Synthesis and ^{68}Ga-radiolabelling of 2-desoxyglucose conjugated macrocyclic chelators.

P. Riss[1], C. Kroll[1], F. Roesch[1]

[1]Institut für Kernchemie, Johannes Gutenberg-Universität, D-55128 Mainz, Germany

Introduction: [^{18}F]FDG is frequently used for the localization and staging of peripheral tumors and multiple other purposes. Although the approved imaging agent is readily available via reliable satellite distribution from local vendors, a generator based alternative would possess the potential to reduce overall cost and logistic effort. It might even increase the overall availability of the most frequently employed PET-examination, the FDG-scan.

This concept has already been examined,[1] e.g. for ^{99m}Tc-labelled ECD-desoxyglucose conjugates. Encouraged by the findings reported by those investigators, we were interested in a ^{68}Ga-labelled analogue for PET. ^{68}Ga provides a high positron abundance of 89 % and an intermediate positron maximum energy. With its half-life (1.13 h) lying perfectly in between the half-lives of the most frequently used ^{11}C (0.33 h) and ^{18}F (1.82 h), it provides excellent decay characteristics as a PET-radiolabel.

Experimental: Multiple mono- and divalent NOTA-desoxyglucose (NOTA-DG) and DOTA-desoxyglucose (DOTA-DG were synthesised from 1,4,7-triazacyclonone and 1,4,7,10-tetraazacyclododecane in good yields. The compounds were labelled with prepurified n.c.a. [^{68}Ga]$GaCl_3$ in aqueuous solution at pH = 2.8. Yields for ^{68}Ga(III) complex formation were in the usual range. The DTPA challenge experiment indicated high complex stability, in a similar range as the congener NOTA.

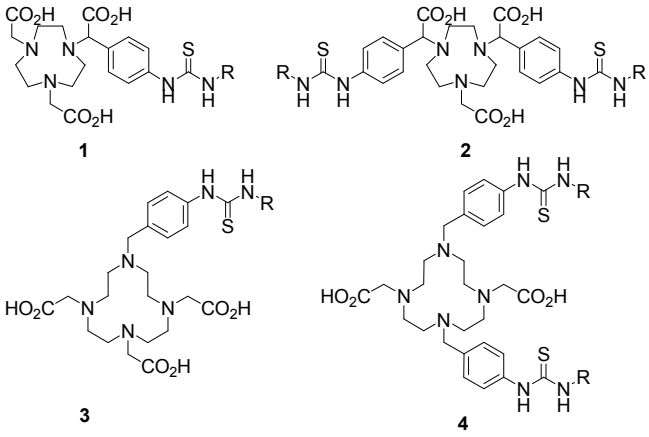
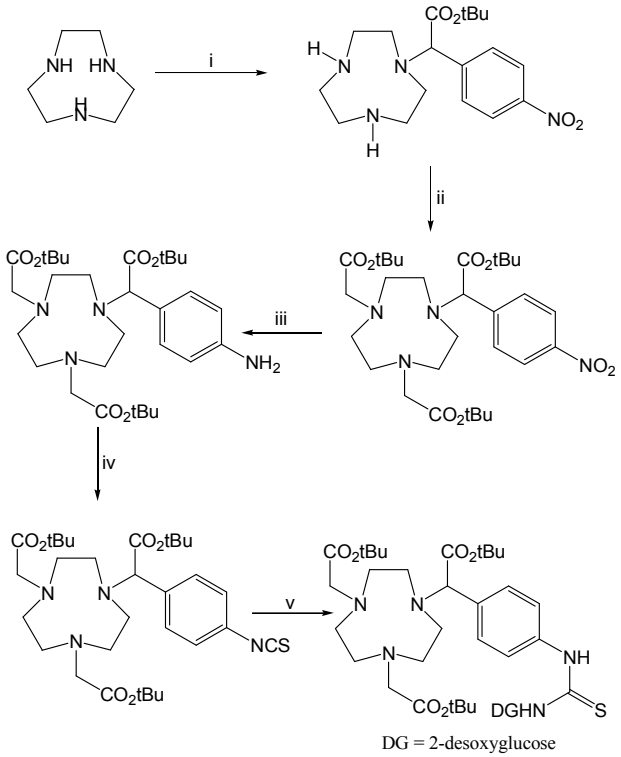


Figure 1. Structures of DG-conjugates



Scheme 1: Synthetic route to tris-tBu-NODAPA-NCS-NHDG[1]. i) CH_2Cl_2, K_2CO_3, RT, 72 h, ii) MeCN, 75 °C, 14 h, iii) Fe, AcOH, 3h; iv) CCl_2S, $CaCO_3$, RT, 14 h.

Results: A series of novel macrocyclic chelator-desoxyglucose conjugates can now be examined for phosphorylation in a commercial glucose-hexokinase assay. If the novel compounds are still recognized by the GluT 1 as a substrate, further systematic imaging studies seem worthwhile.

References

[1] P. J. Riß, C. Kroll, V. Nagel, F. Roesch, *Bioorganic Medicinal Chemistry Letters* **2008,** *18***,** 5364-7

Acknowledgement

The authors are grateful to the Fonds der chemischen Industrie