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$Mn(OAc)_3$-BASED α'-OXIDATIVE ACETOXYLATION OF *N*-TRIFLUOROACETYL VINYLOGOUS AMIDES

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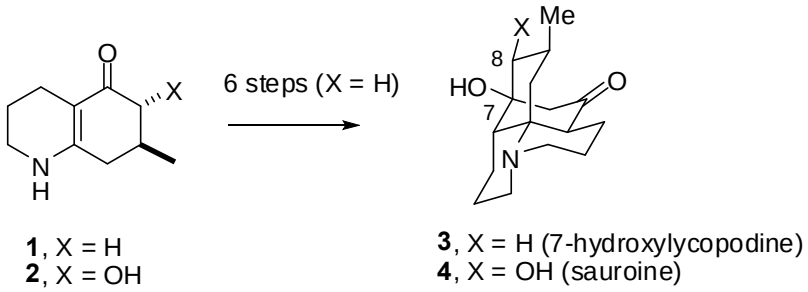
Abstract – Vinylogous amides **1** and **11** are oxidized by dried $Mn(OAc)_3$ in benzene at 90 °C to pyridines **5** and **12**, respectively, whereas the analogous *N*-trifluoroacetyl vinylogous amides **6** and **13** are oxidized by dried $Mn(OAc)_3$ in benzene at 120 °C to give acetates **7** and **14**. The α'-oxo radicals that are generated in this oxidation cyclize to proximal double bonds to give tricylic alkenes such as **20**.

INTRODUCTION

The lycopodium alkaloid sauroine (7,8-dihydroxylycopodine, **4**) was recently shown to improve memory retention in male Wistar rats making it a significant synthetic target (see Scheme 1).[1] We chose to first address the synthesis of the simpler, related alkaloid 7-hydroxylycopodine (**3**) and recently reported a six step synthesis of **3** from vinylogous amide **1**.[2] For the synthesis of sauroine (**4**) we needed to hydroxylate the vinylogous amide **1** in the α'-position to obtain **2**, which could then be elaborated to sauroine (**4**) by the route that was used to prepare **3** from **1**.



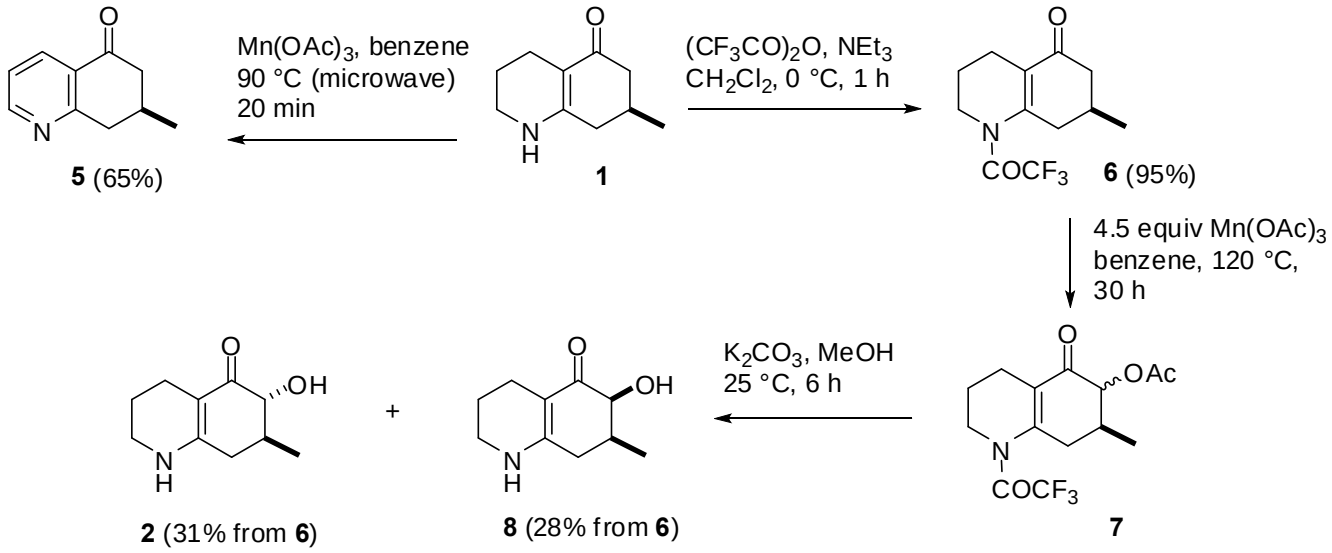
1, X = H
2, X = OH

3, X = H (7-hydroxylycopodine)
4, X = OH (sauroine)

Scheme 1

Dedicated to Professor Ei-ichi Negishi on the occasion of his 77th birthday

Unfortunately, a variety of standard hydroxylation procedures failed to convert **1** to **2** indicating that the chemistry of vinylogous amides such as **1** is quite different from that of enones.[2b] For instance, Watt and Demir developed $Mn(OAc)_3$-based α'-acetoxylations of enones that proceed in high yield with dried $Mn(OAc)_3$ in benzene at reflux.[3] They found that the use of both $Mn(OAc)_3 \cdot 2H_2O$ that had been dried in vacuum over P_2O_5 for several days and benzene at reflux as the solvent was crucial for the success of the α'-acetoxylation. Although only 2 equiv of dried $Mn(OAc)_3$ are required by the stoichiometry, the reaction is heterogeneous and in practice requires 4-6 equiv of dried $Mn(OAc)_3$. This procedure also works well on β-alkoxyenones (vinylogous esters),[3a] but we found that it converted vinylogous amide **1** to pyridine **5** in 65% yield, rather than the desired acetate ester of **2** (see Scheme 2).[2b] Clearly oxidation proceeds at the nitrogen rather than by enolization and formation of the α'-oxo radical. We thought that acylation of the nitrogen should both prevent this undesired oxidation and favor the formation of the required α'-oxo radical by increasing the acidity of the α'-proton.



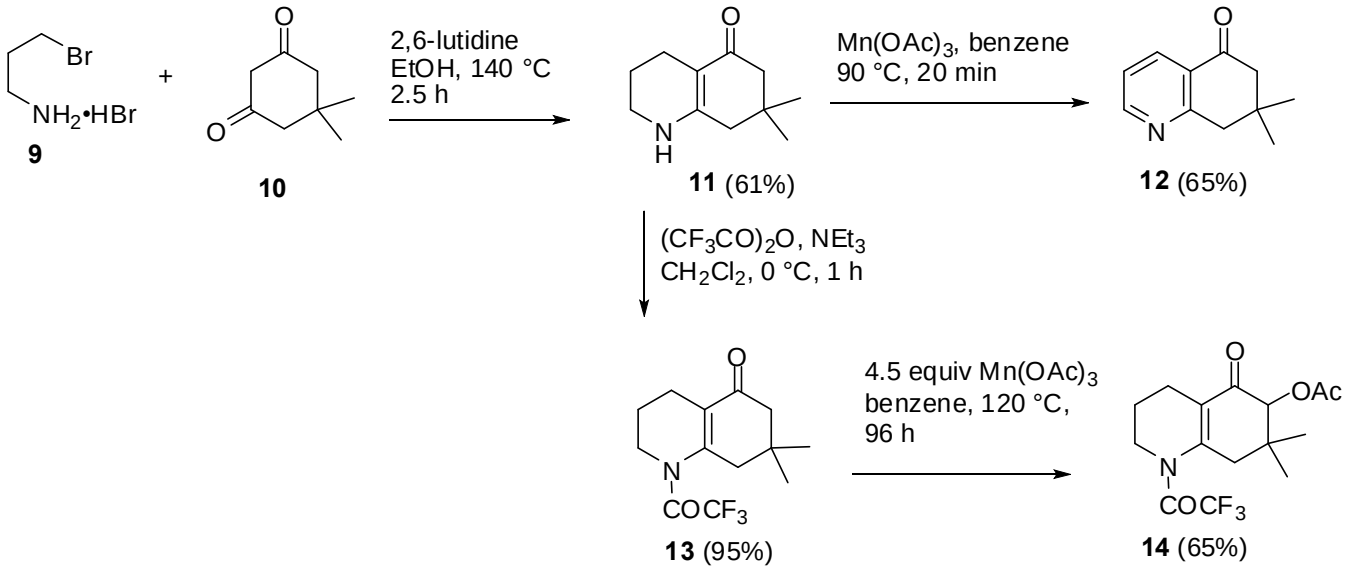
Scheme 2

RESULTS AND DISCUSSION

Electron deficient acyl groups should be the most effective at increasing the acidity of the α'-proton. We therefore treated **1** with trifluoroacetic anhydride and triethylamine in CH_2Cl_2 for 1 h at 0 °C to generate *N*-trifluoroacetyl vinylogous amide **6** in 95% yield.[4] To our delight, we found that oxidation of **6** with dried $Mn(OAc)_3$ in benzene in a sealed tube at 120 °C for 30 h cleanly afforded the desired acetate **7** as an inseparable ~1 : 1 mixture of isomers. This reaction is considerably slower than the α'-acetoxylations of β-alkoxyenones (vinylogous esters), which require 20-48 h in benzene at reflux. The rate determining step is formation of the Mn(III) enolate and the α'-protons of vinylogous imide **6** are probably less acidic

than those of vinylogous esters. Hydrolysis of both the acetate and trifluoroacetamide of **7** with potassium carbonate in MeOH at 25 °C for 6 h gave 31% of the desired trans alcohol **2** and 28% of the undesired cis alcohol **8**. The stereochemistry of the trans isomer **2** was established by the 11.2 Hz coupling between the diaxial methine hydrogens indicating that both the hydroxyl and methyl groups are equatorial.[5] The coupling constant between the methine hydrogens in the cis isomer **8** is 5.2 Hz.[5] The absence of a large coupling constant between the methine hydrogen adjacent to the methyl group and either adjacent methylene hydrogen indicates that in the preferred conformation of **8** the methyl group is axial and the alcohol is equatorial and probably hydrogen bonded to the adjacent carbonyl group.

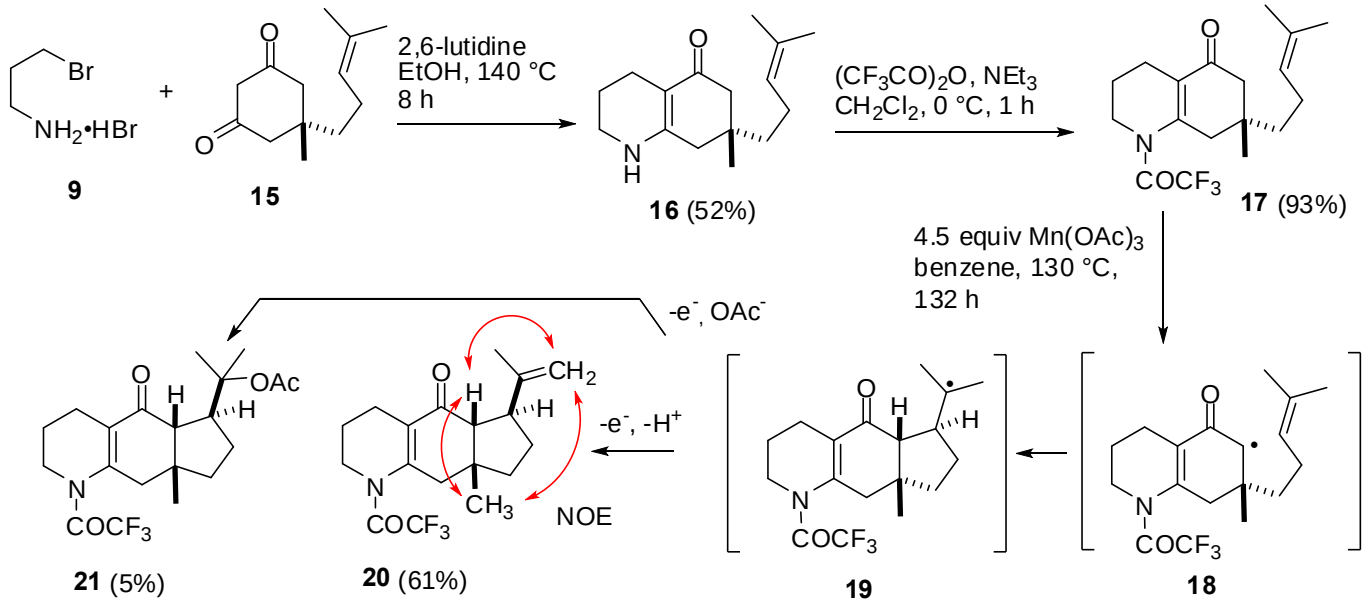
Reaction of 3-bromopropylamine hydrobromide (**9**), dimedone (**10**), and 2,6-lutidine in EtOH in a sealed tube at 140 °C for 2.5 h gave the known vinylogous amide **11**[6] in 61% yield (see Scheme 3). As expected from the conversion of **1** to **5**, oxidation of the unprotected vinylogous amide **11** with dried $Mn(OAc)_3$ in benzene at 90 °C for 20 min afforded pyridine **12**[7] in 65% yield. Trifluoroacetylation of **11** afforded **13** (95%), which was oxidized with dried $Mn(OAc)_3$ in benzene at 120 °C for 96 h to give the desired acetate **14** in 65% yield. The oxidation of **13** is considerably slower than that of **6**, probably as a result of increased steric hindrance due to the second alkyl substituent. Demir recently reported that α'-acetoxylation of enones in 9:1 benzene/HOAc is much faster than in benzene.[8] α'-Acetoxylation of **13** in 9:1 benzene/HOAc is complete in 6 h at 120 °C and 21 h at 90 °C, but is not quite as clean as the slower α'-acetoxylation in benzene at 120 °C.



Scheme 3

In 1996 we reported that cyclization of the α'-keto radical formed by oxidation of enones with $Mn(OAc)_3$ to a proximal double bond is faster than acetoxylation.[9] We therefore investigated whether this was also

the case with *N*-trifluoroacetyl vinylogous amides. Reaction of 3-bromopropylamine hydrobromide (**9**), cyclohexanedione **15**,[10] and 2,6-lutidine in EtOH in a sealed tube at 140 °C for 8 h gave vinylogous amide **16** in 52% unoptimized yield (see Scheme 4). Trifluoroacetylation afforded **17** (93%), which was oxidized with dried $Mn(OAc)_3$ in benzene at 130 °C for 132 h to give the expected tricyclic alkene **20** in 61% yield and tertiary acetate **21** in 5% yield. Oxidation presumably generates α'-oxo radical **18**, which undergoes the expected 5-exo cyclization with the alkene on the convex face to give cis fused tertiary radical **19**, which is oxidized to the cation that loses a proton to yield **20** and reacts with acetate to form **21**. The stereochemistry of the major product **20** was confirmed by the NOEs shown in Scheme 4 and by the coupling pattern of the allylic methine hydrogen (ddd, J = 11.2, 10.4, 7.2 Hz), which is consistent with that expected for this isomer, but not the other three diastereomers. The pyrrolidine-catalyzed intramolecular Michael reaction of ethyl (*E*)-5-(l-methyl-3-oxocyclohexyl)-2-pentenoate gave a single diastereomer corresponding to **20** providing further support for the structure assignment.[11]



Scheme 4

In conclusion, we have shown that vinylogous amides **1** and **11** are oxidized by dried $Mn(OAc)_3$ in benzene at 90 °C to pyridines **5** and **12**, respectively, whereas the analogous *N*-trifluoroacetyl vinylogous amides **6** and **13** are oxidized by dried $Mn(OAc)_3$ in benzene at 120 °C to give acetates **7** and **14**. The α'-oxo radicals such as **18** that are generated in this oxidation cyclize to proximal double bonds to give tricyclic alkenes such as **20**. We are currently exploring the elaboration of hydroxy vinylogous amide **2** to sauroine (**4**).

EXPERIMENTAL

General Experimental Methods. Reactions were conducted in flame- or oven-dried glassware under a nitrogen atmosphere and were stirred magnetically. The phrase "concentrated" refers to removal of solvents by means of a rotary-evaporator attached to a diaphragm pump (15-60 Torr) followed by removal of residual solvents at < 1 Torr with an vacuum pump. Flash chromatography was performed on silica gel 60 (230-400 mesh). Et_3N, pyridine, MeCN and benzene were distilled from CaH_2. $Mn(OAc)_3$•$2H_2O$ was dried over P_2O_5 under vacuum for several days.[3] ^1H and ^{13}C NMR spectra were obtained on a 400 MHz spectrometer in $CDCl_3$ with TMS as internal standard unless specifically indicated. Chemical shifts are reported in δ (ppm downfield from tetramethylsilane). Coupling constants are reported in Hz with multiplicities denoted as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). IR spectra were acquired on an FT-IR spectrometer and are reported in wave numbers (cm^{-1}). High resolution mass spectra were obtained using electrospray ionization (ESI).

2,3,4,6,7,8-Hexahydro-7-methyl-1-trifluoroacetyl-5(1*H*)-quinolinone (6). Trifluoroacetic anhydride (0.56 mL, 4.0 mmol, 2.0 equiv) and NEt_3 (0.67 mL, 5.0 mmol, 2.5 equiv) were added to a solution of **1** (330 mg, 2.0 mmol) in 6 mL of CH_2Cl_2 at 0 °C. The resulting mixture was stirred at 0 °C for 1 h. The reaction was quenched by addition of water (12 mL). The mixture was extracted with CH_2Cl_2 (12 mL × 3). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated. Flash chromatography of the residue on silica gel (6:1 hexanes/EtOAc) gave 496 mg (95%) of **6** as a colorless oil: ^1H NMR 3.90 (br ddd, 1, *J* = 12.8, 3.6, 3.6, H-2), 3.43 (ddd, 1, *J* = 12.8, 10.4, 2.8, H-2), 2.75 (dddd, 1, *J* = 17.6, 10.4, 3.2, 3.2, H-8), 2.65 (br d, 1, *J* = 17.6, H-8), 2.54 (dd, 1, *J* = 12.8, 1.8, H-6), 2.43 (dddd, 1, *J* = 18.4, 6.8, 3.4, 3.4, H-4), 2.30 (ddddd, 1, *J* = 18.4, 8.4, 8.4, 2.4, 2.4, H-4), 2.24-2.13 (m, 1, H-7), 2.14 (dd, 1, *J* = 12.8, 12.8, H-6), 2.08-1.98 (m, 1, H-3), 1.90-1.78 (m, 1, H-3), 1.08 (d, 3, *J* = 6.4); ^{13}C NMR 198.5, 155.8 (q, 1, *J* = 36.4, CF_3CO), 153.2, 124.6, 115.9 (q, 1, *J* = 287, CF_3), 45.4, 45.2 (q, 1, *J* = 4.0, CF_3CONCH_2), 37.3, 30.6, 22.2, 21.0, 20.1; IR 1702, 1663, 1623 (wk), 1202, 1140, 913, 748.

***trans*-2,3,4,6,7,8-Hexahydro-6-hydroxy-7-methyl-5(1*H*)-quinolinone (2) and *cis*-2,3,4,6,7,8-Hexahydro-6-hydroxy-7-methyl-5(1*H*)-quinolinone (8).** A solution of **6** (496 mg, 1.9 mmol) in 20 mL of benzene and dried $Mn(OAc)_3$ (1.98 g, 8.6 mmol, 4.5 equiv) were added to a resealable tube. The reaction mixture was sealed and heated at 120 °C for 30 h. The reaction mixture was cooled to room temperature and 10% aq. $NaHSO_3$ solution (50 mL) was added. The mixture was extracted with EtOAc (50 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to give crude acetate **7** as a ~1:1 mixture of isomers.

To a solution of the residue in 12 mL of MeOH was added powdered K_2CO_3 (1.05 g, 4 equiv). The reaction mixture was stirred at room temperature for 6 h and concentrated. To the residue was added water (30 mL). The mixture was extracted with EtOAc (30 mL × 4). The combined organic layers were

washed with brine, dried over Na_2SO_4, and concentrated. Flash chromatography of the residue on silica gel (100:1:1 EtOAc/MeOH/NEt_3) gave 106 mg (31% from **6**) of **2** as a white solid, followed by 96 mg (28% from **6**) of **8** as a colorless oil.

Data for **2**: mp 212-213 °C; ^{1}H NMR 4.88 (br, 1, NH), 4.30 (br, 1, OH), 3.62 (d, 1, *J* = 11.2, H-6), 3.36-3.20 (m, 2, H-2), 2.45 (br ddd, 1, *J* = 16.0, 6.0, 6.0, H-4), 2.29 (br dd, 1, *J* = 13.6, 4.8, H-8), 2.24 (dd, 1, *J* = 13.6, 13.6, H-8), 2.20 (br dd, 1, *J* = 16.0, 4.8, H-4), 2.04-1.92 (m, 1, H-7), 1.90-1.70 (m, 2, H-3), 1.19 (d, 3, *J* = 6.8); ^{13}C NMR 193.4, 158.9, 101.5, 76.1, 41.5, 36.8, 35.9, 20.6, 18.9, 18.4; IR 3423, 3264, 3108, 1602 (wk), 1570 (wk), 1513, 1264, 978, 749; HRMS (ESI) calcd for $C_{10}H_{16}NO_2$ (MH^+) 182.1181, found 182.1186.

Data for **8**: ^{1}H NMR 4.87 (br, 1, NH), 4.20 (br, 1, OH), 4.18 (d, 1, *J* = 5.2, H-6), 3.37-3.21 (m, 2, H-2), 2.78 (br dd, 1, *J* = 16.0, 5.2, H-8), 2.65-2.53 (m, 1, H-7), 2.50 (br ddd, 1, *J* = 16.0, 5.6, 5.6, H-4), 2.25 (br ddd, 1, 16.0, 6.8, 6.8, H-4), 2.09 (br d, 1, *J* = 16.0, H-8), 1.90-1.70 (m, 2, H-3), 0.92 (d, 3, *J* = 6.8); ^{13}C NMR 192.1, 157.0, 101.1, 73.1, 41.5, 34.9, 33.3, 20.6, 18.6, 11.6; IR 3262 (br), 3089, 1569 (wk), 1514, 1343, 1260, 913, 748; HRMS (ESI) calcd for $C_{10}H_{16}NO_2$ (MH^+) 182.1181, found 182.1179.

2,3,4,6,7,8-Hexahydro-7,7-dimethyl-5(1*H*)-quinolinone (11). A solution of 5,5-dimethylcyclohexane-1,3-dione (**10**) (630 mg, 4.5 mmol), 3-bromopropylammonium bromide (**9**) (1.02 g, 4.7 mmol, 1.04 equiv), and 2,6-lutidine (1.6 mL, 13.5 mmol, 3.0 equiv) in 4 mL of EtOH was added to a resealable tube, which was sealed and heated at 140 °C for 2.5 h. The reaction mixture was cooled to room temperature and 1 M NaOH solution (30 mL) was added. The mixture was extracted with CH_2Cl_2 (30 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to about 5 mL. MeCN (30 mL × 2) was added and the resulting solution was concentrated again. Flash chromatography of the residue on silica gel (100:1:1 EtOAc/MeOH/NEt_3) gave 491 mg (61%) of **11** as a white solid: mp 180-181 °C; ^{1}H NMR 4.41 (br s, 1, NH), 3.26 (br t, 2, *J* = 6.4, H-2), 2.35 (br t, 2, *J* = 6.4, H-4), 2.20 (br s, 2, H-6 or 8), 2.12 (br s, 2, H-6 or 8), 1.80 (tt, *J* = 6.4, 6.4, H-3), 1.04 (s, 6); ^{13}C NMR 193.7, 157.3, 103.4, 50.2, 43.1, 41.6, 32.4, 28.4 (2 C), 21.1, 18.7; IR 3265 (br), 1721, 1668, 1622, 1518 (wk), 1275, 1135, 913, 748. The ^{1}H NMR spectral data are identical to those previously reported.[6]

7,8-Dihydro-7,7-dimethyl-5(6*H*)-quinolinone (12). A solution of **11** (50 mg, 0.28 mmol) in 4 mL of benzene and dried $Mn(OAc)_3$ (292 mg, 1.26 mmol, 4.5 equiv) were added to a resealable tube. The resulting mixture was sealed and heated at 90 °C for 20 min. The reaction mixture was cooled to room temperature and 10% aq. $NaHSO_3$ solution (15 mL) was added. The mixture was extracted with EtOAc (15 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Flash chromatography of the residue on silica gel (100:1:1 EtOAc/MeOH/NEt_3) gave 32 mg (65%) of **12** as a pale yellow oil: ^{1}H NMR 8.71 (dd, 1, *J* = 4.8, 1.8), 8.27 (dd, 1, *J* = 8.0, 1.8), 7.30 (dd, 1, *J* = 8.0, 4.8), 3.05 (s, 2), 2.58 (s, 2), 1.12 (s, 6); ^{13}C NMR 198.1, 162.2, 153.8, 134.5, 127.1, 122.1, 51.9, 46.3, 32.9,

28.2 (2 C); IR, 3070, 1686, 1582, 1300, 1282, 916, 821, 796, 742, 718. The ^{1}H NMR, ^{13}C NMR, and IR spectral data are identical to those previously reported.[7]

2,3,4,6,7,8-Hexahydro-7,7-dimethyl-1-trifluoroacetyl-5(1*H*)-quinolinone (13). Trifluoroacetic anhydride (0.56 mL, 4.0 mmol, 2.0 equiv) and NEt_3 (0.67 mL, 5.0 mmol, 2.5 equiv) were added to a solution of **11** (360 mg, 2.0 mmol) in 6 mL of CH_2Cl_2 at 0 °C. The resulting mixture was stirred at 0 °C for 1 h. The reaction was quenched by addition of water (12 mL). The mixture was extracted with CH_2Cl_2 (12 mL × 3). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated. Flash chromatography of the residue on silica gel (6:1 hexanes/EtOAc) gave 523 mg (95%) of **13** as a colorless oil: ^{1}H NMR 3.66 (dd, 2, *J* = 5.6, 5.6, H-2), 2.70 (dd, 2, *J* = 2.0, 2.0, H-8), 2.38 (dddd, 2, *J* = 6.8, 6.8, 2.0, 2.0, H-4), 2.32 (s, 2, H-6), 1.99-1.91 (m, 2, H-3), 1.06 (s, 6); ^{13}C NMR 198.5, 155.9 (q, 1, *J* = 36.8, CF_3CO), 151.7, 124.2, 115.9 (q, 1, *J* = 287, CF_3), 50.8, 45.2 (q, 1, *J* = 3.8, CF_3CONCH_2), 42.8, 33.7, 27.9 (2 C), 22.4, 20.0; IR 1702, 1664, 1627 (wk), 1199, 1143, 993, 913, 751.

6-Acetoxy-2,3,4,6,7,8-hexahydro-7,7-dimethyl-1-trifluoroacetyl-5(1*H*)-quinolinone (14). A solution of **13** (523 mg, 1.9 mmol) in 20 mL of benzene and dried $Mn(OAc)_3$ (1.98 g, 8.6 mmol, 4.5 equiv) were added to a resealable tube. The reaction mixture was sealed and heated at 120 °C for 96 h. The reaction mixture was cooled to room temperature and 10% aq. $NaHSO_3$ solution (50 mL) was added. The mixture was extracted with EtOAc (50 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Flash chromatography of the residue on silica gel (6:1 hexanes/EtOAc) gave 26 mg (5%) of recovered **13**, followed by 412 mg (65%) of **14** as a white solid: mp 104-105 °C; ^{1}H NMR 5.27 (s, 1, H-6), 3.89 (ddd, 1, *J* = 12.8, 4.0, 4.0, H-2), 3.45 (ddd, 1, *J* = 12.8, 10.4, 2.4, H-2), 3.21 (ddd, 1, *J* = 18.0, 3.4, 3.4, H-8), 2.61 (dd, 1, *J* = 18.0, 1.8, H-8), 2.46 (ddddd, 1, *J* = 18.4, 8.0, 8.0, 2.4, 2.4, H-4), 2.32 (dddd, 1, *J* = 18.4, 6.8, 3.6, 3.6, H-4), 2.22 (s, 3), 2.09-1.99 (m, 1, H-3), 1.93-1.81 (m, 1, H-3), 1.13 (s, 3), 1.00 (s, 3); ^{13}C NMR 192.6, 170.5, 156.0 (q, 1, *J* = 37.2, CF_3CO), 150.7, 123.8, 115.8 (q, 1, *J* = 287, CF_3), 80.1, 45.3 (q, 1, *J* = 3.8, CF_3CONCH_2), 42.7, 38.2, 27.2, 22.0, 20.6, 20.2, 19.4; IR 1748, 1705, 1681, 1628 (wk), 1204, 1152, 913, 749; HRMS (ESI) calcd for $C_{15}H_{19}F_3NO_4$ (MH^+) 334.1266, found 334.1272.

2,3,4,6,7,8-Hexahydro-7-methyl-7-(4-methyl-3-penten-1-yl)-5(1*H*)-quinolinone (16). A solution of 5-methyl-5-(4-methyl-3-penten-1-yl)cyclohexane-1,3-dione (**15**)[10] (400 mg, 1.9 mmol), 3-bromopropylammonium bromide (**9**) (440 mg, 2.0 mmol, 1.05 equiv), and 2,6-lutidine (0.66 mL, 5.7 mmol, 3.0 equiv) in 1.4 mL of EtOH was added to a resealable tube, which was sealed and heated at 140 °C for 8 h. The reaction mixture was cooled to room temperature and 1 M NaOH solution (15 mL) was added. The mixture was extracted with CH_2Cl_2 (15 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to about 5 mL. MeCN (15 mL × 2) was added and the resulting solution was concentrated again. Flash chromatography of the residue on silica gel (25:75:1 hexanes/EtOAc/NEt_3) gave 247 mg (52%) of **16** as a pale yellow oil: ^{1}H NMR 5.07 (br t, 1, *J* = 6.8), 4.72

(br, 1, NH), 3.27 (br t, 2, *J* = 6.0, H-2), 2.37-2.33 (m, 2, H-4), 2.26 (br d, 1, *J* = 16.0, H-6 or 8), 2.26 (br d, 1, *J* = 16.0, H-6 or 8), 2.18 (br d, 1, *J* = 16.0, H-6 or 8), 2.03 (br d, 1, *J* = 16.0, H-6 or 8), 1.98-1.91 (m, 2), 1.80 (tt, 2, *J* = 6.0, 6.0, H-3), 1.67 (br s, 3), 1.59 (br s, 3), 1.37-1.33 (m, 2), 1.03 (s, 3); ^{13}C NMR 193.5, 157.2, 131.6, 124.3, 103.5, 48.5, 41.7, 41.6, 41.5, 35.0, 25.6, 24.8, 22.4, 21.1, 18.7, 17.5; IR 3261 (br), 3072, 1722, 1655, 1571 (wk), 1519, 913, 754; HRMS (ESI) calcd for $C_{16}H_{26}NO$ (MH^+) 248.2014, found 248.2019.

2,3,4,6,7,8-Hexahydro-7-methyl-7-(4-methyl-3-penten-1-yl)-1-trifluoroacetyl-5(1*H*)-quinolinone (17). Trifluoroacetic anhydride (0.17 mL, 1.2 mmol, 2.0 equiv) and NEt_3 (0.20 mL, 1.5 mmol, 2.5 equiv) were added to a solution of **16** (147 mg, 0.60 mmol) in 3 mL of CH_2Cl_2 at 0 °C. The resulting mixture was stirred at 0 °C for 1 h. The reaction was quenched by addition of water (8 mL). The mixture was extracted with CH_2Cl_2 (8 mL × 3). The combined organic layers were washed with water and brine, dried over Na_2SO_4, and concentrated. Flash chromatography of the residue on silica gel (6:1 hexanes/EtOAc) gave 190 mg (93%) of **17** as a colorless oil: ^{1}H NMR 5.05 (br t, 1, *J* = 6.8), 3.73-3.61 (m, 2, H-2), 2.81 (br d, 1, *J* = 17.6, H-8), 2.62 (br d, 1, *J* = 17.6, H-8), 2.41-2.34 (m, 2, H-4), 2.38 (d, 1, *J* = 16.4, H-6), 2.31 (d, 1, *J* = 16.4, H-6), 2.02-1.86 (m, 4, H-3 and C*H*$_2$CH=C), 1.67 (br s, 3), 1.58 (br s, 3), 1.40-1.36 (m, 2), 1.04 (s, 3); ^{13}C NMR 198.4, 155.9 (q, 1, *J* = 36.4, CF_3*C*O), 151.5, 131.2, 124.5, 123.9, 115.9 (q, 1, *J* = 286, *C*F_3), 49.3, 45.2 (q, 1, *J* = 3.8, CF_3CONCH_2), 41.1, 40.8, 36.4, 25.6, 24.7, 22.4, 22.3, 20.0, 17.5; IR 3010, 1738, 1704, 1666, 1628 (wk), 1204, 1143, 914, 752.

(±)-(5a*R*,6*S*,8a*R*)-2,3,4,5a,7,8,8a,9-Octahydro-8a-methyl-6-(1-methylethenyl)-1-trifluoroacetyl-6*H*-cyclopenta[*g*]quinolin-5(1*H*)-one (20) and (±)-(5a*R*,6*S*,8a*R*)-2,3,4,5a,7,8,8a,9-Octahydro-8a-methyl-6-(1-acetoxy-1-methylethyl)-1-trifluoroacetyl-6*H*-cyclopenta[*g*]quinolin-5(1*H*)-one (21). A solution of **17** (103 mg, 0.30 mmol) in 4 mL of benzene and dried $Mn(OAc)_3$ (313 mg, 1.35 mmol, 4.5 equiv) were added to a resealable tube. The reaction mixture was sealed and heated at 130 °C for 132 h. The reaction mixture was cooled to room temperature and 10% aq. $NaHSO_3$ solution (10 mL) was added. The mixture was extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. Flash chromatography of the residue on silica gel (9:1 hexanes/EtOAc) gave 62 mg (61%) of **20** as a colorless oil, followed by 8 mg (8%) of recovered **17**, and 6 mg (5%) of **21** as a white solid.

Data for **20**: ^{1}H NMR 4.79-4.73 (m, 2), 3.92 (br ddd, 1, *J* = 12.8, 4.0, 4.0, H-2), 3.39 (ddd, 1, *J* = 12.8, 10.4, 2.6, H-2), 3.16 (ddd, 1, *J* = 17.6, 3.0, 3.0, H-9), 2.91 (ddd, 1, *J* = 11.2, 10.4, 7.2, H-6), 2.40-2.32 (m, 2, H-4), 2.35 (d, 1, *J* = 11.2, H-5a), 2.28 (d, 1, *J* = 17.6, H-9), 2.15-1.98 (m, 2, H-3, H-7), 1.91-1.79 (m, 1, H-3), 1.77 (br s, 3), 1.74-1.64 (m, 2, H-7, H-8), 1.64-1.52 (m, 1, H-8), 1.14 (s, 3); ^{13}C NMR 199.3, 156.0 (q, 1, *J* = 36.4, CF_3*C*O), 150.4, 145.3, 123.0, 115.9 (q, 1, *J* = 287, *C*F_3), 111.9, 59.0, 50.6, 45.5, 45.2 (q, 1, *J* = 3.8, CF_3CONCH_2), 39.1, 37.1, 29.3, 25.4, 22.5, 20.1, 18.9; IR 3070, 3007, 1737 (wk), 1703, 1660,

1628 (wk), 1203, 1145, 913, 750; HRMS (ESI) calcd for $C_{18}H_{23}F_3NO_2$ (MH^+) 342.1681, found 342.1674. A 2D NOESY experiment showed strong NOEs between H-5a at δ 2.35 and both the alkenyl hydrogens at δ 4.79-4.73 and the upfield methyl group at δ 1.14 and a weak NOE between the alkenyl hydrogens and the upfield methyl group.

Data for **21**: mp 91-92 °C; ^{1}H NMR 3.80 (br ddd, 1, *J* = 13.2, 5.2, 3.0, H-2), 3.50 (ddd, 1, *J* = 13.2, 9.2, 2.8, H-2), 3.07 (ddd, 1, *J* = 18.0, 3.0, 3.0, H-9), 2.88 (ddd, 1, *J* = 10.4, 10.4, 7.2, H-6), 2.57-2.45 (m, 1, H-4), 2.41 (br d, 1, *J* = 18.0, H-9), 2.33 (d, 1, *J* = 10.4, H-5a), 2.25-2.15 (m, 1, H-4), 2.04-1.86 (m, 3, 2 H-3, H-7), 1.92 (s, 3), 1.72-1.56 (m, 2, H-7, H-8), 1.49 (s, 3), 1.47 (s, 3), 1.5-1.4 (m, 1, H-8), 1.13 (s, 3); ^{13}C NMR 201.3, 170.5, 156.0 (q, 1, *J* = 37.2, CF_3CO), 149.6, 123.1, 115.9 (q, 1, *J* = 287, CF_3), 83.8, 57.4, 51.8, 45.9, 45.2 (q, 1, *J* = 3.4, CF_3CONCH_2), 38.7, 36.6, 26.0, 25.3, 24.9, 23.0, 22.5, 22.4, 20.5; IR 1731, 1708, 1666, 1632 (wk), 1205, 1160, 918, 749; HRMS (ESI) calcd for $C_{20}H_{27}F_3NO_4$ (MH^+) 402.1892, found 402.1886.

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