Furo[3,2-*b*]pyridine – a novel privileged scaffold for selective kinase inhibitors and effective modulators of the Hedgehog pathway

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Abstract

We report the identification of the furo[3,2-b]pyridine (FP) core as a novel scaffold for potent and highly selective inhibitors of cdc-like kinases (CLKs) and efficient modulators of the Hedgehog signaling pathway. Initially, a diverse target compound set was prepared by synthetic sequences based on chemoselective metal-mediated couplings, including assembly of the furo[3,2-b]pyridine scaffold via copper-mediated oxidative cyclization. Optimization of the subseries containing 3,5-disubstituted furo[3,2-b]pyridines afforded potent, cell-active and highly selective inhibitors of CLKs. Profiling of the kinase-inactive subset of 3,5,7-trisubstituted furo[3,2-b]pyridines revealed sub-micromolar non-toxic modulators of the Hedgehog pathway.

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