Epand and Scheraga[18] previously reported that a similar polymer, poly(DL-Lys)$_{18}$(L-Val)$_{15}$(DL-Lys)$_{16}$, underwent a conformational transition from β in water to α-helix by the addition of methanol (98%). The observed ellipticity was quite small compared to the values reported herein. Our results are in conflict with this report as shown in Figures 2 and 3.

The infrared spectrum in 98% methanol is nearly identical with that found in water and no conformational change can be detected. Similarly, in Figure 3, a single negative trough is seen at 215–216 nm with $[\theta] = -29,400$ with a cross-over point at ~ 203 nm. The ORD showed a trough at 230 nm ([M] refers to mean residue molar rotation) and a peak at 204 nm ([M] = 38,500). Both these spectra are characteristic of the β form[19] and are similar to that found in H$_2$O (Figure 1). Therefore, it is apparent that no conformational transition of β to α-helix occurred in the valyl block on changing the aqueous solvent to MeOH. Our results agree with the theoretical conformational calculations which indicate that the β form is the most preferred for the valyl residue[15,20,21] in contrast to other studies.[22] This report records the optical properties of a single extended β chain in contrast to previous reports of highly associated β sheets.

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S. Kubota, G. Fasman*

The Graduate Department of Biochemistry, Brandeis University
Waltham, Massachusetts 02154

Nucleoside Complexing. Interligand Interactions between Purine and Pyrimidine Exocyclic Groups and Polyamines. The Importance of Both Hydrogen Bonds and Nonbonding Repulsions

Sir:

Selective attachment of heavy-atom-containing moieties to biopolymers should permit an electron microscopic study of their structure.[1] In particular, the sequence of bases in DNA might be determined if a heavy metal can be selectively bound to one of the four common heterocyclic bases. There are some differences in the coordinating affinity of a given metal ion for the common deoxynucleosides,[2] namely, deoxythymidine (dT), deoxycytidine (dC), deoxyadenosine (dA), and deoxyguanosine (dG). However, these nucleosides are unfortunately not sufficiently different in their coordinating tendencies to allow a meaningful labeling study.[3] Therefore, several alternative approaches to the induction of selectivity have been

tried. These include: (1) specific reaction of a heavy-metal compound (OsO$_4$) with a base (thymine),[4] (2) formation of nucleic acids from covalently bound heavy-metal-labeled precursors (organomercurials[5] of purine and pyrimidine nucleotides), (3) specific organic reactions which introduce a functional group which is then available for binding by a metal ion or complex,[6] and (4) examination of nucleic acids which naturally contain a very few reactive bases (thiouracil).[7] There is presently a great need for a heavy metal label for A. Selective reagents, even those containing only light atoms, are useful in structural studies of nucleic acids.[8]

Recently, we have begun to explore a different approach to selective labeling.[9] We believe that both hydrogen-bonding and nonbonding repulsive interactions between the exocyclic group on the bases and the chelate ligands in metal complexes will lead to selective reactions. In essence, the propensity of *the nucleic acid constituent bases to recognize complementary bases via hydrogen-bonding interactions can be exploited in specific labeling schemes or in the development of specific reagents.*

We now wish to report our studies on the reaction of cis-β-[Co(trien)Cl$_2$]$^+$ (where trien = triethylenetetramine, NH$_2$CH$_2$CH$_2$NHCH$_2$CH$_2$NHCH$_2$CH$_2$NH$_2$) with ^{14}C-labeled dT, dC, dG, and dA. Our reasons for choosing this particular system were as follows. First, the nucleosides are extremely weak ligands,[2] especially toward octahedral complexes, and radiotracer techniques are necessary for detecting complex formation in the presence of excess complex reagent ([Co(trien)Cl$_2$]$^+$). Second, we have previously studied a complex of the purine theophylline (1,3-dimethyl-2,6-dioxopurine).[9] The structure of this complex, trans-[Co(en)$_2$Cl(theophyllinato)]$^+$ (en = ethylenediamine, NH$_2$CH$_2$CH$_2$NH$_2$), revealed that the amino hydrogens of the ethylenediamine ligands are capable of donating a hydrogen bond to the exocyclic oxygen on C(6) of theophylline. This purine was coordinated via N(7), as expected of dG. The trien system offers essentially the same hydrogen-bonding potential as the ethylenediamine complexes. Although preparatively more attractive, the bis(ethylenediamine) complexes usually produce more by-products and react more slowly than the analogous trien complexes.[10]

A schematic representation of the possible interactions between the nucleoside bases and the NH and/or NH$_2$ groups of the coordinated triethylenetetramine ligand is given in Figure 1. Thymine (deprotonated at N(3)) will probably coordinate via N(3). The two exocyclic oxygens (at C(2) and C(4)) are then in a favorable position to hydrogen bond to the NH$_2$ or NH groups of the trien chelate (Figure 1A). The N(3) in the cytosine

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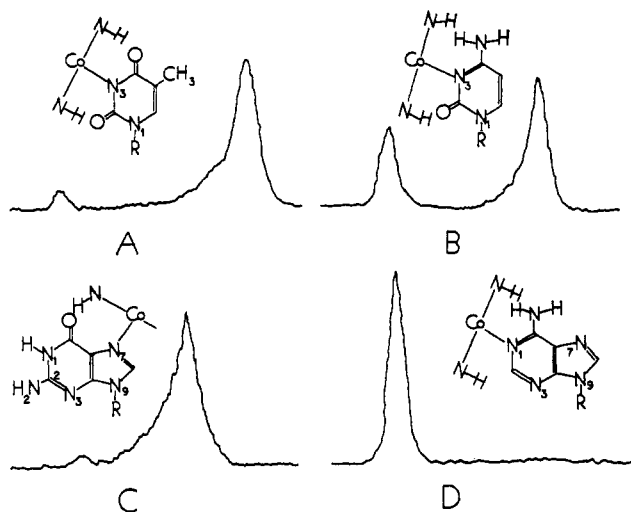
Figure 1. Scan of radioactivity of electrophoretic charts of the reaction mixtures of [Co(trien)Cl₂]Cl (0.1 *M*, pH 7, room temperature) with the nucleosides (after 72 hr) (A) dT (3.4 × 10⁻⁴ *M*), (B) dC (1.9 × 10⁻⁴ *M*), (C) dG (2.2 × 10⁻⁴ *M*), and (D) dA (0.9 × 10⁻⁴ *M*). In every case, the slower moving peak (on the left) moves as the control deoxynucleosides.

base of dC also is the only likely coordination site. Whereas exocyclic oxygen at C(4) is in a favorable position to accept hydrogen bonds (Figure 1B), the exocyclic amino group at C(2) will interact repulsively. Guanine (in dG) will probably coordinate *via* N(7). In such a case, the exocyclic oxygen at C(6) can accept hydrogen bonds (Figure 1C). Alternatively, dG could be deprotonated and coordinate *via* N(1). Interactions similar to those for dC would then be expected. *There are no exocyclic oxygens on the adenine. Only repulsive interactions are expected for coordination of dA via either N(7) or N (1) (Figure 1D).*

Details of the electrophoretic study are given in Table I and some actual scans are given in Figure 1.

Table I. Per Cent Reaction of Deoxyribonucleosides[a] with [Co(trien)Cl₂]Cl

Nucleoside	1 Day	3 Days
	[Co] = 0.025 *M*	
dT	65	65
dG	45	50
dC	10	10
dA	0	0
	[Co] = 0.1 *M*	
dT	85–90	90–95
dG	65	>95
dC	10	65–70
dA	0	0

[a] Nucleoside concentrations are given in the caption to Figure 1.

Clearly, dT and dG, which have only H-bond accepting exocyclic groups, react to the greatest extent. Additionally, dT, which has two H-bond acceptor groups, reacts most rapidly. By contrast, dA did not react, even after 3 weeks. The pyrimidine nucleoside dC, with both exocyclic oxo and amino groups, reacted slowly and to a moderate extent. Furthermore, the complexes formed decompose (to as yet unidentified products), and the complex formed from dC decomposes most rapidly. This decomposition is quite slow;
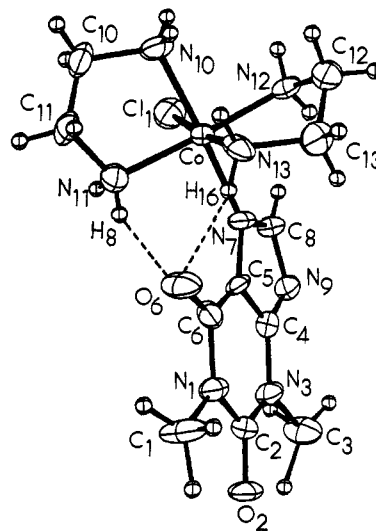

Figure 2. A perspective view of the *cis*-[theophyllinatochlorobis-(ethylenediamine)cobalt(III)]⁺ cation. The interligand hydrogen bonds are indicated by dashed lines.

after 23 days at room temperature ([Co] = 0.1 *M*), approximately one-third of this complex had decomposed.

The clarity of these results prompted us to seek some additional verification of these findings. From the extensive studies on the chemistry of Co(trien) systems, it is known that the trans configuration is not favored.[11] We wished to know then whether hydrogen bond donation to an exocyclic oxygen was possible for a complex with a cis arrangement of ligands. After much difficulty, we were able to separate *cis*-[Co(en)₂(theophyllinato)Cl]Cl from its trans isomer.[12] Crystals containing this cation suitable for X-ray diffraction analysis were difficult to obtain. However, we were finally able to crystallize the complex as the perchlorate salt. The crystals are monoclinic, space group $P2_1/n$, with cell constants $a = 14.878$ (9) Å, $b = 9.108$ (4) Å, $c = 14.286$ (7) Å, and $\beta = 93.91$ (5)°. The crystals grow as monoclinic prisms, and the crystal used in data collection had dimensions 0.10 × 0.10 × 0.25 mm³. Intensity data were collected on a Syntex P1 computer-controlled diffractometer equipped with a graphite-crystal monochromator. The diffractometer was operated in the θ–2θ scan mode and Mo Kα radiation was employed. The structure was solved by standard heavy-atom methods. Full-matrix least-squares refinement, based on 2381 reflections with $I > \sigma(I)$, has led to final unweighted and weighted *R* values of 0.111 and 0.084, respectively. These residuals are somewhat high for counter data due to a complex disordering of the perchlorate anion.[13] Positions for the hydrogen atoms were determined from a difference Fourier map at an intermediate stage in the analysis. The parameters for the hydrogen atoms have not been refined.

The overall geometry of the complex is illustrated in Figure 2. The cobalt atom is octahedrally coordinated with the six coordination sites occupied by the four nitrogen atoms of the ethylenediamine ligands, disposed in a

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cis conformation, a chlorine atom, and N(7) of the theophylline anion. The bond lengths and angles in the complex cation are in good agreement with values found in the trans isomer[9] and will be described in detail elsewhere.[13] The presence of the interligand hydrogen bond system between the chelated ethylenediamine ligands and the carbonyl group at C(6) of the pyrimidine ring (Figure 2 and Table II) is in keeping with our

Table II. Distances (Å) and Angles (deg) in the Interligand Hydrogen Bonds, D–H···A

D	H	A	H···A	D···A	∠D–H···A
N(11)	H(8)	O(6)	2.1	2.942	153
N(13)	H(16)	O(6)	2.0	2.814	158

explanation of the electrophoretic results.

Our immediate objective was the understanding of the basic interaction of complexes with nucleic acid constituents. Our electrophoretic and structural studies indicate that high selectivity can be achieved by taking advantage of the hydrogen bonding and repulsive interactions between incoming nucleosides and coordinated ligands. The cis-β-[Co(trien)Cl₂]Cl reagent may have some utility in the types of studies suggested by Leonard.[8]

(14) (a) Department of Chemistry. (b) Department of Biophysics.

Luigi G. Marzilli,* [14a] Thomas J. Kistenmacher* [14a]
Paul E. Darcy,[14a] David J. Szalda,[14a] Michael Beer* [14b]
Departments of Chemistry and Biophysics,
The Johns Hopkins University
Baltimore, Maryland 21218

## Photolysis of an α-Hydroperoxy Ketone. A Type-II Process Involving the Hydroperoxy Group and 1,2-Dioxetanes

Sir:

Extensive studies of the type-II photolysis of ketones are reported.[1] It is now commonly accepted that C–H hydrogen atom abstraction occurs through a quasi-six-membered ring to give a 1,4-biradical. Considering the ease of hydrogen atom abstraction from hydroperoxides,[2] a facile type-II process might be expected from the photolysis of α-hydroperoxy ketones. In addition closure of the 1,4-biradical produced from an α-hydroperoxy ketone would lead to a 1,2-dioxetane, a unique peroxide that has generated considerable interest recently.[3] To test these proposals, the photolysis of 1,2-diphenyl-2-hydroperoxy-1-propanone (**1**)[4] in carbon

tetrachloride solution was studied. The photolyses were carried out in degassed solutions on a merry-go-round[5] with a 100-W Hanovia high-pressure lamp. A potassium dichromate–potassium carbonate filter solution was used to isolate the 302.5–313.0-nm region.[6]

Benzoic acid and acetophenone are produced in quantitative chemical yield from the photolysis of 0.050–0.50 M solutions of **1**. The yield of the acid was determined by nmr, while the yield of acetophenone was obtained by nmr and glc. These products can be explained by the type-II scheme below (Scheme I). A search

Scheme I
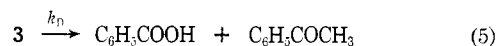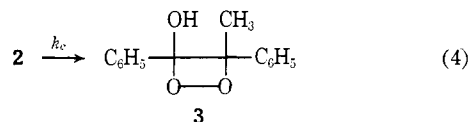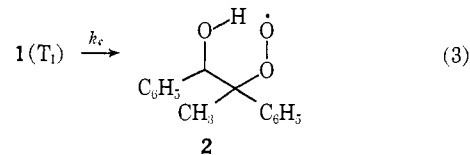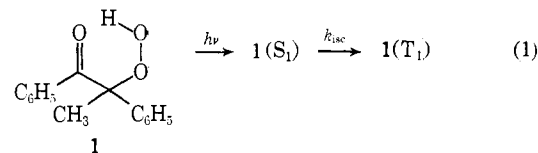
was made for oxygen and 1,2-diphenyl-1-propanone, the products expected from fragmentation of the biradical **2**. Neither of these products was observed where yields greater than 1% would be detected. In part, the lack of fragmentation of **2** could be due to substitution at the α-position in **1**. For example, 10% cyclization occurs with butyrophenone, while α-methyl and α-gem-dimethyl derivatives give 29 and 89% cyclization, respectively.[7] Alternatively, if the activation energies for cyclization and fragmentation of **2** parallel the heats of these reactions, cyclization ($\Delta H_r^\circ \simeq -56$ kcal/mol)[8] would be favored over fragmentation ($\Delta H_r^\circ \simeq -48$ kcal/mol).[8] Conceivably, the hydroperoxy ketone could undergo decomposition by a radical chain process, where an alcohol (1,2-diphenyl-2-hydroxy-1-propanone) and oxygen are among the expected products.[9] Neither of these products was detected. Lastly, energy transfer from **1** to carbon tetrachloride[10] appears unlikely. The expected products from such a process (chloroform, hexachloroethane, and hydrogen chloride) were not detected or produced in a chemical yield no greater than 2%.

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