Crystal structure, Hirshfeld surface analysis, and molecular dynamics simulations of two isostructural N-propargyl-4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinolines

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Abstract

Two new N-propargyl-4-(2-oxopyrrolidin-1-yl)-1,2,3,4-tetrahydroquinoline derivatives (4a and 4b), have been efficiently prepared through a one-pot $InCl_3$-catalyzed cationic Povarov reaction between N-propargylanilines (1a and 1b), formaldehyde (2) and N-vinyl-pyrrolidin-2-one (3). These compounds were characterized by ATR-FTIR spectroscopy, $^{1}H/^{13}C$ NMR spectroscopy, ESI-IT mass spectrometry, and by single-crystal X-ray diffraction. N-propargyl-6-methyl-4-(2′-oxopyrrolidin-1′-yl)-1,2,3,4-tetrahydroquinoline (4a) and N-propargyl-6-chloro-4-(2′-oxopyrrolidin-1′-yl)-1,2,3,4-tetrahydroquinoline (4b) are isostructural and crystallize in space group $P2_1/c$. The crystal structures are characterized by inversion-related interpenetrated helices along the b-axis that form columns along the c-axis. C—H···O, C—H···C, and C—H···π(aryl) for 4a and C—H···O, C—H···Cl, and C—H···π(aryl) for 4b interactions occur within the columns which are connected by C—H···π(propargyl) interactions. These features were further visualized by Hirshfeld surface analysis and energy frameworks calculations and evaluated by the E_{XY} enrichment ratio. Molecular dynamics simulations show that these compounds are promising monoamine oxidase B (MAO-B) inhibitors, since they interact with MAO-B in a similar manner as rasagiline, a drug commonly used in the treatment of Parkinson's and Alzheimer's diseases. © 2021

Author keywords

Cationic Povarov reaction; Crystal structure; Molecular dynamics simulations; Monoamine oxidase B inhibitors; N-propargylamines; Tetrahydroquinoline