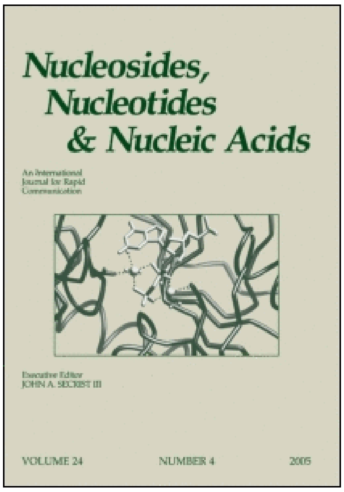

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New 3'-3' Linkers for Alternate Strand Triplex Forming Oligonucleotides

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NEW 3'-3' LINKERS FOR ALTERNATE STRAND TRIPLEX FORMING OLIGONUCLEOTIDES

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ABSTRACT. New solid supports, functionalized with suitably protected 1,2,3-propanetriol and *cis,cis*-1,3,5-cyclohexanetriol, were efficiently prepared and used in the standard automated synthesis of 3'-3' linked ODNs for triplex formation experiments.

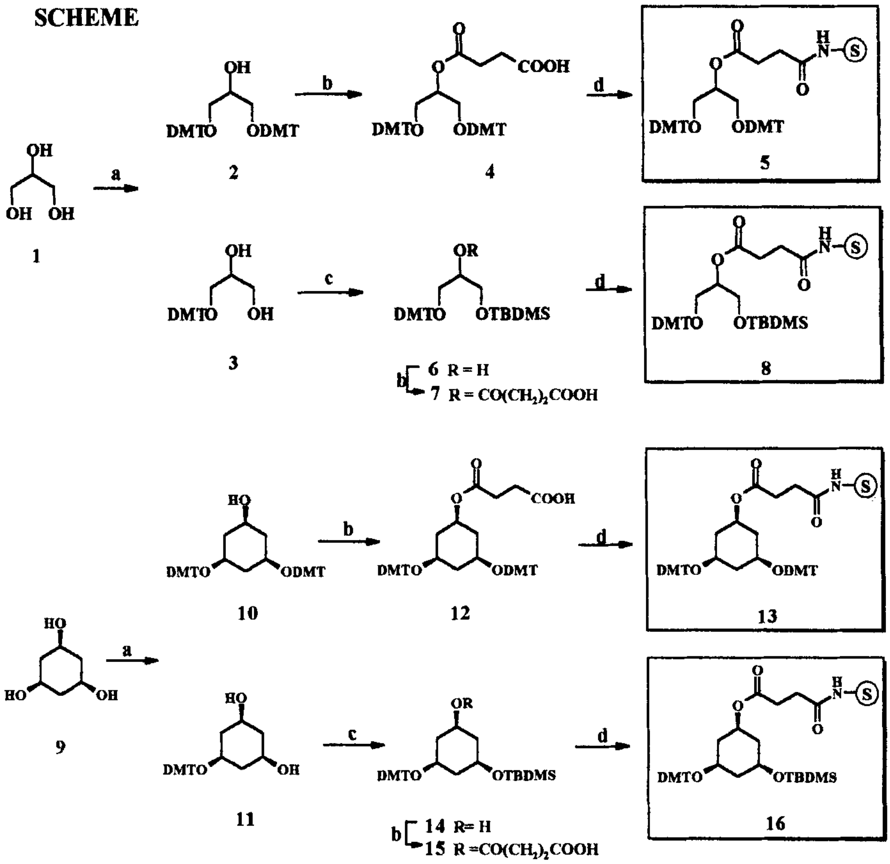
In an effort to design modified ODNs as *antigene agents*[1] able to sequence specifically recognize double stranded DNA fragments of the type $(\text{purine})_m(\text{pyrimidine})_n$, several groups have explored the *alternate strand approach*[2]. This strategy is based on the use of synthetic oligonucleotides simultaneously hybridizing contiguous purine tracts on alternate strands of the target DNA by switching strand at the junction oligopurine-oligopyrimidine of the duplex. In the Hoogsteen triplets recognition mode, a 3'-3' or 5'-5' internucleoside junction has to be introduced in the third strand to allow the required parallel polarity between the two 3'-5' domains of the triple helix forming oligonucleotide (TFO) and the purine tract of the duplex. To covalently connect the two 3'- or 5'-termini of the TFO many linkers have been reported in the literature[2]. We recently[3] studied the potential as alternate strand TFOs of ODNs containing a 3'-3' phosphodiester junction, synthesized by means of a modified Tentagel support linking the first nucleotide through the base.

We here report an easy and convenient synthetic approach to prepare 3'-3' linked ODNs containing a glycerine or a *cis,cis*-1,3,5-cyclohexanetriol unit replacing a nucleoside residue at the 3'-3' inversion site. For the incorporation in the Tentagel support, 1,2,3-propanetriol and 1,3,5-cyclohexanetriol had to be suitably functionalized and protected

(Scheme). Supports **5**, **8**, **13** and **16** were efficiently prepared and used in the synthesis of several sequences following standard automated phosphoramidite methods.

UV thermal denaturation analysis, CD, NMR and molecular mechanics calculations are actually underway to further investigate the behaviour of such triplexes.

SCHEME



a) DMTCl / pyridine; b) succinic anhydride / pyridine; c) TBDMSCl / imidazole / DMF; d) Tentagel resin / DCCI / CH_2Cl_2.

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