

Elution Behavior and Structural Characterization of *N*- and *C*-functionalized DOTA Complexes for the Labelling of Biomolecules

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Two types of lanthanide complexes of 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) for the labelling of biomolecules were investigated by HPLC, MS and NMR spectroscopy. The elution behavior of lanthanide complexes of *N*-functionalized DOTA [1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid-10-maleimidoethylacetamide (nDOTA-Mal) and 1-{2-[4-(maleimido-*N*-propylacetamidobutyl)amino]-2-oxoethyl}-1,4,7,10-tetraazacyclododecane-4,7,10-triacetic acid (nDOTA-Bu-Mal)] and *C*-functionalized DOTA [2-{4-(maleimido-*N*-propylacetamido)benzyl}-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (cDOTA-Bnz-Mal) and 2-(4-isothiocyanatobenzyl)-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (cDOTA-Bnz-NCS)] was compared. *N*-functionalized lanthanide DOTA complexes coelute as required for their use as ICAT-analogous reagents. The complexation of the *C*-functionalized DOTA with lanthanides results in two fractions separable by HPLC. Coelution is observed for the main fractions of the lanthanide complexes. The retention times of the minor fractions show a dependence on the ionic radii of the metal ions. MALDI spectra of lanthanide-DOTA-peptide conjugates including different monoisotopic lanthanides demonstrate the advantage of the mass variations for extensive peptide and protein investigations.

Key words: Macrocycles, Lanthanide DOTA Complexes, HPLC, NMR, ICAT, MeCAT