The major products generated upon irradiation of adamantane under anaerobic conditions[28] were analyzed by GC/MS and determined to be 1-acetyladamantane, 1,3-diacetyladamantane, and 1,3,5-triacetyladamantane. The processes reported here break ground on several fronts. We feel that further detailed evaluation of the energetic and mechanistic features of such processes is warranted.

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(27) For **4**: ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.83 (CH_3), 30.47, 40.56, 41.13, 42.81 (CH_2), 50.25, 51.11, 51.46, 51.60, 52.71, 53.12, 53.12, 53.40, 54.64, 56.78, 58.41 (*C*H), 62.96 (*C*), 209.71 (C=O); MS, m/z 254 (M^+, 19), 239 (M - 15, 59), 211 (M - 43, 100), 197 (M - 57, 7), 183 (M - 71, 19).

(28) Reaction conditions: see Table I, footnote *d*. Reaction run for three 16-h cycles, total time 48 h. Adamantane: MS, m/z 136 (M^+, 100). 1-Acetyladamantane: MS, m/z 178 (M^+, 7), 135 (M - 43, 100), 43 (M - 135, 10). 1,3-Diacetyladamantane: MS, m/z 220 (M^+, 8), 177 (M - 43, 84), 43 (M - 177, 100). 1,3,5-Triacetyladamantane: MS, m/z 262 (M^+, 8), 219 (M - 43, 58), 43 (M - 219, 100).

Sodium Cyanide: A Chemical Probe of the Conformation of DNA Modified by the Antitumor Drug *cis*-Diamminedichloroplatinum(II)

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It is generally accepted that the antitumor drug *cis*-diamminedichloroplatinum(II) (*cis*-DDP) exhibits its toxicity by reacting with DNA. Most of the adducts formed in the reaction of *cis*-DDP with DNA have been identified. The two major adducts arise from intrastrand cross-links between two adjacent guanine residues (d(G*G*) adduct) and between the adjacent adenine and guanine residues (d(A*G*) adduct).[1] Under physiological conditions, the adducts are stable over a large period of time, while in the presence of cyanide ions, most of the bound platinum residues, but not all of them, are rapidly removed.[2] Immunological analysis of the platinated DNA after treatment with cyanide ions suggests a preferential removal of d(G*G*) and the d(A*G*) adducts.[3] Studies of model nucleobase complexes of *cis*-DDP have shown that the conformation of the complexes and the nature of the bases play a key role in the cyanide substitution kinetics.[4] We herewith report that the kinetics of the reaction between cyanide ions and the two major adducts d(G*G*) and d(A*G*) is strongly dependent upon the DNA conformation.

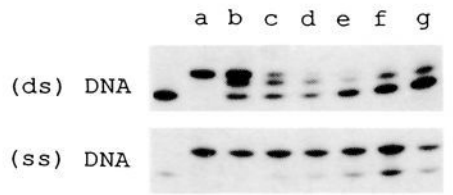

Figure 1. Autoradiogram of a denaturing 24% polyacrylamide gel of the products of the reaction between cyanide ions and ds or ss oligonucleotides containing a single d(G*G*) adduct. The platinated samples ($c \simeq 3 \times 10^{-6}$ M) were incubated at 37 °C and in 0.2 M NaCN, 20 mM Tris·HCl adjusted at pH 8.3 by addition of HCl. At various times, the samples were precipitated with ethanol, washed three times with ethanol, and then electrophoresed. Lanes a-g correspond to the following times of incubation: 0, 0.25, 0.50, 0.75, 1, 1.5, and 2 h for the ds oligonucleotide and 0, 1, 2, 3, 5, 7, and 9 h for the ss oligonucleotide, respectively. The two bands on the left of the autoradiograms correspond to the unplatinated oligonucleotide. The oligonucleotide d(CTTCTCTTCTGGTCTTCTCT) containing a single d(G*G*) adduct is ^{32}P-labeled at the 5′ end.

We first compared the relative resistance of a d(G*G*) adduct either in a single-stranded (ss) oligonucleotide or in a double-stranded (ds) oligonucleotide to the reaction with cyanide ions. The ss oligonucleotide d(CTTCTCTTCTGGTCTTCTCT) was reacted with *cis*-DDP and then ^{32}P labeled at the 5′ end.[5] The corresponding ds oligonucleotide was obtained by mixing the ss oligonucleotide containing a single d(G*G*) adduct with the complementary unplatinated strand. Both the platinated samples were treated with a large excess of cyanide ions. At various times, aliquots were withdrawn and analyzed by gel electrophoresis under denaturing conditions.[6] The ss and ds platinated oligonucleotides behave quite differently (Figure 1). As judged by the disappearance of the starting products (upper bands), cyanide ions are much less reactive with the ss oligonucleotide than with the ds oligonucleotide, the half-lives being 720 and 20 min (precision 10%), respectively. Moreover, only two products (the platinated and the unplatinated oligonucleotides) are detected by gel electrophoresis in the case of the ss oligonucleotide while, in the case of the ds oligonucleotide, three products (the platinated oligonucleotide, the unplatinated oligonucleotide, and an intermediate species) are detected.

Since, in ss and ds oligonucleotides, the two platinated G* residues are in a head-to-head, anti conformation,[7,8] we assume that the difference in the kinetics cannot be due essentially to a different protective effect of the exocyclic oxygens of the platinated bases.[4] The neighboring nucleotide residues could be responsible for a large protective effect in the ss oligonucleotide (structural distortions and even folded back structure (on the 5′ side of the adduct) have been proposed for platinated ss oligonucleotides[8,9]), and/or the double helix, by its surface properties, could favor the

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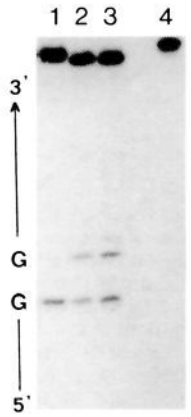

Figure 2. Autoradiogram of a denaturing 24% polyacrylamide gel of the products of the reaction between dimethyl sulfate and the starting product, the intermediate species, and the final product. After 4 h of reaction between cyanide ions and the platinated ds oligonucleotide (same conditions as in Figure 1, but the temperature was 17 °C), the products were separated by gel electrophoresis in a denaturing 24% polyacrylamide gel, eluted from the gel,[6] rehybridized, and then reacted with dimethyl sulfate according to the procedure of Maxam and Gilbert.[10] Lane 1 is relative to the intermediate species, lane 2 to the final product, lane 3 to Maxam–Gilbert specific reaction for the unplatinated ds oligonucleotide, and lane 4 to the starting product.

reaction of cyanide ions with the adducts.

The reaction between cyanide ions and the platinated ds oligonucleotide has been characterized by three sets of experiments. First, a kinetic study was performed at 17 °C. A good fit (not shown) between the experimental and the calculated relative concentrations of the three products was obtained, assuming that the scheme of the reactions is as follows:

$$\text{platinated ds oligonucleotide} \xrightarrow{k_1} \text{intermediate species} \xrightarrow{k_2} \text{unplatinated ds oligonucleotide}$$

The reaction rates $k_1 = 0.28 \pm 0.02$ h^{-1} and $k_2 = 0.27 \pm 0.03$ h^{-1} were calculated by Marquardt's least-squares procedure.

Then, the nature of the intermediate species was studied. The products eluted from the three bands were reacted with dimethyl sulfate according to the procedure of Maxam and Gilbert.[10] The results (Figure 2) show that (a) in the starting product, the two platinated G* residues do not react (the N7's are not accessible); (b) in the final product, the two G residues react; (c) in the intermediate species, the 5′G residue reacts but not the 3′G residue. Thus, in the reaction between cyanide ions and the platinated ds oligonucleotide, cyanide ions react selectively with the 5′G* residues. Within the resulting intermediate species, it is likely that the adduct is *cis*-[Pt(NH$_3$)$_2$(N7-dGuo)CN]$^+$.

Finally, we were interested to know whether subtle conformational changes in a double helix could influence the removal of a d(G*G*) adduct by cyanide ions. We have studied three platinated duplexes obtained by pairing the ss ^{32}P-labeled oligonucleotide containing a single d(G*G*) adduct respectively with the complementary strand and with the complementary strands in which either the 5′ or the 3′C residue complementary to the platinated G* residue was replaced by a T residue. The three platinated duplexes are named by their central two base pairs, i.e., d(G*G*/CC), d(G*G*/TC), and d(G*G*/CT). In the presence of cyanide, the qualitative behavior of the three duplexes was similar. Three bands were detected by gel electrophoresis under denaturing conditions (results not shown). However, the rates of removal of the bound platinum residues were different. At 37 °C, the half-lives of the starting products are 20, 30, and 70 min for the d(G*G*/CC), d(G*G*/CT), and d(G*G*/TC) duplexes, respectively. Recently, we reported that the mismatched T residues induce some distortions in the platinated ds oligonucleotides, the distortions being larger on the side of the mismatched residues.[5] The mismatched T residues paired with the 5′G* residues affect the kinetics more than the mismatched T residues paired with the 3′G* residues, which is in agreement with the selective reactivity of cyanide ions.

We have also compared the relative resistance of a d(A*G*) adduct using an experimental procedure similar to that described for the d(G*G*) adduct, the starting material being the ss oligonucleotide d(CTTCTCTTCTAGTCTTCTCT). By gel electrophoresis, two bands were detected with the ss oligonucleotide and three bands with the ds oligonucleotide (results not shown). The reaction was much slower with the ss oligonucleotide than with the ds oligonucleotide, the half-lives of the starting products being, respectively, 120 min and less than 10 min at 37 °C. Thus, the d(A*G*) adducts behave as the d(G*G*) adducts but are comparatively less stable to the action of cyanide ions.

In conclusion, the reactivity of cyanide ions with the two major adducts d(A*G*) and d(G*G*) depends strongly upon the DNA conformation. Experiments are in progress to determine, in ds natural platinated DNAs, the influence of the sequence on the relative stability of the major adducts in the presence of cyanide ions.

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Zwitterionic Rhodium Complexes as Catalysts for the Hydroformylation of Olefins

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The homogeneous hydroformylation of olefins is a reaction that has attracted great interest, especially in terms of its synthetic utility, as well as studies probing the mechanism of this valuable industrial process.[1] Much of the recent effort has focused on the use of rhodium compounds as catalysts (usually containing phosphine ligands), since some complexes involving this metal exhibit high catalytic activity.[2,3] Despite the latter, the regioselectivity in many cases is not high, including synthetic approaches to commercially important compounds. For example, development of a mild, regiospecific method for the hydroformylation of *p*-isobutylstyrene to 2-(4-isobutylphenyl)propanal would be of significance since subsequent oxidation of the aldehyde[4] affords ibuprofen, one of the best, current, nonsteroidal antiinflammatory agents.[5]

Although numerous neutral and several cationic[6] rhodium complexes have been investigated, there have been no reports, to our knowledge, on the use of zwitterionic rhodium complexes as catalysts for the hydroformylation of olefins. It seemed conceivable that **1**, readily obtained from rhodium chloride, sodium tetraphenylborate, and 1,5-cyclooctadiene in aqueous methanol,[7] might

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