Articles

Syntheses and Structure−Activity Relationships of Taxoids Derived from 14β-Hydroxy-10-deacetylbaccatin III

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A series of new taxoids derived from 14β-hydroxy-10-deacetylbaccatin III was synthesized by means of the β-lactam synthon method. Most of the new taxoids thus synthesized possess excellent cytotoxicity against human ovarian (A121), non-small-cell lung (A549), colon (HT-29), and breast (MCF-7) cancer cell lines, and several of these taxoids show subnanomolar IC_{50} values which are severalfold to 1 order of magnitude better than those of paclitaxel and docetaxel. Modifications at the 3′- and 3′-N-positions exert marked effects on the activity. For the substituents at C-3′, the cytotoxicity decreases in the order 2-furyl ∼ 2-methyl-1-propenyl ≥ 2-methylpropyl > (*E*)-1-propenyl ≥ *n*-propyl > phenyl ≫ 2,2-dimethylpropyl. For the 3′-N substituents, the activity decreases in the order *t*-BuOCO > Ph > *n*-hexanoyl. A significant increase in the cytotoxicity against the doxorubicin-resistant human breast cancer cell line MCF7-R that expresses the multidrug resistance (MDR) phenotype is observed by the proper modification of the substituent at C-10. The observed remarkable effects of the substituents at C-10 on the activity against MCF7-R can be ascribed to the effective inhibition of the binding of these new taxoids to P-glycoprotein that is responsible for MDR.

Introduction

Taxol (paclitaxel)[1] and Taxotère (docetaxel)[2] are currently considered to be two of the most exciting drugs in cancer chemotherapy.[3−7] Both paclitaxel and docetaxel[8−10] exhibit significant antitumor activity against various cancers which have not been effectively treated by existing chemotherapeutic drugs[11,12] through their unique antimitotic mechanism of action.[13] Paclitaxel was approved by the FDA for the treatment of advanced ovarian cancer in December 1992 and for the treatment of breast cancer in April 1994. It is also undergoing clinical trials for other cancers. Docetaxel was approved by the FDA for the treatment of breast cancer in May 1996 and is currently undergoing phase II and III clinical trials for breast and lung cancers worldwide.[3,12] Although both paclitaxel and docetaxel possess potent antitumor activity, recent reports have shown that treatment with these drugs often results in various undesired side effects as well as multidrug resistance (MDR).[12,14] Therefore, it is important to develop new taxoid anticancer agents with fewer side effects, superior pharmacological properties, and improved activity against various classes of tumors.

Extensive studies have been performed in different laboratories on the structure−activity relationships (SAR) of paclitaxel, docetaxel, and their analogs.[3,5,7] As a part of our continuing SAR study of paclitaxel and docetaxel analogs,[15−21] we have been investigating a new series of taxoids derived from 14β-hydroxy-10-deacetylbaccatin III (14β-OH-DAB) isolated from the needles of *Taxus wallichiana* Zucc.[22] The presence of an additional C-14 hydroxyl group in 14β-OH-DAB was found to provide much higher water solubility than the usual 10-deacetylbaccatin III (DAB).[22] Therefore, the new taxoids derived from 14β-OH-DAB might have substantially improved water solubility, bioavailability, and hydrophobicity-related drug resistance.[13] These improved pharmacological properties may well be related to the modification of undesirable toxicity and activity spectra against various cancer types. With those possibilities in mind, we decided to develop a new series of taxoids derived from 14β-OH-DAB. We describe here the syntheses and structure−activity relationships of new taxoids bearing a 14β-OH-baccatin III 1,14-carbonate moiety, which have revealed remarkable effects of substituents at the 3′-, 3′-N-, and 10-positions on cytotoxicities.

Syntheses of New Taxoids

A series of new taxoids were synthesized from 14β-OH-DAB 1,14-carbonate derivatives using the β-lactam synthon method.[23−27] (3*R*,4*S*)-1-Acyl-3-(silyloxy)-4-arylazetidin-2-ones **4** and **5** with extremely high enantiomeric purity were obtained through a chiral ester enolate−imine cyclocondensation developed in these laboratories[23,24] in two steps using TMS-aldimine **2A** or three steps using PMP-aldimine **2B** in 78−80% overall yields eqs 1 and 2). Results are summarized in Table 1.

7-TES-14β-OH-DAB 1,14-carbonate (**8**) (TES = triethylsilyl) was prepared by reacting 14β-OH-DAB (**6**)

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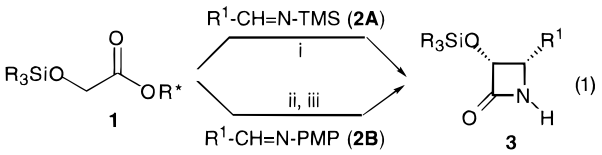
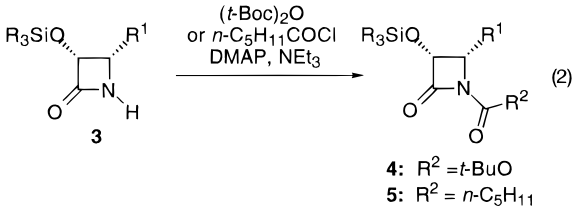
Table 1. β-Lactams **4** and **5**

β-lactam	R^1	R^2	R_3Si	% ee[a]
4a	2-furyl	t-C_4H_9O	i-Pr_3Si	94
4b	$(CH_3)_2C{=}CH$	t-C_4H_9O	i-Pr_3Si	94
4c	(E)-$CH_3CH{=}CH$	t-C_4H_9O	i-Pr_3Si	97
4d	$(CH_3)_3CCH_2$	t-C_4H_9O	Et_3Si	96
5a	phenyl	n-C_5H_{11}	t-$BuMe_2Si$	94
5b	$(CH_3)_2C{=}CH$	n-C_5H_{11}	i-Pr_3Si	96

[a] Determined by chiral HPLC analysis (see the Experimental Section).



i: a) LDA, THF; b) **2A**; c) aq. NH_4Cl.
ii: a) LDA,THF; b) **2B**; c) aq. NH_4Cl;
iii: CAN, $MeCN/H_2O$



with Et_3SiCl in pyridine/DMF at room temperature followed by treatment with phosgene in dichloromethane in 64% yield for the two steps (Scheme 1).

7,10-Bis(TES)-14β-OH-DAB 1,14-carbonate (**9a**) and 10-acyl-14β-OH-DAB 1,14-carbonates **9b**−**g** were prepared by treating baccatin **8** with 1.1 equiv of LiHMDS at −40 °C followed by the addition of either TESCl or an appropriate acyl chloride in freshly distilled THF (Scheme 2). Results are listed in Table 2.

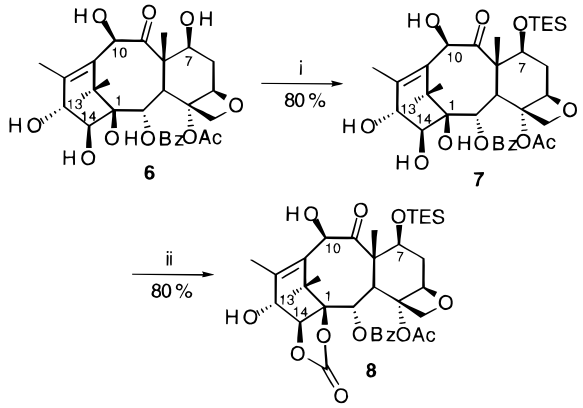
The reactions of baccatin derivatives **9a**−**g** with 1.2 equiv of β-lactam **4** or **5** in the presence of 1.2 equiv of LiHMDS at −40 °C for 30 min gave the corresponding coupling products **10**−**15** in good yields (Scheme 3). The coupling products **10**−**15** were desilylated by treatment with HF−pyridine (70:30) in pyridine/acetonitrile (1:1) at room temperature to yield 3′-dephenyl-3′-(2-furyl)-14β-OH-docetaxel 1,14-carbonates **16a**,**b**, 3′-dephenyl-3′-(2-methyl-1-propenyl)-14β-OH-docetaxel 1,14-carbonates **17a**−**g**, 3′-dephenyl-3′-((*E*)-1-propenyl)-14β-OH-docetaxel 1,14-carbonates **18a**,**b**, 3′-dephenyl-3′-(3,3-dimethylpropyl)-14β-OH-docetaxel 1,14-carbonate **19a**, 3′-*N*-debenzoyl-3′-*N*-hexanoyl-14β-OH-paclitaxel 1,14-carbonate **20a**, and 3′-*N*-debenzoyl-3′-*N*-hexanoyl-3′-dephenyl-3′-(2-methyl-1-propenyl)-14β-OH-paclitaxel 1,14-carbonates **21d**−**f** in good yields. Results are summarized in Table 3.

Several of the 3′-unsaturated analogs (**17**, **18**) were reduced with Pd/C under 1 atm of H_2 to produce the corresponding 3′-saturated taxanes (**22**, **23**) in high yield (Scheme 4). Results are listed in Table 4.

Cytotoxicity of New Taxoids

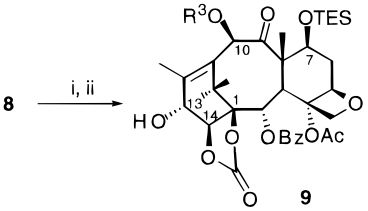
Effect of Substituents at 3′- and 3′-N-Positions on Cytotoxicity. Cytotoxicities of these new taxoids thus synthesized were evaluated *in vitro* against several human cancer cell lines: A121 (ovarian), A549 (non-small-cell lung), HT-29 (colon), MCF-7 (breast), and

Scheme 1[a]



[a] (i) TESCl (9 equiv), pyridine/DMF (1/1), rt; (ii) phosgene, CH_2Cl_2.

Scheme 2[a]



[a] (i) LiHMDS, −40 °C, THF; (ii) R^3Cl or TESCl, −40 °C.

Table 2. 7-TES-10-modified-baccatin III 1,14-Carbonates **9**

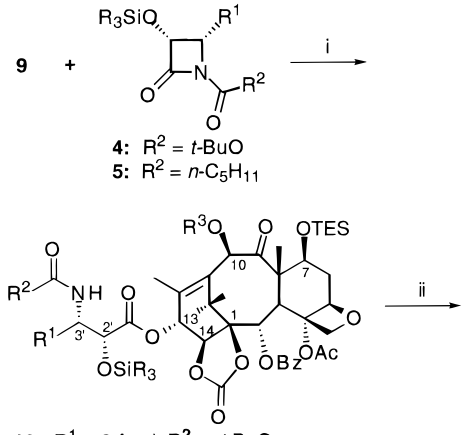
baccatin	R^3	yield[a] (%)
9a	Et_3Si	84
9b	CH_3CO	95
9c	CH_3CH_2CO	74
9d	cyclopropane-CO	91
9e	$(CH_3)_2N$-CO	86
9f	(E)-$CH_3CH{=}CHCO$	54 (79)
9g	CH_3O-CO	65

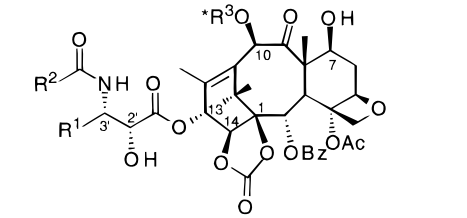
[a] Numbers in parentheses indicate conversion yields based on the consumed **8**.

MCF7-R (doxorubicin-resistant breast). Results are summarized in Tables 5 and 6. The cytotoxicities of paclitaxel, docetaxel, SB-T-1001,[18] SB-T-1011,[19] and SB-T-1012[19] are also shown for comparison. As Tables 5 and 6 show, these new taxoids possess, in general, strong cytotoxicities against human cancer cell lines with clear SAR.

Table 5 shows the SAR of selected new taxoids, summarizing the effects of the substituents at the 3′- and 3′-N-positions, i.e., R^1 and R^2CO, respectively, on cytotoxicity. When R^1 is phenyl (entries 3−5, 10), a *tert*-butoxycarbonyl (*t*-Boc) group is the best substituent as R^2CO among *t*-Boc, benzoyl, and *n*-hexanoyl groups, i.e., the cytotoxicity decreases in the order *t*-Boc ≫ PhCO > n-$C_5H_{11}CO$. It should be noted that 14β-OH-paclitaxel 1,14-carbonate (SB-T-1012) has at least 1 order of magnitude weaker activity than paclitaxel, whereas 14β-OH-docetaxel 1,14-carbonate (SB-T-1011) and 14β-OH-docetaxel (SB-T-1001) possess equivalent or better activity than paclitaxel. It is very clear that 2-furyl as well as alkyl and alkenyl groups, i.e., 2-methyl-1-propenyl, (*E*)-1-propenyl, 2-methylpropyl, and *n*-propyl, substantially increase cytotoxicity (entries 6−8, 12, 13). It is also clear that a 2,2-dimethylpropyl group at the 3′-position markedly decreases cytotoxicity (**19a**, entry 9). Among the new taxoids listed in Table 5, **16a** and

Scheme 3[a]





[a] (i) LiHMDS, −40 °C, THF; (ii) HF−pyridine, pyridine/CH_3CN, rt.

17a exhibit excellent overall cytotoxicity, considerably better than paclitaxel and docetaxel, against different cancer cell lines.

Table 6 summarizes the effects of the substituent at the 10-position on cytotoxicity. As Table 6 clearly shows, the substituent at C-10 exerts a remarkable effect on the activity against the drug-resistant human breast cancer cell line, MCF7-R, i.e., the activity increases, dramatically in some cases (**16a** vs **16b**; **18a** vs **18b**, **22a** vs **22e**), by replacing a free hydroxyl group at C-10 with an acyl group or *N*,*N*-dimethylcarbamoyl group. The activities against normal cancer cell lines are also somewhat influenced by the substituent at C-10, but to a much lesser extent. Three taxoids, **16b** and **17c**−**g**, exhibit subnanomolar IC_{50} values against all normal cancer cell lines examined as well as 10 nM level IC_{50} values against MCF7-R. The taxoid **17f** shows the highest activity against MCF7-R (IC_{50} = 17 nM).

This finding is very important since paclitaxel and docetaxel do not have strong activity against MCF7-R which expresses MDR phenotype (MDR = multidrug resistance). As Table 6 shows, the relative activity indices, i.e, $IC_{50}^{MCF7-R}/IC_{50}^{MCF-7}$, of paclitaxel and docetaxel against MCF7-R in comparison with MCF-7 are 176 and 235, respectively. With this respect, **17b** has the best relative activity index ($IC_{50}^{MCF7-R}/IC_{50}^{MCF-7}$ = 11) while keeping the cytotoxicities against normal cancer cell lines at the lower nanomolar level IC_{50} values. The taxoids **22b**,**d**,**e** also have attractive profiles. The observed remarkable activity against the drug-resistant cancer cells is certainly not restricted to MCF7-R. The taxoid **17b**, for example, shows 1 order of magnitude better activity (IC_{50} = 27 nM) against A2780-DX5 (doxorubicin-resistant human ovarian cancer cell line overexpressing P-glycoprotein) than paclitaxel (IC_{50} = 203 nM) and docetaxel (IC_{50} = 122 nM).

For the observed remarkable effects of the substituents at C-10 on the activity against the drug-resistant cell line MCF7-R, we would like to propose the following hypothesis, although further investigation is necessary to elucidate it: MDR, i.e., the cross-resistance to various structurally different cytotoxic agents, has been shown to be caused by increased outward transport of these agents through the plasma membrane by the action of P-glycoprotein.[28] The photoaffinity label of P-glycoprotein with tritiated photoreactive paclitaxel analog has recently been performed successfully.[29] Thus, it is reasonable to assume that the observed SAR that is unique to MCF7-R is related to the binding ability of these new taxoids to P-glycoprotein. The result that most of the modifications at C-10 we made are tolerated for binding to tubulin, whereas the binding of these taxoids to P-glycoprotein appears to be strongly affected by the structure of the modifier at C-10, implies that the 10-position is crucial for P-glycoprotein to recognize and bind taxoid antitumor agents.[21] Accordingly, it appears that the observed remarkable effects of the substituents at C-10 on the activity against MCF7-R could be ascribed to the effective inhibition of the binding of these new taxoids to P-glycoprotein that is responsible for MDR.

As we recently published,[30] SB-T-1011, developed earlier in our SAR study on the new series of taxoids derived from 14β-OH-DAB, possesses high *in vivo* antitumor activity against a human ovarian tumor xenograft in nude athymic mice. As Table 6 shows, several new taxoids in this series possess 1 order of magnitude better cytotoxicity than SB-T-1011. Therefore, the new series of taxoids reported here warrant further investigation into their *in vivo* antitumor activities against different types of tumors, especially drug-resistant tumors. In fact, several taxoids included here have already been proved to possess excellent antitumor activity against human ovarian A121 tumor xenograft in nude athymic mice. These new taxoids show a clear dose−response, and a couple of these have a maximum tolerated dose (MTD) equivalent to that of paclitaxel (two times as high MTD as that of docetaxel) with much better cytotoxicity than paclitaxel. Further *in vivo* study is actively in progress. These *in vivo* assay results will be published elsewhere. Some of these new taxoids have also been found to cause, indeed, cell cycle arrest at the G2/M phase and lead to apoptosis (confirmed by DNA fragmentation). These results will be published elsewhere.

Conclusion

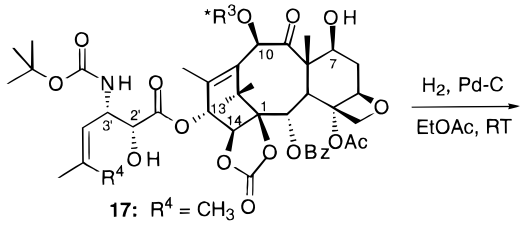
A new series of taxoids are derived from 14β-OH-DAB, and most of these taxoids possess strong cytotoxicities that are better than that of paclitaxel. Several of these taxoids show subnanomolar IC_{50} values against normal human cancer cell lines, A121 (ovarian), A549 (non-small-cell lung), HT-29 (colon), and MCF-7 (breast).

Table 3. Syntheses of Taxoids **16**−**21**

β-lactam	baccatin	coupling product	yield (%)[a]	R^1	R^2	*R^3 (R^3)[b]	taxoid	yield (%)[a]
4a	**9a**	**10a**	78	2-furyl	*t*-Boc	H (Et_3Si)	**16a**	73
4a	**9b**	**10b**	78	2-furyl	*t*-Boc	CH_3CO	**16b**	76
4b	**9a**	**11a**	ni[c]	$(CH_3)_2C{=}CH$	*t*-Boc	H (Et_3Si)	**17a**	90[d]
4b	**9b**	**11b**	80	$(CH_3)_2C{=}CH$	*t*-Boc	CH_3CO	**17b**	73
4b	**9c**	**11c**	82	$(CH_3)_2C{=}CH$	*t*-Boc	CH_3CH_2-CO	**17c**	62
4b	**9d**	**11d**	87	$(CH_3)_2C{=}CH$	*t*-Boc	cyclopropane-CO	**17d**	84
4b	**9e**	**11e**	85	$(CH_3)_2C{=}CH$	*t*-Boc	$(CH_3)_2N$-CO	**17e**	83
4b	**9f**	**11f**	84	$(CH_3)_2C{=}CH$	*t*-Boc	(*E*)-$CH_3CH{=}CH$-CO	**17f**	38
4b	**9g**	**11g**	55	$(CH_3)_2C{=}CH$	*t*-Boc	CH_3O-CO	**17g**	67
4c	**9a**	**12a**	ni[c]	(*E*)-$CH_3CH{=}CH$	*t*-Boc	H (Et_3Si)	**18a**	52[d]
4c	**9a**	**12b**	75	(*E*)-$CH_3CH{=}CH$	*t*-Boc	CH_3CO	**18b**	80
4d	**9a**	**13a**	80	$(CH_3)_3CCH_2$	*t*-Boc	H (Et_3Si)	**19a**	80
5a	**9a**	**14a**	ni[c]	phenyl	*n*-C_5H_{11}	H (Et_3Si)	**20a**	41 (54)[d]
5b	**9d**	**15d**	72	$(CH_3)_2C{=}CH$	*n*-C_5H_{11}	cyclopropane-CO	**21d**	82
5b	**9e**	**15e**	55 (76)	$(CH_3)_2C{=}CH$	*n*-C_5H_{11}	$(CH_3)_2N$-CO	**21e**	54
5b	**9f**	**15f**	50 (65)	$(CH_3)_2C{=}CH$	*n*-C_5H_{11}	(*E*)-$CH_3CH{=}CH$-CO	**21f**	84

[a] Numbers in parentheses indicate conversion yield based on the consumed baccatin **9**. [b] When *R^3 (after deprotection) and R^3 (before deprotection) are different, R^3 (protecting group in these cases) is indicated in the parentheses. [c] ni stands for "not isolated", i.e., the coupling products **11a**, **12a**, and **14a** were carried to deprotection without purification. [d] Yield for two steps.

Scheme 4



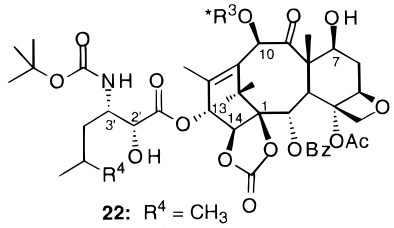


Table 4. Syntheses of 3′-Alkyl Taxoids **22** and **23**

taxoid	R^4	R^1	*R^3	yield (%)
22a	CH_3	$(CH_3)_2CHCH_2$	H	77
22b	CH_3	$(CH_3)_2CHCH_2$	CH_3CO	100
22d	CH_3	$(CH_3)_2CHCH_2$	cyclopropane-CO	91
22e	CH_3	$(CH_3)_2CHCH_2$	$(CH_3)_2N$-CO	75 (94[a])
23a	H	$CH_3(CH_2)_2$	H	90
23b	H	$CH_3(CH_2)_2$	CH_3CO	86

[a] Conversion yield based on the consumed **17e**.

Modifications at the 3′- and 3′-N-positions exert marked effects on the activity. For the substituents at C-3′, the cytotoxicity decreases in the order 2-furyl ∼ 2-methyl-1-propenyl ≥ 2-methylpropyl > (*E*)-1-propenyl ≥ *n*-propyl > phenyl ≫ 2,2-dimethylpropyl. For the 3′-N substituents, the activity decreases in the order *t*-BuOCO > Ph > *n*-hexanoyl. A significant increase in the cytotoxicity against the doxorubicin-resistant human breast cancer cell line MCF7-R is observed with proper modification of the substituent at C-10. It is reasonable to interpret the observed remarkable effects of the substituents at C-10 on the activity against MCF7-R based on the effective inhibition of the binding of these new taxoids to P-glycoprotein that is responsible for MDR. Further investigations into the *in vivo* antitumor activities of these new taxoids are actively underway.

Experimental Section

General Method. Melting points were determined on a Thomas-Hoover capillary apparatus and were not corrected. ^1H (250 MHz), ^{13}C (63 MHz), and 2D NMR spectra were measured using a Bruker AC-250 spectrometer using tetramethylsilane as the internal standard. Infrared spectra were recorded on a Perkin-Elmer Model 1600 FT-IR spectrophotometer with a Hewlett-Packard 7470A plotter using samples as solutions in a liquid cell, neat oil, or KBr disks. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Thin layer chromatography was performed on Merck DC-alufolien with Kieselgel 60F-254. Flash column chromatography was performed using silica gel 60 (230−400 mesh ASTM) from E. Merck. Chiral HPLC analysis for the determination of enantiomeric excess was carried out with a Waters HPLC assembly consisting of a Waters M45 solvent delivery system, a Waters Model 680 gradient controller, and a Waters M440 detector (at 254 nm), equipped with a Spectra Physics Model SP4270 integrator using a Daicel-Chiracel OD chiral column (J. T. Baker), employing hexane/2-propanol (13/1) as the solvent system with a flow rate of 0.2 mL/min. Elemental analyses were performed at M-H-W Laboratories, Phoenix, AZ, and Supersun Technology Analytical Laboratory, Stony Brook, NY. FAB HRMS were performed at UCR Mass Spectrometry Facility, Riverside, CA.

Materials. Chemicals were purchased from Aldrich Chemical Co. and distilled or recrystallized prior to use. (−)-10-(Dicyclohexylsulfamoyl)-D-isoborneol was purchased from Aldrich Chemical Co. (−)-*trans*-2-Phenylcyclohexyl [(triisopropylsilyl)oxy]acetate (**1a**)[24] and (−)-10-(dicyclohexylsulfamoyl)-D-isobornyl [(triisopropylsilyl)oxy]acetate (**1b**)[31] were prepared by literature methods. *N*-TMS-benzaldimine (**2f**)[24] and *N*-TMS-furfuraldimine (**2b**)[32] were prepared using methods previously reported. (3*R*,4*S*)-3-[(Triisopropylsilyl)oxy]-4-(2-furyl)azetidin-2-one (**3a**),[32] 3-[(*tert*-butyldimethylsilyl)oxy]-4-phenylazetidin-2-one (**3e**),[24] and (3*R*,4*S*)-3-[(triisopropylsilyl)-oxy]-4-phenylazetidin-2-one (**3f**)[24] were prepared by literature procedures. 14β-Hydroxy-10-deacetylbaccatin III (14β-OH-DAB) (**7**) was a gift from Indena, SpA, Italy.

Preparation of *N*-(4-Methoxyphenyl)aldimines 2. A typical procedure is given for the preparation of *N*-(4-methoxyphenyl)-3-methyl-2-butenaldimine (**2b**): To a solution of *p*-anisidine (1.072 g, 8.7 mmol), recrystallized twice from EtOH, and anhydrous Na_2SO_4 in dry CH_2Cl_2 (20 mL) was added 3-methyl-2-butenal (1.04 mL, 10.75 mmol). After 1 h, the Na_2SO_4 was filtered off and the solvent was removed to give aldimine **2b** in quantitative yield, which was immediately used in the next step without further purification: ^1H NMR ($CDCl_3$) δ 1.97 (s, 3 H), 1.99 (s, 3 H), 3.78 (s, 3 H), 6.20 (d, J = 7.2 Hz, 1 H), 6.91 (d, J = 7.3 Hz, 2 H), 7.12 (d, J = 7.3 Hz, 2 H), 8.43 (d, J = 7.2 Hz, 1 H).

In the same manner, *N*-(4-methoxyphenyl)-(*E*)-2-butenaldi-

Table 5. Effects of Substituents at 3′- and 3′-N-Positions on Cytotoxicity (IC_{50}, nM)[a]

entry	taxoid	R^1	R^2	A121	A549	HT-29	MCF-7	MCF7-R
1	paclitaxel	phenyl	phenyl	6.1	3.6	3.2	1.7	299
2	docetaxel	phenyl	*t*-BuO	1.2	1.0	1.2	1.0	235
3	SB-T-1001	phenyl	*t*-BuO	3.3	0.8	2.1	1.9	>1000
4	SB-T-1011	phenyl	*t*-BuO	6.2	2.1	1.8	1.8	543
5	SB-T-1012	phenyl	phenyl	105	33	24	11	>1000
6	**16a**	2-furyl	*t*-BuO	0.4	0.5	0.6	0.5	135
7	**17a**	$(CH_3)_2C{=}CH$	*t*-BuO	1.7	0.2	0.5	0.5	54
8	**18a**	(*E*)-$CH_3CH{=}CH$	*t*-BuO	2.6	1.2	1.9	1.6	762
9	**19a**	$(CH_3)_3CCH_2$	*t*-BuO	106	51	52	48	>1000
10	**20a**	phenyl	*n*-C_5H_{11}	330	389	157	13	>1000
11	**21d**	$(CH_3)_2C{=}CH$	*n*-C_5H_{11}	12	18	16	3.2	321
12	**22a**	$(CH_3)_2CHCH_2$	*t*-BuO	1.0	1.8	3.4	2.7	385
13	**23a**	$CH_3(CH_2)_2$	*t*-BuO	2.1	4.4	3.8	4.2	265

[a] The concentration of compound which inhibits 50% (IC_{50}, nM) of the growth of human tumor cell line: A121 (ovarian carcinoma), A549 (non-small-cell lung carcinoma), HT-29 (colon carcinoma), MCF-7 (mammary carcinoma), and MCF7-R (mammarian carcinoma 180-fold resistant to doxorubicin) after 72 h drug exposure according to the method developed by Skehan et al.[34] (see the Experimental Section).

Table 6. Effects of the Substituents at C-10 on Cytotoxicity (IC_{50}, nM)[a]

taxoid	*R^3	A121	A549	HT-29	MCF-7	MCF7-R	MCF7-R/MCF-7
paclitaxel	CH_3CO	6.1	3.6	3.2	1.7	299	176
docetaxel	H	1.2	1.0	1.2	1.0	235	235
SB-T-1011	H	6.2	2.1	1.8	1.8	543	302
SB-T-1012	H	105	33	24	11	>1000	NA
16a	H	0.4	0.5	0.6	0.5	135	270
16b	CH_3CO	0.4	0.5	0.6	0.5	49	96
17a	H	1.7	0.2	0.5	0.5	72	120
17b	CH_3CO	1.5	1.4	2.4	3.3	36	11
17c	CH_3CH_2CO	0.7	0.5	0.6	0.2	26	130
17d	cyclopropane-CO	0.5	0.5	1.0	0.4	28	70
17e	$(CH_3)_2N$-CO	0.7	0.6	1.2	0.4	33	83
17f	(*E*)-$CH_3CH{=}CHCO$	0.8	0.5	1.5	0.4	17	43
17g	CH_3O-CO	0.6	0.5	0.7	0.3	38	127
18a	H	2.6	1.2	1.9	1.6	762	476
18b	CH_3CO	2.4	0.4	3.0	1.6	72	45
21d	cyclopropane-CO	12	18	16	3.2	321	100
21e	$(CH_3)_2N$-CO	4.8	5.5	5.1	1.7	295	56
21f	(*E*)-$CH_3CH{=}CHCO$	17	25	28	2.1	137	65
22a	H	2.5	1.4	4.2	3.0	189	63
22b	CH_3CO	1.2	0.7	1.5	1.1	36	33
22d	cyclopropane-CO	1.1	1.2	3.3	0.7	22	31
22e	$(CH_3)_2N$-CO	0.6	0.6	1.3	0.6	22	37
23a	H	2.1	4.4	3.8	4.2	385	92
23b	CH_3CO	2.3	4.7	4.8	4.6	201	44

[a] See the footnote of Table 5.

mine (**2c**) and *N*-(4-methoxyphenyl)-3,3-dimethylbutanaldimine (**2d**) were prepared and used without further purification.

Asymmetric Synthesis of 4-Substituted (3*R*,4*S*)-3-[(Trialkylsilyl)oxy]azetidin-2-ones 3. Method A: (3*R*,4*S*)-3-[(Triethylsilyl)oxy]-4-(2,2-dimethylpropyl)azetidin-2-one (3d′). To a solution of diisopropylamine (1.16 mL, 8.3 mmol) in THF (15 mL) was added *n*-BuLi (3.33 mL, 8.3 mmol; 2.5 M in hexanes) at 0 °C. The solution was stirred at 0 °C for 30 min followed by the addition of **1a** (2.5 g, 6.4 mmol) in THF (20 mL) at −78 °C over a 1 h period via cannula. The mixture was stirred for 2 h followed by the addition of imine **2d** at −85 °C over a period of 1 h. The reaction mixture was stirred overnight at −85 °C and allowed to slowly warm to room temperature. The reaction was quenched by the addition of aqueous saturated NH_4Cl. The aqueous layer was extracted with ether (2 × 30 mL). The combined organic layers were washed with 3% HCl and brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel (hexanes/EtOAc = 5/1) to give an inseparable mixture of (3*R*,4*S*)-3-[(triisopropylsilyl)-oxy]-4-(2,2-dimethylpropyl)azetidin-2-one (**3d**) and (−)-10-(dicyclohexylsulfamoyl)-D-isoborneol, which was used in the next step without further purification. The chiral HPLC analysis of this mixture showed that the enantiomeric purity of **3d** was 96% ee.

To a solution of a mixture of **3d** and (−)-10-(dicyclohexylsulfamoyl)-D-isoborneol, thus obtained, in THF (23 mL) was added *n*-Bu_4NF (7 mL, 7.03 mmol; 1.0 M in THF) at 0 °C. After 20 min, the solvent was evaporated and the resulting crude oil was purified by column chromatography on silica gel (hexanes/EtOAc = 5/1) to afford 3-hydroxy-4-(2,2-dimethylpropyl)azetidin-2-one (936 mg, 94% yield for two steps) as a white solid: mp 185−186 °C; $[\alpha]^{20}_D$ +51.81° (*c* 8.3, CH_3OH); ^1H NMR (CD_3OD) δ 0.89 (s, 3 H), 1.28 (dd, J = 14.6, 8.0 Hz, 1 H), 1.62 (dd, J = 14.5, 4.0 Hz, 1 H), 3.23 (bs, 1 H), 3.73 (m, 1 H), 4.72 (d, J = 4.7 Hz, 1 H); ^{13}C NMR (CD_3OD) δ 28.75, 29.35, 42.82, 52.72, 76.54, 173.2. Anal. ($C_8H_{15}NO_2$) C, H, N.

To a solution of (3*R*,4*S*)-3-hydroxy-4-(2,2-dimethylpropyl)-azetidin-2-one (600 mg, 3.87 mmol) in DMF (5 mL) and imidazole (0.66 g, 2.5 equiv) was added Et_3SiCl (0.68 mL, 4.06 mmol) with stirring. The mixture was stirred overnight at room temperature, and then additional Et_3SiCl (0.07 mL) was added to complete the reaction. The reaction mixture was diluted with ether and washed with water and 3% HCl. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel (hexanes/EtOAc = 2/1) provided **3d′** (888 mg, 88% yield) as a colorless oil: $[\alpha]^{20}_D$ +36.7° (*c* 2.4, $CHCl_3$); ^1H NMR ($CHCl_3$) δ 0.65 (bq, J = 7.9 Hz, 6 H), 0.92 (s, 9 H), 0.96 (t, J = 7.9 Hz, 9 H), 1.37 (dd, J = 14.7, 8.4 Hz, 1 H), 1.66 (dd, J = 14.7, 3.5 Hz, 1 H), 3.76 (ddd, J = 8.4, 4.7, 3.5 Hz, 1 H), 4.82 (dd, J = 4.7, 2.8 Hz, 1 H), 6.7 (bs, 1 H); ^{13}C NMR ($CDCl_3$) δ 4.67, 6.59, 29.81, 43.35, 52.89, 77.76, 170.13. Anal. ($C_{14}H_{29}NO_2Si$) C, H, N.

Method B: (3*R*,4*S*)-3-[(Triisopropylsilyl)oxy]-4-(2-methyl-1-propenyl)azetidin-2-one (3b). To a solution of *i*-Pr_2NH

(0.93 mL, 6.64 mmol) in dry THF (10 mL) was added *n*-BuLi (2.66 mL, 6.64 mmol; 2.5 M in hexanes) at 0 °C. After stirring for 10 min, the reaction mixture was cooled to −84 °C. A solution of **1a** (2.00 g, 5.12 mmol) in dry THF (5 mL) was added via cannula. After the mixture stirred for an additional 2 h, a solution of imine **2b** (1.65 g, 8.70 mmol) in dry THF (5 mL) was added via cannula. The reaction mixture was stirred for 2 h and then allowed to warm to room temperature overnight with stirring. The reaction was quenched with aqueous saturated NH_4Cl (50 mL), and the mixture was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with 10% aqueous $NaHCO_3$ (100 mL) and brine and then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give the crude product, which was purified by column chromatography (hexanes/EtOAc = 15/1, then 6/1) to give (3*R*,4*S*)-1-(4-methoxyphenyl)-3-[(triisopropylsilyl)oxy]-4-(2-methyl-1-propenyl)azetidin-2-one (1.24 g, 60% yield) as a light yellow oil. The enantiomeric excess of this β-lactam was 94% ee. based on the chiral HPLC analysis: ^{1}H NMR ($CDCl_3$) δ 0.95−1.18 (m, 21 H), 1.64 (s, 3 H), 1.75 (s, 3 H), 4.43 (dd, J = 9.5, 4.7 Hz, 1 H), 4.98 (dd, J = 4.7, 2.3 Hz, 1 H), 5.31 (bd, J = 9.5 Hz, 1 H), 6.25 (bs, 1 H). Anal. ($C_{23}H_{37}NO_3Si$) C, H, N.

To a solution of (3*R*,4*S*)-1-(4-methoxyphenyl)-3-[(triisopropylsilyl)oxy]-4-(2-methyl-2-propenyl)azetidin-2-one (1.01 g, 5.19 mmol) in acetonitrile (90 mL) were added dropwise ammonium cerium(IV) nitrate (10.15 g, 18.5 mmol) in water (135 mL) and additional water (210 mL) over a period of 1.5 h at −5 °C. The mixture was diluted with water (200 mL) and extracted with ethyl acetate (200 mL). The organic layer was washed successively with saturated $NaHCO_3$ (100 mL), saturated $NaHSO_3$ (100 mL), and again with saturated $NaHCO_3$ (100 mL). The organic layer was then dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was submitted to column chromatography on silica gel (hexane/EtOAc = 3:1, then 2:1) affording **3b** (663 mg, 90% yield) as a light yellow solid: mp 85−86 °C; ^{1}H NMR ($CDCl_3$) δ 0.97−1.21 (m, 21 H), 1.68 (d, J = 2.3 Hz, 3 H), 1.19 (d, J = 2.3 Hz, 3 H), 4.43 (dd, J = 9.5, 4.7 Hz, 1 H), 4.98 (dd, J = 4.7, 2.3 Hz, 1 H), 5.31 (d, J = 9.5 Hz, 1 H). Anal. ($C_{16}H_{31}NO_2Si$) C, H, N.

In the same manner, (3*R*,4*S*)-3-[(triisopropylsilyl)oxy]-4-((*E*)-1-propenyl)azetidin-2-one (**3c**) was prepared. **3c:** 72% yield; light yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.01−1.14 (m, 21 H), 1.76 (d, J = 6.4 Hz, 3 H), 4.13 (dd, J = 8.0, 4.7 Hz, 1 H), 4.97 (dd, J = 4.7, 2.3 Hz, 1 H), 5.56 (dd, J = 15.5, 8.0 Hz, 1 H), 5.70 (dq, J = 15.8, 6.4 Hz, 1 H), 5.89 (bs, 1 H). The enantiomeric excess was 97% ee. based on the chiral HPLC analysis.

Preparation of (3*R*,4*S*)-1-(*tert*-Butoxycarbonyl)-3-[(trialkylsilyl)oxy]-4-substituted-azetidin-2-ones 4 and 5. A typical procedure is described for the preparation of (3*R*,4*S*)-1-(*tert*-butoxycarbonyl)-3-[(triisopropylsilyl)oxy]-4-(2-methyl-1-propenyl)azetidin-2-one (**4b**). To a solution of β-lactam **3b** (503 mg, 1.69 mmol), (*N*,*N*-dimethylamino)pyridine (DMAP) (20 mg), and triethylamine (0.71 mL, 5.07 mmol) in dichloromethane (20 mL) at 0 °C was added a solution of di-*tert*-butyl dicarbonate (922 mg, 4.23 mmol) in dichloromethane (5 mL). The reaction mixture was stirred at room temperature for 2 h, and the reaction was quenched with saturated NH_4Cl. The mixture was extracted with ethyl acetate and the organic layer washed with brine, dried over magnesium sulfate, and concentrated *in vacuo*. Purification of the crude product by column chromatography on silica gel (hexanes/EtOAc = 5/1) afforded the *N*-*t*-Boc-β-lactam **4b** (659 mg, 98% yield) as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.02−1.20 (m, 21 H), 1.48 (s, 9 H), 1.77 (d, J = 1.0 Hz, 3 H), 1.79 (d, J = 1.0 Hz, 3 H), 4.75 (dd, J = 9.8, 5.6 Hz, 1 H), 4.98 (d, J = 5.6 Hz, 1 H), 5.28 (dd, J = 9.8, 1.0 Hz, 1 H).

In the same manner, (3*R*,4*S*)-1-(*tert*-butoxycarbonyl)-3-[(triisopropylsilyl)oxy]-4-(2-furyl)azetidin-2-one (**4a**), (3*R*,4*S*)-1-(*tert*-butoxycarbonyl)-3-[(triisopropylsilyl)oxy]-4-((*E*)-1-propenyl)azetidin-2-one (**4c**), and (3*R*,4*S*)-1-(*tert*-butoxycarbonyl)-3-[(triethysilyl)oxy]-4-(2,2-dimethylpropyl)azetidin-2-one (**4d**) were prepared. (3*R*,4*S*)-1-*n*-Hexanoyl-3-[(*tert*-butyldimethylsilyl)oxy]-4-phenylazetidin-2-one (**5a**) and (3*R*,4*S*)-1-*n*-hexanoyl-3-[(triisopropylsilyl)oxy]-4-(2-methyl-1-propenyl)azetidin-2-one (**5b**) were prepared by the reactions of *n*-hexanoyl chloride with 3-[(*tert*-butyldimethylsilyl)oxy]-4-phenylazetidin-2-one (**3g**)[24] and 3-[(triisopropylsilyl)oxy]-4-(2-methyl-1-propenyl)azetidin-2-one (**3b**), respectively, in the presence of triethylamine and DMAP in dichloromethane.

4a: 98% yield; pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 0.87−1.09 (m, 21 H), 1.43 (s, 9 H), 5.10 (d, J = 5.6 Hz, 1 H), 5.14 (d, J = 5.6, 1 H), 6.34−6.38 (m, 2 H), 7.40 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 11.68, 17.39, 17.45, 27.87, 56.17, 77.83, 83.47, 109.75, 110.47, 142.75, 147.76, 147.96, 165.80. Anal. ($C_{21}H_{35}O_5NSi$) C, H, N.

4c: 91% yield; slightly yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.02−1.08 (m, 21 H), 1.48 (s, 9 H), 1.74 (dd, J = 6.4, 1.2 Hz, 3 H), 4.44 (dd, J = 8.6, 5.8 Hz, 1 H), 4.95 (d, J = 5.8 Hz, 1 H), 5.54 (ddd, J = 15.4, 8.6, 1.2 Hz, 1 H), 5.84 (dq, J = 15.4, 6.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 11.76, 17.52, 17.95, 27.97, 61.06, 83.06, 124.80, 132.72, 148.22, 166.07. Anal. ($C_{20}H_{31}NO_4Si$) C, H, N.

4d: 98% yield; colorless oil: $[\alpha]^{20}_D$ +112.4° (*c* 1.14, $CHCl_3$); ^{1}H NMR (250 MHz, $CHCl_3$) δ 0.55 (m, 6 H), 0.80 (s, 9 H), 0.84 (t, J = 8.0 Hz, 9 H), 1.37 (s, 9 H), 1.48 (d, J = 13.5 Hz, 1 H), 1.83 (dd, J = 13.5, 9.4 Hz, 1 H), 3.93 (dd, J = 9.4, 5.8 Hz, 1 H), 4.80 (d, J = 5.8 Hz, 1 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 4.67, 6.59, 28.03, 29.48, 29.66, 38.15, 56.11, 75.82, 83.02, 148.0, 166.2. Anal. Calcd. for $C_{19}H_{37}NO_4Si$: C, 61.41; H, 10.09; N, 3.77. Found: C, 61.65; H, 9.94; N, 3.84.

5a: 72% yield; yellow oil; $[\alpha]^{20}_D$ +87.5° (*c* 0.24, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.17 (s, 3 H), 0.46 (s, 3 H), 0.65 (s, 9 H), 0.88 (bt, 3 H), 1.29−1.35 (m, 4 H), 1.61−1.69 (m, 2 H), 2.65−2.86 (m, 2 H), 5.06 (d, J = 5.8 Hz, 1 H), 5.13 (d, J = 5.8 Hz, 1 H), 7.19−7.33 (m, 5 H). Anal. ($C_{21}H_{33}NO_3Si$) C, H, N.

5b: 89% yield; yellow oil; ^{1}H NMR ($CDCl_3$) δ 0.85−0.92 (m, 3 H), 1.00−1.16 (m, 21 H), 1.25−1.33 (m, 4 H), 1.54−1.68 (m, 2 H), 1.76 (d, J = 0.9 Hz, 3 H), 1.79 (d, J = 0.9 Hz, 3 H), 2.66 (t, J = 7.5 Hz, 2 H), 4.80 (dd, J = 9.6, 6.0 Hz, 1 H), 4.99 (d, J = 6.0 Hz, 1 H), 5.21 (dd, J = 9.6, 0.9 Hz, 1 H).

7-(Triethylsilyl)-14β-hydroxy-10-deacetylbaccatin III (7).[33] To a solution of 14β-OH-DAB (**6**) (800 mg, 1.47 mmol) in pyridine (60 mL) and *N*,*N*-dimethylformamide (60 mL) was added Et_3SiCl (2.50 mL, 14.7 mmol) dropwise via syringe at room temperature. After 4 h, the reaction was quenched by adding ethyl acetate (200 mL) and pyridine was removed by successive washing with aqueous saturated $CuSO_4$ until no color change was observed. The organic layer was washed with water, dried over $MgSO_4$ and concentrated. Silica gel chromatography (hexane/ethyl acetate = 1/1) afforded 7-TES-14β-OH-DAB (**7**) (928 mg, 96% yield) as a white solid: ^{1}H NMR ($CDCl_3$) δ 0.50 (m, 6 H), 0.97 (m, 9 H), 1.21 (s, 3 H), 1.58 (s, 3 H), 1.58 (s, 3 H), 1.73 (s, 3 H), 1.85 (dt, 1 H), 1.99 (s, 3 H), 2.23 (s, 3 H), 2.24 (s, 2 H), 2.47 (ddd, 1 H), 3.94 (d, J = 7.2 Hz, 1 H), 4.14 (d, J = 8.4 Hz, 1 H), 4.32 (d, J = 8.1 Hz, 1 H), 4.41 (d, J = 6.3 Hz, 1 H), 4.84 (t, 1 H), 4.94 (d, J = 8.4 Hz, 1 H), 5.14 (s, 1 H), 5.19 (s, 1 H), 5.58 (d, J = 7.2 Hz, 1 H), 7.40 (t, 2 H), 7.54 (t, 1 H), 8.10 (d, 2 H); ^{13}C NMR ($CDCl_3$) δ 5.1, 6.7, 9.9, 15.1, 19.5, 22.6, 26.8, 37.2, 38.6, 42.7, 47.0, 57.9, 67.9, 72.9, 74.7, 74.8, 76.5, 78.8, 80.7, 84.2, 128.6, 129.4, 130.0, 133.6, 135.1, 141.9, 167.0, 170.7, 210.3; IR ($CDCl_3$) 3465, 2952, 2884, 1725, 1702, 1602, 1443, 1361, 1273, 1237, 1173, 1138, 1102, 1067, 1020, 997, 820, 738, 709 cm^{-1}.

7-(Triethylsilyl)-14β-hydroxy-10-deacetylbaccatin III 1,14-Carbonate (8). To a solution of 7-TES-14β-OH-DAB (**7**)-(600 mg, 0.888 mmol) in dry dichloromethane (100 mL) were added pyridine (1.44 mL, 17.8 mmol) and phosgene (1.01 mL, 1.95 mmol) dropwise via a syringe at 0 °C. After 10 min, the reaction was quenched with aqueous saturated NH_4Cl (20 mL) at 0 °C and the mixture allowed to warm to room temperature. The reaction mixture was extracted with ethyl acetate (200 mL), and the organic layer was washed with water, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel (hexanes/EtOAc = 1/1) afforded **8** (498 mg, 80% yield) as a white solid: mp 139−142 °C; ^{1}H NMR ($CDCl_3$) δ 0.54 (m, 12 H), 0.96 (m, 18 H), 1.04 (s, 3 H), 1.19 (s, 3 H), 1.66 (s, 3 H), 1.84 (dt, 1 H), 2.02 (s, 3 H), 2.24 (s, 2 H), 2.27 (s, 3 H), 2.48 (m, 1 H), 3.90 (d, J = 7.2 Hz, 1 H), 4.13 (d, J = 8.4 Hz, 1 H), 4.27 (d, J = 8.1 Hz, 1 H), 4.41 (dd, J = 6.6 Hz, 1 H), 4.80 (t, 1 H), 4.92 (d, J = 8.4 Hz, 1 H), 5.21 (s, 1 H), 5.60 (d, J = 6.9 Hz, 1 H), 7.43 (t, 2 H), 7.56 (t, 1 H), 8.08 (d, 2 H); ^{13}C NMR ($CDCl_3$) δ 5.2, 5.9, 6.8, 6.9, 10.3, 14.6, 19.4, 22.7, 26.6, 37.3, 38.4, 42.7,

47.2, 58.6, 67.8, 72.8, 74.9, 75.9, 76.7, 78.7, 80.9, 84.0, 128.5, 129.5, 130.0, 133.4, 136.8, 137.9, 167.1, 170.7, 205.8; IR ($CDCl_3$) 3516, 2952, 2876, 1716, 1452, 1367, 1271, 1239, 1143, 1106, 1069, 1003, 985, 866, 820, 738, 709 cm^{-1}.

General Procedure for Modification at the C-10 Position of 7-TES-14β-OH-DAB 1,14-Carbonate (8). A typical procedure is described for the preparation of 7-(triethylsilyl)-10-acetyl-14β-hydroxybaccatin 1,14-carbonate (**9b**): To a solution of **8** (120 mg, 0.17 mmol) in THF (5 mL) was added 1.0 M LiHMDS in hexane (0.20 mL, 0.20 mmol) at −40 °C. After the reaction mixture stirred for 10 min, freshly distilled acetyl chloride (15 μL, 0.30 mmol) was added dropwise at −40 °C. The mixture was allowed to warm to 0 °C over a period of 30 min. The reaction mixture was then concentrated *in vacuo*. Purification by flash chromatography on silica gel (hexanes/EtOAc = 1/1) afforded **9b** (124 mg, 95% yield) as a white solid: ^{1}H NMR ($CDCl_3$) δ 0.51−0.62 (m, 6 H), 0.92 (t, *J* = 7.9 Hz, 9 H), 1.13 (s, 3 H), 1.31 (s, 3 H), 1.71 (s, 3 H), 1.88 (m, 1 H), 2.19 (s, 6 H), 2.30 (s, 3 H), 2.53 (m, 1 H), 2.98 (bs, 1 H), 3.71 (d, *J* = 7.3 Hz, 1 H), 4.19 (d, *J* = 8.3 Hz, 1 H), 4.30 (d, *J* = 8.3 Hz, 1 H), 4.46 (dd, *J* = 10.6, 6.5 Hz, 1 H), 4.79 (d, *J* = 5.7 Hz, 1 H), 4.94 (d, *J* = 8.5 Hz, 1 H), 4.98 (bt, 1 H), 6.08 (d, *J* = 7.3 Hz, 1 H), 6.43 (s, 1 H), 7.47 (t, *J* = 7.6 Hz, 2 H), 7.61 (t, *J* = 7.4 Hz, 1 H), 8.02 (d, *J* = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 5.25, 6.71, 10.07, 14.77, 20.79, 21.63, 22.32, 25.90, 31.57, 36.98, 41.46, 46.61, 58.79, 69.41, 71.97, 72.03, 74.99, 75.98, 80.37, 83.95, 84.00, 88.34, 128.16, 128.89, 129.83, 133.04, 134.14, 141.78, 152.76, 164.78, 169.16, 170.41, 200.70.

In the same manner, **9a**,**c**−**g** were prepared.

7,10-Bis(triethylsilyl)-14β-hydroxy-10-deacetylbaccatin III 1,14-carbonate (9a): Et_3SiCl (0.10 mL, 0.60 mmol) was used instead of an acyl chloride; 84% yield; white solid; mp 145−148 °C; $[\alpha]^{20}_D$ −54.5° (*c* 0.11, $CHCl_3$); ^{1}H NMR ($CDCl_3$); δ 0.49−0.62 (m, 12 H), 0.91−1.05 (m, 18 H), 1.19 (s, 3 H), 1.22 (s, 3 H), 1.79 (s, 3 H), 1.82 (dt, *J* = 9.3 Hz, 1 H), 2.10 (s, 3 H), 2.31 (s, 3 H), 2.49 (m, 1 H), 3.74 (d, *J* = 7.2 Hz, 1 H), 4.19 (d, *J* = 8.4 Hz, 1 H), 4.34 (d, *J* = 8.4 Hz, 1 H), 4.74 (d, *J* = 5.7 Hz, 1 H), 4.95 (d, *J* = 9.3 Hz, 1 H), 5.11 (s, 1 H), 6.02 (d, *J* = 7.2 Hz, 1 H), 7.47 (t, 2 H), 7.60 (t, 1 H), 8.02 (d, 2 H); ^{13}C NMR ($CDCl_3$) δ 5.6, 6.3, 7.2, 7.3, 10.8, 14.7, 21.5, 22.6, 26.1, 37.4, 41.8, 59.1, 70.1, 71.9, 72.8, 76.0, 77.4, 80.7, 84.2, 84.8, 89.1, 128.7, 129.2, 130.2, 134.4, 136.6, 137.3, 153.6, 165.2, 170.7, 205.2. Anal. ($C_{42}H_{62}O_{12}Si_2$) C, H, N.

7-(Triethylsilyl)-10-propanoyl-14β-hydroxy-10-deacetylbaccatin III 1,14-carbonate (9c): 74% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.58 (m, 6 H), 0.91 (m, 9 H), 1.12 (s, 3 H), 1.19 (t, *J* = 7.45 Hz, 3 H), 1.22 (s, 3 H), 1.69 (s, 3 H), 1.86 (t, *J* = 12.0 Hz, 1 H), 2.17 (s, 3 H), 2.27 (s, 3 H), 2.47 (m, 3 H), 3.32 (d, *J* = 5.3 Hz, 1 H), 3.69 (d, *J* = 7.2 Hz, 1 H), 4.17 (d, *J* = 8.4 Hz, 1 H), 4.28 (d, *J* = 8.4 Hz, 1 H), 4.45 (dd, *J* = 10.5, 6.6 Hz, 1 H), 4.77 (d, *J* = 5.7 Hz, 1 H), 4.93 (m, 2 H), 6.05 (d, *J* = 7.2 Hz, 1 H), 6.42 (s, 1 H), 7.45 (t, *J* = 7.9 Hz, 2 H), 7.61 (t, *J* = 7.2 Hz, 1 H), 8.01 (d, *J* = 7.5 Hz, 2 H).

7-(Triethylsilyl)-10-(cyclopropylcarbonyl)-14β-hydroxy-10-deacetylbaccatin III 1,14-carbonate (9d): 91% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.56 (q, *J* = 8.1 Hz, 6 H), 0.85−1.01 (m, 13 H), 1.12 (s, 3 H), 1.30 (s, 3 H), 1.68−1.83 (m, 4 H), 1.85−1.93 (m, 1 H), 2.18 (s, 3 H), 2.27 (s, 3 H), 2.40−2.56 (m, 1 H), 3.30 (d, *J* = 5.5 Hz, 1 H), 3.69 (d, *J* = 7.1 Hz, 1 H), 4.16 (d, *J* = 8.3 Hz, 1 H), 4.29 (d, *J* = 8.3 Hz, 1 H), 4.43 (dd, *J* = 10.4, 6.5 Hz, 1 H), 4.78 (d, *J* = 5.6 Hz, 1 H), 4.90−4.98 (m, 2 H), 6.06 (d, *J* = 7.2 Hz, 1 H), 6.41 (s, 1 H), 7.46 (t, *J* = 7.4 Hz, 2 H), 7.60 (t, *J* = 7.4 Hz, 1 H), 8.01 (d, *J* = 7.4 Hz, 2 H).

7-(Triethylsilyl)-10-(*N*,*N*-dimethylcarbamoyl)-14β-hydroxy-10-deacetylbaccatin III 1,14-carbonate (9e): 86% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.55 (q, *J* = 7.6 Hz, 6 H), 0.90 (t, *J* = 7.6 Hz, 9 H), 1.12 (s, 3 H), 1.30 (s, 3 H), 1.70 (s, 3 H), 1.81−1.91 (m, 1 H), 2.23 (s, 3 H), 2.28 (s, 3 H), 2.44−2.56 (m, 1 H), 2.93 (s, 3 H), 3.06 (s, 3 H), 3.45 (d, *J* = 5.6 Hz, 1 H), 3.70 (d, *J* = 7.2 Hz, 1 H), 4.16 (d, *J* = 8.4 Hz, 1 H), 4.29 (d, *J* = 8.4 Hz, 1 H), 4.44 (dd, *J* = 10.4, 6.5 Hz, 1 H), 4.77 (d, *J* = 5.7 Hz, 1 H), 4.91−4.99 (m, 2 H), 6.06 (d, *J* = 7.2 Hz, 1 H), 6.31 (s, 1 H), 7.46 (t, *J* = 7.4 Hz, 2 H), 7.60 (t, *J* = 7.4 Hz, 1 H), 8.01 (d, *J* = 7.4 Hz, 2 H).

7-(Triethylsilyl)-10-((*E*)-2-butenoyl)-14β-hydroxy-10-deacetylbaccatin III 1,14-carbonate (9f): 54% isolated yield (79% based on the consumed **8**); white solid; ^{1}H NMR ($CDCl_3$) δ 0.55 (t, *J* = 7.6 Hz, 6 H), 0.89 (t, *J* = 7.6 Hz, 9 H), 1.09 (s, 3 H), 1.32 (s, 3 H), 1.70 (s, 3 H), 1.74−1.81 (m, 1 H), 1.91 (dd, *J* = 6.7, 1.3 Hz, 3 H), 2.19 (s, 3 H), 2.27 (s, 3 H), 2.44−2.57 (m, 1 H), 3.53 (d, *J* = 5.5 Hz, 1 H), 3.71 (d, *J* = 7.1 Hz, 1 H), 4.16 (d, *J* = 8.4 Hz, 1 H), 4.29 (d, *J* = 8.4 Hz, 1 H), 4.45 (dd, *J* = 10.3, 6.6 Hz, 1 H), 4.77 (d, *J* = 5.6 Hz, 1 H), 4.94 (m, 2 H), 5.96 (dd, *J* = 15.4, 1.3 Hz, 1 H), 6.07 (d, *J* = 7.1 Hz, 1 H), 6.44 (s, 1 H), 7.09 (dq, *J* = 15.4, 6.8 Hz, 1 H), 7.46 (t, *J* = 7.4 Hz, 2 H), 7.60 (t, *J* = 7.4 Hz, 1 H), 8.01 (d, *J* = 7.4 Hz, 2 H).

7-(Triethylsilyl)-10-(methoxycarbonyl)-14β-hydroxy-10-deacetylbaccatin III 1,14-carbonate (9g): 65% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.58 (m, 6 H), 0.92 (m, 9 H), 1.14 (s, 3 H), 1.29 (s, 3 H), 1.65 (s, 1 H), 1.71 (s, 3 H), 1.90 (m, 1 H), 2.20 (s, 3 H), 2.29 (s, 3 H), 2.53 (m, 1 H), 3.09 (bs, 1 H), 3.67 (d, *J* = 7.1 Hz, 1 H), 3.82 (s, 3 H), 4.17 (d, *J* = 8.5 Hz, 1 H), 4.29 (d, *J* = 8.5 Hz, 1 H), 4.44 (dd, *J* = 10.5, 6.6 Hz, 1 H), 4.78 (d, *J* = 5.6 Hz, 1 H), 4.93 (d, *J* = 8.3 Hz, 1 H), 5.00 (bs, 1 H), 6.07 (d, *J* = 7.2 Hz, 1 H), 6.23 (s, 1 H), 7.46 (t, *J* = 7.4 Hz, 2 H), 7.61 (t, *J* = 7.4 Hz, 1 H), 8.01 (d, *J* = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 5.3, 6.7, 10.0, 14.2, 14.9, 21.1, 21.4, 22.3, 25.7, 30.9, 36.9, 41.3, 46.6, 55.2, 58.6, 60.5, 69.4, 71.7, 72.0, 76.0, 78.4, 80.2, 83.9, 84.1, 88.4, 128.1, 128.9, 129.8, 132.2, 134.2, 143.3, 152.9, 154.7, 164.8, 170.4, 200.5.

General Procedure for the Syntheses of Protected Taxoids 10−15 through the Coupling of β-Lactams 4 and 5 with a Protected Baccatin (9). A typical procedure is described for the preparation of 2′-(triisopropylsilyl)-3′-dephenyl-3′-(2-furyl)-7,10-bis(triethylsilyl)-14β-hydroxydocetaxel 1,14-carbonate (**10a**): 7,10-Bis(TES)-14β-OH-DAB 1,14-carbonate (**9a**) (100 mg, 0.123 mmol) was dissolved in dry THF (8 mL) under nitrogen. The solution was cooled to −45 °C. LiHMDS (0.15 mL; 1.0 M solution in THF) was added dropwise, and the solution was stirred for 2 min. β-Lactam **4a** (75 mg, 0.184 mmol) was then added dropwise, and the mixture was stirred at −45 °C for 7−10 min. The reaction was quenched with saturated NH_4Cl (2 mL); the mixture was extracted with ethyl acetate (2 × 15 mL) and dried over anhydrous $MgSO_4$. After evaporation of the solvent, the residue was purified by column chromatography on silica gel using hexane/EtOAc (4/1) as the eluant to afford the coupling product **10a** (117 mg, 78%) as a white solid: ^{1}H NMR ($CDCl_3$) δ 0.54−0.73 (m, 12 H), 0.93−1.05 (m, 39 H), 1.27 (s, 3 H), 1.32 (s, 3 H), 1.37 (s, 9 H), 1.71 (s, 3 H), 1.86 (s, 3 H), 1.91 (m, 1 H), 2.49 (s, 3 H), 2.53 (m, 1 H), 3.76 (d, *J* = 7.4 Hz, 1 H), 4.21 (d, *J* = 8.5 Hz, 1 H), 4.26 (d, *J* = 8.5 Hz, 1 H), 4.38 (dd, *J* = 6.5, 10.5 Hz, 1 H), 4.82−4.91 (m, 2 H), 5.06 (bs, 1 H), 5.12 (s, 1 H), 5.25 (bd, *J* = 9.5 Hz, 1 H), 5.42 (bd, *J* = 9.5 Hz, 1 H), 6.09 (d, *J* = 7.4 Hz, 1 H), 6.26 (bs, 1 H), 6.35 (bs, 1 H), 6.41 (d, *J* = 6.4 Hz, 1 H), 7.37 (bs, 1 H), 7.46 (t, *J* = 7.4 Hz, 2 H), 7.57 (t, *J* = 7.2 Hz, 1 H), 8.03 (d, *J* = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 5.19, 5.92, 6.81, 6.92, 10.52, 12.39, 13.76, 17.76, 17.79, 21.90, 22.75, 25.63, 28.17, 29.68, 37.11, 41.80, 46.28, 52.80, 58.68, 69.53, 72.39, 73.29, 74.21, 75.09, 76.19, 79.82, 80.49, 80.58, 83.85, 88.07, 107.67, 110.83, 128.14, 128.90, 129.95, 131.33, 133.85, 138.50, 141.92, 151.89, 155.06, 164.85, 170.65, 170.83, 203.96; IR (KBr disk) 3448, 2954, 2872, 1825, 1772, 1731, 1490, 1366, 1243, 1143, 1084 cm^{-1}. Anal. ($C_{63}H_{97}NO_{17}NSi_3$) C, H, N.

In the same manner, **10b**−**15** were prepared. The protected taxoids **11a**, **12a**, and **14a** were used in the next step (deprotection) without spectroscopic characterization.

2′-(Triisopropylsilyl)-3′-dephenyl-3′-(2-furyl)-7-(triethylsilyl)-14β-hydroxy-10-deacetylbaccatin III 1,14-carbonate (10b): 78% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.52−0.63 (m, 12 H), 0.85−1.10 (m, 30 H), 1.28 (s, 3 H), 1.34 (s, 3 H), 1.36 (s, 9 H), 1.73 (s, 3 H), 1.90 (m, 1 H), 2.02 (s, 3 H), 2.19 (s, 3 H), 2.49 (s, 3 H), 2.54 (m, 1 H), 3.73 (d, *J* = 7.4 Hz, 1 H), 4.21 (d, *J* = 8.4 Hz, 1 H), 4.27 (d, *J* = 8.4 Hz, 1 H), 4.45 (dd, *J* = 10.4, 6.5 Hz, 1 H), 4.80−4.90 (m, 2 H), 5.07 (bs, 1 H), 5.23 (bd, *J* = 9.6 Hz, 1 H), 5.42 (bd, *J* = 9.6 Hz, 1 H), 6.10 (d, *J* = 7.4 Hz, 1 H), 6.25 (bs, 1 H), 6.34 (bs, 1 H), 6.43 (m, 2 H), 7.37 (bs, 1 H), 7.47 (t, *J* = 7.3 Hz, 2 H), 7.57 (t, *J* = 7.2 Hz, 1 H), 8.03 (d, *J* = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 5.22, 6.68, 10.12, 12.42, 14.35, 17.78, 20.69, 22.44, 22.69, 25.65, 28.16, 36.99, 41.82, 46.25, 52.78, 58.68, 69.27, 71.92, 73.24, 74.03, 74.24, 76.03, 79.73, 80.52, 80.54, 84.03, 87.84, 107.63, 110.84, 128.01,

128.94, 129.97, 133.92, 134.19, 137.62, 141.93, 151.76, 151.91, 155.09, 164.80, 169.07, 170.52, 170.84, 200.11; IR (KBr disk) 3348, 2954, 2872, 1825, 1731, 1490, 1366, 1237, 1149, 1084 cm^{-1}. Anal. ($C_{59}H_{85}O_{18}NSi_2$) C, H, N.

2′-(Triisopropylsilyl)-3′-dephenyl-3′-(2-methyl-1-propenyl)-7-(triethylsilyl)-10-acetyl-14β-hydroxydocetaxel 1,14-carbonate (11b): 80% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.52−0.61 (m, 6 H), 0.88−0.94 (m, 9 H), 1.03−1.21 (m, 21 H), 1.27 (s, 3 H), 1.33 (s, 3 H), 1.41 (s, 9 H), 1.72 (s, 3 H), 1.74 (s, 3 H), 1.77 (s, 3 H), 1.83−1.94 (m, 1 H), 1.99 (s, 3 H), 2.18 (s, 3 H), 2.50 (m, 1 H), 3.72 (d, J = 7.4 Hz, 1 H), 4.20 (d, J = 8.4 Hz, 1 H), 4.29 (d, J = 8.4 Hz, 1 H), 4.45 (dd, J = 10.2, 6.5 Hz, 1 H), 4.56−4.70 (m, 3 H), 4.86−4.92 (m, 2 H), 5.29 (d, J = 7.8 Hz, 1 H), 6.11 (d, J = 7.4 Hz, 1 H), 6.28 (d, J = 6.6 Hz, 1 H), 6.42 (s, 1 H), 7.45 (m, 2 H), 7.60 (m, 1 H), 8.01 (m, 2 H).

2′-(Triisopropylsilyl)-3′-dephenyl-3′-(2-methyl-1-propenyl)-7-(triethylsilyl)-10-propanoyl-14β-hydroxydocetaxel 1,14-carbonate (11c): 82% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.55 (m, 6 H), 0.91 (m, 9 H), 1.11 (m, 24 H), 1.19 (m, 4 H), 1.22 (s, 3 H), 1.30 (s, 3 H), 1.41 (s, 9 H), 1.69 (s, 3 H), 1.75 (s, 3 H), 1.75 (s, 3 H), 1.77 (s, 3 H), 1.87 (m, 1 H), 2.03 (s, 3 H), 2.47 (m, 5 H), 3.70 (d, J = 7.2 Hz, 1 H), 4.17 (d, J = 9.0 Hz, 1 H), 4.29 (d, J = 9.0 Hz, 1 H), 4.45 (dd, J = 10.5, 6.5 Hz, 1 H), 4.62 (m, 2 H), 4.78 (d, J = 5.7 Hz, 1 H), 4.93 (m, 2 H), 5.25 (d, J = 8.9 Hz, 1 H), 6.09 (d, J = 7.3 Hz, 1 H), 6.27 (d, J = 6.1 Hz, 1 H), 6.43 (s, 1 H), 7.46 (t, J = 7.7 Hz, 2 H), 7.61 (t, J = 7.3 Hz, 1 H), 8.01 (d, J = 7.2 Hz, 2 H).

2′-(Triisopropylsilyl)-3′-dephenyl-3′-(2-methyl-1-propenyl)-7-(triethylsilyl)-10-(cyclopropylcarbonyl)-14β-hydroxydocetaxel 1,14-carbonate (11d): 87% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.55 (q, J = 7.9 Hz, 6 H), 0.86−0.92 (m, 11 H), 0.98−1.16 (m, 29 H), 1.40 (s, 9 H), 1.68−1.77 (m, 10 H), 1.82−1.92 (m, 1 H), 1.99 (s, 3 H), 2.49 (bs, 4 H), 3.70 (d, J = 7.3 Hz, 1 H), 4.19 (d, J = 8.3 Hz, 1 H), 4.27 (d, J = 8.3 Hz, 1 H), 4.43 (dd, J = 10.5, 6.4 Hz, 1 H), 4.54−4.78 (m, 3 H), 4.84−4.92 (m, 1 H), 5.26−5.30 (m, 1 H), 6.09 (d, J = 7.3 Hz, 1 H), 6.27 (d, J = 6.6 Hz, 1 H), 6.42 (s, 1 H), 7.44 (t, J = 7.4 Hz, 2 H), 7.59 (t, J = 7.4 Hz, 1 H), 7.99 (d, J = 7.4 Hz, 2 H).

2′-(Triisopropylsilyl)-3′-dephenyl-3′-(2-methyl-1-propenyl)-7-(triethylsilyl)-10-(*N*,*N*-dimethylcarbamoyl)-14β-hydroxydocetaxel 1,14-carbonate (11e): 85% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.58 (q, J = 7.6 Hz, 6 H), 0.94 (t, J = 7.6 Hz, 9 H), 1.03 (bs, 21 H), 1.24 (s, 3 H), 1.34 (s, 3 H), 1.41 (s, 9 H), 1.65−1.81 (m, 9 H), 1.83−1.92 (m, 1 H), 2.02 (s, 3 H), 2.42 (bs, 4 H), 2.96 (s, 3 H), 3.02 (s, 3 H), 3.71 (d, J = 7.4 Hz, 1 H), 4.20 (d, J = 8.4 Hz, 1 H), 4.27 (d, J = 8.4 Hz, 1 H), 4.44 (dd, J = 10.4, 6.5 Hz, 1 H), 4.53−4.77 (m, 3 H), 4.84−4.96 (m, 2 H), 5.29 (d, J = 7.5 Hz, 1 H), 6.10 (d, J = 7.4 Hz, 1 H), 6.29 (d, J = 6.5 Hz, 1 H), 6.35 (s, 1 H), 7.44 (t, J = 7.4 Hz, 2 H), 7.59 (t, J = 7.4 Hz, 1 H), 8.01 (d, J = 7.4 Hz, 2 H).

2′-[(Triisopropylsilyl)oxy]-3′-dephenyl-3′-(2-methyl-1-propenyl)-7-[(triethylsilyl)oxy]-10-((*E*)-2-butenoyl)-14β-hydroxydocetaxel 1,14-carbonate (11f): 84% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.56 (q, J = 7.6 Hz, 6 H), 0.90 (t, J = 7.6 Hz, 9 H), 1.10 (s, 21 H), 1.26 (s, 3 H), 1.36 (s, 3 H), 1.40 (s, 9 H), 1.70−1.78 (m, 9 H), 1.92 (dd, J = 6.8, 1.3 Hz, 3 H), 2.02 (bs, 4 H), 2.44−2.58 (m, 4 H), 3.73 (d, J = 7.3 Hz, 1 H), 4.21 (d, J = 8.4 Hz, 1 H), 4.28 (d, J = 8.4 Hz, 1 H), 4.46 (dd, J = 10.4, 6.5 Hz, 1 H), 4.53−4.76 (m, 3 H), 4.84−4.94 (m, 2 H), 5.29 (d, J = 7.9 Hz, 1 H), 5.93 (dd, J = 15.6, 1.3 Hz, 1 H), 6.11 (d, J = 7.4 Hz, 1 H), 6.28 (d, J = 6.5 Hz, 1 H), 6.46 (s, 1 H), 7.09 (dq, J = 15.6, 6.8 Hz, 1 H), 7.49 (t, J = 7.4 Hz, 2 H), 7.60 (t, J = 7.4 Hz, 1 H), 8.01 (d, J = 7.4 Hz, 2 H).

2′-(Triisopropylsilyl)-3′-dephenyl-3′-(2-methyl-1-propenyl)-7-(triethylsilyl)-10-(methoxycarbonyl)-14β-hydroxydocetaxel 1,14-carbonate (11g): 55% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.53 (m, 6 H), 0.86 (m, 9 H), 1.09 (s, 21 H), 1.15 (s, 3 H), 1.19 (m, 6 H), 1.31 (s, 9 H), 1.66 (s, 3 H), 1.73 (s, 3 H), 1.77 (s, 3 H), 1.86 (m, 1 H), 1.91 (s, 3 H), 2.34 (s, 3 H), 2.38 (s, 2 H), 2.41 (m, 1 H), 3.81 (d, J = 6.6 Hz, 1 H), 4.15 (d, J = 8.2 Hz, 1 H), 4.26 (d, J = 8.2 Hz, 1 H), 4.41 (s, 1 H), 4.45 (dd, J = 10.6, 6.5 Hz, 1 H), 4.79 (m, 1 H), 4.89 (d, J = 8.9 Hz, 1 H), 5.30 (d, J = 7.7 Hz, 1 H), 5.65 (d, J = 6.6 Hz, 1 H), 6.06 (t, J = 7.2 Hz, 1 H), 6.47 (s, 1 H), 7.40 (t, J = 7.3 Hz, 2 H), 7.54 (t, J = 7.3 Hz, 1 H), 8.01 (d, J = 7.2 Hz, 2 H).

2′-(Triisopropylsilyl)-3′-dephenyl-3′-((*E*)-1-propenyl)-7-(triethylsilyl)-10-acetyl-14β-hydroxydocetaxel 1,14-carbonate (12b): 75% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.58 (q, J = 7.9 Hz, 6 H), 0.90 (t, J = 7.9 Hz, 9 H), 1.04−1.14 (m, 27 H), 1.40 (s, 9 H), 1.71 (s, 3 H), 1.77−1.81 (m, 1 H), 1.98 (s, 3 H), 2.17 (s, 3 H), 2.38−2.49 (m, 4 H), 3.70 (d, J = 7.2 H, 1 H), 4.21 (d, J = 8.4 Hz, 1 H), 4.29 (d, J = 8.4 Hz, 1 H), 4.39−4.52 (m, 1 H), 4.62 (bs, 1 H), 4.80−4.93 (m, 2 H), 5.44−5.62 (m, 1 H), 5.64−5.83 (m, 1 H), 6.10 (d, J = 7.2 Hz, 1 H), 6.29−6.38 (bs, 1 H), 6.41 (s, 1 H), 7.48 (t, J = 7.3 Hz, 2 H), 7.59 (t, J = 7.3 Hz, 1 H), 8.03 (d, J = 7.3 Hz, 2 H).

2′-(Triisopropylsilyl)-3′-dephenyl-3′-(2,2-dimethylpropyl)-7,10-bis(triethylsilyl)-14β-hydroxydocetaxel 1,14-carbonate (13a): 80% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.53−0.77 (m, 12 H), 0.93−1.03 (m, 18 H), 0.96 (s, 9 H), 1.14 (m, 21 H), 1.25−1.35 (m, 2 H), 1.28 (s, 3 H), 1.43 (s, 9 H), 1.54 (s, 3 H), 1.69 (s, 3 H), 1.87 (m, 1 H), 1.88 (s, 3 H), 2.33 (s, 1 H), 2.39 (s, 3 H), 2.54 (m, 1 H), 3.71 (d, J = 6.9 Hz, 1 H), 3.74 (m, 1H), 3.96−4.55 (m, 8 H), 4.84−4.99 (m, 3 H), 5.11 (s, 1 H), 5.13 (s, 1 H), 6.06−6.13 (m, 2 H), 6.14 (d, J = 6.8 Hz, 1 H), 7.43 (m, 2 H), 7.57 (m, 2 H), 8.02 (m, 2 H), 8.10 (d, J = 7.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 5.2, 5.9, 6.8, 6.9, 10.4, 12.2, 12.4, 14.1, 17.9, 18.0, 22.0, 22.6, 25.7, 28.5, 29.8, 30.3, 37.1, 41.9, 42.5, 43.1, 46.2, 52.0, 53.6, 58.8, 69.6, 72.4, 75.0, 75.1, 75.2, 75.4, 75.7, 76.2, 79.4, 79.5, 80.6, 83.8, 87.9, 128.2, 128.8, 129.2, 129.8, 130.3, 131.3, 131.8, 134.0, 134.2, 138.4, 152.2, 153.9, 154.9, 164.8, 170.2, 204.0.

2′-(Triisopropylsilyl)-3′-dephenyl-3′-(2-methyl-1-propenyl)-3′-*N*-hexanoyl-7-(triethylsilyl)-10-(cyclopropylcarbonyl)-14β-hydroxydocetaxel 1,14-carbonate (15d): 72% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.55 (q, J = 7.8 Hz, 6 H), 0.80 (t, J = 6.7 Hz, 3 H), 0.90 (t, J = 7.8 Hz, 9 H), 1.04−1.25 (m, 25 H), 1.29 (s, 3 H), 1.34 (s, 3 H), 1.50−1.58 (m, 2 H), 1.70−1.77 (m, 9 H), 1.84−1.93 (m, 1 H), 2.01 (s, 3 H), 2.04−2.28 (m, 2 H), 2.42−2.55 (m, 4 H), 3.69 (d, J = 7.5 Hz, 1 H), 4.20 (d, J = 8.4 Hz, 1 H), 4.28 (d, J = 8.4 Hz, 1 H), 4.44 (dd, J = 10.6, 6.4 Hz, 1 H), 4.72 (d, J = 4.9 Hz, 1 H), 4.82 (d, J = 7.1 Hz, 1 H), 4.88 (d, J = 8.3 Hz, 1 H), 5.01−5.10 (m, 1 H), 5.37 (d, J = 8.3 Hz, 1 H), 5.51 (d, J = 8.2 Hz, 1 H), 6.09 (d, J = 7.5 Hz, 1 H), 6.31 (d, J = 6.5 Hz, 1 H), 6.42 (s, 1 H), 7.47 (t, J = 7.5 Hz, 2 H), 7.60 (t, J = 7.5 Hz, 1 H), 8.05 (d, J = 7.5 Hz, 2 H).

2′-(Triisopropylsilyl)-3′-dephenyl-3′-(2-methyl-1-propenyl)-3′-*N*-hexanoyl-7-(triethylsilyl)-10-(*N*,*N*-dimethylcarbamoyl)-14β-hydroxydocetaxel 1,14-carbonate (15e): 55% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 0.55 (q, J = 7.6 Hz, 6 H), 0.80 (t, J = 6.7 Hz, 3 H), 0.90 (t, J = 7.6 Hz, 9 H), 1.10 (bs, 25 H), 1.29 (s, 3 H), 1.33 (s, 3 H), 1.43−1.59 (m, 2 H), 1.65−1.76 (m, 9 H), 1.81−1.98 (m, 1 H), 2.00−2.21 (m, 5 H), 2.48 (bs, 4 H), 2.93 (s, 3 H), 3.06 (s, 3 H), 3.71 (d, J = 7.4 Hz, 1 H), 4.20 (d, J = 8.3 Hz, 1 H), 4.28 (d, J = 8.3 Hz, 1 H), 4.45 (dd, J = 10.6, 6.6 Hz, 1 H), 4.72 (d, J = 4.9 Hz, 1 H), 4.82 (d, J = 7.1 Hz, 1 H), 4.90 (d, J = 8.3 Hz, 1 H), 5.00−5.10 (m, 1 H), 5.37 (d, J = 8.1 Hz, 1 H), 5.51 (d, J = 8.2 Hz, 1 H), 6.09 (d, J = 7.4 Hz, 1 H), 6.34 (bs, 2 H), 7.47 (t, J = 7.4 Hz, 2 H), 7.60 (t, J = 7.4 Hz, 1 H), 8.05 (d, J = 7.4 Hz, 2 H).

2′-[(Triisopropylsilyl)oxy]-3′-dephenyl-3′-(2-methyl-1-propenyl)-3′-*N*-hexanoyl-7-(triethylsilyl)-10-((*E*)-2-butenoyl)-14β-hydroxydocetaxel 1,14-carbonate (15f): 50% yield (65% conversion yield); white solid; ^{1}H NMR ($CDCl_3$) δ 0.56 (q, J = 7.6 Hz, 6 H), 0.80 (t, J = 6.7 Hz, 3 H), 0.89 (t, J = 7.6 Hz, 9 H), 1.04−1.22 (m, 25 H), 1.27 (s, 3 H), 1.40 (s, 3 H), 1.68−1.76 (m, 11 H), 1.92 (dd, J = 6.9, 1.4 Hz, 3 H), 2.04 (s, 3 H), 2.35−2.56 (m, 6 H), 3.71 (d, J = 7.4 Hz, 1 H), 4.20 (d, J = 8.3 Hz, 1 H), 4.28 (d, J = 8.3 Hz, 1 H), 4.46 (dd, J = 10.4, 6.4 Hz, 1 H), 4.69−4.96 (m, 4 H), 4.98−5.11 (m, 1 H), 5.36 (d, J = 8.2 Hz, 1 H), 5.53 (d, J = 8.1 Hz, 1 H), 5.96 (dd, J = 15.7, 1.4 Hz, 1 H), 6.09 (d, J = 7.4 Hz, 1 H), 6.32 (d, J = 7.2 Hz, 1 H), 6.46 (s, 1 H), 7.08 (dq, J = 15.7, 6.9 Hz, 1 H), 7.46 (t, J = 7.5 Hz, 2 H), 7.59 (t, J = 7.5 Hz, 1 H), 8.04 (d, J = 7.5 Hz, 2 H).

General Procedure for the Syntheses of Taxoids 16−21 by the Deprotection of Silyl-Protected Taxoids 10−15. A typical procedure is described for the preparation of 3′-dephenyl-3′-(2-methyl-1-propenyl)-10-acetyl-14β-hydroxydocetaxel 1,14-carbonate (**17b**): The protected coupling

product **11b** (170 mg, 0.15 mmol) was dissolved in acetonitrile/pyridine (1/1, 10 mL) and cooled to 0 °C. HF/pyridine (70/30) was added dropwise (0.1 mL/10 mg of reactant). The mixture was stirred at 0 °C for 1 h and then at room temperature overnight. After the disappearance of **11b** on TLC analysis, the reaction was quenched with saturated $CuSO_4$. The reaction mixture was extracted with EtOAc, and the extracts were washed with saturated $CuSO_4$ (2 × 15 mL) and water (2 × 15 mL) and dried over anhydrous $MgSO_4$. Evaporation of the solvent followed by purification of the crude product by flash chromatography (silica gel; hexane/EtOAc = 1/2) afforded taxoid **17b** (128 mg, 73% yield) as a white solid: mp 165−170 °C; $[\alpha]^{20}_D$ −52.6° (*c* 0.038, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3 H), 1.32 (s, 3 H), 1.40 (s, 9 H), 1.70 (s, 3 H), 1.73 (s, 3 H), 1.75 (s, 3 H), 1.88 (s, 3 H), 1.93 (m, 1 H), 2.22 (s, 3 H), 2.43 (s, 3 H), 2.47 (d, *J* = 4.5 Hz, 1 H), 2.55 (m, 1 H), 3.68 (d, *J* = 7.3 Hz, 1 H), 4.19−4.37 (m, 5 H), 4.69 (m, 1 H), 4.80 (d, *J* = 6.9 Hz, 1 H), 4.92 (m, 2 H), 5.22 (d, *J* = 8.7 Hz, 1 H), 6.09 (d, *J* = 7.3 Hz, 1 H), 6.26 (s, 1 H), 6.37 (d, *J* = 6.2 Hz, 1 H), 7.45 (t, 2 H), 7.60 (t, 1 H), 8.00 (d, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.6, 14.9, 18.6, 20.7, 22.3, 22.9, 25.8, 26.0, 28.2, 35.5, 41.7, 45.1, 52.1, 58.7, 69.5, 71.65, 74.2, 74.8, 75.9, 79.7, 80.5, 84.2, 88.1, 119.5, 127.9, 128.9, 129.8, 133.5, 134.2, 139.4, 139.9, 151.9, 156.3, 164.7, 170.4, 170.8, 172.0, 202.1; IR (KBr disk) 3421, 2979, 1824, 1734, 1685, 1508, 1458, 1239, 1165 cm^{-1}. Anal. ($C_{44}H_{56}NO_{16}$) C, H, N.

In the same manner, taxoids **16**−**21** were prepared using the method shown above.

3′-Dephenyl-3′-(2-furyl)-14β-hydroxydocetaxel 1,14-carbonate (16a): 73% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 3 H), 1.31 (s, 3 H), 1.37 (s, 9 H), 1.77 (s, 3 H), 1.86 (m, 1 H), 1.91 (s, 3 H), 2.46 (s, 3 H), 2.56 (m, 1 H), 3.80 (d, *J* = 7.4 Hz, 1 H), 4.22 (d, *J* = 8.5 Hz, 1 H), 4.29 (d, *J* = 8.5 Hz, 1 H), 4.29 (m, 2 H), 4.75−4.84 (m, 2 H), 4.92 (bd, *J* = 8.9 Hz, 1 H), 5.22 (s, 1 H), 5.40 (bd, *J* = 9.4 Hz, 1 H), 5.58 (bd, *J* = 9.4 Hz, 1 H), 6.09 (d, *J* = 7.4 Hz, 1 H), 6.34 (bs, 1 H), 6.38 (bs, 1 H), 6.44 (d, *J* = 6.1 Hz, 1 H), 7.42 (bs, 1 H), 7.49 (t, *J* = 7.4 Hz, 2 H), 7.61 (t, *J* = 7.3 Hz, 1 H), 8.03 (d, *J* = 7.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 10.00, 14.45, 21.96, 22.47, 25.55, 28.19, 36.58, 41.67, 45.98, 51.45, 57.91, 69.31, 71.56, 72.22, 74.08, 74.84, 76.10, 79.64, 80.47, 80.83, 84.09, 88.18, 107.76, 110.81, 127.89, 129.03, 129.98, 134.20, 135.90, 136.43, 142.47, 151.26, 151.99, 155.62, 164.84, 170.77, 171.75, 209.78. Anal. ($C_{42}H_{49}O_{17}N$) C, H, N.

3′-Dephenyl-3′-furyl-10-acetyl-14β-hydroxydocetaxel 1,14-carbonate (16b): 76% yield; white solid; ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 1.33 (s, 3 H), 1.38 (s, 9 H), 1.72 (s, 3 H), 1.89 (m, 4 H), 2.25 (s, 3 H), 2.46 (s, 3 H), 2.56 (m, 1 H), 3.71 (d, *J* = 7.4 Hz, 1 H), 4.25 (d, *J* = 8.5 Hz, 1 H), 4.29 (d, *J* = 8.5 Hz, 1 H), 4.39 (dd, *J* = 10.7, 6.5 Hz, 1 H), 4.79 (bs, 1 H), 4.84 (d, *J* = 6.8 Hz, 1 H), 4.92 (bd, *J* = 8.5 Hz, 1 H), 5.29−5.50 (m, 2 H), 6.10 (d, *J* = 7.4 Hz, 1 H), 6.27 (s, 1 H), 6.34 (bs, 1 H), 6.38 (bs, 1 H), 6.44 (d, *J* = 6.4 Hz, 1 H), 7.42 (bs, 1 H), 7.49 (t, *J* = 7.5 Hz, 2 H), 7.61 (t, *J* = 7.2 Hz, 1 H), 8.04 (d, *J* = 7.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.65, 14.92, 20.75, 22.45, 22.97, 25.90, 28.17, 29.66, 35.46, 41.73, 45.13, 51.48, 58.68, 69.33, 71.70, 72.34, 74.75, 74.82, 75.94, 79.58, 80.52, 80.92, 84.22, 88.07, 107.81, 110.78, 127.89, 128.98, 129.95, 133.67, 134.13, 139.44, 142.48, 151.00, 164.70, 170.73, 170.89, 171.67, 202.07. Anal. ($C_{44}H_{51}O_{18}N$) C, H, N.

3′-Dephenyl-3′-(2-methyl-1-propenyl)-14β-hydroxydocetaxel 1,14-carbonate (17a): 90% yield; colorless film; mp 167−169 °C; $[\alpha]^{20}_D$ −44.4° (*c* 0.45, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3 H), 1.32 (s, 3 H), 1.40 (s, 9 H), 1.70 (s, 3 H), 1.73 (s, 3 H), 1.75 (s, 3 H), 1.88 (s, 3 H), 1.93 (m, 1 H), 2.22 (s, 3 H), 2.43 (s, 3 H), 2.47 (d, *J* = 4.5 Hz, 1 H), 2.55 (m, 1 H), 3.68 (d, *J* = 7.3 Hz, 1 H), 4.19−4.37 (m, 5 H), 4.69 (m, 1 H), 4.80 (d, *J* = 6.9 Hz, 1 H), 4.92 (m, 2 H), 5.12 (s, 1 H), 5.22 (d, *J* = 8.7 Hz, 1 H), 6.09 (d, *J* = 7.3 Hz, 1 H), 6.37 (d, *J* = 6.2 Hz, 1 H), 7.45 (t, 2 H), 7.60 (t, 1 H), 8.00 (d, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.6, 14.9, 18.6, 20.7, 22.3, 22.9, 25.8, 26.0, 28.2, 35.5, 41.7, 45.1, 52.1, 58.7, 69.5, 71.65, 74.2, 74.8, 75.9, 79.7, 80.5, 84.2, 88.1, 119.5, 127.9, 128.9, 129.8, 133.5, 134.2, 139.4, 139.9, 151.9, 156.3, 164.7, 170.8, 172.0, 202.1; IR (KBr disk) 3421, 2979, 1824, 1734, 1685, 1508, 1458, 1239, 1165 cm^{-1}. Anal. ($C_{42}H_{53}NO_{16}$) C, H, N.

3′-Dephenyl-3′-(2-methyl-1-propenyl)-10-propanoyl-14β-hydroxydocetaxel 1,14-carbonate (17c): 62% yield; white solid; mp 165−168 °C; $[\alpha]^{20}_D$ −48.2° (*c* 0.125, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.30 (m, 8 H), 1.35 (s, 3 H), 1.42 (s, 9 H), 1.71 (s, 3 H), 1.75 (s, 3 H), 1.77 (s, 3 H), 1.85 (m, 1 H), 1.90 (s, 3 H), 2.44 (s, 3 H), 2.53 (m, 3 H), 3.69 (d, *J* = 7.3 Hz, 1 H), 4.22 (d, *J* = 8.3 Hz, 1 H), 4.28 (d, *J* = 8.3 Hz, 1 H), 4.33 (s, 1 H), 4.39 (dd, *J* = 10.5, 6.5 Hz, 1 H), 4.70 (m, 1 H), 4.82 (d, *J* = 6.9 Hz, 2 H), 4.93 (d, *J* = 8.3 Hz, 1 H), 5.23 (d, *J* = 8.2 Hz, 1 H), 6.10 (d, *J* = 7.3 Hz, 1 H), 6.27 (s, 1 H), 6.38 (d, *J* = 6.9 Hz, 1 H), 7.45 (t, *J* = 7.9 Hz, 2 H), 7.61 (t, *J* = 7.2 Hz, 1 H), 8.01 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.0, 9.7, 14.2, 15.0, 18.7, 22.4, 23.1, 25.9, 26.0, 27.5, 28.3, 35.4, 41.7, 45.1, 52.2, 58.7, 60.4, 69.5, 71.8, 74.3, 74.6, 75.1, 75.9, 79.7, 80.5, 84.2, 88.2, 119.3, 127.9, 128.9, 129.9, 133.6, 134.2, 139.9, 151.9, 164.7, 170.5, 172.0, 174.3, 202.3. Anal. ($C_{45}H_{59}NO_{16}$) C, H, N.

3′-Dephenyl-3′-(2-methyl-1-propenyl)-10-(cyclopropylcarbonyl)-14β-hydroxydocetaxel 1,14-carbonate (17d): 84% yield; white solid; mp 137−140 °C; $[\alpha]^{20}_D$ −40.0° (*c* 0.30, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.00−1.13 (m, 4 H), 1.28 (s, 3 H), 1.34 (s, 3 H), 1.42 (s, 9 H), 1.70 (s, 3 H), 1.74−1.77 (m, 8 H), 1.89 (s, 3 H), 2.44 (s, 3 H), 2.50−2.57 (m, 1 H), 3.67 (d, *J* = 7.3 Hz, 1 H), 4.04 (bs, 1 H), 4.20−4.42 (m, 4 H), 4.66−4.76 (m, 1 H), 4.82 (d, *J* = 7.0 Hz, 1 H), 4.92 (d, *J* = 9.1 Hz, 1 H), 5.22 (m, 1 H), 6.09 (d, *J* = 7.3 Hz, 1 H), 6.25 (s, 1 H), 6.38 (d, *J* = 5.9 Hz, 1 H), 7.46 (t, *J* = 7.5 Hz, 2 H), 7.61 (t, *J* = 7.5 Hz, 1 H), 8.01 (d, *J* = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.41, 9.62, 12.95, 14.19, 15.01, 18.68, 22.38, 23.11, 25.87, 26.09, 28.03, 28.27, 35.37, 41.70, 45.04, 52.15, 58.71, 60.41, 69.54, 71.81, 74.28, 74.63, 75.03, 75.93, 76.21, 79.75, 80.52, 80.67, 84.25, 88.16, 116.49, 119.33, 127.92, 128.95, 129.88, 133.59, 134.24, 140.05, 151.93, 164.71, 170.46, 172.04, 174.89, 202.40. Anal. ($C_{46}H_{59}NO_{16}$) C, H, N.

3′-Dephenyl-3′-(2-methyl-1-propenyl)-10-(*N*,*N*-dimethylcarbamoyl)-14β-hydroxydocetaxel 1,14-carbonate (17e): 83% yield; white solid; mp 168−171 °C; $[\alpha]^{20}_D$ −63.0° (*c* 0.27, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.24 (s, 3 H), 1.32 (s, 3 H), 1.41 (s, 9 H), 1.67−1.78 (m, 10 H), 1.91 (s, 3 H), 2.44 (s, 3 H), 2.48−2.59 (m, 1 H), 2.95 (s, 3 H), 3.03 (s, 3 H), 3.13 (bs, 1H), 3.68 (d, *J* = 7.4 Hz, 1 H), 4.21 (d, *J* = 8.4 Hz, 1 H), 4.27−4.35 (m, 2 H), 4.41 (bt, 1 H), 4.64−4.77 (m, 1 H), 4.79−4.89 (m, 2 H), 4.95 (d, *J* = 7.9 Hz, 1 H), 5.23 (d, *J* = 8.7 Hz, 1 H), 6.09 (d, *J* = 7.4 Hz, 1 H), 6.21 (s, 1 H), 6.39 (d, *J* = 6.7 Hz, 1 H), 7.46 (t, *J* = 7.5 Hz, 2 H), 7.61 (t, *J* = 7.5 Hz, 1 H), 8.01 (d, *J* = 7.5 Hz, 2 H); ^{13}C NMR (63 MHz, $CDCl_3$) δ 9.47, 15.05, 18.68, 22.38, 23.41, 25.85, 26.24, 28.28, 35.24, 36.06, 36.73, 41.71, 44.98, 52.14, 58.66, 69.63, 72.05, 74.33, 75.03, 75.45, 75.92, 79.82, 80.57, 80.64, 84.43, 88.25, 119.39, 127.95, 128.95, 129.88, 133.83, 134.22, 139.62, 140.41, 151.98, 155.76, 164.71, 170.41, 172.07, 204.19. Anal. ($C_{45}H_{60}N_2O_{16}$) C, H, N.

3′-Dephenyl-3′-(2-methyl-1-propenyl)-10-((*E*)-2-butenoyl)-14β-hydroxydocetaxel 1,14-carbonate (17f): 38% yield; white solid; mp 147−151 °C; $[\alpha]^{20}_D$ −70.0° (*c* 0.20, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3 H), 1.35 (s, 3 H), 1.42 (s, 9 H), 1.71 (s, 3 H), 1.75 (s, 3 H), 1.77 (s, 3 H), 1.90 (s, 3 H), 1.94 (dd, *J* = 6.8, 1.3 Hz, 3 H), 2.11−2.18 (m, 1 H), 2.45 (s, 3 H), 2.49−2.62 (m, 1 H), 3.71 (d, *J* = 7.3 Hz, 1 H), 4.22 (d, *J* = 8.4 Hz, 1 H), 4.27−4.30 (bs, 1 H), 4.32 (d, *J* = 8.4 Hz, 1 H), 4.41 (m, 1 H), 4.67−4.85 (m, 3 H), 4.95 (d, *J* = 7.8 Hz, 1 H), 5.24 (d, *J* = 8.5 Hz, 1 H), 5.98 (dd, *J* = 15.6, 1.3 Hz, 1 H), 6.11 (d, *J* = 7.3 Hz, 1 H), 6.32 (s, 1 H), 6.39 (d, *J* = 7.3 Hz, 1 H), 7.10 (dq, *J* = 15.6, 7.1 Hz, 1 H), 7.46 (t, *J* = 7.4 Hz, 2 H), 7.61 (t, *J* = 7.4 Hz, 1 H), 8.01 (d, *J* = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.65, 14.99, 18.35, 18.69, 22.39, 23.14, 25.87, 26.11, 28.28, 30.15, 35.40, 41.71, 45.04, 52.15, 58.74, 69.56, 71.85, 74.27, 74.55, 75.94, 79.76, 84.26, 88.19, 119.28, 121.22, 128.95, 129.89, 134.25, 140.11, 147.96, 153.85, 164.51, 166.03, 170.22, 171.91, 202.33.

3′-Dephenyl-3′-(2-methyl-1-propenyl)-10-(methoxycarbonyl)-14β-hydroxydocetaxel 1,14-carbonate (17g): 67% yield; white solid; mp 163−165 °C; $[\alpha]^{20}_D$ −53.9° (*c* 0.168, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 3 H), 1.32 (s, 3 H), 1.42 (s, 9 H), 1.75 (m, 6 H), 1.85 (m, 1 H), 1.93 (s, 3 H), 2.45 (s, 3 H), 2.56 (m, 1 H), 3.67 (d, *J* = 7.3 Hz, 1 H), 3.87 (s, 3 H), 4.22 (d, *J* = 8.5 Hz, 1 H), 4.29 (d, *J* = 8.5 Hz, 1 H), 4.32 (d, *J* = 4.8 Hz,

1 H), 4.36 (dd, J = 6.5, 10.9 Hz, 1 H), 4.72 (m, 1 H), 4.83 (m, 2 H), 4.93 (d, J = 8.0 Hz, 1 H), 5.24 (d, J = 8.2 Hz, 1 H), 6.07 (s, 1 H), 6.11 (d, J = 7.5 Hz, 1 H), 6.39 (d, J = 6.1 Hz, 1 H), 7.46 (t, J = 7.3 Hz, 2 H), 7.61 (t, J = 7.2 Hz, 1 H), 8.01 (d, J = 7.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.6, 14.2, 18.7, 22.4, 22.9, 25.9, 28.3, 29.7, 35.5, 41.6, 45.0, 52.2, 55.8, 58.7, 69.5, 71.7, 74.2, 75.0, 75.9, 77.5, 79.7, 80.5, 80.7, 84.2, 88.1, 119.3, 127.9, 129.0, 129.9, 133.1, 134.3, 139.7, 140.8, 151.9, 155.5, 164.7, 170.5, 172.0, 202.5. Anal. ($C_{44}H_{57}NO_{17}$) C, H, N.

3′-Dephenyl-3′-((*E*)-1-propenyl)-14*β*-hydroxydocetaxel 1,14-carbonate (18a): 52% yield (for two steps); white solid; mp 168−172 °C; $[\alpha]^{20}_D$ −42.1° (*c* 0.095, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 3 H), 1.29 (s, 3 H), 1.36 (s, 9 H), 1.71−1.74 (m, 6 H), 1.88 (s, 3 H), 2.01 (s, 3 H), 2.43 (s, 3 H), 2.52 (m, 1 H), 3.77 (d, J = 7.2 Hz, 1 H), 4.18−4.42 (m, 4 H), 4.59 (bs, 1 H), 4.79 (d, J = 6.8 Hz, 1 H), 4.91 (d, J = 8.8 Hz, 1 H), 5.16−5.22 (m, 2 H), 5.54 (dd, J = 15.4, 5.7 Hz, 1 H), 5.74 (dq, J = 15.4, 6.5 Hz, 1 H), 6.07 (d, J = 7.2 Hz, 1 H), 6.39 (d, J = 5.8 Hz, 1 H), 7.46 (t, J = 7.4 Hz, 2 H), 7.59 (t, J = 7.4 Hz, 1 H), 8.00 (d, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.98, 14.17, 14.47, 17.89, 21.89, 22.00, 22.45, 25.60, 28.26, 29.69, 36.55, 41.67, 45.96, 55.10, 57.93, 61.03, 69.36, 71.57, 73.58, 74.10, 74.58, 76.06, 79.64, 80.51, 84.06, 88.16, 126.93, 127.89, 129.00, 129.23, 129.93, 134.19, 136.01, 136.39, 152.25, 155.82, 164.82, 170.53, 172.31, 209.76. Anal. ($C_{41}H_{51}NO_{16}$) C, H, N.

3′-Dephenyl-3′-((*E*)-1-propenyl)-10-acetyl-14*β*-hydroxydocetaxel 1,14-carbonate (18b): 80% yield; white solid; mp 171−175 °C; ^{1}H NMR ($CDCl_3$) δ 1.18 (s, 3 H), 1.20 (s, 3 H), 1.28 (s, 9 H), 1.60 (s, 3 H), 1.63 (d, J = 6.4 Hz, 3 H), 1.70−1.78 (m, 1 H), 1.82 (s, 3 H), 2.11 (s, 3 H), 2.35 (s, 3 H), 2.37−2.48 (m, 1 H), 3.60 (d, J = 7.4 Hz, 1 H), 4.09 (d, J = 8.5 Hz, 1 H), 4.18 (d, J = 8.5 Hz, 1 H), 4.16−4.25 (m, 1 H), 4.28 (d, J = 3.5 Hz, 1 H), 4.42 (bm, 1 H), 4.73 (d, J = 6.8 Hz, 1 H), 4.84 (d, J = 8.3 Hz, 1 H), 5.43 (dd, J = 15.5, 5.7 Hz, 1 H), 5.62 (dq, J = 15.5, 6.4 Hz, 1 H), 5.98 (d, J = 7.4 Hz, 1 H), 6.24 (s, 1 H), 6.25 (bd, 1 H), 7.38 (t, J = 7.5 Hz, 2 H), 7.52 (t, J = 7.5 Hz, 1 H), 7.90 (d, J = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.59, 18.53, 21.57, 24.50, 26.09, 26.54, 29.57, 32.03, 39.70, 45.59, 49.67, 51.74, 52.07, 52.76, 53.10, 53.44, 53.78, 57.32, 58.88, 62.37, 73.34, 74.82, 77.24, 77.91, 78.73, 79.89, 83.74, 84.43, 88.29, 92.15, 131.05, 131.73, 132.62, 132.88, 133.74, 137.38, 138.20, 143.17, 159.80, 168.83, 174.31, 174.71, 176.04, 178.83, 188.72, 191.84, 205.96. Anal. ($C_{43}H_{53}NO_{17}$) C, H, N.

3′-Dephenyl-3′-(2,2-dimethylpropyl)-14*β*-hydroxydocetaxel 1,14-carbonate (19a): 80% yield; white solid; mp 158−161 °C; $[\alpha]^{20}_D$ −38.2° (*c* 0.34, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.99 (s, 9 H), 1.29 (s, 3 H), 1.33 (s, 3 H), 1.40 (s, 9 H), 1.56 (bd, J = 14.5 Hz, 1 H), 1.70 (m, 1 H), 1.80 (s, 3 H), 1.86 (m, 1 H), 1.94 (s, 3 H), 2.48 (s, 3 H), 2.59 (ddd, J = 14.1, 8.0, 3.0 Hz, 1 H), 3.81 (d, J = 7.5 Hz, 1 H), 4.08 (m, 1 H), 4.27 (m, 6 H), 4.80 (m, 1 H), 4.83 (d, J = 6.9 Hz, 1 H), 4.94 (d, J = 7.9 Hz, 1 H), 5.18 (s, 1 H), 6.11 (d, J = 7.4 Hz, 1 H), 6.45 (d, J = 6.5 Hz, 1 H), 7.48 (t, 2 H), 7.62 (t, 1 H), 8.03 (d, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.96, 14.5, 22.0, 25.7, 28.3, 29.8, 30.3, 36.7, 41.6, 44.3, 45.8, 51.2, 57.8, 69.4, 71.6, 74.1, 74.4, 75.6, 76.5, 77.2, 79.7, 80.4, 80.5, 83.9, 88.2, 127.9, 128.9, 129.9, 134.2, 136.1, 136.3, 152.0, 156.2, 164.8, 170.6, 172.4, 209.8. Anal. ($C_{43}H_{58}NO_{15}$) C, H, N.

3′-*N*-Debenzoyl-3′-*N*-*n*-hexanoyl-10-deacetyl-14*β*-hydroxypaclitaxel 1,14-carbonate (20a): 41% yield; white solid; mp 159−163 °C; $[\alpha]^{20}_D$ −9.1° (*c* 0.11, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.81 (t, J = 6.7 Hz, 3 H), 1.20−1.28 (m, 7 H), 1.32 (s, 3 H), 1.55 (bt, J = 6.5 Hz, 2 H), 1.79 (s, 3 H), 1.85 (bs, 1 H), 1.90 (s, 3 H), 2.18−2.29 (m, 2 H), 2.55 (s, 3 H), 2.58−2.62 (m, 1 H), 3.81 (d, J = 7.7 Hz, 1 H), 4.21−4.27 (m, 3 H), 4.78−4.81 (m, 2 H), 4.89 (d, J = 8.2 Hz, 1 H), 5.15 (s, 1 H), 5.73 (dd, J = 9.2, 2.7 Hz, 1 H), 6.08 (d, J = 7.7 Hz, 1 H), 6.37 (d, J = 9.2 Hz, 1 H), 6.52 (d, J = 6.3 Hz, 1 H), 7.33−7.44 (m, 5 H), 7.50 (t, J = 6.9 Hz, 2 H), 7.60 (t, J = 7.1 Hz, 1 H), 8.12 (d, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 10.10, 13.89, 14.31, 22.29, 22.63, 25.25, 25.60, 31.36, 36.52, 36.71, 41.67, 45.95, 54.09, 57.84, 69.36, 71.63, 73.78, 73.93, 74.75, 76.15, 77.21, 79.69, 80.40, 84.07, 88.36, 126.62, 127.79, 128.13, 128.95, 129.01, 130.29, 134.17, 135.49, 136.41, 137.70, 151.91, 165.01, 171.16, 172.20, 173.58, 209.76. Anal. ($C_{45}H_{53}NO_{15}$) C, H, N.

3′-Dephenyl-3′-(2-methyl-1-propenyl)-3′-*N*-debenzoyl-3′-*N*-hexanoyl-10-deacetyl-10-cyclopropyl-14*β*-hydroxypaclitaxel 1,14-carbonate (21d): 81.6% yield; white solid; mp 157−161 °C; $[\alpha]^{20}_D$ −33.3° (*c* 0.36, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.84 (t, J = 6.6 Hz, 3 H), 1.00−1.13 (m, 4 H), 1.19−1.29 (m, 7 H), 1.34 (s, 3 H), 1.52−1.63 (m, 2 H), 1.70 (s, 3 H), 1.74−1.78 (m, 7 H), 1.89 (bs, 4 H), 2.12−2.21 (m, 2 H), 2.45−2.59 (m, 4 H), 3.69 (d, J = 7.5 Hz, 1 H), 4.14−4.28 (m, 2 H), 4.36−4.42 (m, 2 H), 4.83 (d, J = 6.9 Hz, 1 H), 4.92 (d, J = 8.2 Hz, 1 H), 5.00−5.09 (m, 1 H), 5.30 (d, J = 7.3 Hz, 1 H), 5.77 (d, J = 7.7 Hz, 1 H), 6.09 (d, J = 7.5 Hz, 1 H), 6.25 (s, 1 H), 6.41 (d, J = 6.7 Hz, 1 H), 7.48 (t, J = 7.4 Hz, 2 H), 7.61 (t, J = 7.4 Hz, 1 H), 8.06 (d, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.41, 9.68, 12.92, 13.92, 14.92, 18.75, 22.32, 22.47, 23.28, 25.29, 25.87, 26.03, 31.30, 35.34, 36.57, 41.73, 45.04, 50.87, 58.68, 69.54, 71.76, 74.29, 74.58, 75.94, 76.51, 79.71, 80.42, 84.28, 88.37, 118.97, 127.86, 128.97, 130.04, 133.57, 134.23, 139.81, 139.99, 151.93, 164.76, 170.74, 172.13, 174.25, 174.92, 202.36. Anal. ($C_{47}H_{61}NO_{15}$) C, H, N.

3′-Dephenyl-3′-(2-methyl-1-propenyl)-3′-*N*-debenzoyl-3′-*N*-hexanoyl-10-deacetyl-10-(*N*,*N*-dimethylcarbamoyl)-14*β*-hydroxypaclitaxel 1,14-carbonate (21e): 54% yield; white solid; mp 152−156 °C; $[\alpha]^{20}_D$ −45.0° (*c* 0.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.84 (t, J = 6.7 Hz, 3 H), 1.20−1.27 (m, 7 H), 1.33 (s, 3 H), 1.53−1.63 (m, 5 H), 1.70 (s, 3 H), 1.75 (s, 3 H), 1.77 (s, 3 H), 1.91 (bs, 4 H), 2.12−2.21 (m, 2 H), 2.50 (bs, 4 H), 2.96 (s, 3 H), 3.03 (s, 3 H), 3.10 (bs, 1 H), 3.69 (d, J = 7.5 Hz, 1 H), 4.23 (d, J = 8.3 Hz, 1 H), 4.29 (d, J = 8.3 Hz, 1 H), 4.38−4.49 (m, 2 H), 4.83 (d, J = 6.9 Hz, 1 H), 4.95 (d, J = 7.8 Hz, 1 H), 5.00−5.09 (m, 1 H), 5.30 (d, J = 9.0 Hz, 1 H), 5.75 (d, J = 7.7 Hz, 1 H), 6.08 (d, J = 7.5 Hz, 1 H), 6.20 (s, 1 H), 6.42 (d, J = 5.6 Hz, 1 H), 7.48 (t, J = 7.4 Hz, 2 H), 7.61 (t, J = 7.4 Hz, 1 H), 8.06 (d, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.50, 13.94, 15.01, 18.75, 22.32, 22.47, 23.59, 25.30, 25.88, 26.20, 31.33, 35.18, 36.07, 36.58, 36.75, 41.73, 44.95, 50.88, 58.63, 69.61, 72.04, 74.36, 74.71, 75.38, 75.93, 79.79, 80.46, 84.49, 119.00, 128.97, 130.04, 133.80, 134.23, 140.02, 140.22, 151.76, 155.88, 165.02, 170.68, 172.16, 174.19, 204.22. Anal. ($C_{46}H_{62}N_2O_{15}$) C, H, N.

3′-Dephenyl-3′-(2-methyl-1-propenyl)-3′-*N*-hexanoyl-10-((*E*)-2-butenoyl)-14*β*-hydroxydocetaxel 1,14-carbonate (21f): 83.8% yield; white solid; $[\alpha]^{20}_D$ −57.7° (*c* 0.26, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.84 (t, J = 6.7 Hz, 3 H), 1.20−1.28 (m, 7 H), 1.34 (s, 3 H), 1.50−1.63 (m, 2 H), 1.71 (s, 3 H), 1.74 (s, 3 H), 1.77 (s, 3 H), 1.89 (bs, 4 H), 1.94 (dd, J = 7.1, 1.6 Hz, 3 H), 2.13−2.21 (m, 2 H), 2.50−2.62 (m, 4 H), 3.71 (d, J = 7.5 Hz, 1 H), 4.20−4.31 (m, 2 H), 4.36−4.44 (m, 2 H), 4.84 (d, J = 6.9 Hz, 1 H), 4.92−5.08 (m, 2 H), 5.30 (d, J = 8.8 Hz, 1 H), 5.75 (d, J = 7.5 Hz, 1 H), 5.98 (dd, J = 15.6, 1.6 Hz, 1 H), 6.09 (d, J = 7.5 Hz, 1 H), 6.31 (s, 1 H), 6.41 (d, J = 5.7 Hz, 1 H), 7.11 (dq, J = 15.6, 6.9 Hz, 1 H), 7.48 (t, J = 7.4 Hz, 2 H), 7.61 (t, J = 7.4 Hz, 1 H), 8.06 (d, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.69, 13.93, 14.93, 18.35, 18.76, 22.33, 22.48, 23.31, 25.30, 25.88, 26.06, 31.33, 35.39, 36.58, 41.73, 45.04, 50.89, 58.72, 69.55, 71.81, 74.29, 74.48, 74.67, 75.98, 79.73, 80.43, 84.31, 88.37, 119.00, 121.22, 127.86, 128.98, 130.04, 133.62, 134.26, 139.84, 139.99, 147.99, 164.77, 165.95, 170.77, 172.13, 174.22, 202.33.

Syntheses of Taxoids 22 and 23 through Hydrogenation of Taxoids 17 and 18. A typical procedure is described for the preparation of 3′-dephenyl-3′-propyl-14*β*-hydroxydocetaxel 1,14-carbonate (**23a**): A solution **18a** (40 mg, 0.049 mmol) in ethyl acetate (3 mL) was added to 10% PdC (20 mg) under 1 atm of H_2. The mixture was stirred at 40 °C for 36 h. Removal of the catalyst by filtration and removal of the solvent gave **23a** (36 mg, 90%) as a white solid: mp 164−168 °C; ^{1}H NMR ($CDCl_3$) δ 0.98 (t, J = 7.2 Hz, 3 H), 1.25 (s, 3 H), 1.28−1.46 (m, 11 H), 1.62−1.91 (m, 9 H), 2.48−2.60 (m, 4 H), 3.80 (d, J = 7.5 Hz, 1 H), 4.04−4.16 (m, 1 H), 4.21−4.32 (m, 3 H), 4.38 (bs, 1 H), 4.82 (m, 2 H), 4.93 (d, J = 8.3 Hz, 1 H), 5.19 (s, 1 H), 6.10 (d, J = 7.5 Hz, 1 H), 6.45 (d, J = 6.2 Hz, 1 H), 7.48 (t, J = 7.4 Hz, 2 H), 7.61 (d, J = 7.4 Hz, 1 H), 8.03 (d, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.97, 13.99, 14.47, 19.47, 22.05, 22.05, 25.63, 28.24, 33.91, 36.73, 41.70, 45.93, 53.01, 57.87, 69.35, 71.67, 73.09, 74.10, 74.63, 76.09, 79.65, 80.46, 84.01,

88.14, 127.95, 129.01, 129.99, 134.15, 136.04, 136.49, 152.40, 156.95, 165.10, 171.15, 173.88, 209.83.

In the same manner, **22b**,**d**,**e** and **23b** were prepared using the method described above.

3′-Dephenyl-3′-(2-methylpropyl)-14β-hydroxydocetaxel 1,14-carbonate (22a): 77% yield; white solid; mp 161−162 °C; $[\alpha]^{20}_D$ −37.8° (*c* 1.1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 0.97 (d, J = 6.0 Hz, 3 H), 0.99 (d, J = 6.0 Hz, 3 H), 1.25 (s, 3 H), 1.33 (s, 3 H), 1.38 (s, 9 H), 1.66−1.98 (m, 3 H), 1.79 (s, 3 H), 1.93 (s, 3 H), 2.49 (s, 3 H), 2.57 (m, 1 H), 3.81 (d, J = 7.4 Hz, 1 H), 4.05 (m, 1 H), 4.25 (bs, 1 H), 4.23−4.31 (m, 3 H), 4.77 (bd, J = 8.9 Hz, 1 H), 4.83 (d, J = 6.8 Hz, 1 H), 4.94 (d, J = 8.1 Hz, 1 H), 5.18 (s, 1 H), 6.11 (d, J = 7.4 Hz, 1 H), 6.47 (bd, J = 6.2 Hz, 1 H), 7.48 (m, 2 H), 7.62 (m, 1 H), 8.04 (d, J = 7.7 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 10.01, 14.47, 22.07, 22.17, 22.45, 23.23, 24.86, 25.66, 28.24, 29.85, 36.78, 40.35, 41.67, 45.88, 51.87, 57.83, 69.39, 71.68, 73.86, 74.09, 74.59, 76.08, 77.21, 79.67, 80.39, 83.95, 88.16, 127.95, 128.97, 129.95, 134.16, 136.04, 136.37, 151.94, 156.27, 164.85, 170.66, 172.86, 209.84; IR (KBr disk) 3434, 2954, 2930, 1821, 1734, 1713, 1363, 1237, 1088 cm^{-1}. Anal. ($C_{42}H_{55}NO_{16}$) C, H, N.

3′-Dephenyl-3′-(2-methylpropyl)-10-acetyl-14β-hydroxydocetaxel 1,14-carbonate (22b): 100% yield; white solid; mp 158−162 °C; $[\alpha]^{20}_D$ −57.1° (*c* 0.56, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.99 (m, 6 H), 1.29 (s, 3 H), 1.35 (s, 3 H), 1.38 (s, 9 H), 1.72 (m, 6 H), 1.91 (bm, 4 H), 2.26 (s, 3 H), 2.48 (bs, 1 H), 2.56 (s, 3 H), 2.58 (m, 1 H), 3.71 (d, J = 7.4 Hz, 1 H), 4.01 (m, 1 H), 4.10 (m, 1 H), 4.24 and 4.30 (AB quartet, J = 8.7 Hz, 2 H), 4.40 (m, 2 H), 4.75 (d, J = 8.8 Hz, 1 H), 4.87 (d, J = 6.9 Hz, 1 H), 4.94 (d, J = 8.3 Hz, 1 H), 6.09 (d, J = 7.5 Hz, 1 H), 6.26 (s, 1 H), 6.44 (d, J = 6.0 Hz, 1 H), 7.45 (t, 2 H), 7.60 (t, 1 H), 8.00 (d, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.7, 15.0, 20.8, 22.1, 22.5, 23.2, 24.8, 26.0, 28.2, 35.5, 40.4, 41.8, 45.1, 51.7, 58.7, 69.4, 71.7, 73.8, 74.5, 74.8, 75.9, 79.6, 80.4, 84.2, 88.2, 127.9, 129.0, 130.0, 133.5, 134.1, 139.8, 151.8, 156.2, 164.7, 170.6, 170.9, 171.3, 172.9, 202.2; IR ($CDCl_3$) 3422, 2983, 1824, 1732, 1508, 1465, 1243 cm^{-1}. Anal. ($C_{44}H_{58}NO_{16}$) C, H, N.

3′-Dephenyl-3′-(2-methylpropyl)-10-(cyclopropylcarbonyl)-14β-hydroxydocetaxel 1,14-carbonate (22d): 91% yield; white solid; mp 129−133 °C; $[\alpha]^{20}_D$ −40.9° (*c* 0.22, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.88 (dd, J = 6.6, 1.2 Hz, 2 H), 0.95−1.01 (m, 6 H), 1.07−1.12 (m, 2 H), 1.28 (s, 3 H), 1.33−1.43 (m, 14 H), 1.63 (s, 3 H), 1.68−1.83 (m, 5 H), 1.89 (s, 3 H), 2.44−2.60 (m, 4 H), 3.69 (d, J = 7.4 Hz, 1 H), 3.98 (d, J = 6.1 Hz, 1 H), 4.22 (d, J = 8.4 Hz, 1 H), 4.26−4.43 (m, 4 H), 4.72 (d, J = 8.9 Hz, 1 H), 4.85 (d, J = 7.0 Hz, 1 H), 4.93 (d, J = 8.0 Hz, 1 H), 6.09 (d, J = 7.4 Hz, 1 H), 6.25 (s, 1 H), 6.46 (d, J = 6.1 Hz, 1 H), 7.47 (t, J = 7.5 Hz, 2 H), 7.61 (t, J = 7.5 Hz, 1 H), 8.03 (d, J = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.44, 9.70, 12.95, 14.21, 15.08, 22.15, 22.51, 23.26, 24.94, 26.02, 27.96, 28.23, 32.48, 33.97, 35.37, 40.40, 41.76, 45.01, 51.63, 58.68, 69.44, 71.79, 73.85, 74.60, 75.93, 79.64, 80.43, 84.27, 88.22, 127.90, 129.01, 133.55, 134.16, 139.86, 151.91, 156.25, 164.76, 170.63, 172.99, 174.94, 202.38.

3′-Dephenyl-3′-(2-methylpropyl)-10-(*N*,*N*-dimethylcarbamoyl)-14β-hydroxydocetaxel 1,14-carbonate (22e): 75% yield (94% conversion yield); white solid; mp 166−170 °C; $[\alpha]^{20}_D$ −40.5° (*c* 0.37, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.97 (t, J = 5.4 Hz, 6 H), 1.27 (s, 3 H), 1.33 (s, 3 H), 1.39 (bs, 10 H), 1.62−1.72 (m, 5 H), 1.91 (bs, 4 H), 2.47 (s, 3 H), 2.49−2.61 (m, 1 H), 2.96 (s, 3 H), 3.03 (s, 3 H), 3.10 (bs, 1 H), 3.69 (d, J = 7.4 Hz, 1 H), 4.22 (d, J = 8.4 Hz, 1 H), 4.26−4.35 (m, 2 H), 4.36−4.46 (m, 1 H), 4.73 (d, J = 9.0 Hz, 1 H), 4.86 (d, J = 6.9 Hz, 1 H), 4.94 (d, J = 7.7 Hz, 1 H), 6.09 (d, J = 7.5 Hz, 1 H), 6.20 (s, 1 H), 6.46 (d, J = 6.3 Hz, 1 H), 7.47 (t, J = 7.4 Hz, 2 H), 7.60 (t, J = 7.4 Hz, 1 H), 8.02 (d, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.48, 14.20, 15.13, 22.16, 22.51, 23.26, 23.58, 24.85, 26.21, 28.24, 35.21, 36.07, 36.75, 40.43, 41.79, 44.95, 51.62, 58.66, 69.54, 72.07, 73.86, 74.70, 75.41, 75.92, 79.71, 80.49, 84.47, 88.32, 127.95, 128.99, 129.98, 133.81, 134.14, 140.25, 155.79, 156.25, 164.77, 170.58, 172.46, 173.03, 204.19.

3′-Dephenyl-3′-propyl-10-acetyl-14β-hydroxydocetaxel 1,14-carbonate (23b): 86% yield; white solid; mp 158−161 °C; ^{1}H NMR ($CDCl_3$) δ 0.99 (t, J = 7.0 Hz, 3 H), 1.25 (s, 3 H), 1.28 (s, 3 H), 1.36 (s, 9 H), 1.36−1.47 (m, 2 H), 1.63−1.70 (m, 2 H), 1.72 (s, 3 H), 1.90 (d, J = 0.74 Hz, 3 H), 2.25 (s, 3 H), 2.35 (bs, 1 H), 2.49 (s, 3 H), 2.50−2.62 (m, 2 H), 3.71 (d, J = 7.4 Hz, 1 H), 3.83 (bs, 1 H), 4.00−4.10 (m, 1 H), 4.22 (d, J = 8.4 Hz, 1 H), 4.29 (d, J = 8.4 Hz, 1 H), 4.35−4.44 (m, 2 H), 4.76 (d, J = 8.9 Hz, 1 H), 4.86 (d, J = 6.6 Hz, 1 H), 4.93 (d, J = 7.7 Hz, 1 H), 6.11 (d, J = 7.4 Hz, 1 H), 6.27 (s, 1 H), 6.44 (d, J = 6.6 Hz, 1 H), 7.49 (t, J = 7.5 Hz, 2 H), 7.61 (t, J = 7.3 Hz, 1 H), 8.03 (d, J = 7.3 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 9.68 13.95, 14.20, 14.98, 19.44, 20.75, 22.51, 23.11, 25.96, 28.23, 29.69, 33.94, 35.45, 41.79, 45.07, 53.05, 58.74, 60.38, 69.40, 71.75, 73.12, 74.64, 74.78, 75.96, 79.60, 80.34, 80.53, 84.24, 88.12, 127.95, 129.00, 129.98, 133.56, 134.10, 139.72, 151.82, 156.20, 164.76, 170.64, 170.91, 173.06, 202.15.

Cytotoxicity Assay *in Vitro*.[30] Tumor cell growth inhibition was determined according to the method established by Skehan et al.[34] Human tumor cells (A121 ovarian carcinoma, HT-29 colon carcinoma, A549 non-small-cell lung carcinoma, MCF-7 breast carcinoma, and MCF7-R doxorubicin-resistant breast carcinoma) were plated at a density of 400 cells/well in 96-well plates and allowed to attached overnight. These cell lines were maintained in RPMI-1640 medium (Roswell Park Memorial Institute growth medium) supplemented with 5% fetal bovine serum and 5% Nu Serum (Collaborative Biomedical Product, MA). Taxanes were solubilized in DMSO and further diluted with RPMI-1640 medium. Triplicate wells were exposed to various treatments. After 72 h incubation, 100 μL of ice-cold 50% trichloroacetic acid (TCA) was added to each well, and the samples were incubated for 1 h at 4 °C. Plates were then washed five times with water to remove TCA and serum proteins, and 50 μL of 0.4% sulforhodamine B (SRB) was added to each well. Following a 5 min incubation, plates were rinsed five times with 0.1% acetic acid and air-dried. The dye was then solubilized with 10 mM Tris base (pH 10.5) for 5 min on a gyratory shaker. Optical density was measured at 570 nm. The IC_{50} values were then calculated by fitting the concentration−effect curve data with the sigmoid-E_{max} model using nonlinear regression, weighted by the reciprocal of the square of the predicted effect.[35]

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