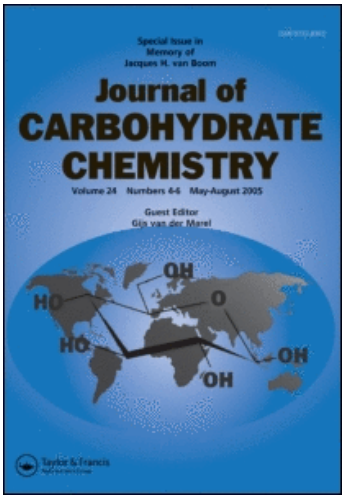


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Communication: Synthesis of Me α-L-Rhap-(13)-2-*O*-Me-α-L-Rhap And Me 2,3,4-Tri-*O*-Me-α-L-Fucp-(13)-α-L-Rhap-(13)-2-*O*-Me-α-L-Rhap : Oligosaccha-Ride Segments of Phenolic Glycolipids in *Mycobacterium Bovis Bcg* and *Tuberculosis Strain Canetti*

Mukund K. Gurjar; G. Viswanadham

To cite this Article Gurjar, Mukund K. and Viswanadham, G.(1991) 'Communication: Synthesis of Me α-L-Rhap-(13)-2-*O*-Me-α-L-Rhap And Me 2,3,4-Tri-*O*-Me-α-L-Fucp-(13)-α-L-Rhap-(13)-2-*O*-Me-α-L-Rhap : Oligosaccha-Ride Segments of Phenolic Glycolipids in *Mycobacterium Bovis Bcg* and *Tuberculosis Strain Canetti*', Journal of Carbohydrate Chemistry, 10: 3, 481 — 485
To link to this Article: DOI: 10.1080/07328309108543923
URL: http://dx.doi.org/10.1080/07328309108543923

J. CARBOHYDRATE CHEMISTRY, 10(3), 481-485 (1991)

COMMUNICATION

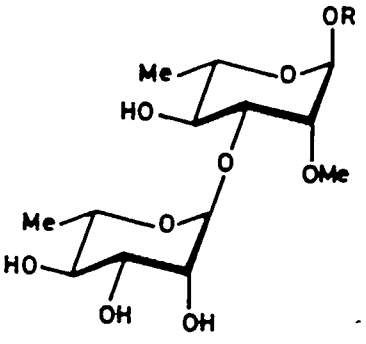
SYNTHESIS OF ME α-L-RHAP-(1→3)-2-O-ME-α-L-RHAP AND ME 2,3,4-TRI-O-ME-α-L-FUCP-(1→3)-α-L-RHAP-(1→3)-2-O-ME-α-L-RHAP : OLIGOSACCHARIDE SEGMENTS OF PHENOLIC GLYCOLIPIDS IN *MYCOBACTERIUM BOVIS BCG* AND *TUBERCULOSIS STRAIN CANETTI*

Mukund K Gurjar* and G Viswanadham

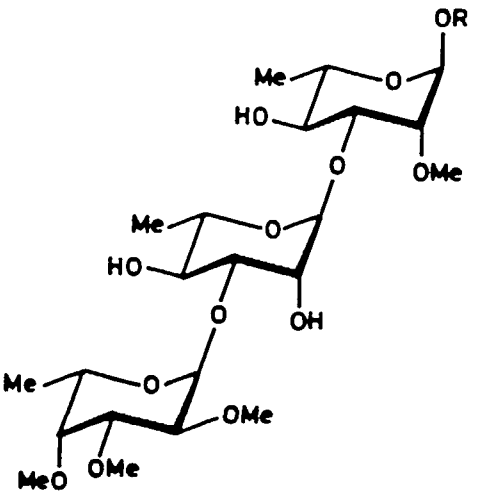
Indian Institute of Chemical Technology, Hyderabad 500 007, India

Received March 26, 1990 - Final form January 9, 1991

The revived interest in phenolic glycolipids of pathogenic mycobacteria is evoked by a widespread[1-3] use of *Mycobacterium (M.) leprae* specific antigen for serodiagnosis of leprosy patients. As a consequence, a few phenolic glycolipids of other mycobacterias were isolated and structurally elucidated. Recently Vercellone and Puzo[4] reported the isolation of new phenolic glycolipids not yet described in *M. bovis* BCG. The combination of sugars in one of the glycolipids was identified as 3-O-(α-L-rhamnopyranosyl)-2-O-methyl-α-L-rhamnopyranoside (1) which is closely related to the trisaccharide segment (2) of *M. tuberculosis* strain Canetti.[5] The latter contains 2,3,4-tri-O-methyl-L-fucopyranosyl monosaccharide α-linked to 3' position of 1. It has been emphasised that new found glycolipids of *M. bovis* BCG could share common epitopes with those of *M. tuberculosis*, thus leading to false positive immunoabsorbent assay tests during screening of tuberculosis patients. In addition, there is concern regarding the involvement of one of the new found glycolipids in the stimulation of T suppressor cells, thus adding to the conflicting results noted in the protection of *M. tuberculosis* by *M. bovis* BCG. In essence the new found phenolic glycolipids of *M. bovis* BCG are associated with interesting but unclear biological profiles. We now report the synthesis of these closely related oligosaccharides, 1 (R = Me) and 2 (R = Me).



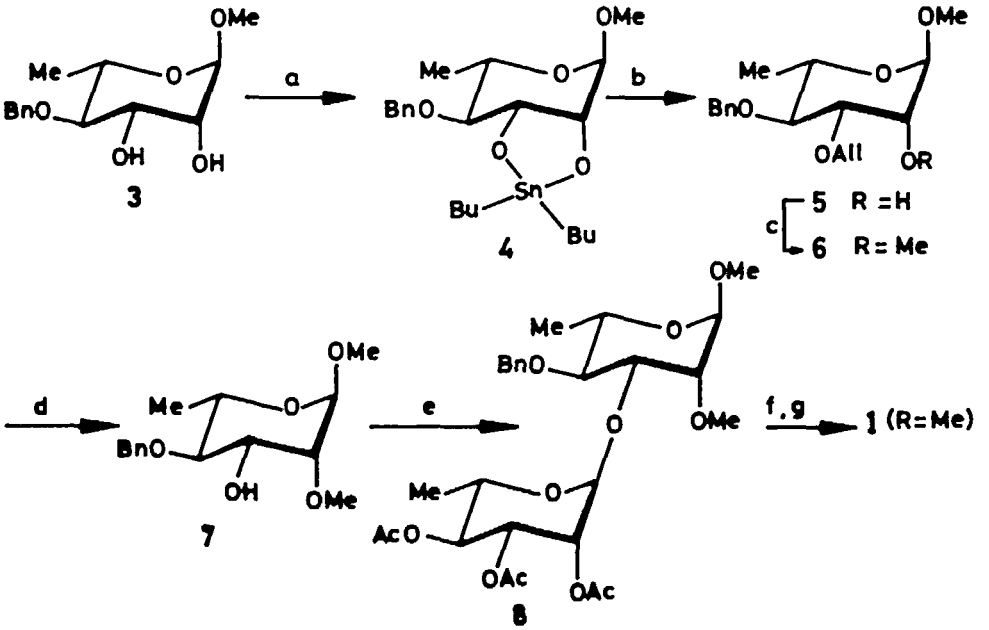
1



2

Methyl 3-O-(α-L-Rhamnopyranosyl)-2-O-methyl-α-L-rhamnopyranoside (1, R = Me)

To initiate the synthetic sequence, methyl 4-O-benzyl-α-L-rhamnopyranoside (3)[6] was selected as the starting material. Subsequent transformation[7] of 3 into the corresponding dibutylstannyl acetal derivative 4 (Bu_2SnO, C_6H_6, Δ, 12 h) followed by reaction with allyl bromide (C_6H_6, Δ, 6 h) selectively blocked the 3 position leading to the formation of compound 5 {$[\alpha]_D^{26}$ -70.7° (c 2.66, chloroform)} (87%). The remaining free hydroxyl group in 5 was methylated (NaH, MeI, THF, 18 h) to give compound 6 {$[\alpha]_D^{26}$ -66.8° (c 1.4, chloroform)} and then the 3-O-allyl group was removed[8] in the presence of Wilkinson's catalyst {$[Rh(PPh_3)_3Cl]$, DABCO, EtOH, C_6H_6, H_2O, Δ, 18 h, $HgCl_2$, HgO, H_2O-MeCOMe, 2 h} to form the aglycone 7 {$[\alpha]_D^{26}$ -38.8° (c 0.5, chloroform)} (73%). The coupling reaction between 7 and tetra-O-acetyl--L-rhamnopyranose[9] was performed[10] in the presence of a catalytic amount of BF_3:OEt_2 (CH_2Cl_2, 0 °C, 2 h). The resulting disaccharide 8 (54%) was deacetylated (NaOMe, MeOH, 18 h, Zemplen) and hydrogenolysed (Pd-C, H_2, EtOAc, 4 h, 1 atm.) to afford 1 (R = Me), {$[\alpha]_D^{26}$ -68.3° (c 0.44, chloroform)} (88%).[11] The stereochemistry at each anomeric centre of 1 was determined by ^1H NMR (300-MHz, $CDCl_3$) [δ_{H-1} 4.74 (singlet) and $\delta_{H-1'}$ 5.03 (singlet)] and ^{13}C NMR (75.47-MHz, CD_3COCD_3) [δ_{C-1} 99.06 and $\delta_{C-1'}$ 103.47 ppm] spectra.

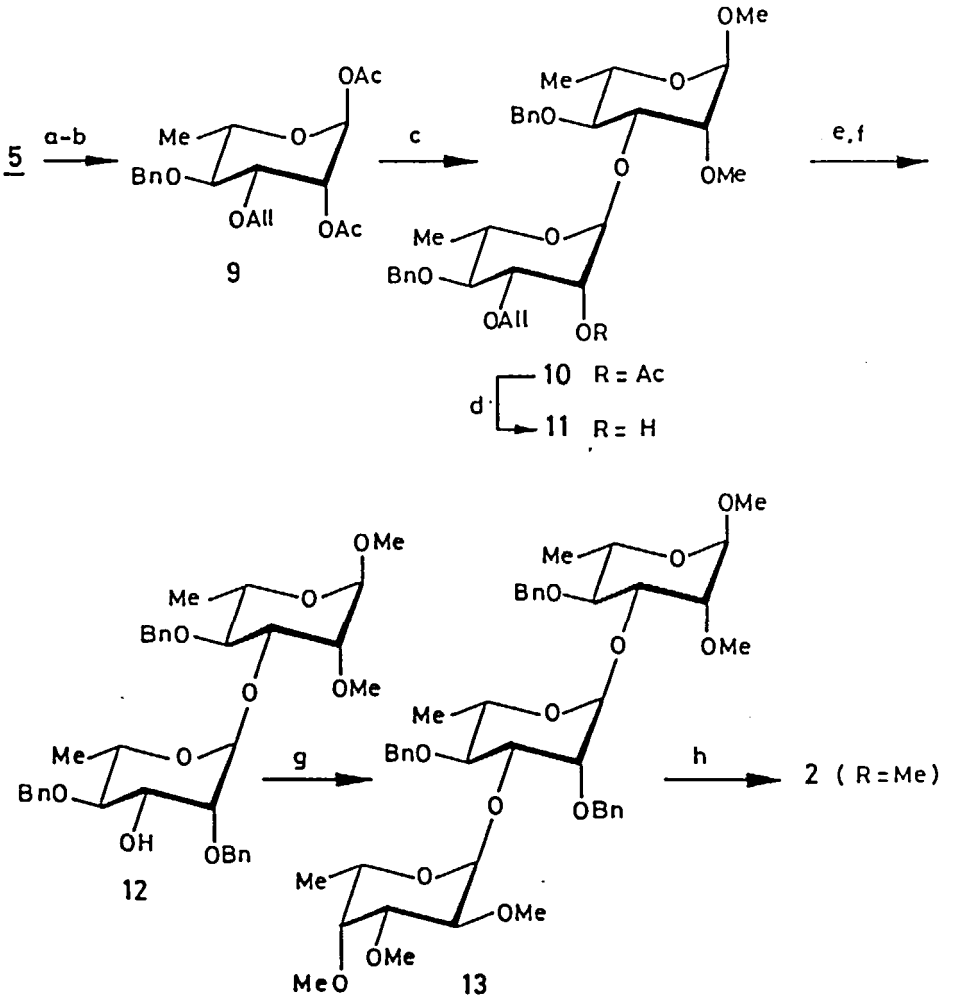


a) $Bu_2Sn{=}O$, C_6H_6, Δ 12h ; b) AllBr, Δ, 6h ; c) NaH, THF, MeI, 18h; d) DABCO, $[Rh(PPh_3)_3]Cl$, EtOH-C_6H_6-H_2O, Δ, 18 h ; $HgCl_2$-HgO, aq.CH_3COCH_3, 1h ; e) $(OAc)_4$-L-RhamP, $BF_3{:}OEt_2$, CH_2Cl_2, 0°C, 2h; f) NaOMe, MeOH, 18h ; g) Pd-C, H_2, EtOAc, 4h

Scheme 1

Methyl 3-*O*-[3-*O*-(2,3,4-Tri-*O*-methyl-α-L-fucopyranozyl)-α-L-rhamnopyranosyl]-2-*O*-methyl-α-rhamnopyranoside (2, R = Me)

Compound 5 was hydrolysed (3N H_2SO_4, dioxan, 100 °C, 6 h) and then acetylated (Ac_2O, Py, 18 h) to give the diacetate 9 (85%). The condensation reaction between 9 and 7 was conducted in the presence of $BF_3{:}OEt_2$ as described above to give the disaccharide 10 (44%) which on deacetylation (NaOMe, MeOH, 18 h, Zemplen) afforded 11 {$[\alpha]_D^{26}$ -29.4° (*c* 0.34, chloroform)}. After benzylation (NaH, BnBr, THF, 18 h) of 11, the allylic substituent was removed with Wilkinson's catalyst to give 12 {$[\alpha]_D^{26}$ -28.2° (*c* 0.22, chloroform)} (70%). Condensation of 12 with 1-*O*-acetyl-2,3,4-tri-*O*-methyl-L-fucopyranose[12] by the same approach ($BF_3{:}OEt_2$, CH_2Cl_2, 0 °C, 2 h) gave rise to the trisaccharide derivative 13 {$[\alpha]_D^{26}$ -39.8° (*c* 0.5, chloroform)} (50%) which on hydrogenolysis (Pd-C, H_2, 24 h, 1 atm.) produced 2 (R = Me) {$[\alpha]^{26}$ -136° (*c* 0.22, methanol)} (75%). The anomeric centres in 2 (R = Me) showed signals in the NMR spectra [^{1}H NMR ($CDCl_3$) $\delta_{H\text{-}1}$



a) 3 NH_2SO_4, dioxane, 100°C, 6h ; b) Ac_2O, Py, RT, 18h; c) 7, BF_3:OEt_2, CH_2Cl_2, 0°C, 2h ; d) NaOMe, MeOH, 18h; e) NaH, THF, BnBr, 18h ; f) $[Rh(PPh_3)_3]$ Cl, DABCO, 12h; $HgCl_2$-HgO, 1h, MeCOMe-H_2O ; g) 1-(OAc)-2,3,4-$(OMe)_3$-L-FucP, BF_3:OEt_2, CH_2Cl_2, 0°C, 2h ; h) Pd-C, H_2, EtOAc, 24h.

Scheme 2

4.72 (singlet), $\delta_{H\text{-}1'}$ 5.04 (singlet) and $\delta_{H\text{-}1''}$ 5.12 (doublet, J = 2.9 Hz) and ^{13}C NMR $\delta_{C\text{-}1}$ 97.45; $\delta_{C\text{-}1'}$ 102.06 and $\delta_{C\text{-}1''}$ 100.72 ppm] which were consistent with the assigned structure.

The authors are indebted to Dr A. V. Rama Rao for his keen interest and encouragement. The research is partly supported by Indo-Soviet ILTP Programme of DST, New Delhi.

REFERENCES AND FOOTNOTES

1. S. W. Hunter, T. Fujiwara, and P. J. Brennan, *J. Biol. Chem.*, **257**, 15072 (1982).

2. H. Gaylord, and P. J. Brennan, *Ann. Rev. Microbial.*, **41**, 645 (1987).

3. J. Gigg, R. Gigg, S. Payne, and R. Conant, *Topics in Lipids Research*; Royal Society: London, 1986, p 119.

4. A. Vercellone, and G. Puzo, *J. Biol. Chem.*, **264**, 7447 (1989).

5. M. Daffe, C. Lacave, M. A. Laneelle, and G. L. Laneelle, *Eur. J. Biochem.*, **167**, 155 (1987); F. Papa, M. Riviere, J. J. Fournie, G. Puzo, and H. David, *J. Clin. Microbiol.*, **25**, 2270 (1987).

6. A. H. Haines, *Carbohydr. Res.*, **10**, 466 (1969).

7. S. David, and S. Hanessian, *Tetrahedron*, **41**, 643 (1985).

8. D. Chatterjee, S. N. Cho, C. Stewart, J. T. Douglas, T. Fujiwara, and P.J. Brennan, *Carbohydr. Res.*, **183**, 241 (1988).

9. V. Pozsgay, and A. Neszmelyi, *Carbohydr. Res.*, **80**, 196 (1980).

10. J. Merino-Albernas, V. Verez-Bencomo, L. Gonzales-Rodriguez, and C. S. Perez-Martinez, *Carbohydr. Res.*, **183**, 175 (1988); H. Paulsen, *Angew. Chem. Int. Ed. Engl.*, **21**, 155 (1982); R. R. Schmidt, *Angew. Chem. Int. Ed. Engl.*, **25**, 212 (1986).

11. Chemical Ionization Mass Spectral data : **1** (R = Me) *m/z* = 338 (M^+), 306, 257, 161, 147, 102, 99, 65; **2** (R = Me) *m/z* 526 (M^+), 494, 380, 349, 335, 316, 189, 157, 99, 65.

12. O. T. Schmidt, W. Mayer, and A. Distelmaier, *Ann. der. Chem.*, **555**, 26 (1943).

IICT Communication No.2569