Synthesis of mucopolysaccharidosis enzyme assay substrates by click chemistry

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Enzyme activity assays play an important role in neonatal diagnostics [1]. The ability to find indications for rare metabolic disorders like mucopolysaccharidoses (MPS) and other lysosomal storage diseases at a very early stage can help to preserve a decent quality of living for affected patients by a timely start of therapy. The use of copper catalyzed click chemistry (CuAAC) allows easy access to enzyme substrates and respective deuterated internal standards towards a tandem-LCMS based enzyme assay.

To measure the activity of galactosamine-6-sulfatase (MPS IVa, Morquio syndrome) substrates were prepared by installing a sulfate moiety at C6 of β-propargyl galactose before the click reaction with various azides. Internal standards were easily prepared using the respective deuterated azides. The performance of these new diagnostic tools in an authentic clinical environment was evaluated by analysis of dried blood spot samples of randomized newborns and patients affected by MPS IVa.