New molecules containing the 1,2,3-triazole moiety as potential HIV-1 Nef inhibitors.

Lucília Zeymer Alves Corrêa[a], Carlos Eduardo M. Salvador[a] and Carlos Kleber Z. Andrade*[a]

[a]*Laboratório de Química Metodológica e Orgânica Sintética (LaQMOS), Instituto de Química, Universidade de Brasília, CP-4478, 70910-970 Brasília-DF, Brasil.*

**ckleber@unb.br*

Keywords: HIV-1 Nef, triazole.

INTRODUCTION

The HIV-1 protein Nef is responsible for the degradation of the cell membrane protein CD4. Ikarugamycin[1] (Figure 1) is a known drug that binds to Nef and blocks its activity.

Based on calculations of the interaction energy between the drug Ikarugamycin and Nef protein, we proposed new molecules with Nef inhibition potential (Figure 2). These new molecules have lower interaction energy values with Nef protein than the drug Ikarugamycin itself. This work describes a short and efficient synthetic route for the target molecules.

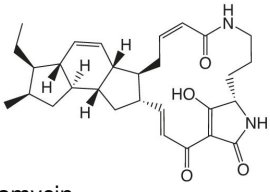


Figure 1. Ikarugamycin.

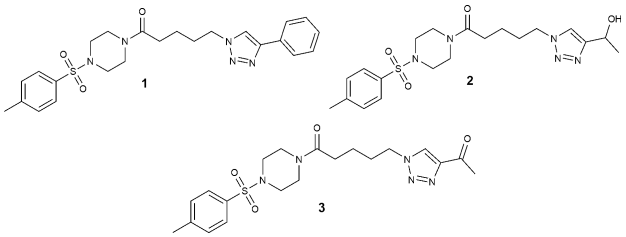
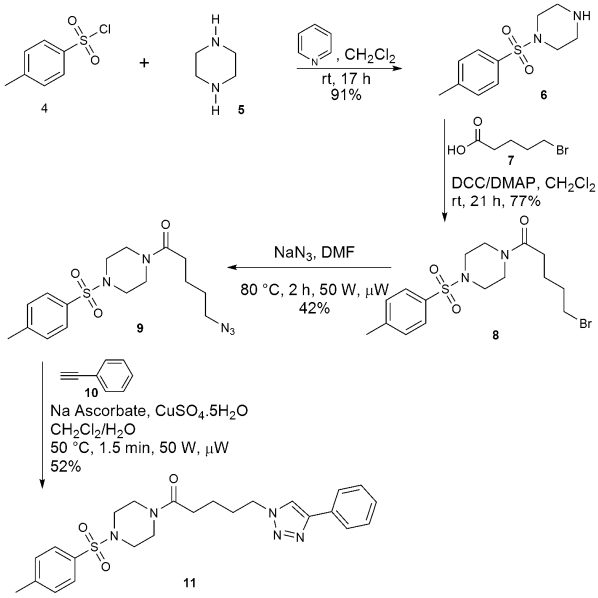


Figure 2. Target molecules.

RESULTS AND DISCUSSION

The synthetic route developed began with sulfonation of piperazine **5** in the presence of pyridine in dichloromethane. The reaction was performed at room temperature for 17 h affording product **6** in high yield (91%). The second step involved the coupling between intermediated **6** and 5-bromovaleric acid **7** in the presence of DCC/DMAP in dichloromethane. The reaction was conducted at room temperature for 21 h giving product **8** in good yield (77%). The following step was performed by a nucleophilic substitution reaction of bromine by azide. The reaction was conducted in the presence of sodium azide in a microwave reactor for 2 h at 80 °C (50 W) giving product **9** in moderate yield (42%).

The last step was performed by a Huisgen cycloaddition reaction (click reaction) between the azide **9** and phenylacetylene **10** in the presence of copper catalyst ($CuSO_4.5H_2O$) and sodium ascorbate. The reaction mixture was subjected to microwave reactor for 1.5 min (50 °C, 50 W) giving product **1** in 52% yield after purification by column chromatography, based on the recovery of the stating material.



Scheme 1. Synthetic route to HIV-1 Nef inhibitors.

CONCLUSION

The synthesis of molecule **1** was successfully performed by a direct synthetic route with moderate to good yields. Subsequent syntheses of molecule **2** and **3** are in progress in our laboratory. Molecules **1-3** will be submitted to *in vitro* tests to evaluate this inhibition activity to HIV-1 virus.

ACKNOWLEDGEMENTS

IQ-UnB, Capes, CNPq and FINEP-CTINFRA n° 0970/01.

REFERENCES

[1] Lama, J. *Curr. HIV Res.* **2003**, *1*, 167.