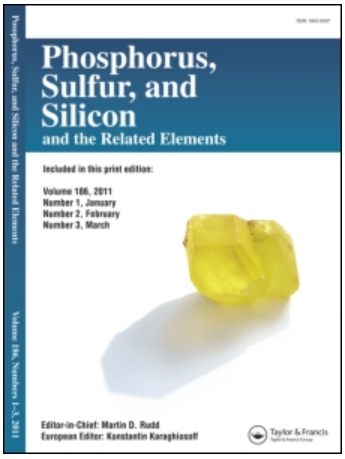


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# SYNTHESIS OF ACYCLO *C*-NUCLEOSIDES: 2-(ALDITOL-1-YL)-5-ALKYLTHIO-1,3,4-THIADIAZOLINES

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# SYNTHESIS OF ACYCLO *C*-NUCLEOSIDES: 2-(ALDITOL-1-YL)-5-ALKYLTHIO-1,3,4-THIADIAZOLINES

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Condensative cyclization of *aldehydo*-sugar *S*-methylhydrazonecarbodithioates and *S*-benzylhydrazonecarbodithioates with acetic anhydride in the presence of pyridine gave the corresponding 3-acetyl-2-(poly-*O*-acetyl-alditol-1-yl)-5-alkylthio-1,3,4-thiadiazolines. De-*O*-acetylation of the latter compounds gave the title acyclo *C*-nucleosides. The compounds prepared were found antimicrobially inactive against *Escherichia coli, Bacillus subtilis, Staphylococcus aureus,* and *Candida albicans*.

*Keywords: aldehydo*-sugar *S*-alkylhydrazonecarbodithioates; 1,3,4-thiadiazoline acyclo *C*-nucleosides; synthesis; structure corroboration; and antimicrobial activity

*C*-Nucleosides are very important class of naturally occurring compounds due to the wide range of biological activities they exhibit.[1–3] Extensive research has, accordingly, been targeted toward the preparation of *C*-nucleosides and their analogs.[1–3] Synthesis of acyclo *C*-nucleosides has also elicited comparable attention[1,2,4,5] as a result of bearing an isosteric relationship with acyclo *N*-nucleosides such as the potent antiviral agent "acyclovir" [9-(2-hydroxyethoxymethyl)guanine].[6] Contributing also to the importance of acyclo *C*-nucleosides was the isolation of the two naturally occurring members pyridindolol {1-[1*R*)-1,2-dihydroxyethyl]-3-hydroxymethyl-9*H*-pyrido[3,4-*b*]indole} from the culture filtrates of *Streptomyces alboverticillatus*[7] and the antibiotic CV-1 [5-hydroxy-4-(D-*arabino*-tetritol-1yl)imidazolidine-2,5-diol] from the culture filtrates of *Streptomyces* Sp. II.[8] Multitudinous pharmaceutical activities[9] and agrochemical[10] applications have been associated with

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the 1,3,4-thiadiazole ring systems, and yet relatively few reports were published dealing with the synthesis of 1,3,4-thiadiazole *C*-nucleosides[11] and their acyclo analogs.[12–14] The synthesis of only one example of condensed 1,3,4-thiadiazole acyclo *C*-nucleosides, namely 6-(alditol-1-yl)-3-aryl-1,2,4-triazolo[3,4-*b*]1,3,4-thiadiazoles, has recently been reported from this laboratory.[15] Continuing our studies on the synthesis and biological activities of acyclo *C*-nucleosides,[13–16] we report in the present article the synthesis and antimicrobial activity of the title compounds.

Treatment of *aldehydo*-sugar acylhydrazones with acid anhydride or acid chlorides caused the cyclization to poly-*O*-acylated 3-acyl-2-(alditol-1-yl)-1,3,4-oxadiazolines[17] rather than the expected poly-*O*-acyl *aldehydo*-sugar *N,N*-diacylhydrazones.[18] Similar condensation-cyclization of *aldehydo*-sugar *S*-methyl hydrazonecarbodithioates[14] **(1a-5a)** and *S*-benzylhydrazone- carbodithioates[14] **(1b-5b)** with acetic anhydride in the presence of pyridine at ambient temperature gave the corresponding 3-acetyl-2-(poly-*O*-acetyl-alditol-1-yl-5-methylthio- **(7a-11a)** and 5-benzylthio-1,3,4-thiadiazolines **(7b-11b)**, respectively. Formation of **7–11** takes place, most probably, by capturing the tautomeric 1,3,4-thiadiazoline structure **(6)** as a result of acetylation of the thiadiazoline ring N3-H and concomittant *O*-acetylation of the alditolyl chain hydroxyls. Compounds **7–11** showed IR absorptions at 1755–1743 (OAc), 1670–1664 (NAc), 1634–1533 (C=N), 1228–1208, 1065–1040, 999–941 $cm^{-1}$ (NCSSR) and lacked the NH and OH absorptions of the parent hydrazones **(1–5)**. UV spectra of **7–11** revealed two absorption maxima at 280–260 and 228–225 nm in contrast to the parent hydrazones which exhibited three maxima at 226–214, 252–248, and 300–294 nm.[14] Mass spectra of **8b**, **9a**, and **11b** showed M+2 peaks at *m/z* 542, 538, and 614, respectively. $^1H$ NMR spectra of **7–11** had signals at δ 6.64–6.25 (thiadiazoline ring C3-H), 5.80–3.90 (alditolyl chain protons), 2.60–2.18 (thiadiazoline N3-Ac), and 2.20–2.00 (alditolyl chain OAc groups). Two structurally noticeable changes took place as a result of cyclization of hydrazones **1–5** to thiadiazolines **7–11** in that (a) the azomethine hydrogen (-CH=N-) in the parent hydrazones absorbed at δ 7.70–7.50[14] and became the thiadiazoline ring C2-H which absorbed at δ 6.64–6.25 and (b) the achiral $sp^2$ azomethine carbon in **1–5** became the thiadiazoline ring C2 chiral carbon in **7–11** and, accordingly, led to the formation of the two diastereoisomeric structures **18** and **19**. Attempt separations of **18** and **19** by fractional crystallization or by column chromatography were unsuccessful.

De-*O*-acetylation of **7–13** with ammonium hydroxide in methanol gave the corresponding 3-acetyl-2-(alditol-1-yl)-5-methylthio- **(13a-17a)** and 5-benzylthio-1,3,4-thiadiazolines **(13b-17b)**. Compounds **13–17** showed IR absorptions at 3475–3315 (OH) and 1685–1659 $cm^{-1}$ (NAc) and three UV absorption maxima at 278–270, 253–247, and 227–216 nm. $^1H$ NMR spectra of **13–17** revealed one-proton doublet signals at δ 6.08–5.15 (thiadiazoline ring C2-H) and one three-proton singlet signal at δ 2.48–1.95 (thiadiazoline N3-Ac).

The 1,3,4-thiadiazoline acyclo *C*-nucleosides **7–17** were tested for their antibacterial activity against the Gram negative bacterium *E. Coli* and the two Gram postive bacteria *B. Subtilis* and *S. aureus* as well as for antifungal activity against *C. albicans* using the agar diffusion method.[19] Unfortunately, none of these compounds was found active.



## EXPERIMENTAL

Melting points were determined using MEL-TEMP-II apparatus and were uncorrected. IR spectra were recorded for KBr discs on a Unicam SP-1025 spectrophotometer. UV spectra were measured with a Unicam SP-1750 spectrophotometer. $^1H$ NMR spectra were carried out at ambient temperature (~25 °C) and at 90 MHz with a Varian EM-390 spectrometer using TMS as an internal standard. Mass spectra were performed at 70 ev on an analytical system consisting of a Du Pont 21–419 mass spectrometer interfaced with a Du Pont 492–094 data-acquision station. Follow up of reactions and checking homogeneity of the prepared compounds were made by TLC on silica gel G (Merck, precoated plates, layer thickness 0.25), used without pretreatment. All ratios of the solvent systems used were v/v; the distance of solvent travel was 5 cm, and the spots were detected by exposure to iodine vapour. Elemental microanalyses were performed in the Microanalyses Unit, Cairo University, Cairo, Egypt.

### 3-Acetyl-2-(poly-*O*-acetyl-alditol-1-yl)-5-methylthio- (7a-11a) and 5-benzylthio-1,3,4-thiadiazolines (7b-11b)

A solution of *aldehydo*-sugar *S*-methylhydrazone-carbodithioate **(1a-5a)** or *aldehydo*-sugar *S*-benzylhydrazonecarbodithioate **1b-5b** (0.01 mole) in anhydrous pyridine (5 ml) was treated with acetic anhydride (30 ml) and stirred at ambient temperature for 24 hours. The mixture was poured into

ice-water and extracted with chloroform. The chloroform extract was washed with 30% aqueous sodium hydrogencarbonate solution and water, dried ($Na_2SO_4$, anhydrous), and evaporated. The residue was crystallized from methanol.

The following compounds were prepared:

### 3-Acetyl-2-(*D-arabino*-1,2,3,4-tetraacetoxybut-1-yl)-5-methylthio-1,3,4-thiadiazoline (7a)

Yield 55%; colorless syrup; TLC in 9:1 chloroform-methanol, $R_f$: 0.62; $\lambda_{max}^{MeOH}$: 260.4 and 225.3 nm; IR: 1749 (OAc), 1667 (CON), 1634 (C=N), 1216, 1043 and 968 $cm^{-1}$ (NCSSMe); $^1H$ NMR ($CDCl_3$): δ 6.64 (d, 1 H, thiadiazoline H), 5.8 (t, 1 H, alditolyl H), 5.62 (dd, 1 H, alditolyl H), 5.50–5.20 (m, 1 H, alditolyl H), 4.59–4.21 (m, 2 H, alditolyl 2 H), 2.64 (s, 3 H, *S*-$CH_3$), 2.60 (s, 3 H, *N*Ac), 2.24 (s, 3 H, *O*Ac), 2.20 (s, 3 H, *O*Ac) and 2.06 ppm (s, 6 H, 2 *O*Ac).

Found : C, 43.8; H, 5.0; N, 6.0%
$C_{17}H_{24}N_2S_2O_9$ required : C, 44.0; H, 5.2; N, 6.0%

### 3-Acetyl-2-(*L-arabino*-1,2,3,4-tetraacetoxybut-1-yl)-5-methylthio-1,3,4-thiadiazoline (8a)

Yield 50%; colorless syrup, TLC in 19:1 chloroform-methanol, $R_f$: 0.62; IR: 1745 (OAc), 1665 (CON), 1531 (C=N), 1220, 1043 and 968 $cm^{-1}$ (NCSSMe); $^1H$ NMR ($CDCl_3$): δ 6.22 (d, 1 H, thiadiazoline H), 5.56–5.53 (dd, 1 H, alditolyl H), 5.45–5.31 (m, 2 H, alditolyl 2 H), 5.09–5.03 (m, 2 H alditolyl 2 H), 2.54 (s, 3 H, *S*-$CH_3$), 2.49 (s, 3 H, *N*Ac), 2.14 (s, 3 H, *O*Ac), 2.12 (s, 3 H, *O*Ac), 2.09 (s, 3 H, *O*Ac), and 2.08 ppm (s, 3 H, *O*Ac); *m/z* 542 (M+2).

Found : C, 44.2; H, 5.5; N, 5.7%
$C_{17}H_{24}N_2S_2O_9$ required : C, 44.0; H, 5.2; N, 6.0%

### 3-Acetyl-2-(*D-galacto*-1,2,3,4,5-pentaacetoxypent-1-yl)-5-methylthio-1,3,4-thiadiazoline (9a)

Yield 62%; m.p., 150–155 °C; TLC in 9:1 chloroform-methanol, $R_f$: 0.67; $\lambda_{max}^{MeOH}$ (log ε): 279.6 (3.99) and 246.6 (3.92) nm; IR: 1775 (OAc), 1664 (CON), 1631 (C=N), 1228, 1045 and 941 $cm^{-1}$ (NCSSMe); $^1H$ NMR

($CDCl_3$): δ 6.3 (s, 1 H, thiadiazoline H), 5.65 (s, 1 H, alditolyl H), 5.30 (m, 3 H, alditolyl H); 4.25 (dd, 1 H, alditol, H), 3.85 (dd, 1 H, alditolyl H); 2.50 (s, 3 H, *S*-$CH_3$); 2.20 (s, 3 H, *N*Ac); 2.10 (s, 6 H, 2 *O*Ac), 2.05 (s, 6 H, 2 *O*Ac) and 2.00 ppm (s, 3 H, *O*Ac); *m/z* 538 (M+2).

Found : C, 45.2; H, 5.0; N, 5.6%

$C_{20}H_{28}N_2S_2O_{11}$ required : C, 44.8; H, 5.2; N, 5.2%

### 3-Acetyl-2-(*D-gluco*-1,2,3,4,5-pentaacetoxypent-1-yl)-5-methylthio-1,3,4-thiadiazoline (10a)

Yield 65%; m.p., 120–122 °C; TLC in 9:1 chloroform-methanol, $R_f$: 0.65; $\lambda_{max}^{MeOH}$ (log ε): 269.0 (4.13) and 228.0 (4.07) nm; IR: 1746 (OAc), 1666 (CON), 1551 (C=N), 1221, 1040 and 941 $cm^{-1}$(NCSSMe).

Found : C, 44.6; H, 5.0; N, 5.1%

$C_{20}H_{28}N_2S_2O_{11}$ required : C, 44.8; H, 5.2; N, 5.2%

### 3-Acetyl-2-(*D-manno*-1,2,3,4,5-pentaacetoxypent-1-yl)-5-methylthio-1,3,4-thiadiazoline (11a)

Yield 65%; m.p., 118–120 °C; TLC in 9:1 chloroform-methanol, $R_f$: 0.64; $\lambda_{max}^{MeOH}$ (log ε): 263.7 (4.08) and 228.3 (4.02) nm; IR: 1751 (OAc), 1669 (CON), 1533 (C=N), 1223, 1045 and 943 $cm^{-1}$ (NCSSMe); $^1H$ NMR ($CDCl_3$): δ 6.25 (d, 1 H, thiadiazoline H), 5.40 (t, 1 H, alditolyl H), 5.18 (dd, 2 H, alditolyl 2 H), 4.95–4.70 (m, alditolyl H), 4.20 (dd, 1 H, alditolyl H), 3.95 (dd, 1 H, alditolyl H), 2.55 (s, 3 H, *S*-$CH_3$), 2.18 (s, 3 H, *N*Ac) and 2.05 ppm (s, 15 H, 5 *O*Ac).

Found : C, 44.6; H, 5.2; N, 5.1%

$C_{20}H_{28}N_2S_2O_{11}$ required : C, 44.8; H, 5.2; N, 5.2%

### 3-Acetyl-2-(*D-arabino*-1,2,3,4-tetraacetoxybut-1-yl)-5-benzylthio-1,3,4-thiadiazoline (7b)

Yield 46%; m.p., 55–60 °C; TLC in 9:1 chloroform-methanol, Rf: 62; $\lambda_{max}^{MeOH}$ (log ε): 261.0 (3.71) and 228.0 (3.81); IR: 1745 (OAc), 1668 (CON), 1533 (C=N), 1208, 1043 and 995 $cm^{-1}$ (NCSSBn); $^1H$ NMR ($CDCl_3$): δ 7.30–7.26 (m, 5 H, aromatic H), 6.31 (d, 1 H, thiadiazoline H), 5.59 (dd, 1 H, alditolyl H), 5.41–5.31 (m, 2 H, alditolyl 2 H), 5.14–5.05

(m, 2 H, alditolyl 2 H), 4.20 (s, 2 H, benzyl $CH_2$), 2.16 (s, 3 H, *N*Ac), 2.10 (s, 3 H, *O*Ac), 2.02 (s, 3 H, *O*Ac), 2.00 (s, 3 H, *O*Ac), and 1.83 ppm (s, 3 H, *O*Ac).

| | |
|---|---|
| Found : | C, 51.2; H, 5.3; N, 5.3% |
| $C_{23}H_{28}N_2S_2O_9$ required : | C, 51.1; H, 5.2; N, 5.2% |

### 3-Acetyl-2-(*L-arabino*-1,2,3,4-tetraacetoxybut-1-yl)-5-benzylthio-1,3,4-thiadiazoline (8b)

Yield 45%; m.p., 82–85 °C; TLC in 9:1 chloroform-methanol, $R_f$: 0.60; $\lambda_{max}^{MeOH}$ (log ε): 280.8 (3.97), 248.7 (4.0) and 227.1 (3.91); IR: 1748 (*O*Ac), 1669 (CON), 1568 (C=N), 1215, 1043 and 995 $cm^{-1}$ (NCSSBn); $^1H$ NMR ($CDCl_3$): δ 7.29–7.20 (m, 5 H, aromatic H), 6.27 (d, 1 H, thiadiazoline H), 5.56 (dd, 1 H, alditolyl H), 5.42–5.28 (m, 2 H, alditolyl 2 H), 5.11–5.00 (m, 2 H, alditolyl 2 H), 4.16 (s, 2 H, benzyl $CH_2$), 2.09 (s, 3 H, *N*Ac), 2.07 (s, 3 H, *O*Ac), 2.05 (s, 3 H, *O*Ac), 2.03 (s, 3 H, *O*Ac), and 1.95 ppm (s, 3 H, *O*Ac).

| | |
|---|---|
| Found : | C, 50.6; H, 4.8; N, 5.4% |
| $C_{23}H_{28}N_2S_2O_9$ required : | C, 51.1; H, 5.2; N, 5.2% |

### 3-Acetyl-2-(*D-galacto*-1,2,3,4,5-pentaacetoxypent-1-yl)-5-benzylthio-1,3,4-thiadiazoline (9b)

Yield 65%; m.p., 75–80 °C ; TLC in 9:1 chloroform-methanol, $R_f$: 0.61; IR: 1748 (*O*Ac), 1668 (CON), 1217, 1045 and 999 $cm^{-1}$ (NCSSBn).

| | |
|---|---|
| Found : | C, 51.3; H, 5.1; N, 4.7% |
| $C_{26}H_{32}N_2S_2O_{11}$ required : | C, 51.0; H, 5.2; N, 4.6% |

### 3-Acetyl-2-(*D-gluco*-1,2,3,4,5-pentaacetoxypent-1-yl)-5-benzylthio-1,3,4-thiadiazoline (10b)

Yield 65%; m.p., 60–65 °C; TLC in 9:1 chloroform-methanol, $R_f$: 0.62; IR: 1744 (*O*Ac), 1670 (CON), 1567 (C=N), 1222, 1065 and 970 $cm^{-1}$ (NCSSBn).

| | |
|---|---|
| Found : | C, 50.7; H, 5.1; N, 4.7% |
| $C_{26}H_{32}N_2S_2O_{11}$ required : | C, 51.0; H, 5.2; N, 4.6% |

### 3-Acetyl-2-(*D-manno*-1,2,3,4,5-pentaacetoxybut-1-yl)-5-benzylthio-1,3,4-thiadiazoline (11b)

Yield 55%; m.p., 157–160 °C; TLC in 9:1 chloroform-methanol, $R_f$: 0.63; $\lambda_{max}^{MeOH}$ (log ε): 263.4 (3.98) and 228.6 (4.10) nm; IR: 1749, 1706 (OAc), 1668 (CON), 1600 (C=N), 1214, 1056 and 995 $cm^{-1}$(NCSSBn); $^1H$ NMR ($CDCl_3$): δ 7.35–7.10 (m, 5 H, aromatic H), 6.30 (d, 1 H, thiadiazoline H), 5.40 (t, 1 H, alditolyl H), 5.20 (dd, 2 H, alditolyl 2 H), 5.10–4.82 (m, 1 H, alditolyl H), 4.30 (s, 2 H, benzyl $CH_2$), 4.20–4.0 (m, 2 H, alditolyl H), 2.25 (s, 3 H, *N*Ac), 2.10 (s, 6 H, 2 *O*Ac), 2.00 (s, 9 H, 3 *O*Ac); *m/z* 612 (M+2).

Found : C, 50.7; H, 5.1; N, 4.8%

$C_{26}H_{32}N_2S_2O_{11}$ required : C, 51.0; H, 5.2; N, 4.6%

### 3-Acetyl-2-(alditol-1-yl)-5-methylthio- (13a-17a) and 5-benzylthio-1,3,4-thiadiazolines (13b-17b)

A solution of **7a-11a** or **7b-11b** (0.001 mole) in methanol (10 ml) was treated with a saturated solution of methanolic ammonia (10 ml) for 24 hours at ambient temperature. Evaporation of the solvent under reduced pressure gave a residue which crystallized from ethanol.

The following compounds were prepared:

### 3-Acetyl-2-(*D-arabino*-1,2,3,4-tetrahydroxybut-1-yl)-5-methylthio-1,3,4-thiadiazoline (13a)

Yield 45%; m.p., 108–110 °C; TLC in 1:1 chloroform-methanol, $R_f$: 0.59; $\lambda_{max}^{MeOH}$ (log ε): 253.8 (3.70), 247.5 (3.7) and 225.7 (3.68) nm; IR: 3351(OH), 1659 (CON), 1548 (C=N); 1083 and 945 $cm^{-1}$(NCSSMe).

Found : C, 36.3; H, 5.6; N, 9.7%

$C_9H_{16}N_2S_2O_5$ required : C, 36.5; H, 5.4; N, 9.5%

### 3-Acetyl-2-(*L-arabino*-1,2,3,4-tetrahydroxybut-1-yl)-5-methylthio-1,3,4-thiadiazoline (14a)

Yield 40%; m.p., 102–105 °C; TLC in 1:1 chloroform-methanol, $R_f$: 0.58; $\lambda_{max}^{MeOH}$ (log ε): 270.0 (3.75), 250.8 (3.74) and 224.7 (3.65) nm; IR: 3357 (OH), 1659 (CON), 1530 (C=N), 1062 and 942 $cm^{-1}$(NCSSMe).

Found : C, 36.9; H, 5.3; N, 9.7%

$C_9H_{16}N_2S_2O_5$ required : C, 36.5; H, 5.4; N, 9.5%

**3-Acetyl-2-(*D-galacto*-1,2,3,4,5-pentahydroxypent-1-yl)-5-methylthio-1,3,4-thiadiazoline (15a)**

Yield 45%; m.p., 198–200 °C; TLC in 1:1 chloroform-methanol, $R_f$: 0.57; $\lambda_{max}^{MeOH}$ (log ε): 274.5 (4.27), 249.9 (4.23) and 216 (sh) nm; IR: 3457 (OH), 1685 (CON), 1649 (C=N), 1078 and 999 $cm^{-1}$ (NCSSMe); $^1H$ NMR [$(CD_3)_2SO$]: δ 5.15 (d, 1 H, CH=N); 4.95–4.75 (m, 2 H, alditolyl H), 2.60 (s, 3 H, *S*-$CH_3$) and 2.48 ppm (s, 3 H, *N*Ac). The rest of the protons were associated with the solvent absorption forming a broad signal at δ 4.50–3.0 ppm.

Found : C, 36.4; H, 5.7; N, 8.6%

$C_{10}H_{18}N_2S_2O_6$ required : C, 36.8; H, 5.5; N, 8.6%

**3-Acetyl-2-(*D-manno*-1,2,3,4,5-pentahydroxypent-1-yl)-5-methylthio-1,3,4-thiadiazole (17a)**

Yield 45%; m.p., 185–188 °C; TLC in 1:1 chloroform-methanol, $R_f$: 0.58; $\lambda_{max}^{MeOH}$ (log ε): 264.3 (4.10) and 227.7 (4.01) nm; IR: 3139 (OH), 1691 (CON), 1646 (C=N), 1119 and 994 $cm^{-1}$ (NCSSMe); $^1H$ NMR [$(CD_3)_2SO$]: δ 5.7 (d, 1 H, CH=N), 5.23–4.95 (m, 3 H, exchangeable 3 OH), 0.195 (s, 3 H, *S*-$CH_3$) and 1.90 ppm (s, 3 H, *N*Ac). The other protons and the hydroxyl protons together with the solvent absorption were gathered in a broad signal at δ 4.0–3.0 ppm.

Found : C, 37.0; H, 5.3; N, 8.5%

$C_{10}H_{18}N_2S_2O_6$ required : C, 36.8; H, 5.5; N, 8.6%

**3-Acetyl-2-(*L-arabino*-1,2,3,4,5-tetrahydroxybut-1-yl)-5-benzylthio-1,3,4-thiadizaoline (14b)**

Yield 40%; m.p., 138–140 °C; TLC in 1:1 chloroform-methanol, $R_f$: 0.57; $\lambda_{max}^{MeOH}$ (log ε): 271.3 (sh), 251.1 (3.63) and 224.1 (3.68) nm; IR: 3275 (OH), 1673 (CON), 1531 (C=N) and 1089 and 991 $cm^{-1}$(NCSSBn).

Found : C, 48.1; H, 5.1; N, 7.0%

$C_{15}H_{20}N_2S_2O_5$ required : C, 48.4; H, 5.4; N, 7.5%

**3-Acetyl-2-(*D-gluco*-1,2,3,4,5-tetrahydroxypent-1-yl)-5-benzylthio-1,3,4-thiadiazoline (16b)**

Yield 60%; m.p., 200–202 °C; TLC in 1:1 chloroform-methanol, $R_f$: 0.56; $\lambda_{max}^{MeOH}$ (log ε): 276.3 (3.71), 251.4 (3.76) and 227.1 (3.61) nm; IR: 3332 (OH), 1662 (CON), 1598 (C=N), 1079 and 944 $cm^{-1}$(NCSSBn); $^1H$ NMR [$(CD_3)_2SO$]: δ 5.30 (d, 1 H, thiadiazoline H); 5.25–4.95 (m, 3 H, exchangeable 3 OH), 4.90 (d, 1 H, alditolyl H), 4.60 (s, 2 H, benzyl $CH_2$); 4.05 (d, 2 H, alditolyl H) and 2.05 ppm (s, 3 H, *N*Ac). The rest of the protons were associated with the solvent absorption forming a broad signal at δ 4.0–3.0 ppm.

Found : C, 47.5; H, 5.7; N, 6.7%

$C_{16}H_{22}N_2S_2O_6$ required : C, 47.8; H, 5.5; N, 7.0%

**3-Acetyl-2-(*D-manno*-1,2,3,4,5-pentahydroxypent-1-yl)-5-benzylthio-1,3,4-thiadiazoline (17b):**

Yield 60%; m.p., 118–120 °C; TLC in 1:1 chloroform-methanol, $R_f$: 0.58; $\lambda_{max}^{MeOH}$ (log ε): 278.1 (3.68), 247.5 (3.58) and 223.5 (3.70) nm; IR: 3360 (OH), 1689 (CON), 1641 (C=N), 1079 and 994 $cm^{-1}$(NCSSBn); $^1H$ NMR [$(CD_3)_2SO$]: δ 7.45–7.10 (m, 5 H, aromatic H), 5.38 (d, 1 H, thiadiazoline), 5.00 (d, 1 H, alditolyl H), 4.60–4.35 (m, 3 H, benzyl $CH_2$ + alditolyl H), 2.0 ppm (s, 3 H, *N*Ac). The rest of the protons were associated with the solvent absorption forming a broad signal at δ 4.3–2.9 ppm.

Found : C, 48.1; H, 5.3; N, 7.4%

$C_{16}H_{22}N_2S_2O_6$ required : C, 47.8; H, 5.5; N, 7.0%

Antimicrobial activity: Sterile nutrient agar (100 ml) was separately inoculated with a 24-h broth culture (1 ml) of *E. Coli, B. Subtilis, S. aureus,* and *C. albicans*. Solutions (30 µl) of the tested compounds were placed in wells (6 mm diameter) cut in the agar media and the plates were incubated at 37 °C (bacteria) or 25 °C (yeast). The diameter of the resulting inhibition zones obtained were measured after 28 h for bacteria and 96 h for the yeast. Inhibition zones of less than 10 mm in diameter were considered to indicate unsatisfactory activity.

All of the prepared compounds developed inhibition zones less than 10 mm in diameter and are, accordingly, devoid of antimicrobial activity.

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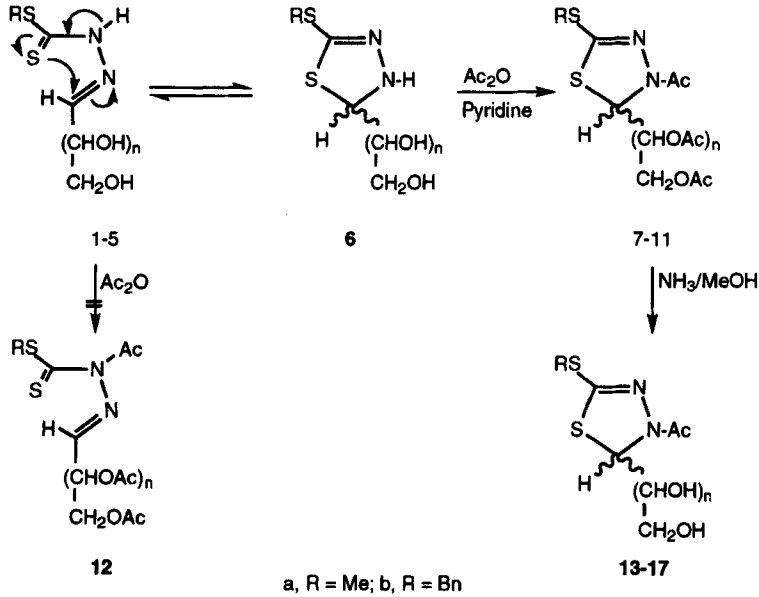
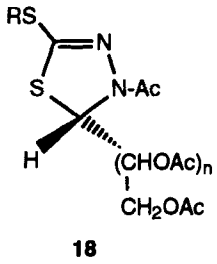


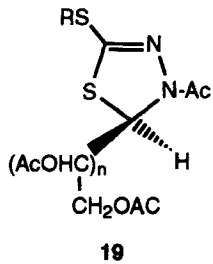

a, R = Me; b, R = Bn

**1, 7, 13,** n = 3, D-*arabino*-tetritol-1-yl
**2, 8, 14,** n = 3, L-*arabino*-tetritol-1-yl
**3, 9, 15,** n = 4, D-*galacto*-pentitol-1-yl
**4, 10, 16,** n = 4, D-*gluco*-pentitol-1-yl
**5, 11, 17,** n = 4, D-*manno*-pentitol-1-yl

SCHEME 1




**18**




**19**