Structural Amendment and Stereoselective Synthesis of Mutisianthol†

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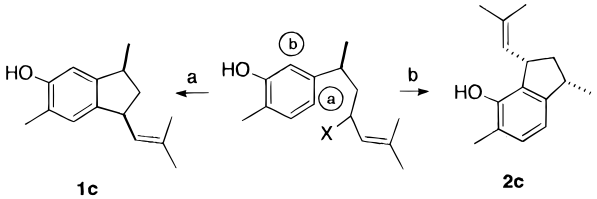
cis-1-(5-Acetoxy-3,6-dimethyl-1-indanyl)-2-methyl-1-propene synthesized from 3,6-dimethyl-1-indanone was found to be different from mutisianthol by spectral comparison. The presence of a high-field signal in the NMR spectrum of the final product and various intermediates, characteristic of the *cis*-1,3-dialkylindanes but absent in the spectrum of the natural terpene, suggests a revision of the structure of mutisianthol to the *trans* isomer. The *trans*-indane which was subsequently obtained indeed exhibits data fully agreeable with mutisianthol. A similar stereochemical revision for jungianol is also indicated.

The isolation of the phenolic sesquiterpene mutisianthol **1c** from the roots of *Mutisia homoeantha* was reported, and its structural assignment was made on the basis of spectroscopic data.[1] Mutisianthol is plausibly derived in nature from an α-curcumene-type precursor by cyclization to form the indane nucleus. Interestingly, an isomer of mutisianthol, jungianol (**2c**), was found in *Jungia malvaefolia*[2] and apparently arises from intramolecular *ortho*-alkylation of the same biogenetic precursor (eq 1). The most intriguing aspect of these terpene molecules is the *cis*-relationship assigned for the two side chains in the five-membered ring of mutisianthol and of jungianol. This feature, suggesting a congested folding of the precursor for the cyclization, attracted our attention to investigate them synthetically.

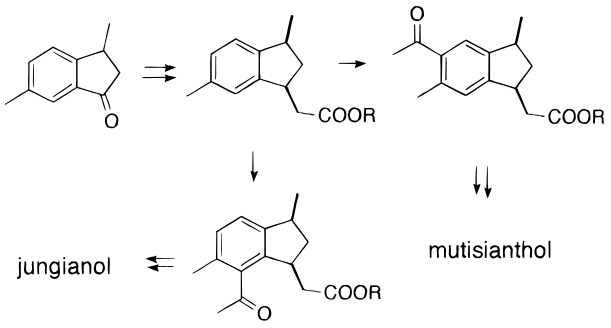


1c **2c**

We proposed to approach both molecules from a central intermediate. Accordingly, the introduction of the oxygen function would be delayed, and the subtarget of our synthesis was a *cis*-1,5-dimethylindan-3-ylacetic ester (Scheme 1). It was hoped that the corresponding carboxylic acid might direct acylation at the peri position and that insertion of an oxygen atom between the acyl group and the aromatic ring would pave the way to jungianol. Alternatively, intermolecular acylation would deliver a ketone suitable for elaboration of mutisianthol.

The starting point of our synthesis was 3,6-dimethyl-1-indanone (**3**) which had been prepared from Rupe's acid.[3] For a shorter ketone preparation we intended to effect benzylic deoxygenation and cyclization of 3-hydroxy-3-(4-methylphenyl)butanoic acid in a tandem fashion,[4] using triethylsilane and trifluoroacetic anhydride. However, the attempt failed as *p*-cymene was the only

Scheme 1



detected product, thus indicating that decarboxylation proceeded far more rapidly than reduction. The primary product of dehydrocymene underwent reduction under the reaction conditions.

By the Reformatsky reaction the indanone was converted into a mixture of the tertiary alcohol **4** and two isomeric unsaturated esters **5** and **6**. It was later found that the in situ dehydration could be avoided if the Reformatsky reaction was carried out in an ultrasonic bath at temperatures below 30 °C; but when the temperature was maintained between 50 to 60 °C, the product was **5**. The transformation of the Reformatsky reaction products involved dehydration of the alcohol/alkene mixtures and catalytic hydrogenation or ionic hydrogenolysis of the alcohol. The two-step procedure furnished only the *cis* compound **7** which was required for the synthesis of the proposed structures of the natural terpenes, whereas the ionic process (CF_3COOH/Et_3SiH)[5] led to a mixture still in favor of the *cis*-isomer (cis:trans =10:1).

The structure of the major product was confirmed by NOE experiments. Concerning the four hydrogen atoms on the five-membered ring, two one-proton multiplets for the methine hydrogens appeared at δ 3.00−3.12 and 3.40−3.50, respectively, one of the methylene hydrogen resonated at δ 2.57, and the other one was hidden under the methyl signals (δ 1.18−1.30), as clearly indicated by integration. Such a relationship was delineated by a ^{1}H−^{1}H COSY experiment, showing coupling of the δ 2.57 peak to the δ 1.18−1.30 multiplet. As nuclear Overhauser effects were also observed on the two methine hydrogens in the same experiment, the δ 2.57 peak can be assigned to the hydrogen *cis* to them. The other

† This paper is dedicated to Professor Dr. D. Seebach on the occasion of his 60th birthday.

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(3) Rupe, H.; Wiederkehr, F. *Helv. Chim. Acta* **1924**, *7*, 654.
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methylene hydrogen atom is *cis* to the methyl group and the acetic ester side chain and shifted upfield due to the strong shielding presumably arising from these two substituents.

At this stage we noticed a possible discrepancy in the NMR data between our synthetic intermediate and those reported for mutisianthol and jungianol. In the described spectra, the signals at the highest field belong to the benzylic methyl group only, and the methylene group appears to absorb at δ 1.93 or 1.98. It seems highly unlikely that the presence of a remote hydroxyl group in the aromatic ring could cause a convergence of the methylene group from that of the magnetically nonequivalent situation we observed. Consequently we examined the spectral data of the natural products more carefully and concluded that these sesquiterpenes might indeed possess the indane skeleton, with the relative configuration of the two side chains revised to *trans*. To resolve this problem, we continued our synthesis work toward **1c** and/or **2c**.

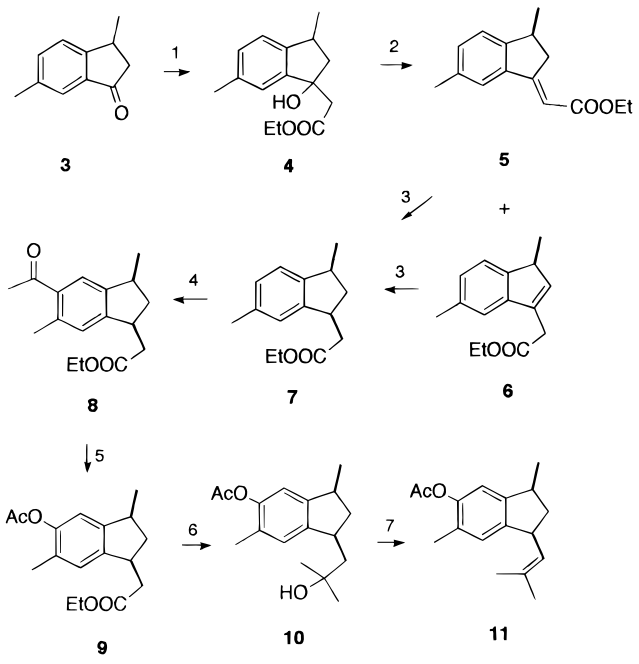
Ester **7** was saponified, and cyclization of the corresponding acid was attempted to deliver a precursor of jungianol. However, the intramolecular acylation was foiled, presumably due to excessive strain of the ring system. The use of a mixed anhydride to induce *peri*-acylation also failed. We then tried to convert the ester to the tertiary alcohol by a Grignard reaction and treat the alcohol with formic acid and concentrated sulfuric acid, expecting the formation of a less strained α-tetralone system. Unfortunately, the Koch−Haaf reaction did not proceed, only dehydration and double bond migration to give an isobutylideneindane were observed.

We redirected our focus to the synthesis of structure **1c**. Accordingly, ester **7** was acetylated to give mainly the 6-acetyl derivative **8**. Reaction of this ketone with *m*-chloroperbenzoic acid led to partial hydrolysis, and the product mixture was reacetylated to afford **9**. Methyllithium attacked both ester functions of the acetate **9**, and it was best to resubmit the product to acetic anhydride treatment to facilitate its isolation as the acetate **10**. Finally, the dehydration of **10** by refluxing with catalytic amount of *p*-toluenesulfonic acid in toluene under a Dean−Stark trap led to **11** (Scheme 2).

The stereochemical structure of **11** was unambiguously established by NMR, including NOE and ^{1}H−^{1}H COSY experiments. There are marked differences in the spectra for this product and mutisianthol, although our compound is the *O*-acetyl derivative of structure **1c**. Since the overall NMR spectral features of mutisianthol support the conclusion of it being an indane having substituents identical to those previously proposed, our results strongly suggest a reassignment of the configuration of C-1 and C-3 of the indane skeleton.

The entry into the *trans*-series was far from straightforward. Numerous attempts at reducing the unsaturated ester to give the *trans*-1,3-disubstituted indane were thwarted; at best an equimolar mixture of the *cis* and *trans* compounds was generated. Finally, we considered that the template effect[6] of a tricarbonylchromium complex might be exploited to provide a solution to the stereoselective reduction leading to the desired intermediate. Accordingly the light-sensitive derivative **12** of the unsaturated ester **5** was prepared following a standard

Scheme 2



Reagents: (1) Zn, $BrCH_2COOEt$, us <30°, 80%; (2) TsOH, PhMe, 110°; (3) H_2, Pd-C, 87%; (4) AcCl, $AlCl_3$, CH_2Cl_2, 86%; (5) MCPBA; Ac_2O, Py, 60%; (6) MeLi; Ac_2O, Py, 60%; (7) TsOH, PhMe, 110°, 80%

protocol;[7] the apparently exclusive formation of one complex was both satisfying and rather surprising (Scheme 3). This complex was reduced with magnesium in methanol.[8] The interesting observation of transesterification under the mild reduction condition to furnish the chromium complex **13** may indicate interaction of the chromium with the ester enolate intermediate, enabling elimination of an alkoxide ion with the formation of a ketene. Such a pathway is possible only when the ester enolate chain is *cis* to the metal. On treatment of **13** with iodine the desired *trans*-ester **14** was obtained. The upfield region of the NMR spectrum of this ester was more consistent with that reported for mutisianthol and jungianol. Synthetic progression toward **1t** then followed the same protocol as described for the *cis*-series, i.e., **14** → **15** → **16** → **17**.

Thus, our work established the relative stereochemical feature of mutisianthol, and by extension jungianol should now be considered to have a *trans*-1,3-indane structure. This synthesis exploited a template effect to exert stereocontrol in the key reduction step. Interestingly, we could isolate only one π-complex **12** in 52% yield, with a structure assigning the bulky metal moiety on the face of the aromatic ring opposite to the benzylic methyl group, by inference from the steric course of the reduction.

Experimental Section

3,6-Dimethyl-1-indanone (3). To a magnetically stirred solution of phosphorus pentoxide (7.27 g) in methanesulfonic acid (72.70 g) was added Rupe's acid (4.00 g, 22.5 mmol) at room temperature. After reaction overnight the mixture was

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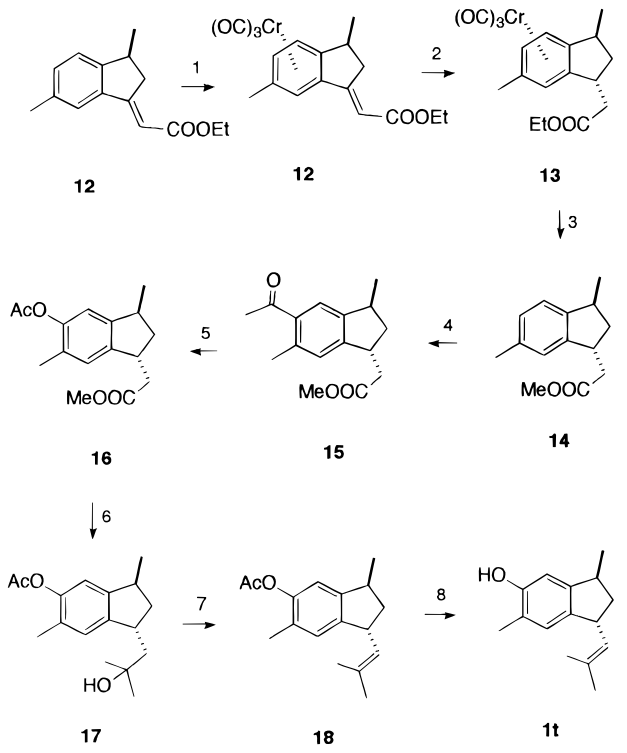
Scheme 3



Reagents: (1) $Cr(CO)_6$, dioxane, 52%; (2) Mg, MeOH, 71%; (3) I_2, THF, 80%; (4) AcCl, $AlCl_3$, CH_2Cl_2, 82%; (5) MCPBA; Ac_2O, Py, 56%; (6) MeLi; Ac_2O, Py, DMAP, 67%; (7) TsOH, PhH, 80°, 85%; (8) $LiAlH_4$, Et_2O, 92%

quenched with water (150 mL), and after 2 h the organic matter was extracted from the aqueous phase with dichloromethane thrice. The combined extracts were washed with brine, dried, evaporated in a rotary evaporator, and chromatographed (eluent: EtOAc/hexane 1:19) to afford the indanone **3** (2.70 g; 75%). IR (film) 1705, 1608 cm^{-1}; ^1H NMR δ 1.36 (3H, d, J = 4.75 Hz), 2.23 (1H, dd, J = 12.7, 2.2 Hz), 2.37 (3H, s), 2.90 (1H, dd, J = 12.7, 4.9 Hz), 3.38 (1H, m), 7.37 (1H, d, J = 5 Hz), 7.41 (1H, d, J = 5 Hz), 7.50 (1H, s); ^{13}C NMR δ 21.0, 21.4, 32.4, 45.7, 123.3, 124.9, 135.9, 136.6, 137.3, 157.4, 206.5; MS m/z 160 (M^+, 98.1), 145 (100), 132 (16.5), 117 (23.7). HRMS (EI) 160.0897 (160.0888 calcd for $C_{11}H_{12}O$).

Ethyl (3,6-Dimethyl-1-hydroxyindanyl)acetate (4). A mixture of indanone **3** (2.00 g, 12.5 mmol), ethyl bromoacetate (2.1 mL, 18.75 mmol), zinc dust (1.64 g, 25 mmol), and iodine (0.60 g) in dioxane (25 mL) was put in a flask under nitrogen and irradiated in an ultrasonic bath (Branson). The bath temperature was kept below 30 °C by occasional addition of ice. After 16 h, the reaction mixture was poured into 150 g of crushed ice containing hydrochloric acid (10 mL). Extraction, evaporation, and chromatography gave the hydroxy ester **4** (2.48 g, 80%). IR (film) 3492, 1726 cm^{-1}; ^1H-NMR δ 1.25 (3H, t, J = 7.1 Hz), 1.31 (3H, d, J = 6.8 Hz), 1.82 (1H, dd, J = 12.8, 9.2 Hz), 2.33 (3H, s), 2.53 (1H, dd, J = 12.8, 7.1 Hz), 2.61 (1H, d, J = 15.6 Hz), 2.74 (1H, d, J = 15.6 Hz), 3.03 (1H, sx, J = 7.3 Hz), 4.18 (2H, q, J = 7.1 Hz), 4.35 (1H, br s), 7.08 (2H, br s), 7.15 (1H, s); ^{13}C-NMR δ 14.0, 19.7, 21.1, 35.4, 44.0, 49.6, 60.6, 79.6, 123.0, 123.1, 129.2, 136.4, 143.5, 146.1, 172.6; MS m/z 248 (M^+, 0.3), 230 (80), 162 (79), 156 (100); HRMS (EI) 248.1411 (248.1413 calcd for $C_{15}H_{20}O_3$).

Ethyl (3,6-Dimethylindanylidene)acetate (5) and Ethyl (3,6-Dimethyl-1-indenyl)acetate (6). To the magnetically stirred chlorotrimethylsilane-activated zinc dust (1.64 g, 25 mmol) in anhydrous tetrahydrofuran (20 mL) was added from a dropping funnel a solution of ethyl bromoacetate (2.10 mL, 18.75 mmol) and indanone **3** (2.00 g, 12.5 mmol) in tetrahydrofuran (20 mL) during 5 min. The mixture was refluxed for 2.5 h, cooled, and concentrated in vacuo. The residue was suspended in dichloromethane (20 mL), placed in an ice bath, and acidified with concd HCl. Layers were separated, the aqueous solution was extracted three more times with the same solvent, and the combined extracts were dried and evaporated. ^1H-NMR showed the presence of hydroxy ester and unsaturated esters; therefore, the mixture was dehydrated in refluxing benzene (30 mL) in the presence of catalytic amount of *p*-toluenesulfonic acid under a Dean−Stark trap for 8 h. The cooled reaction mixture was diluted with ether (20 mL), washed twice with 5% aqueous sodium hydroxide and brine, dried, and concentrated in vacuo. Silica gel chromatography gave **5** and **6** in a combined yield of 70%. The ratio of **5** and **6** was 2:1. The spectral data for **5**: IR (film) 1699, 1627 cm^{-1}; ^1H-NMR δ 1.27−1.35 (6H, m), 2.35 (3H, s), 2.77 (1H, ddd, J = 19.4, 3.7, 2.8 Hz), 3.20−3.40 (1H, m), 3.58 (1H, ddd, J = 19.4, 7.7, 2.6 Hz), 4.20 (2H, q, J = 7.1 Hz), 6.25 (1H, t, J = 2.6 Hz), 7.19 (2H, s), 7.36 (1H, s); ^{13}C-NMR δ 14.4, 21.2, 21.4, 36.9, 40.7, 59.6, 107.4, 121.7, 124.2, 132.1, 136.6, 139.4, 151.4, 161.8, 167.6; MS m/z 230 (M^+, 100), 201 (75), 183 (34), 156 (88); HRMS (EI) 230.1311 (230.1307 calcd for $C_{15}H_{18}O_2$). The spectral data for **6**: IR (film) 1731 cm^{-1}; ^1H-NMR δ 1.26 (3H, t, J = 7.1 Hz), 1.28 (3H, d, J = 7.3 Hz), 2.39 (3H, s), 3.45 (1H, q, J = 7.3 Hz), 3.53 (1H, br s), 4.18 (2H, q, J = 7.3 Hz), 6.34 (1H, s), 7.03 (1H, d, J = 7.5 Hz), 7.14 (1H, s), 7.28 (1H, d, J = 7.5 Hz); ^{13}C-NMR δ 14.1, 16.1, 21.5, 33.9, 43.5, 60.6, 119.9, 122.3, 125.8, 134.8, 135.9, 138.9, 143.8, 146.7, 171.0; HRMS (EI) 230.1310 (230.1307 calcd for $C_{15}H_{18}O_2$).

The following experiment led to **5** only. Zinc dust (1.64 g, 25 mmol), ethyl bromoacetate (2.10 mL, 18.75 mmol), indanone **3** (2.00 g, 12.5 mmol), and a small grain of iodine in anhydrous dioxane (25 mL) was placed under nitrogen in an ultrasonic bath. Irradiation continued for 18 h while the bath temperature was kept between 50−60 °C. The reaction mixture was poured into ice−concd HCl, extracted with dichloromethane (3 × 20 mL), dried, and evaporated. Silica gel chromatography gave **5** (1.73 g, 60%).

Ethyl *cis*-(3,6-Dimethyl-1-indanyl)acetate (7). (a) From **5**/**6** by catalytic hydrogenation. The olefins **5**/**6** (1.50 g, 6.52 mmol) were hydrogenated in ethyl acetate (20 mL) in the presence of Pd−C catalyst (10%, 0.10 g) at atmospheric pressure and room temperature. The catalyst was removed by filtration, the solution was evaporated, and the residue was chromatographed to afford **7** (1.31 g, 87%). IR (film) 1731 cm^{-1}; ^1H-NMR δ 1.18−1.30 (7H, m), 2.32 (3H, s), 2.37 (1H, dd, J = 15.5, 9.2 Hz), 2.57 (1H, dt, J = 12.3, 7.1 Hz), 2.90 (1H, dd, J = 15.4, 5.2 Hz), 3.00−3.12 (1H, m), 3.40−3.50 (1H, m), 4.18 (2H, q, J = 7.1 Hz), 6.95 (1H, s), 7.00 (1H, d, J = 7.7 Hz), 7.07 (1H, J = 7.7 Hz); ^{13}C-NMR δ 14.1, 19.4, 21.1, 37.4, 39.7, 39.8, 42.7, 60.1, 122.7, 123.4, 127.4, 135.7, 145.3, 145.4, 172.6; MS m/z 232 (M^+, 36.3), 186 (16), 158 (48), 144 (100); HRMS (EI) 232.1463 (232.1464 calcd for $C_{15}H_{20}O_2$). (b) From **5**/**6** by ionic hydrogenation. To a magnetically stirred 2:1-mixture of **5**/**6** (0.10 g, 0.434 mmol) and triethylsilane (0.064 g, 0.52 mmol) in dichloromethane (2 mL) was added trifluoracetic acid (0.696 g, 3.04 mmol). Stirring continued overnight, and the reaction mixture was cooled in an ice bath and quenched with 5% sodium bicarbonate solution (2 mL). After dilution with dichloromethane (10 mL), the organic layer was again washed with 5% $NaHCO_3$ solution and brine, dried, filtered, and concentrated. Chromatography furnished (**7**/**7t**) (72.4 mg, 72%) which could not be separated. The ratio of (**7**/**7t**) was determined to be 10:1 by ^1H-NMR. Similar ionic hydrogenolysis of the tertiary alcohol **4** led to a 80% yield of the same **7**/**7t** mixture.

Ethyl *cis*-(5-Acetyl-3,6-dimethyl-1-indanyl)acetate (8). To an acetylating agent prepared from anhydrous aluminum chloride (1.58 g, 11.84 mmol) and acetyl chloride (0.506 g, 6.46 mmol) in dichloromethane (10 mL) was added from a dropping funnel the ester **7c** (1.25 g, 5.38 mmol) in dichloromethane (2 mL) during 5 min. The reaction was run overnight and quenched with crushed ice (to which 5 mL of concd HCl had been added). Dichloromethane extraction workup and chromatography provided the ketone **8** (1.19 g, 86%). IR (neat) 1727, 1675 cm^{-1}; ^1H-NMR δ 1.18−1.37 (7H, m), 2.39 (1H, dd, J = 15, 9 Hz), 2.48 (3H, s), 2.56 (3H, s), 2.53−2.68 (1H, m), 2.56 (3H, s), 2.88 (1H, dd, J = 5.3, 3.15 Hz), 3.05−3.17 (1H, m), 3.55−3.39 (1H, m), 4.18 (2H, q, J = 7 Hz), 6.99 (1H, s),

7.46 (1H, s); ^{13}C-NMR δ 14.2, 19.4, 21.7, 29.5, 37.5, 39.4, 39.9, 42.6, 60.4, 123.9, 126.4, 136.6, 136.9, 145.9, 149.3, 172.4, 201.5; MS *m/z* 274 (M^+, 47), 259 (28), 200 (38), 186 (80), 171 (30), 157 (49), 143 (79), 43 (100); HRMS (EI) 274.1546 (274.1570 calcd for $C_{17}H_{22}O_3$).

Ethyl *cis*-(5-Acetoxy-3,6-dimethyl-1-indanyl)acetate (9). A solution of ketone **8** (1.00 g, 3.65 mmol), *m*-chloroperbenzoic acid (50%, 1.51 g, 4.38 mmol), and *p*-toluenesulfonic acid (0.10 g) in dichloromethane (5 mL) was refluxed for 2 d. The cooled reaction mixture on workup revealed partial hydrolysis of the acetate; therefore, it was acetylated with acetic anhydride (0.365 g) and pyridine (0.289 g) in dichloromethane (5 mL) overnight. Workup by brief treatment with 5% cold NaOH, extraction with dichloromethane, and silica gel chromatography afforded Acetate **9** (0.635 g, 60%). IR (film) 1753, 1727 cm^{-1}; ^{1}H-NMR δ 1.19−1.33 (7H, m), 2.12 (3H, s), 2.29 (3H, s), 2.37 (1H, dd, J = 15.5, 9.1 Hz), 2.52−2.61 (1H, m), 2.86 (1H, dd, J = 15.4, 5.5 Hz), 3.01−3.13 (1H, m), 3.37−3.47 (1H, m), 4.17 (2H, q, J = 7.1 Hz), 6.78 (1H, s), 6.96 (1H, s); ^{13}C-NMR δ 14.2, 16.2, 19.3, 20.8, 37.6, 39.6, 39.8, 42.9, 60.4, 116.5, 125.2, 127.7, 143.1, 147.5, 148.4, 169.5, 172.7; MS *m/z* 290 (M^+, 24), 248 (100), 174 (20), 161 (61); HRMS (EI) 290.1520 (290.1519 calcd for $C_{17}H_{22}O_4$).

***cis*-1-(5-Acetoxy-3,6-dimethyl-1-indanyl)-2-methyl-2-propanol (10).** To a solution of acetate **9** (0.60 g, 2.07 mmol) in anhydrous ether (4 mL) under nitrogen was added during 10 min a solution of methyllithium (1.6 M in ether, 5.43 mL, 8.7 mmol). The resulting mixture was stirred at room temperature for 8 h, quenched with saturated NH_4Cl solution (5 mL), and diluted with ether (20 mL). The product obtained from workup of the organic layer was dissolved in dichloromethane (5 mL) and immediately acetylated with acetic anhydride (0.25 g) and pyridine (0.20 g) overnight. Final workup in the same way as for the isolation of **9** to afford the tertiary alcohol **10** (0.343 g, 60%). IR (film) 1752 cm^{-1}; ^{1}H-NMR δ 1.17−1.25 (1H, m), 1.26 (3H, d, J = 7 Hz), 1.32 (6H, s), 1.54 (1H, dd, J = 14, 9.8 Hz), 2.13 (3H, s), 2.21 (1H, dd, J = 14, 2.7 Hz), 2.29 (3H, s), 2.59−2.68 (1H, m), 3.00−3.13 (1H, m), 6.78 (1H, s), 7.00 (1H, s); ^{13}C-NMR δ 16.2, 19.2, 20.8, 29.7, 30.4, 38.1, 39.4, 45.6, 49.1, 71.2, 116.2, 125.3, 127.4, 145.2, 147.2, 148.1, 169.6; MS *m/z* 276 (M^+, 4), 258 (15), 216 (59), 201 (100), 161 (47); HRMS (EI) 276.1719 (276.1726 calcd for $C_{17}H_{24}O_3$).

***cis*-1-(5-Acetoxy-3,6-dimethyl-1-indanyl)-2-methyl-1-propene (11).** A solution of alcohol **10** (0.276 g, 1 mmol) and *p*-toluenesulfonic acid (0.05 g) in toluene (40 mL) was refluxed under a Dean−Stark trap for 12 h. The cooled reaction mixture was diluted with ether (20 mL), washed with 5% NaOH and brine, and worked up. Silica gel chromatography (eluent: EtOAc/hexane 1:9) furnished **11** (0.198 g, 80%). IR (film) 1754 cm^{-1}; ^{1}H-NMR δ 1.18−1.34 (1H, m), 1.26 (3H, d, J = 10 Hz), 1.75 (3H, s), 1.78 (3H, s), 2.12 (3H, s), 2.30 (3H, s), 2.38−2.48 (1H, m), 3.02−3.10 (1H, m), 3.82 (1H, q, J = 9 Hz), 5.10 (1H, d, J = 8.9 Hz), 6.78 (1H, s), 6.86 (1H, s); ^{13}C-NMR δ 16.1, 18.1, 19.0, 20.8, 25.8, 37.9, 42.7, 44.0, 116.2, 126.1, 127.5, 127.76, 132.8, 144.7, 147.3, 148.1, 169.7; MS *m/z* 258 (M^+, 15.5), 216 (35), 201 (100), 173 (14); HRMS (EI) 258.1626 (258.1621 calcd for $C_{17}H_{22}O_2$).

[Ethyl (3,6-dimethylindanylidene)acetate]tricarbonylchromium (12). A mixture of **5** (0.24 g, 1.04 mmol), chromium hexacarbonyl (0.26 g, 1.18 mmol), and dioxane (6 mL) was placed in a round-bottom flask which was mounted with a condenser. After evacuation and filling with nitrogen in three cycles, the flask was heated in a 150 °C bath for 30 h. On cooling to room temperature the content of the flask was filtered, and the filtrate was evaporated to afford a residue which was chromatographed over silica gel. Elution with 1:10 EtOAc/hexane gave the complex **12** (0.2 g, 52% yield) and unreacted ester (0.05 g). IR (film) 1745 cm^{-1}; ^{1}H-NMR δ 1.22 (3H, d, J = 7.5 Hz), 1.30 (3H, t, J = 8.4 Hz), 2.20 (3H, s), 2.90−2.96 (1H, m), 3.13−3.30 (2H, m), 4.21 (2H, q, J = 7.2 Hz), 5.35 (1H, d, J = 6.6 Hz), 5.46 (1H, d, J = 6.6 Hz), 5.59 (1H, s), 6.07−6.08 (1H, m); ^{13}C-NMR δ −6.4, 14.2, 20.5, 23.3, 36.5, 38.9, 60.0, 87.5, 88.3, 95.3, 104.1, 106.3, 109.8, 121.9, 158.1, 166.4; MS *m/z* 366 (M^+, 25), 310 (10), 282 (70), 210 (100), 141 (36); HRMS (EI) 366.0587 (366.0559 calcd for $C_{18}H_{18}O_5Cr$).

[Methyl *trans*-(3,6-Dimethylindanyl)acetate]tricarbonylchromium (13). Magnesium turnings (28.8 mg, 1.2 mmol) was added to complex **12** (0.2 g, 0.55 mmol) which was dissolved in methanol (5 mL) and cooled in an ice bath to 10 °C. The mixture was stirred for 3 h, poured into 3N HCl (10 mL), and extracted with CH_2Cl_2. The dried extract was concentrated in vacuo to give **13**, after silica gel chromatography (eluent: EtOAc/hexane 1:10) (0.14 g, 71%). IR (film) 1726 cm^{-1}; ^{1}H-NMR δ 1.20 (3H, d, J = 7.2 Hz), 1.95 (2H, m), 2.15 (3H, s), 2.61 (1H, dd, J = 16.5, 7.2Hz), 2.82 (1H, dd, J = 16.5, 7.2Hz), 2.94 (1H, m), 3.60 (1H, quintet, J = 7.2Hz), 3.75 (3H, s), 5.28 (2H, s), 5.34 (1H, s); ^{13}C-NMR δ −4.9, 20.6, 21.4, 36.9, 37.3, 38.3, 39.1, 51.9, 87.9, 91.5, 94.8, 105.7, 116.8, 119.0, 172.9; MS *m/z* 354 (M^+, 3.8), 270 (100), 210 (86), 196 (27); HRMS (EI) 354.0561 (354.0559 calcd for $C_{17}H_{18}O_5Cr$).

Methyl *trans*-(3,6-Dimethyl-1-indanyl)acetate (14). A stirred solution of complex **13** (0.14 g, 0.4 mmol) in THF (2 mL) was cooled to −78 °C, and a solution of iodine (0.35 g in 5 mL THF) was added. After 1 h, the cooling bath was removed and stirring continued for 4 h. The resulting mixture was treated with 10% sodium thiosulfate (3 × 5 mL), dried, and evaporated. Silica gel chromatography afforded **14** (0.07 g, 80%). IR (film) 1739 cm^{-1}; ^{1}H-NMR δ 1.26 (3H, d, J = 6.6 Hz), 1.93−2.09 (2H, m), 2.34 (3H, s), 2.39−2.48 (1H, ddd, J = 15.5, 6Hz), 2.67 (1H, dd, J = 15.6, 6 Hz), 3.25 (1H, sx, J = 6.6 Hz), 3.62 (1H, m), 3.73 (3H, s), 7.01−7.11 (3H, m); ^{13}C-NMR δ 20.2, 21.2, 36.9, 39.7, 39.9, 41.0, 51.4, 123.2, 124.3, 127.8, 136.0, 145.37, 145.4, 173.1. MS *m/z* 218 (M^+, 37.5), 216 (33), 186 (17), 144 (100), 129 (44); HRMS (EI) 218.1306 (218.1306 calcd for $C_{14}H_{18}O_2$).

Methyl *trans*-(5-Acetyl-3,6-dimethyl-1-indanyl)acetate (15). To an acetylating agent prepared from anhydrous aluminum chloride (0.094 g, 0.7 mmol) and acetyl chloride (0.030 g, 0.38 mmol) in dichloromethane (10 mL) was added from a dropping funnel the ester **14** (0.07 g, 0.32 mmol) in dichloromethane (2 mL) during 5 min. The reaction was run overnight and quenched with crushed ice (to which 5 mL of concd HCl had been added). Dichloromethane extraction workup and chromatography provided the ketone **15** (0.072 g, 82%). IR (film) 1739, 1681 cm^{-1}; ^{1}H-NMR δ 1.24 (3H, d, J = 6.9 Hz), 1.91−2.07 (2H, m), 2.36−2.67 (2H, m), 2.44 (3H, s), 2.53 (3H, s), 3.24 (1H, m), 3.58 (1H, m), 3.69 (3H, s), 7.02 (1H, s), 7.47 (1H, s); ^{13}C-NMR δ 20.2, 21.7, 29.6, 37.0, 39.5, 39.7, 40.8, 51.6, 124.4, 127.3, 136.9, 137.1, 145.9, 149.2, 172.8, 201.7. MS *m/z* 260 (M^+, 100), 245 (50), 217 (22), 200 (35), 187 (36), 186 (75); HRMS (EI) 260.1409 (260.1412 calcd for $C_{16}H_{20}O_3$).

Methyl *trans*-(5-Acetoxy-3,6-dimethyl-1-indanyl)acetate (16). A solution of ketone **15** (0.072 g, 0.28 mmol), *m*-chloroperbenzoic acid (50%, 0.12 g, 0.34 mmol), and *p*-toluenesulfonic acid (0.008 g) in dichloromethane (5 mL) was refluxed for 2 d. The cooled reaction mixture on workup revealed partial hydrolysis of the acetate; therefore, it was acetylated with acetic anhydride (0.031 g) and pyridine (0.024 g) in dichloromethane (5 mL) at room temperature overnight. Workup by brief treatment with 5% cold NaOH (2 mL), extraction with dichloromethane, and silica gel chromatography with EtOAc/hexane 1:19 as eluent afforded acetate **16** (0.045 g, 56%). IR (film) 1759, 1732 cm^{-1}; ^{1}H-NMR δ 1.20 (3H, d, J = 6.6 Hz), 1.87−2.08 (2H, m), 2.16 (3H, s), 2.28 (3H, s), 2.37−2.63 (2H, m), 3.22 (1H, m), 3.56 (1H, m), 3.69 (3H, s), 6.79 (1H, s), 7.01 (1H, s); ^{13}C-NMR δ 16.1, 20.0, 20.7, 37.1, 39.3, 39.8, 41.1, 51.5, 116.8, 126.0, 127.9, 143.0, 147.4, 148.5, 169.5, 173.1; MS *m/z* 276 (M^+, 39), 260 (18), 245 (8), 234 (100), 202 (8); HRMS (EI) 276.1364 (276.1361 calcd for $C_{16}H_{20}O_4$).

***trans*-1-(5-Acetoxy-3,6-dimethyl-1-indanyl)-2-methyl-2-propanol (17).** To a solution of acetate **16** (0.045 g, 0.16 mmol) in anhydrous ether (2 mL) under nitrogen was added during 10 min a solution of methyllithium (1.6 M in ether, 0.4 mL, 6.4 mmol). The resulting mixture was stiired at romm temperature for 18 h, quenched with saturated NH_4Cl solution (2 mL), and diluted with ether (10 mL). The product obtained from workup of the organic layer was dissolved in dichloromethane (5 mL) and immediately acetylated with acetic anhydride (0.02 g), pyridine (0.15 g), and DMAP (15 mg) overnight. Workup afforded the tertiary alcohol **17** (0.03 g, 67%). IR (film) 3420, 1738 cm^{-1}; ^{1}H-NMR δ 1.17 (3H, d, J =

6.6 Hz), 1.52 (6H, s), 1.8−2.4 (6H, m), 2.12 (3H, s), 2.31 (3H, s), 3.24 (1H, m), 6.77 (1H, s), 6.99 (1H, s); ^{13}C-NMR δ 20.5, 22.6, 26.4, 26.9, 37.8, 38.6, 42.8, 46.5, 82.4, 116.8, 126.0, 127.8, 144.8, 147.5, 148.2, 169.6; MS *m*/*z* 276 (M^+, 6), 260 (80), 243 (60), 218 (30), 202 (100); HRMS (EI) 276.1721 (276.1726 calcd for $C_{16}H_{24}O_3$).

***trans*-1-(5-Acetoxy-3,6-dimethyl-1-indanyl)-2-methyl-1-propene (18).** A solution of alcohol **17** (0.03 g, 0.11 mmol) and *p*-toluenesulfonic acid (0.005 g) in benzene (10 mL) was refluxed under a Dean−Stark trap for 12 h. The cooled reaction mixture was diluted with ether (20 mL), washed with 5% NaOH and brine, and worked up. Silica gel chromatography (eluent: hexane/EtOAc 10:1) furnished **18** (0.024 g, 85%). IR (film) 1760 cm^{-1}; ^{1}H-NMR δ 1.20 (3H, d, J = 6.6 Hz), 1.73 (3H, s), 1.74 (3H, s), 1.77−1.96 (2H, m), 2.10 (3H, s), 2.29 (3H, s), 3.18 (1H, sx, J = 7.2 Hz), 3.99 (1H, q, J = 8.7 Hz), 5.11 (1H, br d, J =8.7 Hz), 6.78 (1H, s), 6.88 (1H, s); ^{13}C-NMR δ 20.53, 22.63, 26.39, 26.91, 37.78, 38.59, 42.82, 46.49, 82.36, 116.80, 126.03, 127.75, 144.83, 147.45, 148.18, 169.56; MS *m*/*z* 258 (M^+, 50), 218 (36), 216 (85), 210 (100); HRMS (EI) 258.1628 (258.1620 calcd for $C_{17}H_{22}O_2$).

Mutisianthol (1t). A solution of acetate **18** (0.024 g, 0.1 mmol) in anhydrous ether (2 mL) was added to a suspension of lithium aluminum hydride (0.076 g, 0.2 mmol) in ether (2 mL). After stirring at room temperature for 20 min excess reagent was destroyed by addition of EtOAc. The resulting mixture was diluted with ether and treated with 10% HCl. The organic layer was separated, dried, and evaporated. The product was purified by silica gel chromatography (eluent EtOAc/hexane 1:10) to give **1t** (0.02 g, 92%). IR (film) 3600−3000 cm^{-1}; ^{1}H-NMR δ 1.19 (3H, d, J = 7.5 Hz), 1.73 (3H, s), 1.76 (3H, d, J = 4.5 Hz), 1.93 (2H, m), 2.19 (3H, s), 3.18 (1H, sx, J = 5.1 Hz), 3.95 (1H, q, J = 9 Hz), 4.69 (1H, br s), 5.10 (1H, br d, J = 10.5 Hz), 6.60 (1H, s), 6.79 (1H, s); ^{13}C-NMR δ 15.8, 18.1, 20.9, 25.8, 38.0, 41.5, 42.4, 110.1, 121.7, 126.3, 128.6, 131.2, 138.6, 147.8, 152.7; MS *m*/*z* 216 (M^+, 45), 201 (100), 161 (20), 159 (10), 145 (6); HRMS (EI) 216.1522 (216.1514 calcd for $C_{15}H_{20}O$).

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Supporting Information Available: Copies of ^{1}H and ^{13}C-NMR spectra (9 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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