Chemical Science

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

rsc.li/chemical-science

View Article Online
DOI: 10.1039/C6SC04866H

Journal Name

ARTICLE

Expedient Synthesis of Heneicosasaccharyl Mannose Capped Arabinomannan of *Mycobacterium tuberculosis* Cellular Envelope by Glycosyl Carbonate Donors

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Maidul Islam, Ganesh P. Shinde and Srinivas Hotha*

Global incidence of tuberculosis is increasing at an alarming rate and *Mycobacterium tuberculosis* (Mtb) is the causative agent for the tuberculosis, a disease triggering maximum mortality. Lipoarabinomannan (LAM) is one of the major components of the Mtb cellular envelope and is an attractive scaffold for developing anti-tubercular drugs, vaccines and diagnostics. Herein, a highly convergent strategy is developed for the first synthesis of heneicosasaccharyl arabinomannan. Arabinomannan synthesized in this endeavour has several 1,2-*trans* or α-Ara*f* linkages and three 1,2-*cis* or β-Ara*f* linkages end capped with 1,2-*trans* or α-Man*p* linkages. All key glycosidations were performed with alkynyl carbonate glycosyl donors under [Au]/[Ag]-catalysis conditions, which gave excellent yields and stereoselectivity even for the reactions between complex- and branched oligosaccharides. The resultant allyl oligosaccharide was globally deprotected to obtain the heneicosasaccharyl arabinomannan as a propyl glycoside. In summary, the heneicosasaccharyl mannose capped arabinomannan synthesis was achieved in 56 steps with 0.016% overall yield.

Introduction

World-wide resurgence of mycobacterial infections coupled with the emergence of multi-drug and extreme drug resistance placed tuberculosis (TB) as a major public health concern.[1-3] The only available protection against tuberculosis is the BCG vaccine; however, multi-centered clinical trials demonstrated variable efficiency.[4] Tuberculosis infection is caused by *Mycobacterium tuberculosis* (Mtb) with a thick waxy cell wall making the drugs impervious.[5,6] As a consequence, patients suffering from TB are prescribed to long regimen of multiple drugs. Therefore, TB is an ever growing challenge, and novel strategies to diagnose, control or eradicate it are in great demand.

The chemical structure of the waxy cellular envelope has been identified to be a unique glycocalyx comprising mycolic acids, Ara*f*-, Gal*f*-, Man*p*-, Rha*p*- and Inositols.[7-10] Further investigations revealed that the glycocalyx contains trehalose lipids, lipoarabinomannan (LAM), arabinogalactan (AG) and peptidoglycan.[7-10] Of these, structure of LAM was noticed to have a key *C*-3 branched arabinan domain with many α-1→5-linked D-Ara*f*s, and a few β-1→2-linked D-Ara*f*s capped with α-1→2 linked D-Man*p*s at the non-reducing end.[7-10,13] It has been well established that mannose capped LAM (ManLAM) is prevalent in more pathogenic mycobacterial species such as M. tuberculosis, M. leprae, M. bovis.[11-13] ManLAM has been shown to inhibit production of tumor necrosis factor-α (TNF-α) and interleukin-12 (IL-12) by human dendritic cell and

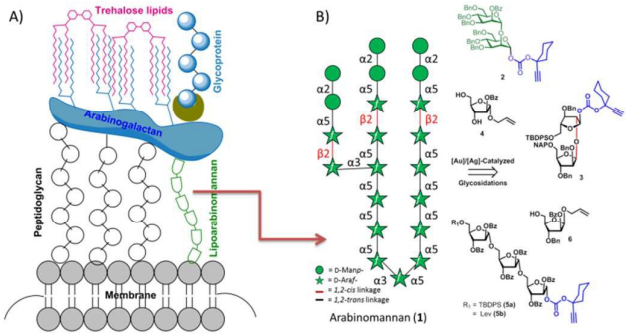


Figure 1. Cartoon representation of the *Mycobacterium tuberculosis* cell wall (A) and retrosynthesis of Heneicosasaccharyl mannose capped arabinan (B).

and macrophages *in vitro* to modulate M. tuberculosis induced macrophage apoptosis.[14,15] Quite recently, a rapid point of care diagnostic kit was developed exploiting the antigenic properties of ManLAM.[16-18] In another study LAM is investigated as a candidate vaccine for the mycobacterial diseases. Thus, non-reducing end portion of LAM is beneficial for various immunological studies, diagnostics and development of carbohydrate-based tuberculosis vaccine.

Owing to the significance of ManLAM, the synthesis of ManLAM and arabinan fragments was attempted over the last two decades.[19-27,44] A recent investigation by Guo's group verified the synthetic and immunological potential of protein conjugated ManLAM fragments.[28] However, far too little attention has been paid to synthesize the large oligomer of the ManLAM. The main aim of the current research has therefore been to synthesize the naturally occurring large

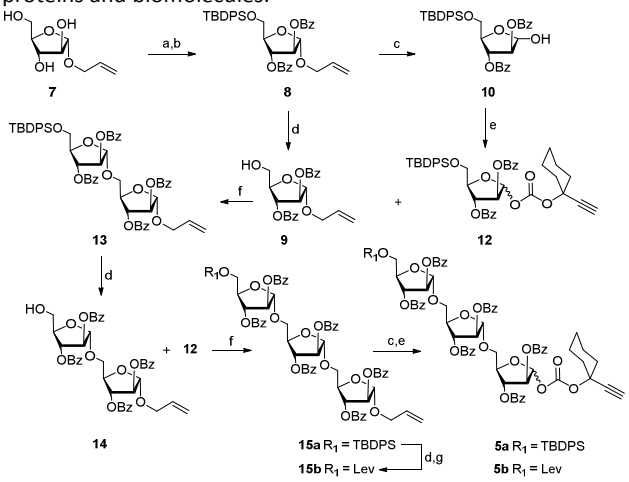
Department of Chemistry, Indian Institute of Science Education and Research, Pune – 411 008, India, s.hotha@iiserpune.ac.in
Electronic Supplementary Information (ESI) available: Experimental procedures, compound characterization data and spectral charts. See DOI: 10.1039/x0xx00000x

View Article Online
DOI: 10.1039/C6SC04866H

oligosaccharide portion of ManLAM such as arabinomannan **1** (figure 1) to facilitate vaccine and diagnostic development.

Results and Discussion

The arabinomannan moiety (**1**) offers enough complexity and challenges for its synthesis in terms of type, number of linkages and asymmetric branching. A careful retrosynthetic disconnection revealed that the target molecule as a propyl glycoside can be synthesized conveniently using two disaccharides (**2**,**3**), two monosaccharides (**4**,**6**) and a trisaccharide (**5**) (Figure 1). Apart from the continued interest,[29-34] alkynyl carbonate donors are chosen as they undergo catalytic activation in the presence of gold and silver salts, fast and high yielding.[35] Neighboring group or reciprocal donor acceptor selectivity assisted synthesis of 1,2-*trans* or α-linkages and stereoelectronics guided 1,2-*cis* or β-Ara*f* was envisioned.[36] Allyl moiety was strategically placed at the anomeric position since it is stable and orthogonal to -OTBDPS, -OBz, -ONAP protecting groups and can be converted to hemiacetals *en route* to the glycosyl donor preparation. In addition, allyl moiety can also be exploited for conjugation of proteins and biomolecules.[37-40]

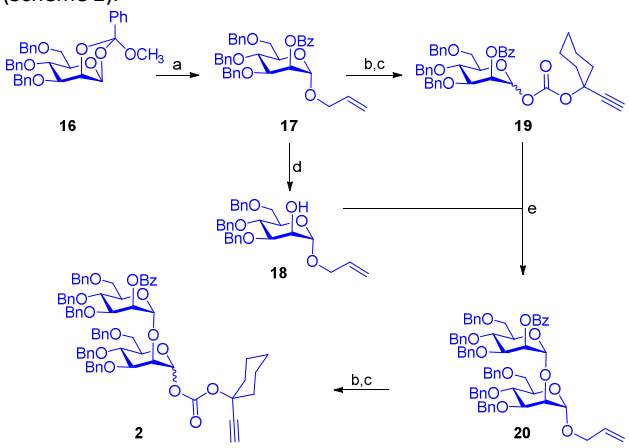


Scheme 1. Reagents: a) TBDPS-Cl, Im., DMF, 0 ^{o}C, 1 h, 82%; b) BzCl, pyridine, DMAP, 0-25 ^{o}C, 5 h, 93%; c) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{o}C, 4 h, 85%; d) HF·py, pyridine, 0-25 ^{o}C, 5 h, 93% for **9**, 91% for **14**, 90% for **15b**; e) 1-ethynylcyclohexyl (4-nitrophenyl) carbonate (**11**), CH_2Cl_2, DMAP, 0-25 ^{o}C, 3 h, 85% for **12**, 83% for **5a** and 85% for **5b** over two steps respectively; f) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite] gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{o}C, 15 min, 95% for **13**, 92% for **15a**; g) Levulinic acid, DIC, DMAP, CH_2Cl_2, 0-25 ^{o}C, 2 h, 95%.

Our synthetic endeavour started with the preparation of triarabinofuranosyl carbonate donor (Scheme 1). Easily accessible allyl arabinofuranoside **7**[41] was converted into fully protected compound **8** by first protecting the *C*-5-OH as silyl ether using TBDPS-Cl followed by the protection of remaining hydroxyls as benzoates with BzCl/py/DMAP. Compound **8** serves as a common building block for the synthesis of both glycosyl donor and acceptor as well. Accordingly, compound **8** has been split into two portions and one portion was converted into the glycosyl acceptor **9** by the treatment of with HF·py in THF whereas the second portion was converted into hemiacetal **10** using $PdCl_2$; subsequently, transformed to glycosyl donor **12** by reacting with easily available ethynyl cyclohexyl (4-nitrophenyl) carbonate **11** (Scheme 1).[47]

The first [Au]/[Ag]-glycosidation between acceptor **9** and donor **12** was successfully performed to afford disaccharide **13** in excellent yields.[35] In continuation, lone silyl ether was deprotected under HF·py conditions to afford acceptor **14** which was glycosylated again with the glycosyl donor **12** under gold/silver catalytic conditions to obtain trisaccharide **15a** as an allyl glycoside. Cleavage of the silyl ether, protection as levulinoate resulted into the other required trisaccharide **15b**. Trisaccharides **15a** and **15b** are respectively converted easily into the triarabinofuranosyl carbonate donors **5a** and **5b** (Scheme 1).[46]

In parallel, allyl mannopyranoside **17** was synthesized from known mannopyranosyl 1,2-orthoester **16**[27] under acidic conditions. Subsequently, allyl glycoside **17** by splitting into two portions and one part was subjected to saponification under Zemplén conditions[42] to afford the acceptor **18** and the other part was converted into the glycosyl donor **19** in two easy steps. The gold/silver assisted glycosidation between the donor **19** and the acceptor **18** underwent uneventfully affording 93% of the disaccharide **20** which was subsequently converted into the other required building block **2** in two steps (Scheme 2).[46]



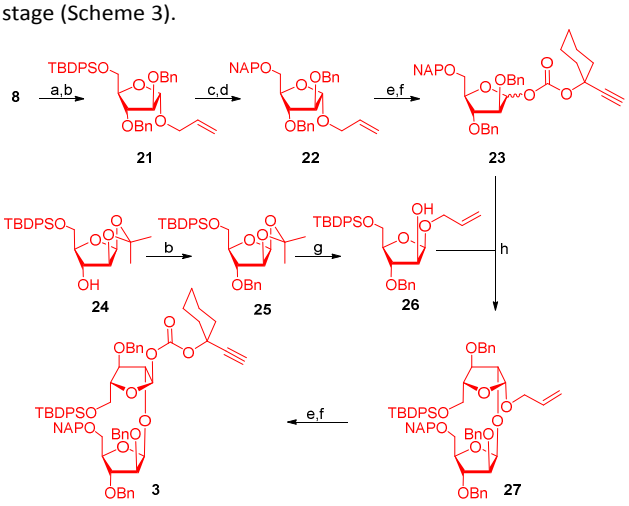
Scheme 2. Reagents: a) PTSA (0.2 eq.), Allyl alcohol, CH_2Cl_2, 4Å MS powder, 25 ^{o}C, 1 h, 86%; b) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 ^{o}C, 4 h, 90% towards **19**; c) **11**, CH_2Cl_2, DMAP, 0-25 ^{o}C, 3 h, 78% for **19**, 83% for **2** over two steps; d) NaOMe, MeOH, 25 ^{o}C, 1 h, 94%; e) 8mol% chloro[tris(2,4-di-*tert*-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 ^{o}C, 15 min, 93%.

Synthesis of the next important 1,2-*cis* disaccharide **3** was initiated with saponification of compound **8** under Zemplén conditions (NaOMe/MeOH); subsequent conversion to benzyl ethers afforded compound **21**. Moving on, the cleavage of the silyl ether using HF·py and protection of the resulting hydroxyl group as NAP ether underwent effortlessly by employing NAP-Br to afford NAP-protected allyl glycoside **22**. Hydrolysis of the allyl glycoside using $PdCl_2$ and conversion to the corresponding donor **23** was achieved in very high yield. In parallel, compound **24** was protected as benzyl ether **25** using NaH/BnBr/DMF and opening of the isopropylidene moiety was

View Article Online
DOI: 10.1039/C6SC04866H

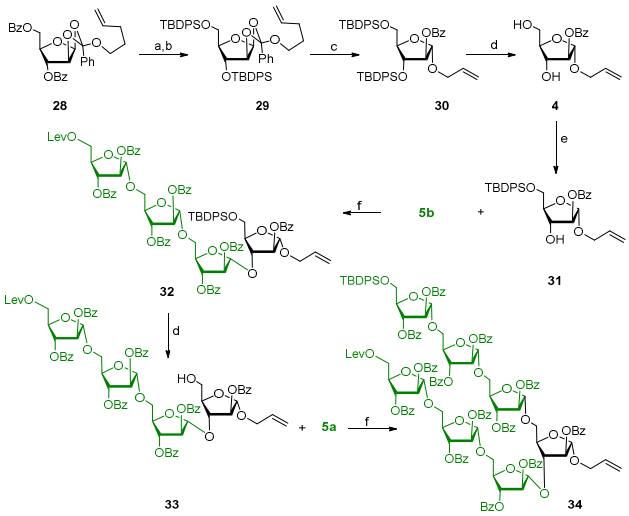
performed in the presence of allyl alcohol under acidic conditions to afford an α,β-mixture of glycosides.

Earlier studies from our group demonstrated that the reciprocal donor acceptor selectivity depends on the reactivity of the nucleophile and the stereoelectonics around the *C*-2 position of the glycosyl acceptor.[36] Accordingly, allyl glycosides were separated by flash silica gel column chromatography and isolated the required 1,2-*cis* disposed allyl glycoside **26**. Glycosyl donor **23** and acceptor **26** were subjected to [Au]/[Ag]-catalysed glycosidation conditions to afford the 1,2-*cis* or β-disaccharide **27** in 92% yield as a single diastereomer further verifying our earlier results.[36,46] Subsequently, the disaccharide **27** was converted into the required glycosyl donor **3** in two steps *viz*. Pd-catalysed hydrolysis of allyl glycoside to hemiacetal followed by its conversion to the ethynylcyclohexyl carbonate by treating with compound **11** and DMAP. Orthogonally cleavable TBDPS and NAP ethers are selected to install mannopyranosyl disaccharide at a later stage (Scheme 3).



Scheme 3. Reagents: a) NaOMe, MeOH, 25 °C, 1 h, 90%; b) NaH, BnBr, TBAI, DMF, 0-25 °C, 1 h, 91% for **21** and 93% for **25**; c) HF·py, pyridine, 0-25 °C, 5 h, 92%; d) NaH, NAPBr, TBAI, DMF, 0-25 °C, 2 h, 90%; e) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 °C, 4 h; f) **11**, DMAP, CH_2Cl_2, 0-25 °C, 3 h, 82% for **23**, 78% for **3** over two steps; g) PTSA (0.2 eq.), Allyl alcohol, CH_2Cl_2, 50 °C, 2 h, 45%; h) 8mol% chloro[tris(2,4-di-*tert*-butylphenyl)phosphite] gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, -78 °C, 5 h, 92%.

Synthesis of another monosaccharide **4** commenced with the saponification of easily accessible **28**[43] under Zemplén conditions (NaOMe/MeOH) followed by its conversion to disilyl ether **29** using TBDPSCl/Im./DMAP in 81% yield over two steps. Acid mediated opening of the 1,2-orthoester in the presence of allyl alcohol afforded the allyl glycoside in 80% yield. Cleavage of the silyl ethers was achieved using HF·py to afford the allyl glycoside **4**, resulting *C*-5 hydroxyl group was protected as its silyl ether to afford the glycosyl acceptor **31**.

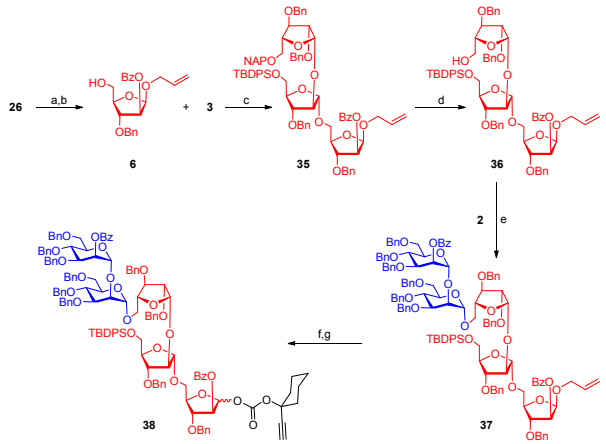


Scheme 4. Reagents: a) NaOMe, MeOH, 25 °C, 1 h, 95%; b) TBDPS-Cl (2.5 eq.), Im., DMF, 0-25 °C, 2 h, 85%; c) PTSA (0.2 eq.), excess allyl alcohol, CH_2Cl_2, 4Å MS powder, 25 °C, 1 h, 80%; d) HF·py, pyridine, 0-25 °C, 6 h, 90% for **4**, 90% for **33**; e) TBDPS-Cl, Im., DMF, 0 °C, 1 h, 80%; f) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH2Cl2, 4Å MS powder, 25 °C, 20 min, 95% for **32** and 92% for **34**.

Synthesis of enough quantities of all identified major partners driven the assembly of ManLAM. Accordingly, glycosyl acceptor **31** and the glycosyl donor **5b** were first glycosylated under gold-silver catalysed glycosidation conditions to afford the tetrasaccharide **32** in excellent yield.[46] Deprotection of the silyl ether using HF·py to obtain **33** and subsequent treatment with glycosyl donor **5a**, 8mol% each of AgOTf and gold-phosphite catalyst in CH_2Cl_2 afforded the required heptasaccharide **34** in 92% yield (Scheme 4).

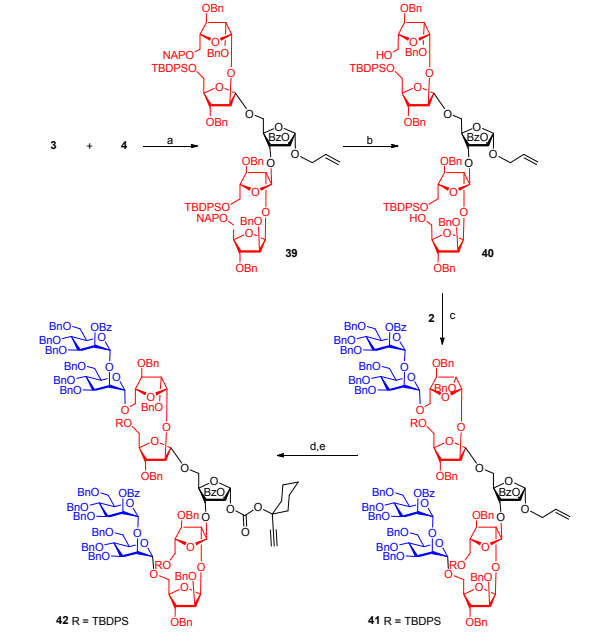
Protection of the *C*-2 hydroxyl group of compound **26** as a benzoate followed by the unblocking of *C*-5 hydroxyl group by the addition of HF·py resulted into the glycosyl acceptor **6**. Subsequently, glycosyl acceptor **6** was treated with the donor **3** under gold-silver catalyzed conditions to afford the required trisaccharide **35**.[35] Diastereoselectivity of the reaction was noticed to be temperature dependent. The diastereomeric ratio swung in favour of the desired α-isomer as the temperature of the reaction was lowered. Best 8:1 ratio (α:β) in favour of desired isomer with an overall yield of 90% (translates to 80% of the trisaccharide **35**) was accomplished at -78 °C that might be due to the presence of bulky 5-*O*-TBDPS moiety (Scheme 5).[36] The naphthyl moiety was deprotected using DDQ, CH_2Cl_2-MeOH (1:4) at 25 °C to obtain the acceptor **36** which was further treated with the mannopyranosyl donor **2** to obtain the pentasaccharide **37** in 76% yield. Two step conversion transformed allyl glycoside **37** into the glycosyl donor **38** in 75% (Scheme 5).

View Article Online
DOI: 10.1039/C6SC04866H



Scheme 5. Reagents: a) BzCl, pyridine, DMAP, 0-25 °C, 5 h, 93%; b) HF·py, pyridine, 0-25 °C, 5 h, 94%; c) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, -78 °C, 5 h, 80% (overall yield 90% with α:β = 8:1); d) DDQ, CH_2Cl_2-MeOH (1:4), 25 °C, 4 h, 82%; e) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 °C, 15 min, 76%; f) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 °C, 4 h; g) **11**, DMAP, CH_2Cl_2, 0-25 °C, 3 h, 75% over two steps.

Glycosidation reaction between donor **3** and acceptor **4** afforded another pentasaccharide **39** as an allyl glycoside in 77% yield in the presence of 8mol% each of Au-phosphite and AgOTf. The stereochemical outcome of glycosidation was noticed to be temperature dependent. Careful analysis of the glycosidation revealed that the mixture of glycosides (α:β = 8:1) is resulting from the *C*-5 position of the acceptor; but, not from the *C*-3 position.



Scheme 6. Reagents: a) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, -78 °C, 5 h, 77% (overall yield 87% with α:β = 8:1); b) DDQ, CH2Cl2-MeOH (1:4), 25 °C, 4 h, 75%; c) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 °C, 15 min, 60%; d) $PdCl_2$, CH_2Cl_2-MeOH (1:4), 25 °C, 4 h; e) **11**, DMAP, CH_2Cl_2, 0-25 °C, 3 h, 76% over two steps.

Gratifyingly, the mixture of pentasaccharides could be separated using flash silica gel column chromatography to obtain 77% of the desired pentasaccharide **39**.[15] Deprotection of NAP-ether was achieved to afford the diol **40** which upon treatment with mannopyranosyl donor **2** gave nonasaccharide **41**. In the ^{13}C NMR spectrum of the nonasaccharide **41**, resonances due to nine anomeric carbons were noticed at δ 98.6, 98.8, 99.7, 99.8, 100.0, 100.5, 105.1, 105.5, and 106.8 ppm. Subsequently, the nonasaccharide was converted into the corresponding carbonate glycosyl donor **42** in 76% yield (Scheme 6).

The final assembly of heneicosaarabinomannan **1** started with the deprotection of silyl ether **34** using HF·py to afford alcohol **43** which was glycosylated with donor **38** using 8mol% each of gold-phosphite and AgOTf to afford dodecassacharide **44** in 85% yield. Twelve characteristic resonances due to anomeric carbons were noticed in the anomeric region (δ 98.7–106.2 ppm) of the spectrum.[46] The lone levulinoate was hydrolysed with hydrazine acetate in THF-MeOH to afford the required glycosyl acceptor **45**.[45] The final glycosidation between acceptor **45** containing twelve saccharide residues and the glycosyl donor **42** containing nine carbohydrate residues was performed in the presence of 8mol% each of Au-phosphite and AgOTf to observe formation of the fully protected heneicosaarabinomannan **46** in 80% yield. In the ^{13}C NMR spectrum of arabinomannan **46**, resonances due to the anomeric carbons were noticed as two sets centred on δ 98.8-100.7 ppm and δ 105.1-107.3 ppm for 21-anomeric carbons (Scheme 7).[4] Oligosaccharide **46** can be subjected to variety of reactions in order to attach biomolecules; however, global deprotection of compound **46** was considered to show that the molecule is stable to conditions employed for the cleavage of protecting groups. Cleavage of the three silyl ethers was carried out using the HF·py, Zemplén debenzoylation resulted in the saponification of eighteen benzoates and the final hydrogenolysis with $Pd(OH)_2/H_2$ caused the deprotection of twenty eight benzyl ethers and reduction of the olefin as well affording the heneicosaarabinomannan (**47**) as its propyl glycoside.

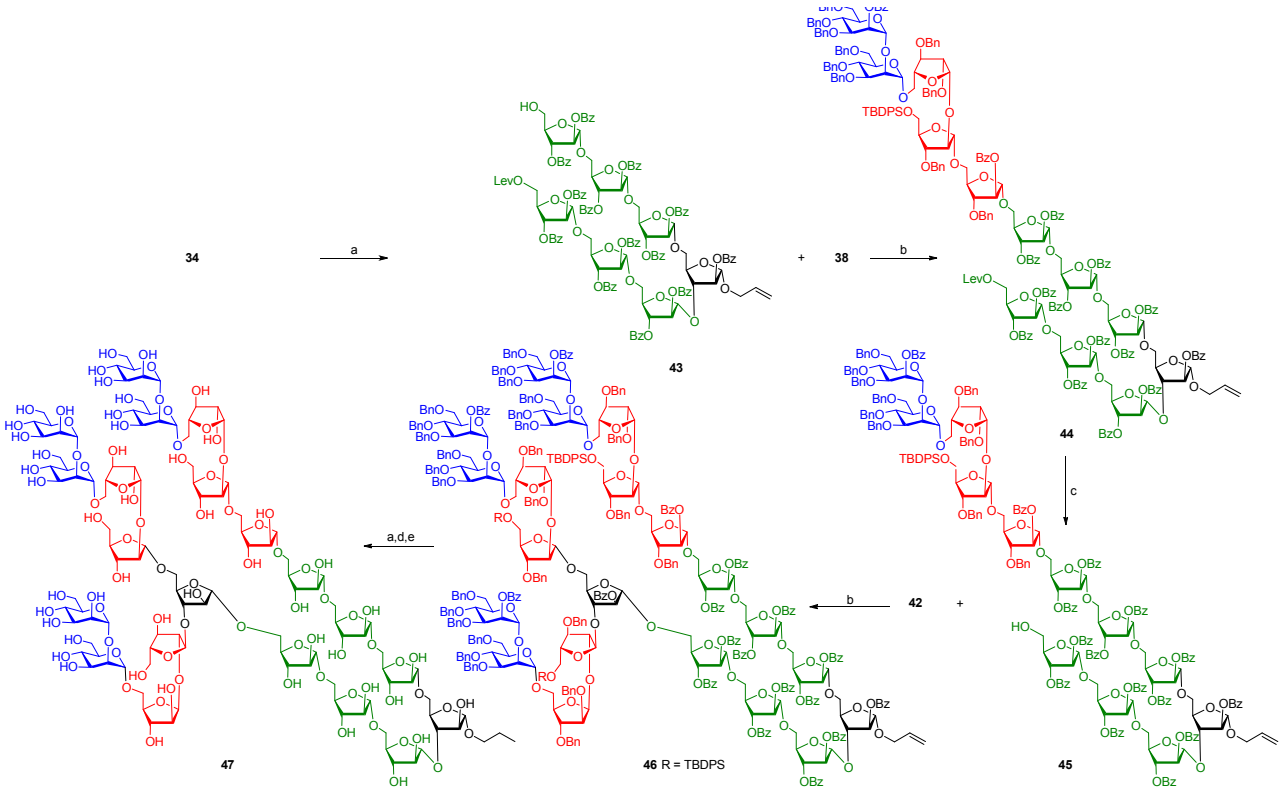
Conclusions

In summary, execution of the highly convergent and modular strategy has led to the first synthesis of branched-, hybrid- and complex- arabinomannan (containing 15-Ara*f* and 6-Man*p*-residues) of *Mycobacterium tuberculosis* cell wall in sufficient amounts for biological explorations with an overall yield of 0.016% yield. Stable alkynyl carbonate glycosyl donors are shown to be versatile glycosyl donors for the synthesis of large oligosaccharides. [Au]/[Ag]-Catalytic conditions are employed for all key glycosylations. 1,2-*cis* Ara*f* and some 1,2-*trans* Ara*f* linkages were installed taking advantage of reciprocal donor-acceptor selectivity. Taken together, the synthesis uses stable reactants, catalytic quantities of noble metal salts; therefore, experimentally less demanding and operationally convenient.

View Article Online
DOI: 10.1039/C6SC04866H

Journal Name

ARTICLE



Scheme 7. Reagents: a) HF·py, pyridine, 0-25 °C, 5 h, 83% for **43**, 80% for **47** ; b) 8mol% chloro[tris(2,4-di-tert-butylphenyl)phosphite]gold, 8mol% AgOTf, CH_2Cl_2, 4Å MS powder, 25 °C, 30 min, 85% for **44** and 80% for **46**; c) Hydrazine acetate, THF-MeOH (4:1), 25 °C, 45 min, 80%; d) NaOMe, MeOH, 25 °C, 15 h, 87%; e) $Pd(OH)_2$, CH_3OH-THF-H_2O (4:3:3), H_2, 36 h, 78%.

Acknowledgements

MI and GPS acknowledge the fellowship from CSIR-UGC-NET. Authors thank financial assistance from DST-SERB-New Delhi [SB/OC/CB-03/2014]. Authors thank DST-FIST funds for high field NMR facility at IISER Pune.

Notes and references

‡ Ara*f* means arabinofuranose; Man*p* means mannospyranose, Im. means imidazole, DMAP means 4-*N*,*N*'-dimethylaminopyridine, THF means tetrahydrofuran, 4Å MS means 4Å molecular sieves.

1 Global Tuberculosis Report http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf?ua=1, 2015.
2 R. M. Coker, *Trop. Med. Int. Health*, 2004, **9**, 25.
3 M. M. Wade, Y. Zhang, *Front. Biosci.*, 2004, **9**, 975.
4 G. Källenius, A. Pawlowski, B. Hamasur, S. V. Svenson, *Trends Microbiol.*, 2008, **16**, 456.
5 X. Hong, A. J. Hopfinger, *Biomacromolecules*, 2004, **5**, 1066.
6 J. Liu, C. E. Barry III, G. S. Besra, H. Nikaido, *J. Biol. Chem.*, 1996, **271**, 29545.
7 G. S. Besra, K.-H. Khoo, M. R. McNeil, A. Dell, H. R. Morris, P. J. Brennan, *Biochem.*, 1995, **34**, 4257.
8 P. J. Brennan, H. Nikaido, *Annu. Rev. Biochem.*, 1995, **64**, 29.
9 A. Lee, S. W. Wu, M. S. Scherman, J. B. Torrelles, D. Chatterjee, M. R. McNeil, K.-H. Khoo, *Biochem.*, 2006, **45**, 15817.
10 G. S. Besra, D. Chatterjee, *In* Tuberculosis: Pathogenesis, Protection and Control, American Society (Ed.: B. R. Bloom), Microbiology Press, Washington, DC, 285-306. 1994.
11 J. B. Torrelles, P. A. Sieling, N. Zhang, M. A. Keen, M. R. McNeil, J. T. Belisle, R. L. Modlin, P. J. Brennan, D. Chatterjee, *Glycobiology*, 2012, **22**, 1118.
12 D. Kaur, M. E. Guerin, H. Skovierová, P. J. Brennan, M. Jackson, *Adv. Appl. Microbiol.*, 2009, **69**, 23.
13 A. K. Mishra, N. N. Driessen, B. J. Appelmelk, G. S. Besra, *FEMS Microbiol. Rev.*, 2011, **35**, 1126.

View Article Online
DOI: 10.1039/C6SC04866H

14 Y. Guérardel, E. Maes, V. Briken, F. Chirat, Y. Leroy, C. Locht, G. Strecker, L. Kremer, *J. Biol. Chem.*, 2003, **278**, 36637.
15 M. Gilleron, N. Himoudi, O. Adam, P. Costant, A. Venisse, M. Rivière, G. Puzo, *J. Biol. Chem.*, 1997, **272**, 117.
16 K. Dheda, M. Ruhwald, G. Theron, J. Peter, W. C. Yam, *Respirology*, 2013, **18**, 217.
17 S. D. Lawn, A. D. Kerkhoff, M. Vogt, R. Wood, *Lancet Infect. Dis.*, 2012, **12**, 201.
18 S. D. Law, *BMC Infectious Diseases*, 2012, **12**, 103.
19 K. N. Jayaprakash, J. Lu, B. Fraser-Reid, *Angew Chem. Int. Ed.*, 2005, **44**, 5894.
20 J. Lu, B. Fraser-Reid, *Chem. Commun.* 2005, 862.
21 B. Fraser-Reid, J. Lu, K. N. Jayaprakash, J. C. Lopez, *Tetrahedron: Asym.* 2006, **17**, 2449.
22 N. M. Podvanyy, P. I. Abronina, K. G. Fedina, N. N. Kondakov, I. Zinin, A. O. Chizhov, V. I. Torgov, V. V. Kachala, L. O. Kononov, *Russ. Chem. Bull.*, 2015, **64**, 1149.
23 K. Sahloul, T. L. Lowary, *J. Org. Chem.* 2015, **80**, 11417.
24 J. Gao, G. Liao, L. Wang, Z. Guo, *Org. Lett.*, 2014, **16**, 988.
25 B. Fraser-Reid, S. R. Chaudhuri, K. N. Jayaprakash, J. Lu, C. V. S. Ramamurty, *J. Org. Chem.*, 2008, **73**, 9732.
26 C. E. Chan, S. Gotze, G. T. Seah, P. H. Seeberger, N. Tukvadze, M. R. Wenk, B. J. Hanson, P. A. MacAry, *Sci. Rep.*, 2015, **5**, 10281.
27 A. Hölemann, B. L. Stocker, P. H. Seeberger, *J. Org. Chem.*, 2006, **71**, 8071.
28 L. Wang, S. Feng, L. An, G. Gu, Z. Guo, *J. Org. Chem.*, 2015, **80**, 10060.
29 S. Hotha, S. Kashyap, *J. Am. Chem. Soc.*, 2006, **128**, 9620.
30 S. R. Vidadala, S. Hotha, *Chem. Commun.* 2009, 2505.
31 G. Sureshkumar, S. Hotha, *Tetrahedron Lett.*, 2007, **48**, 6564.
32 A. K. Kayastha, S. Hotha, *Chem. Commun.*, 2012, **48**, 7161.
33 S. A. Thadke, B. Mishra, S. Hotha, *Org. Lett.*, 2013, **15**, 2466.
34 S. A. Thadke, B. Mishra, S. Hotha, *J. Org. Chem.*, 2014, **79**, 7358.
35 B. Mishra, M. Neralkar, S. Hotha, *Angew. Chem. Int. Ed.*, 2016, **55**, 7786.
36 M. Islam, G. Gayatri, S. Hotha, *J. Org. Chem.* 2015, **80**, 7937.
37 D. P. Nair, M. Podgorski, S. Chatani, T. Gong, W. Xi, C. O. Fenoli, C. N. Bowman, *Chem. Mater.*, 2014, **26**, 724.
38 C. E. Hoyle, C. N. Bowman, *Angew. Chem. Int. Ed.*, 2010, **49**, 1540.
39 B. H. Northrop, R. N. Coffey, *J. Am. Chem. Soc.*, 2012, **134**, 13804.
40 A. B. Lowe, *Polym. Chem.*, 2014, **5**, 4820.
41 P. Finch, G. M. Iskander, A. H. Siriwardena, *Carbohydrate Res.*, 1991, **210**, 319.
42 O. Kanie, Y. Ito, T. Ogawa, *J. Am. Chem. Soc.*, 1994, **116**, 12073.
43 C. V. S. Ramamurty, P. Ganney, C. S. Rao, B. Fraser-Reid, *J. Org. Chem.* 2011, **76**, 2245.
44 M. Joe, Y. Bai, R. C. Nacario, T. L. Lowary, *J. Am. Chem. Soc.*, 2007, **129**, 9885; A. Ishiwata, Y. Ito, *J. Am. Chem. Soc.,* 2011, **133**, 2275.
45 G. J. S. Lohman, P. H. Seeberger, *J. Org. Chem.*, 2004, **69**, 4081.
46 See Supporting information