

Table I

Starting material	Reducing agent	Yield (%)	Cis/trans	Ref
1	LiAlH ₄	73	3.0	12
	Na-DMSO	72	0.11	14
	<i>n</i> -Bu ₃ Sn-H	82	2.5	14
	CH ₃ MgBr	72	2.5	<i>d</i>
	Cr(II)	25	All cis	<i>e</i>
	NaH-HMPT	10-55	0.78	<i>f</i>
6	NaBH ₄	79 ^b	1.8	This work
	<i>n</i> -Bu ₃ Sn-H	84	All cis	14
	Zn-HOAc	95	9	<i>g</i>
	Cr(II)	32	All cis	<i>e</i>
	Na-DMSO	71	0.05	<i>d</i>
	NaBH ₄	90 ^b	1.8	This work
7 ^c	<i>n</i> -Bu ₃ Sn-H	70-84		<i>e</i>
	NaH-HMPT	<i>a</i>		<i>f</i>
	Na- <i>t</i> -AmONa	55		<i>f</i>
	NaBH ₄	80 ^b		This work

^a Reported to afford 3-bromo-2,4-dimethylpenta-1,3-diene (70%).
^b Yield typical of several runs. ^c 1,1-Dibromo-2,2,3,3-tetramethylcyclopropane. ^d C. L. Osborn, T. C. Shields, B. A. Shoulders, C. G. Gardenas, and P. D. Gardner, *Chem. Ind. (London)*, 766 (1965).
^e H. Nozaki, T. Aratani, and R. Noyori, *Tetrahedron*, **23**, 3645 (1967). ^f J. Moreau and P. Canbere, *ibid.*, **27**, 5741 (1971).
^g C. L. Osborn, T. C. Shields, B. A. Shoulders, J. F. Krause, H. V. Cortez, and P. D. Gardner, *J. Amer. Chem. Soc.*, **87**, 3158 (1965).

reactions (Table I). The product distribution for the reaction of sodium borohydride with **1** is similar to that obtained with lithium aluminum hydride,¹² methylmagnesium bromide,¹³ and tri-*n*-butyltin hydride,¹⁴ the latter two of which are most probably radical reactions. A marked contrast is observed, however, with 9,9-dibromobicyclo[6.1.0]nonane (**6**). Whereas tri-*n*-butyltin hydride is reported to give exclusively the cis monobromide, sodium borohydride gave appreciable amounts of the trans compound as well. Consistent with the reaction in Scheme I, this difference can be readily explained by the expected decrease in steric constraints when borohydride is the hydrogen source instead of the more bulky tin hydride.

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Detection of Hydrogen-Deuterium Exchange in Purines by Laser-Raman Spectroscopy. Adenosine 5'-Monophosphate and Polyriboadenylic Acid

Sir:

The phenomenon of hydrogen-deuterium exchange at the 8-C ring position of purines was first detected using nuclear magnetic resonance techniques^{1,2} and has

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since generated considerable attention. In D₂O solutions of purine nucleosides and nucleic acids, the 8-CH group is exchanged slowly by comparison with the near instantaneous rates of exchange of NH and OH groups. At elevated temperatures, however, the "slow" exchange reaction is greatly accelerated.

As a practical application of these results several workers^{3,4} have reported the labeling of DNA with tritium for use in hybridization studies. Tritium labeling has also been exploited in determining the kinetics of the slow exchange reaction⁵ and in demonstrating the dependence of the pseudo-first-order rate constant (k_p) upon the conformational structures of nucleic acids.⁶

In this communication we report the effect of deuterium exchange of the 8-CH group on the laser-Raman scattering spectra of adenosine 5'-monophosphate (5'-rAMP) and polyriboadenylic acid (poly(rA)). At the same time we show that the Raman spectrum provides a far simpler method than tritium labeling for determination of the rate constant in purine nucleotides. In fact the Raman technique described here is so simple that it permits the rapid determination of rate data on different types of nucleic acids very easily.

The present results are of importance for several reasons. First, the spectral effects of isotope exchange at 8-C must be identified so that the Raman technique can be profitably employed in studying the conformational structures of RNA and DNA in D₂O solutions.⁷ At least one Raman investigation has been published recently⁸ in which the conclusions relating to polynucleotide structure might be affected by a further consideration of the exchange reaction. Second, the simplified procedure for measurement of the exchange kinetics that is afforded by Raman spectroscopy makes feasible the study of comparative rates of exchange in different nucleic acids to reveal differences in secondary structure. We shall report our results on polynucleotides in a forthcoming publication. Third, the Raman technique may be of value in studying the accessibility to solvent molecules of purine nucleotides in other biological systems (*e.g.*, cyclic AMP, adenine-containing coenzymes, nucleoproteins, and the like). Finally, the frequency shifts that result from 8-C deuteration are of interest for verifying recent normal coordinate calculations on adenine derivatives.⁹

Poly(rA) (Miles) and 5'-rAMP (Sigma) were dissolved in D₂O (99.8%, Aldrich) at concentrations of 4 and 10% by weight, respectively. Solutions were brought to pD 7 by addition of NaOD and loaded into Raman cells for thermostating at 80° to promote exchange. Raman spectra were recorded at 0° after heating the cells for the intervals specified below. All other

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(7) K. A. Hartman, R. C. Lord, and G. J. Thomas, Jr., in "Physico-Chemical Properties of Nucleic Acids," Vol. 2, J. Duchesne, Ed., Academic Press, New York, N. Y., 1973.

(8) K. G. Brown, E. J. Kiser, and W. L. Peticolas, *Biopolymers*, **11**, 1855 (1972).

(9) M. Tsuboi, S. Takahashi, and I. Harada, ref 7.

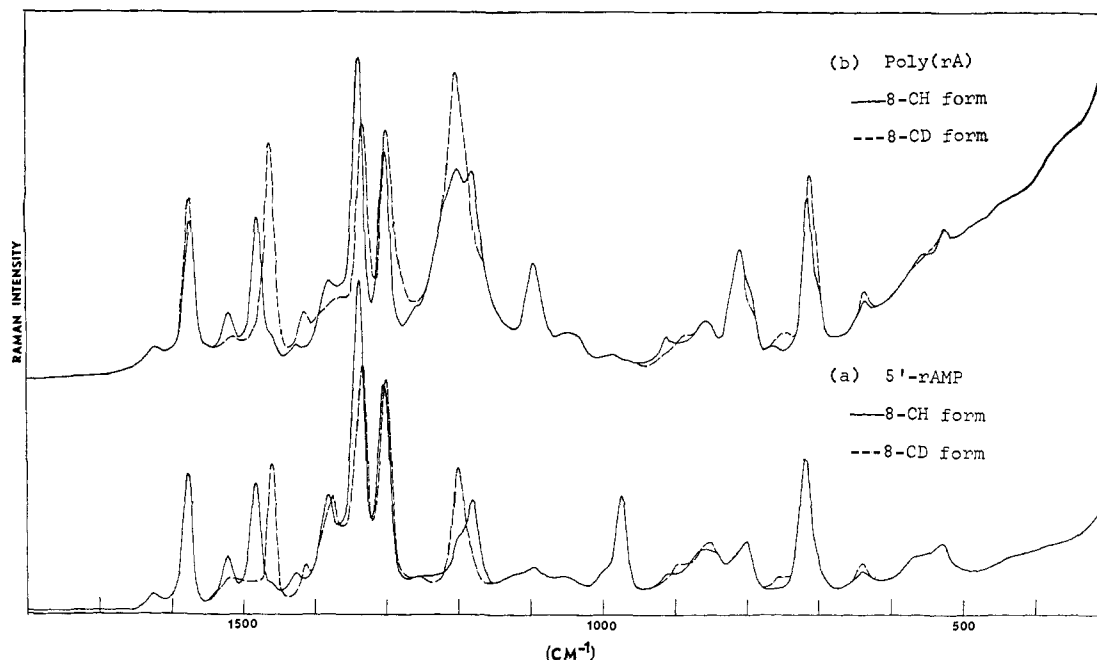


Figure 1. Raman spectra of (a) 5'-rAMP, 10 weight %, and (b) poly(rA), 4 weight %, in D_2O solutions. Solid curves (—) are before exchange of the 8-CH group. Dashed curves (---) are after complete exchange.

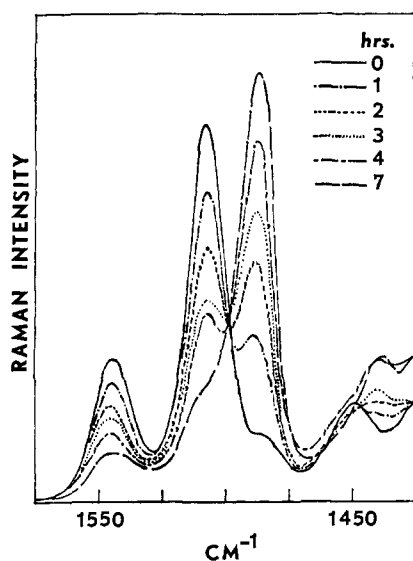


Figure 2. Raman spectra in the region $1450\text{--}1500\text{ cm}^{-1}$ of 5'-rAMP as a function of the time of heating at 80° to promote exchange.

handling was carried out in the cold (4°) in order to minimize further exchanges. Full details of sample handling and instrumentation are given elsewhere.^{7,10}

Figure 1a shows the Raman spectra of 5'-rAMP before and after exchange of the 8-CH group by deuterium. Similar data for poly(rA) are given in Figure 1b. These results implicate the frequencies near 1520, 1485, 1430, 1384, 1344, 1309, 1185, and 915 cm^{-1} in motions of the 8-CH group and those at 1462, 1410, 1378, 1332, 1300, 1201, 895, 850, 750, and 635 cm^{-1} in motions of the 8-CD group. It is clear that the normal vibrations which give rise to the strong Raman scattering of the adenine residue in the region $1200\text{--}1500\text{ cm}^{-1}$ contain

(10) G. C. Medeiros and G. J. Thomas, Jr., *Biochim. Biophys. Acta* 247, 449 (1971).

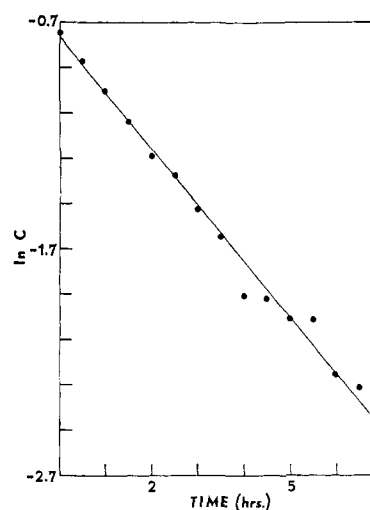


Figure 3. Semilogarithmic plot of the concentration of nonexchanged 5'-rAMP vs. time of heating at 80° . Relative concentrations of nonexchanged and exchanged species were determined from the intensity ratios of 1485 and 1462 cm^{-1} lines, respectively, to the 980-cm^{-1} line.

significant contributions from the in-plane 8-CH deformation. The 8-CH and 8-CD forms of adenine are most easily distinguished by their well-resolved lines at 1485 and 1462 cm^{-1} , respectively.

Figure 2 shows the scattering in the $1400\text{--}1500\text{-cm}^{-1}$ region of 5'-rAMP as a function of the time of heating at 80° . Since the Raman lines at 721 and 980 cm^{-1} are unaffected by the exchange reaction (Figure 1a), either one or both may be used to normalize the Raman intensities at 1485 and 1462 cm^{-1} and thereby to quantitate the extent of exchange in 5'-rAMP.

Accordingly, Figure 3 shows a semilogarithmic plot of the concentration of unreacted material (8-CH) vs. the time of heating. This plot is reasonably linear over the period required to effect "complete" exchange, demon-

strating the pseudo-first-order kinetics. From Figure 3 it is found that k_{ψ} has the value 0.25 hr^{-1} at 80° . This result is in agreement with the values obtained by tritium exchange studies on related adenine derivatives.^{5,6,11} We find the temperature dependence of k_{ψ} gives an activation energy of 23 kcal/mol.

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(11) Note: Attention has been drawn previously to the effects of deuterium exchange at 8-C on the Raman spectra of 5'-rIMP by Medeiros and Thomas¹⁰ and by Hartman, Lord, and Thomas.⁷ We have been informed that similar observations were also made more recently by Erfurth and Peticolas (S. C. Erfurth and W. L. Peticolas, private communication).

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Preparation, Structure, and Reactions of an Organometallic [2.2.1] Propellane, the Bis(triphenylphosphine)platinum Complex of $\Delta^{1,4}$ -Bicyclo[2.2.0]hexene¹

Sir:

The small ring propellanes are of unusual interest with regard to structural and chemical effects at saturated centers.²⁻⁷ In an attempt to prepare a hetero[2.2.1]-propellane, we have examined the reaction of bis(triphenylphosphine)(ethylene)(platinum) (I) with $\Delta^{1,4}$ -bicyclo[2.2.0]hexene (II); the strained ring olefin II should behave like cyclopropene⁸ and displace ethylene from I. The properties of the expected product should show to what extent the presence of platinum modifies structure and reactivity in such small ring propellanes.

The bicyclohexene, II, was prepared as a mixture with 1,2-dimethylenecyclobutane (III) as previously reported.⁹ The product mixture was dissolved in toluene and maintained below -80° to avoid a Diels-Alder reaction between II and III. The platinum complex, I, was added to the toluene solution under nitrogen and the temperature was maintained at -80° for 30 min.

(1) This investigation was supported by a grant from the National Science Foundation.

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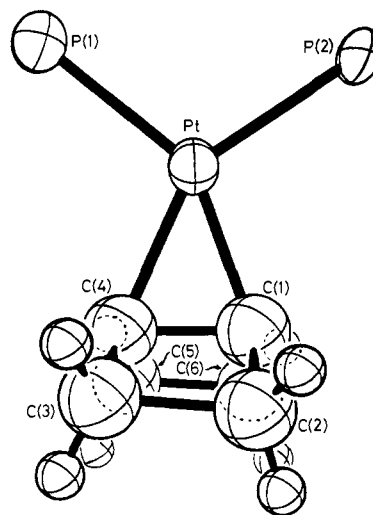
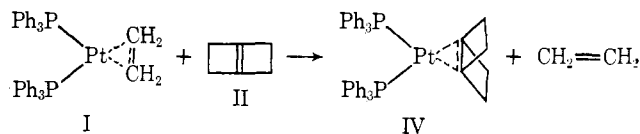


Figure 1. $\text{Pt}(\text{C}_6\text{H}_5)(\text{PPh}_3)_2$ from a viewpoint normal to the Pt, C(1), C(4) plane and above the platinum atom.

Upon warming to -20° , a clear solution was obtained to which two volumes of ether was added. After filtration, clear light-yellow air-stable crystals of bis(triphenylphosphine) ($\Delta^{1,4}$ -bicyclo[2.2.0]hexene)platinum (IV) slowly separated.



The structure of IV was determined by X-ray diffraction, intensity data being collected using a Picker four-circle diffractometer. Crystal data for $\text{Pt}(\text{C}_6\text{H}_5)(\text{PPh}_3)_2$: orthorhombic; $P2_12_12_1$; $Z = 8$; $d_{\text{measd}} = 1.54$ (by flotation), $d_{\text{calcd}} = 1.56 \text{ g/ml}$; $a = 17.726$ (3), $b = 9.748$ (2), $c = 19.724$ (3) Å; $R = 2.8\%$ for 1512 observed reflections. The coordination sphere of platinum and details of the olefin ligand are shown in Figure 1. Important bond lengths (in Å) are: Pt-P(1), 2.29; Pt-P(2), 2.29; Pt-C(1), 2.07; Pt-C(4), 2.14; C(1)-C(4), 1.55; average of other six C-C bond lengths, 1.54. The separation of the olefinic carbon atoms is close to normal for a single σ -bond and the hydrocarbon ligand is significantly bent about the C(1), C(4) vector. The angle between the two four-membered rings is approximately 123° .

Formation of IV provides a means of separating II and III by taking advantage of the higher coordinating power of II toward platinum. The stability of IV makes it a convenient way to store II, since a yet stronger ligand should displace II from the complex. A solution of IV in methylene chloride was treated with an excess of carbon disulfide at 0° and the volatile product was distilled from the reaction mixture. The ^1H nmr spectrum of the distillate (in CD_2Cl_2 solution) at 25° showed a singlet at δ 3.21 which is characteristic of II.⁹ The intensity of this singlet decreased over a period of hours; the cause of this decrease has not been determined as yet, but the product derived from the Diels-Alder reaction of II with 1,2-dimethylene cyclobutane was not found and thus II does not isomerize to III at room temperature. Further proof that the distillate is II was provided by addition of cyclopentadiene; the expected Diels-Alder reaction occurred and the nature