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Synthesis of 2,3-Dihydro-3-hydroxy-2-hydroxylalkylbenzofurans from Epoxy Aldehydes. One-Step Syntheses of Brosimacutin G, Vaginidiol, Vaginol, Smyrindiol, Xanthoarnol, and Avicenol A. Biomimetic Syntheses of Angelicin and Psoralen

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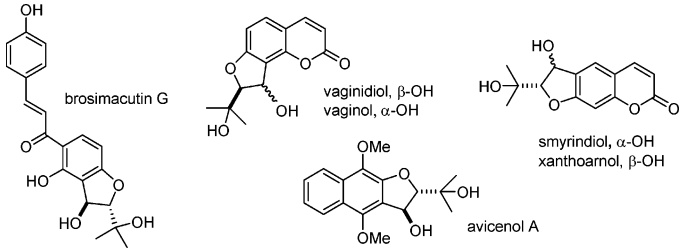

We have developed two practical one-step syntheses of 2,3-dihydro-3-hydroxy-2-hydroxyalkylbenzofurans from readily available optically pure α,β−epoxy aldehydes. Electron-deficient resorcinols react with epoxy aldehydes using either Cs_2CO_3 in DMF or KOH/$CaCl_2$ in MeOH to give adducts **13**, **16**, **18**, **20**, **21**, and brosimacutin G (**6t**). Grignard reagents prepared by low-temperature halogen−metal exchange of acetoxy iodocoumarins **35d** and **40** and acetoxy bromonaphthalene **41** add to epoxy aldehyde (*S*)-**26** to complete the first syntheses of vaginidiol (**7c**), vaginol (**7t**), smyrindiol (**8c**), xanthoarnol (**8t**), and avicenol A (**9t**). Acid-catalyzed fragmentation of vaginidiol or vaginol provides angelicin, while that of smyrindiol or xanthoarnol affords psoralen. In both cases, the trans isomers fragment only twice as fast as the cis isomers, possibly through the intermediacy of a common benzylic cation. This may have implications for the biosynthesis of angelicin and psoralen.

Introduction

The squalene synthase inhibitor bisabosqual A (**1**) was recently isolated from the culture broth of *Stachybotrys* sp. RF-7260.[1] We thought that the tetracyclic skeleton of **1** might be readily accessible with complete control of stereochemistry by an intramolecular inverse electron demand Diels−Alder reaction of quinone methide **2**, which would be generated by dehydration of hydroxy phenol **3** (see Scheme 1). Hydroxy phenol **3** might be available in a single step by addition of the anion formed from resorcinol **4** to the aldehyde of **5** followed by cyclization of the phenol to the epoxide.

The 2,3-dihydro-3-hydroxy-2-(1-hydroxy-1-(methyl)-alkyl)benzofuran moiety of **3** occurs in numerous natural products including brosimacutin G (**6t**),[2,3] the furocoumarins vaginidiol (**7c**),[4−6] vaginol (**7t**),[7] smyrindiol (**8c**),[8−11] and xanthoarnol (**8t**),[12−14] and the naphthofuran avicenol

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(1) (a) Minagawa, K.; Kouzuki, S.; Nomura, K.; Yamaguchi, T.; Kawamura, Y.; Matsushima, K.; Tani, H.; Ishii, K.; Tanimoto, T.; Kamigauchi, T. *J. Antibiot*. **2001**, *54*, 890−895. (b) Minagawa, K.; Kouzuki, S.; Nomura, K.; Kawamura, Y.; Tani, H.; Terui, Y.; Nakai, H.; Kamigauchi, T. *J. Antibiot*. **2001**, *54*, 896−903.

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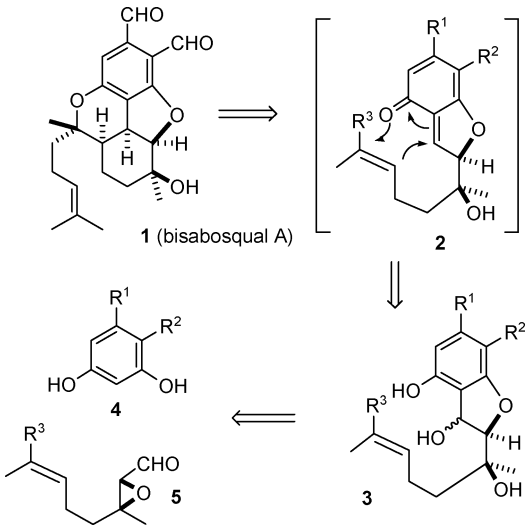
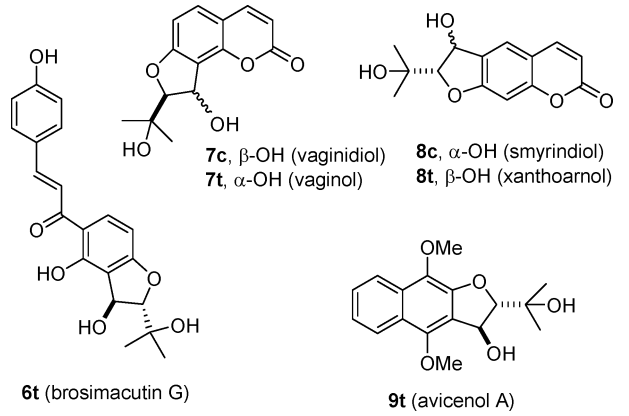
SCHEME 1



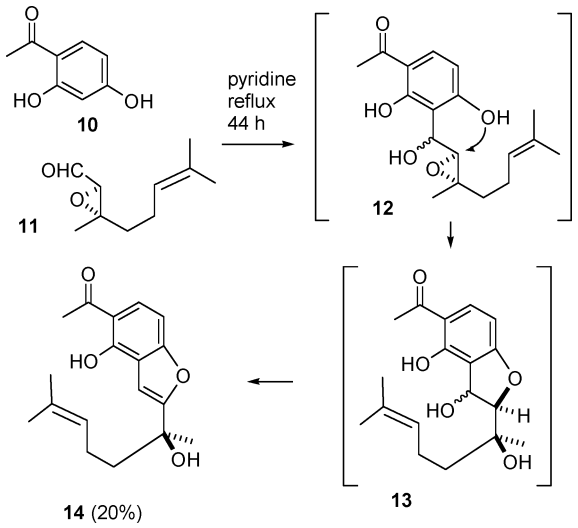
A (**9t**) (see Scheme 2).[15,16] In addition to the free diols, these compounds are often isolated as glycosides or esters.[17,18] Despite the long history of these compounds, the only preparation we are aware of is the partial synthesis of smyrindiol (**8c**) by benzylic oxidation of marmesin to introduce a ketone, which was reduced stereospecifically to give the benzylic alcohol of **8c**.[10] Unsuccessful approaches to vaginol and vaginidiol have been reported.[19]

SCHEME 2



Murphy suggested that **13** was an intermediate in the conversion of **10** and citral epoxide (**11**) to benzofuran **14** in 20% yield by refluxing in pyridine for 2 days (see Scheme 3).[20] Presumably, the phenolate formed from **10** added to the aldehyde to give epoxy alcohol **12**, which cyclized to give **13**. Under these conditions dehydration occurred to give furan **14**. We therefore decided to investigate the reactions of citral epoxide (**11**) with 3,5-dihydroxbenzaldehyde (**15**) and 2,4-dihydroxybenzaldehyde (**19**) under milder conditions that might lead to 2,3-dihydro-3-hydroxybenzofurans without dehydration.

SCHEME 3



Results and Discussion

Citral epoxide (**11**) was prepared with control of relative stereochemistry by oxidation of geraniol with $VO(acac)_2$ to give the epoxy alcohol,[21] which was oxidized to give aldehyde **11** using pyr·SO_3, Et_3N and DMSO in CH_2Cl_2.[22] We surveyed a variety of mild conditions for the coupling and found that reaction of **11** with 3,5-dihydroxybenzaldehyde (**15**) and Cs_2CO_3 in DMF at 25 °C for 3 d afforded 11% of the cis dihydrobenzofuran **16c**, 20% of the trans dihydrobenzofuran **16t**, and 4% of the dehydration product benzofuran **17** (see Scheme 4). The stereochemistry of the products was easily established by the coupling constants, which are between 3.5 and 4.5 Hz for the trans isomers and 5.5 and 6.5 Hz for the cis isomers.[2−18] The regiochemistry of the products was clearly established by the observation of an NOE between the aldehyde proton and only one of the two aromatic hydrogens. HMBC experiments confirmed this assignment. We had anticipated that the initial coupling would occur between the two phenolic hydroxy groups rather than between the phenol and the aldehyde as was observed. However, the formation of **16** and **17** is precedented in the piperidinylmethylation of 3,5-hydroxybenzoic acid with formaldehyde and piperidine at the 2- rather than 4-position.[23]

Shigemasa reported that phenolates of electron deficient resorcinols add to aldehydes efficiently using KOH

(13) Asahara, T.; Sakakibara, I.; Okuyama, T.; Shibata, S. *Planta Med.* **1984**, *50,* 488−492.
(14) Alami, I.; Clérivet, A.; Naji, M.; Van Munster, M.; Macheix, J. J. *Phytochemistry* **1999**, *51*, 733−736.
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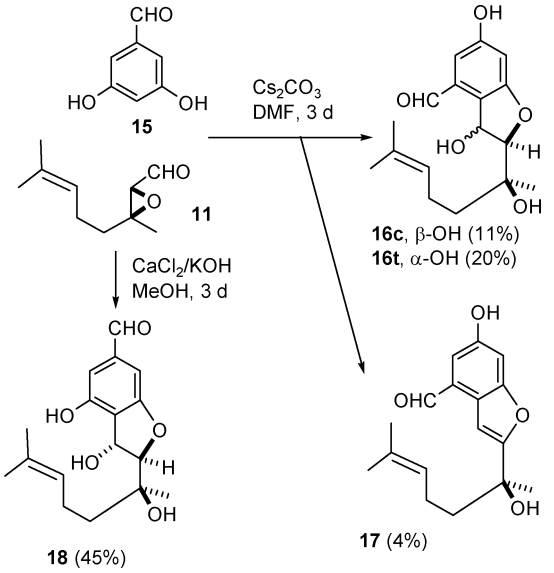
(22) Nacro, K.; Baltas, M.; Escudier, J.; Gorrichon, L. *Tetrahedron* **1996**, *52*, 9047−9056.
(23) Götschi, E.; Jenny, C.; Reindl, P.; Ricklin, F. *Helv. Chim. Acta* **1996**, *79*, 2219−2234.

SCHEME 4



and $CaCl_2$ in MeOH.[24,25] Reaction of **11** and **15** with KOH/$CaCl_2$ in MeOH for 3 d at 25 °C provided 45% of **18** as the sole regio- and stereoisomer. It is noteworthy that the position of attack of the phenolate shifts on changing from Cs to K/Ca as the counterion although the reasons for this and the exclusive isolation of the trans isomer are obscure. We do not think that the solvent plays a crucial role because reaction with KOH/$CaCl_2$ in DMF still gave **18**, while Cs_2CO_3 in MeOH afforded **16** and **17**, but in lower yields.

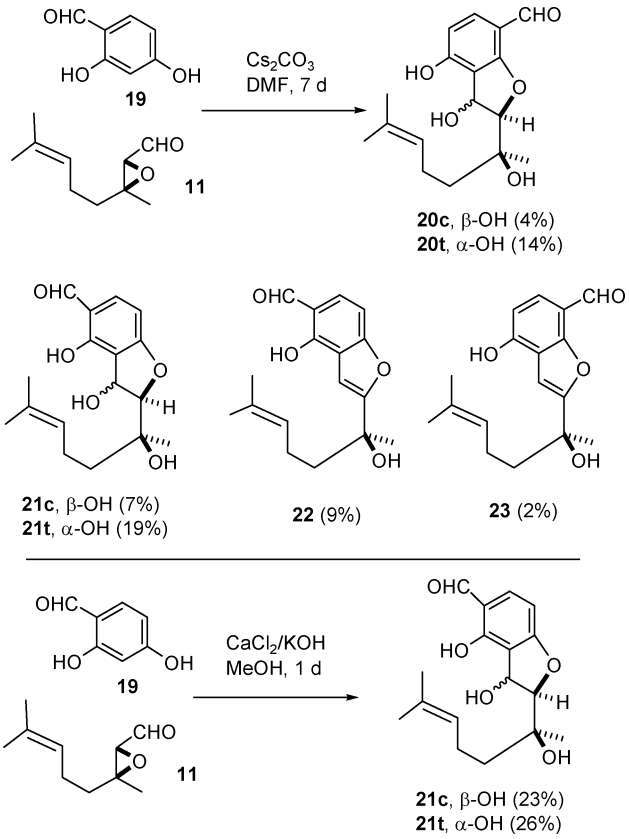
Reaction of 2,4-dihydroxybenzaldehyde (**19**) with **11** using Cs_2CO_3 in DMF for 7 d afforded a mixture of stereo- and regioisomers that were separated to yield dihydrobenzofurans **20c** (4%), **20t** (14%), **21c** (7%), and **21t** (19%) and benzofurans **22** (9%) and **23** (2%) (see Scheme 5). The stereochemistry was established based on coupling constants as described above for **16**. The regiochemistry was tentatively assigned based on polarity behavior. Intramolecular hydrogen bonding makes **21** and **22** much less polar than the regioisomers **20** and **23**, respectively. This assignment was confirmed by the conversion of **21t** to a coumarin (see below). Reaction of **19** and **11** using KOH and $CaCl_2$ in MeOH provided a cleaner reaction mixture containing only **21c** (23%) and **21t** (26%). Similar regioselectivity has been observed with $CaCl_2$ and KOH in the formation of benzopyrans from unsymmetrical resorcinols and α,*β*-unsaturated aldehydes.[24,25] We obtained similar or slightly lower yields of **21c** and **21t** using KOH with either $BaCl_2$, $SrCl_2$, or $LaCl_3$, $Ca(OH)_2$ or $Ba(OH)_2$.

Attempted reaction of 3,5-dihydroxyacetophenone (**24**) with **11** using either Cs_2CO_3 in DMF or KOH and $CaCl_2$ in MeOH gave less than 5% conversion to dihydrobenzofurans (see Scheme 6). Reaction of 2,4-dihydroxyacetophenone (**25**) with **11** using Cs_2CO_3 in DMF also failed, but use of KOH and $CaCl_2$ in MeOH cleanly afforded Murphy's proposed intermediates **13c** (40%) and **13t** (45%) in excellent yield. As previously noted by

(24) Saimoto, H.; Yoshida, K.; Murakami, T.; Morimoto, M.; Sashiwa, H.; Shigemasa, Y. *J. Org. Chem.* **1996**, *61*, 6768−6769.

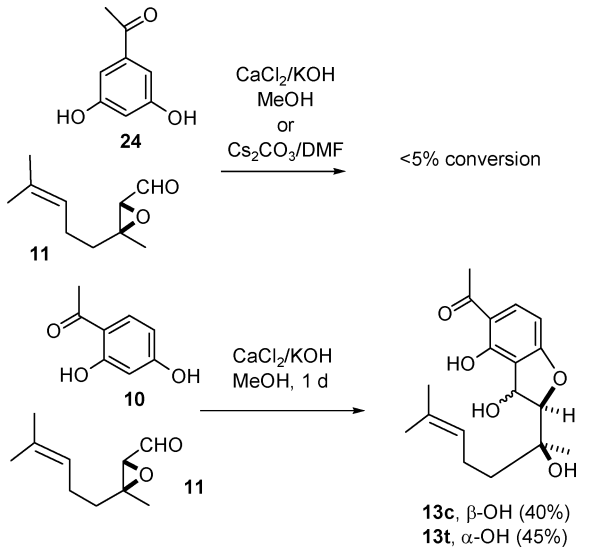
(25) For additional applications and extensions, see: Kang, Y.; Mei, Y.; Du, Y.; Jin, Z. *Org. Lett.* **2003**, *5*, 4481−4484.

SCHEME 5



Shigemasa,[24] the addition of resorcinol phenolates to aldehydes with KOH/$CaCl_2$ requires an electron withdrawing group on the resorcinol. These results indicate that a carboxaldehyde is generally more effective than an acetyl group, although the yields from ketone **10** are higher than those from aldehyde **19** with KOH and $CaCl_2$.

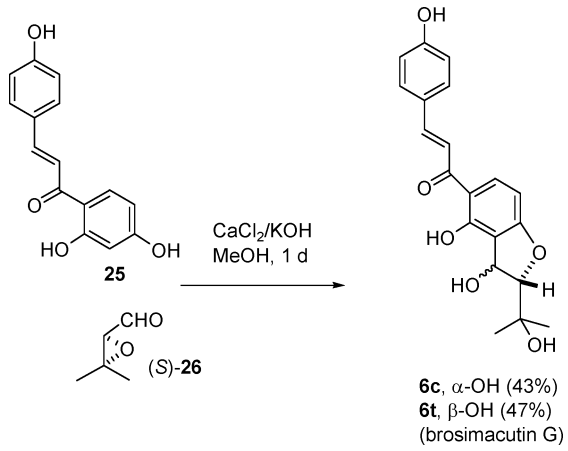
SCHEME 6



Using this chemistry, the first synthesis of brosimacutin G (**6t**) was accomplished in a single step (see Scheme 7). Reaction of **25**[26] and (*S*)-**26**[27] with KOH and $CaCl_2$ in MeOH for 1 d at 25 °C provided 43% of (+)-**6c**

(26) Purchased from Indofine.

SCHEME 7



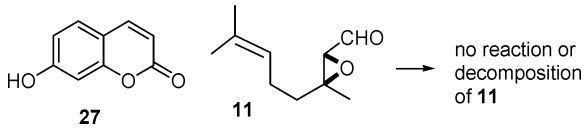
and 47% of (−)-**6t** (brosimacutin G). The rotation for synthetic **6t**, $[\alpha]^{20}_{D}$ −11 to −12 (MeOH) is much larger than for the natural product, $[\alpha]^{20}_{D}$ −0.7 to −1,[2,3] suggesting that the natural product is almost racemic. As expected use of (*R*)-**26**[27] afforded (−)-**6c** and (+)-**6t**.

Having developed procedures that convert epoxy aldehydes and resorcinols to hydroxydihydrofurans **3**, we turned our attention to preparation of quinone methide **2**, which we hoped would undergo an intramolecular inverse electron Diels−Alder reaction to form the tetracyclic core of bisabosqual A (**1**).[28] We knew that tautomerization of the quinone methide to the hydroxy benzofuran would be rapid and irreversible, so that even if we could form the quinone methide, we would only be successful if the Diels−Alder reaction is faster than tautomerization. Heating[29] **21** in toluene at 160 °C for 16 h or at 260 °C for 1 h gave complex mixtures of benzofuran **22** and dienes resulting from dehydration of the side chain tertiary alcohol. No reaction occurred on irradiation at 254 nm of CH_3CN/H_2O solutions of **21**.[30] Treatment of the bis silyl ether of **21t** with CsF in CH_3CN as described by Marino led only to **22**.[31] Other approaches were equally unsuccessful, so we developed a different, successful approach to the tetracyclic core of bisabosqual that we have recently reported.[32]

We now turned our attention to the preparation of vaginidiol (**7c**), vaginol (**7t**), smyrindiol (**8c**), and xanthoarnol (**8t**), in which the dihydrofuran is fused to a coumarin, rather than a benzaldehyde or an acetophenone. Not surprisingly, no reaction occurred between 7-hydroxycoumarin (**27**) and **11** under any of the conditions that were successful for the resorcinols, since these additions are restricted to resorcinols bearing an additional electron withdrawing group (see Scheme 8).[24]

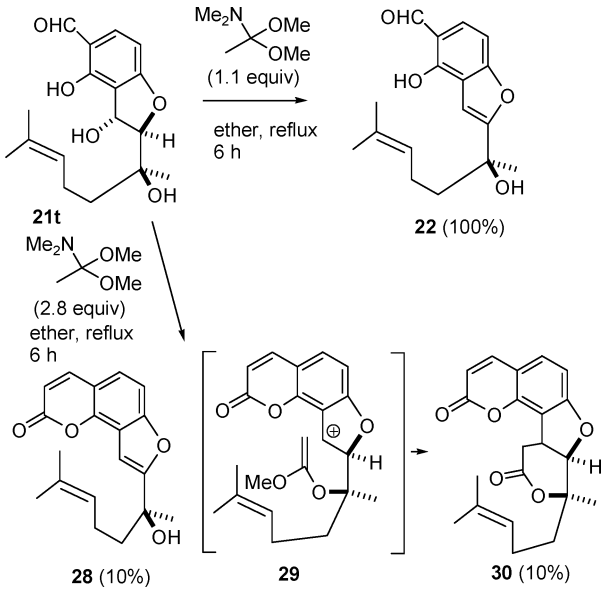
We then tried to develop conditions that would convert hydroxy benzaldehyde **21** to a coumarin without also

SCHEME 8



dehydrating the sensitive 2,3-dihydro-3-hydroxybenzofuran. Yamaguchi reported that the reaction of salicylaldehydes with dimethylacetamide dimethyl acetal in ether at reflux affords coumarins.[33] However, reaction of **21t** with 1.1 equiv of dimethylacetamide dimethyl acetal in ether at reflux afforded only benzofuran **22** resulting from dehydration (see Scheme 9). Reaction of **21t** with 2.8 equiv of dimethylacetamide dimethyl acetal afforded 10% of coumarin **28** and 10% of lactone **30**, which was partially hydrolyzed to the methyl ester on purification. A possible mechanism for the formation of **30** involves trapping a benzylic cation with a ketene acetal as in **29**. Although this is of little synthetic utility, it does unambiguously establish the regiochemistry of **20** to **23**, because **20**, with the phenol and aldehyde groups para to each other, cannot form a coumarin.

SCHEME 9



We briefly examined the synthetic utility of these adducts. Reaction of **19** with (±)-**26**[34] afforded pure **31c** (28%) and **31t** (33%) (see Scheme 10). Treatment of the crude reaction mixture containing both isomers of **31** with dimethylformamide dimethyl acetal in ether at reflux for 6 h effected dehydration, affording benzofuran alcohol **32**[35] (50% over two steps) and isopropenyl benzofuran **33**[35] (7% over two steps). Salicylaldehyde **32** has been converted to the coumarin oroselol[36] by heating with $Ph_3P{=}CHCO_2Et$ in xylene at reflux.[35] Treatment of **31** with acid did not lead to dehydration, but rather loss of

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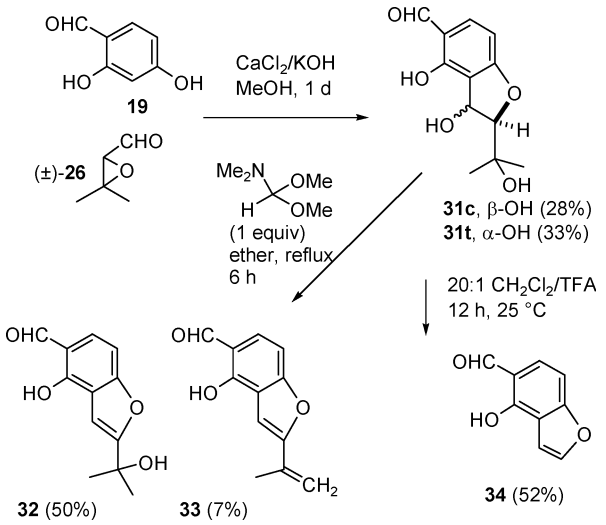
(36) Duffley, R. P.; Stevenson, R. *Synth. Commun.* **1978**, *8*, 175−180.

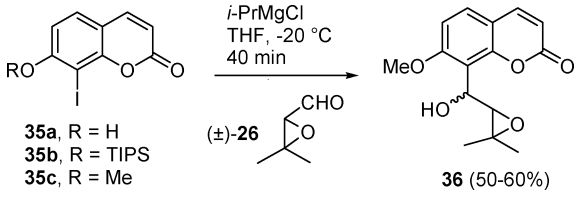
SCHEME 10



acetone and water in a Grob fragmentation to form **34**. This was most effectively accomplished by stirring crude **31** in 20:1 CH_2Cl_2/TFA for 12 h at 25 °C to give **34**[35] (52% over two steps). This fragmentation is probably related to the biosyntheses of psoralen and angelicin, which also occur with the loss of acetone (see below).[12,37]

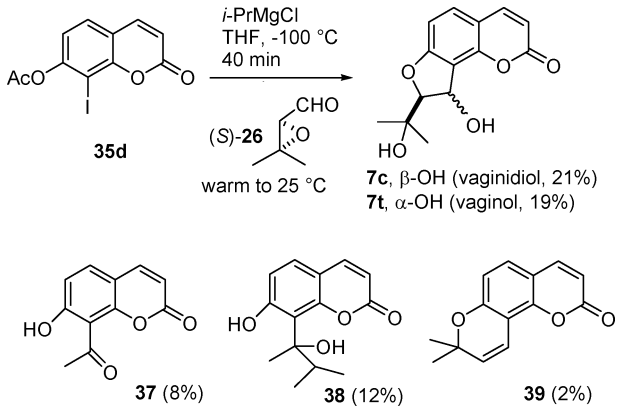
These experiments established that the lactone ring cannot be introduced after the formation of the hydroxydihydrofuran ring without dehydration to give the furan and that the phenolate of 7-hydroxycoumarin does not add to aldehydes. We therefore considered other methods to generate a carbanion from the coumarin that would add to an aldehyde. Iodination of 7-hydroxycoumarin cleanly affords 7-hydroxy-8-iodocoumarin (**35a**),[38] which can be used to generate a carbanion that will add to aldehydes (see Scheme 11). We initially considered the use of $CrCl_2$ and $NiCl_2$ since the organochromium reagent that would be generated should add selectively to an aldehyde. However, reaction of TIPS ether **35b** with $CrCl_2$, $NiCl_2$ and 3-methyl-2-butenal resulted in cleavage of the TIPS group. A similar reaction with methyl ether **35c** partially cleaved the iodide, but resulted in no addition.

SCHEME 11



Knochel has shown that halogen−metal exchange occurs readily with isopropyl Grignard reagents at very low temperatures, even in the presence of functional groups that would not be expected to be compatible with Grignard reagents.[39] Lauret has used this procedure to generate the Grignard reagent from methyl ether **35c**.[40] We were pleased to find that reaction of methyl ether **35c** with isopropylmagnesium chloride in THF at −20 °C for 40 min followed by addition of (±)-**26** provided 50−60% of **36** as a mixture of diastereomers. This indicated that the key carbon−carbon bond could be formed. However, we did not think that cleavage of the methyl ether would be practical in the presence of the epoxide.

SCHEME 12



Fortunately, we found that this sequence worked well with acetate **35d**. Halogen−metal exchange of **35d** with isopropylmagnesium chloride in THF at −100 °C for 1 h, addition of (*S*)-**26** and slow warming to 25 °C over 1 h gave 21% of (+)-vaginidiol (**7c**) and 19% of (+)-vaginol (**7t**), with spectra and optical rotation identical to those reported for the natural products (see Scheme 12).[4−7,41] The formation of (+)-**7c** and (+)-**7t** of known absolute stereochemistry from (*S*)-**26** establishes that the S_N2 substitution of the phenolate on the epoxide (see the conversion of **12** to **13**) occurred with inversion as expected. Byproducts included 15% of recovered **35d**, 8% of ketone **37**,[42] formed by intra- or intermolecular attack of the coumarin Grignard reagent on the acetate protecting group, 12% of **38** and 2% of **39**, which is formed either by a reduction or from 3-methyl-2-butenal present as an impurity in (*S*)-**26**. Addition of isopropylmagnesium chloride to the acetate protecting group will give 3-methyl-2-butanone, which can react with the coumarin Grignard reagent to give **38**. We confirmed the structure of **38** by preparing it in higher yield by addition of 3-methyl-2-butanone, rather than (*S*)-**26**, after halogen−metal exchange. The combined yield of **7c** and **7t** dropped from 40% to about 20% when the halogen−metal exchange was carried out at −78 °C rather than −100 °C.

Although the one-step synthesis of vaginidiol (**7c**) and vaginol (**7t**) in combined 40% yield is very satisfying, the acetate protecting group is not optimal because it reacts with both isopropylmagnesium chloride and the coumarin Grignard reagent. The aryl iodide is very hindered and this reaction is very sensitive to the size of the protecting

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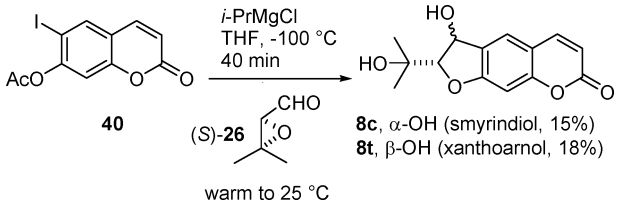
(39) (a) Jensen, A. E.; Dohle, W.; Sapountzis, I.; Lindsay, D. M.; Vu, V. A.; Knochel, P. *Synthesis* **2002**, *4,* 565−569. (b) Vu, V. A.; Bérillon, L.; Knochel, P. *Tetrahedron Lett.* **2001**, *42,* 6847−6850.
(40) Gillmore, A.; Lauret, C.; Roberts, S. M. *Tetrahedron* **2003**, *59,* 4363−4375.
(41) Even though S_N2 reactions under basic conditions should occur at the least substituted carbon, it is conceivable that attack occurred at the tertiary carbon to give a cis or trans dihydrodihydroxybenzopyran. These natural products are known and have very different spectral data: Chen, I.; Chang, C.; Sheen, W.; Teng, C.; Tsai, I.; Duh, C.; Ko, F. *Phytochemistry* **1996**, *41,* 525−530.
(42) Ren, X.; Chen, X.; Peng, K.; Xie, X.; Xia, Y.; Pan, X. *Tetrahedron: Asymmetry* **2002**, *13*, 1799−1804.

SCHEME 13



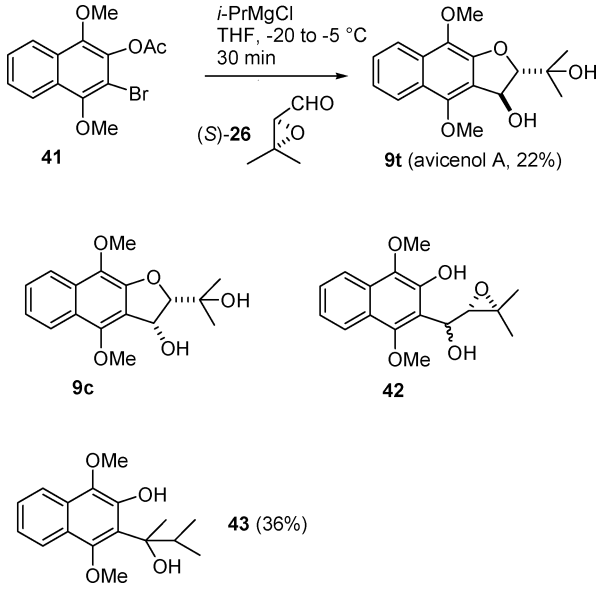
group. Complex mixtures containing little **7** were obtained from the propionate, benzoate or pivaloate esters of phenol **35a**. Reaction of the formate ester[43] of **35a** at −100 °C gave a combined 20% yield of the isomers of **7**. Complex mixtures were obtained with the 1-ethoxyethyl ether of **35a**.

7-Acetoxy-6-iodocoumarin (**40**) was prepared quantitatively from the known phenol[44] with pyridine and Ac_2O in CH_2Cl_2 (see Scheme 13). Halogen−metal exchange of **40** with isopropylmagnesium chloride for 40 min at −100 °C followed by addition of (*S*)-**26** afforded 15% of smyrindiol (**8c**) and 18% of xanthoarnol (**8t**), both with spectral data identical to those reported for the natural products.[8−14] The optical rotation of **8c** is identical to that of smyrindiol. Xanthoarnol (**8t**) has been isolated in racemic form with unassigned relative stereochemistry, although the 4.4 Hz vicinal coupling constant clearly now establishes trans stereochemistry (see above).[12,14] Xanthoarnol has also been isolated as the aglycone of decuroside V with optical rotation similar in magnitude, but opposite in sign, to **8t**.[13]

Reaction of 1,4-dimethoxynaphthalene with TMSBr and $PhI(OAc)_2$ by the procedure of Evans provided 80% of bromo acetate **41** (see Scheme 14).[45] Halogen−metal exchange should be slower with a bromide so it is not surprising that treatment of **41** with isopropylmagnesium chloride in THF at −100 °C and then (*S*)-**26** afforded only traces of **9t**. Fortunately, halogen−metal exchange starting at −20 °C with slow warming to −5 °C over 30 min followed by addition of (*S*)-**26** provided 22% of avicenol A (**9t**) with spectral and optical rotation identical to those reported,[15,16] 20% of an inseparable mixture of **9c** and **42** and 36% of **43**, which was formed analogously to **38**. Halogen−metal exchange with the iodo acetate corresponding to **41** should occur more readily and this might lead to higher yields of **9t**. Reaction of 1,4-dimethoxynaphthalene with TMSI and $PhI(OAc)_2$ gave an unoptimized 11% yield of the iodo acetate corresponding to **41**. However, halogen−metal exchange of the iodide at −100 °C and addition of (*S*)-**26** gave less than 10% of **9t** indicating that the use of bromide **41** is superior.

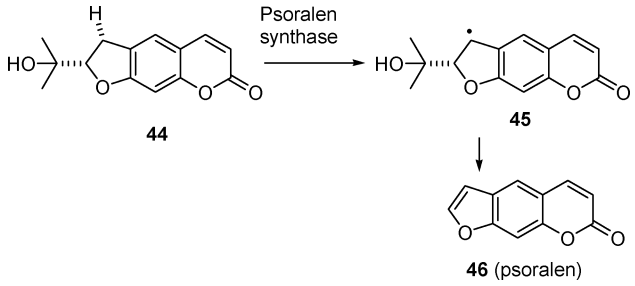
Boland and co-workers showed that psoralen synthase converted marmesin (**44**) to psoralen (**46**) with loss of the hydrogen cis to the side chain.[37] They proposed that oxidation gives radical **45**, which fragments to psoralen (see Scheme 15). Diols **8c** and **8t** were not observed as intermediates. They stated that fragmentation of diol **8** should proceed by an anti elimination. Extensive studies have shown that base-catalyzed elimination of mono-

SCHEME 14



sulfonates of 1,3-diols proceed by anti elimination.[46] The less well studied acid-catalyzed eliminations of 1,3-diols have also been shown to proceed through anti elimination.[47] However, basic or acidic hydrolysis of vaginidin (the tertiary isobutyrate of **7c**) gave angelicin (**47**) quantitatively, indicating that syn elimination is possible.[48]

SCHEME 15



With both isomers of **7** and **8** in hand, we decided to compare the relative rates of anti and syn elimination. Conversion of **7c** in 20:1 CH_2Cl_2/TFA required 3 h for complete syn elimination to give angelicin (**47**)[35] quantitatively (see Scheme 16). The anti elimination of **7t** was approximately twice as fast. Similar differences were observed with **8c** and **8t**. Conversion of **8c** in 20:1 CH_2Cl_2/TFA required 80 min for complete syn elimination to give psoralen (**46**)[49] quantitatively. The anti elimination of **8t** is approximately twice as fast. The small differences in rates for syn and anti elimination suggests that these reactions are not concerted, but proceed by protonation of the secondary alcohol and loss of water to give a common, highly stabilized benzylic carbocation intermediate that loses acetone to form the furan. This carbocation might also be a biosynthetic intermediate.

(43) (a) Muramatsu, I.; Murakami, M.; Yoneda, T.; Hagitani, A. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 244−246. (b) Sōfuku, S.; Muramatsu, I.; Hagitani, A. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2942−2945.

(44) Zubía, E.; Luis, F. R.; Massanet, G. M.; Collado, I. G. *Tetrahedron* **1992**, *48*, 4239−4246.

(45) Evans, P. A.; Brandt, T. A. *J. Org. Chem.* **1997**, *62*, 5321−5326.

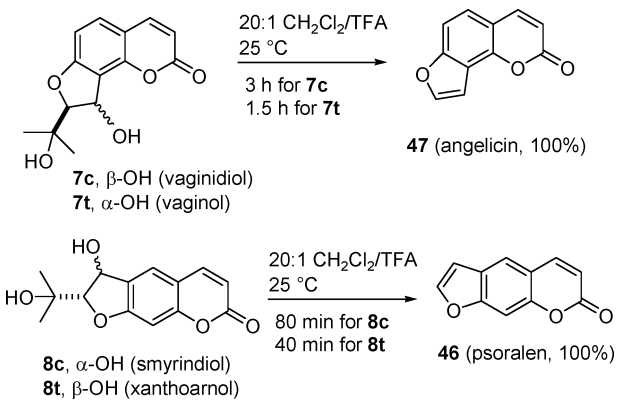
(46) Caine, D. *Org. Prep. Proced. Int.* **1988**, *20*, 1−51.

(47) Maggio, T. E.; English, J., Jr. *J. Am. Chem. Soc.* **1961**, *83*, 968−974.

(48) Seshadri, T. R.; Sood, M. S.; Handa, K. L.; Vishwapaul *Tetrahedron* **1967**, *23*, 1883−1891.

(49) Masuda, T.; Takasugi, M.; Anetai, M. *Phytochemistry* **1998**, *47*, 13−16.

SCHEME 16



In conclusion, we have developed two practical one-step syntheses of 2,3-dihydro-3-hydroxy-2-hydroxyalkylbenzofurans from readily available optically pure α,β-epoxy aldehydes. Electron-deficient resorcinols react with epoxy aldehydes using either Cs_2CO_3 in DMF or KOH/$CaCl_2$ in MeOH to give adducts **13**, **16**, **18**, **20**, **21**, and brosimacutin G (**6t**). Grignard reagents prepared by low-temperature halogen−metal exchange of acetoxy iodocoumarins **35d** and **40**, and acetoxy bromonaphthalene **41** add to epoxy aldehyde (*S*)-**26** to complete the first syntheses of vaginidiol (**7c**), vaginol (**7t**), smyrindiol (**8c**), xanthoarnol (**8t**), and avicenol A (**9t**). Acid-catalyzed fragmentation of vaginidiol or vaginol provides angelicin, while that of smyrindiol or xanthoarnol affords psoralen. In both cases, the trans isomers fragment only twice as fast as the cis isomers, possibly through the intermediacy of a common benzylic cation. This may have implications for the biosynthesis of angelicin and psoralen.

Experimental Section

General Procedure. NMR spectra were recorded at 400 MHz in $CDCl_3$ or in CD_3OD if the compound is not soluble in $CDCl_3$. We used acetone-d_6 for aldehydes that partially formed hemiacetals in CD_3OD.

***cis*-3,6-Dihydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-2,3-dihydrobenzofuran-4-carboxaldehyde (16c), *trans*-3,6-Dihydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-2,3-dihydrobenzofuran-4-carboxaldehyde (16t), and 6-Hydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-benzofuran-4-carboxaldehyde (17).** A solution of citral epoxide (**11**)[22] (125 mg, 0.75 mmol), 3,5-dihydroxybenzaldehyde (**15**) (103 mg, 0.75 mmol), and Cs_2CO_3 (268 mg, 0.83 mmol) in dry DMF (7.5 mL) was stirred under N_2 at 25 °C for 3 d. The reaction was neutralized with 10% citric acid to pH 5−6 and extracted with ether. The combined ether extracts were washed twice with water and brine, dried ($MgSO_4$), and concentrated to yield 178 mg (78%) of crude product. Flash chromatography on MeOH-deactivated silica gel (1:1 hexanes/Et_2O) yielded 20 mg of a 1:1.2 mixture of **17** and **15**, followed by 23 mg of pure **16c**, 5 mg of a 1:2 mixture of **16c** and **16t**, and 43 mg of pure **16t**. Flash chromatography of the first 20 mg fraction on silica gel (4:1 hexanes/EtOAc) gave 9 mg (4%) of pure **17**. The calculated yields are: **16c** (11%), **16t** (20%), and **17** (4%).

Data for **16c**: mp 144−146 °C; ^{1}H NMR (acetone-d_6) 10.09 (s, 1), 9.00 (br s, 1, OH), 6.93 (d, 1, J = 2.2), 6.63 (d, 1, J = 2.2), 5.84 (dd, 1, J = 6.1, 4.9), 5.20 (t, 1, J = 7.4), 5.10 (d, 1, J = 4.9, OH), 4.40 (d, 1, J = 6.1), 4.39 (s, 1, OH), 2.25−2.18 (m, 2), 1.91−1.86 (m, 2), 1.69 (s, 3), 1.65 (s, 3), 1.41 (s, 3); ^{13}C NMR (acetone-d_6) 193.1, 163.6, 161.4, 135.3, 132.3, 126.1, 123.6, 110.8, 104.2, 91.7, 75.1, 71.8, 40.7, 26.4, 24.6, 23.3, 18.2; IR (KBr) 3320, 2925, 1695, 1600, 1150; HRMS (FAB) calcd for $C_{17}H_{22}O_5Na$ (MNa^+) 329.1365, found 329.1364.

Data for **16t**: mp 157−159 °C; ^{1}H NMR (acetone-d_6) 10.12 (s, 1), 8.96 (br s, 1, OH), 6.92 (d, 1, J = 2.2), 6.56 (d, 1, J = 2.2), 5.74 (d, 1, J = 3.7), 5.16 (t, 1, J = 7.0), 4.48 (br s, 1, OH), 4.44 (d, 1, J = 3.7), 3.72 (br s, 1, OH), 2.18 (dt, 2, J = 7.0, 7.0), 1.67 (s, 3), 1.65−1.57 (m, 2), 1.62 (s, 3), 1.21 (s, 3); ^{13}C NMR (acetone-d_6) 193.5, 163.5, 160.6, 134.9, 131.7, 125.5, 123.0, 110.3, 103.4, 97.8, 72.9, 71.7, 39.0, 25.8, 22.6 (2 C), 17.6; IR (KBr) 3200, 2930, 1673, 1587, 1300, 1148; HRMS (DCI/NH_3) calcd for $C_{17}H_{21}O_4$ (M^+ − OH) 289.1440, found 289.1445.

Data for **17**: ^{1}H NMR ($CDCl_3$) 10.04 (s, 1), 7.28 (d, 1, J = 1.8), 7.23 (d, 1, J = 1.8), 7.20 (s, 1), 6.23 (br s, 1, OH), 5.09 (t, 1, J = 7.0), 2.88 (br s, 1, OH), 2.1−1.9 (m, 4), 1.66 (s, 3), 1.62 (s, 3), 1.52 (s, 3); ^{13}C NMR ($CDCl_3$) 191.7, 164.4, 156.1, 153.5, 132.6, 128.7, 123.5, 121.1, 116.3, 104.6, 101.3, 72.5, 41.1, 26.6, 25.6, 23.0, 17.6; IR (neat) 3333, 2920, 1680, 1622, 1331, 1140; HRMS (DCI/NH_3) calcd for $C_{17}H_{21}O_4$ (MH^+) 289.1440, found 289.1436.

***trans*-3,4-Dihydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-2,3-dihydrobenzofuran-6-carboxaldehyde (18).** A solution of citral epoxide (**11**)[22] (110 mg, 0.65 mmol), 3,5-dihydroxybenzaldehyde (**15**) (90 mg, 0.65 mmol), $CaCl_2$ (80 mg, 0.72 mmol), and KOH (81 mg, 1.44 mmol) in MeOH (6.5 mL) was stirred at 25 °C for 3 d. The reaction was neutralized with 10% citric acid to pH 5−6 and extracted with ether. The combined ether extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to yield 183 mg (97%) of crude product. Flash chromatography on MeOH-deactivated silica gel (1:1 hexanes/EtOAc) yielded 90 mg (45%) of pure **18**: mp 155−157 °C; ^{1}H NMR (acetone-d_6) 9.87 (s, 1), 8.88 (br s, 1, OH), 6.93 (s, 1), 6.82 (s, 1), 5.62 (d, 1, J = 3.7), 5.16 (t, 1, J = 7.0), 4.62 (br s, 1, OH), 4.42 (d, 1, J = 3.7), 3.75 (s, 1, OH), 2.19 (dt, 2, J = 7.0, 7.0), 1.67 (s, 3), 1.67−1.59 (m, 2), 1.63 (s, 3), 1.20 (s, 3); ^{13}C NMR (acetone-d_6) 192.4, 163.3, 156.2, 140.6, 131.7, 125.4, 122.8, 110.2, 102.6, 97.8, 73.0, 71.1, 39.1, 25.8, 22.5, 22.4, 17.6; IR (KBr) 3287, 2938, 1679, 1617, 1172; HRMS (FAB) calcd for $C_{17}H_{22}O_5Na$ (MNa^+) 329.1365, found 329.1377.

***cis*-3,4-Dihydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-2,3-dihydrobenzofuran-5-carboxaldehyde (21c), *trans*-3,4-Dihydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-2,3-dihydrobenzofuran-5-carboxaldehyde (21t), 4-Hydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-benzofuran-5-carboxaldehyde (22), *cis*-3,4-Dihydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-2,3-dihydrobenzofuran-7-carboxaldehyde (20c), *trans*-3,4-Dihydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-2,3-dihydrobenzofuran-7-carboxaldehyde (20t), 4-Hydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-benzofuran-7-carboxaldehyde (23).** A solution of citral epoxide (**11**)[22] (283 mg, 1.68 mmol), 2,4-dihydroxybenzaldehyde (**19**) (190 mg, 1.68 mmol), and Cs_2CO_3 (657 mg, 2.02 mmol) in dry DMF (25 mL) was stirred under N_2 at 25 °C for 7 d. The reaction was neutralized with 10% citric acid to pH 5−6 and extracted with ether. The combined ether extracts were washed twice with water and with brine, dried ($MgSO_4$), and concentrated to yield 516 mg (77%) of crude product. Flash chromatography on MeOH-deactivated silica gel (9:1 to 1:1 hexanes/EtOAc) yielded 106 mg of a 1.6:1 mixture of **19** and **22**, followed by 20 mg of pure **21c**, 80 mg of a 1:3 mixture of **21c** and **21t**, 17 mg of a 2:1 mixture of **21t** and **23**, 30 mg of a 8:1:5 mixture of **21t**, **23**, and **20c**, 23 mg of a 1:1:1.5 mixture of **21t**, **20c**, and **20t**, 9 mg of a 1:3.5 mixture of **20c** and **20t**, and 55 mg of pure **20t**, respectively. The calculated yields are: **20c** (4%), **20t** (14%), **21c** (7%), **21t** (19%), **22** (9%), and **23** (2%).

Dihydrobenzofurans **21c** and **21t** were also prepared as follows. A solution of citral epoxide (**11**)[22] (100 mg, 0.6 mmol), 2,4-dihydroxybenzaldehyde (**19**) (84 mg, 0.6 mmol), $CaCl_2$ (73 mg, 0.66 mmol), and KOH (74 mg, 1.32 mmol) in MeOH (6 mL) was stirred at 25 °C for 1 d. The reaction was neutralized with 10% citric acid to pH 5−6 and extracted with ether. The

combined ether extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to yield 180 mg (94%) of crude product. Flash chromatography on MeOH-deactivated silica gel (6:1 hexanes/EtOAc) yielded 44 mg (23%) of pure **21c** and 47 mg (26%) of pure **21t**.

Purification of 18 mg of the 1.6:1 mixture of **19** and **22** by preparative TLC (Silica gel 60 F_{254}, 1:1 hexanes/EtOAc, extracted with MeOH) provided 11.0 mg of **19** and 6.1 mg of **22**. Purification of 23 mg of the 1:1:1.5 mixture of **21t**, **20c**, and **20t** by preparative TLC (Silica gel 60 F_{254}, 1:1 hexanes/EtOAc, extracted with MeOH) provided 5.5 mg of **21t**, 5.6 mg of **20c**, and 8.1 mg of **20t**. Purification of 17 mg of the 2:1 mixture of **21t** and **23** by preparative TLC (Silica gel 60 F_{254}, 1:1 hexanes/EtOAc, extracted with MeOH) provided 10.4 mg of **21t** and 5.1 mg of **23**.

Data for **20c**: ^{1}H NMR (CD_3OD) 9.98 (s, 1), 7.60 (d, 1, J = 8.5), 6.47 (d, 1, J = 8.5), 5.46 (d, 1, J = 6.1), 5.19 (t, 1, J = 7.0), 4.36 (d, 1, J = 6.1), 2.23−2.17 (m, 2), 1.91−1.84 (m, 2), 1.70 (s, 3), 1.66 (s, 3), 1.46 (s, 3); ^{13}C NMR (CD_3OD) 189.0, 166.1, 163.3, 132.7, 130.3, 125.7, 117.9, 114.8, 111.0, 93.0, 75.5, 70.3, 39.8, 26.0, 23.7, 23.2, 17.9; R_f (1:1 hexanes/EtOAc) 0.50; HRMS (DCI/NH_3) calcd for $C_{17}H_{24}NO_4$ (M + NH_3 − OH)$^+$ 306.1705, found 306.1694.

Data for **20t**: mp 125−127 °C; ^{1}H NMR (CD_3OD) 9.95 (s, 1), 7.57 (d, 1, J = 8.5), 6.43 (d, 1, J = 8.5), 5.43 (d, 1, J = 3.9), 5.13 (t, 1, J = 7.0), 4.47 (d, 1, J = 3.9), 2.15 (dt, 2, J = 7.0, 7.0), 1.68 (s, 3), 1.63 (s, 3), 1.61−1.52 (m, 2), 1.21 (s, 3); ^{13}C NMR (CD_3OD) 188.8, 166.7, 164.2, 132.6, 132.5, 125.5, 117.0, 114.1, 111.0, 99.8, 73.0, 71.0, 38.8, 25.9, 22.9, 22.0, 17.7; IR (KBr) 3333, 2930, 1670, 1600, 1260; R_f (1:1 hexanes/EtOAc) 0.40; HRMS (DCI/NH_3) calcd for $C_{17}H_{24}NO_4$ (M + NH_3 − OH)$^+$ 306.1705, found 306.1700.

Data for **21c**: ^{1}H NMR ($CDCl_3$) 11.63 (s, 1, OH), 9.65 (s, 1), 7.42 (d, 1, J = 8.5), 6.55 (d, 1, J = 8.5), 5.59 (d, 1, J = 6.1), 5.16 (t, 1, J = 6.9), 4.34 (d, 1, J = 6.1), 4.12 (br s, 1, OH), 3.77 (br s, 1, OH), 2.23−2.11 (m, 2), 1.97−1.89 (m, 1), 1.84−1.78 (m, 1), 1.70 (s, 3), 1.64 (s, 3), 1.45 (s, 3); ^{13}C NMR ($CDCl_3$) 194.5, 167.4, 160.0, 137.9, 132.2, 123.8, 116.2, 116.1, 104.0, 90.8, 74.5, 69.8, 38.8, 25.7, 24.0, 22.1, 17.7; IR (neat) 3356, 2928, 1648, 1254, 1082; R_f (1:1 hexanes/EtOAc) 0.75; HRMS (DCI/NH_3) calcd for $C_{17}H_{23}O_5$ (MH^+) 307.1545, found 307.1530.

Data for **21t**: mp 134−136 °C; ^{1}H NMR ($CDCl_3$) 11.63 (s, 1, OH), 9.69 (s, 1), 7.44 (d, 1, J = 8.6), 6.51 (d, 1, J = 8.6), 5.62 (d, 1, J = 4.3), 5.12 (t, 1, J = 7.3), 4.51 (d, 1, J = 4.3), 2.62 (s, 1, OH), 2.15 (dt, 2, J = 7.3, 7.3), 1.76 (s, OH), 1.67 (s, 3), 1.66−1.57 (m, 2), 1.62 (s, 3), 1.27 (s, 3); ^{13}C NMR ($CDCl_3$) 194.5, 167.7, 160.4, 137.9, 132.6, 123.8, 116.0, 115.4, 103.6. 97.6, 73.3, 70.3, 37.2, 25.7, 22.4, 21.8, 17.7; IR (KBr) 3324, 2927, 1644, 1252, 1047; R_f (1:1 hexanes/EtOAc) 0.65; HRMS (DCI/NH_3) calcd for $C_{17}H_{23}O_5$ (MH^+) 307.1545, found 307.1541.

Data for **22**: ^{1}H NMR ($CDCl_3$) 11.90 (s, 1, OH), 9.90 (s, 1), 7.42 (d, 1, J = 8.5), 7.10 (d, 1, J = 8.5), 6.82 (s, 1), 5.10 (t, 1, J = 7.0), 2.26 (s, 1, OH), 2.01−1.93 (m, 4), 1.63 (s, 6), 1.54 (s, 3); ^{13}C NMR ($CDCl_3$) 196.0, 162.8, 160.2, 157.5, 132.6, 129.6 123.5, 117.9, 115.5, 104.6, 99.5, 72.2, 41.1, 27.0, 25.6, 22.9, 17.7; R_f (1:1 hexanes/EtOAc) 0.89; HRMS (DCI/NH_3) calcd for $C_{17}H_{19}O_3$ (M^+ − OH) 271.1334, found 271.1340.

Data for **23**: ^{1}H NMR (CD_3OD) 9.95 (s, 1), 7.59 (d, 1, J = 8.5), 6.76 (s, 1), 6.61 (d, 1, J = 8.5), 5.06 (t, 1, J = 7.0), 2.00−1.92 (m, 4), 1.61 (s, 3), 1.56 (s, 3), 1.51 (s, 3); ^{13}C NMR (CD_3OD) 188.7, 164.0, 162.7, 157.5, 132.4, 131.4, 125.1, 120.0, 114.3, 111.3, 100.0, 72.3, 42.5, 26.6, 25.8, 24.0, 17.6; R_f (1:1 hexanes/EtOAc) 0.59; HRMS (DCI/NH_3) calcd for $C_{17}H_{21}O_4$ (MH^+) 289.1440, found 289.1444.

***cis*-3,4-Dihydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-2,3-dihydrobenzofuran-5-acetophenone (13c) and *trans*-3,4-Dihydroxy-2-(1-hydroxy-1,5-dimethyl-4-hexenyl)-2,3-dihydrobenzofuran-5-acetophenone (13t).** A solution of citral epoxide (**11**)[22] (100 mg, 0.6 mmol), 2,4-dihydroxyacetophenone (**10**) (90 mg, 0.6 mmol), $CaCl_2$ (73 mg, 0.66 mmol), and KOH (74 mg, 1.32 mmol) in MeOH (6 mL) was stirred at 25 °C for 1 d. The reaction was neutralized with 10% citric acid to pH 5−6 and extracted with ether. The combined ether extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to yield 180 mg (94%) of crude product. Flash chromatography on MeOH-deactivated silica gel (6:1 hexanes/EtOAc) yielded 76 mg (40%) of pure **13c** and 86 mg (45%) of pure **13t**.

Data for **13c**: ^{1}H NMR ($CDCl_3$) 12.96 (s, 1, OH), 7.70 (d, 1, J = 8.5), 6.49 (d, 1, J = 8.5), 5.63 (dd, 1, J = 6.4, 4.2), 5.17 (t, 1, J = 7.0), 4.37 (d, 1, J = 6.4), 3.38 (s, 1, OH), 3.32 (d, 1, J = 4.2, OH), 2.56 (s, 3), 2.25−2.13 (m, 2), 1.99−1.91 (m, 1), 1.86−1.78 (m, 1), 1.71 (s, 3), 1.65 (s, 3), 1.46 (s, 3); ^{13}C NMR ($CDCl_3$) 202.9, 166.6, 160.9, 134.8, 132.2, 123.9, 116.2, 114.8, 102.9, 90.7, 74.3, 70.2, 38.9, 26.4, 25.7, 24.0, 22.1, 17.7; IR (neat) 3357, 2928, 1640, 1370, 1263; HRMS (FAB) calcd for $C_{18}H_{24}O_5Na$ (MNa^+) 343.1521, found 343.1518.

Data for **13t**: mp 147−148 °C; ^{1}H NMR ($CDCl_3$) 12.94 (s, 1, OH), 7.68 (d, 1, J = 8.8), 6.43 (d, 1, J = 8.8), 5.63 (d, 1, J = 3.9), 5.14 (t, 1, J = 7.0), 4.51 (d, 1, J = 3.9), 2.70 (s, 1, OH), 2.56 (s, 3), 2.17 (dt, 2, J = 7.0, 7.0), 1.81 (s, 1, OH), 1.69 (s, 3), 1.67−1.58 (m, 2), 1.64 (s, 3), 1.28 (s, 3); ^{13}C NMR ($CDCl_3$) 202.9, 166.8, 161.3, 134.7, 132.5, 123.9, 115.5, 114.7, 102.5, 97.4, 73.3, 70.6, 37.1, 26.4, 25.7, 22.4, 21.8, 17.7; IR (KBr) 3310, 2940, 1647, 1257; HRMS (FAB) calcd for $C_{18}H_{24}O_5Na$ (MNa^+) 343.1521, found 343.1535.

(2*S*,3*R*)-1-[2,3-*cis*-3,4-Dihydroxy-2-(1-hydroxy-1-methylethyl)-2,3-dihydrobenzofuran-5-yl]-3-(4-hydroxyphenyl)-*E*-propenone (6c) and Brosimacutin G (6t). A solution of (*S*)-3,3-dimethyloxirane-2-carboxaldehyde ((*S*)-**26**))[27] (20 mg, 0.20 mmol), isoliquiritigenin (**25**)[26] (52 mg, 0.20 mmol), $CaCl_2$ (24 mg, 0.22 mmol), and KOH (25 mg, 0.44 mmol) in MeOH (2 mL) was stirred at 25 °C for 1 d. The reaction was neutralized with 10% citric acid to pH 5−6 and extracted with ether. The combined ether extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to yield 63 mg (90%) of crude product. Flash chromatography on silica gel (20:1 CH_2Cl_2/MeOH) yielded 31 mg (43%) of pure **6c** and 35 mg (47%) of pure **6t**.

Data for **6c**: mp 207−208 °C; $[\alpha]^{20}_D$ +111.2 (*c* 0.5, MeOH); ^{1}H NMR (CD_3OD) 8.12 (d, 1, J = 8.9), 7.82 (d, 1, J = 15.2), 7.64 (d, 2, J = 8.6), 7.63 (d, 1, J = 15.2), 6.85 (d, 2, J = 8.6), 6.54 (d, 1, J = 8.9), 5.51 (d, 1, J = 5.7), 4.33 (d, 1, J = 5.7), 1.51 (s, 3), 1.45 (s, 3); ^{13}C NMR (CD_3OD) 194.0, 168.2, 163.6, 161.8, 146.2, 135.2, 132.0, 131.9, 127.7, 118.2, 117.7, 116.9 (2 C), 116.2, 103.6, 93.2, 73.1, 70.4, 27.1, 26.5; IR (KBr) 3355, 2935, 1640, 1600, 1576, 1240, 1170; HRMS (DCI/NH_3) calcd for $C_{20}H_{21}O_6$ (MH^+) 357.1338, found 357.1345.

Data for **6t**: mp 229−231 °C; $[\alpha]^{20}_D$ −12.2 (*c* 0.55, MeOH), $[\alpha]^{20}_D$ −10.8 (*c* 0.12, MeOH) {lit.[2] $[\alpha]^{22}_D$ −0.7 (c 0.06, MeOH), lit.[3] $[\alpha]^{22}_D$ −1 (c 0.133, MeOH)}; ^{1}H NMR (CD_3OD) 8.11 (d, 1, J = 8.9), 7.82 (d, 1, J = 14.7), 7.64 (d, 1, J = 14.7), 7.63 (d, 2, J = 8.6), 6.85 (d, 2, J = 8.6), 6.51 (d, 1, J = 8.9), 5.48 (d, 1, J = 3.7), 4.38 (d, 1, J = 3.7), 1.26 (s, 3), 1.25 (s, 3); ^{13}C NMR (CD_3OD) 194.0, 168.9, 164.0, 161.7, 146.0, 135.3, 132.0 (2 C), 127.8, 118.3, 117.0 (2 C), 116.9, 116.0, 103.3, 100.2, 71.9, 71.3, 25.3, 25.2; IR (KBr) 3350, 2975, 1640, 1605, 1566, 1250, 1170; HRMS (FAB) calcd for $C_{20}H_{21}O_6$ (MH^+) 357.1338, found 357.1343.

A similar sequence starting with (*R*)-**26** afforded **6c** {$[\alpha]^{22}_D$ −125 (*c* 0.5, MeOH)} and **6t** {$[\alpha]^{22}_D$ +9 (*c* 0.33, MeOH)}.

8-(1-Hydroxy-1,5-dimethyl-4-hexenyl)-2*H*-furo[2,3-*h*]-1-benzopyran-2-one (28), *trans*-8-(1-Hydroxy-1,5-dimethyl-4-hexenyl)-2-oxo-8,9-dihydro-2*H*-furo[2,3-*h*]-1-benzopyran-9-acetic Acid Lactone (30) and Methyl *trans*-8-(1-Hydroxy-1,5-dimethyl-4-hexenyl)-2-oxo-8,9-dihydro-2*H*-furo[2,3-*h*]-1-benzopyran-9-acetate. A solution of **21t** (24 mg, 0.08 mmol) and *N*,*N*-dimethylacetamide dimethyl acetal (0.03 mL, 0.19 mmol) in dry Et_2O (1 mL) was stirred for 6 h at reflux. After cooling, the mixture was neutralized with 10% HCl to pH 4−5 and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with water and saturated $NaHCO_3$, dried ($MgSO_4$), and concentrated to yield 22 mg crude product. Purification of the crude product by preparative

TLC (Silica gel 60 F_{254}, 1:1 hexanes/EtOAc, extracted with MeOH) provided 2.5 mg (10%) of **28** and 2.5 mg (10%) of a 1:2 mixture of **30** and the methyl ester derived from opening the lactone ring of **30**.

Data for **28**: ^{1}H NMR ($CDCl_3$) 7.80 (d, 1, J = 9.5), 7.38 (d, 1, J = 8.6), 7.34 (d, 1, J = 8.6), 6.97 (s, 1), 6.39 (d, 1, J = 9.5), 5.13−5.09 (br, 1), 2.29 (s, 1, OH), 2.04−1.95 (m, 4), 1.66 (s, 3), 1.63 (s, 3), 1.54 (s, 3); ^{13}C NMR ($CDCl_3$) 163.9, 160.8, 157.1, 144.5, 132.8, 123.5, 123.4, 117.7, 114.1, 113.5, 108.5, 107.6, 98.9, 72.3, 41.2, 27.1, 25.6, 22.9, 17.7; IR (neat) 3443, 2926, 1731, 1616, 1446, 1272, 1117; R_f (1:1 hexanes/EtOAc) 0.62; HRMS (DCI/NH_3) calcd for $C_{19}H_{21}O_4$ (MH^+) 313.1440, found 313.1441.

Data for **30**: ^{1}H NMR ($CDCl_3$) 7.65 (d, 1, J = 9.8), 7.36 (d, 1, J = 8.2), 6.86 (d, 1, J = 8.2), 6.24 (d, 1, J = 9.8), 5.15 (t, 1, J = 7.3), 4.36 (d, 1, J = 13.5), 3.88 (ddd, 1, J = 13.5, 12.8, 4.6), 3.76−3.69 (m, 1), 2.86 (dd, 1, J = 17.5, 12.8), 2.23−1.10 (m, 4), 1.69 (s, 3), 1.57 (s, 3), 1.16 (s, 3); R_f (1:1 hexanes/EtOAc) 0.56; HRMS (DCI/NH_3) calcd for $C_{21}H_{23}O_5$ (MH^+) 355.1545, found 355.1553.

Data for the methyl ester derived from opening the lactone ring of **30**: ^{1}H NMR ($CDCl_3$) 7.62 (d, 1, J = 9.5), 7.29 (d, 1, J = 8.2), 6.74 (d, 1, J = 8.2), 6.21 (d, 1, J = 9.5), 5.13 (t, 1, J = 8), 4.61 (d, 1, J = 4.3), 4.14 (ddd, 1, J = 4.3, 3.6, 9.2), 3.72 (s, 3), 3.10 (dd, 1, J = 3.6, 16.7), 2.74 (dd, 1, J = 9.2, 16.7), 2.23−1.10 (m, 4), 1.69 (s, 3), 1.63 (s, 3), 1.16 (s, 3); R_f (1:1 hexanes/EtOAc) 0.56; HRMS (DCI/NH_3) calcd for $C_{22}H_{27}O_6$ (MH^+) 387.1808, found 387.1815.

3,6-Dihydroxy-2-(1-hydroxy-1-methylethyl)-2,3-dihydrobenzofuran-5-carboxaldehyde (31). A solution of (±)-3,3-dimethyloxirane-2-carboxaldehyde (**26**)[34] (165 mg, 1.65 mmol), 2,4-dihydroxybenzaldehyde (**19**) (190 mg, 1.37 mmol), $CaCl_2$ (167 mg, 1.51 mmol), and KOH (169 mg, 3.01 mmol) in MeOH (8 mL) was stirred at 25 °C for 1 d. The reaction was neutralized with 10% citric acid to pH 5−6 and extracted with ether. The combined ether extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to yield 322 mg (90%) of crude product as a 1.2:1 mixture of diastereomers of **31**. Flash chromatography on silica gel (1:1 hexanes/EtOAc) yielded 91 mg (28%) of **31c** and 108 mg (33%) of **31t**.

Data for **31c**: ^{1}H NMR ($CDCl_3$) 11.61 (s, 1, OH), 9.64 (s, 1), 7.41 (d, 1, J = 8.5), 6.51 (d, 1, J = 8.5), 5.56 (d, 1, J = 6.4), 4.30 (d, 1, J = 6.4), 1.50 (s, 3), 1.43 (s, 3); ^{13}C NMR ($CDCl_3$) 194.5, 167.4, 160.1, 137.9, 116.1 (2 C), 104.0, 91.4, 72.2, 70.0, 27.6, 26.3; IR (neat) 3384, 2977, 1644, 1487, 1255, 1090; HRMS (TOF MS ES+) calcd for $C_{12}H_{14}O_5Na$ (MNa^+) 261.0739, found 261.0738.

Data for **31t**: ^{1}H NMR ($CDCl_3$) 11.61 (br s, 1, OH), 9.62 (s, 1), 7.38 (d, 1, J = 8.5), 6.46 (d, 1, J = 8.5), 5.50 (d, 1, J = 4.3), 4.40 (d, 1, J = 4.3), 1.27 (s, 3), 1.22 (s, 3); ^{13}C NMR ($CDCl_3$) 194.5, 167.6, 160.4, 137.9, 116.0, 115.4, 103.6, 98.3, 71.3, 70.4, 25.4, 24.6; IR (neat) 3406, 2979, 1644, 1488, 1256, 1073; HRMS (DCI/NH_3) calcd for $C_{12}H_{15}O_5$ (MH^+) 239.0919, found 239.0920.

4-Hydroxy-2-(1-hydroxy-1-methylethyl)benzofuran-5-carboxaldehyde (32) and 4-Hydroxy-2-(methylethenyl)-benzofuran-5-carboxaldehyde (33). A solution of the crude mixture of **31** (200 mg, ∼0.84 mmol) and *N,N*-dimethylformamide dimethyl acetal (0.12 mL, 0.84 mmol) in dry Et_2O (10 mL) was refluxed for 6 h. After cooling, the mixture was neutralized with 10% HCl to pH 4−5 and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to yield 156 mg of crude product. Flash chromatography on silica gel (10:1 hexanes/EtOAc) yielded 12 mg (7% from **19**) of pure **33** and 93 mg (50% from **19**) of pure **32**.

Data for **32**: mp 72−73 °C; ^{1}H NMR ($CDCl_3$) 11.90 (s, 1, OH), 9.89 (s, 1), 7.42 (d, 1, J = 8.5), 7.11 (dd, 1, J = 8.5, 0.8), 6.80 (d, 1, J = 0.8), 2.14 (s, 1, OH), 1.69 (s, 6); ^{13}C NMR ($CDCl_3$) 196.0, 163.2, 160.1, 157.5, 129.7, 117.8, 115.4, 104.7, 98.5, 69.1, 28.6 (2 C); IR (KBr) 3418, 2975, 1650, 1472, 1321, 1270. The ^{1}H and ^{13}C NMR ($CDCl_3$) spectral data match the literature data.[35]

Data for **33**: mp 91−92 °C (lit.[35] mp 92−93 °C); ^{1}H NMR ($CDCl_3$) 11.93 (s, 1, OH), 9.89 (s, 1), 7.42 (d, 1, J = 8.5), 7.10 (d, 1, J = 8.5), 6.84 (s, 1), 5.78 (s, 1), 5.21 (s, 1), 2.13 (s, 3); ^{13}C NMR ($CDCl_3$) 196.0, 160.1, 157.5, 157.2, 132.2, 130.1, 118.7, 115.5, 113.9, 104.5, 100.5, 19.2; IR (KBr) 3140, 2974, 1657, 1590, 1316, 1280. The ^{1}H and ^{13}C NMR ($CDCl_3$) spectral data match the literature data.[35]

4-Hydroxybenzofuran-5-carboxaldehyde (34). A solution of the crude mixture of **31** (110 mg, ∼0.42 mmol) in 5% TFA/CH_2Cl_2 (5 mL) was stirred at 25 °C for 2 h. The reaction was neutralized with 3 M NaOH to pH 3−4 and extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to yield 60 mg (90%) of crude product. Flash chromatography on silica gel (16:1 hexanes/EtOAc) yielded 41 mg (52% from **19**) of pure **34**: mp 55−56 °C (lit.[35] mp 54−56 °C); ^{1}H NMR ($CDCl_3$) 11.99 (s, 1, OH), 9.90 (s, 1), 7.60 (d, 1, J = 2.1), 7.43 (d, 1, J = 8.5), 7.14 (d, 1, J = 8.5), 7.00 (d, 1, J = 2.1); ^{13}C NMR ($CDCl_3$) 196.0, 160.0, 157.9, 144.9, 129.7, 117.2, 115.4, 104.8, 104.7; IR (KBr) 3150, 2865, 1650, 1590, 1337, 1270. The ^{1}H and ^{13}C NMR ($CDCl_3$) spectral data match the literature data.[35]

***cis*-8,9-Dihydro-9-hydroxy-8-(1-hydroxy-1-methylethyl)-2*H*-furo[2,3-*h*]-1-benzopyran-2-one (Vaginidiol, 7c), *trans*-8,9-Dihydro-9-hydroxy-8-(1-hydroxy-1-methylethyl)-2*H*-furo[2,3-*h*]-1-benzopyran-2-one (Vaginol, 7t), 8-Acetyl-7-hydroxy-2*H*-1-benzopyran-2-one (37), and 7-Hydroxy-8-(1-hydroxy-1,2-dimethylpropyl)-2*H*-1-benzopyran-2-one (38), and 8,8-Dimethyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*′]dipyran-2-one (Seselin, 39).** A solution of 7-acetyloxy-8-iodo-2*H*-1-benzopyran-2-one (**35d**)[38] (252 mg, 0.76 mmol) in dry THF (12 mL) was stirred under N_2 at −100 °C in a diethyl ether/liquid nitrogen bath for 5 min before slowly adding isopropylmagnesium chloride (0.75 mL, 2 M in THF, 1.5 mmol). After 1 h, the exchange was complete (as indicated by TLC) and (*S*)-3,3-dimethyloxirane-2-carboxaldehyde ((*S*)-**26**)[27] was added (240 μL, 2.4 mmol). The reaction was allowed to warm to room temperature over 1 h. The reaction mixture was quenched with MeOH (3 mL), poured into water (30 mL), and extracted with EtOAc. The combined EtOAc extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 302 mg of crude product. Flash chromatography on silica gel (2:1 to 0:1 hexanes/EtOAc) yielded 2.8 mg of **39** (2%), followed by 34 mg of a 2:3 inseparable mixture of **37** (8%) and **38** (12%), 38 mg of **35d** (15%), 40 mg of pure **7c** (21%), 38 mg of pure **7t** (19%), and 141.6 mg of unidentified complex mixtures.

Data for **7c**: mp 175−177 °C (lit.[4] mp 174 °C, lit.[5] mp 166−167 °C, lit[6] mp 168−169 °C); $[\alpha]^{20}_D$ +223 (*c* 0.43, EtOH) {lit.[4] $[\alpha]^{25}_D$ +234.6 (c 1.023, 95% EtOH), lit.[5] $[\alpha]^{20}_D$ +230 (c 0.2, EtOH), lit.[6] $[\alpha]^{25}_D$ +231 (c 0.01, EtOH)}; ^{1}H NMR (acetone-d_6) 7.91 (d, 1, J = 9.8), 7.57 (d, 1, J = 8.5), 6.86 (d, 1, J = 8.5), 6.19 (d, 1, J = 9.8), 5.74 (d, 1, J = 5.5), 4.55 (s, 1, OH), 4.47 (d, 1, J = 5.5), 1.54 (s, 3), 1.45 (s, 3); ^{13}C NMR (acetone-d_6) 164.7, 160.6, 152.8, 145.2, 131.9, 117.9, 114.0, 112.9, 108.2, 92.4, 72.4, 70.3, 27.8, 27.0; IR (KBr) 3347, 1720, 1618, 1406, 1348, 1252, 1115; HRMS (DEI) calcd for $C_{14}H_{14}O_5$ (M^+) 262.0841, found 262.0850.

Data for **7t**: mp 164−166 °C (lit.[7] mp 164−165 °C); $[\alpha]^{20}_D$ +119 (*c* 0.43, EtOH) {lit.[7] $[\alpha]^{24}_D$ +127.6 (c 0.04, EtOH)}; ^{1}H NMR (acetone-d_6) 7.87 (d, 1, J = 9.5), 7.52 (d, 1, J = 8.5), 6.78 (d, 1, J = 8.5), 6.15 (d, 1, J = 9.5), 5.69 (dd, 1, J = 6.1, 3.6), 4.14 (d, 1, OH, J = 6.1), 4.43 (d, 1, J = 3.6), 1.29 (s, 3), 1.25 (s, 3); ^{13}C NMR (acetone-d_6) 165.4, 160.7, 153.2, 145.2, 131.7, 117.5, 113.8, 112.7, 107.9, 100.0, 71.2, 70.7, 26.0, 25.7; IR (KBr) 3367, 1713, 1610, 1402, 1324, 1252, 1120; HRMS (DEI) calcd for $C_{14}H_{14}O_5$ (M^+) 262.0841, found 262.0835.

A similar sequence starting with (*R*)-**26** afforded **7c** {$[\alpha]^{21}_D$ −208 (c 0.35, EtOH)} and **7t** {$[\alpha]^{21}_D$ −117 (c 0.5, EtOH)}.

Data for **37** were determined from the mixture: ^{1}H NMR ($CDCl_3$) 7.66 (d, 1, J = 9.7), 7.52 (d, 1, J = 8.7), 6.91 (d, 1, J = 8.7), 6.28 (d, 1, J = 9.7), 2.97 (s, 3). The ^{1}H NMR ($CDCl_3$) spectral data match the literature data.[42]

Data for **38** were determined from the mixture: ^{1}H NMR ($CDCl_3$) 7.59 (d, 1, J = 9.4), 7.23 (d, 1, J = 8.5), 6.76 (d, 1, J = 8.5), 6.17 (d, 1, J = 9.4), 2.66 (sept, 1, J = 7.0), 1.96 (s, 3), 1.06, (d, 3, J = 7.0), 0.86 (d, 3, J = 7.0).

Data for **39**: ^{1}H NMR ($CDCl_3$) 7.60 (d, 1, J = 9.1), 7.21 (d, 1, J = 8.6), 6.89 (d, 1, J = 10.4), 6.73 (d, 1, J = 8.6), 6.23 (d, 1, J = 9.1), 5.74 (d, 1, J = 10.4), 1.48 (s, 6).

7-Acetoxy-6-iodo-2*H*-1-benzopyranone (40). A solution of 6-iodo-7-hydroxycoumarin[44] (160 mg, 0.55 mmol), pyridine (0.1 mL) and acetic anhydride (0.1 mL) in CH_2Cl_2 (10 mL) was stirred at 25 °C for 18 h. The reaction was washed with 10% HCl and brine, dried ($MgSO_4$) and concentrated to yield 179 mg (98%) of **40**: ^{1}H NMR ($CDCl_3$) 7.95 (s, 1), 7.63 (d, 1, J = 9.5), 7.15 (s, 1), 6.43 (d, 1, J = 9.5), 2.42 (s, 3); ^{13}C NMR ($CDCl_3$) 167.9, 159.6, 154.6, 153.2, 141.5, 137.6, 118.7, 117.1, 111.9, 84.8, 21.2; IR (KBr) 1758, 1717, 1364, 1182, 1147, 1107.

(2*S*,3*R*)-3-Hydroxy-2-(1-hydroxy-1-methylethyl)-2,3-dihydrofuro[3,2-*g*]chromen-7-one (Smyrindiol, 8c) and (2*S*,3*S*)-3-Hydroxy-2-(1-hydroxy-1-methylethyl)-2,3-dihydrofuro[3,2-*g*]chromen-7-one (Xanthoarnol, 8t). A solution of **40** (140 mg, 0.42 mmol) in dry THF (5 mL) was stirred under N_2 at −100 °C in a diethyl ether/liquid nitrogen bath for 5 min before slowly adding isopropylmagnesium chloride (0.42 mL, 2 M in THF, 0.84 mmol). After 1 h, the exchange was complete (as indicated by TLC) and (*S*)-3,3-dimethyloxirane-2-carboxaldehyde ((*S*)-**26**)[27] (120 μL, 1.2 mmol) was added. The reaction was allowed to warm to room temperature over 1 h. The reaction mixture was quenched with MeOH (1 mL), poured into water (10 mL) and extracted with EtOAc. The combined EtOAc extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 220 mg of crude product. Flash chromatography on MeOH-deactivated silica gel (2:1 to 0:1 hexanes/EtOAc) yielded 16.7 mg of **8c** (15%) and 20.4 mg of **8t** (18%).

Data for **8c**: mp 164−166 °C (lit.[9] mp 173−175 °C, lit.[10] mp 166−168 °C); $[\alpha]^{20}_D$ +22.4 (*c* 0.25, $CHCl_3$) {lit.[9] $[\alpha]^{25}_D$ +34 (c 0.0078, DMSO), lit.[10] $[\alpha]^{20}_D$ +24.4 (c 2.8, $CHCl_3$)}; ^{1}H NMR ($CDCl_3$) 7.65 (d, 1, J = 9.5), 7.51 (s, 1), 6.83 (s, 1), 6.25 (d, 1, J = 9.5), 5.38 (dd, 1, J = 6.7, 6.1), 4.44 (d, 1, OH, J = 6.7), 4.36 (d, 1, J = 6.1), 1.60 (s, 3), 1.55 (s, 3); ^{13}C NMR ($CDCl_3$) 162.4, 161.1, 156.7, 143.7, 128.1, 124.8, 113.6, 112.9, 99.0, 90.5, 73.0, 71.8, 28.5, 25.3; IR (KBr) 3423, 1735, 1624, 1570, 1487, 1384, 1128; HRMS (DCI/NH_3) calcd for $C_{14}H_{15}O_5$ (MH^+) 263.0919, found 263.0928. The ^{1}H and ^{13}C NMR ($CDCl_3$) spectral data match the literature data.[10]

Data for **8t**: mp 181−183 °C (lit.[13] mp 152.5−154.0 °C); $[\alpha]^{20}_D$ +37 (*c* 0.4, acetone) {lit.[13] $[\alpha]^{24}_D$ −30.6 (acetone)}; ^{1}H NMR (acetone-d_6) 7.91 (d, 1, J = 9.1), 7.62 (s, 1), 6.71 (s, 1), 6.18 (d, 1, J = 9.1), 5.46 (d, 1, J = 4.3), 4.41 (d, 1, J = 4.3), 1.29 (s, 3), 1.28 (s, 3); ^{1}H NMR (CD_3OD) 7.91 (d, 1, J = 9.5), 7.60 (s, 1), 6.80 (s, 1), 6.22 (d, 1, J = 9.5), 5.35 (d, 1, J = 4.2), 4.36 (d, 1, J = 4.2), 1.29 (s, 3), 1.28 (s, 3); ^{13}C NMR (acetone-d_6) 163.7, 160.1, 156.7, 144.2, 128.4, 125.1, 112.9, 111.9, 98.9, 97.4, 71.3, 70.2, 25.0 (2 C); IR (KBr) 3423, 1733, 1626, 1572, 1489, 1391, 1128; HRMS (DEI) calcd for $C_{14}H_{14}O_5$ (M^+) 262.0841, found 262.0845. The ^{1}H NMR (CD_3OD) spectral data match the literature data.[12−14]

3-(Hydroxy)-1,4-dimethoxy-α-methyl-α-(methylethyl)-2-naphthalenemethanol (43), α-[(3,3-Dimethyloxiranyl)-3-hydroxy-1,4-dimethoxy-2-naphthalenemethanol (42), (2*S*,3*R*)-2,3-Dihydro-3-hydroxy-4,9-dimethoxy-α,α-(dimethyl)naphtho[2,3-*b*]furan-2-methanol (9c), and (2*S*,3*S*)-2,3-Dihydro-3-hydroxy-4,9-dimethoxy-α,α-(dimethyl)naphtho[2,3-*b*]furan-2-methanol (Avicenol A, 9t). A solution of 3-acetoxy-2-bromo-1,4-dimethoxynaphthalene (**41**)[45] (175 mg, 0.53 mmol) in dry THF (8 mL) was stirred under N_2 at −20 °C for 5 min before slowly adding isopropylmagnesium chloride (0.54 mL, 2 M in THF, 1.08 mmol). The solution slowly warmed to −5 °C over 30 min and was then treated with (*S*)-3,3-dimethyloxirane-2-carboxaldehyde ((*S*)-**26**)[27] (150 μL, 1.5 mmol). The reaction was allowed to warm to room temperature over 1 h. The reaction mixture was quenched with MeOH (1 mL), poured into water (10 mL) and extracted with EtOAc. The combined EtOAc extracts were washed with brine, dried ($MgSO_4$), and concentrated to yield 280 mg of crude product. Flash chromatography on silica gel (4:1 hexanes/EtOAc) yielded 84 mg of impure **43**, followed by 34 mg of a 1.5:1 inseparable mixture of **42** (12%) and **9c** (8%), and 20.4 mg of impure **9t**.

Impure **43** (18 mg) was dissolved in 10 mL CH_2Cl_2, which was washed with 1.5 mL of 1 M NaOH. The aqueous layer was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed with saturated NH_4Cl, dried ($MgSO_4$), and concentrated to yield 12 mg of pure **43** (36%).

Purification of 15 mg of impure **9t** by preparative TLC (Silica gel 60 F_{254}, 3:2 CH_2Cl_2/MeOH, extracted with acetone) provided 12 mg of pure **9t** (22%).

Data for **9c** were determined from the mixture: ^{1}H NMR ($CDCl_3$) 8.10 (d, 1, J = 8.1), 8.05 (d, 1, J = 8.1), 7.47 (dd, 1, J = 8.1, 8.0), 7.34 (dd, 1, J = 8.1, 8.0), 5.70 (dd, 1, J = 5.5, 5.5), 4.48 (d, 1, OH, J = 5.5), 4.28 (d, 1, J = 5.5), 4.19 (s, 3), 4.05 (s, 3), 1.60 (s, 3), 1.58 (s, 3).

Data for **9t**: $[\alpha]^{20}_D$ +5.0 (*c* 0.4, $CHCl_3$) {lit.[15] $[\alpha]_D$ 5.1 ($CHCl_3$)}; ^{1}H NMR ($CDCl_3$) 8.05 (d, 2, J = 8.3), 7.47 (dd, 1, J = 8.3, 8.3), 7.36 (dd, 1, J = 8.3, 8.3), 5.70 (dd, 1, J = 6.1, 4.0), 4.44 (d, 1, J = 4.0), 3.96 (s, 3), 3.92 (s, 3), 2.63 (d, 1, OH, J = 6.1), 1.99 (br s, 1, OH), 1.37 (s, 3), 1.34 (s, 3); ^{13}C NMR ($CDCl_3$) 148.7, 147.2, 132.2, 130.4, 126.7, 123.9, 123.5, 122.3, 121.1, 119.8, 97.2, 71.8, 71.4, 61.1, 60.7, 25.6, 24.9; IR (neat) 3417, 1640, 1463, 1416, 1364, 1058; HRMS (DCI/NH_3) calcd for $C_{17}H_{20}O_5$ (M^+) 304.1311, found 304.1313. The ^{1}H and ^{13}C NMR ($CDCl_3$) spectral data match the literature data.[15]

Data for **42** were determined from the mixture: ^{1}H NMR ($CDCl_3$) 8.01 (d, 1, J = 8.6), 7.93 (d, 1, J = 8.6), 7.49 (dd, 1, J = 8.6, 8.0), 7.37 (dd, 1, J = 8.6, 8.0), 5.14 (dd, 1, J = 8.5, 9.5), 3.97 (s, 6), 3.76 (d, 1, OH, J = 9.5), 3.43 (d, 1, J = 8.5), 1.56 (s, 3), 1.55 (s, 3).

Data for **43**: mp 128−129 °C; ^{1}H NMR ($CDCl_3$) 7.98 (br d, 1, J = 8.3), 7.93 (br d, 1, J = 8.3), 7.46 (ddd, 1, J = 8.3, 8.3, 1.2), 7.34 (ddd, 1, J = 8.3, 8.3, 1.2), 3.96 (s, 3), 3.92 (s, 3), 2.52 (sept, J = 6.7), 1.86 (s, 3), 1.00 (d, 3, J = 6.7), 0.89 (d, 3, J = 6.7); ^{13}C NMR ($CDCl_3$) 149.9, 145.9, 137.5, 128.0, 126.3, 125.2, 123.3, 122.9, 122.5, 120.6, 82.1, 63.5, 61.0, 36.5, 27.0, 17.5, 16.6; IR (KBr) 3358, 2970, 1621, 1565, 1444, 1423, 1366, 1334, 1278; HRMS (DEI) calcd for $C_{17}H_{22}O_4$ (M^+) 290.1518, found 290.1520.

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Supporting Information Available: Experimental procedures for the preparation of **11** and **26**; NOE data for many compounds; copies of ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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