REACTIVITY STUDY OF METHYLCYCLOBUTYLKETONES AND CYCLOBUTANONES IN THE OBTENTION OF ANALOGS OF HYDANTOINIC NUCLEOSIDES

Juan A. Caturelli Kuran, Albertina G. Moglioni

Cátedra de Química Medicinal, Departamento de Farmacología, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956, Buenos Aires, (C1113AAD), Argentina.

**e-mail corresponding author*: jacaturelli@ffyb.uba.ar

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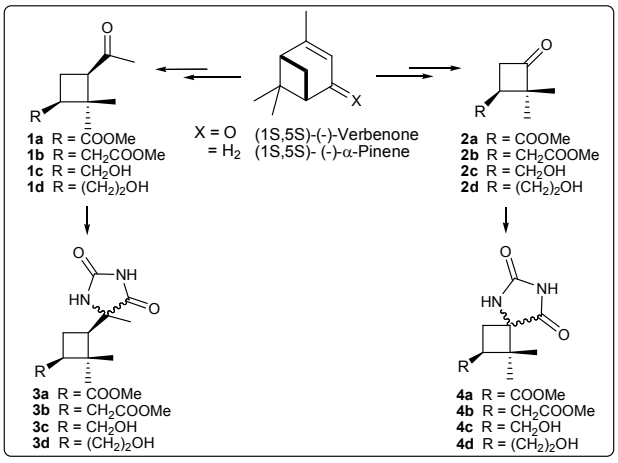
INTRODUCTION

Nucleosidic compounds containing a hydantoinic ring in their structure constitute an interesting group since the discovery of hydantocidin a natural hydantoinic nucleoside.[1] Particularly, there are different timidine analogs, obtained by a ring contraction strategy, with a five-membered heterocycle, namely methylhydantoin. For example, showdomicin is a broad-spectrum antibiotic isolated from *Streptomyces showdoensis*.[2] In this context and supported by our previous experience in the synthesis of 1,2,2,3-tetrasubstituted cyclobutanic derivatives, the reactivity of methylcyclobutylketones **1a-d** and cyclobutanones **2a-d** to obtain hydantoinic compounds was studied.

RESULTS AND DISCUSSION

Intermediates **1a-d, 2a-d** were prepared form (1*S*,5*S*)-α-pinene and (1*S*,5*S*)-(-)-verbenone (Scheme 1).



Scheme 1. Synthetic pathway leading to hydantoinic nucleosides analogs.

The reaction of precursors **1a-b** and **2a-b** with ammonium carbonate and potassium cyanide in a mixture of water and ethanol led to the obtention of the imidazolidinedionic nucleosides analogs **3a-b** and **4a-b** as a mixture in different proportions according to the position of the ketone group in the starting material. A noticeable prevalence for one of them was shown in the case of derivatives **4**. Taking into account that the presence of an hydroximethyl group is mandatory in the development of nucleoside analogs, the reaction was assayed on the precursors **1c-d** and **2c-d,** also prepared from the precursors **1a-b** and **2a-b** respectively.

The results were compared within studied series with those previously obtained[3] for the heterocyclation reaction of thiosemicarbazones, derived from the same precursors, leading to obtain Δ2-1,3,4-thiadiazolines.

CONCLUSION

As had been observed in heterocyclation reactions of cyclobutylmethylketones or cyclobutanones thiosemicarbazones leading to heterocyclic compounds, it could be observed that the differences in the proportions of the obtained products, within the exposed cases, are determined by the position of the sp2 carbon where the cyclization reaction occurs, with respect to the cyclobutanic ring chiral centers.

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