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CHEMICAL OXIDATION OF TAXOIDS WITH *m*-CPBA AND DIMETHYL DIOXIRANE : REGIOSELECTIVE EPOXIDATION OF TAXININE J DERIVATIVES

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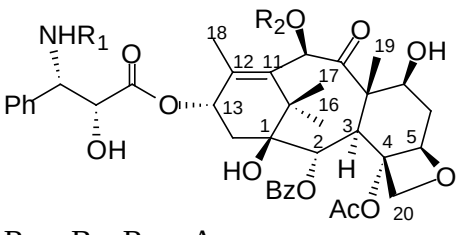
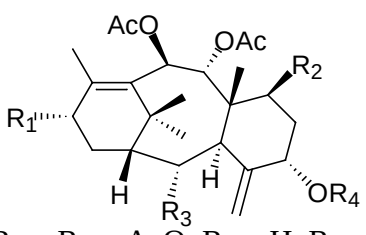
Abstract- Epoxidation of taxinine J derivative (**2c**) with *m*-CPBA afforded a mixture of 4α,20-epoxide (**3**), 4α,20 : 11β,12β-diepoxide (**4**) and 11β,12β-epoxide (**5**). The proportion of the yields was dependent on temperature (**3** : **4** = 80 : 10 at room temperature, **4** : **5** = 68 : 25 at 0-10℃). The reactions of derivatives of taxinine (**2b**) with *m*-CPBA and dimethyldioxirane (DMDO) were also investigated.

Paclitaxel (Taxol, **1a**)[1] and docetaxel (Taxotere, **1b**)[2] have proved to be successful anticancer drugs for the treatment of a variety of malignancies. Both compounds are substrates for P-gp,[3] and increased expression of this protein is a major factor underlying resistance to taxoids.[4] Interestingly, certain natural and semisynthetic taxoids devoid of cytotoxicity and tubulin affinity are powerful inhibitors of P-gp activity, acting as efficient reversing agents and allowing accumulation of paclitaxel in MDR-cancer cells.[5] Among the natural taxoids, 2-deacetoxytaxinine J[6] (**2a**) emerged as the most active member of this class, with potency higher than that of verapamil.[5]



1a, R_1 = Bz, R_2 = Ac
1b, R_1 = Boc, R_2 = H

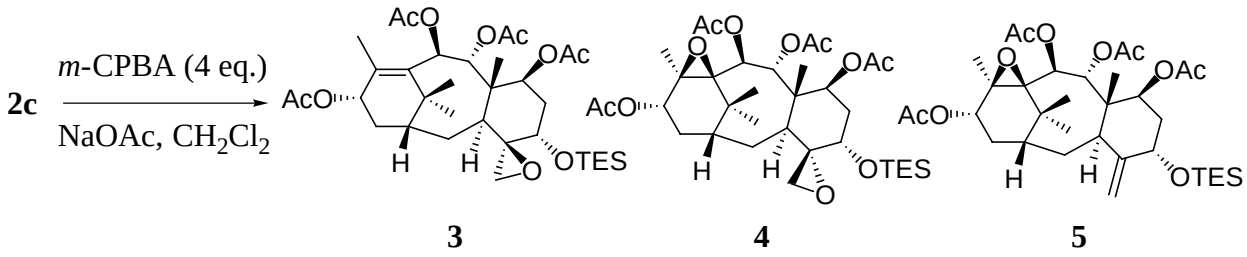


2a, R_1 = R_2 = AcO, R_3 = H, R_4 = cinnamoyl
2b, R_1 = O, R_2 = H, R_3 = AcO, R_4 = cinnamoyl
2c, R_1 = R_2 = AcO, R_3 = H, R_4 = TES

Unlike other cinnamates related to taxine, **2a** does not show cardiac toxicity,[7] and might thus serve as an important starting material for the synthesis of new reversal agents.[8] Consequently, it is important to synthesize the analogs of **2a**. In our previous paper,[9] we reported that hydroxylation of C-1 position of 2-deacetoxytaxinine J derivative (**2c**) had been successfully achieved by a simple chemical oxidation using dimethyldioxirane (DMDO)[10] leading to the 1β-hydroxy-4α,20-epoxide (**6a**) and 1β–hydroxy-4β,20-epoxide (**6b**). Here we report the temperature-dependent regioselective epoxidation of **2c** with *m*-CPBA[11] and the application of our DMDO oxidation to other taxoids that were not able to be oxidized at 1β-position.

Results

1. Reaction of 2c with *m*-CPBA



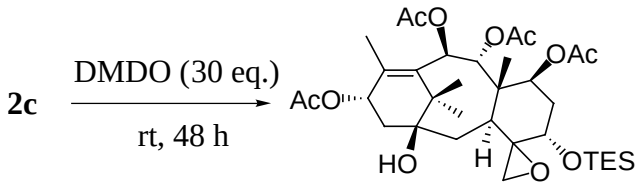
3 **4** **5**

Table 1. Temperature-dependent Regioselectivity on Oxidation of **2c** with *m*-CPBA.

Run	temperature	Yield		
		3	**4**	**5**
1	rt	80%	10%	none
2	0-10℃	none	68%	25%

The oxidation of compound (**2c**) with *m*-CPBA (4 eq.) (Table 1.) at room temperature gave the 4α,20-monoepoxide (**3**) predominantly and a small amount of the diepoxide (**4**).[11(b)]
While the same reaction at 0-10℃ gave 4α,20 : 11β,12β-diepoxide (**4**) mainly and some amount of the 11β, 12β-monoepoxide (**5**).[11(b)] In this case, compound (**3**) was not isolated.

2. Reaction of 2c and taxinine derivatives with *m*-CPBA and DMDO

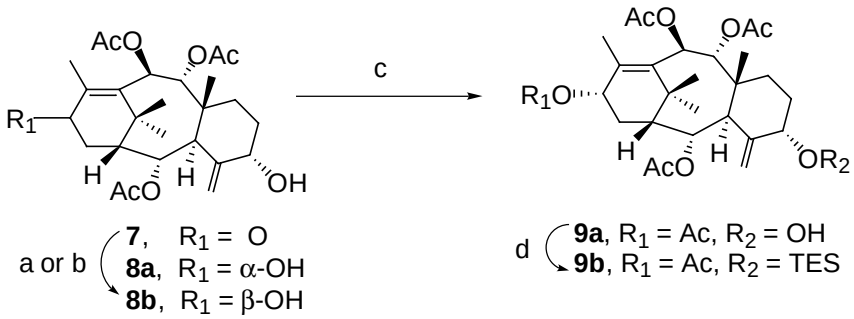


6a, 1β-hydroxy-4α,20-epoxide (45%)
6b, 1β-hydroxy-4β,20-epoxide (51%)

Scheme 1. Regio- and Stereoselective Hydroxylation at C(1) of **2c** with an excess amount of DMDO

On the other hand, the oxidation of **2c** with an excess amount of DMDO gave mixture of 1β-hydroxy-4α,

20-epoxide (**6a**) and 1β-hydroxy-4β,20-epoxide (**6b**) (Scheme 1).[9] The regioselective hydroxylation at C(1) of **2c** with excess DMDO is an interesting finding from the viewpoint of the similarity of biogenesis[13,14] and a synthetic use, so we attempted to apply this method to another type of taxoids prepared from taxinine (**2b**), a major component of the Japanese yew leaves, as follows (Scheme 2): the compound (**7**) [15] was reduced by $NaBH_4$ or $LiBH_4$ to give a mixture of compounds (**8a**)[16] and (**8b**). Next the diol (**8a**) was acetylated selectively at 13-OH to yield 2-acetyltaxinine E (**9a**).[17] Protection of the 5-OH group of **9a** with TES group gave compound (**9b**). We also examined about oxidation of these taxoids with *m*-CPBA .



Scheme 2. Synthesis of 2-acetyltaxinine E (**9a**) and the Related Compound (**9b**).
a) $NaBH_4$, $CeCl_3$, MeOH, (α, 56%; β, 44%). b) $LiBH_4$, THF, (α, 27%; β, 33%).
c) Ac_2O, Py, (**9a**, 88%). d) TESCl, imidazole, DMF, rt, (**9b**, 100%)

As shown in Table 2, none of the compounds could be hydroxylated at the C (1) position even by the use of an excess amount of DMDO or *m*-CPBA. In addition, excess DMDO epoxidized only the exo-double bond of taxoids. The allylic hydroxy groups of compounds (**9a**) and (**7**) were oxidized to carbonyl group (**13a**, **13b**, **14a**, **14b**). Protection of the 5-OH group as TES ether increased β-selectivity in the epoxidation.[11(a),18] On the other hand, *m*-CPBA could epoxidize both 11,12- and 4 (20)-double bonds. Consequently, the 11, 12-double bond was unreactive toward DMDO, which was similar to tendency other electrophilic and nucleophilic addition,[14] but was reactive toward *m*-CPBA.

3. Biological activity

Biological activity of some derivatives were evaluated in *in vitro* cytotoxicity assay against human cancer cell lines (TFK-1), and compound (**4**) was found to be cytotoxic (IC_{50} of **4** / IC_{50} of taxol = 80). While compound (**2c**), (**3**) and (**5**) did not show activity in this assay.

Discussion

1. In a closely related compound of **2c**, it is reported that a change of the functional group could affect the regioselectivity at the 11,12- and 4,20- double bonds,[11(b)] so the reactions (Table 1) above described is the first example of the temperature-dependent change of the regioselectivity. This may be caused by a

conformational change of the substrate depending on temperature.

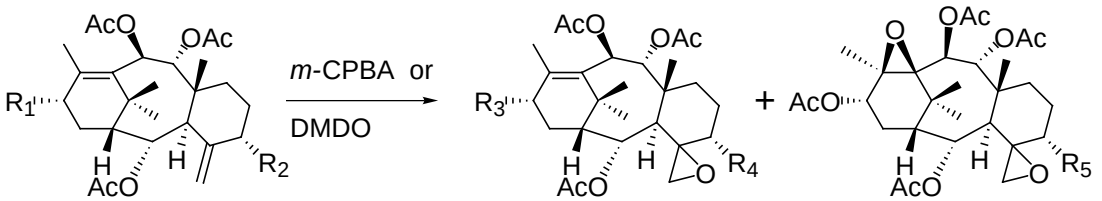
2. Generally, O atom-insertion reaction to C-H bond requires an optimum stereoalignment of the dioxirane attack in the proposed mechanism.[9, 10(a)] These different result about C(1) hydroxylation (Table 2.) in competition with **2c** might be explained by the disadvantage to dioxirane attack caused by additional steric hindrance of the C (2) acetoxy group in **2c**.

3. The proposed relationship of the orientation of 4,20-epoxide with the magnitude of chemical shift differences between the geminal-4,20- epoxide proton of 2-acetoxytaxoids[11(a)][i.e. $\Delta\delta(\alpha)$ $0.5 < \Delta\delta(\beta)$ 1.2] was also observed here, for example $\Delta\delta$ (**11a**) = 0.56 and $\Delta\delta$ (**11b**) = 1.35, $\Delta\delta$ (**12a**) = 0.40 and $\Delta\delta$ (**12b**) = 1.38. A similar relationship could be observed to the 2-dehydroxytaxoids, $\Delta\delta$ (**6a**) = 0 and $\Delta\delta$ (**6b**) = 0.42. While this rule was unapplicable for 5-oxotaxoids; $\Delta\delta$ (**13a**) = 0.66 and $\Delta\delta$ (**13b**) = 0.46, $\Delta\delta$ (**14a**) = 0.65 and $\Delta\delta$ (**14b**) = 0.37.

Table 2. Oxidation Products of Taxinine and Taxinine E Derivatives with DMDO or *m*-CPBA.

Run	Substrate	DMDO yield [% (α/β)]	*m*-CPBA yield [% (α/β)]
1	**9a**	**13a**+**13b** [77(55/22)]	**11a** [72], **17a** [26]
2	**9b**	**12a**+**12b** [64(22/42)]	**12a** (**11a**)[a] [29], **18a**+**18b** (**17b**)[a] [68(40/28)]
3	**7**	**14a**+**14b** [77(55/22)]	**15a**+**15b**[b] [98(97/1)]
4	**10**[b]	**16a**+**16b**[b] [86(41/45)]	

[a] **12a** and **18b** could not be separated with each other, so these structures and yields were estimated from desiyllated **11a** and **17b**, respectively. [b] See ref 11(a).



	R_1	R_2
9a	AcO	OH
9b	AcO	OTES
7	O	OH
10	O	OTES

	R_3	R_4	4, 20-epoxide
11a	AcO	OH	α
12a	AcO	OTES	α
12b	AcO	OTES	β
13a	AcO	O	α
13b	AcO	O	β
14a	O	O	α
14b	O	O	β
15a	O	OH	α
15b	O	OH	β
16a	O	OTES	α
16b	O	OTES	β

	R_5	4, 20-epoxide
17a	OH	α
17b	OH	β
18a	OTES	α
18b	OTES	β

Conclusion

It was found that the change of rection temperature could control a regioselectivity of the epoxidation between the endo- and exo-double bonds of 2-deacetoxytaxinine *J* with *m*-CPBA. The epoxides will be useful for the synthesis of other analogs by reaction with a strong Lewis acid.[19] On the other hand, the regio-selective oxidation at C(1) position by excess DMDO is not useful for 2-acetoxytaxoids because of its additional steric hindrance at C(1) position.

EXPERIMENTAL

General. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian UNITY INOVA 500 spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C in $CDCl_3$, TMS as internal standards). MS spectra (FAB) were recorded on a JEOL The MStation JMS-700 mass spectrometer. Optical rotation was measured on a HORIBA SEPA-300 polarimeter. Merck silica gel 60 (70-230 mesh) was used for column chromatography and Merck silica gel 60 F254 was used for preparative thin-layer chromatography (PTLC).

Materials. Taxinine and 2-deacetoxytaxinine *J* were collected from the needles of the Japanese yew (2 g/kg and 200 mg/Kg). 65 % *m*-CPBA (Tokyo Chemical Industry Co., LTD) was purified to about 100% before use as follow: *m*-CPBA solution in $CHCl_3$ was washed by phosphate buffer (pH 7.5), dried over Na_2SO_4, and concentrated *in vacuo*.

7β,9α,10β,13α-Tetraacetoxy-5α-triethylsilyloxy-taxa-4 (20), 11-diene (**2c**)

The solution of **2** (338 mg, 0.52 mmol), $NH_2OH \cdot HCl$ (338 mg, 4.86 mmol) and NaOAc (672 mg, 8.19 mmol) in EtOH (200 mL) and H_2O (200 mL) was stirred at 80°C for 48 h.[15] The mixture was diluted with $CHCl_3$ (30 mL). The organic layer was washed with a saturated solution of NH_4Cl, 5% $NaHCO_3$, and brine, and dried over Na_2SO_4. The organic layer was concentrated *in vacuo*. The residue was purified by chromatography ($CHCl_3$ / MeOH = 20 / 1), yielding crude alcohol (260 mg). To the solution of crude alcohol (260 mg) and imidazole (49 mg, 0.72 mmol) in DMF (4 mL) was added TESCl (80 mg, 0.53 mmol) and the mixture was stirred for 2h at rt. The mixture was diluted with ether (30 mL). The organic layer was washed with water, a saturated solution of NH_4Cl, and brine, dried over Na_2SO_4. The organic layer was concentrated *in vacuo*. The residue was purified by chromatography ($CHCl_3$ / MeOH = 20/1), yielding **2c** (267 mg, 80%, 2 steps) As amorphous solid; $[\alpha]_D^{20}$ +32° (*c* 0.0075, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.25 (d, 1H, *J* = 11.3 Hz, H-10), 5.97 (m, 1H, H-13), 5.89 (d, 1H, *J* = 11.0 Hz, H-9), 5.65 (dd, 1H, *J* = 5.2, 11.3 Hz, H-7), 5.03 (s, 1H, H-20), 4.75 (s, 1H, H-20), 4.20 (br t, 1H, 5-H), 2.98 (d, 1H, *J* = 6.0 Hz, H-3), 2.56 (ddd, 1H, *J* = 9.6, 9.9, 14.3 Hz, H-14β), 2.15 (d, 3H, *J* = 1.4 Hz, Me-18), 2.05 (s, 3H, Ac), 1.99 (s, 3H, Ac), 1.96 (s, 3H, Ac), 1.91(s, 3H, Ac), 1.85 (m, 2H, H-1, H-2), 1.74 (ddd, 1H, *J* = 2.5, 5.5, 13.5 Hz, H-6α), 1.70 (m, 2H, H-2, H-6), 1.63 (s, 3H, Me-16), 1.16 (s,

3H, Me-17), 1.10 (dd, 1H, *J* = 9.3, 14.3 Hz, H-14α), 0.96-0.92 (m, 9H, TES), 0.81(s, 3H, Me-19), 0.70-0.60 (m, 6H, TES); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.94, 170.37, 169.71, 169.20 (4×Ac), 151.98, 137.84, 133.58, 111.54, 77.11, 73.25, 71.72, 70.81, 70.33, 46.35, 40.89, 39.51, 37.99, 36.02, 31.23, 30.99, 27.89, 27.71, 21.54, 21.46, 21.05, 20.91, 14.72, 13.36, 6.81 (TES), 4.53 (TES); IR (film) ν max ($CHCl_3$) cm^{-1} 3000-2900 (s), 1740 (s, C=O), 1370 (s), 1240 (s), 1020 (s), 750 (s); HRFABMS calcd 634.3534 for $C_{34}H_{54}O_9Si$; found 634.3541.

Preparation of dimethyldioxirane (DMDO)

DMDO solution was prepared and assayed[10(b)] to be 0.075 M solution in acetone.

Reaction by DMDO

Compound (**2c**) (50 mg, 0.079 mmol) was dissolved into DMDO solution (40 mL, 31 eq. as DMDO) and the mixture was left for 48 h at rt. The reaction mixture was concentrated *in vacuo*, and the residue was applied to a TLC (hexane / ethylacetate = 2 / 1) to give **6a**[10] (23 mg, 45%) and **6b**[10] (26 mg, 51%). The same procedure was carried out for **9a**[17], **9b**, **7**[15] and **10**[11(a)].

Reaction of **2c** by *m*-CPBA

To a solution of **2c** (94 mg, 0.15 mmol) in CH_2Cl_2 (5 mL) were added *m*-CPBA (104 mg, 0.60 mmol) and NaOAc (100 mg, 1.2 mmol). The reaction mixture was stirred at rt for 3 h, and then extracted with EtOAc and the extract was washed with a saturated solution of $NaHCO_3$. The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (EtOAc / hexane = 2 / 1) to give **3** (77 mg, 80%) and **4** (10 mg, 10%). The same procedure was carried out at rt for **9a**, **9b** and **7**. Next, to a solution of **2c** (85mg, 0.13 mmol) in CH_2Cl_2 (5 mL) were added *m*-CPBA (94 mg, 0.52 mmol) and NaOAc (100 mg, 1.2 mmol). The reaction mixture was stirred at 0-10℃ for 48 h, and then extracted with EtOAc and the extract was washed with a saturated solution of $NaHCO_3$. The organic layer was dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (EtOAc / hexane = 2 / 1) to give **4** (57 mg, 68%) and **5** (22 mg, 25%).

7β,9α,10β,13α-Tetraacetoxy-4α,20-epoxy-5α-triethylsilyloxy-11-taxene (**3**)

As amorphous solid; $[\alpha]_D$ +95° (*c* 0.0074, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.18 (d, 1H, *J* = 11.0 Hz, H-10), 5.89 (m, 1H, H-13), 5.87 (d, 1H, *J* = 11.0 Hz, H-9), 5.61 (dd, 1H, *J* = 4.5, 11.0 Hz, H-7), 3.32 (br t, 1H, 5-H), 2.75 (m, 1H, H-3), 2.63 (ddd, 1H, *J* = 4.67, 9.62, 14.3 Hz, H-14β), 2.73 (d, *J* = 3.85, 1H, H-20B), 2.37 (d, *J* = 3.85, 1H, H-20B), 2.13 (s, 3H, Me-18), 2.12 (s, 3H, Ac), 2.07 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.03 (m, 1H, H-6β), 1.97 (s, 3H, Ac), 1.78 (m, 1H, H-1), 1.70 (m, 1H, H-6α), 1.60 (m, 1H, H-2β), 1.59 (s, 3H, Me-16), 1.12 (s, 3H, Me-17), 1.10 (m, 1H, H-14α), 1.07 (s, 3H, Me-19), 0.95 (m, 9H, TES), 0.82 (m, 1H, H-2α), 0.62 (m, 6H, TES); ^{13}C-NMR (500 MHz, $CDCl_3$) δ :

170.73, 170.34, 169.65, 169.22, 137.90, 134.57, 130.04, 128.25, 76.69, 73.20, 71.68, 70.51, 69.68, 61.11, 47.81, 46.27, 39.87, 39.59, 35.41, 32.80, 31.38, 30.56, 27.34, 22.76, 21.49, 21.33, 21.02, 20.84, 14.98, 14.30, 6.79, 4.71; IR (film) ν max ($CHCl_3$) cm^{-1}: 2950 (s), 1730 (s, C=O), 1660 (m), 1460 (s), 1430 (s), 1370 (s), 1310 (m), 1240 (s), 1140 (s), 1060 (s), 1020 (s), 990 (s), 960 (s), 900 (w), 820 (m), 800 (m), 750 (s), 660 (m); HR-FABMS calcd for $C_{34}H_{54}O_{10}NaSi$ $(M+Na)^+$ 673.3381, found 673.3382.

7β,9α,10β,13α-Tetraacetoxy-4α,20 : 11β,12β-diepoxy-5α-triethylsilyloxytaxane (**4**)

As amorphous solid; $[\alpha]_D^{20}$ +32°(*c* 0.12, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 5.97 (d, 1H, *J* = 11.3 Hz, H-9), 5.75 (dd, 1H, *J* = 4.7, 11.5 Hz, H-7), 5.45 (d, 1H, *J* = 11.5 Hz, H-9), 5.36 (dd, 1H, *J* = 9.6, 10.2 Hz, H-13), 3.43 (br t, 1H, 5-H), 2.60 (m, 1H, H-3), 2.60 (m, 2H, H-20AB), 2.32 (ddd, 1H, *J* = 9.6, 10.2, 14.8 Hz, H-14β), 2.36 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.01 (s, 3H, Ac), 1.91(m, 1H, H-6β), 2.00 (s, 3H, Ac), 1.86 (s, 3H, Me-18), 1.82 (m, 1H, H-6), 1.78 (m, 1H, H-1), 1.64 (s, 3H, Me-16), 1.50 (dd, 1H, *J* = 4.9, 14.8 Hz, H-2), 1.38 (ddd, 1H, *J* = 1.1, 10.7, 14.8 Hz, H-14α), 1.00 (m, 1H, H-2), 1.14-0.94 (m, 12H, Me-19, TES), 0.73 (s, 3H, Me-17), 0.68 (m, 6H, TES); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.48, 170.11, 169.33, 168.83 (4×Ac), 76.56, 72.54, 72.32, 70.04, 68.93, 65.60, 64.63, 59.08, 47.82, 45.69, 41.97, 39.15, 36.56, 32.26, 31.23, 28.86, 27.00, 21.27, 21.26, 21.17, 20.74, 20.71, 15.18, 13.25, 6.69 (TES), 4.56 (TES); IR (film) ν max ($CHCl_3$) cm^{-1}: 2950 (s), 1750 (s, C=O), 1460 (m), 1430 (s), 1370 (s), 1240 (s), 1140 (w), 1070 (m), 1020 (s), 990 (m), 960 (m), 900 (w), 820 (m), 750 (s), 660 (m); HR-FABMS calcd for $C_{34}H_{54}O_{10}NaSi$ $(M+Na)^+$ 689.3329, found 689.3333.

7β,9α,10β,13α-Tetraacetoxy-11β,12β-epoxy-5α-triethylsilyloxy-4 (20)-taxene (**5**)

As amorphous solid; $[\alpha]_D^{20}$ +21°(*c* 0.053, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.00 (d, 1H, *J* = 11.2 Hz, H-9), 5.76 (dd, 1H, *J* = 5.1, 11.0 Hz, H-7), 5.47 (d, 1H, *J* = 11.4 Hz, H-10), 5.38 (dd, 1H, *J* = 10.2, 11.5 Hz, H-13), 5.16 (br s, 1H, H-20B), 4.89 (d, 1H, *J* = 1.4 Hz, H-20B), 4.31 (dd, 1H, *J* = 2.8, 3.0 Hz 5-H), 2.78 (m, 1H, H-3), 2.32 (ddd, 1H, *J* = 8.8, 9.9, 14.8 Hz, H-14β), 2.11 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.01 (s, 3H, Ac), 2.00 (s, 3H, Ac), 1.86 (m, 2H, H-2), 1.86 (s, 3H, Me-18), 1.80 (m, 1H, H-1), 1.78 (m, 1H, H-6β), 1.75 (m, 1H, H-6α), 1.68 (s, 3H, Me-16), 1.06 (s, 3H, Me-17), 1.16 (dd, 1H, *J* = 10.7, 14.8 Hz, H-14α), 0.85 (s, 3H, Me-19), 0.95 (t, 9H, *J* =7.7 Hz, TES), 0.68 (m, 6H, TES); IR (film) ν max ($CHCl_3$) cm^{-1}: 2950 (s), 1730 (s, C=O), 1660 (m), 1460 (s), 1430 (s), 1370 (s), 1310 (m), 1240 (s), 1140 (s), 1060 (s), 1020 (s), 990 (s), 960 (s), 900 (w), 820 (m), 800 (m), 750 (s), 660(m); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.46, 170.12, 169.51, 168.90 (4×Ac), 150.31, 112.66, 73.42, 72.46, 70.17, 69.50, 65.66, 64.57, 45.45, 42.30, 39.14, 37.62, 35.91, 31.32, 29.31, 27.13, 25.95, 21.34, 21.29, 21.25, 21.20, 20.74, 15.18, 13.18, 6.75 (TES), 4.43 (TES); HR-FABMS calcd 673.3388 for

$C_{34}H_{54}O_{10}NaSi(M+Na)^+$; found 673.3381

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Synthesis of compound (**9a**)[17] and (**9b**)

To a stirred suspension of **7** (3.20 g, 6.71 mmol) and $CeCl_3$ (10 g, 0.16 mmol) in dry MeOH (400 mL) was added $NaBH_4$ (15 g, 2.38 mmol). After 25 min, acetone (10 mL) was added and stirring was continued for additional 15 min. The crude reaction product was isolated with Et_2O in usual manner and purified by chromatography (hexane/ EtOAc = 2/1), yielding pure α-alcohol (**8a**)[16] (1.79 g, 56%) and β-alcohol (**8b**) (1.41g, 46%). To a solution of **8a** (350 mg, 0.73 mmol) in dry pyridine (3 mL) was added Ac_2O (0.11 mL, 2.0 mmol). After the mixture was stirred for 48 h, EtOAc (20 mL) was added. The organic layer was washed with brine, H_2O, saturated solution of $CuSO_4$, H_2O, and brine. The organic layer was concentrated *in vacuo*, yielding **9a** (334 mg, 88%) as amorphous solid. To the solution of **9a** (334 mg, 0.62 mmol) and imidazole (92 mg, 1.2 mmol) in DMF (6 mL) was added TESCl (105 mg, 0.7 mmol). After the mixture was stirred for 2 h at rt, ether (30 mL) was added. The organic layer was washed with water, solution of saturated NH_4Cl, and brine, dried over Na_2SO_4.The organic layer was concentrated *in vacuo*. The residue was purified by chromatography (hexane / EtOAc = 3 / 1), yielding **9b** (394 mg, 100%) as an amorphous solid.

2α,9α,10β-Triacetoxytaxa-4 (20),11-diene-5α,13β-diol (**8b**)

As amorphous solid; $[\alpha]_D^{20}$ +63°(*c* 0.018, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.03 (d, 1H, *J* = 10.4 Hz, H-10), 5.83 (d, 1H, *J* = 10.4 Hz, H-9), 5.48 (dd, 1H, *J* = 1.4, 6.9 Hz, H-2), 5.17 (s, 1H, H-20), 4.69 (s, 1H, H-20), 4.32 (m, 1H, H-13), 4.21 (br s, 1H, 5-H), 3.27 (d, 1H, *J* = 6.9 Hz, H-3), 2.48 (m, 1H, OH-5), 2.18 (br s, 3H, Me-18), 2.16 (m, 1H, H-14), 2.05, 2.04, 2.01 (s, 9H, 3× Ac), 2.03 (m, 2H, H-1, H-14), 1.98 (s, 3H, Ac), 1.87 (m, 1H, H-7), 1.75 (m, 2H, H-6, H-7), 1.65 (s, 3H, Me-16), 1.64 (m, 1H, H-6), 1.29 (s, 3H, Me-17), 0.85 (s, 3H, Me-19); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.11, 169.47 (3×Ac), 147.12, 140.16, 136.31, 114.14, 76.66, 76.15, 73.21, 70.50, 70.04, 56.28, 44.78, 42.16, 36.51, 30.81, 29.74, 26.38, 25.80, 21.50, 21.11, 20.79, 18.91, 17.26; IR ν max ($CHCl_3$) cm^{-1}: 3450 (m, OH), 3000-2900 (m), 1730 (s, C=O), 1440 (m), 1370 (s), 1250 (s), 1020 (s), 980 (s), 900 (m), 760 (s), 660 (m); HR-FABMS calcd for $C_{34}H_{54}O_9Si$ 478.2564, found 478.2565.

2α,9α,10β,13α–Tetraacetoxy-5α-triethylsilyloxytaxa-4 (20),11-diene (**9b**)

As amorphous solid; $[\alpha]_D^{20}$ +29°(*c* 0.015, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.06 (d, 1H, *J* = 10.7 Hz, H-10), 5.95 (ddd, 1H, *J* = 1.2, 8.3, 10.1 Hz, H-13), 5.93 (d, 1H, *J* = 10.7 Hz, H-9), 5.42 (dd, 1H, *J* = 5.1, 2.7 Hz, H-2), 5.11 (s, 1H, H-20A), 4.42 (s, 1H, H-20A), 4.12 (br t, 1H, H-5), 3.36 (d, 1H, *J* = 7.8 Hz, H-3), 2.42 (dt, 1H, *J* = 14.7, 9.5 Hz, H-14β), 2.14 (s, 3H, Ac), 2.09 (d, 3H, *J* = 1.0 Hz, Me-18), 2.04 (s, 3H, Ac), 1.99 (1H, m, H-1), 2.00 (s, 3H, Ac), 1.98 (s, 3H, Ac), 1.83 (dt, 1H, *J* = 13.2,

9.0, H-7), 1.75 (s, 3H, Me-16), 1.70 (dt, 1H, *J* = 13.7, 3.4 Hz, H-7), 1.60 (m, 2H, H-2, H-6), 1.57 (dd, 1H, *J* = 9.8, 15.9 Hz, H-14α), 1.17 (s, 3H, Me-17), 0.96-0.92 (m, 9H, TES), 0.81(s, 3H, Me-19), 0.70-0.60 (m, 6H, TES); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.91, 170.17, 169.88, 169.62 (4×Ac), 146.87, 137.55, 131.91, 113.72, 77.11, 76.52, 72.49, 71.79, 70.44, 48.75, 44.33, 42.89, 37.42, 32.30, 31.35, 27.70, 27.40, 26.83, 21.44, 21.41, 21.03, 20.85, 17.99, 14.61, 6.78 (TES), 4.43(TES); IR (film) ν max ($CHCl_3$) cm^{-1}: 3000-2900 (s), 1740 (s, C=O), 1450 (m), 1370 (s), 1240 (s), 1020 (s), 900 (m), 760 (s), 660 (m); HR-FABMS calcd for $C_{34}H_{54}O_9Si$ 634.3534, found 634.3535.

2α,9α,10β,13α-Tetraacetoxy-4α,20-epoxy-11-taxen-5α-ol (**11a**)

As amorphous solid; $[\alpha]_D^{20}$ +60° (*c* 0.12, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.06 (d, 1H, *J* = 10.3 Hz, H-10), 5.79 (d, 1H, *J* = 10.3 Hz, H-9), 5.79 (m, 1H, H-13), 5.37 (dd, 1H, *J* = 1.0, 4.2 Hz, H-2), 3.47 (d, 1H, *J* = 4.2 Hz, H-3), 3.16 (br t, 1H, H-5), 3.06 (d, *J* = 4.9, 1H, H-20A), 2.67 (ddd, 1H, *J* = 8.8, 10.3, 15.6 Hz, H-14β), 2.50 (d, *J* = 4.9 Hz, 1H, H-20B), 2.29 (m, 1H, OH-5), 2.17 (d, 3H, *J* = 1.4 Hz, Me-18), 2.14 (s, 3H, Ac), 2.14 (m, 1H, H-7), 2.07 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.04 (m, 1H, H-7), 2.01 (s, 3H, Ac), 1.86 (m, 1H, H-6), 1.86 (m, 1H, H-14α), 1.70 (m, 2H, H-1,H-6), 1.69 (s, 3H, Me-16), 1.01 (s, 3H, Me-17), 0.93 (s, 3H, Me-19); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 169.93, 169.87, 169.73, 169.57 (4×Ac), 139.10, 134.16, 76.25, 75.98, 72.26, 72.16, 69.66, 62.93, 51.94, 46.82, 44.03, 37.72, 36.24, 31.70, 28.17, 26.00, 25.63, 25.04, 21.42, 20.91, 20.62, 20.60, 17.55, 15.62; IR (film) ν max ($CHCl_3$) cm^{-1}: 3500 (m), 2950 (s), 1740 (s, C=O), 1460 (m), 1370 (s), 1310 (m), 1240 (s), 1140 (s), 1060 (s), 1020 (s), 990 (s), 960 (s), 900 (w), 820 (m), 760 (s), 660 (m); HR-FABMS calcd for $C_{28}H_{40}O_{10}$(M^+) 536.2619, found 536.2624.

7β,9α,10β,13α-Tetraacetoxy-4β,20-epoxy-11-taxen-5α-ol (**11b**)

As amorphous solid; $[\alpha]_D^{20}$ +73° (*c* 0.038 $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.02 (d, 1H, *J* = 10.7 Hz, H-10), 5.82 (d, 1H, *J* = 10.4 Hz, H-9), 5.75 (ddd, 1H, *J* = 1.1, 4.4, 10.1 Hz, H-13), 5.45 (br d, 1H, *J* = 2.7, H-2), 3.55 (d, *J* = 5.2, 1H, H-20A), 3.17 (d, 1H, *J* = 3.6 Hz, H-3), 2.97 (br t, 1H, H-5), 2.77 (ddd, 1H, *J* = 8.8, 10.4, 15.7 Hz, H-14β), 2.20 (d, *J* = 5.5 Hz, 1H, H-20B), 2.13 (br s, 6H, Me-18, Ac), 2.07 (s, 3H, Ac), 2.01 (s, 3H, Ac), 1.98 (s, 3H, Ac), 1.86 (m, 1H, H-6), 1.85-1.70 (m, 2H, H-7), 1.66 (m, 2H, H-1, H-6), 1.57 (dd, 1H, *J* = 4.7, 15.7, H-14α), 1.65 (s, 3H, Me-16), 1.09 (s, 3H, Me-17), 1.02 (s, 3H, Me-19); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.81, 169.96, 169.87, 169.71 (4×Ac), 139.71, 134.34, 76.37. 76.17, 72.38, 72.30, 69.81, 63.01, 52.08, 46.93, 44.15, 37.84, 36.36, 31.85, 28.31, 26.10, 25.75, 25.16, 21.58, 21.10, 21.07, 21.03, 20.75, 20.74, 17.68, 15.78; IR (film) ν max ($CHCl_3$) cm^{-1}: 3600-3300 (m), 3000 (s), 1730 (s, C=O), 1430 (s), 1370 (s), 1240 (s), 1120 (s), 1020 (s), 960 (s), 920 (s), 900 (m), 750 (s); HR-FABMS calcd for $C_{28}H_{40}O_{10}$(M^+) 536.2619, found 536.2621.

2α,9α,10β,13α-Tetraacetoxy-4α,20-epoxy-5α-triethylsilyloxy-11-taxene (**12a**)

As amorphous solid; $[\alpha]_D^{20}$ +28° (*c* 0.0023, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.05 (d, 1H, *J* = 10.7 Hz, H-10), 5.97 (m, 1H, H-13), 5.87 (d, 1H, *J* = 10.7 Hz, H-9), 5.38 (dd, 1H, *J* = 1.1, 4.7 Hz, H-2), 3.15 (d, 1H, *J* = 4.7 Hz, H-3), 3.05 (br t, 1H, H-5), 2.79 (d, *J* = 5.0, 1H, H-20A), 2.55 (ddd, 1H, *J* = 9.6, 9.6, 14.8 Hz, H-14β), 2.39 (d, *J* = 5.0 Hz, 1H, H-20B), 2.13 (d, 3H, *J* = 1.4 Hz, Me-18), 2.15 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.02 (s, 3H, Ac), 2.00 (s, 3H, Ac), 1.88 (m, 1H, H-7), 1.76 (m, 1H, H-14α), 1.75 (s, 3H, Me-16), 1.74 (m, 1H, H-1), 1.70 (m, 1H, H-7), 1.68 (m, 1H, H-6), 1.60 (ddd, 1H, *J* = 3.6, 4.9, 10.4 Hz, H-6), 1.16 (s, 3H, Me-17), 0.98 (t, 9H, *J* = 3.0 Hz, TES), 0.94 (s, 3H, Me-19), 0.61 (q, 6H, *J* = 3.6 Hz, TES); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 171.92, 170.09, 169.98, 169.84 (4× Ac), 138.94, 132.40, 76.96, 76.66, 73.21, 72.03, 70.44, 61.75, 50.90, 48.34, 44.32, 38.45, 37.26, 31.28, 28.76, 27.82, 27.15, 25.21, 21.68, 21.52, 21.04, 20.77, 18.00, 14.98, 6.93, 4.74; IR (film) ν max ($CHCl_3$) (KBr) cm^{-1}: 3400 (w), 2950(m), 1740 (s, C=O), 1460 (m), 1430 (m), 1370 (s), 1240 (s), 1130 (m), 1030 (m), 980 (m), 950 (m), 920 (w), 820 (w), 800 (w), 740 (m); HR-FABMS calcd for $C_{34}H_{54}O_{10}Si$ (M^+) 650.34830, found 650.3488.

2α,9α,10β,13α-Tetraacetoxy-4β,20-epoxy-5α-triethylsilyloxy-11-taxene (**12b**)

As amorphous solid; $[\alpha]_D^{20}$ +25° (*c* 0.0061, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 5.98 (d, 1H, *J* = 10.7 Hz, H-10), 5.89 (m, 1H, H-13), 5.85 (d, 1H, *J* = 10.4 Hz, H-9), 5.42 (d, 1H, *J* = 3.0 Hz, H-2), 3.46 (d, *J* = 5.2, 1H, H-20A), 2.89 (d, 1H, *J* = 3.9 Hz, H-3), 2.85 (br t, 1H, H-5), 2.59 (ddd, 1H, *J* = 9.3, 9.6, 14.8 Hz, H-14β), 2.16 (s, 3H, Ac), 2.08 (d, *J* = 5.2 Hz, 1H, H-20B), 2.06 (br s, 3H, Me-18), 2.06 (s, 3H, Ac), 2.02 (s, 3H, Ac), 2.00 (s, 3H, Ac), 1.86 (m, 1H, H-6), 1.80-1.70 (m, 3H, H-1, H-7αβ), 1.69 (m, 1H, H-6), 1.69 (s, 3H, Me-16), 1.69 (m, 1H, H-14α), 1.12 (s, 3H, Me-17), 1.06 (s, 3H, Me-19), 0.93 (t, 9H, *J* =7.9 Hz, TES), 0.61 (q, 6H, *J* = 7.9 Hz, TES); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.80, 169.98, 169.90, 168.51 (4×Ac), 138.40, 133.13, 77.38, 76.93, 72.02, 71.85, 70.26, 61.81, 50.73, 48.08, 43.02, 38.41, 37.54, 31.26, 28.41, 27.19, 26.95, 25.33, 21.38, 21.28, 21.04, 20.75, 19.14, 14.96, 6.95, 4.79; IR (film) ν max ($CHCl_3$) cm^{-1}: 2950(m), 1740 (s, C=O), 1660 (m), 1460 (m), 1430 (m), 1390 (m), 1370 (m), 1240 (s), 1040 (s), 820 (m), 750 (m); HR-FABMS calcd for $C_{34}H_{54}O_{10}Si$ (M^+) 650.34830, found 650.3486.

2α,9α,10β,13α-Tetraacetoxy-4α,20-epoxy-11-taxen-5-one (**13a**)

As amorphous solid; $[\alpha]_D^{20}$ +55° (*c* 0.038, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 5.99 (d, 1H, *J* = 10.5 Hz, H-10), 5.90 (d, 1H, *J* = 10.5 Hz, H-10), 5.49 (m, 2H, H-2, H-13), 3.23 (d, 1H, *J* = 4.2, H-3), 3.09 (d, 1H, *J* = 6.1, H-20), 2.72 (ddd, 1H, *J* = 8.3, 10.0, 16.1 Hz, H-14β), 2.61(ddd, 1H, *J* = 2.2, 5.2, 15.9 Hz, H-6β), 2.52 (dd, 1H, *J* = 6.8, 14.4 Hz, H-7β), 2.43 (d, 1H, *J* = 6.1 Hz, H-20), 2.27 (ddd, 1H, *J* = 2.2, 6.8, 13.7 Hz, H-7α), 2.13 (s, 3H, Ac), 2.10 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.03 (s, 3H, Ac), 1.99

(d, 3H, *J* = 1.2, Me-18), 1.86 (m, 2H, H-14α, H-6α), 1.69 (m, 1H, H-1), 1.68 (s, 3H, Me-16), 1.21 (s, 3H, Me-19), 0.97 (s, 3H, Me-17); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 204.36 (C5), 170.60, 169.83, 169.81, 169.65 (4×Ac), 138.63, 135.66, 75.74, 72.09, 71.53, 69.30, 62.96, 50.89, 46.97, 43.51, 42.27, 37.35, 36.31, 32.98, 29.69, 28.50, 25.27, 21.49, 20.98, 20.92, 20.68, 17.89, 16.07; IR (film) ν max ($CHCl_3$) cm^{-1}: 2950 (m), 1730 (s, C=O), 1460 (m), 1370 (s), 1240 (s), 1060 (s), 995 (m), 960 (m), 820 (s), 760 (s), 660 (w); HR-FABMS calcd for $C_{28}H_{38}O_{10}$ (M^+) 534.2463, found 534.2466.

2α,9α,10β,13α-Tetraacetoxy-4β,20-epoxy-11-taxen-5-one (**13b**)

As amorphous solid; $[\alpha]_D^{20}$ +96° (*c* 0.057, $CHCl_3$) ; ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 5.99 (d, 1H, *J* = 10.3 Hz, H-10), 5.89 (d, 1H, *J* = 10.3 Hz, H-9), 5.57 (m, 2H, H-2, H-13), 3.37 (d, 1H, *J* = 6.4, H-20A), 3.21 (d, 1H, *J* = 4.4, H-3), 2.91 (d, 1H, *J* = 6.4, H-20B), 2.85 (ddd, 1H, *J* = 8.3, 10.3, 16.1, H-14β), 2.66 (ddd, 1H, *J* = 7.3, 9.0, 15.1, H-6α), 2.52 (ddd, 1H, *J* = 5.9, 7.3, 15.1, H-6β), 2.10-2.0 (m, 2H, H-7), 2.09, 2.08, 2.03 (s, 9H, 3×Ac), 2.00 (br s, 3H, Me-18), 1.98 (s, 1H, Ac), 1.71 (m, 1H, H-1), 1.65 (s, 3H, Me-16), 1.55 (dd, 1H, *J* = 3.4, 16.1, H-14α), 1.22 (s, 3H, Me-17), 0.98 (s, 3H, Me-19); ^{13}C- NMR (125 MHz, $CDCl_3$) δ : 205.60 (C5), 170.08, 169.96, 169.72, 168.57 (4×Ac), 137.30, 135.71, 76.08, 72.41, 69.29, 69.21, 62.07, 49.13, 47.31, 41.99, 41.70, 36.96, 34.82, 32.80, 29.46, 29.39, 25.63, 21.15, 20.99, 20.91, 20.66, 20.52, 16.43; IR (film) ν max ($CHCl_3$) cm^{-1}: 3000(m), 1730 (s, C=O), 1460 (m), 1370 (s), 1240 (s), 1060 (s), 820 (w), 760 (s), 660 (w); HR-FABMS calcd for $C_{28}H_{38}O_{10}$ (M^+) 534.2463, found 534.2465.

2α,9α,10β-Triacetoxy-4α,20-epoxy-11-taxene-5,13-dione (**14a**)

As amorphous solid; $[\alpha]_D^{20}$ +56° (*c* = 0.016, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.02 (d, 1H, *J* = 10.5 Hz, H-10), 5.99 (d, 1H, *J* = 10.5 Hz, H-9), 5.62 (dd, 1H, *J* = 1.2, 5.6 Hz, H-2), 3.13 (d, 1H, *J* = 6.1, H-20), 2.47 (m, 1H, H-7β), 2.93 (d, 1H, *J* = 4.4, H-3), 2.82 (dd, 1H, *J* = 6.8, 20.0 Hz, H-14β), 2.65 (d, 1H, *J* = 19.8, H-14α), 2.61 (ddd, 1H, *J* = 2.2, 5.1, 16.6 Hz, H-6β), 2.48 (d, 1H, *J* = 6.4, H-20), 2.13 (d, 3H, *J* = 1.2 Hz, Me-18), 2.09 (s, 3H, Ac), 2.06 (s, 6H, 2×Ac), 2.07 (m, 1H, H-1), 1.74 (dt, 1H, *J* = 5.1, 13.9 Hz, H-6α), 1.76 (s, 3H, Me-16), 1.11 (s, 3H, Me-17), 1.23 (s, 3H, Me-19); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 203.86 (C5), 198.86 (C13), 169.78, 169.64, 169.54 (3×Ac), 149.14, 138.60, 74.90, 72.28, 70.58, 62.60, 51.86, 47.55, 43.47, 42.91, 38.23, 36.67, 35.94, 35.84, 29.52, 25.06, 21.48, 20.84, 20.66, 17.99, 14.14; IR (film) ν max ($CHCl_3$) cm^{-1}: 2950 (s), 1740 (s, C=O), 1680 (m), 1430 (w), 1370 (s), 1240 (s), 1060 (s), 820 (m), 760 (s), 660 (m); HR-FABMS calcd for $C_{26}H_{34}O_9$ (M^+) 490.2200, found 490.2204.

2α,9α,10β-Triacetoxy-4β,20-epoxy-11-taxene-5,13-dione (**14b**)

As amorphous solid; $[\alpha]_D^{20}$ +38° (*c* 0.021, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.02 (d, 1H, *J* = 10.3

Hz, H-10), 6.00 (d, 1H, *J* = 10.5 Hz, H-9), 5.70 (dd, 1H, *J* = 1.5, 4.9 Hz, H-2), 3.25 (d, 1H, *J* = 6.3 Hz, H-20A), 2.98 (dd, 1H , *J* =7.1, 19.8 Hz, H-14β), 2.91 (d, 1H, *J* = 4.9 Hz, H-3), 2.88 (d, 1H, *J* = 6.4 Hz, H-20B), 2.61 (ddd, 1H, *J* = 7.8, 8.1, 15.9 Hz, H-6), 2.43 (ddd, 1H, *J* = 6.3, 8.5, 15.9 Hz, H-6), 2.34 (d, 1H, *J* = 19.8 Hz, H-14α), 2.20 (m, 1H, H-1), 2.12 (s, 3H, Ac), 2.07 (s, 3H, Ac), 2.03 (m, 1H, H-7), 2.01 (s, 3H, Ac), 1.99 (d, 3H, *J* = 1.22 Hz, Me-18), 1.73 (s, 3H, Me-16), 1.23 (s, 3H, Me-19), 1.12 (s, 3H, Me-17); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 205.22 (C5), 198.54 (C13), 169.74, 169.65, 168.57 (3×Ac), 150.64, 137.80, 75.25, 72.86, 68.03, 61.34, 49.97, 48.58, 41.96, 41.92, 37.83, 36.82, 36.38, 34.36, 28.72, 25.44, 21.14, 20.88, 20.85, 20.64, 13.94; IR (film) ν max ($CHCl_3$) cm^{-1}: 3400 (w), 2950 (m), 1740 (s, C=O), 1670 (m), 1450 (m), 1430 (s), 1370 (s), 1240 (s), 1140 (s), 1030 (s), 760 (s), 660 (m); HR-FABMS calcd for $C_{26}H_{34}O_9$ (M^+) 490.2200, found 490.2204.

2α,9α,10β,13α-Tetraacetoxy-4α,20 : 11β,12β-diepoxytaxan-5α-ol (**17a**)

As amorphous solid; $[\alpha]_D^{20}$ +12° (*c* 0.019, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 5.93 (d, 1H, *J* = 10.7 Hz, H-9), 5.51(d, 1H, *J* = 3.4 Hz, H-2), 5.42 (d, 1H, *J* = 10.4 Hz, H-10), 5.31 (dd, 1H, *J* = 7.6 Hz, 10.0 Hz, H-13), 3.24 (br s, 1H, H-5), 3.20 (d, *J* = 4.6 Hz, 1H, H-20A), 3.00 (d, 1H, *J* = 3.9 Hz, H-3), 2.56 (d, 1H, *J* = 4.6 Hz, 1H, H-20B), 2.42 (ddd, 1H, *J* = 9.8, 10.0, 15.9 Hz, H-14β), 2.13 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.04 (s, 3H, Ac), 1.90(m, 1H, H-6), 1.89 (m, 2H, H-7, H-6), 1.88 (s, 3H, Me-18), 1.84 (dd, 1H, *J* = 7.6, 15.9 Hz, H-14α), 1.76 (m, 1H, H-6), 1.76 (s, 3H, Me-16), 1.70 (m, 1H, H-7), 1.00 (s, 3H, Me-19), 0.91 (s, 3H, Me-17); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.13, 169.91, 169.88, 168.60 (4×Ac), 77.22, 72.33, 70.48, 68.14, 64.48, 64.38, 61.29, 60.33, 50.11, 49.41, 42.49, 37.87, 36.74, 30.29, 28.06, 26.07, 25.42, 24.86, 21.05, 20.92, 20.67, 20.42, 16.25, 14.03; IR (film) ν max ($CHCl_3$) cm^{-1}:3560 (m), 3500 (m), 2950 (s), 1730 (s, C=O), 1460 (s), 1430 (s), 1370 (s), 1220 (s), 1140 (m), 1060 (s), 1020 (s), 990 (s), 960 (s), 900 (w), 830 (m), 760 (s), 670 (m); HR-FABMS calcd for $C_{28}H_{40}O_{11}$ (M^+) 552.2568, found 552.2570.

2α,9α,10β,13α-Tetraacetoxy-4β,20 : 11β,12β-diepoxytaxan-5α-ol (**17b**)

As amorphous solid; $[\alpha]_D^{20}$ +34° (*c* 0.023, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : (d, 1H, *J* = 11.0 Hz, H-9), 5.57 (d, 1H, *J* = 2.4 Hz, H-2), 5.39 (d, 1H, *J* = 10.7 Hz, H-10), 5.30 (dd, 1H, *J* = 7.8, 10.3 Hz, H-13), 3.59 (d, *J* = 5.1, 1H, H-20A), 2.76 (d, 1H, *J* = 3.1 Hz, H-3), 3.06 (br s, 1H, H-5), 2.48 (ddd, 1H, *J* = 9.8, 10.0, 15.9 Hz, H-14β), 2.29 (d, 1H, *J* = 5.1 Hz, 1H, H-20B), 2.12 (s, 3H, Ac), 2.02 (s, 6H, 2×Ac), 2.00 (s, 3H, Ac), 1.98 (m, 1H, H-6), 1.89 (dd, 1H, *J* = 3.9, 14.1 Hz, H-7), 1.83 (s, 3H, Me-18), 1.77 (m, 1H, H-7), 1.74 (s, 3H, Me-16), 1.77 (m, 1H, H-7), 1.74 (s, 3H, Me-16), 1.70 (m, 1H, H-7), 1.59 (m, 2H, H-1, H-14α), 1.15 (s, 3H, Me-19), 0.94 (s, 3H, Me-17); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 169.98, 169.77, 169.75, 168.45, 77.17, 76.57, 72.30, 70.45, 68.12, 64.47, 64.38, 61.32,

50.17, 49.41, 42.52, 37.91, 36.77, 30.37, 28.12, 26.15, 25.47, 24.93, 21.19, 21.06, 20.80, 20.54, 18.64, 16.37; IR (film) ν max ($CHCl_3$) cm^{-1}: 3700-3200 (m), 3000 (s), 1740 (s, C=O), 1450 (s), 1370 (s), 1310 (m), 1240 (s), 1140 (s), 1040 (s), 920 (s), 835 (m), 800 (m), 760 (s), 660(m); HR-FABMS calcd for $C_{28}H_{40}O_{11}$ (M^+) 650.2568, found 650.2570.

2α,9α,10β,13α-Tetraacetoxy-4α,20 : 11β,12β-diepoxy-5α-triethylsilyloxytaxane (**18b**)

As amorphous solid; $[\alpha]_D^{20}$ +28° (*c* 0.0094, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 5.97 (d, 1H, *J* = 11.0 Hz, H-9), 5.50 (br d, 1H, *J* = 3.2 Hz, H-2), 5.36 (d, 1H, *J* = 11.0 Hz, H-10), 5.36 (dd, 1H, *J* = 9.8, 9.8 Hz, H-13), 3.14 (br s, 1H, H-5), 2.96 (d, *J* = 4.9 Hz, 1H, H-20A), 2.90 (d, 1H, *J* = 4.2 Hz, H-3), 2.39 (d, 1H, *J* = 4.9 Hz, 1H, H-20B), 2.33 (ddd, 1H, *J* = 9.8, 9.8, 15.4 Hz, H-14β), 2.15 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.03 (s, 3H, Ac), 1.88 (m, 1H, H-7), 1.85 (s, 3H, Me-18), 1.82 (m, 1H, H-7), 1.82 (m, 1H, H-14α), 1.78 (s, 3H, Me-16), 1.76 (m, 1H, H-6), 1.75 (m, 1H, H-7), 1.66 (m, 2H, H-1, H-6), 1.03 (s, 3H, Me-17), 1.00-0.94 (m, 12H, Me-19, TES), 0.76 (m, 6H, TES); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.44, 169.87, 169.81, 169.69 (4×Ac), 77.20, 76.75, 72.63, 72.49, 69.53, 64.07, 64.64, 61.37, 50.98, 50.12, 43.75, 37.98, 37.36, 31.11, 28.58, 26.54, 26.51, 24.93, 21.66, 21.26, 20.82, 20.30, 18.02, 15.90, 6.84 (TES), 4.65 (TES); IR (film) ν max ($CHCl_3$) cm^{-1}: 2950 (m), 1740 (s, C=O), 1460 (m), 1370 (s), 1240 (s), 1140 (m), 1030 (m), 980 (s), 960 (s), 890 (w), 820 (m), 800 (w), 750 (m), 670 (w); HR-FABMS calcd for $C_{34}H_{55}O_{11}Si$ $(M+H)^+$ 667.3510, found 667.3517.

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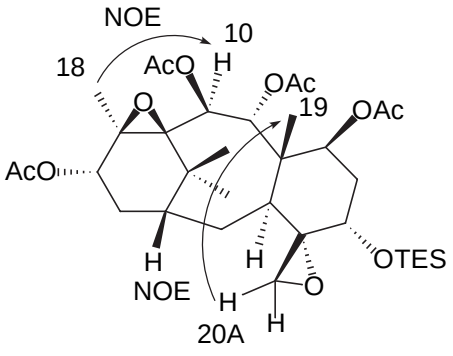

(**4**)

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