# Biocatalytic Generation of Molecular Diversity: Modification of Ginsenoside $Rb_1$ by $\beta$-1,4-Galactosyltransferase and *Candida antarctica* Lipase

Part 4[1])

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A series of specific derivatives of the complex protopanaxadiol glycoside ginsenoside $Rb_1$ (**1**) were prepared by catalysis of two unrelated enzymes: the $\beta$-1,4-galactosyltransferase from bovine colostrum (GalT) and the lipase B from *Candida antarctica* (*Novozym® 435*). Both of the enzymes showed the expected regioselectivity towards specific glucose OH groups (*i.e.*, OH–C(4) for GalT and preferentially the primary OH–C(6) for *Novozym® 435*), accompanied by a nonpredictable 'site selectivity' for the gentiobiose disaccharide unit linked at C(20) of the dammarane skeleton. The galactosylated products **1a**–**e** and the acetylated products **1f**–**h** were isolated by HPLC and fully characterized by extensive MS and NMR analysis.

**Introduction.** – Natural products are still today an unsurpassed source of bioactive compounds, which are useful to improve well-being and the quality of life of humans and constitute a relevant economic resource for the pharmaceutical, cosmetic, and food industries [2]. Chemical modification is currently largely applied to implement the properties of existing materials by modulating their pharmacological activity and/or bioavailability. This approach emulates some of the chemistry that occurs in biological systems, where natural or nonnatural substrates are modified by the action of biocatalysts to generate physiologically active compounds and/or their intermediates, or are deactivated to be expelled from the organism. However, the semi-synthetic chemical approach to natural-products derivatives runs into difficulties when the molecules are labile or when they possess multiple functionalities, as in the case of glycosides. In fact, chemical reactions involving these molecules have often indiscriminate outcomes, resulting in the formation of mixtures of products and by-products. In a way, these protocols can be considered a sort of combinatorial synthesis, offering the opportunity to obtain a large number of derivatives from a single starting material. However, on the other side, they are thwarted by difficulties in the isolation of single products, which usually requires tedious and low-yielding chromatographic procedures.

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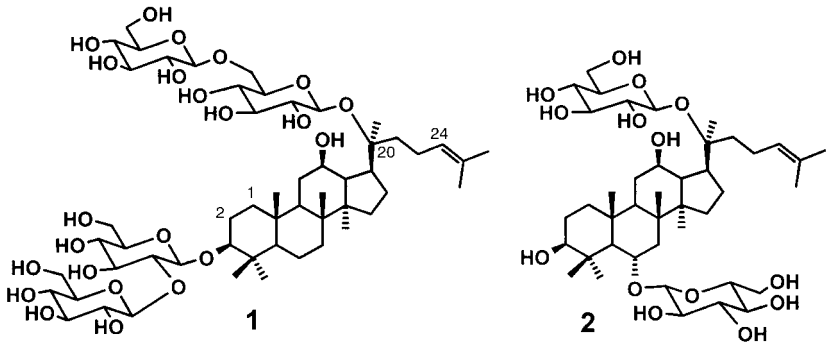
[1]) For Part 3, see [1].

In the last years, it has been shown that biocatalysis offers a number of key advantages over chemical synthesis when working on complex molecules, advantages based on the chemo-, regio-, and stereoselectivity of enzymes and on the possibility to carry out reactions under mild conditions [3]. Even in cases of simple transformations (*e.g.*, an acylation reaction), the chemo- and regioselectivity of the biocatalyst may eliminate several protection-deprotection steps embodied in the chemical route, once the enzyme and the reaction conditions have been carefully selected.

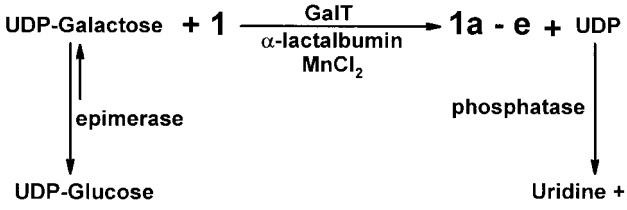
For many years, we have been studying the structural and functional elaboration of several natural compounds, exploiting alternatively the regio- and stereoselectivity of dehydrogenases [4], glycosidases [5], and glycosyltransferases [1][6], and the regioselectivity of hydrolases [7]. As an extension of this work, we report here on the use of two classes of enzymes (hydrolases and glycosyltransferases) for the preparation of a series of specific derivatives of the complex protopanaxadiol glycoside ginsenoside $Rb_1$ (**1**), one of the saponins isolated from *Panax Ginseng* C.A. MEYER, a plant widely used in traditional Chinese medicine [8]. This compound is a dammarane-type triterpene, carrying a gentiobiose unit linked to C(20) and a sophorose unit linked to C(3). The presence of four glucopyranose moieties, carrying 3 primary and 11 secondary OH groups, makes **1** an ideal candidate for the exploitation of biocatalysis to generate a limited array of derivatives having a specific structure. The selected enzymes will furnish derivatives with opposite characteristics, more hydrophilic in the case of glycosyltransferases and more lipophilic in the case of hydrolases, thus allowing generation of a molecular diversity that can be exploited to detect suitable modulations of the bioactivity of the starting product.

**Results and Discussion.** – We started our investigation by submitting ginsenoside $Rb_1$ (**1**) to the catalytic action of the $\beta$-1,4-galactosyltransferase from bovine milk (GalT) [9]. It is well-known that this enzyme, naturally involved in the synthesis of lactose or of *N*-acetyllactosamine from UDP-galactose and glucose or *N*-acetylglucosamine, respectively, is very selective concerning the formation of the new glycosidic bond ($\beta$-1,4-linkage) and can accept a wide variety of aglycone-substituted glucopyranosides. However, in the presence of more than one glucose moiety bearing a free OH–C(4), the reaction outcome is strongly dependant on the structure of the substrate. For instance, we have shown that it is possible to have the selective galactosylation of only one of the two or three possible glucose acceptors of stevioside and steviolbioside [10], while, in the case of the more simple ginsenoside $Rg_1$ (**2**) that contains two glucose moieties, both saccharides were galactosylated, although at different rates [1]. Due to the increased structural complexity of ginsenoside $Rb_1$ (**1**), this compound appeared to be a challenging substrate to get more information on the performance of GalT.

The usual enzymatic cocktail (GalT, epimerase, alkaline phosphatase) was added to a buffered solution of **1** containing UDP-glucose, $\alpha$-lactalbumine, and $MnCl_2$ (*Scheme*, see *Exper. Part*) [1][10]. Due to the low solubility of **1**, 20% DMSO was added because we have demonstrated that this cosolvent is compatible with the activity of this enzyme mixture [11]. The reaction was monitored by TLC and by HPLC, and a complex chromatographic profile was obtained after 5 days of incubation at 37° (*Fig. 1*, 54% overall conversion). The products corresponding to the five HPLC peaks (products



Scheme. *Multi-Enzymatic Protocol Used to Galactosylate Ginsenoside Rb$_1$* (**1**)




**1a**–**e**) were isolated by prep. HPLC and extensively analyzed by the usual 1D and 2D NMR and MS techniques[2]).

The most abundant product **1d** ($t_R$ 16.1 min) showed a quasi-molecular-ion peak $[M-H]^-$ at *m/z* 1269 in its LSI-MS (neg. mode), indicating the presence of one additional hexose moiety compared to **1** ($[M-H]^-$ at *m/z* 1107). The structure of **1d** was established as [*β*-D-Glc*p*-(1 → 2)-*β*-D-Glc*p*-(1 → *O*-3)]-[*β*-D-Gal*p*-(1 → 4)-*β*-D-Glc*p*-(1 → 6)-*β*-D-Glc*p*-(1 → *O*-20)]-protopanaxadiol after extensive spectral analyses.

Accordingly, the $^1$H-NMR spectrum ($CD_3OD$) of **1d** showed 5 *d* at *δ* 4.66, 4.58, 4.43, 4.39, and 4.34 due to anomeric protons of the 5 sugar units, all with a *β*-D-configuration (vicinal coupling constant values between 7.2 and 7.6 Hz). Analysis of the spin systems by $^1$H,$^1$H-COSY and TOCSY experiments disclosed the glucopyranose nature of the sugar units whose anomeric protons were at *δ* 4.66, 4.58, 4.43, and 4.39, whereas the anomeric proton at *δ* 4.34 belonged to the newly introduced galactopyranose moiety because of its connection to the signal at *δ* 3.81 of the equatorial H–C(4).

All the homo- and hetero-2D NMR experiments showed that the sophorose disaccharide moiety linked at C(3) was unaffected, displaying anomeric proton signals at *δ* 4.43 and 4.66 as in the starting material **1**. The attachment of the galactopyranose moiety to OH–C(4) of the external glucose moiety of the gentiobiose disaccharide unit was finally established as follows. The anomeric proton at *δ* 4.58 was shown to be due to H–C(1)(Glc″) because of its connection to C(20) (*δ* 84.99) of the dammarane skeleton (HMBC), and, therefore, the second glucose moiety of the gentiobiose disaccharide unit had its anomeric proton at *δ* 4.39 (H–C(1)(Glc‴)). The anomeric proton of the galactopyranose moiety (*δ* 4.34) (H–C(1)(Glc⁗)) was linked to the last-mentioned signal *via* (C(4)(Glc‴) at *δ* 80.84 and H–C(4)(Glc‴) at *δ* 3.54, as nicely detailed in *Fig. 2*, which reports the relevant plots of the COSY, HMBC, HMQC, and TOCSY experiments of **1d**, and highlight the connectivity from H–C(1)(Gal⁗) to H–C(1)(Glc⁗).

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[2]) The thorough investigation of these products and of other ginsenoside derivatives by ESI-MS$^n$ has already been reported [12].

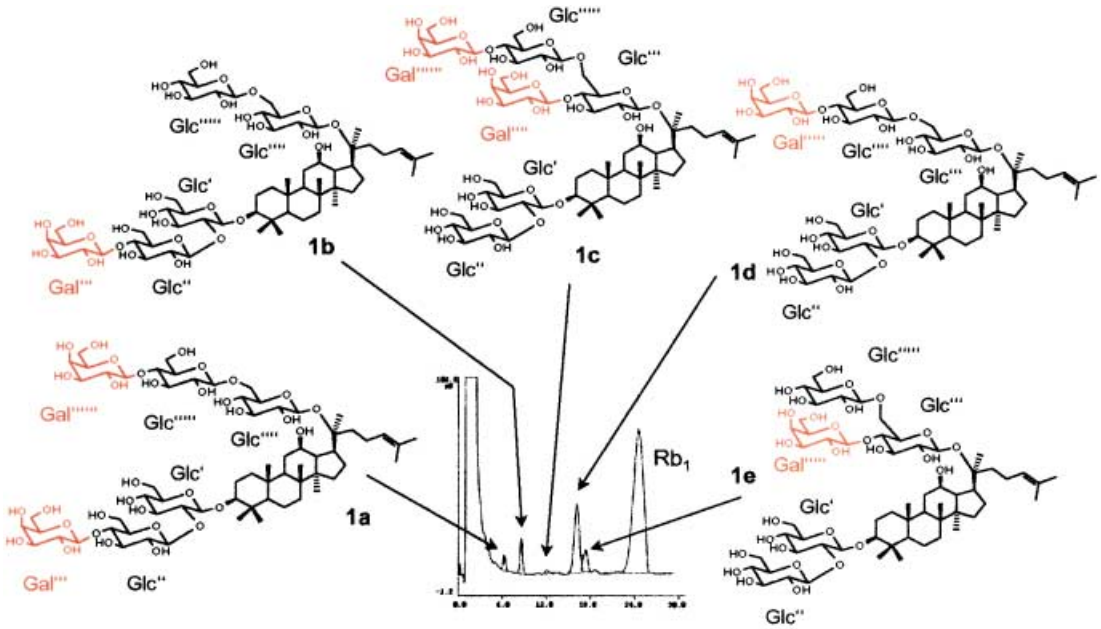



Fig. 1. *HPLC Plot of the GalT-catalyzed galactosylation of* **1**. $t_R$. **1a** 6.2 min, **1b** 8.5 min, **1c** 12.2 min, **1d** 16.1 min, **1e** 17.5 min, and **1** 24.8 min, at *ca.* 40% conversion.

The most retained product **1e** ($t_R$ 17.5 min) was also a monogalactosylated derivative, and NMR analysis similar to that of **1d** showed that the anomeric proton of the galactopyranose unit ($\delta$ 4.50) was linked (HMBC) to the C(4)(Glc‴) ($\delta$ 80.22) belonging to the 'inner' glucopyranose moiety of the gentiobiose unit. Furthermore, H–C(4)(Glc‴) ($\delta$ 3.72) was connected (HMQC) to H–C(1)(Glc‴) ($\delta$ 4.60) *via* TOCSY. Product **1e** was thus recognized as [$\beta$-D-Glc*p*-(1 → 2)-$\beta$-D-Glc*p*-(1 → *O*-3)]-[$\beta$-D-Gal*p*-(1 → 4)-[$\beta$-D-Glc*p*-(1 → 6)]-$\beta$-D-Glc*p*-(1 → *O*-20)]-protopanaxadiol.

In the third mono-galactosylated derivative, product **1b** ($t_R$ 8.5 min), the gentiobiose disaccharide unit was found to be unaffected, and applying the above spectroscopic approach, the galactopyranose moiety was shown to be linked to the terminal glucose unit of the sophorose moiety (see data in the *Exper. Part*). Therefore, **1b** was identified as [$\beta$-D-Gal*p*-(1 → 4)-$\beta$-D-Glc*p*-(1 → 2)-$\beta$-D-Glc*p*-(1 → *O*-3)]-[$\beta$-D-Glc*p*-(1 → 6)-$\beta$-D-Glc*p*-(1 → *O*-20)]-protopanaxadiol.

The two remaining products, products **1a** and **1c** ($t_R$ 6.2 and 12.2 min, resp.), were both di-galactosylated derivatives, as indicated by the quasi-molecular ion peak at *m*/*z* 1431 ([*M* – H]$^-$) in their LSI-MS (neg. mode). Although the isolated amount of these compounds was too low to record structurally significant $^{13}$C-NMR, HMQC, and HMBC spectra and although both contained some unidentified impurities, we could demonstrate that, in case of **1a**, the two galactopyranose units were linked to the terminal glucose units of the sophorose and gentiobiose moieties, respectively, by comparison of its TOCSY plot with those of the fully characterized starting material **1**, of product **1b**, and of product **1d**. *Fig. 3* reports the relevant portion of the TOCSY plots

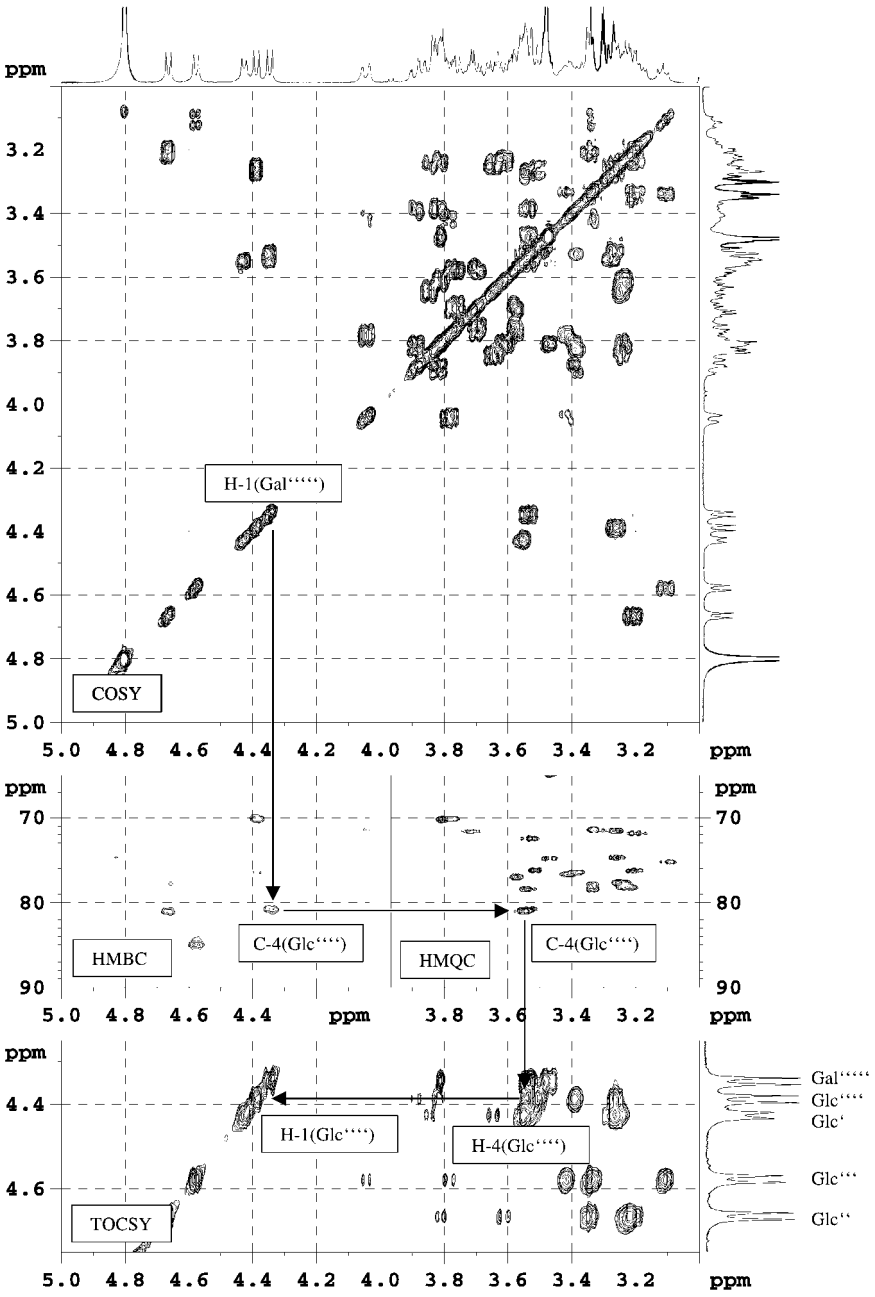



Fig. 2. *Expanded $^1H,^1H$-COSY, HMBC, HMQC, and TOCSY plots of* **1d**, *showing the correlation between H–C(1)(Gal‘‘‘‘) (=*H-1(Gal‘‘‘‘)*) and H–C(1)(Glc‘‘‘) (=*H-1(Glc‘‘‘)*)*

and clearly shows that the contour profile of **1a** is superimposable on that of **1b** and **1d**. Similarly, structure elucidation for product **1c**, which was by far the less-abundant product, was based on the comparison of its TOCSY with those of **1**, **1d**, and **1e**. This indicated that the sophorose unit was unaffected and that the two galactose units were attached to OH–C(4) of each glucose moiety of the gentiobiose unit. In this way, the structures of the di-galactosylated compounds **1a** and **1c** could be established as [β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→2)-β-D-Glc*p*-(1→*O*-3)]-[β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→6)-β-D-Glc*p*-(1→*O*-20)]-protopanaxadiol and as [β-D-Glc*p*-(1→2)-β-D-Glc*p*-(1→*O*-3)]-[β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→6)-[β-D-Gal*p*-(1→4)]-β-D-Glc*p*-(1→*O*-20)]-protopanaxadiol, respectively.

The structures of the isolated products allow us to deduce that GalT has an overwhelming preference for the recognition of the gentiobiose unit linked at C(20): in fact, four of the five isolated compounds carry at least one galactose unit at this 'upper' disaccharide moiety. Additionally, the mono-galactosylated compounds **1b** and **1e** were produced in similar amount, despite that the formation of the latter requires the access to an internal and, in principle, sterically much-more-hindered glucose moiety. Worth mentioning is also the formation of product **1c**, presumably derived from further galactosylation of **1e**, although in very small amounts.

A final comment can be made on the polarity of products **1a**–**e**. Clearly, the 'lower' portion of the derivatives of **1**, which contains the sophorose disaccharide unit, is mainly responsible for the polarity of the molecules. In fact, galactosylation of this portion produces the less-retained compounds in HPLC, thus suggesting a weak interaction of this region of the molecule with the apolar stationary phase.

To obtain new derivatives of ginsenoside $Rb_1$ (**1**), this time possessing a more hydrophobic character, the esterification of **1** by action of hydrolases in organic solvents was investigated. Due to the insolubility of **1** in apolar or moderately polar solvents, only few enzymes of this type could be used in a preliminary screening, and, after experimentation, only the lipase B from *Candida antarctica* (*Novozym® 435*) [13] proved to be able to acylate the substrate with almost complete conversion and selectivity. This finding was in agreement with previous works showing that this enzyme is particularly suitable for the regioselective esterification of complex natural glycosides, the cognate $Rg_1$ (**2**) [14] and the haemolytic saponine digitonin being just two significant examples [15]. Accordingly, acylation reactions were performed by dissolving compound **1** in DMF/THF 1:2 containing vinyl acetate. *Novozym® 435* was added, and the suspension was shaken at 45°. The reaction was very fast, and, after only 4 h, **1** was almost completely converted into two acetylated products **1f** and **1g**, which were isolated and purified by flash chromatography. At variance with the previously reported galactosylated derivatives **1a**–**e**, an unambiguous successful analysis of the NMR spectra of the new compounds could be performed only by taking the spectra in ($D_6$)DMSO, at 45° or at higher temperature. This solvent was unique in suppressing extensive overlapping of signals and in securing good stability of products at the working temperature.

The less-polar and less-abundant compound **1f** was recognized as a di-*O*-acetylginsenoside $Rb_1$ on the basis of its LSI-MS (neg. mode; $[M-H]^-$ ion at 1191) and of its $^1$H-NMR spectrum. Detailed spectral analyses revealed its structure to be 6″,6‴-di-*O*-acetylginsenoside $Rb_1$ (**1f**).

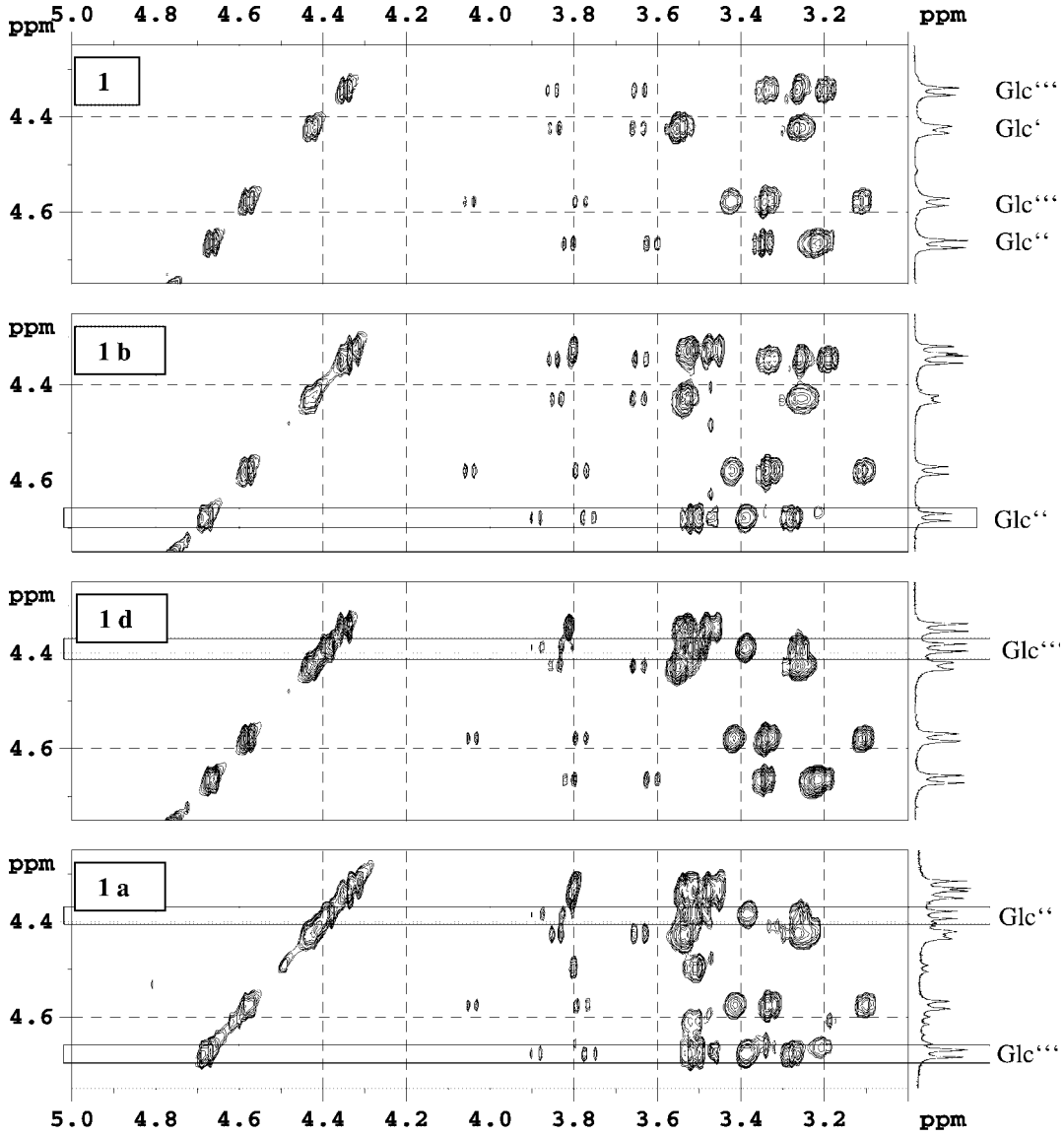
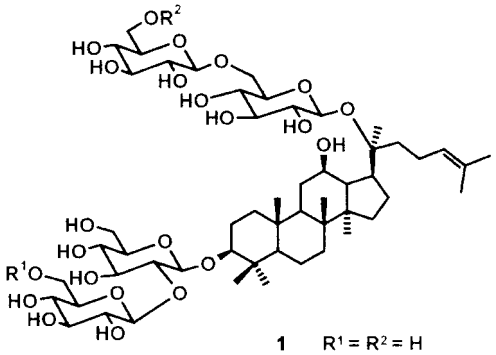



Fig. 3. *TOCSY Plots of compounds* **1**, **1a**, **1b**, *and* **1d**. The spin systems of the glucopyranose moieties carrying a galactosylpyranosyl substituent are outlined.

The $^1$H-NMR spectrum of **1f** showed, among other signals, 2 *s* at $\delta$ 2.00 and 2.02 for the acetate groups and 2 *AB* portions of 2 *ABX* systems at low field, *i.e.*, at $\delta$ 4.25 and 4.02, and 4.19 and 3.98, respectively, for the acetylated oxymethylene protons of two glucose units. To unambiguously locate the positions of attachment of the acetyl residues, the usual detailed NMR study was carried out by means of 1D and 2D techniques, which allowed us to establish the complete direct, vicinal, and long-range H,H and H,C connectivity of both disaccharides **1f** and **1g**. The conclusion of these investigations was that the *AB* portion at $\delta$ 4.25 and 4.02 of **1f** was due to $CH_2(6)$(Glc‘‘‘‘), the oxymethylene protons of the external glucose unit of the ‘upper’ gentiobiose




disaccharide moiety, because these signals were linked to the anomeric H–C(1)(Glc′′′′) at $\delta$ 4.24. In turn, this was connected to C(6)(Glc′′′) at $\delta$ 68.81, the substituted oxymethylene of the internal glucose unit of the gentiobiose moiety. The second acetate group of **1f** was located on the external glucose unit of the 'lower' sophorose disaccharide moiety. In fact, the *AB* portion at $\delta$ 4.19 and 3.98 was correlated to the anomeric proton at $\delta$ 4.47 possessing a long-range interaction with the substituted C(2)(Glc′) whose $^{13}$C-NMR signal was at low field ($\delta$ 80.23) due to the ether linkage to the external glucose.

The more polar and more abundant product, apparently homogeneous on TLC, was recognized as a monoacetate by LSI-MS analysis (neg. mode) showing an $[M-H]^-$ ion at 1149. However, by analyzing its NMR spectrum, it turned out immediately that the isolated product consisted of a mixture of two compounds **1g**/**1h** in a *ca.* 9 : 1 ratio (two acetate signals at $\delta$ 2.02 and 2.00). Separation of these two monoacetates proved to be a difficult task and could be achieved, even if not completely, by prep. HPLC on a *Partisil-10-ODS-3* column in the isocratic mode. The major component **1g** could be isolated in pure form, whereas the minor **1h** was always contaminated by **1g**. The NMR data of the pure, more abundant monoacetate were consistent with the structure of 6′′′′-*O*-acetylginsenoside $Rb_1$ (**1g**). By careful comparison of the NMR spectra of the monoacetate mixture and of the pure monoacetate **1g**, it was possible to detect structurally significant signals (see *Exper. Part*) due to the less-abundant acetate **1h**, indicating that its external glucose unit of the sophorose moiety was acetylated at its primary OH group. Therefore, the structure of 6′′-*O*-acetylginsenoside $Rb_1$ (**1h**) is suggested for the minor acetate.[3])

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[3]) During a detailed investigation of the dammarane saponins of commercial American ginseng (*Panax quinquefolium* L.), *Tanaka* and co-workers [16] isolated a new saponin, named quinquenoside $R_1$ (Q-$R_1$), which was shown to be mono-*O*-acetyl-$Rb_1$. By means of MS and with a view to the acetylation shift in the $^{13}$C-NMR spectra, the acetyl group was located at OH–C(6) of the terminal glucose moiety of the $\beta$-sophorose unit of $Rb_1$. We observe that, because the $^{13}$C-NMR spectrum of $Rb_1$ was taken in ($D_5$)pyridine and, in this solvent, the resonances of C(4), C(5), and C(6) of Glc′, Glc′′, and Glc′′′′ were superimposed ($\delta$ 71.4, 78.0, and 62.6, resp.), the structure proposed by the authors should be the object of a more-detailed investigation.

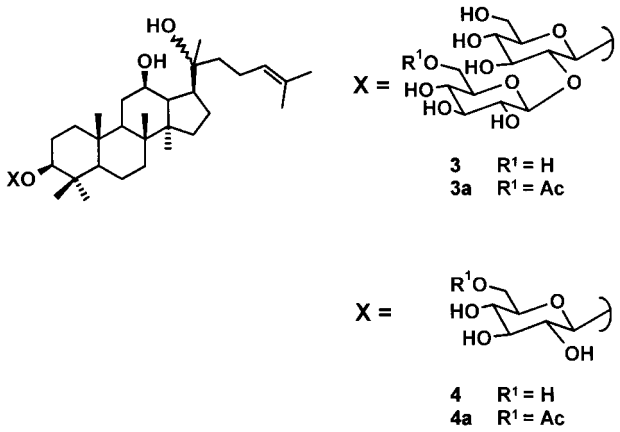
The signals of the acetylated gentiobiose moiety of **1g**, *i.e.*, $CH_2$(6)(Glc‴) at $\delta$ 4.01 and 4.24, H–C(1)(Glc‴) at $\delta$ 4.23, C(6)(Glc‴) at $\delta$ 68.75, $CH_2$(6)(Gl‴) at $\delta$ 3.57 and 3.86, and H–C(1)(Glc‴) at $\delta$ 4.41, were almost superimposible on the signals of the corresponding portion of the diacetate **1f**, while those of the unaffected sophorose unit were equivalent to the respective signals in the starting material **1**.

Therefore, *Novozym® 435* confirmed its regioselectivity for the acylation of primary OH groups of ginsenosides [14], and, more significantly, the 'upper' gentiobiose moiety proved to be more reactive than the 'lower' sophorose unit, as in the previously described biocatalyzed galactosylation. These results, obtained with two completely unrelated enzymes, are quite surprising when compared with the data previously collected with the cognate ginsenoside $Rg_1$ (**2**) [14]. In fact, in the case of **2**, the glucose moiety linked at C(20) was the less-reactive portion of the molecule, and both acetylation and galactosylation took place preferentially at the glucose unit linked at C(6).

This is an additional support to the following general finding made by us and by others: while the regioselectivity of both enzymes towards specific glucose OH groups (strictly speaking, OH–C(4) for GalT and preferentially the primary OH–C(6) for *Novozym® 435*) is the same in different substrates, the capability to discriminate the same moiety (*i.e.*, a glucopyranose) located in different parts of a molecule ('site selectivity') is strongly dependent upon more-subtle structural characteristics that are presently far from well-understood. For instance, the tridimensional structure of the lipase B from *Candida antarctica* has been determined by X-ray analysis [17], and, in the presence of a covalently bound phosphonate inhibitor [18], it has been shown that a narrow cleft limits access to its active site. We have found experimentally that this lipase can accept a large variety of bulky (nonlinearly shaped) and sterically demanding substrates (*i.e.*, ginsenosides, see [14] and this work, and digitonin, see [15]), a clear indication of the enzyme's capability to dynamically modulate its shape around the active site in order to host these compounds. This structural flexibility is obviously a positive factor from a synthetic point of view, but, on the other hand, the present lack of definite rationales for this phenomenon impairs efforts to predict enzymatic site selectivity.

Indirect support for the different reactivities of the two disaccharide moieties of **1** was obtained by inspection of the behavior of the related disaccharide ginsenoside $Rg_3$ (**3**), which contains only the 'lower' sophorose moiety and is formed as a mixture of (20*R*) and (20*S*) epimers by acid hydrolysis of **1** [19]. Galactosylation of **3** gave no detectable reaction products after five days, whereas acetylation under the same conditions as for **1** occurred very slowly, giving *ca.* 5% conversion after 4 h and complete conversion to a monoacetate only after 72 h. The monoacetylation product was recognized as the 6″-*O*-acetylginsenoside $Rg_3$ (**3a**) on the basis of the usual spectroscopic analysis (see *Exper. Part*).

In the same way, we examined the reactivity of the simple 3-*O*-$\beta$-D-glucosyl protopanaxadiol (= ginsenoside $Rh_2$, **4**), prepared by enzymatic hydrolysis of ginsenoside $Rg_3$ (**3**). The enzyme hesperidinase [20][21], $\beta$-glucosidase, cellulase, and $\beta$-galactosidase were tested. Whereas cellulase was uneffective and hesperidinase and $\beta$-glucosidase gave extensive hydrolysis of ginsenoside $Rg_3$, to our surprise, $\beta$-galactosidase promoted a controlled reaction resulting in the formation of a single product identified as ginsenoside $Rh_2$ (**4**). This compound was completely unaffected by GalT but gave the expected 6′-*O*-acetyl derivative **2a** after 72 h incubation with *Novozym® 435*.




In conclusion, we have shown that enzymes from different classes can be successfully used to selectively modify a complex natural compound carrying several reactive functionalities. A limited array of different derivatives was generated from this lead compound. This result derived from a combination of the expected regioselectivity and of a significant and nonpredictable site selectivity of the biocatalysts employed.

## Experimental Part

*General*. UDP-glucose, $\alpha$-lactalbumin from bovine milk, UDP-galactose-4′-epimerase (EC 5.1.3.2; from galactose-adapted yeast), alkaline phosphatase (EC 3.1.3.1; from bovine intestinal mucosa, type VII S), $\beta$-galactosidase (EC 3.2.1.23; from *A. oryzae*) were from *Sigma*. $\beta$-1,4-Galactosyltransferase (EC 2.4.1.22; from bovine colostrum) was either purchased from *Sigma* or purified as described elsewhere [22], and its activity was evaluated in a spectrophotometric assay [23]. *Novozym® 435* was a generous gift from *Novo-Nordisk*. TLC: precoated silica gel *60* $F_{254}$ plates (*Merck*); detection with the *Komarowsky* reagent [24]. Flash chromatography (FC): silica gel *60* (70–230 mesh, Merck). Anal. HPLC: *Jasco* HPLC instrument (model *880-PU* pump, model *870-UV/VIS* detector, $\lambda$ 200 nm); *Licrospher-100-RP-18* (5 µm; *Merck*) reversed-phase anal. column. Prep. HPLC: *Partisil-10-ODS-3* column (*Whatman*). M.p.: *Kofler* apparatus; uncorrected. NMR Spectra: *Bruker 600*, *AMX-500*, and *AC-200*; standard 1D and 2D pulse sequences with appropriate parameters. Mass spectra: *Finnigan MAT 8500*; 4.5 kV Cs beam, negative-ion mode, glycerol as matrix.

*Ginsenoside Rb$_1$* (= *[β-*D*-Glc*p*-(1 → 2)-β-*D*-Glc*p*-(1 → *O*-3)]-[β-*D*-Glc*p*-(1 → 6)-β-*D*-Glc*p*-(1 → O-20)]-protopanaxadiol* = *(3β-,12β)-20-[(6-*O*-β-*D*-Glucopyranosyl-β-*D*-glucopyranosyl)oxy]-12-hydroxydammar-24-en-3-yl 2-*O*-β-*D*-Glucopyranosyl-β-*D*-glucopyranoside*; **1**). Ginsenoside $Rb_1$ (**1**) was isolated by column chromatography ($CHCl_3$/MeOH/$H_2O$ 8:4:0.3) from a root extract of Korean ginseng supplied by *Indena*, Milano (Italy). Amorphous solid. M.p. 186–188°. $^1$H-NMR ($CD_3OD$, 500 MHz): aglycone moiety: 1.00, 1.72 ($CH_2$(1)); 1.71, 1.98 ($CH_2$(2)); 3.20 (H–C(3)); 0.78 (H–C(5)); 1.49, 1.57 ($CH_2$(6)); 1.29, 1.52 ($CH_2$(7)); 1.42 (H–C(9)); 1.25, 1.79 ($CH_2$(11)); 3.71 (H–C(12)); 1.72 (H–C(13)); 1.02, 1.57 ($CH_2$(15)); 1.32, 1.73 ($CH_2$(16)); 2.29 (H–C(17)); 1.00 (Me(18)); 0.91 Me(19); 1.36 (Me(21)); 1.53, 1.80 ($CH_2$(22)); 2.05, 2.12 ($CH_2$(23)); 5.13 (H–C(24)); 1.68 (Me(26)); 1.62 (Me(27)); 1.06 (Me(28)); 0.91 (Me(29)); 0.85 (Me(30)); Glc′: 4.43 (*d*, $J$(1′,2′) = 7.8, H–C(1′)); 3.56 (*dd*, $J$(2′,3′) = 8.9, H–C(2′)); 3.54 (H–C(3′)); 3.27 (H–C(4′)); 3.25 (H–C(5′)); 3.64 (*dd*, $J$(6′a,6′b) = 11.9, $J$(5′,6′a) = 5.2, $H_a$–C(6′)); 3.86 (*dd*, $J$(6′a,6′b) = 9.9, $J$(5′,6′b) = 2.0, $H_b$–C(6′)); Glc″: 4.66 (*d*, $J$(1″,2″) = 7.7, H–C(1″)); 3.21 (*dd*, $J$(2″,3″) = 8.9, H–C(2″)); 3.35 (H–C(3″)); 3.20 (H–C(4″)); 3.25 (H–C(5″)); 3.62 (*dd*, $J$(6″a,6″b) = 11.8, $J$(5″,6″a) = 2.7, $H_a$–C(6″)); 3.82 (*dd*, $J$(5″,6″b) = 1.5, $H_b$–C(6″)); Glc‴: 4.57 (*d*, $J$(1‴,2‴) = 7.8, H–C(1‴)); 3.10 (*dd*, $J$(2‴,3‴) = 9.6, H–C(2‴)); 3.34 (H–C(3‴)); 3.35 (H–C(4‴)); 3.42 (H–C(5‴)); 3.79 (*dd*, $J$(6‴a,6‴b) = 12.1, $J$(5‴,6‴a) = 7.3, $H_a$–C(6‴)); 4.05 (*dd*, $J$(5‴,6‴b) = 1.5, $H_b$–C(6‴)); Glc⁗: 4.36 (*d*, $J$(1⁗,2⁗) = 7.8, H–C(1⁗)); 3.20 (H–C(2⁗)); 3.34

(H–C(3‴)); 3.33 (H–C(4‴)); 3.27 (H–C(5‴)); 3.63 (*dd*, *J*(6‴a,6‴b) = 11.8, *J*(5‴,6‴a) = 3.5, $H_a$–C(6‴)); 3.87 (*dd*, *J*(5‴,6‴b) = 1.5, $H_b$–C(6‴)). $^1$H-NMR ((D$_6$)DMSO, 600 MHz, 45°): aglycone moiety: 0.91, 1.58 ($CH_2$(1)); 1.53, 1.86 ($CH_2$(2)); 3.01 (H–C(3)); 0.68 (H–C(5)); 1.38, 1.48 ($CH_2$(6)); 1.19, 1.48 ($CH_2$(7)); 1.31 (H–C(9)); 1.07, 1.62 ($CH_2$(11)); 3.56 (H–C(12)); 1.55 (H–C(13)); 0.92, 1.55 ($CH_2$(15)); 1.45, 1.78 ($CH_2$(16)); 2.198 (H–C(17)); 1.44, 1.70 ($CH_2$(22)); 1.932, 2.02 ($CH_2$(23)); 5.10 (H–C(24)); 0.76, 0.81, 0.83, 0.89 (Me(18), Me(19), Me(29), Me(30)); 1.24 (Me(21)); 1.64 (Me(26)); 1.56 (Me(27)); 0.98 (Me(28)); Glc′: 4.27 (*d*, *J*(1′,2′) = 7.8, H–C(1′)); 3.32 (H–C(2′)); 3.38 (H–C(3′)); *ca.* 3.10 (H–C(4′), H–C(5′)); 3.43 (*dd*, *J*(6′a,6′b) = 11.8, *J*(5′,6′a) = 3.5, $H_a$–C(6′)); 3.66 (*dd*, *J*(5′,6′b) = 1.5, $H_b$–C(6′)); Glc″: 4.43 (*d*, *J*(1″,2″) = 7.7, H–C(1″)); 3.00 (*dd*, *J*(2″,3″) = 8.9, H–C(2″)); *ca.* 3.12 (H–C(3″)); 3.04 (H–C(4″)); *ca.* 3.15 (H–C(5″)); 3.49 (*dd*, *J*(6″a,6″b) = 11.8, *J*(5″,6″a) = 2.7, $H_a$–C(6″)); 3.62 (*dd*, *J*(5″,6″b) = 1.5, $H_b$–C(6″)); Glc‴: 4.43 (*d*, *J*(1‴,2‴) = 8.2, H–C(1‴)); 2.89 (*dd*, *J*(2‴,3‴) = 9.6, H–C(2‴)); 3.18 (H–C(3‴)); 3.06 (H–C(4‴)); 3.31 (H–C(5‴)); 3.58 (*dd*, *J*(6‴a,6‴b) = 12.1, *J*(5‴,6‴a) = 7.3, $H_a$–C(6‴)); 3.90 (*dd*, *J*(5‴,6‴b) = 1.5, $H_b$–C(6‴)); Glc⁗: 4.24 (H–C(1⁗)); 2.96 (H–C(2⁗)); *ca.* 3.13 (H–C(3⁗)); *ca.* 3.06 (H–C(4⁗)); *ca.* 3.12 (H–C(5⁗)); 3.43 (*dd*, *J*(6⁗a,6⁗b) = 11.8, *J*(5⁗,6⁗a) = 3.5, $H_a$–C(6⁗)); 3.66 (*dd*, *J*(5⁗,6⁗b) = 1.5, $H_b$–C(6⁗')). $^{13}$C-NMR (CD$_3$OD, 50 MHz; values with the same superscript might be interchangeable): aglycone moiety: 40.59[a] (C(1)); 27.25 (C(2)); 91.33 (C(3)); 40.26[a] (C(4)); 57.56 (C(5)); 19.25 (C(6)); 35.86 (C(7)); 40.99[a] (C(8)); 51.10 (C(9)); 37.92 (C(10)); 30.82[b] (C(11)); 71.93 (C(12)); 49.85 (C(13)); 52.41[c] (C(14)); 30.84[b] (C(15)); 27.25 (C(16)); 52.41[c] (C(17)); 84.97 (C(20)); 21.85 (C(21)); 36.79 (C(22)); 23.89 (C(23)); 126.05 (C(24)); 132.28 (C(25)); 25.94 (C(26)); 18.02 (C(27)); 28.41 (C(28)); 16.32, 16.70, 16.73, 17.39 (C(18), C(19), C(29), C(30)); Glc′: 105.40 (C(1′)); 81.11 (C(2′)); 78.52 (C(3′)); 71.60[d] (C(4′)); 77.71 (C(5′)); 62.84[e] (C(6′)); Glc″: 104.51 (C(1″)); 76.32 (C(2″)); 77.93 (C(3″)); 71.93 (C(4″)); 78.33 (C(5″)); 63.12[e] (C(6″)); Glc‴: 98.10 (C(1‴)); 75.29 (C(2‴)); 77.93 (C(3‴)); 71.68[d] (C(4‴)); 76.80 (C(5‴)); 70.25 (C(6‴)); Glc⁗: 104.99 (C(1⁗)); 75.14 (C(2⁗)); 78.33 (C(3⁗)); 71.68[d] (C(4⁗)); 77.93 (C(5⁗)); 61.84 (C(6⁗)). $^{13}$C-NMR ((D$_6$)DMSO, 150 MHz, 45°; values with the same superscript may be interchangeable): aglycone moiety: 38.76 (C(1)); 25.89 (C(2)); 88.35 (C(3)); 38.96 (C(4)); 55.78 (C(5)); 18.73 (C(6)); 34.52 (C(7)); 39.23 (C(8)); 49.36 (C(9)); 36.39 (C(10)); 30.19 (C(11)); 69.18 (C(12)); 48.63 (C(13)); 50.84 (C(14)); 30.19 (C(15)); 25.89 (C(16)); 50.72 (C(17)); 82.42 (C(20)); 21.85 (C(21)); 35.52 (C(22)); 22.40 (C(23)); 125.35 (C(24)); 130.31 (C(25)); 25.58 (C(26)); 17.78 (C(27)); 27.63 (C(28)); 15.70, 15.93, 16.04, 17.05 (C(18), C(19), C(29), C(30)); Glc′: 103.68 (C(1′)); 81.40 (C(2′)); 77.23 (C(3′)); 70.29[a] (C(4′)); 76.30[b] (C(5′)); 61.30[c] (C(6′)); Glc″: 103.91 (C(1″)); 75.30[d] (C(2″)); 76.49 (C(3″)); 70.29[a] (C(4″)); 76.73[b] (C(5″)); 61.16 (C(6″)); Glc‴: 96.62 (C(1‴)); 73.73[e] (C(2‴)); 76.81[b] (C(3‴)); 70.19[a] (C(4‴)); 75.62 (C(5‴)); 68.77 (C(6‴)); Glc⁗: 103.47 (C(1⁗)); 73.90[e] (C(2⁗)); 76.87[b] (C(3⁗)); 70.19[a] (C(4⁗)); 76.88[b] (C(5⁗)); 61.26[c] (C(6⁗)). LSI-MS: 1107 ([*M* – H]$^-$), 945, 783, 621, 459.

*Enzymatic Galactosylation of Ginsenoside Rb$_1$* (**1**). GalT (7 U), epimerase (2 mg, 18 U), alkaline phosphatase (8 µl), and α-lactalbumine (15 mg) were added to 15 ml of 50 mM *Tris* buffer (pH 7.4) containing 20% DMSO, 165 mg of **1** (10 mM), 5 equiv. of UDP-glucose (475 mg, 50 mM), and $MnCl_2$ (25 mM). The soln. was stirred at 30° for five days, adjusting the pH daily with 0.2N NaOH. Reaction outcome was monitored qualitatively by TLC (AcOEt/MeOH/$H_2O$ 9 : 2 : 0.5) and quantitatively by anal. HPLC ($H_2O$/MeCN 82 : 18, flow rate 0.9 ml/min). Purification was performed by prep. HPLC (same eluent, injection of the reaction mixture in several portions, flow rate 5 ml/min): 6 mg (5.2%) of **1a**, 11 mg (5.9%) of **1b**, 3 mg (4.8%) of **1c**, 35 mg (18.7%) of **1d**, and 16 mg (8.6%) of **1e**.

*(3β,12β)-20-{[*O*-β-*D*-Galactopyranosyl-(1 → 4)*-O*-β-*D*-glucopyranosyl-(1 → 6)-β-*D*-glucopyranosyl]oxy}-12-hydroxydammar-24-en-3-yl* O-β-D-*Galactopyranosyl-(1 → 4)*-O-β-D-*glucopyranosyl-(1 → 2)*-β-D-*glucopyranoside* (= *[β-*D*-Gal*p*-(1 → 4)-β-*D*-Glc*p*-(1 → 2)-β-*D*-Glc*p*-(1 → *O*-3)]-[β-*D*-Gal*p*-(1 → 4)-β-*D*-Glc*p*-(1 → 6)-β-*D*-Glc*p*-(1 → *O*-20)]-protopanaxadiol*; **1a**). Amorphous solid. M.p. 261 – 265° (dec.). $^1$H-NMR (CD$_3$OD, 500 MHz; values with the same superscript might be interchangeable): aglycone moiety: 1.00, 1.72 ($CH_2$(1)); 1.71, 1.98 ($CH_2$(2)); 3.20 (H–C(3)); 0.78 (H–C(5)); 1.49, 1.57 ($CH_2$(6)); 1.29, 1.52 ($CH_2$(7)); 1.42 (H–C(9)); 1.25, 1.79 ($CH_2$(11)); 3.71 (H–C(12)); 1.72 (H–C(13)); 1.02, 1.57 ($CH_2$(15)); 1.32, 1.73 ($CH_2$(16)); 2.29 (H–C(17)); 1.00 (Me(18)); 0.91 (Me(19)); 1.36 (Me(21)); 1.53, 1.80 ($CH_2$(22)); 2.05, 2.12 ($CH_2$(23)); 5.13 (H–C(24)); 1.68 (Me(26)); 1.62 (Me(27)); 1.06 (Me(28)); 0.91 (Me(29)); 0.85 (Me(30)); Glc′: 4.43 (*d*, *J*(1′,2′) = 7.8, H–C(1′)); 3.53 (H–C(2′)); 3.53 (H–C(3′)); 3.26 (H–C(4′)); 3.24 (H–C(5′)); 3.64 ($H_a$–C(6′)); 3.85 ($H_b$–C(6′)); Glc″: 4.67 (*d*, *J*(1″,2″) = 7.7, H–C(1″)); 3.28 (H–C(2″)); 3.52 (H–C(3″)); 3.48 (H–C(4″)); 3.39 (H–C(5″)); 3.77 ($H_a$–C(6″)); 3.89 ($H_b$–C(6″)); Gal‴: 4.34[a] (*d*, *J*(1‴,2‴) = 7.8, H–C(1‴)); 3.53 (H–C(2‴)); 3.46 (H–C(3‴)); 3.81 (H–C(4‴)); 3.58 (H–C(5‴)); 3.69 ($H_a$–C(6‴)); 3.77 ($H_b$–C(6‴)); Glc⁗: 4.58 (*d*, *J*(1⁗,2⁗) = 7.8, H–C(1⁗)); 3.11 (H–C(2⁗)); 3.34 (H–C(3⁗)); 3.33 (H–C(4⁗)); 3.42 (H–C(5⁗)); 3.79 (*dd*, *J*(6⁗a,6⁗b) = 11.8, *J*(5⁗,6⁗a) = 3.5, $H_a$–C(6⁗)); 4.04 (*dd*, *J*(5⁗,6⁗b) = 1.8; $H_b$–C(6⁗)); Glc⁗′: 4.39 (*d*, *J*(1⁗′,2⁗′) = 7.8, H–C(1⁗′)); 3.26 (H–C(2⁗′)); 3.51 (H–C(3⁗′)); 3.54 (H–C(4⁗′)); 3.39

(H–C(5‴″)); 3.82 ($H_a$–C(6‴″)); 3.89 ($H_b$–C(6‴″)); Gal‴″: 4.32[a] (*d*, *J*(1‴″,2‴″) = 7.8, H–C(1‴″)); 3.53 (H–C(2‴″)); 3.46 (H–C(3‴″)); 3.81 (H–C(4‴″)); 3.58 (H–C(5‴″)); 3.69 ($H_a$–C(6‴″)); 3.77 ($H_b$–C(6‴″)). LSI-MS: 1431 ($[M-H]^-$, 1269, 1107, 945, 783.

*(3β,12β)-20-[(6-*O*-β-*D*-Glucopyranosyl-β-*D*-glucopyranosyl)oxy]-12-hydroxydammar-24-en-3-yl* O-β-D-*Galactopyranosyl-(1 → 4)*-O-β-D-*glucopyranosyl-(1 → 2)*-β-D-*glucopyranoside* (= *[β-*D*-Gal*p*(1 → 4)-β-*D*-Glc*p-*(1 → 2)*-β-D-*Glc*p-*(1 → *O*-*3)]-[β-*D*-Glc*p-*(1 → 6)*-β-D-*Glc*p-*(1 → *O*-*20)]-protopanaxadiol*; **1b**). Amorphous solid. M.p. 255–259° (dec.). $^1$H-NMR ($CD_3OD$, 500 MHz): aglycone moiety: 1.00, 1.72 ($CH_2$(1)); 1.71, 1.98 ($CH_2$(2)); 3.20 (H–C(3)); 0.78 (H–C(5)); 1.49, 1.57 ($CH_2$(6)); 1.29, 1.52 ($CH_2$(7)); 1.42 (H–C(9)); 1.25, 1.79 ($CH_2$(11)); 3.71 (H–C(12)); 1.72 (H–C(13)); 1.02, 1.57 ($CH_2$(15)); 1.32, 1.73 ($CH_2$(16)); 2.29 (H–C(17)); 1.00 (Me(18)); 0.91 (Me(19)); 1.36 (Me(21)); 1.53, 1.80 ($CH_2$(22)); 2.05, 2.12 ($CH_2$(23)); 5.13 (H–C(24)); 1.68 (Me(26)); 1.62 (Me(27)); 1.06 (Me(28)); 0.91 (Me(29)); 0.85 (Me(30)); Glc′: 4.43 (*d*, *J*(1′,2′) = 7.8, H–C(1′)); 3.53 (*dd*, *J*(2′,3′) = 7.8, H–C(2′)); 3.54 (H–C(3′)); 3.27 (H–C(4′)); 3.24 (H–C(5′)); 3.64 (*dd*, *J*(6′a,6′b) = 11.9, *J*(5′,6′a) = 5.2, $H_a$–C(6′)); 3.85 (*dd*, *J*(5′,6′b) = 2.0, $H_b$–C(6′)); Glc″: 4.67 (*d*, *J*(1″,2″) = 7.7, H–C(1″)); 3.28 (*dd*, *J*(2″,3″) = 8.9, H–C(2″)); 3.52 (H–C(3″)); 3.47 (H–C(4″)); 3.39 (H–C(5″)); 3.77 (*dd*, *J*(6″a,6″b) = 11.8, *J*(5″,6″a) = 2.7, $H_a$–C(6″)); 3.89 (*dd*, *J*(5″,6″b) = 1.5, $H_b$–C(6″)); Gal‴: 4.32 (*d*, *J*(1‴,2‴) = 7.8, H–C(1‴)); 3.52 (H–C(2)); 3.47 (H–C(3‴)); 3.81 (H–C(4‴)); 3.58 (H–C(5‴)); 3.69 (*dd*, *J*(6‴a,6‴b) = 11.8, *J*(5‴,6‴a) = 3.5, $H_a$–C(6‴)); 3.76 (*dd*, *J*(5‴,6‴b) = 1.5, $H_b$–C(6‴)); Glc⁗: 4.58 (*d*, *J*(1⁗,2⁗) = 7.8, H–C(1⁗)); 3.11 (*dd*, *J*(2⁗,3⁗) = 9.6, H–C(2⁗)); 3.34 (H–C(3⁗)); 3.35 (H–C(4⁗)); 3.42 (H–C(5⁗)); 3.78 (*dd*, *J*(6⁗a,6⁗b) = 12.1, *J*(5⁗,6⁗a) = 7.3, $H_a$–C(6⁗)); 4.05 (*dd*, *J*(5⁗,6⁗b) = 1.5; $H_b$–C(6⁗)); Glc⁗⁗: 4.35 (*d*, *J*(1⁗⁗,2⁗⁗) = 7.8, H–C(1⁗⁗)); 3.19 (H–C(2⁗⁗)); 3.34 (H–C(3⁗⁗)); 3.33 (H–C(4⁗⁗)); 3.26 (H–C(5⁗⁗)); 3.64 (*dd*, *J*(6⁗⁗a,6⁗⁗b) = 11.8, *J*(5⁗⁗,6⁗⁗a) = 3.5, $H_a$–C(6⁗⁗)); 3.86 (*dd*, *J*(5⁗⁗,6⁗⁗b) = 1.5, Hb–C(6⁗⁗)). $^{13}$C-NMR ($CD_3OD$, 50 MHz; values with the same superscript might be interchangeable): aglycone moiety: 40.58[a] (C(1)); 27.28 (C(2)); 91.12 (C(3)); 40.58[a] (C(4)); 57.57 (C(5)); 19.29 (C(6)); 35.88 (C(7)); 41.00[a] (C(8)); 51.12 (C(9)); 37.93 (C(10)); 30.79[b] (C(11)); 71.70 (C(12)); 49.85 (C(13)); 52.42[c] (C(14)); 30.76[b] (C(15)); 27.26 (C(16)); 52.93[c] (C(17)); 84.98 (C(20)); 22.50 (C(21)); 36.81 (C(22)); 23.90 (C(23)); 126.04 (C(24)); 132.25 (C(25)); 25.94 (C(26)); 18.02 (C(27)); 28.44 (C(28)); 16.33, 16.71, 16.80, 17.37 (C(18, C(19), C(29), C(30)); Glc′: 105.36 (C(1′)); 81.87 (C(2′)); 78.42 (C(3′)); 71.70[d] (C(4′)); 77.66 (C(5′)); 62.83[e] (C(6′)); Glc″: 104.73 (C(1″)); 76.11 (C(2″)); 76.25 (C(3″)); 81.29 (C(4″)); 76.91 (C(5″)); 62.52[e] (C(6″)); Gal‴: 105.25 (C(1‴)); 72.56 (C(2‴)); 74.83 (C(3‴)); 70.31 (C(4‴)); 77.12 (C(5‴)); 62.52[e] (C(6‴)); Glc⁗: 98.12 (C(1⁗)); 75.32 (C(2⁗)); 77.96 (C(3⁗)); 71.70[d] (C(4⁗)); 76.91 (C(5⁗)); 62.52[e] (C(6⁗)); Glc⁗⁗: 105.01 (C(1⁗⁗)); 75.16 (C(2⁗⁗)); 78.56 (C(3⁗⁗)); 71.70[d] (C(4⁗⁗)); 77.96 (C(5⁗⁗)); 62.83[e] (C(6⁗⁗)). LSI-MS: 1269 ($[M-H]^-$), 1107, 945, 783.

*(3β,12β)-20-({*O*-β-*D*-Galactopyranosyl-(1 → 4)*-O-β-D-*glucopyranosyl-(1 → 6)*-O-*[β-*D*-galactopyranosyl-(1 → 4)]-β-D-glucopyranosyl}oxy)-12-hydroxydammar-24-en-3-yl* 2-O-β-D-*Glucopyranosyl-β-D-glucopyranoside* (= *[β-*D*-Glc*p*-(1 → 2)-β-D-Glc*p*-(1 → *O*-3)]-[β-D-Gal*p*-(1 → 4)-β-D-Glc*p*-(1 → 6)-[β-D-Gal*p*-(1 → 4)]-β-D-Glc*p*-(1 → *O*-20)]-protopanaxadiol*; **1c**). Amorphous solid. $^1$H-NMR ($CD_3OD$/($D_5$)pyridine, 500 MHz): aglycone moiety: 0.98, 1.69 ($CH_2$(1)); 1.65, 1.97 ($CH_2$(2)); 3.16 (H–C(3)); 0.74 (H–C(5)); 1.46, 1.55 ($CH_2$(6)); 1.26, 1.50 ($CH_2$(7)); 1.41 (H–C(9)); 1.22, 1.74 ($CH_2$(11)); 3.75 (H–C(12)); 1.75 (H–C(13)); 0.99, 1.54 ($CH_2$(15)); 1.29, 1.68 ($CH_2$(16)); 2.28 (H–C(17)); 0.91 (Me(18)); 0.91 (Me(19)); 1.35 (Me(21)); 1.51, 1.80 ($CH_2$(22)); 2.01, 2.11 ($CH_2$(23)); 5.11 (H–C(24)); 1.62 (Me(26)); 1.58 (Me(27)); 1.04 (Me(28)); 0.86 (Me(29)); 0.83 (Me(30)); Glc′: 4.45 (*d*, *J*(1′,2′) = 7.8, H–C(1′)); 3.70 (H–C(2′), H–C(3′)); 3.42 (H–C(4′)); 3.39 (H–C(5′)); 3.74 ($H_a$–C(6′)); 3.95 ($H_b$–C(6′)); Glc″: 4.77 (*d*, *J*(1″,2″) = 7.7, H–C(1″)); 3.38 (H–C(2″)); 3.49 (H–C(3″)); 3.39 (H–C(4″)); 3.34 (H–C(5″)); 3.73 ($H_a$–C(6″)); 3.91 ($H_b$–C(6″)); Glc‴: 4.64 (*d*, *J*(1‴,2‴) = 7.8, H–C(1‴)); 3.27 (*dd*, *J*(2‴,3‴) = 9.6, H–C(2‴)); 3.58 (H–C(3‴)); 3.83 (H–C(4‴)); 3.61 (H–C(5‴)); 4.02 ($H_a$–C(6‴)); 4.22 ($H_b$–C(6‴)); Gal⁗: 4.63 (*d*, *J*(1⁗,2⁗) = 7.8, H–C(1⁗)); 3.68 (H–C(2⁗)); 3.58 (H–C(3⁗)); 3.90 (H–C(4⁗)); 3.72 (H–C(5⁗)); 3.79 ($H_a$–C(6)); 3.84 ($H_b$–C(6⁗)); Glc⁗⁗: 4.47 (*d*, *J*(1,2) = 7.8, H–C(1⁗⁗)); 3.40 (H–C(2⁗⁗)); 3.56 (H–C(3⁗⁗)); 3.59 (H–C(4⁗⁗)); 3.35 (H–C(5⁗⁗)); 3.94 ($H_a$–C(6⁗⁗)); 3.97 ($H_b$–C(6⁗⁗)); Gal⁗⁗: 4.43 (*d*, *J*(1⁗⁗,2⁗⁗) = 7.8, H–C(1⁗⁗)); 3.68 (H–C(2⁗⁗)); 3.58 (H–C(3⁗⁗)); 3.90 (H–C(4⁗⁗)); 3.72 (H–C(5⁗⁗)); 3.79 ($H_a$–C(6⁗⁗)); 3.84 ($H_b$–C(6⁗⁗)). LSI-MS: 1431 ($[M-H]^-$), 1269, 1107, 945, 783, 621, 459.

*(3β,12β)-20-{[*O*-β-*D*-Galactopyranosyl-(1 → 4)*-O-β-glucopyranosyl-(1 → 6)*-β-D-glucopyranosyl]oxy}-12-hydroxydammar-24-en-3-yl* 2-O-β-D-*Glucopyranosyl-β-D-glucopyranoside* (= *[β-*D*-Glc*p*-(1 → 2)-β-D-Glc*p*-(1 → *O*-3)]-[β-D-Gal*p*-(1 → 4)-β-D-Glc*p*-(1 → 6)-β-D-Glc*p*-(1 → *O*-20)]-protopanaxadiol*; **1d**). Amorphous solid. M.p. 243–246° (dec.). $^1$H-NMR (MeOD, 500 MHz): aglycone moiety: 1.00, 1.72 ($CH_2$(1)); 1.71, 1.98 ($CH_2$(2)); 3.20 (H–C(3)); 0.78 (H–C(5)); 1.49, 1.57 ($CH_2$(6)); 1.29, 1.52 ($CH_2$(7)); 1.42 (H–C(9)); 1.25, 1.79 ($CH_2$(11)); 3.71 (H–C(12)); 1.72 (H–C(13)); 1.02, 1.57 ($CH_2$(15)); 1.32, 1.73 ($CH_2$(16)); 2.29 (H–C(17)); 1.00 (Me(18)); 0.91 (Me(19)); 1.36 (Me(21)); 1.53, 1.80 ($CH_2$(22)); 2.05, 2.12 ($CH_2$(23)); 5.13 (H–C(24)); 1.68

(Me(26)); 1.62 (Me(27)); 1.06 (Me(28)); 0.91 (Me(29)); 0.85 (Me(30)); Glc′: 4.43 (*d*, *J*(1′,2′) = 7.2, H–C(1′)); 3.55 (H–C(2′)); 3.53 (H–C(3′)); 3.26 (H–C(4′)); 3.24 (H–C(5′)); 3.64 (*dd*, *J*(6′a,6′b) = 11.9, *J*(5′,6′a) = 5.3, $H_a$–C(6′)); 3.85 (*dd*, *J*(5′,6′b) = 1.8, $H_b$–C(6′)); Glc″: 4.66 (*d*, *J*(1″,2″) = 7.8, H–C(1″)); 3.21 (H–C(2″)); 3.35 (H–C(3″)); 3.19 (H–C(4″)); 3.23 (H–C(5″)); 3.62 ($H_a$–C(6″)); 3.82 ($H_b$–C(6″)); Glc‴: 4.58 (*d*, *J*(1‴,2‴) = 7.8, H–C(1‴)); 3.11 (*dd*, *J*(2‴,3‴) = 8.3, H–C(2‴)); 3.34 (H–C(3‴)); 3.33 (H–C(4‴)); 3.42 (H–C(5‴)); 3.79 ($H_a$–C(6‴)); 4.04 (*dd*, *J*(6‴a,6‴b) = 11.6, *J*(5‴,6‴b) = 1.8, $H_b$–C(6‴)); Glc⁗: 4.39 (*d*, *J*(1⁗,2⁗) = 7.8, H–C(1⁗)); 3.26 (H–C(2⁗)); 3.51 (H–C(3⁗)); 3.54 (H–C(4⁗)); 3.39 (H–C(5⁗)); 3.82 (*dd*, *J*(6⁗a,6⁗b) = 12.2, *J*(5⁗,6⁗a) = 3.5, $H_a$–C(6⁗)); 3.89 (*dd*, *J*(5⁗,6⁗b) = 1.5, $H_b$–C(6⁗)); Gal′⁗: 4.34 (*d*, *J*(1′⁗,2′⁗) = 7.6, H–C(1′⁗)); 3.54 (H–C(2′⁗)); 3.47 (H–C(3′⁗)); 3.81 (H–C(4′⁗)); 3.58 (H–C(5′⁗)); 3.70 (*dd*,*J*( 6′⁗a,6′⁗b) = 11.8, *J*(5′⁗,6′⁗a) = 3.5, $H_a$–C(6′⁗)); 3.76 (*dd*, *J*(5′⁗,6′⁗b) = 1.5, $H_b$–C(6′⁗)). $^{13}$C-NMR ($CD_3OD$, 50 MHz; values with the same superscript might be interchangeable): aglycone moiety: 40.59[a] (C(1)); 27.26 (C(2)); 91.33 (C(3)); 40.27[a] (C(4)); 57.56 (C(5)); 19.24 (C(6)); 35.86 (C(7)); 40.99[a] (C(8)); 51.11 (C(9)); 37.93 (C(10)); 30.83[b] (C(11)); 71.94 (C(12)); 49.85 (C(13)); 52.41[c] (C(14)); 30.83[b] (C(15)); 27.26 (C(16)); 52.93[c] (C(17)); 84.99 (C(20)); 22.48 (C(21)); 36.79 (C(22)); 23.90 (C(23)); 126.02 (C(24)); 132.30 (C(25)); 25.98 (C(26)); 18.04 (C(27)); 28.41 (C(28)); 16.33, 16.73 (double), 17.39 (C(18), C(19), C(29), C(30)); Glc′: 105.41 (C(1′)); 81.14[d] (C(2′)); 78.53 (C(3′)); 71.63[e] (C(4′)); 77.71 (C(5′)); 62.86[f] (C(6′)); Glc″: 104.54 (C(1″)); 76.33 (C(2″)); 77.90 (C(3″)); 71.94[e] (C(4″)); 78.34 (C(5″)); 63.13 (C(6′)); Glc‴: 98.13 (C(1‴)); 75.30 (C(2‴)); 77.71 (C(3‴)); 71.70[e] (C(4‴)); 76.80 (C(5‴)); 62.47[f] (C(6‴)); Glc⁗: 104.80 (C(1⁗)); 75.11 (C(2⁗)); 77.87 (C(3⁗)); 80.84[d] (C(4⁗)); 76.48 (C(5⁗)); 62.02[f] (C(6⁗)); Gal′⁗: 105.19 (C(1′⁗)); 72.66 (C(2′⁗)); 74.89 (C(3′⁗)); 74.87 (C(4′⁗)); 76.84 (C(5′⁗)); 62.47[f] (C(6′⁗)). LSI-MS: 1269 ($[M-H]^-$), 1107, 945, 783, 621, 459.

*(3β,12β)-20-({*O*-β-*D*-Galactopyranosyl-(1 → 4)*-O*-[β-*D*-glucopyranosyl-(1 → 6)]-β-*D*-glucopyranosyl}oxy)-12-hydroxydammar-24-en-3-yl 2-O-β-D-Glucopyranosyl-β-D-glucopyranoside* (= *[β-*D*-Glc*p*-(1 → 2)-β-*D*-Glc*p-(1 → O-3)]-{β-*D*-Gal*p-(1 → 4)-[β-*D*-Glc*p-(1 → 6)]-β-*D*-Glc*p-(1 → O-20)}-protopanaxadiol* (**1e**). Amorphous solid. M.p. 245–250° (dec.). $^1$H-NMR ($CD_3OD$, 500 MHz): aglycone moiety: 1.00, 1.72 ($CH_2$(1)); 1.71, 1.98 ($CH_2$(2)); 3.20 (H–C(3)); 0.78 (H–C(5)); 1.49, 1.57 ($CH_2$(6)); 1.29, 1.52 ($CH_2$(7)); 1.42 (H–C(9)); 1.25, 1.79 ($CH_2$(11)); 3.71 (H–C(12)); 1.72 (H–C(13)); 1.02, 1.57 ($CH_2$(15)); 1.32, 1.73 ($CH_2$(16)); 2.29 (H–C(17)); 1.00 (Me(18)); 0.91 (Me(19)); 1.36 (Me(21)); 1.53, 1.80 ($CH_2$(22)); 2.05, 2.12 ($CH_2$(23)); 5.13 (H–C(24)); 1.68 (Me(26)); 1.62 (Me(27)); 1.06 (Me(28)); 0.91 (Me(29)); 0.85 (Me(30)); Glc′: 4.43 (*d*, *J*(1′,2′) = 7.8, H–C(1′)); 3.55 (H–C(2′)); 3.54 (H–C(3′)); 3.27 (H–C(4′)); 3.25 (H–C(5′)); 3.65 (*dd*, *J*(6′a,6′b) = 11.9, *J*(5′,6′a) = 5.4, $H_a$–C(6′)); 3.85 (*dd*, *J*(5′,6′b) = 2.0, $H_b$–C(6′)); Glc″: 4.66 (*d*, *J*(1″,2″) = 7.7, H–C(1″)); 3.21 (H–C(2′)); 3.35 (H–C(3″)); 3.20 (H–C(4″)); 3.24 (H–C(5″)); 3.61 ($H_a$–C(6″)); 3.81 ($H_b$–C(6″)); Glc‴: 4.60 (*d*, *J*(1‴,2‴) = 7.8, H–C(1‴)); 3.20 (*dd*, *J*(2‴,3‴) = 9.6, H–C(2‴)); 3.51 (H–C(3‴)); 3.72 (H–C(4‴)); 3.52 (H–C(5‴)); 3.91 (*dd*, *j*(6‴a,6‴b) = 12.1, *J*(5‴,6‴a) = 3.7, $H_a$–C(5‴)); 4.16 (*dd*, *J*(5‴,6‴b) = 1.5; $H_b$–C(6‴)); Gal⁗: 4.50 (*d*, *J*(1⁗,2⁗) = 7.8, H–C(1⁗)); 3.52 (*dd*, *J*(2⁗,3⁗) = 8.7, H–C(2⁗)); 3.49 (H–C(3⁗)); 3.80 (H–C(4⁗)); 3.61 (H–C(5⁗)); 3.69 (*dd*, *J*(6⁗a,6⁗b) = 12.1, *J*(5⁗,6⁗a) = 7.3, $H_a$–C(6⁗)); 3.75 (*dd*, *J*(5⁗,6⁗b) = 1.5, $H_b$–C(6⁗)); Glc′⁗: 4.41 (*d*, *J*(1′⁗,2′⁗) = 7.8, H–C(1′⁗)); 3.22 (H–C(2′⁗)); 3.34 (H–C(3′⁗)); 3.33 (H–C(4′⁗)); 3.27 (H–C(5′⁗)); 3.63 (*dd*, *J*(6′⁗a,6′⁗b) = 11.8, *J*(5′⁗,6′⁗a) = 3.5, $H_a$–C(6′⁗)); 3.87 (*dd*, *J*(5′⁗,6′⁗b) = 1.5, $H_b$–C(6′⁗)). $^{13}$C-NMR ($CD_3OD$, 50 MHz; values with the same superscript might be interchangeable): aglycone moiety: 40.59[a] (C(1)); 27.26 (C(2)); 91.31 (C(3)); 40.30[a] (C(4)); 57.56 (C(5)); 19.27 (C(6)); 35.88 (C(7)); 41.00[a] (C(8)); 51.12 (C(9)); 37.94 (C(10)); 30.76[b] (C(11)); 71.95 (C(12)); 49.85 (C(13)); 52.41[c] (C(14)); 30.76[b] (C(15)); 27.26 (C(16)); 52.75[c] (C(17)); 85.05 (C(20)); 22.37 (C(21)); 36.82 (C(22)); 23.83 (C(23)); 125.98 (C(24)); 132.29 (C(25)); 25.92 (C(26)); 18.03 (C(27)); 28.40 (C(28)); 16.34, 16.69 (double), 17.42 (C(18), C(19), C(29), C(30)); Glc′: 105.40 (C(1′)); 81.18 (C(2′)); 78.54 (C(3′)); 71.65[d] (C(4′)); 77.71 (C(5′)); 62.86[e] (C(6′)); Glc″: 104.55 (C(1″)); 76.35 (C(2′)); 77.87[f] (C(3″)); 71.95[d] (C(4″)); 78.34 (C(5″)); 63.14[e] (C(6″)); Glc‴: 98.11 (C(1‴)); 70.36 (C(2‴)); 77.71[f] (C(3‴)); 80.22 (C(4‴)); 78.34 (C(5‴)); 68.90 (C(6‴)); Gal⁗: 104.88 (C(1⁗)); 72.66 (C(2⁗)); 74.89 (C(3⁗)); 70.36 (C(4⁗)); 76.84 (C(5⁗)); 62.46[e] (C(6⁗)); Glc′⁗: 104.88 (C(1′⁗)); 75.11 (C(2′⁗)); 77.87[f] (C(3′⁗)); 71.75[d] (C(4′⁗)); 77.87[f] (C(5′⁗)); 62.86[e] (C(6′⁗)). LSI-MS: 1269 ($[M-H]^-$), 1107, 945, 783, 621, 459.

*Enzymatic Acylation of Ginsenoside Rb$_1$* (**1**). Compound **1** (200 mg) was dissolved in a mixture of DMF (8 ml), THF (16 ml) and vinyl acetate (6 ml). *Novozym® 435* (400 mg) was added and the suspension shaken at 45°. The reaction was monitored by TLC ($CHCl_3$/MeOH/$H_2O$ 8 : 5 : 0.4). After 4 h, the starting material was almost completely converted to two products. The enzyme was filtered off, the solvent mixture evaporated, and the crude residue purified by FC ($CHCl_3$/MeOH/$H_2O$ 2 : 1 : 0.1): 60 mg of 6″,6⁗-di-*O*-acetylginsenoside $Rb_1$ (**1f**) and 120 mg of a monoacetate fraction. The monoacetate fraction was recognized to be a 9 : 1 mixture of 6⁗-*O*-acetylginsenoside $Rb_1$ (**1g**) and 6″-*O*-acetylginsenoside $Rb_1$ (**1h**) by anal. HPLC ($H_2O$/MeCN 2 : 1): $t_R$

16.46 min for **1g** and 14.69 min for **1h**. Prep. HPLC allowed the isolation of 46 mg of pure **1g**, whereas **1h** could not be recovered as a pure compound.

*6″,6‴-Di*-O-*acetylginsenoside Rb$_1$* (=*(3β,12β)-20-{[6*-O-*(6*-O-*Acetyl-β*-D-*glucopyranosyl)-β*-D-*glucopyranosyl]oxy}-12-hydroxydammar-24-en-3-yl 2*-O-*(6*-O-*Acetyl-β*-D-*glucopyranosyl)-β*-D-*glucopyranoside*; **1f**): Amorphous solid. M.p. 177–178°. $^1$H-NMR ((D$_6$)DMSO, 600 MHz, 45°): aglycone moiety: 0.92, 1.58 (CH$_2$(1)); 1.56, 1.88 (CH$_2$(2)); 3.01 (H–C(3)); 0.71 (H–C(5)); 1.36, 1.49 (CH$_2$(6)); 1.21, 1.48 (CH$_2$(7)); 1.31 (H–C(9)); 1.08, 1.64 (CH$_2$(11)); 3.56 (H–C(12)); 1.57 (H–C(13)); 0.92, 1.57 (CH$_2$(15)); 1.47, 1.77 (CH$_2$(16)); 2.18 (H–C(17)); 0.71, 0.80, 0.83, 0.90 (Me(18), Me(19), Me(29), Me(30)); 1.25 (Me(21)); 1.47, 1.72 (CH$_2$(22)); 1.92, 2.04 (CH$_2$(23)); 5.09 (H–C(24)); 1.63 (Me(26)); 1.56 (Me(27)); 0.96 (Me(28)); Glc′: 4.27 (*d*, *J*(1′,2′) = 7.8, H–C(1′)); 3.28 (H–C(2′)); 3.38 (H–C(3′)); *ca*. 3.11 (H–C(4′), H–C(5′)); 3.45 (*dd*, *J*(6′a,6′b) = 11.8, *J*(5′,6′a) = 2.1, H$_a$–C(6′)); 3.65 (*dd*, *J*(5″,6″b) = 2.7, H$_b$–C(6′)); Glc″: 4.47 (*d*, *J*(1″,2″) = 7.8, H–C(1″)); 3.03 (H–C(2″)); 3.18 (H–C(3″)); 3.09 (H–C(4″)); 3.32 (H–C(5″)); 3.98 (*dd*, *J*(6″a,6″b) = 11.8, *J*(5″,6″a) = 2.7, H$_a$–C(6″)); 4.19 (*dd*, *J*(5″,6″b) = 5.3, H$_b$–C(6″)); 2.02 (1 Ac); Glc‴: 4.41 (*d*, *J*(1‴,2‴) = 7.8, H–C(1‴)); 2.89 (*dd*, *J*(2‴,3‴) = 9.6, H–C(2‴)); 3.19 (H–C(3‴)); 3.03 (H–C(4‴)); 3.37 (H–C(5‴)); 3.58 (*dd*, *J*(6‴a,6‴b) = 10.5, *J*(5‴,6‴a) = 4.6, H$_a$–C(6‴)); 3.86 (*dd*, *J*(5‴,6‴b) = 2.1, H$_b$–C(6‴)); Glc⁗: 4.24 (*d*, *J*(1⁗,2⁗) = 8.2, H–C(1⁗)); 2.98 (*dd*, *J*(2⁗,3⁗) = 9.6, H–C(2⁗)); 3.16 (H–C(3⁗)); 3.07 (H–C(4⁗)); 3.32 (H–C(5⁗)); 4.03 (*dd*, *J*(6⁗a,6⁗b) = 10.5, *J*(5⁗,6⁗a) = 2.1, H$_a$–C(6⁗)); 4.25 (*dd*, *J*(5⁗,6⁗a) = 4.6, H$_b$–C(6⁗)); 2.00 (1 Ac). $^{13}$C-NMR ((D$_6$)DMSO, 125 MHz, 45°; values with the same superscript might be interchangeable): aglycone moiety: 38.56 (C(1)); 25.42 (C(2)); 87.74 (C(3)); 38.56 (C(4)); 55.10 (C(5)); 18.03 (C(6)); 34.58 (C(7)); 39.10 (C(8)); 48.70 (C(9)); 35.98 (C(10)); 28.98 (C(11)); 68.45 (C(12)); 48.41 (C(13)); 50.35 (C(14)); 30.01 (C(15)); 25.05 (C(16)); 50.35 (C(17)); 82.25 (C(20)); 35.03 (C(22)); 22.40 (C(23)); 124.56 (C(24)); 130.63 (C(25)); 15.85, 16.05, 16.17, 16.27 (C(18), C(19), C(29), C(30)); 20.98 (C(21)); 24.70 (C(26)); 16.83 (C(27)); 26.63 (C(28)); Glc′: 102.51 (C(1′)); 87.78 (C(2′)); 76.50$^a$ (C(3′)); 68.96$^b$ (C(4′)); 75.74$^c$ (C(5′)); 60.34 (C(6′)); Glc″: 103.07 (C(1″)); 74.29 (C(2″)); 75.79$^c$ (C(3″)); 68.96$^b$ (C(4″)); 72.88$^c$ (C(5″)); 62.97 (C(6″)); Glc‴: 95.56 (C(1‴)); 73.00 (C(2‴)); 75.79$^c$ (C(3‴)); 68.98$^b$ (C(4‴)); 76.02$^a$ (C(5‴)); 68.81 (C(6‴)); Glc⁗: 102.75 (C(1⁗)); 72.63$^d$ (C(2⁗)); 75.79$^c$ (C(3⁗)); 69.02$^a$ (C(4⁗)); 72.88$^d$ (C(5⁗)); 62.97 (C(6⁗)); 19.95, 20.01 (*Me*COO); 170.04, 170.08 (Me*C*OO). LSI-MS: 1191 ([*M* – H]$^-$), 1149, 987, 945, 783, 621, 459.

*6⁗*-O-*Acetylginsenoside Rb$_1$* (=*(3β,12β)-20-{[6*-O-*(6*-O-*Acetyl-β*-D-*glucopyranosyl)-β*-D-*glucopyranosyl]-oxy}-12-hydroxydammar-24-en-3-yl 2*-O-*β*-D-*Glucopyranosyl-β*-D-*glucopyranoside*; **1g**): Amorphous solid. M.p. 189–190°. $^1$H-NMR ((D$_6$)DMSO, 600 MHz, 45°): aglycone moiety: 0.91, 1.59 (CH$_2$(1)); 1.55, 1.88 (CH$_2$(2)); 3.02 (H–C(3)); 0.70 (H–C(5)); 1.36, 1.46 (CH$_2$(6)); 1.22, 1.48 (CH$_2$(7)); 1.30 (H–C(9)); 1.05, 1.64 (CH$_2$(11)); 3.58 (H–C(12)); 1.55 (H–C(13)); 0.90, 1.52 (CH$_2$(15)); 1.47, 1.75 (CH$_2$(16)); 2.17 (H–C(17)); 0.75, 0.81, 0.83, 0.89 (Me(18), Me(19), Me(29), Me(30)); 1.24 (Me(21)); 1.45, 1.74 (CH$_2$(22)); 1.94, 2.01 (CH$_2$(23)); 5.10 (H–C(24)); 1.62 (Me(26)); 1.56 (Me(27)); 0.99 (Me(28)); Glc′: 4.27 (*d*, *J*(1′,2′) = 8.0, H–C(1′)); 3.32 (*dd*, *J*(2′,3′) = 9.3, H–C(2′)); 3.38 (H–C(3′)); 3.10 (H–C(4′), H–C(5′)); 3.43 (*dd*, *J*(6′a,6′b) = 11.9, *J*(5′,6′a) = 4.8, H$_a$–C(6′)); 3.66 (*dd*, *J*(5′,6b) = 2.4, H$_b$–C(6′)); Glc″: 4.45 (*d*, *J*(1″,2″) = 7.7, H–C(1″)); 3.00 (H–C(2″)); 3.13 (H–C(3″)); 3.06 (H–C(4″)); 3.18 (H–C(5″)); 3.48 (*dd*, *J*(6″a,6″b) = 11.8, *J*(5″,6″a) = 5.9, H$_a$–C(6″)); 3.62 (*dd*, *J*(5″,6″b) = 2.5, H$_b$–C(6″)); Glc‴: 4.41 (*d*, *J*(1‴,2‴) = 8.2, H–C(1‴)); 2.89 (*dd*, *J*(2‴,3‴) = 9.6, H–C(2‴)); 3.17 (H–C(3‴)); 3.02 (H–C(4‴)); 3.34 (H–C(5‴)); 3.57 (*dd*, *J*(6‴a,6‴b) = 12.1, *J*(5‴,6‴a) = 7.3, H$_a$–C(6‴)); 3.86 (*dd*, *J*(5‴,6‴b) = 2.3, H$_b$–C(6‴)); Glc⁗: 4.23 (*d*, *J*(1⁗,2⁗) = 8.2, H–C(1⁗)); 2.96 (H–C(2⁗)); 3.14 (H–C(3⁗)); 3.06 (H–C(4⁗)); 3.31 (H–C(5⁗)); 4.01 (*dd*, *J*(6⁗a,6⁗b) = 11.5, *J*(5⁗,6⁗a) = 7.5, H–C(6⁗a)); 4.25 (*dd*, *J*(5⁗,6⁗b) = 1.5, H–C(6⁗b)); 2.02 (Ac). $^{13}$C-NMR ((D$_6$)DMSO, 150 MHz, 45°; values with the same superscript might be interchangeable): aglycone moiety: 38.60 (C(1)); 25.73 (C(2)); 87.93 (C(3)); 38.81 (C(4)); 55.27 (C(5)); 18.68 (C(6)); 34.64 (C(7)); 39.18 (C(8)); 48.950 (C(9)); 36.12 (C(10)); 30.08 (C(11)); 68.70 (C(12)); 48.58 (C(13)); 50.61 (C(14)); 30.12 (C(15)); 25.58 (C(16)); 50.64 (C(17)); 82.38 (C(20)); 20.98 (C(21)); 35.34 (C(22)); 22.48 (C(23)); 124.90 (C(24)); 130.42 (C(25)); 25.28 (C(26)); 17.23 (C(27)); 27.12 (C(28)); 16.01, 16.04, 16.18, 16.83 (C(18), C(19), C(29), C(30)); Glc′: 102.70 (C(1′)); 81.95 (C(2′)); 77.01 (C(3′)); 70.11$^a$ (C(4′)); 76.18$^b$ (C(5′)); 61.25 (C(6′)); Glc″: 103.12 (C(1″)); 75.18$^c$ (C(2″)); 76.34 (C(3″)); 70.15$^a$ (C(4″)); 76.50$^b$ (C(5″)); 61.30 (C(6″)); Glc‴: 95.34 (C(1‴)); 73.58 (C(2‴)); 76.25$^b$ (C(3‴)); 70.09$^a$ (C(4‴)); 75.23$^c$ (C(5‴)); 68.75 (C(6‴)); Glc⁗: 102.73 (C(1⁗)); 73.49 (C(2⁗)); 76.53$^b$ (C(3⁗)); 70.02$^a$ (C(4⁗)); 72.57 (C(5⁗)); 63.10 (C(6⁗)); 20.61 (*Me*COO); 170.11 (Me*C*OO). LSI-MS: 1149 ([*M* – H]$^-$), 1107, 987, 783, 621, 459.

*6″*-O-*Acetylginsenoside Rb$_1$* (=*(3β,12β)-20-[(6*-O-*β*-D-*Glucopyranosyl-β*-D-*glucopyranosyl)oxy]-12-hydroxydammar-24-en-3-yl 2*-O-*(6*-O-*Acetyl-β*-D-*glucopyranosyl)-β*-D-*glucopyranoside*; **1h**): Selected $^1$H-NMR data ((D$_6$)DMSO, 600 MHz, 45°): Glc″: 4.47 (*d*, *J*(1″,2″) = 8.2, H–C(1″)); 3.02 (H–C(2″)); 3.18 (H–C(3″)); 3.09 (H–C(4″)); 3.30 (H–C(5″)); 3.98 (*dd*, *J*(6″a,6″b) = 11.8, *J*(5″,6″a) = 5.9, H$_a$–C(6″)); 4.19 (*dd*, *J*(5″,6″b) =

2.5, $H_b$–C(6″)); Glc‴: 4.42 (*d*, *J*(1‴,2‴) = 8.0, H–C(1‴)); 2.89 (*dd*, *J*(2‴,3‴) = 9.6, H–C(2‴)); 3.19 (H–C(3‴)); 3.06 (H–C(4‴)); 3.31 (H–C(5‴)); 3.56 (*dd*, *J*(6‴,a,6‴b) = 12.1, *J*(5‴,6‴a) = 7.3, $H_a$–C(6‴)); 3.90 (*dd*, *J*(5‴,6‴b) = 2.3, $H_b$–C(6‴)); 2.02 (Ac).

*Ginsenoside Rg₃* (= *(3β,12β,20*R*)- and (3β,12β,20*S*)-12,20-Dihydroxydammar-24-en-3-yl 2*-O-*β*-D-*glucopyranosyl*-*β*-D-*glucopyranoside* = *[β*-D-*Glc*p-*(1 → 2)*-*β*-D-*Glc*p-*(1π*O-*3)]*-*protopanaxadiol*; **3**). Ginsenoside $Rb_1$ (**1**; 1 g) was dissolved in 40% AcOH/$H_2O$ (*v*/*v*; 40 ml), and the mixture was stirred for 2 h at 70°. $H_2O$ (50 ml) was added, the mixture extracted 4 times with AcOEt, and the org. phase dried ($Na_2SO_4$) and evaporated. FC (AcOEt/MeOH/$H_2O$ 9 : 2 : 0.5) yielded 466 mg (65%) of **3** as a mixture of (20*R*) and (20*S*) epimers. Amorphous solid. M.p. 146–147°. $^1$H-NMR ((D$_6$)DMSO, 300 MHz, 80°): selected data of the aglycone moiety: 3.08 (H–C(3)); 3.42 (H–C(12)); 5.12, 5.14 (H–C(24)); Glc′: 4.31 (*d*, *J*(1′,2′) = 8.0, H–C(1′)); 3.26 (*t*, *J*(2′,3′) = 8.0, H–C(2′)); 3.40 (*t*, *J*(3′,4′) = 8.0, H–C(3′)); 3.12–3.18 (H–C(4′), H–C(5′)); 3.42 (*dd*, *J*(6′a,6′b) = 11.8, *J*(5′,6′a) = 3.5, $H_a$–C(6′)); 3.67 (*dd*, *J*(5′,6′b) = 1.5, $H_b$–C(6′)); Glc″: 4.52 (*d*, *J*(1″,2″) = 8.0, H–C(1″)); 3.06 (*t*, *J*(2″,3″) = 8.0, H–C(2″)); 3.12–3.18 (H–C(3″), H–C(4″), H–C(5′)); 3.52 (*dd*, *J*(6″a,6″b) = 11.8, *J*(5″,6″a) = 2.7, $H_a$–C(6″)); 3.68 (*dd*, *J*(5″,6″b) = 1.5, $H_b$–C(6″)). $^{13}$C-NMR ((D$_6$)DMSO, 300 MHz, 80°; values with the same superscript might be interchangeable): aglycone moiety: 38.87 (C(1)); 27.43 (C(2)); 88.41 (C(3)); 38.56[a] (C(4)); 55.83 (C(5)); 17.80 (C(6)); 34.57 (C(7)); 39.10[a] (C(8)); 49.59 (C(9)); 36.43 (C(10)); 31.01 (C(11)); 68.87 (C(12)); 47.67, 48.20 (C(13)); 51.04 (C(14)); 31.05, 31.06 (C(15)); 25.55, 26.48 (C(16)); 49.62, 53.41 (C(17)); 70.17, 72.11 (C(20)); 20.98 (C(21)); 34.90 (C(22)); 21.56 (C(23)); 125.26, 125.47 (C(24)); 130.05 (C(25)); 24.70 (C(26)); 16.83 (C(27)); 26.63 (C(28)); 15.85, 16.05, 16.17, 16.27 (C(18), C(19), C(29), C(30)); Glc′: 103.45 (C(1′)); 81.02 (C(2′)); 76.58 (C(3′)); 70.36 (C(4′)); 76.23 (C(5′)); 61.31 (C(6′)); Glc″: 103.45 (C(1″)); 74.95 (C(2″)); 76.60 (C(3″)); 70.38 (C(4″)); 76.23 (C(5″)); 61.31 (C(6″)). LSI-MS: 783 ([*M* – H]$^-$), 621, 459.

*Enzymatic Acetylation of Ginsenoside Rg₃* (**3**): *6″-*O*-Acetylginsenoside Rg₃* (= *(3β,12β,20*R*)- and (3β,12β,20*S*)-12,20-Dihydroxydammar-24-en-3-yl 2*-O-*(6*-O*-Acetyl-β*-D-*glucopyranosyl)-β*-D-*glucopyranoside*; **3a**). Compound **3** (200 mg) was dissolved in a mixture of DMF (5 ml), THF (15 ml), and vinyl acetate (5 ml). *Novozym® 435* (400 mg) was added and the suspension shaken at 45°. After 72 h, **3** was almost completely converted to one product (TLC monitoring ($CHCl_3$/MeOH/$H_2O$ 6 : 2 : 0.3)). The enzyme was filtered off, the solvent mixture evaporated, and the crude residue purified by FC ($CHCl_3$/MeOH/$H_2O$ 2 : 0.5 : 0.1): 137 mg of **3a**. Amorphous solid. M.p. 218–219°. $^1$H-NMR ((D$_6$)DMSO, 600 MHz, 80°): selected data of the aglycone moiety: 3.02 (H–C(3)); 3.38 (H–C(12)); 5.06, 5.08 (H–C(24)); Glc′: 4.27 (*d*, *J*(1′,2′) = 7.8, H–C(1′)); 3.26 (*t*, *J*(2′,3′) = 7.8, H–C(2′)); 3.37 (*t*, *J*(3′,4′) = 7.8, H–C(3′)); 3.09 (H–C(4′), H–C(5′)); 3.41 (*dd*, *J*(6′a,6′b) = 11.5, *J*(5′,6′a) = 5.5, $H_a$–C(6′)); 3.63 (*dd*, *J*(5′,6′b) = 1.0, $H_b$–C(6′)); Glc″: 4.47 (*d*, *J*(1″,2″) = 8.0, H–C(1″)); 3.01 (*t*, *J*(2″,3″) = 8.0, H–C(2″)); 3.17 (*t*, *J*(3″,4″) = 8.0, H–C(3″)); 3.09 (H–C(4″)); 3.30 (*ddd*, *J*(4″,5″) = 7.8, *J*(5″,6″a) = 5.5, *J*(5″,6″b) = 1.0, H–C(5″)); 3.97 (*dd*, *J*(6″a,6″b) = 11.5, $H_a$–C(6″)); 4.16 (*dd*, $H_b$–C(6″)); 2.00 (Ac). $^{13}$C-NMR ((D$_6$)DMSO, 600 MHz, 80°; values with the same superscript might be interchangeable): aglycone moiety: 38.91 (C(1)); 27.43 (C(2)); 88.30 (C(3)); 38.56[a] (C(4)); 55.82 (C(5)); 17.80 (C(6)); 34.58 (C(7)); 39.10[a] (C(8)); 49.62 (C(9)); 36.47 (C(10)); 31.71 (C(11)); 69.89 (C(12)); 47.69, 48.27 (C(13)); 51.05 (C(14)); 31.05, 31.06 (C(15)); 25.85, 26.68 (C(16)); 50.02, 53.01 (C(17)); 70.57, 72.01 (C(20)); 21.78 (C(21)); 34.75 (C(22)); 21.38 (C(23)); 125.22, 125.46 (C(24)); 130.05 (C(25)); 24.58 (C(26)); 16.03 (C(27)); 27.13 (C(28)); 15.65, 16.15, 16.20, 16.38 (C(18), C(19), C(29), C(30)); Glc′: 103.40 (C(1′)); 82.01 (C(2′)); 76.08 (C(3′)); 70.17 (C(4′)); 76.38 (C(5′)); 61.30 (C(6′)); Glc″: 103.88 (C(1″)); 74.94 (C(2″)); 76.80 (C(3″)); 69.89 (C(4″)); 73.86 (C(5″)); 63.74 (C(6″)); 20.57 (*Me*COO); 170.20 (Me*C*OO). LSI-MS: 825 ([*M* – H]$^-$), 783, 621, 459.

*Ginsenoside Rh₂* (= *(3β,12β,20*R*)- and (3β,12β,20*S*)-12,20-Dihydroxydammar-24-en-3-yl-β-*D*-Glucopyranoside;* **4**). A soln. of *β*-galactosidase (100 mg) in phosphate buffer (pH 4.5; 36 ml) was added dropwise into MeOH (10 ml) containing **3** (450 mg). The mixture was shaken for 2 h at 37°, then more *β*-galactosidase was added. After 24 h, the mixture was extracted with 3 × 20 ml AcOEt, the org. phase evaporated, and the residue purified by FC (AcOEt/MeOH/$H_2O$ 9 : 0.7 : 0.2): 129 mg (36%) of **4** as a mixture of (20*R*) and (20*S*) epimers. Amorphous solid. M.p. 139–144°. $^1$H-NMR ($CD_3OD$, 500 MHz): aglycone moiety: 1.02, 1.72 ($CH_2$(1)); 1.71, 1.98 ($CH_2$(2)); 3.21 (H–C(3)); 0.78 H–C(5)); 1.48, 1.56 ($CH_2$(6)); 1.30, 1.51 ($CH_2$(7)); 1.46 (H–C(9)); 1.24, 1.83 ($CH_2$(11)); 3.83 (H–C(12)); 1.74 (H–C(13)); 1.02, 1.56 ($CH_2$(15)); 1.32, 1.74 ($CH_2$(16)); 2.29 (H–C(17)); 0.85, 0.91, 0.92, 1.00 (Me(18), Me(19), Me(29), Me(30)); 1.29 (Me(21)); 1.37, 1.55 ($CH_2$(22)); 1.99, 2.14 ($CH_2$(23)); 5.13 (H–C(24)); 1.66 (Me(26)); 1.61 (Me(27)); 1.07 (Me(28)); Glc′: 4.31 (*d*, *J*(1′,2′) = 7.8, H–C(1′)); 3.18 (*dd*, *J*(2′,3′) = 8.9, H–C(2′)); 3.33 (*dd*, *J*(3′,4′) = 8.6, H–C(3′)); 3.28 (H–C(4′)); 3.25 (H–C(5′)); 3.65 (*dd*, *J*(6′a,6′b) = 11.9, *J*(5′,6′a) = 5.2, $H_a$–C(6′)); 3.83 (*dd*, *J*(5′,6′b) = 2.0, $H_b$–C(6′)). $^{13}$C-NMR ($CD_3OD$, 50 MHz; values with the same superscript might be interchangeable): aglycone moiety:

40.63[a] (C(1)); 27.36 (C(2)); 90.62 (C(3)); 40.23[a] (C(4)); 57.56 (C(5)); 19.26 (C(6)); 35.95 (C(7)); 40.98[a] (C(8)); 51.38 (C(9)); 37.97 (C(10)); 32.03 (C(11)); 71.69 (C(12)); 49.85 (C(13)); 52.59 (C(14)); 32.03 (C(15)); 27.19 (C(16)); 55.12 (C(17)); 74.40 (C(20)); 28.43 (C(21)); 35.95 (C(22)); 23.30 (C(23)); 126.19 (C(24)); 131.97 (C(25)); 25.90 (C(26)); 17.71 (C(27)); 28.43 (C(28)); 16.18, 16.81 (double), 17.15 (C(18), C(19), C(29), C(30)); Glc′: 106.71 (C(1′)); 72.14 (C(2′)); 78.29 (C(3′)); 71.69 (C(4′)); 77.69 (C(5′)); 62.84 (C(6′)). LSI-MS: 621 ([*M* – H]$^-$), 459.

*Enzymatic Acetylation of Ginsenoside Rh$_2$* (**4**): *6′-O-Acetylginsenoside Rh$_2$* (=*(3β,12β,20*R*)- and (3β,12β,20*S*)-12,20-Dihydroxydammar-24-en-3-yl 6-O-Acetyl-β-*D*-Glucopyranoside*; **4a**). To a soln. of **4** (3 mg) in THF (0.5 ml), vinyl acetate (0.1 ml) *Novozym® 435* (10 mg) were added. The mixture was shaken 72 h at 42° (TLC: (AcOEt/MeOH/H$_2$O 9 : 0.7 : 0.2): nearly 100% conversion to a single product). After filtration of the enzyme, the mixture was evaporated: **4a** as a mixture of (20*R*)- and (20*S*)-epimers. Amorphous solid. $^1$H-NMR (CD$_3$OD, 500 MHz): aglycone moiety: 1.02, 1.73 (CH$_2$(1)); 1.71, 1.98 (CH$_2$(2)); 3.22 (H–C(3)); 0.78 (H–C(5)); 1.48, 1.56 (CH$_2$(6)); 1.30, 1.51 (CH$_2$(7)); 1.46 (H–C(9)); 1.24, 1.83 (CH$_2$(11)); 3.83 (H–C(12)); 1.74 (H–C(13)); 1.02, 1.56 (CH$_2$(15)); 1.32, 1.73 (CH$_2$(16)); 2.29 (H–C(17)); 0.84, 0.91, 0.92, 1.00 (Me(18), Me(19), Me(29), Me(30)); 1.28 (Me(21)); 1.37, 1.55 (CH$_2$(22)); 1.99, 2.14 (CH$_2$(23)); 5.13 (H–C(24)); 1.67 (Me(26)); 1.61 (Me(27)); 1.07 (Me(28)); Glc′: 4.30 (*d*, *J*(1′,2′) = 7.8, H–C(1′)); 3.18 (*dd*, *J*(2′,3′) = 8.9, H–C(2′)); 3.31 (*dd*, *J*(3′,4′) = 8.6, H–C(3′)); 3.24 (H–C(4′)); 3.42 (H–C(5′)); 4.21 (H$_a$–C(6′)); 4.33 (H$_b$–C(6′)); 1.96 (Ac). $^{13}$C-NMR (CD$_3$OD, 50 MHz; values with the same superscript might be interchangeable): aglycone moiety: 40.33[a] (C(1)); 27.17 (C(2)); 90.90 (C(3)); 41.06[a] (C(4)); 57.59 (C(5)); 19.27 (C(6)); 35.94 (C(7)); 40.32[a] (C(8)); 51.30 (C(9)); 37.99 (C(10)); 30.90[b] (C(11)); 71.89 (C(12)); 49.86 (C(13)); 52.60 (C(14)); 32.04[b] (C(15)); 27.17 (C(16)); 55.14 (C(17)); 74.41 (C(20)); 28.40 (C(21)); 35.95 (C(22)); 23.30 (C(23)); 126.19 (C(24)); 131.98 (C(25)); 25.87 (C(26)); 17.69 (C(27)); 28.40 (C(28)); 16.18, 16.78 (double), 17.13 (C(18), C(19), C(29), C(30)); Glc′: 106.74 (C(1′)); 75.56 (C(2′)); 78.14 (C(3′)); 71.88 (C(4′)); 77.69 (C(5′)); 62.84 (C(6′)); 20.72 (*Me*COO); 172.68 (Me*C*OO). LSI-MS: 663 ([*M* – H]$^-$), 621, 459.

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