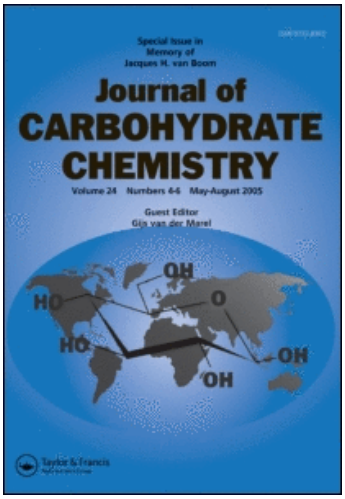

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Synthesis of 3-Deoxy-D-*threo*pentofuranose 5-Phosphate, a Substrate of Arabinose 5-Phosphate Isomerase

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3-Deoxy-D-*threo*pentofuranose 5-phosphate, a substrate of arabinose 5-phosphate isomerase, has been synthesised starting from D-arabinose. Selective protection of the hydroxyl groups at C-1, C-2, and C-5 allowed deoxygenation of position 3 by conversion into a thiocarbamate and radical reduction. Deprotection and phosphorylation of the primary hydroxyl group and final deprotection of the other hydroxyl groups afforded the desired compound.

Keywords Deoxysugars; API; LPS biosynthesis

INTRODUCTION

Arabinose 5-phosphate isomerase (API) converts ribulose 5-phosphate into arabinose 5-phosphate in bacteria. This reaction is the first step of the biosynthesis of KDO (3-deoxy-D-manno-octulosonate), an essential component of LPS (lipopolysaccharide) structure.[1] As a consequence, API activity is fundamental for Gram-negative bacteria survival,[2] which results in it being a relevant pharmacological target for the development of new antibacterial agents.[3,4]

We therefore decided to investigate the structural requirements of the active site of the enzyme in order to design inhibitors with potential antibacterial activity. In particular, we studied several modifications on arabinose 5-phosphate to verify their effect on substrate recognition by the

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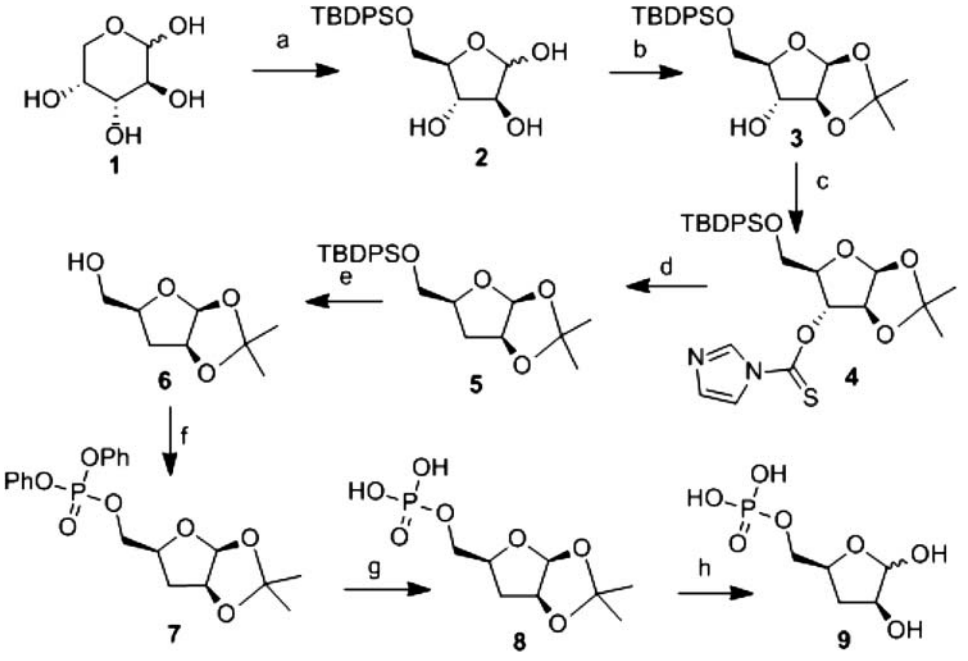
enzyme. In this context, we synthesised a 3-deoxy derivative of the natural substrate, namely 3-deoxy-D-*threo*pentofuranose 5-phosphate, and we verified API ability to recognize and convert it into the corresponding ketose. 3-Deoxy-D-*threo*pentofuranose 5-phosphate has been already reported as a weak API inhibitor,[5] but the synthesis is not described; in this work we demonstrate that this compound is in fact a substrate of this enzyme.

RESULTS AND DISCUSSION

The synthesis of 3-deoxy-D-*threo*pentofuranose 5-phosphate was performed starting from D-arabinose **1** (Sch. 1), which was treated first with *t*-butyldiphenylsilyl chloride (TBDPSC1) in order to protect selectively the primary hydroxyl group affording compound **2**,[6] and then with acetone dimethylacetal in dichloromethane, in the presence of camphorsulphonic acid (CSA), to protect the hydroxyl groups in positions 1 and 2. Those two hydroxyl groups are the only cis-related, in the β-anomer, that can generate the isopropylidene cycle. The obtained 5-*O*-t-butyldiphenylsilyl-1,2-*O*-isopropylidene-β-D-arabinofuranose (**3**)[6,7] has the only hydroxyl group at C-3 deprotected,

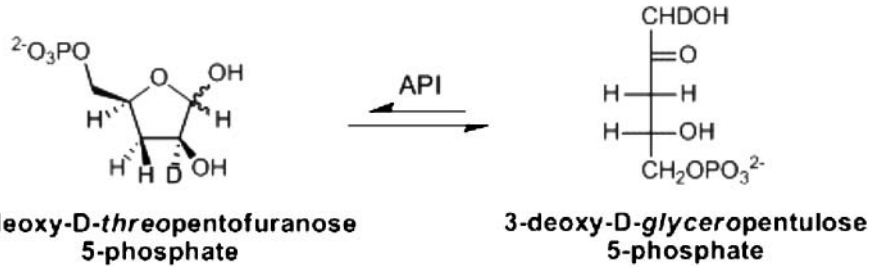


Scheme 1: *Reagents and conditions.* (a) TBDPSCl, Py dry, 4°C, 75% yield; (b) $Me_2C(OMe)_2$, CSA, CH_2Cl_2, 4°C, 63% yield; (c) thiocarbonyldiimidazole, CH_3CH_2Cl, rfx, 80°C; (d) $(Me_3Si)SiH$, AIBN, toluene dry, rfx, 110°C, 69% yield over two steps; (e) TBAF, THF, 91% yield; (f) diphenyl chlorophosphate, Py dry, 80% yield; (g) H_2, PtO_2, MeOH, quantitative yield; (h) H_2O, quantitative yield.

allowing its reduction to hydrogen, exploiting the radical displacement of a thiocarbamate. To this purpose, compound **3** was treated with thiocarbonyldiimidazole in dry dichloroethane at 80°C to afford the carbamate **4**, which was directly treated with $(Me_3Si)_3SiH$ and AIBN in toluene under reflux,[8] affording 5-*O*-*t*-butyldiphenylsilyl-3-deoxy-1,2-*O*-isopropylidene-*β*-D-*threo*pentofuranose **5**[6] in 69% yield over two steps. The deoxygenated compound **5** was then deprotected at the primary hydroxyl group by treatment with tetrabutylammonium fluoride (TBAF) in THF affording 3-deoxy-1,2-O-isopropylidene-*β*-D-*threo*pentofuranose **6** in 91% yield. The primary hydroxyl group of **6** was then converted into a diphenylphosphate by treatment with diphenyl chlorophosphate in dry pyridine (80% yield), and the diphenylphosphate was quantitatively deprotected by treatment with PtO_2 in degassed methanol, affording 3-deoxy-1,2-*O*-isopropylidene-*β*-D-*threo*pentofuranose 5-phosphate **8**. Finally, hydrolysis of the isopropylidene, the last protecting group, afforded 3-deoxy-D-*threo*pentofuranose 5-phosphate **9** in quantitative yield.

STD NMR experiments[9] performed with *Escherichia coli* API[10] showed that 3-deoxy-D-*threo*pentofuranose 5-phosphate **9** is accepted in the active site of the enzyme, and it is isomerized to the corresponding ketose sugar (Sch. 2, Fig. 1). According to our data, positions 1 and 5 of both the deoxy-substrates are fundamental for recognition and binding processes and their affinity for API is lower with respect to the natural substrate. In addition, API-specific activity for arabinose 5-phosphate and for compound **9** was determinated by monitoring the enzymatic reaction by ^{1}H-NMR. The calculated values are $2.306 \pm 0.467 \times 10^{-4}$ and $3.295 \pm 0.165 \times 10^{-5}$, respectively.

These results indicate that 3-OH deletion reduces the binding affinity, even if it does not inhibit isomerisation. This observation can be exploited in order to design and synthesize new API inhibitors as potential antibacterial drugs.



Scheme 2: The reversible isomerization of 3-deoxy-D-*threo*pentofuranose 5-phosphate to 3-deoxy-D-*glycero*pentulose 5-phosphate catalyzed by API. When the reaction is carried out in D_2O, the deuteration of 3-deoxy-D-*glycero*pentulose 5-phosphate at position 1 and of 3-deoxy-D-*threo*pentofuranose 5-phosphate at position 2 occurs.

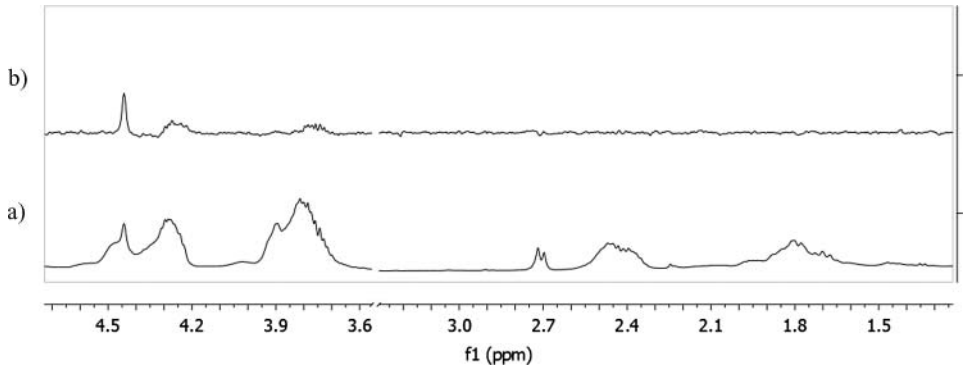


Figure 1: (a) ^{1}H NMR spectrum of API: 3-deoxy-substrate mixture at equilibrium (3-deoxy-D-*threo*pentofuranose 5-phosphate: 3-deoxy-D-*glycero*pentulose 5-phosphate 4:6) NS = 16; (b) STD spectrum of API-substrate mixture at equilibrium, at an API: 3-deoxy-D-*threo*pentofuranose 5-phosphate 1:80 molar ratio and an API: 3-deoxy-D-*glycero*pentulose 5-phosphate 1:120 molar ratio, protein saturation time = 2 s, NS = 2304, on-resonance frequency = 7.9 ppm, off-resonance frequency = 40 ppm. Spectra were recorded on the same sample; the sample was dissolved in PBS, pH 7.3, 5°C.

EXPERIMENTAL

Synthesis

General methods

All solvents were dried with molecular sieves (4 Å, Fluka) for at least 24 h prior to use. When dry conditions were required, the reactions were performed under argon. Thin layer chromatography (TLC) was performed on silica gel 60 F254 plates (Merck) with UV detection, or by using a developing solution of concd. $H_2SO_4/E_1OH/H_2O$ (10:45:45), followed by heating at 180°C. Flash column chromatography was performed on silica gel 230–400 mesh (Merck). Mixtures of petroleum ether (boiling range 40–60°C) and ethyl acetate were used as eluents. ^{1}H, ^{13}C, ^{1}H-^{1}H COSY, and ^{1}H-^{13}C HSQC NMR spectra were recorded with a Varian 400 MHz Mercury instrument at 25°C unless otherwise stated. Chemical shifts are reported in ppm downfield from TMS as internal standard; mass spectra were recorded with a Q-TRAP 2000 instrument (Applied Biosystem). Optical rotations were measured at ambient temperature, using the sodium-D line, with a POLAX-2L electronic polarimeter (ATAGO).

5-O-t-Butyldiphenylsilyl-D-arabinofuranose (2)

To a stirred suspension of D-arabinose (100 mg, 0.666 mmol) in dry Py (2 mL), TBDPSC1 (188 μL, 0.733 mmol) was added dropwise at 0°C under argon atmosphere. Afer 10 min the reaction was stirred at 4°C overnight. Water was added to quench the reaction and the mixture was stirred for 15 min.

The mixture was concentrated under reduced pressure. The product was purified by flash column chromatography (5:5, petroleum ether;EtOAc) affording **2** (194 g, 75% yield) as a yellow oil (mixture of α- and β- anomers). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.83–7.56 (m, 4H, Ar), 7.56–7.27 (m, 6H, Ar), 5.41 (s, 1H, H1), 5.29 (d, 1H, J = 3.8, H1), 4.39–3.57 (m, 5H), 1.21–0.97 (s, 9H, 3 × CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.05, 135.87, 135.83, 132.25, 132.05, 130.43, 130.34, 130.26, 128.25, 128.20, 128.18, 128.01, 103.49, 96.72, 86.74, 82.92, 79.60, 78.03, 77.86, 76.28, 65.01, 64.39, 60.86, 27.10, 26.95, 19.29. MS: m/z = 411.4 $[M+Na]^+$; m/z = 427.4 $[M+K]^+$ Anal. calcd. for $C_{21}H_{28}O_5Si$: C, 64,92; H, 7.26; O, 20.59; Si, 7.23; found C, 64.95; H, 7.24; O, 20.58; Si, 7.24.

5-O-t-*Butyldiphenylsilyl-1,2*-O-*isopropylidene-β*-D-*arabinofuranose (3)*

To a stirred solution of **2** (50 mg, 0.129 mmol) in dry CH_2Cl_2 (2.5 mL), 2,2-dimethoxypropane (24 μL, 0.194 mmol) and camphorsulphonic acid (catalytic amount) were added at 4°C under argon atmosphere. The reaction mixture was stirred overnight at 4°C. After 14 h, Et_3N was added to neutralize the reaction and the mixture was stirred for 15 min. The mixture was concentrated under reduced pressure. The product was purified by flash column chromatography (8:2, petroleum ether:EtOAc) giving **3** (35 mg, 63% yield) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.78–7.59 (m, 4H, Ar), 7.50–7.31 (m, 6H, Ar), 5.89 (d1H, J = 4.0, H1), 4.55 (d, 1H, J = 4.0, H2), 4.43 (d, 1H, J = 1.9, H3), 4.19–3.98 (m, 1H, H4), 3.98–3.72 (m, 2H, 2 × H5), 1.34 (s, 3H, CH_3), 1.29 (s, 3H, 3H, CH_3), 1.10 (s, 9H, 3 × CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.82, 133.35, 130.02, 128.01, 112.76, 105.81, 87.66, 87.29, 87.23, 76.49, 63.86, 27.09, 26.35, 19,45. $[\alpha]_D^{20}$ = –12.1 (c = 1, $CHCl_3$); MS: m/z = 451.4 $[M+Na]^+$; m/z—467.4 $[M + K]^+$ Anal. caled. for $C_{24}H_{32}O_5Si$: C, 67.26; H, 7.53; O, 18.67; Si, 6.55; found: C, 67.22; H, 7.54; O, 18.66; Si, 6.57.

5-O-t-*Butyldiphenylsilyl-3*-O-*(imidazolylthiocarbonyl)-1,2*–O-*isopropylidene-β*-D-threo*pentofuranose (4)*

To a stirred solution of **3** (65 mg, 0.151 mmol) in dry $CH_3CH_2Cl_2$ (2 mL), 1,1′-thiocarbonyldiimidazole (35 mg, 0.197 mmol) was added under argon atmosphere. The reaction mixture was heated at reflux (80°C). After 3 h, the reaction mixture was cooled to r t and the mixture was concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and the organic layer was washed with water.

5-O-t-*Butyldiphenylsilyl-3-deoxy-1,2*-O-*isopyropylidene-β*-D-threo*pentofuranose (5)*

To a stirred solution of crude **4** in dry toluene (2 mL), tris(trimethylsilyl)silane (33 μL, 0.196 mmol) and α,α'-azobisbutyronitrile (9 mg, 0.055 mmol) were added and the resulting solution was heated and stirred at 110°C

under argon atmosphere and refluxed. After 20 min, the mixture was cooled to r t and the mixture was concentrated under reduced pressure. The product was purified by flash column chromatography (9.5:0.5, petroleum ether:EtOAc) affording **5** (42 mg, 69% yield over 2 steps) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ–7.72–7.63 (m, 4H, Ar), 7.46–7.32 (m, 6H, Ar), 5.79 (d, 1H, J = 3.9, H1), 4.79–4.69 (m, 1H, H2), 4.37–4.23 (m, 1H, H4), 3.91–3.73 (m, 2H, 2 × H5), 2.27 (dd, 1H, J = 14.2, 2.4, H3a), 2.15 (ddd, 1H, J = 14.3, 8.1, 6.2, H3b), 1.33 (s, 3H, CH_3), 1.28 (s, 4H, CH_3), 1.06 (s, 9H, 3 × CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.86, 133.74, 129.86, 127.90, 112.33, 106.87, 81.49, 80.96, 66.06, 33.78, 27.20, 27.06, 26.14, 19.46, $[\alpha]_D^{20}$ = –10 (c = 1, $CHCl_3$); MS: m/z = 413.7 $[M+H]^+$, m/z = 435.7 $[M+Na]^+$. Anal. calcd. for $C_{24}H_{32}O_4Si$: C, 69,86; H,7.82; O, 15.51; Si, 6,81; found: C, 69.87; H, 7.84; O, 15.49; Si, 6.80.

*3-Deoxy 1,2-*O*-isopropylidene-β-*D-threo*pentofuranose (6)*

To a stirred solution of **5** in dry THF (2 mL), tetrabutylammonium fluoride 1M in THF (121 μL, 0.121 mmol) was added at r t under argon atmosphere, After 1 h, silica was added and the mixture was conecentrated under reduced pressure. The product was purified by flash column chromatography (9.5:0.5, petroleum ether: $(CH_3)_2CO$) giving **6** (19.3 mg 91% yield) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.81 (d, 1H, J = 3.8, H1), 4.75 (m, 1H, H2), 4.31 (m, 1H, H4), 3.81 (dd, 1H J–11.5, 8.0, IH, H5a), 3.60 (dd, 1H, J = 11.5, 3.9, H5b), 2.19 (ddd, 1H J = 14.7, 8.6, 6.3, H3a), 1.98 (dd, 1H J = 14.2, 3.3, H3b), 1.54 (s, 3H, CH_3), 1.31 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 112.35, 106.67, 81.95, 80.91, 65.23, 33.39, 27.21, 26.13. $[\alpha]_D^{20}$ = +4.9 (c = 1, $CHCl_3$); MS: m/z = 197.2 $[M+Na]^1$. Anal. calcd. for $C_8H_{14}O_4$; C, 55.16; H, 8.10; O, 36.74; found: C, 55.14; H, 8.11; O, 36.70.

*3-Deoxy-1,2-*O*-isopropylidene-β-*D-threo*pentofuranose 5-diphenylphosphate (7)*

To a stirred solution of **6** (220 mg, 1.26 mmol) in dry Py (13 mL), diphenylphosphochloridate (24 μL, 0.194 mmol) was added at 0°C under argon atmosphere. After 1 h, MeOH was added to quench the reaction and the mixture was stirred for 15 min. The mixture was concentrated under reduced pressure. The product was purified by flash column chromatography (6:4, petroleum ether:EtOAc) affording **7** (35 mg, 80% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.41–6.93 (m, 10H, Ar), 5.75 (d, 1H, J = 3.7, H1), 4.64 (bt, 1H, J = 4.1, H2), 4.52–4.38 (m, 1H, J = 9.5, 7.1, H5a), 4.39–4.30 (m, 1H, J = 8.6, 2.4, H4), 4.30–4.21 (m, 1H, J = 9.6, 6.6, H5b), 2.13–1.97 (m, 2H, 2 × H3), 1.46 (s, 3H, CH_3), 1.22 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.31, 130.00, 125.58, 120.32, 112.66, 107.07, 80.57, 79.04, 70.38, 33.63, 27.17, 25.95. ^{31}P NMR (162 MHz, $CDCl_3$) δ –10.96, $[\alpha]_D^{20}$ = +5.9 (c = 1, $CHCl_3$); MS: m/z = 407.3 $[M+H]^+$; m/z = 429.3 $[M+Na]^+$; m/z = 445.3 $[M+K]^+$.

Anal. calcd. for $C_{20}H_{23}O_7P$: C, 59,11; H, 5.70; O, 27.56; P, 7.62; found: C, 59.09; H, 5.71; O, 27.54; P, 7.61.

*3-Deoxy-1,2-*O-*isopropylidene-β-*D-threo*pentofuranose 5-phosphate (8)*

Compound **7** (30 mg, 0.074 mmol) was dissolved in degassed MeOH (3 ml) and PtO_2 was added (16.8 mg). The reaction mixture was stirred under H_2 at r t for 2 h. The catalyst was removed by filtration through Celite and the filtrate was concentrated under reduced pressure, obtaining **8** (19 mg, quantitative yield) as a white solid. ^{1}H NMR (400 MHz, CD_3OD) $\delta = 5.77$ (d, 1H, $J = 3.0$, H1), 4.84–4.67 (m, 1H, H2), 4.44–4.23 (m, IH, H4), 4.23–3.86 (m, 2H, $J = 40.3$, 2 × H5), 2.34–1.94 (m, 2H, $J = 33.4$, 17.6, 2 × H3), 1.51 (s, 3H, CH_3), 1.28 (s, 3H, CH_3). ^{13}C NMR (101 MHz, CD_3OD) δ 112.38, 106.99, 80.75, 79.73, 68.07, 33.10, 26.26, 24.98. ^{31}P NMR (162 MHz, D_2O) δ 1.07. $[\alpha]_D{}^{20} = +5.9$ (c = 1, H_2O); MS: m/z = 255.3 $[M+H]^+$; m/z = 277.3 $[M+Na]^+$; m/z = 293.3 $[M+K]^+$. Anal. calcd. for $C_8H_{15}O_7P$: C, 37.80; H, 5.95; O, 44.06; P, 12.19; found: C, 37.78; H, 5.97; O, 44.02; P, 12.20.

*3-Deoxy-*D-threo*pentofuranose 5-phosphate (9)*

Compound **8** was dissolved in H_2O and the solution was transferred into an NMR-tube. The reaction was monitored by ^{1}H NMR. After 1 h pH was neutralized by adding NaOH 1.0 M and the solution was lyophilized to give **9** in quantitative yield (mixture of α- and β- anomers). ^{1}H NMR (400 MHz, D_2O) $\delta = 5.10$ (s, 1H, H1), 5.02 (d, 1H, $J = 4.3$, H1), 4.26 (m, 1H, H2), 4.18–3.93 (m, 1H, H4), 3.93–3.58 (m, 2H, 2 × H5), 2.38–2.06 (m, 1H, H3a), 1.66–1.35 (m, 1H, H3b). ^{13}C NMR (101 MHz, D_2O) δ 102.23, 95.63, 77.48, 77.24, 75.21, 74.35, 70.83, 67.84, 32.84, 30.94. MS: m/z = 259.1 $[M(disodium\ salt)+H]^+$. Anal. calcd. for $C_5H_{11}O_7P$: C, 28.05; H, 5.18; O, 52.31; P, 14.47; found: C, 28.07; H, 5.19; O, 52.28; P, 14.49.

NMR experiments

Binding studies

The ligand resonances were assigned using ^{1}H-^{1}H COSY and ^{1}H-^{13}C HSQC NMR spectroscopy. A basic 1D-STD sequence was used with the on-resonance frequency of 7.9 ppm and the off-resonance frequency of 40 ppm. A train of Gaussian-shaped pulses of 50 ms each was employed, with a total saturation time of the protein envelope of 2 s. A $T_{1\rho}$ filter of 2 ms was employed to eliminate the background signals from protein. All the samples were dissolved in deuterated PBS at pH 7.3, containing NaCl (300 mM), at 5°C. Total sample volumes were 550 μL. The on-resonance and the off-resonance spectra were acquired simultaneously with the same number of scans. The STD spectrum was

obtained by subtraction of the on-resonance spectrum from the off-resonance spectrum. Subtraction was performed by phase cycling to minimize artifacts arising from magnet and temperature instabilities.[11] Reference experiments of samples containing only the free tested compound itself were performed under the same experimental conditions to verify true ligand binding. The effects observed in the presence of the protein were due to true saturation transfer, as no signal was present in the STD spectra obtained in the reference experiments, except residues from HDO, indicating artifacts from the subtraction of compound signals to be negligible.

Enzymatic assays

API-specific activity was determined as increase of ribulose 5-phosphate H3 or of 3-deoxy-D-glyceropentulose 5-phosphate H3 integral value vs. time per μg of API. Spectra were collected in 33 s time intervals over 673 s. Measurement is the mean of five independent determinations.

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REFERENCES

1. Holst, O. The structures of core regions from enterobacterial lipopolysaccharides—an update. *FEMS Microbiol. Lett.* **2007**, *271*, 3–11.

2. Raetz, C.R.; Whitfield, C. Lipopolysaccharide endotoxins. *Annu. Rev. Biochem.* **2002**, *71*, 635–700.

3. Meredith, T.C.; Aggarwal, p.; Mamat, U.; Lindner, B.; Woodard, R.W. Redefining the requisite lipopolysaccharide structure in *Escherichia coli*. *ACS Chem. Biol.* **2006**, *1*, 33–42.

4. Klein, G.; Lindner, B.; Brabetz, W.; Brade, H.; Raina, S. *Escherichia coli* K-12 suppressor-free mutants lacking early glycosyltransferases and late acyltransferase. *J. Biol. Chem.* **2009**, *284*, 15369–15389.

5. Bingham, E.C.; Gragg, C.E.; Hall, W.R.; Kelsey, J.E.; Mallory, W.R.; Richardson, D.C.; Benedict, C.; Ray, P.H. Inhibition of Arabinose-5-phosphate isomerase. An approach to the inhibition of bacterial lipopolysaccharide biosynthesis. *J. Med. Chem.* **1984**, *27*, 717–726.

6. (a) Ikeda, M.; Bando, H. Preparation of enynes as intermediates for vitamin D3 derivatives. *Jpn. Kokai Tokkyo Koho* **1995**, 12P. (b) Sunagawa, J.; Uenishi, Y.; Kususe, N.; Ito, Y.; Ishiwatari, A.; Akao, H.; Yano, I.; Fujita, Y. Arabinomycolate compounds, their manufacture from cell wall skeleton components of Mycobacterium bovis BCG, and their uses as antitumor agents, etc. *Jpn. Kokai Tokkyo Koho* **2006**, 44pp.

7. (a) Martin, O.R.; Rao, S.P.; El-Shenawy, H.A.; Kurz, K.G.; Cutler, A.B. Unsual 1,5-hydride shifts in lewis acid mediated reactions of benzylated sugars. Synthesis of 3-alkylisochroman derivatives. *J. Org. Chem.* **1988**, *53*, 3287–3292; (b) Fleet, G.W.J.;

Mathews, C.J.; Seijas, J.A.; Vazquez Tato, M.P.; Brown, D.J. Chiral quinuclidines (1-azabicyclo[2.2.2]octanes) from sugars: synthesis of (3S,5S)-quinuclidine-3,5-diol from D-arabinose. *J. Chem. Soc. Perkin Trans 1* **1989**, *5*, 1065–1066; (c) Elliott, R.P.; Fleet, G.W.J.; Vogt, K.; Wilson, F.X.; Wang, Y.; Witty, D.R.; Storer, R.; Myers, P.L.; Wallis, C.J. Attempted ring contraction of α-triflates of 3-azido- and 3-fluoro-γ-lactiones to oxetanes. *Tetrahedron Asymm.* **1990**, *1*, 715–718; (d) Pakulski, Z.; Zamojski, A. The reaction of acctyliron [(η5-C5H5)Fe(CO)(PPh3)(COCH3)] with sugar aldehydes. New synthesis of deoxy sugars. *Tetrahedron* **1995**, *51*, 871–908; (e) Vazquez-Tato, M.P.; Seijas, J.A.; Fleet, G.W.J.; Mathews, C.J.; Hemmings, P.R.; Brown, D. Synthesis of (3S,5S)-quinuclidine-3,5-diol and of [3S-(3α,3aα, 7aα)]-octahydro-2-furo[2,3-c]pyridinol from D-arabinose. *Tetrahedron* **1995**, *51*, 959–974; (f) Mereyala, H.B.; Hotha, S.; Gurjar, M.K. Synthesis of pentaarabinofuranosyl structure motif A of Mycobacterium tuberculosis. *Chem. Comm.* **1998**, *6*, 685–686; (g) Hoeffler, J.-F.; Grosdemange-Billiard, C.; Rohmer, M. Elucidation of the 2-C-methyl-D-erythritol 4-phosphate pathway for isoprenoid biosynthesis: straightforward syntheses of enantiopure 1-deoxy-D-xylulose from pentose derivatives. *Tetrahedron Lett.* **2001**, *42*, 3065–3067; (h) Sorensen, M. H.; Nielsen, C.; Nielsen, P. Synthesis of a bicyclic analogue of AZT restricted in an unusual 04′-Endo conformation. *J. Org. Chem.* **2001**, *66*, 4878–4886; (i) Sharma, G.V.M.; Reddy, V. G.; Radha Krishna, P.; Sankar, A.R.; Kunwar, A.C. Synthesis of spiro carbon linked disaccharides from D-glucose, D- and L-arabinose. *Tetrahedron* **2002**, *58*, 3801–3812; (l) Houseknecht, J.B.; Lowary, T.L. Oligofuranosides containing conformationally restricted residues: synthesis and conformational analysis. *J. Org. Chem.* **2002**, *67*, 4150–4164; (m) Larsen, C.H.; Ridgway, B.H.; Shaw, J.T.; Smith, D.M.; Woerpel, K.A. Stereoselective C-glycosylation reactions of ribose derivatives: electronic effects of five-membered ring oxocarbenium ions. *J. Am. Chem. Soc.* **2005**, *127*, 10879–10884; (n) Khasnobis, S.; Zhang, J.; Angala, S.K.; Amin, A.G.; McNeil, M.R.; Crick, D.C.; Chatterjee, D. Characterization of a specific arabinosyltransferase activity involved in mycobacterial arabinan biosynthesis. *Chem. Biol.* **2006**, *13*, 787–795; (o) Chevallier, O.P.; Migaud, M.E. Investigation of acetyl migrations in furanosides. *Beilstein J. Org. Chem.* **2006**, *2*(14), 1–6; (p) Doboszewski, B.; Herdewijn, P. Carbohydrate-based approach to four enantiomerically pure 2-naphthylmethyl 3-hydroxy-2-methylbutanoates. *Tetrahedron Lett.* **2008**, *49*, 1331–1335; (q) Sattigeri, V.J.; Palle, V.P.; Khera, M.K.; Reddy, R.; Tiwari, M.K.; Soni, A.; Abdul Rauf, A.R.; Joseph, S.; Musib, A.; Dastidar, S.G.; Srivastava, Punit Kumar. Preparation of uronic acid derivatives as metalloproteinase inhibitors. *PCT Int. Appl.* **2008**, 183p. (r) Doboszewski, B.; Herdewijn, P. Carbohydrate chiral-pool approach to four enantiomerically pure 2-naphthylmethyl 3-hydroxy-2-methylbutanoates. *Terahedron***2008**, *64*, 5551–5562; (s) Muraoka, O.; Tanabe, G. Preparation of cyclic sulfonium salt as glycosidase inhibitor. *PCT Int. Appl.* **2008**, 55p.

8. Mathe, C.; Imbach, J.-L.; Gosselin, G. 1,2-Di-*O*-acetyl-5-*O*-benzoyl-3-deoxy-L-*erythro*- pentofuranose, a convenient precursor for the stereospecific synthesis of nucleoside analogues with the unnatural β-L-configuration. *Carbohydr. Res.* **2000**, *323*, 226–229.

9. Meyer, B.; Peters, T. NMR spectroscopy techniques for screening and identifying ligand binding to protein receptors. *Angew. Chem. Int. Ed.* **2003**, *42*, 864–890.

10. Meredith, T.C.; Woodard, R.W. *Escherichia coli* YrbH Is a D-arabinose 5-phosphate isomerase. *J. Biol. Chem.* **2003**, *278*, 32771–32777.

11. Mayer, M.; Meyer, B. Group epitope mapping by saturation transfer difference NMR to identify segments of a ligand in direct contact with a protein receptor. *J. Am. Chem. Soc.* **2001**, *123*, 6108–6117.