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Medicinal chemistry and Agrochemicals

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Synthesis and antiproliferative activity of (+)-muricatacin and two novel conformationally constrained analogues

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(+)-Muricatacin (4, Scheme 1) is naturally occurring γ -lactone that shows *in vitro* antiproliferative activity against some human neoplastic cells. Herein we describe a modified total synthesis of 4 starting from D-xylose, as well as synthesis of two new conformationally constrained (+)-muricatacin mimics (10a and 10b) from D-glucose (Scheme 2). Furanolactone 10b is one-carbon higher homologue of 10a. In the same time, both compounds 10a and 10b might also be considered as dephenylated analogues of (+)-goniofufurone (11), a naturally occurring styryl-lactone, which also demonstrated antitumour activity. Key diols 1 and 7 were converted to targets 4, 10a and 10b by utilizing the same three-step sequence as outlined in the reaction schemes. Results related to antiproliferative activity of 4, 10a and 10b against a number of tumour cells will be presented.

D-Xylose
$$\frac{8 \text{ steps}}{\text{Ref. 1}}$$
 $\frac{\text{OH}}{\text{BnO}}$ $\frac{\text{C}}{\text{BnO}}$ $\frac{\text{C}}{\text{BnO}}$ $\frac{\text{C}}{\text{Ho}}$ $\frac{\text{C}}{\text{Ho}}$

Scheme 1. Reagents and conditions: (a) I₂, imidazole, Ph₃P, CH₃CN, N₂, 90 °C; (b) 1-dodecene, Grubbs cat. 2nd generation, CH₂Cl₂, Ar, rt; (c) H₂, 10% Pd/C, MeOH, rt.

Scheme 2. Reagents and conditions: (a) TFA:H₂O (1:1), rt; (b) Meldrum's acid, Et₃N, DMF, 46–48 °C; (c) I₂, imidazole, Ph₃P, CH₃CN, N₂, 90 °C; (d) 1-undecene for 9a, 1-dodecene for 9b, Grubbs cat. 2nd generation, CH₂Cl₂, Ar, rt; (e) H₂, 10% Pd/C, MeOH, rt.

References

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