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Enantioselective [4 + 2] Cycloadditions of *o*-Quinone Methides: Total Synthesis of (+)-Mimosifoliol and Formal Synthesis of (+)-Tolterodine

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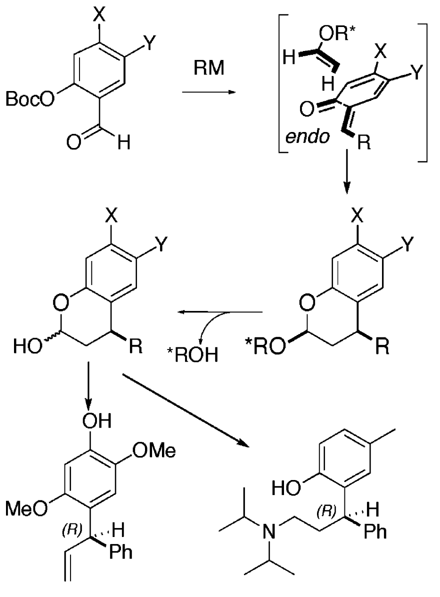
The first example of an enantioselective cycloaddition of an *o*-quinone methide (*o*-QM) with a chiral enol ether is described along with the total synthesis of (+)-mimosifoliol and the formal synthesis of (+)-tolterodine. These syntheses exemplify a three-component, one-pot benzopyran approach for the construction of chiral benzylic junctions. Cycloadditions of various enol ethers and *o*-QMs are examined, and diastereoselectivities >95% are obtained with *trans*-2-phenyl-1-cyclohexanol and 2,2-diphenylcyclopentanol vinyl ethers.

Introduction

Due to the ephemeral nature and high reactivity of most *o*-quinone methides (*o*-QMs), their method for generation determines their ensuing application. Typically, *o*-QMs are generated under Lewis acidic or thermal conditions and result in a mixture of *endo* and *exo* isomers in [4 + 2] cycloadditions.[1] The appearance of *exo* cycloadducts reflect the thermodynamic conditions needed for *o*-QM generation. However, a short time ago, a low-temperature anionic method for *o*-QM generation greatly enhanced the diastereoselectivities of succeeding cycloadditions.[2] *o*-QMs generated in this manner undergo remarkably *endo* selective [4 + 2] cycloadditions with a variety of electron-rich dienophiles.[3] An asymmetric format was explored in the synthesis of (+)-mimosifoliol (**2**) utilizing a chiral vinyl ether and an *o*-QM to create a chiral benzopyran building block.[4] To the best of our knowledge, this is the first reported enantioselective cycloaddition of an *o*-QM with an enol ether. This article describes (1) *o*-QM formation in greater detail, (2) illuminates numerous enol ethers and their syntheses, (3) reports the diastereoselectivities observed from a series of enol ethers and *o*-QMs, and (4) applies the asymmetric method to (+)-tolterodine (**1**), a remedy for urinary incontinence (Scheme 1).

SCHEME 1



(+)-*R*-mimosifoliol (**2**) (+)-*R*-tolterodine (**1**)

o-QM Generation

In the past, methods for *o*-QM generation have been harsh and cumbersome, thus making subsequent diastereoselective reactions unsuitable. For example, Pochini heats 2-[hydroxy(phenyl)methyl]phenol and ethyl vinyl ether (EVE) to 170 °C, and the resulting cycloaddition proceeds with a 3:1 ratio of *endo*/*exo* products.[5] Dufresne thermolyzes 2-phenyl-4-ethyl-1,3,2-benzodioxaborin with EVE at 300 °C and observes a 1:1 mixture of *endo*/*exo* products.[6] Similarly, Chiba uses Lewis acidic conditions with *o*-hydroxybenzyl alcohols and enol ethers to result in a ratio of cycloadducts.[7]

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[1] Van De Water, R. W.; Pettus, T. R. R. *Tetrahedron* **2002**, *58*, 5367–5405.

[2] Van De Water, R.; Magdziak, D.; Chau, J.; Pettus, T. R. R. *J. Am. Chem. Soc.* **2000**, *122*, 6502–6503.

[3] Jones, R. M.; Selenski, C.; Pettus, T. R. R. *J. Org. Chem.* **2002**, *67*, 6911–6915.

[4] Selenski, C.; Mejorado, L.; Pettus, T. R. R. *Synlett* **2004**, 1101–1103.

[5] Arduini, A.; Bosi, A.; Pochini, A.; Ungaro, R. *Tetrahedron* **1985**, *41*, 3095–3103.

[6] Chambers, J. D.; Crawford, J.; Williams, H. W. R.; Dufresne, C.; Scheigetz, J.; Bernstein, M. A.; Lau, C. K. *Can. J. Chem.* **1992**, *70*, 1717–1732.

10.1021/jo048703c CCC: $27.50

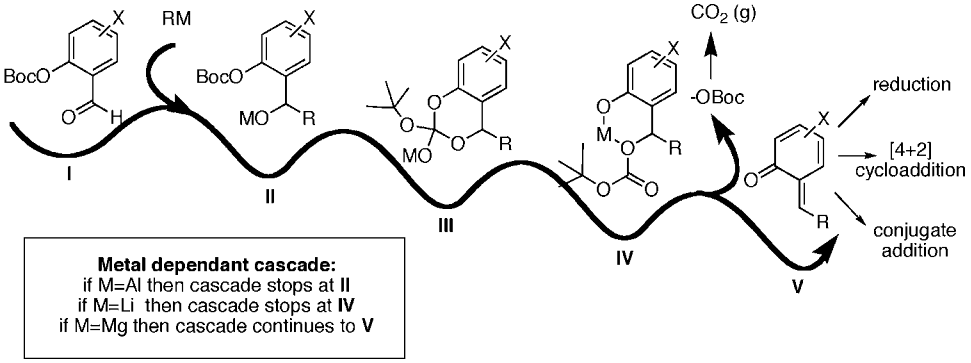

FIGURE 1. *o*-QM cascade.

The following low-temperature, anionic method for *o*-QM generation achieves high *endo*/*exo* ratios for ensuing cycloadditions (Figure 1). It has been proposed *o*-QM formation results from a series of events called the *o*-QM cascade. The cascade begins with the nucleophilic addition of an organometallic reagent to an *o*-Boc salicylaldehyde **I**. The resulting benzyloxy anion **II** attacks the −OBoc carbonate to form a cyclic intermediate **III**, which collapses to form a more stable phenoxide **IV** upon −BOC migration. Under certain circumstances, β-elimination of the −OBoc residue produces an *o*-QM **V**. Cascade incursion is both metal and temperature dependent, presumably reflecting the strength of the oxygen−metal bond and the electrophilicity of the metal cation. For example, an aluminum reagent proceeds to intermediate **II**, whereas a lithium reagent continues to intermediate **IV**. Surprisingly, a magnesium reagent facilitates the final conversion to **V**, an unfavorable event which is energetically offset by entropy, the Lewis acidity of Mg^{2+}, and CO_2 expulsion. The resulting geometry of the *o*-QM olefin is *E* unless a large group is located at the 6-position of the salicylaldehyde.

If an *o*-QM is generated in the presence of a chiral enol ether, it is consumed in a diastereoselective [4 + 2] cycloaddition. The ensuing cycloaddition is governed by four elements: (1) the olefin geometry of the *o*-QM, (2) the facial selectivity of the chiral enol ether, (3) the transition state between the reacting components, and (4) the effect of *o*-QM generation on the product distribution.

Chiral Enol Ethers

After considering the availability and past performace of many enol ethers, enol ethers **3**−**9** were investigated (Figure 2). At first glance, enol ethers may appear flexible and would exhibit poor facial selectivity; however, Houk found the *s-trans* conformation to be preferred during inverse-demand Diels−Alder reactions.[8] The preference is explained on the basis of electrostatic interactions and, to a lesser extent, steric affects. Allylic strain of the vinyl C−H, aryl C−H, and the chiral center limits the conformations of the enol ether and increases the diastereoselectivity during cycloaddition.

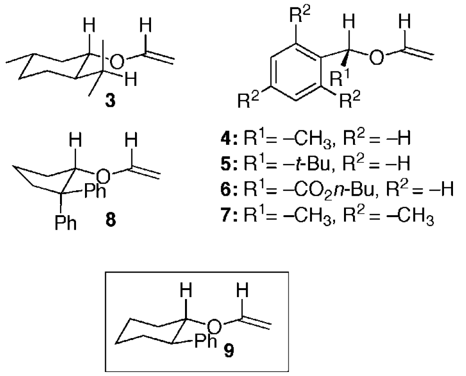

FIGURE 2. Chiral enol ethers examined.

In 1986, Posner surveyed the diastereoselective cycloadditions of enol ethers **3**, **4**, **5**, and **7** with 3-arenesulfonyl-2-pyrone to form [2.2.2]-bicyclic lactone adducts.[9] Enol ether **5** was superior in the cycloaddition proceeding in >90% de and >90% yield. In 1989, Franck reported the cycloaddition of **9** with an isoquinolinium salt in 91% yield and 95% de.[10] In 1990, Denmark investigated **8** and **9** in tandem cycloadditions with nitroalkenes.[11] Enol ether **8** was designed by Denmark, and over the next decade **8** and **9** were used in the syntheses of many alkaloids.[12] In 1991, Thornton surveyed the diastereoselectivities of enol ethers **4** and **5** in high-pressure cycloadditions with 3-hydroxylated-2-pyrones resulting in good yields and a range of diastereoselectivities.[13] In 1994, Dujardin investigated the cycloaddition of **6**, derived from a Fisher esterification of mandelic acid, with various oxabutadienes undergoing cycloadditions in >90% de.[14]

Traditionally, the synthesis of enol ether used toxic reagents, resulted in mediocre yields, and therefore was unappealing for application in total synthesis. The original Watanabe process entails transetherification of *n*-

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[7] Chiba, K.; Hirano, T.; Kitano, Y.; Tada, M. *J. Chem. Soc., Chem. Commun.* **1999**, 691−692.

[8] Liu, J.; Niwayama, S.; You, Y.; Houk, K. N. *J. Org. Chem.* **1998**, *63*, 1064−1073.

[9] Posner, G. H.; Wettlaufer, D. G. *Tetrahedron Lett.* **1986**, *27*, 667−670.

[10] Choudhury, A.; Franck, R. W.; Gupta, R. B. *Tetrahedron Lett.* **1989**, *30*, 4921−4924.

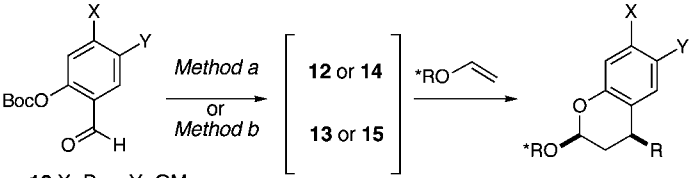
[11] Denmark, S. E.; Senanayake, C. B. W.; Ho, G.-D. *Tetrahedron* **1990**, *46*, 4857−4876.

[12] The following alkaloids were synthesized: (−)-mesembrine, (+)-castanospermine, (−)-hastanecine, (+)-casuarine, (−)-rosmarinecine, (+)-detoxinine, and (+)-australine.

[13] Prapansiri, V.; Thornton, E. R. *Tetrahedron Lett.* **1991**, *32*, 3247−3150.

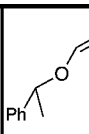
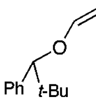
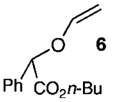
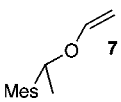
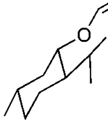
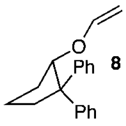
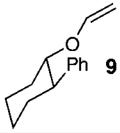
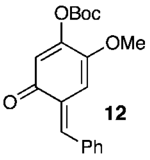
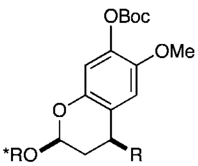
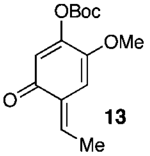
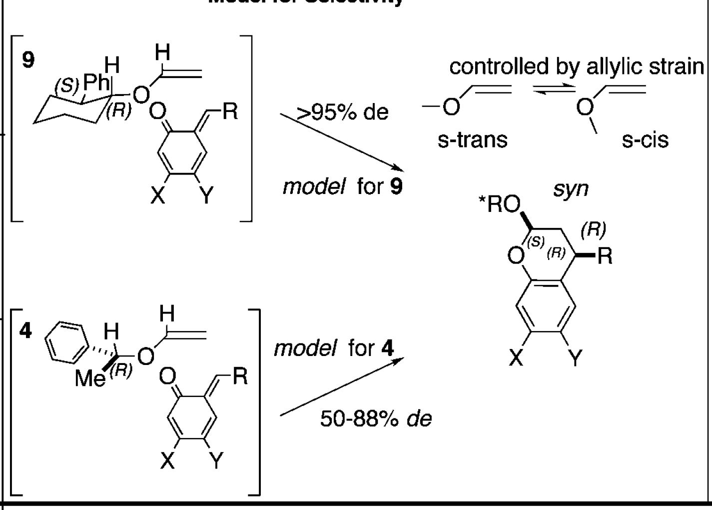
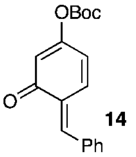
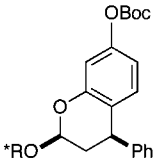
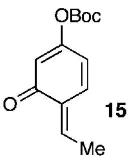
[14] Dujardin, G.; Rossignol, S.; Molato, S.; Brown, E. *Tetrahedron* **1994**, *50*, 9037−9050.

TABLE 1. Diastereoselective Cycloadditions of *o*-QMs and Enol Ethers*



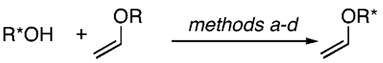
10:X=Boc, Y=OMe
11:X=Boc, Y=H

16- 28

Chiral enol ethers → ***o*-QMs** ↓	 **4**	 **5**	 **6**	 **7**	 **3**	 **8**	 **9**	**Chiral chromans** ↓
 **12**	**16** 88% *de*[a] 90% yield[b]	**17** 11% *de*[a] 63%yield[b]	**18** 4% *de*[a] 70%yield[b]	**19** 25% *de*[a] 58% yield[b]	**20** 45% *de*[a] 60% yield[b]	**21** 95% *de*[a] 66% yield[c]	**22** 95% *de*[a] 69%yield[c]	 **16-22, R=Ph** **23-24, R=Me**
 **13**	**23** 60% *de*[a] 80%yield[b]	**Model for Selectivity** 					**24** 95% *de*[a] 75% yield[c]	
 **14**	**25** 60% *de*[a] 85% yield[b]						**26** 95% *de*[a] 88% yield[c]	 **25-26, R=Ph** **27-28, R=Me**
 **15**	**27** 50% *de*[a] 77% yield[b]						**28** 95% *de*[a] 72% yield[c]	

*Method A: The aldehyde (0.1 M Et_2O) and enol ether (2 equiv) were cooled to −78 °C, the Grignard reagent (1.05 equiv) was added dropwise, and the reaction was warmed to rt over 3 h. Method B: After the aldehyde (0.1 M Et_2O) was cooled to 0 °C the alkyllithium (1.05 equiv) was added dropwise, and the reaction stirred for 15 min and then cooled to −78 °C. The enol ether (2 equiv) was added, followed by the addition of $MgBr_2{\cdot}Et_2O$ (1 equiv). The reaction was warmed to rt over 3 h. [a] Diastereomeric excess. [b] Yield for all diastereomers. [c] Isolated yield for major diastereomer.

SCHEME 2. Enol Ether Synthesis[a]



[a] Key: (a) BVE, cat. $Hg(OAc)_2$, R*OH, 75 °C, 6 h; (b) (i) EVE, CF_3CO_2H, R*OH, 20 °C, 5d; (ii) NEt_3, TMSOTf, 0 °C, CH_2Cl_2, 12 h; (c) BVE, R*OH, cat. $(DPP)Pd(OCOCF_3)_2$, 75 °C, 12 h; (d) $AcOCH{=}CH_2$, R*OH, cat. $[Ir(Cod)Cl]_2$, Na_2CO_3, toluene, 90 °C, 12 h.

butyl vinyl ether (BVE) in the presence of substoichiometric mercuric acetate and a chiral alcohol (Scheme 2, method a).[15] Following the Watanabe method, the syntheses of **3** and **6** result in 60% and 43% yields, respectively. Dujardin subsequently reported a mercury-free two-step preparation of **3** and **6** in 75% and 80% yields, respectively (Scheme 2, method b).[16] Though the method avoids hazardous materials, acetal formation in the first step can take up to 1 week for completion. More recently, Schlaf reported that **4** can be prepared in 83% yield by using an air-stable palladium catalyst; unfortunately, hindered alcohols require lengthy reaction times (Scheme 2, method c).[17] We find the Ishii method to be vastly superior due to short reaction times, high yields, and ease of experimental setup (Scheme 2, method d).[18] In our hands, enol ethers **3** and **4** were readily prepared in 86% and 95% yields, respectively, by heating vinyl acetate, the alcohol, Na_2CO_3, and catalytic $[Ir(cod)Cl]_2$.

Results and Discussion

The diastereoselective cycloadditions of enol ethers **3**−**9** with *o*-QMs **12**−**15** were studied (Table 1). *o*-QMs **12**−

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[15] Watanabe, W. H.; Conlon, L. E. *J. Am. Chem. Soc.* **1957**, *79*, 2828−2833.

[16] Dujardin, G.; Rossignol, S.; Brown, E. *Tetrahedron Lett.* **1995**, *36*, 1653−1656.

[17] Bosch, M.; Schlaf, M. *J. Org. Chem.* **2003**, *68*, 5225−5227.

[18] Okimoto, Y.; Sakaguchi, S.; Ishii, Y. *J. Am. Chem. Soc.* **2002**, *124*, 1590−1591.

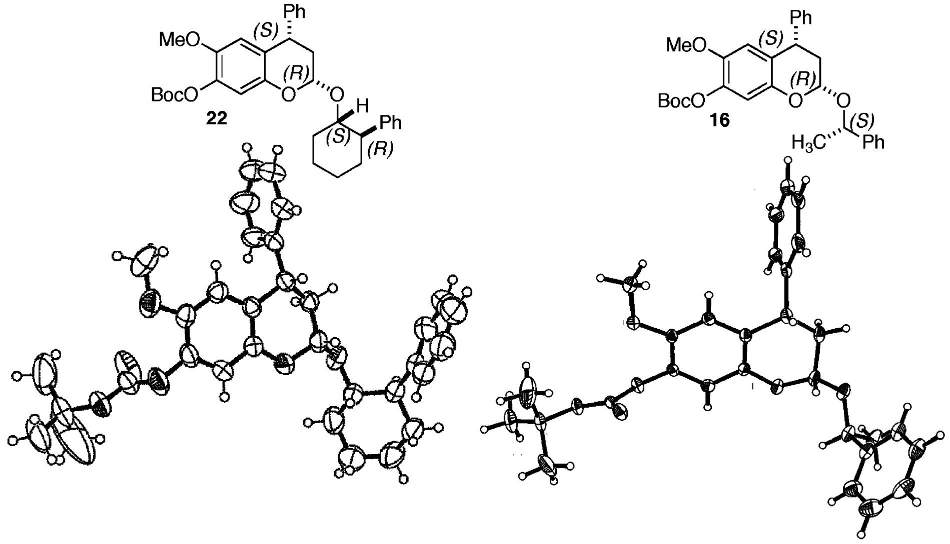
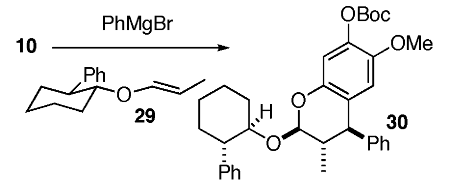


FIGURE 3. Crystal structures of chromans **22** and **16**.

15 were generated by the addition of phenyl or methyl Grignard reagent to *o*-Boc salicylaldehydes **10**[19] or **11**.[20] Enol ethers **3**−**5** and **7**−**9** were prepared by the Ishii method,[18] while enol ether **6** was prepared using the mercury-free procedure[16] by Dujardin. In most cases, method A or B can be used for the syntheses of chromans **16**−**28**. Method B manipulates the metal-dependent cascade shown in Figure 1 and should be used when an enol ether contains functionality prone to nucleophilic attack.

SCHEME 3



When *o*-QM **12** is generated in the presence of menthol vinyl ether (**3**)[21] a cycloaddition ensues to produce **20** in 45% de and 60% yield for all cycloadducts. Menthol vinyl ether (**3**) was the only enol ether to produce *exo* cycloadducts visible in the crude reaction. The *exo* adducts may result from steric interactions corrupting preference for an *endo* transition state. Next, we examined *o*-QM **12** with 1-phenylethanol vinyl ether (**4**),[9] and the resulting cycloaddition proceeded in 90% yield with 88% de. The yield may reflect the compact size of **4**, but the diastereomeric ratio reflects its failure to react exclusively from one face. Unfortunately, the diastereoselectivities (50−60%) and yields (77−85%) associated with products **23**, **25**, and **27** from *o*-QMs **13**−**15** were significantly lower. We anticipated enol ether **5**[9] containing a *tert*-butyl residue might prove more selective; however, the reaction with *o*-QM **12** results in 63% yield and 11% de. The *tert*-butyl group might overpower allylic strain to confer rigidity of the enol ether in regard to the reacting face and the chiral center; therefore, butyl mandelate derived enol ether **6**[21] was examined with a small sp^2 carbonyl group next to the chiral center. While the yield of **18** was 70% the de was a meager 4%; clearly, both *o*-QM faces are accessible for cycloaddition. 1-Mesitylethanol vinyl ether (**7**)[9] was then examined, hoping the large aryl ring might drastically change the selectivity; however, compound **19** arises in 58% yield and 25% de. On the other hand, 2,2-diphenylcyclopentanol vinyl ether (**8**)[22] undergoes cycloaddition with *o*-QM **12** in 66% yield and 95% de; however, its five-step synthesis makes it somewhat unattractive as a chiral building block. The diastereoselectivities of *trans*-2-phenyl-1-cyclohexanol vinyl ether (**9**)[23] are outstanding for all *o*-QMs. The isolated yields of benzopyrans **22**, **24**, **26**, and **28** range from 69 to 88% all in 95% de. Enol ether **9** is a good choice for application in total synthesis because of its high diastereoselective induction, facile construction, and commercial availability of its corresponding alcohol in both enantiomers.

The facial selectivities of enol ethers **4** and **9** during cycloaddition are shown in Table 1. The relative stereochemistries of chromans **16** and **22** were determined by X-ray crystallography (Figure 3). (Note: the crystal structures are shown in their opposite enantiomers) The *syn* relationship between the phenyl residue of the benzopyran and the oxygen substituent of the acetal results from an *endo* transition state. Taking into account pseudoallylic strain and Houk's calculation, the enol ether reacts in the *s-trans* conformation. The *o*-QM undergoes reaction opposite the methyl residue of enol ether **4** and opposite the phenyl residue of enol ether **9**. The *S*-stereocenter of **4** and the 2*R*-stereocenter of **9** induces the *S*-configuration of the resulting benzyl junction. The absolute configuration of the chiral enol ether determines the absolute configuration of the resulting benzopyran. The selectivity model was confirmed by the key cycloadditions of *trans*-2*S*-phenyl-1*R*-cyclohexanol

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[19] Tuttle, K.; Rodriguez, A. A.; Pettus, T. R. R. *Synlett* **2003**, 2234−2237.

[20] Jones, R.; Van De Water, R. W.; Lindsey, C.; Hoarau, C.; Ung, T.; Pettus, T. R. R. *J. Org. Chem.* **2001**, *66*, 3435−3441.

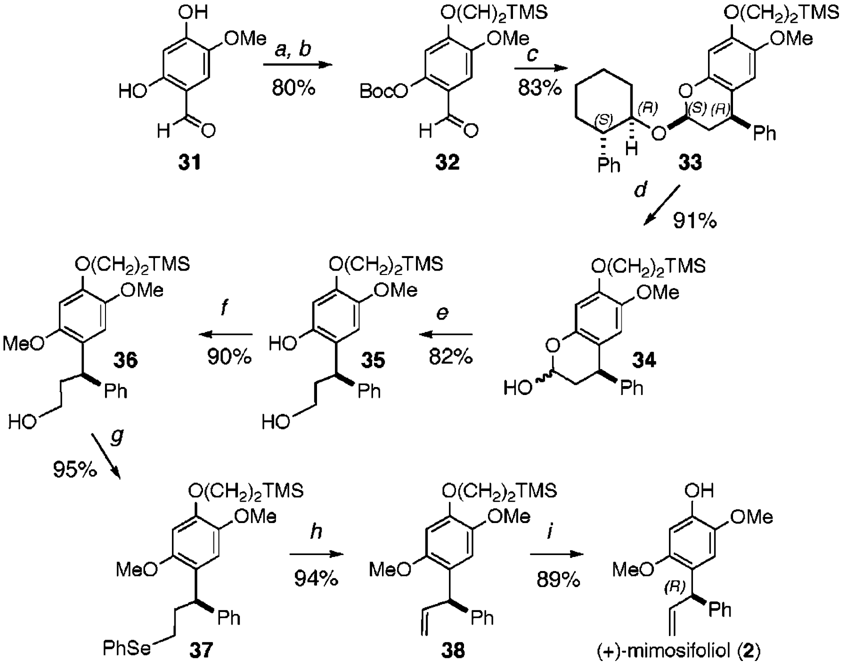
[21] Dujardin, G.; Rossignol, S.; Molato, S.; Brown, E. *Tetrahedron.* **1994**, *50*, 9037−50.

[22] Denmark, S. E.; Schnute, M. E.; Marcin, L. R.; Thorarensen, A. *J. Org. Chem.* **1995**, *60*, 3205−3220.

[23] Denmark, S. E.; Senanayake, B. W. *J. Org. Chem.* **1993**, *58*, 1853−1858.

[24] Reference deleted in proof.

SCHEME 4[a]



[a] Key: (a) $TMS(CH_2)_2OH$ (2 equiv), PPh_3 (2 equiv), DIAD (2 equiv), 1 M THF, 12 h; (b) BOC_2O (1.1 equiv), Hunig's base (0.5 equiv), DMAP (cat.), 0.1 M CH_2Cl_2; (c) PhMgBr (1.05 equiv), (−)-**9** (2 equiv), 0.1 M Et_2O, −78 °C to rt, 3 h; (d) CSA (0.6 equiv), 0.1 M 1:1 H_2O/CH_3CN, 70 °C, 5 h; (e) $LiAlH_4$ (2 equiv), 0 °C, 5 min; (f) CH_2N_2; (g) PhSeCN (1.05 equiv), PBu_3 (1.1 equiv); (h) $NaIO_4$, $NaHCO_3$, 40 °C; (i) CsF (2 equiv), 0.1 M DMF, 160 °C, 6 h.

vinyl ether (−)-**9** with the appropriate *o*-QMs that ultimately created *R*-mimosifoliol (**2**) and *R*-tolterodine (**1**).

From this model, it was concluded that substituted enol ether **29**[23] should also undergo a diastereoselective cycloaddition (Scheme 3). Addition of phenyl Grignard reagent to aldehyde **10**[19] in the presence of enol ether **29** affords benzopyran **30**, creating three chiral centers, with a 60% yield and 95% de.

To demonstrate the usefulness of this process within the context of synthesis, (+)-mimosifoliol (**2**), isolated from the rootwood of *Aeschynomene mimosifolia* Vatke (Leguminosae),[25] was constructed in nine steps with a 35% overall yield (Scheme 4). The synthesis began with the treatment of benzaldehyde **31**[26] under a Mitsunobu protocol (1 M THF, 2 equiv of $TMS(CH_2)_2OH$, PPh_3, and DIAD) followed by carbonate formation (1 M CH_2Cl_2, 1.1 equiv BOC_2O, 0.5 equiv of Hunig's base, cat. DMAP) resulting in the bis-protected aldehyde **32** in 80% yield over two steps. When **32** (0.1 M Et_2O) was subjected to PhMgBr (1.05 equiv) in the presence of enol ether (−)-**9** (2.0 equiv) at −78 °C and warmed over 3 h to room temperature, adduct (+)-**33** arose in 83% yield. Hydrolysis of **33** (0.1 M 1:1 H_2O/CH_3CN, 0.6 equiv of CSA, 70 °C, 6 h) afforded the lactol **34** in 91% yield along with the chiral alcohol. Reduction of lactol **34** (0.1 M THF, 3 equiv of $LiAlH_4$, 0 °C, 5 min), followed by methylation (3 equiv of CH_2N_2, 12 h) afforded the primary alcohol (+)-**36** in 74% yield over two steps. Introduction of the desired alkene was accomplished by the conversion of the primary alcohol **36** into the corresponding selenide **37** (0.1 M THF, 2 equiv of PhSeCN, 2 equiv of PBu_3, rt, 5 h) followed by oxidation (0.5 M 2:1 $MeOH/H_2O$, 2 equiv of $NaIO_4$, 2 equiv of $NaHCO_3$, 40 °C), which resulted in spontaneous *syn*-elimination to form the terminal olefin **38**.[27] Finally, cleavage (0.2 M DMF, 2 equiv of CsF, 160 °C, 6 h) of the $-O(CH_2)_2TMS$ ether afforded synthetic *R*-mimosifoliol (**2**), which is identical in every respect to (+)-**2**[25] isolated from natural sources.

The formal synthesis of(+)-tolterodine (**1**) was achieved in three steps and 65% overall yield (Scheme 5). The synthesis began with *o*-Boc salicylaldehyde **40** available from 2-hydroxy-5-methyl benzaldehyde (**39**) (1 M CH_2Cl_2, 1.1 equiv of BOC_2O, 0.5 equiv of Hunig's base, cat. DMAP) in 95% yield. Aldehyde **40** was subjected to PhMgBr (1.05 equiv) in the presence of enol ether (−)-**9** (2.0 equiv) at −78 °C and then warmed over 3 h to room temperature to afford (+)-**41** in 90% yield as a single diastereomer. The cycloadduct (+)-**41** (0.1 M 1:1 H_2O/CH_3CN, 0.6 equiv of CSA, 70 °C, 6 h) was hydrolyzed to produce lactol **42**[28] in 85% yield. This constitutes a formal synthesis of (+)-tolterodine (**1**) as application of the Botteghi reductive amination with **42** yields the urological drug in 90% yield.[29]

Conclusions

The first examples of enantioselective cycloadditions of *o*-QMs with chiral enol ether **9** have been demon-

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[25] Fullas, F.; Kornberg, L. J.; Wani, M. C.; Wall, M. E. *J. Nat. Prod.* **1996**, *59*, 190−192.

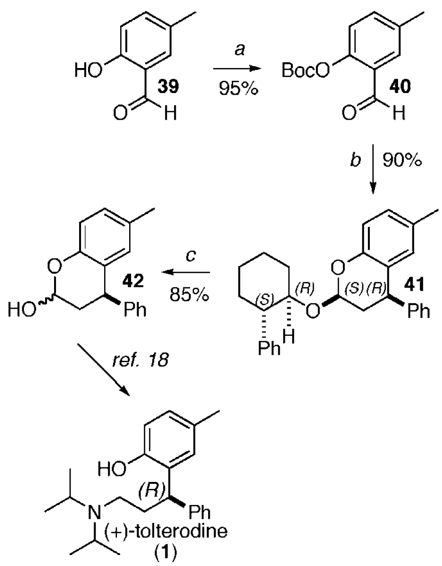
[26] Mali, R. S.; Manekar, A. R.; Tilve, S. G. *Org. Prep. Proced. Int.* **1992**, *24*, 52−54.

[27] Bissel, P.; Nazih, A.; Sablong, R.; Lepoittevin, J.-P. *Org. Lett.* **1999**, *1*, 1283−1285.

[28] Gage, J. R.; Cabaj, J. E. (Pharmacia & Upjohn Co.). US Patent 5,922,914, 1999.

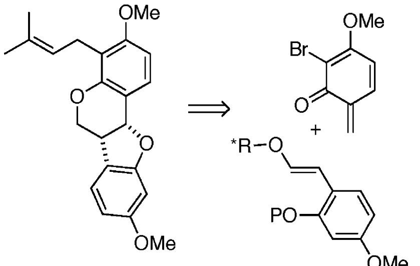
[29] Botteghi, C.; Corrias, T.; Marchetti, M.; Paganelli, S.; Piccolo, O. *Org. Process Res. Dev.* **2002**, *6*, 379−383.

SCHEME 5[a]



[a] (a) BOC_2O (1.1 equiv), Hunig's base (0.5 equiv), DMAP (cat.), 0.1 M CH_2Cl_2; (b) PhMgBr (1.05 equiv), (−)-**9** (2 equiv), 0.1 M Et_2O, −78 °C to rt, 3 h; (c) CSA (0.6 equiv), 0.1 M 1:1 H_2O/CH_3CN, 70 °C, 5 h.

SCHEME 6



bitucarpin A

strated. The cycloadditions of *trans*-2-phenyl-1-cyclohexanol vinyl ether (**9**) with *o*-QMs formulate chiral benzylic junctions in >95% de. The chiral alcohol is recovered by hydrolysis and the resulting lactol can be transformed into any number of useful materials as shown by the syntheses of (+)-tolterodine (**1**) and (+)-mimosifoliol (**2**). We anticipate future asymmetric synthesis of the chiral chroman bitucarpin A (Scheme 6). This compound was isolated from the aerial plants of Mediterranean papilionaceaous plants *Bituminaria morisiana* and *B. bituminosa* and has antimicrobial activity.[30] It is envisioned to set the 3-stereocenter of the chroman adduct by a cycloaddition of the corresponding *o*-QM with a substituted enol ether.

Experimental Section

General Procedure for Chroman Synthesis for Compounds 16−28, 30, 33, and 41. Method A. A flame-dried flask equipped with stir-bar and nitrogen line was charged with an aldehyde (0.1 M Et_2O) and an enol ether (2 equiv). The solution was cooled to −78 °C, and a Grignard reagent (1.05 equiv) was added dropwise. The reaction mixture was warmed to rt over 3 h, quenched with 1 M $NaHCO_3$, and extracted with Et_2O. The ether layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude mixture was then chromatographed through silica gel, eluting with petroleum ether/EtOAc (95:5). **Method B.** A flame-dried flask equipped with a stir bar and nitrogen line was charged with an aldehyde (0.1 M Et_2O) and then cooled to 0 °C. The appropriate organolithium reagent (1.05 equiv) was added dropwise and then stirred for 15 min. The reaction mixture was cooled to −78 °C, and the enol ether (5 equiv) was added, followed by $MgBr_2{\cdot}OEt_2$ (1 equiv). The reaction mixture was warmed to rt over 3 h, quenched with 1 M $NaHCO_3$, and extracted with Et_2O. The ether layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude mixture was then chromatographed through silica gel, eluting with petroleum ether/EtOAc (95:5).

Compound 16. General Procedure for Chroman Synthesis (Method A). ^1H NMR (400 MHz, $CDCl_3$): δ 7.37−7.17 (m, 10H), 6.77 (s, 1H), 6.27 (s, 1H), 5.11−5.06 (q, 1H, J = 6.6 Hz), 5.03−5.00 (m, 1H), 4.07−4.03 (m, 1H), 3.55 (s, 3H), 2.28−2.18 (m, 2H), 1.56 (s, 9H), 1.48 (d, 3H, J = 6.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7, 147.2, 145.5, 144.1, 143.1, 139.7, 128.8, 128.7, 128.6, 127.9, 126.9, 126.6, 123.3, 113.4, 111.6, 96.8, 83.6, 75.3, 56.6, 41.3, 37.5, 27.8, 24.4. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3055, 2984, 1761, 1505, 1419, 1371. HRMS (ESI-TOF) (M$^+$ + Na): *m/z* calcd for $C_{29}H_{32}O_6$ 476.2199, found 476.2204.

Compound 17. General Procedure for Chroman Synthesis (Method A). ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.17 (m, 10H), 6.32 (s, 1H), 6.03 (s, 1H), 5.29−5.27 (m, 1H), 4.18 (s, 1H), 4.12−4.09 (m, 1H), 3.58 (s, 3H), 2.47−2.42 (m 1H), 2.31−2.25 (m, 1H), 1.55 (s, 9H), 0.78 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.6, 146.9, 145.5, 144.5, 140.8, 139.6, 128.7, 128.6, 128.5, 127.3, 127.0, 126.7, 123.0, 113.3, 112.1, 101.2, 91.6, 83.4, 56.7, 40.1, 36.0, 32.1, 27.8, 26.2. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3053, 2972, 2870, 1761, 1504, 1452, 1421, 1394, 1364, 1205, 1151, 11261047, 1007. HRMS (EI): *m/z* calcd for $C_{32}H_{38}O_6$ 518.2668, found 518.2679.

Compound 18. General Procedure for Chroman Synthesis (Method B). ^1H NMR (400 MHz, $CDCl_3$): δ 7.37−7.23 (m, 10H), 6.72 (s, 1H), 6.34 (s, 1H), 5.33 (s, 1H), 5.23−5.20 (m, 1H), 4.15−3.99 (m, 3H), 3.58 (s, 3H), 2.41−2.35 (m, 2H), 1.56 (s, 9H), 1.53−1.48 (m, 2H), 1.27−1.20 (m, 2H), 0.89−0.83 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 151.7, 146.6, 145.9, 144.1, 139.9, 136.0, 128.9, 128.9, 128.8, 128.7, 127.5, 126.9, 123.0, 113.6, 111.7, 97.7, 83.6, 78.9, 65.3, 56.7, 40.5, 36.5, 30.6, 27.8, 19.1, 13.8. IR (CH_2Cl_2, ν_{max} cm^{-1}) 2962, 2932, 2873, 1755, 1732, 1514, 1504, 1446, 1371, 1150, 1049. HRMS (ESI-TOF) (M$^+$ + Na): *m/z* calcd for $C_{33}H_{38}O_8$ 585.2567, found 585.2480.

Compound 19. General Procedure for Chroman Synthesis (Method A). ^1H NMR (400 MHz, $CDCl_3$): δ 7.33−7.17 (m, 5H), 6.82 (s, 2H), 6.75 (s, 1H), 6.29 (s, 1H), 5.58 (q, 1H, J = 7 Hz), 4.95−4.92 (m, 1H), 4.07−4.03 (m, 1H), 3.56 (s, 3H), 2.35 (s, 6H), 2.26 (s, 3H), 2.24−2.17 (m, 2H), 1.56 (s, 9H), 1.52−1.50 (d, 3H, J = 7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.7, 147.3, 145.6, 144.3, 139.7, 137.0, 134.5, 128.8, 128.7, 128.4, 127.0, 123.3, 113.6, 111.6, 96.4, 83.6, 77.5, 71.2, 56.7, 41.2, 37.6, 27.8, 21.0, 20.5, 20.4. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3004, 2979, 2934, 2971, 1760, 1609, 1505, 1464, 1454, 1416, 1371, 1274. HRMS (ESI-TOF) (M$^+$ + Na): *m/z* calcd for $C_{32}H_{38}O_6$ 541.2566, found 541.2558.

Compound 20. General Procedure for Chroman Synthesis (Method A). ^1H NMR (400 MHz, $CDCl_3$): δ 7.33−7.19 (m, 5H), 6.73 (s, 1H), 6.28 (s, 1H), 5.25−5.22 (m, 1H), 4.18−4.14 (m, 1H), 3.56 (s, 3H), 3.45−3.43 (m, 1H), 2.36−2.15 (m, 4H), 1.64−1.57 (m, 2H), 1.55 (s, 9H), 1.49−0.74 (m, 14H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5, 145.6, 144.2, 139.7, 128.8, 128.7, 127.0, 123.3, 113.4, 111.9, 101.3, 83.6, 81.6, 56.7, 48.6, 43.5, 41.8, 37.9, 34.5, 31.9, 27.8, 25.8, 23.5, 22.5, 21.2, 16.5. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2958, 2927, 2870, 1761, 1603, 1505, 1454, 1417, 1371, 1274, 1207. HRMS (EI): *m/z* calcd for $C_{31}H_{42}O_6$ 510.2980, found 510.2972.

Compound 21. General Procedure for Chroman Synthesis (Method A). ^1H NMR (400 MHz, $CDCl_3$): 7.34−7.08 (m, 15H), 6.75 (s, 1H), 6.36 (s, 1H), 4.87−4.85 (m, 1H), 4.84−

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(30) Pistelli, L.; Noccioli, C.; Appendino, G.; Bianchi, F.; Sterner, O.; Ballero, M. *Phytochemistry* **2003**, *64*, 595−598.

4.78 (m, 1H), 3.93−3.90 (m, 1H), 3.61 (s, 3H), 2.33−1.62 (m, 7H), 1.59 (s, 9H) 1.39−1.37 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 147.1, 146.6, 145.5, 145.4, 144.7, 139.7, 128.7, 128.7, 128.5, 128.4, 127.7, 127.2, 126.5, 126.1, 125.7, 122.7, 113.7, 111.9, 100.7, 87.2, 83.6, 60.2, 56.6, 40.3, 36.4, 34.9, 32.1, 27.8, 20.5. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2975, 2937, 1761, 1600, 1504, 1495, 1447, 1415, 1371, 1278. HRMS (EI): *m/z* calcd for $C_{38}H_{40}O_6$ 592.2825, found 592.2806.

Compound 22. General Procedure for Chroman Synthesis (Method A). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.00 (m, 5H), 6.89−6.59 (m, 2H), 4.46−4.44 (m, 1H), 3.70−3.64 (m, 1H), 2.62−2.50 (m, 2H), 2.23−2.21 (m, 1H), 1.92−1.58 (m, 3H), 1.55 (s, 9H), 1.46−1.21 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.3, 152.2, 150.2, 144.5, 128.3, 128.2, 128.0, 126.5, 125.4, 113.6, 110.2, 100.7, 83.9, 51.7, 35.5, 34.9, 33.0, 29.9, 27.9, 27.8, 26.0, 25.5, 21.4. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2990, 2930, 2856, 1757, 1609, 1494, 1370, 1253. HRMS (EI): *m/z* calcd for $C_{27}H_{34}O_5$ 438.2406, found 438.2413.

Compound 23. General Procedure for Chroman Synthesis (Method A). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.22 (m, 5H), 6.73 (s, 1H), 6.70 (s, 1H), 5.02 (q, 1H, $J = 6$ Hz), 4.97−4.94 (m, 1H), 3.80 (s, 3H), 2.90−2.85 (m, 1H), 2.09−2.04 (m, 1H), 1.79−1.72 (m, 1H), 1.57 (s, 9H), 1.48−1.46 (d, 3H, $J = 6$ Hz), 1.40−1.38 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 146.2, 145.7, 143.3, 139.4, 128.7, 127.8, 126.7, 125.6, 112.0, 111.6, 96.4, 83.5, 75.1, 56.9, 35.8, 28.3, 27.9, 24.5, 21.8. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2982, 2934, 1759, 1502, 1454, 1416, 1371, 1277, 1252, 1128, 908. HRMS (EI): *m/z* calcd for $C_{24}H_{30}O_6$ 414.2042, found 414.2058.

Compound 24. General Procedure for Chroman Synthesis (Method A). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30−7.05 (m, 10H), 6.68−6.51 (m, 2H), 4.51−4.48 (m, 1H), 3.72−3.66 (m, 2H), 2.53−2.33 (m, 2H), 1.91−1.62 (m, 3H), 1.55 (s, 9H), 1.49−1.28 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3, 152.1, 150.5, 144.2, 130.0, 128.8, 128.7, 128.3, 128.3, 126.9, 123.5, 113.7, 110.2, 101.4, 84.5, 83.6, 51.6, 41.1, 36.8, 35.0, 32.7, 27.9, 26.0, 25.5. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3057, 2934, 2859, 1757, 1653, 1558, 1497, 1414, 1371. HRMS (ESI-TOF) (M^+ + Na): *m/z* calcd for $C_{32}H_{36}O_5$ 523.2460, found 523.2439.

Compound 25. General Procedure for Chroman Synthesis (Method A). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.16 (m, 10H), 6.79 (s, 1H), 6.66−6.57 (m, 2H), 5.12 (q, 1H, $J = 6$ Hz), 5.10−5.07 (m, 1H), 4.05−4.01 (m, 1H), 2.31−2.18 (m, 2H), 1.57 (s, 9H), 1.51 (d, 3H, $J = 6$ Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3, 152.1, 150.6, 144.0, 143.1, 130.1, 128.8, 128.8, 128.7, 128.0, 127.0, 126.7, 123.5, 113.9, 110.2, 97.3, 83.7, 75.6, 41.1, 37.3, 27.9, 24.5. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3030, 2980, 2934, 1757, 1684, 1599, 1495, 1454, 1371, 1280, 1134, 1043. HRMS (EI) *m/z* calcd for $C_{28}H_{30}O_5$ 446.2093, found 446.2096.

Compound 26. General Procedure for Chroman Synthesis (Method A). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.19 (m, 5H), 6.66 (s, 1H), 6.59 (s, 1H), 4.41−4.39 (m, 1H), 3.77 (s, 3H), 3.65−3.63 (m, 1H), 2.61−2.49 (m, 2H), 2.22−2.20 (m, 1H), 1.91−1.56 (m, 6H), 1.55 (s, 9H), 1.54−1.22 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 146.2, 145.5, 144.5, 139.2, 128.3, 128.2, 126,4, 126.6, 111.8, 111.6, 100.4, 83.8, 83.5, 56.8, 51.7, 35.4, 34.9, 33.0, 28.1, 27.8, 26.0, 25.5, 21.7. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2934, 2858, 1759, 1502, 1416, 1371. HRMS (EI): *m/z* calcd for $C_{28}H_{36}O_6$ 468.2512, found 468.2532.

Compound 27. General Procedure for Chroman Synthesis (Method A). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.12 (m, 6H), 6.73−6.70 (m, 2H), 5.07−5.03 (q, 1H, $J = 6$ Hz), 5.01−4.99 (m, 1H), 2.89−2.85 (m, 1H), 2.09−2.05 (m, 1H), 1.79−1.73 (m, 1H), 1.57 (s, 9H), 1.49−1.47 (d, 3H, $J = 6$ Hz), 1.38−1.37 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.2, 152.2, 150.3, 143.2, 128.7, 128.1, 127.9, 126.7, 125.4, 113.8, 110.2, 96.7, 83.6, 75.2, 35.9, 27.9, 27.8, 24.5, 21.6. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2982, 2932, 1757, 1614, 1591, 1499, 1371, 1278, 1249, 1026. HRMS (EI): *m/z* calcd for $C_{23}H_{28}O_5$ 384.1937, found 384.1941.

Compound 28. General Procedure for Chroman Synthesis (Method A). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.07 (m, 10H), 6.67 (s, 1H), 6.20 (s, 1H), 4.46−4.43 (m, 1H), 3.75−3.71 (m, 1H), 3.66−3.65 (m, 1H), 3.53 (s, 3H), 2.47−2.46 (m, 1H), 2.31−2.30 (m, 1H), 1.90 (m, 6H), 1.55 (s, 9H), 1.51−1.27 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.8, 147.4, 145.4, 144.3, 144.2, 139.6, 128.8, 128.6, 128.3, 128.3, 126.8, 126.5, 123.3, 113.4, 111.7, 101.0, 84.4, 83.6, 56.6, 51.6, 41.4, 37.1, 34.9, 32.7, 27.8, 25.9, 25.5. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3029, 2934, 2858, 1761, 1605, 1483, 1450, 1414, 1371, 1342. HRMS (ESI-TOF) (M^+ + Na): *m/z* calcd for $C_{33}H_{38}O_6$ 553.2566, found 553.2562.

Compound 30. General Procedure for Chroman Synthesis (Method A). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.00 (m, 10H), 6.68 (s, 1H), 6.09 (s, 1H), 4.39−4.37 (m, 1H), 3.78−3.74 (m, 1H), 3.50 (s, 3H), 3.35−3.32 (m, 1H), 2.60−2.53 (m, 1H), 2.47−2.44 (m, 1H), 1.88−1.56 (m, 5H), 1.55 (s, 9H), 1.50−1.31 (m, 3H) 0.18−0.17 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.9, 147.1, 145.5, 144.7, 143.3, 139.5, 129.5, 128.5, 128.4, 128.3, 126.8, 126.4, 124.0, 113.8, 111.4, 105.8, 84.4, 83.5, 56.6, 51.8, 49.6, 40.3, 35.2, 34.2, 27.8, 26.0, 25.5, 14.3. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3051, 2984, 2934, 2858, 1761, 1603, 1504, 1454, 1418, 1371, 1140; HRMS (EI) (M^+ + Na): *m/z* calcd for $C_{34}H_{40}O_6$ 544.2825, found 544.2848.

Compound 32. (a) A flame-dried flask equipped with stirbar and nitrogen line was charged with PPh_3 (2 equiv, 0.5 M THF). The reaction mixture was cooled to 0 °C, and DIAD (2 equiv) was added dropwise. After 20 min, the solution solidified and the phenol **31** (1 equiv) and 2-trimethylsiylethanol (2 equiv) were added. The reaction mixture was stirred overnight at room temperature. Silica gel was added to the reaction mixture and concentrated in vacuo. The reaction mixture was chromatographed with petroleum ether/EtOAc (8:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.41 (s, 1H), 9.69 (s, 1H), 6.99 (s, 1H), 6.44 (s, 1H), 4.20−4.16 (m, 2H), 3.86 (s, 3H), 1.25−1.22 (m, 2H), 0.09 (s, 9H). HRMS (EI): *m/z* calcd for $C_{13}H_{20}O_4Si$ 268.113, found 268.1125. (b) A flame-dried flask equipped with a stir-bar and a nitrogen line containing the phenol (0.1 M CH_2Cl_2) obtained above, Hunig's Base (0.6 equiv), DMAP (0.05 equiv), and BOC_2O (1.2 equiv) was stirred overnight. The reaction was quenched with 1 M NH_4Cl and extracted twice with CH_2Cl_2. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude mixture was then chromatographed on silica gel, eluting with petroleum ether/EtOAc (9:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.06 (s, 1H), 7.32 (s, 1H), 6.69 (s, 1H), 4.19 (t, $J = 8.4$ Hz, 2H), 3.91 (s, 3H), 1.59 (s, 9H), 1.25 (t, $J = 8.4$ Hz, 2H), 0.10 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.2, 154.5, 151.9, 148.3, 147.7, 120.6, 109.7, 106.6, 84.7, 67.3, 56.4, 27.9, 17.7, −1.3. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2956, 2933, 2857, 1761, 1681, 1607, 1512.1, 1275. LRMS (EI): *m/z* calcd for $C_{18}H_{28}O_6Si$ 368, found 368.

Compound 33. General Procedure for Chroman Synthesis (Method A). $[\alpha]_D = +15$ ($c = 0.6$, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26−7.21 (m, 10H), 6.37 (s, 1H), 6.11 (s, 1H), 4.47−4.45 (m, 1H), 4.09−4.05 (t, $J = 8.3$ Hz, 2H), 3.74−3.56 (m, 2H), 3.54 (s, 3H), 2.51−2.45 (m, 1H), 2.35−2.23 (m, 1H), 1.91−1.19 (m, 11H), 0.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 147.5, 144.9, 144.2, 143.7, 128.7, 128.4, 128.2, 127.4, 126.6, 126.4, 115.8, 112.7, 102.2, 101.1, 84.3, 66.3, 56.5, 51.6, 41.0, 37.4, 35.0, 32.7, 25.9, 25.4, 17.9, −1.3. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2934, 2858, 1618, 1600, 1504, 1494, 1407, 1252. HRMS (EI): *m/z* calcd for $C_{33}H_{42}O_4Si$ 530.7697, found 530.2835.

General Procedure for Chroman Hydrolysis for Synthesis of Compounds 34 and 42. A flask containing a stir bar was charged with a chroman (0.1 M 1:1 CH_3CN/H_2O) and CSA (0.6 equiv). While the reaction mixture stirred, THF was added dropwise until the solution became translucent. A water-jacketed reflux condenser open to the atmosphere was connected and the reaction heated to 100 °C for 6 h. The reaction mixture was cooled, quenched with 1 M HCl, and extracted with chloroform. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in vacuo.

Compound 34. General Procedure for Chroman Hydrolysis. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.20 (m, 5H), 6.43 (s, 1H), 6.26 (s, 1H), 5.60−5.58 (m, 1H), 4.27−4.23 (m, 1H), 4.08 (t, *J* = 8.5 Hz, 2H), 3.59 (s, 3H), 2.29−2.23 (m, 1H), 2.17−2.06 (m, 1H), 1.23−1.21 (t, *J* = 8.5 Hz, 2H), 0.07 (s, 2H). HRMS (EI): *m*/*z* calcd for $C_{21}H_{28}O_4Si$ 372.1760, found 372.1767.

Compound 35. The lactol **34** (0.1 M THF) was added to a flame-dried flask equipped with a stir bar and cooled to 0 °C. $LiAlH_4$ (2 equiv) was added to the reaction mixture and stirred for 10 min. The reaction was quenched with 1 M HCl, extracted with chloroform, washed with brine, and dried with Mg_2SO_4. ^1H NMR (400 MHz, $CDCl_3$): δ 7.34−7.20 (m, 5H), 6.47 (s, 1H), 6.43 (s, 1H), 4.53−4.49 (m, 1H), 4.09−4.04 (m, 2H), 3.87−3.82 (s, 1H), 3.66 (s, 3H), 3.57−3.51 (m, 1H), 2.42−2.34 (m, 1H), 2.17−2.06 (m, 1H), 1.26−1.18 (m, 2H), 0.07 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.2, 147.8, 144.2, 144.0, 128.7, 128.3, 126.6, 121.3, 112.8, 103.0, 66.4, 60.9, 56.9, 38.6, 36.7, 18.0, −1.3. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3591, 3319, 2955, 2898, 1618, 1507, 1466, 1450, 1411. HRMS (EI): *m*/*z* calcd for $C_{21}H_{30}O_4Si$ 374.1910, found 374.1907.

Compound 36. The diol **35** was added to a flask containing a stir bar and freshly prepared CH_2N_2 (10 equiv, 0.43 M Et_2O) open to the atmosphere. The reaction was monitored by thin-layer chromatography, and CH_2N_2 was added until the reaction was complete (~12 h). The reaction mixture was concentrated in vacuo and chromatographed on silica gel with petroleum ether/EtOAc (9:1). $[\alpha]_D$ = +41 (*c* = 0.37, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.44−7.16 (m, 5H), 6.68 (s, 1H), 6.47 (s, 1H), 4.53−4.49 (m, 1H), 4.14−4.13 (m, 2H), 3.74 (s, 3H), 3.72 (s, 3H), 2.90−2.87 (m, 2H), 2.45−2.39 (m, 2H), 1.24−1.21 (m, 2H), 0.12 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 147.5, 144.9, 128.5, 128.2, 126.2, 124.7, 113.2, 100.0, 76.7, 66.9, 61.3, 57.1, 57.0, 38.8, 37.9, 18.1, −1.2. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3688, 3053, 2955, 2933, 1607, 1506, 1274. HRMS (EI): *m*/*z* calcd for $C_{22}H_{32}O_4Si$ 388.5726, found 388.2083.

Compound 37. The alcohol **36** (0.1 M) was added to a flame-dried round-bottom flask equipped with a stir bar. PhSeCN (1.05 equiv) and BBu_3 (1.1 equiv) were added to the reaction mixture and allowed to stir for 2 h. The reaction mixture was concentrated in vacuo and chromatographed in petroleum ether/EtOAc (9:1). ^1H NMR (400 MHz, $CDCl_3$): δ 7.44−7.16 (m, 10H), 6.68 (s, 1H), 6.47 (s, 1H), 4.47−4.45 (m, 1H), 4.12−4.08 (m, 2H), 3.74 (s, 3H), 3.72 (s, 3H), 2.86−2.82 (m, 2H), 2.39−2.37 (m, 2H), 1.21−1.17 (m, 2H), 0.077 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.6, 147.5, 144.4, 143.9, 132.5, 130.6, 129.2, 128.5, 128.2, 126.8, 126.2, 124.3, 112.9, 100.0, 66.9, 57.1, 56.7, 43.4, 35.8, 26.1, 18.1, −1.22. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2954, 2904, 1609, 1580, 1507, 1494, 1478, 1466, 1449, 1438, 1400, 1314, 1273, 1250, 1181, 1130. HRMS (EI): *m*/*z* calcd for $C_{28}H_{36}O_3SeSi$ 528.1599, found Se^{76} 524.1630.

Compound 38. The selenide **37** (0.5 M 1:1/H_2O:MeOH) was added to a flask equipped with a stir bar, $NaIO_4$ (1.05 equiv), and $NaHCO_3$ (2 equiv). THF was added dropwise until the reaction became transparent. The reaction was then stirred at 70 °C for 8 h. The reaction was extracted with Et_2O and chromatographed in petroleum ether/EtOAc (95:5). ^1H NMR (400 MHz, $CDCl_3$): δ 7.29−7.19 (m, 5H), 6.69 (s, 1H), 6.52 (s, 1H), 6.32−6.25 (m, 1H), 5.22−5.19 (m, 1H), 5.11−5.09 (m, 1H), 4.95−4.91 (s, 1H), 4.14−4.10 (m, 2H), 3.76 (s, 3H), 3.71 (s, 3H), 1.26−1.19 (m, 2H), 0.08 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.4, 147.6, 143.8, 143.5, 140.8, 128.7, 128.3, 126.2, 123.6, 116.2, 114.1, 100.1, 66.7, 57.0, 57.0, 47.4, 18.1, −1.2. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3053, 2956, 2905, 1608, 1506, 1465, 1448, 1340, 1312, 1250, 1209, 1180. HRMS (EI): *m*/*z* calcd for $C_{22}H_{30}0_3Si$ 370.1960, found 370.1953.

(*R*)-(+)-Mimosifoliol (2). The ether **38** (0.1 M DMF) was added to a flame-dried flask equipped with a stir bar and CsF (2 equiv). The reaction was stirred at 100 °C for 6 h. The reaction was diluted with H_2O, extracted with Et_2O, washed with brine, and dried with $MgSO_4$. $[\alpha]_D$ = +20 (*c* = 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.29−7.17 (m, 5H), 6.64 (s, 1H), 6.57 (s, 1H), 6.31−6.24 (m, 1H), 5.56 (s, 1H), 5.21−5.20 (m, 1H), 5.11−5.09 (m, 1H), 4.94−4.90 (m, 1H), 3.79 (s, 3H), 3.69 (s, 3H).

Compound 40. A flame-dried flask equipped with a stir bar and a nitrogen line containing phenol **39** (0.1 M CH_2Cl_2), Hunig's Base (0.6 equiv), DMAP (0.05 equiv), and BOC_2O (1.2 equiv) was stirred overnight. The reaction was quenched with 1 M NH_4Cl and extracted twice with CH_2Cl_2. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. The crude mixture was then chromatographed on silica gel, eluting with petroleum ether/EtOAc (9:1). ^1H NMR (400 MHz, $CDCl_3$): δ 10.15 (s, 1H), 7.68 (s, 1H), 7.43 (d, 1H, *J* = 8 Hz), 7.15 (d, 1H, *J* = 8 Hz), 2.18 (s, 3H), 1.58 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.1, 151.7, 150.2, 136.6, 136.2, 131.0, 128.0, 123.0, 84.6, 27.9, 20.9. IR (CH_2Cl_2, ν_{max} cm^{-1}): 2980, 2932, 2868, 1761, 1695, 1607, 1585, 1495, 1396, 1371, 1283, 1236, 1148. HRMS (EI) (M^+ + H): *m*/*z* calcd for $C_{13}H_{17}O_4$ 237.1049, found 237.1121.

Compound 41. General Procedure for Chroman Synthesis (Method A). ^1H NMR (400 MHz, $CDCl_3$): δ 7.32−7.07 (m, 10H), 6.90 (d, 1H, *J* = 8 Hz), 6.74 (d, 1H, *J* = 8 Hz), 4.50−4.48 (m, 1H), 3.77−3.66 (m, 2H), 2.51−2.34 (m, 2H), 2.10 (s, 3H), 1.90−1.27 (m, H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.5, 144.7, 144.4, 129.9, 129.7, 128.9, 128.5, 128.3, 128.3, 126.6, 126.5, 125.6, 117.1, 101.0, 84.3, 51.6, 41.3, 37.2, 35.0, 32.8, 26.0, 25.5, 20.7. IR (CH_2Cl_2, ν_{max} cm^{-1}): 3050, 2910, 2805, 1501, 1409. HRMS (EI): *m*/*z* calcd for $C_{28}H_{30}O_2$ 398.2246, found 398.2234.

Compound 42. General Procedure for Chroman Hydrolysis. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.19 (m, 5H), 6.94 (d, 1H, *J* = 8 Hz), 6.77 (d, 1H, *J* = 8 Hz), 6.58 (s, 1H), 5.63 (bs, H), 2.05 (s, 3H). IR (CH_2Cl_2, ν_{max} cm^{-1}): 3410, 3020, 2925, 1605, 1498, 1447, 1205, 1010. HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}O_2$ 240.1150, found 240.1140.

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Supporting Information Available: General methods are provided along with full spectral data (^1H and ^{13}C NMR, IR, and HRMS) for compounds **16**−**33**, **35**−**38**, **40** and **41**; ^1H NMR and HRMS for **34** and **42**; and ^1H NMR spectral data for **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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