SYNTHESIS OF NUCLEOSIDE MONO- AND DIALDEHYDES AS ANTIVIRAL AGENTS (U) ROCHESTER INST OF TECH NY
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UNCLASSIFIED
SYNTHESIS OF NUCLEOSIDE MONO- AND DIALDEHYDES AS ANTIVIRAL AGENTS

Annual Report

John P. Neenan, Ph.D.

15 December 1986

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Rochester Institute of Technology
Rochester, New York 14623

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The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.
**Synthesis of Nucleoside Mono- and Dialdehydes as Antiviral Agents (U)**

- **Seven nucleoside 2', 3'-dialdehydes** were synthesized by periodic oxidation of inosine, 6-methylmercaptopurine riboside, thymine riboside, guanosine, 5'-fluoro-5'-deoxyadenosine, 8-bromoadenosine, and N6,N6-dimethylaminopurine riboside, respectively. The resultant nucleoside dialdehydes, as well as the intermediate 5'-fluoro-5'-deoxyadenosine, were submitted to the USAMRIID antiviral screening program. Antiviral screening is still in progress as of this date. Preparation of the 4', 5'-unsaturated derivative of adenosine dialdehyde is in progress as of this date.
Summary

Prior to the start of this contract, a number of nucleoside 2',3'-dialdehydes were found to have in vitro activity against vaccinia virus, a DNA virus; as well as against RNA viruses of the arena-, bunya-, rhabdo-, and togaviridae families. Based on these findings, the first year of this project was devoted to the synthesis of nucleoside dialdehydes by periodate oxidation of the following starting compounds: inosine, 6-methylmercaptopurine riboside, thymine riboside, guanosine, 5'-fluoro-5'-deoxyadenosine, 8-bromoadenosine, and N⁶, N⁶-dimethylaminopurine riboside. The resultant nucleoside dialdehydes, as well as the intermediate 5'-fluoro-5'-deoxyadenosine, were characterized and submitted to the antiviral screening program at USAMRIID. Work is currently underway on the preparation of the 4',5'-unsaturated derivative of adenosine dialdehyde. This derivative is intended to serve as a precursor to nucleoside monoaldehydes. The limited antiviral screening results obtained thus far on the eight compounds submitted during the first year of this project will also be discussed.
Foreword

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.
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<td>17</td>
</tr>
</tbody>
</table>
Technical Presentation

Background

Prior to the start of this contract, a number of nucleoside dialdehydes had been found to have antiviral activity. Keller and Borchardt reported inhibition of vaccinia virus in vitro by adenosine dialdehyde.\(^1\) The antiviral activity of adenosine dialdehyde has been attributed to its potent inhibition of the enzyme S-adenosyl-L-homocysteine (AdoHcy) hydrolase, with resultant blockage of methylation of the 5'-cap of viral mRNA.\(^4\) Neenan et al. more recently reported in vitro inhibition of a number of RNA viruses in the USAMRIID screening system by adenosine dialdehyde and other nucleoside dialdehydes.\(^5\) Based on these results the series of nucleoside dialdehydes reported herein was synthesized and submitted to the antiviral screening system during this past year (Table I).

Chemistry

Compounds 1-4, 7 and 9 were prepared by periodic acid oxidation\(^6\) of: inosine, 6-methylmercaptopurine riboside, thymine riboside, guanosine, 8-bromoadenosine and \(N^6,N^6\)-dimethylaminopurine riboside, respectively. The requisite nucleoside starting materials were all obtained commercially. Compound 5 was obtained by periodic acid oxidation of 5'-fluoro- 5'deoxyadenosine (6), which had previously been synthesized as a candidate antiviral in a lengthy procedure described by Shen et al.\(^7\) Instead, we prepared 6 in one step from commercially obtained 5'-O-tosyladenosine by method of Kowollik et al.\(^8\) The synthesis of the 4','5'-unsaturated derivative (8) of adenosine dialdehyde, as previously described by Grant and Lehrner\(^9\) is currently underway. An attempt to prepare the dialdehyde derivative of formycin A (10) was unsuccessful.

\[\text{NH}_2\]
\[\text{N} \]
\[\text{C} \]
\[\text{N}_2 \]
\[\text{H} \]
\[\text{N} \]
\[\text{O} \]
\[\text{I} \]
\[\text{HC} \]
\[\text{CH} \]
\[\text{O} \]
\[\text{I} \]
\[\text{O} \]

8

10
Table I. Structures of Compounds Submitted During Reporting Period

<table>
<thead>
<tr>
<th>Compound</th>
<th>Code No.</th>
<th>AVS No.</th>
<th>Name</th>
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<tbody>
<tr>
<td>1</td>
<td>OP-I-19</td>
<td>1915</td>
<td>Inosine-2', 3'-dialdehyde</td>
</tr>
<tr>
<td>2</td>
<td>OP-I-9</td>
<td>1970</td>
<td>6-Methylmercaptopurine riboside-2', 3'-dialdehyde</td>
</tr>
<tr>
<td>3</td>
<td>OP-I-25</td>
<td>1976</td>
<td>Thymine riboside-2', 3'-dialdehyde</td>
</tr>
<tr>
<td>4</td>
<td>JDC-I-18</td>
<td>2151</td>
<td>Guanosine-2', 3'-dialdehyde</td>
</tr>
<tr>
<td>5</td>
<td>OP-I-77</td>
<td>2275</td>
<td>5'-Fluoro-5'-deoxyadenosine-2', 3'-dialdehyde</td>
</tr>
<tr>
<td>6</td>
<td>OP-I-63</td>
<td>2273</td>
<td>5'-Fluoro-5'-deoxyadenosine</td>
</tr>
<tr>
<td>7</td>
<td>OP-I-71</td>
<td>2274</td>
<td>8-Bromoadenosine-2', 3'-dialdehyde</td>
</tr>
<tr>
<td>8</td>
<td>LME-I-39</td>
<td>2543</td>
<td>N6, N6-Dimethylaminopurine riboside-2', 3'-dialdehyde</td>
</tr>
</tbody>
</table>
Biological Results.

As of this report date the only compound that the author has received any antiviral screening data on is compound 3 (AVS 1976). Compound 3 was essentially inactive against vesicular stomatitis virus in L929 cells.

Conclusions and Recommendations.

Once further antiviral data is obtained on the compounds already submitted, conclusions can perhaps be drawn with respect to future target compounds. Nevertheless, recommendations for next year include:

1. Completion of synthesis of compound 8. Once compound 8 is in hand, we will attempt to convert some of it reductively to the 2'- and/or 3'-monoaldehydes. Compound 8 and its monoaldehyde derivatives might be good transition state analogs for the antiviral target enzyme AdoHcy hydrolase.

2. Synthesis of the dialdehyde derivative of tubercidin.

3. Submission of compound 3 to the AIDS screening system. Compound 3 is somewhat similar in structure to azidothymidine (AZT), which is currently being used for treatment of AIDS. Preliminary work in our laboratory (at Rochester) indicates that 3 can inhibit reverse transcriptase.

4. Selection of other target compounds based on antiviral screening results obtained with compounds 1-9 in this report.
Experimental Section

IR spectra were recorded on a Perkin Elmer 681 Infrared Spectrophotometer. 1H NMR spectra were recorded on a Hitachi Perkin Elmer R-600 High Resolution NMR Spectrometer. Chemical shift values are reported in δ relative to Me4Si. UV spectra were recorded on a Varian Cary 219 Spectrophotometer. Mass spectra were obtained in the electron impact mode using a direct insertion probe and recorded on a Hewlett Packard 5995 Gas Chromatograph/Mass Spectrometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

Inosine-2',3'-dialdehyde (1); WR 220 078; NSC 118994

Compound 1 was prepared by modification of the method of Dvonch et al6. To a stirred solution of 3.0 g (11.2 mmol) of inosine in 130 mL of water was added 2.81 g (12.3 mmol) of paraperiodic acid (H5IO6). The reaction mixture was kept in the dark for 50 min and then applied to a 1.4 x 18 cm column of AG l-X8 anion exchange resin (acetate form). The column was washed with water. The self-eluate and washings (320 mL) were found to be free of iodate and periodate by starch iodide test paper and lyophilized to give 2.68 g (84%) of inosine dialdehyde as a flocculent white powder.

Physical and Analytical Data

Melting Point: Dec. > 205°, shrinking at 185°.

Analysis: For C10H10N4O5·H2O (284.24)

<table>
<thead>
<tr>
<th></th>
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<tr>
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<td>42.34</td>
</tr>
<tr>
<td>H</td>
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<td>4.60</td>
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<tr>
<td>N</td>
<td>19.71</td>
<td>19.12</td>
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</table>

Infrared Spectrum:

KBr. Compatible with structure. Broad band at 1100 cm⁻¹ typical of nucleoside dialdehydes.10

NMR:

(D2O) δ 8.70-8.23 (m, 2 H, H-2 and H-8), 6.20-5.07 (several overlapping m, 3 H, H-1', H-2', H-3'), 4.35-3.64 (several overlapping m, 3 H, H-4', 2 H-5').

UV Spectrum: λmax (H2O) 248 nm (ε 12,880)

Thin-layer Chromatography: (Eastman 13254 Cellulose)

<table>
<thead>
<tr>
<th>Eluent</th>
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<tr>
<td>H2O</td>
<td>0.85</td>
<td>Homogeneous</td>
</tr>
<tr>
<td>EtOH-1M NH4OAc (7:3,v/v)</td>
<td>0.73</td>
<td>Homogeneous</td>
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</table>
Compound 2 was prepared by modification of the method of Dvonch, et al. 6 To a stirred suspension of 2.9 g (9.72 mmol) of 6-methylmercaptopurine riboside in 140 mL of water was added a solution of 2.44 g (10.69 mmol) of paraperiodic acid in a few mL of water. The reaction mixture was stirred in the dark for 45 min. and then applied to a 1.4 X 17.5 cm column of Bio-Rad AG 1-X8 anion exchange resin (acetate form). The column was washed with water. The self-eluate and washings (350 mL) were found to be free of iodate and periodate by starch iodide test paper and lyophilized twice to give 2.5 g (87%) of 6-methylmercaptopurine riboside-2',3'-dialdehyde.

**Physical and Analytical Data**

**Melting Point:** 175° (dec), starts shrinking at 120°.

**Analysis:** C_{11}H_{12}N_{4}O_{4}S·H_2O (314.33)

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<td>42.30</td>
</tr>
<tr>
<td>H</td>
<td>4.49</td>
<td>4.83</td>
</tr>
<tr>
<td>N</td>
<td>17.83</td>
<td>17.69</td>
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</table>

**IR Spectrum:**

KBr. Compatible with structure. Broad band at 1100 cm\(^{-1}\) typical of nucleoside dialdehydes. 10

**NMR:**

\((D_2O) \delta 8.94-8.30 (m, 2 \text{ H, H-2 and H-8}), 6.37-5.10 (several overlapping \text{ r}, 3 \text{ H, H-1', H-2', H-3'}), 4.60-3.60 (several overlapping \text{ m, 3 H, H-4'}, 2 \text{ H-5'}) , 2.58 (s, 3 \text{ H, -SCH}_3)\).

**UV Spectrum:** \(\lambda_{max} (H_2O) 291 \text{ nm (e 19,760)}\)

**Thin-Layer Chromatography:** (Eastman 13254 Cellulose)

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<tr>
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<tr>
<td>H_2O</td>
<td>0.78</td>
<td>Homogeneous</td>
</tr>
<tr>
<td>EtOH-1M NH_4OAc (7:3)</td>
<td>0.94</td>
<td>Homogeneous</td>
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Compound 3 was prepared by modification of the method of Dvonch et al. \(^6\). To a stirred solution of 2.35 g (9.10 mmol) of thymine riboside in 100 mL of water was added a solution of 2.28 g (10.01 mmol) of paraperiodic acid in a few mL of water. The reaction mixture was stirred in the dark for 1.5 hr and then applied to a 1.4 X 18 cm column of Bio-Rad AG 1-X8 anion exchange resin (acetate form). The column was washed with water. The self-eluate and washings (310 mL) were found to be free of iodate and periodate by starch iodide test paper and lyphoïlized twice to give 2.27 g (90%) of thymine riboside-2',3'-dialdehyde.

Physical and Analytical Data

**Melting Point:** 140\(^\circ\) starts shrinking
158\(^\circ\) opaque melt
180\(^\circ\) transparent

**Analysis:** For C\(_{10}\)H\(_{12}\)N\(_2\)O\(_6\)·1\(\frac{1}{4}\)H\(_2\)O (278.75)

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<tr>
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<td>43.22</td>
</tr>
<tr>
<td>H</td>
<td>5.25</td>
<td>5.42</td>
</tr>
<tr>
<td>N</td>
<td>10.05</td>
<td>10.03</td>
</tr>
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</table>

**IR Spectrum:**

KBr. Compatible with structure. Broad band at 1100 cm\(^{-1}\) typical of nucleoside dialdehydes.\(^{10}\)

**NMR:**

D\(_2\)O 6 7.86-7.46 (broad, 1 H, H-6), 6.06-4.99 (several overlapping m, 3 H, H-1', H-2', H-3'), 4.46-3.36 (several overlapping m, 3 H, H-4', 2 H-5'), 1.9 (s, 3 H, 5-CH\(_3\)).

**UV Spectrum:** \(\lambda_{max} (H_2O) 264 \text{ nm (e 9,760)}\)
Thin-Layer Chromatography: (Eastman 13254 Cellulose)

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<td>H₂O</td>
<td>0.91</td>
<td>Homogeneous</td>
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<tr>
<td>EtOH–1M NH₄OAc (7:3)</td>
<td>0.87</td>
<td>Homogeneous</td>
</tr>
</tbody>
</table>

Code No.: OP-I-25
Prepared by: S. M. Opitz

Materials:

Thymine riboside
Periodic acid
AG 1-X8 resin (acetate form)
Water

Guanosine-2',3'-dialdehyde (4)

Compound 4 was prepared by modification of the method of Johnson et al.11 To a stirred suspension of 5.7 g (20 mmol) of guanosine in 200 mL of water was added 5.02 g (22 mmol) of periodic acid. The reaction mixture was stirred in the dark at room temperature for 60 min. A 10 g portion of Bio-Rad AG 1-X8 anion exchange resin (acetate form) was then added to the reaction mixture. The resulting slurry was stirred briefly and then allowed to stand for one min. The resin was removed by vacuum filtration, and the procedure was repeated until a total of six 10 g portions of resin has been used and the filtrate was free of iodate and periodate by starch iodide test paper. A 20 g portion of Bio-Rad AG 11-A8 ion retardation resin was then added to the filtrate, slurried for one minute, and then removed by vacuum filtration. The filtrate was lyophilized to give 4.06 g of white powder, which was redissolved in 250 mL of water and treated with 30 g of ion retardation resin, followed by vacuum filtration. The filtrate was lyophilized to give 3.89 g (51%) of guanosine-2',3'-dialdehyde.

Physical and Analytical Data

Melting Point: 150° (dec)

Analysis: C₁₀H₁₁N₅O₅·2³/₄H₂O·1¹/₄CH₃CO₂H (360.80)

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<td>36.42</td>
</tr>
<tr>
<td>H</td>
<td>5.17</td>
<td>4.67</td>
</tr>
<tr>
<td>N</td>
<td>19.41</td>
<td>19.55</td>
</tr>
</tbody>
</table>

IR Spectrum:

KBr. Compatible with structure. Broad band at 1100 cm⁻¹ typical of nucleoside dialdehydes.10
NMR:
Could not obtain. Insoluble in deuterated DMSO; forms gel in D_2O. Only acetate protons were detected at δ 1.9. See ref. 10.

UV Spectrum: \( \lambda_{\text{max}} (\text{H}_2\text{O}) \) 252.5 nm (ε 13,375)

Thin-Layer Chromatography:

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<td>H_2O</td>
<td>0.79</td>
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<td>EtOH-1M NH_4OAc (7:3)</td>
<td>0.80</td>
<td>Homogeneous</td>
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Code No.: JDG-I-18

Prepared by: J. D. Grinnell

Materials:

Guanosine
Periodic Acid
AG 1-X8 resin (acetate form)
AG 11-A8 resin
Water

5'-Fluoro-5'-deoxyadenosine-2',3'-dialdehyde (5)

To a stirred suspension of 2.5g (8.96 mmol) of compound 6 in 150 mL of water was added 2.3g (9.86 mmol) of periodic acid. The reaction mixture was stirred in the dark for 1.5 hr and then applied to a 1.4 X 18 cm column of Bio-Rad AG 1-X8 anion exchange resin (acetate form). The column was washed with water. The self eluate and washings (450 mL) were found to be free of iodate and periodate by starch iodide test paper and lyophilized twice to give 2.45g (90%) of compound 5.

Physical and Analytical Data

Melting Point: > 187° dec

Analysis: For C_{10}H_{10}FN_5O_3·2H_2O (303.25)

<table>
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<tr>
<th></th>
<th>Calcd</th>
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<tr>
<td>C</td>
<td>39.61</td>
<td>39.42</td>
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<tr>
<td>H</td>
<td>4.65</td>
<td>5.05</td>
</tr>
<tr>
<td>N</td>
<td>23.09</td>
<td>22.86</td>
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IR Spectrum:
KBr. Compatible with structure. Broad band at 1100 cm\(^{-1}\) typical of nucleoside dialdehydes.\(^{10}\)
NMR:

$\text{(Me}_2\text{SO-d}_6) \delta 8.70-7.90 \text{ (2 s, 2 H, H-2 and H-8), 7.70-6.80 (m, 2 H, 2 H-6'), 6.10-3.90 (several overlapping m, 6 H, H-1', H-2', H-3', H-4', 2 H-5').}$

UV Spectrum: $\lambda_{max} (\text{H}_2\text{O} 258 \text{ nm (c 15,900).}$

Thin-Layer Chromatography: (Eastman 13254 cellulose)

<table>
<thead>
<tr>
<th>Eluent</th>
<th>Rf</th>
<th>Comment</th>
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<tbody>
<tr>
<td>H$_2$O</td>
<td>0.62</td>
<td>Homogeneous</td>
</tr>
<tr>
<td>EtOH-1M NH$_4$OAc (7:3)</td>
<td>0.75</td>
<td>Homogeneous</td>
</tr>
</tbody>
</table>

Code No.: OP-I-77

Prepared by: S. M. Opitz

Materials:

Periodic acid Sigma lot 34F-0351
AG 1-X8 resin Bio-Rad Control No. 28817
Water triple distilled

5'-Fluoro-5'-deoxyadenosine (6)

Prepared by modification of the general method of Kowollik et al. A stirred solution of 5'-tosyladenosine (5.4 g, 12.8 mmol) in a 1.0 M solution of tetrabutylammonium fluoride (80 mL, 80 mmol) in THF was heated in an oil bath at 48-51° for 25 hr. The solvent was removed on a rotary evaporator. The residue was dissolved in water (500 mL) and applied to a 2.5 X 1.9 cm column of Bio-Rad AG 50W-X8 resin (hydrogen form). The column was washed with water until the eluate was neutral (pH paper). The resin and its contents were transferred to a beaker, stirred with 2M ammonium hydroxide in a warm bath (40-45°) for a few min. The resin was removed by vacuum filtration, and repeatedly washed with 2M ammonium hydroxide until the eluate showed no UV absorption. The combined eluate was lyophilized and to give a yellow powder which was dissolved in warm H$_2$O and kept at 4° overnight. The resultant precipitate was collected by filtration, washed with water and dried under suction. The crude product (2.45 g) was dissolved in 75 mL acetonitrile-water (11:89) and purified on a Waters Prep LC 500A system (column: 57 mm x 30 cm C18 cartridge; mobile phase: 11 vol% acetonitrile in water; flow rate: 100 mL/min; detector: refractive index). Solvents were removed by rotary evaporation under high vacuum to a small volume, followed by lyophilization to give 1.6 g (46%) of compound 6.

Physical and Analytical Data

Melting Point: 204-205° dec.
Analysis: For C_{10}H_{12}FN_{5}O_{3} \cdot 0.5H_{2}O (273.74).

<table>
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<tr>
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<tbody>
<tr>
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<td>43.87</td>
<td>43.77</td>
</tr>
<tr>
<td>H</td>
<td>4.60</td>
<td>4.67</td>
</tr>
<tr>
<td>N</td>
<td>25.58</td>
<td>25.96</td>
</tr>
</tbody>
</table>

IR Spectrum: KBr. Compatible with structure.

NMR:

$$(\text{Me}_{2}\text{SO-d}_{6}) \delta 8.27 \ (s, \ 1 \ H, \ H-8), \ 8.15 \ (s, \ 1 \ H, \ H-2), \ 5.95-5.92 \ (d, \ 1 \ H, \ H-1'), \ 5.63-5.40 \ (2 \ d, \ 2 \ H, \ \text{OH-3'} \ and \ \text{OH-2'}), \ 4.77-4.51 \ (m, \ 3 \ H, \ H-2' \ and \ 2 \ H-5', \ J_{H-5}, \ F = 50 \ Hz), \ 4.29-4.04 \ (m, \ 2 \ H, \ H-3' and \ H-4', \ J_{H-4'}, \ F = 15 \ Hz).$$

UV Spectrum: $\lambda_{\text{max}} (\text{H}_{2}\text{O}) \ 258 \text{ nm} (\epsilon \ 14,670)$

Thin-Layer Chromatography: (Eastman 13254 cellulose)

<table>
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<th>Eluent</th>
<th>Rf</th>
<th>Comment</th>
</tr>
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<tbody>
<tr>
<td>H_{2}O</td>
<td>0.48</td>
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</tr>
<tr>
<td>EtOH-1M NH_{4}OAc (7:3)</td>
<td>0.65</td>
<td>Homogeneous</td>
</tr>
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</table>

Code No.: OP-I-63

Prepared By: S. M. Opitz

Materials:

- 5'-Tosyladenosine Sigma lot 120F-4032
- Tetrabutylammonium fluoride Aldrich lot 00820BP (1.0 M in THF)
- AG 50W-X8 resin, 50-100 mesh (hydrogen form) Bio-Rad control. no. 29996

8-Bromoadenosine-2,3'-dialdehyde (7)

To a stirred suspension of 2.90 g (8.40 mmol of 8-bromoadenosine in 100 mL of water was added 2.11 g (9.24 mmol) of periodic acid. The reaction mixture was stirred in the dark for 1.5 hr and then applied to a 1.4 X 18 cm column of Bio-Rad AG 1-X8 resin (acetate form). The column was washed with water. The self-eluate and washings (400 mL were found to be free of iodate and periodate by starch iodide test paper, and lyophilized three times to give 2.77g (87%) of compound 7.

Physical and Analytical Data

Melting Point: >177° dec
**Analysis:** For C₁₀H₁₀BrN₅O₄ · 2H₂O

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<th>Calcd</th>
<th>Found</th>
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<td>31.92</td>
</tr>
<tr>
<td>H</td>
<td>3.71</td>
<td>3.82</td>
</tr>
<tr>
<td>N</td>
<td>18.42</td>
<td>18.35</td>
</tr>
</tbody>
</table>

**IR Spectrum:**

KBr. Compatible with structure. Broad band at 1100 cm⁻¹ typical of nucleoside dialdehydes.¹⁰

**NMR:**

(Me₂SO-d₆/D₂O) δ 8.17 (s, 1 H, H-2), 6.40-4.60 (several overlapping m, 4 H, H-1', H-2', H-3', H-4'), 3.6 (broad, 2 H, 2 H-5').

**UV Spectrum:** λmax (H₂O) 265 nm (ε 17,320)

**Thin-Layer Chromatography:** (Eastman 13254 cellulose)

<table>
<thead>
<tr>
<th>Eluent</th>
<th>Rf</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂O</td>
<td>0.61</td>
<td>Homogeneous</td>
</tr>
<tr>
<td>EtOH-1M NH₄OAc (7:3)</td>
<td>0.79</td>
<td>Homogeneous</td>
</tr>
</tbody>
</table>

**Code No.:** OP-I-71

**Prepared By:** S. M. Opitz

**Materials:**

- 8-Bromoadenosine Sigma lot 84F-0602
- Periodic acid Sigma lot 34F-0351
- AG 1-X8 resin (acetate form) Bio-Rad control no. 28817

**N₆,N₆-Dimethylaminopurine riboside-2',3'-dialdehyde (9).**

To a stirred suspension of 2.4 g (8.13 mmoles) of N₆,N₆-dimethylaminopurine riboside in 100 mL of water was added 2.04 g (8.95 mmoles) of para-periodic acid. The reaction mixture was stirred in the dark for 2-1/4 hours and then applied to a 1.4 cm x 16.24 cm column of Bio-Rad AG 1-X8 anion exchange resin (acetate form). The column was washed with water. The self-elute and washings (300 mL) were found to be free of iodate and periodate by starch iodide test paper, and were then lyophilized twice to give 2.19 grams (92%) of N₆,N₆-dimethylaminopurine riboside-2',3'-dialdehyde.

**Physical and Analytical Data**

**Melting Point:** 170° (dec), starts shrinking at 120°.
**Analysis:** For $C_{12}H_{15}N_5O_4\cdot2H_2O$ (329.31)

<table>
<thead>
<tr>
<th></th>
<th>Calcd</th>
<th>Found</th>
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<tbody>
<tr>
<td>C</td>
<td>43.77</td>
<td>44.10</td>
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<tr>
<td>H</td>
<td>5.82</td>
<td>5.42</td>
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<tr>
<td>N</td>
<td>21.2</td>
<td>20.70</td>
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</tbody>
</table>

**IR Spectrum:**

KBr. Broad band at 1100 cm\(^{-1}\) typical of nucleoside dialdehydes\(^10\).

**NMR (D\(_2\)O):**

$\delta$ 8.53-8.00 (m, 2 H, H-2, H-8), 6.12-3.94 (several overlapping m, 3 H, H-1', H-2', H-3'), 4.74-3.53 (several overlapping m, 3 H, H-4', 2 H-5'), 3.48-3.24 (t, 6 H, CH\(_3\) dimethylamino group).

**Melting point (°C):**

127° melts, opaque
170° decomposes into yellow liquid
>170° brown, charred solid

**UV Spectrum:** $\lambda_{\text{max}}$ (H\(_2\)O) 274 nm (ε 20,895)

**Mass Spectrum (EI, methanol)**

m/e 293 ($M^+$), 275 ($M^+ - H_2O$), 264 ($M^+ - CHO$)
246 [M - (H\(_2\)O + CHO)], 164 ($N_6,N_6$-dimethyladenine $H^+$)

**Thin-layer Chromatography:** (Eastman 13254 cellulose)

<table>
<thead>
<tr>
<th>Eluent</th>
<th>RF</th>
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</thead>
<tbody>
<tr>
<td>H(_2)O</td>
<td>0.77</td>
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<tr>
<td>EtOH-1 M NH(_4)OAc (7:3)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**Code No.:** LME-I-39

**Prepared by:** L.M. Eckel

**Materials:**

$N_6,N_6$-dimethylaminopurine riboside Sigma lot 88C-0410
paraperiodic acid Sigma lot 34F-0351
anion exchange resin (acetate form) Bio-Rad AG 1-X8 control #28817
Literature Cited


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