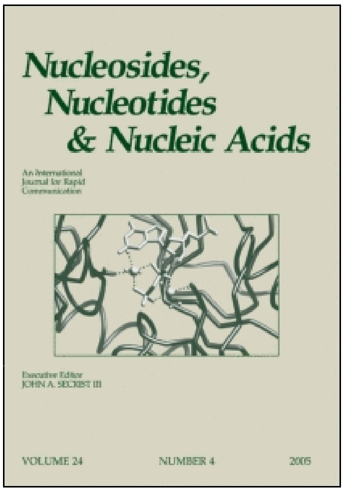


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

# NOVEL SYNTHESIS OF *seco* TYPE OF ACYCLO *C*-NUCLEOSIDES OF 1,2,4-TRIAZOLE AND 1,2,4-TRIAZOLO[3,4-b][1,3,4]THIADIAZINE

El Sayed H. El Ashry[a]; Laila F. Awad[a]
[a] Chemistry Department, Faculty of Science, Alexandria University, Alexandria, Egypt

**To cite this Article** Ashry, El Sayed H. El and Awad, Laila F.(2001) 'NOVEL SYNTHESIS OF *seco* TYPE OF ACYCLO *C*-NUCLEOSIDES OF 1,2,4-TRIAZOLE AND 1,2,4-TRIAZOLO[3,4-b][1,3,4]THIADIAZINE', Nucleosides, Nucleotides and Nucleic Acids, 20: 1, 103 — 116

**To link to this Article: DOI:** 10.1081/NCN-100001440

**URL:** http://dx.doi.org/10.1081/NCN-100001440

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS, 20(1&2), 103–116 (2001)

# NOVEL SYNTHESIS OF *seco* TYPE OF ACYCLO *C*-NUCLEOSIDES OF 1,2,4-TRIAZOLE AND 1,2,4-TRIAZOLO[3,4-b][1,3,4]THIADIAZINE

**El Sayed H. El Ashry* and Laila F. Awad**

Chemistry Department, Faculty of Science, Alexandria University,
Alexandria, Egypt

## ABSTRACT

The *seco* *C*-nucleosides 3-(1,2,3,4,5-penta-*O*-acetyl-D-gluco- and D-galacto-pentitol-1-yl)-1*H*-1,2,4-triazoles (**8** and **9**) were obtained in a one pot by deamination and dethiolation of 4-amino-3-(D-gluco- and D-galacto-pentitol-1-yl)-5-mercapto-1,2,4-triazoles (**1** and **2**), respectively, using sodium nitrite in orthophosphoric acid and subsequent acetylation. Condensation of **1, 2**, and 4-amino-3-(D-glycero-D-gulo-hexitol-1-yl)-5-mercapto-1,2,4-triazole (**12**) with phenacylbromide (**11**) afforded the corresponding 3-(D-gluco-, D-galacto-pentitol-1-yl) and 3-(D-glycero-D-gulo-hexitol-1-yl)-6-phenyl-7*H*-1,2,4-triazolo[3,4-b][1,3,4] thiadiazines (**15, 16**, and **17**). Acetylation of **15–17** gave the penta- and hexa-*O*-acetyl derivatives **18–20**, respectively. The structures were confirmed by using $^{1}$H, $^{13}$C, and 2D NMR spectra, DQFCOSY, HMQC, and HMBC experiments. The favored conformational structures were deduced from the vicinal coupling constants of the protons.

*Key Words*: Seco C-Nucleosides; 1,2,4-Triazoles; 1,2,4-Triazolo[3,4-b][1,3,4] thiadiazines.

## INTRODUCTION

The biological activity of naturally occurring *C*-nucleosides has stimulated extensive research for the synthesis of their analogs (1–3). Various analogs of the

---

*Address correspondence to E.S.H. El Ashry. E-mail: elashry@internetalex.com potent antiviral nucleoside ribavirin (4–13) were prepared because of their broad spectrum of activity against RNA and DNA viruses. Some acyclic *C*-nucleosides of the 1,2,4-triazole have potential biological activities as antiviral (14), herbicides, fungicides, or insecticides (15). A part of our ongoing research program has been devoted to the synthesis of acyclo *N*- and *C*-nucleosides (16,17). The biological activities of various 1,2,4-triazole derivatives (18) and their N-bridged heterocyclic analogs (19) have been extensively studied. Those incorporating the N–C–S linkage as in the skeleton of 1,2,4-triazolo[3,4-b][1,3,4]thiadiazine exhibit a broad spectrum of biological activities (19). Consequently, the attachment of hydrophilic groups such as alditolyl moieties on these ring systems may lead to an enhanced bioavailability and/or improved biological activities. Thus, a novel synthesis of acyclo *C*-nucleosides of the 1,2,4-triazole and its fused ring system analogs is the subject of this paper.

## RESULTS AND DISCUSSION

Our protocol was designed for the construction of nucleosides having the 1,2,4-triazolo[4,3-d][1,2,3,4]thiatriazole ring system **5** by reaction of 3-(D-alditol-1-yl)-4-amino-5-mercapto-1,2,4-triazole (16) (**1, 2**) at 0°C with sodium nitrite in orthophosphoric acid (20) followed by neutralization with sodium hydroxide. The expected product **5** could not be prepared, but products of the triazole type **6** and **7** have been obtained, which could be isolated upon acetylation with acetic anhydride in pyridine whereby the respective crystalline products **8** and **9** were obtained. Their elemental analysis and mass spectral data were not consistent with the expected fused ring products **5**. Their molecular ion peaks in the electron impact mass spectra (EIMS) appeared at *m/z* 429. Moreover, the FABMS of 3-(1,2,3,4,5-penta-*O*-acetyl-D-galacto-pentitol-1-yl)-1*H*-1,2,4-triazole (**9**) showed a protonated molecular ion peak at *m/z* 430 in agreement with the loss of sulfur and two nitrogen atoms from **4** and agreed with the molecular formula $C_{17}H_{23}N_3O_{10}$. The presence of the 1*H*-1,2,4-triazole ring has been confirmed by the appearance of the respective fragment ions possessing a 3-acetoxymethyl group at *m/z* 141 and 3-hydroxymethyl group at *m/z* 98. Their $^1$H NMR spectra exhibited a singlet at the downfield region ($\delta = 8.22$–$8.39$) due to H-5 of the triazole moiety, which agreed with the reported (21) value for that proton on such a ring system. Although the N–H signal could not be observed in deuterochloroform solution, which is usual (22), a broad exchangeable signal of low intensity at $\delta = 7.90$ for that proton could be detected for their solutions in DMSO-$d_6$.

At the higher frequency region in the $^{13}$C NMR spectra of **8** and **9**, signals corresponding to C-3 and C-5 of the triazole moiety were assigned based on their $^1$H–$^{13}$C HMQC experiment, which showed a correlation of H-5 ($\delta = 8.22$–$8.39$) with that of C-5 ($\delta_C = 144.71$–$144.29$). The possibility of that signal to be due to an SH was ruled out from the fact that this signal is not exchangeable by $D_2O$. The C-3 was resonated at $\delta_C = 158.52$–$158.82$. Such assignment was confirmed on the basis of the heteronuclear multiple bond correlation (HMBC) experiment

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

for **9** that showed a correlation of H-1′ of the sugar moiety at $\delta = 6.13$ and C-3 of the triazole moiety, which in turn correlated with H-5 of the triazole moiety. Their 2D NMR spectra ($^1$H–$^1$H DQFCOSY and $^1$H–$^{13}$C HMQC) facilitated the spectral assignment of the sugar moiety. The above data indicated that the isolated products have the structure 3-(1,2,3,4,5-penta-*O*-acetyl-D-alditol-1-yl)-1*H*-1,2,4-triazole (**8** and **9**) whereas the formation of triazolo[4,3-d][1,2,3,4]thiatriazole was ruled out.

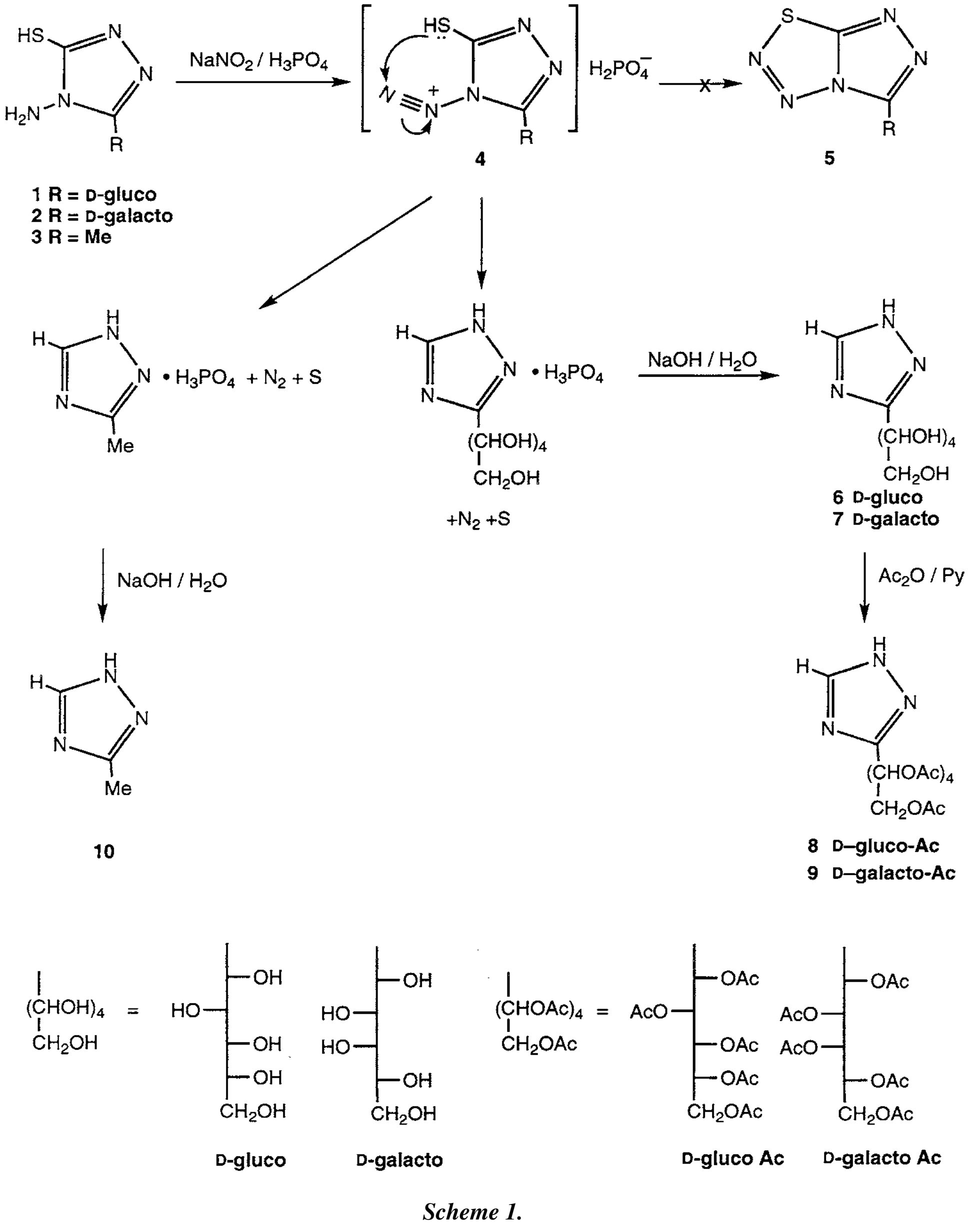
In order to establish that the formation of 3-substituted-1*H*-1,2,4-triazole from 4-amino-5-mercapto-3-substituted-1,2,4-triazole has taken place via the diazotization step and not under the condition of acetylation, the model compound 4-amino-5-mercapto-3-methyl-1,2,4-triazole (23) (**3**) was diazotized under the same reaction conditions whereby it gave **10**, which was identical with an authentic sample (24).

To account for the reaction, diazotization of **1–3** would give the respective diazonium salt **4**, which undergoes loss of two nitrogen atoms in addition to a desulphurization process of the thiol group to give **6, 7**, and **10**, respectively. The unusual desulphurization of the thiol group may involve a thinyl radical as intermediate (25). Although 1-aryloxymethyl-s-triazolo[4,3-d][1,2,3,4]thiatriazoles were reported (20) as products under similar reaction conditions, the respective analogs (**5** in the present work) were not obtained (Scheme 1). To the best of our knowledge, no data are available in literature for the simultaneous removal of the SH and $NH_2$ from 4-amino-5-mercapto-3-substituted-1,2,4-triazole derivatives, in one step, but each of them can be eliminated separately; the thiol group via its oxidation with nitric acid and the amino group via diazotization followed by reductive removal of the diazo group with hypophosphorus acid (26) (Scheme 1).

4-Amino-5-mercapto-1,2,4-triazole ring system is a versatile key intermediate to the synthesis of 1,2,4,triazolo[3,4-b][1,3,4]thiadiazine derivatives (19). Accordingly, the synthesis of the respective new acyclo *C*-nucleoside analogs **16–18** was achieved by condensation of equimolar amounts of 4-amino-3-(D-gluco-D-galacto-pentitol-1-yl and D-glycero-D-gulo-hexitol-1-yl)-5-mercapto-1,2,4-triazole (**1, 2**, and **12**) and phenacylbromide (**11**) in absolute ethanol. The cyclocondensation process can take place either through N-alkylation (route i) or S-alkylation (route ii) to form **13** or **15**, respectively, followed by dehydrative cyclization to give either 3-(D-alditol-1-yl)-7-phenyl-5*H* (**14**) or 6-phenyl-7*H*-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine (**16–18**), respectively (Scheme 2). The latter structures were confirmed from the analysis, their infrared (IR) and $^1$H NMR spectra.

Further verification of ring closure was concluded from their FABMS, which showed protonated molecular ion peaks at *m/z* 367 for **16, 17** and *m/z* 397 for **18**, although the EIMS spectrum of **17** showed the highest molecular ion peak at *m/z* 335, which has resulted from loss of the $CH_2OH$ fragment.

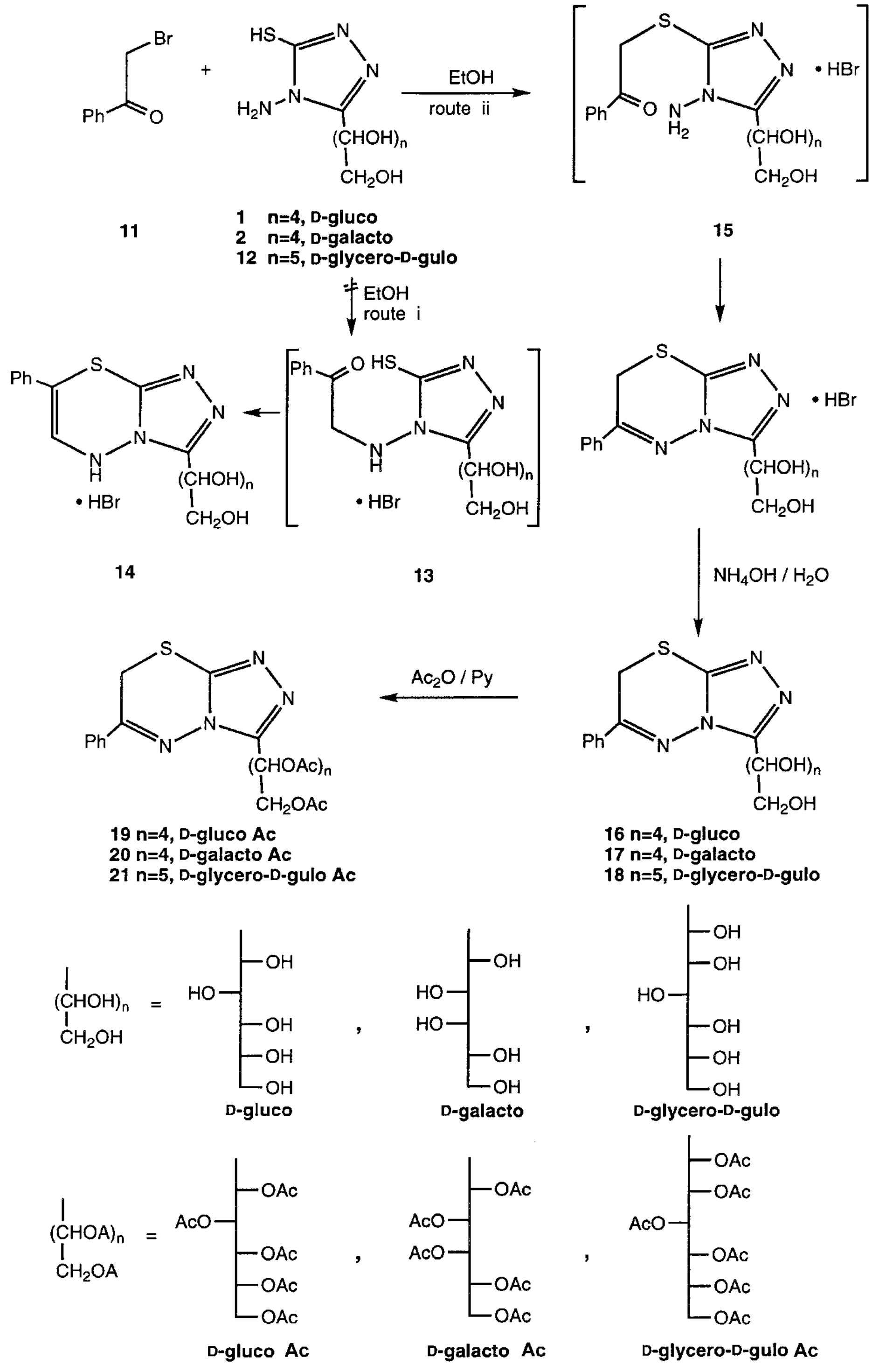
Acetylation of compounds **16–18** with acetic anhydride in pyridine afforded the corresponding peracetylated derivatives **19–21**. Their mass spectra showed molecular ion peaks at *m/z* 576 for both **16** and **17** and 648 for **18**. Subsequent fragmentation of the sugar moieties gave ions at *m/z* 245 and 217 corresponding to B-CHOH$^{+\bullet}$ and the protonated base BH$^+$ (B = heterocyclic ring). The fragmentation route that involved concomitant breaking of N−N and C−C bonds of the 1,3,4-thiadiazine ring system in B−CHOH$^{+\bullet}$ fragment gave the base peak fragment



*Scheme 1.*

at *m/z* 143, which is consistent with literature (27). This result again reveals the stability of the 1,2,4-triazole ring toward electron bombardment (16), which is not the case for the 1,3,4-thiadiazine ring.

Along with other expected signals in $^1$H NMR (600 MHz) spectra of compounds **16–18** measured in DMSO-$d_6$, the $SCH_2$ protons were assigned for two doublets of the AB type spin system at $\delta = 4.32$–$4.34$ and $4.37$–$4.40$ with $J_{gem} = 15.64$–$15.66$ Hz, and for **20** as two doublets ($\delta = 4.36, 4.53$) with $J_{gem} = 15.67$ Hz. The


Br
Ph
O
+
HS
N
N
H2N
N
(CHOH)n
CH2OH
EtOH
route ii
S
N
N
• HBr
Ph
O
N
N
H2
(CHOH)n
CH2OH
11
1 n=4, D-gluco
2 n=4, D-galacto
12 n=5, D-glycero-D-gulo
15
EtOH
route i
Ph
S
N
N
N
N
H
• HBr
(CHOH)n
CH2OH
Ph
O
HS
N
N
N
N
H
• HBr
(CHOH)n
CH2OH
S
N
N
• HBr
Ph
N
N
(CHOH)n
CH2OH
14
13
NH4OH / H2O
S
N
N
Ph
N
N
(CHOAc)n
CH2OAc
Ac2O / Py
S
N
N
Ph
N
N
(CHOH)n
CH2OH
19 n=4, D-gluco Ac
20 n=4, D-galacto Ac
21 n=5, D-glycero-D-gulo Ac
16 n=4, D-gluco
17 n=4, D-galacto
18 n=5, D-glycero-D-gulo
(CHOH)n
CH2OH
=
OH
HO
OH
OH
OH
D-gluco
OH
HO
HO
OH
OH
D-galacto
OH
OH
HO
OH
OH
OH
D-glycero-D-gulo
(CHOA)n
CH2OA
=
OAc
AcO
OAc
OAc
OAc
D-gluco Ac
OAc
AcO
AcO
OAc
OAc
D-galacto Ac
OAc
OAc
AcO
OAc
OAc
OAc
D-glycero-D-gulo Ac

*Scheme 2.*

reported data for simple analogs with such ring system (19,28) showed them as a singlet, but the present results are in accord with that for 5*H*-1,2,4-triazolo[4,3-c][1,3]benzothiazine derivatives (29). Accordingly, the two protons of the methylene group are not equivalent. This is readily realized by the construction of a molecular model for the 3-substituted-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine ring, which showed that the thiadiazine ring is present in a twisted conformation in which C-7 is in a position out of plane whereby H-7 and H-7′ occupy two different planes.

The $^{13}$C NMR spectrum of compounds **16–21** confirmed the assigned structures. At lower frequency region, $SCH_2$ signal was assigned at $\delta_C = 23.00$–$23.90$. Signals corresponding to C-3 and C-8a of compounds **16–18** were resonated at $\delta_C = 154.00$–$154.87$ whereas the C-6 signal appeared upfield ($\delta_C = 140.37$–$140.81$) because of the shielding effect exerted by ring nitrogen and phenyl group. Acetylation of compounds **16–18** was accompanied by an upfield shift of C-3 ($\delta_C = 148.33$–$148.60$) of the peracetylated derivatives **19–21**. The sugar moieties of compounds **16–21** were characterized from their $^1$H–$^1$H DQFCOSY and $^1$H–$^{13}$C HMQC NMR spectroscopic studies.

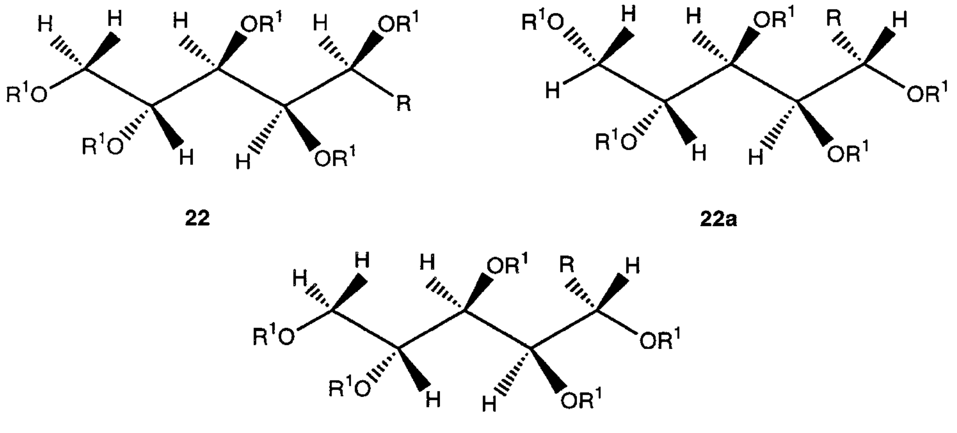
**Conformational analysis.** There has been much interest in the solution conformations of alditols and their derivatives based on $^1$H NMR data (16,30), via the values of the coupling constants.

The planar zigzag conformation **22** of the D-gluco derivatives **8, 16**, and **19** would have a parallel interaction between either the acetoxy groups in **8** and **19** or the hydroxyl groups in **16**, attached at C-1′ and C-3′. Such a planar conformation should show a smaller coupling constant value (<4 Hz) for $J_{1',2'}$ (Tab. 1). However, the observed value ($J_{1',2'} = 7.79$–$8.57$ Hz) indicated the presence of antidisposed protons at C-1′ and C-2′. This required rotation along C-1′–C-2′ bond to give the conformer **22a**. Regarding the terminal hydroxy and acetoxy methyl groups, the observed value for $J_{4',5''}$ (4.68–5.68 Hz) is somewhat small for an antiperiplanar disposition of H-4′ and H-5″ in the acetate derivatives **8** and **19**. This can be alleviated when H-4′ and H-5″ are in a gauche disposition, which would be generated by rotation along

***Table 1.*** Vicinal Coupling Constants in Hertz

| Compound No. | $J_{1',2'}$ | $J_{2',3'}$ | $J_{3',4'}$ | $J_{4',5'}$ | $J_{4',5''}$ | $J_{5',5''}$ | $J_{5',6'}$ | $J_{5',6''}$ | $J_{6',6''}$ |
|---|---|---|---|---|---|---|---|---|---|
| **8**[a] | 7.79 | 3.06 | 8.07 | 3.09 | 5.68 | 12.45 | | | |
| **9**[a] | 2.46 | 9.67 | 2.17 | 5.06 | 7.42 | 11.64 | | | |
| **16**[b,c] | 8.19 | 1.65 | 8.23 | 2.87 | 6.89 | 12.41 | | | |
| **17**[b,c] | 2.19 | 9.15 | 1.56 | 4.97 | – | 9.70 | | | |
| **19**[a] | 8.57 | 2.49 | 8.79 | 2.85 | | | | | |
| **20**[a] | 1.97 | 9.67 | 2.16 | 5.09 | 4.68 | 12.34 | | | |
| **21**[a] | 7.18 | 3.24 | 6.28 | 5.02 | | | 4.98 | 5.97 | 11.77 |

[a] In $CDCl_3$.
[b] In DMSO-$d_6$.
[c] After addition of $D_2O$.



**22** **22a**

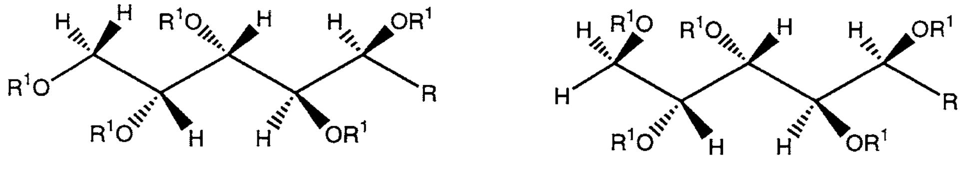
**22b**

***Figure 1.*** Conformation of the D-gluco derivatives **8, 16**, and **19**.

C-4′–C-5′ bond. The observed $J_{4',5'}$ value (2.85–3.09 Hz) reflects that, in the rotamers **22, 22a**, and **22b**, H-4′ and H-5′ have a gauche disposition. The $J_{4',5''} =$ 6.89 Hz in the unprotected sugar **16** indicated that H-4′ and H-5″ could be present in an antiparallel disposition. Consequently, conformer **22a** is the preferred one for the acetyl derivatives whereas **22b** is for the unprotected analogs (Fig. 1).

The coupling constant values of the D-galacto derivatives **9, 17**, and **20** showed that these compounds adopt the favored planar zigzag conformation **23**, which are compatible with other acyclic chains having the D-galacto configuration (16,31). The value of $J_{4',5''}$ (7.42–7.56 Hz) indicated that H-4′ and H-5″ exist in an antiparallel disposition, whereas the $J_{4',5'}$ value (5.06–5.09 Hz) is of intermediate magnitude indicating that H-4′ and H-5′ are not in a gauche arrangement as in **23**. However, rotation around the C-4′–C-5′ bond gives **23a** whereby H-5′ will be in an extended planar zigzag conformation (Fig. 2).

The proton–proton coupling constant values of compound **21** having the D-glycero-D-gulo configuration showed that **21** is not in a simple zigzag conformation as is **24**. Rotation of C-3′–C-4′ to alleviate the 1,3-interaction between the acetoxy groups at C-2′ and C-4′ in the conformer **24** would generate an interaction between



**23** **23a**

***Figure 2.*** Conformation of the D-galacto derivatives **9, 17**, and **20**.

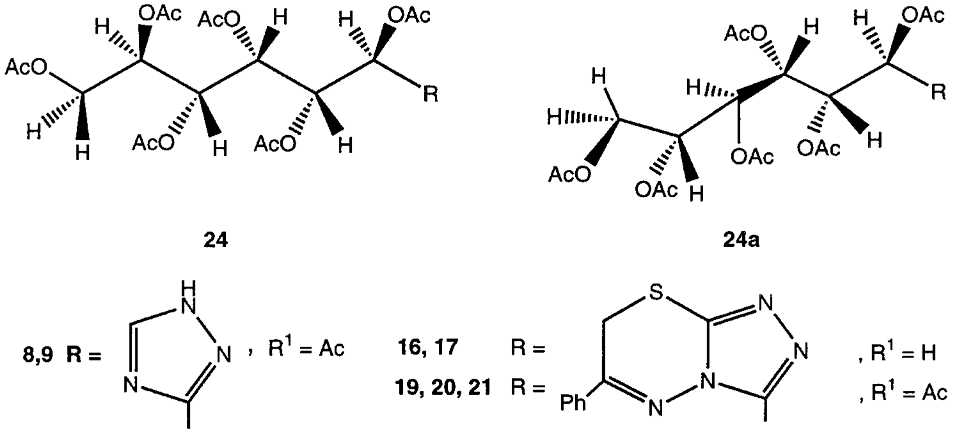


*Figure 3.* Conformation of D-glycero-D-gulo acetyl derivative **21**.

the acetoxy groups at C-3′ and C-5′ as in **24a** and it would also require a larger value of both $J_{3',4'}$ and $J_{4',5'}$, which is not the case. Therefore compound **21** exists in solution in another rotameric state that would justify these coupling constant values (Fig. 3).

## EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus and are uncorrected. IR spectra were recorded with a Unicam SP1025 spectrometer. Mass spectra were recorded using electron ionization (EI) on a Finnigan MAT 312 spectrometer and fast-atom-bombardment (FAB) on a Kratos MS 50 spectrometer. $^1$H NMR and $^{13}$C NMR spectra were recorded with a Bruker AC 270 MHz, Bruker Advance DPX 300 MHz, or a Bruker Advance DRX 600 MHz ($^1$H) and at 62.9 or 75 MHz ($^{13}$C) spectrometers. The chemical shifts are expressed on the $\delta$-scale using $Me_4Si$ as a standard. The $J$-values are given in hertz. The assignment of $^1$H NMR spectra was based on chemical-shift correlation spectra (DQFCOSY). The assignment of $^{13}$C NMR spectra were based on carbon–proton shift-correlation spectra (HMQC) and heteronuclear multiple bond correlation (HMBC). TLC was performed on Merck Silica Gel 60 F254 with detection by charring in sulfuric acid and by UV light. Microanalyses were performed in the Unit of Microanalysis at the Faculty of Science, Alexandria University.

**3-(1,2,3,4,5-Penta-*O*-acetyl-D-alditol-1-yl)-1*H*-1,2,4-triazole (8, 9).** General procedure: A suspension of compound **1** or **2** (0.27 g, 1.01 mmol) in orthophosphoric acid (2–3 mL) was treated with sodium nitrite (5*N*, 7 mL) at 0°C. The solid was dissolved during the addition. The reaction mixture was left for 2 h at 0°C and then left at room temperature overnight. It was neutralized with 10% sodium hydroxide solution and the resulting solution was evaporated under reduced pressure.

The crude product was boiled with ethanol, filtered and the ethanolic solution was evaporated to dryness. The resulting syrup was dissolved in pyridine (3.0 mL) cooled to 0°C and then treated with acetic anhydride (5.0 mL). The reaction mixture was kept overnight at room temperature, poured on ice-cold water, and extracted with methylene chloride. The organic layer was washed with water, dried over anhydrous sodium sulfate and evaporated to give a syrup.

**3-(1,2,3,4,5-Penta-*O*-acetyl-D-gluco-pentitol-1-yl)-1*H*-1,2,4-triazole (8).** The syrup was crystallized from absolute ethanol to give **8** as white crystals (0.22 g, 52%); m.p. 177–178°C; IR (KBr): 3161, 3114 (NH), 1754 (OCO), 1533 $\text{cm}^{-1}$ (C=N); $^1$H NMR (600 MHz) ($CDCl_3$) $\delta$: 1.99, 2.05, 2.06, 2.09, 2.10 (5s, 15H, 5Ac), 4.01 (dd, 1H, $J_{4',5''} = 5.68$ Hz, $J_{5',5''} = 12.45$ Hz, H-5″), 4.21 (dd, 1H, $J_{4',5'} = 3.09$ Hz, H-5′), 5.10–5.13 (m, 1H, H-4′), 5.71 (dd, 1H, $J_{3',4'} = 8.07$ Hz, H-3′), 5.91 (dd, 1H, $J_{2',3'} = 3.06$ Hz, H-2′), 6.11 (d, 1H, $J_{1',2'} = 7.79$ Hz, H-1′), 8.39 (s, 1H, H-5); $^{13}$C NMR ($CDCl_3$) $\delta_C$: 20.57, 20.67, 20.82 (Ac), 67.71 (C-1′), 69.95 (C-2′), 68.69 (C-3′), 68.23 (C-4′), 61.86 (C-5′), 158.82 (C-3), 145.29 (C-5), 169.78, 169.93, 169.99, 170.60 (C=O); EIMS, *m/z* (%): 429 (9, $M^{+\bullet}$), 386 (26, $M^{+\bullet} - Ac^{\bullet}$), 370 (15, $M^{+\bullet} - AcO^{\bullet}$), 356 (26, $M^{+\bullet} - CH_2OAc^{\bullet}$), 327 (71, 370 − $Ac^{\bullet}$), 314 (32, 356 − $C_2H_2O$), 242 (9, 327 − AcOH–$C_2H_2$), 170 (16, 242 – $HCOAc^{\bullet}$), 141 (100, B–$CHOAc^{+\bullet}$), 98 (44, B–$CHO^+H$). Anal. calcd for $C_{17}H_{23}N_3O_{10}$ (429.37): C, 47.55; H, 5.39; N, 9.78. Found: C, 47.26; H, 5.34; N, 9.79.

**3-(1,2,3,4,5-Penta-*O*-acetyl-D-galacto-pentitol-1-yl)-1*H*-1,2,4-triazole (9).** The syrup was chromatographed on silica gel by elution with acetone:toluene (3:1). The fractions enriched with the product were collected and evaporated to give a syrup, which was crystallized from chloroform as white crystals (0.20 g, 48%); m.p. 99–100°C; IR (KBr): 3124 (NH), 1756 $\text{cm}^{-1}$ (OCO); $^1$H NMR (600 MHz) ($CDCl_3$) $\delta$: 1.97, 2.03, 2.14 (3s, 15H, 5Ac), 3.93 (dd, 1H, $J_{4',5''} = 7.42$ Hz, $J_{5',5''} = 11.64$ Hz, H-5″), 4.31 (dd, 1H, $J_{4',5'} = 5.06$ Hz, H-5′), 5.33–5.34 (m, 1H, H-4′), 5.55 (dd, 1H, $J_{3',4'} = 2.17$ Hz, H-3′), 5.61 (dd, 1H, $J_{2',3'} = 9.67$ Hz, H-2′), 6.13 (d, 1H, $J_{1',2'} = 2.46$ Hz, H-1′), 8.22 (s, 1H, H-5); $^{13}$C NMR ($CDCl_3$) $\delta_C$: 20.52, 20.62 (Ac), 66.49 (C-1′), 69.22 (C-2′), 67.80 (C-3′), 67.69 (C-4′), 62.05 (C-5′), 158.52 (C-3), 144.71 (C-5), 169.60, 169.75, 170.24, 170.50 (C=O). FABMS, *m/z* (%): 430 (100, $MH^+$); EIMS, *m/z* (%): 429 (9, $M^{+\bullet}$), 386 (12, $M^{+\bullet} - Ac^{\bullet}$), 370 (6, $M^{+\bullet} - AcO^{\bullet}$), 356 (4, $M^{+\bullet} - CH_2OAc^{\bullet}$), 327 (35, 370 − $Ac^{\bullet}$), 267 (21, 327 − AcOH), 242 (15, 267 − $C_2H_2$), 141 (100, B–$CHOAc^{+\bullet}$), 98 (92, B–$CHOH^+$). Anal. calcd for $C_{17}H_{23}N_3O_{10}$ (429.37): C, 47.55; H, 5.39; N, 9.78. Found: C, 47.09; H, 5.10; N, 9.39.

**3-Methyl-1*H*-1,2,4-triazole (10).** A suspension of **3** (0.64 g, 4.9 mmol) in orthophosphoric acid (5.0 mL) was treated with sodium nitrite (5*N*, 10 mL) at 0°C. The resulting solution was left at 0°C for 2 h and then left overnight at room temperature. The solution was neutralized with 10% sodium hydroxide solution and then evaporated to dryness. The product was extracted with chloroform. The chloroform solution was dried over anhydrous sodium sulfate and evaporated to dryness to give a hygroscopic product **9** (0.2 g, 50%); m.p. 90°C, lit. (14) m.p. 94°C; EIMS, *m/z* (%): 83 (100, $M^{+\bullet}$), 56 (39, $M^{+\bullet} - N2$).

**3-(D-Alditol-1-yl)-6-Phenyl-7*H*-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine (16–18).** General procedure: A mixture of **1, 2**, or **12** (1 mmol) and phenacylbromide (**11**) (1 mmol) in absolute ethanol (25 mL) was heated under reflux for 6 h. The reaction mixture was then left to cool, neutralized with ammonia solution and concentrated. The product was filtered off, washed with water, and crystallized from ethanol to give **16, 17**, or **18**, respectively.

**3-(D-Gluco-pentitol-1-yl)-6-phenyl-7*H*-1,2,4,triazolo[3,4-b][1,3,4]thiadiazine (16).** It was obtained as a white crystalline product (0.3 g, 82%); m.p. 138–140°C; IR (KBr): 3200 (OH), and 1600 $cm^{-1}$ (C=N); $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$: 5.04 (dd, 1H, $J_{1',2'} = 8.45$ Hz, H-1′), 4.33–4.40 (m, 1H, H-2′), 3.13 (t, 1H, $J_{3',4'} = 7.7$ Hz, H-3′), 3.48–3.54 (m, 3H, H-4′, H-5′, H-5″), 5.56 (d, 1H, $J_{1',OH} = 5.73$ Hz, OH-1′), 4.62 (d, 1H, $J_{2',OH} = 6.14$ Hz, OH-2′), 4.31 (d, 1H, $J_{3',OH} = 7.56$ Hz, OH-3′), 4.24 (t, 1H, $J_{4',OH} = 5.68$ Hz, OH-4′), 4.31–4.40 (m, 3H, OH-5′+ $SCH_2$), 7.50–7.58 (m, 3H, Ph–H), 7.95 (d, 2H, Ph–H); $^1$H NMR (DMSO-$d_6$+ $D_2O$) $\delta$: 5.07 (d, 1H, $J_{1',2'} = 8.19$ Hz, H-1′), 4.37 (dd, 1H, $J_{2',3'} = 1.65$ Hz, H-2′), 3.15 (dd, 1H, $J_{3',4'} = 8.23$ Hz, H-3′), 3.54 (t, 1H, $J_{4',5'} = 2.87$ Hz, H-4′), 3.55 (t, 1H, H-5′), 3.37 (dd, 1H, $J_{4',5''} = 6.89$ Hz, $J_{5',5''} = 12.41$ Hz, H-5″), 4.12, 4.19 (2d, 2H, $J_{gem} = 15.60$ Hz, $SCH_2$); $^{13}$C NMR (DMSO-$d_6$) $\delta_C$: 23.31 ($SCH_2$), 66.16 (C-1′), 70.87 (C-2′), 70.79 (C-3′), 71.73 (C-4′), 63.85 (C-5′), 140.81 (C-6), 154.00, 154.75 (C-3, C-8a), 128.01, 129.32, 132.20, 134.05 (Ph); FABMS (DMSO/NBOH), *m/z* (%): 367 (50, $MH^{+\bullet}$), 217 (7, $BH^{+\bullet}$), 77 (39, $Ph^+$). Anal. calcd for $C_{15}H_{18}N_4O_5S$ (336.384): C, 49.16; H, 4.95; N, 15.29. Found: C, 48.93; H, 5.03; N, 14.56.

**3-(D-Galacto-pentitol-1-yl)-6-phenyl-7*H*-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine (17).** It was obtained as white needles (0.27 g, 74%), m.p. 204–205°C; IR (KBr): 3280 (OH) and 1600 $cm^{-1}$ (C=N); $^1$H NMR (600 MHz, DMSO-$d_6$) $\delta$: 5.19–5.23 (m, 2H, H-1′ + OH-1′), 3.93 (t, 1H, $J_{2',3'} = 6.58$ Hz, H-2′), 3.61 (t, 1H, $J_{3',4'} = 8.23$ Hz, H-3′), 3.72 (dd, 1H, $J_{4',5''} = 6.30$ Hz, H-4′), 3.49 (dd, 1H, $J_{4',5'} = 5.14$ Hz, $J_{5',5''} = 10.54$ Hz, H-5′), 3.37–3.40 (m, 1H, H-5″), 4.61 (d, 1H, $J_{2',OH} = 6.51$ Hz, OH-2′), 4.23 (m, 1H, OH-3′), 4.18 (d, 1H, $J_{4',OH} = 7.72$ Hz, OH-4′), 4.43 (t, 1H, $J_{5',OH} = 5.48$ Hz, OH-5′), 4.34, 4.39 (2d, 2H, $J_{gem} = 15.64$ Hz, $SCH_2$), 7.50–7.58 (m, 3H, Ph–H), 7.95 (d, 2H, Ph–H); $^1$H NMR (DMSO-$d_6$ + $D_2O$) $\delta$: 5.15 (d, 1H, $J_{1',2'} = 2.91$ Hz, H-1′), 3.94 (dd, 1H, $J_{2',3'} = 9.15$ Hz, H-2′), 3.58 (dd, 1H, $J_{3',4'} = 1.56$ Hz, H-3′), 3.71 (m, 1H, H-4′), 3.47 (t, 1H, $J_{4',5'} = 4.97$ Hz, $J_{5',5''} = 9.7$ Hz, H-5′), 3.40 (m, 1H, H- 5″), 4.20, 4.27 (2d, 2H, $J_{gem} = 15.55$ Hz, $SCH_2$); $^{13}$C NMR (DMSO-$d_6$) $\delta_C$: 23.31 = ($SCH_2$), 65.66 (C-1′), 71.87 (C-2′), 69.42 (C-3′), 70.24 (C-4′), 63.32 (C-5′), 140.78 (C-6), 154.87 (C-3, C-8a), 127.99, 129.40, 132.21, 133.95 (Ph); FABMS (DMSO/NBOH), *m/z*: (%): 367 (30, $MH^{+\bullet}$); EIMS, *m/z* (%): 335 (26, $M^{+\bullet} - CH_2OH$), 305 (32, $335 - CH_2O$), 275 (50, $305 - CH_2O$), 246 (35, 275 − CHO), 216 (29, $B^{+\bullet}$), 143 (100, $246-PhC{\equiv}NH^+$), 104 ($Ph-C{\equiv}NH^+$), 77 (41, $Ph^+$). Anal. calcd for $C_{15}H_{18}N_4O_5S$ (336.384): C, 49.17; H, 4.95; N, 15.29. Found: C, 49.28; H, 4.56; N, 15.40.

**3-(D-Glycero-D-gulo-hexitol-1-yl)-6-phenyl-7*H*-1,2,4-triazolo[3,4-b][1,3,4]-thiadiazine (18).** It was obtained as white needles (0.25 g, 66%); m.p. 200–202°C; IR (KBr): 3220–3320 (OH) and 1580 $cm^{-1}$(C=N); 1H NMR (600 MHz)

(DMSO-$d_6$) $\delta$: 4.99 (d, 1H, $J_{1',2'} = 9.24$ Hz, H-1′), 4.21 (dd, 1H, $J_{2',3'} = 1.84$ Hz, H-2′), 4.03 (t, 1H, $J_{3',4'} = 2.22$ Hz, H- 3′), 3.52–3.53 (2dd, 2H, $J_{4',5'} = 2.88$ Hz, H-4′, H-5′), 3.58 (dd, $J_{5',6'} = 9.46$ Hz, $J_{6',6''} = 11.67$ Hz, H-6′), 3.39 (dd, 1H, $J_{5',6''} = 4.88$ Hz, H-6″), 5.81 (d, 1H, $J_{1',\mathrm{OH}} = 6.25$ Hz, OH-1′), 4.66 (d, 1H, $J_{2',\mathrm{OH}} = 5.61$ Hz, OH-2′), 4.28 (d, 1H, $J_{3',\mathrm{OH}} = 7.53$ Hz, OH-3′), 4.55 (t, 1H, $J_{4',\mathrm{OH}} = 4.97$ Hz, OH-4′), 4.04 (t, 1H, OH-5′), 4.38 (d, 1H, $J_{6',\mathrm{OH}} = 5.77$ Hz, OH-6′), 4.32, 4.37 (2d, 2H, $J_{\mathrm{gem}} = 15.65$ Hz, $SCH_2$), 7.55–7.60 (m, 3H, Ph–H), 8.00 (d, 2H, Ph–H); $^{13}$C NMR (DMSO-$d_6$) $\delta_C$: 23.00 ($SCH_2$), 64.53 (C-1′), 73.78 (C-2′), 67.17 (C-3′), 71.53 (C-4′), 74.05 (C-5′), 63.15 (C-6′), 140.31 (C-6), 154.34, 154.73 (C-3, C-8a), 127.60, 129.14, 131.94, 133.74 (Ph); FABMS (DMSO/NBOH), *m/z* (%): 397 (38, $MH^{+\bullet}$). Anal. calcd for $C_{16}H_{20}N_4O_6S$ (396.414): C, 48.47; H, 5.08; N, 14.13. Found: C, 48.05; H, 4.74; N, 14.14.

**3-(Penta- and hexa-*O*-acetyl-D-alditol-1-yl)-6-phenyl-7*H*-1,2,4-triazolo [3,4-b][1,3,4]thiadiazine (19–21).** General procedure: To an ice-cold solution of compounds **16, 17**, and **18** (0.3 g) in pyridine (5 mL), acetic anhydride (5 mL) was added. The reaction mixture was left overnight at room temperature and then poured onto ice-cold water.

**3-(1,2,3,4,5-Penta-*O*-acetyl-D-gluco-pentitol-1-yl)-6-phenyl-7*H*-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine (19).** The resulting syrup was extracted with chloroform, washed with water, dried over anhydrous sodium sulfate and evaporated to dryness. The syrup was chromatographed on silica gel. Elution with 3:1 EtOAc-petroleum ether (60–80°C) gave 19 as a syrup (68%); IR (KBr): 1755 cm$^{-1}$ (OCO); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$: 7.93 (d, 2H, Ph–H), 7.59–7.51 (m, 3H, Ph–H), 6.36 (d, 1H, $J_{1',2'} = 8.57$ Hz, H-1′), 6.09 (dd, 1H, $J_{2',3'} = 2.49$ Hz, H-2′), 5.24 (dd, 1H, $J_{3',4'} = 8.79$ Hz, H-3′), 5.10–5.08 (m, 1H, H-4′), 4.17 (dd, 1H, $J_{4',5'} = 2.85$ Hz, $J_{5',5''} = 12.34$ Hz, H-5′), 4.03, 4.02 (2s, 2H, $SCH_2$), 3.99 (t, 1H, $J_{4',5''} = 4.68$ Hz, H-5″), 2.09, 2.08, 2.05, 1.98, 1.96 (5s, 15H, 5 Ac); $^{13}$C NMR ($CDCl_3$) $\delta_C$: 20.37, 20.43, 20.53, 20.67 (Ac), 23.49 ($SCH_2$), 61.39 (C-5′), 64.06 (C-1′), 67.72, 67.77 (C- 3′, C-4′), 69.39 (C-2′), 127.18, 129.14, 132.30, 133.11 (Ph), 141.32 (C-6), 148.52 (C-3), 154.58 (C-8a), 169.36, 169.43, 169.84, 170.44 (C=O); EIMS, *m/z* (%): 576 (35, $M^{+\bullet}$), 517 (11, $M^{+\bullet} - AcO^\bullet$), 474 (16, 517 − $Ac^\bullet$), 415 (29, 474 − $AcO^\bullet$), 371 (16, 415 − $Ac^\bullet$), 329 (31, 371 − $C_2H_2O$), 245 (86, B–$CHOH^+$), 142 (36, 245 − Ph–C≡$NH^+$), 104 (18, PhC≡$NH^+$). Anal. calcd for $C_{25}H_{28}N_4O_{10}S$ (576.564): C, 52.07; H, 4.89; N, 9.71. Found: C, 51.72; H, 4.25; N, 10.25.

**3-(1,2,3,4,5-Penta-*O*-acetyl-D-galacto-pentitol-1-yl)-6-phenyl-7*H*-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine (20).** The solid obtained was filtered off, washed with water, dried and crystallized from ethanol to give **20** (84%); m.p. 205–207°C; IR (KBr): 1740 cm$^{-1}$ (OCO); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$: 7.95 (d, 2H, Ph–H), 7.59–7.61 (m, 3H, Ph–H), 6.31 (d, 1H, $J_{1',2'} = 1.97$ Hz, H-1′), 5.62 (dd, 1H, $J_{2',3'} = 9.67$ Hz, H-2′), 5.56 (dd, 1H, $J_{3',4'} = 2.16$ Hz, H-3′), 5.39–5.34 (m, 1H, H-4′), 4.31 (dd, 1H, $J_{4',5'} = 5.09$ Hz, H-5′), 4.01, 4.00 (2s, 2H, $SCH_2$), 3.96 (dd, 1H, $J_{4',5''} = 7.56$ Hz, $J_{5',5''} = 11.70$ Hz, H-5″), 2.23, 2.15, 2.03, 1.98, 1.84 (5s, 15H, 5Ac); $^1$H NMR (270 MHz, DMSO-$d_6$) $\delta$: 8.05 (d, 2H, Ph–H), 7.63–7.60 (m, 3H, Ph–H), 6.17 (d, 1H, $J_{1',2'} = 2.64$ Hz, H-1′), 5.59 (dd, 1H, $J_{2',3'} = 6.93$ Hz, H-2′), 5.45

(d, 1H, H-3′), 5.26 (m, 1H, H-4′), 4.53, 4.36 (2d, 2H, $J_{gem} = 15.51$ Hz, $SCH_2$), 4.21 (dd, 1H, $J_{4',5'} = 4.29$ Hz, H-5′), 3.98 (dd, 1H, $J_{4',5''} = 9.26$ Hz, $J_{5',5''} = 11.55$ Hz, H-5″); $^{13}$C NMR ($CDCl_3$) $\delta_C$: 20.39, 20.47, 20.57, 20.64, 20.69 (Ac), 23.78 ($SCH_2$), 62.00 (C-5′), 64.43 (C- 1′), 67.77, 76.86 (C-3′, C-4′), 68.14 (C-2′), 127.25, 129.26, 132.31, 133.55 (Ph), 141.17 (C-6), 148.60 (C-3), 154.44 (C-8a); EIMS, *m/z* (%): 576 (13, $M^{+\bullet}$), 517 (5, $M^{+\bullet}$− $AcO^{\bullet}$), 474 (5, 517 − $Ac^{\bullet}$), 415 (11, 474 − $AcO^{\bullet}$), 371 (6, 415 − $Ac^{\bullet}$), 329 (14, 371 − $C_2H_2O$), 288 (11, 329 − $C_2H_2O$), 245 (33, B–$CHOH^+$), 142 (23, 245−PhC≡$NH^+$), 103 (13, PhC≡$N^{+\bullet}$). Anal. calcd for $C_{25}H_{28}N_4O_{10}S$ (576.564): C, 52.07; H, 4.89; N, 9.71. Found: C, 51.64; H, 4.58, N, 9.68.

**3-(1,2,3,4,5,6-Hexa-*O*-acetyl-D-glycero-D-gulo-hexitol-1-yl)-6-phenyl-7*H*-1,2,4-triazolo[3,4-b][1,3,4]thiadiazine (21).** The syrup obtained was extracted with chloroform. The chloroform solution was washed with water, dried over anhydrous sodium sulfate and evaporated to dryness. The resulting syrup was then chromatographed on silica gel. Elution with 3:1 EtOAc:petroleum ether (60–80°C) gave **21** as a syrup (78%); IR (KBr): 1756 $cm^{-1}$ (OCO); $^1$H NMR (300 MHz, $CDCl_3$) $\delta$: 7.89 (d, 2H, Ph–H), 7.59–7.53 (m, 3H, Ph–H), 6.34 (d, 1H $J_{1',2'} = 7.18$ Hz, H-1′), 5.89 (dd, 1H, $J_{2',3'} = 3.24$ Hz, H-2′), 5.75 (dd, 1H, $J_{3',4'} = 6.28$ Hz, H-3′), 5.45 (dd, 1H, $J_{4'.5'} = 5.02$ Hz, H-4′), 5.02 (q, 1H, H-5′), 4,15 (dd, 1H, $J_{5',6'} = 4.98$ Hz, H-6′), 4.15 (dd, 1H, $J_{5',6''} = 5.97$ Hz, $J_{6',6''} = 11.77$ Hz, H-6″), 4.01 (s, 2H, $SCH_2$), 2.10, 2.09, 2.08, 2.03, 1.99, 1.95 (6s, 18H, 6Ac). $^{13}$C NMR ($CDCl_3$) $\delta_C$: 20.47, 20.49, 20.54, 20.60 (Ac), 23.65 ($SCH_2$), 61.14 (C-6′), 64.32 (C-1′), 67.78 (C-3′), 68.72 (C-5′), 69.08 (C-2′), 69.87 (C-4′), 127.35, 129.14, 130.84, 133.49 (Ph), 141.92 (C-6), 148.33 (C-3), 154.29 (C-8a), 169.03, 169.72, 169.89, 170.22 (C=O); EIMS, *m/z* (%) 648 (39, $M^{+\bullet}$), 588 (10, $M^{+\bullet}$ − $AcO^{\bullet}$), 546 (13, 588 − $C_2H_2O$), 487 (22, 546 − $AcO^{\bullet}$), 443 (5, 487 − $C_2H_4O$), 385 (44), 329 (27), 288 (23, B–$CHOAc^{+\bullet}$ − 1), 245 (60, B–$CHOH^+$), 142 (28, B − PhC≡$NH^{+\bullet}$). Anal. calcd for $C_{28}H_{32}N_4O_{12}S$ (648.63): C, 51.84; H, 4.97; N, 8.63. Found: C, 51.89; H, 5.16; N, 9.01.

## ACKNOWLEDGMENTS

The authors thanks Prof. Dr. R. R. Schmidt and Prof. Dr. E. B. Pedersen for making available some of the spectral measurment at Konstanz University and Odense University, also thanks Dr. Armin Geyer for measuring the NMR spectra.

## REFERENCES

1. Watanabe, K.A. The Chemistry of *C*-Nucleosides. In *Chemistry of Nucleosides and Nucleotides;* Townsend, L.B., Ed.; Plenum Press: New York, 1994, Vol. 3, 421–35; Hanessian, S.; Pernet, A.G. Adv. Carbohydr. Chem. Biochem. **1976**, *33*, 111–88.
2. Knutsem, L.J.S. Nucleosides Nucleotides **1992**, *11*, 961–83; Hacksell, U.; Daves, Jr. G.D., Progr. Med. Chem. **1985**, *22*, 2–65; Chu, C.K.; El-Kabbani, F.M.; Thompson, B.B. Nucleosides Nucleotides **1984**, *3*, 1–31.

3. Buchanan, J.G. Fortschr. Chem. Org. Nat. Prod. **1983**, *44*, 243–99; Ogura, H.; Takahashi, H. Yuki Gosei Kagaku Kyokaishi **1980**, *38*, 756–68; Chem. Abstr. **1981**, *94*, 157143n.; James, S.R. J. Carbohydr. Nucleosides Nucleotides **1979**, *6*, 417–65.
4. Just, G.; Ramjeesingh, M. Tetrahedron Lett. **1975**, 985–88; Huynh-Dinh, T.; Igolen, J.; Bisagni, E.; Marquet, J.P.; Civier, A. J. Chem. Soc., Perkin Trans. 1, **1977**, 761–64.
5. Poonian, M.S.; Nowoswiat, E.F. J. Org. Chem. **1980**, *45*, 203–208.
6. Katagiri, N.; Tabei, N.; Atsuumi, S.; Haneda, T.; Kato, T. Chem. Pharm. Bull. **1985**, *33*, 102–109.
7. Sanghvi, Y.S.; Hanna, N.B.; Larson, S.B.; Fujitaka, J.M.; Willis, R.C.; Smith, R.A.; Robins, R.K.; Revankar, G.R. J. Med. Chem. **1988**, *31*, 330–35.
8. Shen, G.Y.; Robins, R.K.; Revankar, G.R. Nucleosides Nucleotides **1991**, *10*, 1707–717.
9. Witkoaski, J.T.; Robins, R.K.; Sidwell, R.W.; Simon, L.N. J. Med. Chem. **1972**, *15*, 1150–154.
10. Sidwell, R.W.; Huffmann, J.H.; Khare, G.P.; Allene, L.B.; Wikowski, J.T.; Robins, R.K. Science **1972**, *177*, 705–706.
11. Smith, R.A.; Kirkpatrick, W. *Ribavirin: A Broad Spectrum Antiviral Agent*; Academic Press: New York, 1980.
12. Sidwell, R.W.; Revankar, G.P.; Robins, R.K. In *Viral Chemotherapy*; Shugar, D., Ed.; Pergamon Press: New York, 1985; Vol. 2.
13. Smith, R.A.; Knight, V.; Smith, J.A.D. *Clinical Applications of Ribavirin*; Academic Press: New York, 1984.
14. Schneller, S.W.; May, J.L.; De Clercq, E. Croat. Chem. Acta **1986**, *596*, 307–11; Chem. Abst. **1987**, *107*, 7490w.
15. Al Masoudi, N.A.; Al Soud, Y.A.; Geyer, A. Tetrahedron **1999**, *55*, 751–58; Al Masoudi, N.A.; Al Soud, Y.A.; Lagoja, I.M. Carbohydr. Res. **1999**, *318*, 67–74.
16. Awad, L.F.; El Ashry, E.S.H. Carbohydr. Res. **1998**, *312*, 9–22; El Ashry, E.S.H.; Awad, L.F.; Winkler, M. J. Chem. Soc., Perkin Trans. 1, **2000**, 829–34.
17. El Ashry, E.S.H.; El Kilany, Y. Adv. Heterocycl. Chem. **1997**, *67*, 391–432; El Ashry, E.S.H.; El Kilany, Y. Adv. Heterocycl. Chem. **1997**, *68*, 1–88; El Ashry, E.S. H.; El Kilany, Y. Adv. Heterocycl. Chem. **1998**, *69*, 129–215.
18. Kitazaki, T.; Tasaka, A.; Tamura, N.; Matsushita, Y.; Hosono, H.; Hayashi, R.; Okonogi, K.; Itoh, K. Chem. Pharm. Bull. **1999**, *47*, 351–59; Holla, B.S.; Shivananda, M.K.; Shenoy, M.S.; Antony, G. Farmaco **1998**, *53*, 531–35.; Kagawa, T.; Kodama, H.; Goto, Y.; Niwano, Y.; Yoshida, M. PCT Int. Appl. WO 99 **1999**, 33,826; Chem. Abst. **1999**, *131*, 87917z; Eissa, A.A.H. Bull. Fac. Pharm. **1998**, *36*, 99–105; Sikorski, J.A. PCT Int. WO 99 **1999**, *14*, *204*; Chem. Abst. **1999**, *130*, 237570b; Sunakawa, K.; Kumasawa, S.; Hoshi, H.; Nagatsuka, T. Jpn. Kokai Tokkyo Koho JP 11 **1999**, *80*, 126; Chem. Abst. **1999**, *130*, 237571c.
19. Zitouni, G.T.; Kaplancikli, Z.A.; Erol, K.; Kilic, F.S. Farmaco **1999**, *54*, 218–23.; Mohan, J.; Kumar, V. Indian J. Chem. **1998**, *37B*, 183–86; Holla, B.S.; Poojary, K. N.; Kalluraya, B.; Gowda, P.V. Farmaco **1996**, *51*, 793–99; Ilhan, E.; Ergenc, N.; Ulusoy, N.; Ötük-Sanis, G. Pharmazie **1996**, *51*, 123–24; Ergenc, N.; Ulusoy, N.; Capan, G.; Ötük-Sanis, G.; Kiraz, M. Arch. Pharm. Pharm. Med. Chem. **1996**, *329*, 427–30; Kalluraya, B.; Chimbalkar, R. Orient. J. Chem. **1995**, *11*, 242–45.; Mohan, J.; Kataria, S. Indian J. Heterocycl. Chem. **1995**, *5*, 143–44; Holla, B.S.; Kalluraya, B.; Sridhar, K.R.; Drake, E.; Thomas, L.M.; Bhandary, K.K.; Levine, M.J. Eur. J. Med.

Chem., **1994**, *29*, 301–308; Sung, K.; Rong Lee, A. J. Heterocyclic Chem. **1992**, *29*, 1101–109.

20. Abd El Samii, Z.K.M.; El Feky, S.A.H. Alex. J. Pharm. Sci. **1994**, *8*, 127–30.
21. Jacquier, R.; Roumestant, M.L.; Viallefont, P. Bull. Soc. Chim. de France **1967**, *7*, 2630–634.
22. Freiberg, W.; Kröer, C.F.; Radeglia, R. Tetrahedron Lett. **1967**, 2109–112.
23. Potts, K.T.; Huseby, R.M. J. Org. Chem. **1966**, *31*, 3528–531.
24. Bryant Bachman, G.B.; Heisey, L.V. J. Am. Chem. Soc. **1949**, *71*, 1985–988.
25. Barrett, G.C. In *Comprehensive Organic Chemistry*; Jones, D.N., Ed.; Pergamon Press: New York, 1979, Vol. 3, 16.
26. Temple, C., Jr., 1,2,4-Triazoles, In *The Chemistry of Heterocyclic Compound;* Montgomery, J.A., Ed.; John Wiley and Sons: New York, 1981; 7–8.
27. El Dawy, M.A.; Omar, A.M.M.E.; Ismail, A.M.; Hazzaa, A.A.B. J. Pharm. Sci. **1983**, *72*, 45–50.
28. Goswani, B.N.; Kataky, J.C.S.; Baruah, J.N. J. Heterocycl. Chem. **1986**, *23*, 1439–442.
29. Szabo, J.; Fodor, L.; Akoto, E.B.; Talpas, G.S.; Bernath, G. Tetrahedron **1992**, *48*, 4957–962.
30. Angyal, S.J.; Le Fur, R. J. Org. Chem. **1989**, *54*, 1927–931; Lewis, D.; Angyal, S.J. J. Chem. Soc., Perkin Trans. 2, **1989**, 1763–767; Lewis, D. J. Chem. Soc., Perkin Trans. 2, **1986**, 467–70; Hawkes, G.R.; Lewis, D. J. Chem. Soc., Perkin Trans. 2, **1984**, 2073–2078; El Ashry, E.S.H.; El Kilany, Y.; Mousaad, A.; Abdel Hamid, H. Gazz. Chim. Ital. **1988**, *118*, 687–90; Mousaad, A.; Awad, L.F.; El Kilany, Y.; El Ashry, E.S.H. Arab. J. Sci. Eng. **1990**, *15*, 105–110; Rashed, N.; El Nember, A.; El Ashry, E.S.H. Spectrosc. Lett. **1993**, *26*, 1817–838.
31. Abdel Rahman, M.M.; El Ashry, E.S.H.; Abdallah, A.A.; Rashed, N. Carbohydr. Res. **1979**, *73*, 103–111; Seldes, A.M.; Gros, E.G.; Thiel, I.M.E.; Deferrai, J.O. Carbohydr. Res. **1979**, *49*, 49–56; Szilagyl, L.; Bognar, R.; Farkas, I. Carbohydr. Res. **1973**, *26*, 305–13; Binkley, W.W.; Diehl, D.R.; Binkley, R.W. Carbohydr. Res. **1971**, *18*, 459–65; Lemieux, R.U.; Stevens, J.D. Can. J. Chem., **1965**, *43*, 2059–2070.

Received June 13, 2000
Accepted September 29, 2000

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

Downloaded At: 12:32 26 January 2011

**Request Permission or Order Reprints Instantly!**

Interested in copying and sharing this article? In most cases, U.S. Copyright Law requires that you get permission from the article's rightsholder before using copyrighted content.

All information and materials found in this article, including but not limited to text, trademarks, patents, logos, graphics and images (the "Materials"), are the copyrighted works and other forms of intellectual property of Marcel Dekker, Inc., or its licensors. All rights not expressly granted are reserved.

Get permission to lawfully reproduce and distribute the Materials or order reprints quickly and painlessly. Simply click on the "Request Permission/Reprints Here" link below and follow the instructions. Visit the U.S. Copyright Office for information on Fair Use limitations of U.S. copyright law. Please refer to The Association of American Publishers' (AAP) website for guidelines on Fair Use in the Classroom.

The Materials are for your personal use only and cannot be reformatted, reposted, resold or distributed by electronic means or otherwise without permission from Marcel Dekker, Inc. Marcel Dekker, Inc. grants you the limited right to display the Materials only on your personal computer or personal wireless device, and to copy and download single copies of such Materials provided that any copyright, trademark or other notice appearing on such Materials is also retained by, displayed, copied or downloaded as part of the Materials and is not removed or obscured, and provided you do not edit, modify, alter or enhance the Materials. Please refer to our Website User Agreement for more details.

**Order now!**

Reprints of this article can also be ordered at

http://www.dekker.com/servlet/product/DOI/101081NCN100001440