Ag⁺-Mediated DNA Base Pairing: Extraordinarily Stable Pyrrolo-dC–Pyrrolo-dC Pairs Binding Two Silver Ions

Hui Mei,†‡ Ingo Röhl,§ and Frank Seela,*†‡

1Laboratory of Bioorganic Chemistry and Chemical Biology, Center for Nanotechnology, Heisenbergstraße 11, 48149 Münster, Germany
2Laboratorium für Organische und Bioorganische Chemie, Institut für Chemie neuer Materialien, Universität Osnabrück, Barbarastraße 7, 49069 Osnabrück, Germany
3Axolabs GmbH, Fritz-Hornschuch-Straße 9, 95326 Kulmbach, Germany

Supporting Information

ABSTRACT: 6-Substituted pyrrolo-dC–pyrrolo-dC mismatches selectively capture silver ions to form extraordinarily stable metal-mediated base pairs. One single modification in a 12-mer duplex causes a ΔT_m increase of 36.0 °C relative to the metal-free mismatched duplex. Spectrophotometric titrations as well as ESI mass spectra confirmed the binding of two silver ions per base pair. The Ag⁺-mediated base pairs may permit the construction of metal-responsive DNA with a very high silver loading.

Metal-mediated base pairs represent a high-tech alternative to Watson–Crick base pairing stabilized by hydrogen bonds. Already in 1952 Katz reported on binding of HgCl₂ to DNA,1a and Eichhorn later performed detailed investigations.1b Likewise, Lee observed that other divalent metal ions such as Zn²⁺ interact with duplex DNA.2 Our laboratory utilized modified 6-aza-uridine as a nucleobase substitute to shift Zn²⁺ binding and duplex stabilization to neutral pH.3 Interactions of silver ions with DNA have been studied extensively by UV–vis and CD spectroscopy and potentiometric titrations.4 Recently, metal ions have been utilized for homo-base-pair formation by conversion of base-pair mismatches into metal-coordinated matching pairs. Accordingly, the groups of Marzilli and Ono transformed the dT–dT mismatch into a stable metal base pair in the presence of Hg²⁺ ions (Figure 1).5 In a similar way, a dC–dC mismatch was converted into a metal base pair using Ag⁺ ions.6 Artificial metal base pairs have been constructed with chelating heterocycles.7,8 For some metal base pairs, replication by the polymerase chain reaction has been demonstrated.9

6-Methylpyrrolo-dC (mePyrdC, 1) can serve as fluorescent substitute for dC as it possesses the same Watson–Crick binding face as the canonical nucleoside. It has been widely used to explore the structure and dynamics of nucleic acids.10,11 Recently, it was demonstrated that a 1–dG base pair stabilizes the DNA duplex structure, and Ag⁺-mediated base pairing between 1 and dC has been used for Ag⁺ sensing.12 Hence, we envisioned that Ag⁺-mediated homo base pairs of mePyrdC might be exceptionally stable, considering that this base pair might bind two silver ions. Further stabilization was expected by functionalization of the pyrrole skeleton. Herein we report on various pyrrolo-dC derivatives such as 1, 6-(2-pyridyl)-pyrrolo-dC (PyPyrdC, 2), and 6-(1-benzyl-1H-1,2,3-triazolyl)-pyrrolo-dC (triazPyrdC, 3) as components of duplex DNA (Figure 1) and the formation of extraordinarily stable Ag⁺-mediated homoe base pairs stabilized by two silver ions.

While compounds 1 and 3 have already been described in the literature,10c compound 2 was synthesized as depicted in Scheme 1. Sonogashira cross-coupling of 4 to give 6 has been reported previously.13 Next, the 4,4’-dimethoxypyrityl group was introduced at the S‘-position and the amino group was blocked with a benzoyl residue, resulting in intermediate 8. Intramolecular cyclization (Cul and Et₃N) resulted in the formation of 5.2,7

Received: May 21, 2013
Published: August 21, 2013
of the pyrrole system, affording nucleoside 9. Compound 9 was either deprotected to give nucleoside 2 or treated with 2-cyanoethyl-N,N-diisopropylphosphoramidochloridite to yield phosphoramidite 10. Phosphoramidite 11 is commercially available, while phosphoramidite 12 was described earlier by our laboratory. All of the compounds were characterized by 1H, 13C, 1H-1H correlations were observed when PyrdC homo base pairs were paired with dG (ΔTm = +15.0 °C) or ed PyrdC derivatives showed similar cant contribution to the stabilization of DNA duplexes, and Table S2 in the SI). For duplexes in which dG was located opposite to the PyrdC derivatives 1–3, the addition of Ag+ ions had no effect on the duplex stability, and thus, formation of metal base pairs can be excluded. On the contrary, duplexes containing PyrdC–dC pairs were stabilized by silver ions. Already the addition of 1 equiv of AgNO3 caused a notable increase in duplex stability (ΔTm = +6.5 to +9.0 °C). Increasing the amount of Ag+ to 2 equiv did not lead to further changes (Table S2 in the SI).

Next, duplexes with PyrdC–PyrdC homo base pairs were studied. The addition of 1 equiv of silver ions induced biphatic melting for duplexes incorporating 1 (ODN-4-ODN-5) or 3 (ODN-8-ODN-9), while an overlap of the two transitions occurred with 2 (ODN-6-ODN-7). Two species coexisted: duplexes without silver ions (lower Tm) and duplexes binding two silver ions (higher Tm) (Table 1). When 2 equiv of Ag+ was added, only the high Tm values were observed (monophatic melting). The most significant Tm increase (ΔTm = +36.0 °C) was observed for the duplex ODN-8-ODN-9 incorporating a tris-PyrdC−tris-PyrdC base pair, representing an unique example of duplex stabilization by a Ag+-mediated base-pair complex. Such a Tm increase (ΔTm = +40.0 °C) was previously observed for a copper ion–salen base pair,7a 7b CD spectra of the duplexes containing PyrdC–PyrdC homo base pairs confirmed the formation of B-type DNA (Figure S19 in the SI).

Then, the stoichiometry of the Ag+-mediated PyrdC–PyrdC base pairs was determined. UV absorption curves were measured as functions of the AgNO3 concentration. Titration of the duplexes ODN-8-ODN-9 (Figure 3a and Figure S5 in the SI) and ODN-6-ODN-7 (Figure S4a,b in the SI) with Ag+ led to significant UV–vis spectral changes. In both cases, three
Table 1. \(T_m\) Values for PyrdC (1–3)-Modified DNA Duplexes in the Presence or Absence of Silver Ions \(^a\)

<table>
<thead>
<tr>
<th>duplex</th>
<th>(T_m) (°C) with n equiv of Ag(^+)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 0)</td>
</tr>
<tr>
<td>5′-d(TAG GT(C) AAT ACT) ODN-1</td>
<td>46.5</td>
</tr>
<tr>
<td>3′-d(CTC CA(G) TTA TGA) ODN-2</td>
<td>26.0</td>
</tr>
<tr>
<td>5′-d(TAG GT(C) AAT ACT) ODN-3</td>
<td>27.5</td>
</tr>
<tr>
<td>3′-d(CTC CA(G) TTA TGA) ODN-4</td>
<td>42.0</td>
</tr>
<tr>
<td>5′-d(TAG GT(G) AAT ACT) ODN-5</td>
<td>33.0</td>
</tr>
</tbody>
</table>

\(^a\)Measured at 260 nm at a heating rate of 1.0 °C/min with single-strand concentrations of 5 \(\mu\)M in buffer [100 mM NaOAc, 10 mM Mg(OAc)\(_2\), pH 7.4] in the presence of various concentrations of AgNO\(_3\) (0–2.0 equiv). \(T_m\) values were calculated from the cooling curves. \(\Delta T_m = (T_m \text{ with } 2 \text{ equiv of Ag\(^+\)}) - (T_m \text{ without Ag\(^+\})\). Biphasic melting.

Figure 3. (a) Spectrophotometric titration of 5 \(\mu\)M ODN-8-ODN-9 with increasing Ag\(^+\) concentration in buffer [100 mM NaOAc, 10 mM Mg(OAc)\(_2\), pH 7.4]. (b) Determinations of the silver/duplex ratio at different wavelengths.

Three silver ions cannot be excluded (Figure S8 in the SI). Possibly because of the low \(T_m\) value of ODN-4-ODN-5 (Table 1), the mass of its Ag\(^+\) complex was not detectable.

Other metal ions were analyzed and showed almost no effect on the duplex stability (Table S3 in the SI). The ability of Ag\(^+\) to bind through the PyrdC–PyrdC mismatches appears to be highly specific and surpasses that of the other tested metal ions.

Only a very few examples of DNA homo-base-pair binding of two silver ions have been described in the literature. In one example reported by Ono, DNA duplexes bearing 5-fluoro-dT mismatches were significantly stabilized by two silver ions at pH 9.0.15 In another context, Hoogsteen base pairs formed by aminobenzimidazole-dT that were slightly stabilized by two silver ions have been described.16 Also, a base pair of 4-thio-dT capturing two silver ions has been reported.17 Our results discussed above indicate that the PyrdC–PyrdC base pairs instantly bind two silver ions in a cooperative manner. It seems that a paucity of silver ions in solution (1 equiv of Ag\(^+\)) leads to the coexistence of two species, one without Ag\(^+\) and the other with two Ag\(^+\), resulting in the observation of biphasic melting (Figure 2).

On the basis of our results, we propose structures of the PyrdC–Ag\(^+\)-PyrdC base pairs (Figure 4, motifs III and IX). We anticipate that the strong binding capability with two silver ions results from the special features of the pyrrolo[2,3-d]pyrimidine moiety, which can form tautomeric structures (motifs I and II) and bind silver ions by salt bridges as well as by metal coordination. Silver ions replace the protons of the pyrrolo[2,3-d]pyrimidine heterocycles and coordinate to the electron pairs of the nearby nitrogens. Similar proximal positioning of silver ions has been reported before18 and is a prerequisite for motif III. Other motifs under participation of heterocyclic substituents are conceivable.

In conclusion, new PyrdC–PyrdC homo base pairs with heteroaromatic 6-substituents that bind Ag\(^+\) ions strongly and specifically in a cooperative way have been designed. These metal-mediated base pairs are among the rare examples where each base pair has the capability to bind two Ag\(^+\) ions. The incorporation of only one \(^{\text{trix}}\)PyrdC–Ag\(^+\)-\(^{\text{trix}}\)PyrdC pair increases the \(T_m\) by 36.0 °C relative to the silver-free mismatched duplex. Further DNA duplex stabilization can be expected when multiple metal-mediated base pairs are
incorporated.19a–e By this means, metal-containing DNA with a very high silver loading (two silver units per base pair) may be constructed.

## EXPERIMENTAL SECTION

**General Methods and Materials.** All of the chemicals and solvents were of laboratory grade as obtained from commercial suppliers and were used without further purification. Thin-layer chromatography (TLC) was performed on TLC aluminum sheets covered with silica gel 60 F254. Flash column chromatography (FC) employed silica gel 60 at 0.4 bar. UV-spectra were recorded on a U-Vis-1 spectrometer. 1H, 13C, and 31P NMR spectra were measured at 300.15 MHz for 1H, 75.48 MHz for 13C, and 121.52 MHz for 31P. The reported δ values are in parts per million relative to MeSi as an internal standard (1H and 13C) or external 85% H3PO4 (31P).

**Molecular Mass Determination by NMR.** The molecular masses of the oligonucleotides were determined by 1H NMR spectroscopy using DEPT-135 and 1H–1H double quantum gated-decoupled spectra.

### EXPERIMENTAL SECTION

**General Methods and Materials.** All of the chemicals and solvents were of laboratory grade as obtained from commercial suppliers and were used without further purification. Thin-layer chromatography (TLC) was performed on TLC aluminum sheets covered with silica gel 60 F254. Flash column chromatography (FC) employed silica gel 60 at 0.4 bar. UV-spectra were recorded on a U-Vis-1 spectrometer. 1H, 13C, and 31P NMR spectra were measured at 300.15 MHz for 1H, 75.48 MHz for 13C, and 121.52 MHz for 31P. The reported δ values are in parts per million relative to MeSi as an internal standard (1H and 13C) or external 85% H3PO4 (31P).

**Molecular Mass Determination by NMR.** The molecular masses of the oligonucleotides were determined by 1H NMR spectroscopy using DEPT-135 and 1H–1H double quantum gated-decoupled spectra.

---

**4-Amino-1-[2-deoxy-β-erythro-pentofuranosyl]-5-(2-pyridylethynyl)pyrimidin-2(1H)-one (7).** Compound 6 (1.36 g, 4.14 mmol) was coevaporated with anhydrous pyridine (2 × 20 mL) before dissolution in anhydrous pyridine (30 mL). Four drops of NaN3-disopropylamide were added. Next, 4,4’-dimethoxytrityl chloride (1.82 g, 5.37 mmol) was added in three portions, and the reaction mixture was stirred at room temperature for 8 h. Finally, MeOH (2 mL) was added, and the mixture was stirred for another 30 min. The reaction mixture was diluted with CH2Cl2 (2 × 80 mL) and extracted with 5% aqueous NaHCO3 solution (100 mL) followed by H2O (80 mL). The organic layer was dried over Na2SO4, and then concentrated. Purification by FC (silica gel, column 15 cm × 3 cm, 20:1-0.05 CH2Cl2/MeOH/Et3N) gave 7 as a light-yellow foam (1.74 g, 67%). TLC (10:1 CH2Cl2/MeOH): Rf = 0.25. UV (MeOH) λmax/nm (ε/mmol L−1 cm−1): 274.5 (15000), 322 (21500). 1H NMR (DMSO-d6, 300 MHz): δ 2.13–2.22 (m, 2H, 2′-H2), 2.27–2.34 (m, 1H, 1′-H), 3.14–3.28 (m, 2H, 5′-H), 3.66 (s, 6H, 2 × OHCH3), 3.97–3.99 (m, 1H, 4′-H), 4.21–4.25 (m, 1H, 3′-H), 5.31 (d, J = 4.2 Hz, 1H, 3′-OH), 6.12 (t, J = 6.6 Hz, 1H, 1′-H), 6.84–6.88 (m, 4H, DMT-H), 7.05 (s, 1H, NH), 7.12–7.42 (m, 1H, DMT-H, pyridyl-H), 7.72–7.78 (m, 1H, pyridyl-H), 7.89 (s, 1H, NH), 8.11 (s, 1H, 6-H), 8.54–8.56 (m, 1H, pyridyl-H). Anal. Calcd for C18H13N2O3C6: C, 70.40; H, 5.42; N, 8.88. Found: C, 70.40; H, 5.42; N, 8.88.

**4-Benzoylamino-1-[2-deoxy-5-0-(4,4’-dimethoxytritylphenylmethyl)-β-erythro-pentofuranosyl]-5-(2-pyridylethynyl)pyrimidin-2(1H)-one (8).** To a solution of 7 (1.37 g, 2.17 mmol) in pyridine (20 mL) was added trimethylsilyl chloride (386 mL, 3.04 mmol) at rt. The mixture was stirred for 20 min and then cooled to 0 °C (ice bath), and benzoyl chloride (303 mL, 2.63 mmol) was added dropwise using a syringe. The ice bath was removed, and the reaction mixture was stirred overnight. Water (5 mL) was added, and the reaction mixture was stirred for another 20 min. Finally, 28% aq. NH4 (1 mL) was added, and the mixture was stirred for another 10 min. The solution was diluted with CH2Cl2 (80 mL) and extracted with 5% aqueous NaHCO3 solution (100 mL) followed by H2O (80 mL). The organic layer was dried over Na2SO4, and then concentrated. Purification by FC (silica gel, column 15 cm × 3 cm, 30:1-0.05 CH2Cl2/MeOH/Et3N) gave 8 as a light-yellow foam (1.74 g, 67%). TLC (10:1 CH2Cl2/MeOH): Rf = 0.25. UV (MeOH) λmax/nm (ε/mmol L−1 cm−1): 236.5 (38900), 310.0 (21100). 1H NMR (DMSO-d6, 300 MHz): δ 2.23 (m, 2H, 5′-H), 2.32–2.34 (m, 2H, 5′-H), 2.66 (s, 6H, 2 × OCH3), 4.04 (m, 1H, 4′-H), 4.28–4.31 (m, 1H, 3′-H), 5.39 (d, J = 4.5 Hz, 1H, 3′-OH), 6.13 (t, J = 6.3 Hz, 1H, 1′-H), 6.84–7.65 (m, 19H, DMT-H, Bz-H, pyridyl-H), 8.32–8.36 (m, 2H, 6-H, pyridyl-H), 8.52 (s, 1H, NH), 8.53 (m, 1H, pyridyl-H). Anal. Calcd for C44H38N4O7: C, 71.92; H, 5.21; N, 7.62. Found: C, 71.78; H, 5.25; N, 7.62.

**6-(2-Pyridyl)-3-[(2-deoxy-5-O-(4,4’-dimethoxytritylmethyl)-β-erythro-pentofuranosyl)pyrrolo[2,3-d]pyrimidin-2(1H)-one (9).** A mixture of compound 8 (594 mg, 0.81 mmol) and CuCl (230 mg, 1.21 mmol) in Et3N (8 mL) and DMF (8 mL) was heated at 60 °C for 24 h. The solvent was evaporated, and the remaining residue was dissolved in CH2Cl2 (80 mL). The organic phase was washed several times with 5% Na2EDTA solution (4 × 100 mL), dried over...
**Table 2. $^{13}$C NMR Chemical Shifts ($\delta$) of Pyrrolo[2,3-d]pyrimidine Derivatives**

<table>
<thead>
<tr>
<th>cmpd</th>
<th>C2b</th>
<th>C2′</th>
<th>C3b</th>
<th>C3′</th>
<th>C4b/C4′</th>
<th>C5</th>
<th>C5′</th>
<th>C6′</th>
<th>C7</th>
<th>C7′</th>
<th>C8′</th>
<th>C8</th>
<th>OCH3</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>153.3</td>
<td>145.8</td>
<td>93.6</td>
<td></td>
<td>163.8</td>
<td>85.6</td>
<td>40.9</td>
<td>70.0</td>
<td>87.5</td>
<td>60.9</td>
<td></td>
<td></td>
<td>81.1</td>
</tr>
<tr>
<td>7</td>
<td>153.2</td>
<td>145.0</td>
<td>93.7</td>
<td></td>
<td>163.8</td>
<td>85.8</td>
<td>40.9</td>
<td>70.6</td>
<td>85.9</td>
<td>63.7</td>
<td></td>
<td></td>
<td>54.9</td>
</tr>
<tr>
<td>8</td>
<td>158.0</td>
<td>149.9</td>
<td>93.5</td>
<td></td>
<td>157.9</td>
<td>86.7</td>
<td></td>
<td>70.2</td>
<td>86.4</td>
<td>63.5</td>
<td></td>
<td></td>
<td>54.9</td>
</tr>
<tr>
<td>9</td>
<td>153.6</td>
<td>137.2</td>
<td>108.7</td>
<td>99.3</td>
<td>148.7</td>
<td>159.4</td>
<td>85.6</td>
<td>69.0</td>
<td>86.7</td>
<td>62.6</td>
<td></td>
<td></td>
<td>54.9</td>
</tr>
<tr>
<td>10</td>
<td>137.3</td>
<td>137.7</td>
<td>108.8</td>
<td>99.7</td>
<td>148.8</td>
<td>159.4</td>
<td>87.1</td>
<td>69.4</td>
<td>87.9</td>
<td>60.9</td>
<td></td>
<td></td>
<td>149.4</td>
</tr>
</tbody>
</table>

Average δ = 153.3, 153.2, 158.0, 153.6, 137.3, 137.7, 108.7, 99.3, 148.7, 159.4, 85.6, 69.0, 87.9, 60.9.

**Notes:**
- Measured in DMSO-d$_6$ at 298 K.
- Tentative.

Na$_2$SO$_4$ filtered, and evaporated to dryness. The residue was purified by FC (silica gel, column 10 cm × 3 cm, 20:1:0.05 CH$_2$Cl$_2$/MeOH/ Et$_3$N), affording compound 9 (275 mg, 54%) as a yellow foam. TLC (10:1 CH$_2$Cl$_2$/MeOH/Et$_3$N): $R_f$ = 0.29. UV (MeOH) $A_{max}$/nm (ε/dm$^3$/mol$^{-1}$·cm$^{-1}$): 235.3 (3300), 273.0 (18400), 369.5 (11300). $^1$H NMR (DMSO-d$_6$, 300 MHz): δ = 2.24 (m, 1H, H-C5), 3.13–3.14 (m, 1H, H-C6), 2.34–3.41 (m, 2H, 5′-H, 3′-H), 3.70–3.71 (m, 2H, 6′-H, 2′-CHO$_3$), 3.69–4.01 (m, 1H, H-C4′), 4.39–4.42 (m, 1H, 1′-H), 5.41 (d, $J$ = 4.8 Hz, 1H, H-C3′), 6.21–6.25 (m, 2H, 1′-H, 5′-H), 6.85–6.91 (m, 4H, DMTr-H), 7.22–7.90 (m, 12H, DMTr-H, pyridyl-H), 8.59–8.60 (m, 1H, pyridyl-H), 8.71 (s, 1H, H-6), 11.79 (s, 1H, NH). Anal. Calcd for C$_{37}$H$_{34}$N$_4$O$_6$: C, 70.46; H, 5.43; N, 8.88. Found: C, 70.29; H, 5.45; N, 8.88.

6-(2-Pyridyl)-2-[2-deoxy-5-O-(4,4′-dimethoxytritylmethyl)-β-D-erythro-pentofuranosyl]pyrrolo[2,3-dipyrimidin-2(3H)-one 3-′(2-Cyanoethyl)-NN′-dissopropyl phosphoramidite (10).

A stirred solution of compound 9 (0.34 g, 0.54 mmol) in anhydrous CH$_2$Cl$_2$ (10 mL) was preflushed with nitrogen and treated with (i-Pr)$_2$NEt (146 µl, 0.86 mmol) followed by 2-cyanoethyl-N,N′-dissopropylphosphoramidochloride (180 µl, 0.81 mmol). The solution was stirred for 35 min at room temperature and then diluted with CH$_2$Cl$_2$ (40 mL) and extracted with 5% aq. NaHCO$_3$ solution (30 mL). The organic layer was dried over Na$_2$SO$_4$ and evaporated to dryness. The residue was purified by FC (silica gel, column 10 cm × 2 cm, 20:1:0.05 CH$_2$Cl$_2$/MeOH/ Et$_3$N), giving 10 (275 mg, 61%) as a light-yellow foam. TLC (25:1:0.05 CH$_2$Cl$_2$/MeOH/Et$_3$N): $R_f$ = 0.26. $^1$H NMR (CDCl$_3$, 300 MHz): 6 = 4.64 (m, 1H, H-C4), 5.01 (d, $J$ = 4.2 Hz, 1H, H-C5), 5.35 (d, $J$ = 4.2 Hz, 1H, H-C6), 5.39 (d, $J$ = 11.5 Hz, 1H, H-C3′), 6.09–6.11 (m, 2H, 1′-H, 5′-H), 6.76–6.80 (m, 4H, DMTr-H), 7.14–7.16 (m, 12H, DMTr-H, pyridyl-H), 8.59–8.60 (m, 1H, pyridyl-H), 8.71 (s, 1H, H-6), 11.79 (s, 1H, NH). Anal. Calcd for C$_{46}$H$_{43}$N$_4$O$_7$: C, 71.4; H, 5.4; N, 8.88. Found: C, 71.2; H, 5.4; N, 8.88.
remove the DMT residues. The detritylated oligomers were purified by reversed-phase HPLC using gradient II: 0–20 min, 0–20% B in A; 20–25 min, 20% B in A; 25–30 min, 20–0% B in A; flow rate = 0.8 mL min⁻¹. The oligomers were desalted on a short column (RP-18, silica gel) using H₂O for elution of the salt, while the oligomers were eluted with 3:2 MeOH/H₂O. The oligonucleotides were lyophilized from a solution, stored at −24 °C. The extinction coefficients ε₅₅₀ (H₂O) of the nucleosides (in dm³ mol⁻¹ cm⁻¹) were: 1,4500 (ODN-1), 107800 (ODN-2), 104300 (ODN-3), 105200 (ODN-4), 101700 (ODN-5), 117900 (ODN-6), 114400 (ODN-7), 121000 (ODN-8), and 117500 (ODN-9). The concentrations of the oligonucleotides were calculated as the sum of the extinction coefficients of the nucleoside constituents.

The extinction coefficients ε₅₅₀ (H₂O) of ODN-1 to ODN-9 were 107800 (ODN-1), 107800 (ODN-2), 104300 (ODN-3), 105200 (ODN-4), 101700 (ODN-5), 117900 (ODN-6), 114400 (ODN-7), 121000 (ODN-8), and 117500 (ODN-9). The concentrations of single-stranded oligonucleotides were determined at 260 nm at 20 °C with corrections for hyperchromicity.

**Electrospray Ionization Mass Spectrometry of Silver—DNA Complexes.** ESI-MS measurements were performed on a quadrupole-time-of-flight mass spectrometer (Q-ToF). The measurement conditions were as follows: end plate offset, −500 V; capillary voltage, 4200 V; desolvation temperature, 180 °C. The resolution based on the full width at half-maximum (fwhm) was at least 28000. For sample preparation, an aqueous solution (v/v) H₂O/MeOH using a T-mixing piece. The resulting total sample ow rate to the ESI source was 100 μL min⁻¹.

**Notes**

We thank Mr. N. Q. Tran for oligonucleotide synthesis, Dr. H. Letzel (Organisch-Chemisches Institut, Universität Münster, Germany) for the measurement of MALDI and ESI mass spectra, Dr. X. Ming for supplying phosphoramidite 12, and Dr. Jens Müller (Institut für Anorganische und Analytische Chemie, Universität Münster, Germany) for the use of his CD spectrometer. We appreciate the continuous support of Dr. P. Leonard and Dr. S. Budow for the preparation of the manuscript. Financial support by ChemBiotech (Münster, Germany) is highly appreciated.

**REFERENCES**


