Synthesis of (−)-Calicoferol B

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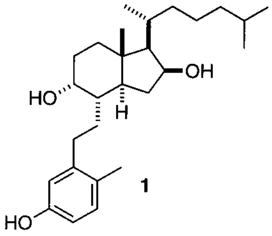
The first total synthesis of (−)-calicoferol B (**III**) is described. The cyclozirconation product **I**, prepared in enantiomerically pure form, was converted into the CD ring chiron **II**. This was coupled with the aromatic A-ring, and then the side chain was constructed with control of relative and absolute configuration to complete the total synthesis of **III**. The first total synthesis of (−)-calicoferol B (**1**) is described. The cyclozirconation product **8**, prepared in enantiomerically pure form, was converted into the CD ring chiron **6**. This was coupled with the aromatic A-ring, and then the side chain was constructed with control of relative and absolute configuration to complete the total synthesis of **1**.

Introduction

Osteopontin (OPN) is one of the major noncollagenous bone matrix proteins produced by osteoblasts and osteoclasts.[1] Substrate-bound OPN promotes attachment of osteoclasts,[2] whereas soluble OPN can alter calcium levels in osteoclasts.[3] These observations suggest that OPN may play a key role both in cell attachment and in controlling subsequent bone cell functions such as resorption. Indeed, it has been observed that OPN knockout mice are resistant to ovariectomy-induced bone resorption compared with wild-type mice.[4] This suggests that induced downregulation of OPN may be an effective strategy for the clinical treatment of osteoporosis.

We had been intrigued by the structural similarity between calicoferol B (**1**), astrogorgiadiol (**2**), and 1α,25-dihydroxyvitamin D_3 ("calcitriol", **3**), the active hormonal form of vitamin D.[5] We recently completed the total synthesis of astrogorgiadiol (**2**),[6] a secosterol isolated from a Japanese marine sponge of the genus *Astrogorgia*,[7] and submitted the synthetic material for screening. Astrogorgiadiol (**2**) was inactive in most of the 1α,25-dihydroxyvitamin D_3 assays. Astrogorgiadiol (**2**) did, however, show remarkable activity in one of them, clearly *downregulating* the production of osteopontin at 30 nM concentration in cell culture.[8] In contrast, 1α,25-dihydroxyvitamin D_3 (**3**) and its other known derivatives dramatically *upregulate* osteopontin production.[5]



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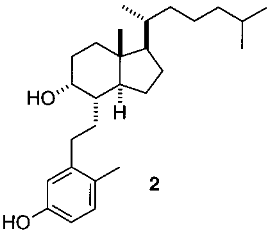

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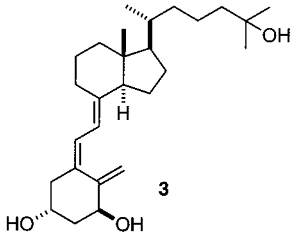

3

The synthetic route to astrogorgiadiol (**2**) that we had established[6] was efficient, but it was not flexible. We have therefore developed an entirely new route (Scheme 1) to this class of vitamin D-like materials. This triply convergent approach allows ready modification of A-ring, D-ring, and side-chain substitution. It was particularly intriguing that semiempirical calculations suggested that the two geometric isomers of **4** should be of approximately equal energy. If this proved to be true, it would be possible to prepare either relative configuration of the side chain from the same precursor. We have taken as our first objective the preparation of calicoferol B (**1**), a

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[1] (a) Butler, W. T.; Ridall, A. L.; McKee, M. D. *Principles of Bone Biology*; Bilezikian, J. P., Raisz, L. G., Rodan, G. A., Eds.; 1997; pp 161−181. (b) Denhardt, D. T.; Noda, M. *J. Cell Biochem.* **1998**, *31*, 92.

[2] (a) Ross, F. P.; Chappel, J.; Alvarez, J. I.; Sander, D.; Butler, W. T.; Farach-Carson, M. C.; Mintz, K. A.; Robey, P. G.; Teitelbaum, S. L.; Cheresh, D. A. *J. Biol. Chem.* **1993**, *268*, 9901. (b) van Dijk, S.; D'Errico, J.; Somerman, M. J.; Farach-Carson, M. C.; Butler, W. T. *J. Bone Miner. Res.* **1993**, *8*, 1499.

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[8] Xu, Y.; Farach-Carson, M. C. Personal communication.

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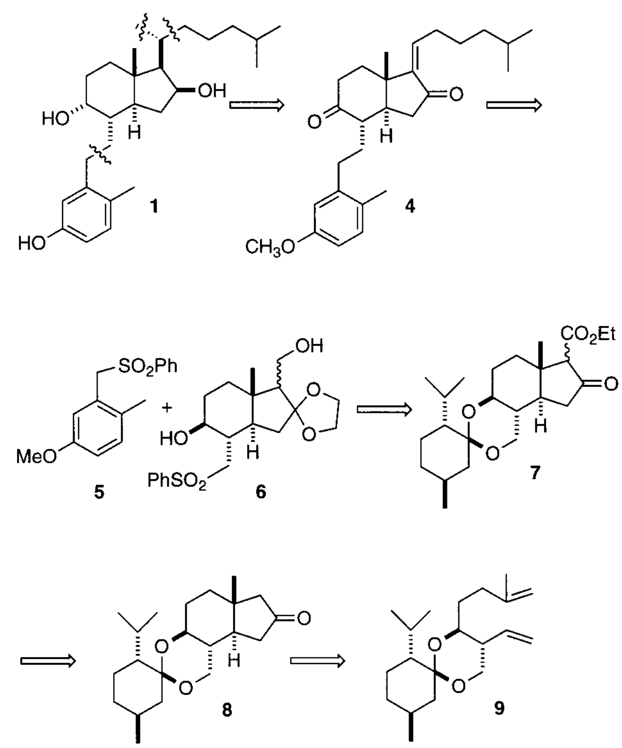
SCHEME 1

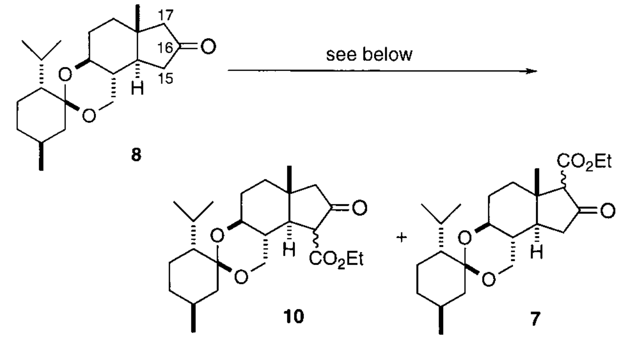


marine secosterol isolated from the gorgonian *Calicogorgia* sp. in 1991 that showed lethality to brine shrimp with an LD_{50} of 2.3 ppm.[9]

Results and Discussion

The key to this approach was the preparation of the bicyclic chiron **6** (Scheme 1). We had already established that cyclozirconation/carbonylation[10,11] of the diene **9** proceeded smoothly to give the crystalline ketone **8**.[12] The immediate task was to differentiate (Scheme 2) the two methylenes flanking the ketone at C(16) (steroid numbering). We expected that the C(15) methylene, being sterically less congested, would be kinetically more acidic than the C(17) methylene. Indeed, exposure of ketone **8** to LDA at −78 °C followed by reaction with ethyl chloroformate gave preponderantly the keto ester **10**.

SCHEME 2[a]



	Reaction conditions	Yield (%)	Ratio (**10**:**7**)[a]
1	LDA, THF,-78 °C; $ClCO_2Et$, -78 °C to rt	65	3.6:1
2	LDA, THF,-100 °C; $ClCO_2Et$, -100 °C to rt	48	4.9:1
3	NaH, Et_2CO_3, DME, EtOH (cat.), reflux	98	1:2

[a] The ratios were determined by ^1H NMR.

Carrying out this same transformation at −100 °C gave an even higher **10**/**7** ratio. In contrast, exposure of ketone **8** to diethyl carbonate in the presence of NaH and a catalytic amount of ethanol in DME gave a 2:1 ratio of the desired keto ester **7** to its regioisomer **10**. The keto esters **10** and **7** could be easily identified by their ^1H NMR spectra. The H(15) signal in keto ester **10** was a doublet with an 13.0 Hz coupling constant at δ 3.04, whereas the H(17) signal in keto ester **7** was a singlet at δ 2.83. The undesired keto ester **10** could be efficiently recycled to the tetracyclic ketone **8**.[13]

Protection (Scheme 3) of the ketone carbonyl group in the desired keto ester **7** with ethylene glycol in the presence of triethyl orthoformate[14] and a catalytic amount of p-TsOH·H_2O produced the ketal **12**, accompanied by an uncharacterized mixture. This mixture was further treated with p-TsOH·H_2O in EtOH to give an additional portion of ketal **12** as well as the diol ketone **11**. Further protection then converted the diol ketone **11** to the desired ketal **12**. Selected benzenesulfonation of the primary alcohol in **12** yielded the monobenzenesulfonate **13**, which was reduced with DIBAL-H to furnish the bicyclic chiron **6**. The transformation of the ketone **8** (Scheme 2) to the monobenzenesulfonate **6** proceeded in 59% overall yield.

The aromatic A-ring synthon **5** was prepared from the commercially available 3-methylanisole (**14**) (Scheme 4). Thus, bromination and benzenesulfonylation of **14** following the procedure of Hoye[15] gave the bromo sulfone **15**. We had originally thought to prepare **5** by direct methylation of **15**, but CH_3MgBr with Cu or Ni catalysts returned only unreacted starting material. The alternative replacement of the bromine with copper(I) cyanide

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(9) Ochi, M.; Yamada, K.; Kotsuki, H.; Shibata, K. *Chem. Lett.* **1991**, 427.

(10) For references to our previous work on intramolecular diene cyclozirconation, see: (a) Nugent, W. A.; Taber, D. F. *J. Am. Chem. Soc.* **1989**, *111*, 6435. (b) Taber, D. F.; Louey, J. P.; Wang, Y.; Nugent, W. A.; Dixon, D. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1994**, *116*, 9457. (c) Taber, D. F.; Wang, Y. *Tetrahedron Lett.* **1995**, *36*, 6639.

(11) For leading references to work by others on intramolecular diene cyclozirconation, see: (a) Rousset, C. J.; Swanson, D. R.; Lamaty, F.; Negishi, E.-i. *Tetrahedron Lett.* **1989**, *30*, 5105. (b) Knight, K. S.; Wang, D.; Waymouth, R. M.; Ziller, J. *J. Am. Chem. Soc.* **1994**, *116*, 1845. (c) Kim, S.; Kim, K. H. *Tetrahedron Lett.* **1995**, *36*, 3725. (d) Mirza-Aghayan, M.; Boukherroub, R.; Etemad-Moghadam, G.; Manuel, G.; Koenig, M. *Tetrahedron Lett.* **1996**, *37*, 3109. (e) Nishihara, Y.; Aoyagi, K.; Hara, R.; Suzuki, N.; Takahashi, T. *Inorg. Chim. Acta* **1996**, *252*, 91. (f) Yamaura, Y.; Hyakutake, M.; Mori, M. *J. Am. Chem. Soc.* **1997**, *119*, 7615. (g) Martin, S.; Brintzinger, H. H. *Inorg. Chim. Acta* **1998**, *280*, 189. (h) Grepioni, F.; Grilli, S.; Martelli, G.; Savoia, D. *J. Org. Chem.* **1999**, *64*, 3679. (i) Yamaura, Y.; Mori, M. *Tetrahedron Lett.* **1999**, *40*, 3221. (j) Campbell, A. D.; Raynham, T. M.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3194. (k) Kasatkin, A. N.; Checksfield, G.; Whitby, R. J. *J. Org. Chem.* **2000**, *65*, 3236.

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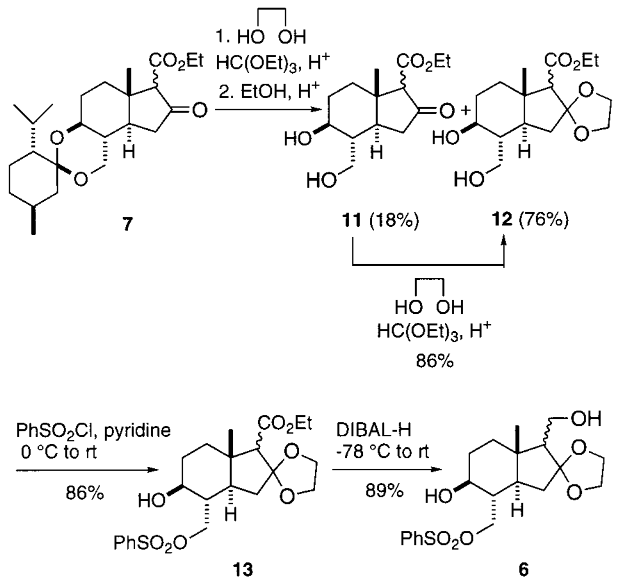
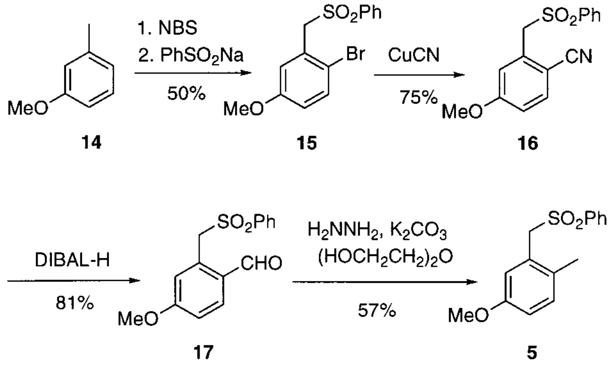
SCHEME 3



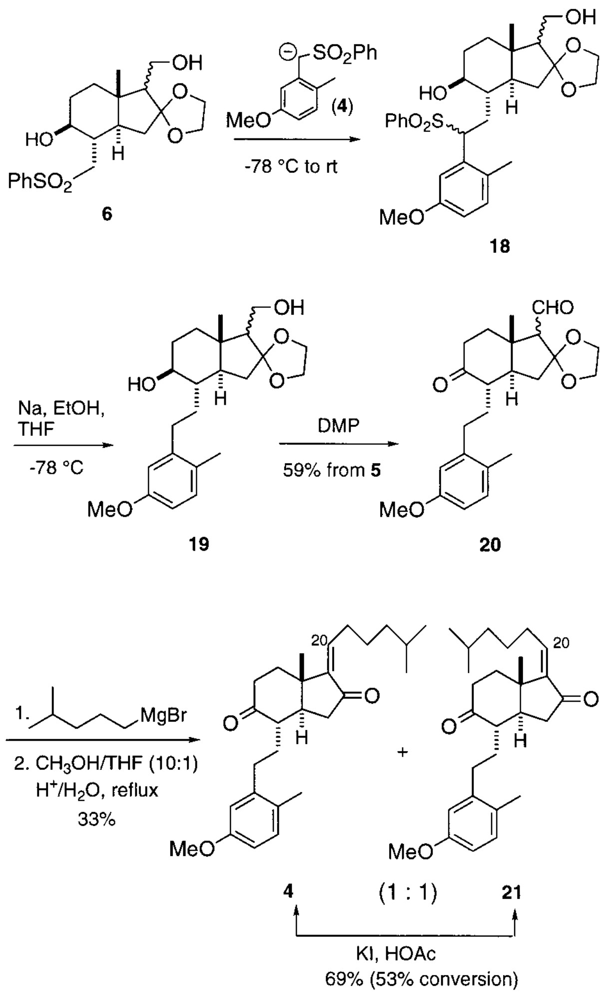
SCHEME 4



proceeded efficiently, to yield the nitrile **16**.[16] Reduction with DIBAL-H to the aldehyde **17** followed by Wolff−Kishner reduction[17] furnished the aromatic A-ring synthon **5**.

Coupling of the bicyclic chiron **6** with the aromatic A-ring synthon **5** gave the sulfone **18** (Scheme 5). Desulfonylation of **18** with Na and ethanol in THF[18] produced the diol **19**, which was oxidized with Dess−Martin periodinane[19] to afford the keto aldehyde **20**. Addition of isohexylmagnesium bromide[20] followed by hydrolysis and dehydration gave the easily separable enones **4** and **21** in the predicted 1:1 ratio.[21] The two enones could readily be identified by their ^{1}H NMR spectra. The H(20) signal of **4** appeared at δ 5.76, whereas the H(20) signal of **21** appeared at δ 6.53. Either enone could be equilibrated efficiently to the ~1:1 mixture by treatment with KI in acetic acid.[22]

SCHEME 5



Based on the literature precedent,[23] we expected that conjugate addition of lithium dimethyl cuprate to enones **4** and **21** would proceed from the α-face. Thus, addition to the desired enone **4** would give the (natural) C(20α) methyl, while addition to the enone **21** would give the epimeric C(20β) methyl. Indeed, conjugate addition of lithium dimethyl cuprate to enone **4** (Scheme 6) gave the dione **22**. Reduction of the dione **22** with L-Selectride afforded the diol **23**, which was demethylated with triethylsilane in the presence of a catalytic amount of tris(pentafluorophenyl)boron[24] followed by desilylation with TBAF to provide the target molecule, (−)-calicoferol B

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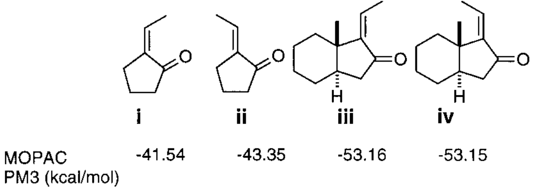
[20] For the preparation of isohexyl bromide, see: Crawforth, J. M.; Fawcett, J.; Rawlings, B. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1721.

[21] Semiempirical calculations (MOPAC PM3) had shown that **ii** is preferred over **i** by a 1.81 kcal/mol, so **ii** should be the predominant product. In contrast, **iii** and **iv** had only a 0.01 kcal/mol difference, suggesting a ~1:1 ratio at equilibrium.



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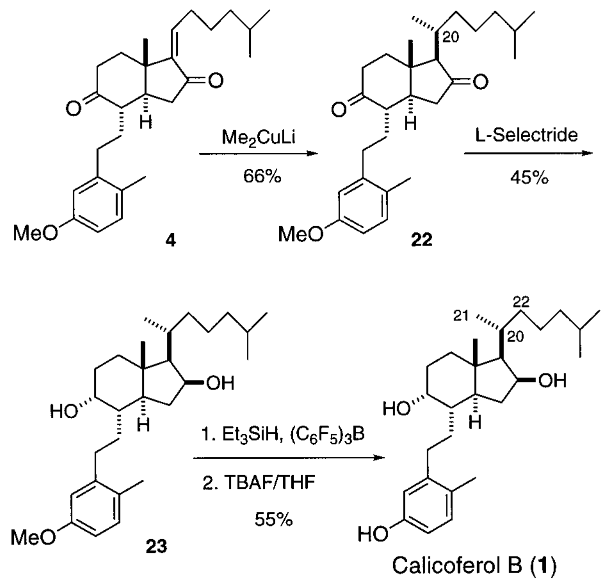
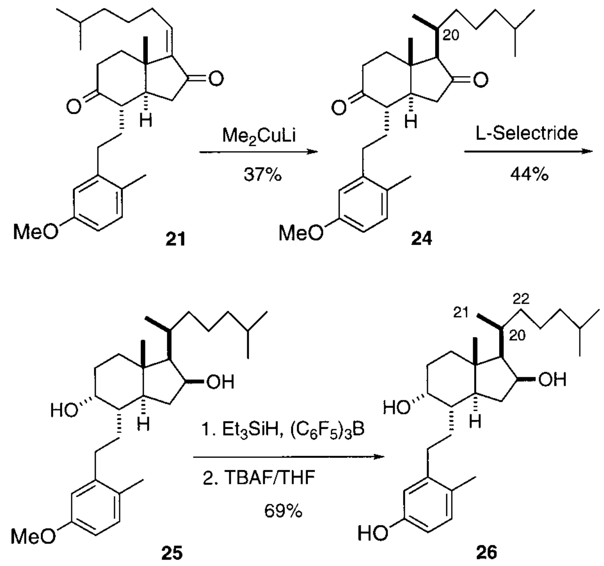
SCHEME 6



SCHEME 7



(**1**). The synthetic (−)-calicoferol B (**1**) was identical to the natural product by ^{1}H and ^{13}C NMR and $[\alpha]_D$ (obsd $[\alpha]_D$ −18.8, *c* 0.08, $CHCl_3$; lit.[9] $[\alpha]_D$ −16.2°, *c* 0.09, $CHCl_3$). The C(20)-*epi*-calicoferol B (**26**) was prepared from the enone **21** in the same manner as described for the preparation of (−)-calicoferol B (**1**) (Scheme 7). The synthetic (−)-calicoferol B (**1**) and its diastereomer **26** were separable on TLC and were not contaminated with each other, demonstrating the stereochemical homogeneity of **22** and of **24**. The identity of the synthetic **1** (and not **26**) with the natural product was established by ^{13}C NMR. The C(21) and C(22) signals of synthetic **1** appeared at δ 18.9 (lit.[9] δ 18.51) and δ 36.9 (lit.[9] δ 36.59), respectively, whereas the corresponding C(21) and C(22) signals of **26** appeared at δ 19.3 and 35.5.

Conclusion

The first total synthesis of (−)-calicoferol B (**1**) has been accomplished. We believe that the triply convergent synthetic strategy described here will offer a general route to the naturally occurring A-ring aromatic B-seco steroids.

Experimental Procedures

General Methods. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained as solutions in deuteriochloroform ($CDCl_3$) unless otherwise noted. ^{13}C multiplicities were determined with the aid of a JVERT pulse sequence, differentiating the signals for methyl and methine carbons as "down" from methylene and quaternary carbons as "up". The infrared (IR) spectra were determined as neat oils. Optical rotations were determined as solutions in chloroform unless otherwise noted. R_f values indicated refer to thin-layer chromatography (TLC) on 2.5 × 10 cm, 250 μm analytical plates coated with silica gel GF and developed in the solvent system indicated. Silica gel (60 Å) was used for flash column chromatography.[25] Tetrahydrofuran (THF) and diethyl ether were distilled from sodium metal/benzophenone ketyl under dry nitrogen. Dichloromethane (CH_2Cl_2) and toluene were distilled from calcium hydride under dry nitrogen. MTBE is methyl *tert*-butyl ether. All reaction mixtures were stirred magnetically, unless otherwise noted.

Keto Esters 10 and 7. To a stirred suspension mixture of diethyl carbonate (205 mg, 1.74 mmol) and NaH (60%, 104 mg, 2.60 mmol) in DME (2 mL) was added a solution of tetracyclic ketone **8** (290 mg, 0.87 mmol) in DME (2.5 mL) followed by EtOH (5 μL) at rt under N_2. The reaction mixture was heated to 90 °C and stirred at 90 °C for 4 h. The reaction mixture was then partitioned between cooled 5% aqueous HCl (10 mL) and MTBE. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed to produce the keto ester **10** (125 mg, 36% from **8**) as a colorless oil: TLC R_f = 0.78 (petroleum ether/MTBE = 7/3); IR (film) 2951, 2869, 1759, 1726, 1457, 1375, 1314, 1264, 1160, 1115, 1030, 925, 855 cm^{-1}; ^{1}H NMR δ 4.15−4.23 (m, 2H), 3.77 (t, *J* = 11.1 Hz, 1H), 3.53−3.62 (m, 2H), 3.04 (d, *J* = 13.0 Hz, 1H), 2.67−2.71 (m, 1H), 1.46−2.45 (m, 15H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.01 (s, 3H), 0.86−0.91 (m, 9H), 0.67 (t, *J* = 12.8 Hz, 1H); ^{13}C NMR δ up 210.3, 169.9, 101.3, 62.6, 61.7, 54.1, 37.9, 37.4, 35.6, 34.8, 27.7, 21.7; down 72.7, 55.5, 50.9, 47.7, 39.4, 29.0, 24.4, 23.7, 22.2, 19.5, 18.8, 14.1; HRMS calcd for $C_{24}H_{38}O_5Na$ (M + Na) 429.2617, found 429.2599. This was followed by the keto ester **7** (218 mg, 62% from **7**) as a colorless oil, TLC R_f = 0.28 (petroleum ether/MTBE = 7/3): IR (film) 2950, 2868, 1764, 1725, 1458, 1370, 1313, 1268, 1181, 1145, 1115, 1031, 925, 854 cm^{-1}; ^{1}H NMR δ 4.16−4.24 (m, 2H), 3.77 (t, *J* = 11.0 Hz, 1H), 3.67 (dd, *J* = 4.6, 11.0 Hz, 1H), 3.51−3.57 (m, 1H), 2.83 (s, 1H), 2.66−2.70 (m, 1H), 1.47−2.45 (m, 15H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.03 (s, 3H), 0.86−0.91 (m, 9H), 0.70 (t, *J* = 12.8 Hz, 1H); ^{13}C NMR δ up 208.9, 167.8, 101.5, 63.1, 60.9, 43.8, 37.4, 35.8, 34.9, 31.7, 27.7, 21.9; down 73.0, 67.1, 51.1, 43.5, 38.8, 29.0, 24.5, 23.7, 22.2, 18.9, 14.9, 14.3; HRMS calcd for $C_{24}H_{38}O_5Na$ (M + Na) 429.2617, found 429.2603.

Keto Esters 10 and 7 from Ethyl Chloroformate and LDA. To a stirred solution of the tetracyclic ketone **8** (45 mg, 0.14 mmol) in dry THF (0.7 mL) was added a 0.5 M lithium diisopropylamide (LDA) solution in THF (0.7 mL, 0.35 mmol) at −78 °C under N_2. After an additional 1 h, ethyl chloroformate (30 mg, 0.28 mmol) was added. The cooling bath was removed, and the reaction mixture was allowed to warm to rt. After an additional 4 h at rt, the reaction mixture was partitioned between cooled 5% aqueous HCl (5 mL) and MTBE. The combined organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed to give the keto ester **10** (13 mg, 51% from **8** based on 47% conversion). This was followed by the tetracyclic ketone **8** (24

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(25) Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

mg) and then the keto ester **7** (3.5 mg, 14% from **8** based on 47% conversion).

Tetracyclic Ketone 7 from Recycling the Keto Ester 10. A stirred suspension mixture of keto ester **10** (25 mg, 0.062 mmol) and LiCl (13 mg, 0.31 mmol) in DMSO/H_2O (0.6 mL, DMSO/H_2O = 9/1, v/v) was heated to reflux for 30 min. After the mixture was cooled to rt, the reaction solvent was removed in vacuo. The residue was chromatographed to give the keto diol (9.5 mg, 78% from **10**) as a colorless oil.

To a stirred solution of the keto diol (219 mg, 1.11 mmol), triethyl orthoformate (327 mg, 2.77 mmol), and (*S*)-(+)-menthone (342 mg, 2.22 mmol) in dry THF (5 mL) was added a catalytic amount of *p*-TsOH·H_2O (21 mg, 0.11 mmol) at rt. After an additional 23 h, the reaction mixture was partitioned between CH_2Cl_2 and, sequentially, saturated aqueous $NaHCO_3$ and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield the tetracyclic ketone **8** (230 mg, 48% from **20**).

Diol Ketone 11 and Diol Ketal 12. To a stirred solution of the keto ester **7** (336 mg, 0.83 mmol), triethyl orthoformate (491 mg, 3.32 mmol), and ethylene glycol (555 mg, 8.28 mmol) in dry CH_2Cl_2 (8.3 mL) was added a catalytic amount of *p*TsOH·H_2O (16 mg, 0.084 mmol) at rt. After an additional 3 days, the reaction mixture was partitioned between EtOAc and, sequentially, saturated aqueous $NaHCO_3$ and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to afford an unknown mixture as a colorless oil. This was followed by the diol ketal **12** (146 mg, 52% from **6**) as a colorless oil, TLC R_f = 0.17 (EtOAc/petroleum ether = 4/1): IR (film) 3406, 2934, 1733, 1458, 1370, 1296, 1178, 1081, 1032 cm^{-1}; ^1H NMR δ 3.62−4.15 (m, 9H), 3.08 (brs, 1H), 2.79 (brs, 1H), 2.68 (s, 1H), 2.18−2.28 (m, 1H), 2.01 (dd, J = 7.8 and 13.5 Hz, *1*H), 1.69−1.90 ($^{\mathrm{m}}$, 5H), 1.43−1.46 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H), 1.12 (s, 3H); 13C NMR δ up 169.6, 116.3, 65.7, 64.2, 59.9, 42.5, 40.5, 35.7, 30.4; down 63.5, 45.1, 43.3, 14.2, 13.4; HRMS calcd for $C_{16}H_{26}O_6Na$ (M + Na) 337.1627, found 337.1616.

To a stirred solution of the unknown mixture in EtOH (5 mL) was added *p*-TsOH·H_2O (5 mg, 0.026 mmol) at rt. After an additional 2 days, the reaction mixture was partitioned between EtOAc and, sequentially, saturated aqueous $NaHCO_3$ and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to give the diol ketal **12** (51 mg, 20% from **7**). This was followed by the diol ketone **11** (40 mg, 18% from **7**) as a colorless oil.

Diol Ketal 12 from Diol Ketone 11. To a stirred solution of the diol ketone **11** (93 mg, 0.34 mmol), $HC(OEt)_3$ (204 mg, 1.38 mmol), and $HO(CH_2)_2OH$ (231 mg, 3.45 mmol) in dry CH_2Cl_2 (3.4 mL) was added a catalytic amount of *p*-TsOH·H_2O (6.5 mg, 0.034 mmol) at rt. After an additional 3 days, the reaction mixture was partitioned between EtOAc and, sequentially, saturated aqueous $NaHCO_3$ and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to give the diol ketal **12** (93 mg, 86% from **11**).

Monobenzenesulfonate 13. To a stirred solution of the diol ketal **12** (160 mg, 0.51 mmol) and pyridine (80 mg, 1.01 mmol) in dry CH_2Cl_2 (5.1 mL) was added benzenesulfonyl chloride (BsCl) (72 mg, 0.41 mmol) at 0 °C under N_2. The reaction mixture was warmed to rt and then stirred for 12 h at rt. The reaction mixture was partitioned between EtOAc and, sequentially, 5% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to provide the monobenzenesulfonate **13** (83 mg, 86% from **12** based on 42% conversion) as a colorless oil: TLC R_f = 0.68 (EtOAc/petroleum ether = 4/1); IR (film) 3510, 2940, 1731, 1448, 1360, 1296, 1187, 1096, 1027, 926, 821, 757 cm^{-1}; ^1H NMR δ 7.86−7.96 (m, 2H), 7.64−7.70 (m, 1H), 7.55−7.60 (m, 2H), 4.40 (dd, J = 3.4 and 9.9 Hz, 1H), 3.51−4.19 (m, 8H), 2.55 (s, 1H), 2.17 (brs, 1H), 1.41−1.97 (m, 7H), 1.25 (t, J = 7.1 Hz, 3H), 1.19−1.29 (m, 1H), 1.09 (s, 3H); ^{13}C NMR δ up 169.5, 135.5, 116.1, 69.2, 65.7, 64.3, 59.8, 42.4, 40.3, 35.6, 30.4; down 133.8, 129.3, 127.8, 69.4, 63.5, 44.7, 42.5, 14.2, 13.1; HRMS calcd for $C_{22}H_{30}O_8SNa$ (M + Na) 477.1559, found 477.1547. This was followed by the diol ketal **12** (93 mg).

Diol Benzenesulfonate 6. To a stirred solution of monobenzenesulfonate **13** (144 mg, 0.32 mmol) in dry THF (10 mL) was added a 1 M solution of DIBAL-H in hexanes (1.6 mL, 1.60 mmol) at −78 °C under N_2. The reaction mixture was warmed slowly to rt over 1 h. After an additional 1 h at rt, the reaction mixture was partitioned between EtOAc and, sequentially, 5% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to afford the diol benzenesulfonate **6** (116 mg, 89% from **13**) as a colorless oil: TLC R_f = 0.11 (EtOAc/petroleum ether = 4/1); IR (film) 3405, 2939, 1732, 1448, 1357, 1187, 1096, 1014, 920, 820, 732 cm^{-1}; ^1H NMR δ 7.85−7.97 (m, 2H), 7.66−7.72 (m, 1H), 7.56−7.60 (m, 2H), 4.34−4.48 (m, 1H), 3.44−3.98 (m, 8H), 1.25−2.71 (m, 11H), 0.78−0.87 (m, 3H); ^{13}C NMR δ up 135.6, 116.8, 69.5, 64.8, 63.2, 58.8, 41.6, 38.9, 35.9, 30.6; down 133.8, 129.2, 127.8, 69.7, 59.9, 44.9, 42.5, 12.8; HRMS calcd for $C_{20}H_{28}O_7SNa$ (M + Na) 435.1453, found 435.1443.

Nitrile 16. To a stirred solution of bromosulfone **15** (5.2 g, 15.6 mmol) in 1-methyl-2-pyrrolidinone (NMP) (120 mL) was added CuCN (7.0 g, 77.8 mmol). The reaction mixture was heated to reflux for 16 h and was then poured into 30% aqueous NH_4OH (300 mL) at 0 °C. After vigorous stirring for 3 h, the mixture was filtered, and the filter cake was partitioned between CH_2Cl_2 and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was recrystallized (EtOAc/petroleum ether = 20/1) to give the nitrile **16** (3.35 g, 75% from 25) as a white solid: TLC R_f = 0.21 (MTBE/petroleum ether = 1/1); mp 144−145 °C; IR (film) 2979, 2845, 2222, 1605, 1500 cm^{-1}; ^1H NMR δ 7.76 (d, J = 7.3 Hz, 2H), 7.70 (t, J = 8.8 Hz, 1H), 7.54 (t, J = 7.8 Hz, 2H), 7.48 (d, J = 8.8 Hz, 1H), 7.13 (d, J = 2.5 Hz, 1H), 6.97 (dd, J = 2.5 and 8.7 Hz, 1H), 4.56 (s, 2H), 3.90 (s, 3H); ^{13}C NMR δ up 162.8, 137.6, 133.8, 117.2, 106.0, 60.7; down 134.50, 134.47, 129.5, 128.9, 117.5, 115.8, 56.0; HRMS calcd for $C_{15}H_{13}O_3NS$ 287.0616, found 287.0611. Anal. Calcd for $C_{15}H_{13}O_3NS$: C, 62.70; H, 4.56; N, 4.87. Found: C, 62.60; H, 4.62; N, 4.98.

Aldehyde 17. To a stirred solution of nitrile **16** (3.92 g, 13.66 mmol) in THF (120 mL) was added a 0.83 M solution of DIBAL-H in hexanes (41.1 mL, 34.15 mmol) at −78 °C. The reaction mixture was stirred and gradually warmed from −78 °C to rt over 2 h. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl and 6 M aqueous HCl (6:1, v/v) at 0 °C. The organic solvent was removed in vacuo, and the residue was then partitioned between EtOAc and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The crude residue was recrystallized (EtOAc/petroleum ether = 20/1) to give the aldehyde **17** (3.22 g, 81% from **16**) as a white solid: TLC R_f = 0.17 (MTBE/petroleum ether = 1/1); mp 114−115 °C; IR (film) 2939, 2841, 1683, 1599, 1571, 1447 cm^{-1}; ^1H NMR δ 9.68 (s, 1H), 7.70−7.72 (m, 2H), 7.65 (d, J = 8.5 Hz, 1H), 7.58−7.61 (m, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.00 (dd, J = 2.5 and 8.5 Hz, 1H), 6.92 (d, J = 2.5 Hz, 1H), 5.05 (s, 2H), 3.85 (s, 3H); ^{13}C NMR δ up 163.3, 138.2, 131.2, 127.9, 57.6; down 190.7, 137.2, 133.9, 128.9, 128.7, 119.4, 114.4, 55.8; HRMS calcd for $C_{15}H_{14}O_4S$ 290.0613, found 290.0605. Anal. Calcd for $C_{15}H_{14}O_4S$: C, 73.43; H, 10.27. Found: C, 73.24; H, 10.52.

Sulfone 5. The aldehyde **17** (2.50 g, 8.62 mmol), hydrazine monohydrate (50.7 g, 862.00 mmol), and K_2CO_3 (42.82 g, 310.32 mmol) were added into diethylene glycol (30 mL) sequentially. The mixture was heated at 180 °C for 5 h and then at 150 °C for another 16 h. The reaction mixture was cooled to rt and then partitioned between EtOAc and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The crude residue was recrystallized (CH_2Cl_2/petroleum ether = 20/1) to give the sulfone **5** (1.35 g, 57% from **17**) as a white solid: TLC R_f = 0.33 (MTBE/petroleum ether

= 1/4); mp 86−87 °C; IR (film) 3062, 2935, 2836, 1612, 1580 cm^{-1}; ^{1}H NMR δ 7.62−7.70 (m, 3H), 7.49 (t, J = 7.8 Hz, 2H), 7.03 (d, J = 8.4 Hz, 1H), 6.79 (dd, J = 2.7 and 8.4 Hz, 1H), 6.56 (d, J = 2.7 Hz, 1H), 4.36 (s, 2H), 3.68 (s, 3H), 2.04 (s, 3H); ^{13}C NMR δ up 157.5, 138.3, 130.2, 127.3, 60.2; down 133.7, 131.4, 128.9, 128.7, 116.5, 115.2, 55.2, 18.3; HRMS calcd for $C_{15}H_{16}O_3SNa$ (M + Na) 299.0718, found 299.0720. Anal. Calcd for $C_{15}H_{16}O_3S$: C, 65.19; H, 5.84. Found: C, 65.16; H, 5.84.

Keto Aldehyde 20. To a stirred solution of sulfone **5** (723 mg, 2.62 mmol) in dry THF (1 mL) was added a 2.5 M solution of *n*-BuLi in hexanes (1.05 mL, 2.62 mmol) at −78 °C under N_2. The reaction mixture was stirred for 30 min, and a solution of diol benzenesulfonate **6** (108 mg, 0.26 mmol) in dry THF (1.6 mL) was then added. The reaction mixture was slowly warmed to rt over 1.5 h and was then stirred at rt for another 6 h. The reaction mixture was partitioned between EtOAc and, sequentially, saturated aqueous NH_4Cl and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to afford the sulfone **18** (123 mg, 88% from **6**) as a colorless oil: TLC R_f = 0.11 (EtOAc/petroleum ether = 4/1).

To a stirred solution of sulfone **18** (70 mg, 0.13 mmol) and EtOH (122 mg, 2.65 mmol) in dry THF (3.5 mL) was added Na (61 mg, 2.65 mmol) at −20 °C under N_2. After an additional 2 h, the unreacted Na was quenched by careful addition of MeOH, and the reaction mixture was then partitioned between EtOAc and, sequentially, saturated aqueous NH_4Cl and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to give the diol **19** (43 mg, 74% from **6**) as a colorless oil: TLC R_f = 0.28 (EtOAc/methylene chloride/petroleum ether = 80/15/5); IR (film) 3406, 2934, 2890, 1733, 1609, 1579, 1503, 1456, 1286, 1252, 1209, 1160, 1083, 1008, 910, 804, 732 cm^{-1}; ^{1}H NMR δ 7.04 (d, J = 8.3 Hz, 1H), 6.64−6.71 (m, 2H), 3.78 (s, 3H), 3.45−4.02 (m, 7H), 2.56−2.63 (m, 2H), 2.24 (S, 3H), 1.22−2.04 (m, 13H), 0.84−0.90 (m, 3H); ^{13}C NMR δ up 157.7, 142.4, 127.8, 117.1, 64.9, 63.2, 59.0, 41.8, 39.9, 36.4, 31.6, 30.3, 30.0; down 130.8, 114.6, 110.4, 74.1, 60.2, 55.2, 48.4, 42.1, 18.4, 13.2; HRMS calcd for $C_{23}H_{34}O_5Na$ (M + Na) 413.2304, found 413.2307.

To a stirred solution of diol **19** (43 mg, 0.11 mmol) in CH_2Cl_2 (4 mL) was added Dess−Martin periodinane (139 mg, 0.33 mmol) at rt. The reaction mixture was stirred for 1.5 h and was then concentrated in vacuo. The residue was chromatographed to provide the keto aldehyde **20** (34 mg, 59% from **6**) as a colorless oil: TLC R_f = 0.18 (petroleum ether/acetone = 9/1); IR (film) 2923, 2876, 1709, 1609, 1579, 1500, 1465, 1298, 1252, 1159, 1084, 1035, 949, 862, 810 cm^{-1}; ^{1}H NMR δ 9.81 (d, J = 1.9 Hz, 1H), 7.04 (d, J = 8.2 Hz, 1H), 6.69 (d, J = 2.7 Hz, 1H), 6.65 (dd, J = 2.7, 8.2 Hz, 1H), 3.98−4.07 (m, 2H), 3.82−3.90 (m, 2H), 3.78 (s, 3H), 2.71 (ddd, J = 4.9, 11.7, 13.3 Hz, 1H), 2.37−2.55 (m, 5H), 2.27 (s, 3H), 2.21 (ddd, J = 1.9, 6.5, 13.2 Hz, 1H), 2.09 (dd, J = 7.1, 13.1 Hz, 1H), 1.51−1.91 (m, 5H), 1.34 (s, 3H); ^{13}C NMR δ up 210.5, 157.7, 141.8, 128.0, 116.6, 65.4, 64.2, 43.3, 41.3, 37.8, 37.1, 31.1, 27.7; down 202.0, 130.9, 114.6, 110.7, 68.6, 55.2, 50.3, 49.0, 18.3, 12.9; HRMS calcd for $C_{23}H_{30}O_5Na$ (M + Na) 409.1991, found 409.2004.

Enones 4 and 21. A stirred solution of keto aldehyde **20** (47.5 mg, 0.12 mmol) in dry THF (6 mL) was titrated with a 0.1 M solution of isohexylmagnesium bromide in THF (1.5 mL, 0.15 mmol) at 0 °C to disappearance of starting material (monitored by TLC). The reaction mixture was then partitioned between EtOAc and, sequentially, saturated aqueous NH_4Cl and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was filtered through a short pad of silica gel with MTBE. Concentration of the filtrate gave a residue that was used in the next step without further purification.

The residue obtained above was dissolved in THF (0.9 mL) followed by the addition of MeOH (9 mL) and 3 M aqueous HCl (1.2 mL). The reaction mixture was heated to reflux for 4.5 h and then cooled to rt. The reaction mixture was neutralized by the addition of saturated aqueous $NaHCO_3$, and the solvent was removed in vacuo. The residue was partitioned between EtOAc and H_2O. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to yield the enone **4** (8 mg, 16% from **20**) as a colorless oil: TLC R_f = 0.37 (petroleum ether/methylene chloride/MTBE = 7/2/1); $[\alpha]^{20}_{D}$ = −61.7 (c = 0.30, CH_2Cl_2); IR (film) 2956, 2926, 2865, 1712, 1639, 1610, 1499, 1458, 1377, 1299, 1252, 1208, 1160, 1109, 1046 cm^{-1}; ^{1}H NMR δ 7.04 (d, J = 8.2 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 6.66 (dd, J = 2.7, 8.2 Hz, 1H), 5.76 (t, J = 7.5 Hz, 1H), 3.78 (s, 3H), 2.45−2.73 (m, 6H), 2.34 (dd, J = 7.2, 17.3 Hz, 1H), 2.27 (s, 3H), 2.09−2.25 (m, 2H), 1.34−2.00 (m, 9H), 1.21 (s, 3H), 1.16−1.25 (m, 1H), 0.86 (d, J = 6.6 Hz, 6H); ^{13}C NMR δ up 210.4, 205.8, 157.8, 145.7, 141.6, 128.0, 43.1, 39.9, 38.51, 38.47, 35.5, 31.1, 27.83, 27.78, 27.1; down 138.1, 131.0, 114.5, 111.1, 55.2, 49.2, 46.9, 27.80, 22.57, 22.53, 19.4, 18.4; HRMS calcd for $C_{27}H_{38}O_3Na$ (M + Na) 433.2719, found 433.2704. This was followed by the enone **21** (8.5 mg, 17% from **20**) as a colorless oil: TLC R_f = 0.35 (petroleum ether/methylene chloride/MTBE = 7/2/1); $[\alpha]^{20}_{D}$ = −41.7 (c = 0.30, CH_2Cl_2); IR (film) 2954, 2921, 2865, 1710, 1644, 1608, 1503, 1455, 1377, 1299, 1252, 1204, 1160, 1102, 1046 cm^{-1}; ^{1}H NMR δ 7.04 (d, J = 8.2 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 6.66 (dd, J = 2.7, 8.2 Hz, 1H), 6.53 (t, J = 7.8 Hz, 1H), 3.78 (s, 3H), 2.45−2.74 (m, 6H), 2.38 (dd, J = 6.9, 17.0 Hz, 1H), 2.27 (s, 3H), 2.17−2.29 (m, 3H), 1.99−2.10 (m, 3H), 1.81−1.86 (m, 1H), 1.65−1.72 (m, 1H), 1.45−1.57 (m, 3H), 1.27 (s, 3H), 1.21−1.25 (m, 1H), 0.87 (d, J = 6.6 Hz, 6H); ^{13}C NMR δ up 210.2, 204.4, 157.8, 145.0, 141.5, 128.0, 43.0, 38.74, 38.68, 38.3, 35.7, 31.0, 28.1, 27.0; down 137.0, 131.0, 114.6, 111.1, 55.2, 49.1, 47.3, 22.51, 22.49, 18.4, 17.8; HRMS calcd for $C_{27}H_{38}O_3Na$ (M + Na) 433.2719, found 433.2715.

Enone 4 from Enone 21. To a stirred solution of enone **22** (6 mg, 0.015 mmol) in HOAc (0.5 mL) was added KI (25 mg, 0.15 mmol) at rt. After an additional 2 days, the reaction solvent was removed in vacuo. The residue was partitioned between MTBE and, sequentially, saturated aqueous $NaHCO_3$ and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to give the enone **4** (2.2 mg, 69% from **21** based on 53% conversion) as a colorless oil. This was followed by the enone **21** (2.8 mg) as a colorless oil.

Dione 22. To a stirred suspension mixture of CuI (38 mg, 0.20 mmol) in dry Et_2O (1.2 mL) was added a 2.2 M solution of MeLi in Et_2O (0.18 mL, 0.40 mmol) dropwise at −20 °C under N_2. After an additional 1 h, the reaction mixture was added a solution of the enone **4** (8 mg, 0.020 mmol) in dry Et_2O (0.8 mL), and the reaction mixture was then stirred for another 1 h at −20 °C. The reaction mixture was partitioned between CH_2Cl_2 and, sequentially, saturated aqueous NH_4Cl and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to provide the dione **22** (5.5 mg, 66% from **4**) as a colorless oil: TLC R_f = 0.40 (petroleum ether/methylene chloride/MTBE = 7/2/1); $[\alpha]^{20}_{D}$ = −85.7 (c = 0.28, CH_2Cl_2); IR (film) 2954, 2921, 2865, 1738, 1709, 1608, 1500, 1464, 1383, 1299, 1252, 1209, 1160, 1104, 1046 cm^{-1}; ^{1}H NMR δ 7.04 (d, J = 8.2 Hz, 1H), 6.70 (d, J = 2.7 Hz, 1H), 6.66 (dd, J = 2.7, 8.2 Hz, 1H), 3.78 (s, 3H), 2.71 (ddd, J = 4.8, 11.6, 13.2 Hz, 1H), 2.28−2.56 (m, 6H), 2.27 (s, 3H), 1.14−2.03 (m, 14H), 1.09 (s, 3H), 1.01 (d, J = 6.4 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H); ^{13}C NMR δ up 216.2, 210.4, 157.8, 141.6, 128.0, 43.2, 39.7, 39.1, 38.4, 35.8, 31.18, 28.01, 24.9; down 131.0, 114.6, 111.0, 67.7, 55.2, 49.1, 48.5, 31.16, 27.94, 22.7, 22.6, 18.7, 18.4, 13.2.

Diol 23. To a stirred solution of dione **22** (5.5 mg, 0.013 mmol) in dry THF (1 mL) was added a 1 M solution of L-Selectride in THF (0.13 mL, 0.13 mmol) at −78 °C. The reaction mixture was slowly warmed to rt over 1.5 h. After an additional 0.5 h at rt, the reaction mixture was partitioned between EtOAc and, sequentially, saturated aqueous NH_4Cl and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to give the diol **23** (2.5 mg, 45% from **22**) as a colorless oil: TLC R_f = 0.28 (petroleum ether/methylene chloride/MTBE = 7/2/1); $[\alpha]^{20}_{D} = -5.6$ (c = 0.13, CH_2Cl_2); IR (film) 3418, 2928, 2865, 1614, 1505, 1456, 1383, 1306, 1251, 1208, 1160, 1102, 1046 cm^{-1}; ^{1}H NMR δ 7.04 (d, J = 8.2 Hz, 1H), 6.72 (d, J = 2.7 Hz, 1H), 6.65 (dd, J = 2.7, 8.2 Hz, 1H), 4.32−4.37 (m, 1H), 4.06 (d, J = 1.3 Hz, 1H), 3.78 (s, 3H), 2.73 (ddd, J = 4.5, 11.2, 13.2 Hz, 1H), 2.43−2.50 (m, 1H), 2.24 (s, 3H), 2.18−2.27 (m, 1H), 1.06−1.78 (m, 20H), 0.99 (d, J = 6.6 Hz, 3H), 0.90 (s, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.6 Hz, 3H); ^{13}C NMR δ up 157.8, 142.3, 127.8, 42.8, 39.5, 36.5, 36.2, 34.2, 31.1, 30.3, 29.9, 24.1; down 130.9, 114.5, 110.8, 71.9, 67.0, 61.3, 55.2, 45.4, 40.4, 29.7, 28.1, 22.8, 22.6, 18.3, 18.2, 12.1; HRMS calcd for $C_{28}H_{46}O_3Na$ (M + Na) 453.3345, found 453.3337.

Calicoferol B (1). To a stirred solution of diol **23** (2.3 mg, 0.0054 mmol) and Et_3SiH (25 mg, 0.22 mmol) in dry CH_2Cl_2 (1 mL) was added a solution of $(C_6F_5)_3B$ (0.6 mg, 0.0012 mmol) in dry CH_2Cl_2 (0.1 mL) at rt under N_2. After an additional 1 h, Et_3N (0.1 mL) was added, and the reaction mixture was filtered through a short pad of silica gel. The filter cake was washed with MTBE, and the filtrate was concentrated. The residue was used in the next step without further purification.

The residue was dissolved in a 1 M solution of TBAF in THF (0.8 mL) at rt. After an additional 24 h, the reaction mixture was partitioned between EtOAc and, sequentially, saturated aqueous NH_4Cl and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was chromatographed to produce the target molecule, (−)-calicoferol B (**1**) (1.2 mg, 55% from **23**), as a colorless oil: TLC R_f = 0.52 (petroleum ether/MTBE = 1/1); $[\alpha]^{20}_{D} = -18.8$ (c = 0.08, $CHCl_3$) (lit.[9] $[\alpha]^{21}_{D} = -16.2$ (c = 0.09, $CHCl_3$)); IR (film) 3379, 2956, 2926, 2865, 1609, 1581, 1504, 1464, 1384, 1292, 1243, 1158, 1102, 1024, 869, 806 cm^{-1}; ^{1}H NMR (C_6D_6) δ 6.95 (d, J = 8.2 Hz, 1H), 6.66 (d, J = 2.6 Hz, 1H), 6.47 (dd, J = 2.6, 8.2 Hz, 1H), 4.04 (ddd, J = 4.4, 7.6, 7.6 Hz, 1H), 3.74 (d, J = 2.5 Hz, 1H), 2.68 (ddd, J = 5.1, 11.9, 13.3 Hz, 1H), 2.35 (ddd, J = 5.3, 11.9, 14.3 Hz, 1H), 2.24 (s, 3H), 1.95−2.04 (m, 2H), 1.05−1.70 (m, 20H), 1.01 (d, J = 6.7 Hz, 3H), 0.95 (d, J = 6.6 Hz, 3H), 0.94 (d, J = 6.6 Hz, 3H), 0.89 (s, 3H); ^{13}C NMR (C_6D_6) δ up 155.3, 143.3, 43.4, 40.3, 37.7, 36.9, 35.0, 31.6, 31.3, 30.7, 25.1; down 131.7, 116.5, 113.3, 71.9, 67.1, 62.1, 45.9, 41.1, 30.5, 28.8, 23.4, 23.2, 18.9, 18.8, 12.8; HRMS calcd for $C_{27}H_{44}O_3Na$ (M + Na) 439.3188, found 439.3186.

Diol 25. The reaction was performed with the enone **21** (7 mg, 0.017 mmol), CuI (32.5 mg, 0.17 mmol), MeLi (2.2 M in THF, 0.16 mL, 0.35 mmol), and dry Et_2O (1.7 mL) in the same manner as described for the preparation of dione **22** to give dione **24** (2.7 mg, 37% from **21**) as a colorless oil: TLC R_f = 0.40 (petroleum ether/methylene chloride/MTBE = 7:2:1).

The reaction was performed with the dione **24** (2.7 mg, 0.0063 mmol), L-Selectride (1 M in THF, 0.13 mL, 0.13 mmol), and dry THF (0.5 mL) in the same manner as described for the preparation of diol **23** to give diol **25** (1.2 mg, 16% from **21**) as a colorless oil: TLC R_f = 0.20 (petroleum ether/methylene chloride/MTBE = 7:2:1); ^{1}H NMR δ 7.04 (d, J = 8.2 Hz, 1H), 6.72 (d, J = 2.7 Hz, 1H), 6.65 (dd, J = 2.7, 8.2 Hz, 1H), 4.30−4.35 (m, 1H), 4.06 (brs, 1H), 3.78 (s, 3H), 2.70−2.77 (m, 1H), 2.42−2.50 (m, 1H), 2.24 (s, 3H), 2.13−2.28 (m, 1H), 1.05−1.90 (m, 20H), 0.98 (d, J = 6.4 Hz, 3H), 0.91 (s, 3H), 0.87 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H).

C(20)-*epi*-Calicoferol B (26). The reaction was performed with the diol **25** (1.2 mg, 0.0028 mmol), Et_3SiH (13 mg, 0.11 mmol), $(C_6F_5)_3B$ (0.3 mg, 0.00059 mmol), and dry CH_2Cl_2 (0.6 mL); Et_3N (0.1 mL); TBAF (1 M in THF, 0.5 mL); in the same manner as described for the preparation of calicoferol B (**1**) to give C(20)-*epi*-calicoferol B (**26**) (0.8 mg, 69% from **25**) as a colorless oil: TLC R_f = 0.40 (petroleum ether/MTBE = 1:1); $[\alpha]^{20}_{D} = +52.8$ (c = 0.053, CH_2Cl_2); IR (film) 3380, 2925, 2858, 1653, 1610, 1497, 1464, 1384, 1257, 1158, 1102, 1024 cm^{-1}; ^{1}H NMR (C_6D_6) δ 6.94 (d, J = 8.2 Hz, 1H), 6.61 (d, J = 2.7 Hz, 1H), 6.44 (dd, J = 2.7, 8.2 Hz, 1H), 3.96 (ddd, J = 4.3, 7.6, 7.6 Hz, 1H), 3.71 (d, J = 2.4 Hz, 1H), 2.68 (ddd, J = 5.0, 12.8, 13.2 Hz, 1H), 2.34 (ddd, J = 5.0, 11.7, 13.3 Hz, 1H), 2.23 (s, 3H), 1.93−2.11 (m, 2H), 1.15−1.70 (m, 19H), 1.07 (dd, J = 4.2, 12.9 Hz, 1H), 0.97 (d, J = 6.4 Hz, 3H), 0.93 (d, J = 7.1 Hz, 6H), 0.92 (s, 3H); ^{13}C NMR (C_6D_6) δ up 155.2, 143.3, 43.4, 40.2, 37.6, 35.5, 35.1, 31.6, 31.3, 30.8, 24.8; down 131.7, 116.4, 113.2, 72.3, 67.0, 62.0, 46.0, 41.2, 30.2, 28.9, 23.4, 23.2, 19.3, 18.9, 12.8; HRMS calcd for $C_{27}H_{44}O_3Na$ (M + Na) 439.3188, found 439.3176.

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Supporting Information Available: ^{1}H and ^{13}C spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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