



Radiochemical Studies Laboratory, Institute of Nuclear & Radiological Sciences & Technology, Energy & Safety, National Center for Scientific Research “Demokritos”



Synthesis and characterization of Gold Nanoparticles and synthesis of a DOTA-derivative for the development of a novel cancer theranostic agent

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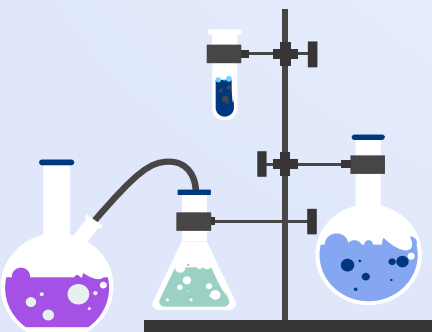
Chemist

PhD Candidate

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Host Supervisor: Dr. Przemysław Koźmiński

Host Institute: Centre of Radiochemistry and Nuclear Chemistry,
Institute of Nuclear Chemistry and Technology



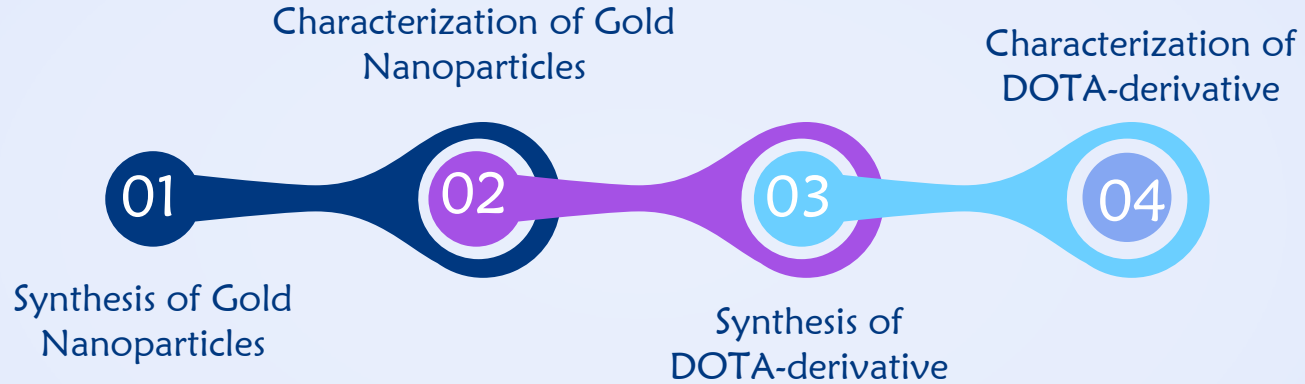
2nd CA17140 STSM Virtual Conference



Thesis Title: «Gold Nanoparticles radiolabeled with α , β and positron emitter radioisotopes for targeted diagnosis and therapy of cancer»

- Prostate cancer → 2nd most common cause of death in men over 60y.o.
- Nanoparticles accumulate passively or actively into specific target organs
- Gold nanoparticles (AuNPs) present beneficiary characteristics (low toxicity, biocompatibility, photothermal therapy etc)
- Gold nanoparticles can be radiolabeled with positron emitting isotopes such as ^{68}Ga (68-Gallium) for diagnosis, beta particles and alpha particles such as ^{177}Lu (177-Lutetium) and ^{225}Ac (225-Actinium) for therapy
- Main goal: Development of radiolabeled nanostructures with therapeutic properties for prostate cancer → functionalization of AuNPs with a molecule that targets the Prostate Specific Membrane Antigen (PSMA)
- Therapeutic efficacy studies

Introduction





01

Synthesis of Gold Nanoparticles

Synthesis of Gold Nanoparticles

Hydrodynamic Diameter: $\sim 20\text{nm}$

Reagents

- $\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$
- $\text{HOC}(\text{COONa})(\text{CH}_2\text{COONa})_2 \cdot 2\text{H}_2\text{O}$

Conditions

- Reflux ($136\text{--}137^\circ\text{C}$)
- Heating for 15 min
- Wrap with aluminum foil
- Leave at RT for a while
- Store in the fridge



Characterization of Gold Nanoparticles

02

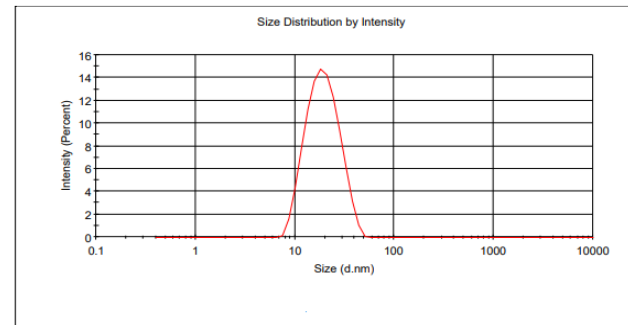
An abstract graphic design on the right side of the slide. It features several organic, teardrop-like shapes in shades of purple, blue, and light blue. A prominent purple shape contains a light blue circle with the number '02' in white. Other shapes in various shades of blue are scattered around, some connected by thin lines, and several solid blue dots of different sizes are also present.

Characterization of Gold Nanoparticles

- Dynamic Light Scattering (DLS) Average size 17.15nm
- Zeta Potential -47.9mV (very stable)

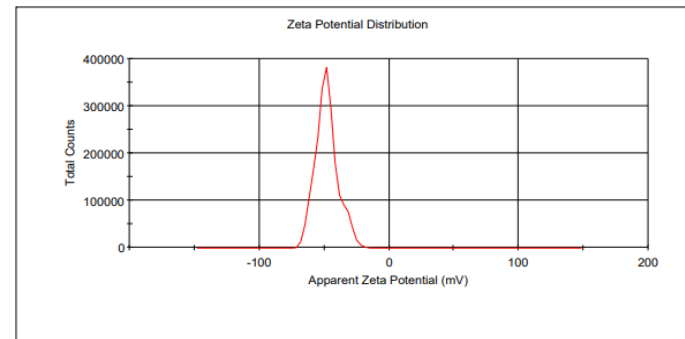


	Size (d.n...	% Intensity:	St Dev (d.n...
Z-Average (d.nm): 17,15	Peak 1: 20,21	100,0	7,438
Pdi: 0,156	Peak 2: 0,000	0,0	0,000
Intercept: 0,880	Peak 3: 0,000	0,0	0,000
Result quality Good			



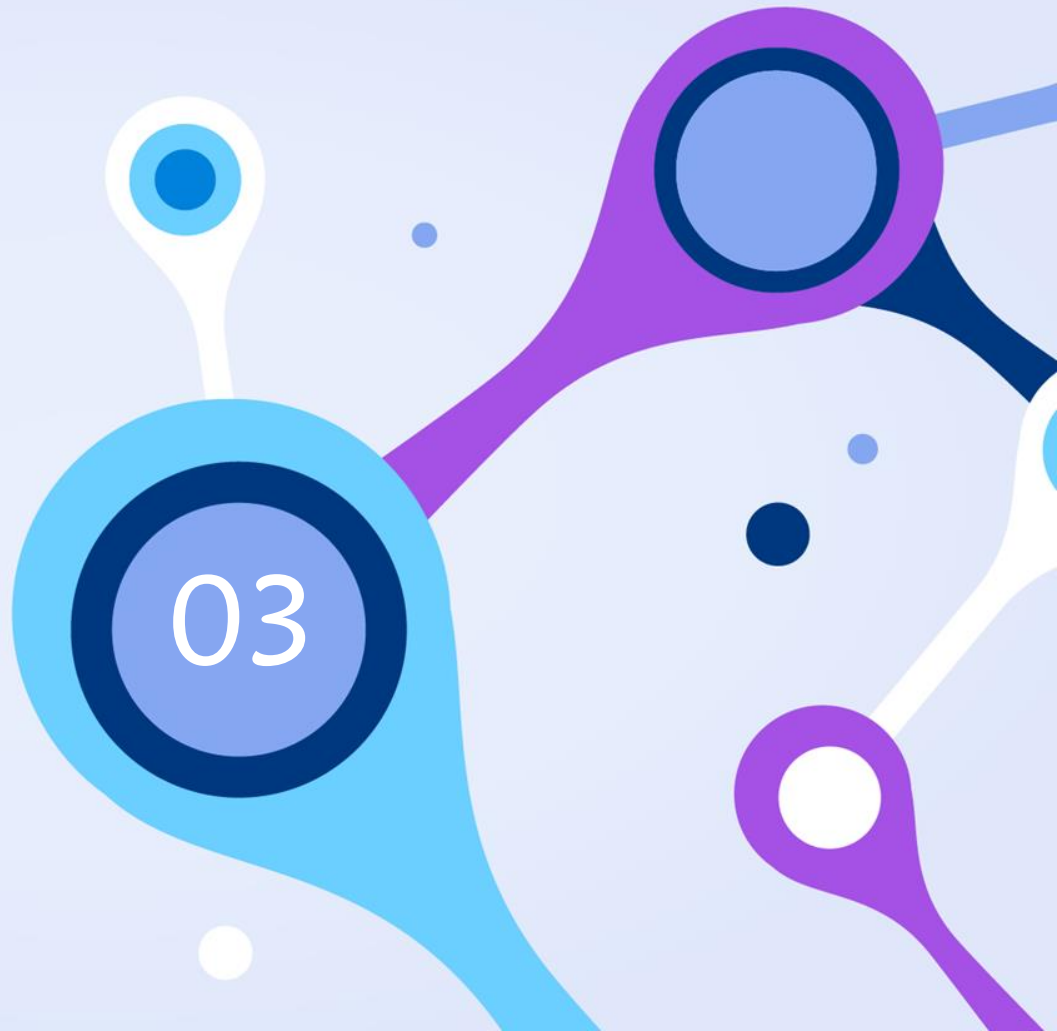
Size Distribution Report

	Mean (mV)	Area (%)	St Dev (mV)
Zeta Potential (mV): -47,9	Peak 1: -47,9	100,0	8,73
Zeta Deviation (mV): 8,73	Peak 2: 0,00	0,0	0,00
Conductivity (mS/cm): 1,13	Peak 3: 0,00	0,0	0,00
Result quality Good			



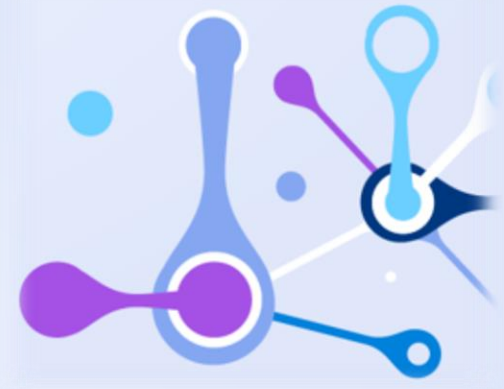
Zeta potential Report

Synthesis of DOTA-derivative



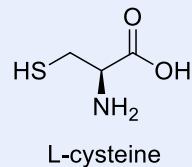
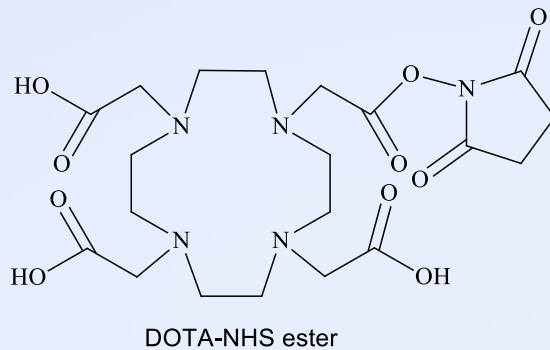
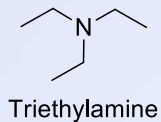
Main purpose of the synthesis:

- Synthesis of a DOTA-derivative with a –SH group
- Easy conjugation with Gold nanoparticles (Au-S bond)
- Functionalization with a PSMA-derivative (synthesized at the Home Institute)
- Radiolabeling through the DOTA-derivative with diagnostic and therapeutic isotopes ^{68}Ga (Gallium-68), ^{177}Lu (Lutetium-177) and ^{225}Ac (Actinium-225) for targeted diagnosis and therapy of Prostate Cancer

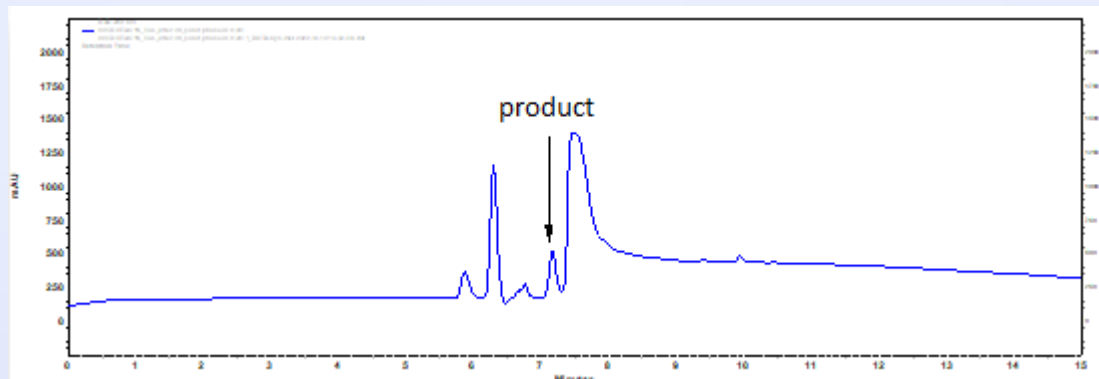
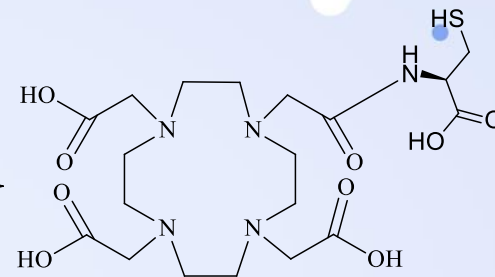


Synthesis of DOTA-derivative

1st method



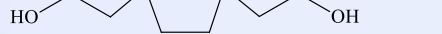
stirring
2-3h, RT



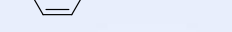
HPLC chromatograph of the reaction mixture at 200nm

Synthesis of DOTA-derivative

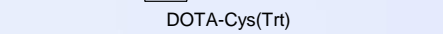
2nd



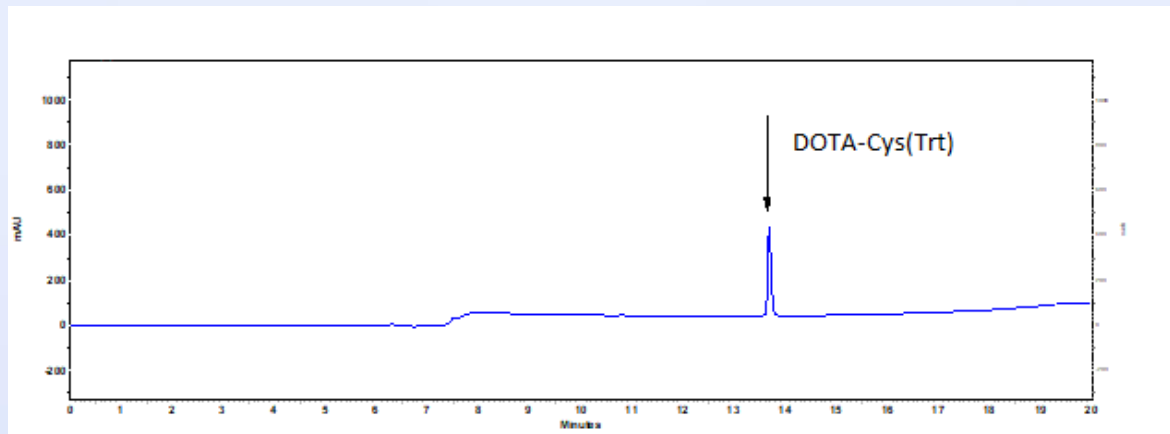
DOTA-NHS-Ester



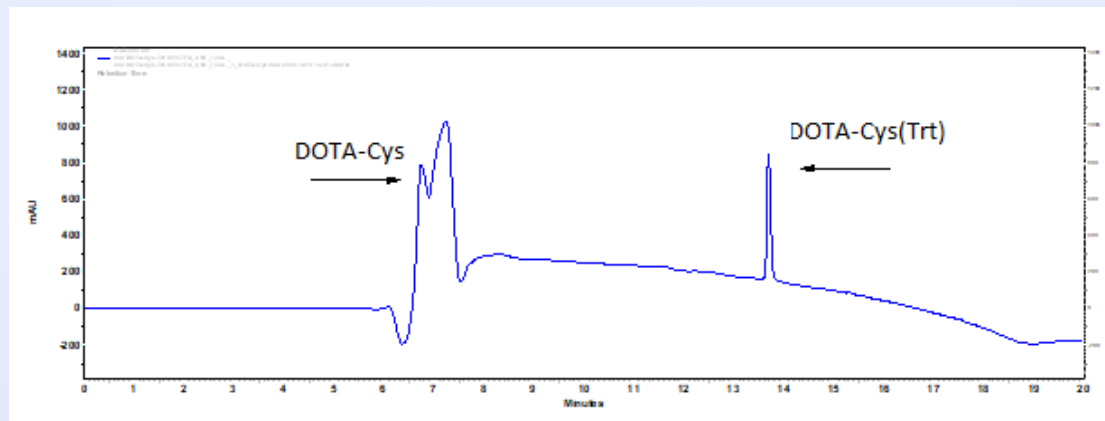
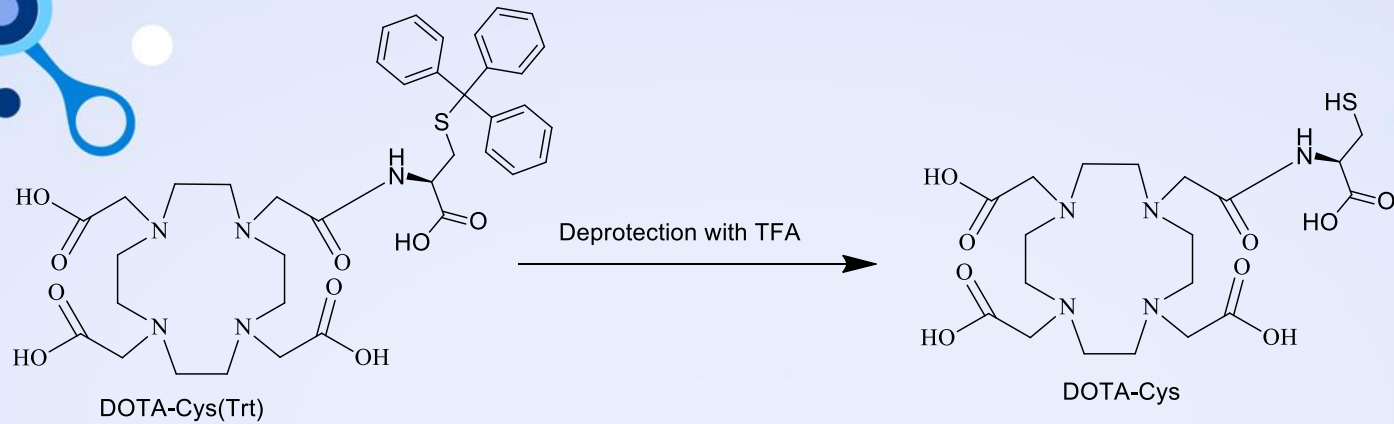
S-Trityl-L-cysteine



DOTA-Cys(Trt)



HPLC chromatograph of the DOTA-Cys(Trt) at 254nm



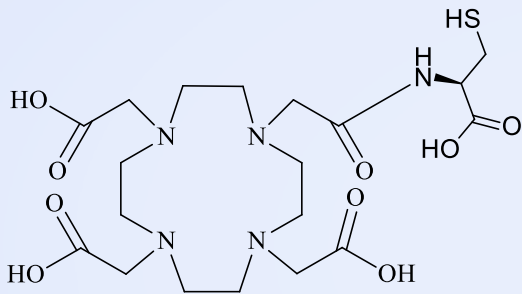
HPLC chromatograph after deprotection with TFA at 200nm



04

Characterization of DOTA- derivatives

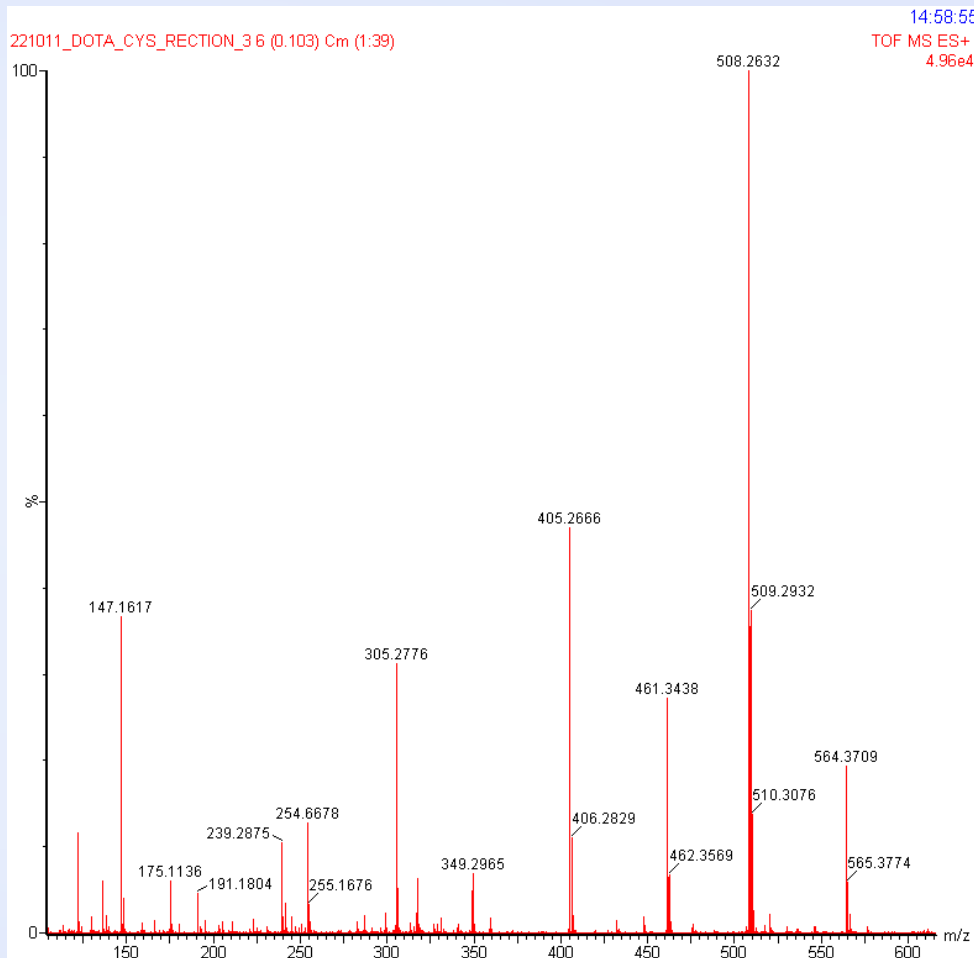
Characterization of DOTA-derivative with Mass Spectrometry (MS)



(R)-2,2',2''-(10-(2-((1-carboxy-2-mercaptoethyl)amino)-2-oxoethyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetic acid

Chemical Formula: $C_{19}H_{33}N_5O_9S$

Molecular Weight: 507.56

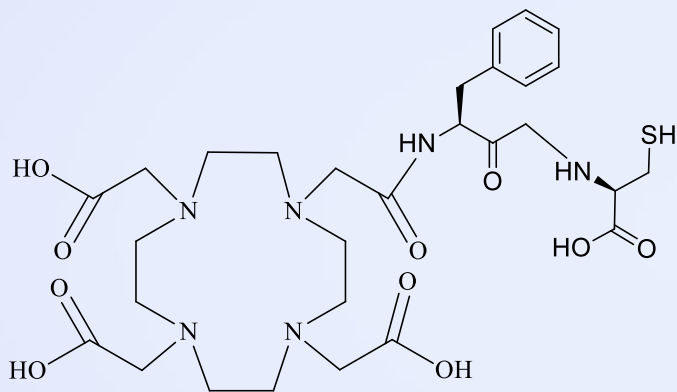


Future Perspectives

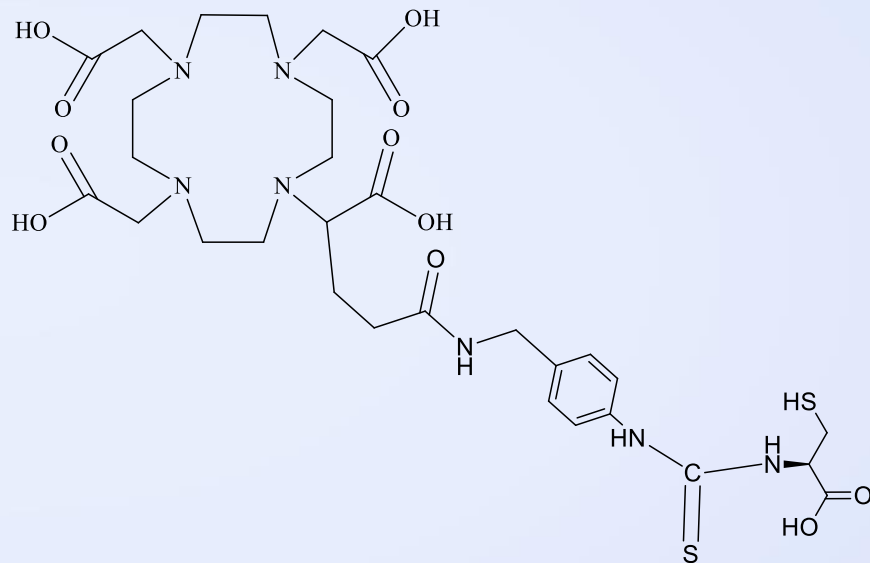


Future Perspectives

Synthesis of two more DOTA-derivatives



2,2',2''-(10-(2-(((S)-4-(((R)-1-carboxy-2-mercaptoethyl)amino)-3-oxo-1-phenylbutan-2-yl)amino)-2-oxoethyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetic acid



2,2',2''-(10-(1-carboxy-4-((4-3-((R)-1-carboxy-2-mercaptoethyl)thioureido)benzyl)amino)-4-oxobutyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triyl)triacetic acid



Acknowledgements



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Thank you very much
for you attention!!!

