# Synthesis of Mesoionic Triazoline Nucleosides

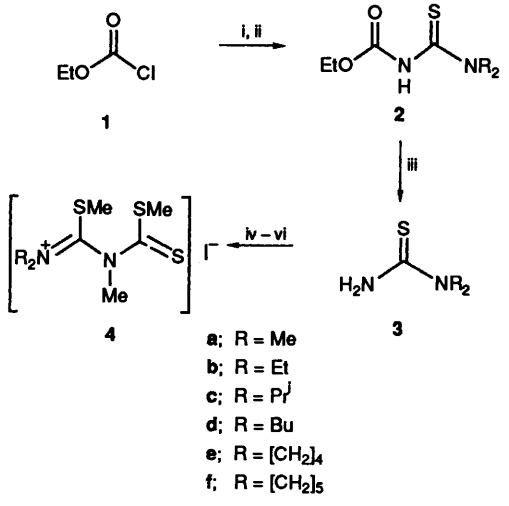
**Masataka Yokoyama,* Toshihiro Ikuma, Nobutoshi Obara and Hideo Togo**
*Department of Chemistry, Faculty of Science, Chiba University, Yayoi-Cho, Chiba City 260, Japan*

A new type of protected mesoionic triazoline nucleoside was synthesized by the reaction of protected 1,2-dideoxy-hydrazino-D-ribose or 1-deoxy-hydrazino-D-ribose with isothiouronium compounds. The three compounds obtained **10a**, **10f** and **16a** were deprotected with tetrabutylammonium fluoride. They showed no activity against HSV-1 virus.

Recently, considerable attention has been given to mesoionic nucleosides [1] ever since the appearance of unnatural nucleosides as potential antiviral agents.[2] The mesoionic nucleosides of purines,[1a] xanthines,[1b] imidazothiazines,[1c] pyridazines,[1d] pyridines[1d] and acyclovir analogues[1e] have been synthesized hitherto. Generally, mesoionic compounds are known to have a variety of biological activities.[3] Thus, in connection with our interest directed towards the synthesis of unnatural nucleosides,[4] we studied the synthesis and biological activities of mesoionic triazoline nucleosides.

## Results and Discussion

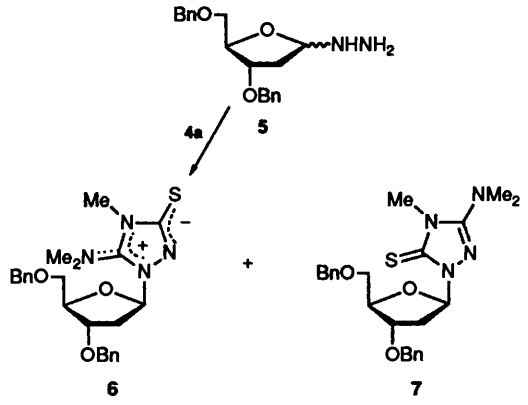
Initially, the isothiouronium method that was reported by us previously[5] was applied to the synthesis of triazoline nucleosides. Several starting materials, isothiouronium compounds **4**, were prepared by the three-step synthesis starting with ethyl chloroformate **1** as shown in Scheme 1.




**Scheme 1.** *Reagents:* i, KSCN; ii, $R_2NH$; iii, HCl; iv, NaH; v, $CS_2$; vi, MeI.

When 1,2,3,3-tetramethyl-1-(methylthio)thiocarbonyl isothiouronium iodide **4a** was allowed to react with 3,5-*O*-dibenzyl-2-deoxy-D-*erythro*-pentofuranosylhydrazine **5** in ethanol at room temperature, the expected mesoionic triazoline nucleoside **6** was obtained in 17% yield together with a small amount of triazoline nucleoside **7** (2%, Scheme 2). However, compound **6** could not, unfortunately, be deprotected by the usual methods (Pd–C, $H_2$ or Na–$NH_3$).

Therefore, a suitable protecting group for the parent dideoxy-1-hydrazino-D-ribose substrate was required for the synthesis of mesoionic nucleosides. Thus, we employed the 2-




**Scheme 2.**

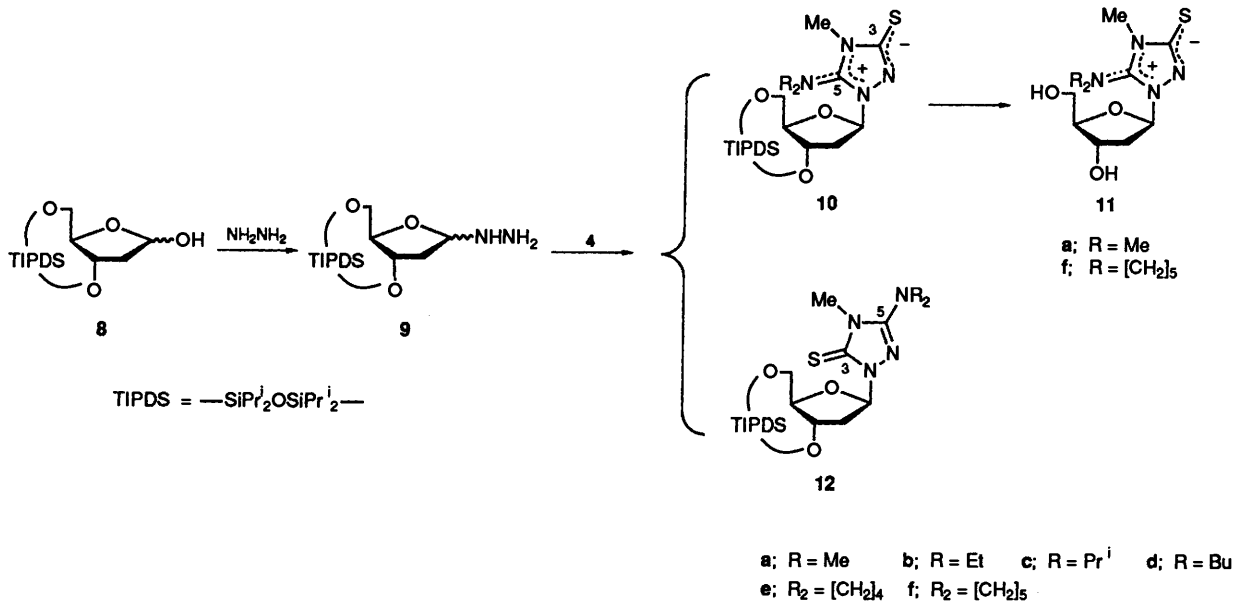
deoxy-3,5-*O*-(tetraisopropyldisiloxane-1,3-diyl)-D-*erythro*-pentofuranosyl-hydrazine **9** derived from 2-deoxy-3,5-*O*-TIPDS-D-*erythro*-pentofuranose **8** in the present reaction. Compound **4a** was allowed to react with compound **9** in the presence of triethylamine in acetonitrile at room temperature to give a mixture of the α- and β-anomer (1:10) of the corresponding mesoionic nucleoside **10a**. Compound **10a** was easily deprotected with tetrabutylammonium fluoride in the usual way to give compound **11a** (Scheme 3).

When the present reaction was performed in refluxing acetonitrile, both TIPDS-protected mesoionic triazoline nucleoside **10a** and triazoline nucleoside **12a** were obtained in 29 and 4% yield, respectively. The structures **10a** and **12a** were determined on the basis of spectroscopic evidence [**10a**: $\delta_C$ 152.1 (C-3), 166.2 (C-5). **12a**: $\delta_C$ 158.5 (C-5), 160.9 (C-3)] (Scheme 3). The stereochemistry of the anomeric carbon was determined by NOE measurements as shown in Fig. 1.

The present reaction was then extended to D-ribofuranosylhydrazine and D-glucopyranosylhydrazine. The reaction of 3,5-*O*-TIPDS-D-ribofuranosylhydrazine **15**, derived from TIPDS-protected D-ribose **14**, with compounds **4** gave the corresponding mesoionic triazoline nucleosides **16** together with a small amount of the corresponding α-anomers. Compound **16a** was deprotected in the usual way to give the corresponding compound **17a** (Scheme 4).

The structure of compounds **16** was determined by the same method as described for compound **10a** (the NOE between 1′-H and 4′-H of compounds **16** was observed). The sugar conformation of compounds **16** is considered to be the *N*-form ($J_{1',2'} \sim 0$ Hz).[6]

The reaction of 2,3;4,6-di-O-TIPDS-D-glucopyranosylhydrazine derived from TIPDS-protected D-glucose with compounds **4** did not give the expected triazoline glycoside, perhaps because of the enforced, less flexible conformer of the sugar moiety caused by TIPDS groups.




Scheme 3.

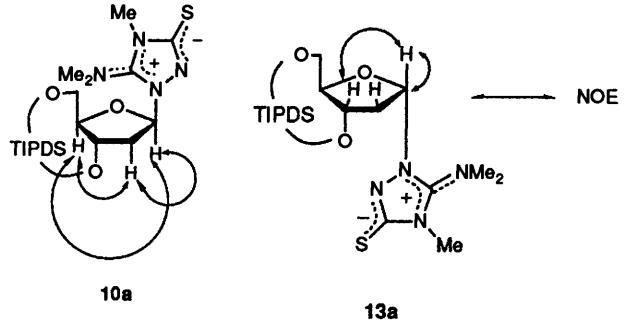
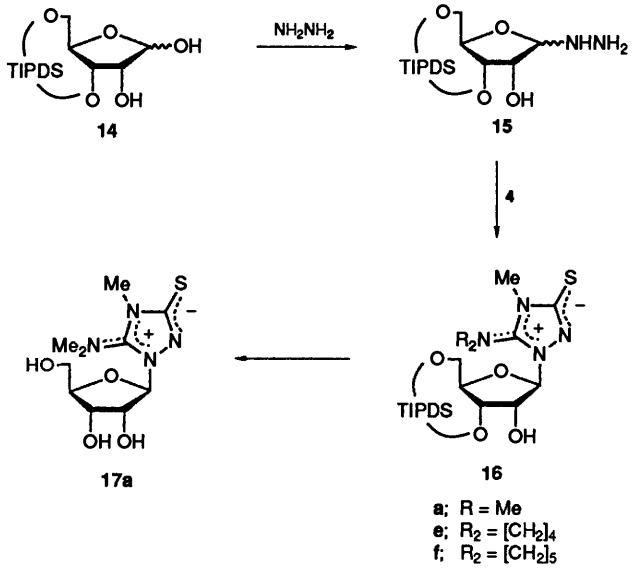



Figure 1.




Scheme 4.

Next, we modified Potts' method[7] for the synthesis of mesoionic triazoline nucleosides bearing alkyl and aryl groups on C-5 of the triazoline ring. Thus 1-(3,5-*O*-benzyl-2-deoxy-D-ribosyl)-4-phenylthiosemicarbazide was employed in this reaction in place of 1,4-diphenylthiosemicarbazide. However, the expected triazoline nucleosides could not be successfully obtained because of many side-reactions.

Among mesoionic triazoline nucleosides prepared by the present reaction, compounds **11a**, **11f** and **17a** were examined for biological activity. The antiviral activities of these compounds were compared with that of acyclovir (ACV). The results show that inhibitory efficacies [50% cytopathogenic effect (CPE)] of these compounds were not observed up to a dose of 100 μg $cm^{-1}$ and, in the case of compound **11a**, cell toxicity was shown at a dose of 50 μg $cm^{-1}$ (*cf.* ACV: 50% CPE at 3 μg $cm^{-1}$; cell toxicity > 750 μg $cm^{-1}$).

In conclusion, several mesoionic triazoline nucleosides were synthesized for the first time by the reaction of TIPDS-protected 2-deoxy-D-*erythro*-pentofuranoyl- or D-ribofuranosyl-hydrazine with isothiouronium compounds; three nucleosides obtained by this method showed no activity against Herpes Simplex Virus (HSV-1) virus.

## Experimental

Microanalysis was performed with a Perkin-Elmer 240 elemental analyser at the Chemical Analysis Center of Chiba University. IR, mass and $^1H$ NMR spectra were measured with Hitachi 215, RMU 6MC, ESP-3T and JEOL-MH-100 spectrometers, respectively. Wakogel C-200 was used for low-pressure liquid chromatography and Wakogel B-5F was used for TLC.

3,3-*Diethyl*-1,2-*dimethyl*-1-[(*methylthio*)*thiocarbonyl*]*isothiouronium Iodide* **4b**.—A mixture of potassium thiocyanate (9.7 g, 0.1 mol), acetone (80 $cm^3$) and ethyl chloroformate **1** (0.1 mol) was refluxed for 2 h and then diethylamine (0.12 mol) was added to the reaction mixture after it had cooled. After being stirred for 1 h the mixture was treated with 6 mol $dm^{-3}$ HCl (200 $cm^{-3}$) and then extracted with ethyl acetate. Evaporation of the extract gave compound **2b** as yellow oil. A mixture of compound **2b** (0.5 mol) and conc. HCl (40 $cm^3$) was heated at 80 °C for 8 h. After being cooled with ice, the reaction mixture was neutralized with ammonium carbonate and then extracted with ethyl acetate. The extract was evaporated to give crude

material, which was then recrystallized from ethanol to afford compound **3b** as white crystals in 55% yield.

To a suspension of NaH (1 g, 42 mmol) in dry tetrahydrofuran (THF) (50 $cm^3$) was added compound **3b** (2.5 g, 19 mmol) under nitrogen. After being refluxed for 1 h, the reaction mixture was cooled with ice and then treated with a solution of $CS_2$ (6 $cm^3$, 100 mmol) in dry THF (30 $cm^3$). The resulting mixture was allowed to warm to the ambient temperature and was then treated with methyl iodide (7 $cm^3$, 112 mmol) and stirred for a further 1 h. The reaction mixture was then condensed to give a white solid, which was extracted with chloroform. The extract was evaporated to give the *salt* **4b** in 61% yield; m.p. 108–109 °C (from ethanol) (Found: C, 28.4; H, 5.1; N, 7.3. $C_9H_{19}IN_2S_3$ requires C, 28.57; H, 5.06; N, 7.40%); $\nu_{max}$ 2950, 2880, 1650 and 1530 $cm^{-1}$; $\delta_H$ 1.35 and 1.45 (6 H, t, *J* 7 Hz, 2 × $CH_2Me$), 2.57 (3 H, s, Me), 2.75 (6 H, s, SMe × 2), 3.69 (2 H, q, *J* 7 Hz, $NCH_2Me$) and 3.89 (2 H, q, *J* 7 Hz, $NCH_2Me$).

3,3-*Di-isopropyl*-1,2-*dimethyl*-1-[(*methylthio*)*thiocarbonyl*]-*isothiouronium iodide* **4c**. This was obtained in 51% yield based on substrate **3c**, m.p. 160–161 °C (from $CH_2Cl_2$–ether) (Found: C, 32.4; H, 5.7; N, 6.9. $C_{11}H_{23}IN_2S_3$ requires C, 32.51; H, 5.70; N, 6.89%); $\nu_{max}$ 2950, 2900, 1560 and 1530 $cm^{-1}$; $\delta_H$ 1.60–1.20 (12 H, m, Me × 4), 2.51 (3 H, s, NMe), 2.73 (6 H, s, SMe × 2) and 4.60–4.10 (2 H, m, CHN × 2).

3,3-*Dibutyl*-1,2-*dimethyl*-1-[(*methylthio*)*thiocarbonyl*]*isothiouronium iodide* **4d**. This was obtained in 62% yield based on substrate **3d**, m.p. 86–87 °C (from $CH_2Cl_2$–ether) (Found: C, 35.9; H, 6.35; N, 6.6. $C_{13}H_{27}IN_2S_3$ requires C, 35.94; H, 6.26; N, 6.45%); $\nu_{max}$ 2920, 2850, 1570 and 1550 $cm^{-1}$; $\delta_H$ 0.98 (6 H, t, *J* 7 Hz, Me × 2), 1.40 (4 H, m, $CH_2$ × 2), 1.70 (4 H, m, $CH_2$ × 2), 2.54 (3 H, s, NMe), 2.74 (6 H, s, SMe × 2) and 3.55 and 3.76 (4 H, t, *J* 6 Hz, $NCH_2$ × 2).

1,3-*Dimethyl*-1-[(*methylthio*)*thiocarbonyl*]-2,2-*tetramethyleneisothiouronium iodide* **4e**. This was obtained in 70% yield based on **3e**, m.p. 119–120 °C (from $CH_2Cl_2$–ether) (Found: C, 28.7; H, 4.6; N, 7.4. $C_9H_{17}IN_2S_3$ requires C, 28.72; H, 4.55; N, 7.44%); $\nu_{max}$ 2950, 1560 and 1530 $cm^{-1}$; $\delta_H$ 2.16–2.40 (4 H, m, $CH_2$ × 2), 2.53 (3 H, s, NMe), 2.72 (6 H, s, SMe × 2) and 3.70–3.92 (4 H, m, $NCH_2$ × 2).

1,3-*Dimethyl*-1-[(*methylthio*)*thiocarbonyl*]-2,2-*pentamethyleneisothiouronium iodide* **4f**. This was obtained in 75% yield based on substrate **3f**, m.p. 123–124 °C (from $CH_2Cl_2$–ether) (Found: C. 30.75; H, 4.8; N, 7.2. $C_{10}H_{19}IN_2S_3$ requires C, 30.77; H, 4.90; N, 7.18%); $\nu_{max}$ 2980, 2920, 1560 and 1530 $cm^{-1}$; $\delta_H$ 1.70–2.00 (6 H, m, $CH_2$ × 3), 2.52 (3 H, s, NMe), 2.72 (6 H, s, $SCH_3$ × 2) and 3.76 and 3.94 (4 H, m, $NCH_2$ × 2).

Compounds **4c–f** were synthesized in the same way as described for compound **4b** and compound **4a** was prepared by our previous method.[5]

3,5-*Di*-O-*benzyl*-2-*deoxy*-D-erythro-*pentafuranosylhydrazine* **5**.—A mixture of methyl 3,5-di-*O*-benzyl-2-deoxy-*erythro*-pentofuranoside[8] (5.1 g, 16 mmol) and 80% aq. acetic acid (59 $cm^3$) was refluxed for 15 min. The reaction mixture was evaporated to give an oil, which was purified by column chromatography on silica gel [eluant AcOEt–hexane (1:2)] to afford white crystals (3.19 g, 66%).

A mixture of the pentofuranose obtained above (0.63 g, 2 mmol), dry methanol (3 $cm^3$) and anhydrous hydrazine (0.64 $cm^3$, 20 mmol) was stirred for 17 h at room temperature. The solvent was removed by an aspirator. The residue was evaporated with dry methanol (4 × 4 $cm^3$) and then under vacuum-pump pressure (1 Torr) below 50 °C to remove excess of hydrazine. A pale yellow syrup was obtained, which was used without purification for the next step.

*Mesoionic* 1-(3′,5′ *Di*-O-*benzyl*-2′-*deoxy*-D-arythro-*pentofuranosyl*)-5-*dimethylamino*-4-*methyldihydro*-1,2,4-*triazole*-3-*thione* **6** *and* 2-(3′,5′-*Di*-O-*benzyl*-2′-*deoxy*-D-erythro-*pentofuranosyl*)-5-*dimethylamino*-4-*methyl*-*dihydro*-1,2,4-*triazole*-3-*thione* **7**.—A mixture of 3,5-dibenzyl-2-deoxy-D-*erythro*-pentofuranose (0.51 g, 1.63 mmol), dry methanol (3 $cm^3$) and hydrazine (16.3 mmol) was stirred at room temperature for 16 h. The resulting mixture was evaporated with dry methanol (4 × 4 $cm^3$) to remove excess of hydrazine, giving a pale yellow oil, to which was added compound **4a** (1.16 g, 3.3 mmol), dry ethanol (15 $cm^3$) and triethylamine (6.5 mmol). The resulting mixture was stirred for 17 h at room temperature, and was then evaporated. After treatment with 0.1 mol $dm^{-3}$ HCl (20 $cm^3$), the residue was extracted with ether. Purification was carried out by LPLC [Wakogel C-300; AcOEt–hexane (1:3)] to give compounds **6** and **7** as oils in 17 and 2% yield, respectively.

For *compound* **6**: (Found: C, 63.35; H, 6.7; N, 12.3. $C_{24}H_{30}N_4O_3S$ requires C, 63.41; H, 6.65; N, 12.32%); *m/z* 454 ($M^+$); $\nu_{max}$ 2910, 2850, 1690 and 1560 $cm^{-1}$; $\delta_H$ 2.34 (2 H, m, 2′-H), 2.61 (3 H, s, NMe), 2.89 (6 H, s, $NMe_2$), 3.61 (2 H, m, 5′-H), 4.30 (1 H, m, 3′-H), 4.39 (1 H, m, 4′-H), 4.52–4.56 (4 H, m, $CH_2Ph$ × 2), 6.06 (1 H, m, 1′-H) and 7.25–7.34 (10 H, m, Ph × 2).

For *compound* **7**: (Found: C, 63.4; H, 6.7; N, 12.1. $C_{24}H_{30}N_4O_3S$ requires C, 63.41; H, 6.65; N, 12.32%); *m/z* 454 ($M^+$); $\nu_{max}$ 2910, 2850, 1730 and 1550 $cm^{-1}$; $\delta_H$ 2.32 (2 H, m, 2′-$H_2$), 2.42 (3 H, s, NMe), 2.93 (6 H, s, $NMe_2$), 3.58 (2 H, m, 5′-H), 4.29 (1 H, m, 3′-H), 4.39 (1 H, m, 4′-H) and 4.52–4.56 (4 H, m, $CH_2Ph$ × 2), 5.98 (1 H, m, 1′-H) and 7.25–7.34 (10 H, m, Ph × 2).

2-*Deoxy*-3,5-O-*TIPDS*-D-erythro-*pentofuranose* **8**.—A mixture of 2-deoxy-D-*erythro*-pentofuranose (670 mg, 5 mmol), dry pyridine (15 $cm^3$) and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (1.6 $cm^3$, 5 mmol) was stirred at −20 °C for 1 h and then kept in a freezer for two days. The reaction mixture was evaporated and the residue was treated with AcOEt–water. The ethyl acetate extract was then treated successively with 1 mol $dm^{-3}$ HCl, water, saturated aq. $NaHCO_3$, saturated aq. NaCl and then dried over anhydrous $Na_2SO_4$. Purification of this extract by LPLC [Wakogel C-300; AcOEt–hexane (1:5)] afforded compound **8** as an oil in 62% yield; $\nu_{max}$ 3350, 2900, 2840 and 1730 $cm^{-1}$; *m/z* 376 ($M^+$).

*Mesoionic* 1-[2-*Deoxy*-3,5-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-D-erythro-*pentofuranosyl*]-5-*dimethylamino*-4-*methyl*-*dihydro*-1,2,4-*triazole*-3-*thione* **10a** *and* 2-[2-*Deoxy*-3,5-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-D-erythro-*pentofuranosyl*]-5-*dimethylamino*-4-*methyldihydro*-1,2,4-*triazole*-3-*thione* **12a**.—A mixture of compound **8** (0.56 g, 1.5 mmol), dry methanol (3 $cm^3$) and hydrazine (15 mmol) was stirred for 16 h at room temperature. The resulting mixture was evaporated with dry methanol to remove excess of hydrazine, giving compound **9** as a pale yellow oil.

A mixture of the above obtained hydrazine **9**, the salt **4a** (1.1 g, 3 mmol), triethylamine (0.8 $cm^3$, 6 mmol) and acetonitrile (5 $cm^3$) was stirred at room temperature for 17 h. The reaction mixture was quenched with 0.1 mol $dm^{-3}$ HCl and was then extracted with ether. Purification was performed by preparative TLC on silica gel [eluant AcOEt–hexane (1:3)] to give compounds **10a** and **13a**, the α-anomer of **10a**, in 39 and 4% yield, respectively. When the above cyclization was carried out in refluxing acetonitrile, compounds **10a** and **12a** were obtained in 29 and 4% yield, respectively.

For *compound* **10a**: (Found: C, 51.1; H, 8.65; N, 10.8. $C_{22}H_{44}N_4O_4SSi_2$ requires C, 51.13; H, 8.58; N, 10.84%); *m/z* 516 ($M^+$); $\nu_{max}$ 2930, 2860 and 1570 $cm^{-1}$; $\delta_H$ 0.9–1.11 (28 H, m, $Pr^i$ × 4), 2.57 and 2.95 (2 H, m, 2′-H), 2.60 (3 H, s, NMe), 2.97 (6 H, s, $NMe_2$), 3.92 and 3.98 (2 H, AB pattern, $J_{5',5'}$ 16, $J_{4',5'}$ 3.7,

4.6 Hz, 5'-$H_2$), 4.07 (1 H, m, 3'-H), 4.44 (1 H, m, 4'-H) and 5.88 (1 H, t, $J_{1',2'}$ 7 Hz, 1'-H).

For *compound* **13a**: (Found: C, 51.1; H, 8.6; N, 10.8%); *m/z* 516 ($M^+$); $\nu_{max}$ 2920, 2850 and 1570 $cm^{-1}$; $\delta_H$ 0.98–1.0 (28 H, m, $Pr^i$ × 4), 1.96 and 2.57 (2 H, m, 2'-$H_2$), 2.65 (3 H, s, NMe), 2.96 (6 H, s, $NMe_2$), 3.36 (1 H, m, 3'-H), 3.86 (1 H, m, 4'-H), 3.73 and 3.95 (2 H, AB pattern, $J_{5',5'}$ 15, $J_{4',5'}$ 1.4, 9.9 Hz, 5'-$H_2$) and 5.48 (1 H, dd, $J_{1',2'}$ 3, 11 Hz, 1'-H).

For *compound* **12a**: (Found: C, 51.05; H, 8.6; N, 10.7%); *m/z* 516 ($M^+$); $\nu_{max}$ 2930, 2850 and 1590 $cm^{-1}$; $\delta_H$ 0.93–1.1 (28 H, m, $Pr^i$ × 4), 2.40 and 2.72 (2 H, m, 2'-$H_2$), 2.48 (3 H, s, NMe), 2.92 (6 H, s, $NMe_2$), 3.85 (2 H, m, 5'-$H_2$), 3.93 (1 H, m, 3'-H), 5.12 (1 H, m, 4'-H) and 5.82 (1 H, d, $J_{1',2'}$ 7 Hz, 1'-H).

*Mesoionic* 1-(2-*deoxy*-3,5-O-*TIPDS*-D-erythro-*pentofuranosyl*)-5-*diethylamino*-4-*methyl*-*dihydro*-1,2,4-*triazole*-3-*thione* **10b**. This was obtained in 10% yield (Found: C, 52.9; H, 8.9; N, 10.15. $C_{24}H_{48}N_4O_4SSi_2$ requires C, 52.90; H, 8.88; N, 10.28%); *m/z* 544; $\nu_{max}$ 2920, 2850 and 1560 $cm^{-1}$; $\delta_H$ 0.9–1.2 (34 H, m, $Pr^i$ × 4, $MeCH_2N$ × 2), 2.42 (2 H, m, 2'-H), 2.57 (3 H, s, NMe), 3.36 (4 H, q, *J* 6 Hz, $MeCH_2N$ × 2), 3.64–4.12 (3 H, m, 3'-H and 5'-$H_2$), 4.30 (1 H, m, 4'-H) and 5.64 (1 H, t, $J_{1',2'}$ 8 Hz, 1'-H).

*Mesoionic* 1-(2-*Deoxy*-3,5-O-*TIPDS*-D-erythro-*pentofuranosyl*)-5-*diisopropylamino*-4-*methyl*-*dihydro*-1,2,4-*triazole*-3-*thione* **10c**. This was obtained in 20% yield (Found: C, 54.6; H, 9.1; N, 9.8. $C_{26}H_{52}N_4O_4SSi_2$ requires C, 54.51; H, 9.15; N, 9.78%); *m/z* 572 ($M^+$); $\nu_{max}$ 2930, 2850 and 1550 $cm^{-1}$; $\delta_H$ 0.9–1.1 [40 H, m, $Pr^i$ × 4, $N(CHMe_2)_2$], 2.50 (5 H, m, 2'-$H_2$ and NMe), 3.30 [2 H, m, $N(CHMe_2)_2$], 3.70 (3 H, m, 3'-H and 5'-H), 4.00 (1 H, m, 4'-H) and 5.80 (1 H, t, $J_{1',2'}$ 8 Hz, 1'-H).

*Mesoionic* 1-(2-*Deoxy*-3,5-O-*TIPDS*-D-erythro-*pentofuranosyl*)-5-*dibutylamino*-4-*methyl*-*dihydro*-1,2,4-*triazole*-3-*thione* **10d**. This was obtained in 15% yield (Found: C, 55.9; H,9.4; N, 9.5. $C_{28}H_{56}N_4O_4SSi_2$ requires C, 55.96; H, 9.39; N, 9.32%); *m/z* 600 ($M^+$); $\nu_{max}$ 2940, 2860 and 1570 $cm^{-1}$; $\delta_H$ 0.80–1.1 (34 H, m, $Pr^i$ × 4, $Me[CH_2]_3N$ × 2), 1.40 (8 H, m, $Me[CH_2]_2$–$CH_2N$ × 2), 2.58 (3 H, s, NMe), 2.60 and 3.00 (2 H, m, 2'-$H_2$), 3.27 (t, 4-H, 6, *J* 6 Hz $Me[CH_2]_2CH_2N$ × 2), 3.66–4.02 (3 H, m, 3'-H and 5'-H), 4.25 (1 H, m, 4'-H) and 5.66 (1 H, t, $J_{1',2'}$ 8 Hz, 1'-H).

*Mesoionic* 1-(2-*deoxy*-3,5-O-*TIPDS*-D-erythro-*pentofuranosyl*)-4-*methyl*-5-*pyrrolidino*-*dihydro*-1,2,4-*triazole*-3-*thione* **10e**. This was obtained in 34% yield (Found: C, 53.05; H, 8.7; N, 10.55. $C_{24}H_{46}N_4OSSi_2$ requires C, 53.10; H, 8.54; N, 10.32%); *m/z* 542 ($M^+$); $\nu_{max}$ 2930, 2860 and 1520 $cm^{-1}$; $\delta_H$ 0.95–1.1 (28 H, m, $Pr^i$ × 4), 1.92 (4 H, m, $CH_2$ × 2), 2.54 and 2.99 (2 H, m, 2'-$H_2$), 2.60 (3 H, s, NMe), 3.41 (4 H, m, $CH_2NCH_2$), 3.93 and 3.97 (2 H, AB pattern, $J_{5',5'}$ 12, $J_{4',5'}$ 3 Hz, 5'-$H_2$), 4.07 (1 H, m, 3'-H), 4.43 (1 H, m, 4'-H) and 5.91 (1 H, t, $J_{1',2'}$ 7 Hz, 1'-H).

*Mesoionic* 1-(2-*deoxy*-3,5-O-*TIPDS*-D-erythro-*pentofuranosyl*)-4-*methyl*-5-*piperidino*-*dihydro*-1,2,4-*triazole*-3-*thione* **10f**. This was obtained in 41% yield (Found: C, 53.9; H, 8.75; N, 10.1. $C_{25}H_{48}N_4O_4SSi_2$ requires C, 53.92; H, 8.69; N, 10.06%); *m/z* 556 ($M^+$); $\nu_{max}$ 2920, 2850 and 1540 $cm^{-1}$; $\delta_H$ 0.93–1.1 (28 H, m, $Pr^i$ × 4), 1.58 (6 H, m, $CH_2$ × 3), 2.56 and 2.95 (2 H, m, 2'-$H_2$), 2.60 (3 H, s, NMe), 3.38 (4 H, m, $CH_2NCH_2$), 3.94 and 3.98 (2 H, AB pattern, $J_{5',5'}$ 13, $J_{4',5'}$ 3 Hz, 5'-$H_2$), 4.06 (1 H, m, 3'-H), 4.43 (1 H, m, 4'-H) and 5.87 (1 H, t, $J_{1',2'}$ 7 Hz, 1'-H).

*Compound* **13f** was obtained in 5% yield (Found: C, 53.95; H, 8.75; N, 10.1. $C_{25}H_{48}N_4O_4SSi_2$ requires C, 53.92; H, 8.69; N, 10.06%); *m/z* 556 ($M^+$); $\nu_{max}$ 2920, 2850 and 1540 $cm^{-1}$; $\delta_H$ 0.98–1.1 (28 H, m, $Pr^i$ × 4), 1.92 (6 H, m, $CH_2$ × 3), 2.58 and 2.99 (2 H, m, 2'-$H_2$), 2.60 (3 H, s, NMe), 3.43 (4 H, m, $CH_2NCH_2$), 3.95 and 3.97 (2 H, AB pattern, $J_{5',5'}$ 12, $J_{4',5'}$ 3 Hz, 5'-$H_2$), 4.08 (1 H, m, 3'-H), 4.44 (1 H, m, 4'-H) and 5.92 (1 H, t, $J_{1',2'}$ 7 Hz, 1'-H).

*Deprotection of Mesoionic* 1-[2-*Deoxy*-3,5-O-(*tetraisopropyldisiloxane*-1,3-*diyl*)-D-erythro-*pentofuranosyl*]-5-*dimethylamino*-4-*methyl*-*dihydro*-1,2,4-*triazole*-3-*thione* **10a** *and* 1-(2-*Deoxy*-3,5-O-*TIPDS*-D-erythro-*pentofuranosyl*)-4-*methyl*-5-*piperidino*-*dihydro*-1,2,4-*triazole*-3-*thione* **10f**.—A mixture of compound **10a** (260 mg, 0.5 mmol), toluene (10 $cm^3$) and tetrabutylammonium fluoride (1 mol $dm^{-3}$ THF soln; 1 $cm^3$) was stirred at room temperature for 30 min. The reaction mixture was added with water and then extracted with ether. The extract was condensed, and the residue was purified by LPLC (Wakogel C-300; AcOEt) to give compound **11a** as an oil in 79% yield (Found: C, 43.7; H, 6.6; N, 20.7. $C_{10}H_{18}N_4O_3S$ requires C, 43.78; H, 6.61; N, 20.42%); *m/z* 274 ($M^+$); $\nu_{max}$ 3300, 2900, 2850, 1725 and 1570 $cm^{-1}$; $\delta_H$ 2.36 (2 H, m, 2'-$H_2$), 2.60 (3 H, s, NMe), 2.89 (6 H, s, $NMe_2$), 3.59 (2 H, br, OH × 2), 4.12–4.36 (3 H, m, 3'-H and 5'-$H_2$), 5.91 (1 H, m, 4'-H) and 6.54 (1 H, d, $J_{1',2'}$ 12 Hz, 1'-H).

Compound **10f** was also deprotected by the same method as mentioned above. Compound **11f** was obtained in 68% yield (Found: C, 49.7; H, 7.1; N, 17.95. $C_{13}H_{22}N_4O_3S$ requires C, 49.66; H, 7.05; N, 17.82%); *m/z* 314 ($M^+$); $\nu_{max}$ 3300, 2900, 2850 and 1530 $cm^{-1}$; $\delta_H$ 1.58 (6 H, m, $CH_2$ × 3), 2.42 (2 H, m, 2'-$H_2$), 2.61 (3 H, s, NMe), 3.08 (2 H, br, OH × 2), 3.30 (4 H, m, $CH_2NCH_2$), 3.59 (2 H, m, 5'-$H_2$), 4.22 (1 H, m, 3'-H), 5.98 (1 H, m, 4'-H) and 6.65 (1 H, d, $J_{1',2'}$ 12 Hz, 1'-H).

3,5-O-*TIPDS*-D-*ribose* **14**.—A mixture of D-ribose (1.5 g, 10 mmol), dry pyridine (49 $cm^3$), and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (3.2 $cm^3$, 10 mmol) was stirred at room temperature overnight. The reaction mixture was treated with water and then extracted with ethyl acetate. The extract was treated successively with 1 mol $dm^{-3}$ HCl, water, saturated aq. $NaHCO_3$ and saturated aq. NaCl. Purification was performed by LPLC [Wakogel C-300; ACOEt–hexane (2:5)] to give compound **14** as an oil in 55% yield; $\nu_{max}$ 3450, 2920, 2850 and 1730 $cm^{-1}$; *m/z* 392 ($M^+$).

*Mesoionic* 5-*Dimethylamino*-4-*methyl*-1-(3,5-O-*TIPDS*-D-*ribosyl*)-*dihydro*-1,2,4-*triazole*-3-*thione* **16a**.—A mixture of compound **14** (860 mg, 2.2 mmol), dry methanol (5 $cm^3$) and hydrazine (22 mmol) was stirred at room temperature overnight. The reaction mixture was evaporated with dry methanol to remove excess of hydrazine, to give compound **15** as a pale yellow oil. A mixture of compound **15**, the salt **4a** (1.5 g, 4.4 mmol), triethylamine (1.2 $cm^3$, 8.8 mmol) and acetonitrile (10 $cm^3$) was stirred at room temperature for 17 h. Purification was performed by the same method as described for the preparation of compound **10a** to afford the *title compound* **16a** as an oil in 23% yield (Found: C, 49.6; H, 8.4; N, 10.5. $C_{22}H_{44}N_4O_5SSi_2$ requires C, 49.59; H, 8.32; N, 10.51%); *m/z* 532 ($M^+$); $\nu_{max}$ 2930, 2850 and 1570 $cm^{-1}$; $\delta_H$ 0.98–1.2 (28 H, m, $Pr^i$ × 4), 2.61 (3 H, s, NMe), 2.92 (6 H, s, $NMe_2$), 3.13 (1 H, s, OH), 3.92–4.04 (3 H, m, 4'-H and 5'-$H_2$), 4.40 (1 H, d, $J_{2',3'}$ 5 Hz, 2'-H), 5.09 (1 H, dd, $J_{2',3'}$ 5, $J_{3',4'}$ 7 Hz, 3'-H) and 5.76 (1 H, s, 1'-H).

The α-anomer of compound **16a** was obtained in 7% yield by the above purification process.

*Mesoionic* 4-*Methyl*-5-*pyrrolidino*-1-(3,5-O-*TIPDS*-D-*ribosyl*)-*dihydro*-1,2,4-*triazole*-3-*thione* **16e**. This was obtained in 11% yield (Found: C, 51.7; H, 8.4; N, 10.1. $C_{24}H_{46}N_4O_5SSi_2$ requires C, 51.58; H, 8.29; N, 10.02%); *m/z* 558 ($M^+$); $\nu_{max}$ 2910, 2850 and 1540 $cm^{-1}$; $\delta_H$ 0.96–1.2 (28 H, m, $Pr^i$ × 4), 1.91–1.93 (4 H, m, $CH_2$ × 2), 3.35–3.37 (4 H, m, $CH_2NCH_2$), 3.96–4.04 (3 H, m, 4'-H and 5'-$H_2$), 4.38 (1 H, d, $J_{2',3'}$ 5 Hz, 2'-H), 5.12 (1 H, dd, $J_{2',3'}$ 5, $J_{3',4'}$ 7 Hz, 3'-H) and 5.80 (1 H, s, 1'-H).

*Mesoionic* 4-*Methyl*-5-*piperidino*-1-(3,5-O-*TIPDS*-D-*ribosyl*)-*dihydro*-1,2,4-*triazole*-3-*thione* **16f**. This was obtained in 11% yield (Found: C, 52.4; H, 8.55; N, 9.9. $C_{25}H_{48}N_4O_5SSi_2$ requires C, 52.41; H, 8.44; N, 9.78%); *m/z* 572 ($M^+$); $\nu_{max}$ 2920, 2850 and 1540 $cm^{-1}$; $\delta_H$ 0.97–1.2 (28 H, m, $Pr^i$ × 4), 1.59–1.61 (6 H, m, $CH_2$ × 3), 2.66 (3 H, s, NMe), 3.15 (1 H, s, OH), 3.32–3.37 (4 H,

m, $CH_2NCH_2$), 3.91–4.04 (3 H, m, 4′-H and 5′-$H_2$), 4.37 (1 H, d, $J_{2',3'}$ 5 Hz, 2′-H), 5.09 (1 H, dd, $J_{2',3'}$ 5, $J_{3',4'}$ 7 Hz, 3′-H) and 5.76 (1 H, s, 1′-H).

*Mesoionic 5-Dimethylamino-4-methyl-1-D-ribosyl-dihydro-1,2,4-triazole-3-thione* **17a**.—Compound **16a** was deprotected in the same way as described for compound **10a**; the *title compound* was obtained in 30% yield as an oil (Found: C, 41.5; H, 6.4; N, 19.4. $C_{10}H_{18}N_4O_4S$ requires C, 41.37; H, 6.25; N, 19.29%); *m/z* 290 ($M^+$); $\nu_{max}$ 3300, 2900, 2850, 2725 and 1570 $cm^{-1}$; $\delta_H$ 1.75 (1 H, br, OH), 2.62 (s, 3 H, NMe), 2.90 (6 H, s, $NMe_2$), 3.36 (1 H, br, OH), 3.66 and 3.93 (2 H, m, 5′-$H_2$), 5.26 (1 H, d, $J_{3',4'}$ 2 Hz, 4-H), 4.48 (1 H, dd, $J_{2',3'}$ 5, $J_{3',4'}$ 2 Hz, 3′-H), 4.76 (1 H, t, $J_{1',2}$ 5, $J_{2',3'}$ 5 Hz, 2′-H), 5.66 (1 H, d, $J_{5',OH}$ 11.3 Hz, 5′-OH) and 5.75 (1 H, d, $J_{1',2'}$ 5 Hz, 1′-H).

2,3;4,6-*Di*-O-*TIPDS*-D-*glucopyanose*.—A mixture of D-glucose (900 mg, 5 mmol), dry pyridine (25 $cm^3$), and 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (3.2 $cm^3$, 10 mmol) was stirred at −30 °C for 30 min and then kept in a freezer overnight. The reaction mixture was worked up in the same way as described for compounds **8** and **14**; the eluant for LPLC was AcOEt–hexane (1:8); the title product was obtained as a foam in 54% yield (α- and β-form 5:2).

α-Form: $\nu_{max}$ 3400, 2920, 2860 and 1460 $cm^{-1}$; $\delta_H$ 0.92–1.1 (56 H, m, $Pr^i$), 3.12 (1 H, d, $J_{1',OH}$ 1.1 Hz, OH), 3.68 (1 H, dd, $J_{2',3'}$ 8.5, $J_{1',2'}$ 4.1 Hz, 2′-H), 3.78 (1 H, m, 5′-H), 3.8 (1 H, dd, $J_{4',5'}$ 8.5, $J_{3',4'}$ 8.5 Hz, 4′-H), 3.91 (1 H, AB pattern, $J_{6',6'}$ 12.7, $J_{5',6'}$ 1.4 Hz, 6′-H), 3.93 (1 H, dd, $J_{2',3'}$ 8.5, $J_{3',4'}$ 8.5 Hz, 3′-H), 4.12 (1 H, AB pattern, $J_{6',6'}$ 12.7, $J_{5',6'}$ 1.9 Hz, 6′-H) and 5.20 (1 H, dd, $J_{1',2'}$ 4.1, $J_{1',OH}$ 1.1 Hz, 1′-H).

β-Form: $\nu_{max}$ 3300, 2920, 2850 and 1460 $cm^{-1}$; $\delta_H$ 0.92–1.1 (56 H, m, $Pr^i$), 2.79 (1 H, d, $J_{1',OH}$ 5.5 Hz, OH), 3.18 (1 H, m, 5′-H), 3.39 (1 H, dd, $J_{2',3'}$ 8.3, $J_{1',2'}$ 7.4 Hz, 2′-H), 3.73 (1 H, dd, $J_{3',4'}$ 9.1, $J_{2',3'}$ 8.3 Hz, 3′-H), 3.88 (1 H, dd, $J_{4',5'}$ 9.1, $J_{3',4'}$ 9.1 Hz, 4′-H), 3.95 (1 H, AB pattern, $J_{6',6'}$ 12.6, $J_{5',6'}$ 1.4 Hz, 6′-H), 4.09 (1 H, AB pattern, $J_{6',6'}$ 12.6, $J_{5',6'}$ 1.9 Hz, 6′-H) and 4.60 (1 H, dd, $J_{1',2'}$ 7.4, $J_{1',OH}$ 5.5 Hz, 1′-H).

*Antiviral Tests against HSV-1 Virus*.—The HSV-1 virus used here was prepared as follows: The HSV-1 virus solution (0.2 $cm^3$/well, 100 plague forming unit/well) with the minimum essential medium (1 $cm^3$/well) containing 1% FCS (serum of calf's embryo) was cultured under an atmosphere containing $CO_2$ (2%) at 37 °C for three days.

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