A Facile Preparation of some Novel Class II Mesoionic Xanthine Acyclonucleosides

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The synthesis of the first examples of Class II mesoionic xanthine acyclonucleosides is described. A series of mesoionic *anhydro*-(8-methoxyalkyl-5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidinium hydroxides), Class II mesoionic analogs isoconjugate with xanthine, were prepared by the thermal condensation of methoxyalkyl-2-aminothiazoles with substituted bis(2,4,6-trichlorophenyl)malonic esters. The methoxyalkyl-2-aminothiazoles were prepared *via* an aromatic nucleophilic substitution reaction between 2-bromothiazole and the appropriate methoxyalkylamine in excess. The resulting 8-methoxyalkyl-substituted mesoionic xanthines were demethylated using iodotrimethylsilane in acetonitrile at room temperature to afford the corresponding mesoionic *anhydro*-(8-hydroxyalkyl-5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidinium hydroxides) as the Class II mesoionic xanthine acyclonucleosides.

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Introduction.

The preparation of a number of mesoionic xanthines and related compounds for use in chemical, spectral and structure-activity studies have previously been reported [1-5]. There exists two major classes of mesoionic purinones and these have been formulated and examined from a quantum chemical standpoint [6,7]. Mesoionic purinones which may be envisioned as being derived from a five-membered mesoionic ring system have been termed class I mesoionic purinones [6] while those derived from a six-membered mesoionic ring system have been termed class II mesoionic purinones [7].

Some mesoionic purinone analogs have demonstrated bacteriostatic and antifungal properties [8,9]. Several mesoionic purinones have been found to exhibit activity as inhibitors of adenosine-3',5'-monophosphate phosphodiesterase [3,10] similar to that of the structurally related theophylline.

Another class of interesting and potentially bioactive compounds are mesoionic xanthine nucleosides. A number of these compounds (Figure 1) were prepared by Schubert, Bass and Glennon [11] for the purpose of exploring general pathways that allow for the preparation of mesoionic nucleosides, as well as to investigate their chemical and spectral properties.

Nucleosides have been broadly defined to include all natural and synthetic compounds that contain a heterocyclic base that is linked through nitrogen or carbon to the 1-position of a sugar [12]. It has been recognized that nucleosides with a modified heterobase or sugar portion can influence some biochemical pathways [13-16]. Several of them have shown biological activity [17], and many have been incorporated into modern drugs [18-24]. Among these, 5-fluorouridine and 5-iodo-2'-deoxyuridine, exhibit antineoplastic activity; 3-deazauridine has pronounced antitumor and antiviral activity; 3'-azido-2',3'-dideoxythymidine (AZT) and dideoxyinosine have shown promise in the treatment of patients infected with HIV. Some examples of mesoionic nucleosides and non-mesoionic acyclonucleosides are depicted in Figure 1. This paper, to our knowledge,

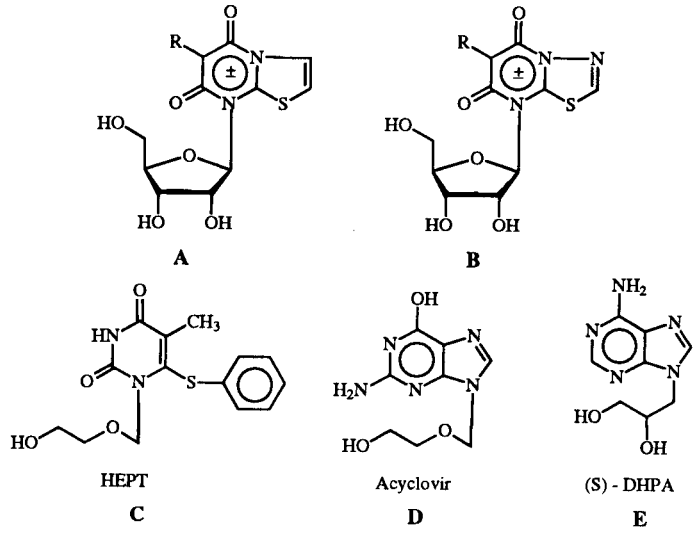
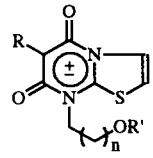


Figure 1. Examples of Some Mesoionic Nucleosides **A** and **B** nnd Non-Mesoionic Acyclonucleosides **C-E**

describes the synthesis of the first known examples of class II mesoionic xanthine acyclonucleosides **6**, and their methoxy precursors **5**, from the condensation of methoxyalkyl-substituted-2-aminothiazoles with bis(2,4,6-trichlorophenyl)malonates and subsequent demethylation with iodotrimethylsilane (Figure 2). The currently accepted nomenclature for mesoionic purinones of type **6** is *anhydro*-(8-hydroxyalkyl-5-hydroxy-7-oxothiazolo[3,2-*a*]-pyrimidinium hydroxide).

Discussion.



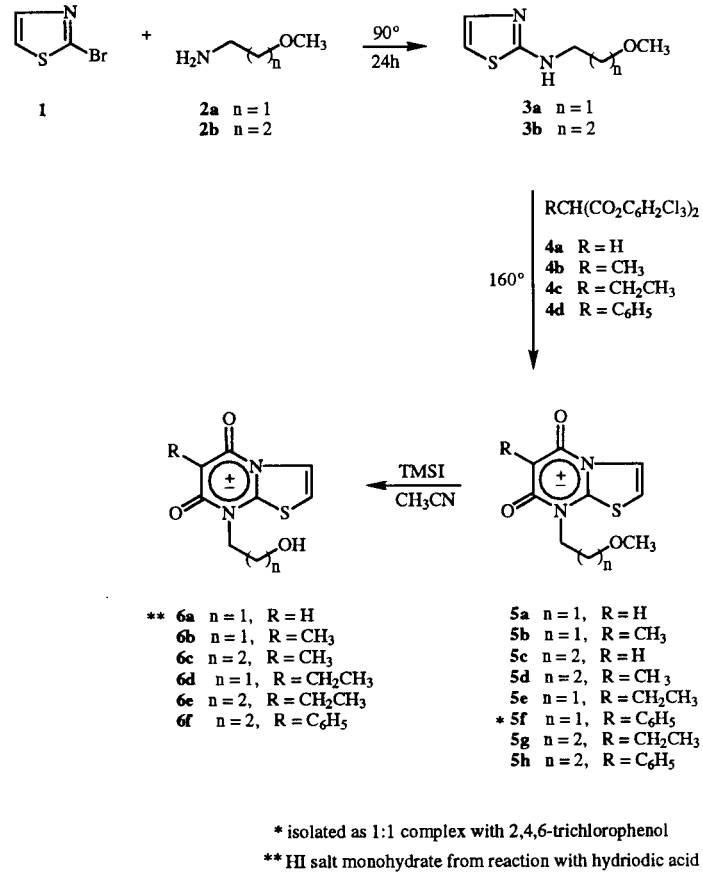
n = 1,2 R = H, CH_3, CH_3CH_2, C_6H_5 R' = H, CH_3

Figure 2. Generalized structural representation of mesoionic xanthine acyclonucleosides **5** and **6**.

2-Methoxyethylamine **2a** or 3-methoxypropylamine **2b** and 2-bromothiazole **1** undergo a nucleophilic substitution reaction to afford the corresponding 2-aminothiazoles **3a** and **3b** (Figure 3). An analogous reaction between 2-bromothiazole and 2-aminoethanol in butanol using sodium carbonate as a neutralizing agent was reported [25] to give exceedingly low yields of the product 2-(2-thiazolylamino)ethanol. Our reactions were performed with excess (4 equivalents) amine in order to drive the reaction to completion and to neutralize the hydrogen bromide that is formed. Triethylamine was tried as an acid trap, but was found to result in greatly reduced yields of product. The crude reaction mixtures were purified by column chromatography on silica-gel using ether as the eluant. This procedure eliminated all of the excess amine and amine salts and generally resulted in 50-70% yields. The relatively low yields may be ascribed to the possibility of protonation of the thiazole ring nitrogen as a process in competition with the protonation of the excess primary methoxyalkylamine. Aminothiazole **3a** was isolated as a viscous oil (picrate, mp 188-190°, ethanol) and aminothiazole **3b** was initially isolated as an oil, but was later crystallized from hexanes (mp 49-50°). Compounds **3a** and **3b** exhibited strong infrared absorption at 1580 cm^{-1} due to the thiazolyl C=N ring stretch and N-H stretching at 3250 cm^{-1}. The analytical and spectral data for compounds **3a** and **3b** are summarized in Tables 1 and 2 respectively.

Thermal condensation of the aminothiazole **3a** or **3b** with an equimolar quantity of the previously reported [26] bis(2,4,6-trichlorophenyl)malonates **4** yielded the 8-methoxyalkyl substituted mesoionic xanthines **5**. The condensations were performed by preparing an intimate mixture (1:1 molar ratio) of the methoxyalkyl-2-aminothiazole **3a** or **3b** and the appropriate bis(2,4,6-trichlorophenyl)malonate **4** and by heating the mixture at 160° for three minutes under a stream of nitrogen. The resulting mesoionic xanthines were obtained by trituration of the cooled melt with anhydrous ether (removal of 2,4,6-trichlorophenol) and filtration of the insoluble solid product. Reactions using malonate **4a** were performed at 125° instead of 160° in order to minimize the formation of polar side products.

Suprisingly, when aminothiazole **3a** was condensed with the phenyl-substituted malonate **4d**, the expected mesoionic xanthine, *anhydro*-(8-methoxyethyl-6-phenyl-5-hydroxy-7-



* isolated as 1:1 complex with 2,4,6-trichlorophenol

** HI salt monohydrate from reaction with hydriodic acid

Figure 3. Preparation of Mesoionic Xanthine Acyclonucleosides

oxothiazolo[3,2-*a*]pyrimidinium hydroxide) **5f**, was not isolated. Instead, however, a 1:1 charge-transfer complex **7** between **5f** and 2,4,6-trichlorophenol was formed (Figure 4). Initially it was erroneously believed that the product was impure and therefore did not give the proper elemental analysis. However, it is well known that 2,4,6-trichlorophenol and related phenols containing electron withdrawing groups are good π-electron acceptors and also form the so called electron donor-acceptor complexes [27]. Since 2,4,6-trichlorophenol is formed in the condensation reaction, it could interact with a good π-donor giving a 1:1 complex. We therefore surmised that the expected **5f** could act as a suitable π-donor. It is interesting to note that quantum chemically based studies by Coburn and co-workers [6,7] had predicted that mesoionic xanthine analogs could function as both electron donors and acceptors and therefore have the potential to participate in charge-transfer modes of bonding. The elemental analysis of **7** supported the idea of a 1:1 complex between the mesoionic xanthine **5f** and 2,4,6-trichorophenol. Additional evidence for complex formation was found in the uv, ir and nmr spectra of **7** (Table 2). The uv spectrum exhibited a charge-transfer band at 312 nm and a residual spectrum quite different from the other analogs of

Table 1
Properties of Compounds **3**, **5** and **6**

	n	R	Yield (%)	Mp (C)	Recrystallization Solvent	Formula	Analyses (%) C	H	N
3a	1	–	47	188-190	EtOH	$C_{12}H_{13}N_5O_8S$ [a]	37.21 (37.29)	3.38 (3.44)	18.08 (18.13)
3b	2	–	76	49-50	Hexanes	$C_7H_{12}N_2OS$	48.81 (48.57)	7.02 (6.97)	16.26 (16.22)
5a	1	H	78	163-164	Acetone	$C_9H_{10}N_2O_3S$	47.78 (47.72)	4.45 (4.45)	12.38 (12.42)
5b	1	CH_3	85	220-221	EtOH/EtOAc	$C_{10}H_{12}N_2O_3S$	49.99 (50.08)	5.03 (5.10)	11.66 (11.56)
5c	2	H	98	133-134	Acetone	$C_{10}H_{12}N_2O_3S$	49.99 (49.80)	5.03 (4.99)	11.66 (11.59)
5d	2	CH_3	87	120-122	EtOH/EtOAc	$C_{11}H_{14}N_2O_3S$	51.96 (51.68)	5.54 (5.60)	11.02 (10.94)
5e	1	CH_3CH_2	76	185-186	EtOH/EtOAc	$C_{11}H_{14}N_2O_3S$	51.96 (52.01)	5.54 (5.52)	11.02 (10.95)
5g	2	CH_3CH_2	76	122-124	EtOAc	$C_{12}H_{14}N_2O_3S$	54.12 (53.94)	5.30 (5.91)	10.53 (10.32)
5h	2	C_6H_5	92	173-175	EtOH/EtOAc	$C_{16}H_{16}N_2O_3S$	60.74 (60.56)	5.10 (5.12)	8.86 (8.78)
6a	1	H	95	149-151	MeCN/EtOAc	$C_8H_{10}N_2O_4S$•HI [c]	26.82 (27.05)	3.10 (3.12)	7.82 (7.84)
6b	1	CH_3	61	205-207	Butanol	$C_9H_{10}N_2O_3S$	47.77 (47.55)	4.46 (4.39)	12.38 (12.23)
6c	2	CH_3	76	183-185	MeCN/EtOH	$C_{10}H_{12}N_2O_3S$	49.99 (50.08)	5.04 (5.09)	11.66 (11.59)
6d	1	CH_3CH_2	66	195-197	Acetone	$C_{10}H_{12}N_2O_3S$	49.99 (49.86)	5.04 (5.07)	11.66 (11.57)
6e	2	CH_3CH_2	69	215-218	EtOH/EtOAc	$C_{11}H_{14}N_2O_3S$	51.95 (51.88)	5.55 (5.58)	11.02 (10.92)
6f	2	C_6H_5	63	192-194	MeCN/MeOH	$C_{15}H_{14}N_2O_3S$	59.58 (59.52)	4.67 (4.68)	9.27 (9.24)
7	1	C_6H_5	80	140-142	EtOAc	$C_{21}H_{17}N_2O_4Cl_3S$ [b]	50.46 (50.18)	3.43 (3.44)	5.6 (5.54)

[a] Reported as picrate. [b] 1:1 Charge transfer complex wtih 2,4,6-trichlorophenol. [c] From reaction with HI.

the series. The ir spectrum showed the presence of a phenolic OH at 3240 cm^{-1}. The nmr showed the presence of an OH at δ 4.88 and the existence of a two proton singlet in the aromatic region at δ 7.31 due to the ring protons of 2,4,6-trichlorophenol. Compound **7** exhibited a sharp melting point, one spot by tlc and was highly colored in the crystalline state. A simple mixture was unequivocally ruled out as a possibility since the complex is completely insoluble in ether (like all mesoionic xanthines) while 2,4,6-trichlorophenol is extremely soluble in ether. Furthermore, it should be emphasized that no complex formation was observed for compound **5h**. This compound is the 8-methoxypropyl homolog of **5f**. The lengthening of the side chain by one carbon is apparently sufficient to cause steric hindrance to the formation of a complex for **5h**.

Compounds **5**, with the exception of **5a** and **5f** were demethylated in anhydrous acetonitrile with iodotrimethylsilane to afford the corresponding *anhydro*-(8-hydroxyalkyl-5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidinium hydroxides) **6**. Compound **6a** was prepared by the action of hydriodic acid on **5a** to give the mesoionic acyclonucleoside as the hydriodic acid salt monohydrate. This structure was confirmed by elemental analysis (Table 1) and by high resolution mass spectral analysis (*m/e* 231.0443, 100%). The *m/e* 231 ion corresponds to the mesoionic xanthine plus hydronium ion ($M + H_3O^+$). The low resolution mass spectrum exhibits a molecular ion at *m/e* 358 and corresponds to the *m/e* 231 ion plus iodide ion.

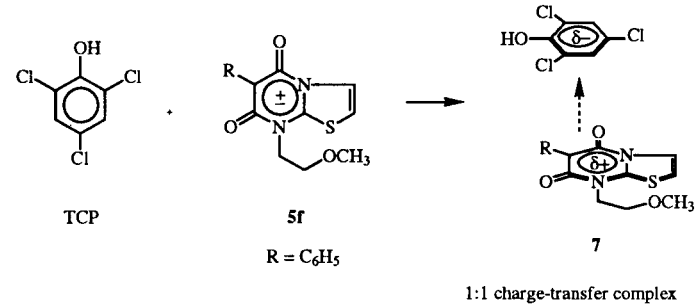


Figure 4. Formation of a 1:1 charge-transfer complex **7** between mesoionic xanthine **5f** and 2,4,6-trichlorophenol

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

Compound	^{1}H-NMR (δ ppm) [a]	UV λ_{max} (nm) [b]	IR (cm^{-1}) [c] νNH	νOH	νC=O
3a	3.32 (s, 3H, OCH_3) 3.48 (brs, 1H, NH) 3.57 (t, 2H, CH_2OC, J = 4.7 Hz) 3.65 (t, 2H, NCH_2, J = 4.7 Hz) 6.59 (d, 1H, SCH, J = 4.4 Hz) 7.22 (d, 1H, SC=CH, J= 4.4 Hz) 7.27 (s, 1H, OH) 8.98 (s, 2H, ArH) [B]	210 250 353 380 (sh)	3250		
3b	1.89 (p, 2H, CCH_2C, J = 6.2 Hz) 3.30 (s, 3H, OCH_3) 3.33 (t, 2H, CH_2OC, J = 6.6 Hz) 3.47 (t, 2H, NCH_2, J = 5.9 Hz) 6.41 (d, 1H, SCH, J = 3.6 Hz) 6.59 (brs, 1H, NH) 7.06 (d, 1H, SC =CH, J = 3.6 Hz) [B]	262	3240		
5a	3.31 (s, 3H, OCH_3) 3.75 (t, 2H, CH_2O, J = 5.0 Hz) 4.24 (t, 2H, NCH_2, J = 5.0 Hz) 4.99 (s, 1H, COCHCO) 7.46 (d, 1H, SCH, J = 5.0 Hz) 8.07 (d, 1H, SC=CH, J = 5.0 Hz) [A]	241 278			1645 1695
5b	1.93 (s, 3H, $ArCH_3$) 3.30 (s, 3H, OCH_3) 3.76 (t, 2H, CH_2O, J = 5.1 Hz) 4.28 (t, 2H, NCH_2, J = 5.1 Hz) 7.43 (d, 1H, SCH, J = 4.9 Hz) 8.08 (d, 1H, SC=CH, J = 4.9 Hz) [A]	245 282			1640 1690
5c	2.04 (p, 2H, CCH_2C, J = 6.5 Hz) 3.30 (s, 3H, OCH_3) 3.47 (t, 2H, CH_2OC, J = 5.7 Hz) 4.17 (t, 2H, NCH_2, J = 7.0 Hz) 4.99 (s, 1H, COCHCO) 7.48 (d, 1H, SCH, J = 4.5 Hz) 8.09 (d, 1H, SC=CH, J = 4.5 Hz) [A]	239 277			1645 1695
5d	1.92 (s, 3H, $ArCH_3$) 2.05 (p, 2H, CCH_2C, J = 6.6 Hz) 3.30 (s, 3H, OCH_3) 3.47 (t, 2H, CH_2OC, J = 5.7 Hz) 4.17 (t, 2H, NCH_2, J = 7.0 Hz) 7.47 (d, 1H, SCH, J = 4.5 Hz) 8.10 (d, 1H, SC=CH, J = 4.5 Hz) [A]	244 282			1645 1690
5e	1.07 (t, 3H, CCH_3, J = 7.3 Hz) 2.48 (q, 2H, $ArCH_2$, J = 7.3 Hz) 3.30 (s, 3H, OCH_3) 3.76 (t, 2H, CH_2O, J = 4.9 Hz) 4.27 (t, 2H, NCH_2, J = 4.9 Hz) 7.43 (d, 1H, SCH, J = 4.5 Hz) 8.08 (d, 1H, SC=CH, J = 4.5 Hz) [A]	246 282			1635 1690
5g	1.07 (t, 3H, CCH_3, J = 7.3 Hz) 2.05 (p, 2H, CCH_2C, J = 7.0 Hz) 2.47 (q, 2H, $ArCH_2$, J = 7.3 Hz) 3.30 (s, 3H, OCH_3) 3.47 (t, 2H, CH_2OC, J = 6.1 Hz) 4.17 (t, 2H, NCH_2, J = 7.0 Hz) 7.46 (d, 1H, SCH, J = 4.6 Hz) 8.10 (d, 1H, SC=CH, J = 4.6 Hz) [A]	245 282			1645 1690
5h	2.05 (p, 2H, CCH_2C, J = 7.3 Hz) 3.27 (s, 3H, OCH_3) 3.46 (t, 2H, CH_2OC, J = 5.6 Hz) 4.19 (t, 2H, NCH_2, J = 6.9 Hz) 7.17 (t, 1H, ArH, J = 7.3 Hz) 7.30 (t, 2H, ArH, J = 7.3 Hz)	250 307			1635 1685

Table 2 (Continued)

Compound	^{1}H-NMR (δ ppm) [a]	UV λ_{max} (nm) [b]	IR (cm^{-1}) [c] vNH	vOH	vC=O
5h	7.44 (d, 1H, SCH, J = 4.7 Hz) 7.52 (d, 2H, ArH, J = 7.2 Hz) 8.12 (d, 1H, SC=CH, J = 4.7 Hz) [A]				
6a	3.43 (s, 1H, COCHCO) 3.76 (t, 2H, CH_2O, J = 5.2 Hz) 4.41 (t, 2H, NCH_2, J = 4.8 Hz) 4.94 (brs, 1H, OH) 6.98 (d, 1H, SCH, J = 4.4 Hz) 7.29 (d, 1H, SC=CH, J = 4.4 Hz) [A]	202 242		3250	1615 1754
6b	1.94 (s, 3H, $ArCH_3$) 3.93 (t, 2H, CH_2O, J = 5.3 Hz) 4.21 (t, 2H, NCH_2, J = 4.8 Hz) 4.88 (brs, 1H, OH) 7.45 (d, 1H, SCH, J = 4.5 Hz) 8.09 (d, 1H, SC=CH, J = 4.5 Hz) [A]	245 282		3300	1640 1690
6c	2.05 (s, 3H, $ArCH_3$) 2.52 (p, 2H, CCH_2C, J = 6.5 Hz) 4.35 (t, 2H, CH_2O, J = 6.2 Hz) 4.69 (t, 2H, NCH_2, J = 5.4 Hz) 4.88 (brs, 1H, OH) 7.86 (d, 1H, SCH, J = 4.4 Hz) 8.42 (d, 1H, SC=CH, J = 4.4 Hz) [A]	223 270 300		3400	1630 1715
6d	1.07 (t, 3H, CCH_3, J = 7.4 Hz) 2.48 (q, 2H, $ArCH_2$, J = 7.4 Hz) 3.93 (t, 2H, CH_2O, J = 5.2 Hz) 4.20 (t, 2H, NCH_2, J = 4.9 Hz) 4.78 (brs, 1H, OH) 7.44 (d, 1H, SCH, J = 4.5 Hz) 8.08 (d, 1H, SC=CH, J = 4.5 Hz) [A]	243 282		3300	1635 1690
6e	1.07 (t, 3H, CCH_3, J = 7.3 Hz) 2.00 (p, 2H, CCH_2C, J = 7.1 Hz) 2.48 (q, 2H, CH_2C, J = 7.4 Hz) 3.65 (t, 2H, CH_2O, J = 5.8 Hz) 4.21 (t, 2H, NCH_2, J = 7.2 Hz) 4.87 (brs, 1H, OH) 7.47 (d, 1H, SCH, J = 4.5 Hz) 8.12 (d, 1H, SC=CH, J = 4.5 Hz) [A]	242 282		3300	1640 1690
6f	1.94 (p, 2H, CCH_2C, J = 6.5 Hz) 3.58 (t, 2H, CH_2O, J = 5.9 Hz) 4.15 (t, 2H, NCH_2, J = 7.3 Hz) 4.78 (brs, 1H, OH) 7.11 (t, 1H, ArH, J = 7.3 Hz) 7.24 (t, 2H, ArH, J = 7.3 Hz) 7.39 (d, 1H, SCH, J = 4.6 Hz) 7.46 (d, 2H, ArH, J = 7.3 Hz) 8.07 (d, 1H, SC=CH, J = 4.6 Hz) [A]	249 293		3300	1635 1685
7	3.33 (s, 3H, OCH_3) 3.78 (t, 2H, CH_2OC, J = 5.1 Hz) 4.29 (t, 2H, NCH_2, J = 4.9 Hz) 4.88 (brs, 1H, ArOH) 7.20 (t, 1H, ArH, J = 7.3 Hz) 7.31 (s, 2H, ArH) 7.33 (t, 2H, ArH, J = 7.3 Hz) 7.44 (d, 1H, SCH, J = 4.7 Hz) 7.55 (d, 1H, ArH, J = 7.3 Hz) 8.12 (d, 1H, SC=CH, J = 4.7 Hz) [A]	209 250 297 312		3240	1640 1690

[a] Measured solvents: [A] CD_3OD. [B] $CDCl_3$. [b] Measured solvent: CH_3OH. [c] Recorded using KBr discs.

Investigations on the biological properties of the mesoionic compounds described in this paper are currently in progress and will be the subject of a further report to be published elsewhere.

EXPERIMENTAL

Melting points were obtained with a Thomas-Hoover 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. Thin layer chromatography (tlc) was performed on tlc plates precoated with silica-gel 13181 (Eastman Kodak Co., Rochester, New York). The visualization of products in thin-layer chromatograms was accomplished by uv detection or iodine development.

Infrared spectra (ir) were recorded using potassium bromide disks on a Perkin-Elmer 1600 FTIR spectrophotometer. Proton magnetic resonance spectra (^{1}H nmr) were obtained with either a General Electric QE-300 or a Bruker WP270SY spectrometer. All ^{1}H nmr spectra were obtained using 5 mm spinning tubes and signals were 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; p, pentet; brs, broad singlet. Ultraviolet spectra (uv) were recorded on a Beckman Acta MVII spectrophotometer using spectrograde methanol. Results are expressed as λ_{max} in nanometers (nm).

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

Preparation of Methoxyalkyl-2-aminothiazoles **3**. General Procedure **A**.

A solution containing 2-bromothiazole **1** (60 mmoles) and the appropriate methoxyalkylamine **2** (240 mmoles) were heated together at 90° for 24 hours. The resulting dark brown solution was cooled to room temperature and chromatographed on silica-gel eluting with ether. The physical and spectral data for compounds **3a** and **3b** are summarized in Tables 1 and 2.

Preparation of Methoxyalkyl-2-aminothiazoles **3**. General Procedure **B**.

The resulting dark brown solution obtained from general procedure **A** was treated with 400 ml 10% sodium carbonate solution and extracted with 400 ml ether. The ether layer was separated and washed twice with 400 ml portions of water. The ether layer was dried over magnesium sulfate, filtered and evaporated to give the methoxyalkyl-2-aminothiazoles as viscous brown oils. The physical and spectral data for compounds **3a** and **3b** are summarized in Tables 1 and 2.

Preparation of *anhydro*-(8-methoxyalkyl-5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidinium hydroxides) **5**. General Procedure.

An intimate mixture of the appropriately substituted bis(2,4,6-trichlorophenyl)malonate **4** (3 mmoles) and methoxyalkyl-2-aminothiazole **3** (3 mmoles) was heated at 160° (125° when using **4a**), under an atmosphere of nitrogen, for 3 minutes. When cool, the resultant gum was triturated with anhydrous ether to afford the crude solid product. Recrystallization from the appropriate solvent (Table 1) gave the analytically pure mesoionic xanthine **5**.

Preparation of *anhydro*-(hydroxyalkyl-5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidinium hydroxides) **6**. General Procedure using Iodotrimethylsilane.

To a solution containing **5** (4 mmoles) in 30 ml anhydrous acetonitrile, was added iodotrimethylsilane (16 mmoles). The stoppered solution was stirred for 24 hours at room temperature and the excess iodotrimethylsilane was destroyed by the dropwise addition of 1 ml of water. The resulting solution was evaporated *in vacuo* and the residue was chromatographed on silica-gel eluting with a 2:1 acetone/ethyl acetate mixture to afford the analytically pure mesoionic xanthine acyclonucleoside **6**. The physical and spectral data for the new compounds **6** are summarized in Tables 1 and 2.

Preparation of *Anhydro*-(8-hydroxyethyl-5-hydroxy-7-oxothiazolo[3,2-*a*]pyrimidinium Hydroxide) **6a** using Hydriodic Acid.

Compound **5a** (0.500 g, 2.21 mmoles) was stirred with 11 ml of 57% unstablized hydriodic acid in a closed flask at 40° for 20 hours. The resulting solution was concentrated to dryness under high vacuum and the solid residue was washed with ethyl acetate several times. The solid was obtained by filtration and was washed with ether and dried to yield 0.638 g of a yellow solid (80% yield based on monohydrate of hydriodic acid salt).

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REFERENCES AND NOTES

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A: (anhydro-8-D-ribofuranosyl)-5-hydroxy-7-oxothiazolo[3,2-*a*]-pyrimidinium hydroxide

B: (anhydro-8-D-ribofuranosyl)-5-hydroxy-7-oxothiadiazolo[3,2-*a*]pyrimidinium hydroxide

C: HEPT = 1-[(2-hydroxyethoxymethyl)-6-phenylthio]thymine

D: Acyclovir = 9-(2-hydroxyethoxymethyl)quanine

E: (*S*)-DHPA = (*S*)-9-(2,3-dihydroxypropyl)adenine

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