Novel series of substituted biphenylmethyl urea derivatives as MCH-R1 antagonists for the treatment of obesity

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Abstract

We have designed and synthesized two novel series of MCH-R1 antagonists based on a substituted biphenylmethyl urea core. SAR was explored, suggesting that optimal binding with the receptor was achieved when the biphenylmethyl group and the linker were substituted on the same nitrogen of the urea moiety. Compound 1-(3'-cyano-4-biphenylmethyl)-3-(2-hydroxy-1,1-dimethylethyl)-1-{2-[1-(4-methylbenzyl)-4-piperidinyl]ethyl}urea 2t showed the best antagonist binding activity to the MCH-R1 with a 43 nM K(i).