The chemical synthesis of MPHPV S4 [α-(2-methoxyphenoxy)-β-hydroxypropiovanillone (S4)] was accomplished from commercially available GGE S1 [(guaiacylglycerol-β-guaiacyl ether (S1))] as shown in Figure 1A. The phenolic OH- and primary OH-groups of S1 were selectively protected with a tert-butyldiphenylsilyl group via silylation with tert-butyldiphenylchlorosilane using the DMAP-TEA method (Chaudhary and Hernandez, 1979) to give S2 in quantitative yield. Oxidation of the remaining free secondary OH-group of S2 with periodinane (Dess and Martin, 1991) afforded the ketone S3 in 90 % yield. Finally, removal of the tert-butyldiphenylsilyl groups with TBAF (tetrabutylammonium fluoride) in THF (Hanessian and Lavallee, 1975) afforded the desired product S4 in 85 % yield.

Figure 1. Chemical synthesis of MPHPV (α-(2-methoxyphenoxy)-β-hydroxypropiovanillone) from GGE. The reagents and reaction conditions used were: a) TEA, DMAP, TBDPSi-Cl, CH₂Cl₂, r.t., 1 h, 97 %; b) Dess–Martin periodinane, 90%; c) TBAHF/THF, r.t. 1 h, 85 %.

The chemical synthesis of HPV-glucopyranoside S14 (3-((β-D-glucopyranosyl)oxy-1-(4-hydroxy-3-methoxyphenyl)-propan-1-one (S14)) is outlined in Figure 2.

Figure 2. Chemical synthesis of HPV-glucopyranose from 4-benzyloxy-3-methoxybenzaldehyde

Compound nomenclature:

S5: 4-Benzyloxy-3-methoxybenzaldehyde; S6: Ethyl diazoacetate; S7: Ethyl 3-(4-benzyloxy-3-methoxyphenyl)-3-oxopentanoate; S8: 3-(4-Benzyloxy-3-methoxyphenyl)-3-hydroxy-propan-1-ol;
S9: 1-(4-Benzylxy-3-methoxyphenyl)-3-(tert-butyldiphenylsilyl)oxy-popan-1-ol;
S10: 1-(4-Benzylxy-3-methoxyphenyl)-3-(tert-butyldiphenylsilyl)oxy-popan-1-one;
S11: 2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl fluoride;
S12: 1-(4-Benzylxy-3-methoxyphenyl)-3-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)oxy-propan-1-one;
S13: 3-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)oxy-1-(4-hydroxy-3-methoxyphenyl)-propan-1-one;
S14: 3-(β-D-glucopyranosyl)oxy-1-(4-hydroxy-3-methoxyphenyl)-propan-1-one (HPV-Glucoside);
The reagents and reaction conditions used were:  
a) 5 mol % NbCl₅, CH₂Cl₂, r.t;  
b) NaBH₄ (4 eq), MeOH, r.t;  
c) TEA, DMAP, TBDPSi-Cl, CH₂Cl₂, r.t.;  
d) Dess–Martin periodinane, 90% ;  
e) BF₃·Et₂O, CH₂Cl₂, r.t., 1.5 h;  
f) AlCl₃·PhNMe₂, CH₂Cl₂, r.t;  
g) NaOCH₃-MeOH, MeOH, r.t., Dowex (H⁺ Form).
In this synthesis, commercially available 4-benzylxy-3-methoxybenzaldehyde (S5) was treated with ethyl diazoacetate (S6) in the presence of NbCl₅ as described for similar aldehydes (Yadav et al., 2005) to give the corresponding β-ketoester S7 in 75 % yield. Chemical modification of S7 via reduction (Chaudhuri et al., 2010), selective silylation (Chaudhary and Hernandez, 1979) and oxidation (Dess and Martin, 1991) afforded compound S10. The silylated derivative S10 was subjected for glycosylation with glycosyl fluoride (S11) (Zagrobelny et al., 2014) using borotrifluoroetherate as promoter (Kunz and Sager, 1985) to afford the protected glucoside S12. S12 was debenzylated (Akiyama et al., 1992) to give S13 from which the acetyl groups linked to the sugar moiety were removed using standard procedures afforded the target glucoside S14. The yield obtained in each of the deprotection steps was low and may be optimized. Structural verification of the synthesized compounds was carried out using electrospray ionisation mass spectrometry and ¹H, ¹³C-NMR experiments.