Notes

Base-Induced Bridge Cleavage of 1,5-Dimethyl-7-oxabicyclo[2.2.1]hept-5-ene Derivatives: A Short Synthesis of an Advanced Intermediate for the A and C Ring Subunits of Taxol

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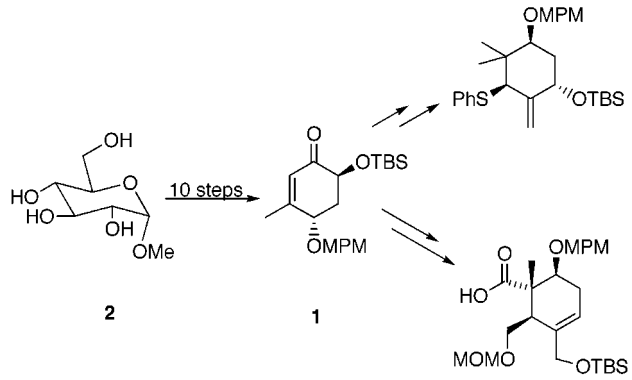
Received May 19, 1998

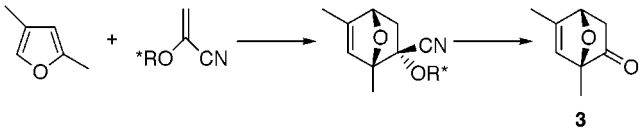
Since the isolation of taxol, this tetracyclic diterpene has attracted tremendous attention due to its great potential in the successful treatment of several types of cancer.[1] On the other hand, the structural complexity of this molecule has stimulated general elegant synthetic approaches,[2] including four total syntheses.[3]

Among the disconnective approaches to the tetracyclic ring systems of taxol,[4] we have focused our attention on two papers of Ermolenko et al.[5] in which the ketone **1** constitutes an advanced intermediate for the synthesis of A and C ring subunits (Scheme 1).

Scheme 1



Scheme 2



The ketone **1** was prepared by Ermolenko et al. in 10 steps from methyl-α-D-glucopyranoside **2**.

In this paper, we wish to account for the synthesis of an analogue of **1** using as a key step a new methodology,[6] developed for us, for the ring opening of 1,5-dimethyl-7-oxanorbornenone **3**. Compound **3** has been previously synthesized by Vogel et al. in optically pure form[7] in two steps, starting from 2,4-dimethylfuran (available in his turn from mesityl oxide in two steps[8]) and 2-canfanoxyacrilonitrile (Scheme 2).

The reaction of compound **3** with $NaBH_4$ in MeOH afforded alcohol **4**. When **4** was treated with LDA in a

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(6) For a preliminary account of this methodology, see: Arjona, O.; Conde, S.; Plumet, J.; Viso, A. *Tetrahedron Lett.* **1995**, *36*, 6157. For a related paper, see: Lautens, M.; Ma, S. *Tetrahedron Lett.* **1996**, *37*, 1727.

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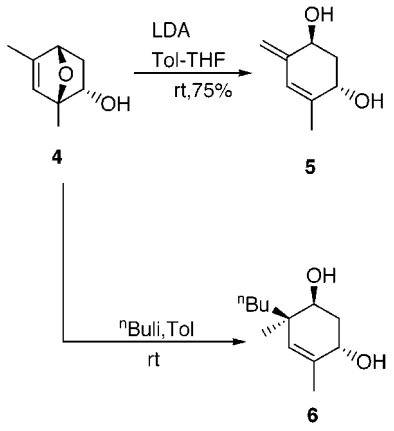
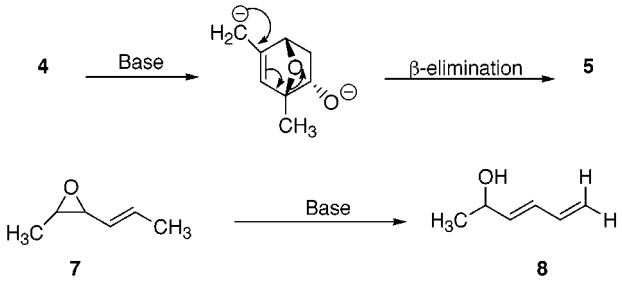
10.1021/jo9809534 CCC: $18.00
Published on Web 12/19/1998

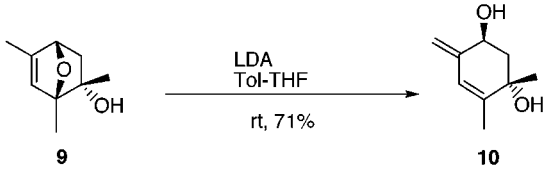
Scheme 3



Scheme 4



Scheme 5



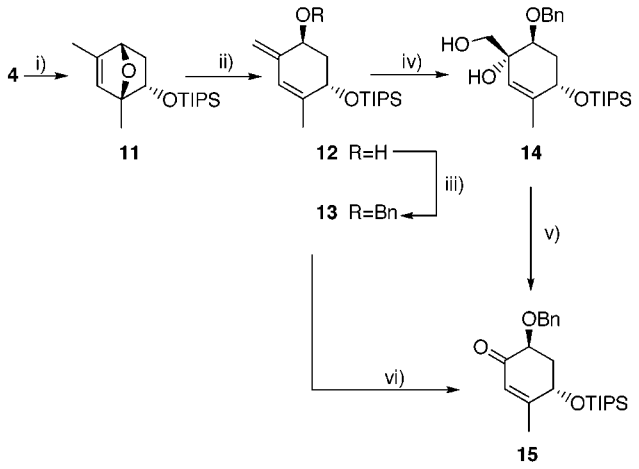
toluene/THF mixture at room temperature, 75% yield of compound **5** was obtained (Scheme 3). The use of these reaction conditions appears to be critical for the success of the process. For instance, when THF alone is used as a solvent, the isolated yield falls to 53%. With ^{n}BuLi as a basic reagent, a mixture of **5** (25%), compound **6**[9] (25%), and starting material (50%) was observed as reaction crude (Scheme 3).

The structure of **5** was confirmed from its spectroscopic data. Thus, in the ^{1}H NMR spectrum (300 MHz), three singlets were observed corresponding to the three vinylic protons at 5.89, 5.24, and 5.05 ppm. The protons attached to the two hydroxy centers appear as two multiplets at 4.50−4.36 and 4.30−4.17 ppm. Finally, the methyl group gives an apparent singlet at 1.82 ppm.

From the mechanistic point of view, this process should occur by deprotonation of the allylic methyl group followed by β-elimination of the oxygen bridge in a reaction, reminiscent of the well-known transformation of acyclic vinyloxiranes in the related dienols,[10] i.e., transformation from **7** to **8** (Scheme 4).

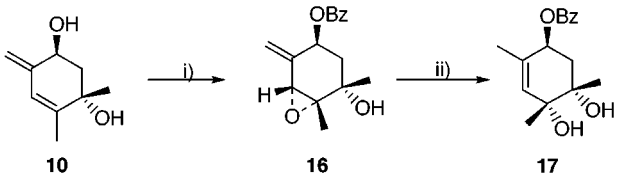
Some derivatives of **4** show the same behavior. For instance, let us take compound **9**, which was obtained

Scheme 6[a]



[a] (i) TIPSOTf, Et_3N, 4-DMPA, CH_2Cl_2, 0 °C, 89%; (ii) LDA, Tol/THF, rt, 87%; (iii) BnBr, NaH, THF, rt, 83%; (iv) OsO_4, acetone−H_2O 8:1, rt, 60%; (v) $NaIO_4$, THF/H_2O 1:1, rt, 100%; (vi) $NaIO_4$, $RuCl_3 \cdot H_2O$, $CH_3CN/CCl_4/H_2O$ 1:1:1.4, rt, 56%.

Scheme 7[a]



[a] (i) a: BzCl, Et_3N, CH_2Cl_2, 0 °C, 70%. b: ^{t}BuOOH, $VO(acac)_2$, C_6H_6, rt, 95%. (ii) H_2, PtO_2, $NaNO_2$, MeOH, rt, 60%.

from **3** by reaction with MeMgBr. This compound, under treatment with LDA (Tol/THF, rt, 71%) gives the expected product **10** (Scheme 5).

Application of this methodology to the synthesis of compounds related to **1** has been achieved in the following way: reaction of **4** with TIPSOTf affords **11**, which in turn gives **12** by the previously described ring-opening methodology. Benzylation of **12** followed by osmilation of the resulting protected diol **13** gives compound **14.** Finally, periodate cleavage of **14** affords **15**, an analogue of **1**. It should be pointed out that the transformation **13** to **15** can be achieved in a single step by reaction of **13** with $NaIO_4/RuCl_3$[11] (Scheme 6).

Another useful transformation based on the above-described ring-opening procedure afforded the synthesis of cyclohexene derivatives with three chiral centers (two quaternary carbon atoms) possesing a well-defined stereochemistry. Thus, benzylation of **10** followed by selective epoxidation of the endocyclic double bond (^{t}BuOOH/C_6H_6, $VO(acac)_2$, 95%)[12] regioselectively afforded epoxide **16**. This was transformed into the monoprotected triol **17** by hydrogenation, using $PtO_2/NaNO_2$ in MeOH anhyd.,[13] with concomitant double bond migration. (Scheme 7).

In summary, a new efficient protocol for the ring opening of 1,5-dimethyl-7-oxanorbornene derivatives has been described. This methodology has been applied to the

(9) Compound **6** arises from the alkylative ring opening of the starting bicyclic by attacking with organolithium reagent position 5 of compound **4**. For leading references, see: Arjona, O.; Fernandez de la Pradilla, R.; Garcia, E.; Martin, A.; Plumet, J. *Tetrahedron Lett.* **1989**, *30*, 6437. (b) Arjona, O.; Fernandez de la Pradilla, R.; Martin, A.; Plumet, J. *Tetrahedron* **1990**, *46*, 8199.

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preparation of an advanced synthetic intermediate for the synthesis of the A and C ring subunits of taxol starting from the ketone **3** (six steps, 36% overall yield, or five steps, 34% overall yield). Moreover, the stereocontrolled synthesis of methyl-substituted cyclohexene derivatives has been also reported.

Experimental Section

General Methods. Reagents and solvents were handled by using standard syringe techniques. Tetrahydrofuran and diethyl ether were distilled over sodium and benzophenone; benzene over sodium; toluene, dichloromethane, and triethylamine over calcium hydride; pyridine over KOH, and acetone over $KMnO_4$. The remaining solvents and chemicals were comercial and used as received. ^1H NMR and ^{13}C NMR were recorded at 250 or 300 MHz. 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. Compound **3** was prepared according with the method of Vogel et al.[7]

(2*S)-1,5-Dimethyl-7-oxabicyclo[2.2.1]hept-5-en-2-ol, 4.** To a solution of **3** (348 mg, 2.52 mmol) in MeOH (4 mL), $NaBH_4$ (143 mg, 3.78 mmol) was added at −20 °C. The mixture was allowed to reach room temperature while stirring for 2 h, and then water was added. The aqueous layer was extracted with AcOEt, dried over $MgSO_4$, and concentrated in vacuo. **4** was obtained after purification by column chromatography (hexane/AcOEt 2:1) as a colorless oil (332 mg, 94%). Data for **4**: ^1H NMR ($CDCl_3$, 250 MHz) δ 5.75 (d, 1H, J = 1.6 Hz), 4.54 (d, 1H, J = 4.9 Hz), 3.94−4.09 (m, 1H), 2.41 (ddd, 1H, J = 12.1, 8.0, 4.9 Hz), 1.90 (d, 3H, J = 1.6 Hz), 1.56 (s, 3H), 1.04 (dd, 1H, J = 12.1, 2.6 Hz); ^{13}C NMR (62.5 MHz) δ 150.6, 127.8, 87.3, 82.1, 76.3, 38.6, 16.8, 13.1; IR ($CHCl_3$) ν 3420, 2980, 2940, 1450, 1390 cm^{-1}. Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.37; H, 8.56.

(1*S,3*S**)-6-Methyl-4-methylencyclohex-5-en-1,3-diol, 5.** To a solution of **4** (70 mg, 0.50 mmol) in THF (1.3 mL) at room temperature, 6 equiv of a 1 M solution of LDA (previously formed from 1 equiv of $^iPr_2NH$ in 0.8 mL/mmol of toluene at 0 °C and 1 equiv of a 1.6 M solution of ^{n}BuLi in hexanes) were added and stirred for 2 h. The reaction was quenched with 5% HCl and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The resulting crude was purified by column chromatography on silica gel (hexane/AcOEt 2:1) to afford 53 mg of **5** (75%) as a white solid. Data of **5**: mp, 105−106 °C; ^1H NMR ($CDCl_3$, 250 MHz) δ 5.89 (s, 1H), 5.24 (s, 1H), 5.05 (s, 1H), 4.36−4.50 (m, 1H), 4.17−4.30 (m, 1H), 1.82 (s, 3H), 1.58−1.74 (m, 2H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 145.6, 138.6, 125.6, 110.8, 68.4, 67.2, 40.3, 20.2; IR ($CHCl_3$) ν 3300, 3020, 2920, 1420 cm^{-1}. Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.47; H, 8.39.

(2*S)-1,5-Dimethyl-2-methyl-7-oxabicyclo[2.2.1]hept-5-en-2-ol, 9.** MeMgBr 3 M in Et_2O (1.33 mL) was added dropwise to a solution of **3** (276 mg, 2 mmol) in THF (5 mL) at 0 °C. The mixture was stirred for 2 h, quenched with NH_4Cl and H_2O, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. **9** (234 mg, 76%) was obtained as a colorless oil after purification by column chromatography (hexane/AcOEt 4:1). Data of **9**: ^1H NMR ($CDCl_3$, 250 MHz) δ 5.79 (d, 1H, J = 1.7 Hz), 4.52 (d, 1H, J = 4.9 Hz), 2.04 (dd, 1H, J = 4.9, 12.5 Hz), 1.88 (d, 3H, J = 1.7 Hz), 1.62 (s, 1H), 1.43 (s, 3H), 1.40 (s, 3H), 1.41 (d, 1H, J = 12.5 Hz); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 149.4, 124.3, 88.9, 81.5, 78.4, 44.9, 24.6, 13.1, 12.8; IR (CH_2Cl_2) ν 3440, 2980, 1450, 1380 cm^{-1}. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.02; H, 8.93.

(1*S,3*S**)-1,6-Dimethyl-4-methylencyclohex-5-en-1,3-diol, 10.** To a solution of **9** (64 mg, 0.42 mmol) in THF (1.1 mL) at room temperature, 6 equiv of a 1 M solution of LDA (previously formed from 1 equiv of $^iPr_2NH$ in 0.8 mL/mmol of toluene at 0 °C and 1 equiv of a 1.6 M solution of ^{n}BuLi in hexanes) were added and stirred for 2 h. The reaction was quenched with 5% HCl and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The resulting crude was purified by column chromatography on silica gel (hexane/AcOEt 2:1) to afford 50 mg of **10** (78%) as a white solid. Data of **10**: mp, 105−107 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.89 (s, 1H), 5.13 (s, 1H), 4.90 (s, 1H), 4.44−4.54 (m, 1H), 2.70−2.80 (m, 1H), 2.45−2.53 (m, 1H), 2.09 (dd, 1H, J = 4.4, 13.0 Hz), 1.80 (s, 3H), 1.72 (dd, 1H, J = 11.7, 13.0 Hz), 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 146.1, 139.8, 126.1, 109.0, 71.5, 66.6, 47.1, 27.7, 17.4; IR ($CHCl_3$) ν 3550, 2990, 2960, 2930, 1440, 1380 cm^{-1}. Anal. Calcd for $C_9H_{14}O_2$: C, 70.08; H, 9.16. Found: C, 69.97; H, 8.92.

(2*S)-1,5-Dimethyl-2-triisopropylsilyloxy-7-oxabicyclo-[2.2.1]hept-5-ene, 11.** To a solution of **4** (340 mg, 2.43 mmol) in CH_2Cl_2 (8 mL) at 0 °C, Et_3N (0.37 mL), DMAP (0.01 equiv)and TIPSOTf (1.1 equiv) were added. The mixture was stirred for 1 h. The reaction was diluted with CH_2Cl_2, and the organic layer was washed with 5% $NaHCO_3$ and NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexane/AcOEt 20:1) to afford 640 mg (89%) of **11** as a colorless oil. Data of **11**: ^1H NMR ($CDCl_3$, 300 MHz) δ 5.67 (d, 1H, J = 1.2 Hz), 4.52 (d, 1H, J = 4.8 Hz), 4.16 (dd, 1H, J = 7.5, 2.4 Hz), 2.27 (ddd, 3H, J = 12.0, 7.5, 4.8 Hz), 1.85 (d, 3H, J = 1.2 Hz), 1.54 (s, 3H), 0.91−1.17 (m, 22H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 147.0, 129.0, 87.5, 82.1, 76.7, 38.7, 17.8, 17.8, 17.8, 17.2, 12.6, 12.1; IR (CH_2Cl_2): ν 3160, 2950, 2880, 1470, 1450, 1400, 1370 cm^{-1}. Anal. Calcd for $C_{17}H_{32}O_2Si$: C, 68.86; H, 10.88. Found: C, 68.72; H, 10.78.

(1*S,5*S**)-5-Triisopropylsilyloxy-4-methyl-2-methylencyclohex-3-en-1-ol, 12.** To a solution of **11** (450 mg, 1.52 mmol) in THF (4 mL) at room temperature, 6 equiv of a 1 M solution of LDA (previously formed from 1 equiv of $^iPr_2NH$ in 0.8 mL/mmol of toluene at 0 °C and 1 equiv of a 1.6 M solution of ^{n}BuLi in hexanes) were added and stirred for 2 h. The reaction was quenched with 5% HCl and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The resulting crude was purified by column chromatography on silica gel (hexane/AcOEt 10:1) to afford 337 mg of **12** (87%) as a colorless oil. Data of **12**: ^1H NMR ($CDCl_3$, 300 MHz) δ 5.82 (s, 1H), 4.97 (s, 1H), 4.82 (s, 1H), 4.38−4.50 (m, 2H), 1.86−1.95 (m, 2H), 1.81 (s, 3H), 1.50−1.55 (m, 1H), 0.93−1.15 (m, 21H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.9, 140.2, 124.4, 110.0, 68.8, 40.8, 20.8, 18.2, 18.2, 18.2, 12.7, 12.7, 12.7, 12.7, 12.7, 12.7; IR ($CHCl_3$) ν 3600, 3450, 2960, 2880, 1470 cm^{-1}. Anal. Calcd for $C_{17}H_{32}O_2Si$: C, 68.86; H, 10.88. Found: C, 68.76; H, 10.80.

(1*S,5*S**)-5-Benzyloxy-1-triisopropylsilyloxy-2-methyl-4-methylencyclohex-2-ene, 13.** To a NaH suspension (162 mg, 4.05 mmol) in THF (10 mL) at room temperature, a solution of **12** (300 mg, 1.01 mmol) in THF (5 mL) was added. After 10 min, BnBr (0.5 mL, 4.05 mmol) was added dropwise, followed by 0.1 equiv of Bu_4NI. The mixture was stirred for 5 h, quenched with NaCl, and extracted with Et_2O. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude was purified by column chromatography (hexane/AcOEt, 10:1) to afford **13** (332 mg, 83%) as a colorless oil. Data of **13**: ^1H NMR ($CDCl_3$, 300 MHz) δ 7.36−7.26 (m, 5H), 5.89 (s, 1H), 4.97 (d, 2H, J = 2.6 Hz), 4.65 (m, 1H), 4.57 (AB system, 2H, J_{AB} = 12 Hz), 4.18 (dd, 1H, J = 6.6, 2.9 Hz), 2.23 (ddd, 1H, J = 12.8, 6.5, 1.6 Hz), 1.97 (ddd, 1H, J = 12.8, 7.3, 2.9 Hz), 1.89 (s, 3H), 1.10 (br s, 21H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 144.2, 142.1, 136.9, 129.0, 128.8, 128.2, 127.7, 124.3, 111.6, 75.2, 68.7, 65.1, 38.8, 20.5, 18.2, 12.8; IR (CCl_4) ν 3080, 2980, 2880, 1650, 1470 cm^{-1}. 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, 14.** A solution of 2.5% OsO_4 in ^{t}BuOH (0.18 mL, 0.015 mmol) was added to a mixture of **13** (280 mg, 0.72 mmol) and Me_3NO (161 mg, 1.45 mmol) in acetone/H_2O (8/1) (5 mL). The reaction was stirred for 6 h. The crude mixture was quenched with $NaHSO_3$ and evaporated under reduced pressure. The crude product was purified by column chromatography (hexane/AcOEt 10:1) to afford a colorless oil characterized as **14** (183 mg, 60%). Data of **14**: ^1H NMR ($CDCl_3$, 300 MHz) δ 7.36−7.28 (m, 5H), 5.15 (s, 1H), 4.58 (AB system, 2H, J_{AB} = 10.8 Hz), 4.32 (dd, 1H, J = 4.5, 3.6 Hz), 4.02 (dd, 1H, J = 4.7, 3.6 Hz), 3.84 (dd, 1H, J = 11.7, 3.0 Hz), 3.30 (dd, 1H, J = 11.7, 10.2 Hz), 3.17 (s, 1H), 2.86 (dd, 1H, J = 10.1, 3.1 Hz), 2.14 (dt, 1H, J = 12.4, 3.6 Hz), 1.94 (dt, 1H, J = 12.4, 4.5 Hz), 1.80 (s, 3H), 1.09 (s, 21H); ^{13}C NMR

($CDCl_3$, 75 MHz) δ 141.1, 139.0, 128.7, 128.1, 127.9, 125.5, 81.1, 72.5, 72.4, 69.1, 65.7, 34.6, 20.9, 18.3, 12.9; IR (CCl_4) ν 3500, 3020, 2980, 1650 cm^{-1}. Anal. Calcd for $C_{24}H_{40}O_4Si$: C, 68.53; H, 9.58. Found: C, 68.41; H, 9.42.

(4*S,6*S**)-6-Benzyloxy-4-triisopropylsilyloxy-3-methylcyclohex-2-en-1-one, 15.** *Method A*. To a solution of **14** (67 mg, 0.16 mmol) in THF/H_2O 1:1 (1 mL), $NaIO_4$ (51 mg, 0.24 mmol) was added. The mixture was stirred for 5 h, quenched with water, and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure to afford **15** as a colorless oil (62 mg, quantitative yield).

Method B. To a well-stirred solution of **13** (49 mg, 0.13 mmol) in a mixture of CH_3CN (0.73 mL), CCl_4 (0.73 mL), and H_2O (1.04 mL), $NaIO_4$ (111 mg, 0.52 mmol) was added. The resulting mixture was allowed to stir for 10 min, and then $RuCl_3 \cdot H_2O$ (1.1 mg, 0.005 mmol) was added. The mixture turned black and was stirred for 2 h. The reaction was quenched with sat. $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and evaporated in vacuo. After purification by column chromatography on silica gel (hexane/AcOEt 6:1), **15** was obtained as a colorless oil (27 mg, 56%). Data of **15**: ^1H NMR ($CDCl_3$, 300 MHz) δ 7.40−7.28 (m, 5H), 5.81 (s, 1H), 4.73 (AB system, 2H, J = 10.8 Hz), 4.71 (dd, J = 5.4, 4.5 Hz, 1H), 4.14 (dd, J = 8.1, 3.9 Hz, 1H), 2.39 (m, 1H), 2.24 (m, 1H), 2.07 (s, 3H), 1.18 (s, 21H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 198.0, 162.8, 138.1, 128.4, 127.9, 127.8, 124.9, 75.7, 72.3, 68.6, 39.4, 21.7, 18.2, 12.7; IR (CCl_4) ν 2925, 2868, 1718, 1678 cm^{-1}. Anal. Calcd for $C_{23}H_{36}O_3Si$: C, 71.09; H, 9.34. Found: C, 70.98; H, 9.18.

(1*S,2*R**,3*R**,5*S**)-5-Benzoyloxy-2,3-epoxy-1,2-dimethyl-4-methylencyclohexan-1-ol, 16.** To a solution of a derivative of **10**, in which the secondary alcohol is protected as benzoyloxy group (30 mg, 0.12 mmol) in C_6H_6 (1.2 mL), *t*-BuOOH was added (0.04 mL, 0.12 mmol), followed by $VO(acac)_2$ (3 mg, 0.01 mmol) at room temperature. The mixture was stirred for 6 h and filtered through florisil. This crude was washed with 10% $Na_2S_2O_5$ and sat. $NaHCO_3$. The aqueous layer was extracted with AcOEt. The organic layer was dried over $MgSO_4$, evaporated under reduced pressure, and purified by column chromatography (hexane/AcOEt 10:1) to afford **16** (31 mg, 95%) as a colorless oil. Data of **16**: ^1H NMR ($CDCl_3$, 300 MHz) δ 7.96 (d, 2H, J = 8.1 Hz), 7.51 (t, 1H, J = 7.2 Hz), 7.38 (t, 2H, J = 7.5 Hz), 5.73 (t, 1H, J = 3.0 Hz), 5.47 (s, 1H), 5.42 (s, 1H), 3.51 (s, 1H), 2.13 (dd, 1H, J = 4.8, 13.9), 1.77 (dd, 1H, J = 6.3, 13.9), 1.42 (s, 3H), 1.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 165.6, 140.4, 133.3, 130.2, 129.7, 129.7, 128.6, 128.6, 119.7, 71.4, 68.7, 65.7, 65.2, 42.3, 26.1, 17.2; IR ($CDCl_3$) ν 3560, 3050, 2980, 1610, 1460 cm^{-1}. Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 69.91; H, 6.47.

(1*R,2*S**,4*S**)-4-Benzoyloxy-1,2,5-trimethylcyclohex-5-en-1,2-diol, 17.** A mixture of **16** (52 mg, 0.19 mmol) and PtO_2/NO_2Na catalyst (1:1, 4:1 mg, 0.1 mmol) in dry MeOH (10 mL) was hydrogenated (5 psi) for 2 h. The reaction mixture was filtered through a short path of Celite with CH_2Cl_2. The solvent was evaporated under reduced pressure and the product was purified by column chromatography (CH_2Cl_2/AcOEt, 1:1) to afford **17** (32 mg, 60%) as a colorless oil. Data of **17**: ^1H NMR ($CDCl_3$, 300 MHz) δ 8.02 (d, 2H, J = 7.8 Hz), 7.56 (t, 1H, J = 7.2 Hz), 7.43 (t, 2H, J = 7.8 Hz), 5.73 (t, 1H, J = 6.6 Hz), 5.50 (s, 1H), 2.42 (dd, 1H, J = 6.0, 14.3 Hz), 2.41 (br s, 1H), 2.20 (br s, 1H), 1.87 (dd, 1H, J = 6.6 Hz, 14.3 Hz), 1.73 (s, 3H), 1.31 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 166.1, 133.3, 132.7, 131.3, 130.4, 129.6, 129.6, 128.4, 128.4, 73.8, 72.4, 71.5, 39.5, 24.5, 24.0, 19.2; IR (CH_2Cl_2): ν 3440, 3060, 2980, 2940, 1720, 1600, 1460 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.49; H, 7.19.

Acknowledgment. This work was supported by the DGICYT (Ministerio de Educación y Cultura, Spain, Grant 96/0641). One of us (M.L.) thanks Universidad Complutense de Madrid for a Grant. We also thank Servicio de Resonancia (U.C.M.) for NMR service.

Supporting Information Available: ^1H NMR spectra copies for compounds **4**, **5**, **9**, **10**, **12**−**17** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO9809534