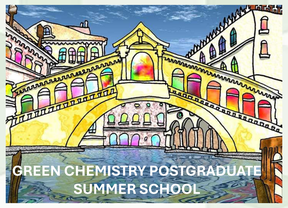

Exploring the potential of Levoglucosenone: from cellulose biomass to the synthesis of aminosugar derivatives

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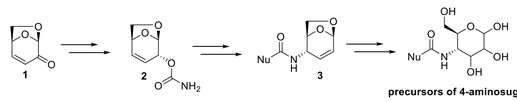
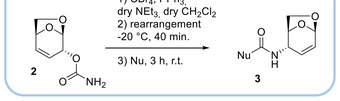
SYNTHESIS OF 4-AMINOSUGAR DERIVATIVES THROUGH ALLYL CYANATE TO ISOCYANATE REARRANGEMENT

The *O*-allyl to *N*-allyl rearrangements are reliable methods for introducing nitrogen moieties on allyl alcohol skeletons with high atom economy and stereocontrol. The allyl cyanate/isocyanate rearrangement[1] is particularly attracting, for several advantages, including use of manageable carbamate precursors and mild metal-free reaction conditions, high degree of stereocontrol and versatility of the resulting isocyanates. The transformation of carbamate to the desired products involves three steps, which are usually performed in one-pot: an initial dehydration of the carbamate to the corresponding elusive cyanate is followed by spontaneous [3,3]-sigmatropic rearrangement to the isocyanate, which is conveniently trapped with a nucleophile to afford the final products. These rearrangement reactions of glycals have recently been reported to afford aminosugars by our research group.[2,3]

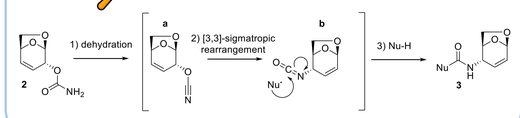
Application of this innovative strategy to levoglucosenone-derived carbamate **2** provided 4-aminosugar derivatives. The rearrangement allowed to install a nitrogen functionality at C-4 to afford the final products **3**. After dihydroxylation of the double bond and opening of the 1,6-bridge, new precursor of 4-aminosugars at C-4 were obtained in a stereocontrolled manner.[7]



Allyl cyanate to isocyanate rearrangement

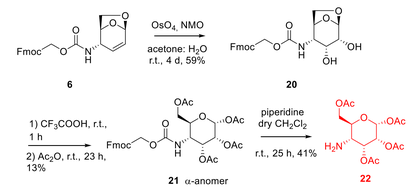


Mechanism of rearrangement

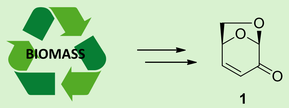


	Nucleophile	Yield	Products
Nu ALCOHOLS (3 eq.)	methanol	63%	4
	propargyl alcohol	70%	5
	9-fluorenylmethanol	60%	6
	3-buten-1-ol	52%	7
	allyl alcohol	45%	8
	phenol	61%	9
	benzyl alcohol	71%	10
	trans-2,4-hexadien-1-ol	55%	11
	octanol	54%	12
	dodecanol	57%	13
Nu AMINES	butylamine (10 eq.)	50%	14
Nu AMINES (3 eq.)	octylamine	47%	15
	propargylamine	31%	16
	dodecylamine	48%	17
Nu THIOLS (3 eq.)	thiophenol	55%	18
	p-thiocresol	52%	19

SYNTHESIS OF 4-AMINOSUGAR DERIVATIVES



LEVOGLUCOSENONE



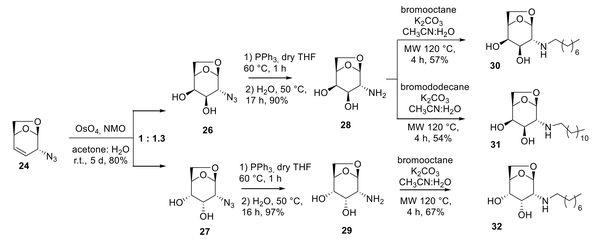
Pyrolysis is one of the most promising technologies for using biomass. In particular, levoglucosenone (1), a small molecule which may be used for the synthesis of biologically relevant compounds, is obtained in 3-7% yield from the pyrolysis of cellulose, as well as of urban and industrial residual materials containing cellulose such as waste paper.[4] For example, this bicyclic ketone allows to obtain aminosugars, compounds widespread in nature possessing a variety of biological roles.[5]

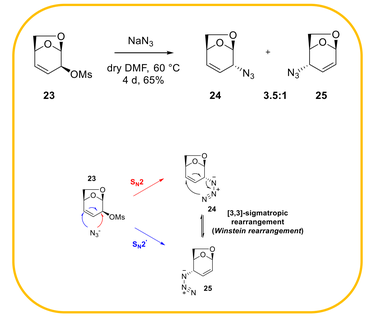
BACTERIAL GROWTH INHIBITION TESTS

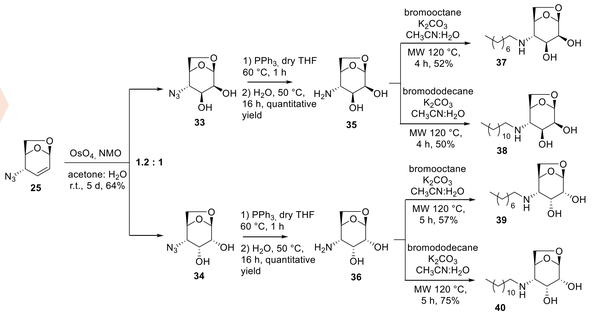
The 4-aminosugar derivatives and the *N*-alkyl aminosugar derivatives have been tested on different bacterial strains including *Escherichia Coli* and *Bacillus Subtilis* thanks to the collaboration with Prof. Massimiliano Marvasi (Department of Biology, University of Florence). *Escherichia Coli* is a Gram-negative that belongs to the *Enterobacteriaceae* family. It's possible to find it mainly in the human intestine. *Bacillus Subtilis* is a Gram-positive that belongs to the *Bacillaceae* family. It is not a human pathogen but can degrade or contaminate food.

SYNTHESIS OF *N*-ALKYL AMINOSUGAR DERIVATIVES

Thanks to the high functionalization of levoglucosenone, we decided to elaborate this compound obtaining an aminosugar scaffold bearing a long lipophilic alkyl chain. For nitrogen insertion we exploited a S_N2 nucleophilic substitution which led to the formation of the desired product 24 and to the corresponding rearranged compound 25 via [3,3]-sigmatropic rearrangement reaction and S_N2' reaction.[6] This has led to the development of two synthetic strategies for obtaining final products with a nitrogen atom substituted for C-2 and C-4. In particular, through a subsequent step of double bond dihydroxylation and *N*-alkylation with a long alkyl chain, the final derivatives were obtained.



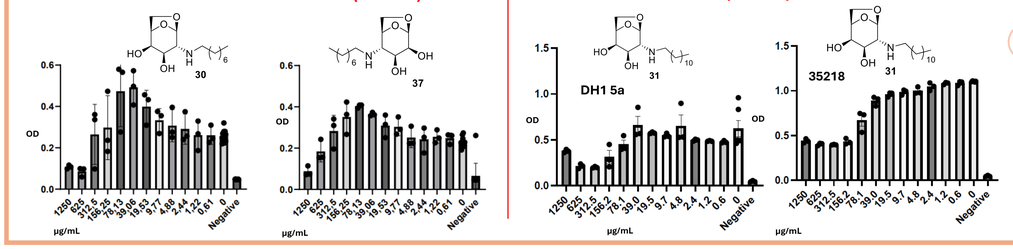




ALL BACTERIAL GROWTH INHIBITION TESTS:

Bacterial strains		41	42	43	44	22	28	29	30	31	37
Bacillus Subtilis ATCC 6633 (Gram +)		-	-	-	-	-	-	-	+	-	+
Escherichia Coli (Gram -)	DH1 5a	-	-	-	-	-	-	-	-	+	-
	35218	-	-	-	-	-	-	-	-	+	-

THE MOST PROMISING LEVOGLUCOSENONE-DERIVATIVE ANTIBACTERIAL AGENTS



FUTURE PERSPECTIVES

- The whole set of novel *N*-alkyl aminosugar compounds will be screened towards bacterial strains.

- New compounds will also be tested on other bacterial strains and the MIC will be evaluated.

ACKNOWLEDGEMENTS

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