Synthesis and the Crystal Structure of 4-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-6-methyl-1,2,4-triazin-3(4*H*)-one 1-Oxide, a Structural Analogue of Thymidine

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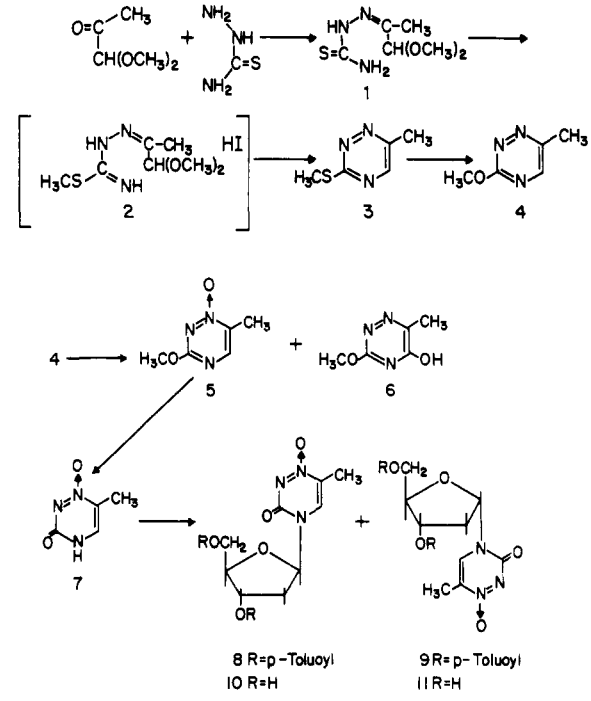
Condensation of pyruvaldehyde dimethyl acetal with thiosemicarbazide, followed by methylation and cyclization, gave 3-(methylthio)-6-methyl-1,2,4-triazine, which was converted to 6-methyl-1,2,4-triazin-3(4*H*)-one 1-oxide by treatment with sodium methoxide and by selective oxidation and hydrolysis. Following silylation, this intermediate was condensed with blocked 2-deoxyribofuranosyl chloride, providing the anomeric nucleoside mixture, which was separated and deblocked to furnish the title compound. X-ray analysis of this nucleoside was carried out to confirm its structure and to study its conformation.

The antimetabolite activity of emimycin,[1,2] which is pyrazin-2(1*H*)-one 4-oxide, suggested the synthesis of other pyrimidine and purine analogues containing a bioisosteric replacement of a carbonyl with the *N*-oxide group. Both ribofuranosyl[2] and deoxyribofuranosyl[3] derivatives of emimycin and a pyrazine *N*-oxide analogue of inosine[4] have been synthesized and shown to possess antibacterial activity. Of interest was the finding[5] that the pyrazine *N*-oxide analogue of thymidine was only weakly active against bacterial cells but was significantly active against leukemia L1210 cells in vitro and in vivo. Similarly, several triazine *N*-oxide derivatives of uracil,[6] uridine,[6] and 2′-deoxyuridine[7] have also been prepared and shown to exhibit antitumor properties. This paper describes the synthesis of *as*-triazine *N*-oxide analogues of thymine (**7**) and thymidine (**10**) (scheme I) and the crystal structure of **10**.

Condensation of thiosemicarbazide with 1,1-dimethoxyacetone gave the corresponding thiosemicarbazone derivative **1**. Methylation of **1** with methyl iodide gave *S*-methyl derivative **2** (Scheme I) which was not isolated but, after an intermediate hydrolysis of the dimethoxy group, cyclized to 3-(methylthio)-6-methyl-1,2,4-triazine (**3**). Compound **3** was formed in trace amounts only if the cyclization was attempted by omitting the hydrolysis step. The formation of **3** as a byproduct (5%) has been reported[8] to occur when *S*-methylthiosemicarbazide is condensed with glyoxal; however, no data concerning **3** have been shown. Conversion of various 3-(methylthio)-1,2,4-triazines to the corresponding 3-methoxy derivatives[8,10] by treatment with sodium methoxide in methanol has recently been reported. A similar treatment of **3**, however, produced only intractable mixtures. A careful monitoring of this reaction revealed that, initially, 3-methoxy-6-methyl-1,2,4-triazine (**4**) was formed; however, this was later destroyed by a reaction with the byproduct sodium methylmercaptide. Oxygen, therefore, was introduced into

Scheme I



the reaction mixture to convert sodium methylmercaptide to a disulfide, and, under these conditions, compound **4** was obtained in fairly good yield (50%). Oxidation of **4** was first attempted by treatment with *m*-chloroperoxybenzoic acid in refluxing benzene, the method that Szekeres et al.[6] used for the preparation of 3-methoxy-1,2,4-triazine 1-oxide. In contrast to 3-methoxy-1,2,4-triazine, oxidation of **4** gave 3-methoxy-6-methyl-1,2,4-triazin-5-(4*H*)-one (**6**), a product of oxidation of the ring. This outcome was not entirely surprising, since it has recently been pointed out that oxidation with peroxy acids of 1,2,4-triazines which are substituted at the 3- and/or 6-position with alkyl or aryl groups and have a hydrogen at the 5-position gives the products oxidized at the ring[9] and that oxidation of N-1 in 3-methoxy-1,2,4-triazine is rather exceptional. We have found that the determining factor in the oxidation of **4** was temperature. Although the compound **6** has always been formed during oxidation of **4** under different conditions, at low temperatures (below 0 °C) a 40% yield of the N-1-oxidized product **5** was obtained. In addition to **5** and **6**, small amounts of isomeric 3-methoxy-6-methyl-1,2,4-triazine 2-oxide (1%) and 3-methoxy-6-methyl-1,2,4-triazine 4-oxide (1.4%) have been isolated from the reaction mixture. The positions of the

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Table I. Positional and Thermal Parameters and Their Estimated Standard Deviations[a]

atom	x	y	z	B(1,1)	B(2,2)	B(3,3)	B(1,2)	B(1,3)	B(2,3)
O(2)	0.2097 (4)	0.6820 (2)	0.5882 (6)	0.0172 (5)	0.00376 (10)	0.0390 (10)	0.0006 (4)	−0.0067 (12)	−0.0013 (6)
O(4)	0.7048 (4)	0.8540 (0)	0.4867 (5)	0.0284 (7)	0.00417 (11)	0.0373 (9)	−0.0007 (5)	0.0132 (13)	0.0094 (6)
O(1′)	0.5732 (3)	0.5950 (2)	1.3129 (4)	0.0196 (4)	0.00302 (9)	0.0221 (7)	0.0006 (4)	0.0089 (9)	−0.0016 (4)
O(3′)	0.5787 (4)	0.3876 (2)	1.0215 (5)	0.0253 (6)	0.00248 (8)	0.0290 (8)	−0.0014 (4)	−0.0003 (11)	−0.0012 (5)
O(5′)	0.9863 (4)	0.5534 (2)	1.2808 (6)	0.0171 (4)	0.00497 (12)	0.0387 (10)	−0.0057 (4)	0.0091 (11)	0.0018 (6)
N(1)	0.5127 (4)	0.6767 (2)	0.9089 (5)	0.0154 (4)	0.00252 (9)	0.0240 (8)	0.0010 (4)	0.004 (1)	−0.0003 (5)
N(3)	0.4593 (4)	0.7675 (2)	0.5228 (5)	0.0211 (6)	0.00298 (10)	0.0243 (8)	0.0025 (4)	−0.001 (1)	−0.0000 (6)
N(4)	0.6437 (4)	0.7974 (2)	0.6232 (5)	0.0214 (6)	0.00261 (9)	0.0253 (8)	0.0028 (4)	0.010 (1)	0.0019 (5)
C(2)	0.3849 (5)	0.7078 (2)	0.6675 (6)	0.0183 (6)	0.0026 (1)	0.0249 (10)	0.0021 (4)	0.001 (1)	−0.0025 (6)
C(5)	0.7724 (5)	0.7714 (2)	0.8681 (6)	0.0160 (6)	0.0027 (1)	0.0291 (10)	0.0022 (4)	0.005 (1)	0.0009 (6)
C(6)	0.7001 (3)	0.7099 (2)	1.0038 (5)	0.0114 (4)	0.0027 (1)	0.0261 (9)	0.0015 (3)	0.004 (1)	0.0009 (5)
C(Me)	0.9744 (5)	0.8134 (3)	0.9603 (8)	0.0175 (6)	0.0036 (1)	0.0463 (15)	−0.0007 (6)	0.008 (2)	0.0046 (8)
C(1′)	0.4286 (4)	0.6101 (2)	1.0641 (6)	0.0151 (5)	0.0028 (1)	0.0266 (9)	0.0002 (5)	0.010 (1)	−0.0004 (6)
C(2′)	0.3913 (4)	0.5245 (2)	0.9157 (7)	0.0139 (5)	0.0030 (1)	0.0287 (10)	−0.0016 (5)	0.001 (1)	−0.0005 (6)
C(3′)	0.5912 (4)	0.4781 (2)	1.0243 (5)	0.0147 (5)	0.0030 (1)	0.0196 (8)	−0.0017 (5)	0.005 (1)	−0.0008 (6)
C(4′)	0.6564 (4)	0.5086 (2)	1.3179 (5)	0.0158 (5)	0.0025 (1)	0.0207 (8)	−0.0012 (4)	0.008 (1)	0.0002 (5)
C(5′)	0.8825 (5)	0.5102 (3)	1.4481 (6)	0.0162 (6)	0.0037 (1)	0.0253 (11)	−0.0012 (5)	−0.002 (1)	0.0004 (7)

atom	x	y	z	B (Å²)	atom	x	y	z	B (Å²)
H(6)	0.774 (6)	0.689 (3)	1.173 (7)	2.5 (7)	H(C3′)	0.698 (5)	0.498 (3)	0.930 (7)	3.2 (9)
H(Me1)	1.050 (6)	0.801 (4)	0.827 (8)	3.9 (10)	H(C4′)	0.589 (5)	0.472 (3)	1.426 (7)	2.6 (7)
H(Me2)	1.044 (6)	0.791 (4)	1.134 (8)	4.1 (10)	H(C5′1)	0.914 (6)	0.541 (3)	1.631 (8)	3.4 (9)
H(Me3)	0.947 (8)	0.875 (4)	0.972 (10)	6.3 (14)	H(C5′2)	0.933 (8)	0.449 (4)	1.482 (11)	6.1 (15)
H(C1′)	0.313 (5)	0.639 (3)	0.103 (7)	2.3 (7)					
H(C2′1)	0.350 (6)	0.534 (3)	0.719 (8)	3.3 (8)	H(O3′)	0.520 (9)	0.365 (5)	0.840 (10)	6.6 (15)
H(C2′2)	0.285 (6)	0.503 (4)	0.984 (8)	4.1 (10)	H(O5′)	1.082 (7)	0.586 (4)	1.375 (9)	4.6 (12)

[a] The form of the anisotropic thermal parameter is $-\exp[-(B(1,1)H^2 + B(2,2)k^2 + B(3,3)L^2 + B(1,2)hk + B(1,3)hl + B(2,3)kl)]$.

N-oxide groups in these compounds were inferred on the basis of chemical shifts in their ^{1}H NMR spectra.[11] Attempts to condense **5** with 3,5-di-*O*-*p*-toluoyl-2-deoxy-D-*erythro*-pentofuranosyl chloride under varying conditions, as well as attempts to hydrolyze it by treatment with methanolic HCl,[6] failed. The 6-methyl derivative **5** was, however, readily converted to 6-methyl-1,2,4-triazin-3-(4*H*)-one 1-oxide (**7**) by treatment with sodium carbonate in methanol–water. Silylation of **7**, followed by condensation with the blocked 2-deoxyribofuranosyl chloride, gave an anomeric mixture of blocked nucleosides **8** and **9** which were separated by chromatography and deblocked by treatment with K_2CO_3 in methanol to give 4-(2-deoxy-β-D-*erythro*-pentofuranosyl)-6-methyl-1,2,4-triazin-3(4*H*)-one 1-oxide (**10**) and its α anomer **11**. The structures of **10** and **11** were derived by elemental analysis and UV and ^{1}H NMR spectra. The structure of **10** was confirmed by X-ray crystallography. Compound **10** did not inhibit the growth of L1210 and HeLa cels in vitro at a 10^{-4} M concentration.

Crystallography

The structure determination is described in the Experimental Section. The atomic parameters are given in Table I, and the bond distances and angles are summarized in Table II. Figure 1 shows a view of the molecule perpendicular to the base plane. (The numbering used here is different from that of the synthetic section, and, it is used mainly to faciliate the comparison with the crystallgraphic work on thymidine and its analogues.) The bond lengths and angles in the sugar moiety of **10** are in good agreement with those found in similar nucleoside structures and need not be discussed in detail. The least-squares plane calculated through all six of the base atoms shows them to lie in a plane (σ(mean) = 0.015 Å) with a maximum deviation from the plane for C(2) of 0.025 Å. The conformation about the glycosidic bond is anti, and the torsion angle χ_{CN} has a very low value 2.6 (8)°. Low χ_{CN} values will introduce short C(6)–H···O(1′) contacts, but in several other nucleosides and nucleotides similar values were also observed: 3.8° in adenosine 3′-

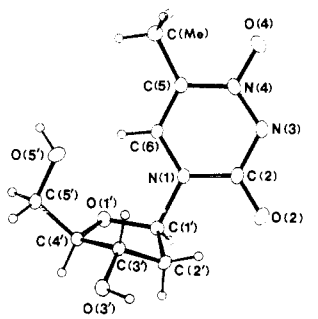

Figure 1. View of **10** perpendicular to the base plane.

Table II. Bond Lengths (Å) and Angles (Degrees) in Compound 10

Bond Lengths

O(2)-C(2)	1.226 (4)	N(3)-N(4)	1.314 (4)
O(4)-N(4)	1.261 (4)	N(3)-C(2)	1.365 (5)
O(1′)-C(1′)	1.408 (4)	N(4)-C(5)	1.386 (4)
O(1′)-C(4′)	1.457 (4)	C(5)-C(6)	1.349 (5)
O(3′)-C(3′)	1.410 (4)	C(5)-C(Me)	1.487 (5)
O(5′)-C(5′)	1.416 (4)	C(1′)-C(2′)	1.520 (2)
N(1)-C(2)	1.396 (4)	C(2′)-C(3′)	1.514 (4)
N(1)-C(6)	1.346 (4)	C(3′)-C(4′)	1.524 (4)
N(1)-C(1′)	1.508 (5)	C(4′)-C(5′)	1.512 (4)

Angles

C(1′)-O(1′)-C(4′)	110.3 (2)	C(6)-C(5)-C(Me)	125.7 (3)
C(2)-N(1)-C(6)	120.0 (2)	N(1)-C(6)-C(5)	121.9 (2)
C(2)-N(1)-C(1′)	117.8 (2)	O(1′)-C(1′)-N(1)	108.4 (2)
C(6)-N(1)-C(1′)	122.1 (2)	O(1′)-C(1′)-C(2′)	106.8 (2)
C(2)-N(3)-C(4)	119.0 (2)	N(1)-C(1′)-C(2′)	112.1 (2)
O(4)-N(4)-N(3)	117.0 (2)	C(1′)-C(2′)-C(3′)	102.6 (2)
O(4)-N(4)-C(5)	118.6 (2)	O(3′)-C(3′)-C(2′)	115.2 (2)
N(3)-N(4)-C(5)	124.3 (2)	O(3′)-C(3′)-C(4′)	108.8 (2)
O(2)-C(2)-N(1)	120.5 (2)	C(2′)-C(3′)-C(4′)	102.3 (2)
O(2)-C(2)-N(3)	120.9 (2)	O(1′)-C(4′)-C(3′)	105.0 (2)
N(1)-C(2)-N(3)	118.6 (2)	O(1′)-C(4′)-C(5′)	109.9 (2)
N(4)-C(5)-C(6)	116.1 (2)	C(3′)-C(4′)-C(5′)	115.9 (2)
N(4)-C(5)-C(Me)	118.2 (2)	O(5′)-C(5′)-C(4′)	111.0 (2)

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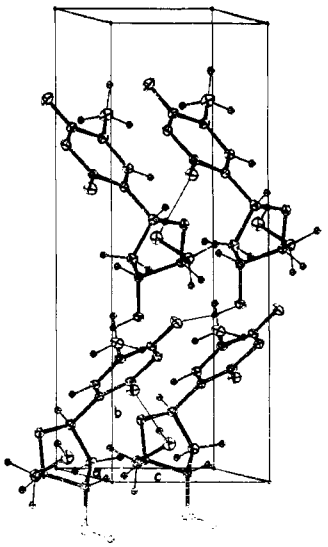

Figure 2. Packing of the molecule in the crystal.

phosphate dihydrate,[12] −2.0° in deoxycytidine hydrochloride,[13] 4.9° in adenylyl-(2′→5′)-uridine tetrahydrate,[14] −5.9° in deoxycytidine 5′-phosphate monohydrate,[15] −1.3° in 3′-(*N*-benzylmethylamino)-3′-(deoxyadenosinyl)oxazolidine.[16] The deoxyribose ring is in the twist C(3′)-endo/C(2′)-exo conformation with O(5′) in the g^+ orientation. The ϕ_{OO} and ϕ_{OC} torsional angles are −69 (1)° and 50 (1)°, respectively. The pseudorotation parameters for the sugar ring[17] are P = 3.9 (8)° and τ_m = 36.1 (5)°, and the displacements of the C(2′) and C(3′) atoms from the planes through the other four ring atoms are −0.519 and 0.537 Å. The packing of the molecules in the crystal and the hydrogen bonds are shown in Figure 2. No stacking between the bases is observed in the crystal. There are two hydrogen bonds, O(5′)···O(2) and O(3′)···O(4) [2.744 (4) and 2.843 (4) Å, respectively], with O···H distances and O–H···O angles being 1.92 (5) Å, 1.96 (5) Å, 159 (3)° and 151 (3)°, respectively. Also there are three intramolecular C–H···O contacts: C(6)–H···O(1′), C(6)–H···O(5′), and C(2′)–H···O(2). The contacts and the angles subtended at the hydrogens are, respectively, 2.25 (4) Å, Å, 2.54 (4) Å, 2.51 (5) Å, 107 (3)°, 129 (3)°, and 113 (4°). There is some justification for interpreting the first contact as a weak hydrogen bond.[18]

Experimental Section

General Methods. ^{1}H NMR spectra were recorded on a Varian LX-100 spectrometer in $CDCl_3$ (Me_4Si). UV spectra were determined on a Cary 14 ultraviolet spectrophotometer, and mass spectra were recorded on a CEC 21-491 double-focusing mass spectrometer using an ionization voltage of 70 eV. Melting points were determined on a Fisher-Johns melting point apparatus and were not corrected. Evaporations were performed under reduced pressure on a rotary evaporator. Thin-layer chromatography was performed on precoated silica gel 60F-25A plates (EM Laboratories, Inc.), and the spots were visualized with a Mineralight UV lamp.

The transparent colorless crystals of **10** ($C_9H_{13}N_3O_5$) are monoclinic and were obtained from a methanol solution. The initial examination and unit cell and space group determinations were performed on a GE XRD-6 diffractometer. The unit cell constants are as follows: a = 6.832 (1) Å, b = 15.550 (1) Å, c = 5.109 (1) Å, β = 105.29 (1)°, V = 523.5 Å^3, Z = 2, d_m = 1.54 g/cm^3, d_x = 1.542 g/cm^3. Intensity data collection was carried out on a CAD-4 diffractometer with Cu Kα radiation. Intensities were measured by ω–2θ scan technique up to θ = 77°. Of the 1116 independent intensities, 1065 had $|F| > 3\sigma$. The data were corrected for anisotropy of absorption by measuring the ψ scan for reflections near $\chi \simeq 90°$. The structure was solved by direct methods and refined by the full-matrix least-squares method to a final R = 0.026 (R_w = 0.046) value. The calculations were performed on a PDP-11/34 computer using the programs in the Enraf-Nonius structure determination package.

1,1-Dimethoxyacetone Thiosemicarbazone (1). A mixture of 1,1-dimethoxyacetone (118 g, 1 mol) and thiosemicarbazide (91 g, 1 mol) in methanol (700 mL) was heated at reflux temperature for 15 min. Toluene (700 mL) was added, and the turbid solution was filtered. The filtrate was evaporated to approximately 400 mL and kept for crystallization at room temperature. The crystals were filtered and washed with toluene: yield 145 g; mp 127–130 °C. Evaporation of the filtrate yielded an additional 30 g of **1**, mass spectrum m/e 191 (molecular ion). Anal. Calcd for $C_6H_{13}N_3O_2S$: C, 37.68; H, 6.85; N, 21.97; S, 16.76. Found: C, 37.50; H, 6.90; N, 21.62; S, 16.82.

3-(Methylthio)-6 methyl-1,2,4-triazine (3). Methyl iodide (150 g) was added to a cold (5–10 °C) solution of compound **1** (191 g, 1 mol) in methanol (600 mL). The reaction mixture was kept at 40–50 °C for 3 h by cooling during the first hour and warming for 2 h. Water (200 mL) was added, and the solution was heated at 55–60 °C for 2 h. Solid $NaHCO_3$ (50 g) was added with stirring, and the mixture was evaporated to a thin syrup. Water (500 mL) was added to this syrup, and the mixture was extracted with $CHCl_3$ (4 × 500 mL and 3 × 100 mL). The combined $CHCl_3$ solution was washed with water (200 mL) and dried (Na_2SO_4). The solution was evaporated and the residue distilled at low pressure (0.1 mmHg). The product was redistilled to yield 69 g of compound **3**: bp 75.5–76 °C (0.35 mmHg); mp 41–42 °C (methanol). The mass spectrum showed a molecular ion at m/e 141. Anal. Calcd for $C_5H_7N_3S$: C, 42.53; H, 4.99; N, 29.76; S, 22.71. Found: C, 42.42; H, 5.03; N, 29.52; S, 22.83.

3-Methoxy-6-methyl-1,2,4-triazine (4). A solution of the 3-methylthio derivative **3** (70.5 g, 0.5 mol) in methanol (2 L) was stirred vigorously at room temperature while a dispersed stream of oxygen was introduced. A solution of sodium methoxide (prepared from 12 g of Na) in methanol (200 mL) was added, and the mixture was stirred at room temperature with continuous introduction of oxygen for 2 days. The solution was neutralized with solid CO_2 and evaporated, and the residue was extracted with $CHCl_2$ (800 mL). The CH_2Cl_2 solution was washed with water (200 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was sublimed at reduced pressure (0.1 mmHg) to give 30 g of compound **4**: mp 72–73 °C (ether); mass spectrum, m/e 125 (molecular ion). Anal. Calcd for $C_5H_7N_3O$: C, 47.99; H, 5.63; N, 33.58. Found: C, 47.76; H, 5.72; N, 33.42.

3-Methoxy-6-methyl-1,2,4-triazine 1-Oxide (5) and 3-Methoxy-6-methyl-1,2,4-triazin-5(4*H*)-one (6). Compound **4** (25 g, 0.2 mol) was dissolved in a mixture of CH_2Cl_2–toluene (300 mL, 2:5 v/v), and the solution was cooled to −10 °C. *m*-Chloroperoxybenzoic acid (85%, 50 g) was added in small portions with stirring and cooling in 6 h. The mixture was allowed to warm to 0 °C and was kept at this temperature for 2 days. The mixture was filtered, and the precipitate was stirred with acetone (150 mL), filtered, and washed with acetone to give 6.7 g of compound **6**, mp 175–176 °C (ethanol). The original filtrate and the acetone filtrates were combined and evaporated to dryness. The residue was stirred with CH_2Cl_2 (500 mL), filtered, and washed with CH_2Cl_2 (50 mL) to give *m*-chlorobenzoic acid (36 g). The combined filtrates were extracted with water (2 × 100 mL). The water solution was washed with CH_2Cl_2 (100 mL) and evaporated to yield additional 8 g of compound **6**. All CH_2Cl_2 solutions were combined, washed with $NaHCO_3$ solution to remove the remaining *m*-chlorobenzoic acid, and dried (Na_2SO_4). The solution was evaporated and the residue crystallized from ethanol to yield 5.8

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g of compound **5**, mp 121–122 °C. The filtrate was evaporated, and the residue was separated by silica gel chromatography in CH_2Cl_2–EtOAc (10:1) to give 5.4 g of **5** and small amounts of isomeric 3-methoxy-6-methyl-1,2,4-triazine 2-oxide (~300 mg) and 3-methoxy-6-methyl-1,2,4-triazine 4-oxide (~400 mg). Mass spectra showed the following: for **5**, molecular ion at *m/e* 141 and major peaks at M – 16 and M – 17 (more abundant than M – 16); for **6**, molecular ion at *m/e* 141; for 3-methoxy-6-methyl-1,2,4-triazine 2-oxide, molecular peak at *m/e* 141; for 3-methoxy-6-methyl-1,2,4-triazine 4-oxide, molecular peak at *m/e* 141. Anal. Calcd for $C_5H_7N_3O_2$ (**5**): C, 42.55; H, 4.99; N, 29.77. Found: C, 42.60; H, 5.10; N, 29.83. Calcd for $C_5H_7N_3O_2$ (**6**): C, 42.55; H, 4.99,; N, 29.77. Found: C, 42.46; N, 5.15; N, 29.61.

6-Methyl-1,2,4-triazin-3(4*H*)-one 1-Oxide (7). A mixture of **5** (5.65 g, 0.04 mol) and Na_2CO_3 (0.7 g) in methanol–water (200 mL, 1:1 v/v) was stirred at 70–75 °C in a closed flask for 24 h. The solution was diluted with water (200 mL) and neutralized with Dowex 50 [H^+]. The mixture was heated to dissolve the precipitated **7** and filtered, and the resin was washed with hot water (~50 mL). The filtrates were cooled to 5 °C and the crystalline product collected by filtration (3.90 g). The filtrate was evaporated to yield an additional 1.0 g of **7**: yield 4.90 g (96.3%); mp 221–222 °C dec. The mass spectrum showed a molecular ion at *m/e* 127 and major peaks at M – 16 and M – 17. Anal. Calcd for $C_4H_5N_3O_2$: C, 37.80; H, 3.96; N, 33.06. Found: C, 37.61; H, 3.98, N, 32.91.

4-(3,5-Di-*O*-*p*-toluoyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-6-methyl-1,2,4-triazin-3(4*H*)-one 1-Oxide (8) and Its α Anomer 9. A mixture of compound **7** (4.5 g, 0.035 mol), trimethylchlorosilane (1 mL), and hexamethyldisilazane (30 mL) was stirred at 100–110 °C until the **7** dissolved (approximately 1 h). Dry toluene (100 mL) was added, and the solution was evaporated. This step was repeated two more times, and the residue was dissolved in dry CH_2Cl_2 (100 mL). A dry mixture of HgO (6.5 g) and $HgBr_2$ (10.5 g) was added, and the mixture was cooled in ice under nitrogen. 2-Deoxy-3,5-di-*O*-*p*-toluoyl-D-*erythro*-pentofuransyl chloride (19 g) in CH_2Cl_2 (150 mL) was added with stirring. The mixture was stirred at 5 °C for 0.5 h and at room temperature for 0.5 h. It was then filtered, and the solids were washed with CH_2Cl_2 (200 mL). The combined filtrates were washed with 20% KI solution (2 × 150 mL) and H_2O (2 × 100 mL) and dried (Na_2SO_4). The solution was evaporated to a crystalline residue which was separated by chromatography on silica gel in CH_2Cl_2–petroleum ether–ether (5:2:1 v/v/v). Evaporation of the appropriate fractions gave 6.05 g of **8**, 4.77 g of **9**, and a mixture (2:3, 2.2 g) of **8** and **9**: compound **8**, mp 191–192 °C; compound **9**, mp 178–179 °C.

4-(2-Deoxy-β-D-*erythro*-pentofuranosyl)-6-methyl-1,2,4-triazin-3(4*H*)-one 1-Oxide (10). A mixture of compound **8** (4.8 g, 0.01 mol) and KOH (400 mg) in methanol was stirred at room temperature for 20 h. The solution was neutralized with a weakly acidic cation exchanger (Amberlite CG-50, H^+) and filtered, and the resin was washed with methanol. The combined filtrates were evaporated to a syrup which was dissolved in ethanol for crystallization: yield 2.23 g; mp 193–194 °C. Anal. Calcd for $C_9H_3N_3O_5$: C, 44.44; H, 5.38; N, 17.27. Found: C, 44.31; H, 5.41; N, 17.17.

4-(2-Deoxy-α-D-*erythro*-pentofuranosyl)-6-methyl-1,2,4-triazin-3(4*H*)-one 1-Oxide (11). Compound **9** (4.8 g, 0.01 mol) was deblocked by following the procedure for preparation of **10**: yield 1.94 g; mp 180–181 °C. Anal. Calcd for $C_9H_{13}N_3O_5$: C, 44.44; H, 5.38; N, 17.27. Found: C, 44.24; H, 5.27; N, 17.16

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Registry No. **1**, 80083-14-3; **3**, 42836-95-3; **4**, 61178-10-7; **5**, 80083-15-4; **6**, 57537-20-9; **7**, 80083-16-5; **8**, 80083-17-6; **9**, 80083-18-7; **10**, 80083-19-8; **11**, 80105-71-1; 1,1-dimethoxyacetone, 6342-56-9; thiosemicarbazide, 79-19-6; 2-deoxy-3,5-di-D-*p*-toluoyl-D-*erythro*-pentofuransyl chloride, 3601-89-6.

Supplementary Material Available: Tables of UV spectral data for compounds **1**, **3–7**, **10**, and **11** and ^1H NMR spectral data for some 1,2,4-triazines (3 pages). Ordering information is given on any current masthead page.

New Synthesis of Spiro Phosphorane by Using Diphenyl Disulfide. A Facile Route to Cyclic Acyloxyphosphoranes from α-Hydroxy Acids

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Five-membered 1,3,2-dioxaphospholanes were subjected to reaction with 1,2- and 1,3-glycols, with 2-(methylamino)ethanol, and with α-hydroxy acids in the presence of diphenyl disulfide to produce various derivatives of spiro oxyphosphoranes **3** and **5**. The reactions were carried out at 0 °C with phosphonite **1a** and at 80 °C with phosphites **1b** and **1c**. Two moles of benzenethiol was isolated from the system by distillation in vacuo. The course of reaction of these ternary systems has reasonably been explained by invoking the intermediacy of a phosphonium benzenethiolate **7**.

Recently, a number of interesting reactions for the syntheses of pentacovalent oxyphosphoranes and their analogues from the corresponding trivalent phosphorus compounds have been reported.[1-4] However, most of these reactions involve some inconveniences, e.g., the employment of dangerous or expensive reagents and the necessity of eliminating concomitant byproducts. In this paper, we describe a new synthetic method for preparation of spiro

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