Synthesis of β-analogues of FR900098 as antimalarials

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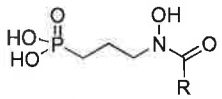
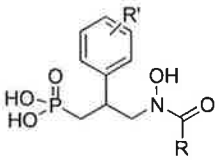
Fosmidomycin (**1**), an antibacterial phosphonate, and its acetyl counterpart FR900098 (**2**) exhibit potent inhibition of DXR, and the former is currently in clinical trials of combination therapies for the treatment of malaria. They thus represent valuable leads, for further optimization in the quest for new antimalarials. Attempts to increase their potency by introducing various aromatic groups in α-position of the phosphonate, yielded analogues with increased cell-based activity.[1,2] Remarkably, substitution at the β-position has hitherto not been explored. In this poster, we present our ongoing efforts towards the synthesis of β-substituted analogues (**3**).



1 R = H
2 R = Me



3 R = H or Me
R' = H, Cl, F, CO_2H, CH_3

[1] Devreux, V.; Wiesner, J.; Jomaa, H.; Rozenski, J.; Van der Eycken, J.; Van Calenbergh, S. *J. Org. Chem.* **2007,** *72*, 3783-3789.

[2] Haemers, T.; Wiesner J.; Van Poecke, S.; Geoman, J. L.; Henschker, D.; Beck, E.; Jomaa, H.; Van Calenbergh, S. *Bioorg. Med. Chem. Lett.* 2006, 16, 1888-1891.