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Synthesis 4-[2-(2-mercapto-4-oxo-4H-quinazolin-3-yl)-ethyl]-benzenesulfonamides with subnanomolar carbonic anhydrase II and XII inhibitory properties (Article)

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Abstract

Condensation of substituted anthranilic acids with 4-isothiocyanatoethyl-benzenesulfonamide led to series of heterocyclic benzenesulfonamides incorporating 2-mercapto-quinazolin-4-one tails. These sulfonamides were investigated as inhibitors of the human carbonic anhydrase (hCA, EC 4.2.1.1) isoforms hCA I and II (cytosolic isozymes), as well as hCA XII (a transmembrane, tumor-associated enzyme also involved in glaucoma-genesis). The new sulfonamides acted as medium potency inhibitors of hCA I (K_Is of 28.5–2954 nM), being highly effective as hCA II (K_Is in the range of 0.62–12.4 nM) and XII (K_Is of 0.54–7.11 nM) inhibitors. All substitution patterns present in these compounds (e.g., halogens, methyl and methoxy moieties, in positions 6, 7 and/or 8 of the 2-mercapto-quinazolin-4-one ring) led to highly effective hCA II/XII inhibitors. These compounds should thus be of interest as preclinical candidates in pathologies in which the activity of these enzymes should be inhibited, such as glaucoma (CA II and XII as targets) or some tumors in which the activity of isoforms CA II and XII is dysregulated. © 2016 Elsevier Ltd

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Author keywords

2-Mercapto-quinazolin-4-one; Carbonic anhydrase; Inhibitor; Sulfonamide; Tail approach

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