nor the reversed face selectivity for 2-bromo- or 2-methylacrolein vs acrolein.

In summary, a variety of physical and chemical data point to transition-state assembly 3 as the most plausible model for the catalytic enantioselective reaction of 2-substituted acroleins with cyclopentadiene.[8,9]

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Synthesis and DNA-Binding Properties of a Cisplatin Analogue Containing a Tethered Dansyl Group

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In the present report we describe the synthesis, fluorescence, and DNA-binding properties of a structural analogue of the platinum antitumor drug cisplatin,[1-5] [Pt(dansen)Cl_2], which contains a tethered dansyl group. The fluorescent properties of the dansyl moiety offer a viable alternative to radiolabeling[6-8] and allow one to monitor by a nondestructive technique[9-12] much lower levels of [Pt(dansen)Cl_2] than cisplatin or its ethylenediamine analogue, [Pt(en)Cl_2]. The structural changes that occur in DNA upon binding of this complex and the ability of the resulting adducts to be recognized by structure-specific recognition proteins[13] mimic properties of cisplatin. Moreover, we have been able to use the fluorescent tag in [Pt(dansen)Cl_2] to observe its covalent binding to plasmid DNA in bacterial cells.

Preparation of the platinum complex containing the dansylated ethylenediamine (dansen) ligand, dichloro((2-((3-dansylpropyl)amino)ethyl)amine)platinum(II) or [Pt(dansen)Cl_2], is outlined in Scheme I. Analytically pure samples were obtained by vapor diffusion of ether into a DMF solution of the complex. The ^{195}Pt NMR chemical shift of [Pt(dansen)Cl_2], δ -2355, is close to the value of δ -2379 for [Pt(en)Cl_2], indicating the presence of two chloride ions and two nitrogen atoms of an ethylenediamine chelate as the ligands.[14,15]

The [Pt(dansen)Cl_2] complex binds covalently to DNA to form bifunctional 1,2-intrastrand cross-links, adducts that display structures analogous to those formed upon binding of cisplatin to duplex DNA.[16] Covalent binding to calf thymus and other

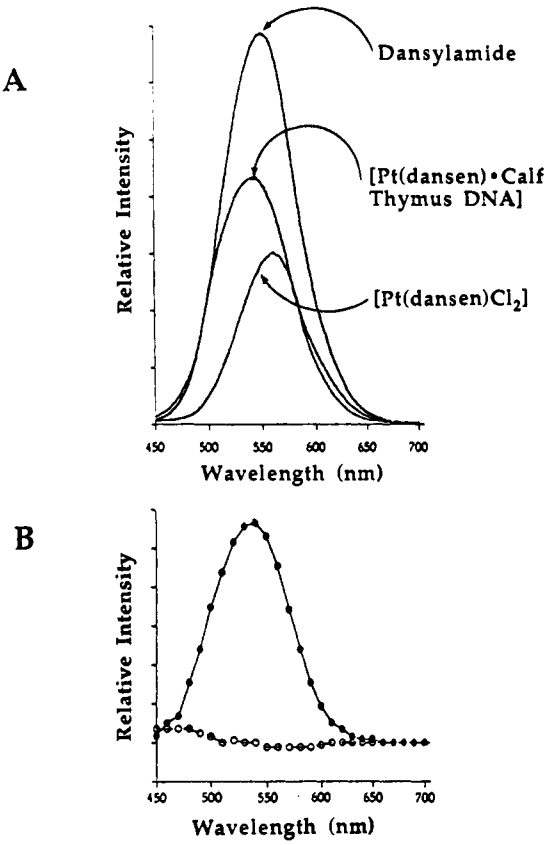
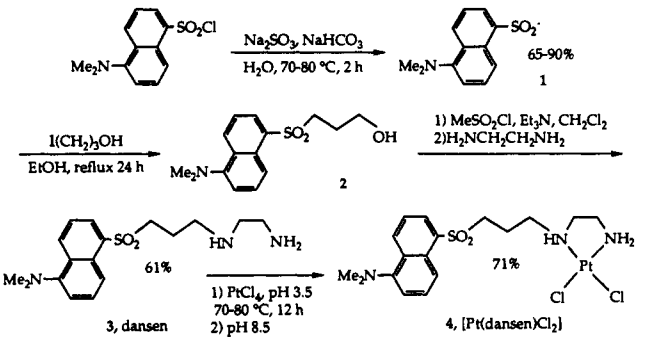


Figure 1. (A) Emission spectra (excitation, 344 nm; excitation bandpass, 5 nm; emission bandpass, 5 nm) of [Pt(dansen)Cl_2], [Pt(dansen)Cl_2] bound to calf thymus DNA at r_b = 0.032, and dansylamide. For all three spectra, the platinum concentration was 3.64×10^{-7} M and the excitation wavelength, 344 nm. (B) Emission spectra (excitation, 344 nm; excitation bandpass, 20 nm; emission bandpass, 20 nm) of pUC19 plasmid DNA recovered from XL1-Blue bacterial cells treated with [Pt(dansen)Cl_2] (●) or free dansen ligand (○). Data were manually digitized and the displayed spectra obtained following subtraction of the typically weak fluorescent background of DNA that becomes significant at the low r_b values used in this experiment.

Scheme I



double-stranded DNAs was demonstrated by platination reactions followed by precipitation or dialysis and subsequent quantitation by atomic absorption or fluorescence spectroscopic analysis. Bifunctional coordination was revealed by analyzing reactions of the diaqua form with the dodecanucleotide d(TCTAGGCCTTCT), which contains a single d(GpG) platinum binding site. Four products having a 1:1 platinum-to-strand ratio were observed (Figure S1, supplementary material) and purified by HPLC. Nuclease and phosphatase digestion analysis[17] revealed the three nucleosides dA, dC, and dT in a 1:4:5 ratio and the absence of unmodified dG (Figure S1). Four peaks corresponding to platinated d(GpG) were also observed. These digestion products

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arise from two diastereomers formed for each of two orientational isomers having the dansyl group located cis to the 3′ or 5′ guanosine of the dinucleoside monophosphate.[17] The absence of a significant intercalative interaction of the dansyl moiety with duplex DNA was demonstrated by unwinding titration experiments, which are sensitive to the mode of binding of platinum compounds.[18] An unwinding angle of 13.5 ± 1.5° was obtained for [Pt(dansen)Cl_2] bound to pUC19 plasmid DNA. This value is essentially identical to those observed for cisplatin and [Pt(en)Cl_2], excluding [Pt(dansen)Cl_2] from the class of complexes that exhibit both covalent and intercalative interactions. Together with the demonstration of bifunctional coordination to single-stranded DNA described above, the results make it extremely unlikely that a combination of monofunctional and intercalative binding modes exists for [Pt(dansen)Cl_2].

Further evidence for the structural similarity of [Pt(dansen)Cl_2]-DNA adducts to those formed by cisplatin was obtained from the ability of the protein HMG1 to bind to restriction fragments modified by the fluorescent analogue. HMG1 binds to DNA modified by platinum complexes that form 1,2-intrastrand d(GpG) or d(ApG) cross-links, as revealed by gel mobility shift assays.[19] Identical band shift studies of DNA modified with [Pt(dansen)Cl_2] indicated that HMG1 also recognizes its DNA adducts (Figure S2).

The emission spectrum of [Pt(dansen)Cl_2] is shown in Figure 1A along with that of dansylamide for comparison. The electronic absorption (dansylamide, λ_{max} 328 nm, ϵ 7060 M^{-1} cm^{-1}; [Pt(dansen)Cl_2], λ_{max} 334 nm, ϵ 5220 M^{-1} cm^{-1}) and emission spectra of the two compounds are not appreciably affected by the presence of a sulfone, rather than a sulfonamide, link in the dansyl moiety. The ratio of emission intensity maxima for dansylamide and [Pt(dansen)Cl_2] at 344 nm, a wavelength where the extinction coefficients are identical, is 0.44. Apparently, the propylene tether prevents efficient quenching of the fluorescence by the platinum metal center. Moreover, the emission spectrum for [Pt(dansen)Cl_2] bound to calf thymus DNA is similar to that for the free complex, as expected in the absence of intercalative binding.

The [Pt(dansen)Cl_2] compound is taken up by bacterial cells in a similar fashion to cisplatin. Figure 1B shows emission spectra for pUC19 plasmid DNA recovered from 100-mL cultures of XL1-Blue *Escherichia coli* treated with 5×10^{-5} M solutions of the complex [Pt(dansen)Cl_2] or with the free ligand dansen in phosphate-buffered saline. An emission band centered at 534 nm was observed for DNA recovered from cultures treated with [Pt(dansen)Cl_2], but not for samples isolated from cultures treated with equimolar concentrations of dansen or cisplatin. In these latter two cases, only a weak background signal due to DNA was observed. Analysis by atomic absorption spectroscopy of pUC19 DNA obtained from platinum-treated cells revealed ratios of bound drug to nucleotide (r_b) of 10^{-4} for cisplatin and 10^{-5} for [Pt(dansen)Cl_2]. Quantitation of [Pt(dansen)Cl_2] in the latter samples by fluorescence spectroscopy agreed with the atomic absorption results, confirming that the ligand remains bound to the platinum center in vivo.

The luminescence, cellular uptake, and DNA binding properties of [Pt(dansen)Cl_2] should facilitate a variety of interesting applications. In particular, this cisplatin analogue might be used to investigate its intracellular distribution, processing by DNA repair enzymes, recognition by HMG-box proteins, and other aspects of its biological chemistry in vivo.[1,13,19] Compounds with similar optical properties, including the structurally uncharacterized compound *cis*-bis(6-aminoquinoline)dichloroplatinum(II),[20] have been employed to follow the compartmental localization of substrates within single cells.[21,22] Applications requiring the analysis of a cisplatin analogue bound to cellular DNA at r_b values considerably lower than those employed in this preliminary study should be possible with [Pt(dansen)Cl_2] or a related compound by laser excitation and recently developed, highly sensitive detection systems.[21,23]

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Supplementary Material Available: Preparation of compounds **1–4** including spectroscopic and analytical data, Figure S1 showing the results of the digestion/HPLC analysis of a dodecanucleotide platinated with [Pt(dansen)Cl_2], and Figure S2 displaying the gel mobility shift of DNA platinated with [Pt(dansen)Cl_2] in the presence of the protein HMG1 (11 pages). Ordering information is given on any current masthead page.

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Synthesis and Characterization of the Neutral Lanthanide Silyl Complexes $(\eta^5\text{-}C_5Me_5)_2LnSiH(SiMe_3)_2$ (Ln = Nd, Sm)

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A number of key advances in transition-metal silicon chemistry have resulted from studies with the early transition metals.[1] In particular, it has been observed that d^0 M–Si σ bonds readily participate in insertion[2] and σ-bond metathesis[3] reactions, which appear to proceed via four-center, concerted additions. This suggests that f-element metal–silicon bonds would also be reactive, since they should be electronically similar to early metal–silicon

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