COMPONENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)-, monosilver salt (Ag sulfamethizole); C₉H₉AgN₄O₂S₂; [24342-31-2]
(2) 4-Morpholinepropanesulfonic acid; C₇H₁₅NO₄S; [1132-61-2]
(3) 4-Morpholinepropanesulfonic acid, sodium salt; C₇H₁₄NNaO₄S; [71119-22-7]
(4) Potassium nitrate; KN0₃; [7757-79-1]
(5) Water; H₂O; [7732-18-5]

ORIGINAL MEASUREMENTS:

PREPARED BY: R. Piekos

VARIABLES:
Hydronium-ion concentration

EXPERIMENTAL VALUES:
Equilibrium values of S² (S = total molar solubility) versus [H₃O⁺] for Ag sulfamethizole in 0.05M 4-morpholinepropanesulfonic acid buffer at 0.1M ionic strength (KN0₃) and 25±0.1°C.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:
Mixt of 100 mg Ag sulfamethizole and 25 or 27 ml of the 4-morpholinepropanesulfonic acid buffer were placed in paraffin-coated vials, adjusted to an ionic strength 0.1M with KNO₃, and rotated end over end in a thermostated bath until equilibrium soly was obtained (3-7 days). After filtration through 20M glass filtering crucibles, the solns were analyzed at 25±0.1°C in paraffin-coated beakers for Ag ions with a silver-ion selective electrode No. 94-16, Orion Res., Cambridge, Mass) standardized at the temp indicated and 0.1M ionic strength. The pH was measured with a triple-purpose pH electrode (Corning Sci. Instruments, Medfield, Mass) standardized using buffers meeting NBS requirements. The buffers were prepd with a total molar concn of 0.05M and adjusted to an ionic strength of 0.1M with KNO₃.

SOURCE AND PURITY OF MATERIALS:
All reagents used were anal or USP grade. Ag sulfamethizole was prepd by the method of Rosenzweig and Fuchs (1) and recrystd from ammonia (2). Water had a sp cond of (1-10) x 10⁻⁷ ohm⁻¹cm⁻¹.
The buffer soln was from US Biochem. Corp., Cleveland, Ohio (purity not specified).

ESTIMATED ERROR:
Soly: not specified.
Temp: ±0.1°C (authors).
pH: accuracy ±0.001 pH unit (authors).

REFERENCES:
COMPONENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-1,3,4-thiadiazol-2-yl)-, monosilver salt (Ag sulfamethizole); C₉H₉AgN₄O₂S₂; [24342-31-2]
(2) Nitric acid; HNO₃; [53081-02-0]
(3) Potassium nitrate; KNO₃; [7757-79-1]
(4) Water; H₂O; [7732-18-5]

ORIGINAL MEASUREMENTS:
Nesbitt, R. U., Jr.; Sandman, B. J.

VARIABLES:

EXPERIMENTAL VALUES:
Comparison of Total Silver Sulfamethizole Molar Solubility, S, Determined by the Method of Known Subtraction with the Molar Concentration of the Silver Ion Determined by Direct Potentiometry of Identical Samples at 25±0.1°C, 0.1M Ionic Strength, in Nitric Acid Buffer

<table>
<thead>
<tr>
<th>pH 1.931</th>
<th>pH 2.565</th>
</tr>
</thead>
<tbody>
<tr>
<td>S x 10⁻⁴</td>
<td>[Ag⁺] x 10⁻⁹</td>
</tr>
<tr>
<td>4.073</td>
<td>4.052</td>
</tr>
<tr>
<td>4.077</td>
<td>4.068</td>
</tr>
<tr>
<td>4.088</td>
<td>4.068</td>
</tr>
<tr>
<td>4.062</td>
<td>4.036</td>
</tr>
<tr>
<td>4.120</td>
<td>4.099</td>
</tr>
<tr>
<td>4.080</td>
<td>4.021</td>
</tr>
<tr>
<td>Mean</td>
<td>4.084</td>
</tr>
<tr>
<td>1.477</td>
<td>1.486</td>
</tr>
<tr>
<td>1.491</td>
<td>1.486</td>
</tr>
<tr>
<td>1.477</td>
<td>1.492</td>
</tr>
<tr>
<td>1.459</td>
<td>1.475</td>
</tr>
<tr>
<td>1.482</td>
<td>1.486</td>
</tr>
<tr>
<td>1.476</td>
<td>1.475</td>
</tr>
<tr>
<td>1.477</td>
<td>1.483</td>
</tr>
</tbody>
</table>

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:
Mixts of 100 mg of Ag sulfamethizole and 25 or 27 ml of the nitric acid buffer were placed in paraffin-coated vials, adjusted to an ionic strength 0.1M with KNO₃, and rotated end over end in a thermostated bath until equilibrium soly was obtained (3-7 days). After filtration through 20M glass filtering crucibles, the solns were analyzed at 25±0.0°C in paraffin-coated beakers for Ag⁺ ions with a silver-ion selective electrode (No.94-16, Orion Res., Cambridge, Mass) standardized at the temp indicated and 0.1M ionic strength. The pH was measured with a triple-purpose pH electrode (Corning Sci. Instruments, Medfield, Mass) standardized using buffers meeting NBS requirements. The nitric acid buffers were prepd by diln to 0.1M HNO₃ and were adjusted to an ionic strength of 0.1M with KNO₃.

SOURCE AND PURITY OF MATERIALS:
All reagents were anal or USP grade. Ag sulfamethizole was prepd by the method of Rosenzweig and Fuchs (1) and recrytd from ammonia (2). Water had a sp cond of (1 - 10) x 10⁻⁷ ohm⁻¹cm⁻¹. The source of the reagents was not specified.

ESTIMATED ERROR: Soly: when tested by one way analysis of variance, the means displayed in the Table were found not to be statistically different at the 1% confidence level (authors).

REFERENCES:
Calculation of the solubility product of Ag sulfamethizole, $K_s$, at $25 \pm 0.1^\circ$C and 0.1M ionic strength

<table>
<thead>
<tr>
<th>pH</th>
<th>$f_o$</th>
<th>$S^2$</th>
<th>$K_s$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.965</td>
<td>1.583 x 10^-4</td>
<td>1.733 x 10^-7</td>
<td>2.74 x 10^-11</td>
</tr>
<tr>
<td>2.102</td>
<td>2.526 x 10^-4</td>
<td>1.051 x 10^-7</td>
<td>2.65 x 10^-11</td>
</tr>
<tr>
<td>2.345</td>
<td>5.448 x 10^-4</td>
<td>4.693 x 10^-8</td>
<td>2.56 x 10^-11</td>
</tr>
<tr>
<td>2.598</td>
<td>1.132 x 10^-3</td>
<td>2.508 x 10^-8</td>
<td>2.85 x 10^-11</td>
</tr>
</tbody>
</table>

Mean $(2.70 \pm 0.12) x 10^{-11}$

$aK_s$ reported as mean ±SD

$a$ from eq. $K_s = f_o S^2$, where $f_o = (1 + \frac{[H_2O^+]}{K_2} + \frac{[H_4O^+]^2}{K_1 K_2})^{-1}$

$S$ is the total molar solubility, and $K_1$ and $K_2$ are the apparent dissociation constants of the $N^4$- (amino) and $N^1$- (amido) hydrogens of sulfamethizole, respectively.

AUXILIARY INFORMATION
COMPONENTS:

ORIGINAL MEASUREMENTS:

VARIABLES:

pH

PREPARED BY:
R. Piekos

EXPERIMENTAL VALUES:

Continued from previous page

\[
\frac{[Ag^+]^2}{[H_3O^+]} \times 10^5
\]

Equilibrium values of \([Ag^+]^2/[H_3O^+]\) versus \([H_3O^+]\) for silver sulfamethizole in nitric acid buffer at 0.1M ionic strength and 25±0.1°C

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

SOURCE AND PURITY OF MATERIALS:

ESTIMATED ERROR:

REFERENCES:
Molar solubility, $S$, of Ag sulfamethizole versus pH at 0.1M ionic strength and 25±0.1°C. Key: 0 calculated from equation

$$S^2 = [\text{Ag}^+]^2 = \frac{[\text{H}_3\text{O}]^+}{K_1} \frac{2}{K_2} + \frac{[\text{H}_3\text{O}]^+}{K_2} K_s$$

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:  

SOURCE AND PURITY OF MATERIALS:  

ESTIMATED ERROR:  

REFERENCES:
COMPONENTS:
(1) Acetamide, N-[4-[[5-methyl-1,3,4-thiadiazol-2-yl]amino][sulfonyl]phenyl]-
(acetyl sulfamethythiadiazole);
C_{11}H_{12}N_{4}O_{3}S_{2}; [39719-87-4]
(2) Water; H_2O; [7732-18-5]

ORIGINAL MEASUREMENTS:
Durel, M. P.; Allinne, M.

VARIABLES:
One temperature: 37°C

EXPERIMENTAL VALUES:

Solubility of acetyl sulfamethythiadiazole in water at 37°C is 0.10 g/liter
(3.2 x 10^{-4} mol dm^{-3}, compiler).

METHOD/APPARATUS/PROCEDURE:
The mixt of acetyl sulfamethythiadiazole
and water was agitated for 24 hours at 37°C.

SOURCE AND PURITY OF MATERIALS:
Source and purity of acetyl sulfamethythiadiazole were not specified.
Distilled water was used.

ESTIMATED ERROR:
Nothing specified.

REFERENCES:
**COMPONENTS:**

1. Acetamide, N-[4-[[[5-methyl-1,3,4-thiadiazol-2-yl]amino]sulfonyl]phenyl]-(acetyl sulfamethylthiadiazole); C_{11}H_{12}N_{4}O_{3}S_{2}; [39719-87-4]
2. Phosphoric acid, disodium salt; Na\_2HPO\_4; [7558-94-4]
3. Water; H\_2O; [7732-18-5]

**VARIABLES:**

One temperature: ca 20\(^\circ\)C; one pH: 8.74

**EXPERIMENTAL VALUES:**

Solubility of acetyl sulfamethylthiadiazole in a 0.705M (10\%) Na\_2HPO\_4 solution of pH 8.74 at room temperature (about 20\(^\circ\)C) is 1.250 g\%

(4.002 \times 10^{-2} \text{ mol dm}^{-3} \text{ solution, compiler}).

**METHOD/APPARATUS/PROCEDURE:**

Acetyl sulfamethylthiadiazole (0.5 g) was dissolved in 10 cm\(^3\) of the 0.705M (10\%) Na\_2HPO\_4 soln, shaken for 2 h at room temp (about 20\(^\circ\)C), and filtered. The filtrate was treated with equal vol of 2N HCl and refluxed for 15 min. After proper diln, a 1-cm\(^3\) aliquot was withdrawn, acidified, cooled, and the sulfonamide content was detd colorimetrically (as sulfamethylthiadiazole) by the Marshall method modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultrasonograph using a glass electrode.

**SOURCE AND PURITY OF MATERIALS:**

Acetyl sulfamethylthiadiazole (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfamethylthiadiazole. The source and purity of the remaining materials were not specified.

**ESTIMATED ERROR:**

Soly: precision ±5\% (author)
Temp: not specified.
PH: ±0.05 pH unit (author)

**REFERENCES:**

**COMPONENTS:**

1. Acetamide, N-[(5-methyl-1,3,4-thiadiazol-2-yl)amino]sulfonyl]phenyl]- (acetyl sulfamethylthiadiazole); C\textsubscript{11}H\textsubscript{12}N\textsubscript{4}O\textsubscript{3}S\textsubscript{2}; [39719-87-4]

2. Phosphoric acid, monopotassium salt; KH\textsubscript{2}P\textsubscript{4}; [7778-77-0]

3. Water; H\textsubscript{2}O; [7732-18-5]

**VARIABLES:**

- One temperature: ca 20°C; one pH: 4.37

**EXPERIMENTAL VALUES:**

Solubility of acetyl sulfamethylthiadiazole in a 0.735M (10%) KH\textsubscript{2}P\textsubscript{4} solution of pH 4.37 at room temperature (about 20°C) is 0.0066 g%

(2.11 x 10\textsuperscript{-4} mol dm\textsuperscript{-3} solution, compiler).

**AUXILIARY INFORMATION**

**METHOD/APPARATUS/PROCEDURE:**

Acetyl sulfamethylthiadiazole (0.5 g) was dissolved in the 0.735M (10%) KH\textsubscript{2}P\textsubscript{4} soln, shaken for 2 h at room temp (about 20°C), and filtered. The filtrate was treated with equal vol of 2N HCl, and refluxed for 15 min. After proper diln, a 1-cm\textsuperscript{3} aliquot was withdrawn, acidified, cooled, and the sulfonamide content was detd colorimetrically by the Marshall method modified by Kimmig (1) using an Authenrieth colorimeter. The pH was detd on an ultraionograph using a glass electrode.

**SOURCE AND PURITY OF MATERIALS:**

Acetyl sulfamethylthiadiazole (source not specified) gave no coloration upon diazotization of its satd soln, thus showing absence of sulfamethylthiadiazole. The source and purity of the remaining materials were not specified.

**ESTIMATED ERROR:**

- Soly: precision ±5% (author)
- Temp: not specified
- pH: ±0.05 pH unit (author)

**REFERENCES:**

COMPONENTS:
(1) Acetamide, N-[4-[[5-methyl-1,3,4-thiadiazol-2-yl]amino]sulfonyl]phenyl]-
(acetyl sulfamethylthiadiazole); C_{11}H_{12}N_{4}O_{3}S_{2}; [39719-87-4]
(2) Phosphoric acid, disodium salt; Na_{2}HPO_{4}; [7558-94-4]
(3) Phosphoric acid, monopotassium salt; K_{2}HPO_{4}; [7778-77-0]
(4) Water; H_{2}O; [7732-18-5]

ORIGINAL MEASUREMENTS:
Krüger-Thiemer, E.

PREPARED BY:
R. Piekos

VARIABLES:
Temperature; pH

EXPERIMENTAL VALUES:

<table>
<thead>
<tr>
<th>Composition of 1/15M phosphate buffer solution</th>
<th>Solubility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Room temp (ca 20°C)</td>
</tr>
<tr>
<td></td>
<td>g% 10^{-3} mol dm^{-3} solution</td>
</tr>
<tr>
<td>Na_{2}HPO_{4}</td>
<td>KH_{2}PO_{4}</td>
</tr>
<tr>
<td>1.0</td>
<td>99.0</td>
</tr>
<tr>
<td>10.0</td>
<td>90.0</td>
</tr>
<tr>
<td>61.1</td>
<td>38.9</td>
</tr>
<tr>
<td>9.5</td>
<td>0.5</td>
</tr>
<tr>
<td>94.7</td>
<td>5.3</td>
</tr>
</tbody>
</table>

^a Calculated by compiler
^b Molar content; 10% buffer solution

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:
Acetyl sulfamethylthiadiazole (0.5 g) was dissolved in 10 cm³ of a buffer soln, shaken
for 2 h at 20°C (or left for 48 h at 37°C),
and filtered at respective temp. The filtrate was treated with equal vol of 2N HCl
and refluxed for 15 min. After proper diln,
a 1-cm³ aliquot was withdrawn, acidified,
cooled, and the sulfonamide content was detd
colorimetrically (as sulfamethylthiadiazole)
by the Marshall method modified by Kimmig
(1) using an Authenrieth colorimeter. The pH was detd on an ultrasonograph using a
glass electrode.

SOURCE AND PURITY OF MATERIALS:
Acetyl sulfamethylthiadiazole (source not
specified) gave no coloration upon diazo-
tization of its satd soln, thus showing
absence of sulfamethylthiadiazole. The
source and purity of the remaining materi-
als were not specified.

ESTIMATED ERROR:
Soly: precision ±5% (author).
Temp: not specified.
pH: ±0.05 pH unit (author).

REFERENCES:
COMPONENTS:
(1) Acetamide, N-4-[[5-methyl-1,3,4-thiadiazol-2-yl]amino]sulfonyl]phenyl]-
(acyetyl sulfamethylthiadiazole); C_{11}H_{12}N_{4}O_{3}S_{2}; [39719-87-4]
(2) Phosphoric acid, disodium salt;
Na_{2}HPO_{4}; [7558-94-4]
(3) Phosphoric acid, monopotassium salt;
KH_{2}PO_{4}; [7778-77-0]
(4) Water; H_{2}O; [7732-18-5]

VARIABLES:

EXPERIMENTAL VALUES:

Solubility of acetyl sulfamethylthiadiazole in buffers of varying mixtures
of Na_{2}HPO_{4}.7H_{2}O (71.6 g/l distilled water; 0.27 mol dm^{-3}, compiler) and
KH_{2}PO_{4} (36.3 g/l distilled water; 0.27 mol dm^{-3}, compiler) at 37{C}.

<table>
<thead>
<tr>
<th>Equilibrium pH</th>
<th>Solubility (based on sulfamethylthiadiazole)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg/100 ml</td>
</tr>
<tr>
<td>4.5</td>
<td>41</td>
</tr>
<tr>
<td>5.0</td>
<td>50</td>
</tr>
<tr>
<td>5.5</td>
<td>71</td>
</tr>
<tr>
<td>6.0</td>
<td>102</td>
</tr>
<tr>
<td>6.3</td>
<td>260</td>
</tr>
<tr>
<td>6.6</td>
<td>630</td>
</tr>
<tr>
<td>7.3</td>
<td>2400</td>
</tr>
</tbody>
</table>

a Calculated by compiler

METHOD/APPARATUS/PROCEDURE:
Solns were prep'd by adding an excess of ace-
ty l sulfamethylthiadiazole to 10 ml of buffer
soln at each pH level in 18 x 150-mm test
tubes, stoppering the tubes, placing them in
water bath at 37{C} with gentle agitation for
24 h. The solute was then hydrolyzed with
5% H_{2}SO_{4} for 1 h to liberate the free sulfon-
amide. One-ml aliquot of the hydrolyzate was
accurately pipetted into a volumetric flask
for diln and analysis. The sulfonamide was
assayed colorimetrically by the method of
Bratton and Marshall as described in detail
by Biamonte and Schneller (1). A standard
curve was prep'd using accurately prep'd stan-
dard solutions.

SOURCE AND PURITY OF MATERIALS:
Neither source nor purity of the reagents
were specified. Distilled water was used.

ESTIMATED ERROR:
Soly: ave values of duplicate runs are
reported (authors).
Temp and pH: not specified.

REFERENCES:
1. Biamonte, A. R.; Schneller, G. E.
COMPONENTS:
(1) Acetamide, N-[4-[[5-(methyl-1,3,4-thiadiazole-2-yl)amino]sulfonyl]phenyl]-N-acetylsulfamethizole; C17H12N4O3S2; [39719-87-4]
(2) Phosphoric acid, disodium salt; Na2HPO4; [7558-94-4]
(3) Phosphoric acid, monopotassium salt; KH2PO4; [7778-77-0]
(4) Water; H2O; [7732-18-5]

VARIABLES:

EXPERIMENTAL VALUES:

<table>
<thead>
<tr>
<th>pH</th>
<th>Solubility at 25°C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg/l</td>
</tr>
<tr>
<td>5.5</td>
<td>200</td>
</tr>
<tr>
<td>7.5</td>
<td>3000</td>
</tr>
</tbody>
</table>

a Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:
Satd solns of N°-acetylsulfamethizole were prep. in phosphate buffers of pH 5.5 and 7.5 at room temp (25°C). The concn of the solute was measured by means of a Spectra Physics 3500B high-performance liquid chromatograph equipped with a column oven (Model 748) and a Pye-Unicam LC-UV spectrophotometric detector. The detector was connected to a l-mV recorder. A stainless steel column (10 cm x 4.6 mm i.d.) was packed with Lichrosorb RPS, 5 μm, obtained from Chrompack. An injection loop of 100 μl was used. The oven temp was 40°C. Detection of the solute was performed at 260 nm.

SOURCE AND PURITY OF MATERIALS:
The source and purity of the materials were not specified.

ESTIMATED ERROR:
The detection limit of the solute by HPLC was 0.5 mg/l (authors). The error in temperature and pH were not specified.

REFERENCES:

ORIGINAL MEASUREMENTS:

PREPARED BY:
R. Piekos