SYNTHESIS OF NEW CARBOCYCLIC *C*-NUCLEOSIDE ANALOGS

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Classical nucleoside analogs include a variety of biologically active compounds, namely those with antiviral and anticancer properties[1]. Since they possess the hemiaminal motif, their chemical and metabolic stability is often limited and the resulting metabolites can be the source of undesired side effects. Significant effort has thus been invested into the identification of more stable substances while preserving the biological activity, e.g. C-nucleosides or carbocyclic N-nucleosides.[1] It is conceivable that, at least in some cases, carbocyclic *C*-nucleosides might be even more robust**.** However, carbocyclic *C*-nucleosides analogs are quite rare and most published syntheses only produced single target compounds[2].

Our recently developed methodology enables flexible preparation of three classes of carbocyclic *C*-nucleoside analogs from common precursors – properly substituted cyclopentanones, which can be prepared racemic (in six steps) or optically pure (in ten steps) from inexpensive norbornadiene.[3] The methodology allows flexible manipulation of individual positions around the cyclopentane ring, namely highly diastereoselective installation of carbo- and heterocyclic substituents at position 1´, orthogonal functionalization of position 5´, and efficient inversion of stereochemistry at position 2´. Newly prepared carbocyclic C-analog of tubercidine, profiled in MCF7 (breast cancer) and HFF1 (human foreskin fibroblasts) cell cultures, is less potent than tubercidine itself, but more selectively toxic towards the tumorigenic cells[3].

This work was supported by projects FP7-PEOPLE-IRG-2008 (grant number 230936) and FNUSA-ICRC (CZ.1.05/1.1.00/02.0123), and by Dr. Alfred and Isabel Bader (private funding).

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