Gold Catalysis: Efficient Synthesis and Structural Assignment of Jungianol and *epi*-Jungianol

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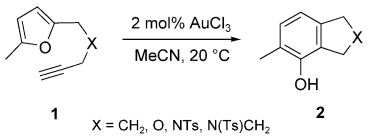
Abstract: Starting from 2-methylfuran and crotonaldehyde, both jungianol and *epi*-jungianol were prepared by a six-step sequence including a gold-catalyzed arene synthesis and a photochemical S_N2-like reduction with lithium aluminum hydride. Not a single protective group was needed in the entire synthesis. With both diastereomers in hand, the stereochemical assignment in the literature could be corrected by means of a thorough ^{1}H NMR spectroscopic analysis and an X-ray diffraction study on an *epi*-jungianol derivative.

Keywords: arenes · cyclization · gold · homogeneous catalysis · terpenoids

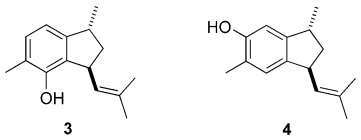
Introduction

Certain substitution patterns of aromatic rings can still present a synthetic problem. We recently reported a gold-catalyzed synthesis of benzoid arenes **2** fused to five- or six-membered rings (Scheme 1).[1–3] This reaction shifts the problem of selective placement of the desired substituents from a benzoid arene to a furan **1**, in which it can easily be controlled. To prove that this strategy to build up the benzoid arene with perfect control of the positions of the substituents can be superior to substitution of the benzoid arene, we sought a synthetic target that had already been approached by the latter strategy and has a close structural relationship to the product of our gold-catalyzed reaction. With such a molecule, one could deliver a proof of principle without the neccessity to perform too many other steps or to carry out only a partial synthesis.

Among some interesting candidates[4] we finally chose jungianol (**3**) as our target molecule. This sesquiterpene was isolated and characterized by Bohlmann et al. in 1977 from *Jungia malvaefolia*, a South American plant.[5] It contains a trisubstituted phenol substructure and two side chains on the five-membered, benzoannelated ring. On the basis of the ^{1}H NMR spectrum Bohlmann et al. assigned the two side chains to be *cis*, while the absolute configuration of the two stereogenic centers is unknown, and the optical rotation was not reported; thus, we did not need to start from enantiomerically pure material. In 1997 Ho et al. tried to synthesize **3** and its isomer mutisianthol (**4**), two natural products that differ only in the position of the phenolic hydroxyl group.[6] Numerous efforts to place the hydroxyl group in the position needed for **3** failed, and only **4** could be prepared from a commercially unavailable starting material in eleven steps with an overall yield of 2.6%. Based on thorough NOE and COSY experiments on the five-membered ring of a precursor of **4** and their synthetic work, Ho et al. proposed a *trans* arrangement of the side chains of **3** rather than the *cis* arrangement suggested by Bohlmann et al.



Scheme 1. Gold-catalyzed phenol synthesis.



So, besides demonstrating the advantages of gold catalysis, we could also clarify the stereochemistry of **3** and related compounds.

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Results and Discussion

We started from the known furans **5** (Scheme 2), which can easily be prepared from 2-methylfuran and Michael acceptors by literature procedures in one step.[7–9] Addition of sodium acetylide to **5a** delivered the secondary propargylic alcohol **6a**. Now we could test the gold catalyst, but with **6a** the catalytic reaction failed, and a gold mirror immediately precipitated. We suspected that the activated secondary alcohol reduced gold(III), but the protection of the hydroxyl group with TBDPS (**6e**) did not help. Hence, we prepared tertiary propargylic alcohol **6c** by the same route, but neither the gold-catalyzed reaction of **6c** nor that of benzyl-protected **6d** succeeded.

We then decided to oxidize alcohol **6a** to the ketone **7a**, for which gold catalysis was successful at room temperature. One might suspect that the products **8a** (45%), **9a** (9%), and **10a** (7%) are formed by a normal, uncatalyzed reaction pathway, but control experiments in which **7a** was heated stepwise to 100 °C in acetonitrile (the solvent of the gold-catalyzed reaction) did not deliver any of the products. Intramolecular [4+2] cycloadditions of furans and alkynes are known, but with a bridge of three carbon atoms the acceptor always sits at the other end of the unsaturated unit, not in the tether.[10] It seems that the transition state is less feasible when the sp^2 carbon atom is in this tether.

The assignment of the constitutional isomers **8a** and **10a** (both tetrasubtituted arenes) is based on the chemical shift of the hydroxyl proton ($\delta = 9.23$ in $CDCl_3$) in **8a** which is quite normal for a hydrogen bond to the carbonyl group, while in **10a** the signal appears at higher field ($\delta = 5.36$ in $CDCl_3$). A crystal structure analysis of **8a** unambigously confirmed this assignment (Figure 1).[11] The structure reveals an O2−O1 distance of 2.8269(0.0024) Å, a H2−O1 distance of 1.9885(0.0388) Å, and an O2-H2-O1 angle of 145.37(3.29)°. Several reports exist on the synthesis of **8a** by a combination of a Fries rearrangement and a Nazarov cyclization.[12–14] However, the compound was somewhat ill-defined (IR data and incomplete list of ^{1}H NMR shifts),[12] and it was not unambiguously proven that the desired *ortho*- and not the *para*-Fries rearrangement[14] led to the product obtained. In contrast to our mild conditions, in these approaches the substrate must tolerate strong Brønstedt and Lewis acids at high temperatures, and the yield is only 18%.

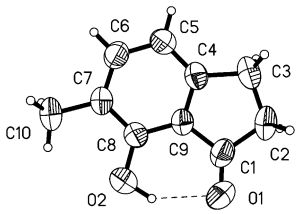


Figure 1. Crystal structure of **8a**.

Compound **9a** is the product of an intramolecular electrophilic attack of the alkynone at the 3-position of the furan ring to give a seven-membered ring. Addition of 2-methyl-1-propenylmagnesium bromide to **8a** delivered **11a**, which can be rationalized as the product of ionization of the intermediate allylic benzylic alcohol followed by intramolecular attack of the phenolic hydroxyl group. This assumption is supported by the observation of spots for other compounds in the TLC of the crude product, which are converted to **11a** upon treatment with mild Lewis acids such as silica gel (cf. the higher yield of **11b**).[12] Once again the structural assignment was proven by an X-ray crystal structure analysis (Figure 2).[11] The benzene ring is approximately planar. The largest torsion angle in this ring is 1.7(2)°. The five-membered ring shows a very small deviation from planarity: ring atom C8 deviates 0.10 Å from the plane through C9/C1/C6/C7. The six-membered ring containing the oxygen atom has a distorted C11 envelope conformation with methyl group C12 in a pseudoaxial position and methyl group

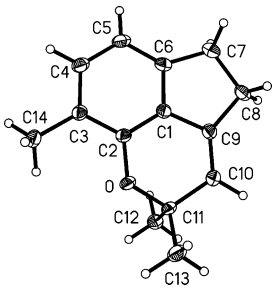
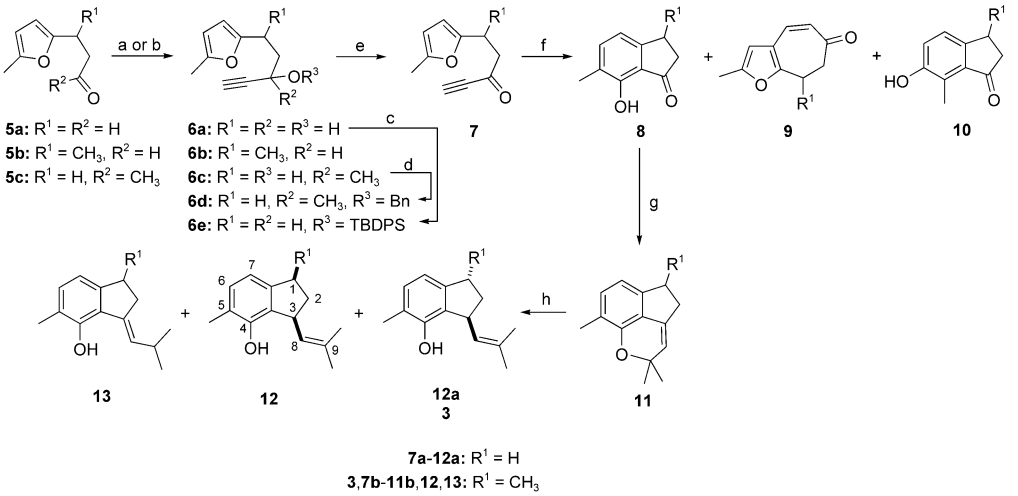


Figure 2. Crystal structure of **11a**.



Scheme 2. Synthesis of jungianol and *epi*-jungianol. a) NaC≡CH, THF, 0 °C; b) BrMgC≡CH, THF, 0 °C; c) TBDPSCl, imidazole, DMF, 0 °C; d) NaH, $PhCH_2Br$, Bu_4NI, THF, heat; e) DMP, CH_2Cl_2, 0 °C → RT; f) $AuCl_3$, CH_3CN, RT; g) $BrMgCH{=}C(CH_3)_2$, THF, 0 °C; then silica gel, CH_2Cl_2, RT; h) LAH, *hv*, Et_2O, RT. DMAP = 4-(dimethylamino)pyridine, DMP = Dess–Martin periodinane, TBDPSCl = *tert*-butyldiphenylsilyl chloride.

C13 in a pseudoequatorial position. The C7–C8 bond length of 1.563(2) Å is slightly longer than the standard C–C single-bond length of 1.54 Å. There are no short intramolecular contacts. The molecules are connected in the crystallographic *a* direction by intermolecular C–H···π(benzene) interactions with H···π distances of 2.79 and 2.83 Å and C–H···π angles of 165 and 155°. Thus, from both enantiomers of the intermediate allylic alcohols the same achiral **11a** is generated.

Now we needed an S_N2-like reduction of the allylic ether substructure of **11a** to form the deconjugated olefin of the final product **12a**. There are several reports in the literature on reduction of a related compound:[15–17] a combination of UV irradiation and lithium aluminum hydride (LAH) was used. As the bond to be cleaved, that between the quarternary allylic carbon atom and the phenolic oxygen atom, is perpendicular to the π system of the olefin, it is a normal, unactivated ether group which does not readily react with LAH. Only after electrocyclic ring opening of the oxacyclohexa-1,3-diene substructure of **11a**, is a reaction possible. The intermediate conjugated dienone then coordinates to LAH, and the hydride is delivered to the *β*-carbon atom via a six-membered transition state to give the deconjugated system of **12a**.

As the sequence worked as desired, we now repeated it with **6b**. Oxidation with DMP delivered the ketone **7b** (77%), which with 2.9 mol% $AuCl_3$ at 0°C again provided three products **8b** (53%), **9b** (2%), and **10b** (3%), but at room temperature **8b** was the only product (75%). Like **8a**, **8b** was prepared before[18, 19] but only characterized by IR and ^{1}H NMR spectroscopy.[18] Our overall yield of 42% for the preparation exceeds the 37% in the literature, and our reaction conditions are much milder.

With 2-methyl-1-propenylmagnesium bromide **8b** then gave a 96% yield of **11b** after treatment of the crude product with silica gel (cf. comments on the formation of **11a** above). Here both diastereomers of the initially formed allylic alcohol convergently delivered **11b**. Finally, LAH reduction under photochemical conditions afforded conjugated isomer **13** (7%)[20] as an undesired by-product and the two diastereomers **12** (68%) and **3** (21%). Thus, the diastereoselectivity-determining step, LAH reduction, had only a moderate *dr* of **12**:**3** = 3.2:1.0, which was not a problem as our major interest was to demonstrate the advantages of gold catalysis in such an approach. Comparison with the ^{1}H NMR data of Bohlmann et al. showed the minor product to be jungianol; the major product thus had to be *epi*-jungianol. With *both* diastereomers in hand, we could now try to resolve the question which is the *cis* and which the *trans* diastereomer. In **12**, the anisochrony of the diastereotopic methylene protons between the two stereogenic centers is pronounced ($\Delta\delta = 1.09$), while in **3** this chemical shift difference is rather small ($\Delta\delta = 0.07$). Usually this would suggest a *cis* configuration for **12**, and a *trans* arrangement for **3**. On the other hand, it is difficult to estimate the influence of the olefinic substituent with its anisotropy and possible conformational preferences. We therefore sought more conclusive arguments for the stereochemical assignment.

Except for 2-H^A,H^B the ^{1}H NMR chemical shifts and coupling constants of the two stereoisomers are very much alike (Table 1), but painstaking analysis of long-range connectivities (from high-resolution spectra with appropriate apodization and long-range COSY experiments), in combination with a NOESY spectrum, allowed a straightforward configurational assignment. In the following, the detailed ratiocination is presented for **12**.

The two aryl proton resonances are each split into a primary doublet ($^3J_{ortho} = 7.4$ Hz). The high field signal at 6.667 ppm is assigned to 7-H on the basis of the +M effect of the 4-hydroxyl substituent, as well as by virtue of the respective long-range coupling patterns of the two multiplets. Diligent apodization resolves a sextet fine structure for the 6-H doublet at 6.985 ppm, while only one long-range coupling (1.2 Hz) becomes apparent for the 7-H doublet. A long-range ^{1}H,^{1}H COSY experiment indeed showed prominent cross-peaks between 6-H and the 4-OH, 3-H, and 5-CH_3 resonances, that is, five coupling partners in all. For 7-H, in contrast, there is only one cross-peak of comparable intensity to the 1-H signal.

These connectivities are verified by selective decoupling, for example, of the phenolic proton, which reduces the fine-structure multiplicity of the two 6-H doublet lines to a perfect quintet. The identical pattern (i.e., a quintet with an apparent splitting of 0.7 Hz) is obtained upon irradiation of 3-H even at fairly high decoupling power. Finally, decoupling of the benzylic 5-CH_3 protons reduces the fine structure to a triplet. In all these selective decoupling experiments, the 1.2 Hz fine splitting of the 7-H resonance remains unimpaired. Selective decoupling of 1-H, on the other hand, leaves the sextet fine structure of the 6-H signal completely untouched (splittings are identical with those in the regular spectrum to within ±0.01 Hz) while the 1.2 Hz splitting of the two 7-H doublet lines is erased completely. The residual line width is distinctly broader, however, than that of the 6-H lines, and this indicates further unresolved small couplings, for example to 5-CH_3, as is also apparent also from the long-range COSY experiment.

Table 1. ^{1}H NMR shifts and coupling constants of **12** and **3**.

	12	**3**
1-H	3.065	3.254
1-CH_3	1.299	1.191
2-H^A	2.423	1.930
2-H^B	1.342	2.004
3-H	3.996	4.171
4-OH	5.930	5.594
5-CH_3	2.189	2.187
6-H	6.984	6.962
7-H	6.666	6.675
8-H	5.346	5.294
9-CH_3(*E*)	1.871	1.870
9-CH_3(*Z*)	1.826	1.799
^3J(1-H,1-CH_3)	6.7	7.1
^3J(1-H,2-H^A)	6.8	3.1
^3J(1-H, 2-H^B)	10.7	8.0
^4J(1-H,7-H)	1.2	< 0.3
^2J(2-H^A,2-H^B)	(−)12.6	(−)12.6
^3J(2-H^A,3-H)	7.1	7.6
^3J(2-H^B,3-H)	10.2	8.0
^3J(3-H,8-H)	10.3	10.3
^3J(6-H,7-H)	7.4	7.4
^4J(6-H,5-CH_3)	0.7	0.7
^5J(6-H,4-OH)	0.7	0.7
^6J(6-H,3-H)	0.7	0.7
^4J(8-H,9-$CH_3^{(E)}$)	1.4	1.4
^4J(8-H,9-$CH_3^{(Z)}$)	1.4	1.4

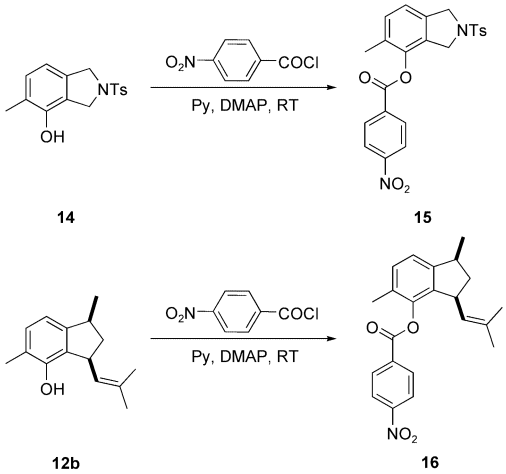
Differentiation between the two *E* and *Z* allylic methyl groups at C-9 rests on a distinct NOESY cross-peak between the 8-H and CH_3 resonances at higher field. Both methyl signals show identical allylic coupling to 8-H (1.4 Hz). Each of the two 8-H vicinal doublet lines ($^3J_{8\text{-H},3\text{-H}} = 10.3$ Hz) is in turn split into a septet, which is reduced to a quartet by irradiation at either of the allylic methyl resonances.

Upon irradiation of 3-H, the originally unstructured phenolic OH resonance is resolved into a clean doublet, the 0.7 Hz splitting of which corresponds exactly to the ^5J coupling constant determined from the 6-H multiplet. Boxed in between the isotropic methyl rotor at C-5 and the isobutenyl group at C-3, the phenolic OH group will be oriented preferentially in the plane of the aromatic ring, and turned away from the *ortho*-methyl group, thus establishing a perfect W pathway for $^5J_\sigma$ coupling to 6-H. Of the NOE contacts established between the phenolic OH group and 3-H, 8-H, the *o*-CH_3 group at C-5, and the two allylic CH_3 groups, that to the vinyl proton at 8-H is the most intense by far. This is as expected for the antiperiplanar conformation of the O–H and the C-4–C-5 bonds derived above, in which the isobutenyl substituent adopts a pseudoequatorial, and 3-H a pseudoaxial position, which in turn is perfect for *para*-benzylic coupling ($^6J_\pi$) between 3-H and 6-H (see above). The most prominent of all NOESY cross-peaks connects the 1-CH_3 and 7-H resonances, and thus definitely establishes a pseudoequatorial orientation of the methyl group. This leaves 1-H in a pseudoaxial position, perfectly aligned with the arene π system, that is, in an optimum orientation for *ortho*-benzylic coupling to 7-H ($^4J_\pi = 1.2$ Hz, see above).

Almost identical, large (> 10 Hz) vicinal coupling constants to both 1-H and 3-H are established for one of the two diastereotopic C-2 methylene protons (2-H^B); the corresponding two vicinal coupling constants of geminal 2-H^A are about 7 Hz. This coupling pattern is feasible only if 2-H^B is oriented pseudo-*trans* to both the methine protons at C-1 and at C-3, and 2-H^A pseudo-*cis*. Taken together, all the NMR evidence collected above is only compatible with a *cis* configuration of the fused five-membered ring in **12**.

For the other diastereomer **3**, the ^{1}H NMR data of the aryl and isobutenyl moieties are almost identical with those of **12**, both with regard to chemical shifts and individual coupling constants (see Table 1). The conformation at C-3 thus appears to be conserved to a high degree. However, inversion of the relative configuration of C-1 and C-3 leaves the 1-CH_3 group in a pseudoaxial and 1-H in a pseudoequatorial position, and the *ortho*-benzylic coupling to 7-H is thus severely attenuated (< 0.3 Hz, as estimated from the line width of the 7-H resonance). Concomitantly, the vicinal coupling constant between 2-H^A and 1-H is reduced to about 3 Hz, in nice agreement with the dihedral angle of 120 – 130° shown by the model. Protons 2-H^A and 2-H^B each adopt an almost eclipsed orientation to one substituent, which apparently results in the almost identical shieldings for the two diastereotopic protons (though with reversed order, see Table 1).

An X-ray crystal structure analysis would confirm this assignment, but all attempts to grow single crystals of the low-melting **12** failed, and **3** is an oil. As a functional group for the preparation of a crystalline derivative the phenolic hydroxyl group is available. 4-Nitrobenzoyl chloride may lead to a crystalline derivative, but phenols are weak nucleophiles. We first tested the conditions for 4-nitrobenzoate formation with the closely related **14**, which we had in stock from mechanistic investigations and obtained, with pyridine as solvent and DMAP as catalyst, 62 % yield of **15** (Scheme 3). Under the same conditions, **12** was transformed into **16** in 69 % yield. As



Scheme 3. Synthesis of crystalline derivatives.

desired, **16** was crystalline, and after some efforts we could obtain single crystals for an X-ray crystal structure analysis (Figure 3).[11] The five-membered ring has an envelope conformation with atom C8 0.37 Å outside the plane through C7/C6/C1/C9. The side groups at C7 and C9 are both in

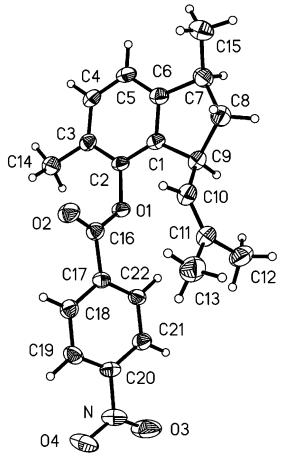


Figure 3. Crystal structure of **16**.

pseudoequatorial positions with respect to the five-membered ring and are *cis*. Both six-membered rings are approximately planar. The angle between the plane of phenyl group C1 – C6 and the plane of the carboxylate group is 76.9°. The angle between the plane of phenyl group C17 – C22 and the plane of the carboxylate group is 15.7°. The angle between the plane of phenyl group C17 – C22 and the plane of the nitro group is 3.9°. The shortest intramolecular contact distances are O1 ··· H22 2.43, O3 ··· H21 2.43, and O4 ··· H19 2.42 Å. The molecules form centrosymmetric dimers connected by two rather short intermolecular C21–H21 ··· Cg interactions with an

H···Cg distance of 2.61 Å and a C-H-Cg angle of 148° (Cg is the centroid of the phenyl ring C1–C6). The crystal packing also shows a second weaker C–H···π interaction and an intermolecular C–H···O interaction.

The natural product jungianol is the *trans* isomer **3**, and the *cis* isomer we prepared as the major product, which Bohlmann et al. had suggested was jungianol, is in fact *epi*-jungianol, as Ho et al. already assumed. With only six steps and a combined yield of 18% (14% for *epi*-jungianol and 4% for jungianol), we have opened an efficient synthetic entry into such systems. Furthermore, it should be noted that the synthesis requires not a single protective group.

Conclusion

Gold catalysis opens a short route to *epi*-jungianol and jungianol, thus once more proving the benefits of this methodology. While both unprotected and protected hydroxyl groups next to the alkyne were not tolerated, carbonyl groups were tolerated in this key step. No protective group is needed in any single step of the whole sequence. The five-membered ring configuration could be definitively assigned for both **12** and **3**. The detailed NMR data in Table 1 will provide a solid reference basis for future assignment of structurally related compounds.

Experimental Section

5-(5-Methyl-2-furyl)pent-1-yn-3-ol (6a): A solution of aldehyde **5a** (16.6 g, 12.0 mmol) in dry THF (50 mL) was added dropwise to a stirred suspension of sodium acetylide (60.0 mL, 18% in light mineral oil, 204 mmol) at 0 °C. The resulting slurry was allowed to warm to room temperature and stirred overnight. The reaction mixture was poured onto ice, saturated with NH_4Cl, and extracted with diethyl ether. The combined organic phases were washed with brine and dried over $MgSO_4$. After removal of the solvents, the residue was purified by column chromatography on silica gel (5% EtOAc/petroleum ether) to give **6a** (6.61 g, 34%). IR (neat): $\tilde{\nu}$ = 3278 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 2.00–2.12 (m, 3H), 2.25 (s, 3H), 2.49 (d, 1H, J = 2.2 Hz), 2.77 (m, 2H), 4.42 (m, 1H), 5.84 (dd, 1H, J = 2.9 Hz, 1.0 Hz), 5.89 (d, 1H, J = 2.9 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.9 (q), 24.1 (t), 36.4 (t), 61.9 (d), 73.7 (d), 84.8 (s), 106.3 (d), 106.4 (d), 151.0 (s), 153.3 (s); MS: m/z (%): 164 [M^+] (58), 146 (8), 109 (12), 95 (100); HRMS: m/z: calcd for $C_{10}H_{12}O_2$ [M^+]: 164.0837, found: 164.0837.

5-(5-Methyl-2-furyl)hex-1-yn-3-ol (6b): Ethynylmagnesium bromide (0.5 M in THF, 35.5 mL, 17.8 mmol) was added to asolution of aldehyde **5b** (1.35 g, 8.87 mmol) in dry THF (20 mL) at −60 °C, and the resulting solution was stirred for 1 h while the temperature was allowed to rise to 0 °C. The reaction mixture was quenched at 0 °C with a saturated aqueous solution of NH_4Cl and warmed to room temperature slowly. The layers were separated, and the aqueous phase was extracted with diethyl ether. The combined organic portions were washed with brine and then dried over $MgSO_4$. After removal of the solvents, the residue was purified by column chromatography on silica gel (10% EtOAc/petroleum ether) to give **5b** (53.9 mg, 4%) and **6b** as a 6:5 mixture of two diastereomers (1.09 g, 73% based on consumed aldehyde **5b**). IR ($CDCl_3$): $\tilde{\nu}$ = 3580, 3281 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.26, 1.27 (d, 3H, J = 7.0 Hz), 1.83–2.18 (m, 3H), 2.25 (s, 3H), 2.46, 2.48 (d, 1H, J = 2.1 Hz), 2.97–3.13 (m, 1H), 4.35 (m, 1H), 5.84 (m, 1H), 5.88, 5.89 (d, 1H, J = 3.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.9 (q), 19.8 (q), 20.0 (q), 30.0 (d), 30.3 (d), 44.1 (t), 44.2 (t), 60.8 (d), 61.1 (d), 73.3 (d), 73.5 (d), 85.16 (s), 85.21 (s), 105.0 (d), 105.3 (d), 106.06 (d), 106.12 (d), 150.9 (s), 151.0 (s), 157.58 (s), 157.64 (s); MS: m/z (%): 178 [M^+] (35), 160 (3), 123 (13), 109 (100); HRMS: m/z: calcd for $C_{11}H_{14}O_2$: 178.0994 [M^+], found: 178.0994.

3-Methyl-5-(5-methyl-2-furyl)pent-1-yn-3-ol (6c): A solution of ketone **5c** (380 mg, 2.50 mmol) in dry THF (3 mL) was added dropwise to a stirred suspension of sodium acetylide (2.50 mL, 18% in light mineral oil, 8.52 mmol) at 0 °C. The resulting slurry was allowed to warm to room temperature and stirred overnight. The reaction mixture was poured onto ice, saturated with NH_4Cl, and extracted with diethyl ether. The combined organic phases were washed with brine and dried over $MgSO_4$. After removal of the solvents, the residue was purified by column chromatography on silica gel (10% diethyl ether/petroleum ether) to give **5c** (34.6 mg, 9%) and **6c** (319 mg, 79% based on consumed ketone **5c**). IR ($CDCl_3$): $\tilde{\nu}$ = 3581, 3282 cm^{-1}; ^1H NMR (300 MHz, CD_3CN): δ = 1.47 (s, 3H), 1.88–1.98 (m, 2H), 2.24 (s, 3H), 2.71 (s, 1H), 2.73–2.80 (m, 2H), 3.44 (s, 1H), 5.89 (dd, 1H, J = 3.0 Hz, 1.0 Hz), 5.92 (d, 1H, J = 3.0 Hz); ^{13}C NMR (126 MHz, CD_3CN): δ = 12.0 (q), 22.7 (t), 28.7 (t), 41.2 (d), 66.2 (s), 70.8 (d), 87.1 (s), 104.9 (d), 105.5 (d), 149.7 (s), 153.3 (s); MS: m/z (%): 178 [M^+] (58), 160 (20), 109 (19), 95 (100); HRMS: m/z: calcd for $C_{11}H_{14}O_2$: 178.0994 [M^+]; found: 178.0994.

2-[3-(Benzyloxy-3-methylpent-4-ynyl]-5-methylfuran (6d): A suspension of alcohol **6c** (214 mg, 1.20 mmol) and sodium hydride (72.0 mg, 3.00 mmol) in dry THF (20 mL) was stirred for 1 h at 40 °C under nitrogen. Benzyl bromide (412 mg, 2.41 mmol) and tetrabutylammonium iodide (0.6 g) were then added and stirring was continued for 1.5 h at 55 °C. The mixture was poured onto ice, saturated with NH_4Cl, and extracted with CH_2Cl_2. The combined organic phases were washed with brine and dried over $MgSO_4$. After evaporation of the solvents, the residue was purified by column chromatography on silica gel (2% EtOAc/petroleum ether) to give **6d** (300 mg, 93%). IR (neat): $\tilde{\nu}$ = 3287, 1053 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.57 (s, 3H), 2.08–2.16 (m, 2H), 2.26 (s, 3H), 2.54 (s, 1H), 2.82–2.90 (m, 2H), 4.62 (d, 1H, J = 11.1 Hz), 4.72 (d, 1H, J = 11.1 Hz), 5.85 (dd, 1H, J = 2.9 Hz, 0.9 Hz), 5.88 (d, 1H, J = 3.0 Hz), 7.28–7.40 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 14.0 (q), 23.7 (t), 26.8 (q), 40.5 (t), 66.8 (t), 73.5 (s), 74.4 (d), 85.1 (s), 105.7 (d), 106.3 (d), 128.0 (d, 2C), 128.7 (d, 2C), 139.4 (s), 150.7 (s), 154.3 (s); MS: m/z (%): 268 [M^+] (9), 160 (32), 145 (86), 109 (35), 95 (49), 91 (100); HRMS: m/z: calcd for $C_{18}H_{20}O_2$: 268.1463 [M^+], found: 268.1462.

***tert*-Butyl-({1-[2-(5-methyl-2-furyl)ethyl]prop-2-ynyl}oxy)diphenylsilane (6e)**: *tert*-Butyldiphenylchlorosilane (1.11 g, 4.00 mmol) was added dropwise under nitrogen to a stirred solution of alcohol **6a** (442 mg, 2.69 mmol) and imidazole (676 mg, 9.93 mmol) in DMF (10 mL) at 0 °C. After stirring for 1 h at room temperature, 10% NaOH was added to quench the reaction, and the resulting solution was extracted with diethyl ether. The combined organic portions were washed with 0.5 N HCl and brine and dried over $MgSO_4$. After evaporation of the solvents, the residue was purified by column chromatography on silica gel (2.5% EtOAc/petroleum ether) to give **6d** (891 mg, 82%). IR ($CDCl_3$): $\tilde{\nu}$ = 3287 cm^{-1}; ^1H NMR (500 MHz, CD_3CN): δ = 1.07 (s, 9H), 1.94–1.98 (m, 2H), 2.18 (s, 3H), 2.64 (d, 1H, J = 2.1 Hz), 2.65–2.73 (m, 2H), 4.46 (dt, 1H, J = 6.2 Hz, 2.0 Hz), 5.78 (d, 1H, J = 2.9 Hz), 5.89 (d, 1H, J = 2.0 Hz), 7.39–7.49 (m, 6H), 7.67 (d, 2H, J = 7.8 Hz), 7.74 (d, 2H, J = 7.8 Hz); ^{13}C NMR (75.5 MHz, CD_3CN): δ = 12.4 (q), 18.7 (s), 23.0 (t), 26.2 (q, 3C), 36.5 (t), 62.9 (d), 73.8 (d), 84.0 (s), 105.6 (d), 105.8 (d), 127.5 (d, 2C), 127.7 (d, 2C), 129.8 (d), 129.9 (d), 133.1 (s), 133.2 (s), 135.6 (d, 2C), 135.7 (d, 2C), 150.2 (s), 153.0 (s); MS: m/z (%): 402 [M^+] (2.5), 345 (100), 199(50), 95 (30); elemental analysis (%) calcd for $C_{26}H_{30}O_2Si$: C 77.57, H 7.51; found: C 77.48, H 7.61.

5-(5-Methyl-2-furyl)pent-1-yn-3-one (7a): Dess–Martin periodinane[21] (3.60 g, 8.49 mmol) was added to a solution of alcohol **6a** (697 mg, 4.24 mmol) in CH_2Cl_2 (40 mL) in portions at 0 °C, and the mixture was stirred at room temperature for 5 h. Water-saturated CH_2Cl_2 was then added to quench the reaction, and the resulting mixture was stirred for 0.5 h. After removing most of the CH_2Cl_2, the residue was purified by column chromatography on silica gel (10% CH_2Cl_2/petroleum ether) to give **7a** (322 mg, 47%). IR ($CDCl_3$): $\tilde{\nu}$ = 3280, 1675 cm^{-1}; ^1H NMR (300 MHz, CD_3CN): δ = 2.23 (s, 3H), 2.92 (s, 4H), 3.72 (s, 1H), 5.90 (br s, 1H), 5.92 (d, 1H, J = 2.9 Hz); ^{13}C NMR (75.5 MHz, CD_3CN): δ = 12.4 (q), 21.7 (t), 43.1 (t), 79.5 (s), 80.8 (d), 106.0 (d, 2C), 150.5 (s), 152.0 (s), 186.0 (s); MS: m/z (%): 162 [M^+] (41), 109 (14), 95 (100); HRMS: m/z: calcd for $C_{10}H_{10}O_2$ [M^+]: 162.0681, found: 164.0680.

5-(5-Methyl-2-furyl)hex-1-yn-3-one (7b): Dess–Martin periodinane[21] (2.00 g, 4.72 mmol) was added to a solution of alcohol **6b** (540 mg, 3.03 mmol) in CH_2Cl_2 (30 mL) in portions at 0 °C, and the mixture was stirred at room temperature for 5 h. Water-saturated CH_2Cl_2 was then

added to quench the reaction, and the resulting mixture was stirred for 0.5 h. After removing most of the CH_2Cl_2, the residue was purified by column chromatography on silica gel (10% CH_2Cl_2/petroleum ether) to give **7b** (410 mg, 77%). IR (neat): $\tilde{\nu}=3262$, 1681 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta=1.27$ (d, 3H, $J=7.0$ Hz), 2.24 (s, 3H), 2.70 (dd, 1H, $J=16.3$, 8.1 Hz), 3.00 (dd, 1H, $J=16.3$, 6.0 Hz), 3.23 (s, 1H), 3.45 (m, 1H), 5.83 (dd, 1H, $J=2.9$, 1.2 Hz), 5.87 (d, 1H, $J=3.0$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta=13.9$ (q), 19.1 (q), 29.5 (d), 51.5 (t), 79.1 (s), 81.8 (d), 105.2 (d), 106.2 (d), 151.1 (s), 156.6 (s), 186.2 (s); MS: *m/z* (%): 176 [M^+] (31), 109 (100); elemental analysis (%) calcd for $C_{11}H_{12}O_2$: C 74.98, H 6.86; found: C 74.62, H 6.92.

7-Hydroxy-6-methylindan-1-one (8a), 2-methyl-7,8-dihydro-6*H*-cyclohepta[*b*]furan-6-one (9a) and 6-hydroxy-7-methylindan-1-one (10a): $AuCl_3$ (46.8 mg, 154 μmol) in CH_3CN (1 mL) was added to a solution of ketone **7a** (500 mg, 3.08 mmol) in CH_3CN (25 mL) at room temperature, and the resulting deep red solution was stirred for 2 h. The reaction mixture was then evaporated under reduced pressure to remove all the solvent. Column chromatography on silica gel (20–40% CH_2Cl_2/petroleum ether) gave **8a** ($R_f=0.4$ in 10% EtOAc/petroleum ether) (225 mg, 45%) and **9a** ($R_f=0.3$ in 10% EtOAc/petroleum ether; 45.0 mg, 9%); further elution with 40% EtOAc/petroleum ether afforded **10a** ($R_f=0.1$ in 10% EtOAc/petroleum ether) (35.8 mg, 7%). **8a**: M.p. 79–80 °C; IR ($CDCl_3$): $\tilde{\nu}=3320$, 1675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta=2.23$ (s, 3H), 2.70 (t, 2H, $J=5.6$ Hz), 3.06 (t, 2H, $J=5.6$ Hz), 6.84 (d, 1H, $J=7.5$ Hz), 7.32 (d, 1H, $J=7.5$ Hz), 9.23 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta=14.1$ (q), 25.4 (t), 36.2 (t), 116.8 (d), 122.2 (s), 122.7 (s), 138.8 (d), 152.6 (s), 155.5 (s), 210.3 (s); MS: *m/z* (%): 162 [M^+] (100); elemental analysis (%) calcd for $C_{10}H_{10}O_2$: C 74.06, H 6.21; found: C 74.07, H 6.23. **9a**: IR ($CDCl_3$): $\tilde{\nu}=1640$, 1570 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta=2.26$ (s, 3H), 2.80–2.86 (m, 2H), 2.91–2.97 (m, 2H), 5.97 (s, 1H), 5.99 (d, 1H, $J=12.1$ Hz), 6.82 (d, 1H, $J=12.1$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta=13.6$ (q), 21.3 (t), 39.3 (t), 108.0 (d), 119.0 (s), 127.4 (d), 134.9 (d), 150.7 (s), 156.5 (s), 200.5 (s); MS: *m/z* (%): 162 [M^+] (100); HRMS: *m/z*: calcd for $C_{10}H_{10}O_2$: 162.0681 [M^+]; found: 164.0681. **10a**: M.p. 169–170 °C; IR (KBr): $\tilde{\nu}=1660$ cm^{-1}; ^1H NMR (300 MHz, CD_3CN): $\delta=2.46$ (s, 3H), 2.59 (m, 2H), 2.96 (t, 2H, $J=5.8$ Hz), 6.97 (s, 1H), 7.06 (d, 1H, $J=8.2$ Hz), 7.17 (d, 1H, $J=8.2$ Hz); ^{13}C NMR (75.5 MHz, CD_3CN): $\delta=9.1$ (q), 23.9 (t), 37.2 (t), 121.4 (d), 122.9 (s), 124.2 (d), 135.1 (s), 147.7 (s), 153.8 (s), 208.0 (s); MS: *m/z* (%): 162 [M^+] (100); elemental analysis (%) calcd for $C_{10}H_{10}O_2$: C 74.06, H 6.21; found: C 73.97, H 6.26.

7-Hydroxy-3,6-dimethylindan-1-one (8b), 2,8-dimethyl-7,8-dihydro-6*H*-cyclohepta[*b*]furan-6-one (9b), and 6-hydroxy-3,7-dimethylindan-1-one (10b): A solution of $AuCl_3$ (200 mg, 2.9% in CD_3CN, 19.1 μmol) was added to a solution of ketone **7b** (47.6 mg, 270 μmol) in CD_3CN at room temperature, and the resulting deep red solution was shaken occasionally over 2 h until the ^1H NMR spectrum showed completion of the reaction. Then the reaction mixture was evaporated and the residue was purified by column chromatography on silica gel (5% EtOAc/petroleum ether) to give **8b** (35.6 mg, 75%). IR (neat): $\tilde{\nu}=3321$, 1671 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=1.37$ (d, 3H, $J=7.1$ Hz), 2.23 (s, 3H), 2.29 (dd, 1H, $J=19.1$, 3.2 Hz), 2.95 (dd, 1H, $J=19.1$, 7.5 Hz), 3.36–3.42 (m, 1H), 6.86 (d, 1H, $J=7.6$ Hz), 7.34 (d, 1H, $J=7.5$ Hz), 9.21 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=14.6$ (q), 21.6 (q), 33.1 (d), 45.7 (t), 115.9 (d), 122.0 (s), 123.2 (s), 139.3 (d), 155.5 (s), 158.1 (s), 210.0 (s); MS: *m/z* (%): 176 [M^+] (100), 161 (92); elemental analysis (%) calcd for $C_{11}H_{12}O_2$: C 75.03, H 6.97; found: C 74.98, H 6.86.

When ketone **7b** (887 mg, 5.03 mmol) was treated with $AuCl_3$ (107 mg, 353 μmol) in CH_3CN at 0 °C for 2 h, purification by column chromatography on silica gel (5% EtOAc/petroleum ether) gave **8b** ($R_f=0.2$, 470 mg, 53%) and **9b** ($R_f=0.1$, 17.4 mg, 2%); further elution with 50% EtOAc/petroleum ether afforded **10b** ($R_f=0.2$ in 10% EtOAc/petroleum ether) (27.7 mg, 3%). **9b**: IR ($CDCl_3$): $\tilde{\nu}=1651$, 1575 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=1.24$ (d, 3H, $J=7.3$ Hz), 2.27 (s, 3H), 2.75 (dd, 1H, $J=15.1$ Hz, 8.4 Hz), 2.89 (dd, 1H, $J=15.1$ Hz, 3.2 Hz), 3.13–3.19 (m, 1H), 5.96 (s, 1H), 5.99 (d, 1H, $J=11.9$ Hz), 6.82 (d, 1H, $J=11.9$ Hz); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=13.6$ (q), 17.0 (q), 28.7 (d), 47.0 (t), 108.3 (d), 117.7 (s), 127.5 (d), 134.8 (d), 150.5 (s), 160.3 (s), 200.3 (s); MS: *m/z* (%): 176 [M^+] (100), 161 (87); HRMS: *m/z*: calcd for $C_{11}H_{11}O_2$: 176.0837 [M^+], found: 176.0837. **10b**: M.p. 138–139 °C; IR (neat): $\tilde{\nu}=3314$, 1677 cm^{-1}; ^1H NMR (500 MHz, CD_3OD): $\delta=1.50$ (d, 3H, $J=7.1$ Hz), 2.39 (dd, 1H, $J=18.9$ Hz, 3.3 Hz), 2.63 (s, 3H), 3.06 (dd, 1H, $J=18.9$ Hz, 7.4 Hz), 3.43–3.49 (m, 1H), 7.25 (d, 1H, $J=8.2$ Hz), 7.37 (d, 1H, $J=8.2$ Hz); ^{13}C NMR (126 MHz, CD_3OD): $\delta=10.9$ (q), 22.7 (q), 33.1 (d), 48.2 (t), 123.6 (d), 124.4 (d), 125.0 (s), 136.1 (s), 154.5 (s), 156.5 (s), 210.8 (s); MS: *m/z* (%): 176 [M^+] (69), 161 (100); HRMS: *m/z*: calcd for $C_{11}H_{11}O_2$: 176.0837 [M^+], found: 176.0837.

2,2,8-Trimethyl-4,5-dihydro-2*H*-cyclopenta[*de*]chromene (11a): A solution of indanone **8a** (162 mg, 1.00 mmol) in dry THF (4 mL) was added dropwise to a solution of 2-methyl-1-propenylmagnesium bromide (0.5 M in THF, 20.0 mL, 10.0 mmol) at 0 °C, and the resulting solution was stirred for 1.5 h. After quenching the reaction with ice, the mixture was filtered through a silica gel pad, which was then thoroughly washed with diethyl ether. The phases of the filtrate were separated, and the aqueous phase was extracted with diethyl ether. The combined organic portions were then washed with brine and dried over $MgSO_4$. After removal of the solvents, the residue was purified by column chromatography on silica gel (2% CH_2Cl_2/petroleum ether) to give **11a** (128 mg, 64%). IR ($CDCl_3$): $\tilde{\nu}=3010$, 1660, 1249, 1025 cm^{-1}; ^1H NMR (500 MHz, CD_3CN): $\delta=1.42$ (s, 6H), 2.11 (s, 3H), 2.71–2.75 (dt, 2H, $J=2.0$ Hz, 6.7 Hz), 2.97 (t, 2H, $J=6.7$ Hz), 5.23 (t, 1H, $J=2.0$ Hz), 6.66 (d, 1H, $J=7.6$ Hz), 6.91 (d, 1H, $J=7.5$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta=13.0$ (q), 27.7 (t), 28.2 (q, 2C), 29.9 (t), 79.2 (s), 115.8 (d), 117.2 (d), 120.3 (s), 125.9 (s), 131.4 (d), 137.1 (s), 140.9 (s), 148.4 (s); MS: *m/z* (%): 200 [M^+] (23), 185 (100); elemental analysis (%) calcd for $C_{14}H_{16}O$: C 83.96, H 8.05; found: C 83.91, H 8.33.

2,2,5,8-Tetramethyl-4,5-dihydro-2*H*-cyclopenta[*de*]chromene (11b): A solution of the indanone **8b** (339 mg, 1.92 mmol) in dry THF (10 mL) was added dropwise to a solution of 2-methyl-1-propenylmagnesium bromide (0.5 M in THF; 40.0 mL, 20.0 mmol) at 0 °C. The resulting solution was stirred for 2 h and then quenched with a saturated aqueous NH_4Cl solution. The layers were separated, and the aqueous phase was extracted with diethyl ether. The combined organic portions were then washed with brine and dried over $MgSO_4$. After removal of the solvents, the residue was dissolved in CH_2Cl_2 (100 mL) and stirred with silica gel (50 g) for 1 h. The mixture was then filtered, and the filtrate was concentrated, purified by column chromatography on silica gel (2.5% CH_2Cl_2/petroleum ether) to give **11b** (396 mg, 96%). IR (neat): $\tilde{\nu}=3037$, 1666, 1259, 1081 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=1.29$ (d, 3H, $J=7.1$ Hz), 1.43 (s, 3H), 1.47 (s, 3H), 2.16 (s, 3H), 2.29 (ddd, 1H, $J=17.0$, 4.7, 2.2 Hz), 2.98 (ddd, 1H, $J=17.0$ Hz, 8.0, 1.9 Hz), 3.38 (dq, 1H, $J=5.1$, 7.2 Hz,), 5.13 (dd, 1H, $J=2.0$ Hz, 2.1 Hz), 6.63 (d, 1H, $J=7.5$ Hz), 6.93 (d, 1H, $J=7.5$ Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta=14.6$ (q), 21.7 (q), 29.7 (q), 30.0 (q), 38.4 (t), 38.8 (d), 79.9 (s), 115.2 (d), 118.0 (d), 121.7 (s), 126.0 (s), 132.2 (d), 136.7 (s), 146.3 (s), 149.1 (s); MS: *m/z* (%): 214 [M^+] (21), 199 (100); elemental analysis (%) calcd for $C_{15}H_{18}O$: C 84.07, H 8.47; found: C 84.19, H 8.54.

5-Methyl-3-(2-methylprop-1-enyl)indan-4-ol (12a): A solution of chromene **11a** (40.1 mg, 200 μmol) in dry diethyl ether (2 mL) was added to a suspension of LAH (90.1 mg, 2.37 mmol) in dry diethyl ether (8 mL) at room temperature. The mixture was irradiated in a quartz flask with stirring for 6 h with a Heraeus TQ 150 mercury lamp. The reaction mixture was then poured onto crushed ice and acidified with dilute HCl until the hydroxides just dissolved. The water layer was extracted with diethyl ether, and the combined organic portions were washed with a saturated solution of Na_2CO_3 and brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel (2% EtOAc/petroleum ether) to give **12a** (36.8 mg, 91%). M.p. 24.5–25.5 °C; IR (neat): $\tilde{\nu}=3468$, 2903, 1580, 1197, 1010, 780 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=1.73–1.81$ (m, 1H), 1.84 (s, 3H), 1.89 (s, 3H), 2.21 (s, 3H), 2.28–2.33 (m, 1H), 2.80–2.93 (m, 2H), 4.09 (dt, 1H, $J_1=7.9$, $J_2=9.6$ Hz), 5.13 (d, 1H, $J=9.4$ Hz), 5.83 (s, 1H), 6.71 (d, 1H, $J=7.4$ Hz), 6.96 (d, 1H, $J=7.4$ Hz); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=15.2$ (q), 18.2 (q), 25.9 (q), 31.9 (t), 34.1 (t), 42.2 (d), 116.1 (d), 122.2 (s), 127.6 (d), 129.6 (s), 129.9 (d), 135.7 (s), 143.2 (s), 151.7 (s); MS: *m/z* (%): 202 [M^+] (56), 187 (55), 147 (100); HRMS: *m/z*: calcd for $C_{14}H_{18}O$: 202.1358 [M^+], found: 202.1357.

1,5-Dimethyl-3-(2-methylprop-1-enyl)indan-4-ol (*epi*-jungianol; 12) and 1,5-dimethyl-3-(2-methylpropylidene)indan-4-ol (13): A solution of chromene **11b** (282 mg, 1.32 mmol) in dry diethyl ether (5 mL) was added to a suspension of LAH (467 mg, 12.3 mmol) in dry diethyl ether (25 mL) at room temperature. The mixture was irradiated in a quartz flask with stirring for 6 h with a Heraeus TQ 150 mercury lamp. The reaction mixture was then poured onto crushed ice and acidified with dilute HCl until the hydroxides just dissolved. The water layer was extracted with diethyl ether, and the combined organic portions were washed with a saturated solution of Na_2CO_3 and brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by preparative TLC (4% EtOAc/petroleum ether)

to give **12** (195 mg, 68%), **3** (60.0 mg, 21%), and **13b** (20.4 mg, 7%). **12**: M.p. 43.5–44.5 °C; IR (neat): $\tilde{\nu}$ = 3481, 2954, 1589, 1204 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.30 (d, 3H, J = 6.8 Hz), 1.34 (ddd, 1H, J = 10.5, 10.5, 12.2 Hz), 1.83 (d, 3H, J = 1.1 Hz), 1.87 (d, 3H, J = 1.2 Hz), 2.19 (s, 3H), 2.43 (ddd, 1H, J = 7.0, 7.0, 12.2 Hz), 3.06 (dm, 1H, J = 10.6 Hz), 4.00 (ddd, 1H, J = 10.2, 10.2, 7.1 Hz), 5.35 (dm, 1H, J = 10.3 Hz), 5.93 (s, 1H), 6.67 (d, 1H, J = 7.3 Hz), 6.99 (d, 1H, J = 7.4 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.6 (q), 18.6 (q), 19.6 (q), 26.4 (q), 38.8 (d), 41.5 (d), 44.1 (t), 115.0 (d), 122.8 (s), 128.1 (d), 129.6 (s), 130.3 (d), 136.4 (s), 148.1 (s), 152.0 (s); MS: m/z (%): 216 [M^+] (46), 201 (49), 161 (100); elemental analysis (%) calcd for $C_{15}H_{20}O$: C 83.28, H 9.32; found: C 82.89, H 9.36. **13**: IR (neat): $\tilde{\nu}$ = 3420, 2957, 1590, 1458, 1247, 804 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.07 (d, 3H, J = 6.7 Hz), 1.07 (d, 3H, J = 6.7 Hz), 1.26 (d, 3H, J = 6.9 Hz), 2.23 (s, 3H), 2.29 (ddd, 1H, J = 2.7, 5.4, 15.9 Hz), 2.58 (dsept, 1H, J = 9.1, 6.7 Hz), 3.01 (ddd, 1H, J = 2.3, 8.3, 15.9 Hz), 3.21 (q, 1H, J = 6.8 Hz), 5.05 (s, 1H), 6.01 (ddd, 1H, J = 9.1, 2.4, 2.4 Hz), 6.73 (d, 1H, J = 7.5 Hz), 6.95 (d, 1H, J = 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 15.5 (q), 21.8 (q), 23.4 (q), 23.5 (q), 30.0 (d), 37.1 (d), 38.6 (t), 116.3 (d), 121.6 (s), 126.9 (s), 130.0 (d), 131.3 (d), 138.6 (s), 150.7 (s), 151.6 (s); MS: m/z (%): 216 [M^+] (59), 201 (100), 173 (31), 161 (80); HRMS: m/z: calcd for $C_{15}H_{20}O$: 216.1514 [M^+], found: 216.1514.

5-Methyl-2-[(4-methylphenyl)sulfonyl]-2,3-dihydro-1*H*-isoindol-4-yl 4-nitrobenzoate (15): *p*-Nitrobenzoyl chloride (249 mg, 1.34 mmol) was added portionwise to a solution of **14** (28.4 mg, 93.7 μmol) in pyridine (10 mL) at 0 °C. Then a catalytic amount of DMAP (ca. 6 mg) was added, and the mixture was stirred at room temperature overnight. The reaction was quenched with water, and the precipitate was collected, dissolved in CH_2Cl_2, and dried over $MgSO_4$. After removal of the solvent, the residue was filtered through a short silica gel column with CH_2Cl_2 as eluent to give **15** (26.1 mg, 62%). M.p. 203–205 °C (decomp); IR (KBr): $\tilde{\nu}$ = 1741, 1513, 1339, 1330, 1248, 1182, 1150, 1062 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.17 (s, 3H), 2.40 (s, 3H), 4.53 (s, 2H), 4.62 (s, 2H), 7.02 (d, 1H, J = 7.7 Hz), 7.18 (d, 1H, J = 7.7 Hz), 7.31 (d, 2H, J = 8.0 Hz), 7.73 (d, 2H, J = 8.3 Hz), 8.36 (d, 2H, J = 8.5 Hz), 8.39 (d, 2H, J = 8.4 Hz); ^{13}C NMR (75.7 MHz, $CDCl_3$): δ = 16.2 (q), 21.9 (q), 52.1 (t), 54.0 (t), 121.0 (d), 124.2 (d), 126.2 (s), 127.9 (d), 129.5 (s), 129.9 (s), 130.3 (d), 131.6 (d), 131.8 (d), 133.9 (s), 134.2 (s), 136.5 (s), 144.2 (s), 151.5 (s), 162.4 (s); MS: m/z (%): 451 [M^+ – H], 3), 297 (100), 150 (73); elemental analysis (%) calcd for $C_{23}H_{20}N_2O_6S$: C 61.05, H 4.46, N 6.19; found: C 60.63, H 4.51, N 5.98.

1,5-Dimethyl-3-(2-methylprop-1-enyl)indan-4-yl 4-nitrobenzoate (16): *p*-Nitrobenzoyl chloride (400 mg, 2.16 mmol) was added portionwise to a solution of **12** (19.2 mg, 88.7 μmol) in pyridine (5 mL) at 0 °C. Then a catalytic amount of DMAP (ca. 6 mg) was added and the mixture was stirred at room temperature overnight. The reaction was quenched with water, and the precipitate was collected, dissolved in CH_2Cl_2,and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel (5% EtOAc/petroleum ether) to give **16** (22.3 mg, 69%). Single crystals for the crystal structure analysis of **16** were grown from dichloromethane/petroleum ether at room temperature. M.p. 142–143 °C; IR (KBr): $\tilde{\nu}$ = 1734, 1517, 1250, 1169, 1063 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.15 (br s, 3H), 1.19–1.35 (m, 1H), 1.33 (d, 3H, J = 6.8 Hz), 1.38 (br s, 3H), 2.19 (s, 3H), 2.41 (ddd, 1H, J = 7.1, 7.1, 12.4 Hz), 3.10–3.15 (m, 1H), 3.91 (br s, 1H), 5.05 (brd, 1H, J = 9.0 Hz), 7.04 (d, 1H, J = 7.6 Hz), 7.14 (d, 1H, J = 7.6 Hz), 8.32 (d, 2H, J = 8.9 Hz), 8.35 (d, 2H, J = 8.9 Hz); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 16.1 (q), 17.7 (q), 17.9 (q), 25.8 (q), 38.4 (d), 42.6 (d), 43.8 (t), 121.3 (d), 123.8 (d), 123.9 (d), 127.9 (s), 130.0 (d), 131.5 (d and s, 2C), 135.4 (s), 137.6 (s), 146.1 (s), 149.4 (s), 150.9 (s), 161.9 (s); MS: m/z (%): 365 [M^+] (29), 199 (100), 150 (26), 215 (9); HRMS: m/z: calcd for $C_{22}H_{23}NO_4$: 365.1627 [M^+], found: 365.1627.

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