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Synthesis And Antitubercular Activities Of S-Glycosyl Mercaptans#

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ABSTRACT

A series of S-glycosyl alkyl thiols (**3-10**) were synthesised by 1,4 - conjugate addition of sulphur nucleophiles to glycosyl olefinic esters (**1**,**2**). The selected compounds (**3**,**4**,**7**,**8**) on oxidation with $KMnO_4$ resulted in quantitative yield of corresponding sulphones (**11**-**14**). The synthesized compounds were screened against M. tuberculosis, though most of the compound exhibited little activity; however one of them (**15**) exhibited good antitubercular activity in vitro for further optimization

KEYWORDS

Tuberculosis;
Conjugate addition;
DBU;
Glycosyl mercaptans.

INTRODUCTION

Tuberculosis, caused by *M.tuberculosis* is a major public health and socioeconomic problem in most of the developing countries[1-3]. About one third of world's population is currently infected with this disease and number is increasing every year[4]. Resistance against the most effective drugs (rifampicin and isoniazid) and their combination, latent tuberculosis and synergy of HIV infection and tuberculosis warrants the introduction of new class of mechanism based antitubercular agents[1, 5-7]. The mycobacterial cell wall consisting of mainly mycolylated arabinogalactan peptidoglycan (mAGP) complex is implicated in its defense as well as in the transport of nutrients and drugs. Therefore, it is an effective and ideal target to design new drugs[8-10]. The cell wall contributes to greater extent towards resistance development against several drugs and due to incredible thickness of the cell wall the antituberculosis treatment is prolonged[11]. The inhibitors of the enzymes involved in the biosynthesis of different

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macromolecules of mAGP complex are being considered to be developed as new candidtaes for the treatment of tuberculosis. A number of inhibitors of arabinosyl transferase[12], galactopyranosyl mutase[13] and mycolyl transferase[14] implicated in the biosynthesis of the above mAGP complex are known today. These inhibitors are either unnatural sugars or natural sugars with appendages and they exhibit moderate to good antitubercular activity. In an ongoing programme to develop new anti-TB drugs, we and others have synthesized certain glycofuranoses and glycopyranoses as antitubercular agents[15-20].

We have very recently reported potent antitubercular activities in a series of glycosyl aminoesters and alcohols bearing alkyl substitutents at the nitrogen atom. As glycosyl amino ester with alkyl chains and many other glycoconjugates with nitrogen atom are known to exhibit very good antitubercular activity[15, 16]. This study prompted to see the effect of 'S' in place of 'N' on antitubercular activity profiles of such compounds. The choice of thioalkyl group is also based on the facts that isoxyl and thioacetazone are known to inhibit the mycolic acid biosynthesis in M. tuberculosis and posses both in vitro and in vivo good antitubercular activity[21, 22]. In this communication we report the conjugate addition of different thiols to the glycosyl olefinic esters and subsequent oxidation of the selected glycosyl sulphides to the respective sulphones. All the synthesized compounds were evaluated for their in vitro antitubercular activities.

RESULTS AND DISCUSSION

Chemistry

The starting glycosyl olefinic ester (1R, 2R, 3S, 4R) ethyl- (3-O-methyl/ benzyl-1, 2-O-isopropylidine-1, 4-pentofuranose-4-yl)-hept-5-enoate (1 and 2) were synthesised by our earlier reported methods[15, 20].

To start with reaction of glycofuranosyl olefinic ester **(1)** with thiophenol in presence of diazabicyclo [5.4.0] undec-7-ene (DBU) led to the formation of ethyl (5,6-dideoxy-1,2-O- isopropylidene-3-O-methyl-5-phenylsulfanyl)-α-D-gluco- and β-L-idoheptofuranuronate **(3)** as a diastereoisomeric mixture (11:9) in good yield (SCHEME 1). The minor and major isomers were isolated by column chromatography and the structures were established on the basis of spectroscopic data and analysis. Similarly, reaction of glycosyl olefinic ester **(1)** with other sulphur nucleophiles viz 4-chlorobenzenemethane thiol, 2-mercapto ethanol, 3-mercapto-1, 2-propan-diol) to above glycosyl olefinic ester **(1)** led to the formation of respective S-aryl or alkyl glycofuranoses **(4-6)** as distereoisomeric mixtures (TABLE 1). Structures of all the above compounds were established on the basis of their spectroscopic data and analysis.

As hydrophobicity or lipophilicity in compounds generally increases the antitubercular activity[23], we were interested to compare the biological activity of 3-O-methyl xylofuranosyl series with those of 3-O-benzyl-xylofuranosyl. Thus conjugate addition of the above sulphur nucleophiles with the glycosyl olefinic ester **(2)** having a 3-O-Benzyl substituent in sugar led to the formation of respective S-aryl or alkyl derivatives**(7-10)** in good yields with better diastereoselectivity. The ratio of major and minor isomers in each case were determined on the basis of ^{1}H NMR spectrum of the respective reaction product and the structures of all the synthesized S-glycosyl mercaptans were established on the basis of their spectroscopic data and analysis. The formation of diastereoisomers was evident from TLC and ^{1}H NMR spectral data. The isomers were separated in few reactions by column chromatography in pure form.

The better diastereoselection in such a conjugate addition of amines to the 3-O-benzyl-glycosyl olefinic esters has already been rationalized during conjugate addition of amines to glycosyl olefinic ester in terms of Felkin- Anh transition state model by us and others[16, 20 and 23]. It is speculated that out of several possible transition states, the transition state shown in figure 1 is most favored; because of the presence of alkene arene II - stacking effect[24], while the latter is absent in the transition state formed from 3-O-methyl glycosyl olefinic ester **(1)**.

The antimicrobial activities associated with sulphones[25-27] prompted us to synthesise sulphones from the glycosyl sulphides. Thus the above glycosyl mercaptans**(3,4,7)** and **(8)** either with mCPBA in AcOH or $KMnO_4$ in CH_2Cl_2 resulted into respective glycosyl sulphones**(11-14)** in almost quantitative yields (TABLE 1). The structures of sulphones were

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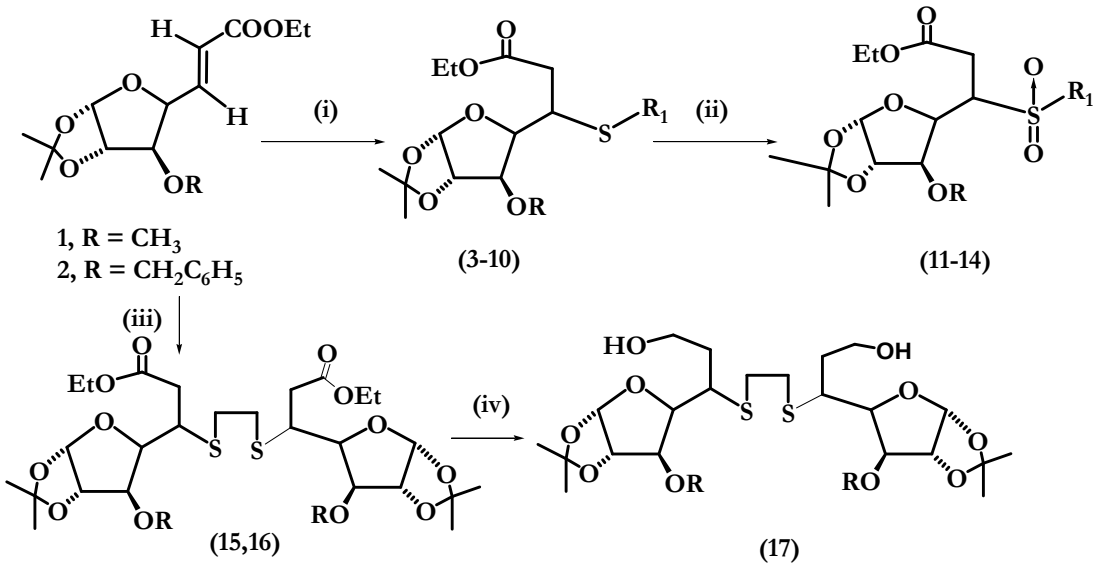


SCHEME 1: Reagents and condition (i) R1SH, DBU, C2H5OH, 8-10h, r.t. (ii) KMnO4, ACOH, 4-6h, r.t. (iii)HS(CH2)2SH, DBU, EtOH, rt, 8h (iv) LiAlH4, THF, 0-rt,2h

established on the basis of their spectroscopic data and analysis. In the ^{13}C NMR spectra of sulphones, the carbon adjacent to SO_2- group (i.e. C-5 and CH_2Ar or Ar) shifted downfield in comparison to their corresponding sulphides, while the carbons at β-position (i.e. C-4 and C-6) were shifted up-field and similar shifting of signals were observed in their ^1H NMR Spectra.

In another experiment, a dimercaptan was used as nucleophile to get S, S-diglycosyl derivatves as shown in SCHEME 1. Thus conjugate addition of 1,2-ethanedithiol to the olefinic esters **(1)** and **(2)** separately as above gave compounds **(15)** and **(16)** respectively, both as a mixture of three diastereomers i.e.compound having β-L-ido (S) configuration at C-

TABLE 1: Synthesis of glycosylated mercapto esters and its corresponding sulphones

Entry	Comp. No.	R	R^1	Major: minor	Yield (%)
1	3	CH_3	C_6H_5-	55:45	90
2	4	CH_3	4-Cl-$C_6H_4CH_2$-	58:42	90
3	5	CH_3	$HOCH_2CH_2$-	54:45	90
4	6	CH_3	$HOCH_2CH(OH)CH_2$-	55:45	90
5	7	$CH_2C_6H_5$	C_6H_5	70:30	90
6	8	$CH_2C_6H_5$	4-Cl-$C_6H_4CH_2$-	71:29	90
7	9	$CH_2C_6H_5$	$HOCH_2CH_2$-	68:32	90
8	10	$CH_2C_6H_5$	$HOCH_2CH(OH)CH_2$-	72:28	90
9	11	CH_3	C_6H_5-	na	92
10	12	CH_3	4-Cl-$C_6H_4CH_2$-	na	90
11	13	$CH_2C_6H_5$	C_6H_5-	na	93
12	14	$CH_2C_6H_5$	4-Cl-$C_6H_4CH_2$-	na	90
13	15	CH_3	SCH_2CH_2-	52:44:6	92
14	16	$CH_2C_6H_5$	SCH_2CH_2-	60:36:4	90
15	17	CH_3	SCH_2CH_2-	na	95
16	19	--	4-Cl-$C_6H_4CH_2$-	60:40	95
17	20	--	4-Cl-$C_6H_4CH_2$-	na	94

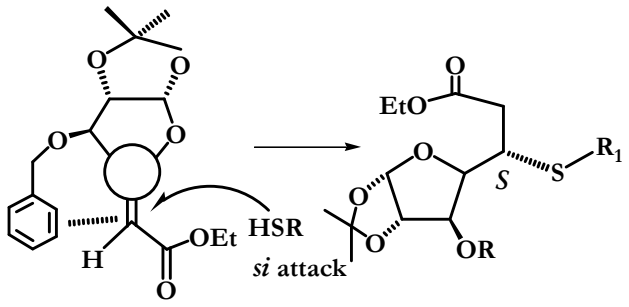


Figure 1: Favorable Felkin-Ahn transition state model leads to diastereoselection

5 in both sugar units, compound having β-L-ido (S) configuration at C-5 in one sugar and α-D-gluco (R) configuration in the other sugar portion and compound having α-D-gluco (R) configuration at C-5 in both sugar units as evident from TLC and ^{1}HNMR spectra of the reaction mixture. The diastereoismers, however, could not be isolated in pure forms even by repeated column chromatography.

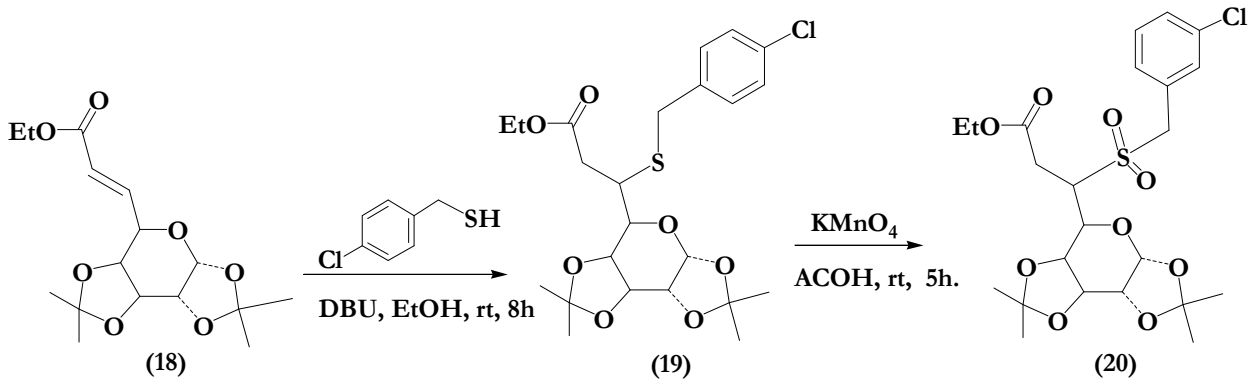
Finally, a glycosyl sulphide and its sulphone having a pyranose ring instead of furanose ring to see the effect of ring size on antitubercualar activity profile. Thus galactopyranosylated olefinic ester **(18)**[28] on reaction with 4-chlorophenyl methanthiol led to the formation of respective S-aryl galactopyranosyl ester **(19)** as a mixture of diastereoisomers, which on subsequent oxidation with $KMnO_4$ in acetic acid led to the formation of galactopyranosyl aryl sulphone **(20)** in good yield (SCHEME 2).

Biology

All of the compounds synthesized were evaluated for their antitubercular efficacy against *M.tuberculosis* H37Ra, *M.tuberculosis* H37Rv and *M. smegmatis* using MABA assay[29] and agar micro dilution method[30] and the results are depicted in TABLE 2. As evident from TABLE 2, except compound **(15)** none of the compounds showed prominent activity against any of the mycobacterial strains. A closer look into the inhibitory potential of these S-glycosyl mercaptans indicated that compounds with terminal hydroxyl functionality in the S-alkyl chain (compounds **(6, 9)** and **(10)**) were more active than those with thiophenyl or substituted thiophenyl or simple S-alkyl derivatives **(3,4,7)** and **(8)**. The conversion of glycosyl sulphides **(3,4,7)** and **(8)** into corresponding sulphones **(11-14)** did not resulted in any enhancement of the biological activities. Introduction of a lipophilic chlorine substituent at 4′- position in the phenyl sulphide glycosyl mercapto esters **(4 and 8)** also did not led to any beneficial effect on antitubercular activity. However, a compound with two sugar moieties, having 3-O-methyl substitutent, flanked by dimercapto ethylene spacer (compound **(15)**) showed significant antitubercular activity. Compound **(15)** causes complete inhibition of M. tuberculosis strain at 6.25 μg/mL. Further, conversion of ester **(15)** to alcohol **(17)** and replacement of 3-O-methyl substitutent (compound **(15)**) with 3-O-benzyl substituent **(16)** resulted in loss of antitubercular activity indicating that carbethoxy group is essential for activity and 3-O-substitutent should not be bulky in the sugar ring.

EXPERIMENTAL

1. Chemistry



SCHEME 2: Synthesis of galactopyranosyl mercaptan

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TABLE 2: Antitubercular activities of glycosylated mercapto and related compounds

Compounds	MIC (μg/mL) *M. tuberculosis* $H_{37}Ra$	MIC (μg/mL) *M.tuberculosis* $H_{37}RV$	MIC (μg/mL) *M.Smegmatis* (ATCC 607)
3	50	50	>12.5
4	>50	>50	>12.5
5	50	>50	>12.5
6	>25	>25	>12.5
7	>100	>100	>12.5
8	>100	>100	>12.5
9	>25	>50	>12.5
10	>50	>50	>12.5
11	>100	>100	>12.5
12	>100	>100	>12.5
13	>100	>100	>12.5
14	>100	>100	>12.5
15	12.5	6.25	>12.5
16	>25.0	>25.0	>12.5
17	25	12.5	>12.5
19	100	> 50	>12.5
20	>100	>100	>12.5
INH	-	0.02	-
RIF	-	0.2	-
ETB	-	2.0	-

1.1 General methods

Thin-layer chromatography was carried out on silica gel (Kiesel 60-F254, Merck) and spots were developed in iodine vapors and also by spraying with 5% sulfuric acid in alcohol followed by heating at 100°C. Column chromatography was carried out on flash silica gel (230-400 mesh, Merck) using the indicated eluent. IR spectra were recorded as thin films on KBr plates with a Perkin-Elmer 881 spectrophotometer. NMR spectra were recorded on Bruker spectrometers 200 and 300 MHz and reference used was $CDCl_3$. Chemical shifts were given as d ppm values and 'J' values were given in Hertz (Hz). Elemental analyses were performed on a Perkin-Elmer 2400 II elemental analyzer. The optical rotations were measured in a 1.0 diameter tube with Jasco dip-140 polarimeter in chloroform. The excess of the reagents or solvents were evaporated under reduced pressure at a bath temperature between the ranges 55 and 60°C.

1.1. Ethyl (5,6-dideoxy-1,2-O-isopropylidene- 3-O-methyl-5- phenyl sulfan- yl)- α- D-gluco and β-L-ido-heptofuranuronate (3)

A solution of (1R, 2R, 3S, 4R) ethyl- [3-O-methyl-1, 2-O-isopropylidene-1, 4-pentofuranose-4-yl]-hept-5-enoate (**(1)**, 2.0 g, 7.35 mmoles), thiophenol (0.76 ml, 7.41 mmoles) and DBU (0.2 ml, 1.32 mmoles) in ethanol (10 ml) was magnetically stirred at room temperature for 10 hours. The solvent was evaporated under reduced pressure and the crude mass thus obtained, was dissolved in ethyl acetate (2 × 100 ml), washed with water (2 × 20 ml) and dried over anhydrous sodium sulphate. Ethyl acetate layer was then evaporated under reduced pressure to get syrup, which latter on column chromatography (SiO_2) using ethyl acetate: hexane (12:88) as eluant afforded the required compound **(3)** as colorless oil (diastereomeric ratio 11:9, Yield 94%). IR (KBr): ν_{max} cm^{-1} 2989, 2933 and 2831 (CH_3 and CH_2 stretching), 1734 (C=O), 1582 (C=C); MS (FAB): 383 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.56 (m, 2H, Ar-H), 7.26 (m, 3H, Ar-H), 5.83 (d, J = 3.8 Hz, 1H, H-1), 4.51 (d, J = 3.7 Hz, 1H, H-2), 4.15 (m,

3H, H-4 and -OCH_2CH_3), 3.81 (d, J = 2.5 Hz, 1H, H-3), 3.38 (m, 1H, H-5), 3.10 (s, 3H, OCH_3), 2.95 and 2.62 (m, 2H, H-6), 1.46 and 1.30 [each s, each 3H, $C(CH_3)_2$], 1.24 (t, J = 7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 171.75 (-COOEt), 133.82, 133.47, 129.18 and 127.97 (Ar-C), 112.05 [$C(CH_3)_2$], 105.38 (C-1), 83.42 (C-2), 82.59 (C-4), 81.48 (C-3), 60.93 (-OCH_2CH_3), 57.31 (OCH_3), 42.96 (C-5), 38.00 (C-6), 27.09 and 26.65 [2×$C(CH_3)_2$], 14.59 (OCH_2CH_3); Anal.calcd for $C_{19}H_{26}SO_6$: C, 59.68; H, 6.80; Found: C, 58.55; H, 7.12 %.

1.2. Ethyl [5-p-chloro-benzylsulfanyl-5,6-dideoxy-1,2-O-isopropylidene- 3-O-methyl]- α-D-gluco and β-L-ido-heptofuranuronate (4)

It was obtained by the reaction of compound **(1)** (1.6 g, 5.88 mmoles) with 4-chlorobenzenemethanethiol (0.78 ml, 5.92 mmoles) in presence of DBU (0.17 ml, 1.12 mmoles) as described above and isolated as colorless oil (diastereomeric ratio 58:42, Yield 92%).

(4a): $[\alpha]_D^{25}$ -72.0 (c 0.075, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2936 and 2854 (CH_3 and CH_2 stretching), 1727 (C=O), 1558 (C=C); MS (FAB): 431 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.26 (m, 4H, Ar-H), 5.84 (d, J = 3.8 Hz, 1H, H-1), 4.54 (d, J = 3.8 Hz, 1H, H-2), 4.16 - 4.08 (m, 3H, H-4 and -OCH_2CH_3), 3.83 (d, J = 3.0 Hz, 1H, H-3), 3.81 (s, 2H, SCH_2), 3.41 (m, 1H, H-5), 3.35 (s, 3H, OCH_3), 2.95 and 2.87 (dd, J = 8.9 Hz and 16.0 Hz, 1H, H-6_A), 2.66 and 2.58 (dd, J = 8.9 Hz and 16.0 Hz, 1H, H-6_B), 1.45 and 1.30 [each s, each 3H, $C(CH_3)_2$], 1.25 (t, J = 7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 171.81 (-COOEt), 137.50, 133.28, 130.80 and 129.05 (Ar-C), 112.03 [$C(CH_3)_2$], 105.47 (C-1), 85.08 (C-2), 82.24 (C-4), 81.35 (C-3), 60.89 (-OCH_2CH_3), 57.78 (OCH_3), 39.64 (C-5), 38.51 (C-6), 35.48 (SCH_2), 27.12 and 26.64[2×$C(CH_3)_2$], 14.61 (OCH_2CH_3); Anal. calcd for $C_{20}H_{27}SO_6Cl$: C, 55.81; H, 6.28; Found: C, 54.65; H, 6.40 %.

(4b): $[\alpha]_D^{25}$ -5.33 (c, 0.075, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2934, 2984 and 2833 (CH_3 and CH_2 stretching), 1733 (C=O), 1597 (C=C); MS (FAB): 431 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.27 (m, 4H, Ar-H), 5.89 (d, J = 3.9 Hz, 1H, H-1), 4.52 (d, J = 3.9 Hz, 1H, H-2), 4.21 - 4.08 (m, 3H, H-4 and -OCH_2CH_3), 3.87 (s, 2H, SCH_2), 3.69 (d, J = 3.2 Hz, 1H, H-3), 3.41 (m, 1H, H-5), 3.38 (s, 3H, OCH_3), 2.77 and 2.69 (dd, J = 4.02 Hz and 16.1 Hz, 1H, H-6_A), 2.56 and 2.48 (dd, J = 9.4 Hz and 16.1 Hz, 1H, H-6_B), 1.44 and 1.31 [each s, each 3H, $C(CH_3)_2$], 1.25 (t, J = 7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 171.84 (-COOEt), 137.67, 133.13, 130.81 and 128.94 (Ar-C), 112.03 [$C(CH_3)_2$], 105.40 (C-1), 85.10 (C-2), 83.14 (C-4), 81.46 (C-3), 60.99 (-OCH_2CH_3), 57.81 (OCH_3), 41.03 (C-5), 37.27 (C-6), 37.13 (SCH_2), 27.16 and 26.69 [2×$C(CH_3)_2$], 14.59 (OCH_2CH_3); Anal. calcd for $C_{20}H_{27}SO_6Cl$: C, 55.81; H, 6.28; Found: C, 54.65; H, 6.40 %.

1.3. Ethyl [5,6-dideoxy-5-hydroxymethylsulfanyl - 1, 2-O- isopropylidene- 3-O-methyl]- α- D-gluco and β-L-ido-heptofuranuronate (5)

It was obtained by the reaction of compound **(1)** (1.5 g, 5.52 mmoles), 2-mercapto-1-ethanol (0.44 ml, 6.28 mmoles) and DBU (0.15 ml, 0.99 mmoles) as described above and isolated as colorless oil (diastereomeric ratio 54:45, Yield 92 %). MS (FAB): 351 $(M+H)^+$; IR (KBr): ν_{max} cm^{-1} 3757, 3465 (OH), 2993 and 2937 (CH_3 and CH_2 stretching), 1727 (C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 5.90 and 5.86 (d, J = 3.9 and 3.8 Hz, 1H, diastereomeric H-1), 4.60 (d, J = 3.8 Hz, 1H, diastereomeric H-2), 4.22 - 4.15 (m, 3H, H-4 and -OCH_2CH_3), 3.90 (d, J = 2.9 Hz 1H, H-3), 3.76 (d, J = 5.4 Hz, 2H, $HOCH_2$), 3.71(d, J = 2.8 Hz 1H, H-3'), 3.43 and 3.39 (each s, each 3H, OCH_3), 3.15 (m, 1H, H-5), 2.82 and 2.56 (m, 4H, H-6 and SCH_2), 2.25 (bs, 1H, OH), 1.49 and 1.32 [each s, each 3H, $C(CH_3)_2$], 1.26 (t, J = 7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 172.50 and 171.91 (-COOEt), 112.05 [$C(CH_3)_2$], 105.34 and 105.04 (C-1), 84.35 and 83.77 (C-2), 83.59 and 83.06 (C-4), 81.50 and 81.10 (C-3), 61.47, 61.37, 61.25 and 61.12 ($HOCH_2$, OCH_2CH_3), 57.82 and 57.40 (OCH_3), 40.63 and 38.83 (C-5), 38.79, 37.48, 36.69 and 35.35 (CH_2 and C-6), 27.11 and 26.60 [2× $C(CH_3)_2$], 14.55 (OCH_2CH_3); Anal.calcd for $C_{15}H_{26}SO_6$: C, 51.43; H, 7.43; Found: C, 50.75; H, 7.17 %.

1.4. Ethyl [5,6-dideoxy-5 (2,3-dihydroxy-propyl sulfanyl)- 1, 2-O- isopropylidene-3-O-methyl]- α-D-gluco and β-L-ido-heptofuranuronate (6)

It was obtained by the reaction of compound **(1)** (1.3 g, 4.78 mmoles), 3-mercapto-1, 2-propa-diol (0.4

ml, 4.80 mmoles) and DBU (0.13 ml, 0.85 mmoles) as described above and isolated as colorless oil (diastereomeric ratio 55:45, Yield 90 %). $[\alpha]_D^{25}$ - 13.0 (c, 0.10, $CHCl_3$); IR(KBr): ν_{max} cm^{-1} 3760 and 3433 (OH), 3020, 2935 and 2881 (CH_3 and CH_2 stretching), 1726 (C=O); MS(FAB): 381 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ5.90 and 5.86 (d, J=3.8 Hz, 1H, diastereomeric H-1), 4.60 (d, J=3.8 Hz, 1H, diastereomeric H-2), 4.17 (m, 3H, H-4 and -OCH_2CH_3), 3.91(m, 2H, CH_2OH), 3.67 (d, J=3.4 Hz, 1H, H-3), 3.42(m, 4H, H-5 and -OCH_3); 2.78 and 2.63 (m, 4H, H-6 and SCH_2), 2.25 (bs, 1H, OH); 1.49 and 1.32[each s, each 3H, $C(CH_3)_2$], 1.25 (t, J= 7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 172.88 and 172.00(-COOEt), 112.21 and 112.10[$C(CH_3)_2$], 105.38 and 105.32(C-1), 84.19 and 83.94(C-2), 82.38 and 83.21 (C-4), 81.15 and 81.42 (C-3), 72.06 and 71.40(CHOH), 65.66 and 65.60 (CH_2OH), 61.31 and 60.78(OCH_2CH_3), 57.46 and 57.87 (OCH_3), 41.65 and 41.02(C-5), 38.72 and 38.55 (SCH_2), 35.81 and 35.64 C-6), 27.12 and 26.60 [2×$C(CH_3)_2$], 14.56 (OCH_2CH_3); Anal.calcd for $C_{15}H_{26}SO_8$: C, 47.37; H, 6.84; Found: C, 48.74; H, 7.12%.

1.5. Ethyl [3-O-benzyl-5,6-dideoxy-1,2-O-iso propylidene- 5- phenyl sulfan -yl]- α- D-gluco and β-L-ido-heptofuranuronate (7)

It was obtained by the reaction of compound **(2)** (2.5 g, 7.18mmoles), thiopheno(0.74ml, 7.22 mmoles) and DBU(021 ml, 1.38 mmoles) as described above and isolated as colourless oil (diastereomeric ratio 70:30, Yield 94 %). $[\alpha]_D^{25}$ - 40.0 (c, 0.162, $CHCl_3$); IR(KBr): ν_{max} cm^{-1} 2984, 2932 and 2874 (CH_3 and CH_2 stretching), 1734(C=O), 1581 (C=C); MS(FAB): 459 $(M+H)^+$; ^1H NMR(200 MHz, $CDCl_3$): δ 7.58 and 7.27(m, 10H, Ar-H), 5.97 and 5.86 (each d, each J=3.7 Hz, 1H, H-1, diastereomeric proton), 4.66 - 4.45 (m, 3H, H-2 and -OCH_2Ar), 4.18 (m, 3H, H-4 and -OCH_2CH_3), 3.83 (d, J = 2.5 Hz, 1H, H-3), 3.43 (m, 1H, H-5), 2.95 and 2.65 (m, 2H, H-6), 1.49 and 1.29 [each s, each 3H, $C(CH_3)_2$], 1.24 (t, J=7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR($CDCl_3$): δ171.71 and 171.22(-COOEt), 135.64, 133.85, 129.30, 129.18, 128.71, 128.63, 128.54, 128.44, 128.16 and 128.02(Ar-C), 112.06 and 112.03[$C(CH_3)_2$], 105.43 and 105.21(C-1), 82.31 and 82.29 (C-2), 82.18 and 82.08 (C-4), 81.82 and 80.39(C-3), 72.63 and 72.06(-OCH_2Ar), 61.00 and 60.88 (-OCH_2CH_3), 44.02 and 42.73(C-5), 38.00 and 36.74(C-6), 27.17, 27.08 and 26.74[2×$C(CH_3)_2$], 14.66 and 14.62(OCH_2CH_3); Anal.calcd for $C_{25}H_{30}SO_6$: C, 65.50; H, 6.55; Found: C, 64.28; H, 6.35%.

1.6. Ethyl [3-O-benzyl- 5- p-chloro-benzylsulfanyl-5,6-dideoxy-1, 2-O- isopropylidene- 3-O-methyl-]- α- D-gluco and β-L-iodo-heptofuran- uronate (8)

It was obtained by the reaction of compound **(2)** (2.2 g, 6.32 mmoles), 4-chlorobenzenemethanethiol (0.84 ml, 6.38 mmoles) and DBU (0.18 ml, 1.38 mmoles) as described above and isolated as colorless oil (diastereomeric ratio 71:29, Yield 92 %).

(8a): $[\alpha]_D^{25}$ - 8.0 (c 0.087, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2970 and 2894 (CH_3 and CH_2 stretching), 1725 (C=O); MS (FAB): 507 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.25 (m, 5H, Ar-H), 7.14 (d, J = 8.6 Hz, 4H, Ar-C), 5.86 (d, J = 3.7 Hz, 1H, H-1), 4.68 (d, J = 11.6 Hz, 1H, OCH_APh), 4.56 (d, J = 3.7 Hz, 1H, H-2), 4.52(d, J = 11.6 Hz, 1H, OCH_BPh), 4.18 - 4.08(m, 4H, H-3, H-4 and -OCH_2CH_3), 3.78 (d, J = 13.1 Hz, 1H, SCH_AAr), 3.68 (d, J = 13.1 Hz, 1H, SCH_BAr), 3.46 (dt, J = 4.4 Hz and 9.0 Hz, 1H, H-5), 2.95 and 2.87(dd, J = 4.5 Hz and 16.0 Hz, 1H, H-6_A), 2.69 and 2.61(dd, J = 8.9 Hz and 16.0 Hz, 1H, H-6_B), 1.44 and 1.29 [each s, each 3H, $C(CH_3)_2$], 1.21 (t, J = 7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR($CDCl_3$): δ 171.80(-COOEt), 137.79, 137.37, 133.26, 130.59, 129.04, 128.89 and 128.08(Ar-C), 112.11 [$C(CH_3)_2$], 105.50 (C-1), 82.52(C-2), 82.41(C-4), 82.12 (C-3), 72.56 (OCH_2Ph), 60.90 (-OCH_2CH_3), 40.02 (C-5), 38.21 (C-6), 34.99 (SCH_2), 27.16 and 26.68 [2× $C(CH_3)_2$], 14.62 (OCH_2CH_3),

(8b): $[\alpha]_D^{25}$ - 38.66(c 0.075, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2980 and 2957(CH_3 and CH_2 stretching), 1725 (C=O); MS (FAB): 507 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.32-7.25 (m, 9H, Ar-H), 5.92 (d, J = 3.8 Hz, 1H, H-1), 4.66 (d, J = 11.7 Hz, 1H, OCH_APh), 4.59 (d, J = 3.8 Hz, 1H, H-2), 4.45 (d, J = 11.7 Hz, 1H, OCH_BPh), 4.17 - 4.05 (m, 3H, H-4 and -OCH_2CH_3), 3.95 - 3.89 (m, 2H, H-3 and SCH_AAr), 3.82 (d, J=13.1Hz, 1H, SCH_BAr), 3.50 - 3.39 (dt, J=3.8Hz and 9.4Hz, 1H, H-5), 2.57 and 2.49 (dd, J=4.0Hz and 15.9 Hz, 1H, H-6_A), 2.41 and 2.33 (dd, J=9.7Hz and 15.9Hz, 1H, H-6_B), 1.45 and 1.31[each s, each 3H, $C(CH_3)_2$], 1.20 (t, J=7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR($CDCl_3$): δ 171.47(-

COOEt), 137.66, 137.47, 133.06, 130.92, 128.88, 128.47 and 128.29 (Ar-C), 112.09 [$C(CH_3)_2$], 105.39 (C-1), 83.61 (C-2), 82.53 (C-4), 82.01 (C-3), 72.18 (OCH_2Ph), 60.96 (-OCH_2CH_3), 40.55 (C-5), 37.17 (C-6), 36.98 (SCH_2), 27.15 and 26.64 [2 × $C(CH_3)_2$], 14.56 (OCH_2CH_3); Anal.calcd for $C_{26}H_{31}SO_6Cl$: C, 61.66; H, 6.13; Found: C, 60.89; H, 6.01 %.

1.7. Ethyl [3-O-benzyl -5,6-dideoxy-5-hydroxy methylsulfanyl - 1, 2-O- isopropylidene]- α- D-gluco and β-L-ido-heptofuranuronate (9)

It was obtained by the reaction of compound **(2)** (0.5 g, 1.44 mmoles), 2-mercapto-1-ethanol (0.105 ml, 1.50 mmoles) and DBU (0.05ml, 0.33 mmoles) as described above and isolated as colorless oil (diastereomeric ratio 58:32, Yield 90 %). $[\alpha]_D^{25}$ - 31.8 (c, 0.13, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 3414 (OH), 2984, 2932 and 2878 (CH_3 and CH_2 stretching), 1728 (C=O), 1649 (C=C); MS (FAB): 427 $(M+H)^+$; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.33 (m, 5H, ArH), 5.93 and 5.89(d, J=3.6 Hz, 1H, diastereomeric H-1), 4.70(d, J=12 Hz, 1H, OCH_APh), 4.65(m, 3H, OCH'_APh, H-2 and H-2'), 4.50 and 4.40(each d, J=12.0 Hz, each 1H, OCH_BPh), 4.21-4.16(m, 6H, diastereomeric OCH_2CH_3 and H-4), 3.86(m, 2H, diastereomeric H-3), 3.72 (m, 4H, CH_2OH, diastereomeric H), 3.45 (m, 2H, H-5) 2.88 -2.69(m, 8H, H-6 and SCH_2), 1.49 and 1.32 [each s, each 3H, $C(CH_3)_2$], 1.25(m, 6H, diastereomeric OCH_2CH_3); ^{13}C NMR($CDCl_3$): δ 172.59 and 171.78 (-COOEt), 137.59, 137.13, 128.94, 128.91, 128.68, 128.59, 128.39 and 128.04(Ar-C), 112.22 and 112.15 [$C(CH_3)_2$], 105.36 and 105.05 (C-1), 83.75 and 83.04 (C-2), 82.31 and 82.12(C-4), 81.85 and 81.34(C-3), 72.19 and 71.99 (OCH_2Ph), 61.44, 61.28, 61.18, 60.79, 41.70, 37.27, 36.64 and 34.82($HOCH_2$, OCH_2CH_3, SCH_2 and C-6), 40.43 and 38.60(C-5), 27.13 and 26.63[2×$C(CH_3)_2$], 14.57(OCH_2CH_3); Anal.calcd for $C_{21}H_{30}SO_7$: C, 59.15; H, 7.04; Found: C, 58.95; H, 7.16 %.

1.8. Ethyl[3-O-benzyl-5,6-dideoxy -5(2,3-dihydroxy-propylsulfanyl)-1, 2-O-isopropyli- dene]-α-D-gluco and β-L-ido-heptofuranuronate (10)

It was obtained by the reaction of compound **(2)** (0.7g, 2.01 mmoles), 3-mercapto-1,2-propa-diol (0.17ml, 2.04 mmoles) and DBU(0.07ml, 0.46 mmoles) as described above and isolated as colorless oil(diastereomeric ratio 72:28, Yield 90%). **(10a)**: $[\alpha]_D^{25}$ -16.0(c, 0.15, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 3684 and 3450 (OH), 3020, 2932 and 2882 (CH_3 and CH_2 stretching), 1726(C=O), 1608(C=C); MS (FAB): 457 $(M+H)^+$; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.33 (m, 5H, Ar-H), 5.89 (d, J=3.6 Hz, 1H, H-1), 4.70-4.58(m, 4H, OCH_2Ph, H-2 and H-4), 3.80 (m, 2H, H-3 and CHOH), 3.52 (m, 2H, CH_2OH), 3.42 (m, 1H, H-5), 2.69-2.55(m, 4H, H-6 and SCH_2), 1.49 and 1.31 [each s, each 3H, $C(CH_3)_2$], 1.25 (t, J=7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 172.80 (-COOEt), 137.5, 128.37, 127.96 and 127.79 (Ar-C), 112.17 [$C(CH_3)_2$], 105.40 (C-1), 83.17 and 83.80 (C-2), 82.42 and 82.35 (C-4), 81.86 and 81.75 (C-3), 72.16 and 72.02 (OCH_2Ph), 70.39 (CHOH), 66.00 and 65.52 (CH_2OH), 61.29 (OCH_2CH_3), 40.15 and 39.28 (C-5), 38.55 and 38.44 (SCH_2), 35.41 and 35.22 (C-6), 27.17 and 26.63 [2×$C(CH_3)_2$], 14.56 (OCH_2CH_3); **(10b):** $[\alpha]_D$ - 29.8 (c, 0,15, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 3540 (OH), 2935 and 2890(CH_3 and CH_2 stretching), 1728 (C=O), 1610(C=C); MS(FAB): 457 $(M+H)^+$; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.32 (m, 5H, Ar-H), 5.93 (d, J=3.8 Hz, 1H, H-1), 4.70 (d, J= 3.8 Hz, 1H, OCH_APh), 4.65 (d, J=3.8 Hz, 1H, H-2), 4.41 (d, J=11.9 Hz, 1H, OCH_BPh), 4.12 (m, 3H, H-4, OCH_2CH_3), 3.85 (d, J=2.4 Hz, 1H, H-3), 3.65 (m, 1H, CHOH), 3.50 (m, 3H, H-5 and CH_2OH), 3.10 (bs, 2H, OH), 2.75 (m, 2H, SCH_2), 2.30 (m, 2H, H-6), 1.50 and 1.32 [each s, each 3H, $C(CH_3)_2$], 1.26 (t, J=7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 171.78 (-COOEt), 137.08, 128.96, 128.65 and 127.94 (Ar-C), 112.28 [$C(CH_3)_2$], 105.01(C-1), 84.05 and 83.40 (C-2), 82.21 and 82.09 (C-4), 81.30 and 81.22 (C-3), 71.99(OCH_2Ph), 71.48 and 70.71 (CHOH), 65.77 and 65.71(CH_2OH), 61.30 (OCH_2CH_3), 41.50 and 40.72(C-5), 37.34, 37.09 and 36.95(SCH_2 and C-6), 27.13 and 26.63[2× $C(CH_3)_2$], 14.58(OCH_2CH_3); Anal.Calcd for $C_{21}H_{30}SO_8$: C, 55.26; H, 6.58; Found: C, 55.12; H, 6.48 %.

1.9. Ethyl [5- benzene sulfonyl- 5,6-dideoxy-1,2-O- isopropylidene- 3-O-methyl]- α- D-gluco and β-L-ido-heptofuranuronate (11)

Compound **(3)** (0.28 g, 0.74 mmoles) dissolved in glacial acetic acid (5 ml), was magnetically stirr with $KMnO_4$ (0.12 g, 0.76 mmoles) at room temperature for 5 hours. Reaction mixture was quenched

by adding few drops of H_2O_2 then it was concentrated under reduced pressure through making azeotropic mixture with alcohol. Crude mass thus obtained was extracted with $CHCl_3$ (2 × 100 ml) and washed with water (10 ml). The organic layer was dried over anhydrous Na_2SO_4, solvent evaporated under reduced pressure to give crude product which on column chromatography (SiO_2) using ethyl acetate: hexane (1:3) afforded compound **(11)** as colorless solid (Yield 92 %). m.p.=142°C; $[\alpha]_D^{25}$ - 31.2 (c , 0.125, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2930 and 2854 (CH_3 and CH_2 stretching), 1736 (C=O), 1630 (C=C); MS (FAB): 415 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ7.98 (d, J=7.2 Hz, 2H, Ph-H), 7.60(m, 3H, Ar-H), 5.75 (d, J=3.8 Hz, 1H, H-1), 4.64- 4.40 (m, 3H, H-2, H-4 and H-5), 4.08 (q, J=7.1 Hz, 2H, -OCH_2CH_3), 3.83 (d, J=3.1 Hz, 1H, H-3), 3.26 (s, 3H, OCH_3), 2.95 (dd, J=5.1 Hz and 17.6 Hz, 1H, H-6_A), 2.77 (dd, J=6.7 Hz and 17.2 Hz, 1H, H-6_B), 1.48 and 1.32 [each s, each 3H, $C(CH_3)_2$], 1.21 (t, J=7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 170.77 (-COOEt), 138.27, 134.38, 129.53 and 129.47 (Ar-C), 112.33[$C(CH_3)_2$], 104.59 (C-1), 84.44 (C-2), 81.88 (C-4), 76.76 (C-3), 61.34 (-OCH_2CH_3), 59.64 (C-5), 57.83 (OCH_3), 31.95 (C-6), 27.17 and 26.61[2×$C(CH_3)_2$], 14.47 (OCH_2CH_3); Anal.calcd for $C_{19}H_{26}SO_8$: C, 55.07; H, 6.28; Found: C, 57.20; H, 6.89%.

1.10. Ethyl [5- p-chloro-phenylmethanesulfonyl - 5,6-dideoxy-1, 2-O- isoprop ylidene- 3-O-methyl]- a**- D-gluco and** b**-L-ido-heptofuranuronate (12)**

It was obtained by the oxidation of compound **(4)** (0.32g, 0.78 mmoles) with $KMnO_4$ (0.125 g, 0.79 mmoles) as described above and isolated as colorless solid. (Yield 90 %). mp=84°C $[\alpha]_D^{25}$ - 72.0 (c 0.075, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2956 and 2884 (CH_3 and CH_2 stretching), 1722 (C=O); MS (FAB): 463 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.38 (m, 4H, Ar-H), 5.83 (d, J=3.7 Hz, 1H, H-1), 4.62 - 4.54 (m, 2H, H-2 and H-4), 4.30 (dd, J=13.0 Hz 2H, CH_2Ar), 4.16 (m, appears as q having J=7.0 Hz, 3H, H-5 and -OCH_2CH_3), 3.83 (d, J=3.0 Hz, 1H, H-3), 3.24 (s, 3H, OCH_3), 3.07 (dd, J=4.6 Hz and 17.9 Hz, 1H, H-6_A), 2.88 (dd, J=7.3 Hz and 17.8 Hz, 1H, H-6_B), 1.49 and 1.31[each s, each 3H, $C(CH_3)_2$], 1.25 (t, J=7.0 Hz, 3H, OCH_2CH_3); ^{13}C NMR($CDCl_3$): δ 171.49 (-COOEt), 135.59, 133.02, 129.38 and 126.15 (Ar-C), 112.58 [$C(CH_3)_2$], 104.77 (C-1), 84.89 (C-2), 81.82 (C-4), 76.74 (C-3), 61.60 (-OCH_2CH_3), 59.24 (SCH_2), 57.93 (C-5), 57.75 (OCH_3), 32.42 (C-6), 27.27 and 26.68 [2 ×$C(CH_3)_2$], 14.55 (OCH_2CH_3), Anal. calcd for $C_{20}H_{27}SO_8Cl$: C, 51.95; H, 5.84; Found: C, 52.66 ; H, 5.49 %.

1.11. Ethyl [5- benzenesulfonyl- 3-O-benzyl- 5,6-dideoxy-1, 2-O- isopropylidene]- α- D-gluco and β-L-ido-heptofuranuronate (13).

It was obtained by the oxidation of compound **(7)** (0.40 g, 0.87 mmoles) with $KMnO_4$ (0.14 g, 0.86 mmoles) as described above and isolated as colorless solid. (Yield 93 %). mp=150°C $[\alpha]_D^{25}$ - 15.6 (c 0.25, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2910 and 2989 (CH_3 and CH_2 stretching), 1732 (C=O), 1624 (C=C); MS (FAB): 491 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.84 (d, J=7.4 Hz, 2H, Ph-H), 7.58 and 7.26 (m, 8H, Ar-H), 5.79 (d, J=3.7 Hz, 1H, H-1), 4.63 (d, J = 11.7 Hz, 1H, OCH_APh), 4.55 (d, J=3.7 Hz, 1H, H-2), 4.51- 4.43 (m, 3H, OCH_BPh, H-4 and H-5), 4.16 (d, J=3.1 Hz, 1H, H-3), 3.95 (q, J=7.0 Hz, 2H, -OCH_2CH_3), 2.99 (dd, J=4.6 Hz and 17.3 Hz, 1H, H-6_A), 2.73 (dd, J=7.2 Hz and 17.3 Hz, 1H, H-6_B), 1.48 and 1.29 [each s, each 3H, $C(CH_3)_2$], 1.15 (t, J=7.0 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 177.72 (-COOEt), 137.99, 137.78, 134.36, 129.57, 129.48, 128.85, 128.27 and 127.99 (Ar-C), 112.41 [$C(CH_3)_2$], 104.72(C-1), 83.44(C-2), 82.57 (C-4), 76.59(C-3), 72.59(OCH_2Ph), 61.27(-OCH_2CH_3), 60.03(C-5), 32.11(C-6), 27.22 and 26.65[2×$C(CH_3)_2$], 14.39(OCH_2CH_3); Anal.calcd for $C_{25}H_{30}SO_8$: C, 61.22 ; H, 6.12 ; Found: C, 62.66 ; H, 6.43 %.

1.12. Ethyl [5- p-chloro-phenylmethanesulfonyl - 3-O-benzyl- 5,6-dideoxy-1, 2-O- isopropylidene]- α- D-gluco and β-L-ido-heptofuranuronate (**14**)

It was obtained by the oxidation of compound **(8)** (0.45 g, 0.89 mmoles) with $KMnO_4$ (0.145 g, 0.92 mmoles) as described above and isolated as colorless solid (Yield 90 %). m.p. =88°C; $[\alpha]_D^{25}$ -33.6 (c, 0.16, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2980 and 2879 (CH_3 and CH_2 stretching), 1725 (C=O); MS (FAB): 539$(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.38 (m, 9H, Ar-H), 6.05(d, J=3.7 Hz, 1H, H-1), 4.68 - 4.62(m, 2H, OCH_APh and H-2), 4.55-4.37(m, 4H, SCH_2Ar,

OCH_BPh and H-4), 4.08-3.94(m, 4H, $-OCH_2CH_3$, H-3 and H-5), 2.75(dd, J=8.8 Hz and 16.9 Hz, 1H, H-6_A), 2.12 (dd, J=2.8 Hz and 16.9 Hz, 1H, H-6_B), 1.53 and 1.35[each s, each 3H, $C(CH_3)_2$], 1.10(t, J = 7.0 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 169.61 (-COOEt), 136.77, 135.56, 133.11, 129.29, 128.96, 128.75, 128.31 and 126.92(Ar-C), 113.05[$C(CH_3)_2$], 105.66 (C-1), 81.67 (C-2), 81.08 (C-4), 79.09(C-3), 71.88 ($-OCH_2Ph$), 61.54 ($-OCH_2CH_3$), 60.88(SCH_2), 56.243(C-5), 29.60(C-6), 27.27 and 26.84[2× $C(CH_3)_2$], 14.26(OCH_2CH_3); Anal.calcd for $C_{26}H_{31}SO_8Cl$: C, 57.99; H, 5.76 Found: C, 57.05; H, 5.58%.

1.13. S^1,S^3-bis- [5-carbethoxymethyl-5-deoxy-1, 2-O-isopropylidene-3-O-methyl-α-D-xylofuranos-5-yl]- 1,2-dimercaptoethane (15)

It was obtained by the reaction of compound **(1)** (2.8 g, 10.29 mmoles) with 1,2-ethane dithiol (0.435 ml, 5.20 mmoles) in presence of DBU (0.4 ml, 2.63 mmoles) as described above and isolated as colorless oil (diastereomeric ratio 52: 44:6, Yield 92 %). **(15a):** $[\alpha]_D^{25}$ - 52.0 (c 0.5, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2932 and 2858 (CH_3 and CH_2 stretching), 1730 (C=O); MS (FAB): 663 $(M+Na)^+$; ^{1}H NMR(200 MHz, $CDCl_3$): δ 5.88 and 5.85 (each d, each J=3.8 Hz, each 1H, H-1, diastereomeric H), 4.58 and 4.55 (each d, each J=3.8 Hz, each 1H, H-2, diastereomeric H), 4.21-4.10(m, 3H, H-4 and $-OCH_2CH_3$), 3.89 and 3.71 (each d, each J=2.8Hz, each 1H, H-3, diastereomeric H), 3.44 and 3.37 (each s, each 3H, OCH_3), 3.40-3.36 (m, 1H, H-5), 2.93-2.56 (m, 4H, H-6 and SCH_2), 1.48 and 1.31 [each s, each 3H, $C(CH_3)_2$], 1.25 (t, J=7.1 Hz, 3H, OCH_2CH_3);
(15b) : $[\alpha]_D^{25}$ - 18.0 (c 0.35, $CHCl_3$); MS (FAB): 663 $(M+Na)^+$; ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.85 (d, J =3.7 Hz, 1H, H-1), 4.59 (d, J=3.7 Hz, 1H, H-2), 4.18 - 4.10 (m, 3H, H-4 and-OCH_2CH_3), 3.90 (d, J =2.7 Hz, 1H, H-3), 3.44 (s, 3H, OCH_3), 3.40 (m, 1H, H-5), 2.90 - 2.73 (m, 4H, H-6 and SCH_2), 1.48 and 1.31 [each s, each 3H, $C(CH_3)_2$], 1.23 (t, J=7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 171.78 (-COOEt), 111.95 [$C(CH_3)_2$], 105.37 (C-1), 83.73 (C-2), 82.72 (C-4), 81.16 (C-3), 60.88 ($-OCH_2CH_3$), 57.74 (OCH_3), 42.59 (C-5), 38.87, 36.24 and 32.24 (C-6 and SCH_2), 27.08 and 26.56 [2×$C(CH_3)_2$], 14.57 (OCH_2CH_3); Anal.calcd for $C_{28}H_{46}S_2O_{12}$: C, 52.60; H, 7.21; Found: C, 51.03; H, 7.69 %.

1.14. S^1,S^3-bis- [3-O-benzyl -5-carbethoxymethyl-5-deoxy-1, 2-O-isopropylidene-α-D-xylofuranos-5-yl]- 1,2-dimercaptoethane (16)

It was obtained by the reaction of compound **(2)** (2.1 g, 6.03 mmoles) with 1,2-ethane dithiol (0.27 ml, 3.22 mmoles) in presence of DBU (0.22 ml, 1.45 mmoles) as described above and isolated as colorless oil (diastereomeric ratio 60: 36: 4, Yield 90 %). $[\alpha]_D^{25}$ - 36.67 (c, 0.15, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2984, 2932 and 2878 (CH_3 and CH_2 stretching), 1732 (C=O); MS (FAB): 443 $(M+H)^+$; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.33 (m, 5H, Ar-H), 5.92 and 5.86 (each d, each J=3.8 Hz, each 1H, H-1, diastereomeric H), 4.69 (d, J=11.4 Hz, 1H, OCH_APh), 4.66-4.54 (m, 5H, H-2, H-2', $OCH_{A'}$, OCH_B and $OCH_{B'}$), 4.24 - 4.10 (m, 8H, H-4, H-4', $-OCH_2$, $-OCH_2$,, H-3 and H3'), 3.46 (m, 2H, H-5 and H-5'), 2.97 - 2.43 (m, 8H, CH_2's), 1.42 and 1.29 [each s, each 3H, $C(CH_3)_2$], 1.25 (t, J=7.0 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 171.83 and 171.33 (-COOEt), 137.75, 127.33, 128.92, 128.54, 128.35, 128.29 and 128.02 (Ar-C), 112.14 [$C(CH_3)_2$], 105.49 (C-1), 82.64, 82.41, 82.19 and 82.09 (C-2, C-3 and C-4),72.47 and 72.13 (OCH_2Ph), 61.03 and 60.84 ($-OCH_2CH_3$), 40.04 and 39.87 (C-5), 38.84, 38.64, 38.07, 37.32, 31.69 and 31.09 (C-6 and SCH_2), 27.23 and 26.68 [2×$C(CH_3)_2$], 14.63 (OCH_2CH_3); Anal. calcd for $C_{21}H_{30}S_2O_{12}$: C, 57.01; H, 6.78; Found: C, 58.55; H, 7.12 %.

1.15. S^1,S^3-bis-[5-deoxy-5-(2'-hydroxy ethyl)- 1,2-O-isopropylidene-3-O-methyl-α-D-xylofuranos-5-yl]- 1,2-dimercaptoethane (17)

A slurry of $LiAlH_4$(0.045g, 1.18 mmoles) in anhydrous tetrahydrofuran(10ml) was magnetically stirred at 0°C for 15 minutes under nitrogen atmosphere. To the stirring reaction mixture a solution of **(15)**(0.75g, 1.13 mmoles), in anhydrous tetrahydrofuran (5ml) was added slowly during 15 min at 0°C. The reaction mixture stirred at the same temperature for ½ hr followed by stirring at 25°C for 1.5 hr. Excess of reducing agent was quenched by adding an aqueous solution of 5 % NaOH and saturated aqueous solution of Na_2SO_4. After 15 minutes, filtered the reaction mixture and the solid cake was washed with more THF. The combined organic layer evaporated under reduced pressure and the crude product was dissolved in ethyl acetate and washed with water. The organic layer dried

(Na_2SO_4) and evaporated under reduced pressure to a get a crude mass, which was purified by column chromatography using CH_3OH: $CHCl_3$(1:49) to give the above title compound **(17)** as colourless oil(Yield 95 %). IR(KBr): ν_{max} cm^{-1} 3434 (OH), 2936 and 2834(CH_3 and CH_2 stretching); ^1H NMR (200 MHz, $CDCl_3$): δ5.88(d, J=3.7 Hz, 1H, H-1), 4.57 (d, J=3.7 Hz, 1H, H-2), 4.07 (dd, J=10.9 Hz and 2.8 Hz, H-4), 3.90 (d, J=3.0 Hz, 1H, H-3), 3.83 (t, J=5.6 Hz, 2H, SCH_2), 3.48 (s, 3H, OCH_3), 3.12(m, 1H, H-5), 1.86(m, 2H, H-6), 1.49 and 1.32 [each s, each 3H, $C(CH_3)_2$]; ^{13}CNMR($CDCl_3$): δ 111.65 and 111.53[$C(CH_3)_2$], 105.08 and 104.59(C-1), 84.04 and 83.84 (C-2), 83.24 and 83.05(C-4), 81.07 and 80.72 (C-3), 60.28 and 60.14(-C-7), 57.55 and 57.37 (OCH_3), 40.73 and 40.53(C-5), 35.75, 31.72 and 31.58(SCH_2), 26.76 and 26.24[2×$C(CH_3)_2$]; Anal.calcd for $C_{24}H_{42}S_2O_{10}$: C, 51.98; H, 7.58; Found: C, 51.24; H, 7.36%.

1.16. Ethyl- 6,7-dideoxy-6-(p-chlorobenzyl-sulfanyl)-L-threo-1,2,3,4-di-O-isopropylidene-α-D-and -β-L-ido-galacto-octapyranuronate (19)

It was obtained by the reaction of compound **(18)** (1.5 g, 4.57 mmoles), 4-chlorobenzenemethanethiol (0.73 ml, mmoles) and DBU (0.15 ml, 0.99 mmoles) as described earlier and isolated as colorless oil (diastereomeric ratio 60:40, Yield 95 %).

Minor isomer (19a): $[\alpha]_D^{25}$ - 7.23 (c ,0.52, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2986 and 2931 (CH_3 and CH_2 stretching), 1730 (C=O); MS (FAB): 487 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.25 (m, 4H, Ar-H), 5.48 (d, J = 4.98 Hz, 1H, H-1), 4.67 - 4.63 (m, 2H, H-3 and H-4), 4.27 (dd, J = 4.98 Hz and 2.0Hz, 1H, H-2), 4.09 (q, J = 7.1 Hz, 2H, -OCH_2CH_3), 3.89 (d, J = 13.0 Hz, 1H, SCH_AAr), 3.78 (d, J = 13.1 Hz, 1H, SCH_BAr), 3.75 (m, 1H, H-5), 3.16 (m, 1H, H-6), 2.90 and 2.81 (dd, J = 4.3 Hz and 16.5Hz, 1H, H-7_A), 2.58 and 2.50 (dd, J = 8.2 Hz and 16.5Hz, 1H, H-7_B), 1.48, 1.36 and 1.30 [each s, each 3H, 4 x $C(CH_3)_2$], 1.23 (t, J = 7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 172.02 (-COOEt), 137.51, 133.14, 130.81 and 128.90 (Ar-C), 109.47 and 109.06 [2 x $C(CH_3)_2$], 97.19 (C-1), 71.57, 71.29, 71.08 and 69.95 (C-2, C-3, C-4, C-5), 60.76 (-OCH_2CH_3), 41.08 (C-6), 38.15 and 36.52 (C-6 and SCH_2), 26.40, 26.33, 25.32 and 24.85 [4 × $C(CH_3)_2$], 14.60 (OCH_2CH_3),

Major isomer (19b): $[\alpha]_D^{25}$ - 70.0 (c 0.4, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2958 and 2926 (CH_3 and CH_2 stretching), 1730 (C=O); MS (FAB): 487 $(M+H)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.25 (m, 4H, Ar-H), 5.55 (d, J =4.98 Hz, 1H, H-1), 4.58 (dd, J = 7.9 Hz and 2.2Hz, 1H, H-3), 4.35 (dd, J=8.0 Hz and 1.4 Hz, 1H, H-4), 4.29 (dd, J=5.0 Hz and 2.3 Hz, 1H, H-2), 4.13 (q, J=7.1 Hz, 2H, -OCH_2CH_3), 3.91(m, 1H, H-5), 3.86 (s, 2H, SCH_2Ar), 3.22 (m, 1H, H-6), 2.84 (dd, J = 16.5 Hz and 4.1 Hz, 1H, H-7_A), 2.65 (dd, J = 16.5 Hz and 8.7 Hz, 1H, H-7_B), 1.47, 1.43, 1.32 and 1.31 [each s, each 3H, 4 × $C(CH_3)_2$], 1.22 (t, J = 7.1 Hz, 3H, OCH_2CH_3); Anal.calcd for $C_{23}H_{31}SO_7Cl$: C, 56.79; H, 6.38; Found: C, 56.15; H, 6.01%.

1.17. Ethyl-6,7-dideoxy-6-(5-p-chlorohenyl-methanesulfon -yl)-L-threo-1,2,3,4-di-O-isopropylidene-α-D-and-β-L-ido-galacto-octapyranuronate (20)

It was obtained by the oxidation of compound **(19)** (0.6 g, 1.23 mmoles) with $KMnO_4$ (0.195 g, 1.23 mmoles) as described above and isolated as colorless solid (Yield 94 %). mp=76°C, $[\alpha]_D^{25}$ - 32.6 (c, 2.5, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 2985 and 2933 (CH_3 and CH_2 stretching), 1738 (C=O); MS (FAB): 542 $(M+Na)^+$; ^1H NMR (200 MHz, $CDCl_3$): δ 7.30 (m, 4H, Ar-H), 5.56 (d, J = 4.95 Hz, 1H, H-1), 4.57 (dd, J = 8.0 Hz and 2.2 Hz, 1H, H-3), 4.33 (m, 2H, H-4 and H-2), 4.12 (q, J=7.1 Hz, 2H, -OCH_2CH_3), 3.98 (s, 2H, SCH_2Ar), 3.75 (m, 1H, H-5), 3.48 (m, 1H, H-6), 2.71 (dd, J=16.5 Hz and 4.1 Hz, 1H, H-7_A), 2.47 (dd, J=16.5 Hz and 8.7 Hz, 1H, H-7_B), 1.48, 1.44, 1.34 and 1.32 [each s, each 3H, 4 x $C(CH_3)_2$], 1.23 (t, J=7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 170.12 (-COOEt), 135.33, 133.13, 129.28 and 127.14(Ar-C), 110.42 and 109.95[2×$C(CH_3)_2$], 96.71(C-1), 71.58, 71.16,70.74(C-2, C-3, C-4), 67.79 (C-5), 61.54 and 61.48(-SO_2CH_2Ar and -OCH_2CH_3), 58.50 (C-6), 29.20 (C-7), 26.34, 26.14, 25.53 and 25.34 [4×$C(CH_3)_2$], 14.33 (OCH_2CH_3); Anal.calcd for $C_{23}H_{31}SO_9Cl$: C, 53.28; H, 5.98; Found: C, 52.98; H, 6.09%.

2. Biology

2.1. Activity against *M. tuberculosis* H_{37}Ra strain

All the compounds synthesized were evaluated for their efficacy against *M.tuberculosis* H_{37}Ra at concentration ranging from 100 μg ml^{-1} to 1.56 μg ml^{-1} using twofold dilutions in the initial screen. Log phase culture of *M.tuberculosis*H_{37} Ra is diluted so as to give

final $OD_{550\ nm}$ of 0.05 in Sauton's medium. In 96 well white plate 190µl of culture is dispensed in each well. A dimethyl sulfoxide(DMSO) solution of test compounds is dispensed to 96 well plates so as to make final test concentration 25µg ml^{-1} (5 µg test compound is dispensed in 10µl of DMSO). Then the plate is incubated at 37°C/5% CO_2 for 5 days. On 5th day 15µl Alamar blue solution is added to the each well of plate. The plate is again incubated overnight at 37°C/5% CO_2 incubator. The fluorescence is read on BMG polar star with excitation frequency at 544 nm and emission frequency at 590 nm. The compounds, which were found active(>90% inhibition as compared with control) at this concentration are then tested at 6 serial dilutions starting from 50 to 3.12µg ml^{-1}[20].

2.2. Activity against *M.tuberculosis* H_{37}Rv strain

Drug susceptibility and determination of MIC of the test compounds/drugs against *M.tuberculosis* H_{37}Rv was performed by agar microdilution method[21] where twofold dilutions of each test compound were added into 7H10 agar supplemented with OADC and organism. A culture of *M.tuberculosis* H_{37}Rv growing on L-J medium was harvested in 0.85% saline with 0.05% Tween-80. A suspension of 1 µg ml^{-1} concentration of extracts/compounds was prepared in DMSO. This suspension was added to (in tubes) 7H10 middle brook's medium (containing 1.7 ml medium and 0.2 ml OADC supplement) at different concentration of compound keeping the volume constant i.e. 0.1 ml. Medium was allowed to cool keeping the tubes in slanting position. These tubes were then incubated at 37°C for 24 h followed by streaking of M.tuberculosis H_{37}Rv (5×10^4 bacilli per tube). These tubes were then incubated at 37°C. Growth of bacilli was seen after 30 days of incubation. Tubes having the compounds were compared with control tubes where medium alone was incubated with H_{37}Rv. The concentration at which complete inhibition of colonies occurred was taken as active concentration of test compound.

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CONCLUSION

In summary, we have synthesized heitherto unprecedented glycosyl sulphides by conjugate addition of mercaptans and thiophenols. The glycosyl sulphides were successfully oxidized to respective sulphones. Two compounds i.e. compound **(15)** and **(17)** were active marginally against the virulent strain of M. tuberculosis with MIC values of 6.25 and 12.5 mg/mL. Other compounds of this series were inactive at this internationally accepted concentration

REFERENCES

[1] R.P.Tripathi, N.Tewari, N.Dwivedi, V.K.Tiwari; Medicinal Research Review, **25**, 1, 93-131 **(2005)**.
[2] C.Dye, S.Scheele, P.Dolin, V.Pathania, M.C.Raviglione; J.Am.Med.Assoc., **282**, 677-686 **(1999)**.
[3] (a) P.Sudre, G.Ten Dam, A.Kochi; Bull.World Health Organ., **70**, 149 **(1992)**.
(b) R.E.Huebner, K.G.Castro; Ann.Rev.Med., **46**, 47 **(1995)**.
[4] (a) A.P.Mendez, M.C.Raviglione, A.Laszlo, N.Binkin, H.L.Rieder, F.Bustreo, D.L.Cohn, C.S.Lambregtsvan Weezenbeek, S.J.Kim, P.Chaulet, P.N.Nunn; Engl.J.Med., **339**, 139 **(1998)**.
(b) A.P.Mendez, M.C.N.Raviglione; Engl.J.Med., **338**, 1641 **(1998)**.
[5] J.Trias, R.Benz; Mol.Microbiol., **19**, 283 **(1994)**.
[6] World Health Organization. Strategic framework to decrease the burden of TB/HIV document WHO/CDS/TB2002, 296, WHO/HIVAIDS/**(2002)**, 2. Geneva, Switzerland: World Health Organization; **(2002)**.
[7] (a) A.Marcos Espinal; The global situation of MDR-TB.Tuberculosis, **83**, 44 - 51 **(2003)**.
(b) T.Amalio, I.Michael; Drugs, **59**, 2, 171-179 **(2000)**.
[8] V.Rao, N.Fujiwara, S.A.Porcelli, M.S.Glickman; J Experimental Medicine, **201**, 4, 535-543 **(2005)**.
[9] (a) T.A.Leski, A.Tomasz, A.Tomasz; J.Bacteriology, **187**, 5, 1815-1824 **(2005)**.
(b) P.J.Brennan, H.Nikaido; Ann.Rev.Biochem., **64**, 2 **(1995)**.
(c) J.S.Blanchard; Ann.Rev.Biochem., **65**, 215 **(1996)**.

Full Paper

(d) M.Daffe, G.Etienne; Tubercl.Lung Dis., **79**, 153 **(1999)**.

[10] I.Chopra, P.Brennan; Tubercle Lung dis, **78**, 2, 89-98 **(1988)**.

[11] L.Cui, X.Ma, K.Sato, K.Okuma, F.C.Tenover, E.M.Mamizuka, C.G.Gemmell, M.N.Kim, M.C.Ploy, S.N.El, V.Ferraz, K.Hiramatsu; J.Clinical Microbiology, **41**, 1, 5-14 **(2003)**.

[12] (a) K.Marotte, T.Ayad, Y.Genisson, G.S.Besra, M.Baltas, J.Prandi; Eur.J.Org.Chem., **14**, 2557-2565 **(2003)**.

(b) B.A.Wolucka, M.R.McNeil, E.Hoffmann, T.Chojnacki, P.J.Brennan; J.Biol.Chem., **269**, 23328 -23335 **(1994)**.

(c) R.E.Lee, K.Mikus¡ova, P.J.Brennan, G.S.Besra; J.Am.Chem.Soc., **17**, 11829-11832 **(1995)**.

[13] (a) J.N.Barlow, J.S.Blanchard; Carbohydrate Res, **328**, 4, 473-480 **(2000)**.

(b) M.S.Scherman, K.A.Winans, R.J.Stern, V.Jones, C.R.Bertozzi, M.R.McNeil; Antimicrob Agents Chemother, **47**, 1, 378-382 **(2003)**.

[14] (a) G.Harth, M.A.Horwitz, D.Tabatadze, P.C. Zamecnik; Proceedings of the National Academy of Sciences, USA, **99**, 24, 15614-15619 **(2002)**.

(b) J.T.Belisle, V.D.Visaa, T.Sievert, K.Takayama, P.J.Brennan, G.S.Besra; Science, **276**, 1420-1422 **(1997)**.

[15] (a) R.P.Tripathi, R.Tripathi, V.K.Tiwari, L.Bala, S.Sinha, A.Srivastava, R.Srivastava, B.S.Srivastava; Eur.J. Med.Chem., **37**, 773 **(2002)**.

(b) V.K.Tiwari, R.P.Tripathi, R.Tripathi, L.Bala, S.Sinha, A.Srivastava, R.Srivastava, B.S.Srivastava; Trends in Carbohydrate Chem., **8**, 67-76 **(2002)**.

[16] (a) D.Katiyar, V.K.Tiwari, N.Tiwari, S.S.Verma, S.Sinha, A.Giakwad, A.Srivastava, V.Chaturvedi, R.Srivastava, B.S.Srivastava, R.P.Tripathi; Eur.J. Med.Chem., **40**, 351-360 **(2005)**.

(b) R.P.Tripathi, V.K.Tiwari, N.Tewari, D.Katiyar, N.Saxena, S.Sinha, A.Gaikwad, A.Srivastava, V.Chaturvedi, Y.K.Manju, R.Srivastava, R.Srivastava, B.S.Srivastava; Bio.Med.Chem., **13**, 5668-5679 **(2005)**.

[17] N.Tewari, V.K.Tiwari, R.C.Mishra, R.P.Tripathi, A.K.Srivastava, R.Ahmad, R.Srivastava, B.S.Srivastava; Bio.Med.Chem., **11**, 2911-2922 **(2003)**.

[18] D.Katiyar, V.K.Tiwari, R.P.Tripathi, A.K.Srivastava, V.Chaturvedi, R.Srivastava, B.S.Srivastava; Bio.Med. Chem., **11**, 4369-4375 **(2003)**.

[19] N.Tewari, V.K.Tiwari, R.P.Tripathi, A.Gaikwad, S.Sinha, A.K.Chaturvedi, P.K.Shukla, R.Srivastava, B.S.Srivastava; Bio.Med.Chem.Lett, **14**, 329-332 **(2003)**.

[20] A.R.Khan, R.P.Tripathi, V.K.Tiwari, R.C.Mishra, V.J.M.Reddy, J.K.Saxena; J.Carbohydrate Chem., **21**, 6, 587-600 **(2002)**.

[21] (a) F.G.Winder, P.B.Collins, D.J.Whelan; Microbiol, **66**, 379-381 **(1997)**.

(b) B.Phetsuksiri, M.Jackson, H.Scherman, M.McNeil, G.S.Besra; J.Biol.Chem., **278**, 53123-53130 **(2003)**.

[22] B.Phetsukiri, A.R.Baulard, A.M.Cooper, D.E. Minnikin, J.D.Douglas, G.S.Besra, P.J.Brennan; Antimicrob.Agents.Chemother., **43**, 1042-1051 **(1999)**.

[23] NT Patil, J.N.Tilekar, D.D.Dhavale; J.Org.Chem., **66**, 1065 **(2001)**.

[24] K.N.Houk, R.Paddon, N.G.Rondon, Y.D.Wu, F.K.Brown, C.D.Spellmeyer, J.T.Metz, Y.L.Li, R.J.Loncharich; Science, **231**, 1108 **(1986)**.

[25] Centrone, A.Charla, T.L.Lowary; Bio-Org and Med.Chem, **12**, 21, 5495-5503 **(2004)**.

[26] B.R.Shinde, N.R.Pai; Indian Drugs, **27**, 1, 32-4 **(1989)**.

[27] (a) J.R.Merchant, A.S.Gupta, P.J.Shah, S.S.Shirali; Chemistry and Industry (London, UK), **10**, 351-2 **(1979)**.

(b) J.R.Merchant, P.J.Shah; Chemistry and Industry, **19**, 791-2 **(1980)**.

(c) J.R.Merchant, N.M.Koshti, A.S.Gupta; Chemistry and Industry, **23**, 955 **(1982)**.

[28] D.Katiyar, R.C.Mishra, R.P.Tripathi; J Carbohydrate Chem., **23**, 1, 49-70 **(2004)**.

[29] L.A.Collins, S.G.Franzblan; Antimicrob.Agents Chemother., **41**, 1004 **(1997)**.

[30] H.Saita, H.Tomioka, K.Sato, T.Yamne, K.Yamashita, K.Hosol; Antimicrob.Agents Chemother., **35**, 542 **(1991)**.