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(54) Title: SUBSTITUTED 8-ARYLQUINOLINE PHOSPHODIESTERASE-4 INHIBITORS

(57) Abstract: Novel substituted 8-arylquinolines represented by Formula (I), or a pharmaceutically acceptable salt thereof, wherein S_1, S_2 and S_3 are independently H, -OH; halogen, -C_1-C_6alkyl, -NO_2, -CN, or -C_1-C_6alkoxy, wherein the alkyl and alkoxy groups are optionally substituted with 1-5 substituents; wherein each substituent is independently a halogen or OH; R_1 is a H, OH, halogen, carbonyl, or -C_1-C_6alkyl, -cycloC_3-C_6alkyl, -C_1-C_6alkenyl, -C_1-C_6alkoxy, aryl, heteroaryl, -CN, -heterocycloC_3-C_6alkyl, -amino, -C_1-C_6alkylamino, -(C_1-C_6alkyl)(C_1-C_6alkyl)amino, -C_1-C_6alkyl(oxy)C_1-C_6alkyl, -C(O)NH(aryl), -C(O)NH(heteroaryl), -SO_nNH(aryl), -SO_nNH(heteroaryl), -SO_nNH(C_1-C_6alkyl), -C(O)N(C_0-C_6alkyl)(C_0-C_6alkyl), -NH-SO_n-(C_1-C_6alkyl), -SO_n-(C_1-C_6alkyl), -(C_1-C_6alkyl)-O-C(CN)-dialkylamino, or -(C_1-C_6alkyl)-SO_n-(C_1-C_6alkal) group, wherein any of the groups is optionally substituted with 1-5 substituents; wherein each substituent is independently a halogen, -OH, -CN, -C_1-C_6alkyl, -cycloC_3-C_6alkyl, -C(O)(heterocycloC_3-C_6alkyl), -C(O)-O-(C_0-C_6alkyl), -C(O)-aryloxy, -C_1-C_6alkoxy, -(C_0-C_6alkyl)(C_0-C_6alkyl)amino, cycloalkyloxy, acyl, acyloxy, -cycloC_3-C_6alkyl, heterocycloC_3-C_6alkyl, aryl, heteroaryl, carbonyl, carbamoyl, or -SO_n-(C_1-C_6alkyl); A is CH, C-ester, or C-R_4; R_2 and R_3 independently is an aryl, heteroaryl, H, halogen, -CN, -C_1-C_6alkyl, heterocycloC_3-$_6$alkyl, -C_1-C_6alkoxy, carbonyl, carbamoyl, -C(O)OH, -C_1-C_6alkyl)-SO_n-(C_1-C_6alkyl), -C(O)N(C_0-C_6alkyl)(C_0-C_6alkyl), or -C_1-C_6alkylacylamino group, wherein any of the groups is optionally substituted with 1-5 substituents, wherein each substituent is independently an aryl, heteroaryl, halogen, -NO_2, -C(O)OH, carbonyl, -CN, -C_1-C_6alkyl, -SO_n-(C_1-C_6alkyl), -SO_n-(aryl), aryloxy, -heteroaryloxy, C_1-C_6alkoxy, N-oxide, -C(O)-heterocycloC_3-C_6alkyl, -NH-cycloC_3-C_6alkyl, amino, -OH, or -(C_0-C_6alkyl)(C_0-C_6alkyl)amino, -C(O)-N(C_0-C_6alkyl)(C_0-C_6alkyl) substituent group, wherein each substituent group independently is optionally substituted with -OH, C_1-C_6alkoxy, -C_1-C_6alkyl, -cycloC_3-C_6alkyl, aryloxy, -C(O)OH, -C(O)O(C_1-C_6alkyl), halogen, -NO_2, -CN, -SO_n-(C_1-C_6alkyl), or -C(O)-N(C_0-C_6alkyl)(C_0-C_6alkyl); one of R_2 and R_3 must be an aryl or heteroaryl, optionally substituted; when R_2 and R_3 are both an aryl or heteroaryl, then R_2 and R_3 may be optionally connected by a thio, oxy, or (C_1-C_4alkyl) bridge to form a fused three ring system; are PDE4 inhibitors.

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