

Exercise Session, 20.11.19

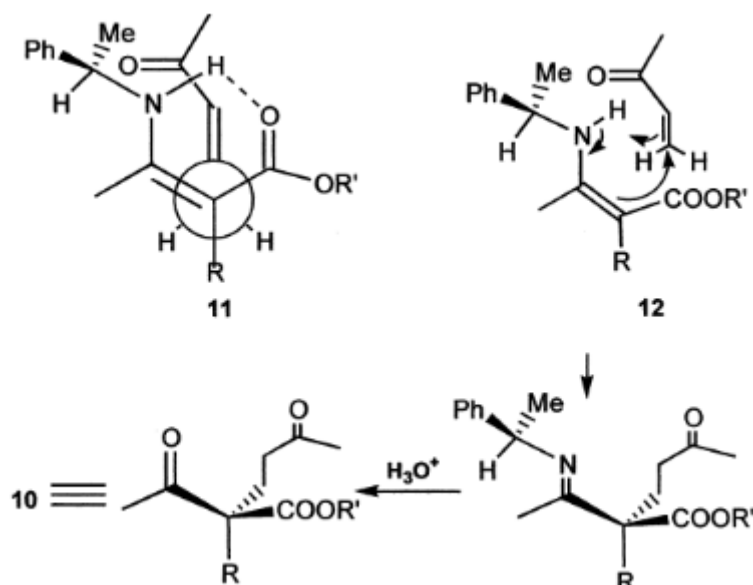
Submitted by M. Gnägi

Question 1

Give the structure of the missing starting material (SM1), explain the synthesis of (-)-53

Answer 1

From: *Tetrahedron Asymmetry* 2001, 12, 765-769 (opposite enantiomer of chiral auxiliary is used in this synthesis)



Question 2

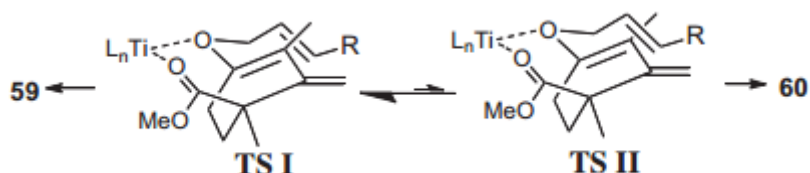
Propose the structure of (-)-59 and explain the stereochemistry
What might the Me_3Al be used for?

Answer 2

The overall transformation is a Claisen Rearrangement (nothing more)

The authors claim that Me_3Al should be used as proton scavenger, what does not make too much sense to me. However, Me_3Al was described to react with $TiCl_4$ to form $TiCl_2Me_2$ (Reetz reagent; especially in DCM, the solvent used here), that might be the true catalyst here;

Explanation for the stereochemistry:



Question 3

What product(s) can you expect from the reaction of 3-lithiated furan with (+)-63?

Explain the selectivity.

How can this lithiated furan be obtained?

Answer 3

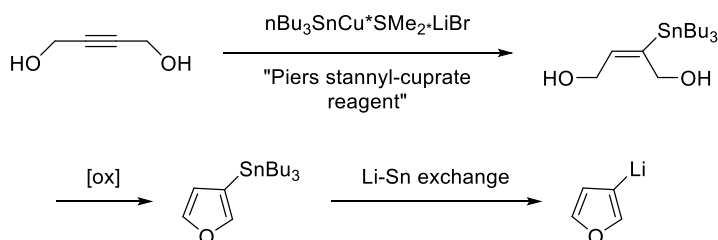
Where the reaction happens should be obvious from the product obtained later; however, only the open keto-alcohol can be reacted further. The product *isolated* however is the hemiacetal.

Ketone: sterically too hindered (claimed by authors)

Ester: Less reactive than lactone

Epoxide: lithiated reagent prefers a hard electrophile

The 3-lithiated furane is obtained by the procedure from Fleming:



Synthesis 1985; 1985(9): 898; DOI: 10.1055/s-1985-31378

Question 4

Propose a solution for the two-step transformation of 71 to 73

Answer 4

BF_3 catalyzed acetal formation; stereoselectivity suggest an $\text{S}_{\text{N}}2$, attack from below controlled by α -ketone stereocenter.

Step 2 is a simple ester hydrolysis.

Question 5

Propose a solution for the three-step transformation of 73 to 75

Answer 5

Double oxidation of alcohol to the acid (2); here Swern and NaClO_2 , NaH_2PO_4

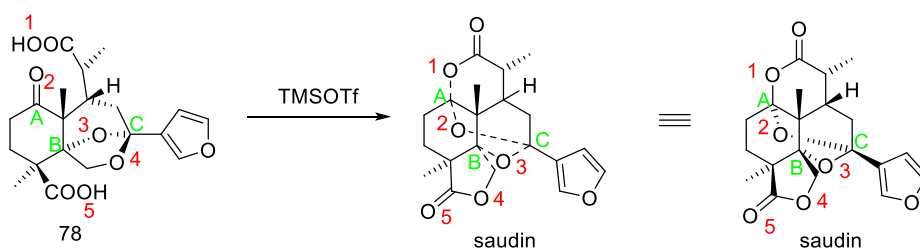
Step three is a formation of mixed anhydride with trifluoroacetic anhydride, that can then be "trapped" by the enol form of the ketone (NaOAc is in the mixture)

Question 6

Propose the stereochemistry in the product Saudin

Answer 6

It seems that the authors are very lucky and the desired compound is favoured in "rearrangement".



B: not changed; C: defined by pre-set geometry of cyclic system. A: acid must thus attack from above.

