Titel des Beitrags: Synthesis of novel 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) derivatives for chemoselective attachment to unprotected polyfunctionalized compounds.

Abstract: A convenient synthesis of novel bifunctional poly(amino carboxylate) chelating agents allowing chemoselective attachment to highly functionalized biomolecules is described. Based on the well known chelator 1,4,7,10-tetraazacyclodecane-1,4,7,10-tetraacetic acid (DOTA), we synthesized novel bifunctional chelating agents bearing additional functional groups by alkylating 1,4,7,10-tetraazacyclododecane (cyclen) with one equivalent of para-functionalized alkyl 2-bromophenyl-acetate and three equivalents of tert-butyl 2-bromoacetate. The resulting compounds, which contain an additional carbonyl or alkyne functionality, allow site specific labeling of appropriately functionalized unprotected biomolecules in a rapid manner via click reactions. This was demonstrated by the attachment of our new DOTA derivatives to the somatostatin analogue Tyr3-octreotate by chemoselective oxime ligation and CuI-catalyzed azide-alkyne cycloaddition. Initial biodistribution studies in mice with the radiometalated compound demonstrated the applicability of the described DOTA conjugation.