UNIVERSITÀ DEGLI STUDI DI MILANO

A Facile Synthesis of α-*N*-*R*ibosyl-Asparagine and α-*N*-Ribosyl-Glutamine Building Blocks

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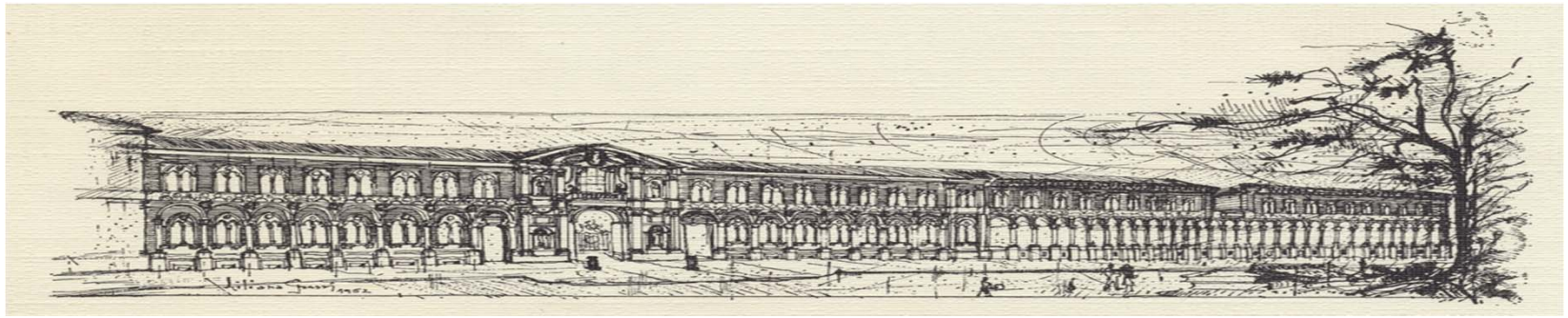
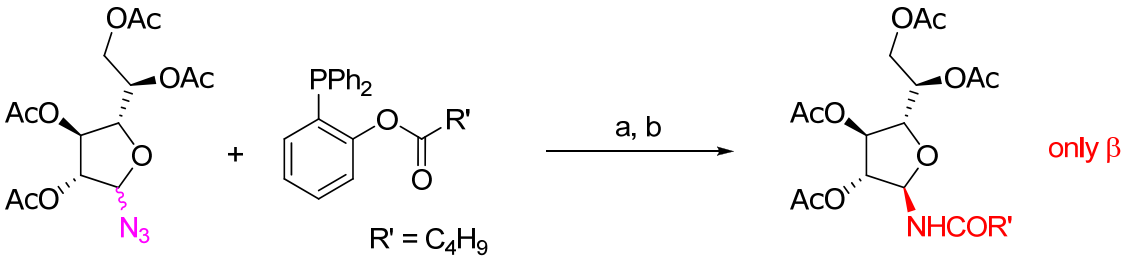


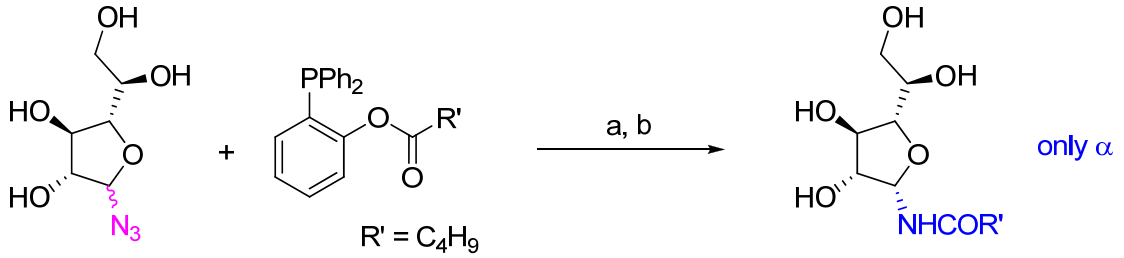
Background: *Staudinger ligation, a stereoselective process*

Tetra-*O*-acetyl furanosyl azides give 1,2-*trans*-amides



a) 70°C, 4h, DMA/DMPU; b) H_2O, 2 h, 70°C

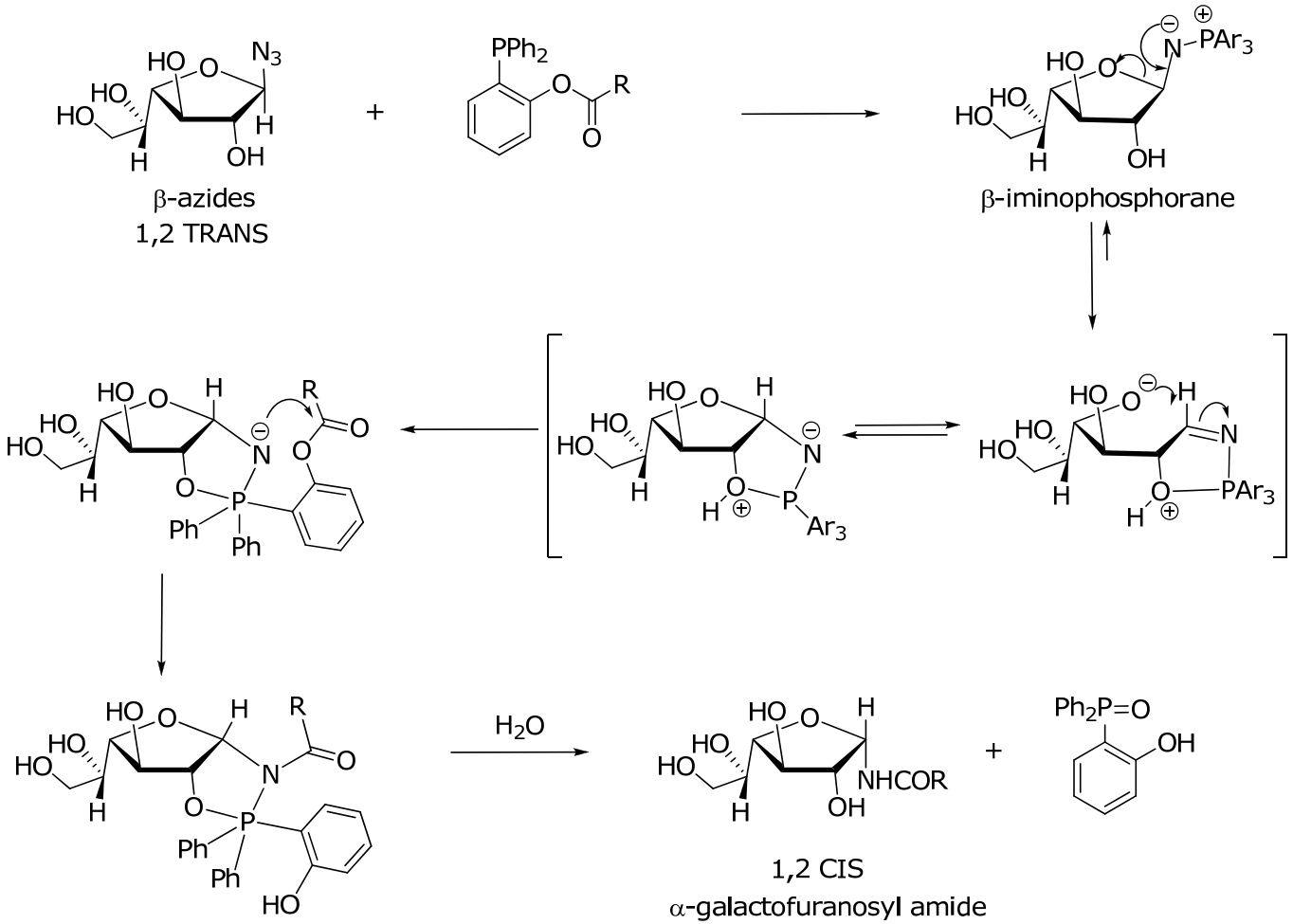
Unprotected furanosyl azides give 1,2-*cis*-amides



a) 70°C, 4h, DMA/DMPU; b) H_2O, 2 h, 70°C

Chem.Eur.J. **2012**, *18*, 6895-6906.
Carbohydr. Res. **2011**, *346*, 465-471.

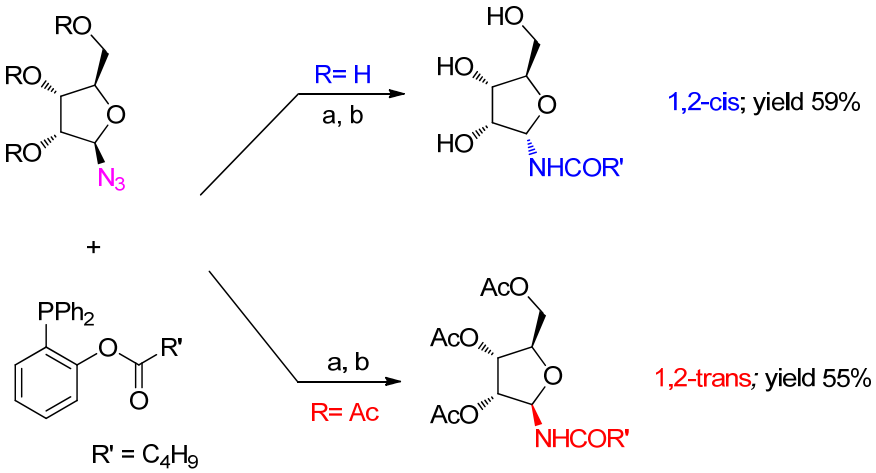
Background: *Proposed mechanism for anomeric inversion in unprotected Galf amides*



Chem.Eur.J. **2012**, *18*, 6895-6906.

Background: *Staudinger ligation, a stereoselective process*

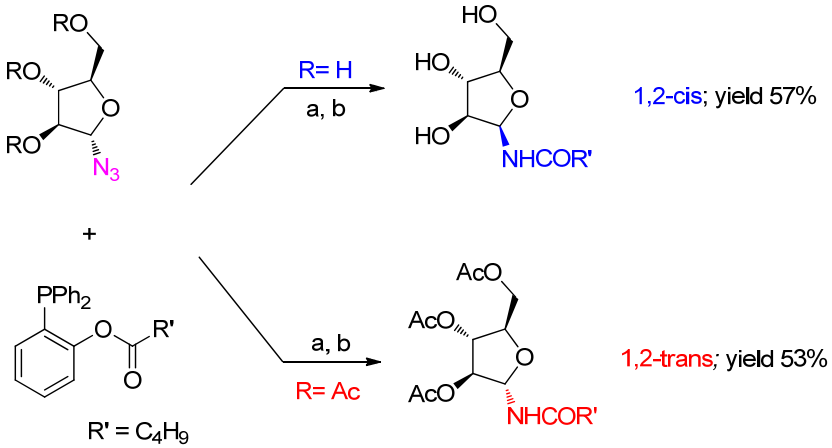
Ribofuranosylamides



a) 70°C, 4h, DMA/DMPU; b) H_2O, 2 h, 70°C

The process is controlled by the configuration and the protection state of the hydroxyl group in position 2

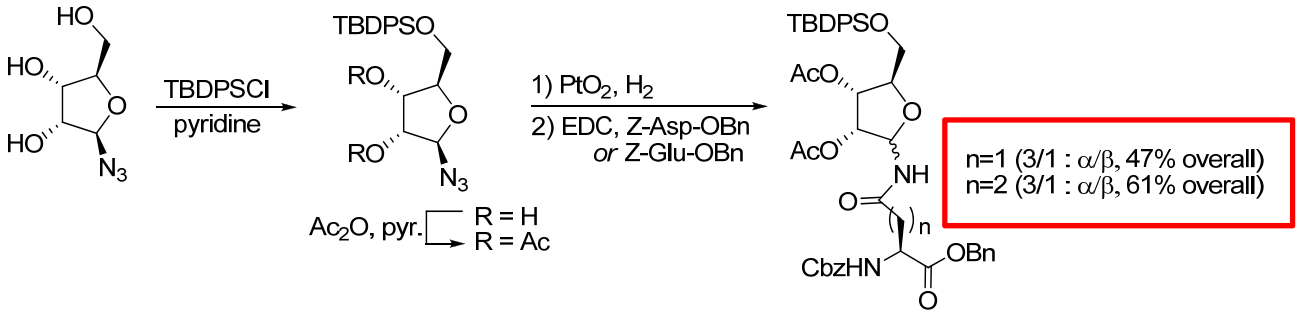
Arabinofuranosylamides



a) 70°C, 4h, DMA/DMPU; b) H_2O, 2 h, 70°C

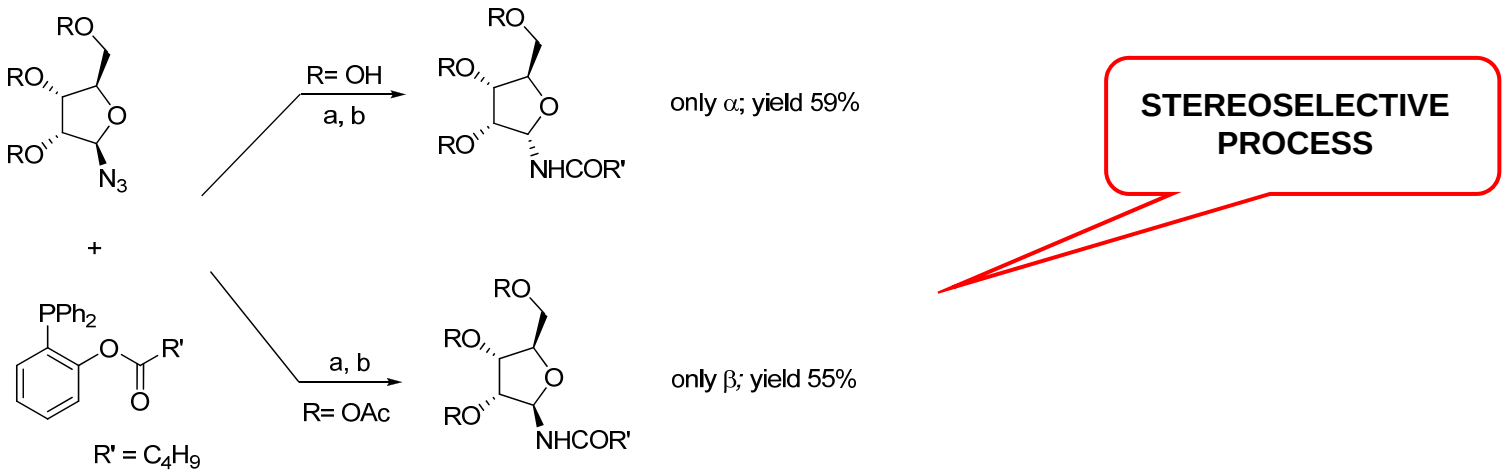
Chem.Eur.J. **2012**, *18*, 6895-6906.

Previous synthesis of ribosylated amino acids



J. Am. Chem. Soc. **2010**, *132*, 5236-5240.

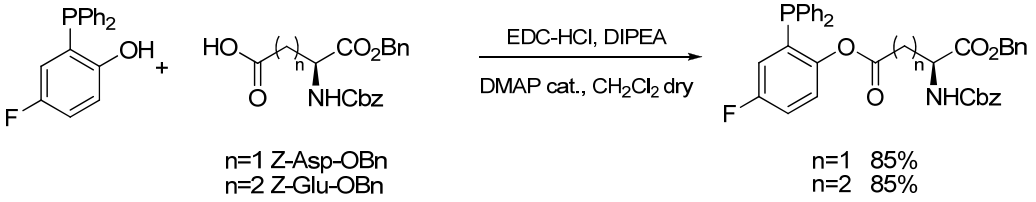
Traceless Staudinger ligation of Ribofuranosyl azides with functionalized phosphines



a) 70°C, 4h, DMA/DMPU; b) H_2O, 2 h, 70°C

Chem.Eur.J. **2012**, *18*, 6895-6906.

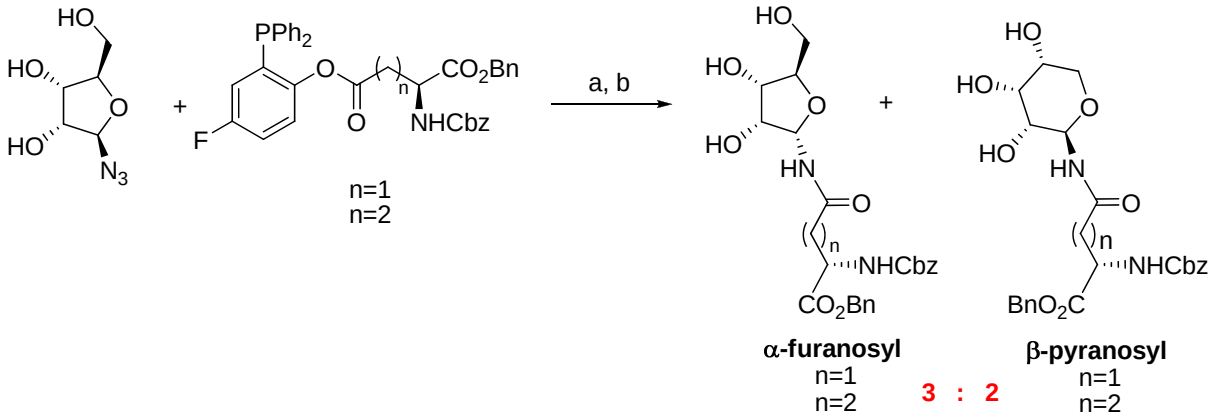
Synthesis of functionalized phosphines



Fluorinated phosphines allowed to obtain excellent aminoacid chain transfer

Chem. Eur. J. **2003**, *9*, 6093-6107;
Eur. J.Org. Chem. **2009**, 5744-5751.

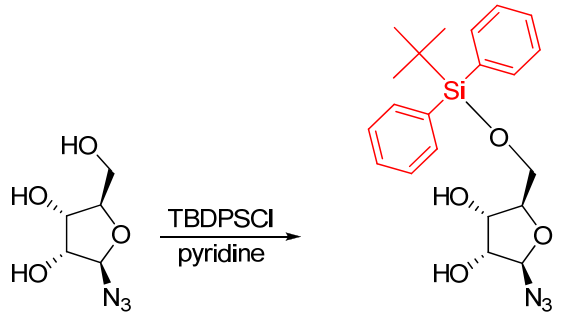
Traceless Staudinger ligation of Ribofuranosyl azides with fluorinated phosphines



The β-pyranosyl isomers obtained in these ligation must derive from ring-expansion occuring after ring-opening process

a) 70°C, 20h, DMA/DMPU 98:2; b) H_2O, 2 h, 70°C

Synthesis of 5-TBDPS-β-Ribofuranosyl azides

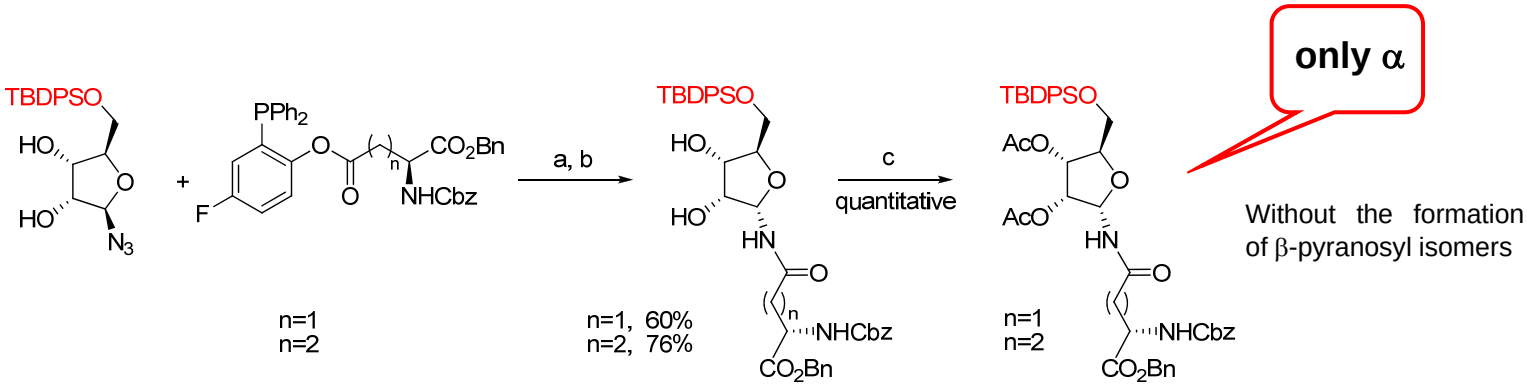


5-TBDPS-β-D-ribofuranosyl azide

Tert-butyldiphenylsilyl ether play a key role for the stereoselectivity and blocks the ring-expansion process

J. Am. Chem. Soc. **2010**, *132*, 5236-5240.

Traceless Staudinger ligation of 5-TBDPS-β-Ribofuranosyl azides with fluorinated phosphines



Without the formation of β-pyranosyl isomers

a) 70°C, 20h, DMA/DMPU 98:2; b) H_2O, 2 h, 70°C; c) Ac_2O, DMAP cat., CH_2Cl_2.

Conclusion:

- **We describe an improved synthesis of α-*N*-*R*ibosyl-Asparagine and α-*N*-Ribosyl-Glutamine Building Blocks.**

- **Application of the Staudinger Traceless Ligation protocol allowed to obtain the ribosylated amino acids from 5-TBDPS-β-Ribofuranosyl azide in good yields and with excellent selectivity for the α anomer.**

Acknowledgements:

This work was supported by the University of Milan (PUR) and Ministero dell'Universita' e della Ricerca (PRIN). Exact mass were obtained from CIGA.