Partial synthesis of 7α and 7β-hydroxy-ent-cyclozonarone and 7-hydroxy-chlorocyclozonarones derivatives

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INTRODUCTION

Sesquiterpenquinone, cyclozonarone (**1**), isolated from *Dictyopteris undulata*[1], has proven antifeedant activity against abalones.

The enantiomer of natural cyclozonarone ((+)-**2**) has shown activity against epimastigotes of *Trypanosoma Cruzi*[2], protozoo responsible for the Chagas disease. We have synthesized (+)-cyclozonarone (**2**) in a previous work [3].

The important bioactivity of these sesquiterpenquinones aroused our interest in the synthesis of both epimers of 7-hydroxycyclozonarone (**3** and **4**) and chlorinated derivatives (**5**).

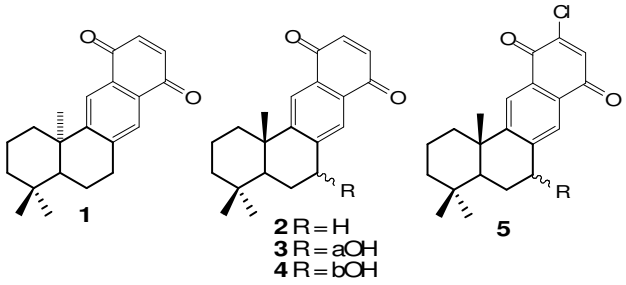


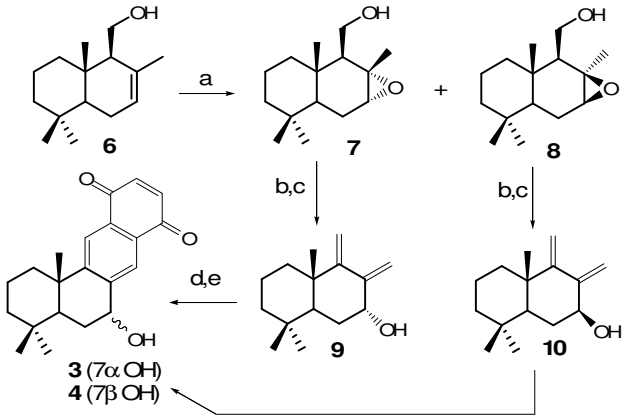
Figure 1. Cyclozonarones ,7-hydroxy cyclozonarones and 7-hydroxy chlorocyclozonarones.

RESULTS AND DISCUSSION

The substrate for the synthetic strategy was (-)-drimenol (**6**) isolated in large amounts from the bark of *Drymis Winteri*[4], which on treatment with *m*-chloroperbenzoic acid gave a mixture of diasteromeric epoxides **7** and **8**.

Epoxide cleavage and mesylic acid elimination with potassium t-butoxide afforded 7α-hydroxy diene (**9**) from **7** and 7β-hydroxy diene (**10**) from **8**.

Both 7-hydroxy dienes (**9** and **10**) were submitted to Diels - Alder reaction with *p*-benzoquinone and further oxidation with DDQ to afford the corresponding 7-hydroxy cyclozonarones (**3** and **4**).



Scheme 1. a) MCPBA, CH_2Cl_2, 70%; b) MsCl, Py, 51%; c) *t*-BuOK, *t*-BuOH, 20%, d) *p*-benzoquinone,C_6H_6,49%,e) DDQ,C_6H_6, 64%.

The same sequence was followed to obtain 7-hydroxychlorocyclozonarones by Diels - Alder reaction with chlorobenzoquinone, readily available by oxidation of chlorohydroquinone.

CONCLUSION

By a simple route, four new ent-cyclozonarone derivatives were successfully obtained, which allows a structure activity relation study. Biological activity tests are under way.

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