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Taxane Diterpenes 4: Autoxidation, Epimerization and Isomerization for the Introduction of Functionality into the Taxane ABC Ring System

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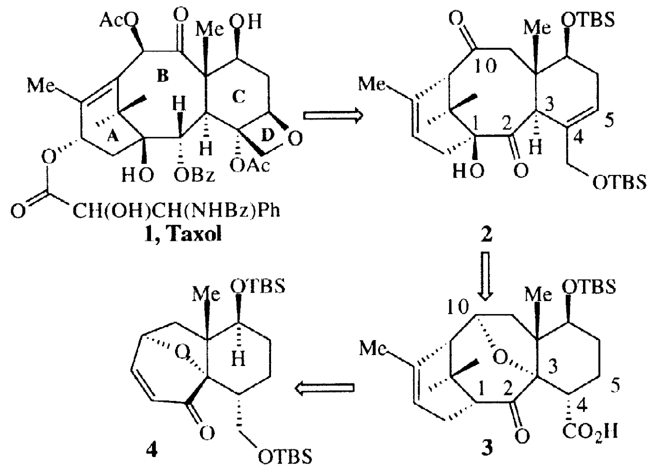
Abstract: The bicyclo[5.4.0]undecenone **4** was converted through a four step sequence involving activation, *gem*-methylcyclopropanation and reductive cleavage into **18**α/β, containing the B/C rings of the taxanes. The A-ring has been attached to the B/C ring system by cyclization of the sulfone-ester **23**α to give **24**. The A-ring was modified to give **29**, which underwent β-elimination of the 3,10-oxido bridge *via* a dianion, followed by transannular hydride shift to give the butenolide **30** and **32**. Autoxidation of **30** gave **33** which was further elaborated into the *trans*-fused B/C adduct **35**. The isomeric 3,10-diones *trans*-**39** and *cis*-**45** undergo autoxidation using *t*-BuOK/THF/O_2/$P(OEt)_3$ to give **2** and **46** respectively without B/C *cis/trans* isomerization.

Introduction

Scheme 1



Efforts to synthesize the antitumor diterpene taxol® **1** [1] have produced an wide variety of strategies for the construction of the core structure,[2] and to-date four total syntheses have been reported.[3a-d] One of the approaches we have adopted involves the conversion of **4** into the ABC skeleton **3**, which now requires β-elimination of the $C_{3,10}$ oxido bridge, hydroxylation at C_1, and double bond isomerization from $C_{3,4}$ to $C_{4,5}$ with establishment of the correct B/C *trans*-ring fusion to arrive at the advanced intermediate **2**, **Scheme 1**.[4] There have been a number of examples of C_1-oxygenation of taxane-type substrates that are summarized in **Scheme 2**. Shea reported that the A/B model **5**, under kinetic deprotonation conditions followed by quenching the $C_{1,2}$ enolate with the Davis oxaziridine gave **6**.[5,6] MM2 calculations indicated that the C_1-H is appropriately aligned [dihedral angle (ϕ) ca. 90°] to the adjacent C=O π-bond to allow direct enolate delocalization without energetically prohibitive conformational changes.[7] In Holtons synthesis of taxol the C_1-hydroxyl was introduced into **7** by C_1-enolate formation in the presence of the acidic β-ketolactone (C_3-H), and the enolate was quenched with (±)-camphorsulfonyl oxaziridine to give **8**.[3a] Wender employed the classical Barton-Gardner autoxidation conditions[8,9] to convert **9** into **10** (after reduction of the C_2 carbonyl group) in his synthesis of taxol.[3d]

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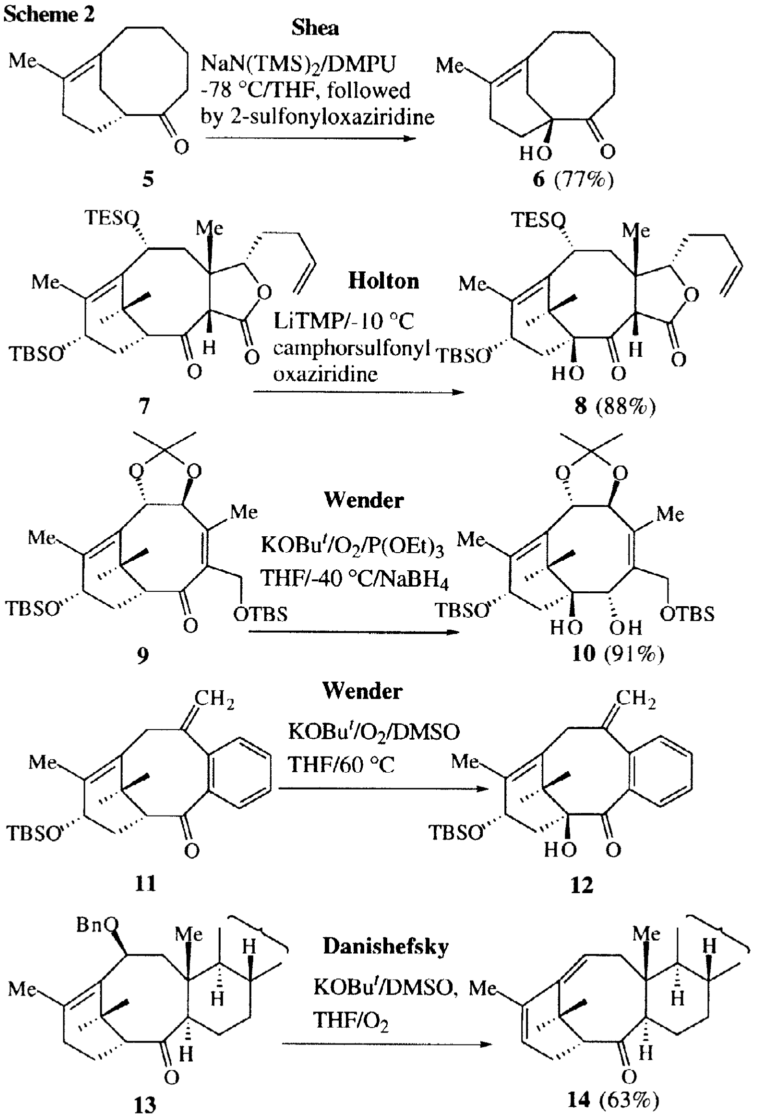
In model studies the conversion of **11** into **12** was described.[10] Danishefsky's application of the autoxidation protocol to **13** (partial structure) resulted in elimination to give **14**, rather than C_1 hydroxylation.[11]

Scheme 2



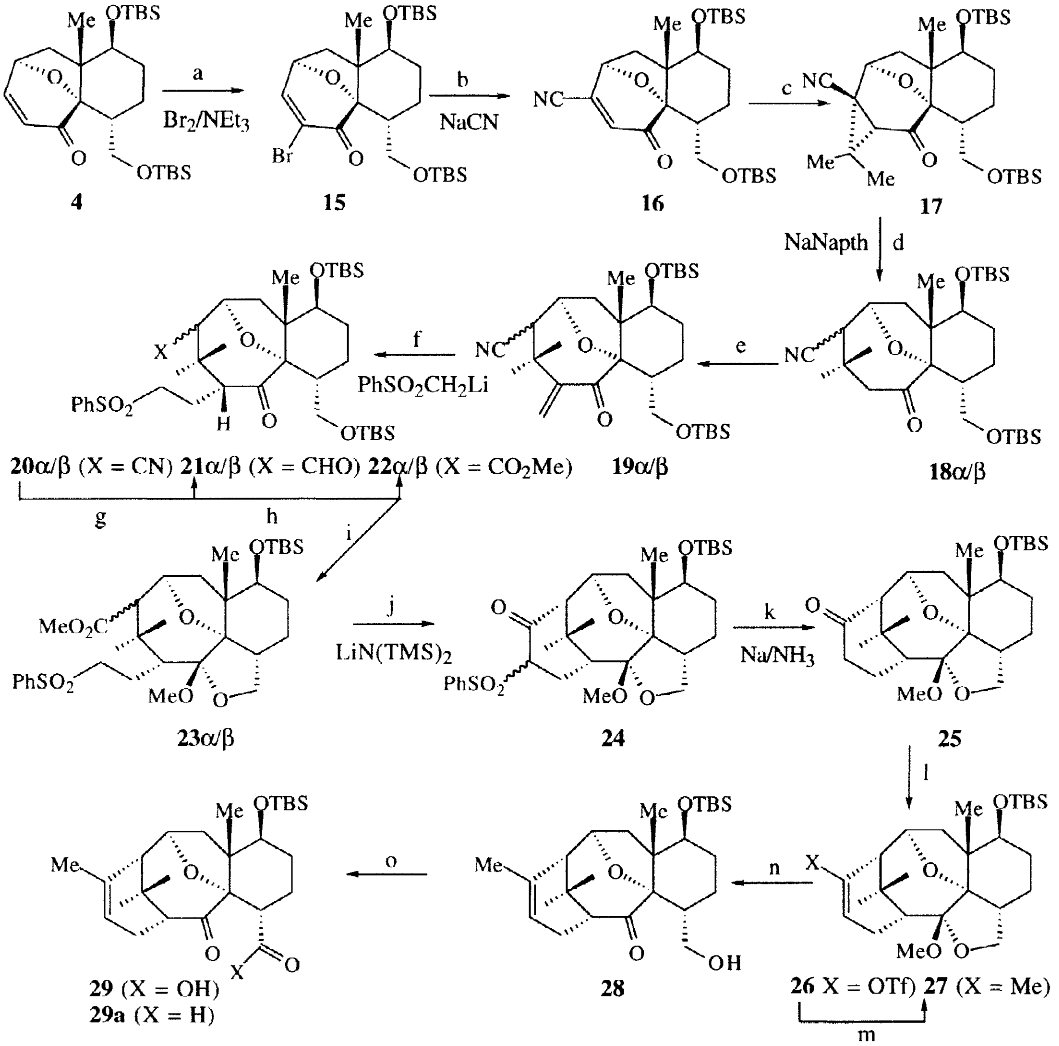
In all of the above cases of successful C_1-hydroxylation the dihedral angle between the C_1-H and the adjacent C=O π-bond is approximately 90°, and therefore allows direct enolate resonance. The failure of the last example parallels our attempt to autoxidize **37** (**Scheme 5**) which also failed, whereas the C_9-ketone **39** was readily oxidized at C_1. Clearly, there are very subtle conformational effects at play that dramatically influence the ease of C_1-enolization.

Synthesis of the Taxane ABC Skeleton

Following the strategy and sequence of transformation we developed for 7-deoxytaxanes,[4] the enone **4** was converted into **15**, which on treatment with sodium cyanide under phase transfer conditions gave **16**, **Scheme 3**. *Gem*-methylcyclopropanation of **16** using isopropylidene triphenylphosphorane[12] gave **17**. Reductive cleavage of the internal cyclopropane bond of **17** with sodium naphthalenide gave a mixture of **18**α

and **18**β (2:1).[13] It was not necessary to separate the C_{11}-epimers until the ring A precursor **23** was reached. The α/β-ratio of the C_{11}-epimers gradually improved in favor of the desired α-epimer in the sequence of transformations from **18** to **22**, presumably due to base catalyzed enolization.

Scheme 3



Conditions:-(a) $Br_2/CCl_4/CH_2Cl_2$/-40 °C/Et_3N/25 °C, **15** (97%). (b) NaCN/*n*-$Bu_4NI/CH_2Cl_2/H_2O$/25 °C/1h, followed by Et_3N/25 °C/18h, **16** (85%). (c) $Me_2C{=}PPh_3$/THF/-78 to 25 °C/3h, **17** (95%). (d) Sodium naphthalenide/THF/-78 °C, **18**α/β (2:1), (95%). (e) $KN(TMS)_2$/25 °C/THF/$(CH_2O)_n$/1 h, **19**α/β (3:1), (82%). (f) $PhSO_2CH_2Li$/THF/-78 °C/1 h, **20**α/β (3:1), (95%). (g) DIBAL-H/CH_2Cl_2/-78 °C/1 h, **21**α/β (3:1). (h) i. $NaClO_2$ ii. K_2CO_3/acetone/MeI, **22**α/β (5:1), (83%). (i) $(MeO)_3CH$/MeOH/PPTS/70 °C/12 h, **23**α (82%). (j) $LiN(TMS)_2$/THF/70 °C/1.5 h, **24**. (k) Na/NH_3/THF/-33 °C, **25** (84% from **23**α). (l) $NaN(TMS)_2$/THF/0 °C/15 min, then *N*-(5-chloro-2-pyridyl)triflimide/0 °C/3 h, **26** (96%). (m) CuI/MeLi/THF/0 °C/48h, **27** (95%). (n) Dioxane/AcOH/50 °C/18 h, **28** (92%). (o) i. Dess-Martin reagent/CH_2Cl_2/1 h. ii. $NaClO_2$/25 °C/1 h, **29**.

Treatment of **18**α/β with paraformaldehyde in the presence of excess $KN(TMS)_2$ resulted in the direct formation of the C_1-exomethylene compound **19**α/β (3:1). Conjugate addition of $LiCH_2SO_2Ph$ to the α,β-unsaturated ketone **19**α/β gave **20**α/β (3:1). The C_2-carbonyl group is too hindered to permit 1,2-addition. The nitrile in **20**α/β proved to be resistant to methanolysis under acidic conditions, but it was readily reduced (DIBAL-H) to the aldehyde **21**α/β (3:1), which was oxidized ($NaClO_2$) and esterified to give the methyl ester

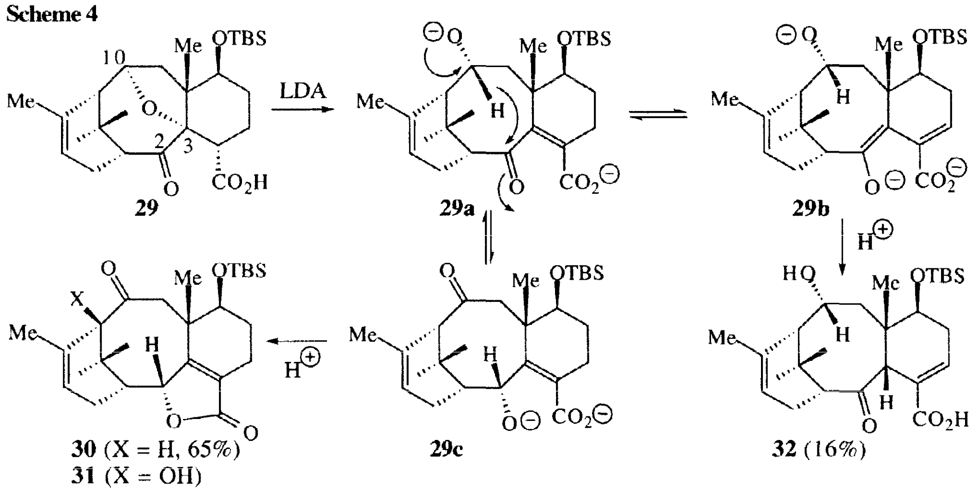
22α/β (5:1), (83%, from **20**α/β). Treatment of **22**α/β with $CH(OMe)_3$/MeOH/PPTS gave the internal ketal **23**α/β, which was recrystallized to provide **23**α (82%) as a single stereoisomer. When a solution of **23**α in THF at 70°C was treated with $LiN(TMS)_2$ (slow addition), it was cleanly converted into **24** ($-SO_2Ph$ epimers), which upon reductive removal (Na/NH_3) of the $-SO_2Ph$ group gave **25**. Direct attempts to cyclize **22**α resulted in a retro-Michael reaction to give phenyl vinyl sulfone and the methyl ester derivative of **18**.

Treatment of **25** with $NaN(TMS)_2$ and quenching with *N*-(5-chloro-2-pyridyl)triflimide gave **26**.[14] Coupling of **26** with $(CH_3)_2CuLi$ was slow, and required careful control of the temperature, but eventually resulted in **27**.[15] Hydrolysis of **27** gave **28**, which was oxidized to the acid **29**.

β-Elimination of the 3,10-Oxido bridge

While it is possible to consider the reductive elimination of the $C_{3,10}$-oxido bridge in **29**, it is advantageous to maintain the current oxidation level through β-elimination. The resulting $C_{3,4}$-double bond in the product should be capable of isomerization (deconjugation) to the $C_{4,5}$-position, and now is ideally situated for the construction of the oxetane functionality. Furthermore, the above isomerization process should also allow for the correct *trans*-B/C ring fusion stereochemistry through thermodynamic equilibration.[16] Also, as a soubrette to this analysis of the various reaction pathways, it was anticipated that the possibility of transannular hydride from C_{10} to C_2 might play a role in the above transformations.

Scheme 4

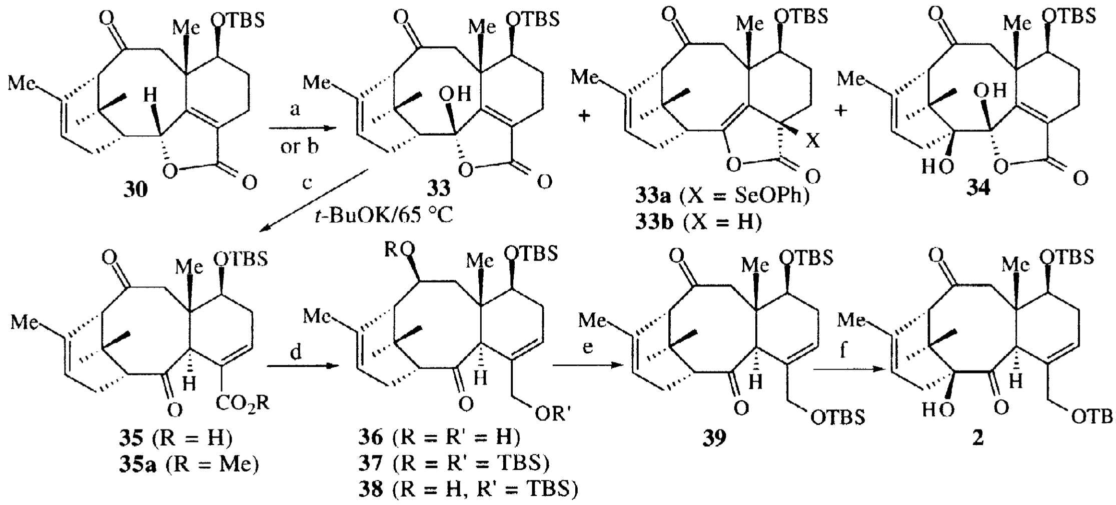


We found that the carboxylate dianion of **29** was necessary for β-elimination of the $C_{3,10}$-oxido-bridge, since the aldehyde or methyl ester derivatives of **29** resulted in C_4-epimerization in both cases. The ketoacid **29**, on treatment with LDA (0-25 °C) underwent β-elimination (*via* the dianion), followed by transannular hydride migration, to give the ketolactone **30**, **Scheme 4**.[17] This series of events serves to exchange oxidation levels between C_{10} and C_2, and provide the correct $C_{2\alpha}$-configuration. Presumably, after β-elimination the alkoxide **29a** undergoes reversible hydride migration to give **29c**, which on protonation leads to **30**.[18] It was found that conducting the above reaction for an extended period (4 days) gave **30** (50%) along with **32** (16%), and **31** (12%) (X-ray), which presumably arises from oxygen leakage and autoxidation of the C_{10} dienolate.[19] The formation of **32** during the extended reaction period (it was not present after 1 day) suggests that equilibration of **29a** and **29c** can slowly lead to the extended enolate **29b**, which on protonation result in **32**. In particular, it should be noted that the B/C rings in **32** are *cis*-fused.

C_1-Autoxidation, C_3/C_4-Double Bond Isomerization and C_3-Epimerization

Since the C_{10} to C_2 transannular hydride shift could not be prevented, it was decided to examine the oxidation of **30** with the expectation that C_2 could be selectively functionalized. The butenolide **30** was treated with $(PhSeO)_2O$[20]/*t*-BuOK/P(OEt)$_3$/THF at 0°C and resulted in conversion into the ketal **33** (72%), (X-ray), **Scheme 5**. Small amounts of the selenoxide **33a** and enol-lactone **33b** (X-ray) could also be isolated. Further exposure of **33a/b** to the above oxidation reaction conditions gave **33**. It was found that treatment of **33** with *t*-BuOK/*t*-BuOH/THF at 65°C cleanly gave the C_4 isomer **35**, which was converted into the methyl ester **35a** (47% overall) (X-ray). It appears that the base-induced deconjugation reactions (at 0-25 °C) leads to *cis*-B/C ring fused compounds, whereas at higher temperatures (>25 °C) the correct *trans*-B/C ring fused stereochemistry is produced.

Scheme 5

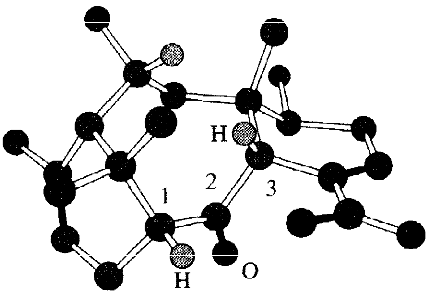


Conditions:-(a) $(PhSeO)_2O$/*t*-BuOK/P(OEt)$_3$/THF/0 °C **33** (72%). (b) *t*-BuOK/THF/O_2/P(OEt)$_3$/-78 °C (**33**, 41% and **34**, 47%). (c) i. *t*-BuOK/THF at 65 °C. ii. K_2CO_3/THF/MeI **35a** (47% from **30**). (d). i. DIBAL-H (92%). ii. TBSCl/Et_3N/DMAP/0 °C, **38** (98%), whereas TBSOTf/Et_3N/0 °C gave **37** (R = TBS) (100%). (e) Dess-Martin on **38**, **39** (100%). (f) *t*-BuOK/THF/O_2/P(OEt)$_3$/52 °C, **2** (31%, 39% based on recovered **39**).

When **30** was exposed to the standard autoxidation conditions of *t*-BuOK/THF/O_2/P(OEt)$_3$ it was transformed into **33** (41%) and **34** (47%) (X-ray). The formation of **34** must have arisen from the open form of **33** which can enolize towards C_1. The ester **35a** was converted into **37** by standard reactions, and exposed to the autoxidation reaction conditions from -78° to 65°C. Under these conditions, that readily autoxidize **30**, **33** and **39** (see also **Scheme 6**), there was no C_1 oxidation observed. In contrast, oxidation of **38** to the 2,10-dione **39**, followed by autoxidation at 52°C gave **2** (31%, 39% based on recovered **39**). The X-ray structure of **32** (B/C *cis*-fused) shows that the C_1 hydrogen atom is 93° to the adjacent C=O bond, and therefore suitably aligned for enolization. The C_3 hydrogen atom is not aligned for enolization (ϕ 174°), although upward movement of the C_2 carbonyl group (ca. 20-30°) allows overlap of the $C_{3(H)}$ σ-bond with the C_2 C=O π-bond.

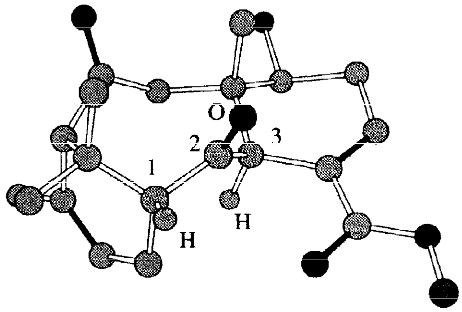
Figure 1, shows the C_1-C_3 portion of **32** taken from the X-ray coordinates. **Figure 2** is the same portion but of **35a** (B/C *trans*-fused), and shows that the C_1(H) has a dihedral angle of 40° to the C=O bond, and the C_3(H) is 167° to C=O bond (from X-ray coordinates).

Figure 1 (32)



C1(H)-C2 dihedral angle 93°
C3(H)-C2 dihedral angle 174°

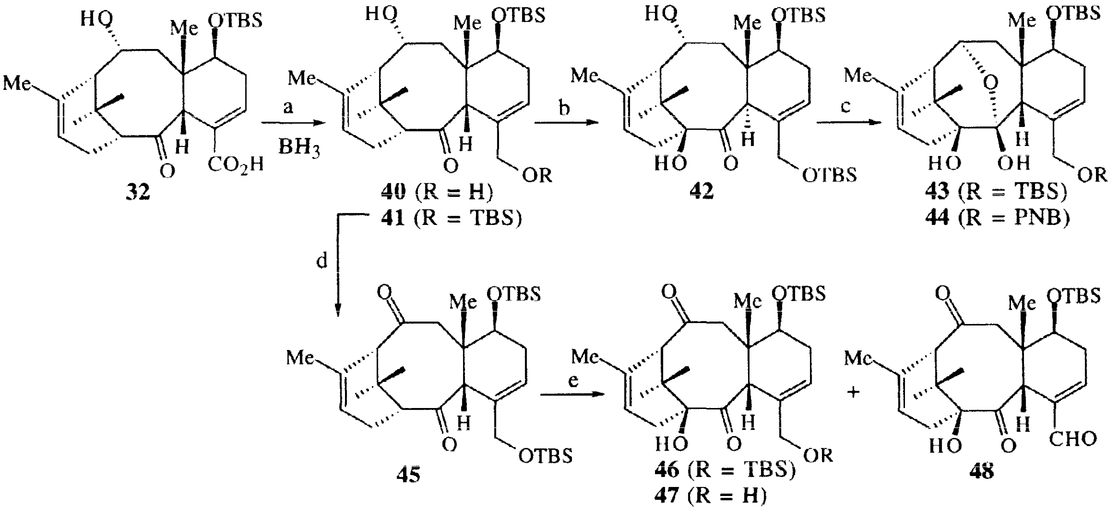
Figure 2 (35a)



C1(H)-C2 dihedral angle 40°
C3(H)-C2 dihedral angle 167°

It appears that the *trans*-B/C compounds are not well aligned for C_1 enolization compared to the *cis*-B/C fused isomers, but nevertheless they do autoxidize at C_1, and more cleanly than the *cis*- compounds. Furthermore, in both the *cis*- and trans- compounds the C_3(H) is badly aligned for enolization but in fact they readily interconvert, **Scheme 6**. Both **Figures 1** and **2** clearly show, the C=O is pointing down in the former and up in the latter. The mid-point between these two extremes is probably a more realistic solution conformation, and is well aligned for enolization towards C_3 in both the *cis*- and *trans*- series.

Scheme 6



Conditions:- (a) BH_3.THF, **40** (70%) followed by TBSCl/Et_3N/DMAP, **41** (84%). (b) *t*-BuOK/THF/O_2/P(OEt)$_3$/-78 ° C (85% of **42** and 10% of **43**). (c) *t*-BuOK/THF at 0-25 °C, **43** (>95%). (d) Dess-Martin **45** (100%). (e) *t*-BuOK/THF/O_2/P(OEt)$_3$/-78 ° to 25 °C, **46** (40%), **47** (24%) and **48** (34%).

While **32** was a minor product in the β-elimination process, **Scheme 4**, it was nevertheless instructive to examine the possibility of introduction of the 1β-hydroxyl group *via* autoxidation of the C_1 enolate. Treatment of **32** with BH_3.THF gave **40** (75%), which was protected as its TBS ether **41** (84%). Exposure of

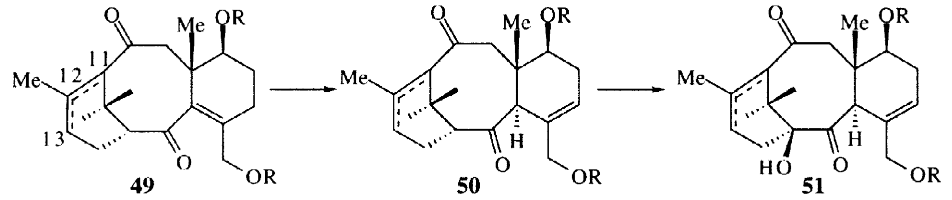
41 to the standard autoxidation conditions (*t*-BuOK/THF/O_2/$P(OEt)_3$/-78 ° to 0 °C) cleanly gave **42** (85%) and **43** (10%). When **42** was further treated with *t*-BuOK/THF/0°-25 °C it was converted into **43** (95%). The structure of **43** was deduced from the derived *p*-nitrobenzoate (PNB) **44** (X-ray). Transannular 2,10-ketalization is only possible when the B/C rings are *cis*-fused (C_2, C=O pointing downwards). Consequently, the only logical structure that can be written for **42** is the *trans*-fused B/C stereoisomer. It appears that B/C *cis-trans* isomerization has taken place during the autoxidation reaction.

Dess-Martin oxidation of **41** gave **45** (C_3 stereoisomer of **39**, **Scheme 5**) which upon autoxidation at -78 °C gave **46**, **47** and **48**. Under these conditions we did not observe any equilibration of **45** into **39**, nor **46** into **2**. It appears that the autoxidation of **45** to give the aldehyde **48** must result from reversible C_4 double bond isomerization to C_3, followed by autoxidation of the extended enolate.

Summary

It is clear from the autoxidation results that the ability to introduce the C_1 hydroxyl group into advanced taxane ABC-ring systems is very structure sensitive, with distant stereochemistry (C_{10}) influencing the reaction outcome at C_1. These results show that taxanes of the type **49** ($\Delta^{12,13}$) should be capable of isomerization to give **50** which on autoxidation will give **51**, **Scheme 7**. It is not a forgone conclusion that the isomeric $\Delta^{11,12}$ substrates will behave in the same fashion, but given the literature results outlined in **Scheme 2**, a favorable prognosis might not be too optimistic. Current research in these laboratories is directed towards this objective.

Scheme 7



Experimental Section

1-Bromo-4α-(*tert*-butyldimethylsilyl)oxymethyl-7β-(*tert*-butyldimethylsilyl)oxy-8β-methyl-3α,10α-oxido-bicyclo[5.4.0^{3,8}]undec-1-ene-2 one 15. Bromine (2.50 mL, 48.5 mmol) was added dropwise, *via* syringe, to a stirred solution of **4** (10:1 diastereomeric mixture) (22.6 g, 48.4 mmol) in dichloromethane (500 mL) at -40°C. After the addition was complete, a persistent yellow coloration was observed. Triethylamine (7.40 mL, 53.1 mmol) was added, *via* syringe, and the resulting solution maintained at -40°C for approximately 15 min. The reaction mixture was warmed to room temperature, concentrated *in vacuo* and the residue partitioned between EtOAc and water. The organic phase was separated and the aqueous phase re-extracted with EtOAc (x 2). The combined extracts were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 5-10% EtOAc/hexanes gave **15** (25.6 g, 97%) as pale yellow solid (10:1 diastereomeric mixture). For pure **15**. IR (NaCl) 2954, 2859, 1700, 1604 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (1H, d, J = 5.3 Hz), 4.68 (1H, t, J = 6.4 Hz), 3.44 (3H, m), 2.75 (1H, m), 2.34 (1H, dd, J = 8.0, 12.8 Hz), 1.92 (1H, m), 1.40-1.66 (3H, m), 0.90 (3H, s), 0.87 (9H, s), 0.86 (9H, s), 0.06 (6H, s), 0.02 (3H, s), 0.01 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.2, 155.3, 121.9, 94.7, 78.2, 72.7, 64.6, 45.5, 44.1, 38.3, 29.5, 26.0 (3C), 25.7 (3C), 23.6, 18.4, 18.0, 15.0, -3.6, -5.0, -5.3, -5.5; HRMS (CI) calcd for $C_{25}H_{46}BrO_4Si_2$ (MH$^+$) 545.2118, found 545.2103.

11-Cyano-4α-(*tert*-butyldimethylsilyl)oxymethyl-7β-(*tert*-butyldimethylsilyl)oxy-8β-methyl-3α,10α-oxidobicyclo[5.4.0^{3,8}]undec-1-ene-2 one 16. A solution of **15** (10:1 diastereomeric mixture) (25.6 g, 46.9 mmol) in dichloromethane (235 mL) was added dropwise over approximately 25 min, *via* a pressure equalizing addition funnel to a vigorously stirred solution of sodium cyanide (2.41 g, 49.2 mmol) and tetra-*n*-butylammonium iodide (1.73 g, 4.68 mmol) in water (117 mL). After 1 h, the organic phase was separated and the aqueous phase re-extracted with dichloromethane (2x50 mL). The combined extracts were treated with triethylamine (13.1 mL, 94.0 mmol), and the resulting solution maintained at room temperature overnight. The reaction mixture was concentrated *in vacuo* and the residue partitioned between EtOAc and water. The organic layer was separated, and the aqueous phase extracted with EtOAc (x2). The combined extracts were washed with brine, dried (MgSO$_4$), and evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 4% EtOAc/hexanes gave in order of elution, minor diastereomer of **16** (2.00 g, 9%). IR (NaCl) 2954, 2859, 1697 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.42 (1H, s), 4.66 (1H, d, *J* = 7.6 Hz), 3.56 (2H, m), 3.38 (1H, t, *J* = 8.8 Hz), 2.81 (1H, dd, *J* = 7.9, 13.1 Hz), 2.54 (1H, m), 1.44-1.76 (5H, m), 0.94 (3H, s), 0.89 (9H, s), 0.85 (9H, s), 0.06 (6H, s), 0.00 (6H, s); ^{13}C NMR (75 MHz, CDCl$_3$) δ 194.1, 137.2, 135.9, 114.7, 93.0, 75.0, 73.3, 64.7, 45.5, 39.0, 35.4, 27.0, 26.0 (3C), 25.8 (3C), 23.3, 19.2, 18.4, 18.1, -4.0, -5.0, -5.3, -5.5; HRMS (CI) calcd for $C_{26}H_{46}NO_4Si_2$ (MH$^+$) 492.2965, found 492.2961.

Major diastereomer **16** (19.7 g, 85%) as a viscous bright yellow oil. IR (NaCl) 2952, 2859, 1696 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 6.45 (1H, s), 4.72 (1H, d, *J* = 7.3 Hz), 3.40-3.51 (3H, m), 2.66 (1H, m), 2.51 (1H, dd, *J* = 8.0, 13.2 Hz), 1.83 (1H, m), 1.59-1.66 (2H, m), 1.47 (1H, m), 1.15 (1H, m), 0.90 (3H, s), 0.88 (9H, s), 0.84 (9H, s), 0.07 (6H, 2 × s), -0.01 (6H, s); ^{13}C NMR (75 MHz, CDCl$_3$) δ 193.5, 137.7, 135.9, 114.6, 94.1, 77.8, 72.5, 64.4, 45.7, 45.2, 37.7, 29.4, 26.0 (3C), 25.8 (3C), 23.3, 18.4, 18.1, 14.7, -3.5, -4.9, -5.4, -5.5; HRMS (CI) calcd for $C_{26}H_{46}NO_4Si_2$ (MH$^+$) 492.2965, found 492.2958.

11β-Cyano-4α-(*tert*-butyldimethylsilyl)oxymethyl-7β-(*tert*-butyldimethylsilyl)oxy-1α,11α-dimethylcyclopropano-8β-methyl-3α,10α-oxido-bicyclo[5.4.0^{3,8}]undec-2-one 17. A solution of *n*-butyllithium (29.6 mL of a 2.5 M solution in hexanes, 74.0 mmol) was added dropwise, *via* syringe, to a stirred suspension of anhydrous isopropyltriphenylphosphonium iodide (33.6 g, 77.7 mmol) in THF (300 mL) at room temperature. After 30 min, the resulting dark red mixture was cooled to -78°C and a solution of **16** (18.2 g, 37.0 mmol) in THF (70 mL) was added dropwise, *via* cannula, maintaining the internal temperature ≤70°C. After a further 30 min, the reaction mixture was warmed to room temperature and stirred for approximately 3 h. The reaction was quenched by the addition of saturated aqueous NH$_4$Cl (40 mL) and the resulting mixture concentrated *in vacuo*. The residue was partitioned between dichloromethane and water, the organic layer separated and the aqueous phase extracted with dichloromethane (× 2). The combined extracts were washed with brine, dried (MgSO$_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with hexanes→4% EtOAc/hexanes gave **17** (18.8 g, 95%) as a colorless solid. IR (NaCl) 2953, 2861, 2236, 1703 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.78 (1H, d, *J* = 6.6 Hz), 3.39 (2H, m), 3.24 (1H, t, *J* = 9.4 Hz), 2.54 (1H, dd, *J* = 7.6, 13.6 Hz), 2.41 (1H, m), 2.02 (1H, s), 1.91

(1H, m), 1.82 (1H, dd, 1.7, 13.7 Hz), 1.58 (4H, m), 1.40 (4H, m), 1.16 (1H, m), 0.92 (3H, s), 0.88 (9H, s), 0.84 (9H, s), 0.06 (3H, s), 0.05 (3H, s), -0.01 (3H, s), -0.02 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.7, 119.0, 92.4, 77.0, 71.8, 65.0, 49.3, 44.9, 41.6, 38.9, 35.2, 30.0, 29.4, 28.9, 26.0 (3C), 25.9 (3C), 22.9, 18.4, 18.1, 16.8, 14.4, -3.6, -4.9, -5.4, -5.4; HRMS (CI) calcd for $C_{29}H_{52}NO_4Si_2$ (MH$^+$) 534.3435, found 534.3436.

11α/β-Cyano-4α-(*tert*-butyldimethylsilyl)oxymethyl-7β-(*tert*-butyldimethylsilyl)oxy-3α,10α-oxido-8β,12,12-trimethyl-bicyclo[6.4.0^{3,8}]dodecan-2-one 18α and **18β**. A solution of freshly prepared sodium naphthalenide (180 mL of a 0.4 M solution in THF, 72.2 mmol) was added dropwise, *via* cannula, to a mechanically stirred solution of **17** (18.8 g, 35.2 mmol) in THF (1.4 L) at -78°C. After the addition was complete, a persistent green/blue coloration was observed. The reaction was quenched by the addition of saturated aqueous NH_4Cl (140 mL) and the resulting mixture warmed to ambient temperature. After concentration *in vacuo*, the residue was partitioned between dichloromethane and water. The organic layer was separated and the aqueous phase extracted with dichloromethane (× 2). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with hexanes→5% EtOAc/hexanes afforded a colorless solid (17.9 g, 95%) which was a 2:1 mixture of **18α** and **18β**. An analytical sample was rechromatographed to give pure **18α** and **18β**.

For isomer **18α**. IR (NaCl) 2952, 2859, 2238, 1711 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.65 (1H, m), 3.52 (1H, dd, *J* = 7.4, 10.2 Hz), 3.37 (2H, m), 3.25 (1H, d, *J* = 11.8 Hz), 3.14 (1H, d, *J* = 4.5 Hz), 2.31 (1H, dd, *J* = 9.2, 14.0 Hz), 2.07 (2H, dm, *J* = 11.7 Hz), 1.44-1.73 (4H, m), 1.26 (3H, s), 1.20 (3H, s), 1.16 (1H, m), 1.08 (3H, s), 0.88 (9H, s), 0.84 (9H, s), 0.06 (3H, s), 0.05 (3H, s), 0.00 (3H, s), -0.01 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.6, 118.4, 93.6, 76.5, 73.7, 64.1, 55.7, 51.4, 45.6, 43.2, 36.3, 34.9, 29.5, 26.0 (3C), 25.9 (3C), 25.1, 23.2, 18.4, 18.1, 12.5, -3.6, -4.9, -5.5 (2C); HRMS (CI) calcd for $C_{29}H_{54}NO_4Si_2$ (MH$^+$) 536.3591, found 536.3575.

For isomer **18β**. IR (NaCl) 2953, 2859, 2238, 1704 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.76 (1H, m), 3.58 (1H, dd, *J* = 6.5, 10.1 Hz), 3.39 (2H, m), 3.26 (1H, d, *J* = 13.7 Hz), 2.70 (1H, s) 2.37 (1H, dd, *J* = 9.3, 13.9 Hz), 2.12 (2H, m), 1.40-1.80 (4H, m), 1.34 (3H, s), 1.27 (1H, m), 1.20 (3H, s), 1.00 (3H, s), 0.88 (9H, s), 0.86 (9H, s), 0.05 (6H, 2 × s), 0.01 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.3, 120.6, 94.5, 77.2, 73.9, 64.3, 55.5, 50.8, 46.8, 42.3, 39.7, 34.5, 32.1, 30.6, 29.48, 26.0 (3C), 25.9 (3C), 23.2, 18.4, 18.1, 12.7, -3.6, -5.0, -5.4 (2C), 1 carbon not found; HRMS (CI) calcd for $C_{29}H_{54}NO_4Si_2$ (MH$^+$) 536.3591, found 536.3572.

11α/β-Cyano-4α-(*tert*-butyldimethylsilyl)oxymethyl-7β-(*tert*-butyldimethylsilyl)oxy-1-ylidene-3α,10α-oxido-8β,12,12-trimethyl-bicyclo-[6.4.0^{3,8}]dodecan-2-one 19α and 19β. Potassium bis(trimethylsilyl)amide (40.9 g, 205 mmol) was added portion wise, over approximately 5 min, to a stirred solution of **18α** and **18β** (2:1) (11.0 g, 20.5 mmol) in THF (820 mL) at room temperature. After 30 min, paraformaldehyde (41.0 g) was added portion wise, over approximately 5 min.; CAUTION - an exothermic reaction was observed. After 1h, the reaction was quenched by the addition of saturated aqueous NH_4Cl (200 mL) and the resulting mixture concentrated *in vacuo*. The residue was partitioned between Et_2O and water, and the resulting biphasic mixture filtered through a short pad of Celite®. The organic phase was separated and the aqueous phase extracted with Et_2O (× 2). The combined extracts were washed with brine, dried

($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over basic alumina eluting with 10% EtOAc/hexanes gave a colorless foam (9.2 g, 82%) which was a 3:1 mixture of **19α** and **19β**. A sample was rechromatographed to give pure **19α** and **19β**.

For isomer **19α**. IR (NaCl) 2953, 2859, 2238, 1685 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76 (1H, s), 5.43 (1H, s), 4.81 (1H, m), 3.52 (1H, dd, *J* = 3.8, 9.3 Hz), 3.43 (1H, dd, *J* = 3.8, 11.7 Hz), 3.31 2H, m), 2.39 (2H, m), 2.01 (1H, m), 1.89 (1H, dd, *J* = 7.5, 13.9 Hz), 1.64 (1H, m), 1.44 (3H, s), 1.40 (3H, s), 1.35 (3H, s), 1.24 (3H, s), 0.87 (9H, s), 0.86 (3H, s), 0.84 (3H, s), 0.06 (6H, s), 0.02 (3H, s), 0.00 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.9, 156.5, 123.6, 118.1, 95.6, 75.0, 74.1, 64.8, 49.9, 45.5, 39.9, 39.3, 37.9, 30.8, 29.6, 28.7, 26.0 (3C), 25.9 (3C), 23.2, 18.4, 18.1, 12.2, -3.6, -4.9, -5.2, -5.4; HRMS (CI) calcd for $C_{30}H_{54}NO_4Si_2$ (MH^+) 548.3591, found 548.3583.

For isomer **19β**. IR (NaCl) 2954, 2859, 2238, 1685 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76 (1H, s), 5.40 (1H, s), 4.80 (1H, m), 3.53 (1H, dd, *J* = 3.7, 9.4 Hz), 3.34-3.42 (2H, m), 2.62 (1H, s), 2.41 (2H, m), 2.00 (1H, m), 1.58 (2H, m), 1.41 (3H, s), 1.36 (4H, m), 1.27 (1H, m), 0.86 (18H, s), 0.79 (3H, s), 0.06 (3H, s), 0.05 (3H, s), 0.03 (3H, s), 0.01 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.0, 157.5, 123.4, 120.5, 95.3, 73.9, 64.9, 49.6, 47.6, 42.3, 39.5, 38.7, 29.5, 26.7, 26.0 (3C), 25.8 (3C), 23.0, 18.4, 18.1, 12.3, -3.6, -5.0, -5.3, -5.4. 2 carbons not found; HRMS (CI) calcd for $C_{30}H_{54}NO_4Si_2$ (MH^+) 548.3591, found 548.3597.

11α/β-Cyano-4α-(*tert*-butyldimethylsilyl)oxymethyl-7β-(*tert*-butyldimethylsilyl)oxy-3α,10α-oxido-1α-(2'-phenylsulfonylethyl)-8β,12,12-trimethylbicyclo[6.4.0^{3,8}]dodecan-2-one 20α and 20β. A solution of *n*-butyllithium (8.70 mL of a 2.5 M solution in hexanes, 21.8 mmol) was added dropwise to a stirred solution of phenylmethylsulfone (3.50 g, 22.4 mmol) in THF (50 mL) at 0°C. After approximately 45 min, the resulting turbid mixture was transferred, *via* cannula, to a stirred solution of the enones **19α** and **19β** (3:1) (10.8 g, 19.7 mmol) in THF (150 mL) at -78°C. After 1 h, the reaction was quenched by the addition of saturated aqueous NH_4Cl (20 mL) and the resulting mixture warmed to room temperature. The volatiles were evaporated and the residue partitioned between dichloromethane and water. The organic phase was separated and the aqueous phase extracted with dichloromethane (× 2). The extracts were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 15-20% EtOAc/hexanes gave **20** (13.2 g, 95%) as a colorless solid which was a 3:1 mixture of separable diastereoisomers.

For isomer **20α**. IR (NaCl) 2953, 2858, 1692 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87-7.97 (2H, m), 7.55-7.69 (3H, m), 4.88 (1H, dd, *J* = 6.4, 9.5 Hz), 3.38 (2H, m), 3.25 (1H, t, *J* = 9.4 Hz), 3.01 (2H, m), 2.81 (1H, s), 2.65 (1H, dd, *J* = 9.5, 14.1 Hz), 2.36 (1H, m), 2.15 (2H, m), 2.00 (1H, m), 1.75 (1H, dd, *J* = 6.4, 14.3 Hz), 1.60 (1H, m), 1.36 (1H, m), 1.26 (3H, s), 1.19 (1H, m), 1.14 (4H, s), 0.88 (9H, s), 0.85 (9H, s), 0.81 (3H, s), 0.07 (3H, s), 0.06 (3H, s), -0.01 (3H, s), -0.02 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.0, 139.4, 134.0, 129.5, 127.9, 120.9, 96.2, 77.0, 75.1, 65.2, 58.5, 55.4, 49.8, 49.4, 44.6, 44.0, 39.6, 39.0, 31.1, 29.5, 26.0 (3C), 25.9 (3C), 23.4, 22.0, 20.4, 18.4, 18.1, 12.5, -3.6, -4.9, -5.2, -5.3. 1 carbon not found; HRMS (CI) calcd for $C_{37}H_{62}NO_6SSi_2$ (MH^+) 704.3836, found 704.3837.

11α/β-Formyl-4α-(*tert*-butyldimethylsilyl)oxymethyl-7β-(*tert*-butyldimethylsilyl)oxy-3α,10α-oxido-1α-(2'-phenylsulfonylethyl)-8β,12,12-trimethyl-bicyclo[6.4.0^{3,8}]dodecan-2-one 21α and 21β. A solution of DIBAL-H (21.0 mL of a 1.0M solution in dichloromethane, 21.0 mmol) was added dropwise over approximately 10 min, *via* syringe, to a stirred solution of **20α** and **20β** (3:1) (9.86 g, 14.0 mmol) in dichloromethane (140 mL) at -78°C. After 1 h, the reaction was quenched by the addition of 1 N HCl (14 mL), warmed to room temperature and partitioned between Et_2O and 1 N HCl. The organic phase was separated and the aqueous phase extracted with Et_2O/dichloromethane (3:2; × 2). The combined extracts were washed with water, brine, dried ($MgSO_4$) and evaporated *in vacuo*. The crude residue was composed of a 3:1 mixture of **21α** and **21β**. A sample was rechromatographed to give pure **21α** and **21β**.

For isomer **21α**. IR (NaCl) 2953, 2858, 1723, 1690 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.92 (1H, d, J = 2.9 Hz), 7.91 (2H, m), 7.55-7.69 (3H, m), 4.93 (1H, dd, J = 6.4, 9.7 Hz), 3.35-3.50 (3H, m), 3.22 (1H, t, J = 9.3 Hz), 3.00 (2H, m), 2.60 (1H, dd, J = 9.7, 14.0 Hz), 2.35 (1H, m), 2.28 (1H, d, J = 3.0 Hz), 2.15 (2H, m), 1.78 (1H, dd, J = 6.5, 14.0 Hz), 1.35 (1H, m), 1.26 (5H, m), 1.00 (3H, s), 0.88 (9H, s), 0.84 (9H, s), 0.80 (3H, s), 0.06 (6H, s), -0.01 (3H, s), -0.03 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.8, 203.3, 139.4, 133.9, 129.5, 128.0, 95.7, 75.2, 73.5, 65.8, 65.3, 60.1, 55.7, 49.3, 43.1, 39.6, 39.1, 30.3, 29.6, 26.0 (3C), 25.9 (3C), 23.5, 21.0, 19.5, 18.4, 18.1, 12.7, -3.6, -4.9, -5.2, -5.3. 2 carbons not found; HRMS (CI) calcd for $C_{37}H_{63}O_7SSi_2$ (MH^+) 707.3833, found 707.3841.

For isomer **21β**. IR (NaCl) 2932, 2858, 1694 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.87 (1H, d, J = 2.8 Hz), 7.91 (2H, m), 7.56-7.67 (3H, m), 4.80 (1H, m), 3.23-3.41 (5H, m), 2.92-3.03 (2H, m), 2.15-2.34 (4H, m), 2.01 (1H, m), 1.61 (1H, m), 1.40 (1H, m), 1.26 (2H, m), 1.14 (3H, s), 0.87 (12H, s), 0.85 (12H, s), 0.05 (6H, s), 0.00 (3H, s), -0.01 (3H, s); HRMS (CI) calcd for $C_{37}H_{63}O_7SSi_2$ (MH^+) 707.3833, found 707.3834.

11α/β-Carbomethoxy-4α-(*tert*-butyldimethylsilyl)oxymethyl-7β-(*tert*-butyldimethylsilyl)oxy-3α,10α-oxido-1α-(2'-phenylsulfonylethyl)-8β,12,12-trimethyl-bicyclo[6.4.0^{3,8}] dodecan-2-one 22α and 22β. A solution of sodium chlorite (15.8 g, 140 mmol; 80%) and sodium phosphate monobasic monohydrate (19.3 g, 140 mmol) in water (35 mL) was added dropwise over approximately 10 min. *via* pressure equalizing addition funnel, to a vigorously stirred solution of the crude **21α** and **21β** in a mixture of 2-methyl-2-butene and *t*-BuOH (1:2; 105 mL) at room temperature. After 1 h, the reaction mixture was poured into Et_2O and the organic phase separated. The aqueous phase was extracted with Et_2O/dichloromethane (3:2; × 2), the extracts washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. IR (NaCl) 2950, 2859, 1693 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (2H, m), 7.56-7.67 (3H, m), 4.86 (1H, dd, J = 6.5, 9.4 Hz), 3.37-3.47 (3H, m), 3.28 (1H, t, J = 9.0 Hz), 3.00 (2H, m), 2.64 (1H, s), 2.61 (1H, dd, J = 10.0, 14.4 Hz), 2.34 (1H, m), 2.17 (2H, m), 1.99 (1H, m), 1.40-1.80 (3H, bm), 1.26 (5H, m), 0.99 (3H, s), 0.88 (9H, s), 0.84 (9H, s), 0.80 (3H, s), 0.05 (6H, s), -0.01 (3H, s), -0.03 (3H, s); HRMS (CI) calcd for $C_{37}H_{63}O_8SSi_2$ (MH^+) 723.3782, found 723.3767.

Anhydrous potassium carbonate (9.67 g, 70.0 mmol) was added, in one portion, to a vigorously stirred solution of the crude acid in dry acetone (140 mL) at room temperature. After approximately 10 min, iodomethane (8.72 mL, 140 mmol; pre-filtered through basic alumina) was added, *via* syringe, and the resulting yellow suspension stirred at ambient temperature for 1 h. The volatiles were evaporated and the residue partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with Et_2O/dichloromethane (3:2; × 2). The extracts were washed with brine, dried ($MgSO_4$) and evaporated *in* *vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 17.5-20% EtOAc/hexanes gave **22α** and **22β** (8.55 g, 83% from **20α** and **20β**) as a colorless foam which was a 5:1 mixture of inseparable diastereoisomers. IR (NaCl) 2952, 2859, 1733, 1690 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.91 (2H, m), 7.55-7.66 (3H, m), 4.76 (1H, dd, *J* = 6.4, 9.6 Hz), 3.74 (3H, s), 3.35-3.74 (3H, m), 3.28 (1H, t, *J* = 9.4 Hz), 2.91-3.02 (2H, m), 2.59 (2H, m), 2.32 (1H, m), 2.14 (2H, m), 1.99 (1H, m), 1.69 (1H, dd, *J* = 6.5, 14.1 Hz), 1.54 (1H, m), 1.29 (2H, m), 1.18 (3H, s), 0.93 (3H, s), 0.87 (9H, s), 0.86 (3H, s), 0.84 (9H, s), 0.04 (6H, s), -0.02 (3H, s), -0.03 (3H, s); ^{13}C NMR (75 MHz, CDCl$_3$) δ 210.5, 174.8, 139.9, 134.2, 129.9, 128.4, 95.8, 78.0, 75.6, 65.8, 62.0, 60.5, 56.2, 52.3, 49.6, 44.7, 40.1, 39.8, 30.8, 30.0, 26.5 (3C), 26.3 (3C), 23.8, 22.1, 20.6, 18.8, 18.5, 13.2, -3.2, -4.5, -4.7, -4.9. 2 carbons not found; HRMS (CI) calcd for $C_{38}H_{65}O_8SSi_2$ (MH$^+$) 37.3939, found 737.3930.

Methyl 1α-(2'-phenylsulfonylethyl)-2β-methoxy-7β-(*tert*-butyldimethylsilyl)oxy-3α,10α-oxido-2α,19α-oxido-8β,12,12-trimethylbicyclo[6.4.0^{3,8}]dodec-11α/β-oate 23α and 23β. Pyridinium *p*-toluenesulfonate (0.15 g, 0.60 mmol) was added, to a stirred solution of **22α** and **22β** (8.51 g, 11.5 mmol) in a mixture of trimethylorthoformate and MeOH (1:1; 116 mL) at room temperature. The resulting solution was heated at 70°C for approximately 12 h. After cooling to ambient temperature, the reaction was quenched by the addition of saturated aqueous NaHCO$_3$ (12 mL) and the volatiles evaporated *in vacuo*. The residue was partitioned between dichloromethane and water, the organic phase separated and the aqueous phase extracted with dichloromethane (× 2). The combined extracts were washed with brine, dried (MgSO$_4$) and evaporated *in vacuo*. Recrystallization of the crude residue from dichloromethane/hexanes afforded **23α** as a single diastereoisomer (5.79 g, 76%).

For isomer **23α**. IR (NaCl) 2952, 1731 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.92 (2H, m), 7.53-7.66 (3H, m), 4.42 (1H, t, *J* = 8.1 Hz), 3.83 (1H, t, *J* = 7.7 Hz), 3.68 (3H, s), 3.60 (1H, dd, *J* = 7.4, 11.3 Hz), 3.49 (1H, dd, *J* = 3.9, 11.1 Hz), 3.09-3.34 (2H, m), 2.94 (3H, s), 1.70-2.08 (5H, m), 1.35-1.61 (6H, m), 1.02 (3H, s), 0.97 (6H, s), 0.86 (9H, s), 0.01 (6H, s); ^{13}C NMR (75 MHz, CDCl$_3$) δ 175.3, 139.0, 133.6, 129.3, 128.4, 111.5, 93.5, 74.7, 74.0, 69.5, 62.8, 59.2, 55.2, 51.6, 50.3, 48.4, 45.0, 40.4, 38.6, 30.7, 29.7, 25.9 (3C), 21.3, 20.8, 19.3, 12.6, -3.8, -4.9. 3 carbons not found; HRMS (CI) calcd for $C_{33}H_{52}O_8SSi$ (MH$^+$) 636.3152, found 636.3146. The mother liquors were concentrated and purified by flash chromatography over silica gel eluting with 17% EtOAc/hexanes to afford **23β** (1.12 g, 15%), and a second batch of **23α** (0.56 g, 8%).

For isomer **23β**. IR (NaCl) 2951, 1735 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.92 (2H, m), 7.55-7.63 (3H, m), 4.47 (1H, q, *J* = 8.3 Hz), 3.87 (1H, t, *J* = 7.8 Hz), 3.59 (3H, s), 3.52 (2H, m), 3.26 (2H, m), 3.00 (3H, s), 2.95 (1H, d, *J* = 8.7 Hz), 2.26 (1H, m), 2.10 (1H, m), 1.73-1.99 (4H, m), 1.38-1.60 (4H, m), 1.10 (3H, s), 1.03 (3H, s), 0.87 (3H, s), 0.86 (9H, s), 0.00 (3H, s), -0.02 (3H, s); ^{13}C NMR (75 MHz, CDCl$_3$) δ 172.6, 139.2, 133.4, 129.2, 128.3, 112.0, 94.1, 73.9, 73.5, 69.2, 58.8, 58.5, 51.1, 50.4, 50.1, 48.5, 38.6, 38.5, 30.8, 28.3, 28.0, 25.9 (3C), 20.5, 19.6, 18.1, 12.2, -3.9, -5.0. 3 carbons not found; HRMS (CI) calcd for $C_{33}H_{52}O_8SSi_2$ (MH$^+$) 636.3152, found 636.3146.

4β,11β-Dihydro-13-phenylsulfonyl-7β-(*tert*-butyldimethylsilyl)oxy-3α,10α-oxido-2α,20α-oxido-2β-methoxy-12-nortaxane-12-one 24. A solution of lithium bis(trimethylsilyl)amide (27.1 mL of a 1 M solution in THF, 27.1 mmol) was added dropwise over approximately 1.5 h, *via* uniform motor driven syringe addition to a vigorously stirred solution of the **23α** (5.76 g, 9.04 mmol) in THF (90 mL) at reflux. After a further 1.5 h, the reaction mixture was cooled to room temperature and the reaction quenched by the addition of saturated aqueous NH_4Cl (20 mL). The resulting mixture was partitioned between dichloromethane and water, the organic phase separated and the aqueous phase extracted with dichloromethane (× 2). The combined extracts were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. IR (NaCl) 2934, 2859, 1717 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.02 (2H, m), 7.52-7.63 (3H, m), 4.58 (1H, m), 4.23 (1H, m), 3.92 (1H, t, J = 7.5 Hz), 3.42 (1H, dd, J = 7.7, 12.2 Hz), 3.32 (1H, dd, J = 4.2, 10.9 Hz), 3.16 (3H, s), 2.76 (1H, dd, J = 8.8, 13.8 Hz), 2.04-2.35 (6H, m), 1.15-1.65 (10H, m), 0.86 (9H, s), 0.82 (3H, s), -0.01 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.4, 139.4, 133.6, 129.5, 128.8, 115.4, 94.9, 77.6, 77.1, 69.9, 69.6, 64.9, 54.3, 53.4, 48.0, 46.3, 41.7, 36.7, 32.7, 30.6, 28.8, 25.9 (3C), 24.5, 18.5, 18.1, 12.1, -3.6, -5.1. 2 carbons not found; HRMS (CI) calcd for $C_{32}H_{49}O_7SSi$ (MH^+) 605.2968, found 605.2960.

4β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-3α,10α-oxido-2α,20-oxido-2β-methoxy-12-nortaxane-12-one 25. A solution of crude **24** in THF (15 mL) was added dropwise, *via* syringe, to a vigorously stirred solution of dry ammonia (75 mL, distilled from sodium metal) over excess sodium metal at -78°C. After approximately 30 min, the reaction mixture was warmed to -33°C and stirred for a further 30 min, adding more sodium if necessary. The reaction mixture was recooled to -78°C and quenched by the successive addition of isoprene (10 mL) followed by saturated aqueous NH_4Cl (10 mL). After warming to room temperature, the volatiles were allowed to evaporate at atmospheric pressure and the residue partitioned between Et_2O/dichloromethane (3:2) and water. The organic phase was separated, the aqueous phase extracted with Et_2O/dichloromethane (3:2; × 2), and the combined extracts washed with brine, dried ($MgSO_4$), and evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 15% EtOAc/hexanes gave **25** (3.51 g, 84%), and 24 (0.87 g, 16%). For **25**. IR (NaCl) 2938, 2859, 1707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.26 (1H, ddd, J = 2.3, 5.4, 9.5 Hz), 3.94 (1H, t, J = 7.1 Hz), 3.52 (1H, dd, J = 7.3, 12.4 Hz), 3.39 (1H, dd, J = 4.1, 10.9 Hz), 3.19 (3H, s), 2.68 (1H, dt, J = 17.4, 10.0 Hz), 2.21-2.39 (4H, m), 1.96-2.14 (4H, m), 1.61 (1H, m), 1.35-1.51 (6H, m), 1.22 (3H, s), 0.95 (3H, s), 0.88 (9H, s), 0.02 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.9, 116.2, 94.4, 78.4, 76.6, 69.7, 64.3, 53.3, 47.7, 45.9, 41.8, 38.1, 37.1, 37.0, 33.7, 30.6, 28.9, 25.9 (3C), 22.0, 18.4, 18.1, 12.1, -3.7, -5.1; HRMS (CI) calcd for $C_{26}H_{45}O_5Si$ (MH^+) 465.3036, found 465.3024.

4β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-2β-methoxy-2α,20-oxido-3α,10α-oxido-12-trifluoromethylsulfonyl-12-nortaxane-12-ene 26. A solution of sodium bis(trimethylsilyl)amide (8.96 mL of a 1M solution in THF, 8.96 mmol) was added dropwise over approximately 15 min, *via* syringe, to a stirred solution of **25** (3.47 g, 7.47 mmol) in THF (60 mL) at 0°C. After 30 min., a solution of *N*-(5-chloro-2-pyridyl)triflimide (4.10 g, 10.4 mmol) in THF (15 mL) was added, *via* syringe, and the resulting mixture maintained at 0°C for 3 h. The mixture was quenched with saturated aqueous NH_4Cl (7.5 mL) and warmed to room temperature. After evaporation of the volatiles *in vacuo*, the residue was partitioned between dichloromethane and water, the organic phase separated and the aqueous phase extracted with dichloromethane (× 2) and EtOAc (× 1). The combined extracts were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. Purification of the residue by flash chromatography over basic alumina eluting with

2.5% EtOAc/hexanes) gave **26** (4.29 g, 96%) as a colorless foam. IR (NaCl) 2938, 1697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72 (1H, t, J = 3.8 Hz), 4.38 (1H, ddd, J = 2.2, 5.0, 9.7 Hz), 3.91 (1H, t, J = 7.3 Hz), 3.42-3.51 (2H, m), 3.16 (3H, s), 2.65 (1H, dd, J = 4.3, 20.0 Hz), 2.39 (1H, dd, J = 3.4, 9.8 Hz), 2.25-2.34 (2H, m), 2.07-2.15 (2H, m), 1.40-1.64 (8H, m), 1.22 (3H, s), 1.17 (3H, s), 0.90 (9H, s), 0.06 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.8, 118.9, 116.1, 94.8, 78.0, 77.9, 70.0, 54.6, 52.7, 47.9, 44.7, 41.8, 38.0, 36.9, 33.5, 30.7, 28.6, 26.0 (3C), 25.6, 18.3, 12.4, -3.5, -5.0. 2 carbons not found; HRMS (CI) calcd for $C_{27}H_{44}F_3O_7SSi$ (MH^+) 597.2529 , found 597.2521.

4β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-2β-methoxy-2α,20-oxido-3α,10α-oxido-taxane-12-ene 27. A solution of MeLi (91.6 mL of a 1.4M solution in Et_2O, 128 mmol) was added dropwise, *via* syringe, to a vigorously stirred suspension of CuI (13.6 g, 71.4 mmol) in THF (50 mL) at -10°C, maintaining the internal reaction temperature ≤ -3°C. After 30 min, a solution of **26** (4.25 g, 7.12 mmol) in THF (20 mL) was added dropwise, *via* cannula, sustaining the internal reaction temperature ≤ 0°C. After 48 h at 0±1°C (cryostat control), the mixture was quenched by the addition of saturated aqueous NH_4Cl (50 mL) and the resulting mixture filtered through a short pad of Celite® eluting with dichloromethane and water. The organic phase was separated from the filtrate and the aqueous phase extracted with dichloromethane (× 2). The combined extracts were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. Purification of the residue by flash chromatography over basic alumina eluting with 2.5% EtOAc/hexanes gave **27** (3.13 g, 95%) as a colorless solid. IR (NaCl) 2933, 2859, 1466 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.39 (1H, m), 4.27 (1H, ddd, J = 2.0, 5.2, 9.8 Hz), 3.90 (1H, t, J = 7.3 Hz), 3.56 (1H, dd, J = 7.3, 12.4 Hz), 3.48 (1H, m), 3.18 (3H, s), 2.41 (1H, dm, J = 19.1 Hz), 2.03-2.30 (5H, m), 1.73 (3H, m), 1.40-1.61 (8H, m), 1.21 (3H, s), 1.02 (3H, s), 0.89 (9H, s), 0.02 (6H, s); HRMS (CI) calcd for $C_{27}H_{47}O_4Si$ (MH^+) 463.3244, found 463.3233.

4β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-20-hydroxy-3α,10α-oxido-taxane-12-ene-2-one 28. A solution of **27** (3.07 g, 6.63 mmol) in dioxane/glacial AcOH/water (2:1:1; 64 mL) was heated at 50°C for 18 h. After cooling the solution to room temperature, the reaction was quenched by addition of saturated aqueous $NaHCO_3$ (50 mL) and the resulting solution concentrated *in vacuo*. The residue was partitioned between dichloromethane and water, the organic phase separated and the aqueous phase extracted with dichloromethane (× 2). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 17.5% EtOAc/hexanes gave **28** (2.74 g, 92%). IR (NaCl) 3521, 2933, 1689 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.45 (1H, m), 4.47 (1H, ddd, J = 2.9, 5.3, 9.5 Hz), 3.69 (1H, dd, J = 1.9, 12.0 Hz), 3.45 (1H, dd, J = 2.8, 11.0 Hz), 3.38 (1H, m), 2.72 (1H, d, J = 10.5 Hz), 2.51-2.58 (2H, m), 2.33 (1H, m), 1.99-2.15 (3H, m), 1.88 (1H, m), 1.77 (3H, d, J = 1.4 Hz), 1.71 (1H, m), 1.47-1.64 (2H, m), 1.24 (3H, s), 1.07 (3H, s), 1.06 (3H, s), 0.88 (9H, s), 0.05 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 219.2, 136.0, 120.8, 96.0, 78.6, 65.6, 61.6, 61.6, 53.0, 42.3, 42.3, 36.1, 35.1, 35.1, 31.7, 30.1, 30.0, 25.9, 25.2, 24.0, 22.9, 18.1, 12.5, -3.5, -4.9. One carbon not found; HRMS (CI) calcd for $C_{26}H_{45}O_4Si$ (MH^+) 3087, found 3083.

4β,11β-Dihydro-4-formyl-7β-(*tert*-butyldimethylsilyl)oxy-3α,10α-oxido-taxane-12-ene-2-one 28a. 1,1,1-Triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one (2.57 g, 6.06 mmol) was added to a stirred solution of **28** (2.47 g, 5.50 mmol) in dichloromethane (55 mL) at room temperature. After 1 h, the mixture was diluted with Et_2O (25 mL) and quenched with a mixture of saturated aqueous $NaHCO_3$/1M $Na_2S_2O_3$ (1:1; 25 mL). After 15 min. of vigorous agitation, the organic phase was separated and the aqueous phase extracted with Et_2O/dichloromethane (3:2; × 2). The combined extracts were washed with water, brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo* to give **28a** which was used directly in the next step. IR (NaCl) 2933, 1724, 1691 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.63 (1H, d, *J* = 3.3 Hz), 5.38 (1H, m), 4.48 (1H, ddd, *J* = 2.9, 5.2, 9.6 Hz), 3.46 (1H, dd, *J* = 3.7, 11.7 Hz), 2.93 (1H, m), 2.51 (1H, dm, *J* = 8.5 Hz), 2.04-2.22 (4H, m), 1.78 (3H, d, *J* = 1.5 Hz), 1.44-1.75 (5H, m), 1.25 (3H, s), 1.09 (3H, s), 1.06 (3H, s), 0.89 (9H, s), 0.06 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.7, 203.0, 135.3, 120.8, 92.7, 78.4, 76.0, 60.6, 54.6, 53.2, 53.1, 36.6, 35.0, 31.8, 30.0, 28.6, 25.9 (3C), 25.7, 23.1, 20.4, 18.2, 12.4, -3.5, -4.9; HRMS (CI) calcd for $C_{26}H_{43}O_4Si$ (MH^+) 447.2931, found 447.2942.

4β,11β-Dihydro-4-carboxy-7β-(*tert*-butyldimethylsilyl)oxy-3α,10α-oxido-taxane-12-ene-2-one 29. A solution of $NaClO_2$ (6.22 g, 55.0 mmol; 80%) and NaH_2PO_4 (7.60 g, 55.0 mmol) in water (14 mL) was added dropwise over approximately 10 min., *via* syringe, to a vigorously stirred solution of the crude **28a** in a mixture of 2-methyl-2-butene and *t*-BuOH (1:2; 42 mL) at room temperature. After 1 h, the mixture was poured into Et_2O and the organic phase separated. The aqueous phase was extracted with Et_2O/dichloromethane (3:2; × 2), the combined extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo.* to give **29**. IR (NaCl) 2953, 1708 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.38 (1H, bs), 4.57 (1H, ddd, *J* = 2.9, 5.0, 9.5 Hz), 3.48 (1H, dd, *J* = 3.9, 11.6 Hz), 3.07 (1H, dd, *J* = 6.0, 12.0 Hz), 2.50 (1H, d, *J* = 8.7 Hz), 2.06-2.34 (4H, m), 1.43-1.86 (8H, m), 1.23 (3H, s), 1.08 (3H, s), 1.06 (3H, s), 0.88 (9H, s), 0.05 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.9, 176.7, 135.0, 121.3, 92.2, 78.8, 75.8, 60.4, 53.2, 53.0, 48.0, 36.6, 34.9, 31.7, 30.0, 28.9, 25.9 (3C), 25.3, 24.1, 23.1, 18.1, 12.5, -3.5, -5.0; HRMS (CI) calcd for $C_{26}H_{43}O_5Si$ (MH^+) 463.2880, found 463.2876.

4β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-2α,20-oxido-20-oxo-taxane-3,12-diene-10-one 30, 31 and 3β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-10α-hydroxy-4-carboxy-taxane-4,12-diene-2-one 32. A solution of *n*-BuLi (1.58 mL of a 2.5M solution in hexanes, 3.95 mmol) was added, *via* syringe, to a stirred solution of diisopropylamine (0.52 mL, 3.97 mmol) in THF (2.4 mL) at -78°C. After approximately 10 min., the resulting suspension was warmed to 0°C and stirred for a further 15 min. The solution was transferred dropwise, *via* cannula, to a stirred solution of the crude **29** (from 0.395 mmol of **28** without purification) in THF (4 mL) at -10°C, maintaining the internal reaction temperature ≤0°C. The resulting mixture was allowed to warm to room temperature and stirred for approximately 4 days. The mixture was quenched with 1 N HCl (2 mL) and partitioned between Et_2O and water. The organic phase was separated and the aqueous phase re-extracted with dichloromethane (× 2) and EtOAc (× 2). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 10-50% EtOAc/hexane furnished in order of elution, **30** (88 mg, 50% from **28**) as a colorless solid. IR (NaCl) 2932, 1759, 1694 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.50 (1H, bs), 5.07 (1H, bd, J = 2.3 Hz), 3.54 (1H, dd, J = 4.6, 7.5 Hz), 2.94 (1H, d, J = 10.5 Hz), 2.43 (2H, m), 2.18-2.32 (4H, m), 1.69-1.76 (3H, m), 1.63 (3H, d, J = 1.4 Hz), 1.19 (3H, s), 1.12 (3H, s), 1.11 (3H, s), 0.88 (9H, s), 0.07 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.5, 172.3, 165.1, 133.2, 129.6, 122.0, 82.1, 76.3, 64.1, 46.7, 44.4, 43.7, 35.0, 33.6, 26.4, 26.2, 25.9 (3C), 24.3, 21.2, 20.2, 18.8, 18.1, -4.0, -4.8; HRMS (CI) calcd for $C_{26}H_{41}O_4Si$ (MH^+) 445.2774, found 445.2779. **31**, (22 mg, 12%). m.p. 148-149° C (from Et_2O/hexane); IR (NaCl) 3487, 2931, 1761, 1691 cm^{-1}; ^1H NMR (300 MHz) δ 5.63 (1H, br s), 5.10 (1H, d, J = 8.5 Hz), 3.93 (1H, s), 3.56 (1H, dd, J = 10.0, 4.5 Hz), 3.14 (1H, d, J = 11.0 Hz), 2.60 (1H, dd, J = 7.5, 2.5 Hz), 2.46-2.19 (4H, m), 1.79-1.63 (3H, m), 1.62 (3H, br s), 1.19 (3H, s), 1.14 (3H, s), 1.04 (3H, s), 0.91 (9H, s), 0.09 (3H, s), 0.05 (3H, s); HRMS (CI) calcd for $C_{26}H_{41}O_5Si$ (MH^+) 461.2723, found 461.2738. **32** (30 mg, 16% from **28**) as a colorless solid. IR (NaCl) 2929, 2857, 1694 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.10 (1H, dd, J = 2.4, 5.1 Hz), 5.51 (1H, bd, J = 3.9 Hz), 4.48 (1H, d, J = 6.0 Hz), 4.13 (1H, s), 3.75 (1H, dd, J = 6.1, 9.0 Hz), 2.97 (1H, d, J = 17.3 Hz), 2.52 (1H, dt, J = 20.0, 5.6 Hz), 2.10-2.26 (3H, m), 1.75 (3H, s), 1.68 (3H, s), 1.60 (3H, s), 1.19 (3H, s), 1.00 (3H, s), 0.87-0.88 (9H, 2 × s), 0.03 (3H, s), -0.03 (3H, s); HRMS (CI) calcd for $C_{26}H_{42}O_5Si$ (M^+) 462.2802, found 462.2785.

11βH-7β-(*tert*-butyldimethylsilyl)oxy-2β-hydroxy-2α,20-oxido-20-oxo-taxane-3,12-diene-10-one 33, 33a and 33b. *t*-BuOK (103 mg, 0.918 mmol) was added to a stirred solution of **30** (82.0 mg, 0.184 mmol) in THF (1.8 mL) at -78°C. After 20 min., the mixture was warmed to 0° C and stirred for a further 20 min. The resulting solution was then transferred dropwise, *via* cannula, to a vigorously stirred suspension of benzene seleninic anhydride (332 mg, 0.992 mmol) in THF (1.8 mL) at 0° C. After 40 min., the resulting mixture was cooled to -78° C and a second portion of *t*-BuOK (103 mg, 0.918 mmol) was added. After 30 min., the mixture was quenched with saturated aqueous NH_4Cl (1 mL), warmed to room temperature and partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with dichloromethane (× 3). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 10-50% EtOAc/hexanes provided **33** (61 mg, 72%) as a colorless solid. IR (NaCl) 3362, 2956, 2858, 1742, 1676 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.46 (1H, bs), 3.47 (1H, dd, J = 1.6, 6.3 Hz), 3.02 (2H, dm, J = 10.5 Hz), 2.38-2.50 (3H, m), 2.10-2.31 (2H, m), 2.02 (1H, d, J = 10.4 Hz), 1.61-1.83 (6H, m), 1.32 (3H, s), 1.26 (3H, s), 1.12 (3H, s), 0.86 (9H, s), 0.07 (3H, s), 0.05 (3H, s); HRMS (CI) calcd for $C_{26}H_{41}O_5Si$ (MH^+) 462.2802, found 462.2785 **33a**, IR (NaCl) 2935, 1781, 1697 cm^{-1}; ^1H NMR (300 MHz) δ 7.61-7.59 (2H, m), 7.42-7.30 (3H, m), 5.58 (1H, br s), 3.07 (1H, dd, J = 11.5, 4.0 Hz), 2.96 (1H, d, J = 11.5 Hz), 2.59 (1H, d, J = 10.0 Hz), 2.50 (1H, s), 2.41-2.25 (4H, m), 2.01-1.96 (1H, m), 1.75-1.66 (2H, m), 1.62 (3H, br s), 1.49 (3H, s), 1.00 (3H, s), 0.92 (9H, s), 0.74 (3H, s), 0.08 (3H, s), 0.00 (3H, s). **33b**, IR (NaCl) 2935, 1782, 1688 cm^{-1}; ^1H NMR (300 MHz) δ 5.64 (1H, br s), 3.20 (1H, dd, J = 13.0, 6.0 Hz), 3.13-3.09 (2H, m), 2.70 (1H, d, J = 10.5 Hz), 2.54 (1H, s), 2.40 (1H, br d, J = 21.0 Hz), 2.27-2.21 (2H, m), 1.76-1.72 (2H, m), 1.67 (3H, br s), 1.42-1.25 (2H, m), 1.12 (3H, s), 1.07 (3H, s), 1.04 (3H, s), 0.88 (9H, s), 0.04 (3H, s), -0.01 (3H, s); HRMS (CI) calcd for $C_{26}H_{41}O_4Si$ (MH^+) 445.2774, found 445.2772.

11βH-7β-(*tert*-butyldimethylsilyl)oxy-1β,2β-dihydroxy-2α,20-oxido-20-oxo-taxane-3,12-diene-10-one 34. *t*-BuOK (18.0 mg, 160 μmol) was added to a stirred solution of **30** (7.0 mg, 15.7 μmol) in THF (0.6 mL) at -78°C. After 30 min., triethylphosphite (27.0 μL, 157 μmol) was added, *via* syringe, and then a gentle stream of dry air was bubbled through the mixture. After 1 h, the resulting mixture was warmed to room temperature, quenched by the addition of saturated aqueous NH_4Cl (0.1 mL) and partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with dichloromethane. The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by thin layer chromatography on silica gel eluting with 30% EtOAc/hexanes (double elution) gave in order of elution, **33** (3.0 mg, 41%) and **34** (3.5 mg, 47%) as a colorless solid. IR (NaCl) 3461, 2933, 1755, 1679 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.37 (1H, bs), 3.48 (1H, dd, *J* = 2.1 Hz, 5.7 Hz), 2.97 (1H, d, *J* = 10.9 Hz), 2.68 (1H, bs), 2.48 (1H, m), 2.15-2.35 (4H, m), 1.63-1.88 (6H, m), 1.30 (3H, s), 1.25 (3H, s), 1.22 (3H, s), 0.86 (9H, s), 0.06 (6H, s); HRMS (CI) calcd for $C_{26}H_{41}O_6Si$ (MH^+) 477.2672, found 477.2667.

3α,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-4-carboxy-taxane-4,12-diene-2,10-dione 35. *t*-BuOK (81.0 mg, 0.811 mmol) was added to a stirred solution of **33** (75.0 mg, 0.163 mmol) in a mixture of THF and *t*-BuOH (5:1; 1.6 mL) at room temperature and the resulting mixture heated at reflux for approximately 12 h. After cooling to room temperature, the reaction was quenched by the addition of 1N HCl (0.5 mL) and partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with dichloromethane (× 3). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*, and the crude product used directly in the next step. **35** IR (NaCl) 2930, 2857, 1691 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.97 (1H, bs), 5.78 (1H, bs), 4.01 (1H, bs), 3.41 (1H, dd, *J* = 6.1, 9.5 Hz), 3.11 (1H, bd, *J* = 19.3 Hz), 2.73 (1H, d, *J* = 10.7 Hz), 2.49 (1H, d, *J* = 10.8 Hz), 2.13-2.45 (5H, m), 1.73 (3H, s), 1.07 (3H, s), 0.97 (12H, s), 0.73 (3H, s), 0.05 (3H, s), 0.01 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.3, 213.2, 171.6, 140.9, 135.3, 131.4, 122.1, 73.4, 64.2, 56.3, 51.6, 48.9, 43.5, 36.8, 32.3, 32.1, 26.7, 25.9 (3C), 25.7, 24.6, 18.1, 11.0, -4.1, -4.7; HRMS (CI) calcd for $C_{26}H_{41}O_5Si$ (MH^+) 461.2723, found 461.2707.

3α,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-4-carbomethoxy-taxane-4,12-diene-2,10-dione 35a. Anhydrous K_2CO_3 (113 mg, 0.818 mmol) was added, in one portion, to a vigorously stirred solution of the crude **35** in dry acetone (1.6 mL) at room temperature. After approximately 10 min., iodomethane (0.510 mL, 8.19 mmol; pre-filtered through basic alumina) was added, *via* syringe, and the resulting pale yellow suspension stirred at ambient temperature for 3 h. The volatiles were evaporated and the residue partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with Et_2O/dichloromethane (3:2; × 3). The combined extracts were washed with brine, dried ($MgSO_4$) and evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 10% EtOAc/hexanes gave **35a** (50 mg, 65%). m.p. 180-181° C (EtOAc/hexanes). IR (NaCl) 2931, 2858, 1693 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.91 (1H, m), 5.81 (1H, bs), 4.04 (1H, m), 3.64 (3H, s), 3.42 (1H, dd, *J* = 6.1, 9.5 Hz), 3.19 (1H, bdd, *J* = 2.4, 19.3 Hz), 2.73 (1H, d, *J* = 10.7 Hz), 2.58 (1H, m), 2.51 (1H, dd, *J* = 1.5, 10.8 Hz), 2.38-2.41 (2H, m), 2.21-2.29 (2H, m), 1.75 (3H, s), 1.09 (3H, s), 0.99 (3H, s), 0.88 (9H, s), 0.77 (3H, s), 0.04 (3H, s), 0.01 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.8, 213.2, 167.3, 139.0, 135.2, 131.9, 122.0, 73.4, 64.2, 56.3, 51.9, 51.7, 48.9, 43.5, 36.7, 32.3, 31.9, 26.6, 25.8 (3C), 25.7, 24.6, 18.0, 11.0, -4.1, -4.8; HRMS (CI) calcd for $C_{27}H_{43}O_5Si$ (MH^+) 475.2880, found 475.2882.

3α,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-10β-hydroxy-4-hydroxymethyl-taxane-4,12-diene-2-one 36. A solution of DIBAL-H (0.290 mL of a 1.0M solution in dichloromethane, 0.290 mmol) was added dropwise over approximately 5 min, *via* syringe, to a stirred solution of **35a** (34.0 mg, 0.716 mmol) in dichloromethane (0.7 mL) at -78°C. After 1 h the reaction was quenched by the addition of 1N HCl (0.2 mL), warmed to room temperature and partitioned between Et_2O and 1N HCl. The organic phase was separated and the aqueous phase extracted with Et_2O/dichloromethane (3:2; × 3). The combined extracts were washed with water, brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 25% EtOAc/hexane afforded **36** (29.5 mg, 92%) as a colorless solid. IR (NaCl) 3401, 2929, 2859, 1689 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.65 (1H, dm, *J* = 3.1 Hz), 5.55 (1H, bs), 4.10 (1H, m), 4.01 (1H, bs), 3.87 (2H, m), 3.66 (1H, dd, *J* = 7.5, 8.4 Hz), 2.38 (3H, m), 2.25 (1H, m), 1.92-2.14 (5H, m), 1.88 (3H, s), 1.35 (3H, s), 1.18 (1H, bs), 1.05 (3H, s), 0.90 (12H, s), 0.08 (3H, s), 0.06 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.0, 136.5, 136.2, 126.3, 121.4, 70.7, 69.2, 65.1, 57.8, 56.2, 51.7, 41.9, 40.6, 35.4, 34.6, 34.1, 25.8 (3C), 25.4, 24.9, 23.2, 18.1, 15.5, -3.5, -5.1; HRMS (EI) calcd for $C_{26}H_{44}O_4Si$ (M^+) 448.3009, found 448.3004.

3α,11β-Dihydro-7β,10β-di(*tert*-butyldimethylsilyl)oxy-4-(*tert*-butyldimethylsilyl)oxymethyl-taxane-4,12-diene-2-one 37. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (15.0 μL, 65.5 μmol) was added, *via* syringe, to a stirred solution of **36** (14.0 mg, 31.2 μmol) and triethylamine (18.3 μL, 0.131 μmol) in dichloromethane (0.3 mL) at 0°C. After approximately 1 h, consecutive portions of triethylamine (18.3 μL, 131 μmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (15.0 μL, 65.5 μmol) were added. After 1 h, the reaction was quenched by the addition of water (0.1 mL), warmed to room temperature and partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with dichloromethane (× 4). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 2.5% EtOAc/hexane furnished **37** (21.0 mg, 100%) as a colorless oil.

3α,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-10β-hydroxy-4-(*tert*-butyldimethylsilyl)oxy methyl-taxane-4,12-diene-2-one 38. *tert*-Butyldimethylsilyl chloride (5.5 mg, 36.5 μmol) was added, in one portion, to a stirred solution of **36** (14.9 mg, 33.2 μmol), *N*, *N*-dimethylaminopyridine (0.4 mg, 3.3 μmol) and triethylamine (10.2 μL, 73.0 μmol) in dichloromethane (0.3 mL) at 0°C. After approximately 1 h, triethylamine (10.2 μL, 73.0 μmol) and *tert*-butyldimethylsilyl chloride (5.5 mg, 36.5 μmol) were added. After a further 1 h, the reaction was quenched by the addition of water (0.1 mL), warmed to room temperature and then partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with dichloromethane (× 4). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 7.5% EtOAc/hexanes provided **38** (18.3 mg, 98%) as a colorless oil. IR (NaCl) 3488, 2927, 2856, 1693 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.59 (1H, d, *J* = 1.9 Hz), 5.54 (1H, bs), 4.09 (1H, m), 3.92 (3H, bs), 3.67 (1H, m), 2.58 (1H, bd, J = 19.5 Hz), 1.86-2.45 (10H, m), 1.34 (3H, s), 1.25 (3H, s), 1.15 (1H, bs), 1.04 (3H, s), 0.86-0.89 (18H, 3 × s), 0.08 (3H, s), 0.06 (3H, s), 0.04 (3H, s), 0.03 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.8, 136.0, 135.7, 122.9, 121.7, 71.1, 69.4, 64.7, 57.6, 56.2, 50.6, 42.1, 40.7, 34.6, 34.2, 29.8, 29.7, 26.1 (3C), 25.9 (3C), 25.4, 25.0, 23.2, 18.1, 15.5, -3.5, -5.0, -5.3. 1 carbon not found; HRMS (EI) calcd for $C_{32}H_{58}O_4Si_2$ (M^+) 562.3874, found 562.3860.

3α,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-4-(*tert*-butyldimethylsilyl)oxymethyl-taxane-4,12-diene-2,10-dione 39. 1,1,1-Triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1*H*)-one (12.8 mg, 30.2 μmol) was added to a stirred solution of **38** (8.5 m g, 15.1 μmol) in dichloromethane (0.3 mL) at room temperature. After approximately 1 h, the reaction was diluted with Et_2O (1.7 mL) and quenched with a mixture of saturated aqueous $NaHCO_3$/1M $Na_2S_2O_3$ (1:1; 1.0 mL). After 15 min. of vigorous agitation, the organic phase was separated and the aqueous phase extracted with Et_2O/dichloromethane (3:2; × 4). The combined extracts were washed with water, brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 5% EtOAc/hexanes gave **39** (8.5 mg, 100%) as a colorless oil. IR (NaCl) 2931, 2858, 1691 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76 (1H, bs), 5.63 (1H, m), 3.99 (1H, bs), 3.81-3.89 (2H, m), 3.43 (1H, dd, J = 5.9, 9.8 Hz), 3.00 (1H, bd, J = 19.7 Hz), 2.69 (1H, d, J = 10.5 Hz), 2.53 (1H, dd, J = 1.2, 9.8 Hz), 2.43 (1H, m), 2.37 (1H, bs), 2.25 (1H, d, J = 6.7 Hz), 1.94-2.20 (2H, m), 1.75 (3H, s), 1.07 (3H, s), 1.00 (3H, s), 0.89 (9H, s), 0.87 (9H, s), 0.75 (3H, s), 0.03-0.04 (9H, 2 × s), 0.00 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 213.4, 136.1, 135.7, 122.2, 121.5, 74.3, 66.7, 64.1, 56.6, 52.8, 49.7, 43.8, 36.7, 32.2, 31.5, 26.6, 26.2 (3C), 25.9 (3C), 25.3, 24.7, 18.7, 18.1, 11.2, -4.0, -4.7, -5.0, -5.2; HRMS (EI) calcd for $C_{32}H_{57}O_4Si_2$ (M^+) 61.3795, found 561.3783.

3α,11β-Dihydro-1β-hydroxy-7β-(*tert*-butyldimethylsilyl)oxy-4-(*tert*-butyldimethylsilyl)oxy methyl-taxane-4,12-diene-2,10-dione 2. *t*-BuOK (1.0 M soln. in THF, 143 μL, 0.143 mmol, 11 eq) and $P(OEt)_3$ (48 μL, 0.30 mmol, 24 eq) were added to a stirred solution of **39** (7 mg, 12.5 μmol) in dry THF (1 mL) at room temperature under argon. A stream of dried O_2 was passed through the bright yellow reaction mixture at 52° C for 7 h. Further portions of *t*-BuOK solution (5x143 μL), $P(OEt)_3$ (4x48 μL) and THF (total reaction volume kept at approx. 1.5 mL) were added during this period. The reaction was cooled to room temperature and saturated aqueous NH_4Cl solution (10 mL) added. The aqueous layer was extracted with CH_2Cl_2 (3x30 mL) and the combined extracts dried ($MgSO_4$) and concentrated *in vacuo* to give a colorless oil (6 mg). Purification by flash column chromatography over silica gel eluting with 5% EtOAc/hexane gave **2** (2.2 mg, 31%; 39% based on recovered **39**) as an oil which solidified on standing; m.p. 90-91° C; $[\alpha]_D^{21}$ +72.5 (c 0.26 in $CHCl_3$); IR (NaCl) 3502, 2930, 1690 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86 (1H, br s), 5.62 (1H, br s), 3.97 (1H, br s), 3.93, 3.83 (2H, ABq, J_{AB} = 11.5 Hz), 3.63 (1H, s), 3.46 (1H, dd, J = 10.0, 6.0 Hz), 2.95, 2.55 (2H, ABq, J_{AB} = 19.5 Hz), 2.93, 2.76 (2H, ABq, J_{AB} = 10.5 Hz), 2.50 (1H, s), 2.22-2.04 (2H, m), 1.73 (3H, s), 1.16 (3H, s), 0.90 (9H, s), 0.89 (9H, s), 0.88 (3H, s), 0.77 (3H, s), 0.053, 0.048, 0.01 (12H, br s and 2 x s); HRMS (CI) calcd. for $C_{32}H_{57}O_5Si_2$ (MH^+) 577.3744, found 577.3727.

3β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-10α-hydroxy-4-hydroxymethyl-taxane-4,12-diene-2-one 40. A solution of BH_3.THF complex (169 μL of a 1M solution in THF, 169 μmol) was added dropwise, *via* syringe, to a stirred solution of **32** (26.0 mg, 56.2 μmol) in THF (0.6 mL) at room temperature. After approximately 1 h, the mixture was quenched by the addition of water (0.2 mL) and then partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with Et_2O/dichloromethane (× 3). The combined extracts were washed with brine, dried ($MgSO_4$) and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 30% EtOAc/hexanes provided **40** (19.0 mg, 75%) as a colorless solid. IR (NaCl) 3453, 2930, 2857, 1681 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.68 (1H, m), 5.51 (1H, m), 4.45 (1H, d, J = 5.9 Hz), 3.85 (2H, d, J = 5.4 Hz), 3.78 (1H, dd, J = 6.2, 9.2 Hz), 2.99 (1H, dd, J = 4.9, 18.2 Hz), 2.33 (1H, dt, J = 18.2, 5.5 Hz), 2.20 (1H, m), 1.90-2.05 (3H, m), 1.75 (3H, s), 1.67 (3H, s), 1.49-1.63 (3H, m), 1.09-1.28 (2H, m), 1.18 (3H, s), 1.02 (3H, s), 0.86 (9H, s), 0.02 (3H, s), -0.03 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.3, 135.4, 133.6, 125.3, 123.5, 69.8, 68.6, 67.9, 57.3, 56.4, 55.0, 41.9, 39.8, 34.8, 34.8, 32.2, 28.7, 26.6, 26.0 (3C), 25.1, 18.1, 17.0, -4.2, -4.8; HRMS (CI) calcd for $C_{26}H_{44}O_4Si$ (M^+) 448.3009, found 48.2992.

3β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-10α-hydroxy-4-(*tert*-butyldimethylsilyl)oxy methyl-taxane-4,12-diene-2-one 41. *tert*-Butyldimethylsilyl chloride (6.7 mg, 44.5 μmol) was added to a stirred solution of the **40** (19.0 mg, 42.3 mmol), 4-*N*, *N*-dimethylaminopyridine (0.5 mg, 4.1 mmol) and Et_3N (12.0 μL, 86.1 μmol) in dichloromethane (0.4 mL) at 0°C. After 1 h, Et_3N (12.0 μL, 86.1 μmol) and *tert*-butyldimethylsilyl chloride (6.7 mg, 44.5 μmol) were added. After a further 30 min, the mixture was quenched with water (0.2 mL) and partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with dichloromethane (× 3). The combined extracts were washed with brine, dried ($MgSO_4$), and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 5% EtOAc/hexanes gave **41** (20.0 mg, 84%) as a colorless solid. IR (NaCl) 3508, 2938, 2856, 1670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.59 (1H, m), 5.51 (1H, m), 4.45 (1H, m), 3.73-3.90 (4H, m), 3.00 (1H, dd, J = 4.6, 18.3 Hz), 2.31 (1H, dt, J = 5.4, 18.0 Hz), 2.17 (1H, m), 2.04 (1H, s), 1.90-1.99 (2H, m), 1.75 (3H, s), 1.66 (3H, s), 1.56 (2H, m), 1.18 (3H, s), 1.01 (3H, s), 0.89 (9H, s), 0.85 (9H, s), 0.01 (6H, s), 0.00 (3H, s), -0.03 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 135.1, 133.6, 123.7, 123.6, 70.0, 68.7, 67.3, 57.4, 55.5, 42.1, 39.8, 34.9, 32.1, 28.8, 26.5, 26.0 (6C), 25.1, 18.1, 17.0, -4.1, -4.8, -5.1, -5.2. 3 carbons not found; HRMS (CI) calcd for $C_{32}H_{59}O_4Si_2$ (MH^+) 563.3952, found 563.3944.

3α,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-1β,10α-dihydroxy-4-(*tert*-butyldimethylsilyl) oxymethyl-taxane-4,12-diene-2-one 42. *t*-BuOK (12.0 mg, 107 μmol) was added to a stirred solution of the **41** (6.0 mg, 10.7 μmol) in THF (0.5 mL) at 0°C. After 30 min, the mixture was cooled to -78°C, triethyl phosphite (18.3 μL, 107 μmol) added, *via* syringe, and a gentle stream of dry air was bubbled through the mixture. After 1 h, the mixture was quenched by the addition of saturated aqueous NH_4Cl (0.2 mL) and warmed to room temperature. The resulting mixture was partitioned between Et_2O and water, the organic phase separated and the aqueous phase extracted with dichloromethane (× 3). The combined organic extract was washed with brine, dried ($MgSO_4$), and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 10% EtOAc/hexanes afforded **42** (5.3 mg, 85%) as a colorless solid. IR (NaCl) 3572, 2930, 2857, 1697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.57 (1H, d, *J* = 4.4 Hz), 5.51 (1H, d, *J* = 4.5 Hz), 4.39 (1H, dd, *J* = 2.5, 7.7 Hz), 3.93 (5H, m), 2.91 (1H, dd, *J* = 5.6, 16.7 Hz), 2.20-2.30 (2H, m), 1.98-2.07 (2H, m), 1.74 (3H, s), 1.41-1.66 (5H, m), 1.24 (3H, s), 1.19 (1H, m), 1.04 (3H, s), 0.88 (9H, s), 0.87 (9H, s), 0.08 (6H, s), 0.04 (3H, s), 0.00 (3H, s); HRMS (EI) calcd for $C_{32}H_{58}O_5Si_2$ (M^+) 578.3823, found 578.3807.

3β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-1β,2β-dihydroxy-2α,10α-oxido-4-hydroxymethyl -taxane-4,12-diene 43. *t*-BuOK (2.4 mg, 21.4 μmol) was added, in one portion, to a stirred solution of **42** (2.3 mg, 4.0 μmol) in THF (0.2 mL) at 0°C. After 30 min the mixture was warmed to room temperature and stirred for approximately 12 h. The mixture was quenched with saturated aqueous NH_4Cl (0.1 mL) and the resulting mixture partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with dichloromethane (× 4). The combined extracts were washed with brine, dried ($MgSO_4$), and the solvent evaporated *in vacuo* to give **43**. IR (NaCl) 3399, 2929 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81 (1H, m), 5.43 (1H, m), 4.35 (1H, dd, *J* = 6.7, 9.3 Hz), 4.19 (1H, d, *J* = 12.5 Hz), 3.97 (2H, m), 3.58 (1H, s), 3.01-3.20 (2H, m), 2.64 (1H, dd, *J* = 12.3, 15.2 Hz), 2.32 (1H, dt, *J* = 18.4, 5.3 Hz), 1.86-2.01 (2H, m), 1.74 (1H, d, *J* = 1.7 Hz), 1.71 (3H, d, *J* = 1.5 Hz), 1.58 (2H, m), 1.51 (3H, s), 1.25 (1H, dm, *J* = 1.7 Hz), 1.13 (3H, s), 0.92 (3H, s), 0.90 (9H, s), 0.05 (3H, s), 0.02 (3H, s); HRMS (EI) calcd for $C_{26}H_{44}O_5Si$ (M^+) 464.2958, found 464.2949.

3β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-1β,2β-dihydroxy-2α,10α-oxido-4-(4'-nitro benzoyl)oxymethyl-taxane-4,12-diene 44. 4-Nitrobenzoyl chloride (1.6 mg, 8.4 μmol) was added to a stirred solution of **43**, *N*, *N*-dimethylaminopyridine (1 micro crystal) and triethylamine (2.3 μL, 16.5 μmol) in dichloromethane (0.2 mL) at 0°C. After approximately 30 min the mixture was quenched by the addition of water (0.1 mL), and the resulting mixture partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with dichloromethane (× 4). The combined extracts were washed with brine, dried ($MgSO_4$), and the solvent evaporated *in vacuo*. Purification of the residue by chromatography over silica gel eluting with 25% EtOAc/hexanes gave **44** (1.9 mg, 79%) as a colorless solid. IR (NaCl) 3511, 2927, 2857, 1722, 1607, 1530 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (2H, d, *J* = 8.8 Hz), 8.21 (2H, d, *J* = 8.8 Hz), 6.02 (1H, m), 5.43 (1H, bs), 4.93 (1H, d, *J* = 12.8 Hz), 4.78 (1H, d, *J* = 12.5 Hz), 4.39 (1H, dd, *J* = 6.5, 9.2 Hz), 3.97 (1H, m), 3.62 (1H, s), 3.00 (1H, m), 2.90 (1H, s), 2.64 (1H, dd, *J* = 12.2, 15.2 Hz), 2.38 (1H, dt, *J* = 18.4, 5.2 Hz), 1.85-2.08 (2H, m), 1.82 (1H, s), 1.71 (3H, s), 1.56 (2H, m), 1.42 (3H, s), 1.09 (3H, s), 0.94 (3H, s), 0.90 (9H, s), 0.06 (3H, s), 0.03 (3H, s); HRMS (EI) calcd for $C_{33}H_{47}NO_8Si$ (MH^+) 613.3071, found 613.3051.

3β,11β-Dihydro-7β-(*tert*-butyldimethylsilyl)oxy-4-(*tert*-butyldimethylsilyl)oxymethyl-taxane-4,12-diene-2,10-dione 45. Dess-Martin reagent (7.8 mg, 18.4 μmol) was added to a stirred solution of **41** (5.2 mg, 9.24 μmol) in dichloromethane (0.2 mL) at room temperature. After approximately 30 min the reaction was diluted with Et_2O (1.8 mL) and quenched with a mixture of saturated aqueous $NaHCO_3$/1M $Na_2S_2O_3$ (1:1, 1.0 mL). After 15 min. of vigorous agitation, the organic phase was separated and the aqueous phase extracted with Et_2O/dichloromethane (3:2; × 4). The combined extracts were washed with water, brine, dried ($MgSO_4$)

and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 3.5% EtOAc/hexanes gave **45** (5.2 mg, 100%) as a colorless solid. IR (NaCl) 2932, 2857, 1691 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.65 (1H, m), 5.58 (1H, m), 3.78-3.95 (4H, m), 3.25 (1H, m), 2.60 (1H, s), 2.51 (1H, d, *J* = 12.0 Hz), 2.21-2.34 (3H, m), 2.10 (1H, dd, *J* = 1.1, 11.8 Hz), 1.95 (1H, m), 1.54 (3H, s), 1.20 (3H, s), 1.04 (3H, s), 0.84 (21H, s), 0.02 (3H, s), 0.01 (3H, s), 0.00 (3H, s), -0.07 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.5, 213.3, 134.9, 132.1, 124.1, 123.3, 70.1, 68.1, 67.5, 56.3, 55.4, 43.8, 41.7, 34.7, 34.6, 31.6, 29.4, 26.0 (3C), 25.9 (3C), 25.5, 23.0, 18.1, 16.4, -4.2, -4.9, -5.1, -5.2. 1 carbon not found; HRMS (CI) calcd for $C_{32}H_{57}O_4Si_2$ (MH^+) 561.3795, found 561.3784.

3β,11β-Dihydro-1β-hydroxy-7β-(*tert*-butyldimethylsilyl)oxy-4-(*tert*-butyldimethylsilyl)oxy methyl-taxane-4,12-diene-2,10-dione 46. *t*-BuOK(10.0 mg, 89.1 μmol) was added to a stirred solution of **45** (5.0 mg, 8.91 μmol) in THF (0.9 mL) at 0°C. After 30 min the mixture was cooled to -78°C, triethyl phosphite (15.3 μL, 89.1 μmol) added *via* syringe, and a gentle stream of dry air was bubbled through the mixture. After 15 min the mixture was quenched with saturated aqueous NH_4Cl (0.45 mL), warmed to room temperature and partitioned between Et_2O and water. The organic phase was separated and the aqueous phase extracted with dichloromethane (× 4). The combined extracts were washed with brine, dried ($MgSO_4$), and the solvent evaporated *in vacuo*. Purification of the residue by flash chromatography over silica gel eluting with 5-20% EtOAc/hexanes afforded in order of elution, **46** (2.5 mg, 40%) as a colorless solid. IR (NaCl) 3377, 2931, 2857, 1696 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.65 (1H, d, *J* = 5.5 Hz), 5.58 (1H, d, *J* = 4.4 Hz), 4.44 (1H, s), 3.98 (4H, m), 3.05 (1H, dd, *J* = 5.8, 17.1 Hz), 2.78 (1H, s), 2.38 (1H, d, *J* = 11.7 Hz), 1.99-2.36 (5H, m), 1.55 (3H, s), 1.37 (3H, s), 1.24 (3H, s), 1.05 (3H, s), 0.86 (9H, s), 0.85 (9H, s), 0.08 (6H, s), 0.04 (3H, s), -0.05 (3H, s); HRMS (CI) calcd for $C_{32}H_{57}O_5Si_2$ (MH^+) 577.3745, found 577.3728.

48 (1.4 mg, 34%) as a colorless solid. IR (NaCl) 3429, 2930, 1672 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.25 (1H, s), 6.98 (1H, dd, *J* = 2.3, 5.1 Hz), 5.61 (1H, d, 5.0 Hz), 4.62 (1H, s), 4.12 (1H, s), 4.01 (1H, dd, *J* = 5.9, 9.0 Hz), 3.14 (1H, dd, *J* = 5.0, 17.1 Hz), 2.83 (1H, s), 2.70 (1H, dt, *J* = 20.6, 5.5 Hz), 2.51 (1H, d, *J* = 12.1 Hz), 2.11-2.36 (4H, m), 1.56 (3H, s), 1.47 (3H, s), 1.29 (3H, s), 1.01 (3H, s), 0.87 (9H, s), 0.07 (3H, s), -0.04 (3H, s); HRMS (CI) calcd for $C_{26}H_{41}O_5Si$ (MH^+) 461.2723, found 461.2727.

47 (1.0 mg, 24%) as a colorless solid. IR (NaCl) 3382, 2928, 2857, 1694 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72 (1H, d, *J* = 4.9 Hz), 5.63 (1H, d, *J* = 5.0 Hz), 4.14 (1H, bs), 3.97 (4H, m), 3.12 (1H, dd, *J* = 5.5, 16.5 Hz), 2.79 (1H, s), 2.42 (1H, d, *J* = 11.8 Hz), 2.29 (1H, dt, *J* = 18.2, 5.4 Hz), 2.12-2.19 (2H, m), 1.97-2.07 (2H, m), 1.77 (1H, dd, *J* = 1.1, 7.9 Hz), 1.55 (3H, s), 1.42 (3H, s), 1.26 (3H, s), 1.06 (3H, s), 0.85 (9H, s), 0.04 (3H, s), -0.05 (3H, s); HRMS (CI) calcd for $C_{26}H_{43}O_5Si$ (MH^+) 463.2880, found 463.2879.

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References and Footnotes

† Author for inquiries concerning the X-ray data.

(1) Paclitaxel is the generic name for Taxol, which is now a registered trademark. For the isolation and structure see: Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2327.

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