

Cholesterol-Lowering

1. Preparation of substituted pyrroleheptanoic acid derivatives as HMG-CoA reductase inhibitors

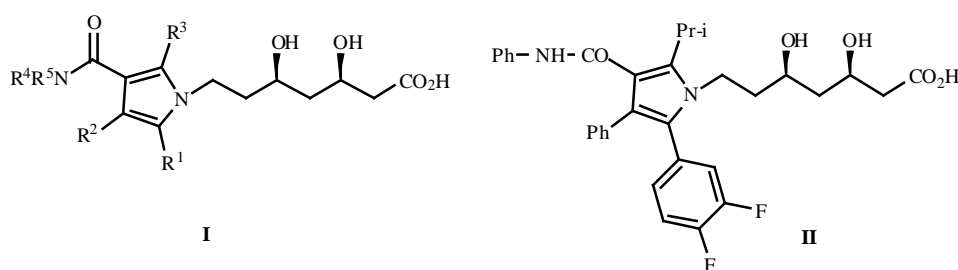
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U.S. Pat. Appl. Publ. US 2004, 102, 511 (CL. 514-422; A61k31/4025) 27 May 2004, IN Appl. 2002/DE1, 176, 21 Nov 2002; 19 pp; C.A. 141(1): 7016y

Abstract: Substituted pyrroleheptanoic acid derivatives **I** [R^1 =(substituted) Ph, cyclohexyl; R^2 (substituted) Ph; R^3 = *iso*-pr, cyclopropyl; R^4 =H, Me; R^5 = (substituted) Ph, pyridyl] were synthesized. These synthetic analogs are inhibitors of HMG-CoA reductase.

Activity and bioassay: Compound **II** exhibited IC_{50} = 6.25 μ M against HMG-CoA reductase, suggesting it to be useful as cholesterol-lowering agent and in the treatment of cholesterol related diseases.

Origin: Synthetic



2. Preparation of non-steroidal FXR agonists

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PCT Int. Appl. WO 2004, 46, 162 (Cl. C07J). 3 Jun 2004 US Appl. PV491.185, 29 Jul. 2003; 75 pp;. C.A. 141(2): 23422h

Abstract: Non-steroidal compounds *N*-aryl-*N*-arylmethyl amido and ureido **I** [E^1 = (C₁-C₈)alkyl, cyclohexyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, Ph, NH(C₁-C₈)alkyl; L^1 , L^2 = H; dashed bond = single bond or double bond; X^1 = CO, CH₂; Y^1 = H, NHZ¹, NH(Z²)Z³, OZ⁴; A^1 = aryl, heterocyclyl etc.; Z^1 = H, Ph, alkyl, benzyl, benzoyl; Z^2 , Z^3 = alkyl; Z^2Z^3 = cycloalkyl; Z^4 = H, oxygen protecting group], and **II** were synthesized

Activity and bioassay: These compounds exhibited farnesoid X receptor (FXR) agonists activity. Compounds with such type of activity are used to treat diseases related to cholesterol, bile acids, and their metabolism and homeostasis. Compound **II** displayed EC_{50} of 72 nM for FXR activity and relative efficacy = 1.70 at 1 mM to 100 mM CDCA in a cell-based assay.

Origin: Synthetic

