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Thiopyran Route to Polypropionates: An Efficient Synthesis of Serricornin

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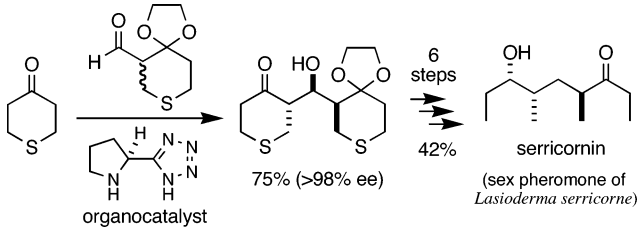
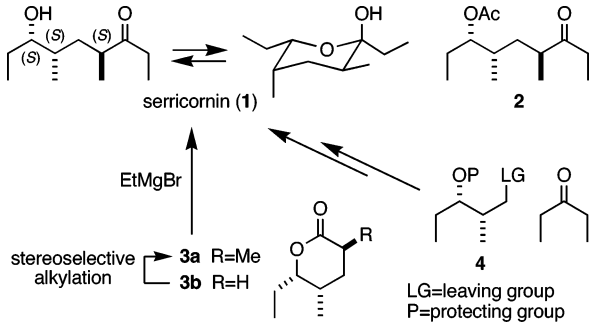


The synthesis of serricornin [(4*S*,6*S*,7*S*)-7-hydroxy-4,6-dimethylnonan-3-one], a sex pheromone produced by the female cigarette beetle (*Lasioderma serricorne* F.), in seven steps from readily available racemic 1,4-dioxa-8-thiaspiro-[4.5]decane-6-carboxaldehyde (**6**) is described. The key steps include enantioselective aldol reaction of **6** with tetrahydrothiopyran-4-one catalyzed by 5-[(2*S*)-pyrrolidine-2-yl]-1*H*-tetrazole to fabricate the tetrapropionate skeleton, stereoselective Li^{s}Bu$_3$BH reduction of the resulting aldol adduct, Barton−McCombie deoxygenation, and Raney nickel desulfurization.

Serricornin (**1**) is the sex pheromone of the female cigarette beetle (*Lasioderma serricorne* F.), a serious pest of cured tobacco leaves and various dried foodstuffs.[1] Because serricornin (**1**) exists as an equilibrium mixture of the ketol and cyclic hemiacetal forms,[2] it is often characterized as the corresponding acetate **2** (Scheme 1). The relative and absolute configuration of **1** was determined from a series of synthetic studies that produced all of the possible stereoisomers of **2**.[3] The attractant activity of **1** is at least 10^3 greater than any of the other stereoisomers, and the (4*S*,6*S*,7*R*)-diastereomer inhibits the activity of **1**.[4] The potential commercial value of **1** has prompted numerous synthetic studies.[5] The large majority of reported

SCHEME 1



stereoselective syntheses of **1** proceed either by addition of EtMgBr to the lactone **3a**[6,7] or by alkylation of 3-pentanone with a suitable derivative of **4**.[8,9]

We have been developing stereoselective stepwise two-directional aldol reactions of **5** and **6** as the foundation of a thiopyran-based synthetic route to polypropionates (Scheme 2).[10] In this regard, we recently reported that (*S*)-proline catalyzes an enantioselective direct aldol reaction of **5** with (±)-**6** that proceeds with dynamic kinetic resolution[11] to give adduct **9**

(1) Chuman, T.; Mochizuki, K.; Mori, M.; Kohno, M.; Kato, K.; Noguchi, M. *J. Chem. Ecol.* **1985**, *11*, 417−434.

(2) Mori, M.; Chuman, T.; Kato, K. *Tetrahedron Lett.* **1984**, *25*, 2553−2556.

(3) (a) Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M.; Nomi, H.; Mori, K. *Agric. Biol. Chem.* **1981**, *45*, 2019−2023. (b) Mori, K.; Nomi, H.; Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M. *Tetrahedron Lett.* **1981**, *22*, 1127−1130. (c) Mori, M.; Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M.; Nomi, H.; Mori, K. *Tetrahedron Lett.* **1982**, *23*, 667−670.

(4) Mochizuki, K.; Chuman, T.; Mori, M.; Kohno, M.; Kato, K. *Agric. Biol. Chem.* **1984**, *48*, 2833−2834. (b) Mori, M.; Mochizuki, K.; Kohno, M.; Chuman, T.; Ohnishi, A.; Watanabe, H.; Mori, K. *J. Chem. Ecol.* **1986**, *12*, 83−89.

(5) Review: Mori, K. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1992; Vol. 9, pp 1−534.

(6) (a) Takeda, Y.; Kobayashi, Y.; Sato, F. *Chem. Lett.* **1985**, 471−472. (b) Kobayashi, Y.; Kitano, Y.; Takeda, Y.; Sato, F. *Tetrahedron* **1986**, *42*, 2937−2943. (c) Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 651−654. (d) Miyashita, M.; Toshimitsu, Y.; Shiratani, T.; Irie, H. *Tetrahedron: Asymmetry* **1993**, *4*, 1573−1578. (e) Pilli, R. A.; Riatto, V. B. *J. Braz. Chem. Soc.* **1998**, *9*, 571−576. (f) Fujita, K.; Mori, K. *Biosci., Biotechnol., Biochem.* **2001**, *65*, 1429−1433. (g) Zlokazov, M. V.; Veselovsky, V. V. *Russ. Chem. Bull., Int. Ed.* **2002**, *51*, 1600−1604.

(7) Other syntheses of lactones **3a** or **3b**: (a) Redlich, H.; Samm, K.; Lenfers, J. B.; Bruns, W. *Carbohydr. Res.* **1988**, *174*, 341−348. (b) Takano, S.; Sekiguchi, Y.; Ogasawara, K. *Heterocycles* **1989**, *29*, 445−448. (c) Nguyen Cong, H.; Mavrov, M. V.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, 1361−1364. (d) Brandaenge, S.; Leijonmarck, H. *Tetrahedron Lett.* **1992**, *33*, 3025−3028. (e) Pilli, R. A.; de Andrade, C. K. Z. *Synth. Commun.* **1994**, *24*, 233−241. (f) Ferreira, J. T. B.; Marques, J. A.; Marino, J. P. *Tetrahedron: Asymmetry* **1994**, *5*, 641−648. (g) Ha, H.-J.; Yim, Y.-G. *Synth. Commun.* **2000**, *30*, 581−586.

(8) Stereoselective alkylation of 3-pentanone with **4** is achieved via the SAMP hydrazone derivative: (a) Mori, K.; Nomi, H.; Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M. *Tetrahedron* **1982**, *38*, 3705−3711. (b) Job, A.; Nagelsdiek, R.; Enders, D. *Collect. Czech. Chem. Commun.* **2000**, *65*, 524−538. Because the (4*R*,6*S*,7*S*)-diastereomer is not biologically active and can be separated from **1** by silica gel chromatography, several authors have employed nonstereoselective alkyations of 3-pentanone with **4** to give ca. 1:1 mixtures of (4*R*) and (4*S*) products: (c) Baker, R.; Devlin, J. A. *J. Chem. Soc., Chem. Commun.* **1983**, 147−148. (d) Hoffmann, R. W.; Ladner, W.; Helbig, W. *Liebigs Ann. Chem.* **1984**, 1170−1179. (e) Mori, K.; Watanabe, H. *Tetrahedron* **1985**, *41*, 3423−3428. (f) Chan, P. C. M.; Chong, J. M.; Kousha, K. *Tetrahedron* **1994**, *50*, 2703−2714. (g) Hayakawa, R.; Shimizu, M. *Synlett.* **1999**, 1298−1300. Other syntheses of **4**: (h) Fujisawa, T.; Tajima, K.; Sato, T. *Chem. Lett.* **1984**, 1669−1672. (i) Oppolzer, W.; Blagg, J.; Rodriguez, I.; Walther, E. *J. Am. Chem. Soc.* **1990**, *112*, 2767−2772. (j) Szurdoki, F.; Novak, L.; Baitz-Gacs, E.; Szantay, C. *Acta Chim. Hung.* **1992**, *129*, 303−309. (k) DiBattista, J. P.; Webster, F. X. *Bioorg. Med. Chem* **1996**, *4*, 423−428.

(9) Other syntheses of **1**: (a) Mori, M.; Chuman, T.; Kato, K.; Mori, K. *Tetrahedron Lett.* **1982**, *23*, 4593−4596. (b) Shimizu, I.; Hayashi, K.; Ide, N.; Oshima, M. *Tetrahedron* **1991**, *47*, 2991−2998. (c) Matteson, D. S.; Singh, R. P.; Schafman, B.; Yang, J.-j. *J. Org. Chem.* **1998**, *63*, 4466−4469.

(10) (a) Ward, D. E.; Man, C. C.; Guo, C. *Tetrahedron Lett.* **1997**, *38*, 2201−2202. (b) Ward, D. E.; Guo, C.; Sasmal, P. K.; Man, C. C.; Sales, M. *Org. Lett.* **2000**, *2*, 1325−1328. (c) Ward, D. E.; Sales, M.; Man, C. C.; Shen, J.; Sasmal, P. K.; Guo, C. *J. Org. Chem.* **2002**, *67*, 1618−1629. (d) Ward, D. E.; Gillis, H. M.; Akinnusi, O. T.; Rasheed, M. A.; Saravanan, K.; Sasmal, P. K. *Org. Lett.* **2006**, *8*, 2631−2634.

(11) Pellissier, H. *Tetrahedron* **2003**, *59*, 8291−8327.

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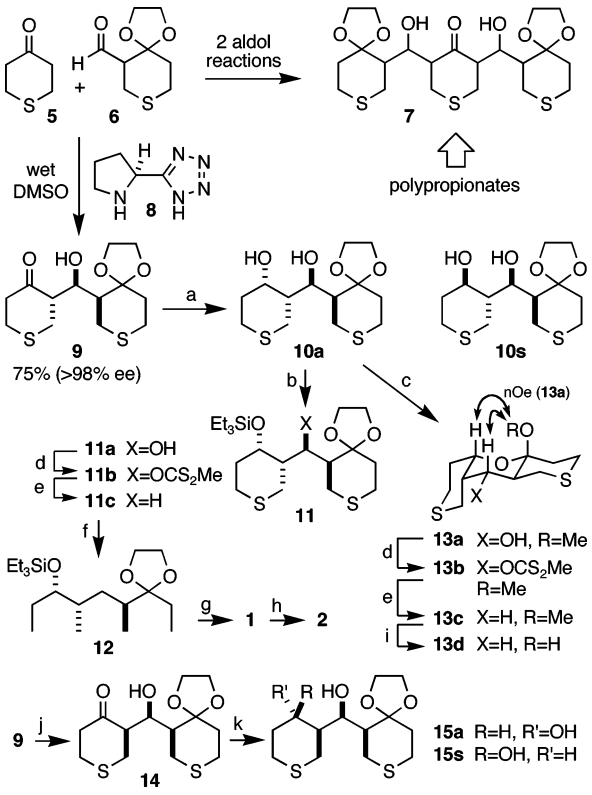
SCHEME 2 [a]



[a] Reagents and conditions: (a) Li^{s}Bu$_3$BH, THF, −78 °C (83%); (b) Et$_3$SiOTf, 2,6-lutidine, CH_2Cl_2, 0 °C (97%); (c) HCl, MeOH (95%); (d) NaH, CS_2, MeI (93%); (e) Bu$_3$SnH, AIBN, PhMe, 110 °C (91−97%); (f) Raney-Ni, EtOH, reflux (82%); (g) HOAc, CH_2Cl_2; (h) AcCl, DMAP, CH_2Cl_2 (72% from **11**) ; (i) HOAc, H_2O, THF, 50 °C (94%); (j) Et_3N, SiO_2, EtOAc (78%, 2 cycles); (k) DIBALH (**14s**, 92%)[10c] or Na(OAc)$_3$BH (**14a**, 92%).

(>98% ee).[12] In this paper, we describe an improved synthesis of **9** and its efficient conversion into serricornin (**1**) and **2**.

Our reported procedure for the (*S*)-proline-catalyzed (0.5 equiv) aldol reaction of **5** (6 equiv) with **6** (1 M in DMSO with 8 equiv of H_2O) gives **9** as a single isomer in 55−60% yield on 1 g scale (Scheme 2).[12] On larger scale the reaction work up is complicated by the need to remove large amounts of **5** by sublimation or chromatography. All attempts to reduce the amount of **5** used in the reaction gave **9** in lower yield and/or enantioselectivity. Interestingly, reactions in the absence of solvent were much less enantioselective than those in DMSO. These reactions were exceedingly slow at room temperature; however, sonication of a mixture of **6**, **5** (1.5 equiv), (*S*)-proline (0.5 equiv), and water (1 equiv) for 60 h at 38 °C gave **9** as the sole aldol diastereomer in 80% yield but in <20% optical purity.[13] We also investigated the more soluble catalyst **8** developed independently by the Ley, Yamamoto, and Arviddson groups.[14] Under optimized conditions (**5**, 2 equiv; DMSO, 1.5 equiv; **8**, 0.2 equiv; room temperature, 8 d), **9** (>98% ee) was obtained in 75% yield from **6** (1 g scale). Reactions run at lower concentrations (e.g., 1 M in DMSO) gave yields of up to 85% but required a large excess of **5** (6−12 equiv).

Aldol adduct **9** contains the complete carbon skeleton of **1**, and the synthesis requires only functional group manipulations: deoxygenation of the alcohol, stereoselective reduction of the ketone, desulfurization, and hydrolysis of the ethylene acetal (Scheme 2). Stereoselective reduction of **9** with DIBALH is known[10c] to give the undesired *syn*-1,3-diol **10s**, and attempted reduction with Na(OAc)$_3$BH[15] (usually 1,3-*anti* selective in these systems)[10c] gave poor selectivity (1:1.5 **10a**:**10s**). The desired *anti*-1,3-diol **10a** was obtained in good yield by reaction of **9** with Li^{s}Bu$_3$BH (Scheme 2).[16] The secondary hydroxy groups in **10a** were readily differentiated by treatment with HCl in methanol to give the cyclic acetal **13a**. Deoxygenation of **13a** was achieved by treatment of its xanthate derivative **13b** with Bu$_3$SnH to give **13c** (80% yield over two steps).[17] Unfortunately, attempted Raney nickel desulfurization of **13c** (or **13d**) was capricious, and we were unable to isolate the desired product in any significant amount.[18]

Alternatively, reaction of diol **10a** with Et_3SiOTf gave the mono silyl ether **11a** in excellent yield (Scheme 2). Barton−McCombie deoxygenation[17] of **11a** gave **11c** that was smoothly desulfurized by treatment with Raney nickel (W-2) in refluxing ethanol to give the desired serricornin derivative **12** (73% over three steps). Exposure of **12** to mild acid gave serricornin (**1**) that was isolated and characterized as the acetate derivative **2** (71% over two steps). The spectral properties and specific rotation of **2** were fully consistent with those reported previously.[1,6]

In summary, serricornin (**1**) was prepared in seven steps from the readily available aldehyde (±)-**6**[10c] (31% overall yield). The key step involves the catalytic enantioselective direct aldol reaction of **6** with **5** that occurs with dynamic kinetic resolution to give adduct **9** in excellent yield and enantiopurity. It is noteworthy that diols **10s**, **15a**, and **15s** are also readily prepared from **9**;[10c,19] thus, the same strategy might be extended to afford each of the possible stereoisomers of **1**.

Experimental Section[20]

(3*S*)-3-[(*R*)-(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]dec-6-yl(hydroxy)-methyl]tetrahydro-4*H*-thiopyran-4-one (9). A solution of ketone **5** (1.25 g, 10.8 mmol), aldehyde **6** (1.01 g, 5.37 mmol), catalyst **8** (145 mg, 1.04 mmol), water (0.10 mL, 0.10 g, 5.6 mmol), and DMSO (0.6 mL) was stirred at room temperature. After 8 days, the brownish semisolid reaction mixture was taken up in ethyl acetate and washed with water. The organic layer was dried over Na_2SO_4, concentrated, and fractionated by FCC (5−10% ethyl

(12) Ward, D. E.; Jheengut, V.; Akinnusi, O. T. *Org. Lett.* **2005**, *7*, 1181−1184.

(13) This constitutes a very convenient procedure for the diastereoselective synthesis of (essentially) racemic **9** that can be used to prepare a C_s symmetric (meso) diastereomer of **7** (see ref 10).

(14) (a) Cobb, A. J. A.; Shaw, D. M.; Ley, S. V. *Synlett.* **2004**, 558−560. (b) Torii, H.; Nakadai, M.; Ishihara, K.; Saito, S.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 1983−1986. (c) Hartikka, A.; Arvidsson, P. I. *Tetrahedron: Asymmetry* **2004**, *15*, 1831−1834. (d) Hartikka, A.; Arvidsson, P. I. *Eur. J. Org. Chem.* **2005**, 4287−4295.

(15) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560−3578.

(16) The relative configuration in **10a** was assigned by ^{1}H NMR based on the H-C-C-H vicinal coupling constants (2.5, 3, 7 Hz) for the thiopyran carbinol proton (HC-4′).

(17) (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. I* **1975**, 1574−1585. (b) McCombie, S. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 8, Chapter 4.2.

(18) The expected products (e.g. **1**) are very volatile. For an example of successful desulfurization of a closely related structure, see ref 8g.

(19) Ward, D. E.; Sales, M.; Sasmal, P. K. *J. Org. Chem.* **2004**, *69*, 4808−4815.

(20) See the Supporting Information for general methods and procedures.

acetate in CH_2Cl_2) to give **9** as a white solid (1.22 g, 75%): $[\alpha]_D$ −48, *c* 1.0, $CHCl_3$ (lit.[12] for **9** of >98% ee: $[\alpha]_D$ −47, *c* 1.0, $CHCl_3$). Spectroscopic data for **9** were identical to that previously reported.[12] The catalyst could be recovered in >80% yield by concentrating the water layers and precipitating the residue from hot MeOH on addition of benzene.

(α*R*,6*S*)-α-[(3*R*,4*S*)-Tetrahydro-4-hydroxy-2*H*-thiopyran-3-yl]-1,4-dioxa-8-thiaspiro[4.5]decane-6-methanol (10a). Li^{s}Bu$_3$BH (1.0 M solution in THF; 10 mL, 10 mmol) was added dropwise via syringe to a stirred solution of ketone **9** (1.03 g, 3.40 mmol) in THF (50 mL) at −78 °C under argon. After 3 h, phosphate buffer (pH = 7.5; 10 mL) and 30% aqueous H_2O_2 (5 mL) were sequentially added. The mixture was allowed to stir for 10 min at 0 °C and then was diluted with cold saturated aqueous Na_2SO_3 (20 mL) and extracted with CH_2Cl_2 (×4). The combined organic layers were dried over Na_2SO_4, concentrated, and fractionated by FCC (30% ethyl acetate in hexane) to give the titled diol as a colorless oil (852 mg, 83%): $[\alpha]_D$ +41 (*c* 3.0, MeOH); IR ν_{max}: 3466 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.35 (1H, ddd, *J* = 1.5, 2, 8.5 Hz), 4.17 (1H, ddd, *J* = 2.5, 3, 4, 7 Hz), 4.13−3.95 (4H, m), 3.31 (1H, d, *J* = 1.5 Hz), 3.12 (1H, d, *J* = 4 Hz), 3.02 (1H, dd, *J* = 11, 14 Hz), 2.97 (1H, ddd, *J* = 3, 11, 14 Hz), 2.85 (1H, dd, *J* = 10, 14 Hz), 2.81 (1H, ddd, *J* = 2.5, 12.5, 14 Hz), 2.71 (1H, ddd, *J* = 3, 3.5, 14 Hz), 2.56 (1H, dddd, *J* = 2, 4.5, 4.5, 14 Hz), 2.39 (1H, dddd, *J* = 1.5, 3, 4, 14 Hz), 2.29 (1H, dd, *J* = 3, 14 Hz), 2.20−2.13 (2H, m), 2.03 (1H, ddd, *J* = 2, 3.5, 11 Hz), 1.97 (1H, dddd, *J* = 2.5, 3, 8.5, 10 Hz), 1.91 (1H, dddd, *J* = 3, 3, 11, 14 Hz), 1.74 (1H, ddd, *J* = 4.5, 12.5, 13.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 110.4 (s), 70.2 (d), 67.0 (d), 64.9 (t), 64.3 (t), 47.0 (d), 43.5 (d), 36.1 (t), 34.1 (t), 26.8 (t), 26.7 (t), 26.2 (t), 23.9 (t); HRMS (EI) *m*/*z* calcd for $C_{13}H_{22}O_4S_2$ 306.0960, found 306.0963.

(α*R*,6*S*)-α-[(3*S*,4*S*)-4-Triethylsilyloxytetrahydro-2*H*-thiopyran-3-yl]-1,4-dioxa-8-thiaspiro[4.5]decane-6-methanol (11a). Et_3SiOTf (0.477 mL, 2.11 mmol) was added to a solution of diol **10a** (615 mg, 2.01 mmol) and 2,6-lutidine (2.40 mL, 2.21 g, 20.6 mmol) in CH_2Cl_2 (100 mL) at 0 °C under argon. After 10 min (reaction complete by TLC), the mixture was diluted with CH_2Cl_2, washed with aqueous $NaHCO_3$, dried over Na_2SO_4, concentrated, and fractionated by FCC (10% ethyl acetate in hexanes) to give the titled product as a colorless liquid (820 mg, 97%): $[\alpha]_D$ +34 (*c* 1.1, benzene); IR ν_{max}: 3526 cm^{-1}; ^{1}H NMR (500 MHz, C_6D_6) δ: 4.58 (1H, m), 4.15 (1H, dd, *J* = 2.5, 10 Hz), 3.51 (1H, ddd, *J* = 7, 7.5, 7.5 Hz), 3.40 (1H, ddd, *J* = 5, 7.5, 7.5 Hz), 3.25 (1H, ddd, *J* = 5, 7.5, 7.5 Hz), 3.16 (1H, ddd, *J* = 3, 13, 13 Hz), 3.15−3.09 (2H, m), 3.08 (1H, dd, *J* = 12, 14 Hz), 2.92 (1H, dd, *J* = 12, 13 Hz), 2.60 (1H, ddd, *J* = 2, 13, 14 Hz), 2.55 (1H, ddd, *J* = 2, 3, 14 Hz), 2.15 (1H, dddd, *J* = 2, 3.5, 4, 14 Hz), 2.06−1.96 (3H, m), 1.91 (1H, dddd, *J* = 3, 3, 5, 14 Hz), 1.86 (1H, ddd, *J* = 2, 3, 10, 13.5 Hz), 1.74−1.67 (2H, m), 1.54 (1H, ddd, *J* = 3.5, 13, 13.5 Hz), 1.03 (9H, t, *J* = 8 Hz), 0.65 (6H, q, *J* = 8 Hz); **^{13}C NMR** (125 MHz, C_6D_6) δ: 111.1 (s), 68.6 (d), 65.4 (d), 64.6 (t), 64.1 (t), 46.3 (d), 46.2 (d), 37.0 (t), 36.3 (t), 27.0 (t), 26.1 (t), 24.0 (t), 22.3 (t), 7.6 (q × 3), 5.8 (t × 3); HRMS *m*/*z* calcd for $C_{19}H_{36}O_4S_2Si$ 420.1824, found 420.1835.

***O*-(*R*)-[(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]decan-6-yl][(3*S*,4*S*)-4-(triethylsilyloxy)tetrahydro-2*H*-thiopyran-3-yl]methyl *S*-Methyl Carbonodithioate (11b).** NaH (50% dispersion in oil; 650 mg, 13.5 mmol) was added to a stirred solution of alcohol **11a** (750 mg, 1.79 mmol) and imidazole (~10 mg) in THF (10 mL) at 0 °C. The mixture was allowed to warm to ambient temperature and, after 30 min, was cooled to 0 °C and CS_2 (1.1 mL, 18 mmol) was added via syringe. The mixture was allowed to warm to ambient temperature and, after 1 h, was cooled at 0 °C and MeI (1.2 mL, 18 mmol) was added via syringe. After 30 min, the reaction was allowed to warm to ambient temperature. After 15 h (reaction complete by TLC), the reaction mixture was cooled to 0 °C and quenched by careful addition of water [**caution**: H_2 evolution]. The mixture was diluted with CH_2Cl_2, washed with water, dried over Na_2SO_4, concentrated, and fractionated by FCC (5−10% ethyl acetate in hexanes) to give the titled xanthate as a yellow oil (850 mg, 93%): $[\alpha]_D$ +90 (*c* 1.6, benzene); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.18 (1H, dd, *J* = 2, 6 Hz), 4.23 (1H, m), 4.12−4.05 (1H, m), 4.01−3.94 (2H, m), 3.87−3.81 (1H, m), 3.14 (1H, dd, *J* = 12.5, 12.5 Hz), 3.07 (1H, ddd, *J* = 3, 13, 13 Hz), 2.99 (1H, dd, *J* = 12, 14 Hz), 2.86 (1H, ddd, *J* = 3, 13, 13.5 Hz), 2.70 (1H, ddd, *J* = 3, 3, 14 Hz), 2.63 (1H, ddd, *J* = 2, 3, 12 Hz), 2.55 (3H, s), 2.46 (1H, dddd, *J* = 3, 3.5, 4, 13.5 Hz), 2.31 (1H, br d, *J* = 12.5 Hz), 2.24−2.19 (2H, m), 2.14−2.08 (2H, m), 1.83 (1H, dddd, *J* = 1.5, 3.5, 13, 14 Hz), 1.68 (1H, ddd, *J* = 4, 13, 13.5 Hz), 1.00 (9H, t, *J* = 7.5 Hz), 0.72−0.63 (6H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 215 (s), 108.8 (s), 81.9 (d), 67.1 (d), 64.7 (t), 64.5 (t), 48.2 (d), 47.5 (d), 36.6 (t), 36.2 (t), 28.4 (t), 27.0 (t), 24.0 (t), 22.1 (t), 19.2 (q), 7.4 (q × 3), 5.6 (t × 3); HRMS (EI) *m*/*z* calcd for $C_{21}H_{38}O_4S_4Si$ 510.1422, found 510.1420.

{(3*S*,4*S*)-3-[(6*S*)-1,4-Dioxa-8-thiaspiro[4.5]decan-6-ylmethyl]-tetrahydro-2*H*-thiopyran-4-yloxy}triethylsilane (11c). Tributylstannane (0.52 mL, 2.0 mmol) was added to a stirred solution of xanthate **11b** (850 mg, 1.67 mmol) in dry toluene (5 mL) under argon. The mixture was heated under reflux, and then AIBN (ca. 15 mg) was added. After 30 min, the reaction was allowed to cool to ambient temperature and then was diluted with H_2O and extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated, and the resulting colorless oil was passed through a short pad of silica gel (eluting first with hexane and then with 5% ethyl acetate in hexane) to afford the titled compound (653 mg, 97%): $[\alpha]_D$ −14 (*c* 1.9, benzene); ^{1}H NMR (500 MHz, C_6D_6) δ: 3.63 (1H, ddd, *J* = 2.5, 2.5, 5.5 Hz), 3.50−3.36 (4H, m), 2.94 (1H, ddd, *J* = 3, 11, 13 Hz), 2.89−2.82 (2H, m), 2.60−2.54 (3H, m), 2.25 (1H, ddd, *J* = 1.5, 3, 13.5 Hz), 2.13 (1H, dddd, *J* = 1.5, 3.5, 5.5, 13 Hz), 1.92 (1H, ddd, *J* = 3, 10.5, 13.5 Hz), 1.88−1.77 (3H, m), 1.71−1.53 (4H, m), 0.98 (9H, t, *J* = 8 Hz), 0.55 (6H, q, *J* = 8 Hz); ^{13}C NMR (125 MHz, C_6D_6) δ: 109.5 (s), 71.5 (d), 64.7 (t), 64.6 (t), 42.5 (d), 40.9 (d), 35.6 (t), 35.3 (t), 31.6 (t), 30.4 (t), 28.1 (t), 27.0 (t), 23.5 (t), 7.3 (q × 3), 4.9 (t × 3); HRMS (EI) *m*/*z* calcd for $C_{19}H_{36}O_3S_2Si$ 404.1875, found 404.1869.

Triethyl[(3*S*,4*S*,6*S*)-6-(2-ethyl-1,3-dioxolan-2-yl)-4-methylheptan-3-yloxy]silane (12). A suspension of freshly prepared Raney-Ni (W-2)[21] (4 mL settled volume) in ethanol (2 mL) was added in one portion to a well-stirred solution of **11c** (282 mg, 0.698 mmol) in methanol (10 mL). The reaction mixture was heated under reflux, and progress was monitored by TLC. Additional Raney-Ni (2 mL settled volume) was added each hour until the reaction was complete (2−3 h). The supernatant was filtered through a pad of Celite, and the residue was suspended in methanol (50 mL) and heated under reflux for several minutes. The supernatant was filtered and the residue treated as above (this process repeated 3 times). The combined filtrates were concentrated and fractionated by FCC (10% ethyl acetate in hexane) to give the titled compound as a clear oil (198 mg, 82%): $[\alpha]_D$ −27 (*c* 1.6, benzene); ^{1}H NMR (500 MHz, C_6D_6) δ: 3.61−3.56 (4H, m), 3.48 (1H, dd, *J* = 5.5, 10 Hz), 1.93 (1H, m), 1.77−1.67 (3H, m), 1.62 (1H, ddd, *J* = 2, 12, 12 Hz), 1.57−1.39 (3H, m), 1.07 (3H, d, *J* = 6.5 Hz), 1.05 (9H, t, *J* = 7.5 Hz), 0.99 (3H, t, *J* = 7.5 Hz), 0.92 (3H, t, *J* = 7.5 Hz), 0.92 (3H, d, *J* = 6.5 Hz), 0.67 (6H, q, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, C_6D_6) δ: 114.7 (s), 79.3 (d), 65.7 (t), 65.6 (t), 37.5 (d), 35.8 (d), 34.9 (t), 27.3 (t), 27.2 (t), 14.5 (q), 14.2 (q), 10.9 (q), 8.2 (q), 7.7 (q × 3), 6.1 (t × 3); HRMS *m*/*z* calcd for $C_{19}H_{40}O_3Si$ 344.2747, found 344.2740.

(3*S*,4*S*,6*S*)-4,6-Dimethyl-7-oxononan-3-yl acetate (2). Acetic acid (21 μL, 0.37 mmol) was added to a stirred solution of **12** (65 mg, 0.19 mmol) in CH_2Cl_2 (3 mL). After 10 min, DMAP (69 mg, 0.57 mmol) and acetyl chloride (0.1 mL, excess) were added. After 15 min, the mixture was diluted with CH_2Cl_2 (10 mL), washed

(21) Mozingo, R. *Org. Synth.* **1941**, *21*, 15−17. (*Coll. Vol. III* **1955**, 181−183.)

with aqueous $NaHCO_3$, dried over Na_2SO_4, concentrated, and fractionated by FCC (pentane and then 5% Et_2O in pentane) to give serricornin acetate (**2**) as a colorless oil (31 mg, 72% yield): $[\alpha]_D$ −20 (*c* 0.3, hexane) (lit.[1,6] −16.1 to −18.7); IR ν_{max}: 2964, 2940, 2886, 1732, 1708, 1462, 1367, 1235, 1104, 1014 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 4.76 (1H, ddd, J = 4.5, 4.5, 8.5 Hz), 2.63 (1H, m), 2.56−2.39 (2H, m), 2.06 (3H, s), 1.68 (1H, m), 1.60−1.46 (3H, m), 1.29 (1H, m), 1.05 (3H, t, J = 7.5 Hz), 1.04 (3H, d, J = 7 Hz), 0.87 (3H, d, J = 7 Hz), 0.86 (3H, t, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 215.3, 171.2, 78.3, 43.7, 36.0, 34.5, 33.8, 24.3, 21.3, 16.8, 14.6, 10.4, 8.0; LRMS (CI, NH_3), *m*/*z* (relative intensity): 246 ($[M + 18]^+$, 27), 229 ($[M + 1]^+$, 7), 189 (41), 169 (100); HRMS *m*/*z* calcd for $C_{13}H_{24}O_3$ 228.1725 (246.2069 for $M + NH_4$), found 246.2063 (CI, NH_3).

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Supporting Information Available: Experimental procedures and spectroscopic data for **13a**−**d**, **14**, and **15a**; ^1H and ^{13}C NMR spectra for all reported compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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