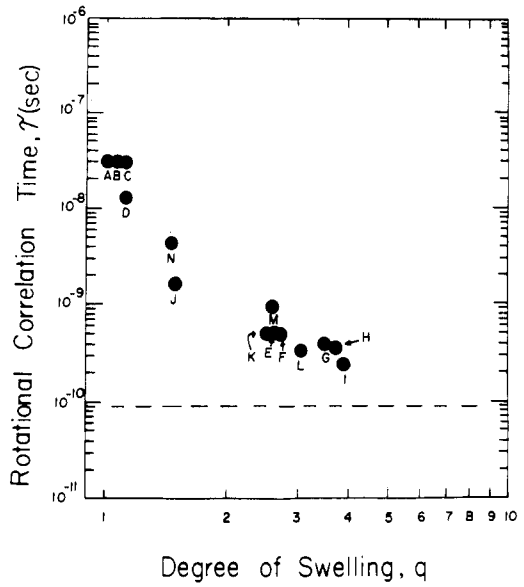
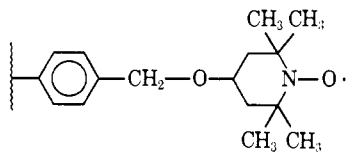


Figure 1. Plot of τ as a function of q for **3** swelled in (A) no solvent, (B) ethanol, (C) 2-propanol, (D) acetonitrile, (E) ethyl acetate, (F) *N*,*N*-dimethylformamide, (G) carbon tetrachloride, (H) dichloromethane, (I) benzene, (J) ethanol in benzene (67% v/v), (K) ethanol in benzene (33% v/v), (L) ethanol in benzene (17% v/v), (M) **4** swelled in benzene, and (N) **5** swelled in benzene; the dashed line (----) represents the value of τ measured for a benzene *solution* of nitroxide polymer **6**.

(0.2 mmol of chlorine/gram of polymer), swelled in *N*,*N*-dimethylformamide (DMF) in the presence of base.[3] Analysis of the resulting nitroxide polymer, **3**,



3, 0.2 mmol of nitroxide/gram of polymer; 2% ring substitution

indicated complete replacement of the chloride ion by the spin label.[4,5] Rotational correlation times, τ, were calculated from observed room temperature electron paramagnetic resonance (epr) spectra.[6-9] The degree of swelling values, q (swelled volume/dry volume), were determined from the measured density of the dry resin and the weight of imbibed solvent.[10,11]

Data obtained for nitroxide polymer **3** swelled in a variety of solvents are presented in Figure 1. A distinct trend can be noted; as the degree of swelling of the polymer increases, the rotational correlation time of the spin-label decreases. In order to ensure the absence of any special solvent effects, we measured the mobility of the label in **3** swelled in different mixtures of benzene and ethanol. Here again, we detected the same trend. Incremental replacement of ethanol by benzene led to both a higher degree of swelling and a correspondingly smaller correlation time. We also found that by increasing the crosslink density of the polystyryl nitroxide to 4%, **4**, and 12%, **5**, the degree of swelling decreased and the correlation time increased.[12] All of the data obtained fall along a smooth curve which asymptotically approaches the value of τ measured for a benzene *solution* of an analogous noncross-linked polystyryl nitroxide, **6**.[12] This plot clearly demonstrates that the rotational motion of the covalently bound spin-label is primarily dependent upon the degree of swelling of the polymer lattice. Although the precise relationship between q and τ has not yet been determined, the results cited here establish that *those solvents which swell polystyrene matrices the most will allow for the greatest mobility of the substrates bound to them.*

Our observation that the physical nature of resin-bound molecules varies substantially with the degree of swelling of the polymer lattice suggests that the chemical nature of such species may be similarly influenced.[13] We are presently carrying out experiments designed to test this hypothesis.

Acknowledgment. We are grateful to the Marquette University Committee on Research and Chemistry Department for their financial support. We thank Dr. Harold M. Swartz for the use of his Varian E-9 spectrometer and Dr. Colin Mailer for assistance in obtaining the epr spectra.

(3) J. S. Brimacombe, B. D. Jones, M. Stacey, and J. J. Willard, *Carbohyd. Res.*, **2**, 167 (1966). The polymer product was filtered, washed with water, ethanol, and ether, and dried under vacuum.

(4) Nitrogen was determined by microanalysis (Midwest Microlab, Indianapolis, Ind.).

(5) Chloromethylation of the polystyrene occurs uniformly, requiring a uniform distribution of the nitroxide along the polymer: R. B. Merrifield and V. Littau in E. Bricas, "Peptides 1968," North Holland Publishing Co., Amsterdam, 1968, p 179.

(6) Each polymer sample was swelled with a given solvent for 24 hr in an epr tube, sealed with a No-Air stopper, and then purged with nitrogen for 10 min.

(7) D. Kivelson, *J. Chem. Phys.*, **27**, 1087 (1957); J. H. Freed and G. K. Fraenkel, *ibid.*, **39**, 326 (1963); S. A. Goldman, G. V. Bruno, and J. H. Freed, *J. Phys. Chem.*, **76**, 1858 (1972); A. T. Bullock, G. G. Cameron and P. M. Smith, *J. Polym. Sci., Part A-2*, **11**, 1263 (1973).

(8) The rigid lattice value of the anisotropic ^{14}N hyperfine splitting used was 32.3 G; this was determined experimentally from **3** in the dry state at 77°K.

(9) Those spectra which appeared as three sharp lines were further analyzed and found to be well behaved; *i.e.*, the quantity (line width)^2 × (amplitude) was constant for all three lines (±1%): G. K. Fraenkel, *J. Phys. Chem.*, **71**, 139 (1967). Correlation times calculated for polystyryl nitroxides containing less than 0.2×10^{-4} mmol of nitroxide/gram of polymer differed from those calculated for **3** by less than a factor of two.

(10) Swelling measurements were made after the nitroxide polymers were equilibrated with a given solvent for at least 24 hr; swelling equilibrium was usually attained within a 2-hr period. Reproducibility was ±5%.

(11) In this calculation it was assumed that the volumes of the polymer and the solvent are additive. The density of **3** was experimentally found to be 0.95 ± 0.03 g/cm^3.

(12) Prepared from the corresponding chloromethylated polymer containing 0.2 mmol of chlorine/gram of polymer.

(13) A recent study dealing with a polystyrene-bound hydrogenation catalyst revealed a marked dependency of the catalyst's activity on the choice of solvent used to swell the polymer: W. Dumont, J. C. Poulin, T. P. Dang, and H. B. Kagan, *J. Amer. Chem. Soc.*, **95**, 8295 (1973).

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8-Azaadenosine. Crystallographic Evidence for a "High-Anti" Conformation around a Shortened Glycosidic Linkage

Sir:

We wish to report the results of our X-ray structural investigation of 8-azadenosine and discuss the effects of the 8-aza substitution on both the glycosidic C–N bond and the torsion angle χ around the glycosidic bond. The structure of this nucleoside is of particular signifi-

Table I. Conformational Parameters in Ortho Azanucleosides

Compound	χ_{CN}, deg	Sugar pucker	Glycosyl C–N (Å)	Intramolecular [N(8),N(6)] ···C(2′)[a] (Å)	Conformation at C(4′)–C(5′)	Ref
6-Azauridine						
Molecule A	82.7	^3E[b]	1.462	2.814	*gt*[b]	10
Molecule B	76.5	^3E	1.473	2.844	*gt*	10
6-Azacytidine	99.1	^3E	1.465	2.758	*gg*	11
8-Azaadenosine	103.6	$^2T_1$	1.445	2.835	*gt*	This work
Tubercidin	73.0	$^2T_1$	1.438	3.066[c]	*gt*	12
Formycin[d]	109.5	$^2T_1$	1.501[d]	2.870	*gt*	5
cis-ATD[e]	132.4[f]		1.459[e]	2.776[f]		7
Formycin HBr	Syn	$^2T_3$			*gt*	4
Virazole[d,g] (V1)	10.4	$^3T_2$			*gg*	13
Virazole[d,g] (V2)	119.0	$_2T^1$			*gt*	13
Pyrazomycin A[d,g]	Syn					14
Pyrazomycin B[d,g,h]	Syn					15

[a] N(8) for azapurines, N(6) for azapyrimidines. [b] Symbols are explained in M. Sundaralingam, *J. Amer. Chem. Soc.*, **93**, 6644 (1971), for the sugar pucker and in E. Shefter and K. N. Trueblood, *Acta Crystallogr.*, **18**, 1065 (1965), for the conformation at the C(4′)–C(5′) bond. [c] A C···C distance. [d] C–C glycosyl bond. [e] Both enantiomers present. [f] Calculated from the coordinates reported in the reference. Value of χ_{CN} pertains to the enantiomer analogous to a β-D nucleoside. The other enantiomer is syn with χ_{CN} = 227.6°. [g] A substituted imidazole nucleoside. [h] An α-nucleoside.

cance since it belongs to the general category of 8-azapurine nucleosides, *e.g.*, formycin and 8-azaguanosine, whose carcinostatic and biophysical properties have been studied extensively.[1-3]

Many biological properties of 8-azapurine nucleosides, *e.g.*, formycin, 8-azaadenosine, and 8-azaguanosine, have been studied by Ward and coworkers,[1-3] who have shown that the anomalous behavior of these nucleosides can be explained by assuming that they adopt the syn conformation around the glycosidic bond as observed[4] in the crystal of formycin hydrobromide and further that they have a low barrier to syn–anti conversion. However, it has been pointed out[5] that many anomalous properties of formycin and its polymers can be explained equally well by assuming the intermediate anti–syn conformation (called "high-anti") observed in the crystal of formycin monohydrate. In addition, 8-azaadenosine has some significant properties as a substrate for adenosine deaminase.[6] In the present communication we have compared our structural results for 8-azaadenosine with those for related compounds in order to throw some light on the structure–function relationship. Crystal structures of two related 8-aza nucleosides have been published: formycin,[4,5] which has a C–C glycosidic bond and is a diazole, and *cis*-1-(6-acetoxymethyltetrahydro-2-pyranyl)-5,6-dichlorobenzotriazole or *cis*-ATD,[7] which, like 8-azaadenosine, is a triazole but has a substituted benzene ring in place of the pyrimidine ring and a substituted six-membered pyranyl ring in place of the five-membered ribose. This, however, is the first structural study of a true 8-azapurine nucleoside.

Long, thin (1 × 0.15 × 0.05 mm) needles of 8-azaadenosine monohydrate were grown from aqueous solution from material kindly supplied by Dr. J. A. Montgomery. The material crystallizes in the space group $P2_12_12_1$ of the orthorhombic system with a = 17.150 (9), b = 9.840 (4), and c = 7.423 (5) Å. The intensity data (1029 above 3σ) were collected on a Picker FACS-I automatic diffractometer equipped with a graphite monochromator, using Mo Kα radiation. At the present stage of refinement the R factor (on F) is 0.049. Details of the structure analysis will be published elsewhere.

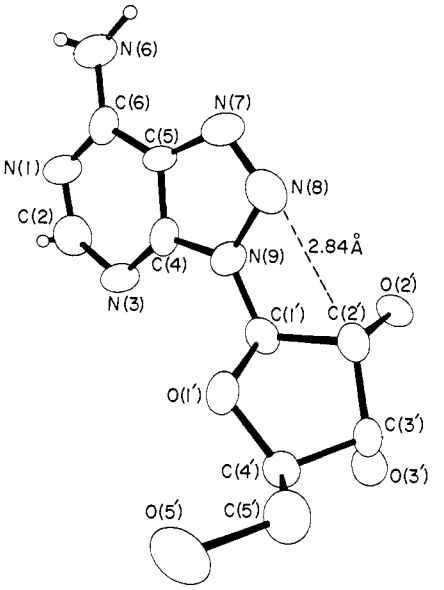

Figure 1. View of the 8-azaadenosine molecule. The thermal ellipsoids of the hydrogen atoms have been reduced artificially, and hydrogen atoms on the sugar have been omitted for clarity.

A view of the 8-azaadenosine molecule, showing the conventional numbering system, is shown in Figure 1. The glycosidic torsion angle, χ_{CN},[8] describing the relative orientation of the sugar and base moieties[9] for the 8-azaadenosine molecule is 103.6°. A comparison of

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(5) P. Prusiner, T. Brenan, and M. Sundaralingam, *Biochemistry*, **12**, 1196 (1973).
(6) L. N. Simon, R. J. Bauer, R. L. Tolman, and R. K. Robins, *Biochemistry*, **9**, 573 (1970).
(7) J. Fayos and S. Garcia-Blanco, *Acta Crystallogr., Sect. B*, **28**, 2863 (1972).
(8) M. Sundaralingam, *Biopolymers*, **7**, 821 (1969).
(9) J. Donohue and K. N. Trueblood, *J. Mol. Biol.*, **2**, 363 (1960).

the χ values for all ortho azanucleosides (8-azapurine or 6-azapyrimidine nucleosides)[4,5,7,10-15] is presented in Table I and shows that with one exception they lie either in the intermediate "high-anti" region ($\chi_{mean} \approx 100$) or in the syn region. The lone exception is that one of the two known forms of virazole[13] is in the anti conformation while the other adopts the "high-anti" conformation; virazole, however, has much more conformational freedom than the other nucleosides listed in Table I. It should be noted, however, that the syn conformation for the two pyrazomycins is stabilized by strong intramolecular hydrogen bonding between a base hydroxyl and O(5′) in pyrazomycin A (the β-anomer) and the same hydroxyl and O(2′) in pyrazomycin B (the α-anomer). In formycin hydrobromide the formycin cation is protonated at N(1). It is clear, however, that the unsubstituted ortho azanucleosides favor the intermediate "high-anti" region rather than the syn region. The main intramolecular interactions in those 8-azapurine nucleosides which exist in the "high-anti" χ region are between N(8) of the base and C(2′) of the sugar (and its attached hydrogen H(2′)) (see Table I); in 8-azaadenosine, the N(8)···C(2′) and N(8)···H(2′) separations are 2.835 (7) and 2.34 (5) Å, respectively, and the N(8)···H(2′)–C(2′) angle is approximately 100°. This is similar to the situation found for 6-azapyrimidine nucleosides, 6-azauridine[10] and 6-azacytidine,[11] where two of the severest intramolecular interactions are between the same two sugar atoms, namely, C(2′) and H(2′), and N(6) of the base.

Sundaralingam[16] has shown that the glycosidic bond in purine nucleosides (average value 1.465 Å) is shorter than that in pyrimidine nucleosides (1.495 Å). A comparison of the glycosidic bond lengths for 8-azaadenosine (1.445 Å) with those of 6-azauridine (1.468 Å)[10] and 6-azacytidine (1.465 Å)[11] suggests that this trend carries over to the ortho azanucleosides but that the bonds are shorter in the latter group than in the normal nucleosides. This general shortening of the glycosidic bond in ortho azanucleosides may not be related to the ortho-aza substitution, since tubercidin does not have this feature, but instead may be a function of the "high-anti" conformation around the glycosidic bond as suggested by Sundaralingam.[17,18]

Other stereochemical parameters of interest in 8-azaadenosine are similar to those in formycin. Thus, the puckering of the ribose ring is C(2′)-endo, C(1′)-exo, $^2T_1$, which, as noted by Sundaralingam, is slightly different from that normally observed ($^2T_3$) in purine nucleosides. The conformation of the C(5′)–O(5′) bond around the extracyclic bond C(4′)–C(5′) is gauche-gauche as in formycin. The hydrogen bonding scheme is also similar to that of formycin with the exception that N(7), which is not protonated in 8-azaadenosine, does not form the donor hydrogen bond N(7)–H···O-(3′) found in formycin. In 8-azaadenosine N(7) does not participate in any hydrogen bonding.

The observed "high-anti" (intermediate between syn and anti) conformation of 8-azaadenosine may explain its weakened binding (relative to adenosine) to adenosine deaminase,[6] since this enzyme is inactive on nucleosides in the syn conformation but active on nucleosides in the anti conformation.[19]

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Retardation of the Ferric Ion Catalyzed Decomposition of Hydrogen Peroxide by an Iron(II) Diimine Complex

Sir:

Much interest has been devoted to the study of the ferric ion catalyzed decomposition of hydrogen peroxide,[1,2] and also to the retardation of this reaction by organic substrates.[3]

We now report a striking retardation of the ferric ion catalyzed decomposition of hydrogen peroxide by an iron(II) complex,[4] tris(glyoxal bis(methylimine))iron-(II), $Fe(GMI)_3^{2+}$. While in the retardation of the reaction by organic substrates evidence was presented that the organic compound acts as an HO· radical trap,[3] in this case we believe that $Fe(GMI)_3^{2+}$ acts as an HO_2· radical trap. In the reaction of hydrogen peroxide with other diimine complexes of iron(II), such as tris(1,10-phenanthroline)iron(II) and tris(2,2′-bipyridine)iron(II),[2,5] the complexes undergo dissociation and the respective bis and mono complexes of iron(III) catalyze the decomposition of hydrogen peroxide,[6,7] contrary to what is observed in the present case.

It is known that $Fe(GMI)_3^{2+}$ can only be oxidized reversibly to $Fe(GMI)_3^{3+}$ at high acid concentration[8] (*e.g.*, 10 *M* H_2SO_4). At lower acid concentration, disproportionation reactions of the ferric complex occur, leading to the formation of ligand-oxidized complexes.[9] The formal electrode potential of the couple $Fe(GMI)_3^{3+}|Fe(GMI)_3^{2+}$ is 1.02 V *vs.* sce in 4.0 *M* H_2SO_4 and increases as the acid concentration decreases. This behavior is similarly observed in the

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