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SYNTHESIS OF MODIFIED ANALOGUES OF TAXOL C, D SUBUNITS FROM FURAN

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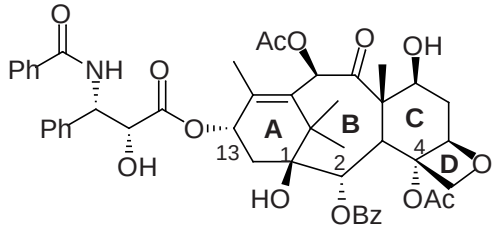
Abstract-The synthesis of two modified analogues of the C,D subunits of taxol, using a furan derivative as precursor, is reported.

Dedicated to Professor James P. Kutney on occasion of his 70th birthday.

INTRODUCTION

Taxol, a potent antitumor agent isolated from the bark of *Taxus brevifolia*,[1] has become one of the most important members in a new class of chemotherapeutic agents which inhibits cell growth by interacting with microtubules (Scheme 1).[2] Due to its novel mode of action and complex structure as well as its low natural availability, taxol remains of great synthetic interest for organic chemists. At this time, six total syntheses of taxol and some synthetic approaches have been reported.[3]

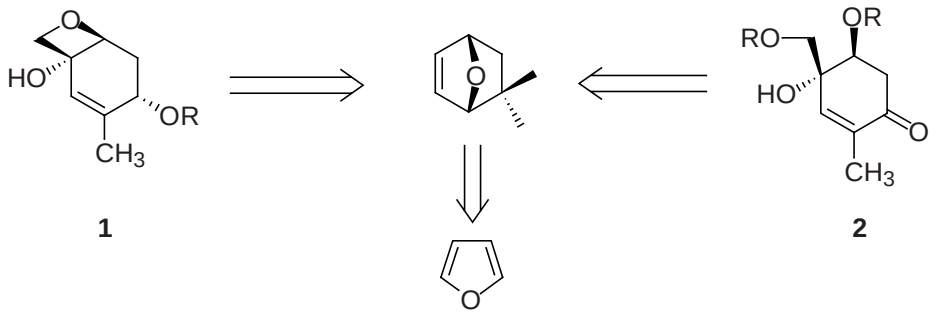
In order to obtain simpler analogues with better therapeutic profiles, extensive studies have been made on structure-activity relationship to find out the minimal structural requirements to maintain microtubule binding.[4] These studies have established that the C-13 side chain, the oxygenated groups at C-2 and C-4 and the oxetane ring are essential for biological activity.[5] The importance of this last functionality has promoted the synthesis and study of D-secotaxol analogues[6] and recently, Dubois has prepared the first taxol analogue with a modified D-ring which is active on microtubules.[7]



Taxol

Scheme 1

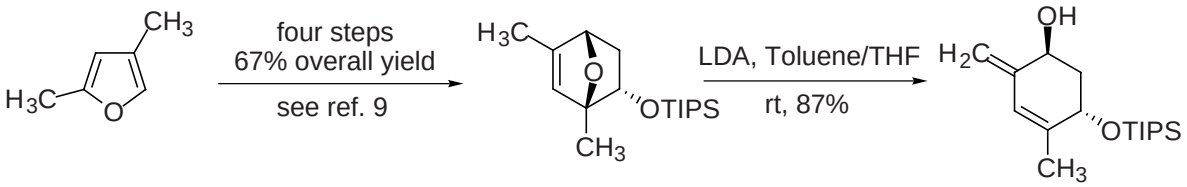
In this paper we wish to report our synthetic efforts focused on the preparation of modified analogues of taxol C,D-subunits. In this way, compounds (**1**) and (**2**) will be prepared *via* 7-oxanorbornene derivatives easily obtained from furan through Diels-Alder cycloadditions (Scheme 2).[8]



1 **2**

Scheme 2

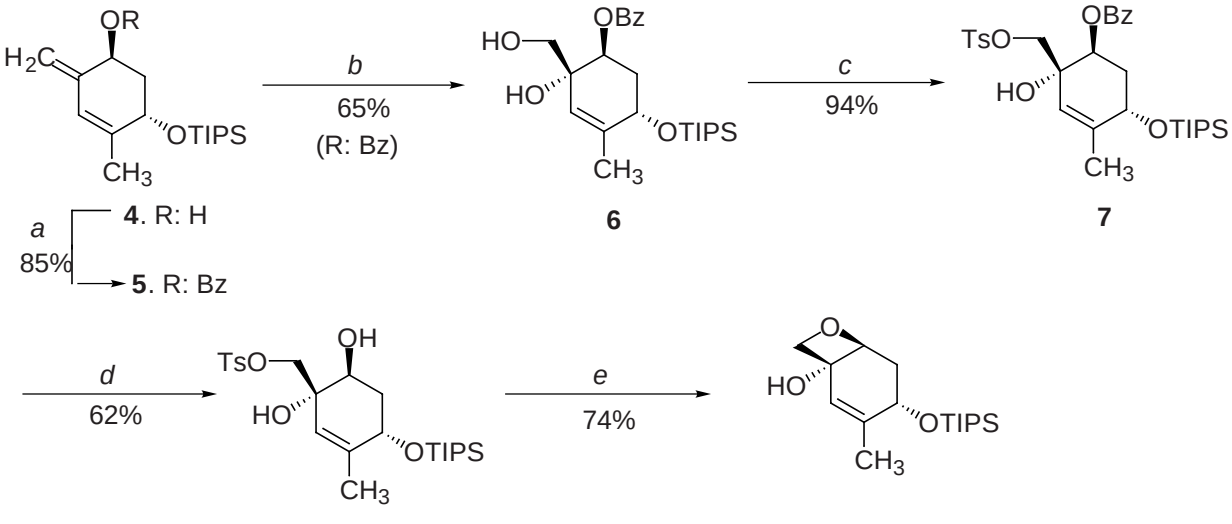
In a previous study, the synthesis of diene (**4**) was accomplished in five steps from 2,4-dimethylfuran in 58% overall yield.[9] The key step of this process consisted of an LDA-mediated ring opening of 7-oxanorbornene derivative (**3**) to afford **4** (Scheme 3).[10]



3 **4**

Scheme 3

Protection of the hydroxyl group in **4** and catalytic bishydroxylation of the exocyclic double bond in the resulting compound (**5**), afforded **6**. Treatment with TsCl followed by hydrolysis of the benzoyl functionality, using K_2CO_3, gave rise to diol (**8**). Final transformation of **8** into the oxabicyclic derivative (**9**), employing NaH, permitted the formation of this modified subunit of taxol C,D rings (Scheme 4).

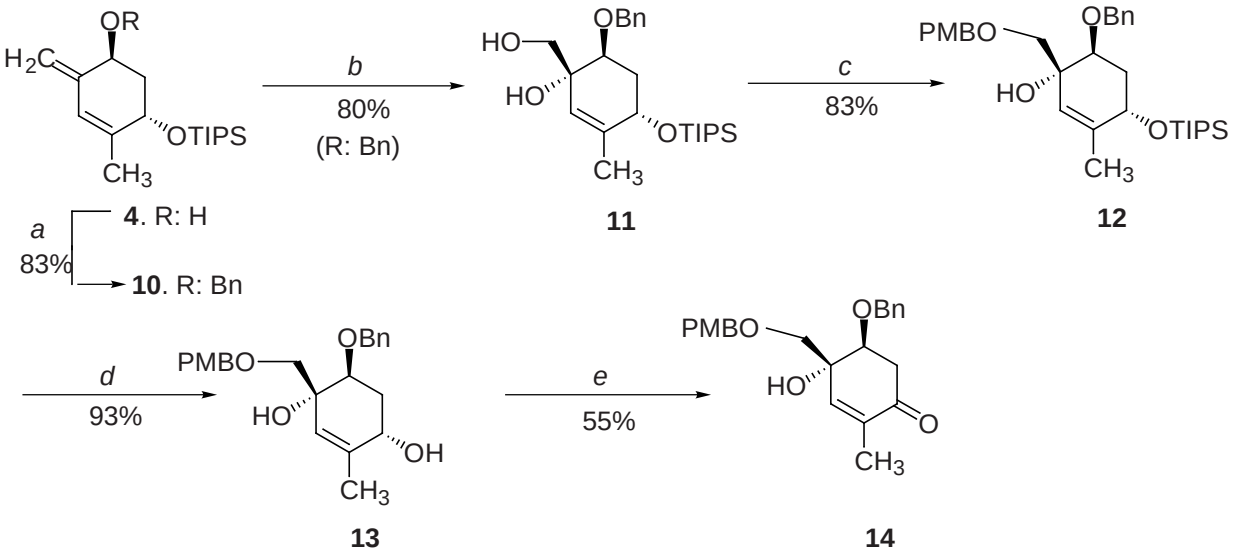


8 **9**

Key. *a*) BzCl, Et_3N, DMAP, CH_2Cl_2, rt; *b*) OsO_4, Me_3NO, acetone/H_2O 8/1, rt; *c*) TsCl, Py, rt; *d*) K_2CO_3, MeOH/H_2O 5/1, 0^oC; *e*) NaH, THF, rt.

Scheme 4

On the other hand, the synthesis of compound (**14**) was achieved in five steps from diene (**4**) according to the sequence displayed in Scheme 5. Catalytic bishydroxylation of benzyl derivative (**10**), followed by protection of the primary hydroxyl group in the resulting **11**, afforded compound (**12**). Deprotection of the silyl ether derivative (**12**), using TBAF, and further oxidation of the allylic alcohol (**13**) under the Swern's conditions,[11] gave rise to the desired compound (**14**).



Key. *a*) BnBr, TBAI, NaH, THF, rt; *b*) OsO_4, Me_3NO, acetone/H_2O 8/1, rt; *c*) PMBCl, TBAI, NaH, THF, rt; *d*) TBAF, THF, rt; *e*) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78°C to 0°C.

Scheme 5

In summary, a stereodivergent synthesis of two modified analogues, compounds (**9**) and (**14**), of the C,D subunits of taxol has been described using a furan derivative as precursor.

EXPERIMENTAL

General Methods. Reagents and solvents were handled by using standard syringe techniques. Tetrahydrofuran and ether were distilled over sodium and benzophenone; benzene over sodium; toluene, dichloromethane and triethylamine over calcium hydride; pyridine over KOH, acetone over $KMnO_4$. The remaining solvents and chemicals were comercial and used as received. ^1H NMR and ^{13}C NMR were recorded at 300 and 75 MHz, respectively. Flash chromatography was performed using 230-400 mesh silica gel. Analytical TLC was carried out on silica gel plates. Melting points are uncorrected. Elemental analyses were performed at the Universidad Complutense de Madrid.

(1*S, 5*S**)-5-Benzoyloxy-1-triisopropylsilyloxy-2-methyl-4-methylenecyclohex-2-ene (5).** To a solution of **4** (490 mg, 1.60 mmol) in CH_2Cl_2 (10 mL) at rt, Et_3N (0.92 mL, 6.4 mmol), BzCl (0.77 mL, 6.4 mmol) and a catalytic amount of DMAP were added consecutively. After stirring for 4 h the reaction was quenched with saturated aqueous solution of NaCl and extracted with AcOEt. The organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by silica gel

chromatography eluting with hexanes/ ethyl acetate (10:1) afforded **5** (563 mg, 85%) as a colorless oil. IR (CCl_4) υ 2880, 1720, 1650, 1370. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.02 (s, 21H), 1.92 (s, 3H), 2.04 (ddd, 1H, J= 11.4, 7.2, 3.3 Hz), 2.22 (ddd, 1H, J= 11.7, 7.2, 4.2 Hz), 4.61 (t, 1H, J= 5.7 Hz), 4.96 (s, 1H), 5.07 (s, 1H), 5.90 (br s, 2H), 7.38-8.12 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.8, 18.1, 20.6, 38.1, 68.4, 70.7, 113.0, 124.5, 128.3, 129.0, 130.6, 131.4, 132.9, 135.3, 140.7, 144.2, 165.7. Anal. Calcd for $C_{24}H_{36}O_3Si$: C, 71.95; H, 9.06. Found: C, 72.23; H, 8.88.

(1*R, 4*S**, 6*S**)-6-Benzoyloxy-1-hydroxymethyl-4-triisopropylsilyloxy-3-methylcyclohex-2-en-1-ol (6).** To a solution of **5** (105 mg, 0.26 mmol) in a mixture of acetone/water 8/1 (3 mL) at rt, Me_3NO (58 mg, 0.52 mmol) and OsO_4 (2.5 % solution in *t*-BuOH, 0.065 mL, 0.005 mmol) were added. The reaction was stirred for 12 h, quenched with a saturated aqueous solution of $NaHSO_3$, and concentrated under reduced pressure. Further purification using flash chromatography (hexanes/ ethyl acetate, 4:1) afforded **6** as a colorless oil (72 mg, 65%). IR (CCl_4) υ 3500, 2980, 1720, 1610. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10 (s, 21H), 1.88 (s, 3H), 2.28-2.36 (m, 2H), 2.97 (dd, 1H, J= 9.6, 4.4 Hz), 3.19 (d, 1H, J= 1.5 Hz), 3.40 (dd, 1H, J= 11.9, 9.6 Hz), 3.57 (dd, 1H, J= 12.0, 4.4 Hz), 4.62 (dd, 1H, J= 7.3, 6.6 Hz), 5.24 (d, 1H, J= 1.5 Hz), 5.29 (br s, 1H), 7.45-7.96 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.8, 18.2, 20.4, 33.9, 65.3, 68.1, 70.7, 73.8, 122.1, 128.5, 129.7, 133.6, 137.0, 144.5, 167.3. Anal. Calcd for $C_{24}H_{38}O_5Si$: C, 66.32; H, 8.81. Found: C, 66.21; H, 8.95.

(1*R,4*S**,6*S**)-6-Benzoyloxy-4-triisopropylsilyloxy-3-methyl-1-(*p*-toluenesulfonyloxy)-methylcyclohex-2-en-1-ol (7).** Diol (**6**) (34 mg, 0.08 mmol) was dissolved in pyridine (1 mL) at rt and TsCl (48 mg, 0.25 mmol) was added. After stirring for 5 h the reaction mixture was hydrolyzed with water and 0.5 N aqueous solution of HCl. The organic layers were extracted with CH_2Cl_2 and dried over $MgSO_4$. Purification by silica gel column chromatography (hexanes/ ethyl acetate, 2:1) and concentration under reduced pressure afforded 44 mg (94%) of **7** as a colorless oil. IR (CCl_4) υ 3500, 1720, 1580, 1370. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.13 (br s, 21H), 1.98 (s, 3H), 2.20-2.30 (m, 1H), 2.39 (s, 3H), 2.42-2.50 (m, 1H), 3.19 (br s, 1H), 4.17 (syst. AB, 2 H, J_{AB}= 9.6 Hz), 4.46 (dd, 1H, J= 6.0, 5.6 Hz), 5.37 (d, 1H, J= 1.2 Hz), 5.45 (dd, 1H, J= 7.5, 2.4 Hz), 7.24-7.56 (m, 4H), 7.65-7.79 (m, 3H), 7.92-7.99 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.6, 18.1, 20.6, 21.6, 33.7, 67.9, 70.5, 72.0, 73.6, 121.5, 127.9, 128.4, 129.6, 129.7, 132.2, 133.2, 137.2, 143.9, 144.8, 165.8. Anal. Calcd for $C_{31}H_{44}O_7SSi$: C, 63.23; H, 7.53. Found: C, 63.14; H, 7.49.

(1*S, 2*R**, 5*S**)-5-Triisopropylsilyloxy-2-(*p*-toluensulfonyloxymethyl)-4-methylcyclohex-3-ene-1,2-diol (8).** A solution of **7** (36 mg, 0.06 mmol) in a mixture of MeOH/H_2O 5/1 (1 mL) was cooled to 0 ºC. K_2CO_3 (89.8 mg, 0.65 mmol) was added and the mixture was stirred for 30 min. After quenching using water and extraction with CH_2Cl_2, the organic layers were dried over $MgSO_4$. Concentration under reduced pressure and purification *via* flash chromatography (hexanes/ ethyl acetate, 4:1), afforded **8** (19 mg, 62%) as a colorless oil. IR (CCl_4) υ 3500, 1740, 1600, 1470. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10 (br s, 21H), 1.59 (br s, 1H), 1.80 (s, 3H), 2.00-2.05 (m, 1H), 2.29-2.32 (m, 1H), 2.45 (s, 3H), 4.06-4.10 (m, 1H), 4.11 (syst. AB, 2H, J_{AB}= 10.3 Hz), 4.41 (t, 1H, J =5.9 Hz), 5.16 (s, 1H), 7.58 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.7, 18.1, 20.6, 21.7, 36.2, 68.1, 70.4, 71.9, 73.2,

121.6, 128.0, 129.9, 137.1, 143.9, 145.2. Anal. Calcd for $C_{24}H_{40}O_6SSi$: C, 59.47; H, 8.32. Found: C, 59.63; H, 8.14.

(1*R, 4*S**, 6*S**)-1-Hydroxy-4-triisopropylsilyloxy-3-methyl-7-oxabicyclo[4.2.0]oct-2-ene (9).** To a suspension of NaH (60% mineral oil suspension, 5 mg, 0.12 mmol) in THF (1 mL) at rt, were added 15 mg (0.03 mmol) of **8** and the reaction mixture was stirred for 2 h. The reaction was then quenched with a 0.5 N aqueous solution of HCl and extracted with Et_2O. The organic layers were dried over $MgSO_4$. Concentration under reduced pressure afforded a crude, which after purification by flash chromatography (hexanes/ ethyl acetate, 1:1), yielded 7.1 mg (74%) of **9** as a colorless oil. IR (CCl_4) υ 3580, 2980, 1370, 1040. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.09 (br s, 21H), 1.82 (s, 3H), 1.87 (m, 1H), 1.97-2.08 (m, 1H), 3.65 (syst. AB, 2H, J_{AB}= 11.4 Hz), 4.14 (dd, 1H, J= 10.3, 3.9 Hz), 4.33 (t, 1H, J= 4.0 Hz), 5.26 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.7, 18.2, 21.2, 36.6, 68.6, 68.9, 69.5, 72.3, 128.4, 142.3. Anal. Calcd for $C_{17}H_{32}O_3Si$: C, 65.33; H, 10.32. Found: C, 65.12; H, 10.13.

(1*S,5*S**)-5-Benzyloxy-1-triisopropylsilyloxy-2-methyl-4-methylencyclohex-2-ene (10).** To a suspension of NaH (60% mineral oil suspension, 162 mg, 4.05 mmol) in THF (10 mL) at rt, a solution of **4** (300 mg, 1.01 mmol) in THF (10 mL) was added. After stirring for 10 min, BnBr (0.5 mL, 4.05 mmol) and a catalytic amount of TBAI were added. The reaction mixture was stirred for 5 h, quenched with a saturated aqueous solution of NaCl and extracted with ether. The organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford a crude, which after purification by flash chromatography (hexanes/ ethyl acetate, 10:1), yielded 332 mg (83%) of **10** as a colorless oil. IR (CCl_4) υ 3080, 2980, 1650, 1470. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10 (br s, 21H), 1.89 (s, 3H), 1.97 (ddd, 1H, J= 12.8, 7.3, 2.9 Hz), 2.23 (ddd, 1H, J= 12.8, 6.5, 1.6 Hz), 4.18 (dd, 1H, J = 6.6, 2.9 Hz), 4.57 (syst. AB, 2H, J_{AB}= 12.0 Hz), 4.65 (m, 1H), 4.97 (s, 1H), 4.98 (s, 1H), 5.89 (s, 1H), 7.26-7.36 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.8, 18.2, 20.5, 38.8, 65.1, 68.7, 75.2, 111.6, 124.3, 127.7, 128.2, 129.0, 136.9, 142.1, 144.2. Anal. Calcd for $C_{24}H_{38}O_2Si$: C, 74.55; H, 9.91. Found: C, 74.42; H, 9.76.

(1*R, 4*S**, 6*S**)-6-Benzyloxy-1-hydroxymethyl-4-triisopropylsilyloxy-3-methylcyclohex-2-en-1-ol (11).** To a solution of **10** (280 mg, 0.72 mmol) in a mixture of acetone/water 8/1 (5 mL) at rt, Me_3NO (161 mg, 1.45 mmol) and OsO_4 (2.5 % solution in *t*-BuOH, 0.18 mL, 0.015 mmol) were added. The reaction was stirred for 10 h, quenched with a saturated aqueous solution of $NaHSO_3$, and concentrated under reduced pressure. Further purification using flash chromatography (hexanes/ ethyl acetate, 8:1) afforded **11** as a colorless oil (244 mg, 80%). IR (CCl_4) υ 3500, 3020, 2980, 1650. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.09 (s, 21H), 1.80 (s, 3H), 1.94 (dt, 1H, J= 12.4, 4.5 Hz), 2.14 (dt, 1H, J= 12.4, 3.6 Hz), 2.86 (dd, 1H, J= 10.1, 3.1 Hz), 3.17 (s, 1H), 3.30 (dd, 1H, J= 11.7, 10.2 Hz), 3.84 (dd, 1H, J= 11.7, 3.0 Hz), 4.02 (dd, 1H, J= 4.7, 3.6 Hz), 4.32 (dd, 1H, J= 4.5, 3.6 Hz), 4.58 (syst. AB, 2H, J_{AB}= 10.8 Hz), 5.15 (s, 1H), 7.28-7.36 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.9, 18.3, 20.9, 34.6, 65.7, 69.1, 72.4, 72.5, 81.1, 125.5, 127.9, 128.1, 128.7, 139.0, 141.1. Anal. Calcd for $C_{24}H_{40}O_4Si$: C, 68.53; H, 9.58. Found: C, 68.44; H, 9.50.

(1*R, 4*S**, 6*S**)-6-Benzyloxy-4-triisopropylsilyloxy-1-(*p*-methoxybenzyloxymethyl)-3-methylcyclohex-2-en-1-ol (12).** To a suspension of NaH (60% mineral oil suspension, 7.6 mg, 0.19

mmol) in THF (1 mL) at rt, 40 mg (0.10 mmol) of **11**, 0.02 mL of PMBCl (0.14 mmol) and 3.3 mg (0.01 mmol) of TBAI were added. The reaction mixture was stirred for 9 h and then quenched with water. The crude was extracted with AcOEt, dried over $MgSO_4$ and concentrated under reduced pressure to afford, after purification *via* flash chromatography (hexanes/ ethyl acetate, 20:1), 42 mg (83%) of **12** as a colorless oil. IR (CCl_4) υ 3500, 2960, 1620, 1510. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.12 (s, 21H), 1.81 (s, 3H), 2.02 (m, 1H), 2.11 (m, 1H), 2.68 (br s, 1H), 3.59 (syst. AB, 2H, J_{AB}= 8.8 Hz), 3.80 (s, 3H), 4.41-4.53 (m, 4H), 4.58 (syst. AB, 2H, J_{AB}= 12 Hz), 5.26 (s, 1H), 6.86 (m, 2H), 7.26-7.33 (m, 7H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.8, 18.3, 20.5, 33.3, 55.3, 68.5, 71.9, 73.1, 76.6, 78.1, 81.7, 113.7, 123.5, 126.9, 127.6, 128.5, 129.4, 132.0, 142.7, 144.2, 155.9. Anal. Calcd for $C_{32}H_{48}O_5Si$: C, 71.07; H, 8.95. Found: C, 71.21; H, 9.10.

(1*S, 4*R**, 6*S**)-6-Benzyloxy-1-(*p*-methoxybenzyloxymethyl)-3-methylcyclohex-2-ene-1,4-diol (13).** To a solution of **12** (51 mg, 0.09 mmol) in THF (1 mL) at rt, TBAF (0.47 mL, 0.45 mmol) was added and the mixture was stirred over 24 h. After quenching the reaction with a saturated aqueous solution of NaCl and extraction with ether, the organic layers were dried over $MgSO_4$. Concentration under reduced pressure and purification *via* flash chromatography (hexanes/ ethyl acetate, 2:1) afforded **13** (34 mg, 93%) as a white solid. mp 107-108 ºC. IR (CCl_4) υ 3650, 1640, 1580, 1370. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.82 (s, 3 H), 1.89-2.02 (m, 1H), 2.22-2.30 (m, 1H), 2.80 (br s, 1H), 3.56 (syst. AB, 2H, J_{AB}= 8.8 Hz), 3.80 (s, 3H), 4.10-4.25 (m, 2H), 4.49 (s, 2H), 4.58 (syst. AB, 2H, J_{AB}= 11.8 Hz), 5.32 (d, 1H, J= 1.1 Hz), 6.86 (m, 2H), 7.26-7.36 (m, 7H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.0, 32.7, 55.3, 67.9, 69.2, 71.8, 71.9, 72.2, 72.9, 113.7, 124.7, 127.2, 127.9, 128.3, 129.4, 138.4, 141.2, 159.3. Anal. Calcd for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.79; H, 7.28.

(4*R, 5*S**)-5-Benzyloxy-4-hydroxy-2-methyl-4-(*p*-methoxybenzyloxymethyl)-cyclohex-2-en-1-one (14).** To a solution of $(COCl)_2$ (0.035 mL, 0.39 mmol) in CH_2Cl_2 (2 mL) at -78 ºC, DMSO (0.025 mL, 0.48 mmol) was added and the mixture was stirref for 30 min. A solution of **13** (34 mg, 0.09 mmol) in 1 mL of CH_2Cl_2 was added and stirring was maintained for an additional hour. Finally, 0.1 mL of Et_3N (0.7 mmol) was added at -78ºC and the reaction mixture was allowed to warm to 0ºC. After stirring for 3 h at this temperature, it was quenched with a saturated aqueous solution of NaCl and extracted with CH_2Cl_2. The organic layers were dried over $MgSO_4$. Concentration under reduced pressure and purification *via* flash chromatography (hexanes/ ethyl acetate, 2:1) afforded **14** (19 mg, 55%) as a colorless oil. IR (CCl_4) υ 3650, 1680, 1610, 1060. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.79 (s, 3H), 2.67 (dd, 1H, J= 16.6, 7.4 Hz), 2.90 (dd, 1H, J= 16.6, 3.9 Hz), 2.95 (s, 1H), 3.68 (syst. AB, 2H, J_{AB}= 9.3 Hz), 3.80 (s, 3H), 3.95 (m, 1 H), 4.50 (s, 2 H), 4.58 (syst. AB, 2H, J_{AB} =12.5 Hz), 6.43 (s, 1H), 6.87 (m, 2H), 7.24-7.32 (m, 7H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.6, 39.5, 55.3, 66.8, 71.9, 73.5, 76.6, 78.6, 113.9, 127.5, 127.7, 127.9, 128.4, 129.6, 137.9, 144.3, 145.5, 159.5, 197.4. Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.19; H, 6.81.

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REFERENCES

1. M. C. Wani, H. L. Taylor, M. E. Wall, P. Coggon, and A. T. McPhail, *J. Am. Chem. Soc.*, 1971, **93**, 2325.
2. P. B. Schiff, J. Fant, and S. B. Horwitz, *Nature*, 1979, **277**, 665.
3. a) K. C. Nicolaou, W. M. Dai, and R. Kiplin, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 15. b) K. C. Nicolaou, P. G. Nantermet, H. Ueno, R. K. Guy, E. A. Couladouros, and E. J. Sorensen, *J. Am. Chem. Soc.*, 1995, **117**, 624. c) R. A. Holton, C. Somoza, F. Liang, P. D. Boatman, C. C. Smith, Y. Suzuki, S. Tang, K. K. Murthi, and J. H. Liu, *J. Am. Chem. Soc.*, 1994, **116**, 1597. d) S. J. Danishefsky, J. J. Masters, W. B. Young, L. B. Snyder, D. K. Jung, W. G. Bornman, C. A. Coburn, and M. J. Di Grandi, *J. Am. Chem. Soc.*, 1996, **118**, 2843. e) P. A. Wender, N. F. Badham, T. E. Glass, J. B. Houze, D. Lee, P. L. McGrane, T. P. Mucciaro, H. Paulsen, A. J. Shuker, and K. Tomooka, *J. Am. Chem. Soc.*, 1997, **119**, 2755. f) T. Mukaiyama, M. Hasegawa, I. Shiina, and H. Sakoh, *Chem. Lett.*, 1998, 1 and references therein. g) I. Kuwajima, H. Kusama, T. Nishimori, R. Hara, and K. Morihira, *J. Am. Chem. Soc.*, 1998, **120**, 12980. h) H. Kusama, T. Nishimori, N. Nakamura, and I. Kuwajima, *J. Am. Chem. Soc.*, 2000, **122**, 3811.
4. For general reviews on taxoid chemistry, see: a) Taxol: Science and Application, ed. by M. Suffness, CRC Press, New York, 1995. b) Taxane Anticancer Agents: Basic Science and Current Status, ed. by I. G. Georg, T. T. Chen, I. Ojima, and D. M. Vyas, ACS Symposium Series 583, American Chemical Society, Washington, 1995. c) The Chemistry and Pharmacology of Taxol and its Derivatives, ed. by V. Farina, Elsevier, Oxford, 1995.
5. a) D. G. I. Kingston, *Trends Biotechnol.*, 1994, **12**, 222. b) A. Datta, L. R. Jayasinghe, and G. I. Georg, *J. Med. Chem.*, 1994, **37**, 4258. c) S. H. Chen, J. F. Kadow, V. Farina, C. R. Fairchild, and K. A. Johnston, *J. Org. Chem.*, 1994, **59**, 6156. d) S. H. Chen and V. Farina, Paclitaxel Chemistry and Structure Activity Relationships. In The Chemistry and Pharmacology of Taxol and its Derivatives, ed. by V. Farina, Elsevier, New York, 1995, 165. e) M. M. Wang, B. Cornett, J. Nettles, D. C. Liotta, and J. P. Snyder, *J. Org. Chem.*, 2000, **65**, 1059. f) L. F. He, P. G. F. Jagtap, D. G. I. KIngston, H. J. Shen, G. A. Orr, and S. B. Horwitz, *Biochemistry*, 2000, **39**, 3972.
6. a) W. F. Berkowitz and A. S. Amarasekara, *Tetrahedron Lett.*, 1985, **26**, 3663. b) G. Clark, M. M. Nikaido, and J. Lin, *J. Org. Chem.*, 1987, **52**, 3745. c) C. K. Sha, S. J. Lee, and W. H. Tseng, *Tetrahedron Lett.*, 1997, **38**, 2725. d) J. Dubois, L. Bricard, D. Guenard, and F. Gueritte, *J. Org. Chem.*, 1997, **62**, 6631. e) T. Takahashi, Y. Hirose, H. Iwamoto, and T. Doi, *J. Org. Chem.*, 1998, **63**, 5742. f) D. G. I. Kingston, F. D. Ramdayal, A. A. L. Gunatilaka, and M. H. Sarragiotto, *J. Org. Chem.*, 1999, **64**, 2694. g) D. Bourgeois, J. Y. Lallemand, A. Pancrazi, and J. Prunet, *Synlett*, 1999, 1555.
7. J. Dubois, S. Thoret, F. Gueritte, and D. Guenard, *Tetrahedron Lett.*, 2000, **41**, 3331.
8. P. Vogel, J. Cossy, J. Plumet, and O. Arjona, *Tetrahedron*, 1999, **55**, 13521.
9. O. Arjona, S. Conde, J. Plumet, and A. Viso, *Tetrahedron Lett.*, 1995, **36**, 3043.
10. O. Arjona, M. L. León, and J. Plumet, *J. Org. Chem.*, 1999, **64**, 272.
11. A. J. Mancuso, and D. Swern, *Synthesis*, 1981, 165.