why *cis*-dichlorodiammineplatinum(II), in addition to being a useful anticancer agent, is an activator of other anticancer drugs.[11]

The title molecule is of further interest in that recent studies have shown that $K(PtCl_3Me_2SO)$ complexes directly and efficiently to the base functions of denatured DNA.[12] One to one complexation is observed with cytosine, guanine, and thymine bases, while 1:2 complexation is observed for the adenine bases. This difference in the complexation behavior of the adenine bases is clearly consistent with the structure reported here and provides a potentially useful method for sequencing the adenine bases in DNA using electron microscopy.[12]

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Colin James Lyne Lock,* Robert Anthony Speranzini Graham Turner

Institute for Materials Research, McMaster University Hamilton, Ontario, Canada L8S 4M1

John Powell

Lash-Miller Chemical Laboratories, University of Toronto Toronto, Ontario, Canada M5S 1A1

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Resonance Raman Spectra of Liganded and Unliganded Carp Hemoglobin in Both R and T States

Sir:

Unliganded mammalian hemoglobins (Hb) adopt a thermodynamically stable conformation exhibiting a low ligand affinity, denoted the T state. The binding of oxygen and other ligands or oxidation is usually accompanied by a transition to a different, high affinity, conformation, denoted the R state, and the cooperative ligand-binding properties of hemoglobin are a consequence of the reversible transition between these two forms.[1] The nature of the transduction mechanism whereby ligation or oxidation of the pentacoordinate ferroheme controls this conformational equilibrium, and reciprocally, whereby the protein conformation determines the apparent ligand affinity at the heme, is a matter of keen interest.[2]

The most widely known and completely articulated proposal is the "trigger mechanism" elaborated by Perutz[1,3] following suggestions of Williams[4] and Hoard.[5] It includes a proposed coupling between protein conformation and the spin state and position of iron: the five-coordinate high-spin Fe(II) of an unliganded heme in Hb lies substantially out of the mean porphyrin plane and is considered to be held in a stressed state by tension exerted through the protein. Upon oxygenation, the Fe atom becomes low spin and moves into the porphyrin plane with a concomitant release to tension. However, this mechanism has been seriously questioned, and other views of the nature of the stresses (forces) on the heme group and resulting strains (deformations) have been presented.[2,6] We here report a resonance Raman (RR) spectroscopic study of deoxy- and cyanomet-Hb from the carp which shows no evidence of heme strain upon changing protein conformation.

At neutral pH, carp (*cyprinus carpio*) hemoglobin shows cooperative effects characteristic of a T $\rightleftarrows$ R switch upon ligation. However, at low pH, particularly in the presence of organic phosphates, both unliganded and liganded forms remain in the T state, whereas at high pH, both forms adopt the R conformation.[7] Therefore, it is possible to induce a change between T and R merely by changing the pH, providing a unique opportunity to examine in both low and high affinity conformations the properties of both liganded and unliganded hemes.

Resonance Raman spectroscopy provides a particularly sensitive probe of heme properties. A number of vibrational bands have been correlated to heme spin and oxidation state.[8] The underlying cause of observed variations in vibrational frequencies is perturbations in the porphyrin structure, variously considered to be doming occurring upon motion of the metal-atom[8] and changes in the diameter of the porphyrin "central hole".[9] In either case, these "structure-sensitive" Raman bands provide a means of investigating whether changes in protein conformation can indeed induce strains in the heme prosthetic group.

We have obtained[10] RR spectra of carp deoxy-Hb in the T state, pH 5.8 with 4mM inositol hexaphosphate (IHP), and in the R state, pH 8.8, usually at 4° in order to improve protein stability. Figure 1 presents the high-frequency region of the RR spectra obtained with laser frequencies near the visible (5145 Å) and Soret (4579 Å) heme absorptions; Table I lists the frequencies of the structure-sensitive bands for both the

Table I. Frequencies of Structure-Sensitive RR Bands for Hb and Cyanomet-Hb

Deoxy-Hb			Cyanomet-Hb		
	Carp[b,c]			Carp[c]	
Human[a]	T state[d]	R state[e]	Human[a]	T state[d]	R state[e]
1358 (p) vs	1354 (B,Q)	1355 (B,Q)	1374 (p) vs	1372 (B,Q)	1371 (B,Q)
1473 (p) m	1471 (B,Q)	1469 (B,Q)	1508 (p) m	1504 (B,Q)	1505 (B,Q)
1546 (dp) m	1545 (Q)	1544 (Q)	1564 (dp) m	1560 (Q)	1561 (Q)
1552 (ap) s	1557 (Q)[f]	1559 (Q)[f]	1588 (ap) s	1590 (Q)	1588 (Q)
1565 (p) m	1564 (B)	1565 (B)	1583 (p) m	1584 (B)	1586 (B)
1607 (dp) s	1604 (B,Q)	1603 (B,Q)	1642 (dp) vs	1642 (B,Q)	1641 (B,Q)

[a] Vs = very strong, s = strong, m = medium, p = polarized, dp = depolarized, ap = anomalously polarized; ref 8a. [b] Spectra taken at 4 °C. [c] B = 4579-Å excitation; Q = 5145-Å excitation; vs and s bands—estimated reproducibility, ±1 cm^{-1}; m bands—estimated reproducibility, ±2 cm^{-1}. [d] ~1.2 mM in heme, 0.1 M phosphate-citrate, pH 5.8, plus 4 mM IHP. [e] ~1.2 mM in heme, 0.1 M Tris, pH 8.8. [f] This feature appears as a shoulder in spectra with the abscissa expanded, and is clearly resolved from the adjacent (1545 cm^{-1}) peak in successive spectra taken with parallel and perpendicular orientation of the polaroid analyzer.

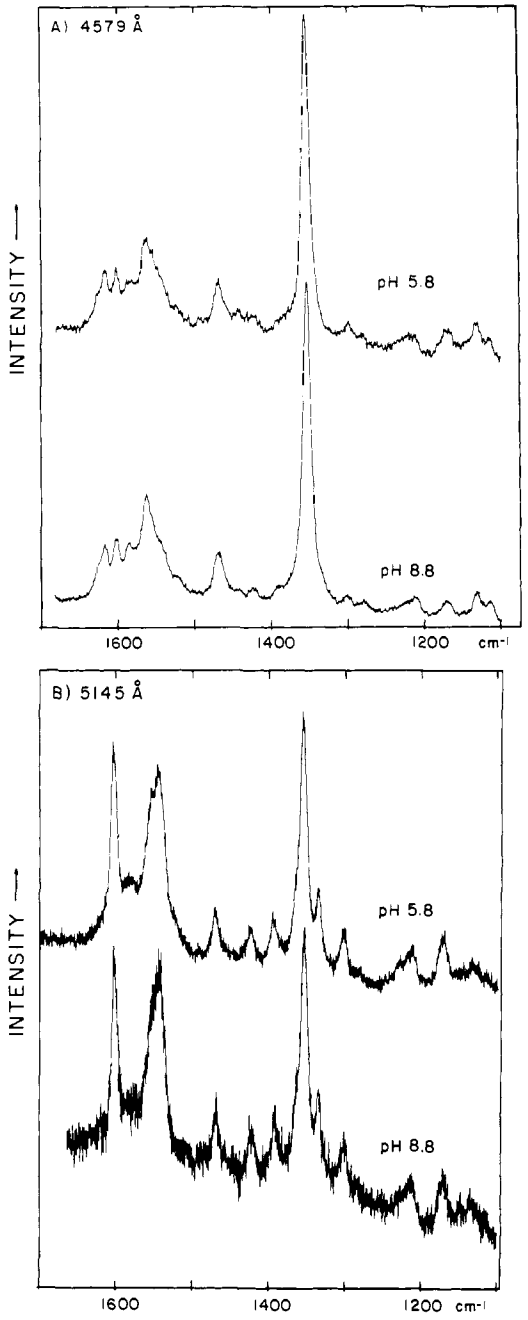

Figure 1. High-frequency resonance Raman spectra of carp deoxyhemoglobin: (A) 4579-Å (35 mW power, 4.5 cm^{-1} slits, 23 °C) and (B) 5145-Å (60 mW power, 3.7 cm^{-1} slits, 4 °C) excitation is shown. Upper spectra, T state, 0.1 M phosphate-citrate, pH 5.8, plus 4 mM IHP; lower spectra, R state, 0.1 M Tris, pH 8.8. A backscattering geometry (180°), Ar ion laser excitation, and spinning glass cells were used.[10] Differences between spectra at 23 and 4 °C were 3 cm^{-1} or less.

T and R states, as well as those for T state human deoxy-Hb.[8a] Within experimental error (see footnote *c*, Table I), there is no change in the frequencies or intensities of the structure-sensitive bands[11] or of any other band between 100 and 1700 cm^{-1}.

Carp carbonmonoxy-Hb also exhibits a pH-induced change between T and R states. Because Hb(CO) is photosensitive, and thus difficult to study by RR, we have examined the structural analogue, cyanomet-Hb. In this liganded Hb, the occurrence of an R-T conformational transition is evidenced by the large optical difference spectra induced by the addition of IHP at pH 5.8.[7e,12] The RR spectra of carp cyanomethemoglobin in R state, pH 8.8, and in the T state, pH 5.8 plus 4 mM IHP, have been obtained. Peak positions of the structure-sensitive bands, as well as those of human R-state cyanomet-Hb,[8a] are listed in Table I. The RR spectra of the ferric, low-spin, carp cyanomet-Hb show the substantial differences from those of the ferrous high-spin, deoxy-Hb observed in human hemoglobin.[8a] Again, for bands between 100 and 1700 cm^{-1} we find no shift in peak positions or significant changes in intensities upon the pH-induced change in protein conformation (Table I).

Therefore, although the heme-ligand affinities and binding rates differ by one to two orders of magnitude in T and R states, and the optical spectra of both unliganded and cyanomet hemes are altered, frequencies of the observed RR bands which are believed to be heme-structure sensitive are not affected. The postulate of significant strain on an unliganded T-state ferroheme would suggest that the strain would be released in the R state with a concomitant alteration of structure. Conversely, it might be imagined that a liganded heme would undergo strain if the protein were changed from the R to the T form. However, neither for a liganded nor an unliganded heme do we find the structure-sensitive bands to indicate that the change in the protein environment alters the heme geometry. Recent RR studies of chemically modified hemoglobins[13,14] and an EXAFS study of a mutant human Hb[6f] have reached the same conclusion regarding unliganded Hb. The changes in electronic spectra observed upon changing protein conformation[3e] may arise in part from perturbations of the excited state; indeed, it has been shown that the geometry of the excited state of a metalloporphyrin is sensitive to the protein structure.[15] To within the limitations of RR and EXAFS, there is at present no direct evidence of differential protein-induced *ground-state* heme strain.[16,17]

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(11) In one of five samples at pH 8.8, the 1354 cm^{-1} peak showed a small high-frequency shoulder. This shoulder was only seen in one spectrum under 4579-Å excitation and not with 5145-Å excitation, and is believed to be a result of partial protein denaturation.
(12) These difference spectra, originally attributed to changes in optical ab-

sorption by the cyanoferriheme (ref 7e), in fact result from a release of CN^- (Q. H. Gibson, private communication). This release we attribute to a decrease in affinity for CN^- upon transition from the high-affinity R state to the low-affinity T state.
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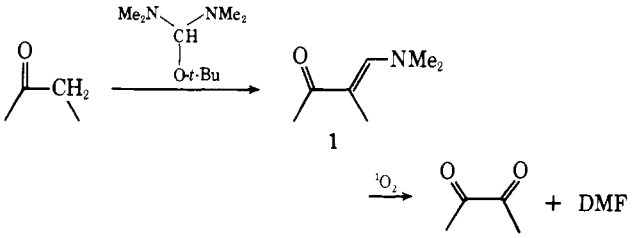
(16) This conclusion does not apply to Hb(NO), (see A. Szabo and L. D. Barron, *J. Am. Chem. Soc.*, **97**, 660 (1975)), which has substantially different properties due to the strong trans effect of NO. See ref 3e.
(17) As a further probe of porphyrin properties, epr measurements have been initiated.

D. M. Scholler, B. M. Hoffman,* D. F. Shriver*
Department of Chemistry, Northwestern University
Evanston, Illinois 60201
Received August 16, 1976

A Novel Method for Converting Ketones to α-Diketones. The Reaction of Enamino Ketones with Singlet Oxygen[1]

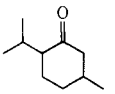
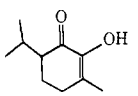
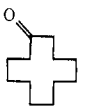
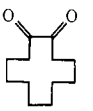
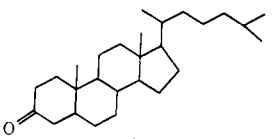
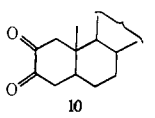
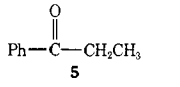
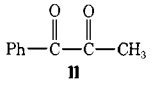
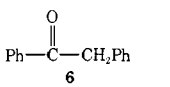
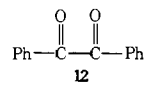
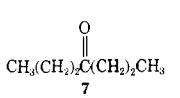
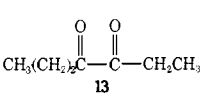
Sir:

The oxidation of a methylene group α to a ketone to form an α-diketone is an important functional group transformation which has many applications in organic synthesis.[2] Conventional reagents for accomplishing this transformation, including selenium dioxide[3a] or alkyl nitrites in acid or base,[3b] often lead to further oxidation or side reactions because of the strong reaction conditions employed. Other methods involving α-halogenation or α-oxygenation followed by further oxidation,[4] or α-formylation followed by dithiane formation and hydrolysis[2] may be limited to special systems.



We now report a new method for conversion of a ketone to an α-diketone, which is generally applicable and *mild enough to use on complex systems containing sensitive functional groups.* The procedure consists of the transformation of the ketone to the enamino ketone (**1**) by reaction with an alkoxybis(dimethylamino)methane (a reactive derivative of DMF)[5,6] followed by cleavage of the carbon-carbon double bond using singlet oxygen.[7-14] The fact that one does not need to isolate the intermediate (**1**) lends simplicity to the method, as outlined below. Table I lists the ketones oxidized, reaction conditions, and products. The high yields in the conversion of menthone (**2**) and cholestanone (**4**) to the corresponding diones **8** and **10** may be contrasted with the reported poor results in the use of selenium dioxide.[15] Of particular interest is the oxidation of ketone **14**, an intermediate in a current natural product synthesis.[16] Conversion of **14** to **15** took place in 85% yield under the conditions outlined below despite the presence in the molecule of several sensitive functional groups in a strained tricyclic system.

Table I. Conversion of Ketones to Diketones

Ketone	Enamino ketone[c]	α-Diketone[d]	Overall yield, %
 **2**	a, 55 °C, 24 h	b	 **8**	81
 **3**	a, 60 °C, 24 h	b	 **9**	82
 **4**	a, 55 °C, 18 h	b	 **10**	87
 **5**	a, 55 °C, 18 h	b	 **11**	68
 **6**	a, 55 °C, 3 h	b	 **12**	89
 **7**	a, 55 °C, 24 h	b	 **13**	74

[a] Reaction of the ketone with a slight excess of *tert*-butoxybis(dimethylamino)methane. Reaction times were determined by the disappearance of the IR carbonyl absorption of the starting ketone. [b] Photooxygenation of the enamino ketone in methylene chloride at −78 °C using 3–5 mg of bisacenapthalenethiophene and a Sylvania DWY 650-W lamp (workup involved repeated washing with water, drying, removal of the sensitizer with charcoal, filtering, concentrating, and drying in vacuo to give pure α-diketone). [c] All enamino ketones have been isolated, characterized, and photooxygenated to give the same products as those formed in the one-step conversion described. [d] All α-diketones were identified by IR, NMR, comparison with authentic material, and/or elemental analysis.