

Carbohydrates, amides, and triazoles: on the way to foldamers

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Oligopeptides arising from synthetic sugar amino acids exhibit interesting self-assembling structures in solution, and were intensively studied as peptidomimetics.¹ After the discovery of click synthesis of 1,2,3-triazoles,² the latter were studied as amide bond isosteres as they exhibit similar spatial arrangement and geometry.³

We have synthesized hybrid **1** which contains two carbohydrate-based molecular scaffolds, and amide functionality that can participate in the hydrogen bond formation. It also contains C-terminal alkyne along with masked N-terminal azide for differentiated copper-catalyzed azide alkyne cycloadditions.

Iterative cycloaddition reaction - azidation sequence using this hybrid allows the synthesis of oligomeric saccharopeptide **2** which has both the amide and triazole linkers between carbohydrate cores.

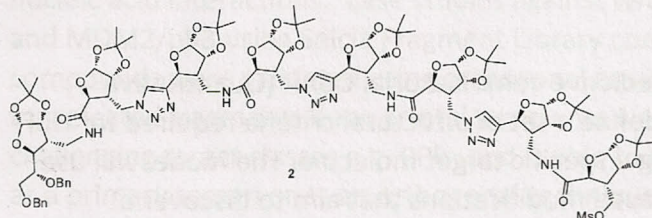
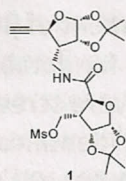


Fig.1. Structures of hybrids.

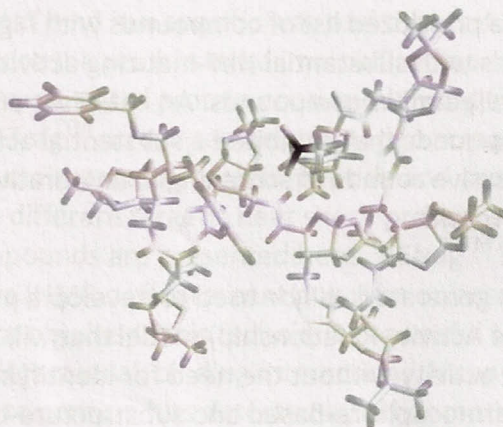


Fig. 2. Structure of octamer **2** after MD

The structure of oligomer **2** was studied by NMR. Using ROESY spectra distances between adjacent protons were calculated and used as the constraints for the molecular dynamics studies. They showed that the rotation of triazole-linked fragments is restricted and thus no regular secondary structure is formed. Conformation of the molecule after the MD is shown in figure 2.

[1] Claridge, T. D. W.; Long, D. D.; Baker, C. M.; Odell, B.; Grant, G. H.; Edwards, A. A.; Tranter, G. E.; Fleet, O. W. J.; Smith, M. D. *J. Org. Chem.* **2005**, *70*, 2082-2090.

[2] Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2596-2599.

[3] Angell, Y.; Chen, D.; Brahimi, F.; Saragovi, H. U.; Burgess, K. *J. Am. Chem. Soc.* **2008**, *130*, 556-565.