Synthesis of (±)-Okicenone and (±)-Aloesaponol III

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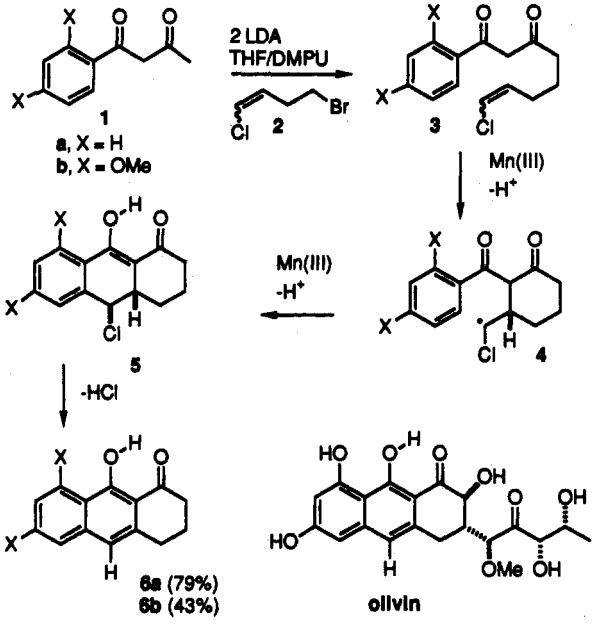
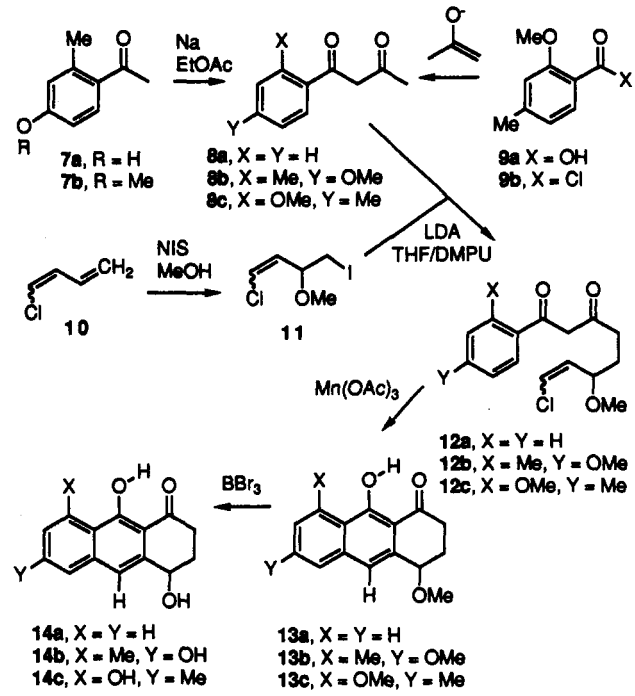
We recently reported that chlorine substituents on the alkene control the regioselectivity of the cyclization of 5-hexenyl and 6-heptenyl radicals generated by oxidation of an acetoacetate ester or 1,3-diketone with $Mn(OAc)_3 \cdot 2H_2O$.[1] One-electron oxidation of benzoylacetone derivative **3a**, containing a chlorine on the terminal double-bond carbon, gives α-chloro radical **4a** that adds to the aromatic ring to give **5a** after a second one-electron oxidation. Loss of hydrogen chloride leads to naphthol **6a** in 79% yield. The chlorine substituent plays two crucial roles in the conversion of **3a** to **6a**. Steric effects from the chlorine slow down the 7-endo cyclization thereby favoring the 6-exo cyclization to give **4a**. No tricyclic products are obtained from the deschloro analogue of **3a**. Secondly, spontaneous loss of hydrogen chloride from **5a** leads directly to the desired naphthol **6a**.



An analogous oxidative cyclization of **3b** leads to 43% of **6b**,[1] a model for the synthesis of olivin, the aglycon of the aureolic acid antitumor antibiotic olivomycin.[2] The required substrate **3b** is easily prepared in 68% yield by alkylation of the dianion of benzoyl acetone **1b** with **2**.[3]

The antitumor antibiotic okicenone (**14b**), which was recently isolated from *Streptomyces* sp. KO-3599, shows cytocidal activity against mammalian tumor cells in vitro with IC_{50} levels of 0.53–11 μg/mL.[4] Aloesaponol III (**14c**) was isolated from the young subterranean stems of *Aloe saponaria* Haw.[5] Both of these targets appeared to be well suited for preparation by oxidative free-radical cyclization of chloroalkenes **12b** and **12c**. The successful synthesis of the olivin model **6b** demonstrates that this reaction will tolerate substituents on the benzene ring of **12**.



The new feature of these targets is the benzylic hydroxyl group. In principle, this can be introduced after the formation of the tricyclic ring system. Oxidative cyclization of **12** with an allylic methoxy group appeared to be more attractive for several reasons. This strategy is more convergent than a linear approach. The more highly functionalized iodide **11** is, surprisingly, much easier to prepare than **2**, which must be prepared by a four-step homologation of 1,3-dichloropropene.[3] Finally, examination of the oxidative cyclization of **12** will further define the scope and limitations of this dihydroanthracenone synthesis.

We chose to carry out a model study using **12a** with an unsubstituted aromatic ring. Addition of NIS to 1-chloro-1,3-butadiene[6] (**10**) in MeOH affords 72% of **11** as a 6:1 mixture of *Z*- and *E*-isomers.[7] Alkylation of the dianion of benzoylacetone (prepared from 2 equiv of LDA and 2 equiv of DMPU in THF) with **11** at 0 °C provides 72% of the alkylated dione **12a**. Oxidative cyclization of **12a** with 2 equiv of $Mn(OAc)_3 \cdot 2H_2O$ in HOAc can be carried out at various temperatures. We found that the best yield of **13a** (60%) is obtained when the reaction is carried out rapidly (6 min) at reflux (120 °C). The byproducts appear to be oligomeric and cannot be characterized. The use of

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(7) This reaction has been previously reported using HgO and I_2 in MeOH. Petrov, A. A.; Sopov, N. P. *Z. Obshch. Khim.* **1945**, *15*, 981; *Chem. Abstr.* **1946**, *40*, 6406[7].

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KOAc as a buffer has no effect on the yield of **13a**. Deprotection[8] of the benzylic methyl ether is easily accomplished by treatment of **13a** with 3 equiv of BBr_3 in CH_2Cl_2 (−78 to 0 °C) yielding 95% of the desired dihydroxy ketone **14a**.

The synthesis of okicenone (**14b**) was carried out analogously. Methylation[9b] of **7a** with potassium carbonate and methyl iodide in acetone gives **7b**[9a] quantitatively. Claisen condensation of ketone **7b** with sodium in ethyl acetate[10] provides 79% of the requisite substituted benzoylacetone **8b**. Alkylation of the dianion of **8b** with 11 yields 78% of **12b**. Oxidative cyclization of **12b** (2 equiv of $Mn(OAc)_3 \cdot 2H_2O$, HOAc, 120 °C, 6 min) affords 42% of **13b** and 11% of recovered **12b**. Deprotection of both methyl ethers of **13b** with BBr_3 provides 67% of (±)-okicenone (**14b**) whose spectral data are identical to those reported.[4]

This procedure is also successful for the preparation of aloesaponol III (**14c**). Carboxylic acid **9a** was converted to the acid chloride **9b** and added to the enolate of acetone[11] affording 71% of substituted benzoylacetone **8c**. Alkylation of the dianion of **8c** with 11 yields 56% of **12c**. Oxidative cyclization of **12c** (2 equiv of $Mn(OAc)_3 \cdot 2H_2O$, HOAc, 120 °C, 6 min) affords 31% of **13c**. Deprotection of both methyl ethers of **13c** with BBr_3 provides 70% of (±)-aloesaponol III (**14c**) whose spectral data are identical to those reported.[5]

Okicenone (**14b**) and aloesaponol III (**14c**) have both been synthesized for the first time from substituted benzoyl acetones using a three-step route that further demonstrates the utility of oxidative free-radical cyclization for the preparation of highly oxygenated dihydroanthracenones.

Experimental Section

NMR spectra were recorded at 300 MHz in $CDCl_3$ unless otherwise indicated. Chemical shifts are reported in δ and coupling constants in Hz. $Mn(OAc)_3 \cdot 2H_2O$ was purchased from Aldrich. All alkylations and oxidative cyclizations were run under N_2.

4-Methoxy-2-methylacetophenone (7b).[9] A mixture of 4-hydroxy-2-methylacetophenone (6.03 g, 40 mmol), iodomethane (2.82 mL, 45 mmol), K_2CO_3 (8.4 g, 60 mmol), and acetone (65 mL) was heated at reflux overnight and cooled to rt. The solution was filtered, and the filtrate was concentrated in vacuo. The residue was diluted with ether (50 mL). The solution was washed with water (2 × 20 mL), dried ($MgSO_4$), and concentrated in vacuo to give 6.54 g (100%) of crude **7b** which was used without purification: ^1H NMR 7.75 (br d, 1, J = 8.5), 6.75 (br d, 1, J = 8.5), 6.73 (br s, 1), 3.84 (s, 3), 2.57 (s, 3), 2.54 (s, 3); ^{13}C NMR 199.4, 161.8, 142.1, 132.5, 129.8, 117.4, 110.5, 55.2, 29.0, 22.5; IR (neat) 2967, 2927, 2838, 1673, 1603, 1566, 1248.

1-(4-Methoxy-2-methylphenyl)-1,3-butanedione (8b) was prepared by the literature procedure for the preparation of a **8c**.[10] Crude 4-methoxy-2-methylacetophenone (**7b**) (3.3 g, 20 mmol) was dissolved in EtOAc (5.3 g, 60 mmol). Sodium metal (0.62 g, 27 mmol) was added. The mixture was stirred at 0 °C for 16 h and rt for 4 h. The mixture was diluted with water (30 mL) and 3 N HCl solution (7 mL) and extracted with ether (2 × 50 mL). The ether layers were washed with saturated $NaHCO_3$ solution (20 mL), dried ($MgSO_4$), and concentrated in vacuo to give 4.16 g of crude **8b**. Flash chromatography (20:1 hexane–EtOAc) gave 3.25 g (91% based on recovery of 13.6% **7b**) of **8b** as a 15:1 mixture of enol and keto tautomers: ^1H NMR (enol) 16.8 (s, 1), 7.48 (br d, 1, J = 8.8), 6.74 (br s, 1), 6.73 (br d, 1, J = 8.8), 5.75 (s, 1), 3.81 (s, 3), 2.51 (s, 3), 2.13 (s, 1); ^{13}C NMR (enol) 191.1, 188.3, 161.4, 139.9, 130.4, 128.3, 116.9, 110.9, 99.8, 55.1, 25.1, 21.4; ^1H NMR (keto) 7.70 (br d, 1, J = 9.0), 4.02 (s, 2), 3.83 (s, 3), 2.57 (s, 3), 2.27 (s, 3); ^{13}C NMR (keto) 162.4, 143.2, 132.8, 117.8, 110.7, 56.7, 55.2, 30.4, 22.6; IR (neat) 3000, 2960, 2927, 2817, 1720, 1650–1550 (br), 1240. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.98; H, 6.80.

1-(2-Methoxy-4-methylphenyl)-1,3-butanedione (8c). To a solution of 2-methoxy-4-methylbenzoic acid (**9a**) (1.38 g, 8.3 mmol) in anhydrous ether (5 mL) was added oxalyl chloride (1.6 mL, 18 mmol). The solution was heated at reflux for 1 h, and the solvent was removed in vacuo to give acid chloride **9b** (1.55 g) as a slightly yellow liquid. To a solution of **9b** in THF (10 mL) at −78 °C was added dropwise a solution of the enolate of acetone[1,11] (prepared from 17 mmol of LDA and 17 mmol of acetone in 35 mL of THF at −78 °C) over 20 min. The solution was stirred at −78 to −60 °C for 1 h. The solvent was removed, and the residue was diluted with ether (80 mL). The ether solution was washed with 10% HCl solution (15 mL), saturated $NaHCO_3$ solution (15 mL), and brine (15 mL), dried ($MgSO_4$), and concentrated in vacuo to afford crude **8c** (1.90 g). Flash chromatography (6:1 hexane–EtOAc) gave 1.20 g (71%) of pure **8c** as a 3:1 mixture of enol and keto tautomers: mp 51.5–52.5 °C (lit.[10] mp 52 °C); ^1H NMR (enol) 16.34 (s, 1), 7.78 (br d, 1, J = 7.9), 6.81 (br d, 1, J = 7.9), 6.74 (br s, 1), 6.45 (br s, 1), 3.87 (s, 3), 2.36 (s, 3), 2.15 (s, 3); ^{13}C NMR (enol) 194.2, 181.1, 158.4, 143.9, 130.0, 121.5, 121.0, 112.2, 101.3, 55.4, 26.0, 21.7; ^1H NMR (keto) 7.76 (br d, 1, J = 7.9), 4.0 (s, 2), 3.84 (s, 3), 2.22 (s, 3); ^{13}C NMR (keto) 158.9, 145.9, 130.9, 121.7, 112.1, 58.8, 55.2, 30.2, 21.8; IR (KBr) 2971, 1606, 801, 720.

1-Chloro-4-iodo-3-methoxy-1-butene (11).[7] To 1-chloro-1,3-butadiene (**10**)[6] (Z:E = 6:1, 0.83 g, 9.3 mmol) in methanol (15 mL) was added NIS (1.70 g, 7.18 mmol) in portions. The solution was stirred at rt for 2 h. The methanol was evaporated in vacuo. The residue was diluted with petroleum ether (70 mL). The solution was filtered, and the filtrate was washed with water (3 × 20 mL), dried ($MgSO_4$) and evaporated in vacuo to give 1.62 g (72%) of crude **11** which was used without purification: ^1H NMR (Z:E = 6:1) 6.33 (dd, 1, J = 7.4, 1.2, Z), 6.30 (dd, 1, J = 13.3, 0.8, E), 5.82 (dd, 1, J = 13.3, 7.8, E), 5.74 (dd, 1, J = 7.4, 8.1, Z), 4.25 (dddd, 1, J = 1.2, 8.1, 5.2, 6.0, Z), 3.69 (ddt, 1, J = 0.8, 7.8, 5.9, E), 3.37 (s, 3, Z), 3.35 (s, 3, E), 3.26 (d, 1, J = 10.7, 5.2, Z), 3.23 (dd, 1, J = 10.7, 6.0, Z), 3.21 (d, 2, J = 5.9, E); ^{13}C NMR 131.9 (E), 131.2 (Z), 122.64 (Z), 122.57 (E), 79.4 (E), 75.3 (Z), 56.9 (Z + E), 7.8 (E), 7.1 (Z); IR (neat) 3076, 2988, 2931, 2897, 2823, 1624, 1351, 1285, 1104.

8-Chloro-6-methoxy-1-phenyl-7-octene-1,3-dione (12a) was prepared from LDA (4.8 mmol of n-BuLi, 4.8 mmol of diisopropylamine in 10 mL of THF), 1-benzoylacetone (**8a**) (2 mmol), DMPU (4.8 mmol), and **11** (2 mmol) as described below for **12b** giving 999 mg of crude **12a**. Flash chromatography (20:1 hexane–EtOAc) gave 37 mg (11%) of **8a** followed by 406 mg (72%, 81% based on recovered **8a**) of **12a** as a 20:1 mixture of enol and keto tautomers: ^1H NMR (enol, mainly Z) 16.12 (s, 1), 7.92 (m, 2), 7.52 (m, 3), 6.28 (dd, 1, J = 7.4, 1.2), 6.19 (br s, 1), 5.70 (dd, 1, J = 7.4, 8.5), 4.28 (m, 1), 3.31 (s, 3), 2.58 (dt, 1, J = 15.5, 6.6), 2.51 (dt, 1, J = 15.5, 6.5), 1.96 (m, 2); ^{13}C NMR (enol, mainly Z) 196.5, 182.7, 134.8, 132.2, 132.1, 128.5, 126.9, 121.4, 96.1, 75.4, 56.6, 34.9, 30.1; ^1H NMR (keto) 4.11 (s, 2), 3.28 (s, 3); ^{13}C NMR (keto) 133.4, 128.7, 128.6, 121.0, 96.2, 79.2, 56.5, 56.4, 34.8, 30.8; IR (neat) 2930, 2823, 1603, 1460. Anal. Calcd for $C_{15}H_{17}O_3Cl$: C, 64.17; H, 6.10. Found: C, 63.94; H, 5.98.

8-Chloro-6-methoxy-1-(4-methoxy-2-methylphenyl)-7-octene-1,3-dione (12b). To a stirred solution of LDA (14.75 mmol of n-BuLi and 15.1 mmol of diisopropylamine) in THF (10 mL) at 0 °C was added a solution of **8b** (1.24 g, 6 mmol) in THF (2 mL). The resulting solution was stirred for 30 min at 0 °C. DMPU (1.7 mL, 15 mmol) and fresh 1-chloro-4-iodo-3-methoxy-1-butene (**11**) (1.65 g, 6.7 mmol) in THF (1 mL) were added. The resulting solution was stirred at 0 °C for 10 min and rt for 3 h. The mixture was diluted with water (50 mL) and 1 N HCl solution (50 mL) and extracted with ether (3 × 50 mL). The ether layers

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were dried ($MgSO_4$) and concentrated in vacuo to give 2.98 g of crude **12b**. Flash chromatography (8:1 hexane–EtOAc) gave 0.174 g of recovered **8b** (14%) followed by 1.508 g of pure **12b** (78%, 90% based on recovered **8b**) as a 15:1 mixture of enol and keto tautomers: ^1H NMR (enol, mainly *Z*) 16.12 (s, 1), 7.49 (br d, 1, J = 9.3), 6.75 (br s, 1), 6.73 (br d, 1, J = 9.3), 6.27 (dd, 1, J = 7.3, 1.0), 5.87 (s, 1), 5.69 (dd, 1, J = 7.3, 8.4), 4.28 (m, 1), 3.83 (s, 3), 3.31 (s, 3), 2.52 (s, 3), 2.51 (m, 2), 1.95 (m, 2); ^{13}C NMR (enol, mainly *Z*) 194.0, 187.8, 164.4, 140.0, 132.2, 130.5, 128.3, 121.4, 116.9, 111.0, 99.4, 75.5, 56.5, 55.3, 34.4, 30.3, 21.4; ^1H NMR (keto) 7.73 (d, 1, J = 9.4), 6.22 (dd, 1, J = 7.3, 1.0), 4.03 (s, 2), 3.84 (s, 3), 3.24 (s, 3), 2.58 (s, 3); ^{13}C NMR (keto) 133.0, 121.3, 117.8, 110.7, 75.3, 56.6, 56.0, 55.2, 38.9, 28.2, 22.6; IR (neat) 2931, 2823, 1719, 1667, 1604, 1245. Anal. Calcd for $C_{17}H_{21}O_4Cl$: C, 62.87; H, 6.52. Found: C, 62.96; H, 6.48.

8-Chloro-6-methoxy-1-(2-methoxy-4-methylphenyl)-7-octene-1,3-dione (12c) was prepared from LDA (10.0 mmol of n-BuLi, 10.0 mmol of diisopropylamine in 20 mL of THF), **8c** (0.955 g, 4.64 mmol), DMPU (10 mmol), and **11** (1.40 g, 5 mmol) as described above for **12b** giving 1.94 g of crude **12c**. Flash chromatography (8:1 hexane–EtOAc) gave 290 mg (30%) of recovered **8c** followed by 848 mg (56%, 80% based on recovered **8c**) of **12c** as a 15:1 mixture of enol and keto tautomers: ^1H NMR (enol, mainly *Z*) 16.31 (s, 1), 7.79 (br d, 1, J = 8.0), 6.81 (br d, 1, J = 8.0), 6.74 (br s, 1), 6.47 (s, 1), 6.25 (br d, 1, J = 7.4), 5.68 (dd, 1, J = 7.4, 8.5), 4.25 (m, 1), 3.87 (s, 3), 3.29 (s, 3), 2.55 (m, 2), 2.36 (s, 3), 1.89 (m, 2); ^{13}C NMR (enol, mainly *Z*) 196.8, 180.3, 158.3, 143.8, 132.0, 129.9, 121.3, 121.1, 120.8, 112.1, 100.8, 75.3, 56.3, 55.3, 34.9, 30.0, 21.6; ^1H NMR (keto, mainly *Z*) 7.75 (br d, 1, J = 8.1), 6.23 (br d, 1, J = 7.5), 5.65 (dd, 1, J = 7.5, 8.3), 4.02 (s, 2), 3.83 (s, 3), 3.26 (s, 3); ^{13}C NMR (keto, mainly *Z*) 204.0, 193.3, 158.8, 145.8, 132.1, 130.7, 123.8, 121.6, 121.0, 100.9, 75.1, 57.9, 56.3, 55.1, 38.4, 27.9, 21.7; IR (neat) 2933, 2823, 1717, 1668, 1614, 1257. Anal. Calcd for $C_{17}H_{21}O_4Cl$: C, 62.87; H, 6.52. Found: C, 62.58; H, 6.25.

3,4-Dihydro-9-hydroxy-4-methoxy-1(2*H*)-anthracenone (13a) was prepared from **12a** (309 mg, 1.1 mmol), HOAc (100 mL), and $Mn(OAc)_3 \cdot 2H_2O$ (730 mg, 2.4 mmol) as described below for **13b** giving 320 mg of crude **13a**. Flash chromatography (6:1 hexane–EtOAc) gave 160 mg (60%) of pure **13a**: ^1H NMR 14.2 (s, 1), 8.42 (br d, 1, J = 8.3), 7.76 (br d, 1, J = 8.1), 7.64 (ddd, 1, J = 1.3, 6.9, 8.1), 7.52 (ddd, 1, J = 1.2, 6.9, 8.3), 7.23 (br s, 1), 4.44 (dd, 1, J = 2.9, 5.1), 3.40 (s, 3), 3.11 (ddd, 1, J = 18.2, 5.6, 11.1), 2.64 (ddd, 1, J = 18.2, 4.8, 4.6), 2.40 (dddd, 1, J = 5.1, 4.6, 5.6, 13.6), 2.26 (dddd, 1, J = 2.9, 4.8, 11.1, 13.6); ^{13}C NMR 204.5, 163.2, 136.8, 135.6, 130.4, 127.5, 125.8, 125.0, 124.3, 117.7, 109.9, 76.3, 56.0, 33.4, 27.9; IR (neat) 3060, 2920, 1620, 1385, 1250, 1080. Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.37; H, 5.82. Found: C, 74.37; H, 5.73.

3,4-Dihydro-9-hydroxy-4,6-dimethoxy-8-methyl-1(2*H*)-anthracenone (13b). A solution of **12b** (530 mg, 1.63 mmol) and $Mn(OAc)_3 \cdot 2H_2O$ (1.082 g, 3.92 mmol) in HOAc (100 mL) was heated to 120 °C for 6 min. As soon as the color changed from dark to light brown, the solution was cooled in a cold water bath. The mixture was diluted with water (350 mL) and extracted with EtOAc (2 × 150 mL). The organic layers were washed with saturated $NaHCO_3$ (3 × 100 mL) and dried ($MgSO_4$). Removal of the solvent in vacuo gave 0.710 g crude of **13b**. Flash chromatography (8:1 hexane–EtOAc) gave 58 mg of recovered **12b** (11%) followed by 196 mg of pure **13b** (42%, 47% based on recovered **12b**) as a yellow oil: ^1H NMR 15.00 (s, 1), 7.05 (s, 1), 6.88 (d, 1, J = 2.7), 6.86 (br s, 1), 4.37 (dd, 1, J = 3.2, 5.0), 3.90 (s, 3), 3.39 (s, 3), 3.05 (ddd, 1, J = 5.7, 10.4, 18.0), 2.90 (s, 3), 2.60 (ddd, 1, J = 4.9, 5.0, 18.0), 2.33 (dddd, 1, J = 13.5, 5.7, 5.0, 5.0), 2.24 (dddd, 1, J = 13.5, 10.4, 4.9, 3.2); ^{13}C NMR 203.6, 167.2, 160.5, 141.6, 141.0, 136.2, 120.2, 119.0, 117.4, 109.1, 105.1, 76.4, 56.1, 55.2, 33.4, 27.9, 24.8; IR (neat) 2934, 2821, 1607, 1463, 1378, 1165. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.08; H, 6.22.

3,4-Dihydro-9-hydroxy-4,8-dimethoxy-6-methyl-1(2*H*)-anthracenone (13c) was prepared from **12c** (163 mg, 0.50 mmol), HOAc (40 mL), and $Mn(OAc)_3 \cdot 2H_2O$ (320 mg, 1.15 mmol) as described above for **13b** giving 160 mg of crude **13c**. Flash chromatography (10:1 hexane–EtOAc) gave 18 mg of recovered **12c** (11%) followed by 44 mg of pure **13c** (31%, 35% based on recovered **12c**) as a light yellow solid: mp 121.0–122.0 °C; ^1H NMR 15.24 (s, 1), 7.10 (br s, 1), 7.05 (br s, 1), 6.70 (br s, 1), 4.38 (dd, 1, J = 3.1, 5.1), 4.02 (s, 3), 3.39 (s, 3), 3.08 (ddd, 1, J = 5.7, 10.5, 18.1), 2.61 (ddd, 1, J = 4.9, 4.9, 18.1), 2.48 (s, 3), 2.31 (dddd, 1, J = 13.6, 5.1, 4.9, 5.7), 2.25 (dddd, 1, J = 13.6, 10.5, 4.9, 3.1); ^{13}C NMR 203.8, 166.1, 159.6, 142.0, 140.0, 136.4, 120.1 (2C), 117.3, 109.7, 108.5, 76.4, 56.2, 56.1, 33.5, 27.8, 22.2; IR (neat) 2942, 2824, 1620, 1577, 1381.

3,4-Dihydro-4,9-dihydroxy-1(2*H*)-anthracenone (14a) was prepared from **13a** (24 mg, 0.1 mmol) and BBr_3 (0.3 mL, 1 M in CH_2Cl_2) in CH_2Cl_2 (1 mL) as described below for the preparation of **14b** except that the temperature was raised from −78 to 0 °C over 1 h. Normal workup as described below gave 30 mg of crude **14a**. Flash chromatography (10:1 and then 1:1 hexane–EtOAc) gave 22 mg (95%) of pure **14a** as a yellow oil: ^1H NMR 14.16 (s, 1), 8.39 (br d, 1, J = 8.4), 7.71 (d, 1, J = 8.2), 7.61 (ddd, 1, J = 1.3, 6.9, 8.2), 7.49 (ddd, 1, J = 1.3, 6.9, 8.4), 7.30 (br s, 1), 4.98 (dd, 1, J = 3.7, 6.7), 3.05 (ddd, 1, J = 5.2, 8.7, 18.1), 2.67 (ddd, 1, J = 5.0, 7.2, 18.1), 2.30 (dddd, 1, J = 3.7, 5.0, 8.7, 13.3), 2.20 (dddd, 1, J = 6.7, 5.2, 7.2, 13.3), 2.00 (br s, 1); ^{13}C NMR 204.1, 163.2, 139.2, 137.3, 130.5, 127.5, 125.9, 124.7, 124.4, 115.9, 109.5, 68.0, 34.1, 30.8; IR (neat) 3406, 2950, 1625. Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.46; H, 5.24.

(±)-Okicenone (14b). To a solution of **13b** (86 mg, 0.3 mmol) in CH_2Cl_2 (1 mL) was added BBr_3 (1.2 mL, 1 M in CH_2Cl_2) at −78 °C. The solution was warmed to rt and stirred for 3 h. The mixture was poured into water (5 mL). The resulting solution was stirred for 1 h and extracted with CH_2Cl_2 (4 × 10 mL). Removal of the solvent in vacuo gave a yellow solid. The solid was hydrolyzed with a solution of THF (4 mL) and saturated $NaHCO_3$ (4 mL) at rt for 2 h. The mixture was extracted with CH_2Cl_2 (4 × 10 mL). The organic layers were dried ($MgSO_4$) and concentrated in vacuo to give 98 mg of a yellow solid. Flash chromatography (4:1 hexane–EtOAc and then EtOAc) gave 58 mg of **14b** as a yellow solid. Recrystallization from MeOH provided 51 mg (67%) of pure **14b** as a pale yellow solid: mp 240 °C dec; ^1H NMR (CD_3OD) 7.10 (d, 1, J = 0.9), 6.84 (d, 1, J = 2.5), 6.77 (dq, 1, J = 2.5, 0.9), 4.83 (br dd, 1, J = 3.6, 7.8), 2.91 (ddd, 1, J = 4.9, 7.9, 17.9), 2.66 (ddd, 1, J = 5.0, 8.2, 17.9), 2.25 (dddd, 1, J = 12.9, 3.6, 5.0, 7.9), 2.10 (dddd, 1, J = 12.9, 4.8, 8.2, 7.8); ^{13}C NMR (CD_3OD) 205.2, 168.1, 160.6, 143.7, 143.0, 141.7, 121.4, 118.9, 116.9, 109.8, 109.7, 68.9, 35.7, 32.4, 25.3; IR (KBr) 3372, 3178, 1623, 1592, 1500, 1458, 1376, 1329, 1276, 1238, 1163, 1110, 1044, 1026, 939, 909, 881, 855, 804; UV (MeOH) λ_{max} (ϵ) 377 (1100), 330 (800), 317 (900), 272 (6000), 224 (2100); (basic MeOH) 399 (2700), 293 (2000), 274 (4400) nm. The ^1H, ^{13}C NMR, IR, and UV spectra are identical to those of natural okicenone.[4]

(±)-Aloesaponol III (14c) was prepared from **13c** (14 mg, 0.050 mmol) and BBr_3 (0.2 mL, 1 M in CH_2Cl_2) in CH_2Cl_2 (1 mL) as described above for the preparation of **14b** except that the temperature raised from −78 °C to rt for 2 h. Normal workup as described above gave 14 mg of crude **14c**. Flash chromatography (2:1 hexane–EtOAc and then EtOAc) gave 9 mg (70%) of pure **14c** as a yellow solid: mp 230 °C dec; ^1H NMR 16.21 (s, 1), 9.69 (s, 1), 7.15 (s, 1), 7.01 (br s, 1), 6.74 (br s, 1), 4.95 (dd, 1, J = 6.4, 3.6), 3.07 (ddd, 1, J = 18.2, 8.7, 5.3), 2.70 (ddd, 1, J = 18.2, 6.9, 5.0), 2.44 (s, 3), 2.28 (m, 2), 1.89 (br s, 1); ^{13}C NMR 203.5, 166.2, 157.9, 144.1, 139.4, 138.8, 118.8, 116.2, 113.4, 111.4, 108.0, 67.7, 33.3, 30.9, 22.1; IR (KBr) 3386, 1639, 1381, 1156; UV (MeOH) λ_{max} (ϵ) 401 (7300), 307 (3800), 298 (4200), 268 (38 000), 225 (22 000); MS (18 eV) m/z (relative intensity) 258 (M^+, 1.3), 240 (95), 225 (23), 212 (8), 211 (8), 197 (15). The ^1H NMR, IR, UV, and mass spectral data are identical to those of natural aloesaponol III.[5]