recrystallization from a hexane/ethanol (1:1 v/v) mixture, afforded 4,4′-difluoro-1,1′-bibicyclo[2.2.2]octane (**6**, X = F) as a white microcrystalline solid (2.3 g, 90.6%): mp 278–280 °C; ^{1}H NMR ($CDCl_3$) δ 1.63 (24 H, s, CH_2CH_2); ^{13}C NMR (see Table IV). Anal. Calcd for $C_{16}H_{24}F_2$: C, 75.59; H, 9.45. Found: C, 75.29; H, 9.84.

Preparation of Some 4-Substituted 4′-Fluoro-1,1′-bibicyclo[2.2.2]octanes as Mixtures (6, X = H, Cl, Br, I, and CH_3). Initially, we set out to prepare 4-iodo-4′-fluoro-1,1′-bicyclo[2.2.2]octane (**6**, X = I) as an appropriate precursor for synthesizing a fairly extensive series of system **6**. However, this goal was thwarted when an attempt to prepare this compound in quantity by treatment of 4-hydroxy-4′-iodo-1,1′-bibicyclo[2.2.2]octane with sulfur tetrafluoride at room temperature in the usual manner afforded the difluoro derivative (**6**, X = F) almost quantitatively. At this stage of our investigation, a cost–benefit analysis led us to restrict our efforts to a more limited range of compounds obtainable as mixtures from the readily available difluoro compound (**6**, X = F).

By use of the procedure of Olah et al.,[51] 4,4′-difluoro-1,1′-bicyclo[2.2.2]octane was treated with ca. 1 equiv of iodotrimethylsilane to afford a mixture containing 4-iodo-4′-fluoro-1,1′-bibicyclo[2.2.2]octane (**6**, X = I; ca. 32%), 4,4′-diiodo-1,1′-bibicyclo[2.2.2]octane (ca. 4%), and unreacted starting material (ca. 64%). Samples of the sublimed mixture were then treated appropriately with Li/*t*-BuOH/THF,[52] ICl,[53] or Br_2[54] to provide mixtures containing the parent system (**6**, X = H), the chloro–fluoro (**6**, X = Cl) and bromo–fluoro (**6**, X = Br) derivatives, respectively. Treatment of the difluoro precursor (**6**, X = F) with a limited quantity of trimethylaluminium as previously described[34b] gave a mixture containing the methyl–fluoro derivative (**6**, X = CH_3), 4,4′-dimethyl-1,1′-bibicyclo[2.2.2]octane, and unreacted starting material. All the aforementioned mixtures were unambiguously characterized by VPC analysis and ^{13}C NMR (Table IV). Spectra assignments for the various compounds were facilitated by the characteristic ^{13}C–^{19}F coupling constants in the bicyclo[2.2.2]octane ring system as well as by the fact that, except for bridgehead positions, additivity of substituent effects on chemical shifts work very well for 1,4-disubstituted bicyclo[2.2.2]octanes. The availability[55] of authentic samples of 1,1′-bibicyclo[2.2.2]octane (mp 234–236 °C; ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 34.06 (C1,1′), 24.75 (C2,2′), 26.18 (C3,3′), 23.79 (C4,4′)) and 4,4′-dimethyl-1,1′-bibicyclo[2.2.2]octane (mp 182–184 °C (lit.[56] mp 184–185 °C); ^{13}C NMR ($CDCl_3$, relative Me_4Si) δ 34.48 (C1,1′), 25.59 (C2,2′), 33.55 (C3,3′), 27.16 (C4,4′), 28.14 (CH_3)) allowed ^{13}C NMR spectra to be calculated for all the appropriately substituted bibicyclo[2.2.2]octanes. These agreed well with all the observed spectra.

Registry No. **5** (X = H), 116263-68-4; **5** (X = Br), 116263-70-8; **5** (X = Cl), 116263-73-1; **5** (X = CH_3), 116263-76-4; **5** (X = NO_2), 116263-86-6; **5** (X = CN), 116263-87-7; **5** (X = COOH), 116263-88-8; **5** (X = $COOCH_3$), 116263-89-9; **5** (X = $COCH_3$), 116263-90-2; **5** (X = CHO), 116263-91-3; **5** (X = CH_2OH), 116263-92-4; **5** (X = COCl), 116263-93-5; **5** (X = OH), 116263-94-6; **5** (X = I), 116263-95-7; **5** (X = NH_2), 116263-96-8; **5** (X = $Sn(CH_3)_3$), 116263-97-9; **5** (X = D), 116278-40-1; **6** (X = F), 116263-80-0; **6** (X = I), 116263-81-1; **6** (X = Cl), 116263-83-3; **6** (X = H), 116263-82-2; **6** (X = CH_3), 116263-84-4; **6** (X = Br), 116263-85-5; 9-acetoxytriptycene, 97733-14-7; 9-hydroxytriptycene, 73597-16-7; 9,10-dibromoanthracene, 523-27-3; 9,10-dibromotriptycene, 795-42-6; 9-bromo-10-hydroxytriptycene, 116263-69-5; 9-bromo-10-chloroanthracene, 22273-72-9; 9-bromo-10-chlorotriptycene, 116263-71-9; 9-chloro-10-hydroxytriptycene, 116263-72-0; 9-methyl-10-methoxyanthracene, 21992-33-6; 9-methyl-10-methoxytriptycene, 116263-74-2; 9-hydroxy-10-methyltriptycene, 116263-75-3; 1-acetyl-4-methoxybicyclo[2.2.2]octane, 116263-77-5; 4-methoxybicyclo[2.2.2]octane-1-carboxylic acid, 773-34-2; 1-acetoxy-4-methoxybicyclo[2.2.2]octane, 116263-78-6; 1,4-diiodobicyclo[2.2.2]octane, 10364-05-3; 1-iodo-4-methoxybicyclo[2.2.2]octane, 74467-18-8; 1-acetoxy-4-iodobicyclo[2.2.2]octane, 74467-16-6; 4-iodobicyclo[2.2.2]octan-1-ol, 74467-17-7; 4,4′-dimethoxy-1,1′-bibicyclo[2.2.2]octane, 74467-39-3; 4-hydroxy-4′-iodo-1,1′-bibicyclo[2.2.2]octane, 74467-40-6; 4,4′-diacetoxy-1,1′-bibicyclo[2.2.2]octane, 116278-39-8; 4,4′-dihydroxy-1,1′-bibicyclo[2.2.2]octane, 116263-79-7.

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Conformational Transmission in Nucleotides Containing Trigonal Bipyramidal Phosphorus as the Internucleoside Linkage

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A set of nucleotide analogues containing a stable trigonal bipyramidal phosphorus (P^V TBP) moiety (**5**–**11**) has been developed, and their conformational properties were studied with 300- and 500-MHz ^{1}H NMR. In the solvent acetone-d_6, it is found that the conformation of the model compounds is determined by a hydrogen bond between the backbone atom $O_{5'}$ and the base proton H_6 (pyrimidine base) or H_8 (purine base), resulting in a preference for the standard gauche(+) conformation around the $C_{4'}$–$C_{5'}$ bond. In the hydrogen bond disrupting solvent DMSO-d_6, the P^V TBP nucleotides **5**–**8** clearly show conformational transmission, i.e., a preference for the unusual gauche(−) (g^-) rotamer around the $C_{4'}$–$C_{5'}$ bond is found. This structural distortion opposes stacking of the bases, as is confirmed by the observation that the preference for g^- is strongest for **7** and **8**, in which stacking is eliminated. The present results provide support to our earlier proposition that formation of P^V TBP locations in DNA can lead to a marked change of the secondary structure (Buck, H. M. *Recl. Trav. Chim. Pays-Bas* **1980**, *99*, 181).

In the past years we developed and firmly established a concept for conformational transmission in a variety of trigonal bipyramidal phosphorus (P^V TBP) compounds.[1] It was shown that the construction of specific ligands

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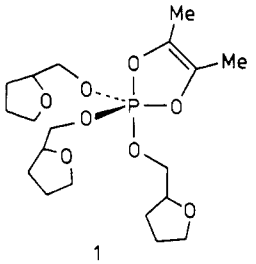
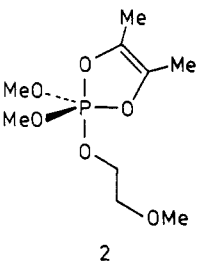
Chart I

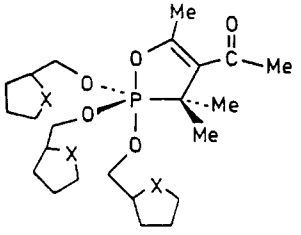


1

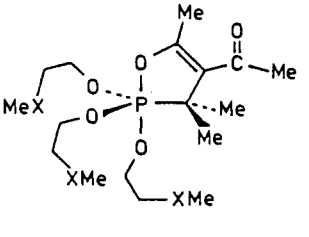


2

directly linked to phosphorus as P^V–O–C–C–O(R) makes it possible to select a different conformational behavior around the C–C linkage for equatorial or axial position in the TBP. Compounds **1** and **2** are typical model compounds used to study the conformational transmission effect in our previous work (Chart I). A pronounced trans orientation of both oxygens is found for the axial sites, whereas the well-known gauche arrangement has an equatorial preference.[2] The introduction of the concept of conformational transmission is based on the observation that in the corresponding P^{IV} tetrahedral compounds (P^{IV}–O–C–C–O(R)) the gauche arrangement of both oxygens is unique, whereas after introduction of an extra (similar) ligand the P^V TBP with its (chemically) different sites selects the conformational change from gauche to trans via exchange of axial and equatorial positions respectively. The addition of an extra ligand which is reflected in the intrinsic chemical-bonding properties of a P^V TBP configuration[3] results in an enhanced electron density on the axial oxygens directly linked to phosphorus. In its turn this effect is transmitted in a conformational change around the C–C linkage via an increased Coulombic repulsion between both oxygens leading to a trans orientation. Very recently, de Keijzer et al. investigated the impact of conformational transmission on the rate of intramolecular ligand exchange in P^V TBP model systems (pseudorotation).[4] With variable-temperature ^{13}C NMR on the monocyclic P^V TBP compounds **3a,b** and **4a,b** it



3a: X = O
3b: X = $C(H_2)$

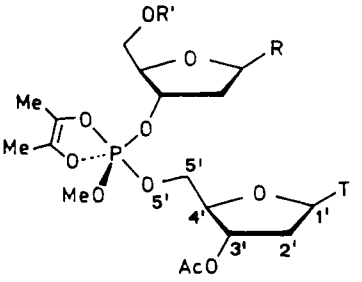


4a: X = O
4b: X = $C(H_2)$

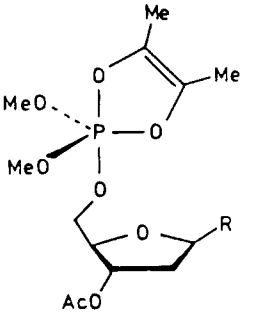
was established that pseudorotation in **3a** and **4a** is 2–4 times faster than in **3b** and **4b**. With the acceptance of the intermediacy of a square pyramid in controlling the pseudorotation, it could be shown that conformational transmission in the basal ligands in the square pyramid is responsible for lowering of the activation barrier for pseudorotation by 2–3 kJ/mol. In previous publications,[1] we have regularly emphasized that the concept of conformational transmission might be of significance in activating phosphorylated biomolecules. A straightforward example has been given by Meulendijks et al.[1c,5] in their studies on conformational transmission in model systems for phospholipids. For monomeric phospholipid models in solution, it was found that going from P^{IV} toward P^V TBP results in a structural change in the glyceryl fragment leading to stronger van der Waals interaction between the two acyl chains.[1c] Precise conclusions could be drawn for a set of phospholipid analogues in the solid state, which have been studied with cross polarization MAS ^{13}C NMR. It was observed that conformational transmission results in a more downfield ^{13}C chemical shift for the ω-methyl groups and a reduced cross polarization optimal contact time, which show that the chain ends are forced into a more proximate position. Based on these results, the suggestion was put forward that conformational transmission might be of importance for controlling ion transport in phospholipid bilayers.[5]

Now we will offer a detailed study of the impact of P^V TBP locations in the backbone of nucleotides for conformational transmission on the level of single-strand phosphate-methylated DNAs in various solvents. The P^V TBP nucleotides **5–11** (Chart II) were chosen as representative model systems. The selection of phosphate-methylated DNAs is necessary to guarantee stable P^V TBPs. The presentation of the results will be discussed with the

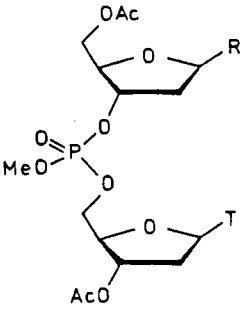
Chart II. P^V Nucleotide Structures Studied in This Work and Their P^{IV} Counterparts



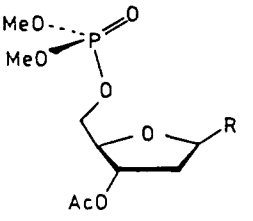
5: R = T, R′ = Ac
6: R = T, R′ = CPh_3
7: R = H, R′ = Ac
8: R = H, R′ = CPh_3



9: R = T
10: R = A
11: R = N^4-acetyl-C



12: R = T
13: R = H



14: R = T
15: R = A
16: R = N^4-acetyl-C

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(2) For **1** in acetone-d_6 at 276 K, it was shown that axial and equatorial locations in the P^V TBP correspond with 68 and 20% O–O trans, respectively. See ref 1a.

(3) See, for instance: (a) Holmes, R. R. *Pentacoordinated Phosphorus*; ACS Monograph 175, 176; American Chemical Society: Washington, DC, 1980; Vol. I, II. (b) Hamerlinck, J. H. H.; Schipper, P.; Buck, H. M. *J. Org. Chem.* **1983**, *48*, 306.

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Table I. Experimental Coupling Constants $J_{4'5'}$ and $J_{4'5''}$ Measured in DMSO-d_6 (Left) or Acetone-d_6 (Right) and the Calculated Time-Averaged Rotamer Populations around the $C_{4'}$–$C_{5'}$ Bond[a]

	DMSO-d_6					acetone-d_6				
compd	$J_{4'5'}$, Hz	$J_{4'5''}$, Hz	$x(g^+)$	$x(g^t)$	$x(g^-)$	$J_{4'5'}$, Hz	$J_{4'5''}$, Hz	$x(g^+)$	$x(g^t)$	$x(g^-)$
5	6.7	6.0	0.20	0.23	0.48	2.4	2.6	0.87	0.13	0.00
6	6.8	5.7	0.22	0.28	0.50	2.5	2.6	0.86	0.14	0.00
7	7.5	5.5	0.19	0.22	0.59	3.0	2.8	0.79	0.15	0.06
8	8.0	5.1	0.19	0.16	0.65	2.9	2.7	0.81	0.14	0.05
9	3.8	3.1	0.70	0.15	0.15	2.4	2.2	0.90	0.10	0.00
10	3.6	4.0	0.61	0.25	0.14	3.0	3.7	0.70	0.24	0.06
11	3.7	3.1	0.70	0.15	0.15	2.4	2.2	0.90	0.10	0.00
12	3.7	3.1	0.71	0.18	0.11	2.8	2.6	0.83	0.13	0.04
13	3.8	3.8	0.63	0.25	0.12	3.0	3.2	0.75	0.19	0.06
14	3.5	3.5	0.68	0.20	0.12	3.0	2.9	0.78	0.16	0.06
15	3.7	3.1	0.70	0.15	0.15	4.4	4.4	0.50	0.27	0.23
16	3.4	3.5	0.68	0.20	0.12	2.9	2.9	0.80	0.14	0.06

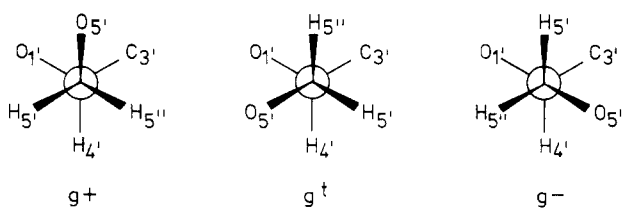
[a] Data refer to the 3'-residue in the case of the nucleotides 5–8 and 12, 13.

different contributions of the bioorganic ligands leading to a relaxed P^V TBP structure.

Methods

Synthesis of 5–16. The model compounds 5–8 (P^V TBP) and 12 and 13 (P^{IV}) were synthesized from the corresponding phosphite triester (P^{III}) nucleotides via reaction with butanedione, and ozone/oxygen, respectively. The precursor P^{III} nucleotides were prepared from 5'-protected thymidine 3'-(methyldiisopropylphosphoramidite) (in the case of 5, 6, and 12), or 5'-protected 1',2'-dideoxyribose 3'-(methyldiisopropylphosphoramidite) (in the case of 7, 8, and 13), in a tetrazole-catalyzed coupling reaction in dry pyridine. Standard column chromatography using Woelm silica gel as the stationary phase and dry butanone as eluent afforded these compounds in the pure form in moderate yields (vide infra). In all cases, ^{31}P NMR clearly confirmed the formation of the P^{III} nucleotides, each of which exists as a mixture of two diastereomers. For 5–8, it was observed that the ^{31}P NMR spectrum consists of a single line. This proves that stereomutation around the P^V TBP is rapid on the NMR time scale.[6] The model compounds 9–11 and 14–16 were prepared by phosphorylation of the corresponding 3'-*O*-acetylated nucleosides with dimethoxy-(*N*,*N*-dimethylamino)phosphine, leading to the 5'-P^{III} precursors. Purification of these compounds was also accomplished with chromatography on a silica gel column with dry butanone as eluent.

Conformational Analysis. The structural aspects of 5–16 were investigated with 300- and 500-MHz ^1H NMR. Conformational analysis was focused on the $C_{4'}$–$C_{5'}$ bonds, as well as on the sugar moieties. $C_{4'}$–$C_{5'}$ conformations are described in terms of a time-averaged distribution over the staggered rotamers gauche(+) (g^+), gauche–trans (g^t), and gauche(–) (g^-). The rotamer populations were calculated



from the experimental proton–proton coupling constants $J_{4'5'}$ and $J_{4'5''}$ with the help of the empirically generalized Karplus equation of Altona et al.[7] The conformation of the sugar rings in nucleotides is generally treated as a two-state equilibrium between a $C_{2'}$-endo and a $C_{3'}$-endo type puckered ring form.[8] In principle, five vicinal proton–proton coupling constants are available to monitor the sugar conformation ($J_{1'2'}$, $J_{1'2''}$, $J_{2'3'}$, $J_{2''3'}$, and $J_{3'4'}$). In various cases, however, it proved impossible to determine accurate values for $J_{2'3'}$, $J_{2''3'}$, and/or $J_{3'4'}$, due to one of the following reasons: (i) collapse of $H_{2'}$ and $H_{2''}$ in the NMR spectra; (ii) overlap of the $H_{2'}$ or $H_{2''}$ spectral pattern with the residual signal of the solvent DMSO-d_6; (iii) overlap of $H_{4'}$ and the $H_{5'}/H_{5''}$ spectral pattern. In order to arrive at a uniform treatment for all model compounds, we used the formula $x(C_{2'}\text{-endo}) = (J_{1'2'} + J_{1'2''} - 9.8)/5.9$, as developed by Rinkel et al.[9] This method allows one to estimate the conformational equilibrium of the sugar ring in DNA nucleotides with a fair accuracy, on the basis of $J_{1'2'}$ and $J_{1'2''}$ exclusively. For the nucleotides 5, 6, and 12, the assignment of the $H_{1'}$ patterns to the upper and lower residue was performed with homonuclear decoupling experiments, based on the fact that the connectivity sequence phosphorus–H_3–$H_{2'/2''}$–$H_{1'}$ only exists for the upper residue.

Results and Discussion

The solvents acetone-d_6 and DMSO-d_6 have been chosen to study the conformational aspects of the model systems 5–16. Acetone-d_6 was found to be an unsuitable solvent to study conformational transmission, since hydrogen bonding between the backbone atom $O_{5'}$ and H_6 of thymidine or cytosine, or H_8 of adenine, strongly fixes the $C_{4'}$–$C_{5'}$ conformation in the g^+ rotamer (Figure 1).[10] The formation of the $O_{5'}$–base hydrogen bond was perfectly prevented in DMSO-d_6, which enabled us to establish the impact of conformational transmission on the molecular structure of our model systems in an unequivocal way.

Conformation of 5–16 in DMSO-d_6. Table I (left) summarizes the experimental coupling constants $J_{4'5'}$ and $J_{4'5''}$ and the calculated rotamer distributions around the $C_{4'}$–$C_{5'}$ bond for 5–16 in the solvent DMSO-d_6. Inspection

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(8) Saenger, W. *Principles of Nucleic Acid Structure*; Springer: New York, 1984.

(9) (a) Rinkel, L. J. Thesis, State University of Leiden, 1987. (b) Rinkel, L. J.; Altona, C. *J. Biomol. Struct. Dyn.* **1987**, *4*, 939.

(10) It is well-known that the $C_{4'}$–$C_{5'}$ conformation in nucleotides is determined in part by hydrogen bonding between $O_{5'}$ and the base proton H_6 (pyrimidine) or H_8 (purine). See: (a) Yathindra, N.; Sundaralingam, M. *Biochemistry* **1973**, *12*, 297. (b) Rubin, J.; Brennan, T.; Sundaralingam, M. *Biochemistry* **1972**, *11*, 3112. (c) Sundaralingam, M. *Structure and Conformation of Nucleic Acids and Protein–Nucleic Acids Interactions*; Sundaralingam, M., Rao, T., Eds.; University Park: Baltimore, 1975; p 487. (d) Amidon, G. L.; Anik, S.; Rubin, J. *Ibid.* pp 729–744. (e) Taylor, R.; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 5063.

Table II. Experimental Coupling Constants $J_{1'2'}$ and $J_{1'2''}$ Measured in DMSO-d_6 (Left) or Acetone-d_6 (Right) and the Calculated Population of the $C_{2'}$-Endo Puckered Form of the 2'-Deoxyribose Ring

	DMSO-d_6			acetone-d_6		
compd	$J_{1'2'}$, Hz	$J_{1'2''}$, Hz	$x(C_{2'}$-endo)	$J_{1'2'}$, Hz	$J_{1'2''}$, Hz	$x(C_{2'}$-endo)
5 5'-residue	7.0	6.8	0.68	6.9	6.9	0.68
5 3'-residue	7.9	7.5	0.95	7.4	7.0	0.78
6 5'-residue	7.0	6.7	0.66	6.7	6.5	0.58
6 3'-residue	8.0	7.5	0.97	7.6	7.1	0.83
7 3'-residue	7.8	7.6	0.95	7.7	7.1	0.85
8 3'-residue	7.9	7.4	0.93	7.5	7.3	0.85
9	7.9	7.0	0.86	8.0	7.4	0.95
10	7.7	7.2	0.86	7.7	7.0	0.83
11	7.9	7.1	0.88	8.0	7.4	0.95
12 5'-residue	7.0	6.9	0.70	7.0	6.8	0.68
12 3'-residue	7.2	7.0	0.75	7.7	7.2	0.86
13 3'-residue	7.2	7.0	0.75	7.4	7.4	0.85
14	7.6	7.0	0.81	7.5	7.0	0.80
15	7.4	6.9	0.76	7.6	7.0	0.81
16	7.5	7.0	0.80	7.5	7.0	0.80

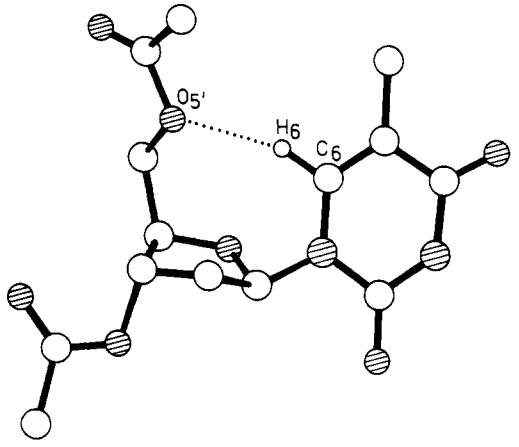
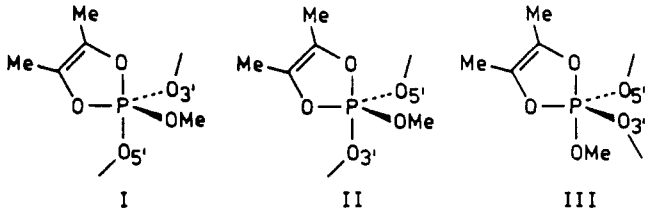


Figure 1. Part of the X-ray crystal structure of 3',5'-di-*O*-acetylthymidine,[18] in which the g^+ conformation is stabilized via hydrogen bonding between $O_{5'}$ and H_6. Hetero atoms (O, N) are shaded, and hydrogen atoms have been omitted for clarity.

of these data shows that the P^V TBP nucleotides **5**–**8** have dominant populations of g^-, which corresponds with trans orientation of $O_{5'}$ and $O_{1'}$ (vide supra); $x(g^-)$ varies form 0.48 to 0.65 for **5**–**8**. The P^{IV} structures **12** and **13**, on the other hand, display a clear preference for the well-known g^+ conformation, in which $O_{5'}$ is gauche with respect to $O_{1'}$ ($x(g^+)$ = 0.71 and 0.63 for **12** and **13**, respectively). The occurrence of conformational transmission in **5**–**8** implies that $O_{5'}$ is preferentially located in the axis of the P^V TBP, i.e., structure I ($O_{5'}$ axial, $O_{3'}$ equatorial) prevails over the



two possible alternatives, II ($O_{3'}$ axial, $O_{5'}$ equatorial) and III ($O_{3'}$ and $O_{5'}$ equatorial). The preference of I over II correlates with quantum chemical model calculations by van Lier et al.[11] which showed that $O_{5'}$ axial, $O_{3'}$ equatorial is approximately 8 kJ/mol more stable than $O_{3'}$ axial, $O_{5'}$ equatorial. From Dreiding molecular models, it seems clear that III is unfavorable with respect to I and II (no quantum chemical calculations have been performed). These results provide strong support for our original proposition[12] that formation of P^V TBP in the DNA backbone can substantially perturb the DNA secondary structure via a rotation around the $C_{4'}$–$C_{5'}$ linkage from g^+ toward g^-. The P^V TBP systems **7** and **8**, in which base stacking is eliminated since the 5'-base is replaced by hydrogen, are of further interest. Comparison with **5** and **6** reveals that the preference for g^- is most pronounced in the absence of stacking (**7** and **8**; $x(g^-)$ = 0.59 and 0.65, respectively; **5** and **6**, $x(g^-)$ = 0.48 and 0.50, respectively), i.e., conformational transmission opposes the regular stacking of adjacent bases.

The data on the P^V TBP nucleotides **9**–**11** show that a high preference exists for the g^+ conformation (Table I). The explanation for the absence of conformational transmission in these systems rests on the fact that $O_{5'}$ is preferentially located in an equatorial position in the TBP.[13] The similarity of the $C_{4'}$–$C_{5'}$ rotamer populations of **9**–**11** and the P^{IV} counterparts **14**–**16** is in line with our earlier work, in which a close resemblance was found for 5'-tetrahydrofurfuryl, and tetrahydrofurfuryl in an equatorial location in a P^V TBP.[1a] It must be concluded that the 5'-P^V TBP nucleotides **9**–**11** are in fact inadequate models to study conformational transmission in DNA structures.

The conformational data on the sugar rings in **5**–**16** are summarized in Table II (left). These data clearly show a preference for the $C_{2'}$-endo puckered form of the ring. Conformational transmission upon going from P^{IV} (**12**, **13**) toward P^V TBP (**5**–**8**) results in a slight increase of $x(C_{2'}$-endo) for the 3'-residue. The apparent preference for the conformational combination g^- ($C_{4'}$–$C_{5'}$ bond) and $C_{2'}$-endo (sugar ring) corresponds with the conclusion of Remin[14] that a $g^-/C_{3'}$-endo conformation is highly unfavorable.

Conformation of 5–16 in Acetone-d_6. The experimental coupling constants $J_{4'5'}$ and $J_{4'5''}$ measured in acetone-d_6, as well as the calculated rotamer populations of g^+, g^t, and g^-, are listed in Table I (right). Inspection of these data shows that none of the P^V TBP systems display conformational transmission. In fact, it appears that increasing the phosphorus coordination from P^{IV} to P^V TBP results in a slight *increase* of the g^+ rotamer populations. For example, it is found for the P^V TBP systems **5**–**8** in acetone-d_6 that $x(g^+)$ ranges from 0.85 to 0.91, while $x(g^+)$

(11) van Lier, J. J. C.; Koole, L. H.; Buck, H. M. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 148.

(12) Buck, H. M. *Recl. Trav. Chim. Pays-Bas* **1980**, *99*, 181.

(13) A single bulky substituent on a P^V TBP structure prefers an equatorial location. See, for instance: Luckenbach, R. *Dynamic Stereochemistry of Pentacoordinated Phosphorus and Related Elements*; Georg Thieme Verlag: Stuttgart, 1973.

(14) Remin, M. *J. Biomol. Struct. Dyn.* **1984**, *2*, 211.

= 0.70 and 0.72 for the P^{IV} counterparts **12** and **13**, respectively. These data suggest that conformational transmission is prevented by the formation of a hydrogen bond between $O_{5'}$ and H_6 of thymine (vide supra). The extreme situation represents the 5′-P^V TBP compound **9** with $x(g^+) = 0.90$. The data in Table II (right) show that the conformational equilibria of the sugar rings in **5–16** in acetone-d_6 are heavily biased toward the $C_{2'}$-endo form.

Concluding Remarks

The results obtained with the model compounds **5–11** illustrate several novel and revealing aspects of conformational transmission in nucleotide structures. First, it is clear that the solvent is of importance in determining whether or not conformational transmission will occur. Apparently, it is a prerequisite for conformational transmission that a hydrogen bond disrupting solvent such as DMSO is used.[15] Otherwise, the $C_{4'}$–$C_{5'}$ conformation is determined by an $O_{5'}$–base hydrogen bond, leading to an exclusive preference for the g^+ conformation. Secondly, it follows from a comparison of the data on **5**, **6**, and **12** with those of **7**, **8**, and **13** that conformational transmission opposes stacking of adjacent bases.

The present results provide support to our earlier suggestion that conformational changes in natural DNA can also be achieved by activation of the backbone phosphates via a P^{IV} into P^V TBP transition.[1a,b,12] Two points must be made in extrapolating the present data to conformational transitions in natural DNA: (i) The P^V TBP compounds **5–11** are neutral species, whereas the transient P^V TBP system formed in natural DNA has two negatively charged oxygens bound to phosphorus. Quantum chemical calculations performed by van Lier et al.,[11] and more recently by de Keijzer et al.,[4] have shown that conformational transmission occurs in both charged and neutral P^V TBPs. These data strengthen our original point that neutral P^V TBP structures (which are stable enough for experimental studies) can be used as models for unstable transient P^V TBPs as formed in our proposed mechanism for conformational transmission in natural DNA. (ii) The present study refers to DMSO-d_6 or acetone-d_6 as the solvent, whereas natural DNA is usually in an aqueous environment. The instability of the systems **5–11** has precluded direct conformational studies in protic media (e.g., CD_3OD or D_2O). However, since it is known that hydrogen-bonding interactions in aqueous solution are relatively weak due to competition of water molecules for hydrogen-bonding donor and acceptor sites (ref 8, p 126), it must be expected that the conformational transmission effect is also operative in water as the solvent.

Experimental Section

^1H NMR spectra were recorded in the Fourier transform (FT) mode on a Bruker CXP 300 (300 MHz)[16] or a Bruker AM 500 (500 MHz)[17] spectrometer. Tetramethylsilane was used as the internal standard. Appropriate spectral windows (10–15 ppm) were chosen, and Fourier transformation was usually performed with 32K data points. ^{31}P NMR spectra were run in the FT mode on a Bruker HX 90 (36.4 MHz) or on a Bruker AC 200 (80.9 MHz) spectrometer. Woelm silica gel was used for column chromatography. All melting and boiling points are uncorrected.

5′-*O*-Acetylthymidine. Acetic anhydride (2.45 g, 24 mmol) was added over 30 min to a magnetically stirred solution of thymidine (4.84 g, 20 mmol) in 150 mL of dry pyridine. The reaction mixture was stirred for 3 h, after which the solvent was evaporated under reduced pressure with moderate heating (40 °C). The last traces of pyridine were removed by coevaporation with toluene. Thin-layer chromatography (TLC) of the residual gum, using butanone as eluent, revealed the presence of four different compounds, i.e., 3′,5′-di-*O*-acetylthymidine (R_f 0.51), 3′-*O*-acetylthymidine (R_f 0.37), 5′-*O*-acetylthymidine (R_f 0.17), and unreacted thymidine ($R_f \approx 0$). Repeated column chromatography afforded 5′-*O*-acetylthymidine as a white solid in 28% yield (1.60 g): mp 134–137 °C; ^1H NMR (acetone-d_6) δ 1.87 (3 H, s, 6-Me), 2.12 (3 H, s, Ac), 2.34–2.42 (2 H, m, $H_{2'/2''}$), 4.02–4.12 (2 H, m, $H_{5'/5''}$), 4.19 (1 H, m, $H_{4'}$), 5.32 (1 H, m, $H_{3'}$), 6.33 (1 H, dd, $H_{1'}$), 7.66 (1 H, s, H_6). Anal. Calcd for $C_{12}H_{16}O_6N_2$: C, 50.70; H, 5.63; N, 9.86. Found: C, 50.5; H, 5.8; N, 10.1.

3′-*O*-((*N*,*N*-Diisopropylamino)methoxyphosphino)-5′-*O*-acetylthymidine. 5′-*O*-Acetylthymidine (1.42 g, 5 mmol) was added with stirring to a mixture of 100 mL of dry chloroform and 10 mL of dry diisopropylethylamine. After the addition, the reaction flask was thoroughly flushed with argon and sealed with a rubber septum. After the mixture was stirred for 2 h, dropwise addition of chloro(*N*,*N*-diisopropylamino)methoxyphosphine (1.03 g, 5.2 mmol) was started. The resulting yellow solution was stirred for 2 h and diluted with 250 mL of ethyl acetate (prewashed with $NaHCO_3$). Repeated washing with 100-mL portions of a saturated NaCl solution in water, and finally with pure water, drying on Na_2SO_4, and evaporation of all volatile material afforded a yellowish oil, which was transferred to a silica gel column. Elution with a mixture of *n*-hexane/dichloromethane/triethylamine (45:45:10, v/v/v) yielded an oily product with R_f 0.34. Coevaporation with dry dichloromethane yielded the desired product as a slightly colored foam (1.52 g, 68%): mp 106–109 °C; ^1H NMR (acetone-d_6) δ 0.90–1.25 (12 H, m, Me diisopropyl), 1.58 (3 H, s, 6-Me), 2.12 (3 H, s, Ac), 2.52–2.56 (2 H, m, $H_{2'/2''}$), 3.38 (3 H, d, POMe, J = 11 Hz), 3.96–4.09 (2 H, m, $H_{5'/5''}$), 4.24 (1 H, m, $H_{4'}$), 4.80 (1 H, m, $H_{3'}$), 6.44 (1 H, dd, $H_{1'}$), 7.68 (1 H, s, H_6); ^{31}P NMR (acetone-d_6) δ 154.8 and 154.1 (ratio 1:0.91). Anal. Calcd for $C_{19}H_{32}N_3PO_7$: C, 51.23; H, 7.19; N, 9.44. Found: C, 50.7; H, 7.2; N, 9.7.

5′-*O*-(3′-*O*-Acetylthymidyl) 3′-*O*-(5′-*O*-Acetylthymidyl) Methyl Phosphite. 3′-*O*-Acetylthymidine (0.80 g, 2.46 mmol) and 3′-*O*-((*N*,*N*-diisopropylamino)methoxyphosphino)-5′-*O*-acetylthymidine (0.94 g, 2.11 mmol) were dissolved with stirring in 15 mL of dry pyridine. 1*H*-Tetrazole (0.24 g, 3.2 mmol) was added, and the reaction mixture was stirred for 4 h. Thorough evaporation of the pyridine afforded a yellow syrup, which was transferred to a 10-cm-long silica gel column. Elution with butanone yielded a slightly colored foam (R_f 0.32). ^{31}P NMR indicated the presence of two diastereomers with δ 145.8 and 145.2 (acetone-d_6): ^1H NMR (acetone-d_6) δ 1.53 and 1.58 (2 × 3 H, s, Me base), 1.95 and 2.00 (2 × 3 H, s, Ac), 2.08–2.35 (4 H, m, $H_{2'/2''}$), 3.32 (3 H, d, OMe, J = 11 Hz), 3.36–3.52 (4 H, m, $H_{5'/5''}$), 4.06 and 4.16 (2 × 1 H, m, $H_{4'}$), 4.56 and 4.71 (2 × 1 H, m, $H_{3'}$), 6.35 and 6.42 (2 × 1 H, dd, $H_{1'}$), 7.58 and 7.62 (2 × 1 H, s, H_6). Anal. Calcd for $C_{25}H_{33}N_4PO_{13}$: C, 52.08; H, 5.73; N, 9.72. Found: C, 51.9; H, 5.6; N, 9.6.

2-(3′-*O*-(5′-*O*-Acetylthymidyl))-2-(5′-*O*-(3′-*O*-acetylthymidyl))-2-methoxy-4,5-dimethyl-1,3,2λ^5-dioxaphosphole (5). This compound was prepared by the addition of 1 equiv of freshly distilled butanedione to a cooled (0 °C) solution of *5′-O-(3′-O-acetylthymidyl) 3′-O-(5′-O-acetylthymidyl)* methyl phosphite in a 5-mm NMR sample tube. After 30 min, ^{31}P NMR indicated complete conversion of the phosphite into the pentacoordinated phosphorus structure of **5**: ^{31}P NMR (acetone-d_6) δ −48.3 (s); ^1H NMR (acetone-d_6) δ 8.4 (2 H, br s, NH), 7.68 and 7.60 (2 × 1 H, s, H_6), 6.20 (1 H, t, $H_{1'}$ (5′-residue)), 6.12 (1 H, t, $H_{1'}$ (3′-residue)), 5.80 (1 H, m, $H_{3'}$ (3′-residue)), 5.32 (1 H, m, $H_{3'}$ (5′-residue)), 4.23 (2 H, m, $H_{4'}$), 4.18–4.14 (2 H, m, $H_{5'/5''}$ (3′-residue)), 3.75 (3 H, d, OCH_3, J = 12.9 Hz), 3.68 (2 H, m, $H_{5'/5''}$ (5′-residue)), 1.86 (6 H, s, CH_3 dioxaphosphole), 2.42–2.21 (4 H, m, $H_{2'/2''}$), 2.12 and 2.10 (2 × 3 H, s, acetyl), 1.90 and 1.87 (2 × 3 H, s, 5-CH_3).

5′-*O*-(3′-*O*-Acetylthymidyl) 3′-*O*-(5′-*O*-Acetylthymidyl) Methyl Phosphate (12). This compound was prepared by bubbling NO_2 gas through a cooled (0 °C) solution of *5′-O-(3′-O-acetylthymidyl) 3′-O-(5′-O-acetylthymidyl)* methyl phosphite in a 5-mm NMR sample tube. ^{31}P NMR indicated complete

(15) Conformational transmission was also observed with the model compounds **5–8** in the hydrogen bond disrupting solvent $[(CH_3)_2N]_3P{=}O$. See: Normant, H. *Bull. Soc. Chim. Fr.* **1968**, *2*, 791.

(16) NMR facility at the Eindhoven University of Technology.

(17) Dutch National hf 500/200 NMR facility at Nijmegen, The Netherlands.

conversion of the phosphite into **12**: ^{31}P NMR (acetone-d_6) δ 0.2 and 0.8.

2-(3′-*O*-(5′-*O*-Tritylthymidyl))-2-(5′-*O*-(3′-*O*-acetylthymidyl))-2-methoxy-4,5-dimethyl-1,3,2λ^5-dioxaphosphole (6). This compound was prepared by the addition of 1 equiv of freshly distilled butanedione to a cooled (0 °C) solution of *5′-O-(3′-O-acetylthymidyl) 3′-O-(5′-O-tritylthymidyl)* methyl phosphite[18] in a 5-mm NMR sample tube. After 20 min, ^{31}P NMR indicated quantitative conversion of the phosphite into the pentacoordinated phosphorus structure of **6**: ^{31}P NMR (acetone-d_6) δ −50.3 (s); ^{1}H NMR (acetone-d_6) δ 8.2 (2 H, br s, NH), 7.52 and 7.51 (2 × 1 H, s, H_6), 7.92–7.14 (15 H, m, aromatic H), 6.21 (1 H, t, $H_{1'}$ (5′-residue)), 6.16 (1 H, t, $H_{1'}$ (3′-residue)), 5.78 (1 H, m, $H_{3'}$ (3′-residue)), 5.22 (1 H, m, $H_{3'}$ (5′-residue)), 4.20 (2 H, m, $H_{4'}$), 4.17–4.12 (2 H, m, $H_{5'/5''}$ (3′-residue)), 3.72 (3 H, d, OCH_3, J = 12.8 Hz), 3.40 (2 H, m, $H_{5'/5''}$ (5′-residue)), 1.90 (6 H, s, CH_3 dioxaphosphole), 2.28–2.20 (4 H, m, $H_{2'/2''}$), 2.10 (3 H, s, acetyl), 1.88 and 1.84 (2 × 3 H, s, 5-CH_3).

5′-*O*-Acetyl-1′,2′-dideoxyribose. 1′,2′-Dideoxyribose[19] (5.9 g, 50 mmol) was reacted with acetic anhydride (6.1 g, 60 mmol) according to the procedure that was described for 5′-*O*-acetylthymidine (vide supra). Repeated column chromatography using butanone as eluent finally afforded the desired product as a viscous oil with R_f 0.38 in 17% yield (1.38 g). Detection was effected by exposure to iodine vapor: ^{1}H NMR (acetone-d_6) δ 1.58–2.35 (2 H, m, $H_{2'/2''}$), 2.13 (3 H, s, Ac), 3.16–4.30 (6 H, m, $H_{1'/1''}$, $H_{3'}$, $H_{4'}$, $H_{5'/5''}$). Anal. Calcd for $C_7H_{12}O_4$: C, 52.52; H, 7.50. Found: C, 51.8; H, 7.6.

3′-*O*-((*N*,*N*-Diisopropylamino)methoxyphosphino)-5′-*O*-acetyl-1′,2′-dideoxyribose. This compound was synthesized from 5′-*O*-acetyl-1′,2′-dideoxyribose (1.20 g, 7.5 mmol) and chloro-(*N*,*N*-diisopropylamino)methoxyphosphine (1.58 g, 8.0 mmol) according to the procedure that was given for 3′-*O*-((*N*,*N*-diisopropylamino)methoxyphosphino)-5′-*O*-acetylthymidine (vide supra). Purification as described yielded the desired product as a foam, mp 96–101 °C, in 52% yield (0.78 g): ^{1}H NMR (acetone-d_6) δ 1.12 (12 H, m, isopropyl), 1.4–2.4 (2 H, m, $H_{2'/2''}$), 2.10 (3 H, s, Ac), 3.0–4.40 (8 H, m, $H_{1'/1''}$, $H_{3'}$, $H_{4'}$, $H_{5'/5''}$, 2 × isopropyl); ^{31}P NMR (acetone-d_6) δ 154.2 and 153.7 (ratio 1:0.88). Anal. Calcd for $C_{14}H_{28}PNO_5$: C, 52.34; H, 8.72; N, 4.36. Found: C, 51.6; H, 8.4; N, 5.0.

5′-*O*-(3′-*O*-Acetylthymidyl) 3′-*O*-(5′-*O*-Acetyl-1′,2′-dideoxyribosyl) Methyl Phosphite. This compound was prepared in a coupling reaction of 3′-*O*-acetylthymidine (620 mg, 2.2 mmol) and 3′-*O*-((*N*,*N*-diisopropylamino)methoxyphosphino)-5′-*O*-acetyl-1′,2′-dideoxyribose (640 mg, 2 mmol) as described for *5′-O-(3′-O-acetylthymidyl) 3′-O-(5′-O-acetylthymidyl)* methyl phosphite (vide supra). The product was obtained as a colorless glass. ^{31}P NMR indicated the presence of two diastereomers with δ 144.9 and 144.6 (acetone-d_6): yield, 360 mg (36%); ^{31}P NMR (acetone-d_6) δ 145.2 and 144.9. Anal. Calcd for $C_{20}H_{29}N_2PO_{11}$: C, 47.62; H, 5.75; N, 5.56. Found: C, 46.8; H, 5.7; N, 5.9.

2-(3′-*O*-(5′-*O*-Acetyl-1′,2′-dideoxyribosyl))-2-(5′-*O*-(3′-*O*-acetylthymidyl))-2-methoxy-4,5-dimethyl-1,3,2λ^5-dioxaphosphole (7). This compound was prepared by the addition of 1 equiv of freshly distilled butanedione to a cooled (0 °C) solution of 5′-*O*-(3′-*O*-acetylthymidyl) 3′-*O*-(5′-*O*-acetyl-1′,2′-dideoxyribosyl) methyl phosphite in a 5-mm NMR sample tube. After 30 min, ^{31}P NMR proved quantitative conversion into **7**: ^{31}P NMR (acetone-d_6) δ −49.0 (s); ^{1}H NMR (acetone-d_6) δ 8.9 (1 H, br s, NH), 7.60 (1 H, s, H_6), 6.19 (1 H, t, $H_{1'}$ (3′-residue)), 5.80 (1 H, m, $H_{3'}$ (3′-residue)), 5.28 (1 H, m, $H_{3'}$ (5′-residue)), 4.23 (1 H, m, $H_{4'}$ (5′-residue)), 4.18 (1 H, m, $H_{4'}$ (3′-residue)), 4.10–3.92 (2 H, m, $H_{1'}$ (5′-residue)), 3.82 (3 H, d, OCH_3, J = 13.0 Hz), 3.68 (2 H, m, $H_{5'/5''}$ (3′-residue)), 1.82 (6 H, s, CH_3 dioxaphosphole), 2.32–2.22 (4 H, m, $H_{2'/2''}$), 2.13 and 2.05 (2 × 3 H, s, acetyl), 1.87 (3 H, 5-CH_3).

5′-*O*-(3′-*O*-Acetylthymidyl) 3′-*O*-(5′-*O*-Acetyl-1′,2′-dideoxyribosyl) Methyl Phosphate (13). This compound was obtained by bubbling a stream of ozone/oxygen through a cooled (0 °C) solution of 5′-*O*-(3′-*O*-acetylthymidyl) 3′-*O*-(5′-*O*-acetyl-1′,2′-dideoxyribosyl) methyl phosphite in a 5-mm NMR sample tube. ^{31}P NMR indicated complete oxidation of the phosphite after 2 min of reaction time: ^{31}P NMR (acetone-d_6) δ 0.1 and 0.6.

5′-*O*-(3′-*O*-Acetylthymidyl) 3′-*O*-(5′-*O*-Trityl-1′,2′-dideoxyribosyl) Methyl Phosphite. This compound was obtained after a coupling reaction of 3′-*O*-acetylthymidine (1.28 g, 4.5 mmol) and 3′-*O*-((*N*,*N*-diisopropylamino)methoxyphosphino)-5′-*O*-trityl-1′,2′-dideoxyribose (2.00 g, 4.0 mmol) as described for *5′-O-(3′-O-acetylthymidyl) 3′-O-(5′-O-acetylthymidyl)* methyl phosphite (vide supra). The product was obtained as a foam. ^{31}P NMR indicated the presence of two diastereomers with δ 145.9 and 145.0 (acetone-d_6). Yield: 1.04 g (37%).

2-(3′-*O*-(5′-*O*-Trityl-1′,2′-dideoxyribosyl))-2-(5′-*O*-(3′-*O*-acetylthymidyl))-2-methoxy-4,5-dimethyl-1,3,2λ^5-dioxaphosphole (8). This compound was prepared by the addition of 1 equiv of freshly distilled butanedione to a cooled (0 °C) solution of 5′-*O*-(3′-*O*-acetylthymidyl) 3′-*O*-(5′-*O*-trityl-1′,2′-dideoxyribosyl) methyl phosphite in a 5-mm NMR sample tube. After 30 min, ^{31}P NMR proved complete conversion into **8**: ^{31}P NMR (acetone-d_6) δ −50.3 (s); ^{1}H NMR (acetone-d_6) 8.7 (1 H, br s, NH), 7.58 (1 H, s, H_6), 8.12–7.20 (15 H, m, aromatic H), 6.13 (1 H, t, $H_{1'}$ (3′-residue)), 5.72 (1 H, m, $H_{3'}$ (3′-residue)), 5.22 (1 H, m, $H_{3'}$ (5′-residue)), 4.33 (1 H, m, $H_{4'}$ (5′-residue)), 4.22 (1 H, m, $H_{4'}$ (3′-residue)), 3.80 (3 H, d, OCH_3, J = 13.2 Hz), 3.78–3.70 (2 H, m, $H_{1'}$ (5′-residue)), 3.41 (2 H, m, $H_{5'/5''}$ (5′-residue)), 1.81 (6 H, s, dioxaphosphole), 2.41–2.19 (4 H, m, $H_{2'/2''}$), 2.15 (3 H, s, acetyl), 1.88 (3 H, s, 5-CH_3).

3′-*O*-Acetylthymidine 5′-(Dimethyl phosphite). A solution of dimethoxy(*N*,*N*-dimethylamino)phosphine (14.9 mmol, 1.95 g) in 25 mL of dry 1,4-dioxane was added dropwise to a stirred and heated (80 °C) solution of 3′-*O*-acetylthymidine (2.00 g, 7.1 mmol) and tetrazole (250 mg) in 50 mL of dry 1,4-dioxane. After 3 h, TLC using butanone as eluent indicated complete conversion into a product with R_f 0.64. The reaction mixture was concentrated in vacuo, and the resulting glass was chromatographed on a silica gel column: yield, 1.6 g, 60%; ^{1}H NMR (acetone-d_6) δ 1.87 (3 H, d, CH_3 base), 2.12 (3 H, s, Ac), 2.34–2.42 (2 H, m, $H_{2'/2''}$), 3.58 (6 H, d, OMe), 4.02–4.14 (2 H, m, $H_{5'/5''}$), 4.19 (1 H, m, $H_{4'}$), 5.32 (1 H, m, $H_{3'}$), 6.33 (1 H, t, $H_{1'}$), 7.66 (1 H, s, H_6); ^{31}P NMR (acetone-d_6) δ 145.1.

2-(3′-*O*-Acetylthymidine)-2,2-dimethoxy-4,5-dimethyl-1,3,2λ^5-dioxaphosphole (9). This compound was prepared by the addition of 1 equiv of freshly distilled butanedione to a cooled (0 °C) solution of 3′-*O*-acetylthymidine 5′-(dimethyl phosphite) in a 5-mm NMR sample tube. After 30 min, ^{31}P NMR indicated complete conversion of the phosphite into the pentacoordinated phosphorus structure of **9**: ^{31}P NMR (acetone-d_6) δ −44.1; ^{1}H NMR (acetone-d_6) δ 8.9 (1 H, br s, NH), 7.68 (1 H, s, H_6), 6.16 (1 H, t, $H_{1'}$), 5.30 (1 H, m, $H_{3'}$), 4.30 (1 H, m, $H_{4'}$), 4.28–3.23 (2 H, m, $H_{5'/5''}$), 3.80 (6 H, d, OCH_3, J = 13.2 Hz), 2.50–2.32 (2 H, m, $H_{2'/2''}$), 1.82 (6 H, s, CH_3 dioxaphosphole), 1.90 (3 H, s, 5-CH_3).

2′-Deoxy-3′-*O*-acetyladenosine 5′-(Dimethyl phosphite). This compound was prepared from dimethoxy(*N*,*N*-dimethylamino)phosphine (0.35 g, 2.6 mmol) and 2′-deoxy-3′-*O*-acetyladenosine (0.5 g, 1.7 mmol) according to the procedure that was described for the preparation of 3′-*O*-acetylthymidine 5′-(dimethyl phosphite). Chromatography on a Woelm silica gel column using dry butanone/triethylamine (95:5 v/v) afforded the product as a yellowish glass (R_f 0.41): yield, 315 mg, 48%; ^{1}H NMR (acetone-d_6) δ 2.11 (3 H, s, Ac), 2.65 (1 H, m, $H_{2''}$), 3.12 (1 H, m, $H_{2'}$), 3.38 (6 H, dd, OMe), 4.10 (2 H, m, $H_{5'/5''}$), 4.30 (1 H, m, $H_{4'}$), 5.52 (1 H, m, $H_{3'}$), 6.54 (1 H, dd, $H_{1'}$), 8.36 (1 H, s, H_2), 8.40 (1 H, s, H_8); ^{31}P NMR (acetone-d_6) δ 145.5.

2-(3′-*O*-Acetyl-2′-deoxyadenosyl)-2,2-dimethoxy-4,5-dimethyl-1,3,2λ^5-dioxaphosphole (10). This compound was prepared from 2′-deoxy-3′-*O*-acetyladenosine 5′-(dimethyl phosphite) and butanedione according to the procedure that was described for the preparation of **9**: ^{31}P NMR (acetone-d_6) δ −46.2; ^{1}H NMR (acetone-d_6) δ 8.2 and 8.1 (2 × 1 H, H_2/H_8), 7.2 (2 H, br s, NH_2), 6.04 (1 H, t, $H_{1'}$), 5.22 (1 H, m, $H_{3'}$), 4.52 (1 H, m, $H_{4'}$), 4.31–3.92 (2 H, m, $H_{5'/5''}$), 3.78 (6 H, d, OCH_3, J = 13.0 Hz), 2.31–2.14 (2 H, m, $H_{2'/2''}$), 1.88 (6 H, s, CH_3 dioxaphosphole).

2-(3′-*O*,*N*^{4}-Diacetyl-2′-deoxycytidyl)-2,2-dimethoxy-4,5-dimethyl-1,3,2λ^5-dioxaphosphole (11). This compound was prepared from 2′-deoxy-3′-*O*,*N*^{4}-diacetylcytidine 5′-(dimethyl phosphite) and butanedione according to the procedure that was

(18) The synthesis of this phosphite was described previously. See: Koole, L. H.; van Genderen, M. H. P.; Buck, H. M. *J. Am. Chem. Soc.* **1987**, *109*, 3916.

(19) Hoffer, M. *Chem. Ber.* **1960**, *93*, 2777.

described for **9**: ^{31}P NMR (acetone-d_6) δ -45.7; ^{1}H NMR (acetone-d_6) δ 8.0 (1 H, br s, NH), 7.80 (1 H, d, H_6), 6.18 (1 H, dd, $H_{1'}$), 5.83 (1 H, d, H_5), 5.32 (1 H, m, $H_{3'}$), 4.23 (1 H, m, $H_{4'}$), 4.35-4.30 (2 H, m, $H_{5'/5''}$), 3.80 (6 H, d, OCH_3, J = 13.0 Hz), 2.41-2.28 (2 H, m, $H_{2'/2''}$), 1.90 (6 H, s, CH_3 dioxaphosphole).

3'-*O*-Acetylthymidine 5'-(Dimethyl phosphate) (14). An ozone/oxygen stream was passed through a cooled (0 °C) solution of 500 mg of 3'-*O*-acetylthymidine 5'-(dimethyl phosphite) in 10 mL of anhydrous dichloromethane. After 20 min, TLC using butanone as eluent indicated complete conversion of the phosphite into **14** (R_f 0.30): ^{31}P NMR (acetone-d_6) δ 6.9; ^{1}H NMR (acetone-d_6) δ 8.8 (1 H, br s, NH), 8.15 (1 H, s, H_6), 6.23 (1 H, dd, $H_{1'}$), 5.32 (1 H, m, $H_{3'}$), 4.32 (1 H, m, $H_{4'}$), 4.18-4.06 (2 H, m, $H_{5'/5''}$), 3.85 (6 H, d, OCH_3, J = 11.3 Hz), 2.41-2.30 (2 H, m, $H_{2'/2''}$), 2.05 (3 H, s, acetyl), 1.87 (3 H, s, 5-CH_3).

2'-Deoxy-3'-*O*-acetyladenosine 5'-(Dimethyl phosphate) (15). This compound was prepared from 2'-deoxy-3'-*O*-acetyladenosine 5'-(dimethyl phosphite) according to the procedure that was given for **14**. The product was obtained as a colorless glass (R_f 0.14, eluent butanone/triethylamine, 95:5 v/v): ^{31}P NMR (acetone-d_6) δ 6.7; ^{1}H NMR (acetone-d_6) δ 8.3 and 8.25 (2 × 1 H, s, H_2/H_8), 7.04 (2 H, br s, NH), 6.12 (1 H, dd, $H_{1'}$), 5.55 (1 H, m, $H_{3'}$), 4.37 (1 H, m, $H_{4'}$), 4.20-4.07 (2 H, m, $H_{5'/5''}$), 3.78 (6 H, d, OCH_3, J = 11.2 Hz), 2.38-2.27 (2 H, m, $H_{2'/2''}$), 2.18 (3 H, s, acetyl).

2'-Deoxy-3'-*O*,*N*^{4}-diacetylcytidine 5'-(Dimethyl phosphite). This compound was synthesized from dimethoxy(*N*,*N*-dimethylamino)phosphine (0.51 g, 3.8 mmol) and 2'-deoxy-3'-*O*,*N*^{4}-diacetylcytidine (0.6 g, 1.9 mmol) by following the procedure that was described for 3'-*O*-acetylthymidine 5'-(dimethyl phosphite). Chromatography on a Woelm silica gel column using dry butanones as eluent yielded the product as a colorless glass (R_f 0.46): yield, 420 mg (55%).

2'-Deoxy-3'-*O*,*N*^{4}-diacetylcytidine 5'-(Dimethyl phosphate) (16). This compound was prepared from 2'-deoxy-3'-*O*,*N*^{4}-diacetylcytidine 5'-(dimethyl phosphite), according to the procedure that was given for **14**. This product was isolated as a slightly colored glass (R_f 0.12; eluent butanone): ^{31}P NMR (acetone-d_6) δ 5.9; ^{1}H NMR (acetone-d_6) δ 8.3 (1 H, br s, NH), 7.75 (1 H, d, H_6), 6.20 (1 H, dd, $H_{1'}$), 5.90 (1 H, d, H_5), 5.42 (1 H, m, $H_{3'}$), 4.38 (1 H, m, $H_{4'}$), 4.19-4.06 (2 H, m, $H_{5'/5''}$), 3.81 (6 H, d, OCH_3, J = 11.3 Hz), 2.41-2.17 (2 H, m, $H_{2'/2''}$).

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Studies on the Conformation of 5,15-Diarylporphyrins with (Arylsulfonyl)oxy Substituents[1]

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Dimeso-substituted octaalkylporphyrins, carrying an (arylsulfonyl)oxy group at the ortho position of the two (meso) phenyl groups, were synthesized from dipyrrolylmethanes and aldehydes. On account of a ^{1}H NMR upfield shift in $CDCl_3$ solution of 2-5 ppm for the aryl protons, a folded conformation is assumed in which the substituted aryl groups lie right above and below the porphyrin plane. In $CDCl_3/CF_3COOH$ solution the upfield shifts are absent. The results of low-temperature ^{1}H NMR measurements and ring-current calculations agreed with our assumptions. The sulfonyloxy group promotes folding of the molecule more than the ester, sulfonyl, sulfinyl, thio, or methylene group. In zinc porphyrins carrying anthraquinone substituents, intramolecular coordination was observed. ΔG, ΔH, and ΔS values for the various conformational equilibria were calculated from the NMR data. We suggest van der Waals interactions with a contribution of charge transfer as the driving force for the folding of the molecule.

The mechanism of the charge separation step in photosynthesis is the subject of continuing investigations, mostly on porphyrins, preferably with well-defined geometries.[2] In the course of our synthetic work in this field we prepared a 5,15-diaryl-2,3,7,8,12,13,17,18-octamethylporphyrin, carrying a tosylate group in the β-position of an ethoxy side chain, attached at the ortho (meso) aryl position, i.e. **6b** (Figure 1). The ^{1}H NMR spectrum of this compound in $CDCl_3$ solution showed an unexpectedly large upfield shift for the aromatic tosylate protons: 2.03 and 3.06 ppm for H2',H6' and H3',H5', respectively, compared to the δ values of a reference compound, the corresponding aldehyde RCHO (**7b**) used in the synthesis (Scheme I). In the following we use $\Delta\delta$ values, defined as δ for a proton in the aldehyde **7**, $-\delta$ for the corresponding proton in the porphyrin **6** (see for numbering of the protons Figure 1).[3] Since upon 10-fold dilution of a solution of **6b** we did not observe a significant change of δ values, we exclude intermolecular association and explain the observed shifts

(1) Part of this work has been described in a preliminary communication: Sanders, G. M.; van Dijk, M.; Koning, G. P.; van Veldhuizen, A.; van der Plas, H. C. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 243, and in Sanders, G. M.; van Dijk, M.; van Veldhuizen, A.; van der Plas, H. C. *J. Chem. Soc., Chem. Commun.* **1986**, 1311.

(2) See for some recent references: Hunter, C. A.; Nafees Meah, M.; Sanders, J. K. M. *J. Chem. Soc., Chem. Commun.* **1988**, 692. Schmidt, J. A.; McIntosh, A. R.; Weedon, A. C.; Bolton, J. R.; Connolly, J. S.; Hurley, J. K.; Wasielewski, M. R. *J. Am. Chem. Soc.* **1988**, *110*, 1733. Sanders, G. M.; van Dijk, M.; van Veldhuizen, A.; van der Plas, H. C. *J. Chem. Soc., Chem. Commun.* **1986**, 1311 and the references cited in these articles.

(3) The use of, e.g., the *p*-(mesoaryl)-substituted isomer of **6a** as reference compound instead of the aldehyde RCHO **7a** did not make a significant difference.

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