Table III. B-Ring/A-Ring Ratios for Reactions of Substituted Anthracenes with Benzyne[a]

Substituted anthracene	Benzyne precursor[b]	B ring/A ring
9,10-Dimethoxy	C	*Ca.* 28
9,10-Dimethoxy	D	*Ca.* 14
1,4-Dimethoxy	C	2.4
1,4-Dimethoxy	D	3.5
1,4-Dimethoxy	C[c]	2.6
1,4-Dimethoxy	C[d]	2.6
1,4-Dimethoxy	C[e]	3.2
9-Cyano	C	3.7
9-Cyano	D	3.5
9,10-Diphenyl	C	0.08
9,10-Diphenyl	D	0.09

[a] See footnote *a* of Table II. [b] See footnote *b* of Table II. [c] See footnote *d* of Table II. [d] See footnote *f* of Table II. [e] See footnote *g* of Table II.

erating benzyne have now been checked in addition to the limited number examined previously.[1]

The role of iodobenzene most likely involves the formation of weak complexes with the anthracenes, thus causing the anthracenes to become less reactive with the electrophilic benzyne. Moreover, weak complexes are consistent with the small amount of energy required to cause the observed changes. The absence of an effect upon the relative reactivities for 9-phenylanthracene and 9,10-diphenylanthracene (Table II) indicates that complexes may only be formed with the more electron-rich anthracenes. This point is confirmed by the B/A ratios for 9,10-dimethoxy-, 1,4-dimethoxy-, 9,10-diphenyl-, and 9-cyanoanthracenes (Table III). No effect is observed for 9,10-diphenyl- and 9-cyanoanthracene B/A ratios for a change from 2-carboxybenzenediazonium chloride to diphenyliodonium-2-carboxylate as benzyne precursor. However, as noted earlier, for 1,4-dimethoxyanthracene the B/A ratio increases and for 9,10-dimethoxyanthracene the ratio decreases when changing the benzyne precursor in the same manner. These results show that iodobenzene is definitely involved with the anthracenes, and not with benzyne itself as has been observed for silver ion.[9] The idobenzene complexes are most likely weak charge-transfer complexes.

These observations show the pronounced effect that iodobenzene has upon the *observed* reactivity of benzyne with anthracenes. Thus a new general approach for the control of highly reactive species is available in which changes can be effected by proper conditions of complexing agent, solvent, and temperature.

(9) L. Friedman, *J. Am. Chem. Soc.*, 89, 3071 (1967).

Bruce H. Klanderman, Thomas R. Criswell
Research Laboratories, Eastman Kodak Company
Rochester, New York 14650

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The Conformation of Nucleosides and Nucleotides. An Application of the Nuclear Overhauser Effect

Sir:

Knowledge of the conformation of nucleosides and nucleotides about the C-1′,N-9 bond (the glycosidic bond) has become important to an assessment of the conformation of polynucleotides. Trueblood[1] has considered the question and has established a convention for expressing that conformation in terms of a torsion angle (ϕ_{CN}) that denotes the relative positions of the sugar and the base about the glycosidic bond. The two extreme conformations demonstrated by **1** and **2** in the purine riboside series are designated *anti* and *syn*, respectively.

Conformational analysis of the glycosidic bond in the purine riboside series has been difficult in view of the apparently low energy barriers to rotation about that bond.[2] Considerable experimental work has been done using optical rotatory dispersion,[3–6] but no good index of conformation has been found.

Reported in the present communication are nuclear Overhauser effect (NOE) measurements that represent a more direct approach to the conformation problem and that support the view that purine ribosides are conformationally mobile.

The nuclear Overhauser effect[7,8] is observed during nuclear magnetic double resonance experiments and allows the detection of nuclear–nuclear mutual relaxation processes. One observes an enhancement of the absorption intensity of one member of a pair of spatially proximate nuclei as an effect of irradiating the other. Kaiser[9] was the first to report an intermolecular NOE in a protonic system when he studied the mutual interaction of chloroform and cyclohexane, whereas Anet[10] first reported the intramolecular counterpart. Recently, the NOE has been employed in the study of several structural and configurational problems.[11–18]

Examination of molecular models shows that H-8 of the purine nucleosides would be an ideal conformational probe if it were to be observed during a double-resonance experiment of the above type. It is not spin coupled to any other proton, yet its spatial dimensions with respect to other protons in the same molecule allow differentiation among other extreme conformations.[19] For example, in the *anti* conformation H-8 and H-1′ are approximately 3.4 Å apart,[20] whereas in the *syn* conformation the two atoms are 1.8 Å apart.

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(1) J. Donohue and K. N. Trueblood, *J. Mol. Biol.*, 2, 363 (1960).

(2) A. E. V. Haschemeyer and A. Rich, *ibid.*, 27, 369 (1967).

(3) T. R. Emerson, R. J. Swan, and T. L. V. Ulbricht, *Biochem. Biophys. Res. Commun.*, 22, 505 (1966).

(4) M. Ikehara, M. Kaneko, K. Muneyama, and H. Tanaka, *Tetrahedron Letters*, 3977 (1967).

(5) W. A. Klee and S. H. Mudd, *Biochemistry*, 6, 988 (1967).

(6) D. W. Miles, S. J. Hahn, R. K. Robins, M. J. Robins, and H. Eyring, *J. Phys. Chem.*, 72, 1483 (1968).

(7) I. Solomon, *Phys. Rev.*, 99, 559 (1955).

(8) I. Solomon and N. Bloembergen, *J. Chem. Phys.*, 25, 261 (1956).

(9) R. Kaiser, *ibid.*, 39, 2435 (1963).

(10) F. A. L. Anet and A. J. R. Bourn, *J. Am. Chem. Soc.*, 87, 5250 (1965).

(11) M. C. Woods, I. Miura, Y. Nakadaira, A. Terahara, M. Maruyama, and K. Nakanishi, *Tetrahedron Letters*, 321 (1967).

(12) N. Abe, R. Onoda, K. Shiragata, T. Kato, M. C. Woods, Y. Kitahara, K. Ro, and T. Kurihara, *ibid.*, 1993 (1968).

(13) M. C. Woods, I. Miura, A. Ogiso, M. Kurabayashi, and H. Mishima, *ibid.*, 2009 (1968).

(14) M. C. Woods, H.-C. Chiang, Y. Nakadaira, and K. Nakanishi, *J. Am. Chem. Soc.*, 90, 522 (1968).

(15) R. W. Franck and K. Yanagi, *J. Org. Chem.*, 33, 811 (1968).

(16) J. G. Colson, P. T. Lansbury, and F. D. Saeva, *J. Am. Chem. Soc.*, 89, 4987 (1967).

(17) R. H. Martin and J. C. Nouls, *Tetrahedron Letters*, 2727 (1968).

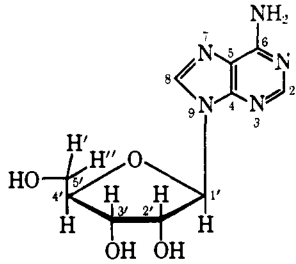
(18) J. C. Nouls, P. Wollost, J. C. Braekman, and G. van Binst, *ibid.*, 2731 (1968).

(19) Dipole–dipole interactions are distance dependent and T_1 is related to the sixth power of distance in the case of rigid intramolecular interactions and the third power of a size parameter in the case of variable distances (intra- as well as intermolecular). See J. G. Powles, *Ber. Bunsenges. Phys. Chem.*, 67, 328 (1963).

(20) Measured as internuclear distance on Dreiding models using pyramidal N-9.

In addition, the *syn* conformation brings H-8 closer to H-2′, -3′, -5′, and -5″ than it is in the *anti* form.

Three models were chosen for examination, 2′,3′-isopropylideneguanosine (**3**), 2′,3′-isopropylideneadenosine (**4**), and 2′,3′-isopropylidine-3,5′-cycloguanosine (**5**).[21] The latter model was chosen to allow measurements on a conformationally rigid system, and the isopropylidine derivatives were chosen to minimize conformational mobility of the furan ring. Dimethyl sulfoxide solvent was chosen to minimize intermolecular association.[22]



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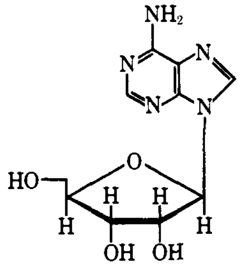

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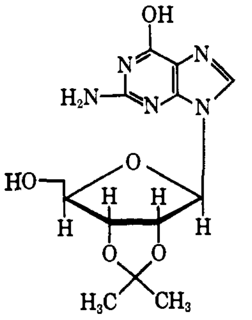

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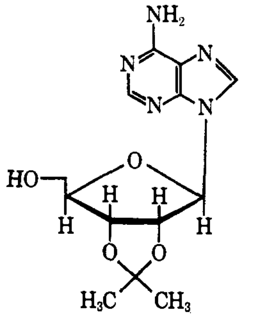

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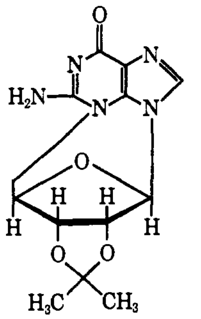

5

Table I. Results of Double-Resonance Experiments

Model	Proton irradiated[a] (mV at 20 db)[b]	Proton obsd	% enhancement
2′,3′-Isopropylidine-3,5′-cycloguanosine (0.27 *M*)	H-8 (200)	H-1′	26
	H-1′ (200)	H-8	39
	H-2′ and H-3′ (125 each)	H-8	1
2′,3′-Isopropylideneadenosine (0.58 *M*)	H-1′ (150)	H-8	23
	H-2′ (150)	H-8	9
	H-3′ (150)	H-8	3
	H-5′ and H-5″ (150)	H-8	4
	H-1′ (150)	H-2	0
2′,3′-Isopropylidineguanosine (0.44 *M*)	H-8 (200)	H-1′	20
	H-1′ (150)	H-8	12
	H-2′, and H-3′ (50 each)	H-8	12
	H-5′ and H-5″ (125)	H-8	10
	H-4′ (125)	H-8	2

[a] Assignments according to L. Gatlin and J. C. Davis, *J. Am. Chem. Soc.*, **84**, 4464 (1962), and R. A. Sandmann, University of Wisconsin, unpublished work. [b] Optimum H_2 intensity levels determined by variation over a wide range of values and choosing the one that gave maximum enhancement.

Results of the double-resonance experiments are shown in Table I. A typical experiment[23] involved first establishing a "standard" trace of the resonance of an appropriate proton by observing the resonance band while a second field in a signal-free part of the spectrum was turned on. Then the appropriate proton signal was observed while an H_2 field was imposed at the frequency of a second proton. The effect of the H_2 irradiation was expressed as the percentage peak height difference[24] between the "standard" and the experimental trace. A positive enhancement greater than 4% was taken as evidence for a nuclear Overhauser effect.[25]

It is clear from Table I that H-8 interacts with only H-1′ in the cyclonucleoside **5** and is noninteracting with H-2′ and H-3′ in that same model. It is also seen that H-8 interacts with H-1′, H-2′, H-5′, and/or H-5″ in the guanosine model (**3**). It is clear from the results tabulated for isopropylideneadenosine that H-8 and H-1′ interact. The enhancements of the H-8 resonance observed when the remaining protons are irradiated allow the assignment of an H-8,H-2′ interaction, but no other interaction can be named for certain. It is seen, though, that the *anti* range of conformations is less favored in the adenosine case than in the guanosine case, a difference that was not anticipated. Thus it appears possible that both *syn*-like and *anti*-like conformations are allowed for both nucleosides under the experimental conditions, but that quantitative differences exist.

Experiments are under way on a variety of models testing further structural effects as well as solvent, concentration, and temperature effects.

Phillip A. Hart, Jeffrey P. Davis[26]
Department of Pharmaceutical Chemistry, School of Pharmacy
University of Wisconsin, Madison, Wisconsin 53706

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(21) Prepared according to R. E. Holmes and R. K. Robins, *J. Org. Chem.*, **28**, 3483 (1963); **3** and **4** commercially available.

(22) L. Katz and S. Penman, *J. Mol. Biol.*, **15**, 220 (1966).

(23) A Varian HA-100 nmr spectrometer run in frequency-sweep mode was used. Coaxial sample tubes were used to minimize possible additional relaxation mechanisms by the hexamethyldisilizane reference standard. Samples were degassed by multiple freeze–pump–thaw cycles.

(24) Peak-height comparisons are valid as no significant signal width variations were observed.

(25) The 4% error is a measure of the poorest reproducibility obtained, not an average deviation.

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