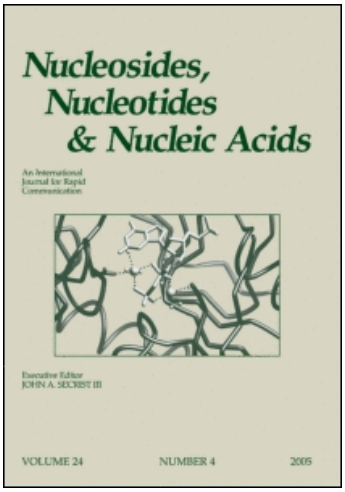

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Glycerol-Furcated Oligonucleotides: Synthesis and Aggregation

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To cite this Article Rosemeyer, H. , Feiling, E. , Nierling, Wolfgang and Seela, F.(1999) 'Glycerol-Furcated Oligonucleotides: Synthesis and Aggregation', Nucleosides, Nucleotides and Nucleic Acids, 18: 6, 1563 — 1564
To link to this Article: DOI: 10.1080/07328319908044784
URL: http://dx.doi.org/10.1080/07328319908044784

NUCLEOSIDES & NUCLEOTIDES, 18(6&7), 1563-1564 (1999)

GLYCEROL-FURCATED OLIGONUCLEOTIDES: SYNTHESIS AND AGGREGATION

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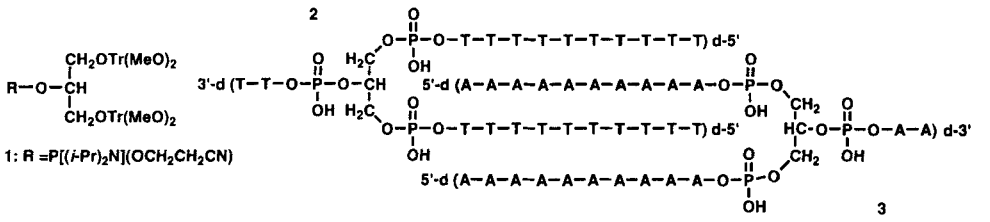
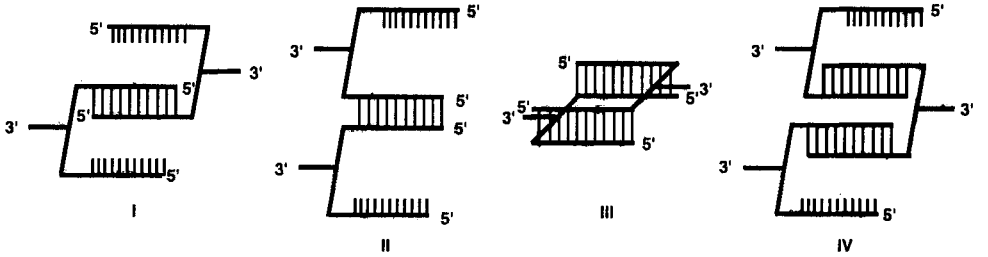
ABSTRACT: The synthesis of the bi-furcated complementary oligonucleotides **2** and **3** is described and their complex formation is studied as a function of their molar ratio and ionic strength by means of temperature-dependent UV- and CD spectroscopy as well as by dynamic light scattering. Structural proposals for the different aggregates are given.

The role of branched RNA's as intermediates of RNA splicing [1] has initiated the synthesis of branched oligonucleotides which have found application as poly-labelled DNA probes [2]. We report on the bi-furcated oligomers **2** and **3** with glycerol as a flexible ramification point. They were prepared by solid-phase synthesis applying the phosphoramidite **1**. Their composition was confirmed by MALDI-TOF mass spectrometry.



Temperature-dependent UV- and CD measurements of an equimolar mixture of **2** and **3** (3 μM, each, 10 mM Na-cacodylate, 10 mM $MgCl_2$, 100 mM NaCl, pH 7) showed a duplex formation with a T_m value of 36°C and a thermal hypochromicity (H, 5-80°C) of 30 % which is similar to the data of $d(A_{10})•d(T_{10})$ [3]. The CD spectra resemble those of homomeric oligo(dA)•oligo(dT). From concentration-dependent T_m measurements as well as from fitting of individual melting curves to a two-state model the thermodynam-

ics of duplex formation ($\Delta H° = -78$ kcal/mol, $\Delta S° = -225$ cal/K mol) were evaluated. Also these data correspond to calculated values of $d(A_{10})•d(T_{10})$ [4]. This imlies the formation of either aggregate I or II and disclosure of structure III. A 2:1 mixture (**2**: 4 μM; **3**: 2 μM) exhibits a similar T_m value as a 1:1 mixture (37°C) making structure IV unlikely.



Enhancement of the $MgCl_2$ concentration to 110 mM raises the T_m value of both, the 2:1- (**2**: 6 μM; **3**: 3 μM; $T_m = 49°C$) and the 1:1 mixture of the oligomers (**2**, **3**: 3 μM, each, $T_m = 47°C$). Cooling a 2:1 mixture of **2•3** below ≈ 40°C results in a reversible precipitation of a fluffy oligonucleotide material which does neither happen in the case of equimolar mixtures nor at low Mg^{2+} ion concentrations. Dynamic light scattering (FIG.) on a 2:1 mixture (**2**: 6 μM; **3**: 3 μM) shows that down to 49°C an ideal solution with a diffusion coefficient, $D_{app.,z}(q,c)$, of 4.5 μm^2/sec exists. Between the T_m (49°C) and 44°C the light scattering intensity increases drastically indicating the formation of large but still soluble particals. Below 44°C the precipitation of a condensed DNA phase occurs (Ψ-DNA) [5].

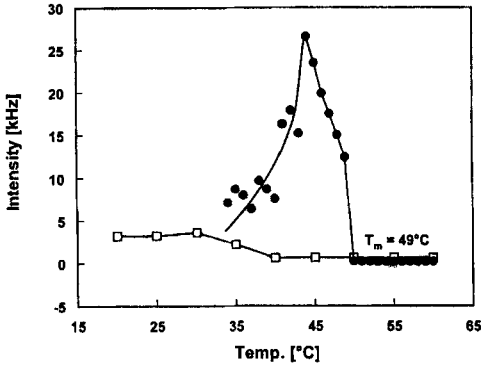


FIG. Dynamic light scattering of **2** (6 μM) + **3** (3 μM) (•••) as well as of an equimolar mixture (3 μM, each, □□□).

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