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The first example of a one-step synthesis of 2′-O-acetyl aryl-D-glucopyranosides

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ABSTRACT

A selective acidic system for partial deacetylation of phenolic D-glucopyranosides per-acetates has been developed that allows synthesis of the corresponding 2′-O-acetyl-D-glucosides. Many disadvantages of generally used methods for preparing such mono-acyl derivatives involving multistep procedures or the use of enzymes are avoided. The ion at *m*/*z* 289 in mass spectra of their TMS derivatives indicates a particular and characteristic fragmentation pattern of these 2′-O-acetyl derivatives of D-glucopyranosides. Quantum-chemical calculations applying B3LYP/TZVP level of theory revealed the stability of 2′-O-acetyl glucopyranoside if compare with 3′-, 4′- and 6′- O-acetyl glucopyanosides.
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1. Introduction

Phenyl glycosides of the family Salicaceae are responsible for the pharmacological activity of willow and aspen bark—a folk medicine herbal remedy used in the treatment of rheumatism, pain, fever and opistorchiasis.[1] Many of these glycosides contain one acetyl group in 2′-hydroxyl of glucose moiety,[2] e.g., 2′-O-acetylsalicin,[3] 2′-O-acetylsalicortin.[4] Monoacetyl derivatives of natural phenyl glycosides are interesting in phytochemistry as important secondary metabolites of higher plants and specific chemotaxonomic markers.[5] They are also of interest for medicinal chemistry since metabolism of monoacetylated glucose and glycosides differs from unprotected glucose derivatives.[6] Although 2′-O-acetyl derivatives of phenolic glycosides are of current importance, they are also of low accessibility.

Direct introduction of an acyl group to a carbohydrate generally leads to 6′-O-acyl derivatives since a primary alcohol group is the most sterically accessible and thus reactive.[7,8] Selectivity of the direct acylation procedure is particularly low and formation of different di-O-acyl derivatives is observed.[9] One more disadvantage is acetyl group migration[8,10] especially if basic conditions are used.[11] Many different methods for partial acylation of carbohydrates have been applied: multistep protection procedures,[12] enzymatic synthesis[13] or partial hydrolysis of fully acylated carbohydrates.[14] Methods for partial hydrolysis, as enzymatic as chemical, often provide selective hydrolysis of 6′-O-acetyl groups (the 6′-ester group at the primary position being the most accessible) or lead to di-acetates,[15] the 4′-acetate[16] and the 3′-O acetate.[17] Thus, despite the variety of different synthetic methods, there are not many procedures for obtaining 2′-O-acetyl derivatives. In some cases 2′-O-acyl group is the most labile.[18]

In the present work we developed a method for the partial hydrolysis of per-acetates of aryl glucopyranosides that allows isolation of their 2′-O-acetyl derivatives in one step. The suggested acidic system for partial hydrolysis provides 2′—selectivity without hydrolysis of the glycosidic bond and avoids the time-consuming route using various protective groups or enzymatic methods.

2. Results and discussion

The initial substrates are per-acetates of phenolglycosides **1**–**8**, which can be obtained from both natural sources and by synthetic means.[19]

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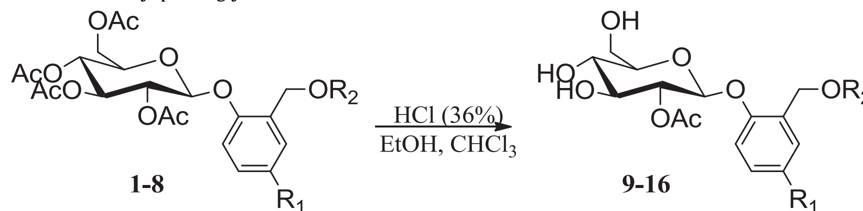
Table 1
Results of the selective synthesis of 2′-monoacetyl phenolglycosides **9–16**



Initial compound	Structure of the initial compound	Product	Structure of the product	Yield, %
1	R_1=OAc, R^2=benzoyl	**9**	R_1=OH, R_2=benzoyl	40
2	R_1=OAc, R_2=3-methoxy-4-acetoxy benzoyl	**10**	R_1=OH R_2=3-methoxy-4-hydroxy benzoyl	20
3	R_1=H, R_2=3-methoxy-4-acetoxy benzoyl	**11**	R_1=H, R_2=3-methoxy-4-hydroxy benzoyl	20
4	R_1=H, R_2=*trans*-cinnamoyl	**12**	R_1=H, R_2=*trans*-cinnamoyl	24
5	R_1=OAc, R_2=*trans*-cinnamoyl	**13**	R_1=OH, R_2=*trans*-cinnamoyl	12
6	R_1=OAc, R_2=2-acetoxy benzoyl	**14**	R_1=OH, R_2=2-hydroxy benzoyl	11
7	R_1=benzoyloxy, R_2=benzoyl	**15**	R_1=benzoyloxy, R_2=benzoyl	11
8	R_1=OAc, R_2=3,4-acetoxy-*trans*-cinnamoyl	**16**	R_1=OH, R_2=3,4-dihydroxy-*trans*-cinnamoyl	25

We established that the most suitable system for the selective removal of acetyl groups is as follows: 9.8 M hydrochloric acid (0.5 mL)–EtOH (1.5 mL)–$CHCl_3$ (0.5 mL). A 0.175 mM of per-acetyl glycoside was treated with this mixture at 30 °C for 8–13 h. In some cases an auxiliary addition of 2–3 drops of chloroform to achieve homogeneity of the reaction mixture is required. Yields of monoacetates **9–16** are 10–40% (Table 1), the remaining substances are fully deprotected glycosides, which can easily be separated from target products **9–16** and subjected to a new cycle of the acetylation—deacetylation procedure.

As a result, selective acetyl groups cleavage leads to a single monoacetyl product that could easily be separated from the non-acetylated glycoside by chromatographic means.

The position of the acetyl groups of resulting monoacetates was established by NMR analysis and comparison with literature data. Thus, for salireposide monoacetate **9** H-2′ signal at 4.77 ppm (dd, $J_{3',4'}$=9.6, 8.2, MHz) is shifted 1.2–1.5 ppm downfield from the position of glucose ring protons and from the H-2′ signal of unprotected slireposide.[20] In addition, NMR data (both ^{13}C and ^{1}H) of glucose moiety for 2′-O-benzoyl salicin[21] and 2′-O-acetyl salicin[3] measured in DMSO-d_6 is in good agreement with our samples measured in the same solvent whereas NMR data of e.g. 3′-O-acetyl salicin, isolated from *S. pseudo-lasiogyne*[22] differs significantly. For position confirmation of the acetyl group, we performed HMBC analysis (Fig. 1), which showed correlation between H-2′ proton with glucose ring carbons at δ_H 4.77 (H-2′)/δ_C 73.9 (C-3′); 99.7

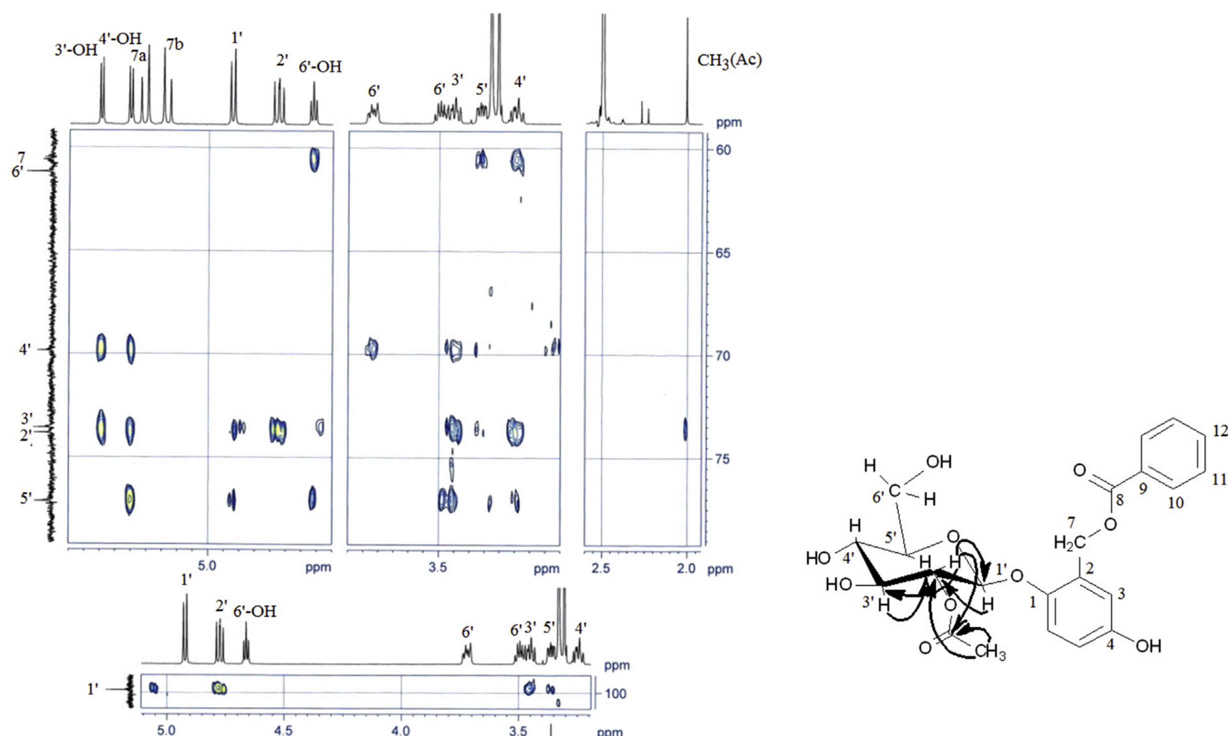


Fig. 1. HMBC spectral data of glucose moiety and key correlations of 2′-O-acetyl salireposide **9**.

Table 2
Comparison of ^{1}H NMR chemical shifts of 2′-O-acetylsalireposide **9**, measured at 600 MHz in DMSO-d_6 and calculated by DFT/B3LYP/TZVP

	3	5	6	7	10	11	12	1′	2′	3′	4′	5′	6′	Ac
Calc, MHz	7.17	6.61	7.42	6.83 4.28	8.66 8.31	7.67 7.54	7.76	4.91	4.42	3.59	3.53	3.53	3.77 3.86	2.10
Exp, MHz	6.79	6.66	7.05	5.12 5.20	8.00	7.49	7.68	4.92	4.76	3.45	3.24	3.36	3.50 3.71	2.01

(C-1′). The same data was obtained for glycosides **14** and **15** (see supplementary data). In addition, ^{1}H NMR data of 2′-O-acetyl salireposide **9** is in good agreement with calculated DFT/B3LYP/TZVP results (Table 2). All these arguments indicate that **9** is 2′-O-acetyl salireposide.

Specific fragmentation in the mass-spectra of trimethylsilyl derivatives of monoacetates in GC–MS analysis shows a prominent peak at m/z 289 (see supplementary data), rationalized as probably due to initial splitting of the glycosidic bond[23] followed by loss of TMS-OH (mass 90) and ketene (mass 42).

Thus, the specific ion m/z 289 in the mass-apectra of TMS-derivatives is notably useful for the identification of natural and synthetic 2′-O-acetyl glucopyranosides.

Factors of such hydrolytic stability of 2′-O-acetyl glucopyranosides comparasing to 3′- and 4′-Oacetylated glucopyranosides are not clear yet. It is more likely that hydrolitic attac at 2′-O-acetyl group is inhibited by the steric hindrance of the aglycone. Also thermodinamic factors should be taken into account. Thus, DFT calculations of all the four possible monoacetyl isomers of **9** using B3LYP/TZVP level of theory and using conductor-like screening model (COSMO) with a dielectric constant of 24.852 simulating ethanol revealed the most relative thermodinamic stability of 2′-O-acetate (Table 3). The results of DFT calculations do not contradict to experimental data although do not explain it. Neverthless, the fact of different hydrolitic stability of monoacetyl derivatives requires further investigation that is beyond the scope of this paper.

3. Experimental section

3.1. General experimental procedures

Melting points, which are uncorrected, were determined using MP50 Melting point system (Mettler toledo). UV spectroscopic data were obtained with SF-102 spectrophotometer. IR spectra were recorded with IR Fourier spectrophotometer Spectrum BX II using KBr disks. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker-300 MMX spectrometer at 300 and 75.5 MHz, respectively, in $CDCl_3$, DMSO-d_6 and MeOD-d_4 with TMS as an internal standard or on Bruker DRX-600 (^{1}H: 600 MHz, ^{13}C: 150 MHz) in DMSO-d_6 in the same conditions. The chemical shifts are given in δ (parts per million) and the spin–spin coupling constants (J) in hertz. GC–MS analysis was performed using Agilent 7890A/5975C GC/MSD instrument, electron energy 70 eV. The ion source temperature was 230 °C, with the quadrupole temperature 150 °C and evaporator temperature 315 °C, employing a 30.000×0.25 mm×0.25 μm HP–5MS fused-silica capillary column. Helium was used as carrier gas at a constant flow of 1 mL/min and an inlet temperature of 315 °C. The column temperature mode: 2 min at 70 °C, 70–315 °C (10 °C/min), and 25 min at 315°C. All samples for GC–MS were prepares as trimethylsililated derivatives. Accurate mass measurement was performed on an Agilent 1200 series LC system coupled with micrOTOF-Q (Bruker) mass spectrometer. TLC were performed using plates Silufol-UV 254 and Sorbfil-UV 254 using chloroform–ethanol 4:1 mixture as eluent. Silica gel MN Kieselgel 60 0.04–0.063 mm was used for column chromatography. Commercially available solvents were used after drying with $CaCl_2$. Ethanol was a commercial grade of 96% purity. Per-acetylated glycosides (**1**–**8**) were obtained according to the method described earlier.[18]

Table 3
The relative energies of 2′-O-acetyl salireposide **9** isomers calculated by B3LYP/TZVP COSMO simulating EtOH. The energy of the lowest isomer (2′-O-acetyl salireposide **9**) is the reference energy

Isomer	Relative energy kcal mol^{-1}
2′-O-acetyl	0
3′-O-acetyl	0.55
4′-O-acetyl	6.32
6′-O-acetyl	0.74

3.2. Calculation details

The molecular structures of the four isomers of 2′-O-acetylsalireposide **9** were optimized at the density functional theory (DFT)[24] level using the B3LYP[25] functional and TZVP[26] basis set and using the conductor-like screening model (COSMO)[27] with a dielectric constant of 24.852 simulating Ethanol for considered solvent effects. Nuclear magnetic shieldings were calculated at the DFT/B3LYP/TZVP level of theory for only 2′-O-acetyl salireposide in gas phase. All calculations were carried out in Gaussian-09[28] Rev. D. 01 quantum chemical package.

3.3. Procedure for a typical hydrolysis reaction

A 0.175 mM of per-acetyl glycoside was treated with the mixture of 9.8 M hydrochloric acid (0.5 mL)–EtOH (1.5 mL)–CHCl3 (0.5 mL). The reaction mixture was stirred and incubated at 30 °C for 4–22 h, evaporated to dryness in a vacuum and the product was isolated employing column chromatography by gradient elution using chloroform and chloroform–ethanol mixture (from ratio 9:1 to 4:1). Analytical samples were purified by recrystallization from water, ethanol or acetone. Purity was determined by HPLC or GC–MS after derivatisation by HMDS in pyridine and thrifluoroacetic acid.[29]

3.3.1. 2′-O-Acetyl-salireposide (9)

2′-O-acetyl-salireposide (**9**) was obtained by hydrolysis of pentaacetyl-salireposide (**1**). Reaction time 4 h, crystallization from water gave colorless crystals, yield 40%, mp 192–194 °C. UV λ_{max} (H_2O) 226, 284 nm; IR (KBr): 3090, 1720, 1480, 1380, 1280, 1210, 1085, 805, 710 cm^{-1}; ^{1}H NMR (DMSO-d_6, 600 MHz) δ: 2.01 (3H, s, Ac); 3.24 (1H, m, H-4′); 3.36 (1H, m, H-5′); 3.45 (1H, m, H-3′); 3.50 (1H, m, H-6′a); 3.71 (1H, m, H-6′b); 4.66 (1H, m, OH-6′); 4.76 (1H, dd, J=9.6, 8.2, MHz, 1H, H-2′); 4.92 (1H, d, J=8.1, Hz, H-1′); 5.12 (1H, d, J=13.1, Hz, H-7a); 5.20 (1H, d, J=13.1, Hz, H-7b); 5.25 (1H, d, J=5.5, Hz, OH-4′); 5.34 (1H, d, J=5.5, Hz, OH-3′); 6.66 (1H, dd, J=8.8, 2.9, Hz, H-5); 6.79 (1H, d, J=2.7, Hz, H-3); 7.05 (1H, d, J=8.9, Hz, H-6); 7.55 (2H, m, H-10, H-13); 7.68 (1H, m, H-12); 8.00 (2H, dd, J=8.4, 1.2, Hz, H-10, H-14) ppm; ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 20.8 (CH_3, Ac); 60.6 (CH_2, C –6′) 61.2 (CH_2, C-7); 69.9 (CH, C –4′); 73.6 (CH, C –2′); 73.9 (CH, C –3′); 77.2 (CH, C –5′); 99.7 (CH, C –1′); 114.8 (CH, C –3); 115.3 (CH, C –5); 117.7 (CH, C-6); 126.3 (C, C-2);

128.9 (2×CH, C −11, C −13); 129.3 (2×CH, C −10, C −14); 129.6 (C, C −9); 133.5 (CH, C −12); 147.3 (C, C-1); 152.7 (C, C-4); 165.5 (C=O, C-8); 169.4 (C=O, Ac) ppm. HRESIMS *m/z* 447.1298 (calcd for $C_{22}H_{24}O_{10}$ ([M-H$^+$]$^-$) 447,1291).

3.3.2. *2-(2′-O-Acetyl-β-D-glucopyranosyloxy)-5-hydroxy-benzyl(3-methoxy-4-hydroxy)benzoate (2′-O-acetyl-vanolloyl-salirepin) (**10**)*

2-(2′-O-acetyl-β-D-glucopyranosyloxy)-5-hydroxy-benzyl(3-methoxy-4-hydroxy)benzoate (2′-O-acetyl-vanolloyl-salirepin) (**10**) was obtained by hydrolysis of 2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyloxy)-5-acetoxy-benzyl(3-methoxy-4-acetoxy)benzoate (hexaacetyl-vanilloyl-salirepin) (**2**). Reaction time 8 h. Crystallization from water gave colorless crystals, yield 20%, mp 169–175 °C. UV λ_{max} (H_2O) 265, 292 nm; ^{1}H NMR (DMSO-d_6, 300 MHz) δ: 2.04 (3H, s, Ac); 3.24–3.33 (2H, m, H-4′, H-5′); 3.45 (2H, m, H-3′, H-6′a); 3.70 m (1H, H-6′b); 3.84 (3H, s, OCH_3); 4.66 (1H, m, OH-6′); 4.78 m (1H, H-2′); 4.89 (1H, d, *J*=7.8, Hz, H-1′); 5.06–5.19 (2H, m, CH_2, H-7); 5.24 (1H, d, *J*=5.1, Hz, OH-4′); 5.34 (1H, d, *J*=5.4, Hz, OH-3′); 6.64 (1H, dd, *J*=2.7, 8.7 Hz, H-5); 6.75 (1H, s, H-5); 6.88 (1H, d, *J*=7.8 Hz, H-13); 7.03 (1H, d, *J*=8.7 Hz, H-6); 7.48 (1H, s, H-10); 7.49 (1H, d, *J*=8.7 Hz, H-14) ppm; ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ: 20.1 (CH_3, Ac); 55.3 (OCH_3); 60.8 (2xC H_2, C 6′,C-7); 69.9 (C H, C −4′); 73.6 (C H, C −2′); 73.9 (C H, C −3′); 77.0 (C H, C −5′); 99.9 (C H, C −1′); 112.6 (CH, C-10); 114.4 (C H, C-13); 114.9 (CH, C-3); 115.1 (C H, C-5); 117.8 (C H, C −6); 120.8 (C, C −9); 123.8 (CH, C-14); 126.9 (C, C-2); 147.1 (CH, C-11); 147.5 (C, C −1); 151.6 (C, C −12); 152.7 (C, C-4); 165.2 (C=O, C-8); 169.1 (C=O, Ac) ppm; HRESIMS 493.1349 (calcd for $C_{23}H_{26}O_{12}$ ([M-H$^+$]$^-$) 493,1346).

3.3.3. *2-(2′-O-Acetyl-β-D-glucopyranosyloxy)-benzyl(3-methoxy-4-hydroxy)benzoate (2′-O-acetyl-vanolloyl-salicin) (**11**)*

2-(2′-O-acetyl-β-D-glucopyranosyloxy)-benzyl(3-methoxy-4-hydroxy)benzoate (2′-O-acetyl-vanolloyl-salicin) (**11**) was obtained by hydrolysis of 2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyloxy)-benzyl(3-methoxy-4-acetoxy)benzoate (pentaacetyl-vanilloyl-salicin) (**3**). Reaction time 8.5 h, crystallization from water, yield 20%, mp 136–137 °C. UV λ_{max} (H_2O) 264, 292 nm; IR (KBr): 3420, 2890, 1720, 1610, 1520, 1500, 1460, 1430, 1380, 1290, 1230, 1090, 1040, 760 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) δ: 1.99 (3H, s, Ac); 3.36–3.39 (DMSO) (2H, H-4′, H-5′); 3.43–3.51 (2H, m, H- 3′, H-6′a); 3.728 (1H, d, *J*-9.9 Hz, H-6′b); 3.82 s (3H, OCH_3); 4.80–4.86 (2H, m, H-1′, H-2′); 5.14 (2H, m, CH_2, H-7); 6.86 (1H, d, *J*=8.1 Hz, H-13); 7.03 (1H, t, *J*=7.5 Hz, H-4); 7.19 (1H, d, *J*=8.4 Hz, H-6); 7.29 (1H, d, *J*-7.5, Hz, H-5); 7.35 (1H, d, *J*=7.5 Hz, H-3); 7.47 (1H, s, H-10); 7.49 (1H, d, *J*=7.5 Hz, H-14) ppm; ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ: 20.8 (CH_3, Ac); 55.8 (OCH_3); 60.6 (C H_2, C 6′); 60.9 (CH_2, C-7); 69.7 (C H, C −4′); 73.4 (C H, C −2′); 73.8 (C H, C −3′); 77.0 (C H, C −5′); 98.3 (C H, C −1′); 112.5 (CH, C-10); 115.2 (2×CH, C-13, C-6); 120.4 (C, C −9); 122.3 (C H, C-4); 123.5 (C H, C-14); 125.1 (CH, C-2); 128.5 (C, C-3); 129.5 (CH, C-5); 147.2 (C, C −11); 151.6 (C, C −12); 154.3 (C, C-1); 165.4 (C=O, C-8); 169.2 (C=O, Ac) ppm; HRESIMS 477.1413 (calcd for $C_{23}H_{26}O_{11}$ ([M-H$^+$]$^-$) 477,1397).

3.3.4. *2-(2′-O-Acetyl-β-D-glucopyranosyloxy)-benzyl-trans-cinnamoate (2′-O-acetyl-cinnamoyl-salicin) (**12**)*

2-(2′-O-acetyl-β-D-glucopyranosyloxy)-benzyl-*trans*-cinnamoate (2′-O-acetyl-cinnamoyl-salicin) (**12**) was obtained by hydrolysis of 2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyloxy)-benzyl-*trans*-cinnamoate (tetraacetyl-cinnamoyl-salicin) (**4**). Reaction time 8 h, yield 24%. Mp 165–170 °C. UV λ_{max} (H_2O) 278 nm; IR (KBr): 3500, 2890, 1720, 1640, 1500, 1460, 1380, 1310, 1260, 1240, 1080, 1050, 770, 750 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) δ: 2.03 (3H, s, Ac); 3.24–3.32 (DMSO) (1H, m, H-4′); 3.47–3.55 (3H, m, H-3′, H-5′, H-6′a); 3.71 (1H, m, H-6′b); 4.67 (1H, m, OH-6′); 4.80 (1H, m, 1H, H-2′); 5.03 (1H, d, *J*=8.1, Hz, H-1′); 5.07–5.16 (2H, m, H-7); 5.28 (1H, d, *J*=5.1, Hz, OH-4′); 5.38 (1H, d, *J*=5.5, Hz, OH-3′); 6.68 (1H, d, *J*=15.9 Hz, H-9); 7.01 (1H, t, *J*=7.5 Hz, H-4); 7.18 (1H, d, *J*=8.1 Hz, H-6); 7.31 (1H, d, *J*=7.5 Hz, H-3); 7.35 (1H, m, H-5); 7.42 (3H, m, H-13, H-14, H-15); 7.67 (1H, d, *J*=16.2 Hz, H-10); 7.72 (2H, m, H-12, H-16) ppm; ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ: 20.8 (CH_3, Ac); 60.4 (C H_2, C 6′); 60.6 (CH_2, C-7); 69.7 (C H, C −4′); 73.2 (C H, C −2′); 73.7 (C H, C −3′); 77.0 (C H, C −5′); 98.1 (C H, C −1′); 114.9 (C H, C −6); 117.8 (CH, H-9); 122.1 (C H, C −4); 124.7 (C, C-2); 128.2 (2xC H, C −12, C-16); 128.9 (3xC H, C −5, C −13, C-15); 129.4 (CH,C-3); 130.5 (C H, C −14); 134.0 (C, C-11); 144.7 (CH, C-10); 154.5 (C, C −1); 166.0 (C=O, C-8); 169.1 (C=O, Ac) ppm; HRESIMS 481.1451 (calcd for $C_{24}H_{26}O_9$ ([M+Na$^+$]$^+$) 481,1469).

3.3.5. *2-(2′-O-Acetyl-β-D-glucopyranosyloxy)-5-hydroxybenzyl-trans-cinnamoate (2′-O-acetyl-cinnamoyl-salirepin) (**13**)*

2-(2′-O-acetyl-β-D-glucopyranosyloxy)-5-hydroxybenzyl-*trans*-cinnamoate (2′-O-acetyl-cinnamoyl-salirepin) (**13**) was obtained by hydrolysis of 2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyloxy)-5-acetoxybenzyl-*trans*-cinnamoate (pentaacetyl-cinnamoyl-salirepin) (**5**) Reaction time 8 h, yield 12%. Mp 174–176 °C. UV λ_{max} (H_2O) 282 nm; IR (KBr) 3500, 2900, 1730, 1710, 1635, 1500, 1470, 1380, 1260, 1210, 1085, 1050, 1000, 770, 680 cm^{-1}; ^{1}H NMR (DMSO-d_6, 300 MHz) δ: 2.05 (3H, s, Ac); 3.23 (DMSO) (1H, m, H-4′); 3.24–3.33 (3H, m, H-3′, H-5′, H-6′a); 3.72 (1H, m, H-6′b); 4.65 (1H, m, OH-6′); 4.77 (1H, m, 1H, H-2′); 4.89 (1H, d, *J*=8.1, Hz, H-1′); 4.97–5.10 (2H, m, H-7); 5.23 (1H, d, *J*=4.8, Hz, OH-4′); 5.33 (1H, d, *J*=5.1, Hz, OH-3′); 6.66–6.74 (3H, m, H-3, H-5, H-9); 7.02 (1H, d, *J*=9.0 Hz, H-6); 7.43 m (3H, H-13, H-14, H-15); 7.68 (1H, d, *J*=15.9 Hz, H-10). 7.73 (2H, m, H-12, H-16) ppm; ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ: 20.08 (3H, CH_3, Ac); 60.7 (2xC H_2, C 6′, C-7); 69.8 (C H, C −4′); 73.42 (C H, C −2′); 74.0 (C H, C −3′); 77.0 (C H, C −5′); 99.6 (C H, C -1′); 114.9 (C H, C −5); 115.3 (CH, C-3); 117.3 (C H, C −6); 117.9 (CH, H-9); 126.1 (C, C-2); 128.1 (2xC H, C −12, C-16); 128.9 (2xC H, C −13, C-15); 130.5 (CH,C-14); 134.0 (C H, C −11); 144.9 (C, C −1); 147.1 (CH, C-10); 152.5 (CH, C-4); 166.0 (C=O, C-8); 169.2 (C=O, Ac) ppm. HRESIMS 509.1231 (calcd for $C_{24}H_{26}O_{10}$ 509.1220 [M+Cl$^-$]$^-$).

3.3.6. *2-(2′-O-Acetyl-β-D-glucopyranosyloxy)-5-hydroxybenzyl (2-hydroxy)benzoate (2′-O-acetyl-salicyloyl-salirepin) (**14**)*

2-(2′-O-acetyl-β-D-glucopyranosyloxy)-5-hydroxybenzyl (2-hydroxy)benzoate (2′-O-acetyl-salicyloyl-salirepin) (**14**) was obtained by hydrolysis of 2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyloxy)-benzyl(2-acetoxy)benzoate (hexaacetyl-salicyloyl-salirepin) (**6**). Reaction time 10 h, yield 11%, mp 189–198 °C. UV λ_{max} (H_2O) 228, 299 nm; IR (KBr): 3490, 3340, 2875, 1740, 1680, 1485, 1390, 1300, 1250, 1210, 1090, 1000, 760 cm^{-1}; ^{1}H NMR (DMSO-d_6, 600 MHz) δ: 2.00 (3H, s, Ac); 3.23 (1H, m, H-4′); 3.35–3.38 (1H, m H-3′); 3.43–3.46 (1H, m, H-5′); 3.46–3.50 (1H, m, H-6′a); 3.70–3.73 (1H, m, H-6′b); 4.66 (1H, m, OH-6′); 4.75 (1H, m, 1H, H-2′); 4.92 (1H, d, *J*=8.4, Hz, H-1′); 5.16 (1H, d, *J*=13.1, Hz, H-7a); 5.22 (1H, d, *J*=13.1, Hz, H-7b); 5.25 (1H, d, *J*=4.8, Hz, OH-4′); 5.34 (1H, d, *J*=5.1, Hz, OH-3′); 6.69 (1H, dd, *J*=2.7; 9.0 Hz, H-5); 6.81 (1H, d, *J*=2.7, Hz, H-3); 6.95 (1H, t, *J*=7.8, 1.2, Hz, H-13); 7.00 (1H, d, *J*=7.8, Hz, H-11); 7.04 (1H, d, *J*=8.7, Hz, H-6); 7.52 (1H, td, *J*=7.2, 1.2, Hz H-12); 7.80 (1H, dd, *J*=7.5, 1.2, Hz, H-14) ppm; ^{13}C NMR (DMSO-d-6, 150 MHz) δ: 20.09 (3H, CH_3, Ac); 60.6 (C H_2, C 6′); 61.5 (CH_2, C −7); 69.9 (C H, C −4′); 73.5 (C H, C −2′); 73.8 (C H, C −3′); 77.0 (C H, C −5′); 99.4 (C H, C -1′); 113.0 (C H, C −9); 114.9 (C-3); 115.5 (C H, C −5); 117.2 (CH, C-11); 117.6 (CH, C-6); 119.4 (C H, C −13); 125.7 (C, C −2); 130.0 (CH, C-14); 135.7 (CH, C-12); 147.4 (C, C −1); 152.5 (C, C −4); 160.0 (C, C-10); 168.2 (C=O, C-8); 169.3 (C=O, Ac) ppm; HRESIMS 499.0994 (calcd for $C_{22}H_{24}O_{11}$ ([M+Cl]$^-$) 499,1007).

*3.3.7. 2-(2′-O-Acetyl-β-D-glucopyranosyloxy)-5-benzoyloxy-benzyl benzoate (2′-O-acetyl-benzoyl-salireposide) (**15**)*

2-(2′-O-acetyl-β-D-glucopyranosyloxy)-5-benzoyloxy-benzyl benzoate (2′-O-acetyl-benzoyl-salireposide) (**15**) was obtained by hydrolysis of 2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyloxy)-5-benzoyloxy-benzyl benzoate (tetracetyl-benzoyl-salireposide) (7). Reaction time 22 h, yield 11%, mp 212–215 °C. UV λ_{max} (H_2O) 229, 276 nm; IR (KBr): 2940, 1720, 1505, 1500, 1380, 1260, 1250, 1195, 1080, 1060, 1000, 915, 900, 810, 700 cm^{-1}. ^1H NMR (DMSO-d_6, 600 MHz) δ: 1.98 (3H, s, Ac); 3.28–3.38 (DMSO) (1H, m, H-4′); 3.48–3.56 (3H, m H-3′, H-5′, H-6′a); 3.72 (1H, m, H-6′b); 4.72 (1H, m, OH-6′); 4.82 (1H, m, 1H, H-2′); 5.18 (1H, d, *J*=13.1, Hz, H-7a); 5.21 (1H, d, *J*=9.0, Hz, H-1′); 5.26 (1H, d, *J*=13.0, H-7b); 5.31 (1H, d, *J*=5.4, Hz, OH-4′); 5.39 (1H, d, *J*=5.5, Hz, OH-3′); 7.28 (2H, m, H-5, H-6); 7.34 (1H, d, *J*-2.3, Hz, H-3); 7.52 (2H, m, H-11, H-13); 7.58 (2H, dd, *J*-8.1, 7.62, Hz, H-18, H-20); 7.65 (1H, t, *J*=7.4, Hz, H-12); 7.73 (1H, d, *J*=7.5, Hz, H-19); 7.99 (2H, d, *J*=8.1, 1.1, Hz, H-10,H-14); 8.11 (2H, d, *J*=8.1, 1.1, Hz, H-17, H-21) ppm; ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 20.8 (CH_3, Ac); 60.3 (CH, C –6′) 61.0 (CH, C-7); 69.8 (CH, C –4′); 73.5 (CH, C –2′); 73.8 (CH, C -3′); 77.2 (CH, C –5′); 98.4 (CH, C –1′); 116.2 (CH, C-6); 122.2 (CH, C-3); 122.8 (CH, C-5); 128.9 (2×CH, C-11, C-13); 129.0 (2×CH, C-18, C-20); 129.3 (3×CH, C-9, C-10, C-14); 129.9 (3×CH, C-16, C-17, C-21); 133.5 (CH, C-12); 134.1 (CH, C-19); 145.2 (C, C-4); 153.3 (C, C-1); 168.1 (C=O, C-15); 169.1 (C=O, C-8); 175.0 (C=O, Ac) ppm; HRESIMS 575.1521 (calcd for $C_{29}H_{28}O_{11}$ ($[M+Na^+]^+$) 575,1529).

*3.3.8. 2-(2′-O-Acetyl-β-D-glucopyranosyloxy)-5-hydroxy-benzyl–(3,4-dihydroxy)-trans-cinnamoate (2′-O-acetyl-caffeoyl salirepin) (**16**)*

2-(2′-O-acetyl-β-D-glucopyranosyloxy)-5-hydroxy-benzyl–(3,4-dihydroxy)-*trans*-cinnamoate (2′-O-acetyl-caffeoyl salirepin) (**16**) was obtained by hydrolysis of 2-(2′,3′,4′,6′-tetra-O-acetyl-β-D-glucopyranosyloxy)-5-acetoxy-benzyl (3,4-diacetoxy) -*trans*-cinnamoate (heptaacetyl-caffeoyl-salirepin) (8)¶. Reaction time 7.5 h, yield 25%. Mp 150–155 °C. UV λ_{max} (EtOH) 245, 299, 332 nm; IR (KBr): 3140, 1720, 1700, 1605, 1460, 1380, 1270, 1210, 1080, 1050, 1000, 805 cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz) δ: 2.05 (3H, s, Ac); 3.06–3.46 (DMSO); 4.74 (1H, m, H-2′); 4.88 (1H, d, *J*=8.4, Hz, H-1′); 4.95–5.07 (2H, m, H-7); 6.30 (1H, d, *J*=15.3 Гц, H-9); 6.64 (1H, dd, *J*=8.1, 1.5 Hz, H-5); 6.71 (1H, d, *J*=2.7 Hz, H-3); 6.74 (1H, d, *J*=8.1 Hz, H-15); 7.00–7.07 (3H, m, H-6, H-12, H-16); 7.49 (1H, d, *J*=15.9 Hz, H-10) ppm; ^{13}C NMR (DMSO-d_6, 75.5 MHz) δ: 21.0 (CH_3, Ac); 60.1 (CH_2, C-6′); 60.7 (C H_2, C –7); 69.8 (CH, C-4′); 73.4 (CH, C-2′); 73.8 (CH, C-3′); 77.0 (CH, C-5′); 99.6 (CH, C-1′); 113.5 (CH, C-12); 113.5 (CH=CH, C-9); 114.9 (CH, C-5); 115.1 (CH, C-3); 115.9 (CH, C-15); 117.5 (CH, C-6); 121.5 (CH, C-16); 125.3 (CH, C-11); 126.4 (C, C-2); 145.6 (C, C-1, CH=CH, C-10); 147.1 (CH, C-13); 148.8 (C, C-14); 152.5 (C, C-4); 166.3 (C=O, C-8); 169.5 (C=O, Ac) ppm; HRESIMS 541.1111 (calcd for $C_{24}H_{26}O_{11}$ ($[M+Cl^-]^-$) 541.1118)

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Supplementary data

Supplementary data (NMR spectra of compounds **9**–**16**, including HMBC, mass-spectra of TMS derivatives **9**–**11** and geometries of isomers listed in Table 2) related to this article can be found at http://dx.doi.org/10.1016/j.carres.2015.03.017.

References

1. Pobłocka-Olech L, van Nederkassel AM, Vander Heyden Y, Krauze-Baranowska M, Glod D, Baczek T. *J Sep Sci* 2007;**30**:2958. Pat. RF No 2162701/ Burkova V.N., et.all. 14.03. 2000.
2. Boeckler GA, Gershenzon J, Unsicker SB. *Phytochem* 2011;**72**(13):1497.
3. Reichardt PB, Merken HM, Clausen TP, Wu J. *J Nat Prod* 1992;**55**(7):970.
4. Kolehmainen J, Roininen H, Julkunen-Tiitto R, Tahvanainen J. *J Chem Ecol* 1994;**20**(9):2455.
5. Steele JW. *J Chromatogr A* 1973;**84**(2):315.
6. (a) Reeves RE, Coulsont RA, Hernandeaz T, Blouin F. *J Am Chem Soc* 1957;**79**(22):604;
   (b) Lee M, Lee SH, Kang J, Yang H, Jeong EJ, Kim HP, Kim Y Ch, Sung SH. *Molecules* 2013;**18**(9):10484.
7. (a) Liang PH, Lu YJ, Tang TH. *Tetrahedron Lett* 2010;**51**:6928;
   (b) Wu Q, Lu D, Cai Y, Xue X, Chen Z, Lin X. *Biotech Lett* 2001;**23**:1981.
8. Haines AH. *Adv Carbohydr Chem Biochem* 1976;**33**:11.
9. (a) Dasgupta F, Hay GW, Szarek WA. *Carbohydr Res* 1983;**114**:153;
   (b) Li X, Li Z, Zhang P, Chen H, Ikegami Sh. *Synth Comm* 2007;**37**:2195.
10. Bonner W. *J Org Chem* 1959;**24**(9):1388.
11. Roslund MU, Aitio O, Warnå J, Maaheimo H, Murzin D Yu, Leino R. *J Am Chem Soc* 2008;**130**:8769.
12. Lehtila RL, Lehtila JO, Roslunda MU, Leino R. *Tetrahedron* 2004;**60**:3653.
13. (a) Kennedy JF, Kumar H, Panesar PS, Marwaha SS, Goyal R, Parmar A, Kaur S. *J Chem Technol Biotechnol* 2006;**81**:866;
    (b) Ferreira L, Ramons MA, Gil MH, Dordick JS. *Biotechnol Prog* 2002;**18**:986;
    (c) Park S, Kazlauskas RJ. *J Org Chem* 2001;**66**:8395;
    (d) Ikeda I, Klibanov AM. *Biotech Bioeng* 1993;**42**:788;
    (e) Park HG, Do JH, Chang HN. *Biotech Bioproc Eng* 2003;**8**:1.
14. (a) Moen AR, Anthonsen T. *Biocat Biotransform* 2009;**27**(3):226;
    (b) Biely P, Côté GL, Kremnicky L, Weisleder D, Greene RV. *Biochim Biophys Acta* 1996;**1298**(2):209;
    (c) Haines AH. *Adv Carbohydr Chem Biochem* 1981;**339**:13–70.
15. Biely P, Côté GL, Kremnický L, Greene RV, Tenkanen M. *FEBS Lett* 1997;**420**:12.
16. Biely P, Côté GL, Kremnicky L, Greene RV, Dupont C, Kluepfel D. *Streptomyces lividans FEBS Lett* 1996;**396**:257.
17. Kučár Š, Zámocký J, Zemek J, Anderle D, Matulova M. *Collect Czechoslov Chem Commun* 1984;**49**(8):1780.
18. Ishido H, Sakairi N, Sekiya M, Nakazaki N. *Carbohydr Res* 1981;**97**(1):51.
19. (a) Belyanin ML, Stepanova EV, Ogorodnikov VD. *Carbohydr Res* 2012;**363**:66;
    (b) Stepanova EV, Belyanin ML, Filimonov VD. *Carbohydr Res* 2014;**388C**:105.
20. Ahmad VU, Abbasi MA, Zubair M, Fatima N, Farooq U, Choudhary MI. *Helv Chim Acta* 2004;**87**(1):67.
21. Mizuno M, Kato M, Misu Ch, Iinuma M, Tanaka T. *J Nat Prod* 1991;**54**(5):1447.
22. Yang H, Lee SH, Sung SH, Kim J, Kim Y Ch. *Planta Med* 2013;**79**(01):78.
23. (a) Pearl IA, Darling SF. *Phytochem* 1968;**7**(5):831;
    (b) Denekamp Ch, Sandlers Y. *J Mass Spectrom* 2005;**40**(8):1055.
24. Casida M. *Recent advances in density functional methods. Part I.* Singapore: World Scientific; 1999.
25. Lee C, Yang W, Parr RGD. *Phys Rev B* 1988;**37**:785.
26. Schaefer A, Horn H, Ahlrichs R. *J Chem Phys* 1992;**97**:2571.
27. Klamt A, Schüürmann G. *J Chem Soc, Perkin Trans 2* 1993:799.
28. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, et al. *Gaussian 09, Revision A.1.* Wallingford CT: Gaussian, Inc.; 2009.
29. Khoddami A, Wilkes MA, Roberts TH. *Molecules* 2013;**18**:2328.