The Synthesis and Properties of New Carbohydrate-Modified Mesoionic Thiazolo[3,2-*a*]pyrimidine-5,7-dione Acyclonucleosides

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The synthesis of the first examples of Class II mesoionic thiazolopyrimidine acyclonucleosides (MTA) incorporating the 2,3-dihydroxypropyl moiety as the sugar simulator is described. First, 2-bromothiazole was reacted with excess 1-amino-2,3-propanediol acetonide *via* an aromatic nucleophilic substitution reaction to yield 1-(2-thiazolylamino)-2,3-propanediol acetonide. This acetonide intermediate was condensed at 160° with substituted bis(2,4,6-trichlorophenyl) malonic esters to form a series of protected acyclonucleosides termed *anhydro*-(8-((2,2-dimethyl-1,3-dioxolan-4-yl)methyl)-5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidinium hydroxides) which differ in their 6-position substituent. Deprotection of these acyclonucleosides using *p*-toluenesulfonic acid catalyst in methanol at 65° yielded the desired Class II MTA, *anhydro*-(8-(2,3-dihydroxypropyl)-5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidinium hydroxides).

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Introduction.

Class I mesoionic purinones are defined as five-membered ring mesoionic compounds fused to a pyrimidine ring while Class II systems possess a mesoionic six-membered pyrimidine ring fused to a five-membered ring [1]. Various investigators including ourselves have previously reported the synthesis as well as spectral, chemical, biological and/or biochemical properties of many Class II mesoionic xanthines, a subclass of mesoionic purinones [2]. For example, some derivatives demonstrated antimicrobial activity including bacteriostatic, antifungal, antiprotozoal or antischistosomal activity [3] while others were also recently reported to possess platelet aggregation inhibitory activity [4]. In addition, several of the previously studied compounds and some new derivatives, including nucleoside analogs (Figure 1), were shown to be inhibitors of adenosine 3',5'-cyclic monophosphate (cyclic AMP) phosphodiesterase (PDE) [5] and antagonists of adenosine receptors [6].

Previous work from our laboratory [2g] detailed the preparation of class II MTA which possess monohydroxyalkyl substituents as the modified sugar portion of the acyclonucleosides and which structurally may be envisioned as hybrid analogs of HEPT and acyclovir

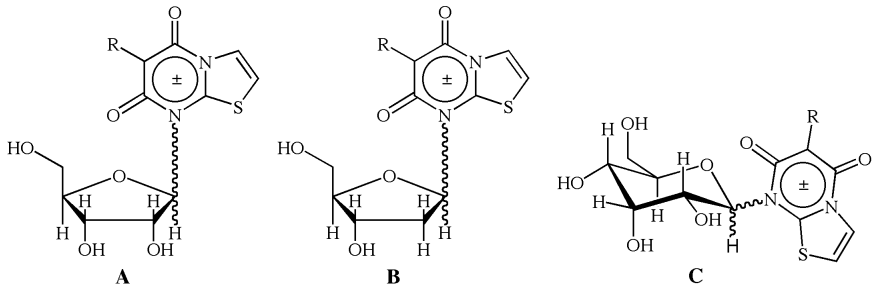


Figure 1. Nucleoside analogs produced by modification of the aglycon.

These studies revealed significant structure-activity relationships (SAR) between the presence or absence of certain mesoionic ring substituents and antimicrobial effects. One interesting aspect of these compounds is that a wide range of alkyl functional group substitution at position N-8 is tolerated while antimicrobial efficacy is maintained. In addition, present in the N-8 substituent is a ready handle which allows synthetic manipulation, including the attachment of a suitable acyclic chain of atoms to yield a class of compounds called acyclonucleosides [2g]. Thus, the mesoionic ring system can be viewed as an aglycon base that, when bonded to a sugar moiety, forms a nucleoside analog [6-8]. Important bioactive examples of acyclonucleosides are 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio)thymine (HEPT), an HIV reverse transcriptase inhibitor [7]; acyclovir and ganciclovir, FDA-approved antiviral agents effective against herpesvirus [8,9]; and (S)-9-(2,3-dihydroxypropyl)adenine((S)-DHPA), an inhibitor of RNA and DNA viruses [10,11] (Figure 2).

(Figure 2). These mesoionic compounds exhibited significant *in vivo* anti-trypanosomal activity in a mouse model system [2h] *and in vitro* antiproliferative activity in C3H/10T1/2 CL8 mouse embryo model system [2i]. Encouraged by these results and to explore the impor-

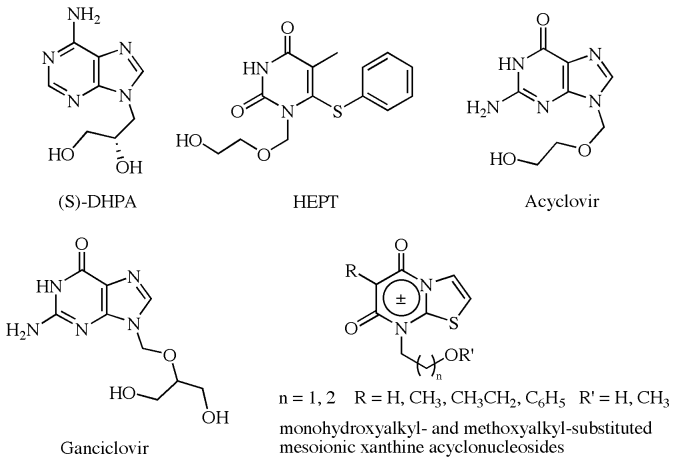
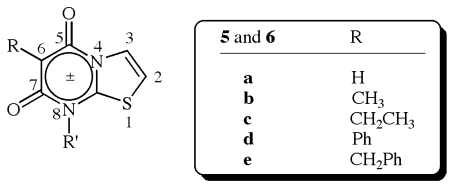


Figure 2. Nucleoside analogs which use an acyclic chain as the sugar simulator.

tance of the *N*-8-dihydroxy alkyl functionality of **6**, we sought to synthesize other analogs of these HEPT-acyclovir-type hybrid compounds (Figure 3) and determine their biological activity.



R' = (2,2-dimethyl-1,3-dioxolan-4-yl)methyl (**5**) or 2,3-propanediol (**6**)

Figure 3. Generalized structural representation of mesoionic xanthine acyclonucleosides **5** and **6**.

Furthermore, Glennon and co-workers synthesized the first examples of Class II mesoionic xanthine nucleosides with either a ribose or a glucose substituent occupying the N-8 position of the mesoionic thiazolo[3,2-*a*]pyrimidine base (Figure 1) and studied their chemical and spectral properties [12]. These compounds were designed as mesoionic analogs of well-known chemotherapeutics developed by synthetic modification of the aglycon part of the nucleoside, including 2'-deoxy-5-fluorouridine, an antineoplastic agent [9]; 2'-deoxy-5-iodouridine, an antiviral drug [10]; and 3-deazauridine which has antitumor and antiviral properties [11].

Of special interest in the present work is the dihydroxypropyl (DHP) substituent which is shown in Figure 2 in the structure for (S)-DHPA as the acyclic side chain attached to the base guanine at the 9 position. DHP was chosen as the sugar simulator in the title MTA for the following reasons: 1) the greater activity observed for the DHP moiety relative to other hydroxylated side chains attached to the 9 position of an adenine or 6-hydroxyaminopurine heterobase [13,14]; 2) the success of the strategy of keeping a portion of the natural ribose sugar ring which is illustrated by (S)-DHPA, a broad-spectrum antiviral agent, and by acyclovir, a potent antiherpetic drug. DHPA preserves the base-C(1)-C(2)-C(3) portion whereas acycloguanosine retains the base-C(1)-0-C(4)-C(5) fragment of their respective natural nucleosides [15]. The marked success of the DHP and (hydroxyethoxy)methyl (HEM) moieties as ribose simulators is evidenced in different ways. The HEM moiety can be "activated" through phosphorylation by cellular kinase to generate *in situ* potent nucleotide drug forms [16] whereas the DHP moiety along with the adenine base effectively inhibit S-adenosylhomocysteine hydrolase [17]; 3) extensive structure-activity relationships studies for xanthines as antagonists for adenosine receptors have shown that *n*-propyl moieties at the 1 and 3 positions confer higher potency than methyl or ethyl at both A_1- and A_2-adenosine receptors [18,19]; 4) like many other xanthines, mesoionic purinone analogs show low water solubility which hampers pharmacological study of them. Therefore, it is hoped that the attachment of the DHP group to the mesoionic heterocycle will enhance hydrogen bonding and result in improved water solubility [19].

As part of our continuing interest in the chemistry of mesoionic nucleoside analogs as potential therapeutic agents, we now report the synthesis and properties of 1) the first examples of Class II MTA to incorporate the 2,3-dihydroxypropyl moiety (**6**) and 2) their acetonide precursors (**5**) (Figure 3). The currently accepted nomenclature for the mesoionic xanthine ring system of **5** and **6** is *anhydro*-(5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidine hydroxide). For the fused ring system of **5** and **6**, the substituents (R') at the N-8 position are (2,2-dimethyl-1,3-dioxolan-4-yl)methyl and 2,3-dihydroxypropyl respectively (Figure 3) while the C-6 substituent (R) is either hydrogen, methyl, ethyl, phenyl, or benzyl.

Results and Discussion.

The standard practical method for construction of the mesoionic thiazolo[3,2-*a*]pyrimidine-5,7-dione ring system involves condensation of a substituted bis(2,4,6-trichlorophenyl) malonate (**4**) with a 2-amino-1,3-thiazole at ~160° [2g]. One could conceivably prepare compound **6** directly in this manner by condensation of 1-(thiazolylamino)-2,3-propanediol with malonates **4**. However problems were envisioned because the reaction pathway is thought to involve a ketene as an intermediate [20]. If 1-(thiazolylamino)-2,3-propanediol was heated with **4** the OH groups present could add to the ketene molecule in competition with NH-bond or nitrogen-atom addition [21]. To avoid such problems it was decided to prepare the protected diol, 1-(thiazolylamino)-2,3-propanediol acetonide (**3**), which was subsequently condensed with **4** to form **5**.

The target compounds **6** could then be formed by deprotection of **5** (Figure 4).

The synthetic strategy for **3** was similar to that which we previously employed for the preparation of the monohy-

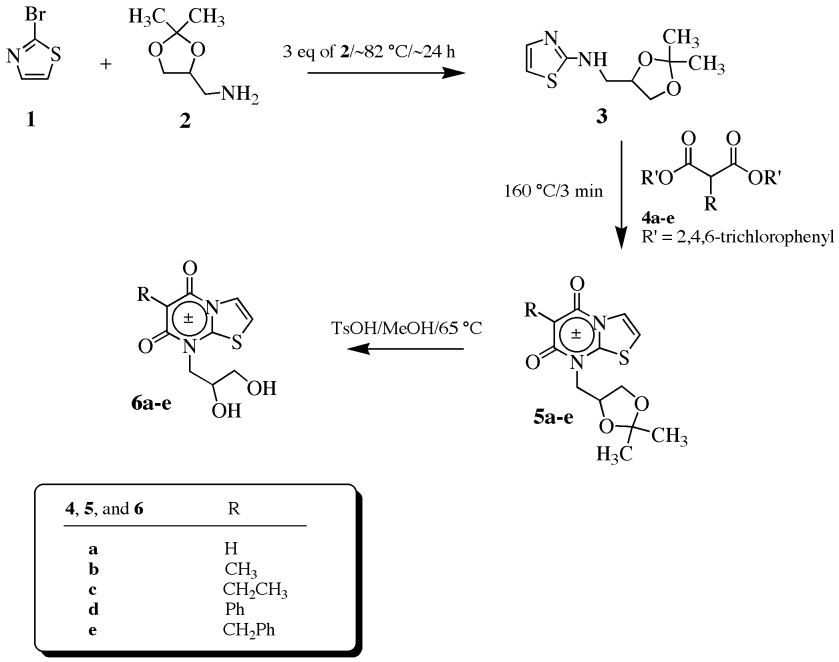


Figure 4. Synthesis of the Mesoionic Xanthine Acyclonucleosides.

Table 1

Properties of Compounds **3**, **5**, and **6**

Compound	R	Yield (%)	Mp (°C)	Purification method [a]	Formula	Analyses: % Theory (% Found) C	H	N
3	—	60	90-90.5	water or silica gel-ether	$C_9H_{14}N_2O_2S$	50.44 (50.30)	6.58 (6.66)	13.07 (12.92)
5a	H	77	165-166	silica gel-chloroform-acetone	$C_{12}H_{14}N_2O_4S$	51.05 (51.03)	5.00 (5.04)	9.92 (9.82)
5b	CH_3	84	133-135	silica gel-chloroform-acetone	$C_{13}H_{16}N_2O_4S$	52.69 (52.73)	5.44 (5.45)	9.45 (9.38)
5c	CH_3CH_2	79	150-153	silica gel-chloroform-acetone	$C_{14}H_{18}N_2O_4S$	54.18 (54.24)	5.85 (5.87)	9.03 (8.97)
5d	C_6H_5	38	213-215	silica gel-chloroform-acetone then toluene	$C_{18}H_{18}N_2O_4S$	60.32 (60.13)	5.06 (5.10)	7.82 (7.69)
5e	$C_6H_5CH_2$	38-79	225-227	ether trituration	$C_{19}H_{20}N_2O_4S$	61.27 (61.21)	5.41 (5.45)	7.52 (7.45)
6a	H	35	194-195 [b]	methanol	$C_9H_{10}N_2O_4S$	44.62 (44.76)	4.16 (4.16)	11.56 (11.43)
6b	CH_3	31	221-223	methanol	$C_{10}H_{12}N_2O_4S$	46.87 (46.62)	4.72 (4.77)	10.93 (10.74)
6c	CH_3CH_2	52	195-197	silica gel-acetone	$C_{11}H_{14}N_2O_4S$	48.88 (48.99)	5.22 (5.21)	10.36 (10.36)
6d	C_6H_5	78	220-223	methanol	$C_{15}H_{14}N_2O_4S$	56.59 (56.48)	4.43 (4.49)	8.80 (8.72)
6e	$C_6H_5CH_2$	38	155-159	acetone trituration	$C_{16}H_{16}N_2O_4S$	57.82 (57.61)	4.85 (4.79)	8.43 (8.33)

[a] Indicates a crystallization solvent, liquid chromatographic conditions, a trituration solvent, or a combination. [b] Mp of sample after recrystallization from methanol.

Table 2
Spectral Data of Compounds **3**, **5**, and **6**

Compound	R	^{1}H-NMR (δ ppm) [a]	UV λ_{max} (nm) [b]	IR (cm^{-1}) [c]		
				νC=N	νOH	νC=O
3	—	1.33 (s, 3H, CH_3)	261.4	1560 (s)		
		1.45 (s, 3H, CH_3)				
		3.17-4.67 (m, 5H, CH_2CHOCH_2O)				
		5.7 (br s, 1H, NH)				
		6.52 (d, 1H, SCH, J = 3.9 Hz)				
		7.30 (d, 1H, SC=CH, J = 3.9 Hz)				
5a	H	1.31 (s, 3H, CH_3)	277.8			1684 (m)
		1.40 (s, 3H, CH_3)	244.0			1654 (s)
		3.53-4.77 (m, 5H, CH_2CHOCH_2O)				
		5.13 (s, 1H)				
		7.05 (d, 1H, SCH, J = 5.0 Hz)				
		8.17 (d, 1H, SC=CH, J = 4.0 Hz)				
5b	CH_3	1.30 (s, 3H, CH_3)	283.0			1672 (m)
		1.38 (s, 3H, CH_3)	248.0			1633 (s)
		2.01 (s, 3H, CH_3)				
		3.57-4.80 (m, 5H, CH_2CHOCH_2O)				
		7.03 (d, 1H, SCH, J = 5.0 Hz)				
		8.21 (d, 1H, SC=CH, J = 4.6 Hz)				
5c	CH_3CH_2	1.07 (t, 3H, CH_3)	283.2			1684 (m)
		1.30 (s, 3H, CH_3)	248.4			1672 (m)
		1.38 (s, 3H, CH_3)				1626 (s)
		2.58 (q, 2H, CH_2)				
		3.57-4.83 (m, 5H, CH_2CHOCH_2O)				
		7.00 (d, 1H, SCH, J = 5.0 Hz)				
		8.22 (d, 1H, SC=CH, J = 5.0 Hz)				
5d	C_6H_5	1.33 (s, 3H, CH_3)	328.2			1666 (m)
		1.44 (s, 3H, CH_3)	254.4			1624 (s)
		3.57-4.90 (m, 5H, CH_2CHOCH_2O)				
		7.05 (d, 1H, SCH, J = 5.0 Hz)				
		7.20-7.97 (m, 5H, C_6H_5)				
		8.30 (d, 1H, SC=CH, J = 5.0 Hz)				
5e	$C_6H_5CH_2$	1.30 (s, 3H, CH_3)	282.6			1676 (m)
		1.38 (s, 3H, CH_3)	248.8			1627 (s)
		3.87 (s, 2H, CH_2)				
		3.53-4.83 (m, 5H, CH_2CHOCH_2O)				
		6.95 (d, 1H, SCH, J = 5.0 Hz)				
		7.13-7.70 (m, 5H, C_6H_5)				
		8.17 (d, 1H, SC=CH, J = 5.0 Hz)				
6a	H	3.12-5.36 (m, 7H, $CH_2CHOHCH_2OH$)	277.8		3327 (br)	1670 (m)
		4.70 (s, 1H)	245.5			1636 (s)
		7.51 (d, 1H, SCH, J = 5.0 Hz)	240.4			
		8.06 (d, 1H, SC=CH, J = 5.0 Hz)				
6b	CH_3	1.80 (s, 3H, CH_3)	283.2		3398 (br)	1654 (m)
		3.23-5.37 (m, 7H, $CH_2CHOHCH_2OH$)	249.8		3285 (br)	1624 (s)
		7.50 (d, 1H, SCH, J = 5.0 Hz)	244.2			
		8.08 (d, 1H, SC=CH, J = 5.0 Hz)				
6c	CH_3CH_2	0.98 (t, 3H, CH_3)	282.8		3369 (br)	1664 (m)
		2.35 (q, 2H, CH_2)	250.4			1633 (s)
		3.2-5.4 (m, 7H, $CH_2CHOHCH_2OH$)	244.6			
		7.48 (d, 1H, SCH, J = 5.0 Hz)				
		8.05 (d, 1H, SC=CH, J = 5.0 Hz)				
6d	C_6H_5	3.13-5.40 (m, 7H, $CH_2CHOHCH_2OH$)	291.2		3434 (br)	1653 (m)
		6.97-7.93 (m, 5H, C_6H_6)	249.6		3290 (br)	1623 (s)
		7.53 (d, 1H, SCH, J = 5.0 Hz)				
		8.15 (d, 1H, SC=CH, J = 5.0 Hz)				
6e	$C_6H_5CH_2$	3.23-5.40 (m, 7H, $CH_2CHOHCH_2OH$)	283.2		3331 (br)	1670 (m)
		3.67 (s, 2H, $ArCH_2$)	251.0		3250 (br)	1612 (s)
		7.03-7.5 (m, 5H, C_6H_5)	244.8			
		7.50 (d, 1H, SCH, J = 5.0 Hz)				
		8.08 (d, 1H, SC=CH, J = 5.0 Hz)				

[a] Measured using solvents: deuteriochloroform (acetonides and **3**) or dimethyl-d_6 sulfoxide (diols); [b] Measured using solvents: acetonitrile (acetonides and **3**) or water (diols); [c] Recorded using KBr discs.

droxyalkyl derivatives [2g] and involved an aromatic nucleophilic substitution reaction between 2-bromothiazole substrate (**1**) and 1-amino-2,3-propanediol acetonide (**2**). The amine **2** can be readily prepared in three steps starting from the commercially available solketal precursor [22].

In order to increase the rate of reaction and to buffer the reaction against the hydrobromic acid that is produced it was necessary to use excess amine to prepare **3**. Thus a three-to-one initial molar ratio of nucleophile **2** to electrophile **1** was used. We have found previously that a temperature of around 80-90° afforded analogs of the desired **3** in yields of 50% or greater within 24 hours [2g,23]. In the present study, after about 24 hours at ~80°, the proton magnetic resonance (pmr) spectrum indicated clean conversion to the desired product to the extent of 25%. Three different modifications of the latter procedure failed to improve on this method. In the first modification the mixture was heated at ~90-100° using a 10% excess of sodium bicarbonate for ~1 day. Pmr data indicated a similar percent conversion thus ruling out any sodium hydrogencarbonate effect on percent yield. In the second attempt, a 4:1 ratio of amine to thiazole was used as the mixture was heated at 100-110° in a capped pyrex test tube until no more **1** was observed (tlc, 54 hours). The reaction contents became very dark red and viscous by this time and the effort required to purify the material by column chromatography was relatively large while the percent yield was only marginally better by 8%. The third modification was different from the first only in that a longer reaction time of four days was used. As expected the longer reaction time was counterproductive and gave a 10% lower yield.

Thermal condensation of the aminothiazole **3** with an equimolar to 5% molar excess amount of the previously reported [24] bis(2,4,6-trichlorophenyl)malonates **4** provides a facile entry to the hitherto unreported 8-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl] substituted mesoionic xanthines **5**. The condensations were performed as previously described [2g] by preparing an intimate mixture (~1:1 molar ratio) of the (2,2-dimethyl-1,3-dioxolan-4-yl)methyl-2-aminothiazole **3** and the appropriate bis(2,4,6-trichlorophenyl)malonate **4** and then heating the mixture at *ca* 160° for three minutes. Unlike previously reported [2f], a stream of nitrogen was not employed. This use of nitrogen originated with Coburn and Glennon [2f] as a method to improve the yield in the condensation reaction of **4a** with 2-ethylaminothiazole. With the exception of the benzyl-substituted compound **5e** and in contrast to previous experience [2f] the resulting mesoionic xanthines could not be purified by trituration of the cooled melt with diethyl ether. Analytically pure **5e** was obtained by this trituration method. The other protected MTA were easily purified by column chromatographyand then (if necessary) by either recrystallization or trituration to yield analytically pure compounds.

Compounds **5** were deprotected to obtain the diols **6** by heating a methanol solution of **5** under reflux with a catalytic amount of *p*-toluenesulfonic acid in a manner similar to that reported by other workers [25] who used pyridinium *p*-toluenesulfonate as the catalyst. These reactions could be easily monitored by thin-layer chromatography using acetone eluant. There is an apparent variation of the percent yields of the diols **6** with R group. Since we did not attempt to optimize the yields we are not in a position to suggest why the yields vary or if there is a real steric and/or electronic effect caused by the R group in the product-forming step.

Now that a straight-forward method for synthesizing the mesoionic acyclonucleosides has been accomplished it is desired to assay their biological properties in future work.

EXPERIMENTAL

Melting points were obtained with a Thomas-Hoover melting-point apparatus and are uncorrected. All compounds were prepared using starting materials obtained from either commercially available sources or made by standard literature procedures. Reagent grade solvents were used in all reactions and column chromatographic separations. Column chromatographic separations were performed using 60-200 mesh silica gel. Thin-layer chromatography (tlc) was performed on sheets coated with silica gel adsorbent with fluorescent indicator (Kodak Chromagram sheet / 13181). The visualization of products in thin-layer chromatograms was accomplished under uv light (254 nm) or by staining with iodine vapors.

Infrared spectra (ir) were recorded using potassium bromide pellets on a JASCO FT/IR-410 spectrophotometer. Proton magnetic resonance spectra (^{1}H nmr) were obtained on a Varian EM-360L NMR spectrometer. 60-MHz ^{1}H NMR spectra were obtained in deuterated solvents using 5-mm spinning tubes with signals referenced to internal tetramethylsilane (TMS). Coupling constants (J) are given in Hertz. The ^{1}H nmr signals are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br s, broad singlet. Uv spectra were recorded on a Spectronic 1201 spectrophotometer using water or acetonitrile as solvent. Results are expressed as λ_{max} in nanometers (nm).

Elemental analyses were performed by Atlantic Microlab Inc., Atlanta, Georgia.

(2,2-Dimethyl-[1,3]dioxolan-4-ylmethyl)-thiazol-2-yl-amine (**3**).

To a round-bottomed flask containing 47.0 g (0.358 mole) of *C*-(2,2-dimethyl-[1,3]dioxolan-4-yl)-methylamine (**2**) was added 19.6 g (0.120 mole, 10.8 ml) of 2-bromothiazole (**1**). The magnetically-stirred mixture was heated to approximately 84° for ~26 hours. After cooling to room temperature the dark orange reaction mixture was dissolved in ether (150 ml) and washed with water (3 x 150 ml) to remove unchanged amine **2**. The ether layer was separated, dried with magnesium sulfate, filtered, and evaporated to leave 14.23 g of a dark orange oil containing some crystals. The oil solidified on standing. Proton nmr indicated a mixture of 2-bromothiazole (**1**) and the desired secondary amine (**3**) in a 3:1 ratio. Unchanged 2-bromothiazole was removed by steam distillation using 50 ml of water. The residue was allowed

to cool to room temperature and **3** crystallized as a white solid which was isolated for mp, spectral, and elemental analyses. The physical and spectral data for this analytically pure product are summarized in Tables 1 and 2. The remaining material in the distillation pot was extracted with ether. The ether layer was separated, dried (magnesium sulfate), and poured through a column of silica gel (2.5 x 13 cm) prepacked with diethyl ether. Saturation of the aqueous extracts with sodium chloride resulted in an oil separating out that after sitting over-night formed crystals, which were isolated by vacuum filtration and rinsed with water. The crystals were dissolved in ether and the solution was dried (magnesium sulfate), filtered, and evaporated. The total yield of **3** was 3.93 g, which is 60% of the 25% conversion of **1** to **3** observed by proton nmr.

General Procedure for the Preparation of *Anhydro*-(8-[(2,2-Dimethyl[1,3]dioxolan-4-yl)methyl]-5-hydroxy-7-oxothiazolo-[3,2-*a*]pyrimidinium hydroxides) (**5**).

An intimate mixture of 1.400 mmoles of (2,2-Dimethyl-[1,3]dioxolan-4-ylmethyl)-thiazol-2-yl-amine (**3**) and 1.400 to 1.470 mmoles of the appropriately substituted bis(2,4,6-trichlorophenyl)malonate (**4**) was heated at 160° for 3 minutes. After cooling the dark oil was purified on silica gel (50 g in a 2.5 cm id glass chromatography column) prepacked in chloroform for all five derivatives except **5e**, the 6-benzyl derivative, which could be isolated by simple trituration of the crude condensation product with diethyl ether. Elution of the column with chloroform removed the 2,4,6-trichlorophenol by-product. When the 2,4,6-trichlorophenol by-product had eluted as judged by TLC (50% EtOAc/50% hexanes eluant, R_f = 0.40) the eluting solvent for the column was switched to acetone or an acetone/chloroform mixture to obtain the desired product. The product isolated in this manner was fairly pure as judged by proton nmr. Further purification of the chromatographed products was performed in all cases except for the unsubstituted derivative, **5a**, to get pure solids for CHN and melting point analysis: the methyl and ethyl derivatives, **5b** and **5c**, were triturated with diethyl ether to induce crystallization from the oil; the phenyl derivative, **5d**, was recrystallized from toluene.

General Procedure for the Preparation of *Anhydro*-(8-(2,3-Dihydroxypropyl)-5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidinium Hydroxides) (**6**).

Compound **5** (0.9 mmole) was dissolved in methanol (*ca*. 30 ml). To this solution a catalytic amount of *p*-toluenesulfonic acid (5-12 mg) was added. The magnetically-stirred solution was heated under reflux. Reaction progress was monitored by tlc using acetone eluant. The reaction was stopped when the reactant spot at an R_f of ~0.7 was no longer or barely visible (typically ~2 hours). In general, the compounds could be easily isolated by evaporation of the methanol and the 2,2-dimethoxypropane by-product under reduced pressure and then trituration of the oil with acetone, by crystallization from the cooled methanol solvent, or by elution through a silica gel column using acetone as eluant. The 6-H (**6a**), 6-phenyl (**6d**) and the 6-methyl (**6b**) diols were crystallized from the reaction mixture. The 6-benzyl (**6e**) diol was isolated by evaporation of the methanol mixture under reduced pressure and then trituration of the oil with acetone. The 6-H diol (**6a**) was also isolated in this manner and then further purified for mp and elemental analysis by recrystallization from methanol. The 6-ethyl diol (**6c**) was purified by eluting the methanol reaction mixture through a column of silica gel using acetone eluant.

Acknowledgments.

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