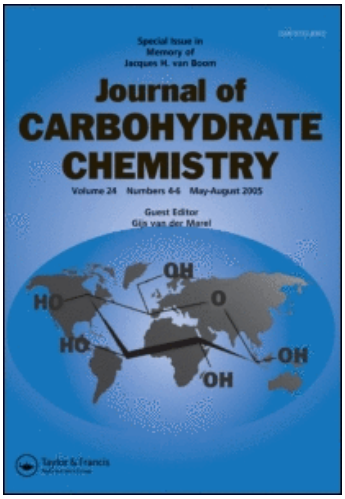

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

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To cite this Article Shaban, Mohammed A. E. , Nasr, Adel Z. and Taha, Mamdouh A. M.(1995) 'Synthesis of 1,3,4-Thiadiazole and 1,2,4-Triazole acyclo *C*-Nucleosides', Journal of Carbohydrate Chemistry, 14: 7, 985 — 994
To link to this Article: DOI: 10.1080/07328309508005390
URL: http://dx.doi.org/10.1080/07328309508005390

J. CARBOHYDRATE CHEMISTRY, 14(7), 985-994 (1995)

SYNTHESIS OF 1,3,4-THIADIAZOLE AND 1,2,4-TRIAZOLE ACYCLO *C*-NUCLEOSIDES

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Received November 16, 1994 - Final Form May 8, 1995

ABSTRACT

Reaction of 4-arylthiosemicarbazides (**1**) with 2,3,4,5-tetra-*O*-acetylgalactaroyl dichloride(**2**) gave the corresponding 2,3,4,5-tetra-*O*-acetylgalactaroyl-bis(4-aryl-thiosemicarbazides (**3**). The latter compounds underwent dehydrative cyclization by heating with phosphoryl chloride to give 1,2,3,4-tetra-*O*-acetyl-1,4-bis(5-arylamino-1,3,4-thiadiazol-2-yl)*galacto*-tetritols (**4**) which afforded, upon de-*O*-acetylation with methanolic ammonia, the corresponding 1,4-bis(5-arylamino-1,3,4-thiadiazol-2-yl)-*galacto*-tetritols (**5**). Compounds **3** were also cyclodehydrated, in a different way, with concomitant de-*O*-acetylation upon treatment with ethanolic sodium ethoxide to give 1,4-bis(4-aryl-5-thioxo-1,2,4-triazol-3-yl)*galacto*-tetritols (**6**). Acetylation of **6** with acetic anhydride in the presence of pyridine afforded 1,2,3,4-tetra-*O*-acetyl-1,4-bis(1-acetyl-4-aryl-5-thioxo-1,2,4-triazol-3-yl)*galacto*-tetritols (**7**) . Compounds **3a, 3b** and **6a-c** showed no antibacterial activity against *Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa,* or *Staphylococcus aureus* and showed weak to moderate antifungal activity against *Aspergillus terreus* and *Candida albicans*.

INTRODUCTION

Synthesis of 1,3,4-thiadiazoles and 1,2,4-triazoles is of importance since many of their members possess various biological activities. These activities range from amoebicidal,[1] antiviral,[2] insecticidal,[3] antitumor,[4] and antiinflammatory[5] for 1,3,4-thiadiazoles to antifungal,[6] herbicidal[7,8] and neurotensin antagonists[9] for 1,2,4-triazoles. In addition, the synthesis[10] of *C*-nucleosides and their acyclo analogues has

also attracted the attention of many investigators due to their documented biological activities.[11]

Speculating that incorporation of 1,3,4-thiadiazole or 1,2,4-triazole moieties into acyclo *C*-nucleoside structures may enhance their biological activities as a result of facilitating penetration into biological systems, and continuing our work on the synthesis[12-18] of acyclo *C*-nucleoside analogues, we describe in this article the synthesis of the title compounds.

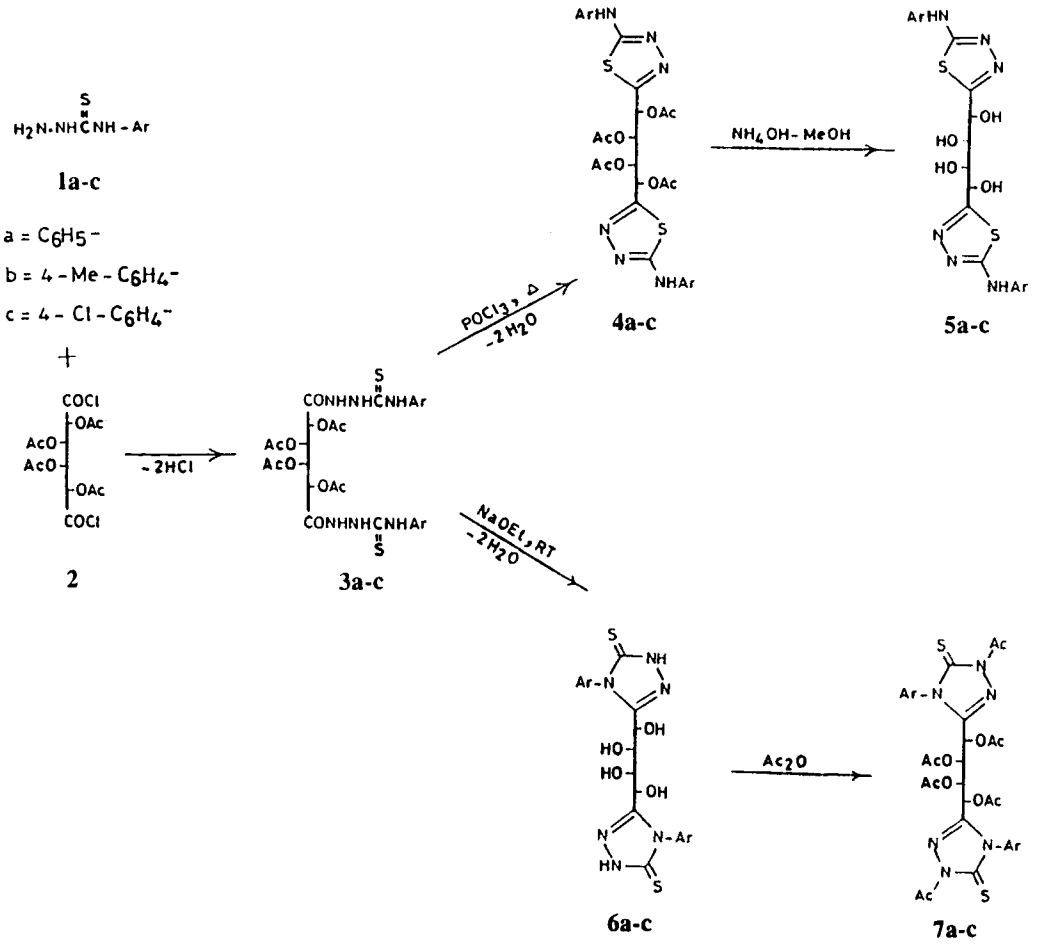
RESULTS AND DISCUSSION

Condensation of two equivalents of 4-arylthiosemicarbazides, namely: 4-phenyl-thiosemicarbazide (**1a**), 4-(*p*-methylphenyl)thiosemicarbazide (**1b**) and 4-(*p*-chloro-phenyl)thiosemicarbazide (**1c**) with one equivalent of 2,3,4,5-tetra-*O*-acetyl galactaroyl dichloride[19] (**2**) gave products which showed IR-absorptions characteristic of NH, OAc and CON. The ^{1}H NMR spectra of the condensation products showed, in addition to the expected aromatic proton signals, six NH protons (exchangeable), four C2-H to C5-H protons and four *O*-acetyl group protons. The condensation products were, therefore, proposed as 2,3,4,5-tetra-*O*-acetylgalactaroyl-bis(4-aryl-thiosemicarbazides) (**3a-c**) (Scheme 1).

1-Acyl-4-arylthiosemicarbazides are known to undergo dehydrocyclization to give 2-alkyl-5-arylamino-1,3,4-thiadiazoles.[20-22] Applying such dehydrocyclization to **3a-c** with boiling phosphoryl chloride gave the corresponding 1,2,3,4-tetra-*O*-acetyl-1,4-bis(5-arylamino-1,3,4-thiadiazol-2-yl)*galacto*-tetritols **4a-c**. The IR spectra of **4a-c** showed NH, OAc and C=N absorptions and lacked the amide absorption bands present in the spectra of the parent bisthiosemicarbazides **3a-c**. The ^{1}H NMR spectra of **5a-c** revealed, in addition to the aromatic protons, two NH protons (exchangeable), four C2-H to C5-H protons and four *O*-acetyl group protons. The mass spectrum of **5a** showed the molecular ion peak at *m/z* 640 in addition to characteristic fragments at *m/z* 597 (M– Ac) (**8**), *m/z* 580 (M– AcOH) (**9**), *m/z* 537 (**8**–AcOH) (**10**), *m/z* 249 (B-CH=$\overset{+}{O}$Ac) (**11**) and *m/z* 206, this last peak corresponding to the heterocyclic base carrying a protonated formyl group (B-CH=$\overset{+}{O}$-H) (**12**) (B=1,3,4-thiadiazolyl nucleus) (Scheme 2). This fragment is diagnostic of *C*-nucleoside structures.[23]

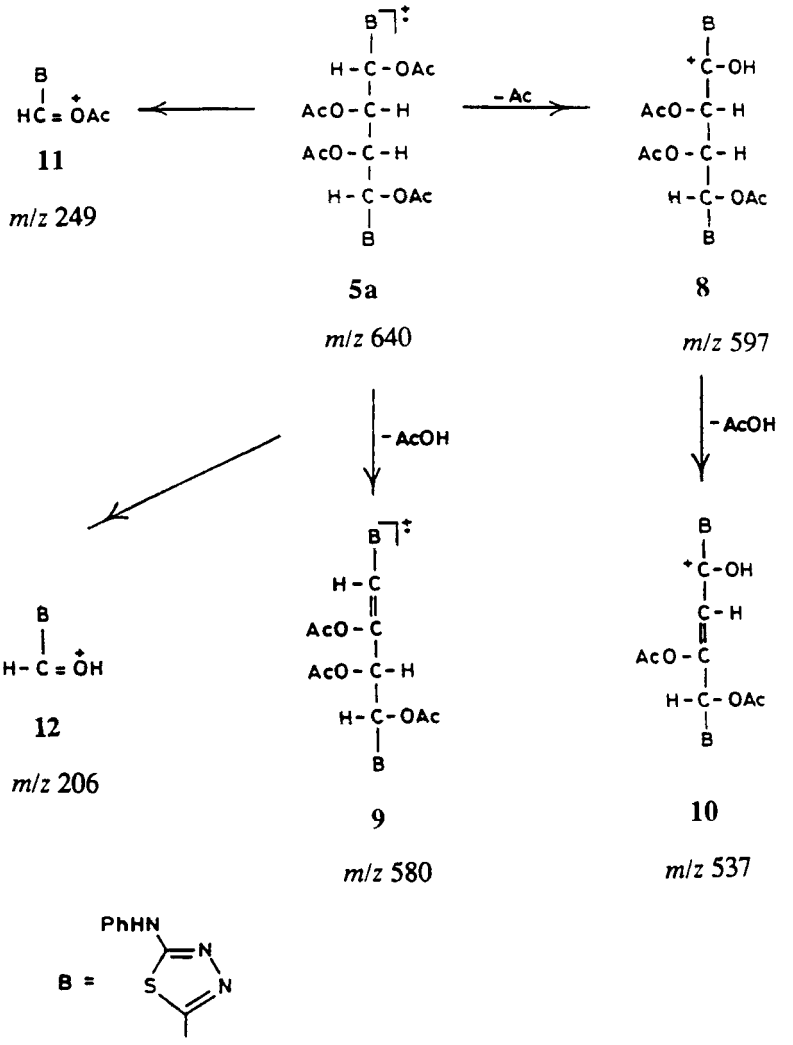
De-*O*-acetylation of **4a-c** with a saturated solution of methanolic ammonia at ambient temperature gave the corresponding unprotected acyclo *C*-nucleosides: 1,4-bis(5-arylamino-1,3,4-thiadiazol-2-yl)*galacto*-tetritols **5a-c**.

1-Acyl-4-arylthiosemicarbazides were reported to undergo base catalyzed dehydrocyclization to afford 3-alkyl-4-aryl-5-thioxo-1,2,4-triazoles.[22,24,25] Cyclization



Scheme 1

of **3a-c** by treatment with sodium ethoxide in ethanol at room temperature gave products that analyzed correctly for two water molecules less than the unacetylated bis-thiosemicarbazides. The IR spectra of the products showed absorption bands at 3368-3343 (OH), 3289-3281 (NH) and 1623-1600 (C=N). These data are in agreement with 1,4-bis(4-aryl-5-thioxo-1,2,4-triazol-3-yl)*galacto*-tetritols **6a-c**. ^{1}H NMR spectra of compounds **6a-c** in $(CD_3)_2SO$ revealed an exchangeable imino proton at 9.10-8.97 and absence of SH proton signals, thus indicating their existence as the thione tautomers.



Scheme 2

Acetylation of **6a-c** with acetic anhydride in the presence of pyridine at room temperature resulted in acetylation of the tetritoldi-1,4-yl chain hydroxyls as well as NH of both of the 1,2,4-triazole rings, giving 1,2,3,4-tetra-*O*-acetyl-1,4-bis(1-acetyl-4-aryl-5-thioxo-1,2,4-triazol-3-yl)*galacto*-tetritols **7a-c**. The IR spectra of the latter compounds showed OAc, NAc and C=N absorptions and lacked the NH and OH absorptions present in the spectra of parent compounds **6a-c**. Beside the aromatic and the tetritolyl protons, the ^{1}H NMR spectra of **7a-c** showed signals of four *O*-acetyl and two N-acetyl groups.

Compounds **3a, 3b,** and **6a-c** were evaluated for antibacterial activity *in vitro* against *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* and for antifungal activity against *Aspergillus terreus* and *Candida albicans* using the agar diffusion method.[26] All of these compounds showed no inhibition of bacterial growth at a concentration of 2 mg/mL. At this concentration, however, **3a** showed no inhibitory activity, while **3b** and **6a-c** showed weak to moderate inhibitory activity against both fungal strains .

In conclusion, this investigation demonstrated the utility of 2,3,4,5-tetra-*O*-acetylgalactaroyl-bis(4-arylthiosemicarbazides) as synthons for the preparation of 1,3,4-thiadiazole and 1,2,4-triazole acyclo *C*-nucleosides by choosing the proper cyclo-dehydrating agent .

EXPERIMENTAL

General methods. Melting points were determined using a MEL-TEMP II melting point apparatus in open glass capillaries and are uncorrected. The infrared spectra (IR) were recorded using potassium bromide discs on a Pye-Unicam SP 1025 spectrophotometer. Proton magnetic resonance (^{1}H NMR) spectra on a Varian EM390 spectrometer. Mass spectra were performed on Du Pont 21-419 mass spectrometer interfaced with a Du Pont 492-094 data-acquisition system. The homogeneity of products and the progress of reactions were checked by TLC on plates precoated with silica gel G (Merck; layer thickness 0.25 mm), used without pretreatment. TLC plates were visualized by exposure to iodine for a few minutes. Elemental microanalyses were preformed at the Microanalytical Laboratory, Department of Chemistry, University of Manchester, Manchester, England or at the Microanalysis Unit, Cairo University, Cairo, Egypt.

General procedure for the preparation of 2,3,4,5-tetra-*O*-acetylgalactaroyl-bis(4-arylthiosemicarbazides) (3a-c). A solution of **2**[19] (10 mmol) in dry benzene (30 mL) was added gradually to a stirred solution of the appropriate 4-aryl-thiosemicarbazide (**1a-c**) (20 mmol) in dry pyridine (10 mL) at ambient temperature. After stirring the mixture for one hour, the solvent was evaporated under reduced pressure and the syrupy residue was crystallized from ethanol.

The following compounds were prepared:

2,3,4,5-Tetra-*O*-acetylgalactaroyl-bis(4-phenylthiosemicarbazide)(3a). Yield: 80%, mp 207 °C; TLC in 9:1 $CHCl_3$-MeOH, R_f: 0.58; IR (KBr) 3209 (NH), 1749 (OAc), 1690 (CONH) cm^{-1}; ^{1}H NMR [$(CD_3)_2SO$] δ10.33, 9.60, 9.03 (3s, broad, 2H each, exchangeable, NH), 7.57-6.90 (m, 10H, aromatic H), 5.60, 5.37 (2s, 2H each, tetritoldi-1,4-yl H), 2.17, 2.03 (2s, 6H each, OAc)

Anal. Calcd for $C_{28}H_{32}N_6O_{10}S_2 \cdot 2H_2O$ (712): C, 47.2 ; H, 5.1; N 11.8 . Found: C, 47.4 ; H, 4.9 ; N, 11.6 .

2,3,4,5-Tetra-*O*-acetylgalactaroyl-bis[4-(*p*-methylphenyl)thiosemicarbazide] (3b). Yield: 77 %, mp 210 °C; TLC in 9:1 $CHCl_3$-MeOH, R_f : 0.60; IR (KBr) 3212 (NH), 1746 (OAc), 1690 (CONH) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ10.30, 9.80, 8.70 (3s, broad, 2H each, exchangeable, NH),7.27, 7.00 (2d, 4H each, 8H, aromatic H), 5.50, 5.10 (2s, 2H each, tetritoldi-1,4-yl H), 2.23 (s, 6H, CH_3), 2.13, 1.97 (2s, 6H each, OAc).

Anal. Calcd for $C_{30}H_{36}N_6O_{10}S_2$ $2H_2O$ (740): C, 48.6 ; H ,5.4 ; N ,11.4. Found: C, 48.3; H, 5.2; N, 11.1 .

2,3,4,5-Tetra-*O*-acetylgalactaroyl-bis[(4-*p*-chlorophenyl)thiosemicarbazide] (3c). Yield: 75%, mp 220 °C; TLC in 9:1 $CHCl_3$-MeOH, R_f : 0.60; IR (KBr) 3176 (NH), 1757 (OAc), 1665 (CONH) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ10.53, 9.97, 9.43 (3s, broad, 2H each, exchangeable, NH), 7.63, 7.37 (2d, 4 H each, aromatic H), 5.67, 5.27 (2s, 2H each, tetritoldi-1,4-yl H), 2.23, 2.14 (2s, 6H each, OAc).

Anal. Calcd for $C_{28}H_{30}N_6O_{10}S_2Cl_2 \cdot 2H_2O$ (781): C, 43.0; H, 4.4 ; N, 10.8. Found: C, 43.2; H, 4.2; N, 10.5 .

General procedure for the preparation of 1,2,3,4-tetra-*O*-acetyl-1,4-bis(5-arylamino-1,3,4-thiadiazol-2-yl)*galacto*-tetritols (4a-c). A mixture of the respective **3a-c** (2 mmol) and phosphoryl chloride (25 mL) was heated under reflux for 1h. After attaining ambient temperature, the mixture was poured onto a cold saturated solution of $NaHCO_3$ and the product which separated was filtered, wasned with H_2O, dried and crystallized from ethanol.

The following compounds were prepared:

1,2,3,4-Tetra-*O*-acetyl-1,4-bis(5-phenylamino-1,3,4-thiadiazol-2-yl)*galacto*-tetritol (4a). Yield: 71%, mp 262 °C; TLC in 9:1 $CHCl_3$-MeOH, R_f : 0.61; IR (KBr) 3238 (NH), 1749 (OAc), 1593 (C=N) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ10.3 (s, 2H, exchangeable, NH), 7.60-6.77 (m, 10H, aromatic H), 6.10,5.53 (2s, 2H each, tetritoldi-1,4-yl H), 2.10, 2.03 (2s, 6H each, OAc).

Anal. Calcd for $C_{28}H_{28}N_6O_8S_2$ (640): C, 52.5; H, 4.4; N, 13.1. Found: C, 52.4; H, 4.3; N, 13.1 .

1,2,3,4-Tetra-*O*-acetyl-1,4-bis[5-(*p*-methylphenyl)amino-1,3,4-thiadiazol-2-yl]*galacto*-tetritol (4b). Yield : 71%, mp 282 °C; TLC in 9:1 $CHCl_3$-MeOH, R_f: 0.60; IR (KBr) 3240 (NH), 1756 (OAc), 1611 (C=N) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ10.23 (s, 2H, exchangeable, NH), 7.40-7.03 (2d, 4 H, each aromatic H), 6.13, 5.57(2s, 2H each, tetritoldi-1,4-yl H), 2.27 (s, 6H, CH_3), 2.13, 2.07 (2s , 6H each, OAc) .

Anal. Calcd for $C_{30}H_{32}N_6O_8S_2$ (668): C, 53.9; H, 4.8; N, 12.6. Found: C, 54.1; H, 4.9; N, 12.8 .

1,2,3,4-Tetra-*O*-acetyl-1,4-bis[5-(*p*-chlorophenyl)amino-1,3,4-thiadiazol-2-yl]*galacto*-tetritol (4c). Yield: 64%, mp 287 °C; TLC in 9:1 $CHCl_3$-MeOH, R_f : 0.63; IR (KBr) 3240 (NH), 1755 (OAc), 1613 (C=N) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ7.73-7.43 (2d, H each, aromatic H), 6.27, 5.70 (2s, 2 H each, tetritoldi-1,4-yl H); 2.23, 2.20 (2s, 6H each, OAc) .

Anal. Calcd for C_{28} H_{26} N_6 O_8 S_2 Cl_2 (709): C, 47.4; H, 3.7; N, 11.8. Found: C, 47.6; H, 3.8; N, 12.1 .

General procedure for the preparation of 1,4-bis(5-arylamino-1,3,4-thiadiazol-2-yl)*galacto*-tetritols (5a-c). A solution of the appropriate **4a-c** (2 mmol) in methanol (50 mL) was treated with a concentrated methanolic ammonia solution (20 mL) and kept at room temperature for 16 h. The mixture was concentrated under reduced pressure and the product was crystallized from water - ethanol.

The following compounds were prepared :

1,4-Bis(5-phenylamino-1,3,4-thiadiazol-2-yl)*galacto*-tetritol (5a). Yield: 64%, mp 305 °C; TLC in 1:1 $CHCl_3$-MeOH, R_f: 0.59; IR (KBr) 3368 (OH), 3281 (NH), 1600 (C=N) cm^{-1}, ^1H NMR [$(CD_3)_2$ SO] δ 9.67(s, 2H, exchangeable, NH), 7.70-6.73 (m, 10H, aromatic H), 5.8, 5.17 (2d, 2H each, exchangeable, OH), 4.97, 3.80 (2d, 2H each, tetritol-1,4-yl H) .

Anal. Calcd for C_{20} H_{20} N_6 O_4 S_2 (472): C, 50.8; H, 4.2; N, 17.8. Found: C, 51.1; H, 4.3; N, 17.9 .

1,4-Bis[5-(*p*-methylphenyl)amino-1,3,4-thiadiazol-2-yl]*galacto*-tetritol (5b). Yield: 64%, mp 318 °C; TLC in 1:1 $CHCl_3$-MeOH, R_f: 0.58; IR (KBr) 3350 (OH), 3289 (NH), 1603 (C=N) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ 9.83 (s, 2H, exchangeable, NH), 7.30, 7.10 (2s, 4H each, aromatic H), 5.73, 5.17 (2d, 2H each, exchangeable, OH), 4.90, 3.90 (2d, 2H each, tetritol-1,4-yl H), 2.33 (s, 6H, CH_3) .

Anal. Calcd for C_{22} H_{24} N_6 O_4 S_2 (550): C, 52.8; H, 4.8; N, 16.8. Found: C, 52.6; H, 4.6; N, 16.9 .

1,4-Bis[5-(*p*-chlorophenyl)amino-1,3,4-thiadiazol-2-yl]*galacto*-tetritol (5c). Yield: 55%, mp 298 °C; TLC in 1:1 $CHCl_3$-MeOH, R_f: 0.58; IR (KBr) 3343 (NH), 3288 (NH), 1623 (C=N) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ10.27 (s, 2H, exchangeable, NH); 7.57, 7.30 (2d, 4H each, aromatic H), 6.0-5.73 (m, 2H , exchangeable, OH), 5.20-4.80 (m, 4H, 2 exchangeable, OH+ tetritoldi-1,4-yl H) . The other two tetritoldi-1,4-yl protons were associated with the solvent to give a broad signal at δ 3.27 ppm .

Anal. Calcd for C_{20} H_{18} N_6 O_4 S_2 Cl_2 (541): C, 44.4 ; H, 3.3; N, 15.5. Found: C, 44.5; H, 3.4; N, 15.7.

General procedure for the preparation of 1,4-bis(4-aryl-5-thioxo-1,2,4-thiadiazol-3-yl)*galacto*-tetritols (6a-c). A mixture of the appropriate **3a-c** (2 mmol)

and freshly prepared 0.05 M sodium ethoxide (100 mL) was stirred for 16 h at ambient temperature. The resulting solution was stirred with Dowex-50 cation exchange resin (5 mL, H^+ form) for 20 min, the resin was filtered and the filtrate was concentrated to half its volume. The product which separated was filtered and crystallized from water - ethanol.

The following compounds were prepared :

1,4-Bis(4-phenyl-5-thioxo-1,2,4-triazol-3-yl)*galacto*-tetritols (6a). Yield: 64%, mp: 198-200 °C (dec.); TLC in 1:1 $CHCl_3$-MeOH, R_f: 0.57; IR (KBr) 3381(OH), 3283 (NH), 1667 (C=N) cm^{-1} ; ^1H NMR [$(CD_3)_2$ SO] δ 7.70-6.80 (m, 10H, aromatic H), 4.50, 4.27 (2d, 2H each, tetritoldi-1,4-yl H) . The hydroxyl and imino protons were associated with the solvent to give a broad signal at δ 3.8 ppm .

Anal. Calcd for $C_{20}H_{20}N_6O_4S_2$ (541): C, 50.8; H, 4.2; N, 17.8. Found: C, 50.7; H, 4.1; N, 17.8.

1,4-Bis[4-(*p*-methylphenyl)-5-thioxo-1,2,4-triazol-3-yl]*galacto*-tetritols (6b) Yield: 64%, mp: 220-222 °C (dec.); TLC in 1:1 $CHCl_3$-MeOH, R_f: 0.56; IR (KBr) 3280 (NH+OH), 1655 (C=N) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ 8.97 (1*s*, 2H, exchangeable, NH), 7.27, 6.90 (2d, 4H each, aromatic H); 2.20 (s, 6H, CH_3) . The protons of the tetritoldi-1,4-yl chain were associated with the solvent to give a broad signal at δ 4.1 ppm .

Anal. Calcd for $C_{22}H_{24}N_6O_4S_2$ (500): C, 52.8; H, 4.8; N, 16.8. Found: C, 52.9; H, 4.8; N, 17.0.

1,4-Bis[4-(*p*-chlorophenyl)-5-thioxo-1,2,4-triazol-3-yl]*galacto*-tetritols (6c). Yield: 55%, mp: 208-210 °C (dec.); TLC in 1:1 $CHCl_3$-MeOH, R_f: 0.59 ; IR: (KBr) 3306 (NH+OH), 1663 (C=N) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO]δ 9.10 (1s, 2H, exchangeable, NH), 7.5, 7.2 (2d, 4H each, aromatic H), 5.60-5.30, 5.03-4.70 (2m, 2H each, exchangeable, OH), 4.6-4.07 (m, 4H, tetritoldi-1,4-yl) .

Anal. Calcd for $C_{20}H_{18}N_6O_4S_2Cl_2$ (541): C, 44.4; H, 3.3; N, 15.5. Found: C, 44.2; H, 3.1; N, 15.7 .

General procedure for the preparation of 1,2,3,4-tetra-*O*-acetyl-1,4-bis(1-acetyl-4-aryl-5-thioxo-1,2,4-triazol-3-yl)*galacto*-tetritols (7a-c). A mixture of the respective **6a-c** (2 mmol), pyridine (5 mL) and acetic anhydride (10 mL) was stirred for 16 h at ambient temperature. The mixture was then concentrated under reduced pressure and the syrupy residue obtained was washed with water and dried. Compounds **7a-c** were all syrupy products that could not be crystallized as yet.

The following compounds were prepared :

1,2,3,4-Tetra-*O*-acetyl-1,4-bis(1-acetyl-4-phenyl-5-thioxo-1,2,4-triazol-3-yl)-*galacto*-tetritols (7a). Yield: 62%, TLC in 9:1 $CHCl_3$-MeOH, R_f: 0.61; IR (KBr)

1751(OAc), 1683(NAc), 1593 (C=N) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ 7.5-7.0 (m, 10H, aromatic H), 5.97, 5.30 (2s, 2H each, tetritoldi-1,4-yl H), 2.03 (s, 6H, NAc); 1.23 (s, 12H, OAc).

Anal. Calcd for $C_{32}H_{32}N_6O_{10}S_2$ (724): C, 53.0; H, 4.4 ; N, 11.6. Found: C, 53.3; H, 4.2; N, 11.4 .

1,2,3,4-Tetra-*O*-acetyl-1,4-bis[1-acetyl-4-(*p*-methylphenyl)-5-thioxo-1,2,4-triazol-3-yl]*galacto*-tetritols (7b). Yield: 57%, TLC in 9:1 $CHCl_3$-MeOH, R_f: 0.6; IR (KBr) 1760(OAc), 1690(NAc), 1605 (C=N) cm^{-1}; ^1H NMR [$(CD_3)_2$ SO] δ 7.30-7.17 (2d, 4H each, aromatic H), 6.30, 6.10 (2s, 2H each, tetritoldi-1,4-yl 4H), 2.47 (s, 6H, NAc), 2.33 (s, 6H , CH_3), 2.17, 2.30 (2s, 6H each, OAc).

Anal. Calcd for $C_{34}H_{36}N_6O_{10}S_2$ (752): C, 54.3; H, 4.8; N, 11.2. Found: C, 54.5; H, 4.6; N, 11.5.

1,2,3,4-Tetra-*O*-acetyl-1,4-bis[1-acetyl-4-(*p*-chlorophenyl)-5-thioxo-1,2,4-triazol-3-yl]*galacto*-tetritols (7c). Yield: 50%; TLC in 9:1 $CHCl_3$-MeOH, R_f: 0.63; IR (KBr) 1749 (OAc), 1685(NAc), 1593 (C=N) cm^{-1} ; ^1H NMR [$(CD_3)_2$ SO] δ 7.37, 7.07 (2d, 4H each, aromatic H), 5.97, 5.30 (2s, 2H each, tetritoldi-1,4-yl H), 2.57 (1s, 6H, NAc), 2.07 , 2.00 (2s, 6H each, OAc).

Anal. Calcd for $C_{32}H_{30}N_6O_{10}S_2Cl_2$ (793): C, 48.4; H, 3.8; N, 10.6. Found: C, 48.6; H, 3.6; N, 10.8.

Antimicrobial Screening. A solution (15 μL) of **3a, 3b**, or **6a-c** (2 mg) in dimethyl sulfoxide (2 mL) was aseptically transferred onto sterile discs of Whatman filter paper (5 mm diameter). The discs were placed onto the surface of the inoculated agar plates. Bacteria-inoculated plates were incubated at 37 °C for 24 h while fungi-inoculated plates were incubated at 25 °C for 96 h. A disc impregnated with dimethyl sulfoxide (15 μL) was used as a control for each microorganism. The diameter of the inhibition zones was taken as a measure of the antimicrobial activity.

ACKNOWLEDGMENT

Our thanks are due to Dr. Hanan Ghozlan, Department of Botany and Microbiolgy, Faculty of Science, Alexandria University for performing the antimicrobial activities.

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