

SYNTHESIS AND INVESTIGATION OF Ag-NHC COMPLEXES WITH CYTOTOXIC PROPERTIES TOWARDS CELL LINES MODELLING ACUTE MYELOID LEUKEMIA

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Synthetic route design and method development^[1-4] previously performed in Bjørsvik research group disclosed the NHC-Ag complexes, *N*-1-phenyl-*N*-3-methyl-4-methylimidazol-2-ylidene silver iodine NHC-I and *N*-1-phenyl-*N*-3-methyl-4-heptylimidazol-2-ylidene silver iodine NHC-II (Figure 1).^[5] These compounds were proven to possess a profound effect on the two human cell lines HL60 and MOLM-13 both modelling acute myeloid leukemia (AML).

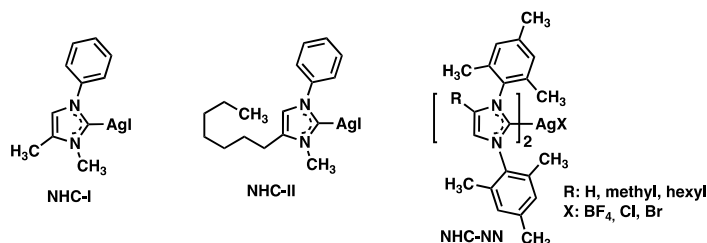


Figure 1: Structures of synthesized NHC-Ag complexes

New NHC-Ag complexes (NHC-NN, Figure 1) containing more bulky substituents on the imidazole ring nitrogen atoms both with and without alkylated backbones have been synthesized with the goal to further investigate how the cytotoxic effect is influenced by substitution pattern of the imidazole scaffold. Three main factors were investigated: (1) bulky groups on the imidazole nitrogen atoms, (2) variation of the alkyl chain installed on the backbone, and (3) installing the lipophilic alkyl group on another (other than the backbone) of the molecular framework.

The syntheses of target molecules involved various multicomponent reactions (MCR), *N*3-alkylation or *N*3-arylation, reductions, Sonogashira coupling reactions, amidation and ultimately the target imidazolium salts have been complexed to silver using silver(I) oxide or silver(I) nitrate.

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[5] A. H. Sandtorv, C. Leitch, S. L. Bedringaas, B. T. Gjertsen, H. -R. Bjørsvik, *ChemMedChem*, **2015**, 10, 1522-1527.