ΔH_{12} is not sufficient to pump two protons.[6] This observation contradicts those reports indicating that two protons are pumped per photocycle. However, our results are consistent with those experimental studies that indicate that the number of protons pumped per photocycle is approximately equal to $\sim 0.6/\Phi_1$ (see discussion in refs 5 and 16-19).

In closing, we note that the revised assignments for Φ_1 and Φ_2 affect not only ΔH_{12} but also the value of χ_K (the fraction of the K photoproduct in the photostationary state) and the calculated spectrum of K. Our previous value of χ_K (λ = 500 nm) of 0.46 increases to 0.53 (Table II, ref 6) on the basis of $\Phi_1/\Phi_2 = 0.68$, which is equal within experimental error to the 510-nm value of 0.56 reported in ref 14. A recalculated K spectrum based on our bR spectrum and our K - bR difference spectrum assuming $\Phi_1/\Phi_2 = 0.68$ is nearly identical with that shown in ref 14. This means that our raw spectroscopic data are consistent with those presented in ref 14, and this observation supports the use of our raw spectroscopic data to assign the partition functions that appear in eqs 1-3 as a function of Φ_1 and Φ_2. The fact that our photocalorimetry data are more consistent with a ratio of $\Phi_1/\Phi_2 = 0.45$ versus the revised value of $\Phi_1/\Phi_2 = 0.68$ is reflected in our least-squares regression by a $\sim$1.5-fold percentage increase in the standard deviation for our revised enthalpy (11.6 ± 3.4 (29%) kcal mol^{-1}) relative to the standard deviation associated with our previous assignment (15.9 ± 3.2 (20%) kcal mol^{-1}).

Acknowledgment. This work was supported in part by a grant to R.R.B. from the National Institutes of Health (GM-34548).

Registry No. Hydrogen ion, 12408-02-5.

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New Strategy for the Synthesis of Oligodeoxynucleotides Bearing Adducts at Exocyclic Amino Sites of Purine Nucleosides

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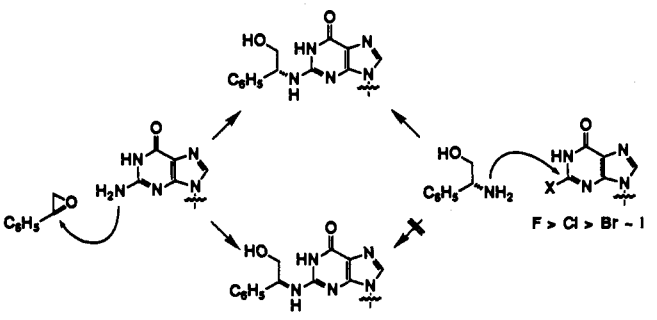
Received November 30, 1990

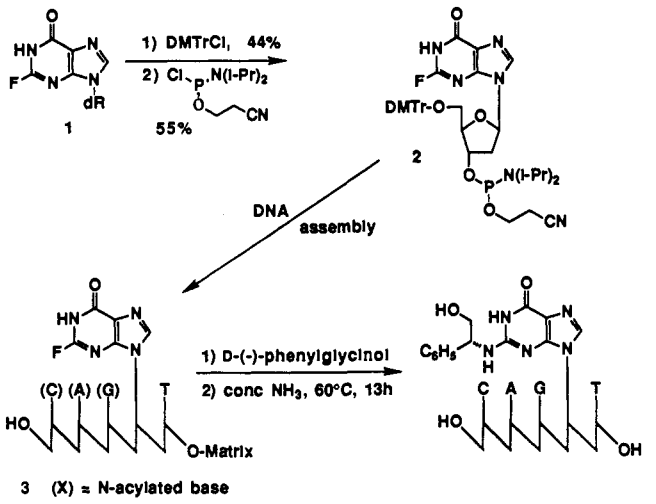
An understanding of the structure and conformation of nucleic acid-mutagen adducts is essential to the elucidation of events involved in chemical carcinogenesis. Conformations can be established by NMR spectroscopy[1] and X-ray crystallography[2] using oligonucleotides containing structurally defined adducts; these oligomers can also be used for site-specific mutagenesis studies.[3] Oligodeoxynucleotides bearing specifically linked carcinogens have been prepared by enzymatic or chemical assembly of the oligomer using an adducted nucleoside,[4] adduction of an oligomer containing only one reactive site,[5] or chromatographic separation of the mixture resulting from reaction of a mutagen with several sites in an oligomer.[6] Herein we report a novel postoligomerization strategy that provides complete regiochemical and stereochemical control of adduction. In this method the natural polarity of reaction, i.e., with the heterocyclic base as the nucleophilic species and the adducting moiety as electrophile, is reversed. Thus, an amino derivative of the mutagen is used to displace halogen from the appropriate halo-substituted heterocyclic species. Modified deoxynucleotides have been prepared previously by such strategies,[7] but their conversion to oligodeoxynucleotides poses formidable problems if the adduct contains reactive functional groups which must be protected during oligomer synthesis.

The key to the present method is that the displacement reaction is carried out while the oligomer is still attached to the solid support.[8] Styrene adducts at guanine N^2 and adenine N^6 were chosen for the initial demonstration of this strategy. Styrene is metabolically oxidized to the epoxide, which is mutagenic and carcinogenic.[9] Reaction of the epoxide with DNA occurs at a variety of sites, involving both ends of the epoxide and with varied stereochemical results.[10] Reaction at guanine N^2 occurs solely at the α carbon of styrene oxide but is not stereospecific; deoxyadenosine adducts have not yet been observed but may be present as minor products.

Scheme I



Scheme II



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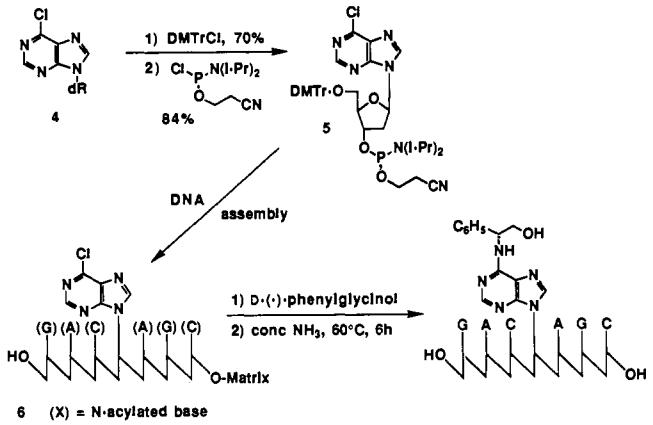
Scheme III



6 (X) = N-acylated base

2-Fluorodeoxyinosine (**1**) was used for preparation of the guanine N^2 adduct because the fluorine is more easily displaced than chlorine or bromine.[11] It could be converted to the adducted deoxynucleoside (Scheme I) by treatment with D-(-)-phenylglycinol (3 equiv, DMSO, 5.5 days, 65 °C, 39%). For incorporation into oligonucleotides (Scheme II), nucleoside **1** was converted to 5′-*O*-(dimethoxytrityl) 3′-*O*-phosphoramidite derivative **2**.[12] The target oligonucleotide 5′-CAG-(**1**)-T-3′ was synthesized on a 1.3-μmol scale by the normal automated solid-phase protocol except that **2** was used in twice the normal excess (i.e., 20 equiv) and the reaction time for addition of this nucleoside was extended to 10 min from the usual 1.5. The matrix beads were treated with D-(-)-phenylglycinol (50 mg, 0.050 mL of MeOH, 3 days, 50 °C). The mixture was washed with Et_2O to remove excess phenylglycinol and treated with concentrated NH_4OH (13 h, 60 °C) to remove protective groups. The modified oligomer, 5′-d(CAG-$G^{2\text{-styr}}$-T)-3′, was purified by SAX ion-exchange chromatography (NH_4OAc/20% EtOH) followed by passage through Sephadex G-15. The structure was confirmed by ^1H NMR; the spectrum was similar to that of unmodified 5′-d(CAGGT)-3′ except for the presence of the phenylglycinol moiety (aromatic protons at δ 7.3-7.4, α-H triplet at δ 5.2). The yield has not yet been fully optimized and is approximately one-third that obtained for *unadducted* oligomer after similar purification. The synthetic method represents an attractive strategy for preparation of oligodeoxynucleotides bearing structurally defined adducts containing reactive functional groups and readily yields the large quantities required for structural studies.

We have extended the method to preparation of N^6 adducts on adenine. Chloro nucleoside **4**[13] was employed as the halonucleoside component. It reacts readily with D-(-)-phenylglycinol to give the adenine N^6 adduct (DMF, 32 °C, 1 day, 59%). 5′-*O*-(Dimethoxytrityl) 3′-*O*-phosphoramidite derivative **5** was prepared uneventfully from **4** and was employed in the synthesis of 5′-d(GAC-$A^{6\text{-styr}}$-AGC)-3′ as shown in Scheme III. The reaction of D-(-)-phenylglycinol with oligomer containing the chloro-substituted adenine precursor was somewhat faster than with oligomer containing 2-fluorodeoxyinosine; the overall yields of the two syntheses were comparable. The synthesis was carried out on a 10-μmol scale. In the NMR spectrum of the oligomer the aromatic protons of the phenylglycinol are at δ 7.3-7.1, and the α-H is at δ 5.31. The structures of the modified oligomers were supported by enzymatic degradation to give the component nucleosides in the expected ratios.[14]

The merits of the halonucleoside strategy for synthesis of styrene oxide adducted oligomers are that it permits assembly with complete regiospecificity of site of adduction in the DNA and with equally complete stereospecificity at the α position of the styrene moiety, since the site of reaction in the oligomer is determined by the placement of the halonucleoside and the configuration of the α position of the styrene moiety is determined by the choice of phenylglycinol enantiomer. Moreover, delaying adduction until after the oligomer has been assembled avoids the need to invoke complex strategies for differential protection and deprotection of the hydroxyl groups in the styrene and deoxyribose moieties during oligomer assembly. We feel that this postoligomerization methodology will be applicable to synthesis of oligomers adducted with a wide variety of mutagens and carcinogens including polycyclic aromatic hydrocarbons where strong economic advantage is provided by late introduction of the costly carcinogen moiety.

Acknowledgment. Generous support of this project by USPHS Grants ES00267 and ES05509 and a fellowship to L.Z. from the Chemical Industry Institute of Toxicology are gratefully acknowledged.

Supplementary Material Available: Structural characterization of new compounds and chromatographic data (8 pages). Ordering information is given on any current masthead page.

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Cluster of Clusters. Structure of a Novel Cluster $[(Ph_3P)_{10}Au_{13}Ag_{12}Br_8](SbF_6)$ Containing an Exact Staggered-Eclipsed-Staggered Metal Configuration. Evidence of Icosahedral Units as Building Blocks

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Received November 13, 1990

Fivefold symmetry, which is not allowed crystallographically, has been found in quasicrystals.[1] The latter have long-range orientational order but only quasiperiodic translational order. Pentagonal or icosahedral packing (pip) is also quite common in clusters[2] and fine particles[3] where the crystallographical constraints are partially or completely lifted. Pip has also been implicated in the early stages of cluster growth and for structure units in amorphous materials.[4]

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