Design and Synthesis of Antitumor Acylfulvenes

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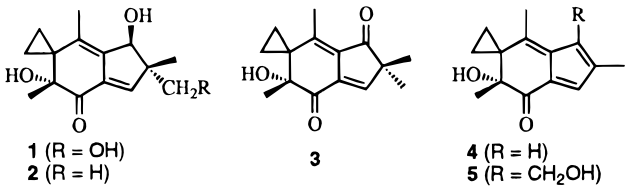
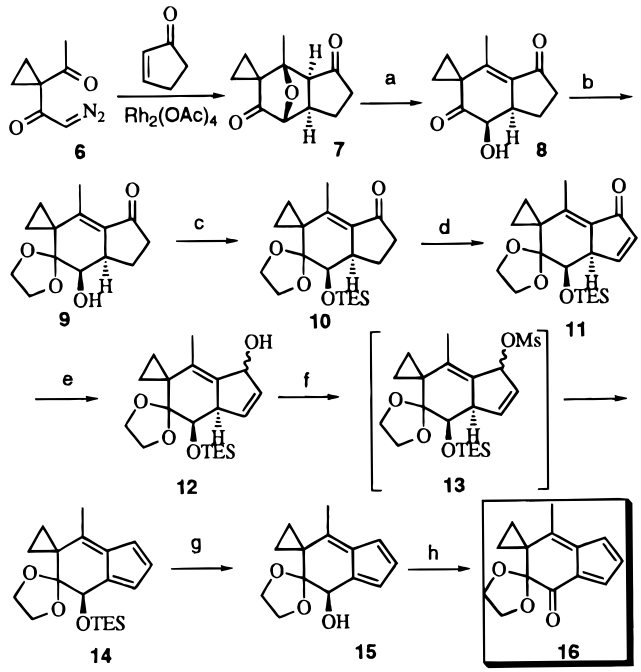
Acylfulvenes are a new class of potent antitumor compounds derived from the toxic sesquiterpene illudin S (**1**).[1,2] The latter and illudin M (**2**) are produced in cultures of the basidiomycete *Omphalotus illudens*.[3] These two compounds also possess antitumor activity but were found to have a poor therapeutic index when tested *in vivo*, particularly in solid tumor systems. Studies on the mechanism of toxicity of illudins have led to the preparation of illudin derivatives with greatly improved therapeutic index compared to the parent compounds. Thus, first-generation analog dehydroilludin M (**3**)[4] showed better efficacy against human metastatic MV 522 lung carcinoma xenografts (established in 4-week-old athymic Balb/c nu/nu mice) than nine known anticancer agents including cisplatin, cytoxan, and paclitaxel. Its efficacy was comparable to that of mitomycin C.[5] The efficacy of second-generation analog acylfulvene **4** exceeded that of dehydroilludin M and mitomycin C.[6] Although these compounds prolonged life span in the MV 522 model, they did not induce regression of the primary tumor implants. However, a third-generation analog (hydroxymethyl)-acylfulvene (HMAF, **5**) caused complete tumor regression in all animals at the maximum tolerated dose of 10 mg/kg (iv) three times per week for 3 weeks. This resulted in increased life span of more than 150%.[7] HMAF has also been found to exhibit outstanding activity against breast, colon, and skin cancer cell lines derived from human tumors. This compound is now undergoing clinical trials.[8]



We postulate that analogs possessing a concatenation of functional groups as found in illudins will exhibit toxic and antitumor properties. Therefore, we have been interested in a total synthetic approach to illudins as a way of preparing a wide variety of analogs.[9] In this connection the recently reported 1,3-dipolar cycloaddition reaction of Padwa et al.[10] seems particularly suitable for constructing the illudin skeleton. Two papers have appeared on the use of this method to prepare dehydroilludin M and related bicyclic analogs.[11,12] We have focused on the preparation of acylfulvene analogs since HMAF possesses the greatest efficacy among illudin derivatives. In this report the synthesis of acylfulvenes lacking the two methyl groups present in **4** is described.

Scheme 1[a]



[a] (a) K_2CO_3, *i*-PrOH, rt, 1 week; (b) cat *p*-TsOH, large excess ethylene glycol, benzene, rt, 24 h; (c) Py, TESCl, N_2, 60 °C, 0.5 h; (d) $(PhSeO)_2O$, PhCl, 95 °C, N_2, 0.5 h; (e) $CeCl_3 \cdot 7H_2O$, MeOH, excess $NaBH_4$, rt, 0.5 h; (f) CH_2Cl_2, Et_3N, MsCl, rt, 5 min; (g) cat *p*-TsOH, acetone, water, rt, 5 min; (h) PDC, CH_2Cl_2, rt, 1 h.

The starting compound for our synthesis (Scheme 1) is the adduct obtained from the 1,3-dipolar cycloaddition of a cyclic carbonyl ylide **6** and cyclopentenone.[10] In our hands the pure diastereomer **7** was obtained in more than 40% yield.

Intermediate **7** was very sensitive to basic conditions, even potassium carbonate in methanol at room temperature caused extensive decomposition. We found that potassium carbonate in 2-propanol at room temperature could selectively cleave the oxy bridge. The relative stereochemistry depicted in **8** was indicated by X-ray crystallographic analysis. Another novel reaction was

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(4) McMorris, T. C.; Kelner, M. J.; Wang, W.; Estes, L. A.; Montoya, M. A.; Taetle, R. *J. Org. Chem.* **1992**, 57, 6876−6883.
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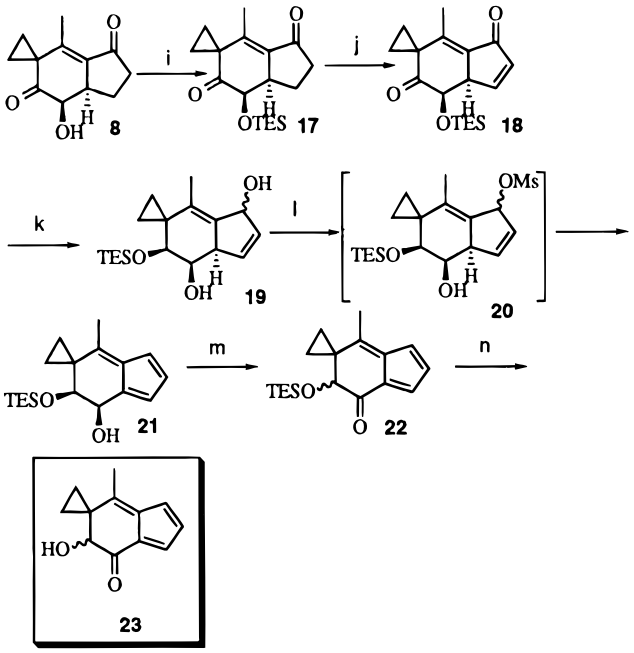
(6) Kelner, M. J.; McMorris, T. C.; Estes, L. A.; Montoya, M. A.; Starr, R.; Samson, K.; Taetle, R. *Cancer Res.* **1995**, 55, 4936−4940.
(7) Kelner, M. J.; McMorris, T. C.; Estes, L. A.; Wang, W.; Samson, K. M.; Taetle, R. *Investigational New Drugs* **1996**, 14, 161−167.
(8) Unpublished data provided by MGI Pharma Inc., Minneapolis, MN. This company has been licensed by the University of California to develop illudin analogs for treating tumors. U.S. Patents 5,439,-936; 5,439,942; 5,523,490; and 5,563,176 on these compounds have been issued to the University of California, and several more are pending.
(9) For previous synthesis of illudins, see: Matsumoto, T.; Shirahama, H.; Ichihara, A.; Shin, H.; Kagawa, S.; Sakan, F.; Matsumoto, S.; Nishida, S. *J. Am. Chem. Soc.* **1968**, 90, 3280−3281.
(10) Padwa, A.; Sandanayaka, V. P.; Curtis, E. A. *J. Am. Chem. Soc.* **1994**, 116, 2667−2668.
(11) Kinder, F. R.; Bair, K. W. *J. Org. Chem.* **1994**, 59, 6965−6967.
(12) Kinder, F. R.; Wang, R. M.; Bauta, W. E.; Bair, K. W. *Bioorg. Med. Chem. Lett.* **1996**, 6, 1029−1034.

S0022-3263(97)00141-2 CCC: $14.00

Scheme 2[a]



[a] (i) Py, TESCl, N_2, 60 °C, 0.5 h; (j) $(PhSeO)_2O$, PhCl, 95 °C, N_2, 0.5 h; (k) $CeCl_3 \cdot 7H_2O$, MeOH, excess $NaBH_4$, 25 °C, 0.5 h; (l) CH_2Cl_2, Et_3N, MsCl, rt, 5 min; (m) Dess−Martin reagent, CH_2Cl_2, rt, 0.5 h; (n) acetone, water, cat *p*-TsOH, rt, 0.5 h.

selective acetal formation, accomplished by reacting **8** with a large excess of ethylene glycol and a catalytic amount of *p*-toluenesulfonic acid in benzene at room temperature. An almost quantitative yield of the monoacetal **9** was obtained. Normal conditions (a limited amount of ethylene glycol, reflux with the continued removal of water) resulted in low yields. Benzene and ethylene glycol formed two layers. While starting material **8** was more soluble in ethylene glycol, the product **9** was more soluble in benzene which, presumably, made the selective formation of acetal **9** favorable. We believe these conditions may be generally useful since selective protection of ketones is often difficult.

In order to form the fulvene structure the hydroxyl group in **9** was protected as the triethylsilyl (TES) derivative **10**, which was reacted with phenylseleninic anhydride in chlorobenzene at 95 °C for 30 min, yielding the dienone **11** in 78%. 1,2-Reduction of the ketone gave the corresponding alcohol **12**, which was then mesylated. The product **13** was unstable on workup and, on chromatography, the fulvenes **14** and **15** were isolated. Removal of the TES group in **14** gave more **15** for a combined yield of 82%. Finally, oxidation of **15** with pyridinium dichromate afforded acylfulvene analog **16** in 72% yield.

Another acylfulvene analog (**23**) was synthesized in the following manner (Scheme 2). The hydroxyl group in intermediate **8** (from Scheme 1) was protected as the TES ether, and a double bond was introduced in the five-membered ring of **17** by reaction with phenylseleninic anhydride in chlorobenzene (60% yield). Reduction of the diketone yielded the diol **19**, in which the TES group had migrated to the newly formed hydroxyl group. Mesylation of the allylic hydroxyl group followed by chromatographic workup gave the fulvene **21** (90% yield). Dess−Martin oxidation of **21** and removal of the TES protecting group gave the acylfulvene **23** in 92% yield.

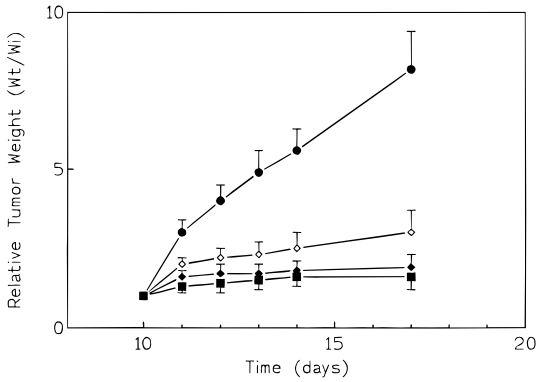


Figure 1. Efficacy of acylfulvene analog **16**, compared to mitomycin C, in the human lung MV522 multidrug resistant (gp 170+) metastatic tumor model.[6] MV522 cells were injected subcutaneously at 10 million cells per animal and treatment was delayed for 7 days until the tumors were palpable. The drug was administered iv daily for 5 days. Key: controls, 20% DMSO/saline (●); mitomycin C, 1.6 mg/kg, nontoxic (◇); mitomycin C, 2.0 mg/kg, toxic to animals (◆); analog **16**, 8 mg/kg, nontoxic (■).

The *in vitro* activity of analogs **16** and **23** in the MV 522 adenocarcinoma cell line has been examined. Both analogs were observed to have very similar toxicity to that of acylfulvene **4** on short (2 h) or long (48 h) exposure of cells to these compounds.[6] More importantly, analog **16** has been found to have similar *in vivo* activity to that of mitomycin C in mice implanted with MV522 cells (Figure 1). The toxicity exhibited by **16** and **23** is predicted by our hypothesis of the mechanism of toxicity of illudins.[2] Compound **16** is particularly interesting because it shows that a chiral center is not necessary for toxicity. Also, a tertiary hydroxyl group is not essential; a readily displaced heteroatom (*i.e.*, acetal oxygen) can serve equally well. Further data on *in vitro* and *in vivo* activity of these and other analogs will be reported elsewhere.

In conclusion, the total synthesis of two acylfulvene analogs with good anticancer activity was accomplished. An overall yield of 36% was achieved for the eight-step synthesis of acylfulvene **16**, and 35% yield was achieved for the seven-step synthesis of acylfulvene **23** from starting material **7**.

Experimental Section

General. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were measured at 300 and 75 MHz, respectively. High-resolution mass spectra were determined at the University of Minnesota Mass Spectrometry Service Laboratory. All chromatography was carried out with silica gel (Davisil 230-425 mesh, Fisher Scientific) and solvents ethyl acetate and hexanes in varying proportions were used. Analytical TLC was carried out on Whatman 4420 222 silica gel plates. Reactions were routinely monitored by TLC. Yields were calculated by taking into account recovered starting materials.

Compound 8. To a stirred solution of **7**[10] (2.83 g, 13.7 mmol) and 2-propanol (500 mL) was added K_2CO_3 (8 g, 58.0 mmol) at 25 °C. The mixture was stirred for 7 days and then partitioned between EtOAc and water. The organic extract was washed with saturated NH_4Cl and dried over $MgSO_4$. Then EtOAc was removed and the crude product was chromatographed to give 1.88 g of **7** and 0.78 g of **8** (82%) as a white solid: mp 183−5 °C; IR (KBr) 3369, 2995, 1696, 1616, 1407 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (m, 1H), 1.38 (m, 1H), 1.68 (m, 1H), 1.88 (m, 1H), 2.00 (s, 3H), 2.16 (m, 2H), 2.46 (m, 2H), 3.21 (m, 1H), 4.06 (d, J = 2.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 206.1, 204.8, 147.5, 128.0, 72.0, 42.2, 39.5, 32.1, 21.7, 19.4, 18.6, 11.7; MS *m/z* 206 (M^+), 177,

150, 147; HRMS for $C_{12}H_{14}O_3$ calcd 206.0943, found 206.0944. The structure was confirmed by X-ray crystallographic analysis.

Compound 9. *p*-Toluenesulfonic acid (12 mg, 0.063 mmol) was added to a stirred solution of **8** (107 mg, 0.519 mmol) in a mixture of ethylene glycol (3.04 g, 49 mmol) and benzene (10 mL) at 25 °C which was then stirred for 24 h. The mixture was partitioned between EtOAc and saturated $NaHCO_3$. The organic layer was washed with saline, dried over $MgSO_4$, and concentrated to an oil which was chromatographed to give 5 mg of **8** and 118 mg of **9** (95%) as a colorless oil: IR (KBr) 3469, 2952, 2892, 1757, 1690, 1616, 1374 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (m, 3H), 1.36 (m, 1H), 1.88 (d, J = 2.7 Hz, 3H), 1.96 (m, 2H), 2.36 (m, 2H), 3.19 (m, 1H), 3.78 (m, 1H), 4.00 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 205.4, 148.3, 128.3, 108.9, 67.9, 65.6, 64.5, 41.9, 39.3, 26.8, 20.8, 12.8, 11.5, 6.22; MS *m*/*z* 250 (M^+), 221, 193, 177; HRMS for $C_{14}H_{18}O_4$ calcd 250.1205, found 250.1201.

Compound 10. To a stirred solution of **9** (8.0 mg, 0.032mmol) and pyridine (0.5 mL) was added TESCl (0.1 mL, 0.25 mmol) under N_2. The reaction mixture was stirred at 60 °C for 30 min and then concentrated to an oil. The crude product was purified by chromatography to give 13 mg of **10** (quantitative) as a colorless oil: IR (KBr) 2959, 2885, 1710, 1610, 1454, 1414 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.62 (q, J = 7.8 Hz, 6H), 0.94 (m, 11H), 1.28 (m, 1H), 1.83 (m, 2H), 1.87 (d, J = 2.4 Hz, 3H), 2.35 (m, 2H), 3.13 (m, 1H), 3.75 (d, J = 3.3 Hz, 1H), 4.01 (m, 4H); ^{13}C ($CDCl_3$) δ 205.6, 148.8, 128.8, 109.5, 69.1, 65.3, 64.7, 43.3, 39.5, 27.4, 21.5, 12.9, 11.6, 6.8, 6.5, 4.8; MS *m*/*z* 364 (M^+), 336, 291, 219, 161; HRMS for $C_{20}H_{32}O_4Si$ calcd 364.2070, found 364.2070.

Compound 11. A solution of **10** (13 mg, 0.0357 mmol) and phenylseleninic anhydride (13 mg, 0.0361 mmol) in chlorobenzene (0.5 mL) was stirred at 95 °C for 0.5 h under N_2. The solution was then concentrated and chromatographed to give 4.9 mg of **10** and 7.0 mg of **11** (78%) as a colorless oil: IR (KBr) 2959, 2878, 1716, 1683, 1622, 1454 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.54 (q, J = 6.3 Hz, 6H), 0.89 (m, 10H), 1.27 (m, 2H), 1.57 (m, 1H), 1.93 (s, 3H), 3.79 (s, 1H), 4.00 (m, 4H), 6.30 (dd, J = 2.4, 6 Hz, 1H), 7.28 (dd, J = 2.1, 6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 195.9, 154.7, 146.9, 137.7, 127.5, 109.5, 69.2, 65.5, 64.6, 47.4, 28.0, 12.8, 11.1, 7.1, 6.7, 5.0; MS *m*/*z* 362 (M^+), 333, 289, 187, 159, 87; HRMS for $C_{20}H_{30}O_4Si$ calcd 362.1913, found 362.1919.

Compound 15. To the solution of **11** (20 mg, 0.055 mmol) and $CeCl_3 \cdot 7H_2O$ (35 mg, 0.094 mmol) in MeOH (1 mL) was added $NaBH_4$ (excess). The mixture was stirred for 15 min at 25 °C and then more $NaBH_4$ was added. After 15 min of stirring, the mixture was partitioned between Et_2O and saturated NH_4Cl. The ether extract was dried over $MgSO_4$ and concentrated to give crude product **12** as a pale yellow oil.

To the solution of the above crude product **12** in CH_2Cl_2 (1 mL) was added Et_3N (20 μL, 0.143 mmol) and MsCl (20 μL, 0.258 mmol), respectively, at 25 °C. It was stirred for 5 min. Then the mixture was partitioned between Et_2O and saturated $NaHCO_3$. The ether extract was washed with saline and dried over $MgSO_4$. After concentration, it was chromatographed to give **14** and **15** as a yellow gum.

To the solution of the above compound **14** in acetone (2 mL) and water (1 mL) was added some *p*-TsOH at room temperature. The mixture was set aside for 5 min and partitioned between Et_2O and saturated $NaHCO_3$. Then the ether extract was washed with saline and dried over $MgSO_4$. After concentration and chromatography, it was mixed with the above product **15** to give a total 10.5 mg of a yellow gum: IR (KBr) 3456, 2912, 2885, 1730, 1636, 1441 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75 (m, 1H), 1.10 (m, 2H), 1.24 (m, 1H), 1.88 (s, 3H), 2.34 (d, J = 6.9 Hz, 1H), 3.95 (m, 2H), 4.06 (m, 2H), 4.68 (d, J = 5.7 Hz, 1H), 6.34 (m, 1H), 6.42 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 152.0, 139.8, 134.6, 130.5, 125.3, 117.9, 111.9, 71.3, 67.0, 66.1, 31.5, 16.4, 9.5, 6.6; MS *m*/*z* 232 (M^+), 215, 189, 160, 145; HRMS for $C_{14}H_{16}O_3$ calcd 232.1099, found 232.1093.

Compound 16. A solution of **15** (7.3 mg, 0.031 mmol) and pyridinium dichromate (26 mg, 0.069 mmol) in CH_2Cl_2 (1 mL) was stirred for 1 h at 25 °C. The mixture was diluted by Et_2O and then filtered. The concentrated crude product was chromatographed to give 5.2 mg of **16** (72%) as yellow crystals: mp 138−140 °C; IR (KBr) 2959, 2892, 1683, 1616, 1549 cm^{-1}; 1H NMR ($CDCl_3$) δ 1.14 (m, 2H), 1.35 (m, 2H), 2.06 (s, 3H), 4.02 (m, 2H), 4.16 (m, 2H), 6.63 (dd, J = 2.4, 4.8 Hz, 1H), 6.76 (d, J = 4.8 Hz, 1H), 7.39 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 187.6, 159.6, 140.3, 135.4, 131.0, 127.9, 124.8, 106.2, 66.0 (OCH_2CH_2O), 33.4, 16.9, 12.9; MS *m*/*z* 230 (M^+), 202, 158; HRMS for $C_{14}H_{14}O_3$ calcd 230.0942, found 230.0948; UV λ_{max} (methanol) 230 nm (ϵ 6543), 330 (ϵ 3484).

Compound 17. To a solution of **8** (37 mg, 0.18 mmol) in pyridine (3 mL) was added TESCl (0.25 mL, 0.624 mmol). The mixture was stirred at 60 °C for 0.5 h under N_2. After concentration and chromatography, 50 mg (87%) of **17** was obtained as a colorless oil: IR (KBr) 2952, 2872, 1703, 1622, 1461 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.58 (q, J = 7.8 Hz, 6H), 0.97 (m, 10H), 1.25 (m, 2H), 1.58 (m, 1H), 1.85 (m, 2H), 1.98 (s, 3H), 2.42 (m, 2H), 3.09 (broad, 1H), 4.01 (d, J = 3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 206.0, 205.0, 147.0, 128.6, 72.6, 43.0, 39.6, 32.1, 21.4, 19.6, 18.0, 11.5, 6.5, 4.5; MS *m*/*z* 320 (M^+), 291, 259; HRMS for $C_{18}H_{28}O_3Si$ calcd 320.1808, found 320.1803.

Compound 18. A solution of **17** (278 mg, 0.869 mmol) and phenylseleninic anhydride (320 mg, 0.889 mmol) in chlorobenzene (2.5 mL) was stirred at 95 °C for 0.5 h under N_2. The mixture was then concentrated and chromatographed to give 58.7 mg of **17** and 131.2 mg of **18** (60%) as a colorless gum: IR (KBr) 2952, 2878, 1730, 1690, 1636, 1454 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.52 (q, J = 7.8 Hz, 6H), 0.85 (t, J = 7.8 Hz, 9H), 1.20 (m, 1H), 1.36 (m, 1H), 1.69 (m, 1H), 1.82 (m, 1H), 2.06 (s, 3H), 3.58 (s, 1H), 4.26 (d, J = 2.4 Hz, 1H), 6.45 (dd, J = 2.1, 6 Hz, 1H), 7.33 (dd, J = 2.1, 6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 205.9, 195.3, 153.2, 144.3, 139.4, 127.7, 72.1, 47.3, 32.4, 20.1, 19.7, 11.4, 6.4, 4.4; MS *m*/*z* 318 (M^+), 289, 261; HRMS for $C_{18}H_{26}O_3Si$ calcd 318.1651, found 318.1658.

Compound 21. To a solution of **18** (9.5 mg, 0.0299 mmol), and $CeCl_3 \cdot 7H_2O$ (58.5 mg, 0.157 mmol) in MeOH (0.3 mL) was added $NaBH_4$ (excess) at 25 °C. It was stirred for 30 min. Then the mixture was partitioned between Et_2O and saturated NH_4Cl. The ether extract was dried by $MgSO_4$ and concentrated to give crude product **19** as a pale yellow oil.

To the solution of above **19** in CH_2Cl_2 (0.2 mL) was added Et_3N (5 μL, 0.036 mmol) and MsCl (5 mL, 0.097 mmol) at 25 °C. The mixture was stirred for 5 min and then partitioned between Et_2O and saturated $NaHCO_3$. The ether extract was washed with saline and dried over $MgSO_4$. After concentration, it was chromatographed to give 8.2 mg of **21** (90%) as a yellow gum: IR (KBr) 3557, 3449, 2946, 2878, 1716, 1643, 1461 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.66 (q, J = 7.8 Hz, 6H), 0.87 (m, 2H), 0.98 (t, J = 7.8 Hz, 9H), 1.26 (m, 2H), 1.86 (s, 3H), 2.55 (d, J = 3.9 Hz, 1H), 3.24 (broad s, 1H), 4.94 (d, J = 2.1 Hz, 1H), 6.35 (m, 2H), 6.46 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 150.7, 140.0, 133.2, 130.4, 125.7, 117.5, 78.7, 69.7, 28.2, 15.7, 11.6, 10.3, 6.8, 5.0; MS *m*/*z* 304 (M^+), 287, 275; HRMS for $C_{18}H_{28}O_2Si$ calcd 304.1859, found 304.1860.

Compound 22. A solution of **21** (1.2 mg, 3.95 mmol) and Dess−Martin reagent (2.2 mg, 5.19 μmol) in CH_2Cl_2 (0.2 mL) was stirred for 30 min at 25 °C. The mixture was partitioned between Et_2O and 10% Na_2SO_3. Then the ether extract was washed with saline and dried over $MgSO_4$. After concentration, it was chromatographed to give 1.1 mg of **22** (92%) as a yellow gum: IR (KBr) 2952, 2872, 1690, 1610, 1549 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.71 (q, J = 7.8 Hz, 6H), 0.85 (m, 1H), 0.97 (t, J = 7.8 Hz, 9H), 1.21 (m, 2H), 1.45 (m, 1H), 2.08 (s, 3H), 4.50 (s, 1H), 6.66 (dd, J = 2.4, 5.0 Hz, 1H), 6.72 (d, J = 5.0 Hz, 1H), 7.25 (broad s, 1H); ^{13}C NMR ($CDCl_3$) δ 193.3, 161.2, 140.7, 131.8, 131.2, 128.3, 122.8, 32.9, 17.1, 12.5, 10.3, 6.9, 5.2; MS *m*/*z* 302 (M^+), 273, 245; HRMS for $C_{18}H_{26}O_2Si$ calcd 302.1702, found 302.1710; UV λ_{max} 227 (ϵ 15 612), 323 nm (ϵ 10 720).

Compound 23. To a solution of **22** (9.0 mg, 0.0298 mmol) in acetone (0.8 mL) and H_2O (0.4 mL) was added a trace of *p*-TsOH. The mixture was stirred for 30 min. Then it was partitioned between Et_2O and saturated $NaHCO_3$. The ether extract was washed with saline and dried over $MgSO_4$. After concentration, it was chromatographed to give **23** (quantitative yield) as a yellow gum: IR (KBr) 3449, 3013, 2925, 1663, 1609, 1441 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 (m, 1H), 1.25 (m, 1H), 1.36 (m, 1H), 1.44 (m, 1H), 2.12 (s, 3H), 3.82 (d, J = 2 Hz, 1H), 4.55 (d, J = 2 Hz, 1H), 6.70 (dd, J = 2.7, 5.1 Hz, 1H), 6.81 (t, 1H), 7.32 (broad s, 1H); ^{13}C NMR ($CDCl_3$) δ 194.2, 162.2, 140.9, 132.7, 131.4, 126.5, 124.1, 74.6, 32.8, 17.0, 12.7, 10.3; MS *m*/*z* 188 (M^+), 160, 145; HRMS for $C_{12}H_{12}O_2$ calcd 188.0837, found 188.0840; UV λ_{max} (methanol) 227 (ϵ 13 626), 323 nm (ϵ 7474).

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Supporting Information Available: ^{1}H NMR for all new compounds reported (12 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.

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