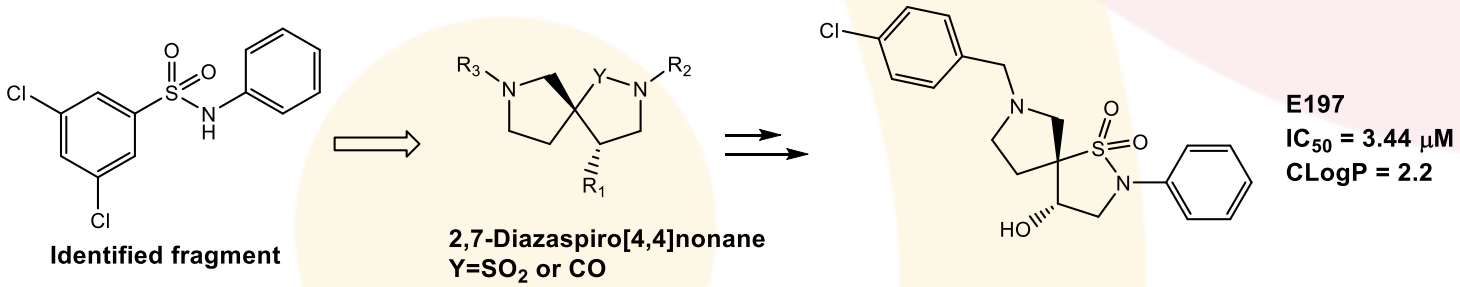
2,7-Diazaspiro[4,4]nonane derivatives, original N-arylsufonamides compounds featuring a diazaspiro[4,4]nonane nucleus that inhibit the exchange factor DOCK5

Exchange factor DOCK5 is an essential part of the bone resorption activity of osteoclasts and a major drug target in anti-osteoporosis drug research. From an identified arylsulfonamide fragment, EDELRIS developed and synthesized a unique small-molecule compound library based on the diaza[4,4]nonane nucleus.



The library was tested on DOCK5, and after further medicinal chemistry optimization of hits, the spiro-compound **E197** was identified as an important lead-molecule as it protected mice from ovariectomy-induced bone loss without affecting bone formation. Also, **E197** is efficient on both mouse and human DOCK5 and can prevent mouse and human osteoclast activity.

Novel 2,7-Diazaspiro[4,4]nonane derivatives to inhibit mouse and human osteoclast activities and to prevent bone loss in ovariectomized mice without affecting bone formation. DOI: 10.1021/acs.jmedchem.0c01201

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