



# MADRID

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Centro de Investigaciones Biológicas - CSIC



## BIENNIAL MEETING OF THE CHEMICAL BIOLOGY GROUP XII CARBOHYDRATE SYMPOSIUM

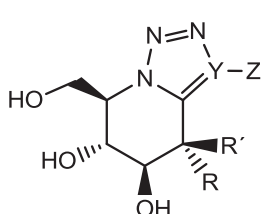


## Intramolecular [3+2] Cycloaddition of Fused Azolo-Azepanes from Azido Monosaccharide Derivatives

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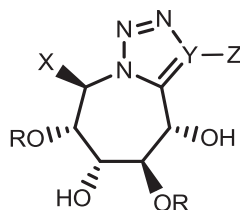
Bicyclic aromatic compounds have shown an enhanced potency as inhibitors and therefore a number of tetrazoles, triazoles and imidazoles, fused to pyranoses and furanoses have been synthesized.<sup>[1]</sup> The glucotetrazole **2** was designed as a bicyclic neutral transition state analogue inhibitor of  $\beta$ -glucosidases and glycogen phosphorylase. The mannose analogue **3** is an inhibitor of mannosidases and the glucotriazole **4** is a competitive inhibitor of glycogen phosphorylase. In previous experiences, we have synthesized polyhydroxyazepane derivatives with amide, aminomethyl or hydroxymethyl groups, starting from epoxyamides.<sup>[2]</sup> Now, with the aim of obtaining new inhibitors, we are interested in the formation of bicyclic compounds with azepanes fused to azoles (**5,6,7**). Azoles are profusely found in bioactive products but few tetrazoles<sup>[3]</sup> and triazoles fused to polyhydroxyazepanes have been reported to be evaluated as inhibitors.



2: R=OH, R'=H, Y=C, Z=CO<sub>2</sub>H

3: R=H, R'=OH, Y=N, Z=

4: R=OH, R'=H, Y=N, Z=



5: X=H, Y=C, Z=CO<sub>2</sub>Et

6: X=H, Y=N, Z=

7: X=CH<sub>2</sub>OH, Y=N, Z=



The methodology carried out to form the heterocyclic ring is based on intramolecular [3+2] cycloaddition of azido monosaccharide derivatives containing ciano or other unsaturated groups.

In order to elucidate the mechanism of formation of the bicyclic products, a quantum chemical topological study has been carried out.

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### References

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[2] Oña, N.; Romero-Carrasco, A.; Pino-González, M. S. *Tetrahedron: Asymmetry* **2013**, *24*, 156 and references therein.  
[3] Paz, N. R.; Santana, A. G.; Francisco, C. G.; Suárez, E.; González, C. C. *Org. Lett.* **2012**, *14*, 3388.

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