

# Extension of the PNA world by functionalized PNA monomers eligible candidates for inverse Diels Alder Click Chemistry

Manfred Wiessler, Waldemar Waldeck, Ruediger Pipkorn, Christian Kliem, Peter Lorenz, Heinz Fleischhacker, Manuel Hafner, Klaus Braun

### Abstract :

Progress in genome research led to new perspectives in diagnostic applications and to new promising therapies. On account of their specificity and sensitivity, nucleic acids (DNA/RNA) increasingly are in the focus of the scientific interest. While nucleic acids were a target of therapeutic interventions up to now, they could serve as excellent tools in the future, being highly sequence-specific in molecular diagnostics. Examples for imaging modalities are the representation of metabolic processes (Molecular Imaging) and customized therapeutic approaches ("Targeted Therapy"). In the individualized medicine nucleic acids could play a key role; this requires new properties of the nucleic acids, such as stability. Due to evolutionary reasons natural nucleic acids are substrates for nucleases and therefore suitable only to a limited extent as a drug. To use DNA as an excellent drug, modifications are required leading e.g. to a peptide nucleic acid (PNA). Here we show that an easy substitution of nucleobases by functional molecules with different reactivity like the Reppe anhydride and pentenoic acid derivatives is feasible. These derivatives allow an independent multi-ligation of functionalized compounds, e.g. pharmacologically active ones together with imaging components, leading to local concentrations sufficient for therapy and diagnostics at the same time. The high chemical stability and ease of synthesis could enhance nucleic chemistry applications and qualify PNA as a favourite for delivery. This system is not restricted to medicament material, but appropriate for the development of new and highly efficient drugs for a sustainable pharmacy.

### Key Word :

Click Chemistry, Diels Alder Reactioninvers (DARinv), Peptide Nucleic Acid (PNA), PNA building block functionalization

*Volume 7, Number 4, - 2010*