was added 88.7 mL of *n*-butyllithium (2.45 M in hexane). The reaction mixture was stirred at room temp for 1 h, then cooled to −78 °C, and 34.7 g (0.217 mol) of bromine was added dropwise. The mixture was allowed to warm to room temperature and was stirred for 1 h. Water was then added carefully at 0 °C. The ether layer was separated, washed with water and brine, and dried over anhydrous Na_2SO_4. Removal of the solvent and fractional distillation yielded 25.5 g (81%) of 3-bromoveratrole: bp 70 °C (0.5 mm) (lit[17] bp 111–113 °C (9 mm)); NMR ($CHCl_3$) δ 3.86 (s, 3 H), 3.87 (s, 3 H), 6.80–7.12 (m, 3 H).

General Procedure for the Preparation of Benzocyclobutenones. A mixture of 1 equiv of bromoarene, 2 equiv of $NaNH_2$, and 2 equiv of 1,1-dimethoxyethylene in THF (approximately 3 mL/mmol of bromoarene) was stirred at reflux. In those cases where no solvent was used (see Table I), 1 equiv of bromoarene was stirred with 2 equiv of $NaNH_2$ and 4 equiv of 1,1-dimethoxyethylene at 75–80 °C. Typically 0.5–5.0 g of bromoarene was employed in this study. The reaction mixtures gradually turned brown, and the reaction was judged complete when no bromoarene could be observed by gas chromatography. Even within multiple runs employing the same bromarene the reaction time varied widely, necessitating monitoring each reaction by gas chromatography. The reaction mixture was allowed to cool to room temperature and water was added carefully to destroy excess $NaNH_2$. The products were isolated by extraction with ether. The combined ether extracts were then washed with water and brine and dried over anhydrous Na_2SO_4. Removal of the solvent left a brown oil, which was distilled under reduced pressure to provide the pure ketal.

Hydrolysis of the ketal was effected by stirring in THF–water (5:1) containing a trace of HCl for 2 h. Most of the THF was removed in vacuo and the residue extracted with ether. The combined ether extracts were then washed with water and brine and dried over anhydrous Na_2SO_4. Removal of the ether afforded quantitatively the pure benzocyclobutenone.

The mixtures of regioisomers (**4c** and **4d**; **7c** and **7d**) were separated on a column of silica gel (Merck, 70–230 mesh) with ether–hexane as eluant.

Spectral Data for Benzocyclobutenones and Their Dimethyl Ketals.[12] **1a**: IR (neat) 2920, 2819, 1595, 1454, 1330, 1278, 1243, 1206, 1151, 1133, 1113, 1083, 1054, 1033, 850, 754, 720 cm^{-1}; NMR ($CDCl_3$) δ 3.37 (s, 2 H), 3.45 (s, 6 H), 7.20–7.38 (m, 4 H).

2a: IR (neat) 2923, 2820, 1600, 1474, 1438, 1340, 1270, 1234, 1204, 1149, 1131, 1101, 1078, 1030, 940, 868, 843, 768, 735 cm^{-1}; NMR ($CDCl_3$) δ 3.30 (s, 2 H), 3.47 (s, 6 H), 3.85 (s, 3 H), 6.37 (d, J = 8 Hz, 1 H), 6.82 (d, J = 7 Hz, 1 H), 7.29 (dd, J = 7, 8 Hz, 1 H).

5a: IR (neat) 2936, 2832, 1591, 1485, 1433, 1330, 1258, 1234, 1200, 1170, 1133, 1110, 1055, 1026, 991, 856, 830, 800, 744, 709 cm^{-1}; NMR ($CDCl_3$) δ 3.32 (s, 2 H), 3.42 (s, 6 H), 3.84 (s, 3 H), 4.03 (s, 3 H), 6.74 (d, J = 8 Hz, 1 H), 6.88 (d, J = 8 Hz, 1 H).

5b: mp 86–87 °C (petroleum ether); IR ($CHCl_3$) 3030, 3005, 2953, 2837, 1759 (C=O), 1603, 1583, 1490, 1454, 1435, 1410, 1350, 1268, 1258, 1179, 1128, 1066, 1049, 995, 970, 846, 808, 655 cm^{-1}; NMR ($CDCl_3$) δ 3.87 (s, 5 H, OCH_3, CH_2), 4.21 (s, 3 H), 6.94 (d, J = 8 Hz, 1 H), 7.04 (d, J = 8 Hz, 1 H).

7c: mp 68–69 °C (petroleum ether); IR ($CHCl_3$) 3020, 2925, 1759 (C=O), 1610, 1585, 1482, 1336, 1223, 1161, 1148, 1029, 967, 921 cm^{-1}; NMR ($CDCl_3$) δ 2.41 (s, 3 H), 3.93 (s, 2 H), 7.11–7.45 (m, 3 H).

7d: mp 53–54 °C (petroleum ether) (lit[13] mp 53–54 °C); IR ($CHCl_3$) 3007, 2920, 1750 (C=O), 1587, 1482, 1405, 1322, 1254, 1228, 1218, 1201, 1162, 1142, 1006, 971, 698 cm^{-1}; NMR ($CDCl_3$) δ 2.37 (s, 3 H), 391 (s, 2 H), 7.10–7.35 (m, 3 H).

8a: IR ($CHCl_3$) 3004, 2933, 2895, 2830, 1500, 1458, 1302, 1218, 1150, 1130, 1092, 1074, 1038, 946, 912, 837, 815 cm^{-1}; NMR ($CDCl_3$) δ 3.19 (s, 2 H), 3.41 (s, 6 H), 5.91 (s, 2 H, OCH_2O), 6.72 (s, 1 H), 6.79 (s, 1 H).

8b: mp 120–121 °C (petroleum ether); IR ($CHCl_3$) 3030, 3000, 2920, 2892, 1748 and 1757 (C=O), 1590, 1501, 1464, 1288, 1159, 1120, 1033, 948, 901, 858 cm^{-1}; NMR ($CDCl_3$) δ 3.75 (s, 2 H), 6.06 (s, 2 H, OCH_2O), 6.76 (s, 1 H), 6.95 (s, 1 H).

Base-Induced Cleavage of Benzocyclobutenones 2b, 5b, and 8b. The benzocyclobutenone (100 mg) was stirred in 15 mL of 10% aq NaOH at 60 °C for 2 h. The mixture was cooled to room temperature and acidified with concentrated hydrochloric acid. The resultant crystalline product was collected by filtration, rinsed with water, and air dried to afford the corresponding pure phenylacetic acid **14**–**16** in quantitative yield. The spectral and physical properties of each sample were identical with those of commercially available samples.

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Registry No. **1**, 108-86-1; **1a**, 81447-53-2; **1b**, 3469-06-5; **2**, 578-57-4; **2a**, 81447-54-3; **2b**, 66947-60-2; **3**, 2398-37-0; **4**, 104-92-7; **4a**, 81447-55-4; **4b**, 81447-56-5; **4c**, 55171-77-2; **4d**, 22246-27-1; **5**, 5424-43-1; **5a**, 81447-57-6; **5b**, 81447-58-7; **6**, 2859-78-1; **7**, 95-46-5; **7a**, 81447-59-8; **7b**, 81447-60-1; **7c**, 81447-61-2; **7d**, 62708-44-5; **8**, 108-37-2; **8a**, 81447-62-3; **8b**, 81447-63-4; **14**, 1798-09-0; **15**, 93-40-3; **16**, 1878-65-5; 1,1-dimethoxyethylene, 922-69-0.

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Benzocyclobutenones as Synthons for the Synthesis of C-11 Oxygenated Diterpenoids. Application to the Total Synthesis of (±)-Taxodione

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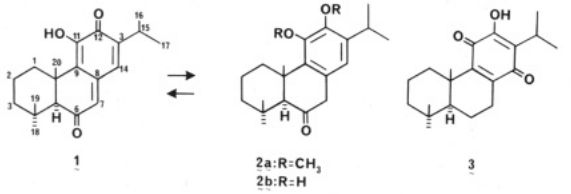
An efficient ten-step total synthesis of racemic taxodione is described. Key steps involve the regiospecific synthesis of benzocyclobutenone **8** via a [2 + 2] cycloaddition (**6** to **8**) and a regioselective base-catalyzed opening of benzocyclobutenol **13** to afford enone **16**.

In 1968 Kupchan et al., reported[1] the isolation of an interesting quinone methide diterpene, taxodione (**1**), from extracts off *Taxodium distichum* Rich (Taxodiaceae). This compound exhibited significant activity in vivo against Walker intramuscular carcinosarcoma 256 in rats and in vitro against cells derived from human carcinoma of the nasopharnyx (KB). In addition, Kupchan reported the conversion of taxodione to the octahydro-

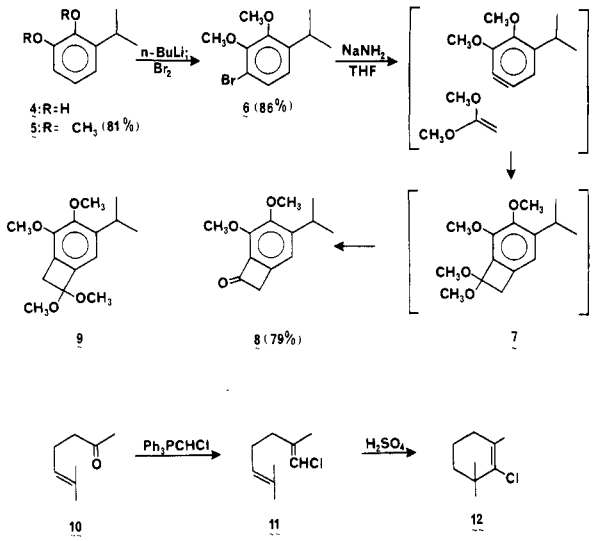


1 **2a**: R = CH_3; **2b**: R = H **3**

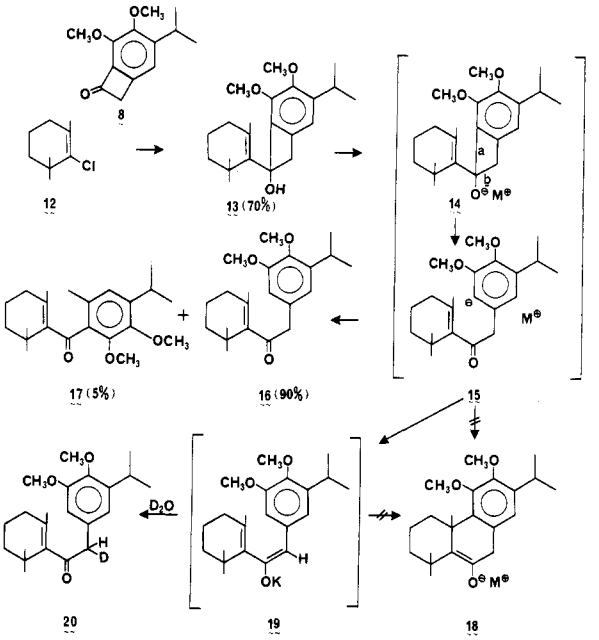
(1) (a) Kupchan, S. M.; Karim, A.; Marcks, C. *J. Am. Chem. Soc.* **1968**, *90*, 5923; (b) Kupchan, S. M.; Karim, A.; Marcks, C. *J. Org. Chem.* **1969**, *34*, 3912.

0022-3263/82/1947-2396$01.25/0

Scheme I



Scheme II



phenanthrones **2a** and **2b** by catalytic hydrogenation followed by alkylation of the resultant catechol with methyl iodide. Later, Mori[2a] and Matsumoto[2b] demonstrated that these steps could be reversed. Thus, demethylation of **2a** with BBr_3 afforded **2b**, which underwent air oxidation on silica gel to regenerate taxodione in high yield. To date, five syntheses of taxodione have been reported.[2a-e] Although each involves interesting chemistry, it is highly unlikely that any one of them can be employed to increase substantially the world's supply of this interesting substance for further biological evaluation. In this paper we report the shortest and most efficient synthesis of taxodione to date. The methodology employed should also be applicable to other ring C aromatic octahydrophenanthrenes bearing an oxygen substituent at C-11, of which there is a growing number [e.g., royleanone (**3**)[3]].

The ease and efficiency with which the Kupchan degradation product **2a** was converted back to taxodione as noted above[2a,b] prompted us to select it as our penultimate target. Our point of departure was commercially available isopropylcatechol (**4**, Scheme I), which was methylated with dimethyl sulfate to afford the corresponding veratrole (**5**) in 81% yield. Exclusive bromination at the 6-position could be effected by orthometalation with *n*-butyllithium, followed by quenching with bromine to provide **6** in 86% yield. According to the procedure reported in the preceding paper in this issue,[4] bromoarene **6** was dehydrobrominated with sodium amide in refluxing tetrahydrofuran in the presence of 1,1-dimethoxyethylene to afford ketal **7**. In agreement with our previous observations,[4] none of the regioisomeric ketal **9** could be detected in the crude reaction mixture by gas chromatography or 200-Mz ^1H NMR spectroscopy. The crude ketal was hydrolyzed directly to the desired benzocyclobutenone **8** (mp 56–57 °C) in 79% overall yield after silica gel chromatography. Commercially available 6-methyl-5-hepten-2-one (**10**) was converted by the method of Köbrich[5] to the known vinyl chloride **12**. The latter substance was metalated efficiently with lithium dispersion (2% sodium) in ether and was then added dropwise to a cooled (−78 °C) solution of benzocyclobutenone **8** in tetrahydrofuran. The resultant mixture was then quenched at −78 °C with acetic acid and allowed to warm to room temperature. In this fashion pure benzocyclobutenol (**13**) was obtained in 70% yield after recrystallization. When exposed to potassium *tert*-butoxide in *tert*-butyl alcohol for 5 min at room temperature, benzocyclobutenol **13** (Scheme II) underwent cleavage of the four-membered ring predominantly along bond a to provide, after chromatography, a 90% yield of crystalline enone **16**; a small amount (~5%) of isomeric enone **17** corresponding to cleavage of bond b was also isolated. This outcome was in accord with the prediction that the transition state for cleavage of bond a would be stabilized inductively by the adjacent methoxy group. Originally, we had hoped that the intermediate alkoxide might be coaxed to rearrange directly to tricyclic enolate **18** either by a concerted 1,3 shift[6] of bond a or by a two-step mechanism involving cleavage of bond a to produce enone **15**, which could condense intramolecularly in a Michael fashion[7] to afford enolate **18**. However, generation of alkoxide **14** under a wide variety of reaction conditions including solvent variation (from hexane to HMPA), temperature (−78 to 85 °C), and counterion (M = Li, Na, K, MgBr, CuRLi) failed to induce direct conversion of **14** to **18**. Rather, cleavage of either bond a or b was observed leading to various ratios of **16** and **17** in high yield. The probable course of reaction in the transformation of **13** to **16** was determined by treating alcohol **13** with potassium hydride in dry dimethoxyethane followed by quenching with D_2O at 0 °C. Under these conditions one deuterium was incorporated α to the ketone in the position shown in formula **20** as determined by the ^1H NMR and mass spectra of **20**. Thus it would appear that proton abstraction (**15** to **19**) is the preferred fate of **15** rather than intramolecular Michael addition (**15** to **18**) and also that the resultant trienolate anion **19** is probably not of the proper geometry to undergo electrocyclic ring closure.

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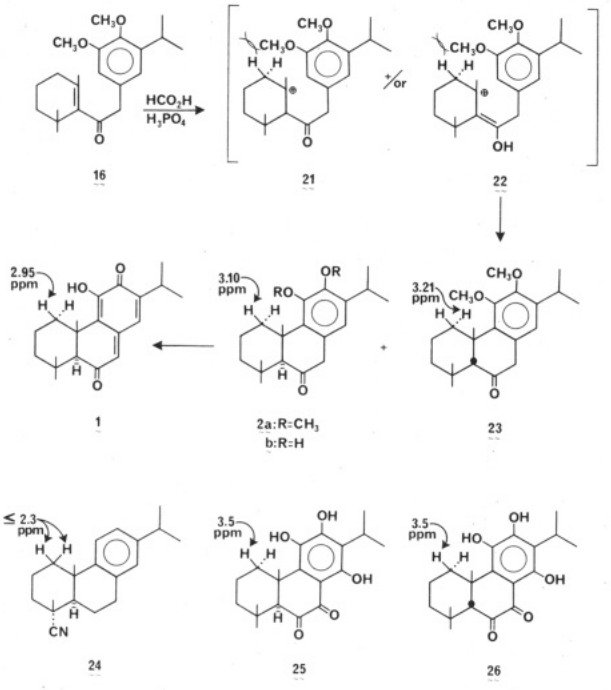
Scheme III



We were not particularly concerned about our inability to effect the direct conversion of **13** to tricyclic ketone **2a** under basic conditions since it appeared eminently reasonable that such a transformation could be achieved under acidic conditions via an intramolecular Friedel–Crafts reaction. This apparently straightforward transformation proved to be much more difficult than we had anticipated. Conditions that had been employed previously to effect analogous cyclizations such as aluminum trichloride,[8] polyphosphoric acid,[9] or irradiation in the presence of acidic catalysts[10] failed with this system. After considerable experimentation it was found that treatment of enone **16** with a 3:1 mixture of formic and phosphoric acids[11] for 5 h at reflux gave a 66% yield of tricyclic ketones **2a** and **23** in a ratio of 3:2, respectively. Support for the cis stereochemistry of the AB ring fusion of **23** (Scheme III) was provided from the ^{1}H NMR spectrum, which showed characteristic signals[12] at 0.38 ppm for the C-18 methyl and 0.93 ppm for the C-19 methyl groups. No doubt steric factors contribute to the difficulty encountered in this cyclization. Inspection of models reveals that in the transition state for cyclization of cations **21** and/or **22** considerable steric compression between the C-1 methylene and C-11 methoxyl must occur. This close prximity is clearly evident in the ^{1}H NMR spectra of the cyclized products of this reaction (**2a** and **23**). In the absence of a nearby oxygen at C-11 the chemical shift of the C-1 equatorial (and axial) proton is in the neighborhood of 2.3 ppm or less (e.g., abietonitrile, **24**). In **2a** and **23** values of 3.1 and 3.2 ppm, respectively, were observed for the C-1 equitorial proton. Similar dramitic deshielding has been observed[13] for related C-11 oxygenated diterpenes such as Coleon V (**25**) and its C-4 epimer (**26**). It shoudl be noted that the C-1 equitorial proton of taxodione itself (**1**) also displays a considerable downfield chemical shift (2.95 ppm), a heretofore unreported spectral feature of this natural product. In all cases studied, under acidic conditions a mixture of both substances was produced. Completion of the synthesis followed the literature procedure.[2b] Thus, **2a** was demethylated with boron tribromide to afford **2b**, which was oxidized to (±)-taxodione by absorption onto silica gel followed by elution with benzene. The synthetic material was identical (TLC, IR, mass spectrum, and 200-MHz ^{1}H NMR spectrum in $CDCl_3$ and benzene-d_6) with an authentic sample kindly provided by Professor Takashi Matsumoto.

Experimental Section

Infrared spectra were recorded on Beckmann IR 4210 and Perkin-Elmer 297 spectrophotometers. ^{1}H and ^{13}C NMR spectra were taken on a Bruker WP-200 spectrometer using tetramethylsilane as internal standard. Mass spectra were determined on an AEI-MS 9 mass spectrometer. Melting points were taken on a Thomas-Hoover apparatus and are uncorrected. Gas chromatographic analyses were performed on a Hewlett-Packard 5710A chromatograph (flame ionization detector) fitted with an 8 ft × $^1/_8$ in. OV-17 on an Anakrom ABS 100/110 column. THF and diethyl ether was distilled from sodium–benzophenone.

3-Isopropylveratrole (5). To a stirred mixture of 100 g (0.66 mol) of 3-isopropylcatechol (**4**) and 4 g of sodium hydrosulfite ($Na_2S_2O_4$) dissolved in 1 L of methanol at 40 °C under a N_2 atmosphere were added alternately, in eight portions each, potassium hydroxide (104 g of 85% KOH, 1.58 mol, in 150 mL of water) and dimethyl sulfate (199.1 g, 1.58 mol). A vigorous exothermic reaction was observed during addition of the dimethyl sulfate. After the addition was complete (45 min), the reaction mixture was refluxed for 3 h. Most of the methanol was removed under reduced pressure, and the residue was extracted with ether. The ether extract was washed with 10% aqueous KOH, water, and brine and dried over Na_2SO_4. Removal of the solvent afforded a brown oil, which was distilled to yield 96.5 g (81%) of pure isopropylveratrole, bp 65 °C (0.5 mm) [lit.[14] bp 84 °C (3 mm).

1-Bromo-2,3-dimethoxy-4-isopropylbenzene (6). The procedure employed was identical with that described in the preceding paper[4] for the preparation of 3-bromoveratrole. Thus, 30.0 g (0.167 mol) of **5** was metalated with 102 mL of *n*-butyllithium (2.45 mol in hexane) in 29.1 g (0.25 mol) of TMEDA and 250 mL of ether. The mixture was quenched with bromine (40.0 g, 0.25 mol) and the crude product purified by distillation to provide 37.1 g (86%) of pure **6**: bp 90 °C (0.9 mm); ^{1}H NMR ($CDCl_3$) δ 1.20 (d, J = 7 Hz, 6 H), 3.28 (m, J = 7 Hz, 1 H), 3.87 (s, 6 H), 6,86 (d, J = 9 Hz, 1 H), 7.23 (d, J = 9 Hz, 1 H).

5,6-Dimethoxy-4-isopropylbenzocyclobutenone (8). The procedure used was essentially that described in the previous paper.[4] Thus, 5.0 g (19.3 mmol) of bromoarene 6, 1.15 g (38.6 mmol) of $NaNH_2$, and 3.40 g (38.6 mmol) of 1,1-dimethoxyethylene in 50 mL of THF were refluxed with stirring under a N_2 atmosphere until complete disappearance of the starting bromoarene was observed by gas chromatography (about 24 h). The reaction mixture was cooled, and H_2O was added carefully to destroy the excess $NaNH_2$. The mixture was then acidified with concentrated HCl and the mixture stirred for 2 h at room temperature to ensure complete hydrolysis of the ketal. The product was isolated by extraction with ether, washing with H_2O then brine, and drying over $NaSO_4$. Removal of the solvent afforded a brown solid which was chromatographed on silica gel with ether–hexane to provide 3.35 g (79%) of pure **8**: mp 56–57 °C (petroleum ether); IR ($CHCl_3$) 2957, 2925, 2864, 1760 (C=O), 1599, 1569, 1465, 1455, 1446, 1309, 1282, 1230, 1165, 1070, 1042, 1005, 973, 920, 865, 655 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.23 (d, J = 7 Hz, 6 H), 3.40 (m, J = 7 Hz, 1 H), 3.78 (s, 3 H), 3.84 (s, 2 H), 4.19 (s, 3 H) 6.93 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 23.3 (q), 27.9 (d), 50.5 (t), 60.5 (q), 60.8 (q),

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(14) Edwards, J. D.; Cashaw, J. L. *J. Org. Chem.* **1955**, *20*, 847.

112.7 (d), 131.5 (s), 144.3 (s), 145.7 (s), 146.7 (s), 152.1 (s), 183.5 (s); exact mass calcd for $C_{13}H_{16}O_3$ 220.1099 (found 220.1107).

1-(1,3,3-Trimethylcyclohexenyl)-4-isopropyl-5,6-dimethoxybenzocyclobutenol (13). Under an argon atmosphere, 0.139 g (20 mmol) of lithium dispersion containing 2% sodium was washed from its oily coating by stirring briefly with cyclohexane, allowing the lithium to rise to the surface, and removing the underlying solvent via syringe. Ether (15 mL) and 0.547 g (3.62 mmol) of 1,3,3-trimethylcyclohexenyl chloride (**12**) were added to the lithium, and the mixture was heated to reflux with stirring. After 1.25 h, a hydrolyzed aliquot from the mixture was analyzed by gas chromatography, which showed that metalation was complete. Stirring was then stopped and the mixture allowed to cool. The solution below the unreacted lithium was taken up by syringe and added slowly dropwise to a stirred solution of benzocyclobutenone **8** (0.536 g, 2.44 mmol) in 30 mL of THF at −78 °C under a N_2 atmosphere. Stirring was continued at −78 °C for 1 h and then quenched by a slow dropwise addition of acetic acid (0.24 g, 4.0 mmol) dissolved in 2 mL of THF. The mixture was allowed to warm to room temperature; water was added and the product isolated by extraction with ether. The ether extracts were washed with water and brine and dried over Na_2SO_4. Removal of the solvent left a solid mass which was recrystallized from petroleum ether to yield 0.588 g (70%) of **13**: mp 105 °C; IR ($CHCl_3$) 3420, 2940, 2920, 2855, 1603, 1575, 1463, 1410, 1378, 1355, 1338, 1309, 1271, 1224, 1198, 1167, 1069, 1025, 991, 969, 946, 905, 845, 831, 813, 749 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (d, J = 7 Hz, 6 H), 1.20 (s, 3 H), 1.23 (s, 3 H), 1.35 (s, 3 H), 1.43 (m, 2 H), 1.55 (m, 2 H), 1.95 (m, 2 H), 2.16 (s, exchanges with D_2O, 1 H), 3.24 and 3.45 (AB quartet, J = 14 Hz, 2 H) 3.35 (m, J = 7 Hz, 1 H), 3.74 (s, 3 H), 3.98 (s, 3 H), 6.61 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.4 (t), 20.9 (q), 24.0 (q), 27.3 (d) 29.0 (q), 29.6 (q), 36.1 (s), 36.3 (t), 43.9 (t), 52.6 (t), 59.2 (q), 61.3 (q), 83.4 (s), 114.6 (d), 130.2 (s), 136.5 (s), 138.7 (s), 141.0 (s), 146.0 (s), 146.5 (s), 148.0 (s); exact mass calcd for $C_{22}H_{32}O_3$, 344.2351 (found 344.2367).

Enones 16 and 17. To a stirred solution of 100 mg (0.45 mmol) of benzocyclobutenol **13** in 5 mL of *t*-BuOH was added 100 mg (0.9 mmol) of potassium *tert*-butoxide. After 5 min of stirring at room temperature, water was added, and the product was isolated by extraction with ether. The combined organic extracts were washed with water and then brine and dried over Na_2SO_4. Removal of the solvent afforded a partially crystalline mass which was chromatographed on silica gel (ether–hexane) to yield 90 mg (90%) of pure enone **16**: mp 45–46 °C (petroleum ether); IR ($CHCl_3$) 2955, 2925, 2862, 2844, 2814, 1695 (C=O), 1590, 1491, 1465, 1432, 1383, 1373, 1343, 1314, 1302, 1230, 1190, 1150, 1072, 1052, 1017, 982, 787 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08, (s, 6 H), 1.20 (d, J = 7 Hz, 6 H), 1.45 (m, 2 H), 1.55 (s, 3 H), 1.65 (m, 2 H), 1.96 (t, 2 H), 3.79 (s, 2 H), 3.80 (s, 3 H), 3.85 (s, 3 H), 6.64 (d, J = 2 Hz, 1 H), 6.66 (d, J = 2 Hz, 1 H); exact mass calcd for $C_{22}H_{32}O_3$, 344.2351 (found 344.2361). Also isolated from the chromatography was 5 mg (5%) of enone **17**: IR (film) 2960, 2932, 2865, 2822, 1643 (C=O), 1599, 1560, 1452, 1398, 1379, 1369, 1332, 1302, 1291, 1270, 1246, 1070, 1055, 1049, 1027, 980, 933, 900, 869, 849, 829, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.16 (s, 6 H), 1.20 (d, J = 7 Hz, 6 H), 1.52 (s, 3 H), 1.55 (m, 2 H), 1.70 (m, 2 H), 2.11 (t, 2 H), 2.27 (s, 3 H), 3.30 (m, J = 7 Hz, 1 H), 3.75 (s, 3 H), 6.77 (s, 1 H).

Ketones 2a and 23. Enone 16 (50 mg, 0.16 mmol) was stirred in a mixture of 3 mL of formic acid and 1 mL of phosphoric acid at 115 °C for 5 h under a N_2 atmosphere. Water was added to the cooled reaction mixture and the product isolated by extraction with ether. The combined ether extracts were washed with water, aqueous sodium bicarbonate, water again, and brine and dried over Na_2SO_4. Removal of the solvent afforded a light brown oil which was chromatographed on silica gel (ether–hexane) to yield 21 mg (41%) of pure trans-fused ketone **2a**: mp 101–102 °C (lit.[2b] mp 102–103.5 °C); IR ($CHCl_3$) 2957, 2926, 2864, 1724 (C=O), 1604, 1559, 1466, 1448, 1404, 1386, 1376, 1353, 1318, 1253, 1230, 1175, 1065, 1038, 1024, 804 cm^{-1}; ^1H NMR ($CDCl_3$) δ ca. 1.0–1.8 (m, 5 H), 1.02 (s, 3 H, C-18 methyl), 1.19 and 1.21 (2d, each J = 7 Hz, each 3 H, **Me**$_2$CH), 1.26 (s, 3 H, C-19 methyl), 1.35 (s, 3 H, C-20 methyl), 2.61 (s, 1 H, C-5 proton), 3.10 (br d, J = 13 Hz, 1 H, C-1 β-proton), 3.26 (m, J = 7 Hz, 1 H, Me$_2$C**H**), 3.36 and 3.69 (2d, each 20 Hz, each 1 H, C-7 CH_2), 3.78 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 6.61 (s, 1 H, C-14 proton); exact mass calcd for $C_{22}H_{32}O_3$, 344.2351 (found 344.2346). Also isolated from the chromatography was 12 mg (25%) of pure cis-fused ketone (**23**): IR (film) 2955, 2925, 2845, 1700 (C=O), 1600, 1558, 1460, 1405, 1389, 1368, 1310, 1241, 1060, 1020, 985, 942, 862, 836 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.38 (s, 3 H, C-18 methyl), 0.93 (s, 3 H, C-19 methyl), ca. 1.0–1.6 (m, 5 H), 1.15 (s, 3 H, C-20 methyl), 1.19 and 1.20 (2d, each J = 7 Hz, each 3 H, **Me**$_2$CH), 1.95 (s, 1 H, C-5 proton), 3.21 (br d, $J \simeq$ 14 Hz, 1 H, C-1 eq proton), 3.28 (m, J = 7 Hz, 1 H, Me$_2$C**H**), 3.46 and 3.62 (2d, each J = 21 Hz, each 1 H, C-7 methylene), 3.82 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 6.63 (s, 1 H, C-14 proton).

Catechol 2b was prepared from **2a** by demethylation with boron tribromide according to the literature procedure.[2b] IR (Film) 3470, 2960, 2930, 2870, 1702 (C=O), 1623, 1570, 1491, 1464, 1458, 1439, 1420, 1389, 1379, 1363, 1312, 1289, 1083, 1072, 1051, 1026, 968, 909, 849, 732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H, C-18 methyl), ca. 1.05–1.85 (m, 5 H), 1.24 and 1.26 (2d, each J = 7 Hz, each 3 H, **Me**$_2$CH), 1.28 (s, 3 H, C-19 methyl), 1.35 (s, 3 H, C-20 methyl), 2.64 (s, 1 H, C-5 proton), 3.00 (m, J = 7 Hz, 1 H), 3.19 (br d, J = 11 Hz, 1 H, C-1 β proton), 3.36 and 3.70 (2d, J = 20 Hz, each 1 H, C-7 methylene), 4.68 (s, 1 H, O**H**), 5.81 (s, 1 H, O**H**), 6.40 (s, 1 H, C-14 proton).

(±)-Taxodione (1) was prepared from **2b** according to the literature procedure.[2b] IR (film) 3320, 2954, 2920, 2861, 1680 (C=O), 1640, 1623, 1610, 1596, 1462, 1420, 1387, 1360, 1350, 1288, 1240, 1223, 1187, 1175, 1161, 1150, 1140, 1050, 1025, 976, 902, 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ ca. 0.90–1.80 (m, 5 H), 1.12 (s, 3 H, C-18 methyl), 1.16 and 1.18 (2d, each J = 7 Hz, each 3 H, **Me**$_2$CH), 1.27 (s, 6 H, C-19 and C-20 methyls) 2.60 (s, 1 H, C-5 proton), 2.95 (br d, J = 11 Hz, 1 H, C-1 β proton, 3.08 (m, J = 7 Hz, 1 H), 6.20 (s, 1 H, C-7 proton), 6.88 (s, 1 H, C-14 proton), 7.56 (s, 1 H, O**H**); ^1H NMR (C_6D_6) δ ca. 0.90–1.70 (m, 5 H), 0.97 and 1.02 (2d, each J = 7 Hz, each 3 H, **Me**$_2$CH), 1.17 (s, 3 H, C-18 methyl), 1.25 (s, 3 H, C-19 methyl) 1.38 (s, 3 H, C-20 methyl), 2.31 (s, 1 H, C-5 proton), 2.99 (br d, $J \simeq$ 13 Hz, C-1 β proton), 5.82 (s, 1 H, C-7 proton), 6.35 (s, 1 H, C-14 proton), 7.64 (s, 1 H, O**H**); exact mass calcd for $C_{20}H_{26}O_3$, 314.1882 (found 314.1879).

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