INTRODUCTION
Sansalvamide A (San A, 1) is a natural product isolated from a marine fungus (*Fusarium ssp.*). This cyclic depsipeptide exhibits a potent anticarcinogenic activity on multiple cancer cell lines. In continuing our research on the synthesis of peptoids with potential pharmacological activity, we decided to perform the synthesis of cyclic depsipeptoid analogues of San A (2a-b, Figure 1) based on a strategy previously developed in our group by combination of Ugi and Passerini reactions. To the best of our knowledge, the synthesis of cyclic depsipeptoids has not yet been explored.

Figure 1. Sansalvamide A (1) and its depsipeptoid analogues (2).

RESULTS AND DISCUSSION
The aim of our study was to develop a general strategy for the synthesis of cyclic pentadepsipeptides, as shown in Scheme 1. This strategy is based on: (a) formation of a peptoid via Ugi reaction; (b) ester hydrolysis; (c) formation of an acyclic tetradepsipeptoid scaffold in the Passerini reaction; (d) deprotection of the amine/acid and (e) a macrocyclization step via Ugi reaction. Peptoid 7 was prepared in 81% yield by an Ugi 4-component reaction (U-4CR) using benzylamine 3, paraformaldehyde 4, N-Boc-glycine 5 and methyl isocyanooacetate 6 (Scheme 1) using microwave (MW) irradiation for 3 min (45 °C, 150 W). Peptoid 7 was hydrolyzed after basic treatment (LiOH, THF/H2O) to give the corresponding acid in quantitative yield. Acid 8 was employed in a Passerini reaction with isobutyraldehyde 9 and tert-butyl isocyanooacetate 10, under µW irradiation for 4 min (60 °C, 40 W) affording the acyclic tetradepsipeptoid 11 in 61% yield.

![Scheme 1. Synthesis of cyclic pentadepsipeptoid analogues of San A (2a-b).](image)

A fast and general synthetic route was developed for the synthesis of cyclic pentadepsipeptides via consecutive multicomponent reactions.

CONCLUSION

A fast and general synthetic route was developed for the synthesis of cyclic pentadepsipeptides via consecutive multicomponent reactions.

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REFERENCES

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