(24) Melting points were determined using a Mel-Temp capillary melting point apparatus and are corrected. IR spectra were obtained from Nujol mulls using a Beckman Model IR-8 spectrophotometer. All chemical analyses were performed by M-H-W Laboratories, Garden City, Mich. Bismuth(III) triacetate (**1**) was prepared from bismuth oxide (**2**) following the procedure of Rigby[3] as modified by Wickham et al.[4] White crystals of **1** and all carboxylic acids used were dried under reduced pressure for 24 h prior to use. All solvents were distilled from $CaSO_4$ and then stored over "Linde" type molecular sieves (4–8 mesh).

Stereoselective Synthesis of (−)-Estafiatin[1]

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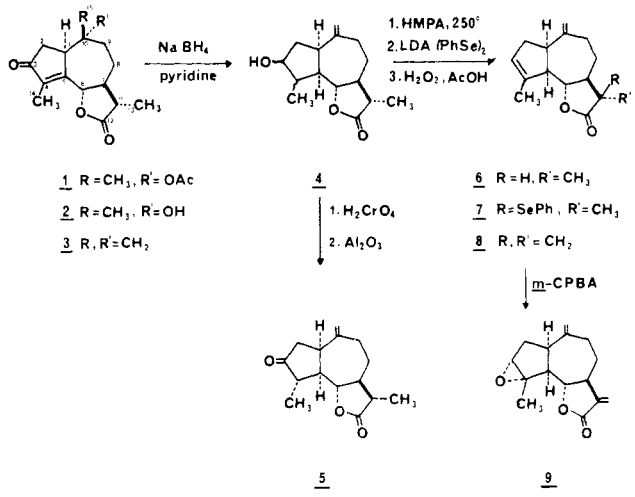
(−)-Estafiatin (**9**), a constituent of the medicinally useful bitter herb *Artemisia mexicana*, was isolated and structurally elucidated by Sanchez-Viesca and Romo.[2] We wish to report a short, stereoselective synthesis from α-santonin of (−)-estafiatin.

The key intermediate in the synthesis was the trisubstituted olefin **6**, which was secured as outlined below. α-Santonin was converted to *O*-acetylisophotosantonic lactone (**1**), which in turn was transformed via the alcohol **2** to the dienone lactone **3** using slightly modified literature procedures.[3] The introduction of the C-10 exocyclic methylene at this point was deemed necessary because it was felt that this conversion would be difficult to achieve later in the synthesis.[4] However, this in turn required a suitable method for reducing the enone function in **3** in the presence of the exocyclic methylene to give a cis-fused guaianolide. Of the reducing agents examined, the infrequently used combination of sodium borohydride in pyridine[5] proved to be by far the most effective in accomplishing this reduction, selectively producing alcohols **4**. This mixture of epimeric alcohols was converted for characterization by oxidation[6] and equilibration to ketone **5** (dihydroestafiatone[2,7]), which has been isolated from *Arctotis revoluta*.[7] Additional evidence that the hydride addition had produced the cis ring fusion was provided by the conversion of *O*-acetylisophotosantonic lactone (**1**) by the above sequence of reactions to the known acetoxy ketone (**5**, where

replaces the exocyclic methylene).[3c]

As had been expected from observations made in similar systems,[3c,8] conversion of alcohols **4** to the trisubstituted olefin **6** proved to be difficult. Several methods[3c,9] yielded only the disubstituted Δ^2-olefin; however, high-temperature dehydration in hexamethylphosphoric triamide[10] afforded a mixture of tri- and disubstituted olefins (ca. 1.4/1), which could be readily separated on silver nitrate impregnated silica gel. Although the spectral properties of trisubstituted olefin **6** closely resembled those of the known[11] isomeric trans-fused (1α, 5β) compound, obvious differences could be seen, especially in the C-6 hydrogen chemical shifts (3.82 and 4.27 ppm, respectively).

Conversion of the α-methyl lactone in **6** to the corresponding α-methylene lactone was readily accomplished by α-phenylselenenylation and oxidation.[12] Selective epoxidation of the resulting triene **8**[13] produced a major epoxide isomer **9** (ca. 80% by NMR), easily separated by crystallization, whose melting point, rotations, and spectral properties were in complete agreement with those of (−)-estafiatin.[2,14] The epoxide in estafiatin thus can be assigned the α configuration on the reasonable assumption that the major product in the



epoxidation of triene **8** is produced by approach of the peracid from the considerably less hindered α face.

Experimental Section

Solvents were redistilled prior to use. Tetrahydrofuran and diisopropylamine were distilled from lithium aluminum hydride, and hexamethylphosphoric triamide (HMPA) was distilled under vacuum from calcium hydride. Reaction products were isolated by addition of water followed by extraction with the solvent indicated and drying over anhydrous sodium sulfate.

Thin-layer chromatography was performed on Merck $60F_{254}$ (0.25 mm) sheets which were visualized with molybdatophosphoric acid in ethanol. Merck 230–400 mesh silica gel 60 was employed for column chromatography. A Beckman acculab 4 spectrophotometer was used to record IR spectra, and a Jeol PMX-60 spectrometer was used for the NMR spectra (Me_4Si as the internal reference). Mass spectra were obtained on an MS-30 AEI mass spectrometer (70 eV, direct insertion probe). Optical rotations were determined on a Perkin-Elmer 141 polarimeter ($CHCl_3$, *c* 1). Microanalyses were performed by the Central Service of the CNRS, Lyon.

Dienone Lactone 3. *O*-Acetylisophotosantonic lactone[3] (6.5 g, 21 mmol) was added to 1.2 L of 5% aqueous potassium hydroxide with stirring. After 1.25 h the reaction mixture was washed with ethyl acetate and acidified with 18% hydrochloric acid and the product was isolated with ethyl acetate, to provide 6.5 g of crude alcohol **2**. This material was dissolved in 20 mL of THF and cooled to −45 °C. A cold (−45 °C) solution of THF (20 mL), pyridine (20 mL), and thionyl chloride (20 mL) was added followed by stirring for 10 min. After addition to cold water–ether, the reaction mixture was thoroughly extracted with ether which was washed with aqueous sodium carbonate, water, and brine to furnish 4.5 g of an oil. This oil was chromatographed on silica gel using 30% ethyl acetate–hexane to afford 3.3 g of the dienone lactone **3**, whose properties were in accord with those reported in the literature.[3b]

Alcohols 4 and Dihydroestafiatone 5. Dienone lactone **3** (2.9 g, 12 mmol) in 50 mL of pyridine was added to a stirred solution of sodium borohydride (2.9 g, 76 mmol) dissolved in 37 mL of pyridine.[5] The resulting dark brown solution was stirred at 17 °C for 24 h followed by addition of 5 mL of water and an additional 1 h of stirring. The reaction mixture was slowly poured into 10% aqueous HCl–ether and the ether extract (concentrated to 250 mL) was added to a solution of 27 g of KIO_3 in 450 mL of water. After stirring for 15 h, the ether phase was washed successively with 5% sodium thiosulfate, water, 10% HCl, saturated sodium bicarbonate, and brine, dried over anhydrous sodium sulfate, and concentrated to give 2.0 g of brown oil.

The crude alcohol mixture (1.0 g, 4.0 mmol), dissolved in 50 mL of ether, was cooled to 0 °C and treated dropwise with a chromic acid solution[6] (540 drops, ~40 mmol). After 1 h at 0 °C and 1 h at 16 °C, the solution was extracted with ether, which was washed with saturated sodium bicarbonate and brine, dried, and concentrated. The resulting oil was stirred for 2 h with 6 g of activity I basic alumina in $CHCl_3$ and then chromatographed on silica gel using 30% ethyl acetate–hexane to afford 650 mg of dihydroestafiatone (**5**).[2,7] Recrystallization from ether–hexane gave colorless needles: mp 80–81 °C; $[\alpha]^{24}_D$ +139°; IR (Nujol) 3080, 1770, 1745, 1645, 995, 900 cm^{-1}; NMR ($CHCl_3$) δ 4.90 (s, 1 H), 4.59 (s, 1 H), 3.89 (broad t, *J* = 8 Hz, 1 H), 1.25 (d, *J* = 7 Hz, 6 H); mass spectrum *m/e* 248 (M^+).

Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.27; H, 8.24.

The 2,4-dinitrophenylhydrazone was synthesized in the usual manner: mp 200–201 °C; $[\alpha]^{21}_D$ +225°.

Regeneration of Alcohols 4. A sample of dihydroestafiatone (**5**) (100 mg, 0.40 mmol) was dissolved in 5 mL of methanol at 0 °C under nitrogen and treated with sodium borohydride (70 mg, 1.8 mmol). After stirring for 1.5 h, water was added and the product was isolated with ether to give 94 mg of alcohols **4** as a colorless oil: IR (film) 3420, 3090, 1760, 1640, 900 cm^{-1}; NMR ($CDCl_3$) δ 4.86 (s, 2 H), 1.16 (d, J = 7 Hz, 3 H).

Trisubstituted Olefin 6 and Disubstituted Δ^2-Olefin. A 327-mg (1.3 mmol) sample of alcohols **4** (from sodium borohydride reduction of dihydroestafiatone) was dissolved in 45 mL of HMPA and heated at 250 °C for 50 min.[10] The cooled reaction mixture was then diluted with water and exhaustively extracted with hexane. The resulting oil (228 mg) was chromatographed on 45 g of 10% silver nitrate–silica gel with 10% ethyl acetate–hexane to furnish trisubstituted olefin **6** as an oil (82 mg), which could be further purified by bulb-to-bulb distillation (80 °C (0.25 mm)): $[\alpha]^{21}_D$ +46°; IR (film) 3080, 3040, 1780, 1640, 990, 900, 810 cm^{-1}; NMR (CCl_4) δ 5.36 (broad s, 1 H), 4.73 (broad s, 2 H), 3.82 (pseudo t, J = 8 Hz, 1 H), 1.83 (broad s, 3 H), 1.15 (d, J = 6 Hz, 3 H); mass spectrum m/e 232 (M^+).

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.61; H, 8.80.

The disubstituted Δ^2-olefin (73 mg) was eluted in subsequent fractions. Recrystallization from hexane provided colorless needles: mp 77.5–79 °C; $[\alpha]^{21}_D$ −41°; IR (Nujol) 3070, 3040, 1760, 1630, 1455, 980, 900 cm^{-1}; NMR (CCl_4) δ 5.58 (broad d, J = 6 Hz, 1 H), 5.30 (dd, J = 2 and 6 Hz, 1 H), 4.72 (broad s, 1 H), 4.60 (broad s, 1 H), 3.83 (pseudo t, J = 9 Hz, 1 H), 3.33 (broad d, J = 10 Hz, 1 H), 1.16 (d, J = 7 Hz, 3 H); mass spectrum m/e 232 (M^+).

Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.45; H, 8.67.

In general, the crude alcohol mixture **4** from the $NaBH_4$–pyridine reduction of dienone **3** was dehydrated directly to produce a comparable mixture of olefins in somewhat lower yield.

Triene 8. Trisubstituted olefin **6** (117 mg, 0.50 mmol) in 0.5 mL of THF was added dropwise over 30 min to a solution of lithium diisopropylamide [from n-BuLi (0.75 mmol, hexane removed) and diisopropylamine (0.77 mmol) in THF (1.5 mL)] at −78 °C under nitrogen.[12] The resulting mixture was stirred for 20 min after which a solution of diphenyl diselenide (234 mg, 0.75 mmol) and HMPA (134 mg, 0.75 mmol) in 0.5 mL of THF was rapidly added. After 20 min at −78 °C and 1.5 h at −35 °C the reaction was quenched with 0.1 N HCl and the crude product was isolated with ether. Chromatography on silica gel using 10% ethyl acetate–hexane gave 147 mg of **7** as a crystalline solid: NMR (CCl_4) δ 7.56–7.00 (m, 5 H), 5.40 (broad s, 1 H), 4.83 (s, 1 H), 4.76 (s, 1 H), 3.95 (pseudo t, J = 9 Hz, 1 H), 1.82 (broad s, 3 H), 1.43 (s, 3 H).

The phenylseleno compound **7** (147 mg, 0.38 mmol) was dissolved in 2 mL of THF containing 0.06 mL of acetic acid and treated at 0 °C with 0.28 mL of 30% H_2O_2. After stirring for 0.5 h, the reaction mixture was poured into cold saturated sodium bicarbonate. Isolation with ether gave an oil which was chromatographed on silica gel using 5% ethyl acetate–hexane to give 75 mg of triene **8**, further purified by bulb-to-bulb distillation: mp 37–40 °C; $[\alpha]^{21}_D$ +113°; IR (film) 3090, 3050, 1765, 1655, 1640, 1005, 900, 820 cm^{-1}; NMR (CCl_4) δ 5.95 (d, J = 3 Hz, 1 H), 5.37 (broad s, 1 H), 5.26 (d, J = 3 Hz, 1 H), 4.78 (s, 2 H), 3.86 (pseudo t, J = 9 Hz, 1 H), 1.83 (broad s, 3 H); mass spectrum m/e 230 (M^+).

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.05; H, 7.71.

(−)-Estafiatin (9). To a solution of triene **8** (60 mg, 0.26 mmol) in 5 mL of chloroform at −8 °C was added m-chloroperbenzoic acid (85%, 154 mg, 0.76 mmol) in three portions over 20 min. The temperature was slowly allowed to increase to 5 °C over 2.25 h. The reaction mixture was then washed with 10% sodium hydroxide and brine, dried, and concentrated under reduced pressure. Chromatography on silica gel using 10% ethyl acetate–hexane afforded 41 mg of an ca. 4:1 (by NMR) mixture of two epoxides, from which 26 mg of pure estafiatin was obtained by crystallization from ether–hexane: mp 104.5–105.5 °C; $[\alpha]^{21}_D$ −10°, $[\alpha]^{24}_{578}$ −15°, $[\alpha]^{24}_{546}$ −15°, $[\alpha]^{24}_{436}$ − 28°, $[\alpha]^{24}_{365}$ −60° (lit.[2] mp 104–106 °C; $[\alpha]^{20}_D$ −9.9°, $[\alpha]^{24}_{578}$ −13.9°, $[\alpha]^{24}_{546}$ −16.1°, $[\alpha]^{24}_{436}$ −30.6°, $[\alpha]^{24}_{365}$ −59.6°); IR (Nujol) 3080, 3020, 1760, 1660, 1645, 1150, 990, 910, 820 cm^{-1}; NMR ($CDCl_3$) δ 6.10 (d, J = 3 Hz, 1 H), 5.36 (d, J = 3 Hz, 1 H), 4.85 (s, 1 H), 4.79 (s, 1 H), 4.00 (dd, J = 8 and 10 Hz, 1 H), 3.30 (s, 1 H), 1.59 (s, 3 H); mass spectrum m/e 246 (M^+).

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.03; H, 7.48.

The pyrazoline derivative was synthesized with diazomethane, mp 118 °C dec [lit.[2] mp 120 °C dec].

Estafiatin was also synthesized in comparable yield by epoxidation of the trisubstituted olefin **6** followed by the introduction of the α-methylene group.

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Registry No.—**1**, 7759-23-1; **2**, 1618-98-0; **3**, 23811-43-0; **4**, 68151-24-6; **5**, 38142-65-3; **6**, 38236-17-8; **7**, 68151-25-7; **8**, 68151-26-8; **9**, 10180-89-9.

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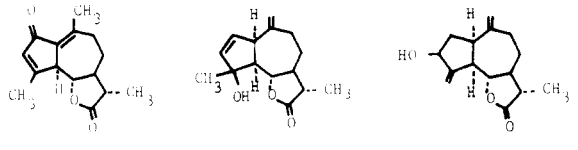

oxidation [P. A. Grieco, *ibid.*, **37**, 2363 (1972)], and treatment with sodium acetate.

An Improved Preparation of Sulfinate Salts and Their Michael Addition to Enones[1]

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Arylsulfinic acids and their salts are available from the corresponding arylsulfonyl chlorides by zinc reduction.[2] On the other hand, aliphatic sulfinic acids and their salts are not easily prepared. The most common method is metal reduction of sulfonyl chlorides as with the aryl systems, but the yields are much lower and the reaction product is contaminated with other sulfur compounds.[2] Another preparation involves the reaction of Grignard reagents and organolithiums with sulfur dioxide, but this also suffers from competing side reactions.[2,3]

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