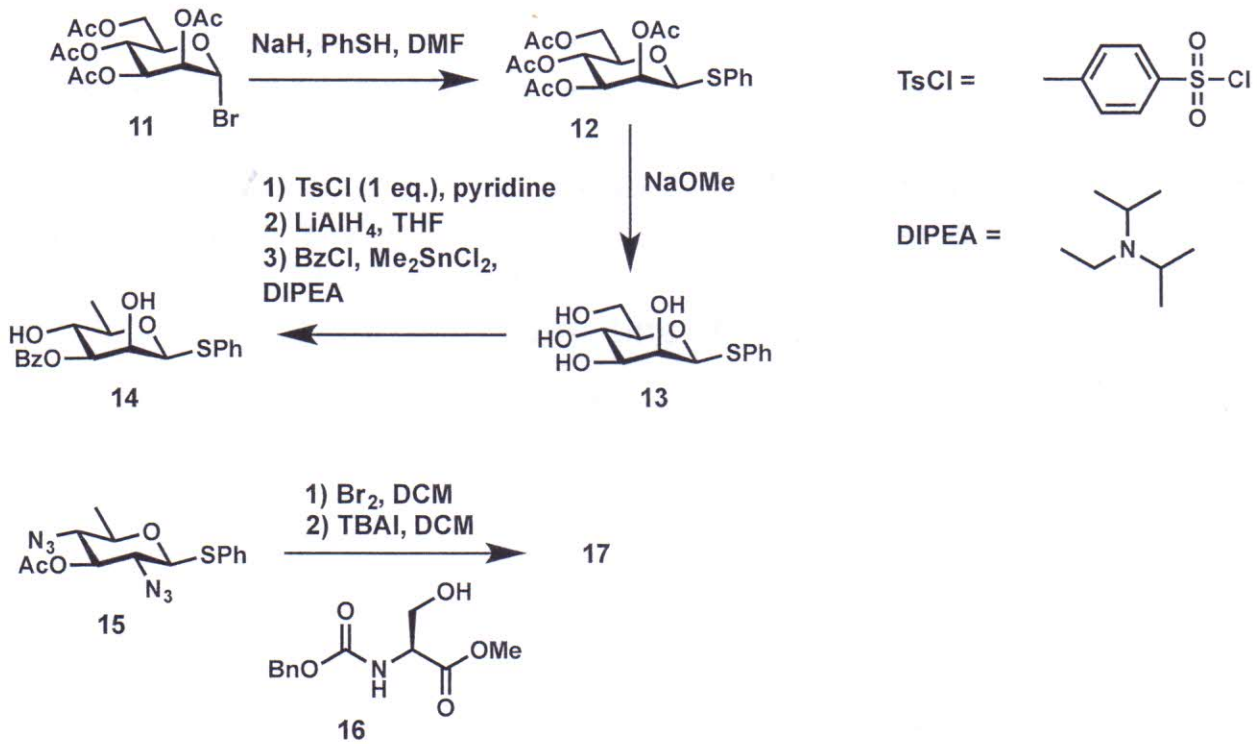
The group of Meier published the following synthesis towards prokaryotic nucleoside diphosphate glycopyranose **10**.



a) Draw the structures, including the stereochemistry of the intermediates, that are isolated during the route of synthesis in which **1** is converted to **2**.
b) Draw the structures, including the stereochemistry of the intermediates, that are isolated during the route of synthesis in which **2** is converted to **3**.
c) Fully acetylated monosaccharide **3** is subjected to two procedures leading to the corresponding anomeric phosphate monoesters. One procedure leads to solely the alpha anomer the other procedure to solely the beta anomer.
Draw the structures, including the stereochemistry of the intermediates toward both anomeric phosphates **6**.
d) Give a synthetic procedure for the transformation of phosphorus trichloride into amidite **4**.
e) Give a synthetic procedure for the transformation of amidite **4** into dibenzyl phosphate **5**.
f) Give a synthetic procedure for the transformation of guanosine into acetylated derivative **7**.
g) Give conditions with which **7** and **8** can be convered into **9**.
h) Reaction of **6** (select one anomer) and **9** gives pyrophosphate **10**.
Draw the structure of **10** and give the mechanism of the corresponding reaction.

Problem 2 (20 points)

Below the synthesis of a D-rhamnose building block is shown.
A) Provide the mechanism for the transformation of bromide **11** into thioglycoside **12**. Explain the stereochemistry of the reaction.
B) After removal of the acetyl groups, the tetraol **13** is treated with the reagents shown to give partially protected rhamnose **14**. Provide the mechanism of the reactions involved and explain the observed regiochemistry.
C) In the synthesis of a *Neisseria meningitidis* glycopeptide (**17**), the coupling reaction of **15** and **16** is performed. How would you synthesize the partially protected amino acid **16**?
D) Provide a mechanism of the reactions involved in the coupling step and a rationale for the stereoselectivity in the steps.



Problem 3 (30 points)

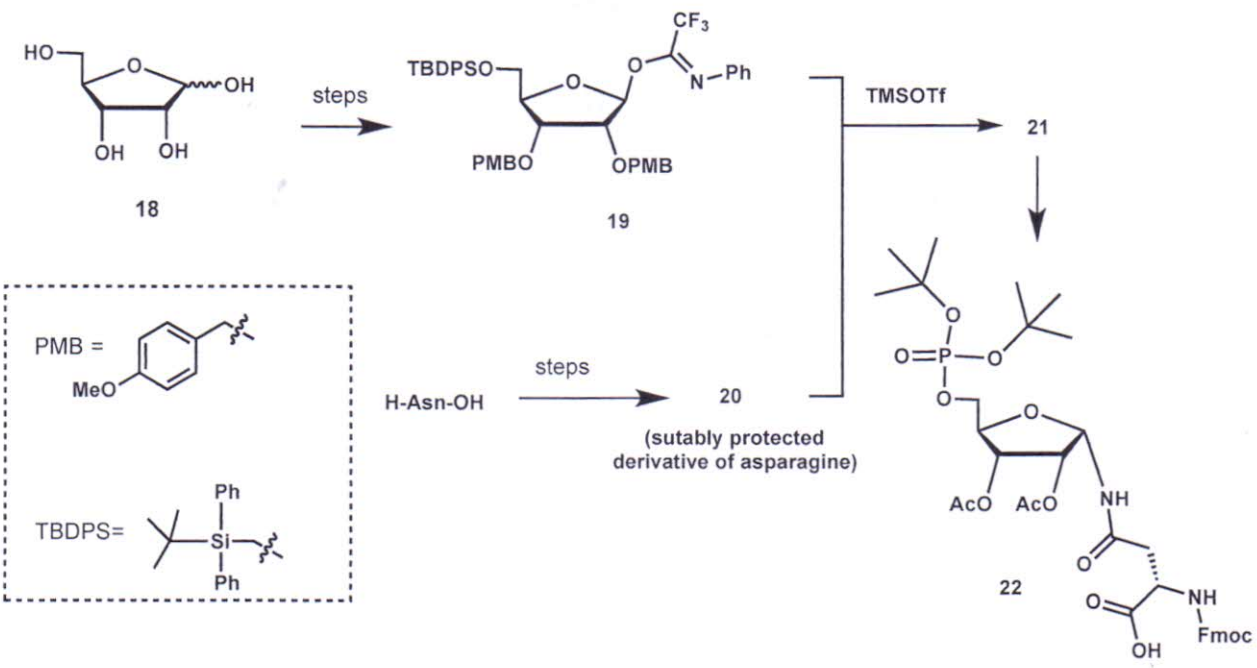
Ribosylated peptide **23** has been prepared via Fmoc solid phase peptide synthesis making use of building block **22**.

A) Provide a (multi-step) synthetic scheme for the preparation of ribofuranosyl donor **19** from D-ribose.

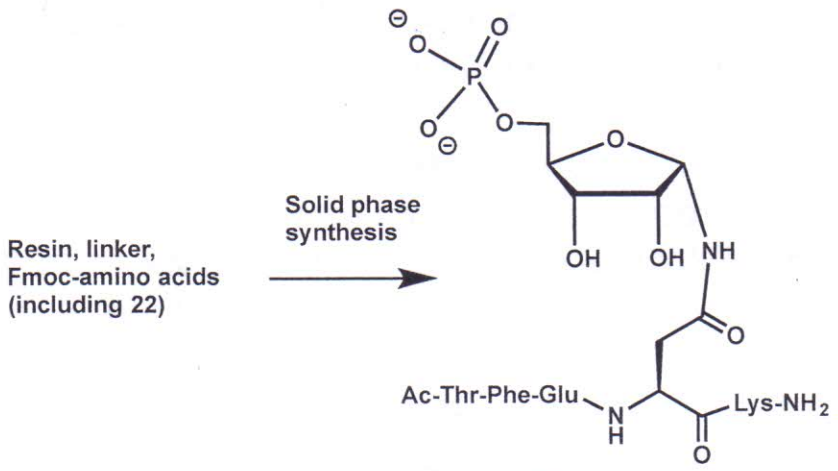
B) Provide a (two-step) synthetic scheme for the preparation of an appropriately protected asparagine building block **20** that can be glycosylated on its side chain with donor **19**.

C) Draw the structure of **21** that is produced in the TMSOTf catalysed glycosylation of **19** and **20**.

D) Provide a (multi-step) synthetic scheme for the preparation of phosphoribofuranosylated asparagine derivative **22** from **21**.



E) Suggest a solid-phase synthesis of compound **23** from suitably protected amino acid building blocks (including **22**). Draw the protected derivatives of all necessary amino acids, show the structure of the linker. Give the reagents and conditions necessary to build up the peptide chain and give the reagents for the final deprotection.



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