$1/4J_{CD}$ between 90 and 180° pulses.

While other workers have extended the INEPT technique to include observed nuclei with spins greater than half[5] and polarization transfer from nuclei with $I = {}^1/_2$ other than ^1H,[6] we believe this is the first report of the adaptation of the polarization transfer from deuterium.

While utilization for ^{13}C observation is described, this experiment is expected to be especially useful for nuclei such as ^{15}N, since polarization transfer will result in signal enhancement and eliminates problems associated with the negative NOE of ^{15}N. Furthermore, in most instances protons attached to nitrogen are generally exchangeable, allowing facile monitoring of ^2H exchange.

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The Antitumor Drug *cis*-$[Pt(NH_3)_2Cl_2]$ Forms an Intrastrand d(GpG) Cross-Link upon Reaction with $[d(ApGpGpCpCpT)]_2$

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The primary target responsible for the cytotoxicity of the antitumor drug *cis*-$[Pt(NH_3)_2Cl_2]$ (*cis*-DDP) is believed to be DNA.[1,2] It is therefore of interest to determine the stereochemistry of *cis*-DDP adducts of DNA. Spectroscopic studies of the binding of *cis*-DDP to mono-[3] and dinucleotides[4] reveal the heterocyclic nitrogen atoms of the purine and pyrimidine bases to be the most favorable DNA binding sites, with N7 of guanine being the most preferred kinetically.[5] Using nucleases, we showed previously that *cis*-DDP binds to regions of DNA rich in $(dG)_n{\cdot}(dC)_n$ ($n \geq 2$) sequences, a result consistent with the formation of intrastrand cross-links between nearest neighbor guanine or cytosine bases.[6] This conclusion was recently supported by ^1H NMR studies of di-[4] and tetranucleotides[7] containing such sequences. Intrastrand cross-linking of two guanines separated by one or more bases has also been demonstrated.[8] In the present investigation we have examined the reaction of *cis*-$[Pt(NH_3)_2Cl_2]$ with the self-complementary deoxyribohexanucleoside pentaphosphate, $[d(ApGpGpCpCpT)]_2$. As shown here, the isolated product contains an intrastrand *cis*-diammineplatinum(II)-d(GpG) cross-link, confirming at the hexanucleotide level the lesion believed to be significant on DNA. The results are of potential value in elucidating the mechanism of action of platinum antitumor drugs.

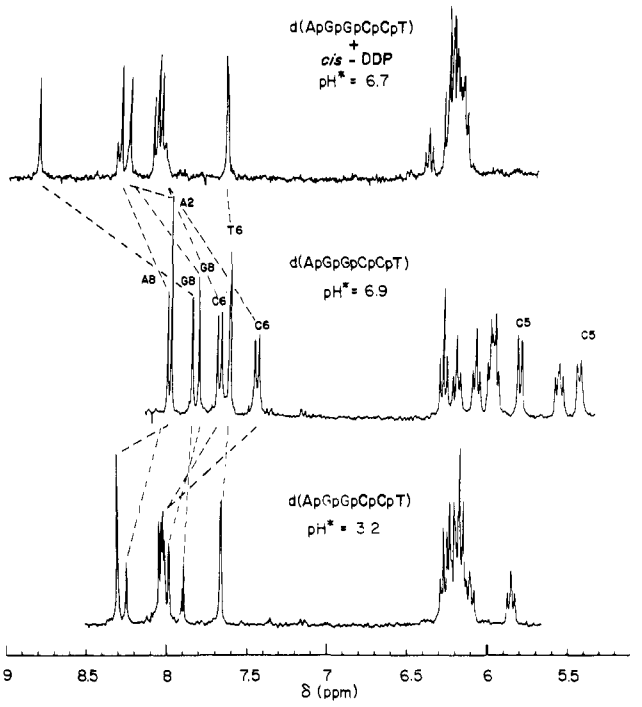

Figure 1. Downfield regions of 300-MHz ^1H NMR spectra (9.0–5.0 ppm) of $[d(ApGpGpCpCpT)]_2$ (3.5 mM duplex, 35 °C, no buffer) and its *cis*-DDP adduct (2.5 mM strand, 70 °C [see caption to Figure 2], no buffer). The central guanine H8 and cytosine H6 resonances are tentatively assigned as the more downfield peaks. The symbol pH* signifies uncorrected meter readings for samples in D_2O.[18]

Deoxyribohexanucleoside pentaphosphate was synthesized by a previously reported solid-phase procedure.[9,10] *cis*-DDP (3.33 mM) was allowed to react with 0.75 equiv of 10^{-3} M $[d(ApGpGpCpCpT)]_2$ (K^+ form) in the dark at 37 °C for 144 h in unbuffered aqueous solution, pH 6.0–6.7. ^1H NMR studies[11] showed that the unmodified oligonucleotide retains considerable duplex structure under these conditions. The mixture was separated by reverse-phase high-performance liquid chromatography.[12] One main product and unreacted starting material accounted for >95% of the total optical density at 260 nm. The retention time of the platinated oligonucleotide was shorter than

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(11) Sequential melting of the deoxyribohexanucleoside pentaphosphate was monitored by observing the G-C amino protons (^1H NMR, Redfield water supression technique) involved in duplex H-bonding as a function of temperature as well as the transition midpoints of the temperature-dependent chemical shifts of the nonexchangeable base protons (3.5 mM duplex, 5 mM phosphate, 1 mM EDTA). The latter experiment showed the transition midpoint to be 55 ± 4 °C for the GpGpCpC core and a much lower transition midpoint (~30 °C) for the A-T base pairs. The duplex-to-strand transition was found to be noncooperative, a result confirmed by temperature-dependent UV and CD studies. Thus at 37 °C, partial duplex structure is still present. Full details will be reported at a later date.
(12) Waters μBondapak C-18 column, 30 × 0.78 cm; dual pump system, pump A, 0.1 M NH_4OAc, pH 6.5; pump B, 0.1 M NH_4OAc/CH_3CN (1:1), pH 6.5; primary linear gradient, 5–60% B, 43 min, 2 mL/min; secondary linear gradient, 15–35% B, 30 min, 2 mL/min. Under these conditions the oligonucleotide would be expected to be in single stranded form.

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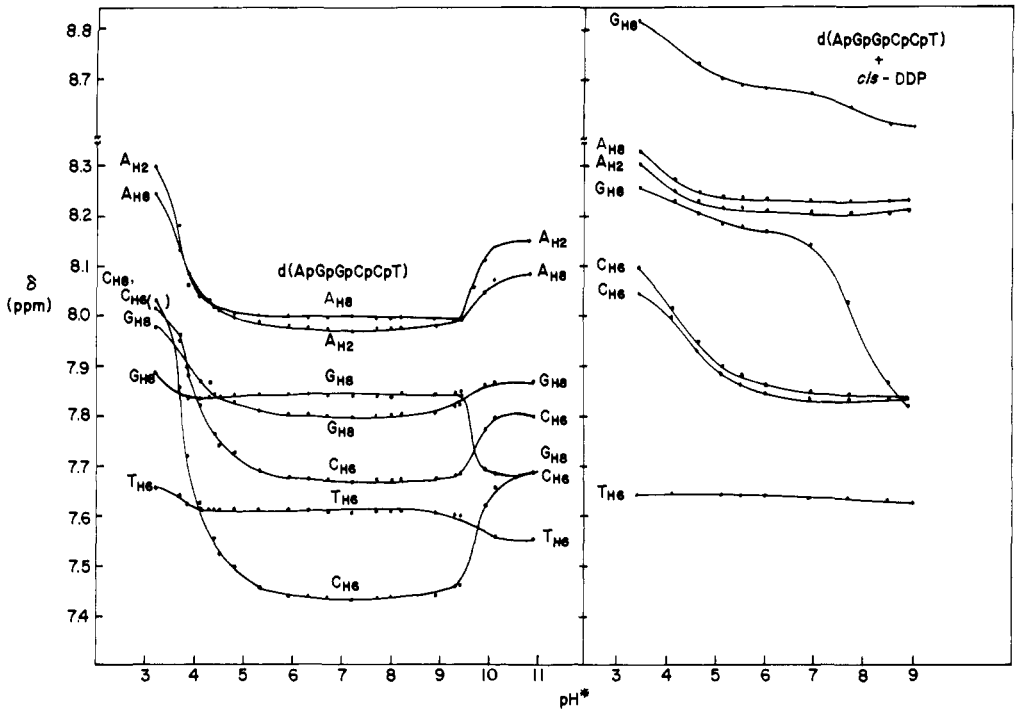

Figure 2. Chemical shift (δ) vs. pH* of the nonexchangeable base protons of D_2O solutions of $[d(ApGpGpCpCpT)]_2$ (3.5 mM, 35 °C) and its *cis*-DDP adduct (2.5 mM, 70 °C). The pyrimidine resonances of the latter sample show no chemical shift changes with temperature over the range $35 < T < 70$ °C while the purine resonances show a slight temperature-dependent chemical shift change of up to 0.1 ppm. Tetramethylammonium chloride was used as the internal standard (δ 3.180).

that of the unmodified oligomer, as expected from the hydrophilic nature of the *cis*-diammineplatinum(II) moiety. The analytical data revealed the presence of one platinum atom per d(ApGpGpCpCpT) strand.[13]

Figure 1 displays the ^1H NMR spectra of the free and platinated oligonucleotides lyophilized and redissolved in D_2O. The latter spectrum demonstrates the purity and single stranded character of the isolated product. The single stranded nature of the adduct was deduced from the very similar appearance (except for H8 of G, vide infra) of the spectra of the platinated and low pH* unplatinated oligonucleotides. Since divalent platinum binds covalently to the bases,[3,4,14] its binding sites can be determined from plots of the pH* dependence of the chemical shifts of the nonexchangeable base protons for both the unplatinated and platinated oligonucleotide (Figure 2). The sigmoidal curves reflect protonation or deprotonation of the pyrimidine or purine ring nitrogen atoms.[4,7,8] For the unplatinated oligomer we observe at low pH* the characteristic protonation at N1 of adenine (pK_a = 3.7), N3 of cytosine (pK_a = 4.5), and N7 of guanine (pK_a = 2.3).[15] Deprotonation of guanine N1 (pK_a = 10) and thymine N3 (pK_a = 9.8) is evident in the pH* 10 region[15] from the characteristic decrease in the chemical shifts of the central guanine H8 and thymine H6 protons, respectively. Opposite shifts of the central and adjacent guanine H8 resonances at high pH* reflect the sequence-dependent nearest neighbor base stacking variations in the strand form,[16] the combined effects of which produce the observed chemical shift profiles.

Upon binding of *cis*-DDP, all nonexchangeable base protons shift to lower magnetic field (Figure 2). The behavior of the base protons is entirely analogous to that of the free oligonucleotide at low pH*. The only observed shifts from pH* 5 to 9 are assigned to the deprotonation of N1 of guanine. The apparent pK_a (8.0) for the deprotonation of guanine N1 is substantially less than for the unmodified oligonucleotide (9.8). Such a decrease in the pK_a of N1 is characteristic of guanine complexes in which *cis*-DDP is bound at the N7 position.[4,7,8,17] The chemical shift changes at pH* 4.5 rule out the N3 atoms of the cytosine residues as platinum binding sites. These results, coupled with the characteristic 0.3–0.9-ppm downfield shift of guanine H8 observed upon Pt(II) binding to N7,[4,7] reveal that *cis*-diammineplatinum(II) is chelated to the N7 atoms of the adjacent guanine residues.

The significant downfield shifting upon platination of resonances belonging to bases not directly bound to platinum is interesting. This behavior is best exhibited by the cytosine H6 resonances. In the unmodified oligomer, the two H6 resonances are in significantly different environments (-purine-cytosine-pyrimidine- vs. -pyrimidine-cytosine-pyrimidine), as reflected by their chemical shifts. Upon platination, however, both H6 protons are in similar environments and both are shifted considerably downfield. The terminal bases show similar but less dramatic effects. The resemblance (Figure 1) between the spectrum of the platinated oligonucleotide and that of the unmodified oligomer at low pH, conditions where the normal base stacking is disrupted,[16] suggests that a significant degree of base unstacking accompanies the binding of *cis*-DDP. In order to obtain additional stereochemical information, we are presently engaged in a full conformational analysis of $[d(ApGpGpCpCpT)]_2$ and its *cis*-diammineplatinum(II) adduct.

(13) A solution of the *cis*-diammineplatinum(II) adduct was analyzed for Pt by carbon rod atomic absorption spectroscopy. From the UV absorption at 260 nm, a molar extinction coefficient of approximately 36 000/(mol of Pt) was calculated. Although this value is larger than that for the unplatinated oligonucleotide (duplex form, $\epsilon_{260} \sim 24{,}500$) the difference is expected since bound platinum destabilizes the duplex structure[7] (vide infra). An adduct having two Pt atoms per strand would have a calculated ϵ_{260} of ~72 000, which is unreasonably large.

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In summary, we have demonstrated that *cis*-$[Pt(NH_3)_2Cl_2]$ reacts with the self-complementary oligonucleotide, [d-(ApGpGpCpCpT)]$_2$, to yield a structure with an intrastrand cross-link between two N7 atoms of adjacent guanine residues. Substantial conformational changes accompany this binding. The platinated hexanucleotide does not form a duplex structure.

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Registry No. *cis*-$[Pt(NH_3)_2Cl_2]$, 15663-27-1; d(ApGpGpCpCpT), 83026-06-6.

Photodisproportionation of (μ-Oxo)bis[(tetraphenylporphinato)iron(III)]

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Strategies for photochemical solar energy conversion in solution have relied almost exclusively on the generation of long-lived charge-transfer excited states that undergo bimolecular redox quenching.[1-4] This approach precludes the choice of potential photocatalysts whose excited states are either nonemitting (and hence short lived) or dissociative. Unfortunately, most transition-metal complexes appear to fall into one or both of these categories.[5,6]

We propose an alternative strategy in which the photocatalyst dissociates from an excited state that may react in the strong coupling limit[7] or even predissociate. The key requirement for uphill thermodynamics is that one photoproduct be either a stronger oxidant or a stronger reductant than the starting compound. The requirement for the potential to recycle as a catalyst is that the products not be reactive radicals. A reaction likely to meet these criteria is a photodisproportionation[8] of the form

$$M\text{–}O\text{–}M \xrightarrow{h\nu} M{=}O + M$$

We report here the first recognized example of this mechanism for potentially storing energy.

Several transition metals exhibit the M–O–M[10-14] structure, and many of these have known complexes of both M and M=O forms.[15-19] Recently Balch and co-workers have postulated the ferryl complex of tetraphenylporphine (FeOTPP),[16,17] and the ferrous complex (FeTPP) is well-known and characterized in many solvents.[18,19] Bartocci and co-workers have recently demonstrated that alcohol complexes of Fe^{III} porphyrins do photochemistry[20] that, according to Brault and co-workers, originates with O → Fe charge transfer.[21] One might expect analogous photochemistry from the title compound, $(FeTPP)_2O$,[16] where the alcoholic R group is replaced by FeTPP.

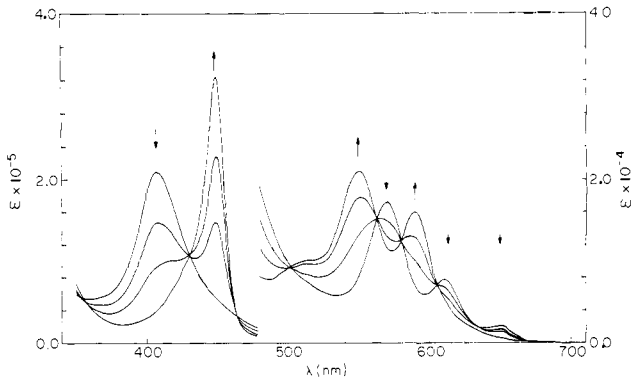

Figure 1. Spectral changes of a benzene solution of 0.2 M PPh_3, and 9 × 10^{-6} M $(FeTPP)_2O$ upon irradiation with a 450-W medium-pressure Hg lamp fitted with a Corning 0-51 cutoff filter. Spectra taken at t = 0, 15, 30, and 158 min.

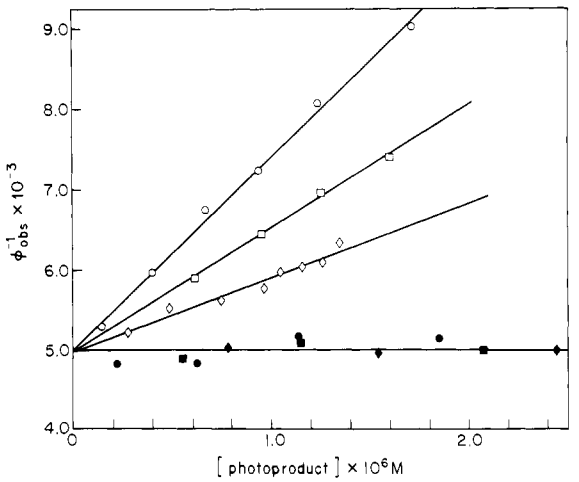

Figure 2. Inverse of the observed quantum yield for appearance of photoproduct vs. photoproduct concentration at $I_0 \simeq 2 \times 10^{-9}$ einstein and initial $[(FeTPP)_2O] \simeq 9 \times 10^{-6}$ M: (○) $[PPh_3]$ = 0.1 M; (□) $[PPh_3]$ = 0.15 M, (◇) $[PPh_3]$ = 0.25 M in benzene; (●) $[PPh_3]$ = 0.1 M; (■) $[PPh_3]$ = 0.15 M; (◆) $[PPh_3]$ = 0.2 M in pyridine. Pyridine data points go to 4 × 10^{-6} M but are truncated for purpose of display. All lines are least-squares fits.

Irradiation into the Soret band of a rigorously degassed benzene or pyridine solution of $(FeTPP)_2O$ leads to no observable spectral changes in the UV–visible or infrared spectrum.[22] If an excess

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