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SYNTHESIS OF THE AMIDITE REAGENT TO BUILT BIPYRIDINE UNITS INTO DNA BACKBONE

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Abstract – A new amidite reagent (**9**) containing 6,6'-bis(acylamino)-2,2'-bipyridine unit was synthesized in moderate yields by a dependable eight step procedure. The unit should work as a metal ion-directed conformational modulator when it is built into the backbone of synthetic DNAs.

INTRODUCTION

Various functional groups have been chemically attached to biomolecules to create bioconjugates with desired functions.[1] DNA is an attractive material for making functional molecules because of its programmability for molecular recognition, ease of chemical modification, and moderate chemical stability. The development of genome chemistry has made it possible to synthesis a large number of DNA conjugates, which have been applied not only in the area of genomics[2] but also in engineering works,[3] such as in making unique nanostructures.

Recently, functional DNA molecules such as deoxyribozymes,[4] aptamers,[5] and antisense DNAs[6] have been extensively studied. Prescript higher ordered structures are critical for these single stranded-DNAs to express their right function. Therefore, the techniques to control their structures reversibly should be

useful for modulation of the corresponding functions. If the chemical groups that changes their conformation by certain stimuli are built into the backbone of the functional DNAs, we could regulate the functions secondarily by controlled conformational change of the DNAs. The strategy is general in the sense that it targets the conformation rather than each particular function.

Here we present the synthesis of the amidite reagent carrying the ligand, 6,6'-bis(acylamino)-2,2'-bipyridine unit. We can build the ligand into any position in DNA backbone with this amidite reagent using automated DNA synthesizer. This ligand was reported to form square planar complex with Cu(II) or Co(II) to yield cisoid conformation.[7] It means that we could bend the DNA by adding certain metal ions through transoid-cisoid transformation. That is, the unit should work as a metal ion-directed conformation modulator of DNA (Figure 1).

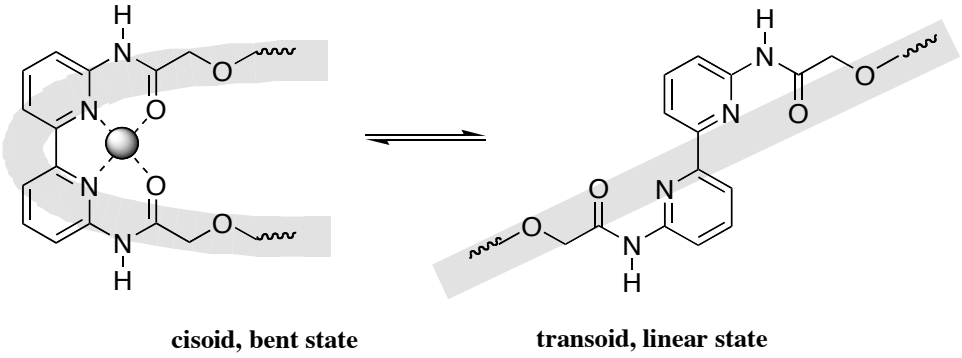
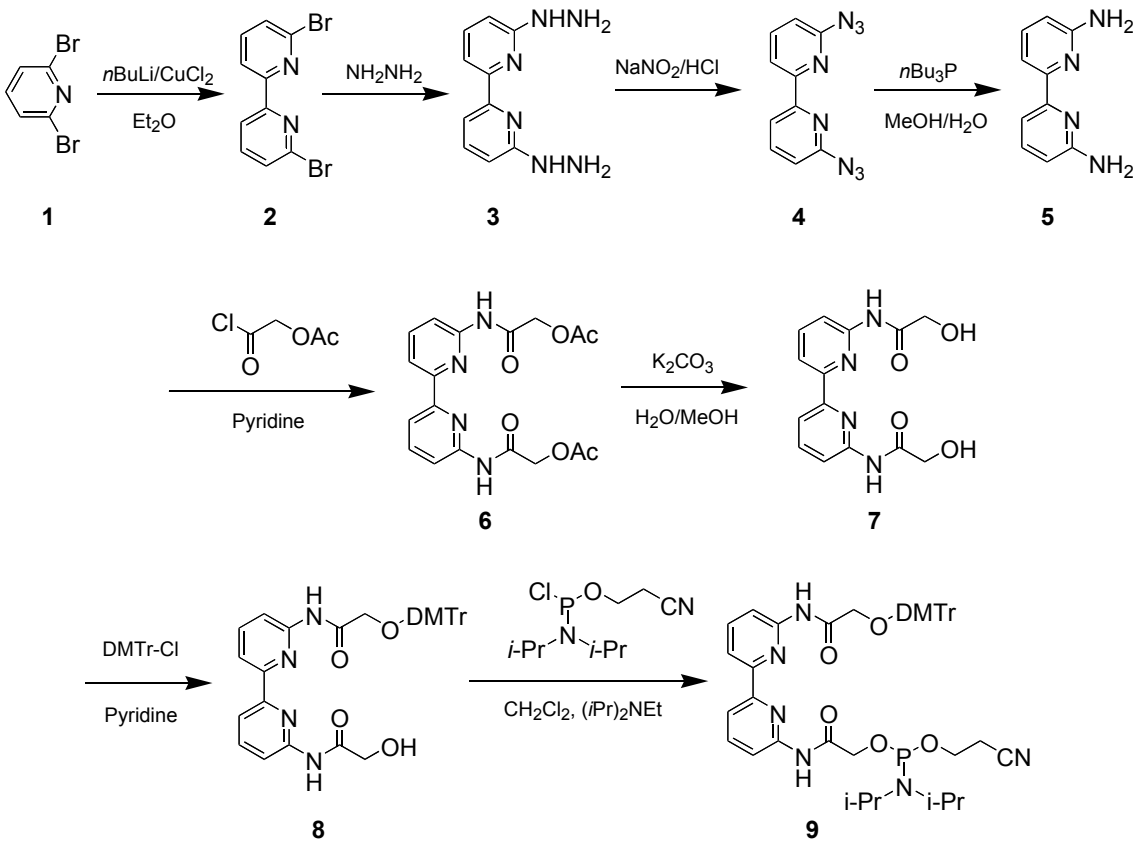


Figure 1. Metal ion-directed conformational modulater of DNA

RESULTS AND DISCUSSION

The 6,6'-bis(acylamino)-2,2'-bipyridine-based amidite reagent was synthesized according to Scheme. Generally a diol is the key compound when one designs the synthetic scheme of an amidite reagent. One of its hydroxyl groups is tritylated by 4,4'-dimethoxytrityl chloride, and then the other is phosphitylated by chloro(diisopropylamino)(β-cyanoethoxy)phosphine to form the desired structure of amidite reagent directly used for an automated DNA synthesizer. Here the bipy diol (**7**) was synthesized as the key compound by acetoxyacetylation of the diaminobipyridine (**5**) and subsequent hydrolysis.

The diaminobipyridine (**5**) was prepared in four steps from 2,6-dibromopyridine (**1**) basically according to the procedures previously described.[8, 9] The intermediates (**2**, **3**, and **4**) were obtained in reasonable yields, 50, 96, and 90 %, respectively. The procedure for the synthesis of **5** from **4** was modified from that of the literature.[9] We used a reductant tri-*n*-butylphosphine in MeOH-H_2O (7:3) instead of phosphonium salt.[10] It improved significantly the yield, up to 83 %, even under the mild conditions (room temperature, 5 h).



Scheme. Synthesis of amidite (**9**)

The diaminobipyridine (**5**) was acylated with acetoxyacetyl chloride in pyridine to afford the diacetate ester (**6**). The compound (**6**) was obtained as a white powder in 79 % yield. It was then hydrolyzed quantitatively in 10 % $K_2CO_{3\,aq}$-MeOH solution to afford the diol (**7**) as a white powder.

Both of the hydroxyl groups in **7** are the primary. They are supposed to have the same reactivity during the tritylation with 4,4'-dimethoxytrityl chloride. Therefore, to obtain the monotritylated alcohol (**8**) in a good yield, the reaction conditions such as feeding ratio of **7** and 4,4'-dimethoxytrityl chloride, reaction time, and temperature were critical. The crude product was chromatographed on a silica gel column with dichloromethane-diethylamine (100:1) to give **8** as a pale yellow powder with no decomposition during the chromatography. The reaction at 60°C for 1 h gave **8** in 56 % yield without significant formation of the bistritylated byproduct even when about more than twice moles of 4,4'-dimethoxytrityl chloride was used. Elongation of the reaction time up to 24 h under the same conditions resulted in a decrease in the yield of **8** and the formation of the bistritylated byproduct only in *ca*. 20 % yield. The reaction rate was rather slower than that expected from the literatures.[11] The characteristics of the reaction show the reaction is more chemoselective for the formation of **8** than the initially expected, owing to some inhibition of the second tritylation. The bipyridyl moiety of the monotritylated product (**8**) is much more basic than the solvent pyridine, because the protonated form is stabilized by making intramolecular

hydrogen bonding with another nitrogen, N-H···N, in its cisoid conformation.[12] Therefore, the hydrogen chloride liberated during the reaction may form a salt preferentially with the bipyridyl moiety of **8**. According to the density functional theoretical method (B3LYP/6-31G(d)), dihedral angles of N-C-C-N in bipyridine center were calculated to be 180° (transoid) and 6.8° (cisoid) for **8** and protonated **8**, respectively. That is, **7** in transoid conformation reacts with a trityl chloride to form **8** and then **8** would flip its conformation to take cisoid form with the assistance of the protonation. The cationic bipyridyl moiety and cisoid conformation of the protonated **8** may prevent the further attack of the reagent $DMTr^+$ by electrostatic repulsion and steric hindrance, respectively.

The amidite (**9**) was prepared by phosphitylation of **8** with chloro(diisopropy1amino)-(β-cyanoethoxy)phosphine. It was obtained as a white powder in 55 % yield. This yield is lower than those of the corresponding reactions in the literatures.[11] The steric hindrance should decrease the rate of phosphitylation. The long reaction time and the low solubility of **8** in the solvent (dichloromethane) would make **9** and chloro(diisopropy1amino)(β-cyanoethoxy)phosphine easy to be degraded by residual water.

The structures of the new compounds (**6** – **9**) obtained in this study were confirmed fully by ^{1}H and ^{13}C NMR, IR spectra, and elemental analyses. Thus, we could prepare the target amidite (**9**) in reasonable yield with a sufficient purity for the use to a DNA synthesizer.

EXPERIMENTAL

Dibromobipyridine (**2**)[8] 2,6-dibromopyridine (**1**) (4.02 g, 17.0 mmol) was suspended in anhydrous ether (20 mL) at -70°C (acetone-dry ice) under an atmosphere of Argon. To the mixture, a hexane solution of *n*-butyllithium (1.6 M, 13 mL, 20.8 mmol) was added slowly *via* an addition funnel to keep the temperature. The suspension gradually dissolved and the color of the solution turned into yellow. Anhydrous copper dichloride (1.14 g, 8.5 mmol) was then added into the solution with vigorous stirring. After 30 min the dry air was infused into the flask, and the mixture was stirred again for 15 min. After the color of the solution turned into green, 20 mL of 6 M hydrochloric acid was added to the solution. The resulting white solid was filtered and washed with 0.5 M hydrochloric acid. The product was used for the next step synthesis without further purification, because NMR study showed the purity more than 99 %.

Yield 2.66 g (50 %); white powder, mp 223-225 °C; ^{1}H NMR ($CDCl_3$), δ 8.36 (2H, d, J = 7.8 Hz, Bipy-3,3'), 7.64 (2H, t, J = 7.8 Hz, Bipy-4,4'), and 7.47 (2H, d, J = 7.8 Hz, Bipy-5,5'); ^{13}C NMR ($CDCl_3$), δ 155.8 (C), 141.8 (C), 139.5 (CH), 128.8 (CH), and 120.3 (CH); IR (KBr) ν 3077, 1573, 1543, 1419, 1376, 1154, 1123, 1072, 985, 785, 707, 625, and 479 cm^{-1}.

Dihydrazinobipyridine (**3**)[9] Dibromobipyridine (**2**) (0.85 g, 2.7 mmol) was suspended in 16 mL (330 mmol) of hydrazine hydrate under an atmosphere of argon. The mixture was heated to dissolve **2** and refluxed for 6 h. After cooling to rt, the resulting yellow solid was collected and washed with small amount of water. The product was used for the next step synthesis without further purification, because NMR study showed the purity more than 99 %.

Yield 0.56 g (96 %); flaky yellow crystal; mp 205-207 °C; ^{1}H NMR (DMSO-d_6), δ 7.4-7.6 (4H, m, Bipy-3,3' and Bipy-4,4'), 6.69 (2H, dd, J = 7.1, 1.8 Hz, Bipy-5,5'), and 4.16 (6H, br s, NH); ^{13}C NMR (DMSO-d_6), δ 161.3 (C) 153.8 (C), 137.6 (CH), 109.6 (CH), and 106.8 (CH); IR (KBr) ν 3326, 3256, 3033, 1582, 1450, 1390, 1305, 1271, 1168, 1002, 985, 90, 736, 634, 606, and 467 cm^{-1}.

Diazidobipyridine (**4**)[9] Dihydrazinobipyridine (**3**) (0.30 g, 1.4 mmol) was suspended in 4 mL of conc. HCl in ice bath under an atmosphere of argon. To the solution, an aqueous solution of $NaNO_2$ (1.58 g, 22.9 mmol in 20 mL of water) was added slowly *via* addition funnel. The suspension gradually dissolved to give a pale yellow clear solution. After the addition was completed, the solution was allowed to warm to rt and stirred for an additional 6 h. The solution was then basified (pH 10-11) with 10 % NaOH and the resulting white precipitate was collected and washed with copious amount of water. The product was used for the next step synthesis without further purification, because NMR study showed the purity more than 99 %.

Yield 0.30 g (90 %); white powder; mp 192-193 °C; ^{1}H NMR (DMSO-d_6), δ 8.52 (2H, dd, J = 1.8, 7.1 Hz, Bipy-3,3') and 8.0-8.2 (4H, m, Bipy-4,4', 5,5'); ^{13}C NMR (DMSO-d_6), δ 117.6 (CH), 120.8 (CH), 127.7 (C), 133.1 (CH), and 148.5 (C); IR (KBr) ν 3452, 3092, 1632, 1562, 1520, 1497, 1417, 1386, 1365, 1344, 1286, 1249, 1183, 164, 1123, 1096, 1038, 1004, 922, 808, 797, 750, 661, 600, 559, and 513 cm^{-1}.

Diaminobipyridine (**5**)[10] Diazidobipyridine (**4**) (0.37 g, 1.6 mmol) was added into 10 mL of mixture of methanol-water (7:3) under an atmosphere of argon. To the suspension, tri-*n*-butylphosphine (1.0 mL, 4.1 mmol) was added, and the solution was stirred for 5 h at room temperature. The solution was concentrated to dryness in vacuo. The oily residue was washed with hexane and chromatographed on a silica gel column with ethyl acetate (R_f 0.4). Recrystallization from ethyl acetate afforded **5** as a yellow crystal.

Yield 0.24 g (83 %); light yellow crystal; mp 182-184 °C; ^{1}H NMR (acetone-d_6), δ 7.62 (2H, d, J = 7.3 Hz, Bipy-3,3'), 7.47 (2H, t, J = 8.3 Hz, Bipy-4,4'), 6.53 (2H, d, J = 7.8 Hz, Bipy-5,5'), and 5.39 (4H, s, NH_2); ^{13}C NMR (acetone-d_6), δ 159.9 (C), 155.7 (C), 138.4 (CH), 110.4 (CH), and 108.9 (CH); IR (KBr) ν 3408, 3298, 3122, 1659, 1615, 1537, 1483, 1452, 1328, and 789 cm^{-1}; *Anal.* Calcd for $C_{10}H_{10}N_4$: C 64.50, H 5.41, N 30.09. Found: C 64.49, H 5.57, N 28.23.

Diacetate ester (**6**) Diaminobipyridine (**5**) (0.42 g, 2.3 mmol) was dissolved in 3 mL of anhydrous pyridine under an atmosphere of Argon. To the solution, acetoxyacetyl chloride (0.75 mL, 6.8 mmol) was added slowly in ice bath and then the solution was stirred for 2 h. The solution was diluted with 10 mL of dichloromethane and washed with water. The organic phase was separated, dried with anhydrous $MgSO_4$, and concentrated to dryness under reduced pressure. The residue was washed with a small amount of chloroform to give a white powder. The product was used for the next step synthesis without further purification, because elemental analysis and NMR study showed the purity more than 99 %.

Yield 0.683 g (79 %); white powder, mp 241-244°C; ^{1}H NMR (DMSO-d_6) 10.70 (2H, s, NH), 8.04 (4H, d, J = 6.8 Hz, Bipy-3,3', Bipy-5,5'), 7.96 (2H, t, J = 6.8 Hz, Bipy-4.4'), 4.79 (4H, s, CH_2), and 2.13 (6H, s, CH_3); ^{13}C NMR (DMSO-d_6) 170.0 (CO), 166.4 (C), 153.3 (C), 150.9 (C), 139.3 (CH), 116.1 (CH), 113.9 (CH), 62.4 (CH_2), and 20.3 (CH_3); IR 3283, 1727, 1697, 1590, 1567, 1539, 1431, 1396, 1373, 1360, 1297, 1281, 1244, 1191, 1149, 1071, 794, 754, and 738 cm^{-1}; *Anal.* Calcd for $C_{18}H_{18}N_4O_6$: C 55.96, H 4.70, N 14.50. Found: C 55.45, H 4.82, N 14.13.

Diol (**7**) Diacetate ester (**6**) (0.77 g, 2.0 mmol) was dissolved in 10 mL of methanol. To the solution, 10 % aqueous solution of K_2CO_3 (10 mL) was added and then the solution was stirred for 2 h at rt. The white precipitate was collected and washed with copious amount of water. The product was used for the next step synthesis without further purification, because elemental analysis and NMR study showed the purity more than 99 %.

Yield 0.582 g (97%); white powder; mp 260-262°C; ^{1}H NMR (DMSO-d_6) 8.10 (2H, d, J = 8.0 Hz, Bipy-5,5'), 8.03 (2H, d, J = 8.0 Hz, Bipy-3,3'), 7.92 (2H, t, J = 8.0 Hz, Bipy-4,4'), and 4.10 (4H, s, CH_2); ^{13}C NMR (DMSO-d_6) 170.8 (CO), 153.2 (C), 150.2 (C), 138.7 (CH), 115.9 (CH), 113.2 (CH), and 61.6 (CH_2); IR (ATR) 3397, 3358, 1666, 1585, 1568, 1529, 1432, 1377, 1326, 1287, 1232, 1203, 1068, 796, 704, and 696 cm^{-1}; *Anal.* Calcd for $C_{14}H_{14}N_4O_4$: C 55.63, H 4.67, N 18.53. Found: C 54.87, H 4.65, N 18.15.

Monotrityl alcohol (**8**)[11] Diol (**7**) (0.40 g, 1.3 mmol) was added into 2 mL of anhydrous pyridine under an atmosphere of Argon. To the suspension, 4,4'-dimethoxytrityl chloride (0.88 g, 2.5 mmol) were added and then the suspension was stirred for 1 h at 60°C. The reaction was quenched by an addition of methanol (1 mL) and triethylamine (0.7 mL, *ca.* 5 mmol). The reaction mixture was diluted with 10 mL of dichloromethane and then washed twice with 5 % aqueous NaOH (100 mL). The organic phase was dried with anhydrous $MgSO_4$ and concentrated in vacuo. The residue was subjected to silica gel column chromatography (dichloromethane : diethylamine = 100 : 1) and the fraction of R_f 0.2 was collected. The

fraction was concentrated to dryness in vacuo and the residue was washed with dichloromethane and ether to give a pale yellow crystal. Recrystallization from propanol afforded **8** as a pale yellow crystal.

Yield 0.45 g (56 %); pale yellow crystal; mp 249-251°C; ^{1}H NMR (DMSO-d_6) δ 9.96 (1H, s, NH), 9.75 (1H, s, NH), 8.14 (1H, d, J = 6.8 Hz, Bipy-3), 7.91-8.05 (5H, m, Bipy), 7.48 (2H, d, J = 7.3 Hz, DMTr), 7.36 (2H, t, J = 7.3 Hz, DMTr), 7.34 (4H, d, J = 8.8 Hz, DMTr), 7.28 (1H, t, J = 7.3 Hz, DMTr), 6.93 (4H, d, J = 8.8 Hz, DMTr), 5.81 (1H, t, J = 5.9 Hz, OH), 4.09 (2H, d, J = 5.9 Hz, CH_2), 3.89 (2H, s, CH_2), and 3.73 (6H, s, OCH_3); ^{13}C NMR (DMSO-d_6) δ 171.4 (CO), 168.1 (CO), 158.2 (C), 153.4 (C), 153.2 (C), 150.7 (C), 150.5 (C), 144.5 (C), 139.5 (CH), 139.4 (CH), 135.1 (C), 129.7 (CH), 128.0 (CH), 127.6 (CH), 126.9 (CH), 116.1 (CH), 116.0 (CH), 113.8 (CH), 113.5 (CH), 113.3 (CH), 86.5 (C), 63.8 (CH_2), 61.6 (CH_2), and 55.0 (CH_3); IR (ATR) ν 3372, 1689, 1608, 1585, 1568, 1512, 1440, 1377, 1341, 1295, 1255, 1178, 1152, 1078, 1035, 993, 829, 803, 771, 727, and 704 cm^{-1}; *Anal.* Calcd for $C_{35}H_{32}N_4O_6$: C 69.52, H 5.33, N 9.27. Found: C 68.72, H 5.60, N 9.12.

Amidite (**9**)[11] Monotrityl alcohol (**8**) (0.20 g, 0.33 mmol) was suspended in 5 mL of anhydrous dichloromethane under an atmosphere of Argon. Additional diisopropylethylamine (0.29 mL, 1.69 mmol) dissolved **8** to give a clear pale yellow solution within 5 min. To the solution, chloro(diisopropylamino)-(β-cyanoethoxy)phosphine (0.19 mL, 0.83 mmol) was added and the solution was stirred for 2 h. Analysis by TLC indicated the presence of a new component and disappearance of **8**. The reaction mixture was diluted with 5 mL of dichloromethane, washed twice with 5 % aqueous $NaHCO_3$ (10 mL), dried with anhydrous $MgSO_4$, and concentrated in vacuo. The residue was purified by chromatography on silica gel (dichloromethane : ethyl acetate : triethylamine = 100 : 50 : 1). The component of R_f 0.9 was collected and concentrated to dryness in vacuo. The residual white powder was dissolved in 3 mL of dichloromethane and poured into a cold hexane at -70°C to precipitate the desired product (**9**) as a colorless powder.

Yield 0.146 g (55 %); white powder; mp 132-134°C, ^{1}H NMR ($CDCl_3$), δ 9.08 (1H, s, NH), 9.05 (1H, s, NH), 8.27 (1H, d, J = 8.3 Hz, Bipy), 8.17 (1H, d, J = 7.3 Hz, Bipy), 8.15 (1H, d, J = 8.3 Hz, Bipy), 8.08 (1H, d, J = 7.3 Hz, Bipy), 7.88 (1H, t, J = 8.3 Hz, Bipy), 7.81 (1H, t, J = 8.3 Hz, Bipy), 7.49 (2H, d, J = 7.3 Hz, DMTr), 7.25-7.39 (7H, m, DMTr), 6.87 (4H, d, J = 8.8 Hz, DMTr), 4.27-4.39 (2H, m, $POCH_2$), 3.90-3.99 (4H, m, $COCH_2$), 3.73-3.83 (8H, m, OCH_3, NCH), 2.70 (2H, dt, J = 1.9, 6.4 Hz, CH_2CN), and 1.29 (12H, dd, J = 6.8, 14.2 Hz, CH_3); ^{13}C NMR ($CDCl_3$) δ 168.6 (CO), 158.9 (C), 153.8 (C), 153.7 (C), 150.0 (C), 143.8 (C), 139.3 (CH), 139.2 (CH), 134.8 (C), 130.0 (CH), 128.2 (CH), 128.0 (CH), 127.3 (CH), 117.3 (CN), 117.1 (CH), 116.9 (CH), 114.1 (CH), 114.2 (CH), 113.5 (CH), 88.0 (C), 64.1 (CH_2), 63.5 (d, $^2J_{CP}$ = 17.0 Hz, CH_2), 58.8 (d, $^2J_{CP}$ = 13.9 Hz, CH_2), 55.3 (OCH_3), 43.6 (d, $^2J_{CP}$ = 12.2 Hz, CH),

24.7 (m, CH_3), and 20.5 (d, $^3J_{CP}$ = 7.3 Hz, CH_2); ^{31}P NMR ($CDCl_3$) □ 151.45; IR (KBr) □ 3392, 2969, 2933, 1699, 1609, 1585, 1570 1518, 1440, 1377, 1297, 1253, 1179, 1078, 1039, 981, 829, and 801 cm^{-1}; *Anal.* Calcd for $C_{44}H_{49}N_6O_7P$: C 65.66, H 6.14, N 10.44. Found: C 64.29, H 5.92, N 10.20.

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REFERENCES

1. G. T. Harmanson, '*Bioconjugate Techniques*', Academic Press, New York, 1996.
2. for example S. Tyagi, *Nat. Biotechnol.,* 1996, **14**, 303; P. Zhang, T. Beck, and W, Tan, *Angew. Chem., Int. Ed.*, 2001, **40**, 402; B. Dubertret, M. Calame, and A. J. Libchaber, *Nat. Biotechnol.*, 2001, **19**, 365; H. K. Kuhn, V. V. Demidov, J. M. Coull, M. J. Fiandaca, B. D. Gildea, and M. D. Frank-Kamenetskii, *J. Am. Chem. Soc.*, 2002, **124**, 1097; T. Ihara, S. Tanaka, Y. Chikaura, and A. Jyo, *Nucleic Acids Res.*, 2004, **32**, e105; T. Ihara, T. Fujii, M. Mukae, Y. Kitamura, and A. Jyo, *J. Am. Chem. Soc.*, 2004, **126**, 8880.
3. for example '*Nanobiotechnology*' (Part III DNA-based Nanostructures), ed. by C. M. Niemeyer and C. A. Mirkin, Wiley-VCH, Weinheim, 2004, pp. 227-342, and refs therein.
4. G. M. Emilsson and R. R. Breaker, *Cell. Mol. Life Sci.*, 2002, **59**, 596; A. Jäschke, *Curr. Opin. Struct. Biol.*, 2001, **11**, 321.
5. M. Rimmele, *ChemBioChem*, 2003, **4**, 963.
6. J. Kurreck, *Eur. J. Biochem.*, 2003, **270**, 1628.
7. K. Araki, T. Kuboki, M. Yamada, and S. Shiraishi, *J. Chem. Soc., Chem. Commun.*, 1992, 1060; J. P. Schneider and J. W. Kelly, *J. Am. Chem. Soc.*, 1995, **117**, 2533.
8. J. E. Parks, B. E. Wagner, and R. H. Holm, *J. Organomet. Chem.*, 1973, **56**, 53; T. Garber and D. P. Rillema, *Syn. Commun.*, 1990, **20**, 1233.
9. J. P. Schneider, R. S. Topgi, and J. W. Kelly, *Syn. Commun.*, 1992, **22**, 1033.
10. L. Horner and A. Gross, *Liebig Ann. Chem.*, 1955, **591**, 117; W. S. Mungall, G. L. Greene, G. A. Heavner, and R. L. Letsinger, *J. Org. Chem.*, 1975, **40**, 1659; M. Vaultier, N. Knouzi, and R. Carrie, *Tetrahedron Lett.*, 1983, **24**, 763; H. Suzuki and K. Takaoka, *Chem. Lett.*, 1984, 1733.

11. Y. Saito, A. Nyilas, and L. A. Agrofoglio, *Carbohydr. Res.*, 2001, **331**, 83; L. M. Easterwood, E. A. Veliz, and P. A. Beal, *J. Am. Chem. Soc.*, 2000, **122**, 11537; A. K. Ogawa, Y. Wu, D. L. McMinn, J. Liu, P. G. Schultz, and F. E. Romesberg, *J. Am. Chem. Soc.*, 2000, **122**, 3274; D. J. Hurley, S. E. Seaman, J. C. Mazura, and Y. Tor, *Org. Lett.*, 2002, **4**, 2305; H. Molrales-Rojas and E. T. Kool, *Org. Lett.*, 2002, **4**, 4377; R. L. Letsinger and T. Wu, *J. Am. Chem. Soc.*, 1995, **117**, 7323.
12. S. T. Howard, *J. Am. Chem. Soc.*, 1996, **118**, 10269.