The design and synthesis of inhibitors of *Mycobacterium tuberculosis* thymidylate kinase (*Mt*TMPK)

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Thymidylate kinase (TMPK) phosphorylates thymidine 5'-monophosphate (dTMP) and has been proposed as an attractive target for *Mycobacterium tuberculosis* (Mt).[1] By mimicking the structure of the substrate (dTMP), we have previously discovered different series of nucleoside analogues with *Mt*TMPK inhibitory activities in a micromole range.[2] Based on recently reported potent piperidin-3-yl-thymine inhibitors of Gram-positive bacterial TMPK,[3] we report a series of isomeric *N*-benzyl-substituted piperidin-4-yl-thymine analogues, some of which demonstrate potent *Mt* TMPK inhibitory activity. Towards this end a convenient and high-yield synthesis was developed to access 1-substitued thymine derivatives.

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