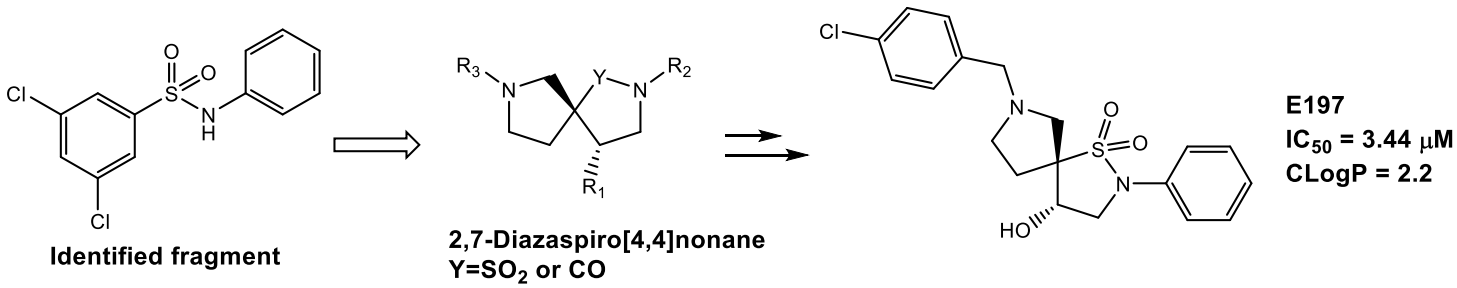
Original N-aryl sulfonamide compounds featuring a diazaspiro[4,4]nonane nucleus: Inhibition of the exchange factor DOCK5

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**. **E197** protects mice from ovariectomy-induced bone loss without affecting bone formation. Also, **E197** is efficient on both mouse and human DOCK5 and prevents human and mouse osteoclast activity.

Original publication: 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