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# Structural diversification of taxanes by whole-cell biotransformation

Jungui Dai [a,*], Runjiang Qu [b], Jian-hua Zou [a], Xiaoguang Chen [b,*]

[a] Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College (Key Laboratory of Biosynthesis of Natural Products, Ministry of Public Health; Key Laboratory of Bioactive Substances and Resources Utilization of Chinese Herbal Medicine, Ministry of Education), 1 Xian Nong Tan Street, Beijing 100050, People's Republic of China

[b] Department of Pharmacology, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, 1 Xian Nong Tan Street, Beijing 100050, People's Republic of China

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ABSTRACT

The structural diversification of four 4(20),11(12)-taxadienes (sinenxan A and its two derivatives, and yunanxane) by microbial/plant whole-cell enzymatic transformation has been achieved; 53 derivatives have been obtained, and 41 of them are new compounds. The occurred reactions exhibited diversity, including hydroxylation, epoxidation, oxidation, hydrolysis, acylation, O-alkylation, O-glycosylation, rearrangement, etc. In addition, one chemical derivative, 9α-cinnamoyl sinenxan A from one enzymatic product 9α-hydroxyl sinenxan A, displayed significant reversal activity toward three MDR tumor cell lines (A549/taxol, KB/VCR, and HCT-8).

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## 1. Introduction

While semisynthetic chemical methods have proven useful to approach many natural product derivatives, these techniques run into difficulties with molecules that are labile or those with functional groups that require protection. However, biocatalytic derivatization offers a number of advantages over chemical synthesis when working with complex molecules and offers a general approach toward a synthetic derivatization strategy.[1] Accordingly, biocatalysis complements chemosynthesis. When biocatalysis is used alone or in combination with synthetic organic transformations, it provides access to derivatives not readily accessible by chemical synthetic means alone. In principle, the microbial/plant whole cells possess a variety of enzymes, which can catalyze various chemical reactions and can be used for derivatization of natural and non-natural compounds. Thus, an enzymatic approach could directly produce not only numerous compounds for pharmacological evaluation, but it could also yield potential alternatives for further chemical modification.

The treatment of cancer with chemotherapeutic drugs is frequently hindered by either intrinsic or acquired resistance of the tumor cells. In both cases, the tumor can become refractory to a variety of antineoplastic drugs of varying structures and mechanisms of action, a process termed multi-drug resistance (MDR). Although MDR can develop by several different mechanisms, a common cause is believed to be overexpression of an Mr 170,000 plasma membrane glycoprotein (P-gp), a transporter protein that acts as an energy-dependent drug efflux pump, preventing adequate intracellular accumulation of a broad range of cytotoxic drugs.[2]

Many natural taxanes and chemical derivatives with MDR-reversal activity have been reported.[3] Inspired by these results, we have been investigated the MDR-reversal activity of our patented natural taxanes [sinenxan A (**1**) and its analogs, which are 4(20),11(12)-taxadienes with *C*-14 oxygenated substituents from cell cultures of *Taxus* in high yield] and their derivatives produced by systematic enzymatic and/or chemical modifications.[4] Herein, we briefly report the structural diversification by enzymatic approach of two major metabolites of *Taxus* cells (**1**, and yunnanxane **2**) and those derivatives of **1** lacking the C-14 or C-2 functional group (**3** and **4**). We also describe the MDR-reversal activity of one chemo-enzymatic derivative (**58**) toward three MDR cell lines with P-gp overexpression.

## 2. Results and discussion

Incubation of **1** [2α,5α,10β,14β-tetraacetoxy-taxa-4(20),11(12)-diene] with 15-day-old suspended cultured cells of *Asparagus officinalis* for 6 days afforded three products (Fig. 1, **5**–**7**). Of them, **7** is a new compound identified as 6α-hydroxy-10-oxo-2α,5α,14β-triacetoxy-taxa-4(20),11-diene on the basis of its physical and spectroscopic data analyses. It is an unusual taxane, probably

* Corresponding authors. Tel.: +86 10 63165195; fax: +86 10 63017757 (J.D.); tel.: +86 10 63165207; fax: +86 10 63017757 (X.C.).
*E-mail addresses:* jgdai@imm.ac.cn (J. Dai), chxg@imm.ac.cn (X. Chen).

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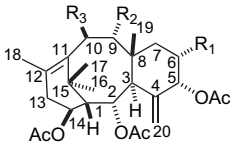


**1** $R_1$=$R_2$=H, $R_3$=OAc
**5** $R_1$=$R_2$=H, $R_3$=OH
**6** $R_1$=$R_3$=OH, $R_2$=H
**7** $R_1$=$R_2$=OH, $R_3$= =O

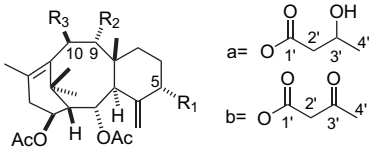
**Figure 1.** The structures of **1** and its transformed products (**5**–**7**) by suspension cultured cells of *A. officinalis*.

biosynthesized from **1** through specific 10-deacetylation (**5**) followed by regio- and stereospecific hydroxylation at the 6α position (**6**) and selective oxidation of the 10β-ol.

Cyclodextrins (CDs) are a group of naturally occurring cyclic oligosaccharides derived from starch with six, seven, or eight glucose residues linked by α(1→4) glycosidic bonds in a cylinder-shaped structure and are denominated α-, β- and γ-cyclodextrin, respectively. The central cavity of CDs is hydrophobic, whereas the rims of the surrounding walls are hydrophilic. This hydrophobic cavity forms inclusion complexes with a wide range of organic guest molecules, which leads to enhancement of the solubility, stability, and bioavailability of guest molecules in the aqueous environment. In our previous report, we observed that co-administration of β-CD with substrate in biotransformations can influence the biotransformation mode, resulting in some new enzymatic reactions.[4f] In the absence of β-CD, only one product (**5**) was obtained from the biotransformation of **1** by a suspension of cultured *Platycodon grandiflorum* cells. However, when β-CD was added with the substrate to the *Platycodon* cell cultures, six additional products (**8**–**13**) except for **5** were obtained (Fig. 2). Compounds **8** and **9** are two products of **1**, which have been reported before,[5] and **10**–**13** are four new compounds. In this biocatalysis process, **8** might be the biosynthetic intermediate of **10**–**13**, which might be biosynthesized via ester transfer mediated by utilizing β-hydroxyacylCoA and β-ketoacylCoA or 10-deacetylation. The results suggested that the substrate goes, in the presence of β-CD, into the organelles of the cells where there are many different enzymes catalyzing the various transformations. We observed a considerable difference in the reaction modes of these biotransformations in the presence and in the absence of β-CD. Obviously, the difference in the reaction mode means that each step of taxane biotransformation takes place in different compartments in the cells.

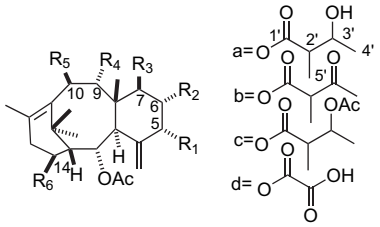
Based on the above results and revelation, the biotransformation of **2** by fungus *Absidia coerulea* in the presence of β-CD has also been investigated. Compared with the results in the absence of β-CD,[4c] eight other products (Fig. 3, **17** and **21**–**27**) except for products **14**–**16** and **18**–**20**[4c] were obtained, and one additional type of reaction (acylation) was observed. As a result, acetylation of the 3′-OH yielded **21** and oxalylation of the 10-OH gave **26**. Thus, this experiment gives further evidence that the use of β-CD in biotransformation can bring about greater structural diversification of a substrate.

Introduction of a hydroxyl group to the molecular skeleton of **1** and its analogs at different positions except at the C-1 and C-13 positions has been achieved previously.[2,4f,5b,6] Because the steric



**5** $R_1$=OAc, $R_2$=H, $R_3$=OH **11** $R_1$=a, $R_2$=H, $R_3$=OH
**8** $R_1$=OH, $R_2$=H, $R_3$=OAc **12** $R_1$=b, $R_2$=H, $R_3$=OAc
**9** $R_1$=$R_3$=OAc, $R_2$=OH **13** $R_1$=b, $R_2$=H, $R_3$=OH
**10** $R_1$=a, $R_2$=H, $R_3$=OAc

**Figure 2.** The transformed products of **1** by suspension cultured cells of *P. grandiflorum* in the presence of β-cyclodextrin.



**2** $R_1$=$R_5$=OAc, $R_2$=$R_3$=$R_4$=H, $R_6$=a
**14** $R_1$=$R_5$=OAc, $R_2$=$R_3$=$R_4$=H, $R_6$=b
**15** $R_1$=$R_5$=OAc, $R_2$=$R_3$=H, $R_4$=OH, $R_6$=a
**16** $R_1$=OAc, $R_2$=$R_3$=$R_4$=H, $R_5$=OH, $R_6$=a
**17** $R_1$=OAc, $R_2$=$R_3$=H, $R_4$=$R_5$=OH, $R_6$=a
**18** $R_1$=$R_5$=OAc, $R_2$=OH, $R_3$=$R_4$=H, $R_6$=a
**19** $R_1$=$R_5$=OAc, $R_2$=$R_4$=H, $R_3$=OH, $R_6$=a
**20** $R_1$=OAc, $R_2$=$R_4$=H, $R_3$=$R_5$=OH, $R_6$=a
**21** $R_1$=$R_5$=OAc, $R_2$=$R_3$=$R_4$=H, $R_6$=c
**22** $R_1$=OAc, $R_2$=$R_3$=$R_4$=H, $R_5$=OH, $R_6$=b
**23** $R_1$=$R_5$=OAc, $R_2$=$R_4$=H, $R_3$=OH, $R_6$=b
**24** $R_1$=OH, $R_2$=$R_3$=$R_4$=H, $R_5$=OAc, $R_6$=a
**25** $R_1$=$R_5$=OAc, $R_2$=OH, $R_3$=$R_4$=H, $R_6$=b
**26** $R_1$=OAc, $R_2$=$R_3$=$R_4$=H, $R_5$=d, $R_6$=a
**27** $R_1$=OAc, $R_2$=$R_5$=OH, $R_3$=$R_4$=H, $R_6$=a

**Figure 3.** The transformed products of **2** by *A. coerulea* in the presence of β-cyclodextrin.

hindrances of *C*-2 or *C*-14 oxygenated substituents might be responsible for the lack of substitution at C-1 and C-13, the acetoxyl groups at the C-14 or C-2 were eliminated. The corresponding compounds **3** and **4** were obtained, and they have subsequently been used as substrates for the bioconversion by several fungal and plant cultured cells, thereby extending the diversity of this class of compounds.

Two species of fungi, *A. coerulea* and *Mucor genevensis*, which have been employed for the biotransformation of **1** and other taxanes,[4c,e] have been selected for the bioconversion of **3**. Compound **3** was very active when incubated with *A. coerulea*, and 12 products (Fig. 4, **28**–**39**) were obtained and identified. In this bioprocess, several types of reactions were involved, such as deacetylation (**28**, an intermediate probably in the formation of all products), acylation (**29** and **31**), O-alkylation (**30**), epoxidation (**32**), hydroxylation (**34**–**36**, **38**, and **39**), rearrangement (**33**, **34**, and **38**), and hydrogenation (**35** from **38**). The hypothetical biosynthetic pathway has been proposed (Fig. 4). The initial reaction was probably the 10-deacetylation (yielded **28**) followed by other types of reactions. The typical 7β hydroxylation in the bioconversion of **1** and its analogs with this fungus[4f] was not observed in this experiment, a similar result was observed in the biotransformation of **3** by *Ginkgo* cells, with the 9α hydroxylation as its typical reaction,[4d,6] suggesting the requirement of a *C*-14 oxygenated functional group for these two enzymatic reactions. Although C-13 hydroxylation (**34**, **36**, and **39**) was observed in this experiment, analyses of NOE difference spectral data and spin–spin coupling established that the stereochemistry of the OH group is β-orientation, which is not a 'natural' configuration, indicating that there existed different stereoselectivities of responsible enzymes between fungus *A. coerulea* and *Taxus* plants. Furthermore, among the obtained compounds were several types of taxanes that have not been found in natural *Taxus* plants before, such as the 18-hydroxylated products (**35** and **38**), 18-oxo derivative (**37**), 12(18)- and 12(13)-olefin (**33**, **34**, and **38**, rearranged products).

Bioconversion of **3** with *M. genevensis* yielded five products (**28**, **32**, **36**, **43**, and **48**, Fig. 5). Compounds **28**, **32**, and **36** have been obtained from bioconversion of **3** by *A. coerulea*, and **43** and **48** are two new products yielded from this process. The original reaction also may be the selective hydrolysis of the *C*-10 acetyl group, followed by epoxidation (**32**), hydroxylation (**36**), O-alkylation (**48**), and O-glucosidation (**43**) to biosynthesize the corresponding

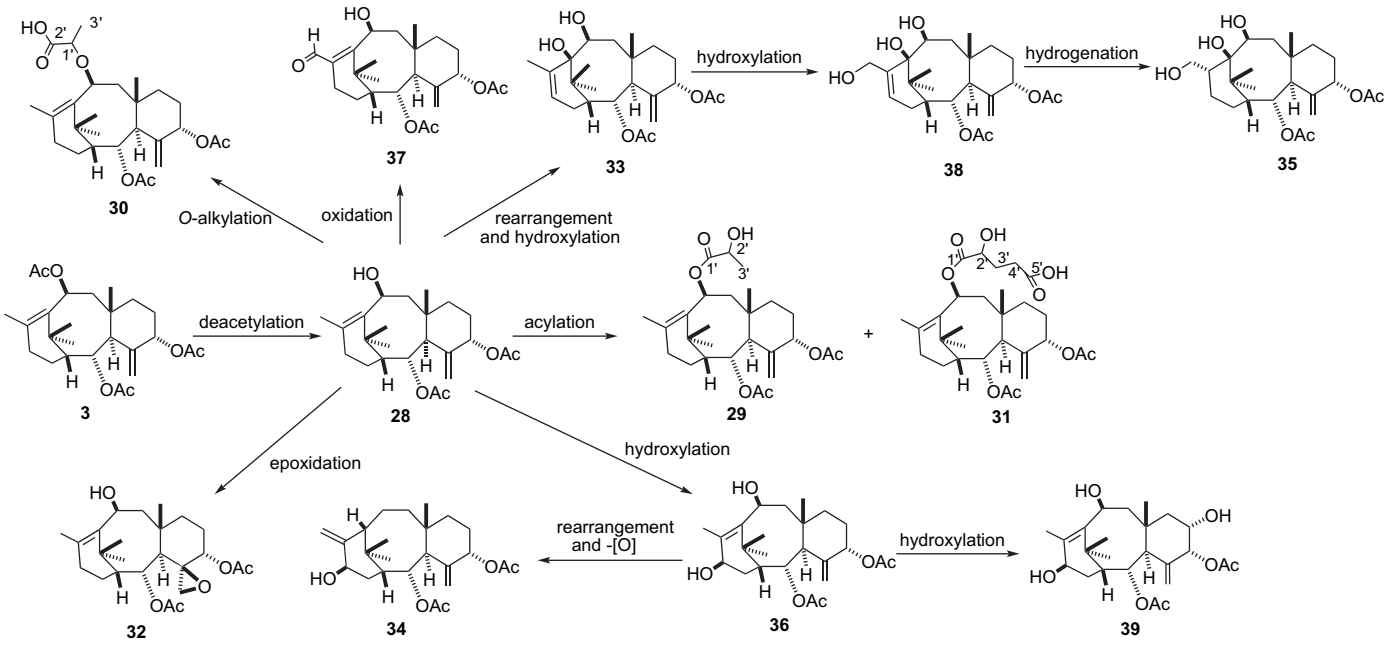



**Figure 4.** The proposed biosynthetic pathway of **3** and its products by *A. coerulea*.

products. Few reports other than the production of the 7β-*O*-glycosides have appeared on the taxane glycosides isolated from natural *Taxus* plants. 10-Deacetylation and epoxidation of the 4(20) double bond, two typical reactions of this kind in taxanes mediated by *M. genevensis*, were both observed,[4e] indicating the substrate specificity of the responsible enzymes.

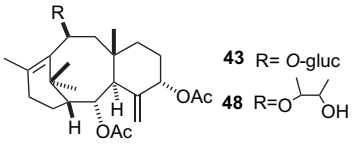



**Figure 5.** The new transformed products (**43** and **48**) of **3** by *M. genevensis*.

In our laboratory, several cultured plant cell suspensions were in hand, such as *A. officinalis*, *Catharanthus roseus*, *Phytolacca acinosa*, and *P. grandiflorum*. Among them, cell suspensions of *C. roseus* and *P. grandiflorum* have been employed for the bioconversion of **1**.[5a,7] They were used as biocatalysts for the transformation of **3** in this experiment for structural diversification. As expected, several structurally different products were obtained, especially with *Asparagus* cells as biocatalyst. In the bioconversion of **3** by *Asparagus* cells, products **28**, **40**, **42**, and **44**–**47** were obtained, and the proposed biosynthetic pathway is shown in Figure 6. Oxidation of *C*-10 alcohol was also observed in the bioconversion of **1** by *Asparagus* cells, indicating that this may be a typical reaction of these types of taxanes catalyzed by *Asparagus* cells. Only a few 11(12) epoxy taxanes have been isolated from *Taxus* plants. Epoxidation of the

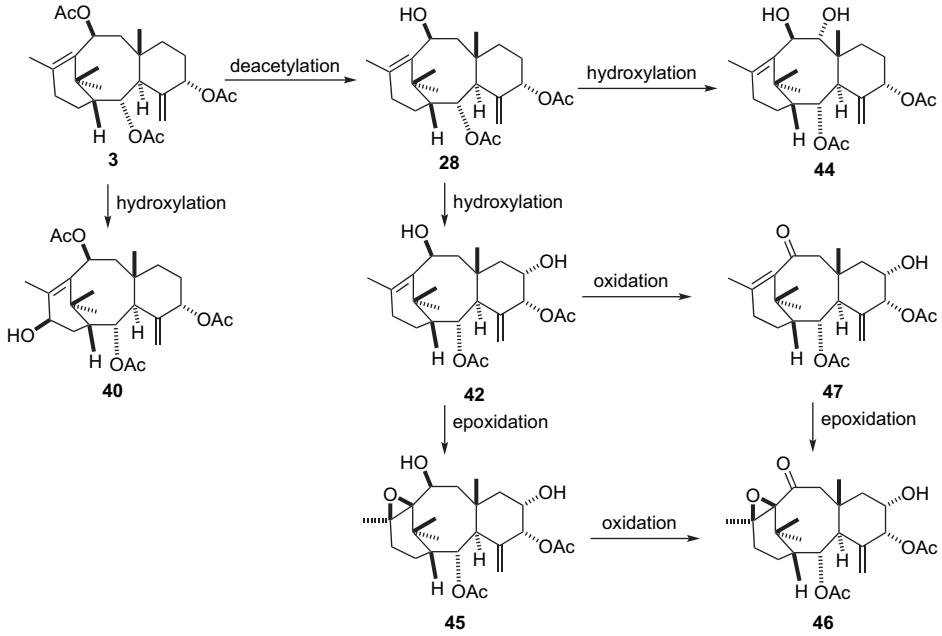



**Figure 6.** The proposed biosynthetic pathway of **3** by suspension cultured cells of *A. officinalis*.

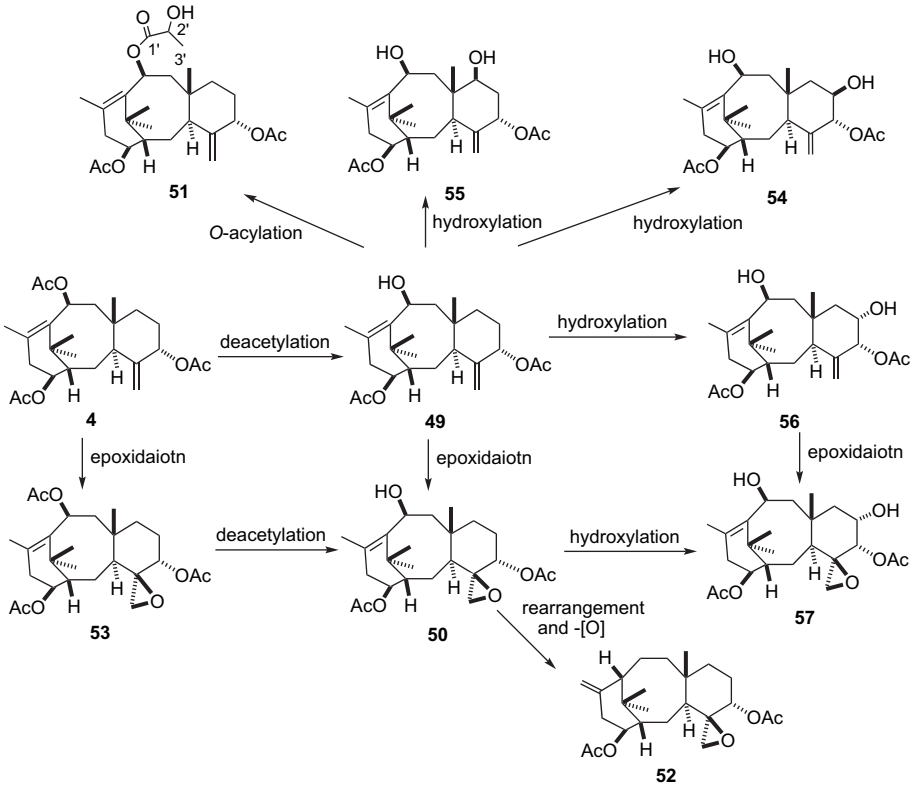
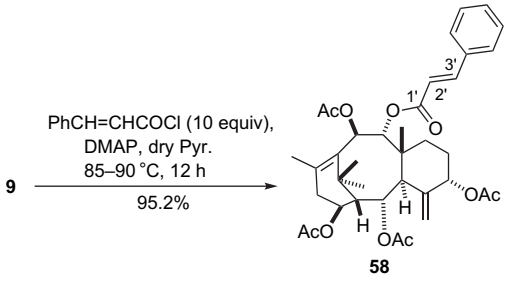



**Figure 7.** The proposed biosynthetic pathway of **4** by the fungus *A. coerulea.*

11(12) double bond is the first reported reaction in the bioconversion of taxanes and may serve as a probe to investigate the biosynthesis of this type of taxane in *Taxus* plants. In the bioconversion of **3** by *Catharanthus* cells (products **28**, **41**–**43**), the triggered reaction may also be the 10-deacetylation, and subsequently, the other reactions, 10-O-butanylation (**41**[8]), 6α-hydroxylation, and 10-O-glycosidation, took place. The products **36** and **40** were obtained from the biotransformation by *Phytolacca* cells, and the products **28**, **42**, and **44** from the biotransformation by *Platycodon* cells.

10-Deacetylation and epoxidation of the 4(20) exocyclic double bond were the two basal reactions in the bioconversion of **4** by fungus *A. coerulea*. The other following reactions included 10-acylation (**51**), elimination of C-10 hydroxyl group, rearrangement of $\Delta^{11(12)}$ to $\Delta^{12(18)}$ double bond (**52**), and hydroxylation (6α, or 6β, or 7β, **56**, **57**, **54**, and **55**). As a result, nine new compounds have been obtained. A plausible biosynthetic pathway is shown in Figure 7. The typical 7β hydroxylation of taxanes by this fungus was observed in this bioprocess, but it was not observed when **3** was used as substrate, which further suggests that the existence of the C-14 functional group is necessary for this specific hydroxylation. Except for 6α hydroxylation of **3** and **4**, 6β hydroxylation was observed by the same fungus only with **4** as substrate, also suggesting that structurally different substrates lead to different stereo-selective reactions.

On the basis of the above enzymatic derivatization, further chemical modifications of some of the products have been carried out. Most of the derivatives from the two synthetic approaches have been subjected to biological evaluation for the reversal activity toward three MDR tumor cell lines (A549/taxol, KB/VCR, and HCT–8) with P-gp overexpressing phenotype. A549/taxol and KB/VCR tumor cell lines are two acquired one, and HCT-8 is an intrinsic one. Several of the novel derivatives displayed potent activity. Especially, one 'combined' derivative (**58**) from **9** via chemical cinnamoylation of the 9α hydroxyl group (Scheme 1) effectively enhanced the cytotoxic activity of the anticancer agents (paclitaxel and vincristine) in the MDR tumor cell lines (Table 1). The $IC_{50}$ values of the antitumor agents were reduced by as much as 99% when **58** (5–10 μM) was co-administered to the MDR tumor cell lines, a decrease in $IC_{50}$ comparable to that obtained with 10 μM verapamil.




**Scheme 1.** Chemical synthesis of **58** from **9**.

## 3. Conclusions

In summary, this paper reports the successful structural derivatization of four 4(20),11(12)-taxadienes by enzymatic synthesis, although the expected hydroxylations of C-1 and 13α did not occur. Totally, 53 derivatives have been obtained, and of them, 41 are new compounds. The reactions exhibited diversity, which resulted in structurally diverse products. In addition, the results also indicated that the addition of β-CD may lead to more structurally varied derivatives. Furthermore, a variety of derivatives have been chemically synthesized following the introduction of functional group to the starting materials, and one 'combined' derivative with potent MDR-reversal activity is reported. These results indicate that bioconversion by whole-cell of fungi and/or plants is a versatile means of introducing diversity into compounds. We also provide

**Table 1**
MDR-reversal activity of compound **58** in MDR cell lines A549/taxol, KB/VCR, and HCT-8[a]

| Concn (μM) | % Reduction[b] | | |
|---|---|---|---|
| | A549/taxol | KB/VCR | HCT-8 |
| Compound **58** | | | |
| 1.0 | 23.1 | 90.5 | 56.5 |
| 2.5 | 24.2 | 96.2 | 96.2 |
| 5.0 | 98.6 | 99.1 | 98.8 |
| 7.5 | 99.3 | 99.6 | 99.4 |
| 10.0 | 99.6 | 99.7 | 99.5 |
| Verapamil | | | |
| 10 | 99.4 | 99.1 | 99.5 |

[a] A549/taxol: an MDR subline of human lung adenocarcinoma cell line A549; KB/V: an MDR subline of human oropharyngeal epidermoid carcinoma cell line KB; HCT-8: an intrinsic MDR human colorectal adenocarcinoma cell line.
[b] % Reduction=[1−$IC_{50}$(reversal agent+antitumor agent)/$IC_{50}$(antitumor agent)]×100; antitumor agent is paclitaxel for A549/taxol and HCT-8, and vincristine for KB/VCR.

a successful example of the application of the combined chemo-enzymatic approach to lead compound discovery in the process of drug R&D.

## 4. Experimental section

### 4.1. General experimental procedures

Optical rotations were obtained using a Horiba SEPA-200 polarimeter. IR spectra were taken on a Hitachi 270-30 spectrometer in $CHCl_3$. $^1H$ NMR (500 MHz) and $^{13}C$ NMR (125 MHz) spectra were recorded with a Varian Unity-PS instrument using $CDCl_3$ or $CD_3OCD_3$ as solvent and reference. $^1H$ NMR and $^{13}C$ NMR assignments were determined by $^1H$–$^1H$ COSY, DEPT, HMQC, and HMBC experiments. HRFABMS were carried out on a JEOL-HX 110 FAB-mate instrument and HRESIMS on a VG ZabSpec mass spectrometer. Semipreparative HPLC was performed on a Shimadzu LC-6A HPLC instrument with a YMC Prep-sil or Pre-ODS (25 cm×10 mm i.d., 5 μm) stainless steel column and a Shimadzu RID-10A detector. Si gel (230–300 mesh) was employed for flash column chromatography and analytical TLC plates (Si gel 60 $F_{254}$, QinDao Oceanic Chemicals, China) were visualized by spraying with 10% $H_2SO_4$ (in EtOH) followed by heating at 105 °C.

### 4.2. Substrates

Sinenxan A [2α,5α,10β,14β-tetraacetoxy-taxa-4(20),11-diene, **1**] and yunnanxane [2α,5α,10β-triacetoxy-14β-(3-hydroxy-2-methyl)-butyryloxy-taxa-4(20),11-diene, **2**] were isolated from callus cultures (Ts-19 strain) of *Taxus chinensis*. The substrates **3** [2α,5α,10β-triacetoxy-taxa-4(20),11-diene] and **4** [5α,10β,14β-triacetoxy-taxa-4(20),11-diene] were prepared following previously described literature procedures.[9] The structures of all substrates were characterized by $^1H$ NMR, $^{13}C$ NMR, and MS spectral analyses, and the purities were >95% by HPLC analysis. The substrates were dissolved in acetone/EtOH before use for biotransformation.

### 4.3. Biotransformation of 1 by suspension cultured cells of *A. officinalis*

The fresh seedlings of *A. officinalis* L. (Liliaceae) were purchased from the supermarket, in May 2004. Young stems were used to initiate calli. The explants were disinfected by immersing in 70% EtOH for 30 s, followed by immersing in saturated calcium hypochlorite solution for 15 min, washed five times with sterilized water, then cut into small pieces (about 1.0 cm in length), and aseptically transferred to Murashige and Skoog's medium (MS) supplemented with 0.5 mg/L naphthalene acetic acid (NAA), 0.5 mg/L 6-benzylaminopurine (6-BA), and 0.2 mg/L 2,4-dichlorophenoxy acetic acid (2,4-D). The pH of the medium was adjusted to 5.8 before autoclaving at 121 °C for 20 min. The calli initiated from all the explants within 4 weeks of cultivation in the dark at (25±2) °C. The callus cultures were maintained under the same cultural conditions by sub-culturing every 4 weeks. After five generations, 3-week-old friable calli were used for initiation of suspension cultures. Cell suspension cultures were sub-cultured every 3 weeks at the inoculum size of 5.0 g/L dry weight in 500-mL Erlenmeyer flask with 150 mL fresh medium and incubated on a rotary shaker at 110 rpm in the dark at (25±2) °C for the biotransformation use. On the cultural day 15th, 500 mg of **1** in 6.0 mL acetone was distributed into 30 flasks of cell cultures. After additional 6 days of incubation, the cell cultures were filtered under vacuum, the filtrate was extracted with EtOAc three times, and concentrated in vacuum at 40 °C to give 750 mg of residue. The cell cultures were extracted with EtOAc thrice by sonication to afford 560 mg of residue. The combined residue was fractionated by Si gel column chromatography eluting with a gradient of *n*-hexane/EtOAc (19/1–100% EtOAc) to yield five fractions. Fractions 3 and 4 were further separated by semipreparative HPLC to afford 250 mg of **1** (50%), 100 mg of **5** (ca. 20%), 10 mg of **7** (ca. 2%), and 25 mg of **6** (ca. 5%). Among these products, compound **7** is a new compound.

#### *4.3.1. 6α-Hydroxy-10-oxo-2α,5α,14β-triacetoxy-taxa-4(20),11-diene (**7**)*

White powder; $[\alpha]_D^{20}$ +105.2 (*c* 0.167, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3624, 3016, 2932, 1732, 1682, 1434, 1374, 1340, 1252, 1122, 1038 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 2.05–2.07 (1H, m, overlapped, H-1), 5.43 (1H, dd, *J*=2.6, 6.6 Hz, H-2), 3.08 (1H, d, *J*=6.6 Hz, H-3), 5.08 (1H, d, *J*=4.6 Hz, H-5), 3.82 (1H, ddd, *J*=1.2, 4.6, 5.6 Hz, H-6), 1.68 (1H, dd, *J*=5.6, 14.6 Hz, H-7β), 1.49 (1H, dd, *J*=1.2, 14.6 Hz, H-7α), 2.51 (1H, d, *J*=14.2 Hz, H-9β), 2.44 (1H, d, *J*=14.2 Hz, H-9α), 2.91 (1H, dd, *J*=9.3, 18.8 Hz, H-13β), 2.42–2.56 (1H, m, overlapped, H-13α), 5.32 (1H, dd, *J*=5.3, 9.0 Hz, H-14), 1.20 (3H, s, H-16), 1.36 (6H, s, H-17 and H-19), 1.80 (3H, s, H-18), 5.26 (1H, s, H-20a), 4.88 (1H, s, H-20b), 2.17, 2.05, 1.98 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 57.97 (d, C-1), 69.81 (d, C-2), 47.44 (d, C-3), 141.22 (s, C-4), 79.60 (d, C-5), 72.88 (d, C-6), 46.57 (t, C-7), 40.18 (s, C-8), 59.85 (t, C-9), 206.59 (s, C-10), 142.66 (s, C-11), 135.45 (s, C-12), 37.69 (t, C-13), 69.69 (d, C-14), 36.20 (s, C-15), 26.09 (q, C-16), 29.71 (q, C-17), 22.82 (q, C-18), 25.14 (q, C-19), 113.91 (t, C-20), 21.34, 21.24, 21.12 [q, OAc ($CH_3$)], 170.99, 170.17, 169.98 [s, OAc (CO)]; HREIMS *m*/*z* $[M+H]^+$ 477.2464 (calcd 477.2488 for $C_{26}H_{37}O_8$).

### 4.4. Biotransformation of 1 by suspended cells of *P. grandiflorum* in the presence of β-cyclodextrin

The procedure of tissue and cell culture of *P. grandiflorum* (JACQ.) A.DC. (Campanulaceae) was performed as described previously.[7] First, **1** (500 mg in 2 mL EtOH) was added into saturated β-cyclodextrin solution (2000 mg in 50 mL medium) and stirred 48 h, and distributed into the flasks with cell cultures. The procedures of incubation, collection, extraction, concentration, and fractionation by open Si gel column chromatography were performed as described as before.[7] Further purification by normal phase semipreparative HPLC afforded 245 mg of substrate (ca. 50%), 50 mg of **5** (ca. 10%), 5 mg of **8** (ca. 1%), 25 mg of **9**–**11** (ca. 5%), and 10 mg of **12** and **13** (ca. 2%). Among them, **10**–**13** are new compounds.

#### *4.4.1. 2α,10β,14β-Triacetoxy-5α-(3-hydroxy-butyryl)oxytaxa-4(20),11-diene (**10**)*

White powder; $[\alpha]_D^{20}$ +38.6 (*c* 0.26, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3556, 2940, 1730, 1646, 1608, 1452, 1374, 1246, 1226, 1210, 1174, 1106, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.88 (1H, d, *J*=2.0 Hz,

H-1), 5.35 (1H, dd, *J*=2.2, 6.3 Hz, H-2), 2.88 (1H, d, *J*=6.8 Hz, H-3), 5.32 (1H, t, *J*=2.4 Hz, H-5), 1.75–1.85 (2H, m, H-6), 1.92–2.06 (1H, m, overlapped, H-7β), 1.21–1.29 (1H, m, overlapped, H-7α), 2.38 (1H, dd, *J*=12.2, 14.9 Hz, H-9β), 1.60–1.68 (1H, m, overlapped, H-9α), 6.06 (1H, dd, *J*=5.6, 12.2 Hz, H-10), 2.85 (1H, dd, *J*=9.0, 14.9 Hz, H-13β), 2.38–2.45 (1H, m, overlapped, H-13α), 4.95 (1H, dd, *J*=4.9, 9.3 Hz, H-14), 1.66 (3H, s, H-16), 1.12 (3H, s, H-17), 2.08 (3H, s, H-18), 0.84 (3H, s, H-19), 5.29 (1H, s, H-20a), 4.86 (1H, s, H-20b), 2.05, 2.04, 2.02 [3H each, OAc ($CH_3$)], 2.59 (1H, dd, *J*=8.3, 16.1 Hz, H-2′a), 2.52 (1H, dd, *J*=3.7, 16.1 Hz, H-2′b), 4.26 (1H, ddq, *J*=3.7, 8.3, 6.3 Hz, H-3′), 1.29 (3H, d, *J*=6.3, H-4′); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 58.98 (d, C-1), 70.55 (d, C-2), 42.16 (d, C-3), 142.11 (s, C-4), 78.56 (d, C-5), 28.95 (t, C-6), 33.81 (t, C-7), 39.70 (s, C-8), 43.88 (t, C-9), 70.03 (d, C-10), 135.41 (s, C-11), 134.73 (s, C-12), 39.51 (t, C-13), 70.71 (d, C-14), 37.37 (s, C-15), 25.44 (q, C-16), 31.62 (q, C-17), 21.04 (q, C-18), 22.48 (q, C-19), 117.21 (t, C-20), 21.50, 2×21.48 [q, OAc ($CH_3$)], 170.19, 170.04, 170.28 [s, OAc (CO)], 171.88 (s, C-1′), 43.80 (t, C-2′), 64.45 (d, C-3′), 22.71 (q, C-4′); HRESIMS *m*/*z* $[M+H]^+$ 549.3080 (calcd 549.3064 for $C_{30}H_{45}O_9$).

*4.4.2. 10β-Hydroxy-2α,14β-diacetoxy-5α-(3-hydroxy-butyryl)oxy-taxa-4(20),11-diene (**11**)*

White powder; $[\alpha]_D^{20}$ +34.2 (*c* 0.08, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3624, 3544, 3032, 2940, 1730, 1454, 1376, 1236, 1224, 1210, 1104, 1022 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz) δ 1.88 (1H, d, *J*=2.0 Hz, H-1), 5.36 (1H, dd, *J*=2.4, 6.6 Hz, H-2), 2.88 (1H, d, *J*=6.4 Hz, H-3), 5.32 (1H, t, *J*=2.7 Hz, H-5), 1.75–1.85 (2H, m, H-6), 1.85–1.97 (1H, m, overlapped, H-7β), 1.20–1.28 (1H, m, overlapped, H-7α), 2.36 (1H, dd, *J*=12.0, 14.9 Hz, H-9β), 1.60–1.68 (1H, m, overlapped, H-9α), 5.10 (1H, dd, *J*=5.6, 11.7 Hz, H-10), 2.85 (1H, dd, *J*=9.3, 19.0 Hz, H-13β), 2.43 (1H, dd, *J*=4.9, 19.0 Hz, H-13α), 4.95 (1H, dd, *J*=5.0, 9.3 Hz, H-14), 1.72 (3H, s, H-16), 1.19 (3H, s, H-17), 1.97 (3H, s, H-18), 0.84 (3H, s, H-19), 5.28 (1H, s, H-20a), 4.86 (1H, s, H-20b), 2.04, 2.02 [3H each, OAc ($CH_3$)], 2.60 (1H, dd, *J*=8.3, 16.1 Hz, H-2′a), 2.51 (1H, dd, *J*=3.9, 15.9 Hz, H-2′b), 4.25 (1H, ddq, *J*=3.9, 8.3, 6.4 Hz, H-3′), 1.29 (3H, d, *J*=6.4 Hz, H-4′); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 59.16 (d, C-1), 70.67 (d, C-2), 41.96 (d, C-3), 142.24 (s, C-4), 78.68 (d, C-5), 29.02 (t, C-6), 33.95 (t, C-7), 39.70 (s, C-8), 47.15 (t, C-9), 67.37 (d, C-10), 138.73 (s, C-11), 132.41 (s, C-12), 39.56 (t, C-13), 70.91 (d, C-14), 37.51 (s, C-15), 25.43 (q, C-16), 31.97 (q, C-17), 21.19 (q, C-18), 22.56 (q, C-19), 117.15 (t, C-20), 21.51, 21.45 [q, OAc ($CH_3$)], 170.23, 169.98 [s, OAc (CO)], 171.86 (s, C-1′), 43.82 (t, C-2′), 64.46 (d, C-3′), 22.73 (q, C-4′); HRESIMS *m*/*z* $[M+H]^+$ 507.2968 (calcd 507.2960 for $C_{28}H_{43}O_8$).

*4.4.3. 2α,10β,14β-Triacetoxy-5α-(3-oxo-butyryl)oxy-taxa-4(20),11-diene (**12**)*

White powder; $[\alpha]_D^{20}$ +39.3 (*c* 0.30, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3460, 3008, 2936, 1726, 1644, 1438, 1402, 1370, 1340, 1312, 1254, 1214, 1150, 1106, 1020 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz) δ 1.88 (1H, d, *J*=1.7 Hz, H-1), 5.35 (1H, dd, *J*=2.4, 6.4 Hz, H-2), 2.85 (1H, d, *J*=6.4 Hz, H-3), 5.36 (1H, br s, H-5), 1.79–1.89 (2H, m, H-6), 1.94 (1H, ddd, *J*=5.9, 13.2, 13.2 Hz, H-7β), 1.20–1.30 (1H, m, H-7α), 2.37 (1H, dd, *J*=12.4, 14.9 Hz, H-9β), 1.58–1.64 (1H, m, overlapped, H-9α), 6.03 (1H, dd, *J*=5.6, 12.2 Hz, H-10), 2.72 (1H, dd, *J*=9.3, 19.0 Hz, H-13β), 2.42 (1H, dd, *J*=4.9, 19.0 Hz, H-13α), 4.95 (1H, dd, *J*=4.9, 9.3 Hz, H-14), 1.65 (3H, s, H-16), 1.11 (3H, s, H-17), 2.03 (3H, br s, H-18), 0.84 (3H, s, H-19), 5.30 (1H, s, H-20a), 4.89 (1H, s, H-20b), 2.05, 2.04, 2.02 [3H each, OAc ($CH_3$)], 3.64 (1H, d, *J*=15.6 Hz, H-2′a), 3.49 (1H, d, *J*=15.8 Hz, H-2′b), 2.33 (3H, s, H-4′); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 58.94 (d, C-1), 70.49 (d, C-2), 42.30 (d, C-3), 141.79 (s, C-4), 79.41 (d, C-5), 28.74 (t, C-6), 33.78 (t, C-7), 39.66 (s, C-8), 43.86 (t, C-9), 70.00 (d, C-10), 135.52 (s, C-11), 134.48 (s, C-12), 39.62 (t, C-13), 70.54 (d, C-14), 37.34 (s, C-15), 25.42 (q, C-16), 31.66 (q, C-17), 20.92 (q, C-18), 22.48 (q, C-19), 117.61 (t, C-20), 21.48, 21.41, 21.03 [q, OAc ($CH_3$)], 170.22, 170.01, 169.99 [s, OAc (CO)], 166.34 (s, C-1′), 50.42 (t, C-2′), 200.60 (s, C-3′), 30.17 (q, C-4′); HRESIMS *m*/*z* $[M+H]^+$ 547.2918 (calcd 547.2908 for $C_{30}H_{43}O_9$).

*4.4.4. 10β-Hydroxy-2α,14β-diacetoxy-5α-(3-oxo-butyryl)oxy-taxa-4(20),11-diene (**13**)*

White powder; $[\alpha]_D^{20}$ +21.5 (*c* 0.16, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3036, 2944, 1732, 1644, 1606, 1374, 1314, 1230, 1148, 1104, 1024 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz) δ 1.87 (1H, d, *J*=2.2 Hz, H-1), 5.36 (1H, dd, *J*=2.2, 6.4 Hz, H-2), 2.86 (1H, d, *J*=6.4 Hz, H-3), 5.35 (1H, br s, H-5), 1.80–1.90 (2H, m, H-6), 1.80–1.86 (1H, m, H-7β), 1.20–1.28 (1H, m, H-7α), 2.28–2.40 (1H, m, overlapped, H-9β), 1.68 (1H, dd, *J*=5.4, 11.7 Hz, H-9α), 5.08 (1H, dd, *J*=5.6, 11.7 Hz, H-10), 2.70 (1H, dd, *J*=9.3, 19.0 Hz, H-13β), 2.42 (1H, dd, *J*=5.0, 9.3 Hz, H-13α), 4.96 (1H, dd, *J*=5.0, 9.3 Hz, H-14), 1.72 (3H, s, H-16), 1.18 (3H, s, H-17), 1.92 (3H, s, H-18), 0.84 (3H, s, H-19), 5.29 (1H, s, H-20a), 4.89 (1H, s, H-20b), 2.04, 2.02 [3H each, OAc ($CH_3$)], 3.64 (1H, d, *J*=15.9 Hz, H-2′a), 3.48 (1H, d, *J*=15.9 Hz, H-2′b), 2.33 (3H, s, H-4′); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 59.12 (d, C-1), 70.65 (d, C-2), 42.11 (d, C-3), 141.94 (s, C-4), 79.52 (d, C-5), 28.80 (t, C-6), 33.91 (t, C-7), 39.66 (s, C-8), 47.13 (t, C-9), 67.34 (d, C-10), 138.82 (s, C-11), 132.15 (s, C-12), 39.66 (t, C-13), 70.69 (d, C-14), 37.48 (s, C-15), 25.41 (q, C-16), 32.02 (q, C-17), 21.18 (q, C-18), 22.58 (q, C-19), 117.54 (t, C-20), 21.49, 21.41 [q, OAc ($CH_3$)], 170.07, 169.94 [s, OAc (CO)], 166.33 (s, C-1′), 50.47 (t, C-2′), 200.73 (s, C-3′), 30.17 (q, C-4′); HRESIMS *m*/*z* $[M+H]^+$ 505.7314 (calcd 505.7309 for $C_{28}H_{41}O_8$).

### 4.5. Biotransformation of 2 by fungus *A. coerulea* in the presence of β-cyclodextrin

The cultural procedure of *A. coerulea* IFO 4011 was performed as described previously.[4c] Substrate **2** (500 mg in 2 mL EtOH) was added into saturated β-cyclodextrin solution (2000 mg in 50 mL cultural medium), stirred for 48 h, and then distributed into the flasks with the cell cultures. The procedures of incubation, collection, extraction, concentration, and fractionation by open Si gel column chromatography were performed as described before[4c] and seven fractions were afforded: 10 mg of **21** (ca. 2%) was obtained from fraction 1; 21.0 mg of **14a** and **14b** (a pair of isomers, ca. 4%), 240 mg of **2** (ca. 48%) from fractions 2 and 3; 6 mg of **22** (a pair of isomers, ca. 1.2%) from fraction 3; 14 mg of **23** (ca. 2.8%)from fraction 3; 3.8 mg of **24** (ca. 0.9%) from fraction 3; 37 mg of **15** (ca. 7.4%) from fractions 3 and 4; 39 mg of **16** (ca. 7.8%), 2.0 mg of **17** (trace), 46 mg of **19** (ca. 9.2%) and 3.2 mg of **25** (ca. 0.6%) from fraction 4; 20 mg of **26** (ca. 5%) from fractions 4 and 5; 13 mg of **18** (ca. 2.6%) from fraction 5; 14 mg of **20** (ca. 2.8%) and 5 mg of **27** (ca. 1.0%) from fractions 5 and 6, by further semipreparative HPLC. Among these products, **17** and **21**–**27** are the eight new compounds.

*4.5.1. 9α,10β-Dihydroxy-2α,5α-diacetoxy-14β-(3-hydroxy-2-methyl-butyryl)oxy-taxa-4(20),11-diene (**17**)*

White powder; $[\alpha]_D^{20}$ +45.0 (*c* 0.313, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3624, 2992, 2944, 1732, 1644, 1456, 1376, 1320, 1242, 1220, 1168, 1114, 1048, 1004 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz) δ 1.87 (1H, d, *J*=2.2 Hz, H-1), 5.37 (1H, dd, *J*=2.2, 6.4 Hz, H-2), 2.93 (1H, d, *J*=6.4 Hz, H-3), 5.31 (1H, br s, H-5), 1.79–1.85 (1H, m, overlapped, H-6β), 1.68–1.74 (1H, m, overlapped, H-6α), 1.75–1.81 (1H, m, overlapped, H-7β), 1.46–1.52 (1H, m, overlapped, H-7α), 4.09 (1H, d, *J*=9.5 Hz, H-9), 4.79 (1H, d, *J*=9.5 Hz, H-10), 2.85 (1H, dd, *J*=9.0, 19.0 Hz, H-13β), 2.37–2.45 (1H, m, overlapped, H-13α), 4.94 (1H, dd, *J*=4.6, 9.0 Hz, H-14), 1.66 (3H, s, H-16), 1.20 (3H, s, H-17), 2.00 (3H, br s, H-18), 1.04 (3H, s, H-19), 5.31 (1H, s, H-20a), 4.87 (1H, s, H-20b), 2.18, 2.02 [3H each, s, OAc ($CH_3$)], 2.38–2.42 (1H, m, overlapped, H-2′), 3.86 (1H, dq, *J*=6.8, 6.3 Hz, H-3′), 1.21 (3H, d, *J*=6.9 Hz, H-4′), 1.16 (3H, d, *J*=7.6 Hz, H-5′); $^{13}$C NMR ($CDCl_3$, 125 MHz) δ 59.09 (d, C-1), 70.05 (d, C-2), 44.21 (d, C-3), 141.94 (s, C-4), 78.75 (d, C-5), 28.54 (t, C-6), 26.05 (t, C-7), 44.44 (s, C-8), 78.42 (d, C-9), 72.06 (d, C-10),

136.55 (s, C-11), 134.37 (s, C-12), 39.61 (t, C-13), 70.76 (d, C-14), 37.37 (s, C-15), 26.02 (q, C-16), 31.82 (q, C-17), 21.30 (q, C-18), 17.62 (q, C-19), 117.58 (t, C-20), 21.94, 21.39 [q, OAc ($CH_3$)], 169.83, 169.78 [s, OAc (CO)], 174.81 (s, C-1′), 47.01 (d, C-2′), 69.52 (d, C-3′), 20.87 (q, C-4′), 14.04 (q, C-5′); HREIMS *m*/*z* $[M]^+$ 536.2992 (calcd 536.2985 for $C_{29}H_{44}O_9$).

*4.5.2. 2α,5α,10β-Triacetoxy-14β-(3-acetoxy-2-methyl-butyryl)oxy-taxa-4(20),11-diene (**21**)*

White powder; $[\alpha]_D^{20}$ +31.9 (*c* 0.440, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 2996, 2936, 1730, 1646, 1456, 1376, 1244, 1224, 1174, 1106, 1070, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.86 (1H, d, *J*=2.2 Hz, H-1), 5.33 (1H, dd, *J*=2.2, 6.4 Hz, H-2), 2.92 (1H, d, *J*=6.3 Hz, H-3), 5.29 (1H, br s, H-5), 1.77–1.84 (2H, m, H-6), 1.90–1.98 (1H, m, overlapped, H-7β), 1.18–1.26 (1H, m, overlapped, H-7α), 2.38 (1H, dd, *J*=11.9, 14.9 Hz, H-9β), 1.63 (1H, dd, *J*=5.6, 14.9 Hz, H-9α), 6.06 (1H, dd, *J*=5.6, 14.9 Hz, H-10), 2.80 (1H, dd, *J*=9.3, 19.0 Hz, H-13β), 2.39 (1H, dd, *J*=4.4, 19.0 Hz, H-13α), 5.02 (1H, dd, *J*=4.4, 9.0 Hz, H-14), 1.66 (3H, s, H-16), 1.11 (3H, s, H-17), 2.09 (3H, br s, H-18), 0.84 (3H, s, H-19), 5.26 (1H, s, H-20a), 4.83 (1H, s, H-20b), 2.17, 2.06, 2.04, 2.02 [3H each, OAc ($CH_3$)], 2.67 (1H, dq, *J*=7.0, 7.3 Hz, H-2′), 5.20 (1H, dq, *J*=7.0, 6.6 Hz, H-3′), 1.27 (3H, d, *J*=6.4 Hz, H-4′), 1.15 (3H, d, *J*=7.0 Hz, H-5′); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 59.13 (d, C-1), 70.50 (d, C-2), 42.09 (d, C-3), 142.20 (s, C-4), 78.25 (d, C-5), 28.90 (t, C-6), 33.81 (t, C-7), 39.65 (s, C-8), 43.84 (t, C-9), 70.05 (d, C-10), 135.36 (s, C-11), 134.53 (s, C-12), 39.20 (t, C-13), 70.82 (d, C-14), 37.19 (s, C-15), 25.37 (q, C-16), 31.87 (q, C-17), 21.43 (q, C-18), 22.45 (q, C-19), 116.95 (t, C-20), 21.91, 21.36, 20.91, 20.52 [q, OAC ($CH_3$)], 170.23, 169.94, 169.74 [s, OAc (CO)], 160.05 [s, 3′-OAc (CO)], 172.23 (s, C-1′), 44.71 (d, C-2′), 71.49 (d, C-3′), 17.04 (q, C-4′), 12.83 (q, C-5′); HREIMS *m*/*z* $[M]^+$ 604.3252 (calcd 604.3247 for $C_{33}H_{48}O_{10}$).

*4.5.3. 10β-Hydroxy-2α,5α-diacetoxy-14β-(3-oxo-2-methyl-butyryl)oxy-taxa-4(20),11-diene (**22**, a pair of isomers)*

White powder; IR $\nu_{max}$ ($CHCl_3$): 3620, 2944, 1732, 1610, 1456, 1376, 1320, 1244, 1204, 1104, 1072, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.85 (1H, d, *J*=2.2 Hz, H-1), 5.363 and 5.350 (1H, dd, *J*=2.2, 5.6 Hz, H-2, **22a** and **22b**), 2.914 and 2.906 (1H, d, *J*=5.6 Hz, H-3, **22a** and **22b**), 5.28 (1H, br s, H-5), 1.75–1.85 (2H, m, H-6), 1.87–1.93 (1H, m, H-7β), 1.16–1.24 (1H, m, H-7α), 2.30–2.40 (1H, m, H-9β), 1.75–1.81 (1H, m, H-9α), 5.10 (1H, dd, *J*=5.6, 11.7 Hz, H-10), 2.824 and 2.806 (1H, dd, *J*=9.3, 19.0 Hz, H-13β, **22a** and **22b**), 2.36–2.50 (1H, m, H-13α), 5.038 and 5.029 (1H, dd, *J*=5.1, 9.8 Hz, H-14, **22a** and **22b**), 1.72 (3H, s, H-16), 1.137 and 1.154 (3H, H-17), 1.98 (3H, s, H-18), 0.84 (3H, s, H-19), 5.26 (1H, s, H-20a), 4.822 and 4.820 (1H, s, H-20b, **22a** and **22b**), 2.171, 2.167, 2.043, and 2.036 [3H each, s, OAc ($CH_3$), **22a** and **22b**], 3.48 (1H, q, *J*=7.3 Hz, H-2′), 1.334 and 1.320 (3H, s, H-4′, **22a** and **22b**), 2.233 and 2.218 (3H, d, *J*=7.1 Hz, H-5′, **22a** and **22b**); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 59.20 and 59.16 (d, C-1, **22a** and **22b**), 70.53 and 70.46 (d, C-2, **22a** and **22b**), 41.95 (d, C-3), 142.29 (s, C-4), 78.32 (d, C-5), 28.95 (t, C-6), 33.95 and 33.92 (t, C-7, **22a** and **22b**), 47.12 (t, C-9), 67.36 (d, C-10), 138.65 (s, C-11), 132.22 and 132.10 (s, C-12, **22a** and **22b**), 39.32 and 39.21 (t, C-13, **22a** and **22b**), 71.89 (d, C-14), 37.34 (s, C-15), 25.30 (q, C-16), 31.99 (q, C-17), 21.05 (q, C-18), 22.54 (q, C-19), 116.90 (t, C-20), 22.54, 21.38 [q, OAc ($CH_3$)], 169.94 and 169.78, 169.47 and 169.38 [s, OAc (CO), **22a** and **22b**], 171.00 (s, C-1′), 53.64 and 53.54 (d, C-2′, **22a** and **22b**), 202.00 (s, C-3′), 21.44 (q, C-4′), 12.71 (q, C-5′); HRFABMS *m*/*z* $[M+Na]^+$ 541.2759 (calcd 541.2778 for $C_{29}H_{42}O_8Na$).

*4.5.4. 7β-Hydroxy-2α,5α,10β-triacetoxy-14β-(3-oxo-2-methyl-butyryl)oxy-taxa-4(20),11-diene (**23**, a pair of isomers)*

White powder; IR $\nu_{max}$ ($CHCl_3$): 3624, 2944, 1734, 1646, 1606, 1458, 1376, 1318, 1244, 1224, 1210, 1156, 1102, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.82 (1H, br s, H-1), 5.34 and 5.33 (1H, dd, *J*=2.4, 5.6 Hz, H-2, **23a** and **23b**), 2.66–2.70 (1H, m, H-3), 5.27 (1H, br s, H-5), 2.00–2.04 (1H, m, overlapped, H-6α), 1.60–1.66 (1H, m, overlapped, H-6β), 3.83 (1H, dd, *J*=5.1, 11.7 Hz, H-7), 2.12–2.10 (1H, m, overlapped, H-9β), 2.02–2.08 (1H, m, overlapped, H-9α), 5.90 (1H, dd, *J*=5.4, 12.2 Hz, H-10), 2.32–2.40 (1H, m, H-13β), 2.76 and 2.74 (1H, dd, *J*=3.4, 19.0 Hz, H-13α, **23a** and **23b**), 4.94 and 4.93 (1H, dd, *J*=6.6, 12.0 Hz, H-14, **23a** and **23b**), 1.62 (3H, s, H-16), 1.04 and 1.03 (3H, s, H-17, **23a** and **23b**), 1.97 (3H, s, H-18), 0.69 (3H, s, H-19), 5.23 (1H, s, H-20a), 4.842 and 4.840 (1H, s, **23a** and **23b**), 2.110 and 2.106, 2.03, 1.990 and 1.982 [3H each, s, OAc ($CH_3$), **23a** and **23b**], 3.413 and 3.405 (1H, q, *J*=7.3 Hz, H-2′, **23a** and **23b**), 2.157 and 2.147 (3H, s, H-4′, **23a** and **23b**), 1.267 and 1.253 (3H each, s, H-5′, **23a** and **23b**); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 58.91 and 58.87 (d, C-1, **23a** and **23b**), 69.94 and 69.87 (d, C-2, **23a** and **23b**), 40.60 (d, C-3), 140.83 and 140.77 (s, C-4, **23a** and **23b**), 77.57 (d, C-5), 36.94 (t, C-6), 68.94 and 68.91 (d, C-7, **23a** and **23b**), 44.38 and 44.35 (s, C-8, **23a** and **23b**), 37.26 and 37.25 (t, C-9, **23a** and **23b**), 69.50 (d, C-10), 135.90 and 135.80 (s, C-11, **23a** and **23b**), 134.74 and 134.62 (s, C-12, **23a** and **23b**), 39.28 and 39.16 (t, C-13, **23a** and **23b**), 71.52 (d, C-14), 36.93 (s, C-15), 25.30 (q, C-16), 31.67 (q, C-17), 21.39 and 21.34 (q, C-18, **23a** and **23b**), 16.54 (q, C-19), 118.06 and 118.03 (t, C-20, **23a** and **23b**), 21.45, 21.42, 21.13 [q, OAc ($CH_3$)], 169.90 and 169.52, 169.52 and 169.51, 169.43 and 169.35 [s, OAc (CO), **23a** and **23b**] 170.51 (s, C-1′, **23a** and **23b**), 53.58 and 53.55 (d, C-2′, **23a** and **23b**), 203.43 (s, C-3′), 21.74 (q, C-4′), 12.71 and 12.68 (q, C-5′, **23a** and **23b**); HREIMS *m*/*z* $[M]^+$ 576.2938 (calcd 576.2935 for $C_{31}H_{44}O_{10}$).

*4.5.5. 5α-Hydroxy-2α,10β-diacetoxy-14β-(3-hydroxy-2-methyl-butyryl)oxy-taxa-4(20),11-diene (5-deacetyl yunnanxane, **24**)*

White powder; $[\alpha]_D^{20}$ +108.1 (*c* 0.033, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1732, 1458, 1376, 1252, 1226, 1218, 1104, 1018 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.86 (1H, d, *J*=2.0 Hz, H-1), 5.35 (1H, dd, *J*=2.2, 6.3 Hz, H-2), 3.21 (1H, d, *J*=6.1 Hz, H-3), 4.20 (1H, t, 2.7 Hz, H-5), 1.68–1.78 (2H, m, H-6), 1.67–1.73 (1H, m, overlapped, H-7β), 1.12–1.18 (1H, m, overlapped, H-7α), 2.28–2.36 (1H, m, overlapped, H-9β), 1.61 (1H, dd, *J*=5.6, 14.9 Hz, H-9α), 6.11 (1H, dd, *J*=5.6, 12.2 Hz, H-10), 2.81 (1H, dd, *J*=9.3, 19.0 Hz, H-13β), 2.30–2.36 (1H, m, overlapped, H-13α), 5.09 (1H, dd, *J*=4.7, 9.3 Hz, H-14), 1.66 (3H, s, H-16), 1.12 (3H, s, H-17), 2.08 (3H, br s, H-18), 0.81 (3H, s, H-19), 5.12 (1H, s, H-20a), 4.76 (1H, s, H-20b), 2.05, 2.03 [3H each, OAc ($CH_3$)], 2.41 (1H, dq, *J*=7.1, 6.4 Hz, H-2′), 3.86 (1H, dq, *J*=6.4, 6.4 Hz, H-3′), 1.21 (3H, d, *J*=6.4 Hz, H-4′), 1.16 (3H, d, *J*=7.3 Hz, H-5′); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 59.17 (d, C-1), 70.85 (d, C-2), 39.99 (d, C-3), 147.48 (s, C-4), 76.29 (d, C-5), 30.92 (t, C-6), 33.04 (t, C-7), 40.03 (s, C-8), 43.77 (d, C-9), 70.31 (d, C-10), 135.73 (s, C-11), 134.55 (s, C-12), 39.27 (t, C-13), 70.31 (d, C-14), 37.32 (s, C-15), 25.38 (q, C-16), 31.82 (q, C-18), 20.83 (q, C-18), 22.22 (q, C-19), 113.64 (t, C-20), 21.49, 21.42 [q, OAc ($CH_3$)], 170.22, 169.89 [s, OAc (CO)], 175.00 (s, C-1′), 46.94 (d, C-2′), 69.52 (d, C-3′), 20.86 (q, C-4′), 14.03 (q, C-5′); HRESIMS *m*/*z* $[M+Na]^+$ 543.2931 (calcd 543.2934 for $C_{29}H_{44}O_8Na$).

*4.5.6. 6α-Hydroxy-2α,10β-diacetoxy-14β-(3-oxo-2-methyl-butyryl)oxy-taxa-4(20),11-diene (**25**, a pair of isomers)*

White powder; IR $\nu_{max}$ ($CHCl_3$): 3616, 2944, 1732, 1456, 1376, 1242, 1216, 1058, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.88 (1H, d, *J*=2.2 Hz, H-1), 5.358 and 5.344 (1H, dd, *J*=2.2, 6.6 Hz, H-2, **25a** and **25b**), 2.87–2.91 (1H, m, H-3), 5.43 (1H, br s, H-5), 3.88–3.98 (1H, m, H-6), 1.82 (1H, dd, *J*=12.2, 12.2, H-7β), 1.56 (1H, dd, *J*=5.4, 13.0 Hz, H-7α), 2.32–2.38 (1H, m, H-9β), 1.67–1.71 (1H, m, H-9α), 6.03 (1H, dd, *J*=5.6, 12.0 Hz, H-10), 2.83–2.87 (1H, m, H-13β), 2.40–2.48 (1H, m, H-13α), 5.041 and 5.031 (1H, dd, *J*=5.1, 9.8 Hz, H-14, **25a** and **25b**), 1.65 (3H, s, H-16), 1.09 and 1.08 (3H, s, H-17, **25a** and **25b**), 2.11 (3H, br s, H-18), 0.87 (3H, s, H-19), 5.38 (1H, s, H-20a), 4.92 (1H, s, H-20b), 2.225 and 2.115, 2.054, 2.054 and 2.044 [3H each, s, OAc ($CH_3$), **25a** and **25b**], 3.44–3.52 (1H, m, H-3′), 2.224 and 2.214 (3H, s, H-4′, **25a** and **25b**), 1.335 and 1.321 (3H, d, *J*=7.3 Hz, H-5′, **25a** and **25b**); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 58.85 and 58.81 (d,

C-1, **25a** and **25b**), 70.07 and 70.02 (d, C-2, **25a** and **25b**), 41.25 (d, C-3), 139.93 (s, C-4), 80.30 (d, C-5), 69.14 (d, C-6), 42.20 (t, C-7), 37.99 (s, C-8), 43.50 (t, C-9), 69.80 (d, C-10), 135.47 (s, C-11), 134.69 (s, C-12), 39.26 and 39.14 (t, C-13, **25a** and **25b**), 71.53 (d, C-14), 37.19 (s, C-15), 25.30 (q, C-16), 31.65 (q, C-17), 21.00 (q, C-18), 23.34 (q, C-19), 119.71 (t, C-20), 21.39, 21.39, 21.33 [q, OAc ($CH_3$)], 170.97, 170.12 and 169.84, 169.46 and 169.24 [s, OAc (CO)], 172.00 (s, C-1′), 53.57 (d, C-2′), 204.00 (s, C-3′), 30.93 (q, C-4′), 12.72 and 12.65 (q, C-5′, **25a** and **25b**); HRFABMS *m/z* $[M+Na]^+$ 599.2830 (calcd 599.2833 for $C_{31}H_{44}O_{10}Na$).

#### 4.5.7. 2α,5α-Diacetoxy-14β-(3-hydroxy-2-methyl-butyryl)oxy-taxa-4(20),11-dien-10β-oxalic acid ester (**26**)

White powder; $[\alpha]_D^{20}$ +20.2 (*c* 0.587, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2992, 2940, 1732, 1648, 1456, 1244, 1174, 1106, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.94 (1H, d, *J*=2.0 Hz, H-1), 5.36 (1H, dd, *J*=2.2, 6.6 Hz, H-2), 2.90 (1H, d, *J*=6.6 Hz, H-3), 5.30 (1H, br s, H-5), 1.76–1.86 (2H, m, H-6), 1.92–2.02 (1H, m, H-7β), 1.23–1.31 (1H, m, H-7α), 2.54 (1H, dd, *J*=12.5, 14.6 Hz, H-9β), 1.75 (1H, dd, *J*=5.6, 14.9 Hz, H-9α), 6.17 (1H, dd, *J*=5.6, 12.0 Hz, H-10), 2.86 (1H, dd, *J*=9.3, 19.3 Hz, H-13β), 2.39–2.47 (1H, m, overlapped, H-13α), 5.03 (1H, dd, *J*=4.6, 9.3 Hz, H-14), 1.70 (3H, s, H-16), 1.12 (3H, s, H-17), 2.11 (3H, s, H-18), 0.87 (3H, s, H-19), 5.29 (1H, s, H-20a), 4.83 (1H, s, H-20b), 2.19, 2.04 [3H each, OAc ($CH_3$)], 2.38–2.46 (1H, m, overlapped, H-2′), 3.90 (1H, dq, *J*=6.9, 6.3 Hz, H-3′), 1.15 (3H, d, *J*=7.3 Hz, H-4′), 1.22 (3H, d, *J*=6.3 Hz, H-5′); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 58.93 (d, C-1), 70.47 (1H, C-2), 42.11 (d, C-3), 141.85 (s, C-4), 78.19 (d, C-5), 28.84 (t, C-6), 33.86 (t, C-7), 39.75 (s, C-8), 43.37 (t, C-9), 73.86 (d, C-10), 134.37 (s, C-11), 136.35 (s, C-12), 39.46 (t, C-13), 70.64 (d, C-14), 31.16 (s, C-15), 25.15 (q, C-16), 37.16 (q, C-17), 21.39 (q, C-18), 22.39 (q, C-19), 117.21 (t, C-20), 21.88, 20.96 [q, OAc ($CH_3$)], 170.30, 169.93 [s, OAc (CO)], 174.91 (s, C-1′), 46.96 (d, C-2′), 69.81 (d, C-3′), 14.03 (q, C-4′), 20.73 (q, C-5′), 157.57 (s, C-1″), 158.22 (s, C-2′); HRESIMS (positive) *m/z* $[M]^+$ 593.2968 (calcd 593.2962 for $C_{33}H_{45}O_{11}$), $[M+Na]^+$ 615.2788 (calcd 615.2782 for $C_{33}H_{44}O_{11}Na$).

#### 4.5.8. 6α,10β-Dihydroxy-2α,5α-diacetoxy-14β-(3-hydroxy-2-methyl-butyryl)oxy-taxa-4(20),11-diene (**27**)

White powder; $[\alpha]_D^{20}$ +70.2 (*c* 0.153, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2944, 1732, 1458, 1376, 1216, 1026 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.90 (1H, d, *J*=2.2 Hz, H-1), 5.37 (1H, dd, *J*=2.4, 6.7 Hz, H-2), 2.89 (1H, d, *J*=6.6 Hz, H-3), 5.43 (1H, d, *J*=3.9 Hz, H-5), 3.90–3.98 (1H, m, H-6), 1.75–1.81 (1H, m, H-7β), 1.50–1.60 (1H, m, H-7α), 2.34 (1H, dd, *J*=11.7, 14.9 Hz, H-9β), 1.71 (1H, dd, *J*=5.6, 14.9 Hz, H-9α), 5.10 (1H, dd, *J*=5.6, 11.7 Hz, H-10), 2.84 (1H, dd, *J*=9.0, 18.8 Hz, H-13β), 2.38–2.44 (1H, m, overlapped, H-13α), 5.04 (1H, dd, *J*=4.9, 9.3 Hz, H-14), 1.72 (3H, s, H-16), 1.19 (3H, s, H-17), 2.00 (3H, s, H-18), 0.87 (3H, s, H-19), 5.38 (1H, s, H-20a), 4.91 (1H, s, H-20b), 2.25, 2.02 [3H each, OAc ($CH_3$)], 2.40 (1H, dq, *J*=6.6, 7.1 Hz, H2′), 3.86 (1H, dq, *J*=6.6, 6.1 Hz, H-3′), 1.21 (3H, d, *J*=6.1 Hz, H-4′), 1.17 (3H, d, *J*=7.3 Hz, H-5′); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 59.10 (d, C-1), 70.26 (d, C-2), 41.06 (d, C-3), 140.07 (s, C-4), 80.43 (d, C-5), 69.55 (d, C-6), 46.72 (t, C-7), 47.03 (s, C-8), 42.29 (t, C-9), 67.23 (d, C-10), 132.39 (s, C-11), 138.76 (s, C-12), 39.51 (t, C-13), 70.78 (d, C-14), 37.97 (s, C-15), 25.31 (q, C-16), 32.06 (q, C-17), 20.90 (q, C-18), 23.46 (q, C-19), 119.64 (t, C-20), 21.76, 21.38 [q, OAc ($CH_3$)], 171.08, 169.82 [s, OAc (CO)], 174.85 (s, C-1′), 46.72 (d, C-2′), 69.22 (d, C-3′), 14.06 (q, C-4′), 21.61 (q, C-5′); HRFABMS (positive) *m/z* $[M+H]^+$ 537.3078 (calcd 537.3063 for $C_{29}H_{45}O_9$).

### 4.6. Biotransformation of 3 by fungus *A. coerulea*

The cultural procedure of *A. coerulea* IFO 4011 was performed as described previously.[4c] Compound **3** (450 mg) was dissolved in acetone (4.5 mL), distributed among nine 1000-mL Erlenmeyer flasks of cell cultures of *A. coerulea* with pipette, and incubated for additional 7 days, after which time the cultures were filtered, and the cell cultures were thoroughly washed with EtOAc. The pooled filtrate was saturated with NaCl and extracted five times with EtOAc. All the extracts were pooled, dried with anhydrous $Na_2SO_4$, and concentrated under vacuum at 40 °C to give 1.01 g of residue. The dried cell cultures were extracted three times by sonication with EtOAc, the given extracts were pooled, and concentrated under vacuum at 40 °C to afford 0.34 g of residue. The combined extract was chromatographed on a Si gel column eluting gradiently with *n*-hexane/EtOAc (hexane/EtOAc=9/1 to 100% EtOAc) to give seven fractions. Further separation was performed by semi-preparative HPLC, and afforded 88.7 mg of **3** (ca. 19.7%), 132.8 mg of **28**[7] (ca. 30.7%), 7.2 mg of **29** (ca. 1.6%), 19.4 mg of **30** (ca. 4.3%), 8.3 mg of **31** (ca. 1.8%), 13 mg of **32** (ca. 5%), 5.4 mg of **33** (ca. 1%), 5.0 mg of **34** (ca. 1%), 9.4 mg of **35** (ca. 2%), 24 mg of **36** (ca. 6%), 5 mg of **37** (ca. 1%), 10 mg of **38** (ca. 2%), and 4.5 mg of **39** (ca. 1%). Except **28**, the other products are new compounds.

#### 4.6.1. 2α,5α-Diacetoxy-10β-(2-hydroxy-propionyl)oxy-taxa-4(20),11-diene (**29**)

White powder; $[\alpha]_D^{20}$ +34.0 (*c* 0.483, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3560, 3040, 2932, 1728, 1452, 1374, 1244, 1204, 1124, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.81–1.83 (1H, m, H-1), 5.38 (1H, dd, *J*=2.0, 6.1 Hz, H-2), 3.07 (1H, d, *J*=6.1 Hz, H-3), 5.27 (1H, t, *J*=2.7 Hz, H-5), 1.78–1.86 (2H, m, H-6), 2.01–2.07 (1H, m, H-7β), 1.24 (1H, ddd, *J*=3.2, 3.4, 13.4 Hz, H-7α), 2.43 (1H, dd, *J*=12.4, 14.7 Hz, H-9β), 1.56–1.64 (1H, m, overlapped, H-9α), 6.16 (1H, dd, *J*=5.6, 12.2 Hz, H-10), 2.40–2.50 (1H, m, overlapped, H-13β), 1.99–2.05 (1H, m, overlapped, H-13α), 1.90–1.98 (1H, m, overlapped, H-14β), 1.67–1.73 (1H, m, overlapped, H-14α), 1.60 (3H, s, H-16), 1.05 (3H, s, H-17), 2.10 (3H, s, H-18), 0.87 (3H, s, H-19), 5.26 (1H, s, H-20a), 4.90 (1H, s, H-20b), 2.13, 2.04 [3H each, OAc ($CH_3$)], 4.26 (1H, q, *J*=6.9 Hz, H-2′), 1.43 (3H, d, *J*=6.9 Hz, H-3′); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 51.98 (d, C-1), 72.13 (d, C-2), 41.16 (d, C-3), 143.19 (s, C-4), 78.67 (d, C-5), 28.92 (t, C-6), 33.69 (t, C-7), 39.71 (s, C-8), 43.74 (t, C-9), 72.38 (d, C-10), 133.59 (s, C-11), 138.18 (s, C-12), 30.16 (t, C-13), 18.16 (t, C-14), 37.00 (s, C-15), 25.25 (q, C-16), 31.71 (q, C-17), 21.17 (q, C-18), 22.45 (q, C-19), 116.58 (t, C-20), 21.95, 21.58 [q, OAc ($CH_3$)], 169.78, 169.75 [s, OAc (CO)], 175.13 (s, C-1′), 66.73 (d, C-2′), 20.34 (q, C-3′); HRESIMS (positive) *m/z* $[M+H]^+$ 477.2864 (calcd 477.2852 for $C_{27}H_{41}O_7$), $[M+Na]^+$ 499.2678 (calcd 499.2672 for $C_{27}H_{40}O_7Na$).

#### 4.6.2. 2α,5α-Diacetoxy-taxa-4(20),11-dien-10β-O-propanoic acid (**30**)

White powder; $[\alpha]_D^{20}$ +11.3 (*c* 1.293, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3624, 2940, 1720, 1644, 1450, 1374, 1252, 1138, 1108, 1004 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.77–1.79 (1H, m, overlapped, H-1), 5.37 (1H, dd, *J*=2.0, 6.3 Hz, H-2), 3.03 (1H, d, *J*=6.1 Hz, H-3), 5.26 (1H, t, *J*=2.7 Hz, H-5), 1.73–1.83 (2H, m, H-6), 1.90–1.96 (1H, m, H-7β), 1.19–1.27 (1H, m, H-7α), 2.37 (1H, dd, *J*=11.7, 14.6 Hz, H-9β), 1.65–1.71 (1H, m, overlapped, H-9α), 4.82 (1H, dd, *J*=5.4, 11.7 Hz, H-10), 2.42–2.50 (1H, m, H-13β), 1.98–2.06 (1H, m, H-13α), 1.87–1.93 (1H, m, H-14β), 1.67–1.73 (1H, m, H-14α), 1.59 (3H, s, H-16), 1.09 (3H, s, H-17), 1.89 (3H, br s, H-18), 0.85 (3H, s, H-19), 5.24 (1H, s, H-20a), 4.88 (1H, s, H-20b), 2.10, 2.03 [3H each, OAc ($CH_3$)], 4.10 (1H, q, *J*=7.1 Hz, H-1′), 1.45 (3H, d, *J*=7.1 Hz, H-3′); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 51.99 (d, C-1), 72.30 (d, C-2), 41.26 (d, C-3), 143.33 (s, C-4), 78.84 (d, C-5), 28.93 (t, C-6), 33.81 (t, C-7), 39.57 (s, C-8), 45.00 (t, C-9), 74.53 (d, C-10), 134.57 (s, C-11), 138.43 (s, C-12), 30.34 (t, C-13), 18.17 (t, C-14), 36.96 (s, C-15), 24.98 (q, C-16), 31.67 (q, C-17), 21.33 (q, C-18), 22.40 (q, C-19), 116.42 (t, C-20), 21.93, 21.59 [q, OAc ($CH_3$)], 169.82, 169.79 [s, OAc (CO)], 70.60 (d, C-1′), 178.00 (s, C-2′), 18.79 (q, C-3′); HRESIMS (positive) *m/z* $[M+H]^+$ 477.2856 (calcd 477.2852 for $C_{27}H_{41}O_7$), $[M+Na]^+$ 499.2681 (calcd 499.2672 for $C_{27}H_{40}O_7Na$).

*4.6.3. 2α,5α-Diacetoxy-taxa-4(20),11-dien-10β-O-carbonyl-(4-hydroxy)-butanoic acid (**31**)*

White powder; $[\alpha]_D^{20}$ +22.4 (*c* 0.553, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 3464, 2956, 1720, 1452, 1374, 1234, 1216, 1150, 1110, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.81–1.83 (1H, m, H-1), 5.37 (1H, dd, *J*=2.0, 6.1 Hz, H-2), 3.05 (1H, d, *J*=6.1 Hz, H-3), 5.27 (1H, t, *J*=2.9 Hz, H-5), 1.75–1.85 (2H, m, H-6), 1.95–2.01 (1H, m, overlapped, H-7β), 1.20–1.26 (1H, m, H-7α), 2.36–2.44 (1H, m, overlapped, H-9β), 1.59 (1H, dd, *J*=5.6, 14.5 Hz, H-9α), 6.15 (1H, dd, *J*=5.6, 12.2 Hz, H-10), 2.48–2.58 (1H, m, overlapped, H-13β), 2.04–2.12 (1H, m, overlapped, H-13α), 1.88–1.96 (1H, m, overlapped, H-14β), 1.65–1.71 (1H, m, overlapped, H-14α), 1.58 (3H, s, H-16), 1.05 (3H, s, H-17), 2.08 (3H, s, H-18), 0.86 (3H, s, H-19), 5.26 (1H, s, H-20a), 4.90 (1H, s, H-20b), 2.13, 2.03 [3H each, s, OAc ($CH_3$)], 4.25 (1H, dd, *J*=5.6, 8.8 Hz, H-2′), 2.48–2.52 (1H, m, H-3′a), 2.18–2.22 (1H, m, H-3′b), 2.35–2.45 (2H, m, H-4′), 6.13 (1H, br s, 5′-OH); $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 51.94 (d, C-1), 72.09 (d, C-2), 41.12 (d, C-3), 143.12 (s, C-4), 78.64 (d, C-5), 28.89 (t, C-6), 33.66 (t, C-7), 39.70 (s, C-8), 43.71 (t, C-9), 72.29 (d, C-10), 133.36 (s, C-11), 138.46 (s, C-12), 30.16 (t, C-13), 18.16 (t, C-14), 37.04 (s, C-15), 25.38 (q, C-16), 31.85 (q, C-17), 21.22 (q, C-18), 22.45 (q, C-19), 116.64 (t, C-20), 21.93, 21.57 [q, OAc ($CH_3$)], 2×169.75 [s, OAc (CO)], 171.09 (s, C-1′), 55.53 (d, C-2′), 24.78 (t, C-3′), 29.27 (t, C-4′), 177.69 (s, C-5′); HRESIMS (positive) *m*/*z* $[M+H]^+$ 535.2912 (calcd 535.2907 for $C_{29}H_{43}O_9$), $[M+Na]^+$ 557.2735 (calcd 557.2727 for $C_{29}H_{42}O_9Na$).

*4.6.4. 2α,5α-Diacetoxy-10β-hydroxy-4β,20-epoxy-taxa-11(12)-ene (**32**)*

White powder: $[\alpha]_D^{20}$ +95.7 (*c* 0.527, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3624, 2948, 1732, 1458, 1374, 1314, 1236, 1118, 1068, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.62 (1H, br s, H-1), 5.36 (1H, dd, *J*=1.0, 3.7 Hz, H-2), 2.72 (1H, d, *J*=3.6 Hz, H-3), 4.18 (1H, t, *J*=2.7 Hz, H-5), 2.00–2.04 (1H, m, H-6α), 1.60–1.68 (1H, m, H-6β), 1.89 (1H, ddd, *J*=3.9, 12.9, 12.9 Hz, H-7β), 1.28 (1H, ddd, *J*=3.4, 3.4, 12.9 Hz, H-7α), 2.33 (1H, dd, *J*=12.0, 14.9 Hz, H-9β), 1.57 (1H, dd, *J*=5.6, 15.1 Hz, H-9α), 5.08 (1H, dd, *J*=5.6, 12.0 Hz, H-10), 2.49 (1H, ddd, *J*=4.7, 12.5, 12.5 Hz, H-13β), 1.96–2.04 (1H, m, overlapped, H-13α), 2.00–2.10 (1H, m, overlapped, H-14β), 1.64–1.72 (1H, m, overlapped, H-14α), 1.60 (3H, s, H-16), 1.10 (3H, s, H-17), 1.94 (3H, br s, H-18), 1.08 (3H, s, H-19), 3.48 (1H, d, *J*=5.4 Hz, H-20a), 2.25 (1H, d, *J*=5.4 Hz, H-20b), 2.13, 1.96 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 51.34 (d, C-1), 71.65 (d, C-2), 35.98 (d, C-3), 59.85 (s, C-4), 78.34 (d, C-5), 24.55 (t, C-6), 32.98 (t, C-7), 38.37 (s, C-8), 47.55 (t, C-9), 67.63 (d, C-10), 137.74 (s, C-11), 135.52 (s, C-12), 30.43 (t, C-13), 18.73 (t, C-14), 37.86 (s, C-15), 25.31 (q, C-16), 31.74 (q, C-17), 21.36 (q, C-18), 22.95 (q, C-19), 50.17 (t, C-20), 21.73, 21.36 [q, OAc ($CH_3$)], 169.34, 168.95 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* $[M+H]^+$ 421.2586 (calcd 421.2590 for $C_{24}H_{37}O_6$), $[M+Na]^+$ 443.2410 (calcd 443.2410 for $C_{24}H_{36}O_6Na$).

*4.6.5. 2α,5α-Diacetoxy-10β,11-dihydroxy-taxa-4(20),12(13)-diene (**33**)*

White powder; $[\alpha]_D^{20}$ +22.9 (*c* 0.0011, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1724, 1442, 1374, 1236, 1208, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.64–1.66 (1H, m, overlapped, H-1), 5.57 (1H, br d, *J*=5.2 Hz, H-2), 3.59 (1H, br s, H-3), 5.23 (1H, br s, H-5), 1.68–1.80 (2H, m, H-6), 1.70–1.76 (1H, m, overlapped, H-7β), 1.18–1.26 (1H, m, overlapped, H-7α), 2.34 (1H, dd, *J*=12.0, 15.0 Hz, H-9β), 1.76–1.84 (1H, m, overlapped, H-9α), 4.09 (1H, dd, *J*=4.0, 12.0 Hz, H-10), 5.80 (1H, br s, H-13), 2.32 (1H, dd, *J*=6.4, 13.2 Hz, H-14β), 2.06–2.14 (1H, m, H-14α), 1.41 (3H, s, H-16), 1.08 (3H, s, H-17), 1.86 (3H, s, H-18), 0.85 (3H, s, H-19), 5.21 (1H, s, H-20a), 5.09 (1H, s, H-20b), 2.09, 2.05 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 51.46 (d, C-1), 71.78 (d, C-2), 40.64 (d, C-3), 143.90 (s, C-4), 78.71 (d, C-5), 28.53 (t, C-6), 29.69 (t, C-7), 41.39 (s, C-8), 47.03 (t, C-9), 70.82 (d, C-10), 76.00 (s, C-11), 136.41 (s, C-12), 129.26 (d, C-13), 24.74 (t, C-14), 32.78 (s, C-15), 21.90 (q, C-16), 30.74 (q, C-17), 18.08 (q, C-18), 21.60 (q, C-19), 115.42 (t, C-20), 2×21.69 [q, OAc ($CH_3$)], 169.93, 169.69 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* $[M+Na]^+$ 443.2412 (calcd 443.2410 for $C_{24}H_{36}O_6Na$).

*4.6.6. 2α,5α-Diacetoxy-13β-hydroxy-taxa-4(20),12(18)-diene (**34**)*

White powder; $[\alpha]_D^{20}$ −57.4 (*c* 0.011, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3616, 3034, 2938, 1726, 1440, 1372, 1234, 1204, 1012 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.90 (1H, br s, H-1), 5.51 (1H, br d, *J*=6.0 Hz, H-2), 3.29 (1H, d, *J*=6.0 Hz, H-3), 5.31 (1H, br s, H-5), 1.71–1.85 (2H, m, overlapped, H-6), 1.75–1.85 (1H, m, overlapped, H-7β), 1.14–1.22 (1H, m, overlapped, H-7α), 2.00–2.08 (1H, m, overlapped, H-9β), 1.26–1.34 (1H, m, overlapped, H-9α), 1.70–1.90 (2H, m, overlapped, H-10), 2.77 (1H, dd, *J*=7.2, 8.8 Hz, H-11), 4.95–4.99 (1H, m, overlapped, H-13), 2.41 (1H, dd, *J*=8.1, 14.4 Hz, H-14β), 1.76–1.84 (1H, m, H-14α), 1.25 (3H, s, H-16), 1.13 (3H, s, H-17), 5.06 (1H, br s, H-18a), 5.04 (1H, br s, H-18b), 0.96 (3H, s, H-19), 5.33 (1H, s, H-20a), 4.97 (1H, s, H-20b), 2.09, 2.05 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 53.19 (d, C-1), 71.01 (d, C-2), 44.78 (d, C-3), 142.86 (s, C-4), 77.99 (d, C-5), 29.11 (t, C-6), 32.11 (t, C-7), 40.27 (s, C-8), 33.85 (t, C-9), 39.08 (t, C-10), 62.80 (d, C-11), 152.08 (s, C-12), 70.09 (d, C-13), 29.69 (t, C-14), 36.06 (s, C-15), 23.12 (q, C-16), 30.70 (q, C-17), 102.72 (t, C-18), 20.87 (q, C-19), 115.86 (t, C-20), 21.51, 21.29 [q, OAc ($CH_3$)], 169.85, 169.72 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* $[M+K]^+$ 443.3549 (calcd 443.3546 for $C_{24}H_{36}O_5K$).

*4.6.7. 2α,5α-Diacetoxy-10β,11,18-trihydroxy-taxa-4(20)-ene (**35**)*

White powder; $[\alpha]_D^{20}$ −15.5 (*c* 0.021, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3616, 2932, 1726, 1440, 1376, 1234, 1206, 1024 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.85–1.87 (1H, m, overlapped, H-1), 5.50 (1H, d, *J*=6.0 Hz, H-2), 3.52 (1H, br s, H-3), 5.30 (1H, s, H-5), 1.78–1.86 (2H, m, overlapped, H-6), 2.02–2.10 (1H, m, overlapped, H-7β), 1.30–1.38 (1H, m, overlapped, H-7α), 2.12–2.24 (1H, m, overlapped, H-9β), 1.88–1.96 (1H, m, overlapped, H-9α), 3.42–3.50 (1H, m, overlapped, H-10), 2.86–2.94 (1H, m, H-12), 1.80–1.92 (2H, m, overlapped, H-13), 2.00–2.12 (1H, m, overlapped, H-14β), 1.80–1.88 (1H, m, overlapped, H-14α), 1.36 (3H, s, H-16), 1.25 (3H, s, H-17), 3.38–3.42 (2H, m, overlapped, H-18), 0.95 (3H, s, H-19), 5.30 (1H, s, H-20a), 4.98 (1H, s, H-20b), 2×2.03 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 53.64 (d, C-1), 71.96 (d, C-2), 43.15 (d, C-3), 142.98 (s, C-4), 78.19 (d, C-5), 29.09 (t, C-6), 33.83 (t, C-7), 39.85 (s, C-8), 38.50 (t, C-9), 55.18 (d, C-10), 67.50 (s, C-11), 36.88 (d, C-12), 26.56 (t, C-13), 19.41 (t, C-14), 37.91 (s, C-15), 24.01 (q, C-16), 29.85 (q, C-17), 64.78 (t, C-18), 20.76 (q, C-19), 115.96 (t, C-20), 21.53, 21.48 [q, OAc ($CH_3$)], 169.67, 169.61 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* 443.3542 $[M-H_2O+Na]^+$ (calcd 443.3546 for $C_{24}H_{36}O_6Na$).

*4.6.8. 2α,5α-Diacetoxy-10β,13β-dihydroxy-taxa-4(20),11-diene (**36**)*

White powder; $[\alpha]_D^{20}$ +15.0 (*c* 0.45, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1724, 1442, 1374, 1236, 1208, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.98 (1H, d, *J*=2.4 Hz, H-1), 5.42 (1H, dd, *J*=2.4, 6.8 Hz, H-2), 2.91 (1H, d, *J*=6.8 Hz, H-3), 5.26 (1H, br s, H-5), 1.75–1.85 (2H, m, H-6), 1.84–1.96 (1H, m, overlapped, H-7β), 1.18–1.26 (1H, m, overlapped, H-7α), 2.43 (1H, dd, *J*=11.7, 14.6 Hz, H-9β), 1.60–1.72 (1H, m, overlapped, H-9α), 5.07 (1H, dd, *J*=5.6, 11.7 Hz, H-10), 4.28 (1H, dd, *J*=3.9, 9.3 Hz, H-13), 2.23 (1H, dd, *J*=9.5, 15.6 Hz, H-14β), 2.02–2.14 (1H, overlapped, H-14α), 1.65 (3H, s, H-16), 1.34 (3H, s, H-17), 2.03 (3H, s, H-18), 0.88 (3H, s, H-19), 5.25 (1H, s, H-20a), 4.81 (1H, s, H-20b), 2.10, 2.04 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 57.03 (d, C-1), 71.12 (d, C-2), 42.03 (d, C-3), 143.36 (s, C-4), 78.68 (d, C-5), 29.04 (t, C-6), 33.96 (t, C-7), 39.75 (s, C-8), 46.40 (t, C-9), 68.17 (d, C-10), 143.12 (s, C-11), 134.31 (s, C-12), 70.92 (d, C-13), 30.30 (t, C-14), 36.80 (s, C-15), 25.33 (q, C-16), 36.96 (q, C-17), 18.93 (q, C-18), 22.57 (q, C-19), 116.36 (t, C-20), 22.00, 21.57 [q, OAc ($CH_3$)], 169.72, 169.68 [s, OAc (CO)]; HRESIMS (positive) *m*/*z*

$[M+H]^+$ 421.2590 (calcd 421.2590 for $C_{24}H_{37}O_6$), $[M+Na]^+$ 443.2410 (calcd 443.2410 for $C_{24}H_{36}O_6Na$).

#### 4.6.9. 2α,5α-Diacetoxy-10β-hydroxy-18-oxo-taxa-4(20),11(12)-diene (**37**)

White powder; $[\alpha]_D^{20}$ +1.8 (*c* 0.011, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3618, 3014, 2936, 1724, 1440, 1376, 1232, 1214, 1012 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.77–1.79 (1H, m, overlapped, H-1), 5.39 (1H, br d, *J*=6.0 Hz, H-2), 2.83 (1H, d, *J*=6.0 Hz, H-3), 5.18 (1H, br s, H-5), 1.73–1.83 (2H, m, H-6), 2.02–2.14 (1H, m, H-7β), 1.15–1.25 (1H, m, overlapped, H-7α), 2.50 (1H, dd, *J*=12.2, 14.7 Hz, H-9β), 1.75–1.85 (1H, m, overlapped, H-9α), 5.71 (1H, dd, *J*=6.4, 11.6 Hz, H-10), 3.00 (1H, dd, *J*=8.0, 15.0 Hz, H-13β), 2.30–2.40 (1H, m, H-13α), 1.94–2.06 (1H, m, overlapped, H-14a), 1.60–1.68 (1H, m, H-14b), 1.77 (3H, s, H-16), 1.21 (3H, s, H-17), 1.15 (1H, s, H-18), 0.87 (3H, s, H-19), 5.24 (1H, s, H-20a), 4.84 (1H, s, H-20b), 2.20, 2.07 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 53.42 (d, C-1), 71.45 (d, C-2), 41.01 (d, C-3), 142.94 (s, C-4), 77.88 (d, C-5), 21.91 (t, C-6), 28.63 (t, C-7), 39.43 (s, C-8), 45.98 (t, C-9), 64.66 (d, C-10), 141.76 (s, C-11), 140.00 (s, C-12), 32.73 (t, C-13), 17.23 (t, C-14), 38.99 (s, C-15), 25.06 (q, C-16), 30.75 (q, C-17), 187.25 (d, C-18), 22.78 (q, C-19), 116.40 (t, C-20), 21.53, 21.45 [q, OAc ($CH_3$)], 170.77, 170.00 [s, OAc (CO)]; HRESIMS (positive) *m/z* $[M+Na]^+$ 441.2250 (calcd 441.2253 for $C_{24}H_{34}O_6Na$); $[M+K]^+$ 457.3342 (calcd 457.3338 for $C_{24}H_{34}O_6K$).

#### 4.6.10. 2α,5α-Diacetoxy-10β,11β,18-trihydroxy-taxa-4(20),12(13)-diene (**38**)

White powder; $[\alpha]_D^{20}$ −0.4 (*c* 0.026, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1724, 1442, 1374, 1236, 1208, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.72 (1H, br s, H-1), 5.56 (1H, d, *J*=5.5 Hz, H-2), 3.31 (1H, br s, H-3), 5.23 (1H, s, H-5), 1.63–1.73 (2H, m, H-6), 1.50–1.60 (1H, m, H-7β), 1.16–1.24 (1H, m, H-7α), 2.46–2.54 (1H, m, H-9β), 1.80–1.88 (1H, m, H-9α), 4.14 (1H, dd, *J*=6.5, 14.0 Hz, H-10), 6.16 (1H, s, H-13), 2.40 (1H, dd, *J*=5.0, 19.5 Hz, H-14β), 2.14–2.26 (1H, m, overlapped, H-14α), 1.40 (3H, s, H-16), 1.25 (3H, s, H-17), 4.49 (1H, d, *J*=11.0 Hz, H-18a), 4.07 (1H, d, *J*=11.5 Hz, H-18b), 1.10 (3H, s, H-19), 5.23 (1H, s, H-20a), 5.09 (1H, s, H-20b), 2×2.09 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 51.11 (d, C-1), 71.61 (d, C-2), 40.70 (d, C-3), 143.54 (s, C-4), 78.66 (d, C-5), 28.47 (t, C-6), 29.71 (t, C-7), 41.62 (s, C-8), 47.19 (t, C-9), 71.88 (d, C-10), 77.28 (s, C-11), 139.51 (s, C-12), 134.19 (d, C-13), 24.84 (t, C-14), 34.07 (s, C-15), 21.73 (q, C-16), 29.70 (q, C-17), 65.19 (q, C-18), 31.94 (q, C-19), 115.75 (t, C-20), 2×21.58 [q, OAc ($CH_3$)], 2×169.79 [s, OAc (CO)]; HRESIMS (positive) *m/z* 459.2364 $[M+Na]^+$ (calcd 459.2359 for $C_{24}H_{36}O_7Na$).

#### 4.6.11. 2α,5α-Diacetoxy-6α,10β,13β-trihydroxy-taxa-4(20),11(12)-diene (**39**)

White powder; $[\alpha]_D^{20}$ +9.0 (*c* 0.0010, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1724, 1442, 1374, 1236, 1208, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.97–1.99 (1H, m, overlapped, H-1), 5.43 (1H, dd, *J*=2.4, 6.8 Hz, H-2), 2.94 (1H, d, *J*=7.0 Hz, H-3), 5.03 (1H, br s, H-5), 3.89 (1H, br s, H-6), 1.96–2.04 (1H, m, overlapped, H-7β), 1.16–1.24 (1H, m, overlapped, H-7α), 2.33 (1H, dd, *J*=11.7, 14.6 Hz, H-9β), 1.68 (1H, dd, *J*=5.6, 14.0 Hz, H-9α), 4.96–5.08 (1H, m, overlapped, H-10), 4.28 (1H, dd, *J*=3.9, 9.3 Hz, H-13), 2.25 (1H, dd, *J*=9.5, 15.6 Hz, H-14β), 2.02–2.18 (1H, m, overlapped, H-14α), 1.66 (3H, s, H-16), 1.38 (3H, s, H-17), 1.97 (3H, s, H-18), 1.10 (3H, s, H-19), 5.41 (1H, s, H-20a), 4.93 (1H, s, H-20b), 2.21, 2.16 [3H each, OAc ($CH_3$)]; HRESIMS (positive) *m/z* $[M+Na]^+$ 459.2357 (calcd 459.2359 for $C_{24}H_{36}O_7Na$); $[M+K]^+$ 475.3446 (calcd 475.3444 for $C_{24}H_{36}O_7K$).

### 4.7. Biotransformation of 3 by fungus *M. genevensis*

The culture of fungus *M. genevensis* JCM 10585 was performed as described previously.[4e] Compound **3** (250 mg) was dissolved in 2.5 mL acetone, and distributed among 20 500-mL Erlenmeyer flasks of 2-day-old cell cultures and incubated for additional 7 days. After which time, the cultures were filtered under reduced pressure. The cell cultures (by sonication) and the filtrate were extracted with EtOAc three times. The extract was pooled and dried over anhydrous $Na_2SO_4$, then concentrated under vacuum, and afforded 650 mg of residue. The giving residue was subjected onto an open Si gel chromatographic column eluting gradiently with *n*-hexane/acetone to afford eight fractions. Each fraction was further separated and purified by normal phase semipreparative HPLC and yielded 96.9 mg of **3** (substrate, 38.8%), 8.0 mg of **48** (ca. 3.2%), 72.2 mg of **28** (ca. 28.9%), 7.9 mg of **32** (ca. 3.2%), 4.6 mg of **36** (ca. 1.9%), and 4.8 mg of **43** (ca. 1.9%). Among them, **43** and **48** are the two new compounds.

#### 4.7.1. 2α,5α,14β-Triacetoxy-10β-O-(β-D-glucopyranosyl)-taxa-4(20),11(12)-diene (**43**)

White powder; $[\alpha]_D^{20}$ −4.7 (*c* 0.247, MeOH); IR $\nu_{max}$ (MeOH): 3700, 3624, 3028, 2404, 1714, 1608, 1518, 1478, 1424, 1370, 1208, 1106, 1080, 1020 $cm^{-1}$; $^1H$ NMR ($CD_3OCD_3$, 500 MHz) δ 1.74 (1H, br s, H-1), 5.44 (1H, dd, *J*=1.8, 5.4 Hz, H-2), 3.14 (1H, d, *J*=5.9 Hz, H-3), 5.22 (1H, br s, H-5), 1.73–1.83 (2H, m, H-6), 1.97–2.07 (1H, m, overlapped, H-7β), 1.15–1.23 (1H, m, H-7α), 2.36 (1H, dd, *J*=12.2, 14.9 Hz, H-9β), 1.59 (1H, dd, *J*=5.4, 14.9 Hz, H-9α), 5.32 (1H, dd, *J*=5.1, 12.2 Hz, H-10), 2.50 (1H, ddd, *J*=4.6, 11.7, 17.8 Hz, H-13β), 2.10–2.20 (1H, m, H-13α), 1.96–2.06 (1H, m, overlapped, H-14β), 1.68 (1H, ddd, *J*=4.6, 10.5, 15.5 Hz, H-14α), 1.63 (3H, s, H-16), 1.12 (3H, s, H-17), 2.02 (3H, s, H-18), 0.86 (3H, s, H-19), 5.23 (1H, s, H-20a), 4.93 (1H, t, *J*=1.5 Hz, H-20b), 2.11, 1.99 [3H each, OAc ($CH_3$)], 4.34 (1H, d, *J*=7.8 Hz, H-1′), 3.20–3.32 (1H, m, H-2′), 3.30–3.44 (2H, m, H-3′ and H-4′), 3.18–3.24 (1H, m, H-5′), 3.85 (1H, ddd, *J*=2.9, 5.6, 11.5 Hz, H-6′a), 3.67 (1H, ddd, *J*=5.6, 6.6, 11.7 Hz, H-6′b), 4.15 (1H, d, *J*=6.6 Hz, 2′-OH), 4.17 (1H, d, *J*=7.1 Hz, 3′-OH), 4.10 (1H, d, *J*=3.9 Hz, 4′-OH), 3.58 (1H, dd, *J*=5.8, 6.8 Hz, 6′-OH); $^{13}C$ NMR ($CD_3OCD_3$, 125 MHz) δ 53.27 (d, C-1), 72.73 (d, C-2), 42.22 (d, C-3), 144.93 (s, C-4), 79.21 (d, C-5), 29.71 (t, C-6), 34.48 (t, C-7), 40.25 (s, C-8), 45.51 (t, C-9), 72.32 (d, C-10), 139.57 (s, C-11), 135.37 (s, C12), 30.94 (t, C-13), 18.99 (t, C-14), 37.74 (s, C-15), 25.18 (q, C-16), 31.73 (q, C-17), 21.47 (q, C-18), 22.88 (q, C-19), 116.48 (t, C-20), 21.88, 21.47 [q, OAc ($CH_3$)], 169.83, 169.75 [s, OAc (CO)], 99.55 (d, C-1′), 74.83 (d, C-2′), 78.58 (d, C-3′), 71.94 (d, C-4′), 77.45 (d, C-5′), 62.95 (t, C-6′); HRESIMS (positive) *m/z* $[M+H]^+$ 567.3169 (calcd 567.3169 for $C_{30}H_{47}O_{10}$), $[M+Na]^+$ 589.2989 (calcd 589.2989 for $C_{30}H_{46}O_{10}Na$).

#### 4.7.2. 2α,5α-Diacetoxy-taxa-4(20),11(12)-dien-10β-O-(butan-2-ol)-ether (**48**)

White powder; $[\alpha]_D^{20}$ +18.5 (*c* 0.05, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3624, 3028, 2986, 1728, 1438, 1376, 1230, 1222, 1216, 1150, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.79–1.81 (1H, m, H-1), 5.38 (1H. dd, *J*=2.0, 6.1 Hz, H-2), 3.07 (1H, d, *J*=5.9 Hz, H-3), 5.27 (1H, t, *J*=2.9 Hz, H-5), 1.75–1.85 (2H, m, H-6), 1.92–2.04 (1H, m, H-7β), 1.20 (1H, ddd, *J*=3.4, 3.4, 13.2 Hz, H-7α), 2.37 (1H, dd, *J*=12.0, 14.9 Hz, H-9β), 1.54–1.66 (1H, m, overlapped, H-9α), 4.78 (1H, dd, *J*=5.4, 12.0 Hz, H-10), 2.45 (1H, ddd, *J*=4.4, 11.5, 18.8 Hz, H-13β), 2.05–2.15 (1H, m, H-13α), 2.02–2.10 (1H, m, H-14β), 1.62–1.74 (1H, m, overlapped, H-14α), 1.63 (3H, s, H-16), 1.11 (3H, s, H-17), 1.97 (3H, s, H-18), 0.85 (3H, s, H-19), 5.24 (1H, s, H-20a), 4.88 (1H, br s, H-20b), 3.26 (1H, dq, *J*=6.6, 6.8 Hz, H-1′), 3.58 (1H, dq, *J*=6.6, 6.7 Hz, H-2′), 1.16 (3H, d, *J*=6.4 Hz, H-3′), 1.13 (3H, d, *J*=6.1 Hz, H-4′), 2.12, 2.03 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 52.28 (d, C-1), 72.44 (d, C-2), 41.26 (d, C-3), 143.51 (s, C-4), 78.87 (d, C-5), 28.99 (t, C-6), 33.85 (t, C-7), 39.61 (s, C-8), 45.99 (t, C-9), 77.04 (d, C-10), 136.10 (s, C-11), 135.81 (s, C-12), 30.19 (t, C-13), 18.21 (t, C-14), 36.98 (s, C-15), 25.30 (q, C-16), 31.57 (q, C-17), 21.97 (q, C-18), 22.56 (q, C-19), 116.36 (t, C-20), 71.41 (d, C-1′), 72.35 (d, C-2′), 18.80 (q, C-3′), 15.46 (q, C-4′), 21.62, 21.60 [q, OAc ($CH_3$)], 169.82, 169.72 [s, OAc

(CO)]; HRESIMS (positive) $m/z$ $[M+Na]^+$ 499.3043 (calcd 499.3031 for $C_{28}H_{44}O_6Na$).

### 4.8. Biotransformation of 3 by suspension cultured cells of *C. roseus*

Cell suspension cultures of *C. roseus* (L.) G. Don (Apocynaceae) were cultivated as described before.[5a] On the cultural day 15th, 65 mg of **3** in 2.4 mL acetone was distributed into eight flasks of cell cultures. After additional 6 days of incubation, the cell cultures were filtered and washed with EtOAc three times. The pooled filtrate was extracted with EtOAc three times and concentrated in vacuum at 40 °C to give 89 mg of residue. The residue was fractionated by Si gel column chromatography eluting gradiently with *n*-hexane/EtOAc (1/1 and 100% EtOAc) to yield two fractions. The resulting fractions were further separated by normal phase semipreparative HPLC. Finally, 20 mg of **3** (substrate, 30.8%), 9.5 mg of **28** (ca. 14.6%) and 2.3 mg of **41** (ca. 3.5%),[8] 5.2 mg of **42** (ca. 8%), and 5.0 mg of **43** (ca. 7.7%) were obtained. Among these products, **42** is a new compound.

*4.8.1. 6α,10β-Dihydroxy-2α,5α-diacetoxy-taxa-4(20),11-diene (**42**)*

White powder; $[\alpha]_D^{20}$ +27.4 (*c* 0.380, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3624, 3028, 2952, 1728, 1642, 1604, 1428, 1374, 1210, 1124, 1102, 1080, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.82 (1H, br s, H-1), 5.39 (1H, dd, *J*=2.2, 6.4 Hz, H-2), 3.12 (1H, d, *J*=6.2 Hz, H-3), 5.03 (1H, br s, H-5), 3.90 (1H, m, H-6), 1.96–2.08 (1H, m, H-7β), 1.49 (1H, br d, *J*=15.7 Hz, H-7α), 2.25 (1H, dd, *J*=12.0, 14.9 Hz, H-9β), 1.70 (1H, dd, *J*=5.6, 14.9 Hz, H-9α), 5.04 (1H, dd, *J*=5.6, 11.7 Hz, H-10), 2.45 (1H, ddd, *J*=5.6, 12.5, 12.5 Hz, H-13β), 2.00–2.10 (1H, m, H-13α), 1.90–2.00 (1H, m, H-14β), 1.62–1.74 (1H, m, H-14α), 1.66 (3H, s, H-16), 1.12 (3H, s, H-17), 1.91 (3H, s, H-18), 1.06 (3H, s, H-19), 5.40 (1H, s, H-20a), 5.01 (1H, s, H-20b), 2.14, 2.04 [3H each, s, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 51.94 (d, C-1), 71.91 (d, C-2), 40.62 (d, C-3), 139.64 (s, C-4), 82.09 (d, C-5), 70.24 (d, C-6), 41.24 (t, C-7), 39.51 (s, C-8), 47.42 (t, C-9), 67.70 (d, C-10), 137.32 (s, C-11), 134.70 (s, C-12), 30.07 (t, C-13), 18.26 (t, C-14), 37.18 (s, C-15), 25.29 (q, C-16), 32.02 (q, C-17), 21.32 (q, C-18), 25.45 (q, C-19), 120.01 (t, C-20), 21.72 and 169.70 (q and s, 2-OAc), 21.59 and 169.50 (q and s, 5-OAc); HRFABMS (positive) $m/z$ $[M+Na]^+$ 443.2416 (calcd 443.2410 for $C_{24}H_{36}O_6Na$).

### 4.9. Biotransformation of 3 by suspension cultured cells of *P. acinosa*

Cell suspension cultures of *P. acinosa* Roxb. (Phytolaccaceae) were cultivated as described before.[10] On the cultural day 15th, 87.5 mg of **3** in 2.1 mL acetone was distributed into seven flasks of cell cultures. After additional 6 days of incubation, the cell cultures were filtered and washed with EtOAc three times. The pooled filtrate was extracted with EtOAc three times and concentrated in vacuum at 40 °C to afford 317 mg of residue. The residue was fractionated by Si gel column chromatography eluting gradiently with *n*-hexane/EtOAc (9:1 and 100% EtOAc) to yield four fractions: 56.9 mg (65%) of **3**, 1.9 mg of **40** (ca. 2.2%), and 2.4 mg of **36** (ca. 2.8%) were obtained in the further purification by normal phase semipreparative HPLC **40** as a new compound.

*4.9.1. 13β-Hydroxy-2α,5α,10β-triacetoxy-taxa-4(20),11-diene (**40**)*

White powder; $[\alpha]_D^{20}$ +20.5 (*c* 0.04, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1724, 1442, 1374, 1236, 1208, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 2.01 (1H, d, *J*=1.7 Hz, H-1), 5.42 (1H, dd, *J*=2.4, 6.6 Hz, H-2), 2.91 (d, *J*=6.8 Hz, H-3), 5.27 (1H, t, *J*=2.9 Hz, H-5), 1.75–1.85 (2H, m, H-6), 1.92–2.04 (1H, m, H-7β), 1.21–1.29 (1H, m, H-7α), 2.46 (1H, dd, *J*=12.0, 14.6 Hz, H-9β), 1.56–1.68 (1H, m, overlapped, H-9α), 6.02 (1H, dd, *J*=5.6, 12.2 Hz, H-10), 4.30 (1H, dd, *J*=3.9, 9.5 Hz, H-13), 2.22 (1H, dd, *J*=9.5, 15.4 Hz, H-14β), 2.04–2.12 (1H, m, H-14α), 1.59 (3H, s, H-16), 1.29 (3H, s, H-17), 2.14 (3H, s, H-18), 0.88 (3H, s, H-19), 5.26 (1H, s, H-20a), 4.81 (1H, s, H-20b), 2.11, 2.06, 2.04 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 58.85 (d, C-1), 71.01 (d, C-2), 42.27 (d, C-3), 142.96 (s, C-4), 78.54 (d, C-5), 28.98 (t, C-6), 33.84 (t, C-7), 39.76 (s, C-8), 43.21 (t, C-9), 70.74 (d, C-10), 140.01 (s, C-11), 136.45 (s, C-12), 70.69 (d, C-13), 30.05 (t, C-14), 36.73 (s, C-15), 25.39 (q, C-16), 36.55 (q, C-17), 18.77 (q, C-18), 22.52 (q, C-19), 116.42 (t, C-20), 22.00, 21.56, 21.44 [q, OAc ($CH_3$)], 170.20, 2×169.67 [s, OAc (CO)]; HRFABMS (positive) $m/z$ $[M+Na]^+$ 485.2524 (calcd 485.2516 for $C_{26}H_{38}O_7Na$).

### 4.10. Biotransformation of 3 by suspension cultured cells of *P. grandiflorum*

Cell suspension cultures of *P. grandiflorum* were cultivated as described before.[5a] On the cultural day 15th, 65 mg of **3** in 2.4 mL of acetone was distributed into eight flasks of cell cultures. After additional 6 days of incubation, the cell cultures were filtered and washed with EtOAc three times. The pooled filtrate was extracted with EtOAc three times and concentrated in vacuum at 40 °C to afford 108 mg of residue. The residue was fractionated by Si gel column chromatography eluting gradiently with *n*-hexane/EtOAc (1:1 and 100% EtOAc) to yield two fractions. The resulting fractions were further separated by normal phase semipreparative HPLC to afford 23 mg of **3** (38.5%), 18.2 mg of **28** (ca. 28.0%), 0.9 mg of **44** (ca. 1.4%), and 6.3 mg of **42** (ca. 9.9%). Among them, **44** is a new compound and only $^1H$ NMR spectra data are obtained because of insufficient amount.

*4.10.1. 9α,10β-Dihydroxy-2α,5α-diacetoxy-taxa-4(20),11-diene (**44**)*

White powder; $[\alpha]_D^{20}$ +208.9 (*c* 0.06, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3624, 3028, 1728, 1642, 1428, 1374, 1214, 1106, 1078, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.77 (1H, br s, H-1), 5.41 (1H, dd, *J*=2.0, 5.9 Hz, H-2), 3.10 (1H, d, *J*=5.9 Hz, H-3), 5.28 (1H, br s, H-5), 1.75–1.85 (2H, m, H-6), 1.88–1.98 (1H, m, overlapped, H-7β), 1.50–1.58 (1H, m, overlapped, H-7α), 4.10 (1H, d, *J*=9.5 Hz, H-9), 4.79 (1H, d, *J*=9.5 Hz, H-10), 2.46 (1H, ddd, *J*=4.6, 12.0, 12.0 Hz, H-13β), 1.90–2.00 (1H, m, H-13α), 2.00–2.10 (1H, m, H-14β), 1.56–1.64 (1H, m, H-14α), 1.60 (3H, s, H-16), 1.13 (3H, s, H-17), 1.97 (3H, s, H-18), 1.05 (3H, s, H-19), 5.29 (1H, s, H-20a), 4.96 (1H, t, *J*=1.5 Hz, H-20b), 2.12, 2.03 [3H each, OAc ($CH_3$)]; HRFABMS (positive) $m/z$ $[M+Na]^+$ 443.2414 (calcd 443.2410 for $C_{24}H_{36}O_6Na$).

### 4.11. Biotransformation of 3 by suspension cultured cells of *A. officinalis*

Cell suspension cultures of *A. officinalis* were cultivated as described before. On the cultural day 15th, 125 mg of **3** in 2.0 mL of acetone was distributed into 10 flasks of cell cultures. After additional 6 days of incubation, the pooled filtrate was extracted with EtOAc thrice and concentrated in vacuum at 40 °C to give 272 mg of residue. The cell cultures were extracted with EtOAc thrice by sonication to afford 200 mg of residue. The combined residue was fractionated by Si gel column chromatography eluting with a gradient of *n*-hexane/EtOAc (19:1 to 100% EtOAc) to yield five fractions: 28.4 mg of substrate **3** (22.8%) was recovered by re-crystallization from fraction 1 (35.6 mg) and 19.2 mg of **28** (ca. 15.4%) was obtained from fraction 2 (36.2 mg). The other fractions were further separated by semipreparative HPLC to give **44** (0.5 mg, trace), **40** (1.4 mg, ca. 1.1%), **47** (2.0 mg, ca. 1.6%), **46** (1.5 mg, ca. 1.1%), **42** (3.0 mg, ca. 2.4%), and **45** (4.5 mg, ca. 3.6%). Among these products, **45**–**47** are the three new compounds.

*4.11.1. 6α,10β-Dihydroxy-2α,5α-diacetoxy-11(12)β-epoxy-taxa-4(20)-ene (**45**)*

White powder; $[\alpha]_D^{20}$ −0.9 (*c* 0.367, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 3036, 2940, 1728, 1456, 1374, 1242, 1224, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.61–1.63 (1H, m, H-1), 5.53 (1H, dd, *J*=2.0, 5.8 Hz, H-2), 2.81 (1H, br d, *J*=5.6 Hz, H-3), 5.16 (1H, br s, H-5), 3.94 (1H, ddd, *J*=1.7, 4.2, 4.2 Hz, H-6), 2.05–2.15 (1H, m, H-7β), 1.50 (1H, dt, *J*=15.1, 1.6 Hz, H-7α), 2.38 (1H, dd, *J*=12.2, 15.6 Hz, H-9β), 1.72–1.80 (1H, m, overlapped, H-9α), 3.86 (1H, dd, *J*=5.4, 12.2 Hz, H-10), 2.02–2.14 (1H, m, overlapped, H-13β), 1.74–1.86 (1H, m, overlapped, H-13α), 2.00–2.12 (1H, m, H-14β), 1.68–1.76 (1H, m, H-14α), 1.71 (3H, s, H-16), 0.91 (3H, s, H-17), 1.71 (3H, s, H-18), 1.14 (3H, s, H-19), 5.49 (1H, s, H-20a), 5.20 (1H, t, *J*=1.5 Hz, H-20b), 2.14, 2.05 [3H each, s, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 49.41 (d, C-1), 71.85 (d, C-2), 42.95 (d, C-3), 138.88 (s, C-4), 82.16 (d, C-5), 70.12 (d, C-6), 41.03 (t, C-7), 38.73 (s, C-8), 46.05 (t, C-9), 69.76 (d, C-10), 66.17 (s, C-11), 62.62 (s, C-12), 25.93 (t, C-13), 18.07 (t, C-14), 37.19 (s, C-15), 25.39 (q, C-16), 31.33 (q, C-17), 24.14 (q, C-18), 25.34 (q, C-19), 120.92 (t, C-20), 21.60, 21.55 [q, OAc ($CH_3$)], 169.56, 169.30 [s, OAc (CO)]; HRFABMS (positive) *m*/*z* $[M+Na]^+$ 459.2368 (calcd 459.2359 for $C_{24}H_{36}O_7Na$).

*4.11.2. 6α-Hydroxy-10-oxo-2α,5α-diacetoxy-11(12)β-epoxy-taxa-4(20)-ene (**46**)*

White powder; $[\alpha]_D^{20}$ −12.3 (*c* 0.03, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 3036, 2940, 1728, 1456, 1374, 1242, 1224, 1022 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.82 (1H, br s, H-1), 5.68 (1H, dd, *J*=1.5, 5.6 Hz, H-2), 3.11 (1H, d, *J*=5.6 Hz, H-3), 5.16 (1H, d, *J*=3.4 Hz, H-5), 3.84–3.92 (1H, m, H-6), 1.78 (1H, dd, *J*=5.4, 15.4 Hz, H-7β), 1.56–1.64 (1H, m, H-7α), 2.96 (1H, d, *J*=15.9 Hz, H-9β), 2.47 (1H, d, *J*=15.9 Hz, H-9α), 1.88–2.08 (4H, m, overlapped, H-13 and H-14), 1.51 (3H, s, H-16), 0.96 (3H, s, H-17), 1.49 (3H, s, H-18), 1.31 (3H, s, H-19), 5.43 (1H, br s, H-20), 5.18 (1H, s, H-20b), 2.15, 2.06 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 47.70 (d, C-1), 71.15 (d, C-2), 44.18 (d, C-3), 139.82 (s, C-4), 80.70 (d, C-5), 71.30 (d, C-6), 44.11 (t, C-7), 39.73 (s, C-8), 58.80 (t, C-9), 204.82 (s, C-10), 70.66 (s, C-11), 60.54 (s, C-12), 24.33 (t, C-13), 17.70 (t, C-14), 34.94 (s, C-15), 26.59 (q, C-16), 30.02 (q, C-17), 23.55 (q, C-18), 25.34 (q, C-19), 117.71 (t, C-20), 21.42, 21.38 [q, OAc ($CH_3$)], 169.88, 169.83 [s, OAc (CO)]; HRFABMS (positive) *m*/*z* $[M+Na]^+$ 457.2212 (calcd 457.2203 for $C_{24}H_{36}O_6Na$).

*4.11.3. 6α-Hydroxy-10-oxo-2α,5α-diacetoxy-taxa-4(20),11-diene (**47**)*

White powder; $[\alpha]_D^{20}$ +75.7 (*c* 0.133, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2940, 1730, 1680, 1374, 1238, 1228, 1214, 1024 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.99–2.01 (1H, m, H-1), 5.46 (1H, dd, *J*=2.2, 6.4 Hz, H-2), 3.26 (1H, d, *J*=6.4 Hz, H-3), 5.10 (1H, d, *J*=4.4 Hz, H-5), 3.82 (1H, ddd, *J*=1.2, 4.4, 5.6 Hz, H-6), 1.71 (1H, dd, *J*=6.1, 15.1 Hz, H-7β), 1.53 (1H, dd, *J*=1.2, 14.6 Hz, H-7α), 2.51 (1H, d, *J*=14.4 Hz, H-9β), 2.46 (1H, d, *J*=14.4 Hz, H-9α), 2.47–2.57 (1H, m, H-13β), 2.10–2.18 (1H, m, H-13α), 1.98–2.10 (1H, m, H-14β), 1.90–1.98 (1H, m, H-14α), 1.32 (3H, s, H-16), 1.12 (3H, s, H-17), 1.78 (3H, s, H-18), 1.36 (3H, s, H-19), 5.25 (1H, br s, H-20a), 4.88 (1H, br s, H-20b), 2.15 [3H, 5-OAc ($CH_3$)], 1.98 [3H, 2-OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 50.65 (d, C-1), 71.27 (d, C-2), 46.38 (d, C-3), 142.01 (s, C-4), 79.90 (d, C-5), 72.86 (d, C-6), 46.30 (t, C-7), 40.24 (s, C-8), 59.91 (t, C-9), 206.48 (s, C-10), 141.59 (s, C-11), 137.91 (s, C-12), 28.32 (t, C-13), 18.08 (t, C-14), 35.85 (s, C-15), 26.05 (q, C-16), 29.75 (q, C-17), 23.03 (q, C-18), 25.31 (q, C-19), 113.57 (t, C-20), 170.87 and 21.20 (s and q, 5-OAc), 170.01 and 21.34 (s and q, 2-OAc); HRFABMS (positive) *m*/*z* $[M+Na]^+$ 441.2258 (calcd 441.2253 for $C_{24}H_{34}O_6Na$).

### 4.12. Biotransformation of 4 by *A. coerulea*

The cultural procedure of *A. coerulea* IFO 4011 was performed as described previously.[4c] Compound **4** (340 mg) was dissolved in acetone (4.5 mL), distributed among nine 1000-mL Erlenmeyer flasks of 2-day-old cell cultures of *A. coerulea* and incubated for additional 7 days. After which time the mycelium was filtered and thoroughly washed with EtOAc. The pooled filtrate was saturated with NaCl and extracted five times with EtOAc. All the extracts were pooled, dried over anhydrous $Na_2SO_4$, and concentrated under vacuum at 40 °C to give 640 mg of residue. The dried mycelium was extracted three times by sonication with EtOAc, the obtained extracts were pooled, and concentrated under vacuum at 40 °C to afford 417 mg of residue. The combined extract was chromatographed on a Si gel column eluting gradiently with *n*-hexane/EtOAc (9/1 to 100% EtOAc) to yield four fractions: 47.0 mg of **4** (substrate, ca. 13.8%) was recovered from fractions 2 and 3 by re-crystallization. Further purification was performed by normal phase semi-preparative HPLC and afforded 35.0 mg of **49** (ca. 10.3%), 126.2 mg of **50** (ca. 37.1%), 11.2 mg of **51** (ca. 3.3%), 2.6 mg of **52** (ca. 0.7%), 15.6 mg of **53** (ca. 5%), 35 mg of **54** (ca. 10%), 2.5 mg of **55** (ca. 0.7%), 6.3 mg of **56** (ca. 2%), and 7.5 mg of **57** (ca. 2%). All of these products are new compounds.

*4.12.1. 10β-Hydroxy-5α,14β-triacetoxy-taxa-4(20),11(12)-diene (**49**)*

White powder; $[\alpha]_D^{20}$ +71.2 (*c* 0.420, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3624, 2940, 1728, 1442, 1374, 1244, 1216, 1160, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.78–1.80 (1H, m, H-1), 1.88–1.96 (1H, m, H-2α), 1.65–1.73 (1H, m, H-2β), 2.66 (1H, d, *J*=6.1 Hz, H-3), 5.34 (1H, br s, H-5), 1.73–1.83 (2H, m, H-6), 1.90–2.00 (1H, m, H-7β), 1.17–1.25 (1H, m, H-7α), 2.28 (1H, dd, *J*=12.4, 14.4 Hz, H-9β), 1.61 (1H, dd, *J*=5.4, 14.4 Hz, H-9α), 5.14 (1H, dd, *J*=5.4, 11.7 Hz, H-10), 2.57 (1H, dd, *J*=9.0, 18.8 Hz, H-13β), 2.50 (1H, dd, *J*=5.6, 18.8 Hz, H-13α), 4.62 (1H, dd, *J*=5.6, 9.0 Hz, H-14), 1.56 (3H, s, H-16), 1.17 (3H, s, H-17), 1.94 (3H, s, H-18), 0.70 (3H, s, H-19), 5.14 (1H, s, H-20a), 4.86 (1H, s, H-20b), 2.08 (3H, s, 5-OAc), 2.03 (3H, s, 14-OAc); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 51.92 (d, C-1), 26.24 (t, C-2), 36.99 (d, C-3), 149.12 (s, C-4), 76.26 (d, C-5), 27.97 (t, C-6), 33.99 (t, C-7), 38.34 (s, C-8), 47.52 (t, C-9), 67.78 (d, C-10), 140.41 (s, C-11), 132.06 (s, C-12), 39.25 (t, C-13), 74.33 (d, C-14), 39.10 (s, C-15), 25.85 (q, C-16), 31.85 (q, C-17), 21.08 (q, C-18), 21.71 (q, C-19), 169.77 and 21.80 (s and q, 5-OAc), 170.65 and 21.52 (s and q, 14-OAc); HRESIMS (positive) *m*/*z* $[M+H]^+$ 405.2645 (calcd 405.2641 for $C_{24}H_{37}O_5$), $[M+Na]^+$ 427.2458 (calcd 427.2461 for $C_{24}H_{36}O_5Na$).

*4.12.2. 5α,14β-Diacetoxy-10β-hydroxy-taxa-4β,20-epoxy-11(12)-ene (**50**)*

White powder; $[\alpha]_D^{20}$ +115.3 (*c* 1.907, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1726, 1442, 1372, 1322, 1232, 1200, 1150, 1104, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.63 (1H, br d, *J*=4.2 Hz, H-1), 1.40 (1H, ddd, *J*=3.0, 4.9, 16.4 Hz, H-2α), 1.21 (1H, ddd, *J*=2.4, 5.6, 16.3 Hz, H-2β), 2.40 (1H, dd, *J*=2.4, 4.6 Hz, H-3), 4.37 (1H, t, *J*=2.7 Hz, H-5), 2.01–2.09 (1H, m, H-6β), 1.64–1.72 (1H, m, H-6α), 1.88 (1H, dd, *J*=3.9, 13.7 Hz, H-7β), 1.29 (1H, ddd, *J*=2.2, 3.7, 13.2 Hz, H-7α), 2.25 (1H, dd, *J*=12.0, 14.7 Hz, H-9β), 1.52 (1H, dd, *J*=5.4, 14.7 Hz, H-9α), 5.09 (1H, dd, *J*=5.4, 12.0 Hz, H-10), 2.63 (1H, ddd, *J*=1.2, 5.3, 18.6 Hz, H-13β), 2.43 (1H, dd, *J*=9.3, 18.6 Hz, H-13α), 4.74 (1H, dd, *J*=5.4, 9.5 Hz, H-14), 1.50 (3H, s, H-16), 1.16 (3H, s, H-17), 1.93 (3H, d, *J*=1.3 Hz, H-18), 0.93 (3H, s, H-19), 3.10 (1H, d, *J*=3.9 Hz, H-20a), 2.37 (1H, d, *J*=3.9 Hz, H-20b), 2.08 (3H, s, 5-OAc), 2.05 (3H, s, 14-OAc); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 51.83 (d, C-1), 21.72 (t, C-2), 32.51 (d, C-3), 59.43 (s, C-4), 75.51 (d, C-5), 24.95 (t, C-6), 33.49 (t, C-7), 37.84 (s, C-8), 47.76 (t, C-9), 67.56 (d, C-10), 140.95 (s, C-11), 132.17 (s, C-12), 38.75 (t, C-13), 72.98 (d, C-14), 39.66 (s, C-15), 25.64 (q, C-16), 31.65 (q, C-17), 21.15 (q, C-18), 22.65 (q, C-19), 48.04 (t, C-20), 169.25 and 21.57 (s and q, 5-OAc), 170.94 and 21.48 (s and q, 14-OAc); HRESIMS (positive) *m*/*z* $[M+H]^+$ 421.2596 (calcd 421.2590 for $C_{24}H_{37}O_6$), $[M+Na]^+$ 443.2416 (calcd 443.2410 for $C_{24}H_{36}O_6Na$).

*4.12.3. 5α,14β-Diacetoxy-taxa-10β-(2-hydroxy-propionyl)oxy-4(20),11(12)-diene (**51**)*

White powder; $[\alpha]_D^{20}$ +53.1 (*c* 0.747, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3552, 3036, 2936, 1730, 1452, 1372, 1258, 1128, 1018 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.78–1.80 (1H, m, H-1), 1.92–1.98 (1H, m, overlapped, H-2α), 1.69 (1H, ddd, *J*=2.4, 6.6, 15.6 Hz, H-2β), 2.65 (1H, br d, *J*=5.9 Hz, H-3), 5.35 (1H, t, *J*=2.7 Hz, H-5), 1.74–1.84 (2H, m, H-6), 1.98–2.06 (1H, m, H-7β), 1.23 (1H, ddd, *J*=3.5, 3.5, 13.9 Hz, H-7α), 2.37 (1H, dd, *J*=12.4, 14.1 Hz, H-9β), 1.58 (1H, dd, *J*=5.9, 14.1 Hz, H-9α), 2.61 (1H, dd, *J*=9.3, 19.0 Hz, H-13β), 2.52 (1H, dd, *J*=5.1, 19.0 Hz, H-13α), 4.62 (1H, dd, *J*=5.1, 9.3 Hz, H-14), 1.50 (3H, s, H-16), 1.09 (3H, s, H-17), 2.10 (3H, s, H-18), 0.72 (3H, s, H-19), 5.16 (1H, s, H-20a), 4.87 (1H, br s, H-20b), 2.10 (3H, s, 5-OAc), 2.03 (3H, s, 14-OAc), 4.26 (1H, q, *J*=6.8 Hz, H-2′), 1.44 (3H, d, *J*=6.8 Hz, H-3′); $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 51.77 (d, C-1), 26.28 (t, C-2), 37.19 (d, C-3), 148.79 (s, C-4), 76.09 (d, C-5), 27.90 (t, C-6), 33.94 (t, C-7), 38.91 (s, C-8), 44.26 (t, C-9), 72.55 (d, C-10), 136.61 (s, C-11), 135.40 (s, C-12), 39.24 (t, C-13), 74.02 (d, C-14), 38.42 (s, C-15), 25.84 (q, C-16), 31.46 (q, C-17), 21.49 (q, C-18), 20.92 (q, C-19), 113.09 (t, C-20), 169.73 and 21.79 (s and q, 5-OAc), 170.63 and 21.64 (s and q, 14-OAc), 175.08 (s, C-1′), 66.73 (d, C-2′), 20.38 (q, C-3′); HRESIMS (positive) *m*/*z* $[M+H]^+$ 477.2861 (calcd 477.2852 for $C_{27}H_{41}O_7$), $[M+Na]^+$ 499.2676 (calcd 499.2672 for $C_{27}H_{40}O_7Na$).

*4.12.4. 5α,14β-Diacetoxy-4β,20-epoxy-taxa-12(18)-ene (**52**)*

White powder; $[\alpha]_D^{20}$ +32.3 (*c* 0.009, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2934, 1726, 1440, 1374, 1320, 1232, 1202, 1154, 1104, 1018 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.89 (1H, d, *J*=6.0 Hz, H-1), 1.48 (1H, dd, *J*=3.5, 7.0 Hz, H-2α), 1.20–1.28 (1H, m, overlapped, H-2β), 2.57 (1H, br s, H-3), 4.43 (1H, s, H-5), 1.19–1.29 (2H, m, H-6), 1.98–2.06 (1H, m, overlapped, H-7β), 1.75–1.81 (1H, m, overlapped, H-7α), 2.04–2.12 (1H, m, overlapped, H-9β), 1.32–1.44 (1H, m, overlapped, H-9α), 1.70–1.86 (2H, m, H-10), 2.70 (1H, dd, *J*=4.5, 12.0 Hz, H-11), 2.78 (1H, d, *J*=18.5 Hz, H-13β), 3.08 (1H, dd, *J*=7.5, 18.5 Hz, H-13α), 4.92 (1H, d, *J*=7.0 Hz, H-14), 1.19 (3H, s, H-16), 1.07 (3H, s, H-17), 4.95 (1H, s, H-18a), 4.73 (1H, s, H-18b), 1.05 (3H, s, H-19), 3.12 (1H, d, *J*=4.0 Hz, H-20a), 2.53 (1H, d, *J*=4.0 Hz, H-20b), 2.06, 2.04 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 50.94 (d, C-1), 20.14 (t, C-2), 36.19 (d, C-3), 58.76 (s, C-4), 75.03 (d, C-5), 29.71 (t, C-6), 24.50 (t, C-7), 37.98 (s, C-8), 33.30 (t, C-9), 40.08 (t, C-10), 64.31 (d, C-11), 145.49 (s, C-12), 38.22 (t, C-13), 71.60 (d, C-14), 36.69 (s, C-15), 23.89 (q, C-16), 31.94 (q, C-17), 105.18 (t, C-18), 21.24 (q, C-19), 48.59 (t, C-20), 21.49, 21.22 [q, OAc ($CH_3$)], 170.36, 169.37 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* $[M+K]^+$ 443.3638 (calcd 443.3636 for $C_{24}H_{36}O_5K$).

*4.12.5. 5α,10β,14β-Triacetoxy-4β,20-epoxy-taxa-11(12)-ene (**53**)*

White powder; white powder; $[\alpha]_D^{20}$ +75.0 (*c* 0.052, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1726, 1442, 1372, 1322, 1232, 1200, 1150, 1104, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.65 (1H, br d, *J*=4.5 Hz, H-1), 1.40 (1H, ddd, *J*=3.0, 4.9, 16.4 Hz, H-2α), 1.14–1.22 (1H, m, H-2β), 2.38–2.42 (1H, m, H-3), 4.39 (1H, br s, H-5), 2.00–2.08 (1H, m, H-6β), 1.65–1.75 (1H, m, H-6α), 2.00 (1H, dd, *J*=3.0, 13.0 Hz, H-7β), 1.28–1.36 (1H, m, H-7α), 2.30 (1H, dd, *J*=12.0, 14.7 Hz, H-9β), 1.50 (1H, dd, *J*=5.5, 15.0 Hz, H-9α), 6.07 (1H, dd, *J*=5.0, 12.0 Hz, H-10), 2.64 (1H, dd, *J*=4.0, 18.5 Hz, H-13β), 2.46 (1H, dd, *J*=9.5, 19.0 Hz, H-13α), 4.75 (1H, dd, *J*=5.0, 9.0 Hz, H-14), 1.49 (3H, s, H-16), 1.11 (3H, s, H-17), 2.06 (3H, s, H-18), 0.95 (3H, s, H-19), 3.10 (1H, d, *J*=3.9 Hz, H-20a), 2.39 (1H, d, *J*=3.9 Hz, H-20b), 2.10, 2.06, 2.05 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 51.71 (d, C-1), 21.74 (t, C-2), 32.81 (d, C-3), 59.41 (s, C-4), 75.43 (d, C-5), 24.92 (t, C-6), 33.43 (t, C-7), 37.93 (s, C-8), 44.54 (t, C-9), 70.41 (d, C-10), 137.62 (s, C-11), 134.53 (s, C-12), 38.73 (t, C-13), 72.86 (d, C-14), 39.56 (s, C-15), 25.68 (q, C-16), 31.29 (q, C-17), 21.00 (q, C-18), 22.61 (q, C-19), 48.07 (t, C-20), 21.57, 2×21.47 [q, OAc ($CH_3$)], 170.94, 170.22, 169.25 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* $[M+Na]^+$ 485.2518 (calcd 485.2516 for $C_{26}H_{38}O_7Na$).

*4.12.6. 5α,14β-Diacetoxy-6β,10β-dihydroxy-taxa-4(20),11(12)-diene (**54**)*

White powder; $[\alpha]_D^{20}$ +49.2 (*c* 0.021, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 3014, 1724, 1440, 1372, 1322, 1232, 1200, 1150, 1104, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.75 (1H, br d, *J*=4.0 Hz, H-1), 1.95 (1H, dd, *J*=5.5, 16.0 Hz, H-2β), 1.77 (1H, dd, *J*=6.5, 15.0 Hz, H-2α), 2.69 (1H, d, *J*=6.0 Hz, H-3), 5.12 (1H, br s, H-5), 3.93 (1H, br s, H-6), 2.00–2.08 (1H, m, H-7β), 1.65 (1H, br d, *J*=14.5 Hz, H-7α), 2.18 (1H, dd, *J*=12.0, 15.0 Hz, H-9β), 1.65 (1H, dd, *J*=5.0, 15.0 Hz, H-9α), 5.07 (1H, dd, *J*=5.0, 11.5 Hz, H-10), 2.58 (1H, dd, *J*=9.0, 18.5 Hz, H-13β), 2.50 (1H, dd, *J*=5.0, 18.5 Hz, H-13α), 4.64 (1H, dd, *J*=5.0, 9.0 Hz, H-14), 1.55 (3H, s, H-16), 1.17 (3H, s, H-17), 1.92 (3H, s, H-18), 1.92 (3H, s, H-19), 5.31 (1H, s, H-20a), 5.05 (1H, br s, H-20b), 2.11, 2.04 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 51.94 (d, C-1), 26.61 (t, C-2), 36.73 (d, C-3), 146.33 (s, C-4), 79.33 (d, C-5), 70.20 (d, C-6), 41.41 (t, C-7), 39.12 (s, C-8), 47.99 (t, C-9), 67.82 (d, C-10), 140.57 (s, C-11), 132.02 (s, C-12), 39.28 (t, C-13), 74.37 (d, C-14), 38.17 (s, C-15), 25.86 (q, C-16), 31.83 (q, C-17), 21.09 (q, C-18), 24.75 (q, C-19), 116.42 (t, C-20), 21.56, 21.51 [q, OAc ($CH_3$)], 170.68, 169.44 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* $[M+Na]^+$ 443.2412 (calcd 443.2410 for $C_{24}H_{36}O_6Na$); $[M+K]^+$ 459.3497 (calcd 459.3495 for $C_{24}H_{36}O_6K$).

*4.12.7. 5α,14β-Diacetoxy-7β,10β-dihydroxy-taxa-4(20),11(12)-diene (**55**)*

White powder; $[\alpha]_D^{20}$ +51.4 (*c* 0.09, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1726, 1442, 1372, 1322, 1232, 1200, 1150, 1104, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.77 (1H, br s, H-1), 1.98–2.06 (1H, m, overlapped, H-2β), 1.70–1.78 (1H, m, overlapped, H-2α), 2.56 (1H, d, *J*=7.0 Hz, H-3), 5.43 (1H, br s, H-5), 2.04–2.12 (1H, m, overlapped, H-6β), 1.60–1.68 (1H, m, overlapped, H-6α), 3.88 (1H, dd, *J*=5.0, 11.5 Hz, H-7), 2.24 (1H, dd, *J*=5.0, 16.5 Hz, H-9β), 1.95 (1H, dd, *J*=7.0, 16.5 Hz, H-9α), 5.11 (1H, dd, *J*=5.0, 11.5 Hz, H-10), 2.48–2.56 (2H, m, H-13), 4.60 (1H, dd, *J*=6.0, 8.5 Hz, H-14), 1.57 (3H, s, H-16), 1.15 (3H, s, H-17), 1.91 (3H, s, H-18), 0.62 (3H, s, H-19), 5.19 (1H, s, H-20a), 4.94 (1H, br s, H-20b), 2.09, 2.04 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 51.67 (d, C-1), 25.74 (t, C-2), 35.71 (d, C-3), 147.46 (s, C-4), 75.86 (d, C-5), 36.45 (t, C-6), 69.54 (d, C-7), 39.22 (s, C-8), 40.55 (t, C-9), 67.27 (d, C-10), 140.65 (s, C-11), 131.84 (s, C-12), 39.19 (t, C-13), 74.09 (d, C-14), 31.91 (s, C-15), 25.86 (q, C-16), 31.76 (q, C-17), 21.13 (q, C-18), 15.67 (q, C-19), 113.95 (t, C-20), 21.65, 21.49 [q, OAc ($CH_3$)], 170.67, 169.55 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* $[M+Na]^+$ 443.2412 (calcd 443.2410 for $C_{24}H_{36}O_6Na$), $[M+K]^+$ 459.3496 (calcd 459.3495 for $C_{24}H_{36}O_6K$).

*4.12.8. 5α,14β-Diacetoxy-6α,10β-dihydroxy-taxa-4(20),11(12)-diene (**56**)*

White powder; $[\alpha]_D^{20}$ +66.6 (*c* 0.027, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1726, 1442, 1372, 1322, 1232, 1200, 1150, 1104, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 1.74–1.78 (1H, m, H-1), 1.92–2.00 (1H, m, overlapped, H-2β), 1.66–1.74 (1H, m, overlapped, H-2α), 2.64 (1H, d, *J*=6.6 Hz, H-3), 5.50 (1H, d, *J*=10.0 Hz, H-5), 3.89–3.97 (1H, m, H-6), 1.82 (1H, dd, *J*=12.0, 12.0 Hz, H-7β), 1.50–1.58 (1H, m, overlapped, H-7α), 2.24 (1H, dd, *J*=12.0, 15.0 Hz, H-9β), 1.61–1.71 (1H, m, overlapped, H-9α), 5.12 (1H, dd, *J*=5.0, 11.5 Hz, H-10), 2.50–2.58 (2H, m, H-13), 4.61 (1H, dd, *J*=5.0, 9.0 Hz, H-14), 1.58 (3H, s, H-16), 1.17 (3H, s, H-17), 1.95 (3H, s, H-18), 0.73 (3H, s, H-19), 5.27 (1H, s, H-20a), 4.99 (1H, br s, H-20b), 2.17, 2.04 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 51.87 (d, C-1), 25.72 (t, C-2), 36.16 (d, C-3), 147.15 (s, C-4), 78.54 (d, C-5), 68.50 (d, C-6), 42.44 (t, C-7), 39.09 (s, C-8), 47.22 (t, C-9), 67.62 (d, C-10), 140.52 (s, C-11), 132.11 (s, C-12), 39.22 (t, C-13), 74.24 (d, C-14), 37.04 (s, C-15), 25.83 (q, C-16), 31.85 (q, C-17), 21.14 (q, C-18), 22.75 (q, C-19), 115.56 (t, C-20), 21.62, 21.49 [q, OAc ($CH_3$)], 170.89, 169.68 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* $[M+Na]^+$ 443.2410

(calcd 443.2410 for $C_{24}H_{36}O_6Na$), $[M+K]^+$ 459.3498 (calcd 459.3495 for $C_{24}H_{36}O_6K$).

*4.12.9. 5α,14β-Diacetoxy-6α,10β-dihydroxy-taxa-4β,20-epoxy-11(12)-ene (**57**)*

White powder; $[\alpha]_D^{20}$ +74.7 (*c* 0.0033, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3620, 2936, 1726, 1442, 1372, 1322, 1232, 1200, 1150, 1104, 1020 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.62 (1H, br s, H-1), 1.40 (1H, dd, *J*=4.0, 16.5 Hz, H-2β), 1.11 (1H, dd, *J*=3.5, 15.0 Hz, H-2α), 2.36 (1H, d, *J*=2.0 Hz, H-3), 4.58 (1H, d, *J*=3.5 Hz, H-5), 4.23 (1H, ddd, *J*=4.5, 4.5, 12.0 Hz, H-6), 1.84 (1H, dd, *J*=12.5, 14.5 Hz, H-7β), 1.58–1.66 (1H, m, overlapped, H-7α), 2.24 (1H, dd, *J*=12.5, 14.5 Hz, H-9β), 1.58–1.66 (1H, m, overlapped, H-9α), 5.09 (1H, dd, *J*=5.5, 12.0 Hz, H-10), 2.66 (1H, dd, *J*=5.0, 18.5 Hz, H-13β), 2.42 (1H, dd, *J*=5.5, 18.5 Hz, H-13α), 4.73 (1H, dd, *J*=5.5, 9.5 Hz, H-14), 1.51 (3H, s, H-16), 1.18 (3H, s, H-17), 1.95 (3H, s, H-18), 0.98 (3H, s, H-19), 3.12 (1H, d, *J*=4.0 Hz, H-20a), 2.43 (1H, d, *J*=4.0 Hz, H-20b), 2.16, 2.06 [3H each, OAc ($CH_3$)]; $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 51.81 (d, C-1), 21.36 (t, C-2), 31.82 (d, C-3), 59.65 (s, C-4), 77.00 (d, C-5), 66.06 (d, C-6), 41.83 (t, C-7), 39.68 (s, C-8), 47.65 (t, C-9), 67.50 (d, C-10), 141.01 (s, C-11), 132.32 (s, C-12), 38.75 (t, C-13), 72.91 (d, C-14), 38.20 (s, C-15), 25.64 (q, C-16), 31.69 (q, C-17), 21.36 (q, C-18), 23.83 (q, C-19), 47.75 (t, C-20), 21.48, 21.23 [q, OAc ($CH_3$)], 171.00, 170.35 [s, OAc (CO)]; HRESIMS (positive) *m*/*z* $[M+Na]^+$ 459.2541 (calcd 459.2539 for $C_{24}H_{36}O_7Na$).

## 4.13. Cinnamoylation of 8

Into 5-mL egg-plant flask, 21 mg of **9**, 40 mg of DMAP, and 72 mg of cinnamoyl chloride were added and dissolved with 1.1 mL of dry pyridine at 85–90 °C by stirring. Monitored by TLC, the reaction was quenched after 12 h of incubation by adding 15 mL saturated NaCl aq and extracted with EtOAc (4×15 mL). The extract was washed with 1 M HCl (3×10 mL) until the pH decreased beneath 5, subsequently with satd $NaHCO_3$ aq (3×15 mL) until the pH reached 7–8, then with satd NaCl aq (2×10 mL), dried over anhydrous $NaSO_4$, and concentrated to afford 53 mg of residue. The residue was directly subjected onto normal phase semipreparative HPLC eluting with the mobile phase (*n*-hexane/EtOAc=7/3) at the flow rate of 5 mL/min. Then, 25 mg of **58** (95.2%) was obtained.

*4.13.1. 2α,5α,10β,14β-Tetraacetoxy-9α-cinnamyloxy-taxa-4(20),11(12)-diene (**58**)*

White powder; $[\alpha]_D^{20}$ 36.1 (*c*, 2.41, $CHCl_3$); IR $\nu_{max}$ ($CHCl_3$): 3028, 2968, 2456, 1734, 1638, 1582, 1454, 1404, 1374, 1332, 1312, 1246, 1224, 1164, 1114, 1072, 1018 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 1.97 (1H, d, *J*=2.2 Hz, H-1), 5.47 (1H, dd, *J*=2.2, 6.6 Hz, H-2), 3.01 (1H, d, *J*=6.6 Hz, H-3), 5.32 (1H, br s, H-5), 1.84–1.92 (1H, m, H-6β), 1.70–1.78 (1H, m, H-6α), 1.76–1.88 (2H, m, H-7), 5.95 (1H, d, *J*=10.3 Hz, H-9), 6.16 (1H, d, *J*=10.3 Hz, H-10), 2.87 (1H, dd, *J*=9.3, 19.0 Hz, H-13β), 2.46 (1H, dd, *J*=4.9, 19.0 Hz, H-13α), 4.99 (1H, dd, *J*=4.9, 9.0 Hz, H-14), 1.77 (3H, s, H-16), 1.14 (3H, s, H-17), 2.18 (3H, br s, H-18), 0.90 (3H, s, H-19), 5.35 (1H, s, H-20a), 4.89 (1H, s, H-20b), 2.20, 2.06, 2.02 [3H each, s, OAc ($CH_3$)], 6.42 (1H, d, *J*=16.1 Hz, H-2′), 7.69 (1H, d, *J*=16.1 Hz, H-3′), 7.50–7.56 (2H, m, Ph-*o*-H), 7.35–7.43 (3H, m, Ph-*p*-H, Ph-*m*-H); $^{13}C$ NMR ($CDCl_3$, 125 MHz) $\delta$ 58.53 (d, C-1), 69.94 (d, C-2), 44.19 (d, C-3), 141.41 (s, C-4), 78.37 (d, C-5), 28.37 (t, C-6), 27.42 (t, C-7), 44.58 (s, C-8), 76.94 (d, C-9), 72.32 (d, C-10), 134.14 (s, C-11), 132.89 (s, C-12), 39.48 (t, C-13), 70.27 (d, C-14), 37.07(s, C-15), 25.81 (q, C-16), 31.66 (q, C-17), 21.09 (q, C-18), 17.34 (q, C-19), 118.14 (t, C-20), 21.85, 21.42, 21.39, 21.09 [q, 4×OAc ($CH_3$)], 170.25, 169.96, 169.76, and 169.71 [s, 4×OAc (CO)], 166.10 (s, C-1′), 117.37 (d, C-2′), 145.60 (d, C-3′), 137.32 (s, C-4′), 128.17 (d, Ph-*o*-C), 128.91 (d, Ph-*p*-C), 130.51 (d, Ph-*m*-C). HRESIMS (positive) *m*/*z* $[M+Na]^+$ 673.2981 (calcd 673.2989 for $C_{37}H_{46}O_{10}Na$).

## 4.14. Evaluation of MDR-reversal activity of 58 in vitro

The human non-small cell lung cancer (NSCLC)-lung adenocarcinoma cell line A549, the human mouth epidermal carcinoma human (KB) cell line, and HCT-8 human colorectal adenocarcinoma cell line were maintained in the Department of Pharmacology, Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College. The drug-resistant subline of A549/taxol was established by culturing the cells with gradually increasing concentrations of paclitaxel. The drug-resistant subline of KB/VCR was established by culturing the cells with gradually increasing concentrations of vincristine. The HCT-8 human colorectal adenocarcinoma cell line is an intrinsic MDR cell line. The MDR tumor cells were incubated in medium RPMI 1640 supplemented with 10% fetal bovine serum, 100 U/mL of penicillin, and 100 μg/mL of streptomycin at 37 °C in a humidified atmosphere of 5% $CO_2$ in air. Cells were subcultured twice every week by digesting with mixture of 0.025% trypsin and 0.01% EDTA solution. Cell proliferation was measured by 3-(4,5-dimethylthiazo-2-yl)-2,5-diphenytetrazolium bromide (MTT) dye reduction method. Briefly, $1\times10^4$ viable cells (100 μL) were plated into each well of 96-well plates and left to attach to the plate for 24 h, after which time, the medium was changed to the one containing or lacking test reversal agents or antitumor agents (paclitaxel or vincrinstine dissolved in 100 μL of DMSO). The medium was eliminated after 72 h of incubation and 100 μL of fresh serum-free medium with 0.5 mg/mL of MTT and incubated for 4 h. The medium was then removed and 150 μL of DMSO was added to each well to dissolve the dark blue crystals by shaking in a mini-shaker. Absorbances were measured with a Wellscan MK3 microtitre plate reader (Labsystems Dragon) at test and reference wavelengths of 570 and 450 nm, respectively. The median drug concentration for 50% inhibition ($IC_{50}$) of tumor cell growth was determined by plotting the logarithm of the drug concentration against the growth rate (percentage of control) of treated cells.

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## Supplementary data

The copies of $^1H$ and/or $^{13}C$ NMR spectra for new compounds. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.06.062.

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