Figure 1. Relative energies (kcal/mol) of the ground states and the excited states of the n → π* transition of acetone in CCl₄ and H₂O solvent.

Table I. Heats of Solution (ΔH_s) of Benzophenone and Enthalpies of Transfer of Benzophenone from Hexane to Other Solvents ($\delta\Delta H^{\text{ground state}}$ (hexane → solvent)) in kcal/mol

Solvent	Dielectric constant[a]	Dipole moment,[b] D	$\Delta H_s{}^c$	$\delta\Delta H^{\text{ground state}}$ (hexane → solvent)
Hexane	1.9	0.0	6.53	0.00
Carbon tetra-chloride	2.2	0.0	4.54	−1.99
Benzene	2.3	0.0	4.18	−2.35
Methyl acetate	7.3	1.7	4.59	−1.94
Acetonitrile	3.9	3.4	5.31	−1.22
Chloroform	4.9	1.1	2.45	−4.08
Ethanol	25.7	2.9	5.56	−0.97

[a] From C. Marsden and S. Mann, "Solvents Guide," Interscience, New York, N. Y., 1963. [b] From A. L. McClelan, "Tables of Experimental Dipole Moments," W. M. Freeman, San Francisco, Calif., 1963. [c] Molar heat of solution (integral), measured using an LKB 8700 calorimeter, benzophenone concentration 0.006–0.03 M, all values better than ±0.1 kcal/mol.

Table II. The Solvent Blue Shift ($\delta\Delta E^{n\rightarrow\pi^*}$ (hexane → solvent)) and the Energy of Transfer of the Benzophenone n → π* Excited State from Hexane to Other Solvents ($\delta\Delta H^{\text{excited state}}$ (hexane → solvent)) in kcal/mol[a]

Solvent	λ_{max},[b] nm	$\delta\Delta E^{n\rightarrow\pi^*}$ (hexane → solvent)	$\delta\Delta H^{\text{excited state}}$ (hexane → solvent)
Hexane	347.10	0.00	0.00
Carbon tetra-chloride	344.11	0.72	−1.27
Benzene	343.05	0.97	−1.38
Methyl acetate	342.11	1.20	−0.74
Acetonitrile	338.87	2.00	0.78
Chloroform	333.70	2.46	−1.62
Ethanol	333.11	3.46	2.49

[a] $\delta\Delta H^{\text{excited state}}$ (hexane → solvent) = $\delta\Delta H^{\text{ground state}}$ (hexane → solvent) + $\delta\Delta E^{n\rightarrow\pi^*}$ (hexane → solvent). [b] From ref 4.

tetrachloride, benzene and chloroform) exhibit a similar solvent effect on the ground state and on the excited state, with the effect on the latter being somewhat damped in each case. This similarity in solvation of the ground and excited states has the effect of diminishing the magnitude of the solvent blue shift in these cases. It should be noted that the greatest solvent blue shift, here as in other examples of the n → π* transition, is
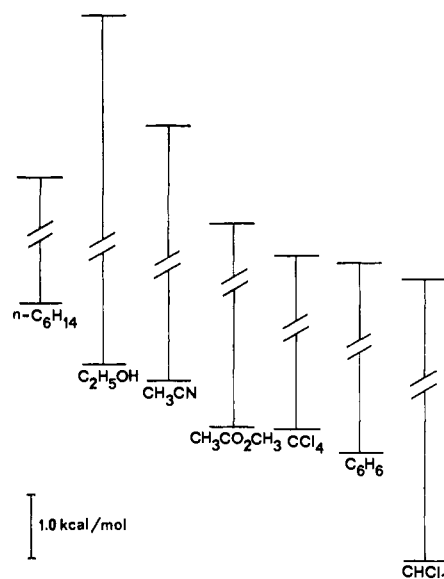

Figure 2. Relative energies of the ground states and the excited states of the n → π* transition of benzophenone in seven solvents.

observed for the H bonding solvent (ethanol); however, contrary to accepted views, this is clearly not a ground state effect. The effect on the excited state (2.49 kcal/mol) is 2.5 times greater than the effect on the ground state (−0.97 kcal/mol), the solvent effect on the excited state thus making the major contribution to the blue shift. On the other hand chloroform solvent, which exhibits by far the greatest degree of ground state solvation and should, therefore, on the basis of accepted reasoning, produce by far the greatest solvent blue shift, has in fact a blue shift which is considerably smaller than that produced by ethanol.

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Dehalogenations with Sodium Borohydride. Evidence for a Free Radical Reaction

Sir:

Reduction of alkyl and aryl halides with sodium borohydride is well known and has been reported, variously, to proceed via an SN1 process,[1] an SN2 process, or nucleophilic attack on halogen[2] depending on the structure of the halide. Only recently has evidence appeared suggesting dehalogenation by a free radical path.[3] In the course of our recent examination of the reaction of α-bromocyclopropyl trifluoroacetates[4] with hydride reagents to afford cyclopropanols,[5] it became apparent that gem-dibromocyclopropanes are appreciably reactive toward sodium borohydride as well, affording high yields of the corresponding mono-

(1) H. B. Bell and H. C. Brown, J. Amer. Chem. Soc., 88, 1473 (1966).
(2) H. M. Bell, C. W. Vanderslice, and A. Spehar, J. Org. Chem., 34, 3923 (1969).
(3) The photoreduction of iodobenzene in the presence of sodium borohydride proceeds with quantum yields in excess of unity; J. A. Barltrop and D. Bradbury, J. Amer. Chem. Soc., 95, 5085 (1973).
(4) J. T. Groves and K. W. Ma, Tetrahedron Lett., 5225 (1973).
(5) J. T. Groves and K. W. Ma, Tetrahedron Lett., 909 (1974).

bromides under the appropriate conditions. Our preliminary examination of this reaction supports a free radical chain reaction.

Thus, to a solution of 3 g of 7,7-dibromonorcarane (1) in 25 ml of dimethylformamide,[6] a 3 molar equiv of sodium borohydride was added while the mixture was exposed to air. The mixture was then stirred vigorously under an inert atmosphere. Within 10 min the mixture warmed spontaneously.[7] After 48 hr the reaction mixture was poured into 150 ml of water and extracted with ether to afford 1.58 g (79%) of *cis*- and *trans*-7-bromonorcarane (2a and 2b) in a ratio of 64:36. No starting material remained, and only trace amounts of norcarane were observed.

Evidence for the radical nature of this reaction is based upon several observations. There is, typically, a 5–10 min induction period and the reaction is inhibited by oxygen. Indeed, a reaction mixture in ethanol could be stirred in air for more than 12 hr with no material change in composition. Upon replacing the air with argon a vigorous reaction ensued with evolution of hydrogen. The reaction is also inhibited to a lesser extent by chloroform.

When the reaction was run with sodium borohydride in methanol-d_4, negligible deuterium was incorporated into the product. Conversely, reaction with sodium borodeuteride afforded deuterated 2, although at a significantly slower rate.[6] Accordingly, the new cyclopropyl hydrogen derives from the borohydride and not from the solvent. From competition experiments with borohydride–borodeuteride mixtures, we find an appreciable hydrogen isotope effect (k_H/k_D = 4.4), apparently the largest boron–hydrogen isotope effect reported to date.[8]

Further evidence regarding the mechanism of this reaction is obtained when 1 is reduced with sodium borohydride in the presence of iodobenzene.[9] Although the reaction of sodium borohydride with iodobenzene alone is negligible, even over prolonged periods, reaction of iodobenzene in the presence of 1 gave benzene and *bromo*benzene in addition to 2 (relative amounts 4:1:10.7). One compelling interpretation of this result is that a reactive intermediate is formed during the reaction of sodium borohydride with 1 which is also capable of abstracting iodine from iodobenzene. The resultant phenyl radical can either abstract hydrogen from borohydride to give benzene or bromine from 1 to afford bromobenzene. From the relative amounts of the products formed it is apparent that 1 is 4.3 times more reactive than iodobenzene toward this reactive intermediate.

Less clear is the nature of the initiation step. We have considered the possibility that this reaction may be mediated by an impurity in the sodium borohydride. However, commercial or analytical grade sodium borohydride, whether twice recrystallized or not, gave

essentially the same results. Oxygen seems to play some role in the initiation process. When a carefully degassed solution of 1 and sodium borohydride in ethanol were mixed, no reaction took place. Introduction of air or oxygen failed to cause reaction but addition of 15 μl of bromoform initiated reduction.

A mechanism consistent with these findings, involving a free radical chain process in bromocyclopropyl radicals (3) and borane radical anion (4), is shown in Scheme I.[10]

Scheme I
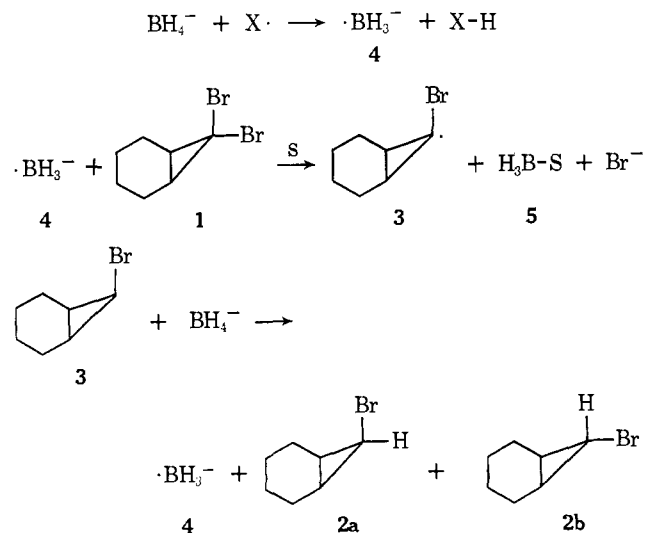
Evidence for the formation of borane derives from examination of the ^{11}B nmr spectrum of the reaction mixture in DMF which reveals the presence of trimethylamine borane (δ 8.0, q, J_{B-H} = 98 Hz)[11] and a second minor borane adduct (δ 14.1, q, J_{B-H} = 98 Hz) in amounts nearly equivalent to the amount of 1 reduced. The observed evolution of greater than stoichiometric amounts of hydrogen in hydroxylic solvents is expected to result from solvolysis of the borane solvate complex 5.

Chloromethane and other relatively unhindered alkyl halides have been reported to undergo dehalogenation with sodium borohydride *via* an SN2 process.[2] The reported high reactivity of carbon tetrachloride, affording both chloroform and methylene chloride, seems anomalous. In light of the results reported here a free radical reaction would seem at least as attractive. Evidence for this alternative is derived from product analyses of the reduction of carbon tetrachloride in the presence of iodobenzene. In addition to the expected products we find an 8:1 mixture of benzene and chlorobenzene. Thus, in analogy to the reaction of 1 in the presence of iodobenzene, the formation of benzene and chlorobenzene may be economically explained in terms of a chain reaction with chain transfer steps.

We have compared product distributions for this reaction with results obtained with other dehalogenation

(6) In addition to DMF, the reaction could be run in THF, diglyme, alcohols, and aqueous acetonitrile. Product yields in methanol were substantially reduced by reaction of borohydride with the solvent.

(7) After 15–30 min the exotherm subsided although only half of the starting material had been reduced.

(8) (a) R. E. Davis, C. L. Kibby, and C. G. Swain, *J. Amer. Chem. Soc.*, 82, 5950 (1960); (b) R. E. Dessy and E. Grannen, Jr., *ibid.*, 83, 3953 (1961); (c) R. E. Davis, E. Bromels, and C. L. Kibby, *ibid.*, 84, 885 (1962); (d) E. S. Lewis and R. H. Grinstein, *ibid.*, 84, 1158 (1962); (e) R. E. Davis and R. E. Kenson, *ibid.*, 89, 1384 (1967); (f) S. S. White, Jr., and H. C. Kelly, *ibid.*, 92, 4203 (1970).

(9) Relative amounts 1:1:2 in refluxing 6% aqueous acetonitrile.

(10) The halogen removal step may be viewed as a direct abstraction process or electron transfer to the cyclopropyl bromide followed by dissociation to form an alkyl radical, bromide ion, and borane.

(11) (a) Lit., δ 8.1, q, J_{B-H} = 98 Hz: D. F. Gaines and L. Schaeffer, *J. Amer. Chem. Soc.*, 86, 1505 (1964). (b) Diborane has been reported to react with DMF at 0° to form this product; V. N. Konoplev and V. D. Krasnoperova, *Zh. Neorg. Khim.*, 11, 2047 (1966).

Table I

Starting material	Reducing agent	Yield (%)	Cis/trans	Ref
1	LiAlH₄	73	3.0	12
	Na–DMSO	72	0.11	14
	n-Bu₃Sn–H	82	2.5	14
	CH₃MgBr	72	2.5	d
	Cr(II)	25	All cis	e
	NaH–HMPT	10–55	0.78	f
	NaBH₄	79ᵇ	1.8	This work
6	n-Bu₃Sn–H	84	All cis	14
	Zn–HOAc	95	9	g
	Cr(II)	32	All cis	e
	Na–DMSO	71	0.05	d
	NaBH₄	90ᵇ	1.8	This work
7ᶜ	n-Bu₃Sn–H	70–84		e
	NaH–HMPT	a		f
	Na-t-AmONa	55		f
	NaBH₄	80ᵇ		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.

(12) C. W. Jefford, D. Kirkpatrick, and F. Delay, *J. Amer. Chem. Soc.*, **94**, 8905 (1972).
(13) D. Seyferth and B. Prokai, *J. Org. Chem.*, **31**, 1702 (1966).
(14) D. Seyferth, H. Yamasaki, and D. L. Alleston, *J. Org. Chem.*, **28**, 703 (1963).

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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 techniques¹,² and has

(1) M. P. Schweizer, S. I. Chan, G. K. Helmkamp, and P. O. P. Ts'o, *J. Amer. Chem. Soc.*, **86**, 696 (1964).

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 workers³,⁴ 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_ψ) 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

(2) C. D. Jardetzky and O. Jardetzky, *J. Amer. Chem. Soc.*, **82**, 222 (1960).
(3) K. R. Shelton and J. M. Clark, *Biochem. Biophys. Res. Commun.*, **33**, 850 (1968).
(4) F. Doppler-Bernardi and G. Felsenfeld, *Biopolymers*, **8**, 733 (1969).
(5) M. Tomasz, J. Olson, and C. M. Mercado, *Biochemistry*, **11**, 1235 (1972).
(6) R. N. Maslova, E. A. Lesnik, and Y. M. Varshavskii, *Mol. Biol.*, **3**, 728 (1969) (english translation, *Mol. Biol. (USSR)*, **3**, 575 (1969)).
(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.