Certain Novel Ribofuranosyl Phosphates Derived from 5-Phospho-α-D-ribofuranosyl-1-pyrophosphate: Synthesis, Structure, and Alkaline Hydrolytic Reactivities

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5-Phospho-α-D-ribofuranosyl 1,2-cyclic monophosphate was synthesized from 5-phospho-α-D-ribofuranosyl-1-pyrophosphate. Alkaline hydrolysis of the cyclic monophosphate yielded the hitherto unreported D-ribofuranosyl 2,5-bisphosphate and α-D-ribofuranosyl 1,5-bisphosphate (a natural metabolite in red blood cells, and a primer for phosphopentomutase). Extensive NMR (^1H, ^{13}C, and ^{31}P) data on the cyclic phosphate and on the related α-D-ribofuranosyl 1,2-cyclic monophosphate (see ref 3) are consistent with a C3-endo ribofuranosyl conformation. The five membered phosphodiester rings in both α-D-ribofuranosyl 1,2-cyclic monophosphate and 5-phospho-α-D-ribofuranosyl 1,2-cyclic monophosphate are also puckered, the P atom forms dihedral angles of 153° to C1–H and 113° to the C2–H atom. Molecular mechanics calculations were consistent with the structure deduced from the NMR data.

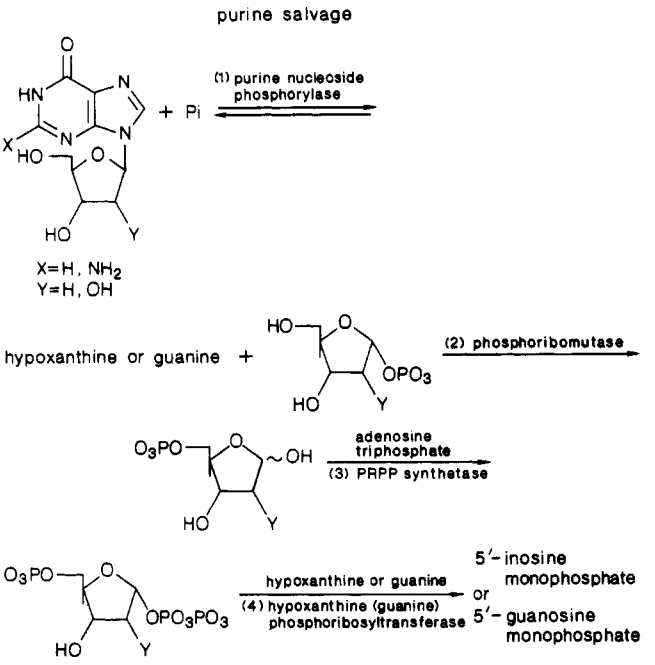
Introduction

Evidence for the importance of the purine salvage pathway (Scheme I) in physiology has been rapidly accumulating of late,[1a,b] especially with the discovery that genetic defects[2] in the enzymes in steps 1 and 4 of the pathway are directly responsible for certain diseases. In order to study the biochemistry of these diseases, potential inhibitors, activators, and primers should be made available synthetically. In a previous paper, we reported the synthesis, NMR properties and acid and alkaline hydrolytic mechanisms for some ribofuranosyl 1,2-cyclic and glucopyranosyl-1,2-cyclic monophosphates.[3] We here summarize the synthesis, structure, and hydrolytic stability of some other sugar phosphates of direct or potential importance to this pathway, all derived from commercially available 5-phospho-α-D-ribofuranosyl-1-pyrophosphate (**1**, itself a substrate for the enzymes in steps 3 and 4): 5-phospho-α-D-ribofuranosyl 1,2-cyclic monophosphate (**2**, a potential inhibitor for enzymes 3 and/or 4), α-D-ribofuranosyl 1,5-bisphosphate (**3**, a primer for the enzyme in step 2, the phosphopentomutase[4]), and D-ribofuranosyl 2,5-bisphosphate (**4**, a possible activator for the pathway in analogy with the role of fructose 2,6-bisphosphate as a metabolic regulator[5]). While compound **3** had been reported in human red blood cells,[6] no efficient chemical synthesis has been forthcoming to date. Compounds **2** and **4** are totally novel. In the meantime, with the help of multinuclear NMR analysis and molecular modeling assisted by molecular mechanics calculations, we can suggest for the first time structures for the very interesting bicyclic, highly strained phosphodiesters related to compound **2**.

Results and Discussion

Synthesis. Former attempts to synthesize compound **3** employed enzymatic approaches and were greatly hampered by the formation of several products that were difficult to separate on a synthetic scale. On the basis of

Scheme I



the early report by Tener and Khorana,[7] we decided to pursue synthesis of **3** from compound **1**, via the cyclic phosphate **2**. Equations 1 and 2 summarize the conditions (see next paragraph). Advantage was taken of the fact that the boronate affinity column Affigel 601[8] can selectively bind *vic* cis-diols and as a consequence can separate compounds **3** and **4**. Also the separation is rapid enough to allow isolation of compounds such as **3**, possessing a labile anomeric phosphate linkage.

Initially, the reaction between compound **1** and dicyclohexylcarbodiimide was carried out in the presence of *n*-butanol, formamide, and 2 N NH_4OH. After ca. 2.5 h reaction time, two compounds were formed according to ^{31}P NMR: **2** and 5-*N*-phosphoureido-α-D-ribofuranosyl 1,2-cyclic monophosphate (i.e., the dicyclohexyl urea phosphoramidate derivative at the 5-phosphoryl group of compound **2**). Descending thin-layer chromatography in 1-propanol/NH_3/H_2O (6:1:3) was capable of separating the

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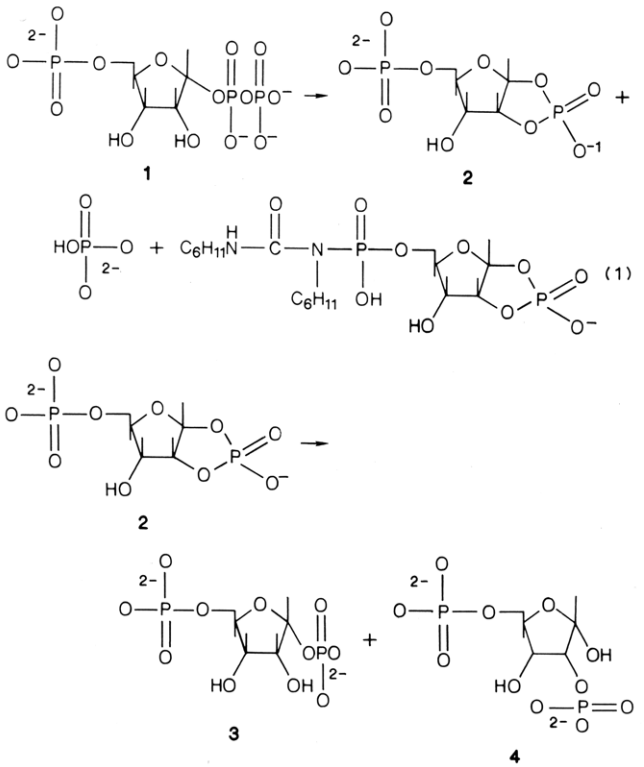

two compounds (Figure 1). After chromatography, two thin strips from the sides of the paper were cut out and sprayed with ammonium molybdate reagent to reveal phosphate-containing areas. The developed strips were used as guides to cut out the appropriate areas of the untreated portion of the chromatogram. The phosphate esters were eluted from the paper with water and lyophilized. Addition of a base stronger than NH_4OH, e.g., triethylamine, inhibited the formation of the urea derivative,[9] but also decreased the rate of the reaction and led to the decomposition of compound **1** to **3**, ribose-5-phosphate, inorganic pyrophosphate and phosphate, thereby decreasing the yield of compound **2**.

Multinuclear NMR Studies. ^{13}C and ^{31}P NMR parameters are listed in Tables I and II for some selected compounds.

The J_{H1-H2} coupling constant provides a convenient means for monitoring the average conformation of the ribose ring. The simplest interpretation of such data places the most stable envelope-type conformations in the C2-endo or C3-endo classes (with the C2 atom or the C3 atom out of the plane formed by the other four ring atoms and on the same side of the plane as is the C5–CH_2 substituent[10,11]). Compiled values for this coupling constant are 6.9 and 1.7 Hz for the C2-endo and C3-endo conformations, respectively.[12] The observed values are 4.1–4.2 Hz for both compound **2** and for α-D-ribofuranosyl 1,2-cyclic phosphate **5** and reflect either a rapidly interconverting mixture of the two conformers or indicate the breakdown of such correlations when applied to these highly strained bicyclic systems. It is relevant to mention, however, that raising the temperature to 50 °C did not change the appearance of the coupling patterns or constants. The three bond $J_{H1-C1-O1-P}$ and $J_{H2-C2-O2-P}$ coupling constant are very different: 17.4 and 4.4 Hz, respectively (Figure 1), and suggest an unsymmetrical and nonplanar cyclic phosphate

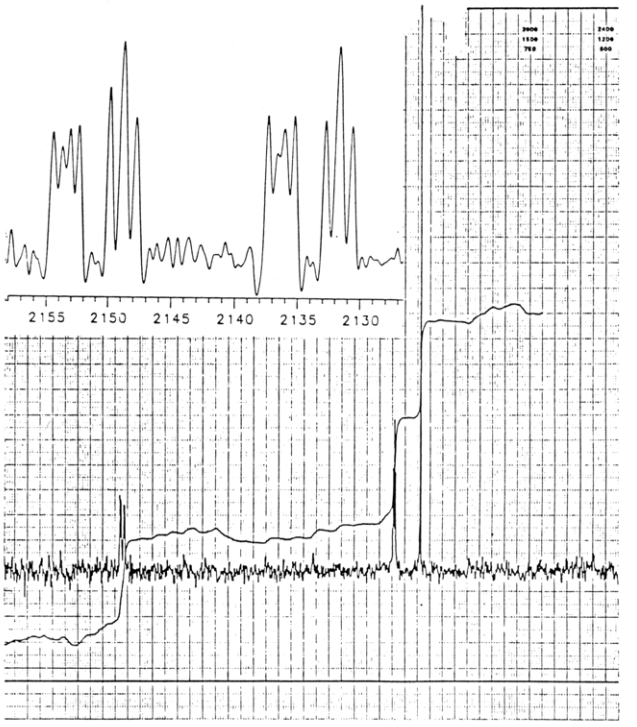

Figure 1. ^{31}P NMR (81.03 MHz) spectrum of 5-phospho-α-D-ribofuranosyl 1,2-cyclic monophosphate at pH 8.0 in 90/10 H_2O/D_2O. The large upfield singlet is internal P_i for chemical shift reference. The inset is an expansion of the low-field multiplet at 200 MHz for ^{31}P (500-MHz nominal ^1H frequency) and corresponds to the P atom in the cyclic phosphate.

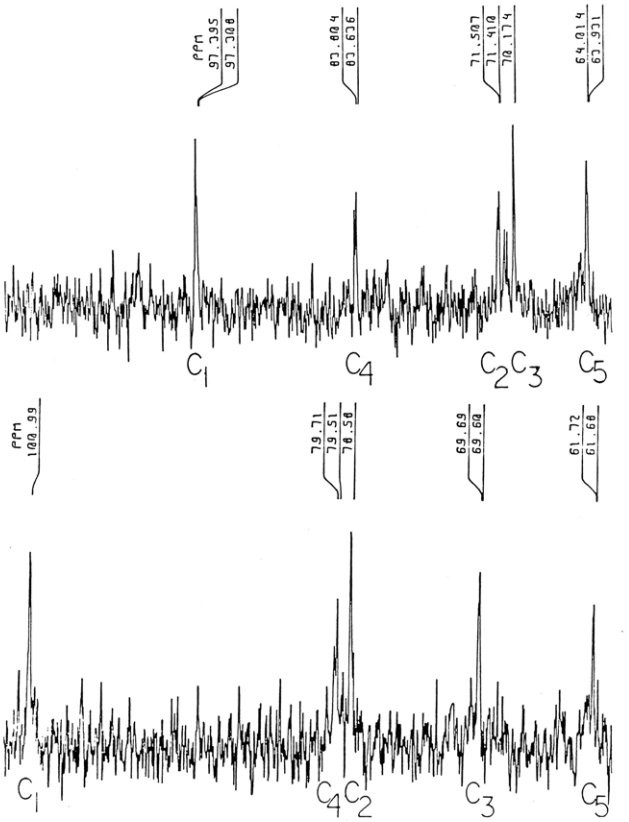

Figure 2. ^{13}C NMR (50.13 MHz) spectrum of α-D-ribofuranosyl 1,5-bisphosphate (top) and 5-phospho-α-D-ribofuranosyl 1,2-cyclic monophosphate in 90/10 H_2O/D_2O referenced against external tetramethylsilane.

ring. From these coupling constants one can deduce dihedral angles of 153° and 113°, respectively, based on a J_{gauche} = 1.8 Hz and J_{anti} = 20.9 Hz[13,14] and the Karplus-

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Table I. ^{13}C Chemical Shifts[a] and ^{31}P–^{13}C Coupling Constants of Ribofuranosyl Phosphates

		chemical shift, ppm					coupling constants, Hz				
compd	pH	C(1)	C(2)	C(3)	C(4)	C(5)	PC(1)	PC(2)	PC(3)	PC(4)	PC(5)
α-D-ribofuranosyl-1-phosphate	8.01	96.7	71.1	69.4	83.5	61.0	4.4	5.6			
5	8.0	101.1	78.4	69.7	80.3	59.7	4.1		6.3		
D-ribose 2-phosphate	8.0	93.6	73.0	67.9	73.4	63.0		6.8	12.3		
D-ribose 5-phosphate	8.0	101.3	75.5	70.8	82.0	64.5				3.7	4.0
2	8.0	101.0	78.6	69.6	79.6	61.7	3.1		4.3	10.3	
3	8.0	97.4	71.5	70.2	83.7	63.7	4.4	4.9		8.5	4.2
4	8.0	100.4	77.2	70.0	81.4	64.1	8.2	3.0	5.2	6.4	8.1

[a] Chemical shifts are downfield from external Me_4Si. Chemical shifts are accurate to ±0.1ppm.

Table II. ^{31}P Chemical Shifts and ^{31}P–^{1}H Coupling Constants for Ribofuranosyl Phosphates

		^{31}P chemical shift,[a] ppm			coupling constants, Hz				
compd	pH	1-P	2-P	5-P	$^3J_{P-H_1}$	$^3J_{P-H_2}$	$^4J_{P-H_3}$	$^4J_{P-H_4}$	$^3J_{P-H_5}$
α-D-ribofuranosyl-1-phosphate	8.0	−0.23			6.5				
5	8.0	+17.0			17.0	4.4	1.2	1.1	
D-ribose 2-phosphate	8.0		+1.56						
D-ribose 5-phosphate	8.0			+1.38					4.0
2	8.0	+17.0		+1.32	17.2	4.5			4.9
3	8.0	−0.22		+1.32	6.5				5.0
4	8.0		+1.50	+1.32					4.9

[a] Referenced from internal P_j downfield (+) or upfield (−).

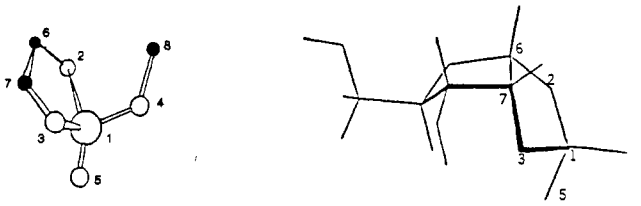
type relationship developed by Lapper and Smith.[15]

The ^{13}C NMR data are also informative concerning the conformation of the cyclic phosphates. On cyclization of the 1-phosphates to the 1,2-cyclic phosphates the chemical shift of C1 is shifted downfield by ca. 4 ppm and that of C2 by ca. 7 ppm (Figure 2). Interestingly, the $J_{C3-C2-O2-P}$ coupling constant is rather large (5–7 Hz), characteristic of an anti rotamer along the C2–O2 bond and as expected for a C3-endo conformation.[16,17]

Hydrolytic Lability of 2. Alkaline hydrolysis of compound **2** at 21 °C in 0.1 N NaOH leads to the formation of compounds **3** and **4** in a 25 to 75 ratio (Figure 3) with a half-life of 50 min, compared to 34-min half-life for hydrolysis of compound **5** under the same conditions. Presumably, ring opening in **2** takes place by hydroxide attack at P, as demonstrated for the alkaline hydrolysis of **5**.[3]

Molecular Mechanics Studies of the Conformation of α-D-Ribofuranosyl 1,2-Cyclic Monophosphates 5. The starting structure of compound **5** was constructed by employing standard bond lengths and angles for the ribose and those of Steitz and Lipscomb obtained for methyl ethylene phosphate[18a,b] for the cyclic phosphate ring. Molecular mechanics calculations were performed with the SYBYL software provided by Tripos Associates, St. Louis, MO, on an Evans and Sutherland PS 300 or NEC terminal and by employing Allinger's program (Xmaximin).[19a,b] To test the validity of the approach, the structure of methyl ethylene phosphate was first minimized starting with the X-ray crystallographic coordinates. Table III demonstrates the results of this study. The agreement between the X-ray structure and the theoretically predicted one is satisfactory overall. Next, the structure of **5** was minimized. The resulting structure is shown in Figure 4, the

Table III. Bond Angles Calculated for Methyl Ethylene Phosphate and Compound 5



bond	obsd[18] angle	calcd angle	calcd angle
O(2)–P(1)–O(3)	98.1	99.2	100.7
O(2)–P(1)–O(4)	106.1	107.5	102.7
O(2)–P(1)–O(5)	117.7	116.3	117.8
O(3)–P(1)–O(4)	110.4	104.1	102.8
O(3)–P(1)–O(5)	115.3	119.4	116.1
O(4)–P(1)–O(5)	108.6	109.2	114.6
C(6)–O(2)–P(1)	112.4	112.3	109.6
C(7)–O(3)–P(1)	114.4	111.0	104.9
C(7)–C(6)–O(2)	106.5	106.9	105.5
C(6)–C(7)–O(3)	105.8	107.5	105.1

[a] The numbering assignment for the atoms in α-D-ribofuranosyl 1,2-cyclic phosphate is the same as in methyl ethylene phosphate for comparison.

Table IV. Comparison of Calculated and Experimental Dihedral Angles in α-D-Ribofuranosyl 1,2-Cyclic Phosphate

dihedral angle	calcd[a]	exptl[b]
H(1)–C(1)–O(2)–P(1)	135.7	153.0
H(2)–C(2)–O(3)–P(1)	95.3	113.0
C(3)–C(2)–O(3)–P(1)	148.5	152.5

[a] Molecular mechanics II. [b] Deduced from NMR coupling constants, see text.

Table V. Bond Distances Calculated for Methyl Ethylene Phosphate and Compound 5

	methyl ethylene phosphate distance, Å		ribose 1,2-cyclic phosphate distance, Å calcd
bond	obsd	calcd	
P(1)–O(2)	1.59	1.60	1.58
P(1)–O(3)	1.58	1.60	1.58
P(1)–O(4)	1.54	1.59	1.59
P(1)–O(5)	1.45	1.40	1.41
O(2)–C(6)	1.44	1.46	1.45
O(3)–C(7)	1.42	1.46	1.46
C(6)–C(7)	1.56	1.54	1.53

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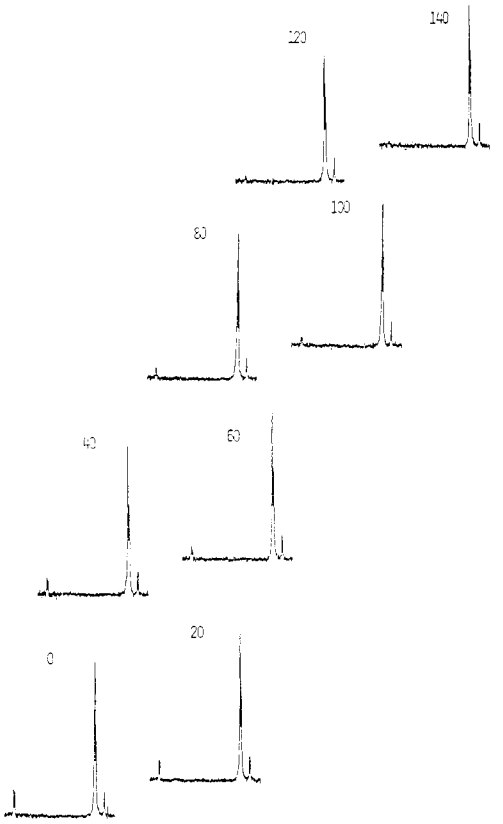

Figure 3. The time course of alkaline hydrolysis of 5-phospho-α-D-ribofuranosyl 1,2-cyclic monophosphate at pH 12.5, 21 °C, monitored by ^{31}P NMR, at the time (minutes) indicated. The lowest field multiplet represents the cyclic phosphate P atom in the starting material, the highest one the 1-phosphate in the α-D-ribofuranosyl 1,5-bisphosphate product, whereas the large resonance is a composite of all 5-phospho and 2-phospho groups.

dihedral angles for a C3-endo ribofuranosyl structure predicted by theory vs those deduced from the NMR data are listed in Table IV. A comparison of internal ring angles and bond lengths found experimentally for methyl ethylene phosphate and calculated by molecular mechanics for compound **5** are given in Table V. For compound **5** the key O1–P–O2 angle is predicted to be 9° less than the tetrahedral value.

This angle contraction accounts for the very high rate of alkaline hydrolysis of **5**,[3] in accord with early studies on five-membered ring cyclic phosphates by Westheimer and his co-workers.[20] Equally interesting is the theoretical prediction for a highly puckered and unsymmetrical cyclic phosphate ring, consistent with the three-bond P–H coupling constant data. As Figure 4 demonstrates, both five-membered rings are subject to significant ring puckering.

In summary, novel sugar phosphates, some with potential and some with already proven biological importance, have been synthesized and isolated in significant yields. Extensive multinuclear NMR and molecular mechanics calculations led to a consistent structure for the α-D-ribofuranosyl 1,2-cyclic monophosphates, a hitherto little studied class of compounds.

Experimental Section

General. All nuclear magnetic resonance spectra were recorded on an IBM WP 200-SY spectrometer (unless otherwise noted): proton at 200.13 MHz [chemical shifts in D_2O recorded in ppm downfield from internal 4,4-dimethyl-4-silapentane-1-sulfonic acid, sodium salt (DSS)]; phosphorus at 81.026 MHz [chemical shifts (in 90/10 v/v H_2O/D_2O containing 10 mM EGTA) in ppm from internal HPO_4^{2-} at pH 8.0]; carbon at 50.31 MHz [chemical shifts (in D_2O) in ppm downfield from an external capillary of tetramethylsilane (Me_4Si)].

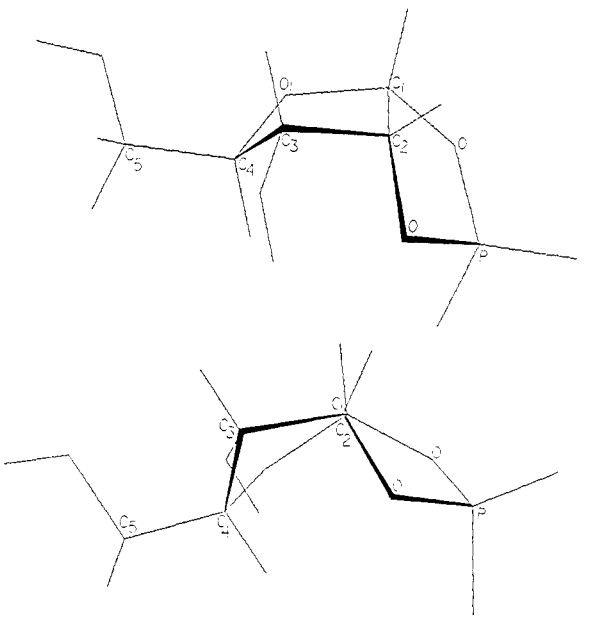

Figure 4. Optimum conformation of α-D-ribofuranosyl 1,2-cyclic monophosphate calculated with the molecular mechanics II program as viewed from two directions but the ribose O1 atom far from the viewer. The top picture shows the C3-endo sugar conformation and the highly puckered cyclic phosphodiester. The bottom view is along the C2–C1 bond, the C2 atom being closer to the viewer.

The R_f of all ribofuranosyl phosphates studied was determined by paper chromatography, carried out on Whatman 31 E/T paper (0.53 mm, fast flow rate) by using the solvent mixture 1-propanol/NH_3/H_2O (6:1:3). Prior to developing the chromatograms, the paper was first washed with 1 N HCl and then with distilled water. The phosphate compounds were detected by spraying with ammonium molybdate reagent.[21]

Materials. 5-Phospho-α-D-ribofuranosyl-1-pyrophosphate, tetrasodium salt (PRPP), was purchased from Sigma Chemical Co., St. Louis, MO. Dicyclohexylcarbodiimide (DCC), triethylamine, and other chemical reagents were high purity materials obtained from Aldrich Chemical Co., Milwaukee, WI. Affigel-601 was from Bio Rad Laboratories, Richmond, CA. Whatman chromatography paper 31 E/T was from Whatman, Inc., Hillsboro, OR. All deuteriated solvents, chemical shift standards, and deuterium oxide were from Stohler Isotope Co., NY.

5-Phospho-α-D-ribofuranosyl 1,2-Cyclic Monophoshate (2). Dicyclohexylcarbodiimide (0.200 g, 0.969 mmol) was dissolved in 6 mL of *tert*-butyl alcohol under vigorous stirring followed by the addition of 2 mL of triethylamine. The flask was warmed gently, and then 100 mg of 5-phospho-α-D-ribofuranosyl-1-pyrophosphate tetrasodium salt in 3 mL of H_2O was added over 5 min. The mixture was kept under gentle reflux for 4.5 h. Next, the solution was allowed to cool to room temperature and extracted with 7 mL of ether, and the aqueous layer was immediately freeze-dried. To the remaining residue 10 mL of dry methanol was added, the solution was stirred for 1 min, and the solid was separated, while the methanolic solution was concentrated at a rotary evaporator. Addition of a second 10-mL portion of dry methanol to the residue resulted in the total precipitation of traces of P_i and dicyclohexylurea. The methanolic solution was evaporated once more, and then the residue was dissolved in 2 mL of water. The pH of this solution was adjusted to 7.0 with triethylamine, and the solution was then freeze-dried, yielding compound **2** as an off-white powder (0.035 g, 35%): R_f (6:1:3 *n*-propanol/NH_3/H_2O) 0.26; ^1H NMR (D_2O/DSS, pH_{app} 8.0) δ 5.93 ppm (dd, 1 H, J = 4.1, 17.1

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Hz, C1H), 4.89 (dd, 1 H, J = 4.4, 8.3 Hz, C2H), 3.93–4.2 (m, 4 H, C3H, C4H, C5H's). Anal. Calcd for $C_5H_9P_2O_{10}\cdot(C_2H_5)_3NH^+\cdot0.5H_2O$: C, 32.84; H, 6.76. Found: C, 33.05; H, 6.27.

Synthesis of α-D-Ribofuranosyl 1,5-Bisphosphate 3 and D-Ribofuranosyl 2,5-Bisphosphate 4 by Alkaline Hydrolysis of Compound 2. 2 (40 mg, 0.1 mmol) was dissolved in 2 mL of 0.1 N NaOH, and the course of hydrolysis was monitored by ^{31}P NMR. After the hydrolysis of 2 was completed (ca. 2.5 h), the solution was lyophilized. The residue was dissolved in 2.5 mL of cyclohexylammonium bicarbonate (0.2 M, pH 8.0) and applied to a polyacrylamide boronate column[8] (Affigel 601, 0.5 × 9 cm), which had been previously washed with 25 mL of doubly distilled water, followed by 6 mL of cyclohexylammonium bicarbonate. The first fraction to elute with 12 mL of cyclohexylammonium bicarbonate contained ribose 2,5-bisphosphate. Compound 3 was eluted with a further 20 mL of water. The pH of the aqueous solution containing compound 3 was immediately adjusted to 8.0 with 0.1 N NaOH. Lyophilization of both eluates yielded white fluffy powders. Compound 3 was isolated as a hygroscopic tetra sodium salt (10 mg, 25%): R_f (7:1:2 isopropyl alcohol/NH_3/H_2O) 0.05–0.1. Anal. Calcd for $C_5H_8P_2O_{11}\cdot4Na\cdot2.5H_2O$: C, 13.55; H, 2.38. Found: C, 13.20; H, 2.14. Compound 4 was isolated as a hygroscopic tetrakis(cyclohexylammonium) salt (25 mg, 44.64%): R_f (7:1:2 isopropyl alcohol/NH_3/H_2O) 0.05–0.1. Anal. Calcd for $C_5H_8P_2O_{11}\cdot4C_6H_{11}NH_3^+\cdot2H_2O$: C, 46.89; H, 9.22; N, 7.54. Found: C, 46.68; H, 8.92; N, 7.72.

Synthesis of D-Ribofuranosyl 2,5-Bisphosphate 4 by Acid Hydrolysis of Compound 2. Compound 2 (20 mg, 0.05 mmol) was dissolved in 2.5 mL of 0.1 N HCl. The time course of hydrolysis was monitored to completion by ^{31}P NMR spectroscopy. Next, the solution was lyophilized, and the residue was treated as above by chromatography on the Affigel 601 column in cyclohexylammonium bicarbonate and then lyophilized. Recovery of D-ribofuranosyl 2,5-bisphosphate ranged from 90% to 95% of the theoretical yield.

Determination of the Rate of Alkaline Hydrolysis of Compound 2. The alkaline hydrolysis of compound 2 was carried out in triplicate in 0.1 N NaOH. Solutions were prepared by dissolving the appropriate amounts of material in 1.4 mL of standard base solution. D_2O (0.1 mL) was added, and the resulting mixture was transferred to a 10-mm NMR tube, which then was fitted with a Teflon vortex suppressor. The tube was placed in the probe, and spectra were accumulated at the times indicated using an automated program. The reaction was monitored at 21 °C, the ambient temperature of the probe. The hydrolysis was allowed to proceed until all starting material was consumed. Electronic integration was employed to determine the fraction of starting material remaining at different time intervals. First-order kinetics were obeyed to at least three half-lives.

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Registry No. 1·4Na, 87372-47-2; 2·Et_3N, 113599-16-9; 3·4Na, 113599-17-0; 4·4(c-$C_6H_{11}NH_2$), 113599-19-2; 5, 90275-35-7.

Nucleophilic Addition to Olefins. 22.[1] Kinetics of Hydrolysis of the Piperidine and Morpholine Adducts of Benzylideneacetylacetone in 50% Me_2SO–50% Water

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Benzylideneacetylacetone reacts with piperidine and morpholine to form a pH-dependent mixture of anionic adducts, $PhCH(R_2N)C(COCH_3)_2^-$ (T_A^-), and zwitterionic adducts, $PhCH(R_2NH^+)C(COCH_3)_2^-$ ($T_A^\pm$), which slowly hydrolyze to benzaldehyde, acetylacetone (or its anion), and R_2NH. A kinetic study of this hydrolysis in 50% Me_2SO–50% water shows that at high pH carbon protonation of T_A^-, to form $PhCH(R_2N)CH(COCH_3)_2$ (T_A^0), is rate-limiting while at intermediate pH carbon protonation of $T_A^\pm$, to form $PhCH(R_2NH^+)CH(COCH_3)_2$ (T_A^+), is co-rate-limiting with intramolecular proton transfer, $T_A^\pm \rightarrow T_A^0$ (Scheme I). At low pH the enol form of T_A^+ becomes an important intermediate (Scheme II). Rate and equilibrium constants for the various elementary steps leading from $T_A^\pm$ and T_A^- to T_A^0 were determined or estimated and a lower limit for the rate constant of breakdown of T_A^0 into $PhCH{=}N^+R_2$ and $CH(COCH_3)_2^-$ was estimated. Comparison of the kinetic behavior of benzylideneacetylacetone adducts with that of amine adducts of four other PhCH=CXY-type olefins shows both similarities and important differences which are discussed in detail. It appears that there are two major factors that determine whether formation of T_A^0 or its breakdown is rate-limiting. One is crowding, which enhances breakdown and slows proton transfer. The other is the sensitivity of the intrinsic barriers to resonance effects in the carbanion that is formed in the breakdown of T_A^0 on the one hand and that which is formed in the deprotonation of T_A^0 on the other. The smaller sensitivity to this factor in the breakdown reaction tends to make breakdown rate-limiting for systems where resonance in the carbanion is modest and to make proton-transfer rate-limiting where this resonance is strong.

The reaction of benzylideneacetylacetone (BAA) with piperidine and morpholine in aqueous Me_2SO leads to hydrolytic cleavage of the olefin into benzaldehyde, acetylacetone (AA) or its anion (AA^-), and the respective amine. The mechanism comprises a number of steps with some of the intermediates accumulating to measurable concentrations. The first two steps occur on a relatively rapid time scale (stopped-flow) and involve the nucleophilic addition of the amine, to form a zwitterionic adduct ($T_A^\pm$), which is in rapid acid–base equilibrium with its anionic form (T_A^-). At high amine concentration and high pH the equilibrium favors $T_A^\pm$ and T_A^- over the substrate, and $T_A^\pm$ and T_A^- can be characterized by their UV spectra.[2] A kinetic study of reaction 1 has been reported recently.[2]

The present paper describes the kinetics of the conversion of $T_A^\pm$ and T_A^- into benzaldehyde, acetylacetone or its anion, and amine. This is a much slower reaction

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(2) Bernasconi, C. F.; Kanavarioti, A. *J. Am. Chem. Soc.* **1986**, *108*, 7744.

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