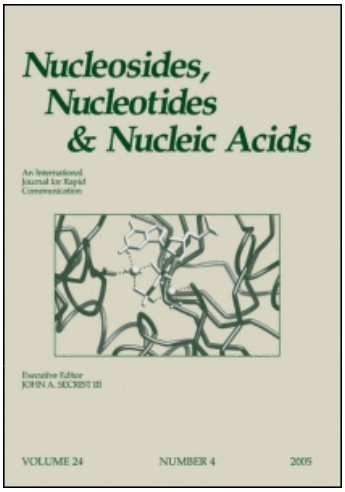

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Synthesis of an Asymmetrically Substituted AZA Crown Ether as Metal and Amino Acid Binding Site in DNA Conjugates

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ABSTRACT

Crown ether **4** as a receptor core for protonated primary amines such as amino acids has been synthesized and incorporated into oligodeoxynucleotides as dangling ends.

Key Words: Aza crown ether; Amino acid binding.

A very limited number of binding sites for organic molecules have been incorporated into oligonucleotides. Functionalised crown ethers have special interest in terms of host-guest chemistry.[1] Their selectivity for metal cations of different sizes and complexation of organic molecules such as amines and amino acids is a starting point for promising applications. It is noteworthy that especially triaza crown ethers show a remarkable affinity for protonated primary amines.[2]

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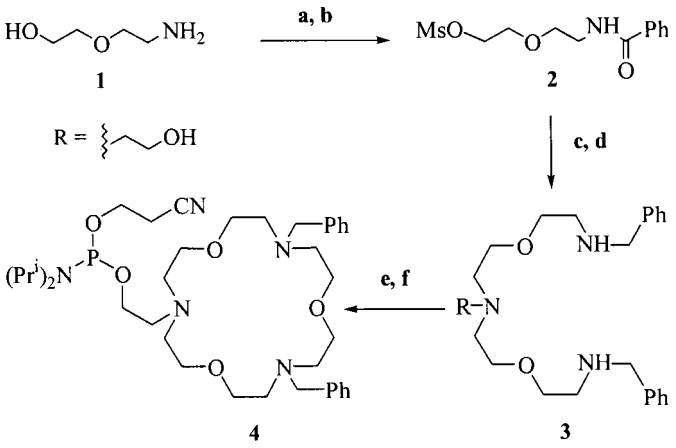

Scheme 1. a) $(PhCO)_2O$, EtOH, reflux, 90%; b) MsCl, pyridine, 80%; c) RNH_2, NEt_3, MeCN, 70%; d) $LiAlH_4$, THF, 90%; e) $TsO(CH_2)_2O(CH_2)_2OTs$, Na_2CO_3, MeCN, 50%; f) $NC(CH_2)_2OP(Cl)N(^iPr)_2$, $(^iPr)_2NEt$, CH_2Cl_2, 50%.

We here report synthesis of an appropriately modified triaza crown ether compatible with automated synthesis using the phosphoramidite approach. Commercially available **1** was treated with benzoic anhydride and subsequently mesylated to give building block **2**. Treatment of **2** with 2-aminoethanol afforded a diamide. Reduction of the diamide led to the triamine **3** suitable for subsequent macrocyclization reaction.[3] Accordingly, treatment of the triamine **3** with diethylene glycol ditosylate led to a macrocycle which was subsequently converted into the phosphoramidite **4** (Sch. 1).

Compound **4** was successfully incorporated (monomer **X**) into two complementary 9-mer sequences [5′-d(**X**CGT ATA GTG) and 3′-d(**XG**$^{\mathbf{Me}}$**C**$^{\mathbf{L}}$**A T**$^{\mathbf{L}}$**AT**$^{\mathbf{L}}$ CAC, $^{\mathbf{Me}}$**C**$^{\mathbf{L}}$ and **T**$^{\mathbf{L}}$ are LNA monomers). Data on the complexation behaviour with amines and T_m values will be reported in due course.

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