Preparation of Pyrrolidone-Gabosine Derivatives by γ-Lactamization

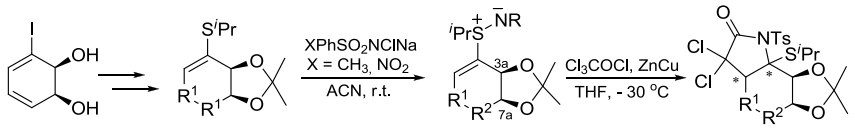
Vilela, G. D.[a], Pandolfi, E.[b], Schapiro, V.[b], Silveira, G. P.[a]

[a]*Dep. de Química Orgânica, IQ –UFRGS, Porto Alegre, Brasil*
[b]*Dpto de Química Orgánica, UdelaR, Montevideo, Uruguay guilherme.vilela@ufrgs.br*

Preparation of pyrrolidones have attracted the scientific community because the abundance of bioactive molecules bearing this structure. In our ongoing program to the development of new agents to combat infections caused by ESKAPE panel of pathogens[1], we proposed the synthesis of pyrrolidone derivatives by the γ-lactamization reaction[2].

Asymmetric diols, such as **1**, have being used as chiral pools to synthesize naturally occurring epoxyquinoids[3]. In the course of our collaboration, we envisioned that **1** could be used to transfer chirality to prepare chiral sulfilimines.

Reaction of sulfides **2** and **3** with chloramine-T (X=CH_3), or nosylchloramine (X=NO_2), in acetonitrile at room temperature, gave sulfilimines **4**, **5**, and **6** as diasteriomeric mixtures (a:less polar + b:more polar spots on TLC) which were separated by flash chromatography as pure diasterioisomers **4a/b**, **5a/b**, and **6a/b** (Scheme).



Scheme: preparation of chiral sulfilimines **4-6** and pyrrolidones **7-8** by γ-lactamization reaction.

Sulfilimine **6a** had its absolute configuration determined by X-ray crystallography as (*R*)-(3a*S*,7a*S*). Double doublets related to the isopropyl group on ^{1}H NMR spectra present a pattern of coupling constants (*J*): sulfilimines **4a**, **5a**, and **6a** (also less spots on TLC) show *J* of 6.5 Hz; meanwhile, *J* to **4b**, **5b**, and **6b** (more polar spots on TLC) are 6.8-6.9 Hz (Figure). These behaviors suggest that **4a** and **5a** also present (*R*)-(3a*S*,7a*S*), while **4b**, **5b**, and **6b** have (*S*)-(3a*S*,7a*S*) absolute configurations.

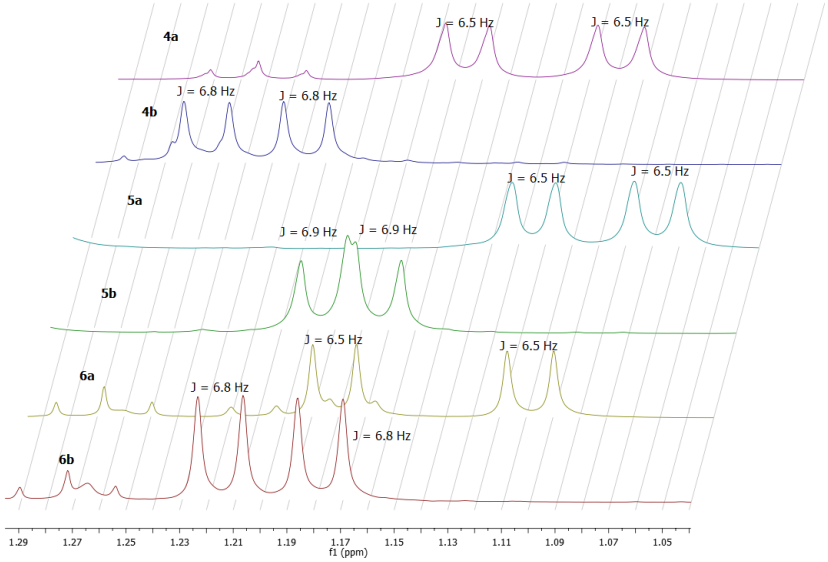


Figure: ^{1}H NMR spectra to sulfilimines **4-6**.

Finally, reaction of sulfilimines **4** and **5** with trichloroacetyl chloride, in presence of ZnCu and dry THF at –30 °C, gave the pyrrolidones **7** and **8**. Unfortunately, nosyl sulfilimines **6** did not afford the expected pyrrolidone after γ-lactamization reaction.

[1]Silva, E.E.; Pereira, P.A.; Londero, N.; Azeredo, J.B.; Braga, A.L; Silveira, G.P.; *39ª RASBQ* **2016**, MED052.
[2]Silveira, G.P.; Marino, J.P. *J. Org.Chem*. **2013**, *78*, 3379.
[3]Pandolfi, E.; Schapiro, V.; Heguaburu, V.; Labora, M. *Curr. Org. Synth*. **2013**, *10*, 2.