Molecules Of Life

26-06-2017

time: 3 hours

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

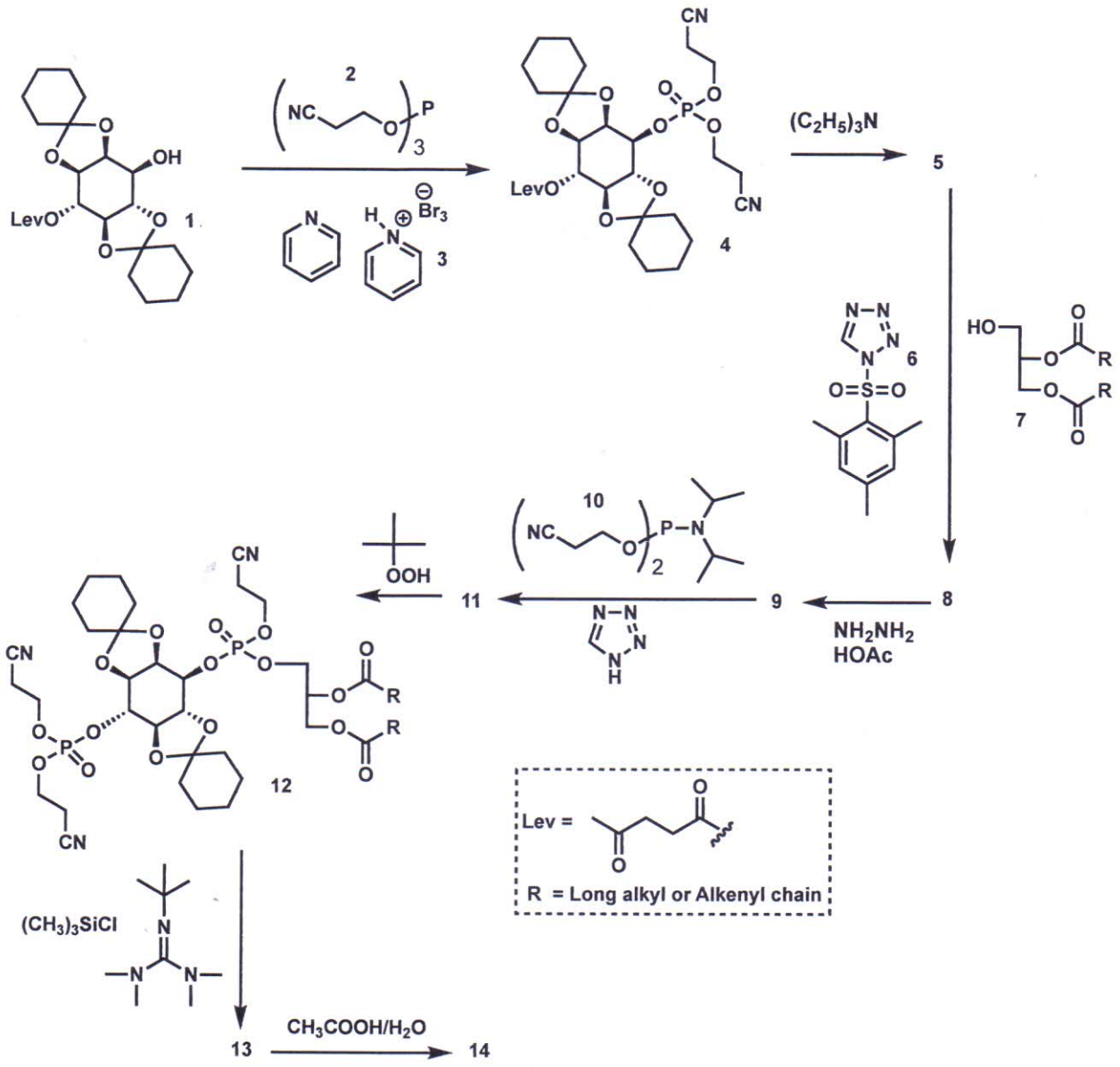
Each answer must be provided with the number of the corresponding question

Give your answer sheets a number

(The maximum points for every question is indicated)

Question 1. *(25 points)*

The group of Gaffney recently published the following reactions toward phosphatidylinositol 4-phosphate (**14**) (Org. Biomol. Chem. 2015, 13, 2001).

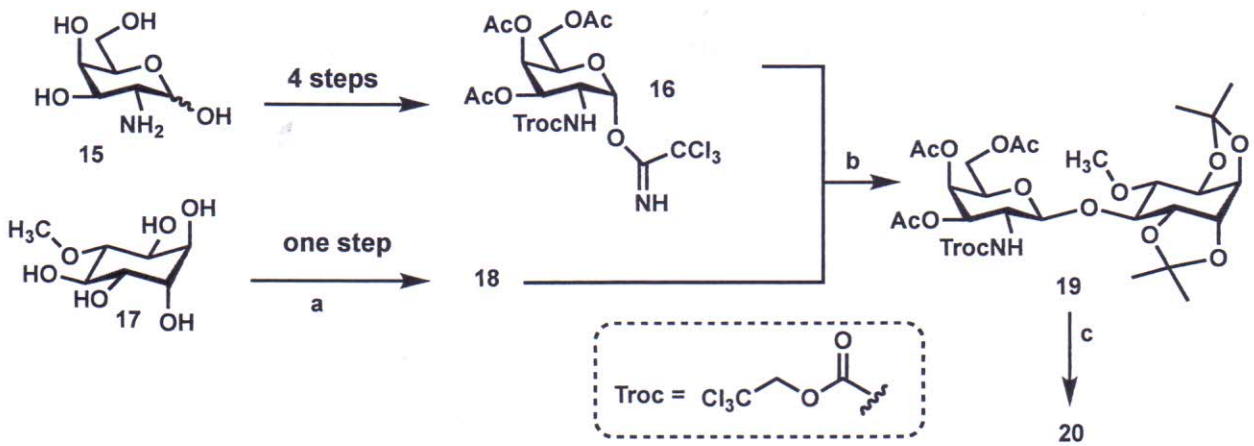


a) Give the mechanism of the transformation of **1** into **4** with the aid phosphite **2** and perbromine **3** (a source of Br_2).
b) Draw the structures of the products **5**, **8**, that are isolated during the conversion of **4** into **8**.
c) Give the mechanism of the removal of the levulinoyl group (i.e. conversion of **8** into **9**).

d) Give a synthetic procedure for the synthesis of **10**, using phosphorus trichloride.
e) Draw the structure of **11** and describe the mechanisms of the two step transformation of **9** into **12**.
f) Draw the structure of **13** and give the mechanism of the conversion of **12** into **13**.
g) Draw the structure of **14**.

Question 2. *(20 points)*

The group of Huang (J. Med. Chem. 2003, 46, 3283) has described the synthesis of a putative insulin mediator (**20**). Part of the synthetic scheme is shown below.

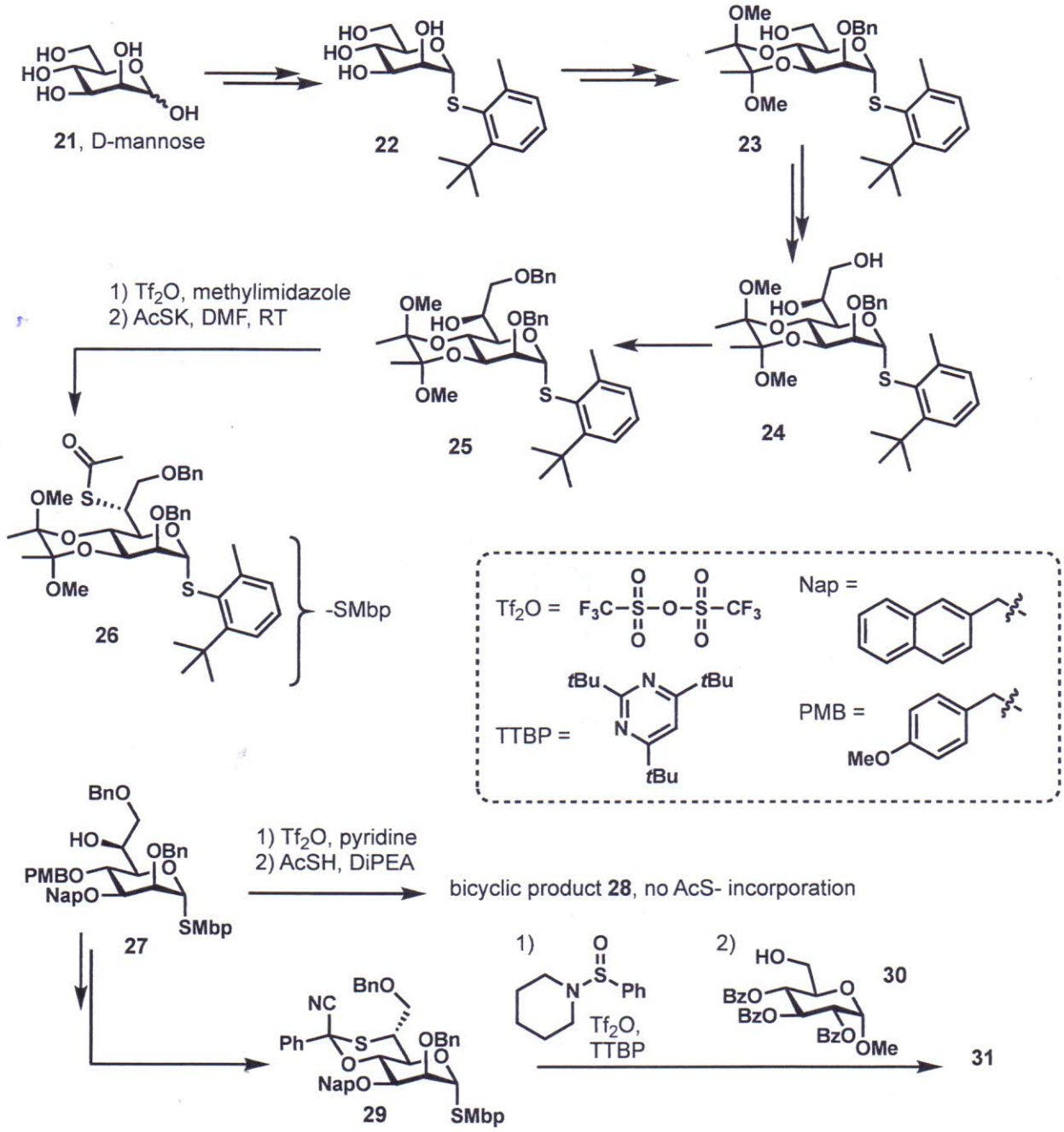


a) Give a synthetic route to fully protected donor **16** using galactosamine (**15**) as starting compound.
b) Draw the structure of **18** that can be obtained from D-pinitol (**17**), using conditions **a**. Give these conditions **a** and explain the regioselectivity of this transformation.
c) Condensation of **16** and **18** gave **19**. Give these conditions **b** and explain the stereoselectivity of this reaction.
d) Removal of all protective groups (procedure **c**) in **19** led to the isolation of **20**. Draw the structure of **20** and give the reaction conditions of procedure **c**.

Question 3 (*25 points*)

Depicted below is part of the synthesis of a mannoheptosyl donor, reported by Picard and Crich (Tetrahedron 2013, *69*, 5501).

a) Provide the reagents and conditions to transform D-mannose **21** into thioglycoside **22**.
b) How would you synthesize **23** from **22**? Explain the regiochemistry of the steps involved in this transformation.
c) Which steps/reagents would you use to transform **24** into **25**?
d) To introduce the sulfur functionality in the molecule **25** can be transformed into **26** as shown. When analogous compound **27** is treated with similar conditions a biclyclic product (**28**) is obtained without incorporation of the thioacetate moiety. What product is formed? Explain the differences in these two reactions (**25** to **26** *vs* **27** to **28**)
e) Finally **29** is obtained and treated with the reagents and compound **30** shown. Give the mechanism of the reactions leading to product **31**.


21, D-mannose
22
23
24
25
1) Tf2O, methylimidazole
2) AcSK, DMF, RT
26
-SMbp
Tf2O =
TTBP =
Nap =
PMB =
27
1) Tf2O, pyridine
2) AcSH, DiPEA
bicyclic product 28, no AcS- incorporation
29
1)
Tf2O,
TTBP
2)
30
31