after evaporation of the solvent was purified by two passes through a Chromatatron silica gel plate, using first 4:1 hexane–ethyl acetate and then 10:1 CH_2Cl_2–hexane. The yield of **15** was 16 mg (12%): ^1H NMR δ 1.19 (t, J = 7.1 Hz, 3 H), 3.34 (s, 3 H), 3.89 (d, J = 8.7 Hz, 1 H), 4.06 (m, 2 H), 4.58 (d, J = 8.7 Hz, 1 H, exchanged with D_2O), 7.2–7.5 (m, 5 H); ^{13}C NMR δ 14.0, 38.2, 62.0, 69.2, 127.7, 128.6, 129.8, 141.6, 168.1, 170.0; MS 237 (M^+, 10), 164 (M – CO_2Et, 16), 134 (M – CH(OH)CO_2Et, 100); HR-MS calcd 237.10015, found 237.0961.

Registry No. **3a**, 38118-69-3; **3b**, 124069-95-0; **3c**, 38118-73-9; **3d**, 124069-96-1; **3e**, 124069-97-2; **4a**, 124043-91-0; **4b**, 124070-01-5; **4c**, 124070-02-6; **4d**, 124070-03-7; **4e**, 124070-04-8; **9**, 124069-98-3; **10**, 124070-05-9; **11**, 22760-66-3; **12**, 124070-06-0; **14**, 124069-99-4; **15**, 124070-00-4; PhNHMe, 100-61-8; PhNHPh, 122-39-4; *m*-$ClC_6H_4NHCH_2Ph$, 50798-95-3; *m*-$NO_2C_6H_4NHCH_2Ph$, 33334-94-0; $PhNH_2$, 62-53-3; *p*-$MeC_6H_4SO_2N_3$, 941-55-9; Rh_2OAc_4, 15956-28-2; *N*,2-dimethyl-4-methoxyaniline, 86735-53-7; 1,2,3,4-tetrahydroquinoline, 635-46-1; diketene, 674-82-8.

Synthesis of (±)-Frullanolide: An Application of Radical Closure

Derrick L. J. Clive* and Antonio C. Joussef

Chemistry Department, University of Alberta, Edmonton, Alberta, Canada T6G 2G2

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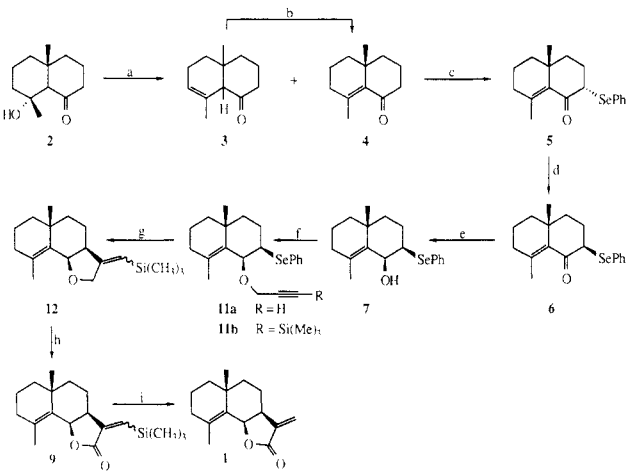
The sesquiterpene, frullanolide (**1**), is an allergy-producing substance that occurs in certain plants of the *Frullania* genus.[1] Several syntheses of this compound have been described;[2] we report here a new route in which radical cyclization is the essential step for constructing the α-methylene γ-lactone unit.

The bicyclic ketone **4** (Scheme I) is a known compound,[3] and its carbon skeleton represents a substructure of frullanolide. We sought, therefore, to develop a method, applicable to ketone **4**, for generating the γ-lactone[4] of the natural product.

A mixture of the isomeric ketones **3** and **4** was prepared along the lines described in the literature via the racemic tertiary alcohol **2**.[3] We used *p*-toluenesulfonic acid for catalytic dehydration of the intermediate tertiary alcohol **2** and, in contrast to the reported[3] use of thionyl chloride, this procedure gives the conjugated isomer **4** as the major product. The two ketones are separable by flash chromatography, and the minor component **3** can be isomerized to the desired ketone **4** by the action of rhodium trichloride trihydrate, optimally, in 2:8 ethanol–benzene at reflux. The equilibration gives a mixture of **3** and **4** in a 1:2 ratio, and the required material can be isolated easily.

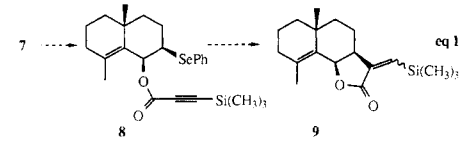
Kinetic deprotonation of **4**, and treatment of the enolate with phenylselenenyl chloride, affords the α-(phenylseleno) ketone **5**. When this, in turn, is deprotonated and reprotonated with saturated aqueous ammonium chloride, it is converted into the β-isomer **6**, which has the phenylseleno group in the equatorial conformation required for the next step. This involves reduction of the carbonyl so as to generate alcohol **7**. Reduction of α-(phenylseleno) ketones is known[5] to present difficulties as there is a tendency for the phenylseleno group to be lost and, of several common hydride reducing agents that we examined, only diisobutylaluminum hydride was effective.[5]

Scheme I[a]



[a] (a) 76% from 3-(4-oxopentyl)-2-cyclohexen-1-one; (b) $RhCl_3 \cdot 3H_2O$; (c) LDA; PhSeCl; 82%; (d) LDA; NH_4Cl; 71% from **4**; (e) DIBAL; 70%; (f) NaH; 3-bromo-1-(trimethylsilyl)-1-propyne; 69% of **11b**; (g) Ph_3SnH, AIBN; (h) CrO_3–pyridine; 52% from **11b**; (i) PhSH, Et_3N; Bu_4NF, methylacrylate; 68% from **9**.

We had intended to acylate the alcohol (**7** → **8**; eq 1) so that the synthesis could be completed by radical cyclization of the resulting ester (**8** → **9** → **1**; eq 1). Analogous clo-



sures of simple crotonic[6] and propiolic[7] esters are known, but the method could not be applied here because we were unable to acylate the hydroxyl group. We treated alcohol **7** in ether or dichloromethane with propiolic acid, DCC, and DMAP[8] but observed only loss of the phenylseleno group. 3-(Trimethylsilyl)-2-propynoic acid[9] and 3-(phenylthio)-2-propenoic acid[10] failed to react under similar conditions, or when the standard[11] procedure using 2-chloro-*N*-methylpyridinium iodide was applied.

We also examined the possibility of using (phenylseleno) alcohol **10** (eq 2), which was readily made by DIBAL reduction of **5**. However, application of the Mitsunobu reaction with 3-(trimethylsilyl)-2-propynoic acid or with 3-(phenylthio)-2-propenoic acid was not successful. The

(1) (a) Knocke, H.; Ourisson, G.; Perold, G. W.; Foussereau, J.; Maleville, J. *Science* **1969**, *166*, 239. (b) Perold, G. W.; Muller, J.-C.; Ourisson, G. *Tetrahedron* **1972**, *28*, 5797.

(2) (a) Greene, A. E.; Muller, J.-C.; Ourisson, G. *Tetrahedron Lett.* **1972**, 2489. (b) Greene, A. E.; Muller, J.-C.; Ourisson, G. *J. Org. Chem.* **1974**, *39*, 186. (c) Still, W. C.; Schneider, M. J. *J. Am. Chem. Soc.* **1977**, *99*, 948. (d) Kido, F.; Maruta, R.; Tsutsumi, K.; Yoshikoshi, A. *Chem. Lett.* **1979**, 311. (e) Kido, F.; Maruta, R.; Tsutsumi, K.; Yoshikoshi, A. *J. Am. Chem. Soc.* **1979**, *101*, 6420. (f) Semmelhack, M. F.; Brickner, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3945. (g) Petragnani, N.; Ferraz, H. M. C.; Yonashiro, M. *Synthesis* **1985**, 27.

(3) Näf, F.; Decorzant, R.; Thommen, W. *Helv. Chim. Acta* **1975**, *58*, 1808.

(4) (a) Grieco, P. A. *Synthesis* **1975**, 67. (b) Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94. (c) Petragnani, N.; Ferraz, H. M. C.; Silva, G. V. J. *Synthesis* **1986**, 157.

(5) Jacobi, P. A.; Kaczmarek, C. S. R.; Udodong, U. E. *Tetrahedron* **1987**, *43*, 5475. Other reducing reagents, such as $NaBH_4$, $NaBH(OAc)_3$, LAH, L-Selectride, $NaBH_4$–$CeCl_3 \cdot 6H_2O$ caused appreciable loss of the phenylseleno group.

(6) Clive, D. L. J.; Beaulieu, P. L. *J. Chem. Soc., Chem. Commun.* **1983**, 307.

(7) Cheshire, D. R. Ph.D. Thesis, University of Alberta, 1987. Haaima, G.; Weavers, R. T. *Tetrahedron Lett.* **1988**, *29*, 1085.

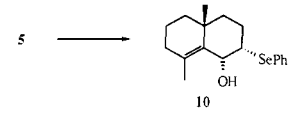
(8) (a) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522. (b) Ziegler, F. E.; Berger, G. D. *Synth. Commun.* **1979**, *9*, 539.

(9) Nicolaou, K. C.; Li, W. S. *J. Chem. Soc., Chem. Commun.* **1985**, 421.

(10) Proust, S. M.; Ridley, D. D. *Aust. J. Chem.* **1984**, *37*, 1677.

(11) Saigo, K.; Usui, M.; Kikuchi, K.; Shimada, E.; Mukaiyma, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1863.

0022-3263/90/1955-1096$02.50/0



10 eq 2

former experiment gave the trimethylsilyl ether corresponding to **10** ($OSiMe_3$ instead of OH in eq 2), while only starting alcohol **10** was recovered from the latter.

We were, however, able to alkylate the hydroxyl group of **7** with 3-bromo-1-(trimethylsilyl)-1-propyne[12] to form the acetylenic ether **11b** (see Scheme I). Some loss of the silicon protecting group occurs during the alkylation, but we did not replace the silicon unit as the yield of **11b** was satisfactory. Radical closure of **11a** was unpromising,[13] but closure of **11b** gave the desired heterocycle **12** as a mixture of geometric isomers, and oxidation with Collins' reagent led to lactone **9**. The synthesis was then completed by removing the silicon protecting group.[14]

Experimental Section

General. The same experimental techniques were used as reported previously.[15]

3-(4-Oxopentyl)-2-cyclohexen-1-one.[3] This compound was prepared (80% yield) by reaction of the Grignard reagent[16] derived from 2-(3-bromopropyl)-2-methyl-1,3-dioxolane[17-19] with 3-ethoxy-2-cyclohexenone.

3,4,4a,5,6,8a-Hexahydro-4a,8-dimethyl-1(2*H*)-naphthalenone (3) and 3,4,4a,5,6,7-Hexahydro-4a,8-dimethyl-1(2*H*)-naphthalenone (4).[3] Methyllithium (1.4 M in ether, 47.3 mL, 66.16 mmol) was added over about 10 min to a stirred and cooled (−78 °C) suspension of copper(I) iodide[20] (6.3 g, 33.08 mmol) in ether (136 mL). The cold bath was exchanged for one at −15 °C, and, after 15 min, the original cold bath (−78 °C) was replaced. A solution of the above diketone (4.91 g, 27.28 mmol) in ether (73 mL) was added with stirring over about 20 min. The mixture was stirred at −78 °C for a further 1.5 h and then at ice-bath temperature for 1 h, and it was then poured into ice-cold hydrochloric acid (400 mL, 1 N) and stirred for 15 min. The mixture was adjusted to pH 8 (concentrated ammonium hydroxide), and the aqueous phase was extracted with ether (2 × 100 mL). The combined extracts were washed with water (2 × 100 mL), dried (Na_2SO_4), and evaporated. The residue in benzene (400 mL), containing *p*-toluenesulfonic acid monohydrate (10 g) and 3-Å molecular sieves, was stirred and refluxed for 4 h under argon. The mixture was filtered, washed with saturated aqueous sodium bicarbonate (2 × 100 mL) and water (2 × 100 mL), dried ($MgSO_4$), and evaporated. Flash chromatography (carried out three times) of the residue over silica gel (5 × 20 cm) with 3% ethyl acetate–hexane afforded **3** (1.08 g, 22%) and **4** (2.60 g, 54%). Compound **3** was a pale yellow, homogeneous (TLC, silica, 3% ethyl acetate–hexane) oil: FT-IR ($CHCl_3$ cast) 1711, 1640, 797 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.00 (s, 3 H), 1.13–1.24 (quintet, J = 6.5 Hz, 1 H), 1.40–1.55 (sextet, J = 6.5 Hz, 2 H), 1.61 (br s, $W_{1/2}$ = 5.2 Hz, 3 H), 1.74–1.92 (m, 3 H), 1.96–2.23 (m, 2 H), 2.28 (t, J = 6.5 Hz, 2 H), 2.55 (br s, 1 H), 5.51 (br s, 1 H); exact mass, m/z calcd for $C_{12}H_{18}O$ 178.1358, found 178.1357. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.94; H, 10.14.

Compound **4** was a white, homogeneous (TLC, silica, 3% ethyl acetate–hexane) solid: mp 45–47 °C; FT-IR ($CHCl_3$ cast) 1689, 1627 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.99 (s, 3 H), 1.36–1.50 (m, 1 H), 1.53–1.70 (m, 5 H), 1.74 (s, 3 H), 1.80–2.13 (m, 4 H), 2.31 (ddd, J = 15.0, 12.5, 7.5 Hz, 1 H), 2.44–2.54 (m, 1 H); exact mass, m/z calcd for $C_{12}H_{18}O$ 178.1358, found 178.1360. Anal. Calcd for $C_{12}H_{18}O$; C, 80.85; H, 10.18. Found: C, 80.94; H, 10.19.

Isomerization of 3 to 4. A solution of **3** (80 mg, 0.449 mmol) in 20% ethanol–benzene (8 mL), containing a catalytic amount of rhodium trichloride trihydrate (ca. 2 mg) was refluxed for 28 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 18 cm) with 5% ethyl acetate–hexane afforded a mixture (79 mg, 0.443 mmol, 99%) of **4** and **3** in a ratio (^1H NMR) of 2:1. This procedure was used to recycle compound **3** from previous experiments, and the desired isomer **4** was isolated by flash chromatography over silica gel with 3% ethyl acetate–hexane.

(2*R*,*cis*)- and (2*S*,*cis*)-3,4,4a,5,6,7-Hexahydro-4a,8-dimethyl-2-(phenylseleno)-1(2*H*)-naphthalenone (6) and (2*R*,*trans*)- and (2*S*,*trans*)-3,4,4a,5,6,7-Hexahydro-4a,8-dimethyl-2-(phenylseleno)-1(2*H*)-naphthalenone (5). A solution of **4** (248 mg, 1.39 mmol) in THF (2 mL plus 0.5 mL as a rinse) was injected over 5 min into a stirred solution of LDA [from diisopropylamine (0.24 mL, 1.7 mmol) and *n*-butyllithium (1.59 M in hexanes, 1.05 mL, 1.65 mmol)] in THF (10 mL) at −78 °C. Stirring was continued for 15 min, and phenylselenenyl chloride (350 mg, 1.83 mmol) in THF (1 mL) was then injected in one portion. The mixture was stirred for 20 min at −78 °C and transferred by cannula over 20 min to a stirred and cooled (−78 °C) solution of LDA, prepared on the same scale as described above. Stirring was continued at −78 °C for 30 min, and the reaction was quenched with saturated aqueous ammonium chloride (10 mL). The mixture was allowed to warm to room temperature and was then extracted with ether (3 × 30 mL). The combined extracts were washed with brine (50 mL) and water (3 × 50 mL), dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (3 × 18 cm) with 4% ethyl acetate–hexane yielded the β isomer **6** (330 mg, 71%) as a homogeneous (TLC, silica, 5% ethyl acetate–hexane) orange oil, and the α isomer **5** (54 mg, 12%) as a homogeneous (TLC, silica, 5% ethyl acetate–hexane), pale yellow solid. The β isomer **6** had the following properties: FT-IR ($CHCl_3$ cast) 1678, 1625 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.96 (s, 3 H), 1.30–1.48 (m, 1 H), 1.52–1.60 (m, 5 H), 1.74 (s, 3 H), 2.00–2.20 (m, 4 H), 4.18 (dd, J = 12.5, 7.5 Hz, 1 H), 7.20–7.35 (m, 3 H), 7.55–7.60 (m, 2 H); exact mass, m/z calcd for $C_{18}H_{22}OSe$ 334.0836, found 334.0833. Anal. Calcd for $C_{18}H_{22}OSe$: C, 64.86; H, 6.65; O, 4.80. Found: C, 64.94; H, 6.74; O, 4.92.

The α isomer **5** had the following properties: mp 70–73 °C; FT-IR ($CHCl_3$ cast) 1673, 1625 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.0 (s, 3 H), 1.41–1.70 (m, 5 H), 1.73 (s, 3 H), 1.81 (dt, J = 14.0, 4.0 Hz, 1 H), 2.05–2.25 (m, 3 H), 2.55 (ddt, J = 14.0, 4.5, 4.0 Hz, 1 H), 3.91 (dt, J = 4.5, 1.5 Hz, 1 H), 7.20–7.35 (m, 3 H), 7.50–7.61 (m, 2 H); exact mass, m/z calcd for $C_{18}H_{22}OSe$ 334.0836, found 334.0835. Anal. Calcd for $C_{18}H_{22}OSe$: C, 64.86; H, 6.65; O, 4.80. Found: C, 64.70; H, 6.69; O, 5.07.

[1*R*-(1α,2α,4aα)]- and [1*S*-(1α,2α,4aα)]-1,2,3,4,4a,5,6,7-Octahydro-4a,8-dimethyl-2-(phenylseleno)-1-naphthalenol (7). Diisobutylaluminum hydride (1.0 M solution in hexane, 4.66 mL, 4.66 mmol) was added over 35 min to a stirred and cooled (−78 °C) solution of **6** (775 mg, 2.33 mmol) in toluene (28 mL). Stirring was continued for a further 3 h at −78 °C, and then methanol (5 mL) was added followed by aqueous acetic acid (50% v/v, 2 mL). The cold bath was then removed, and, after 2 h, the solvents were evaporated. The residue was extracted with 10% ethyl acetate–hexane (3 × 20 mL), and the combined organic extracts were washed with water (2 × 20 mL), dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (4 × 18 cm) with 5% ethyl acetate–hexane afforded **7** (546 mg, 70%) as a homogeneous (TLC, silica, 5% ethyl acetate–hexane), pale yellow oil: FT-IR ($CDCl_3$ cast) 3470, 1625 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.18–1.33 (m, 5 H), 1.41 (dt, J = 13.0, 3.5 Hz, 1 H), 1.50–1.84 (series of m, 7 H), 1.88–2.10 (m, 2 H), 2.22 (dq, J = 13.0, 3.5 Hz, 1 H), 2.23 (br s, 1 H), 3.33 (ddd, J = 13.0, 4.0, 3.0 Hz, 1 H), 4.71 (br s, 1 H), 7.22–7.30 (m, 3 H), 7.52–7.61 (m, 2 H); exact mass, m/z calcd for $C_{18}H_{24}OSe$ 336.0992, found 336.1000. Anal. Calcd for $C_{18}H_{24}OSe$: C, 64.47; H, 7.26. Found: C, 64.48; H, 7.14.

(2*R*,*trans*)- and (2*S*,*trans*)-3,4,4a,5,6,7-Hexahydro-4a,8-dimethyl-2-(phenylseleno)-1(2*H*)-naphthalenone (5). A solution of **4** (178.14 mg, 1 mmol) in THF (2 mL) was added over 30 min to a stirred and cooled (−78 °C) solution of LDA [from

(12) Miller, R. B. *Synth. Commun.* **1972**, *2*, 267.
(13) Cf.: Srikrishna, A. *J. Chem. Soc., Chem. Commun.* **1987**, 587.
(14) Bachi, M. D.; Bosch, E. *Tetrahedron Lett.* **1988**, *29*, 2581.
(15) Clive, D. L. J.; Boivin, T. L. B. *J. Org. Chem.* **1989**, *54*, 1997.
(16) Weill-Raynal, J. *Synthesis* **1969**, 49.
(17) Joss, U.; Schaltegger, H. *Helv. Chim. Acta* **1969**, *52*, 2465.
(18) Cannon, G. A.; Ellis, R. C.; Leal, J. R. *Org. Synth.* **1951**, *31*, 74.
(19) Johnson, W. M. *Chem. Abstr.* **1949**, *43*, 678i.
(20) (a) Kauffman, G. B.; Teter, L. A. *Inorg. Synth.* **1963**, *7*, 10. (b) Linstrumelle, G.; Krieger, J. K.; Whitesides, G. M. *Org. Synth.* **1976**, *55*, 108.

diisopropylamine (0.26 mL, 1.85 mmol) and *n*-butyllithium (1.59 M in hexanes, 1.06 mL, 1.69 mmol)] in THF (4 mL). Stirring was continued for a further 1.5 h at −78 °C and phenylselenenyl chloride (400 mg, 2.09 mmol) in THF (1 mL) was added in one portion. The cold bath was exchanged for one at −30 °C and, after 2 h, the reaction was quenched with glacial acetic acid (112 μL). Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 18 cm) with 4% ethyl acetate–hexane afforded **5** (273 mg, 82%) and **6** (46 mg, 14%).

[1*R*-(1α,2α,4aβ)]- and [1*S*-(1α,2α,4aβ)]-1,2,3,4,4a,5,6,7-Octahydro-4a,8-dimethyl-2-(phenylseleno)-1-naphthalenol (10). Diisobutylaluminum hydride (1.0 M solution in hexane, 2.65 mL, 2.65 mmol) was added over 20 min to a stirred and cooled (−78 °C) solution of **5** (493 mg, 1.48 mmol) in toluene (17 mL). Stirring was continued for a further 1 h at −78 °C, and then methanol (3 mL) was added, followed by aqueous acetic acid (50% v/v, 1 mL). The cold bath was then removed and, after 2 h, the solvents were evaporated. The residue was extracted with 10% ethyl acetate–hexane (3 × 20 mL), and the combined organic extracts were washed with water (2 × 20 mL), dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (2 × 18 cm) with 5% ethyl acetate–hexane afforded **10** (350 mg, 70%) as a homogeneous (TLC, silica, 5% ethyl acetate–hexane), pale yellow oil: FT-IR ($CHCl_3$ cast) 3470, 1650 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.07 (s, 3 H), 1.24–1.45 (m, 3 H), 1.54–2.15 (m, including a singlet at 1.76, 9 H), 2.18–2.34 (m, 1 H), 2.48 (d, J = 4.5 Hz, 1 H), 3.76 (dt, J = 7.5, 3.0 Hz, 1 H), 4.53 (br dd, J = 4.5, 3.0 Hz, 1 H), 7.20–7.32 (m, 3 H), 7.51–7.14 (m, 2 H); exact mass, m/z for $C_{18}H_{24}OSe$ 336.0992, found 336.1000. Anal. Calcd for $C_{18}H_{24}OSe$: C, 64.47; H, 7.26. Found: C, 64.72; H, 6.94.

[1*R*-(1α,2α,4aα)]- and [1*S*-(1α,2α,4aα)]-1,2,3,4,4a,5,6,7-Octahydro-4a,8-dimethyl-2-(phenylseleno)-1-[[3-(trimethylsilyl)-2-propynyl]oxy]naphthalene (11b) and [1*R*-(1α,2α,4aα)]- and [1*S*-(1α,2α,4aα)]-1,2,3,4,4a,5,6,7-Octahydro-4a,8-dimethyl-2-(phenylseleno)-1-(2-propynyloxy)-naphthalene (11a). Sodium hydride (60% dispersion in oil, 59.2 mg, 1.48 mmol) was added in one portion to a stirred solution of **7** (330 mg, 0.985 mmol) in THF (15 mL). Stirring at room temperature was continued for 20 min, and then 3-bromo-1-(trimethylsilyl)-1-propyne[12] (565 mg, 2.96 mmol) in THF (5 mL) was added rapidly. The mixture was heated at 60–62 °C for 21 h, and the solvent was then evaporated. Flash chromatography of the residue (carried out twice) over silica gel (2 × 18 cm) with hexane afforded the desilylated product **11a** (26 mg, 7%) as a colorless, homogeneous (TLC, silica, 2% ethyl acetate–hexane) oil, starting material **7** (36 mg, 11%), and **11b** (304 mg, 69%), which was a pale yellow, homogeneous (TLC, silica, hexane) solid: mp 93–94 °C; FT-IR ($CDCl_3$ cast) 3060, 2180, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.20 (s, 9 H), 1.22 (s, 3 H), 1.25–1.38 (dt, J = 13.0, 4.0 Hz, 2 H), 1.48 (dt, J = 13.0, 4.0 Hz, 1 H), 1.55–1.68 (dt, J = 13.0, 3.5 Hz, 2 H), 1.68–1.93 (m, including a singlet at 1.80, 5 H), 1.98–2.12 (m, 2 H), 2.37 (dq, J = 13.2, 3.5 hz, 1 H), 3.27 (ddd, J = 13.2, 4.0, 3.2 Hz, 1 H), 3.97 and 4.12 (AB q, J = 16.0 Hz, 2 H), 4.93 (d, J = 3.2 Hz, 1 H), 7.20–7.33 (m, 3 H), 7.54–7.67 (m, 2 H); exact mass, m/z calcd for $C_{24}H_{34}OSeSi$ 446.1544, found 446.1545. Anal. Calcd for $C_{24}H_{34}OSeSi$: C, 64.69; H, 7.69. Found: C, 64.04; H, 7.74.

Compound **11a** had the following properties: FT-IR ($CHCl_3$ cast) 3060, 2928, 1640 cm^{-1}; ^1H NMR (C_6D_6, 300 MHz) δ 1.03 (dq, J = 13.0, 3.5 Hz, 2 H), 1.14 (s, 3 H), 1.25 (dt, J = 13.0, 3.5 Hz, 1 H), 1.37 (dt, J = 13.0, 3.5 Hz, 2 H), 1.40–1.60 (m, including a singlet at 1.53, 4 H), 1.62–1.79 (m, 2 H), 1.90 (dq, J = 13.5, 3.5 Hz, 1 H), 2.01 (t, J = 2.5 Hz, 1 H), 2.54 (dq, J = 13.5, 3.5 Hz, 1 H), 3.23 (ddd, J = 13.0, 4.3, 3.2 Hz, 1 H), 3.75 and 3.94 (AB q, J = 15.5, 2.5 Hz, 2 H), 5.00 (d, J = 3.2 Hz, 1 H), 6.93–7.03 (m, 3 H), 7.55–7.62 (m, 2 H); exact mass, m/z for $C_{21}H_{26}OSe$ 374.1149, found 374.1150. Anal. Calcd for $C_{21}H_{26}OSe$: C, 67.55; H, 7.02; O, 4.29. Found: C, 67.43; H, 7.02; O, 4.59.

(*Z*)- and (*E*)-[3a*R*-(3aα,5aβ,9bα)]- and (*Z*)- and (*E*)-[3a*S*-(3aα,5aβ,9bα)]-3a,4,5,5a,6,7,8,9b-Octahydro-5a,9-dimethyl-3-[(trimethylsilyl)methylene]naphtho[1,2-*b*]furan-2(3*H*)-one (9). Triphenyltin hydride (132 mg, 0.377 mmol) in benzene (5 mL) and AIBN (2 mg, 0.0125 mmol) in the same solvent (5 mL) were added simultaneously over 8 h by double syringe pump to a stirred, refluxing solution of **11b** (140 mg, 0.314 mmol) in benzene (25 mL). Refluxing was continued for a further 6 h, and the solvent was then evaporated. Flash chromatography of the residue over silica gel (2 × 18 cm) with 2% ethyl acetate–hexane yielded a mixture of two products (111 mg), which was dissolved in dichloromethane (5 mL) and added over about 5 min to a stirred slurry of pyridine (0.64 mL, 7.89 mmol) and chromium trioxide (640 mg, 6.4 mmol) in dichloromethane (6.5 mL).[21] After 10 min (TLC control, silica, 5% ethyl acetate–hexane), the mixture was filtered through a pad of silica gel (2 × 3 cm), with dichloromethane (20 mL). The solvent was evaporated, and flash chromatography of the residue over silica gel (1 × 18 cm) with 2% ethyl acetate–hexane afforded the *E* and *Z* isomers of silyl lactone **9**: The *E* isomer (42 mg, 44%) was a colorless, homogeneous (TLC, silica, 2% ethyl acetate–hexane) oil: FT-IR ($CDCl_3$ cast) 1758, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.20 (s, 9 H), 1.08 (s, 3 H), 1.22–1.39 (m, 2 H), 1.41–1.53 (m, 2 H), 1.57–1.70 (m, 3 H), 1.76 (s, 3 H), 1.77–1.89 (m, 1 H), 2.06–2.13 (m, 2 H), 2.93–3.01 (m, 1 H), 5.19 (d, J = 5.5 Hz, 1 H), 6.79 (d, J = 1.0 Hz, 1 H); exact mass, m/z calcd for $C_{18}H_{28}O_2Si$ 304.1859, found 304.1851. The *Z* isomer (8.0 mg, 8%) was a white, homogeneous (TLC, silica, 2% ethyl acetate–hexane) solid: mp 90–94 °C; FT-IR ($CDCl_3$ cast) 1760, 1645 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.21 (s, 9 H), 1.08 (s, 3 H), 1.17–1.52 (m, 4 H), 1.58–1.69 (m, 3 H), 1.75 (s, 3 H), 1.77–1.90 (m, 1 H), 2.04–2.13 (m, 2 H), 2.73–2.85 (m, 1 H), 5.27 (d, J = 6.0 Hz, 1 H), 6.32 (d, J = 1.1 Hz, 1 H); exact mass, m/z calcd for $C_{18}H_{28}O_2Si$ 304.1859, found 304.1873. Anal. Calcd for $C_{18}H_{28}O_2Si$: C, 71.00; H, 9.27. Found: C, 70.22; H, 9.29.

[3a*R*-(3aα,5aβ,9bα)]- and [3a*S*-(3aα,5aβ,9bα)]-3a,4,5,5a,6,7,8,9b-Octahydro-5a,9-dimethyl-3-methylenenaphtho[1,2-*b*]furan-2(3*H*)-one [(±)-Frullanolide (1)]. A solution of the (*E*)- and (*Z*)-silyl lactones **9** (29.0 mg, 0.095 mmol), thiophenol (97.7 μL, 0.95 mmol), and triethylamine (132.4 μL, 0.95 mmol) in THF (4 mL) was stirred for 51 h at room temperature.[14] Evaporation of the solvent and flash chromatography of the residue over silica gel (1 × 18 cm) with 5% ethyl acetate–hexane afforded a mixture of isomers of the thiophenol adduct (32.8 mg, 0.08 mmol), which was dissolved in dry THF (4 mL). Tetrabutylammonium fluoride on silica gel (Fluka, 1.16 mmol of F^-/g, 138 mg, 0.16 mmol) and methyl acrylate (72 μL, 0.80 mmol) were added to this solution, and the mixture was stirred for 1 h.[14] Evaporation of the solvent and flash chromatography of the residue over silica gel (1 × 15 cm) with 5% ethyl acetate–hexane afforded (±)-frullanolide (**1**) (15.0 mg, 68%) as a white solid: mp 93–93.5 °C [lit.[2g] mp 93–93.5 °C]; FT-IR ($CDCl_3$ cast) 1760, 1660, 1640, 1285, 1145 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.08 (s, 3 H), 1.22–1.52 (m, 4 H), 1.59–1.74 (m, 3 H), 1.76 (s, 3 H), 1.78–1.89 (m, 1 H), 2.08–2.13 (m, 2 H), 2.91–2.99 (m, 1 H), 5.26 (d, J = 6.0 Hz, 1 H), 5.57 (d, J = 1.0 Hz, 1 H), 6.16 (d, J = 1.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75.47 MHz) δ 18.26, 19.43, 25.16, 25.90, 32.76, 33.24, 37.97, 39.24, 41.34, 75.97, 120.13, 128.65, 138.57, 142.41, 171.00; exact mass, m/z calcd for $C_{15}H_{20}O_2$ 232.1463, found 232.1457. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.29; H, 8.46.

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Registry No. (±)-**1**, 62860-37-1; (±)-**2**, 124127-97-5; (±)-**3**, 124127-98-6; (±)-**4**, 62335-54-0; (±)-**5**, 124127-99-7; (±)-**6**, 124128-00-3; (±)-**7**, 124128-01-4; (±)-**8**, 124128-02-5; (±)-(*E*)-**9**, 124128-03-6; (±)-(*Z*)-**9**, 124128-10-5; **9** thiophenol adduct, 124128-08-1; (±)-**10**, 124128-04-7; (±)-**11a**, 124128-05-8; (±)-**11b**, 124128-07-0; (±)-(*E*)-**12**, 124128-06-9; (±)-(*Z*)-**12**, 124128-09-2; $BrCH_2C{\equiv}CSiMe_3$, 38002-45-8; 2-(3-bromopropyl)-2-methyl-1,3-dioxolane, 24400-75-7; 3-ethoxy-2-cyclohexenone, 5323-87-5; 3-(4-oxopentyl)-2-cyclohexen-1-one, 57232-69-6.

Supplementary Material Available: Full data for characterization of 3-(4-oxopentyl)-2-cyclohexen-1-one and ^{13}C NMR spectral data for all compounds (where not already provided) (3 pages). Ordering information is given on any current masthead page.

(21) Okabe, M.; Abe, M.; Tada, M. *J. Org. Chem.* **1982**, *47*, 1775.