Synthesis, citotoxicity activity of new Cyclozonarone angular isomer

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INTRODUCTION

Among the great variety of natural products, found in plants, algae and sea sponge, we can find compounds that have a quinonic/hydroquinonic moiety united to a terpenic skeleton. Natural (-)-cyclozonarone (1), is a drimanic benzoquinone derivative isolated from algae Dintyopteris undulata that possesses a powerful feeding-deterrant activity towards young abalones1 furthermore shows anticancer activity.2 The absolute configuration of 1 was establish through a six-step route, starting from natural (-) polygodial, leading us to the synthetic enantiomer (+)-cyclozonarone (2), that showed antileishmania activity.3 Later, (-)-cyclozonarone was synthesized starting from (+)-albicanol.4 Both routes of synthesis were based on the Diels-Alder reaction.

RESULTS AND DISCUSSION

In this work, we described to the synthesis of an angular isomer of (+)-cyclozonarone. The compound 6 was synthesized using as synthetic strategy the Diels-Alder cycloaddition reaction between diene 5 and p-benzoquinone, in a sequence of six steps from confertifoline 3 (Scheme 1). Furthermore we reported herein the in vitro testing of 2 and 6 to include normal and tumor cell lines in order to determine the broadness of the activity. The antitumoral activities of compounds were assayed against two cells lines (DU-145 and PC-3) (Table 1).

CONCLUSION

In summary, we described here the synthesis of a new cyclozonarene isomer and anticancer evaluation of ent-cyclozonarone and its angular isomer. As compared with the tumor cell lines analyzed, we found ent-cyclozonarone had major antitumoral effect (Table 1). The comparison of the respective IC50 showed that normal cells were less sensitive to 2 and 6 compounds.

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