Thiomonosaccharide derivatives from D-mannose

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The 24th International Electronic Conference on Synthetic Organic Chemistry

· INTRODUCTION

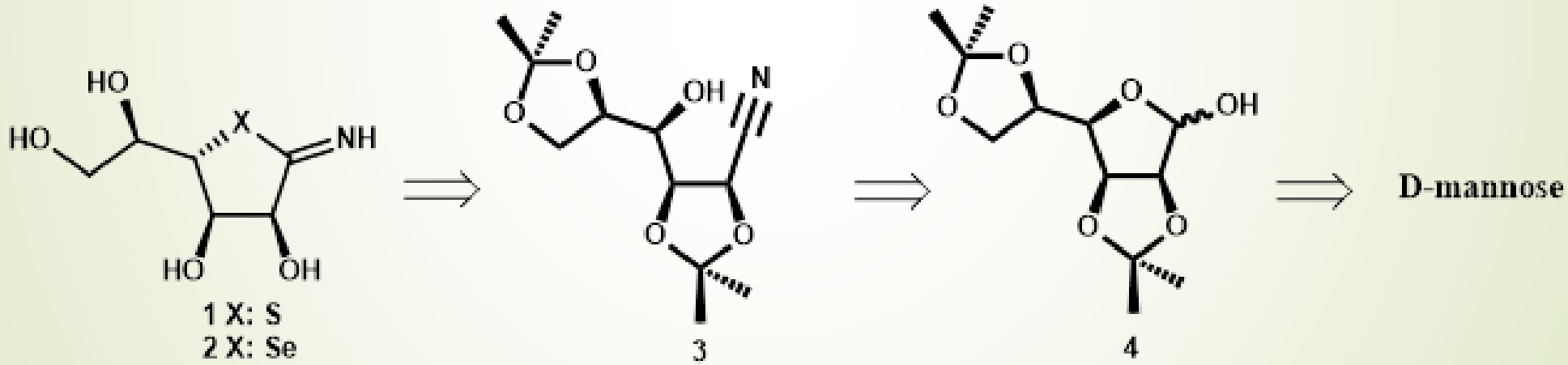
- Glycosidase inhibitors and other enzyme inhibitors plays important roles in the biochemical processing of biopolymers containing carbohydrates. The biological relevance of sulfur containing carbohydrates is gaining substantial attention, especially in the medicinal and synthetic chemistry [1].
- A number of selenium compounds obtained from monosaccharides have shown biological activity [2].

[1] Yoshikawa, M., Murakami, T., Shimada, H., Matsuda, H., Yamahara, J., Tanabe, G., Muraoka, O., *Tetrahedron Lett*., **1997**, 38, 8367-8370.

[2] Pinto, B. M., Liu, H., *J. Org. Chem*. **2005**, 70, 753-755

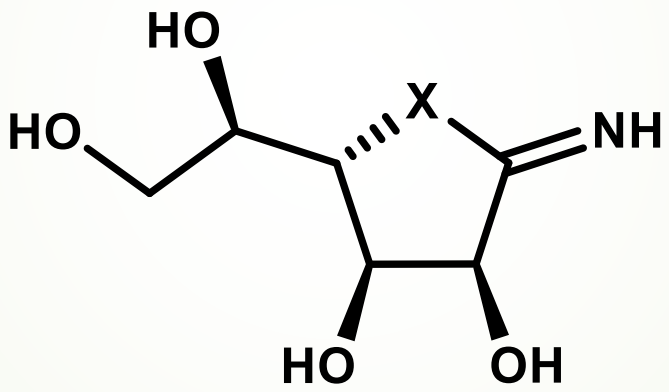
· INTRODUCTION

- Now, our objective is to obtain thio and selenium monosaccharide analogous derivatives, such as **1** and **2**.



· INTRODUCTION

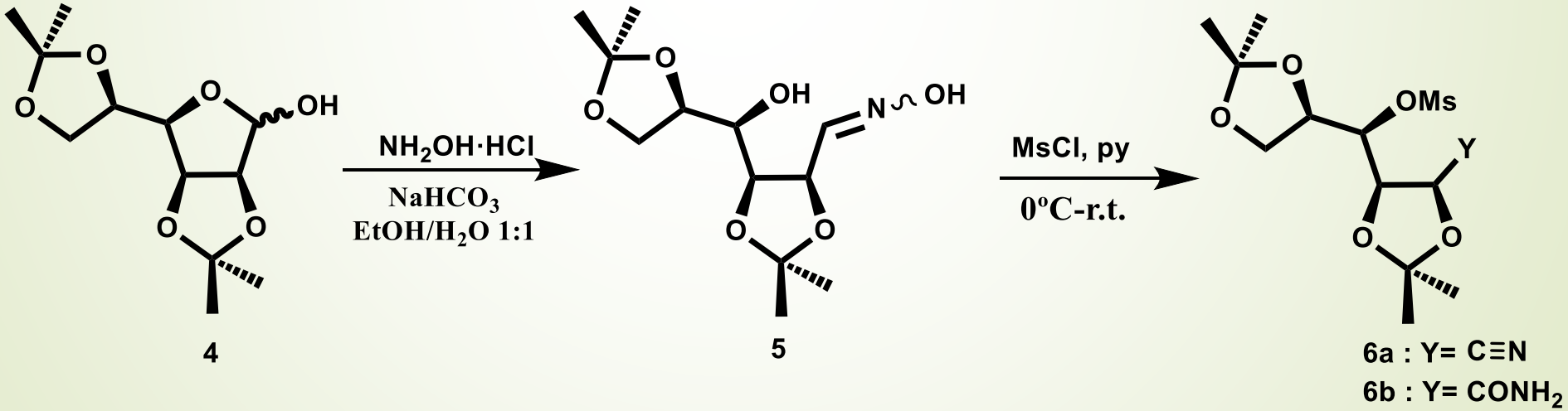
- To our knowledgement, no compounds of this type have been previously synthesized. The incorporation of both heteroatoms S or Se and N could improve the possible biological activity.



1 X: S
2 X: Se

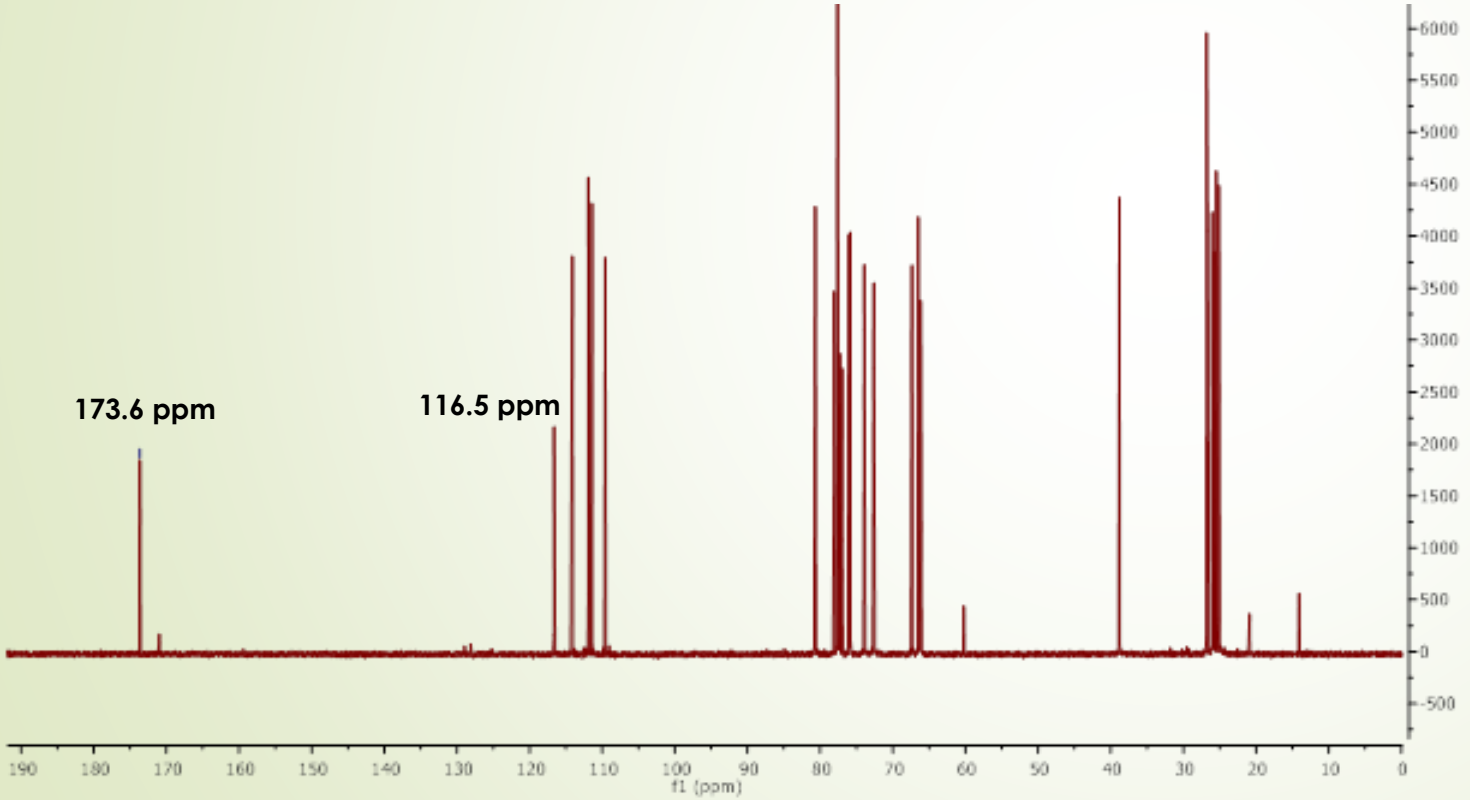
· RESULTS AND DISCUSSION

- In order to transform the aldehyde directly in a nitrile group, we tested several procedures. The best choice was the conversion in the oxime **5**, which could lead to the nitrile.
- To convert the hydroxyl groups in a good leaving group, we tried to introduce the tosyl group, but without good results. Therefore, we decided to introduce the mesyl group with satisfactory results. We obtained a mixture of nitrile **6a** and the related amide **6b**.



· RESULTS AND DISCUSSION

- Figure 1: **^{13}C-NMR** ($CDCl_3$, 100MHz) of the mixture "nitrile/amide" **6**

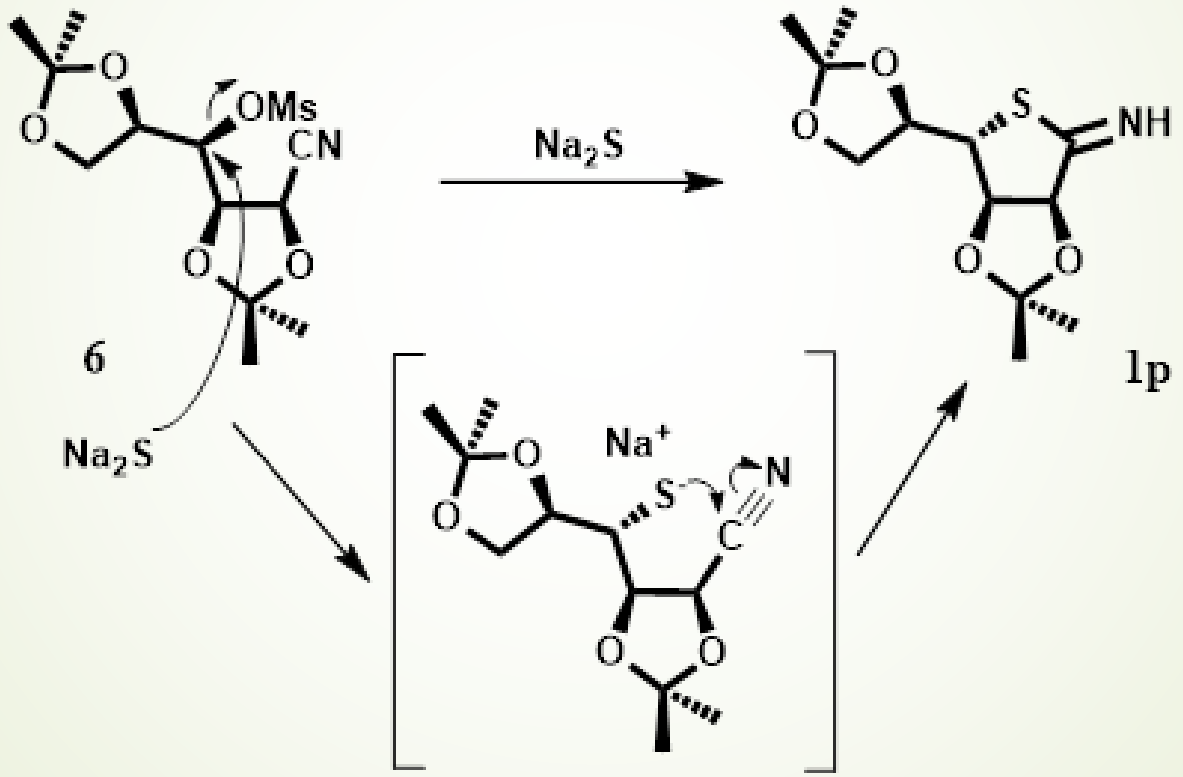


In ^{13}C-NMR spectrum can be observed the peaks 173.9 ppm and 116.5 ppm belonging to amide and to nitrile groups, respectively.

This mixture is used in the following reaction. The amide is transformed in nitrile in the reaction media.

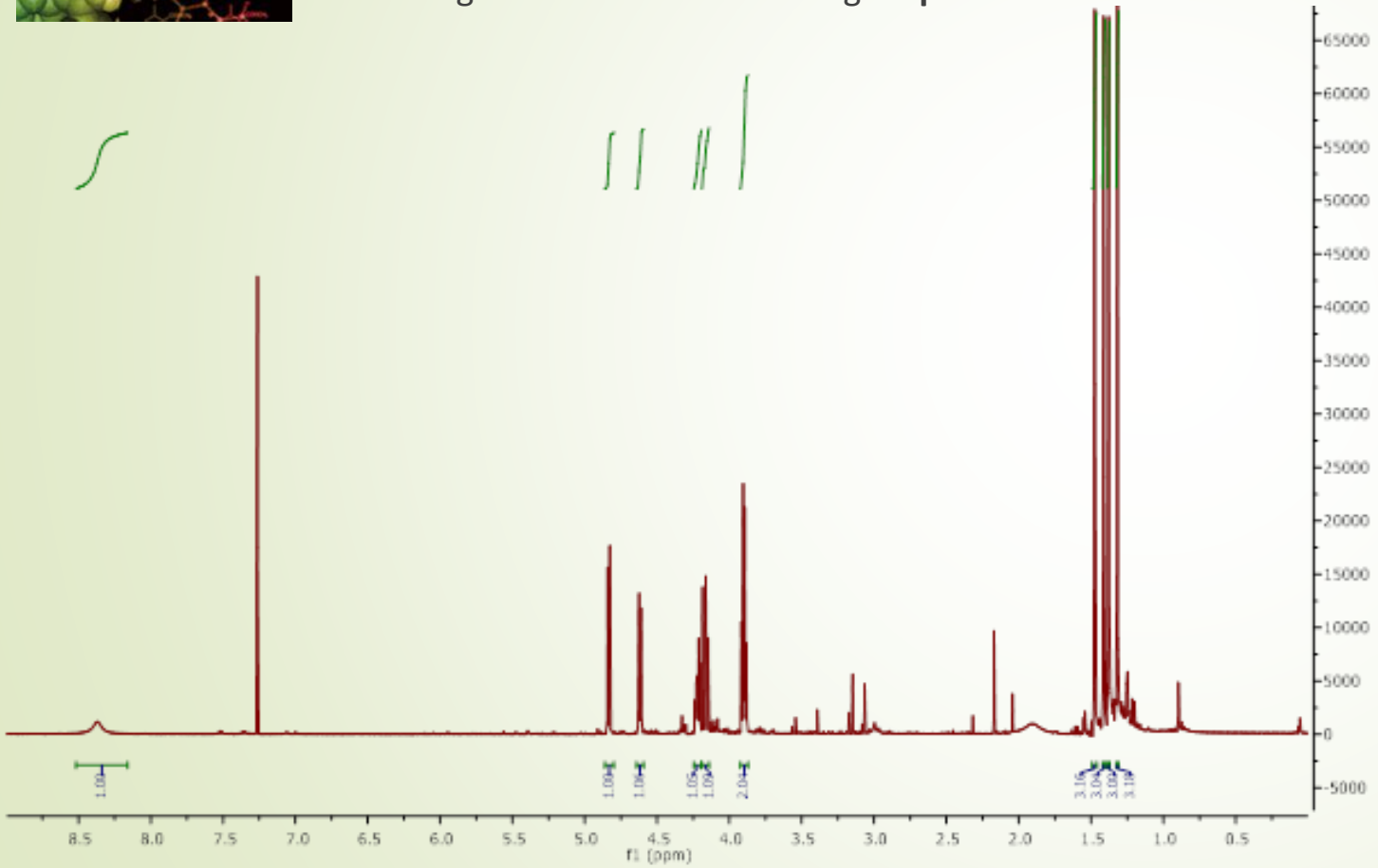
· RESULTS AND DISCUSSION

- The following reaction was the synthesis of the thiosugar **1p**



· RESULTS AND DISCUSSION

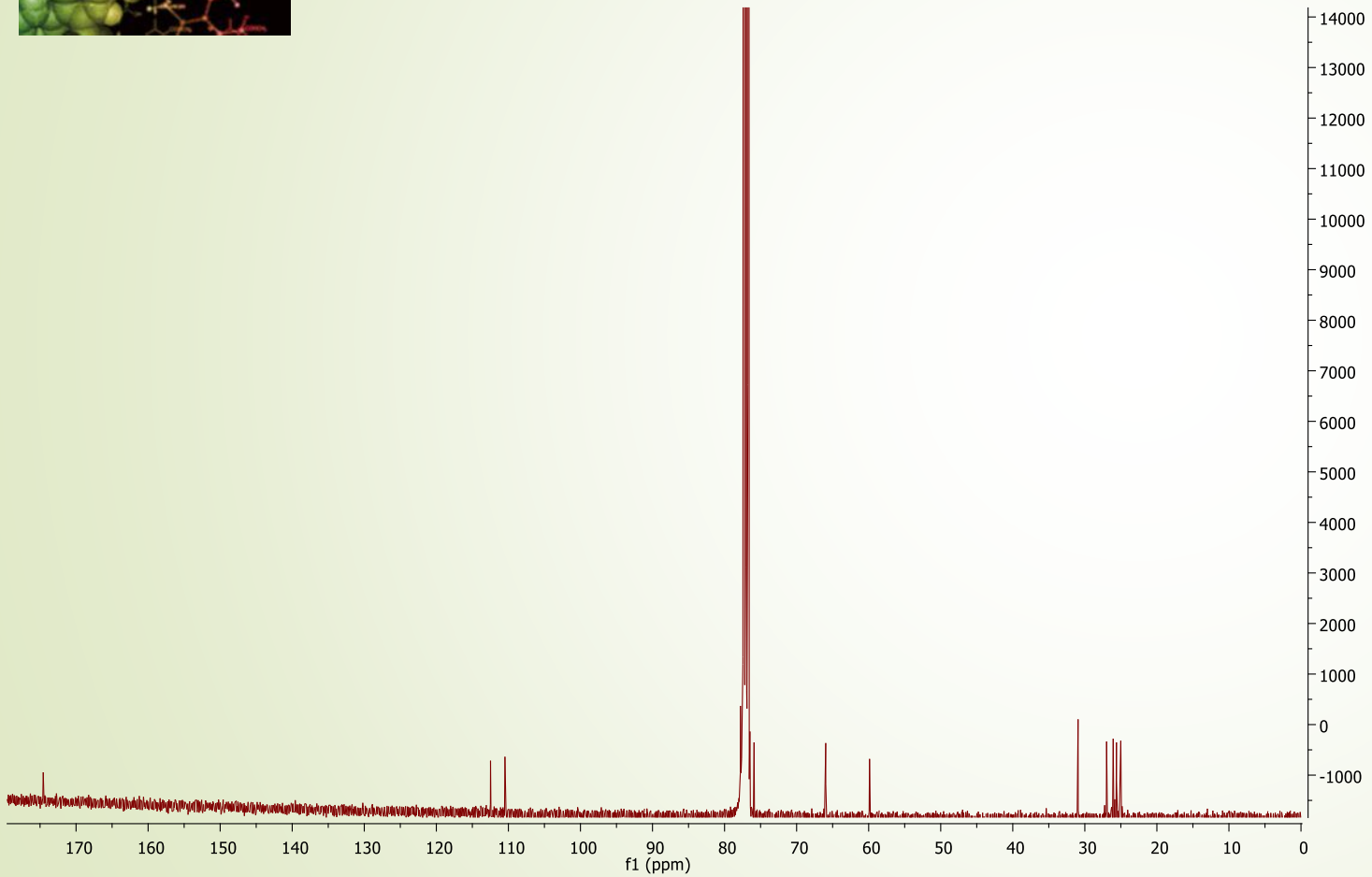
- Figure 2: ^{1}H-NMR of thiosugar **1p**



In ^{1}H-NMR spectrum, we can observe the disappearance of signal 3.04 ppm corresponding to mesyl group of **6**. At 4.83 y 4.62 ppm, two "d" are showed with *J*=5.5 Hz, (H-2 and H-3 respectively). The inversion of configuration at C-4 can be corroborated with $J_{3,4}$ = 0 Hz. At 8.37 ppm a broad singlet is correlated with C=NH proton.

· RESULTS AND DISCUSSION

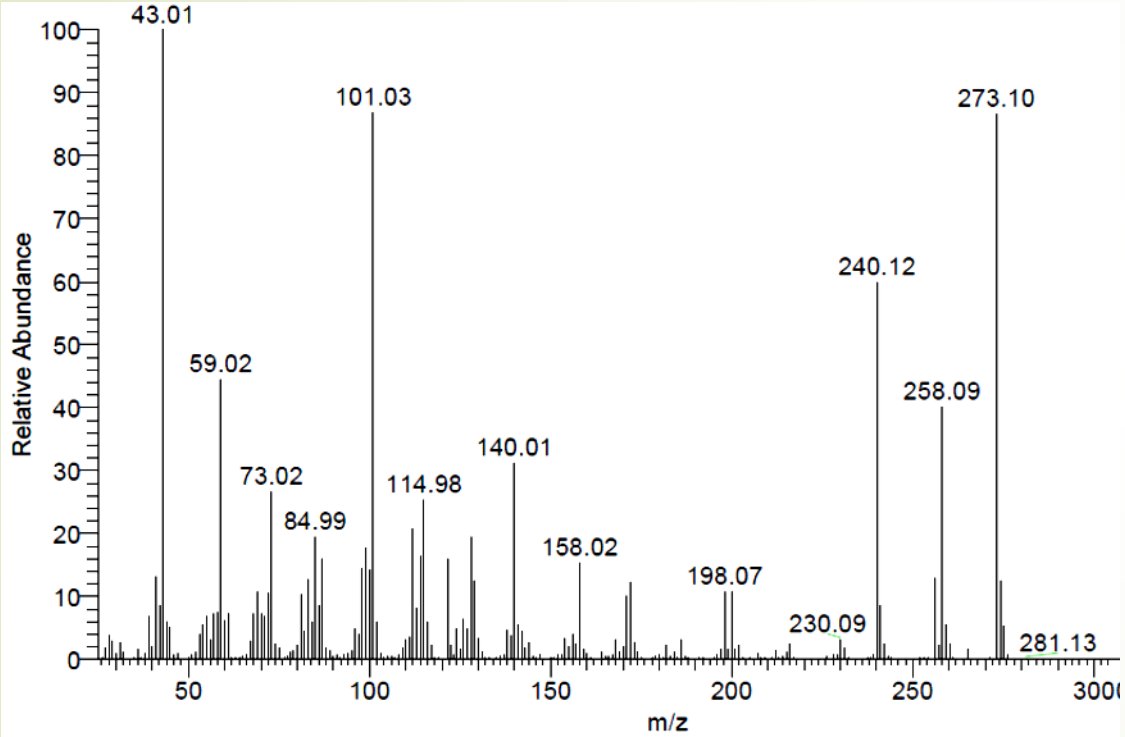
- Figure 3: ^{13}C-NMR of thiosugar **1p**



Comparing ^{13}C-NMR spectra of compound **1p** and the mesylated **6**, we can observe the disappearance of the peaks corresponding to nitrile *sp* carbon (116.5 ppm) and methyl of mesyl group (38.8 ppm). This is an evidence of the mesylate displacement by the sulfur anion and further attack to the nitrile carbon. The new structure can be confirmed by a new signal at 174.5 ppm which is in accordance with imine sp^2 carbon.

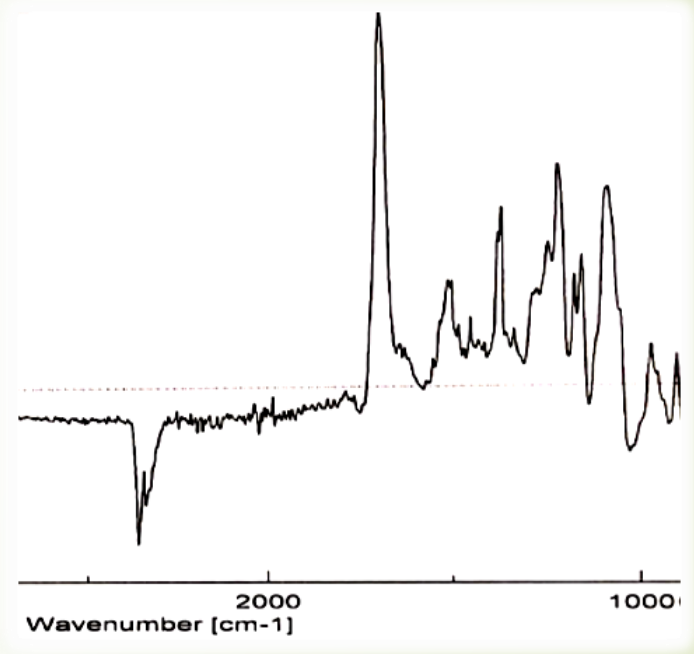
· RESULTS AND DISCUSSION

- Figure 4: (ESI) mass spectrum of thiosugar **1p**



High resolution mass spectra (ESI) showed the molecular ion $(M+H)^+$: 274.11041)

- Figure 5: IR spectrum of thiosugar **1p**



In the infrared spectra (IR) we can observe the band corresponding to C=N tension, which uses to appear at $\nu_{C=N}$= 1700-1615 cm^{-1}.

· CONCLUSIONS

- In summary, we have synthesized a new compound of a new family of heterosugars containing sulfur and nitrogen. The structural elucidation is based in NMR analyses, IR and Mass spectra data. The synthetic method is suitable for the insertion of selenium. The corresponding selenium derivatives are under study and will be reported as soon as possible.