Diastereoselective Total Synthesis of (±)-Basiliolide B and (±)-*epi*-8-BasiliolideB

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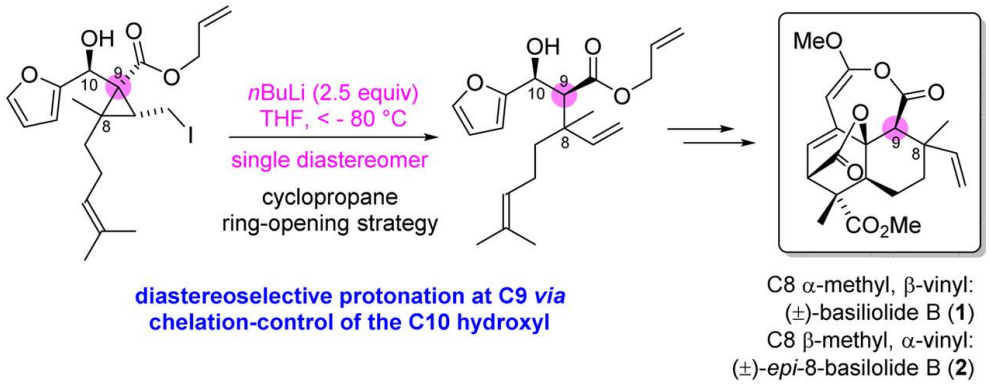
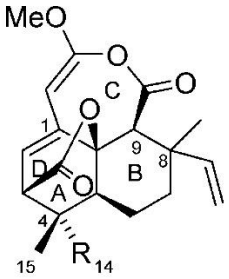
ABSTRACT: The C8 and C9 stereogenic centers of the basiliolide/transtaganolide family have been established stereoselectively using a cyclopropane ring-opening strategy, which has been studied by DFT calculations of a variety of lithium-chelating models. The highly functionalized intermediates obtained in this strategy were successfully employed for the diastereoselective total synthesis of (±)-basiliolide B and (±)-*epi*-8-basiliolide B. The decalin core with a lactone bridge was constructed via a 2-pyrone Diels−Alder (DA) cycloaddition, and the unprecedented seven-membered acyl ketene acetal was established by a biomimetic intramolecular O-acylation cyclization

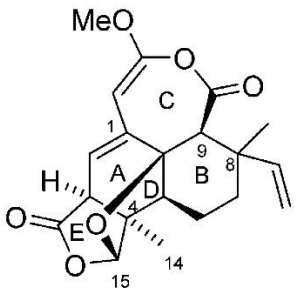


INTRODUCTION

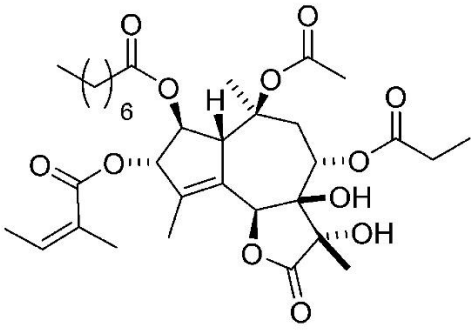
Basiliolides and transtaganolides, shown in Figure 1, are C-19 dilactone terpenolides isolated separately in 2005 from *Thapsiagarganica* L. (San Basilio, Sardinia) and *Thapsia transtagana* Brot. (Bouznika, Morocco) respectively.[1,2] These relatednatural products show inhibitory activity against sacro- and endoplasmic reticulum Ca^{2+}-ATPases (SERCA).[3] Thapsigargin, a sesquiterpene lactone isolated from *Thapsia garganica* L. in 1978, is a well-known SERCA inhibitor,[4] which binds to the E2conformation, the open form of SERCA, and leads to a dead- end complex.[5] Despite the structural differences, it has been proposed that basiliolides and transtaganolides are reversible SERCA inhibitors with similar modes of actions as those of thapsigargin.[3] The skeletons of basiliolides and transtaganolidesshare the same tricyclic core, the ABC ring, which contains a unique seven-membered acyl ketene acetal ring, the C ring, fused with a *trans*-decalin, the AB ring. The major structural differences among the members are the position of the lactone bridge, the oxidation states of the germinal dimethyl groups (C14 and C15) at C4, and the con*fi*guration of the all-carbon quaternary stereogenic center at C8.



R = CH_3, C8-(*R*): basiliolide A1 (transtaganolide D)
R = CH_3, C8-(*S*): basiliolide A2 (transtaganolide C)
R = CO_2CH_3, C8-(*R*): basiliolide B (**1**)
R = CO_2CH_3, C8-(*S*): *epi*-8-basilolide B (**2**)
R = CH_2OAc, C8-(*R*): basiliolide C



C8-(R*)*: transtaganolide A
C8-(*S*): transtaganolide B



thapsigargin

Figure 1. Structures of the basiliolide/transtaganolide family and thapsigargin.

The biosynthesis of members of the basiliolide/trans- taganolide family has been studied quite intensively.[6–10] It is generally believed that the ABD tricyclic ring system of transtaganolide E and F, the *seco* acid derivatives of trans- taganolide D/basiliolide A1 and transtaganolide C/basiliolide A2 respectively, is established via an enolate Claisen rearrange-ment and an intramolecular 2-pyrone Diels–Alder (DA) cycloaddition sequence[6] (Figure 2). This biogenetic pathway has been demonstrated independently by Johansson/Sterner[8] and by Stoltz,[9] and both sequences provided a roughly 2:1 diastereoisomeric mixture at C8. On the basis of the optical rotation comparison study, Stoltz proposed a nonenzymatic enloate Claisen rearrangement,[9d] which is contradicted by Johansson/Sterner's enzymatic proposal.[8a] The biosynthesis of the novel C ring, however, is more controversial, and in this connection, different biosynthetic pathways have been proposed.[2,6,8a] As shown in Figure 2, the seven-membered acyl ketene acetal moiety of the C ring could be constructed by *O*-methylation[2] of an acid anhydride (III) (path a), intra-molecular *O*-acylation[6,8a] of transtaganolide E and F (path b), or oxidation followed by electrocyclic ring opening of thecoisolated coumarin (IV) (path c).[2,6,9d] Recently, an attempt to synthesize the C ring by *O*-acylation of transtaganolide E and Fhas been reported to be very diffcult.[8b] Due to the fact that the embedded cyclic acyl ketene acetal moiety of the C ring can be readily hydrolyzed under acidic or basic conditions, the *seco* acid derivatives have been hypothesized to be the hydrolysis products of the basiliolides or transtaganolides. Formation of the C ring was *fi*rst

accomplished with reasonable yields by Stoltz's group by a formal [5 + 2] annulation process,[9c–e] and they completed the first total synthesis of (±)-basiliolide B in only seven steps with 1.1% overall yield.[9c] In the course of a biomimetic study of the basiliolide/transtaganolide family, our group previously demonstrated that the C ring of basiliolide B can be established by a biomimetic intramolecular *O*-acylationof the *seco* derivative.[10b] In the present paper, we report the details of this biomimetic study and the total synthesis ofbasiliolide B (1) and its *epi*-8 derivative (2), as well as a theoretical study of the diastereoselective synthesis of the C8 all-carbon quaternary stereogenic center by cyclopropane ring opening and protonation.

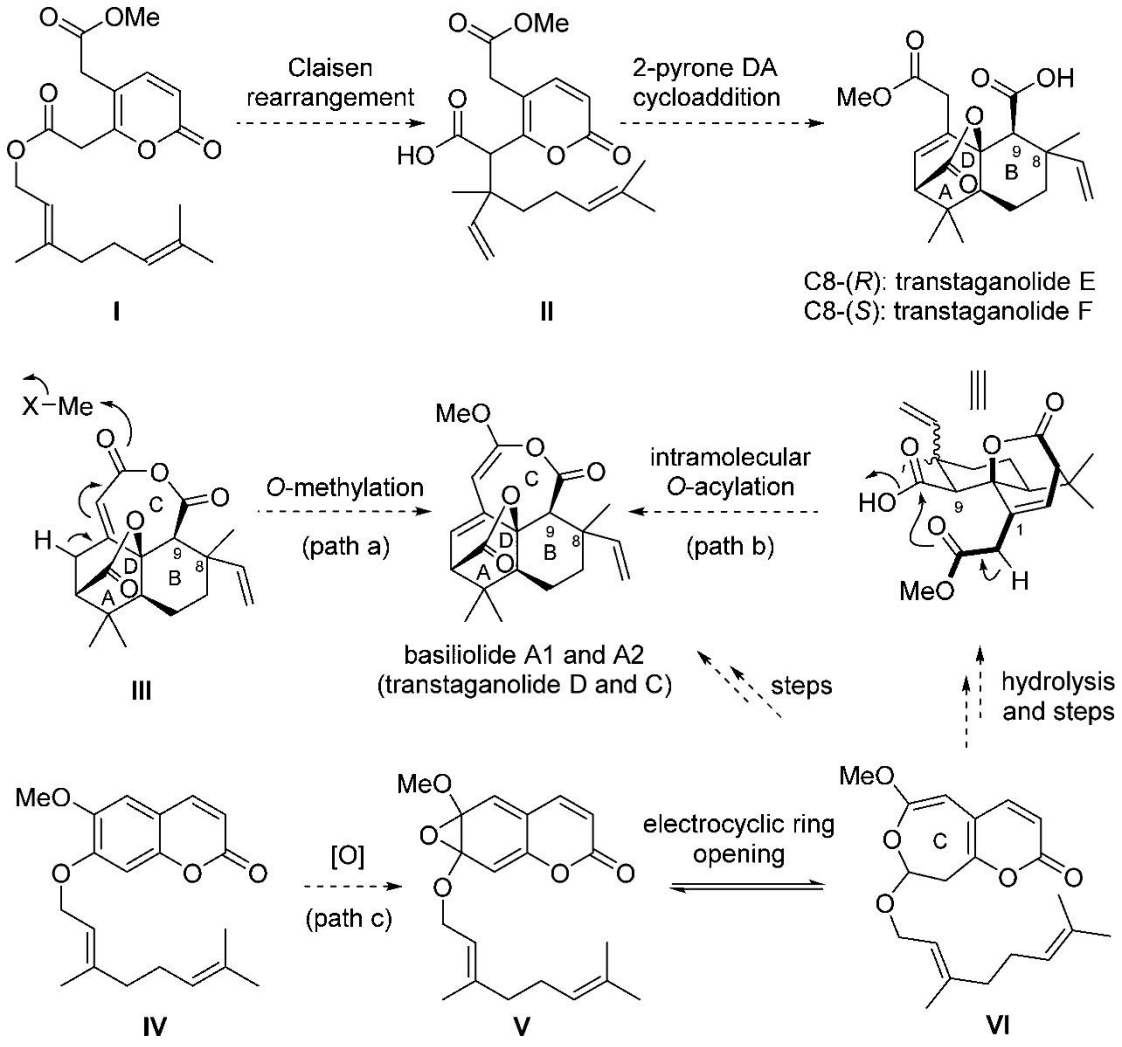


Figure 2. Biosynthesis proposals for the basiliolide/transtaganolide family.

RESULTS AND DISCUSSION

1. Establishment of Stereogenic Centers at C8 and C9 by a Cyclopropane Ring-Opening Strategy.

Although anumber of synthetic reports on the ABD tricyclic core have been reported, the enolate Claisen rearrangement is the onlymethod that has been used to establish stereogenic centers at the all-carbon quaternary carbon C8 and at C9 (Figure 3a),[7c,8,9c–e] which provided only poor to modest diastereose- lectivity, and the isolation of C8 diastereoisomers requires HPLC purification. Accordingly, we have designed a highly diastereoselective cyclopropane ring-opening strategy to establish the stereogenic centers at C8 and C9. As shown inFigure 3b, the cyclopropane (IX) can be readily obtained byintramolecular cyclopropanation of VII followed by opening ofthe lactone ring. Cyclopropane ring opening of IX is expected to provide X with high diastereoselectivity under either radical or lithium−halogen exchange conditions.

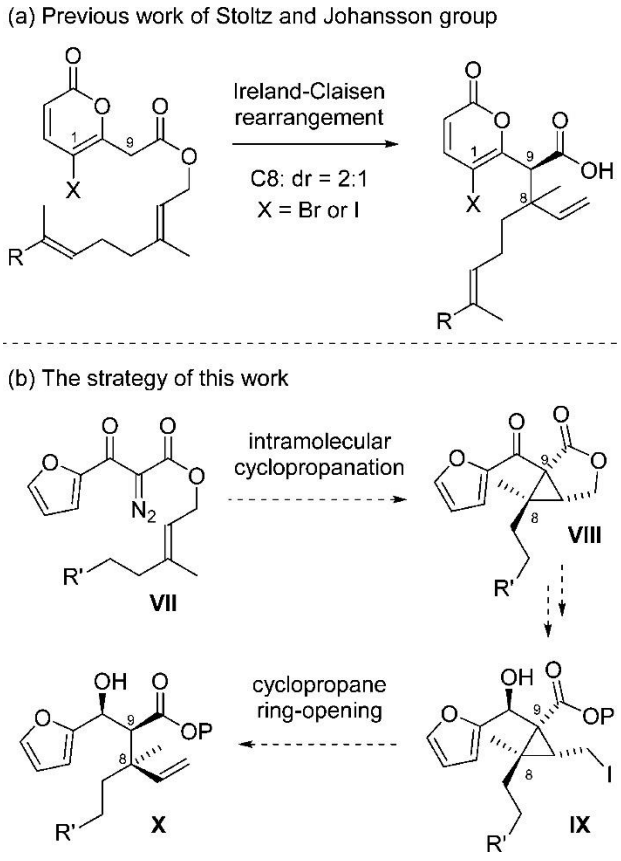
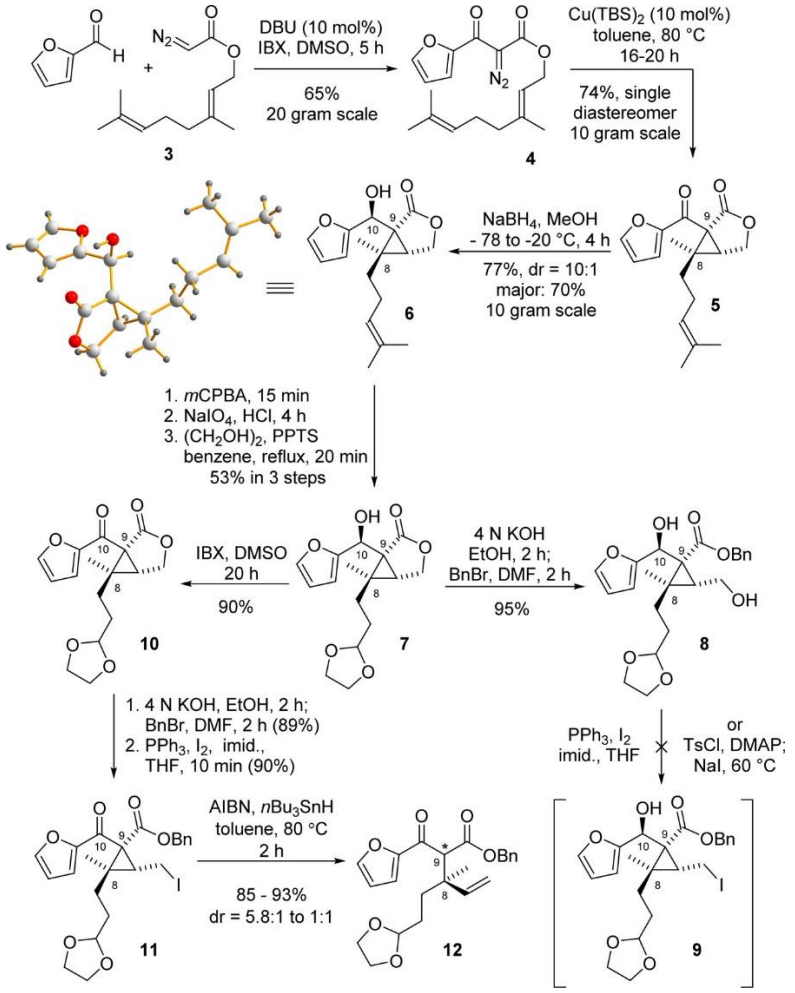


Figure 3. Strategies for construction of stereogenic centers at C8 and C9.

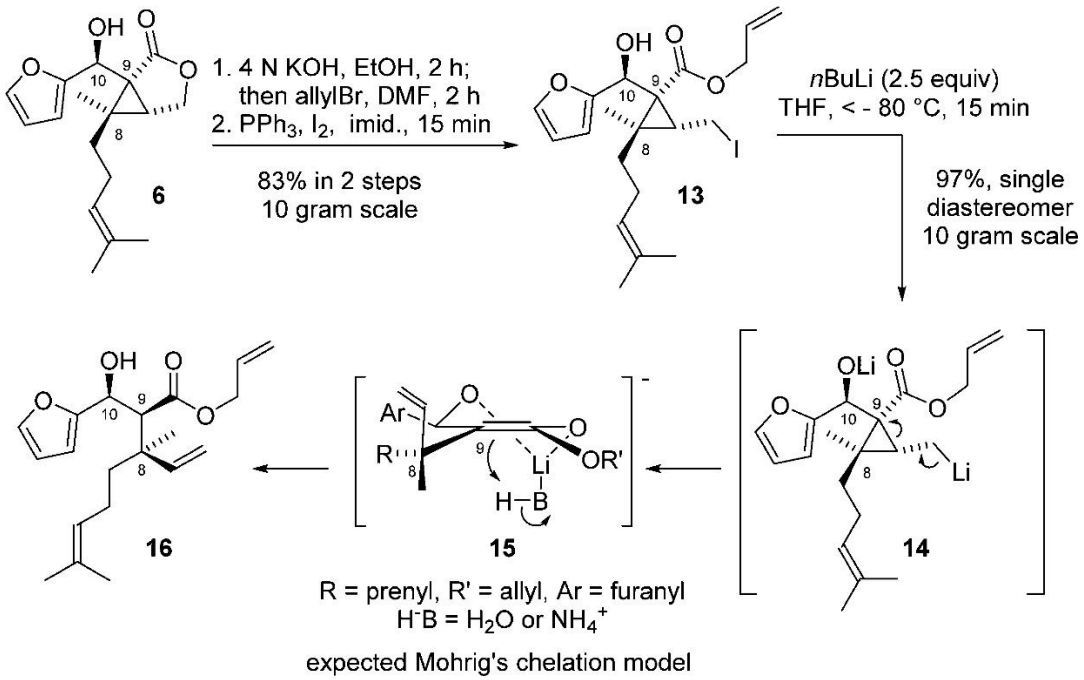
To investigate the diastereoselectivity of the cyclopropane ring-opening reactions under radical conditions, synthesis of substrates 9 and 11 began with the oxidative coupling of furan-2-carbaldehyde with the diazoacetate (3)[11] (Scheme 1). Taking advantage of common Rh and Cu catalyzed reactions,[12] intramolecular cyclopropanation of 4 was optimized with the $Cu(TBS)_2$ catalyst[13] in toluene at 80 °C, which gave 5 as a single diastereoisomer in 74% yield. Subsequent $NaBH_4$ reduction at low

temperature led to 6 with very good diastereoselectivity (dr = 10:1), and the major diastereoisomer was fully characterized by X-ray crystallography.[14] This three- step sequence can be repeated on a decagram scale with high yields. Since the alkene moiety of 6 could be potentially cyclized with the radical generated at C8 after the cyclopropanering opening, it was then converted to a cyclic acetal of 7 by epoxidation, oxidative cleavage, and acetal formation, a three- step procedure which provides a 53% overall yield. Hydrolysisof the lactone in 7 followed by esterification provided 8 in 89%yield. However, iodination of 8 with PPh_3/I_2/imidazole gave only a trace amount of the expected product (9) which was detected by LC-MS. Tosylation of 7 followed by iodination with sodium iodide in acetone at 60 °C resulted in only a traceamount of the iodide product (9) with complete consumptionof the tosylate intermediate, suggesting that 9 may not be stable under the iodination conditions. In a separate approach, the C10 hydroxyl in 7 was oxidized to the ketone and the corresponding lactone (10) was converted to its benzyl ester using the same procedures as was used for 8. Iodination of thisbenzyl ester using PPh_3/I_2/imidazole afforded the iodide (11) smoothly at 0 °C. With AIBN/nBu$_3$SnH in toluene at 80 °C,11 underwent a cyclopropane ring-opening reaction to give theexpected product (12) in very good yield (85−93%), but with awide range of dr values (5.8:1 to 1:1). This spread of dr valuescould be due to the high possibility of epimerization at C9 of 12.

Scheme 1. Cyclopropane Ring Opening under Radical Conditions

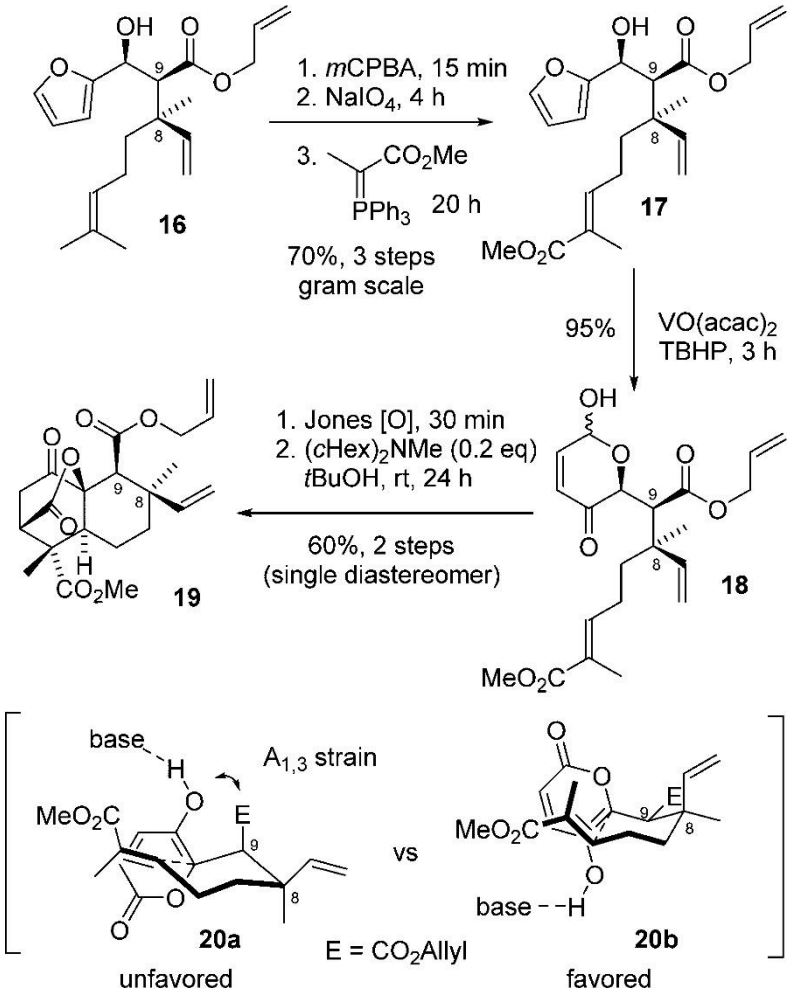


Scheme 2. Cyclopropane Ring Opening by Lithium−Halogen Exchange



In view of the inconsistent results obtained under radical conditions, we investigated whether the cyclopropane ring could be opened by halogen−lithium exchange. It was expectedthat the enolate generated *in situ* could be protonated diastereoselectively by Mohrig's chelation model (15).[15] To examine this hypothesis, 13 was prepared by hydrolysis of the lactone in 6, followed by esteri*fi*cation and iodination (Scheme 2). After an extensive study on the effects of organolithium andtemperature,[16] the optimal conditions were found to include using *n*-BuLi (2.5 equiv) below −80 °C, which provided the expected product (16) as a single diastereoisomer in excellent yield. Formation of the elimination side product was not observed under these conditions. The relative con*fi*gurations of 16 were determined by 2D NMR studies of a derivative of the DA product (19 in Scheme 3) after several transformations. This cyclopropane ring-opening strategy established the stereogenic centers at C8, C9, and C10 of 16 from furan-2- carbaldehyde and diazoacetate (3) in six steps on decagram scales with good overall yields.

Scheme 3. Construction of the Decalin Core via Base-Catalyzed 2-Pyrone DA Cycloaddition



2. A Theoretical Study on the Diastereoselective Protonation

Density functional theory (DFT) calculations were conducted to study the remarkable diastereoselectivity of the protonation of the enolate (15). Asymmetric protonation of enolates normally occurs under kinetic control,[17] and the current substrate (15) is unlikely to be an exception. Accordingly we focused on the transition states of the protonation process in which the stereogenic center at C9 is formed. As shown in Figure 4, the two transition state structures TS-S and TS-R could lead to diastereoisomers C9-(S) and C9-(R) respectively. In order to avoid the distraction posed by conformational space of irrelevant side chains, the model was built up by replacing the C8 moiety with a *tert*-butylgroup and the allyl ester with a methyl ester. The protonsource, H_2O, was envisaged to be guided by the lithium ion of enolate 15. Inspired by Collum's elegant work on elucidation ofstructures of organolithium compounds,[18] we propose that two lithium ions are presented with the alkoxide and the enolate moieties, with the oxygen atom of the alkoxide moiety serving as a bridge. THF solvent molecules are accommodated atunsaturated sites of the lithium ions.

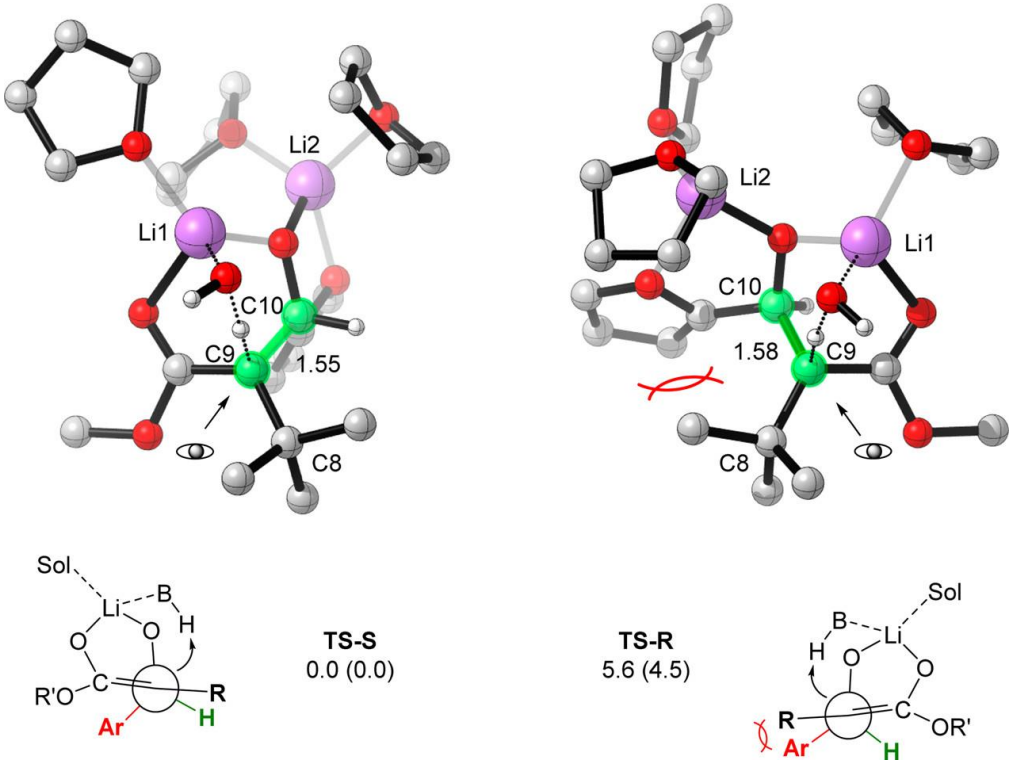


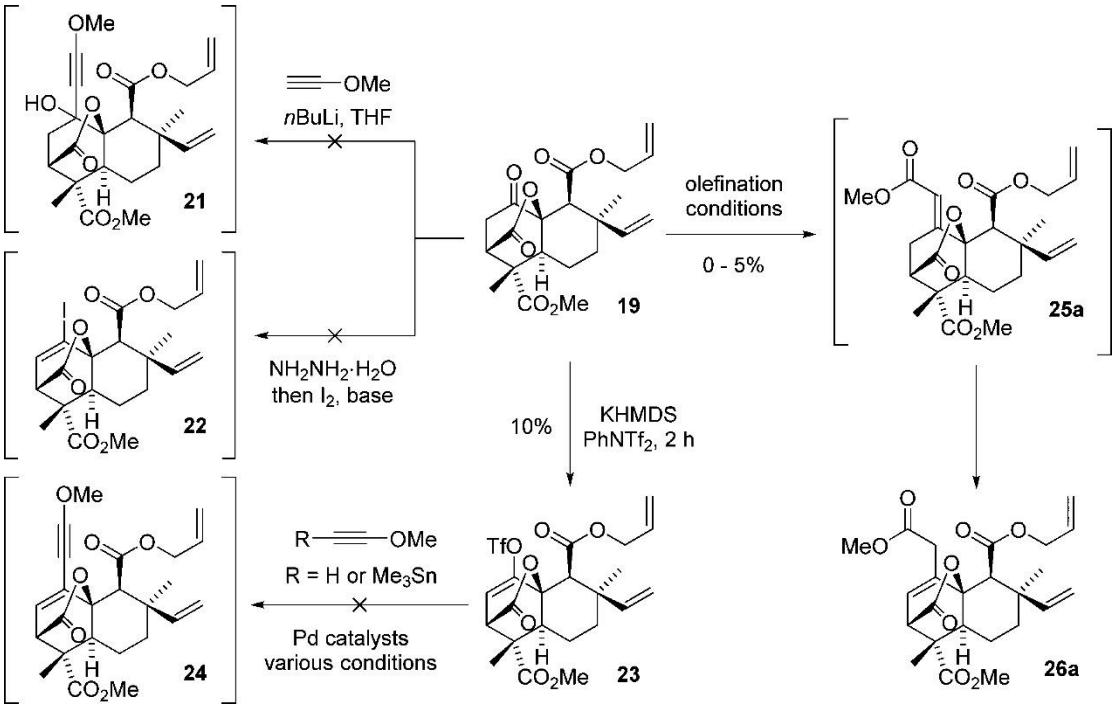
Figure 4. Optimized transition state structures for protonation and their Newman projections along the highlighted (green) C9–C10 bond.Irrelevant hydrogen atoms are omitted for clarity. Relative free energies (energies) are in kcal/mol.

Based on this model, the desired transition state, TS-S, was calculated to be 5.6 kcal/mol lower in free energy than TS-R. Asymmetric information from the adjacent stereogenic center C10 is transferred to the enolic carbon C9 via the coordinating Li1. As depicted in the Newman projection in Figure 4, the chelation of lithium ions confines the enolic double bond to adopt a bisecting conformation. As a result, the bulky R group at C9 is eclipsed by either the H atom (TS-S) or the furan (TS-R) at the adjacent stereogenic center (C10). As indicated bythe elongated C9−C10 bond in TS-R (1.58 Å), the repulsive interaction between the R group and the furan serves to destabilize TS-R. Unlike the asymmetric protonation of acyclic enols bearing an adjacent chiral center,[19] the chelation of the lithium ions enforces the conformational preference which alsois inherent in the core six-membered ring. We also found that replacing the proton source with NH_3 or removal of Li2 did notaffect the preference (Figure S1).[20] The results of this study indicate that the chirality at C8 is not the cause for the high diastereoselectivity of the protonation step, but steric hindranceplays an important role.

3. Biomimetic 2-Pyrone DA Cycloaddition.

With compound 16 in hand, oxidative cleavage of the alkene, followed by ole*fi*nation, afforded 17 in good yield (Scheme 3). Upon treatment with $VO(acac)_2$/TBHP, the furan alcohol moiety undergoes an Achmatowicz rearrangement[21] providing 18 as a mixture of lactol diastereoisomers. Jones oxidation of 18gave the corresponding 2*H*-pyran-2,5-dione, which was expected to rearrange to 5-hydroxy-2-pyrone and undergo DA cycloaddition with a catalytic amount of dicyclohexyl- methylamine (*c*Hex_2NMe) in *tert*-butyl alcohol.[10a,22] This base- catalyzed DA reaction afforded the *endo* product (19) as asingle diastereoisomer. The *endo*-transition state (20b), in which the $A_{1,3}$ strain between the hydroxyl and ester moiety can be avoided, was considered to be more favorable. The relative con*fi*gurations of 19 were determined by 2D NMR studies.

Scheme 4. Strategies for Ketone Functionalization of 19



Ketone functionalization of the DA product (19) was studiedusing various strategies. As shown in Scheme 4, nucleophilic addition of the methoxyethyne anion with 19 failed to result inthe expected product (21), but gave instead a mixture of lactone-opening and ester hydrolysis side products. Treatment with hydrazine followed by iodine did not provide the vinyl iodide (22). The ketone (19) was converted to vinyl triflate 23, but only in 10% yield. Unfortunately, Pd-catalyzed cross- coupling of 23 with methoxyethyne or its trimethylstannane derivative[23] resulted in hydrolysis of the triflate moiety at high temperatures. A variety of ole*fi*nation conditions were alsoinvestigated. As shown in Table 1, decomposition of the ketone was observed under a variety of Horner−Wadsworth− Emmons (HWE) olefination conditions (entries 1−3). Ketone 19 was found to be unreactive with methyl-2-trimethylphos-phoranylidene)acetate in re*fl*uxing benzene or toluene (entry4), and it decomposed

slowly in refluxing mesitylene (entry 5). Switching to methyl 2-(tri-*n*-utylphosphoranylidene)acetate[24] in refluxing toluene also resulted in no reaction (entry 6). A trace amount of the ole*fi*nation product (25 or 26) was observed by LC-MS after refluxing with chlorobenzene (entry 7), and raising the reaction temperature to 150 °C with refluxing mesitylene afforded the olefination product 26 in only5% yield (entry 8).

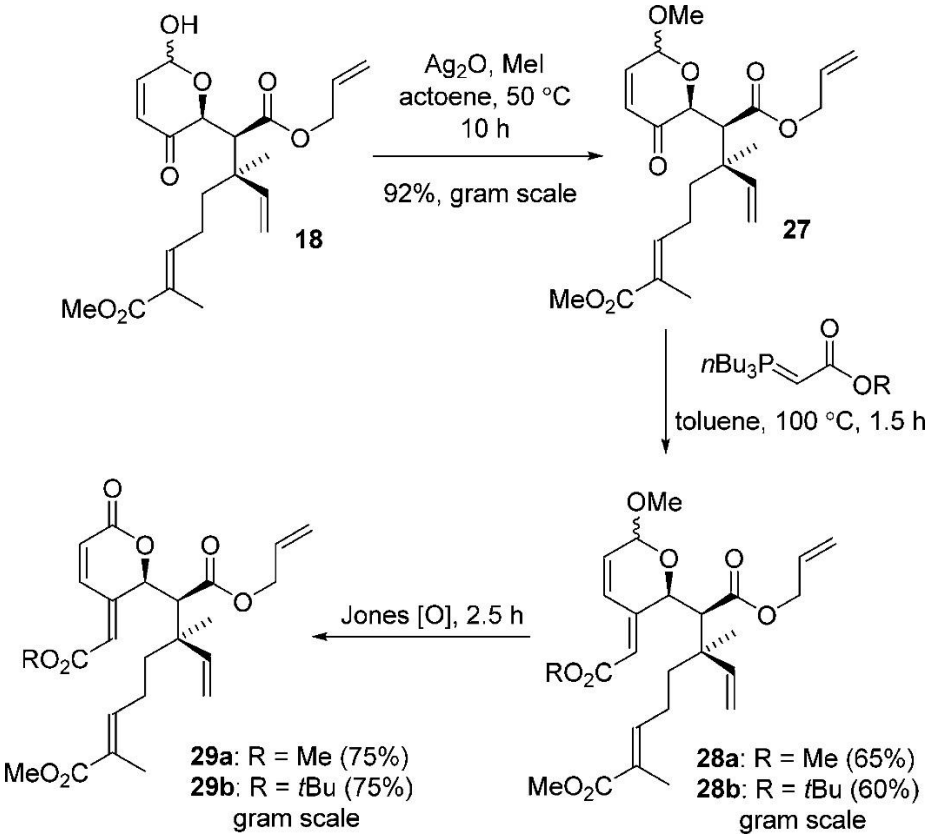
Table 1. Olefination Conditions for Converting 19 to 25a or26a[a]

entry	olefination conditions	yield [b]
1	$(MeO)_2P(O)CH_2CO_2Me$, DIEA, LiCl, THF, 60 °C, 2 h	—[c]
2	$(MeO)_2P(O)CH_2CO_2Me$, DBU, LiCl, THF, 60 °C, 2 h	—[c]
3	$(MeO)_2P(O)CH_2CO_2Me$, NaH, THF, rt, 1 h	—[c]
4	$Ph_3P{=}CHCO_2Me$, benzene or toluene, reflux, 3 d	—[d]
5	$Ph_3P{=}CHCO_2Me$, mesitylene, reflux, 3 d	—[c]
6	$nBu_3P{=}CHCO_2Me$, toluene, reflux, 3 d	—[c]
7	$nBu_3P{=}CHCO_2Me$, cholobenzene, reflux, 3 d	trace[e]
8	$nBu_3P{=}CHCO_2Me$, mesitylene, reflux, 3 d	5%

[a]The general procedures were followed. [b]Isolated yields (%) after silica gel flash column chromatography. [c]Decomposition of 19. [d]No reaction. [e]Observed in LC-MS.

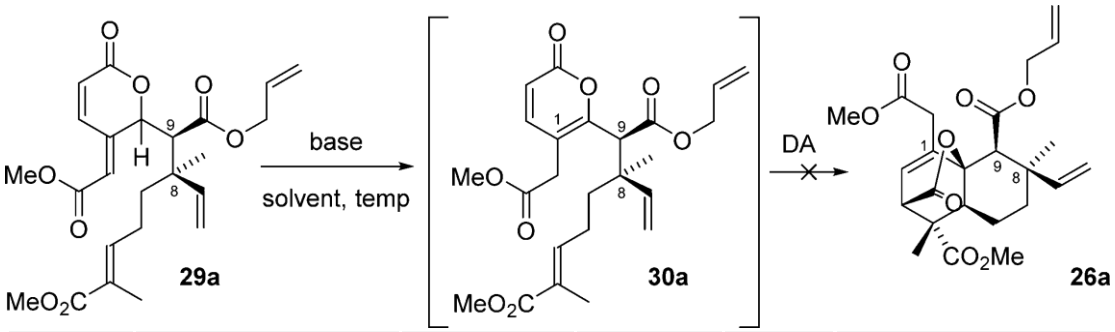
Since the results of the above study indicated that the ketone moiety of 19 was too hindered for functionalization, we decidedto switch the synthetic sequence and carry out the ole*fi*nation before the DA cycloaddition. After methylation of the lactol moiety of 18, ole*fi*nation of 27 was studied intensively with a variety of experimental conditions (Scheme 5). However, the ketone (27) was also found to be too hindered for ole*fi*nation and decomposition of the substrate was observed with a variety of phosphonate/base systems or triphenylphosphine-based stabilized ylides. Methyl and *tert*-butyl 2-(tri-*n*-butylphos- phoranylidene)acetate[24] were *fi*nally found to be e*ff*ective for ole*fi*nation of 27 in toluene at 100 °C and a*ff*orded the expected (*E*)-ole*fi*ns (28a, 28b) in good yields. The methyl lactol moieties were then oxidized with Jones reagent directly tolactones 29a and 29b.[24]

Scheme 5. Synthesis of the 2-Pyrone DA CycloadditionPrecursors 29a and 29b



According to our previous study, compound 29a is expected to equilibrate to the 2-pyrone (30a) and undergo a one-pot 2- pyrone DA cycloaddition under basic conditions. However, treatment with (cHex)$_2$NMe or DIPEA in t-BuOH or toluene resulted in no reaction either at room temperature or in re*fl*uxing toluene (entries 1−4, Table 2). Use of t-BuOK/THF led to decomposition of the substrate (entry 5). Changing the base to DBU in toluene induced epimerization at C9 providing 30a as a 1:1 diastereoisomeric mixture (entry 6). The epimerization at C9 can be suppressed with DABCO[26] at 70°C, which afforded the 2-pyrone (30a) as a single diastereoisomer (entry 8).

Table 2. Attempts of Equilibration and DA Cycloaddition in a One-Pot Reaction[a]

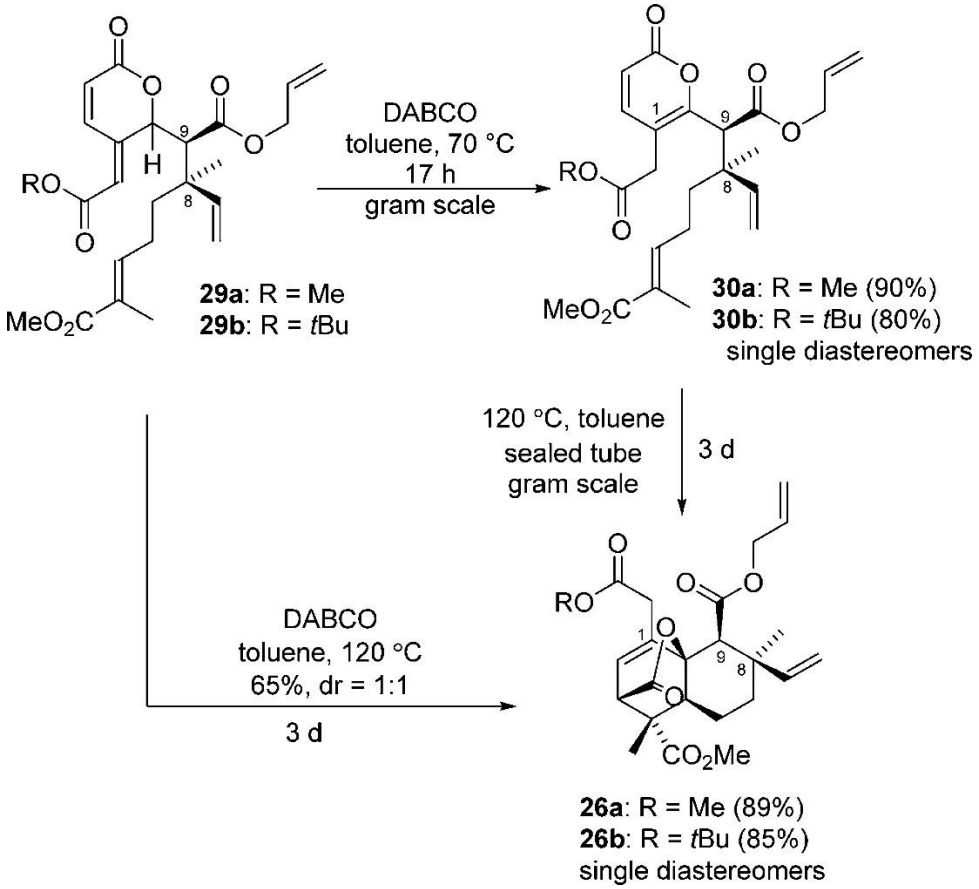


entry	base	solvent	temp	time	yield[b] (dr)
1	(*c*Hex)$_2$NMe	*t*BuOH	rt	2 d	–[c]
2	(*c*Hex)$_2$NMe	*t*BuOH	60 °C	2 d	–[c]
3	(*c*Hex)$_2$NMe	toluene	120 °C	1 d	–[c]
4	DIPEA	toluene	120 °C	1 d	–[c]
5	*t*BuOK	THF	rt	1 d	–[d]
6	DBU	toluene	rt	2 h	90% (1:1)
7	DABCO	toluene	90 °C	14 h	85% (5:1)
8	DABCO	toluene	70 °C	17 h	90% (single)

[a]The general procedures were followed. [b]Isolated yields (%) after silica gel flash column chromatography. [c]No reaction. [d]Decomposition of 29a.

Compound 29a and 29b were then converted to the 2- pyrone (30a, 30b) using the above-mentioned optimal conditions, in which epimerization at C9 was not observed (Scheme 6). Intramolecular DA cycloaddition of the 2-pyrone (30a or 30b) with toluene at 120 °C in a sealed tube was optimized and a*ff*orded the DA products (26a, 26b) in 85– 89% yield as single diastereoisomers without formation of the decarboxylation side product.[27] The relative con*fi*gurations of the DA products 26a and 26b were determined by 2D NMR. Compounds 29a and 29b can also be converted to the DA products 26a and 26b in a one-pot reaction in a sealed tube with DABCO at 120 °C. However, these one-pot conditions generally gave lower yields and led to the formation of 1:1 diastereoisomeric mixtures.

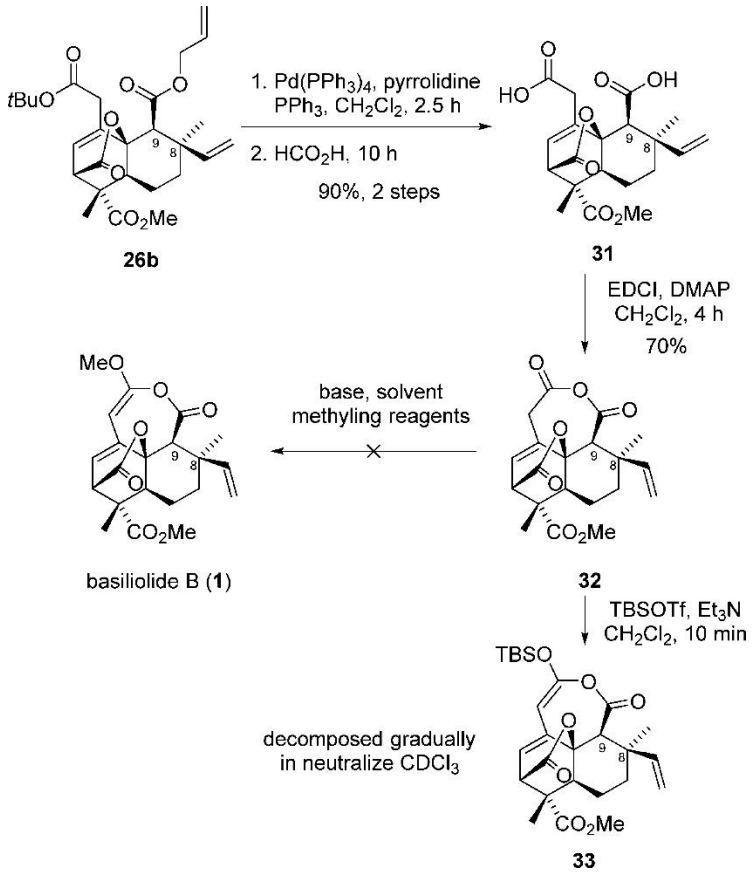
Scheme 6. DA Cycloaddition of 2-Pyrones 30a and 30b



4. Biomimetic Synthesis of the C-Ring and Total Synthesis of Basiliolide B (1).

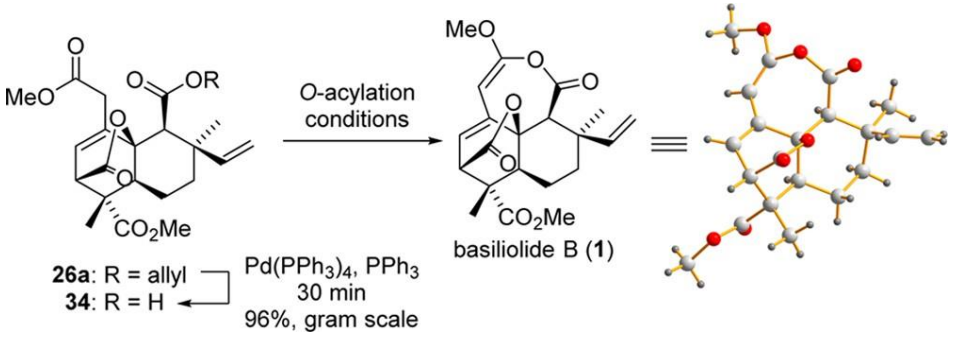
With the DA products 26a and 26b in hand, the biomimetic synthesis of the 7-methoxy-4,5-dihydro-3*H*-oxepin-2-one, the C ring, by *O*-methylation was investigated. As shown in Scheme 7, hydrolysis of the allyl and*tert*-butyl esters of 26b provided the diacid (31), which can be converted to the acid anhydride (32) in refluxing acetic anhydride[28] or thionyl chloride with sodium carbonate.[29] However, these conditions gave yields of only 5−40% and theresults are inconsistent as a result of the instability of 32 underthese reaction conditions. On the other hand, the acid anhydride (32) is suffciently stable for silica gel chromatography and NMR studies. Finally, optimal results were achievedwith EDCI/DMAP, which consistently afforded good yields of 32. Subsequently, *O*-methylation of 32 using a variety of methylating reagents, including CH_2N_2, $TMSCHN_2$,[30] CH_3I, CH_3OTf, and $(MeO)_3BF_4$,[31] with different bases was studied comprehensively. The acid anhydride (32) was found to be unreactive with mild bases, such as TEA and DIPEA, but highlyunstable with strong bases, such as NaH/KH, KHMDS, LDA, and LTMP, with which it gave a mixture of unidentified side products. Upon treatment of TBSOTf/Et_3N, the acid anhydride (32) was converted to the silyl ketene acetal (33), which is unstable. Hydrolysis of the cyclic silyl ketene acetal moiety in neutralized $CDCl_3$ was observed by NMR studies.

Scheme 7. Study of C Ring Formation via O-Methylation.



The disappointing results of the O-methylation strategy prompted investigation of formation of the C ring by an intramolecular O-acylation strategy. Allyl ester deprotection of26a provided the *seco* acid derivative (34), which was used as the substrate in an extensive study of O-acylation conditions. As shown in Table 3, activating the acid moiety of 34 with $SOCl_2$/Et_3N or $(COCl)_2$/2,6-lutidine failed to give any O-acylation product (entries 1−2). Use of t-BuCOCl/DIPEA led to decomposition of 34 (entry 3). Using TFAA with NaOAcresulted in no reaction (entry 4), but switching the base to Et_3N led to a trace amount of basiliolide B, observed in LC-MS(entry 5). We *fi*nally found that 34 undergoes intramolecular O-acylation using Tf_2O/Et_3N, resulting in the natural product basiliolide B, but only 5−10% yields were obtained in CH_2Cl_2 (entries 6−7). After a detailed study of the e*ff*ects and solvents(entries 8−10), optimal conditions were found using Tf_2O/TEA in toluene from −78 to 0 °C, which a*ff*orded(±)-basiliolide B (1) in 92% yield (entry 10). The structure of the synthetic natural product was characterized unambigu- ously by X-ray crystallography.[14] This result strongly suggestedthat the *seco* acid derivative (34) could be a potential biosynthetic precursor of basiliolide B (1).

Table 3. Study of the C Ring Formation via Intramolecular O-Acylation[a]



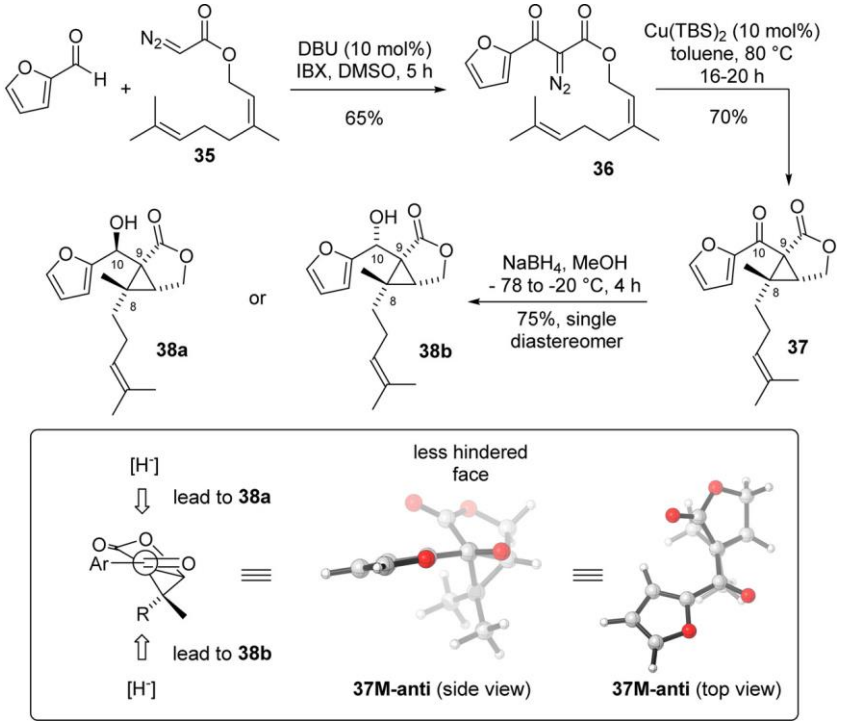
entry	*O*-acylation condition	yield[b]
1	$SOCl_2$, Et_3N, CH_2Cl_2, 0 °C, 1 h	—[c]
2	$(COCl_2)$, 2,6-lutidine, CH_2Cl_2, 40 °C, 1 h	—[c]
3	*t*BuCOCl, DIPEA, CH_2Cl_2, 40 °C, 30 min	—[d]
4	TFAA, NaOAc, CH_2Cl_2, 0 °C, 1 h	—[c]
5	TFAA, Et_3N, CH_2Cl_2, 0 °C, 1 h	trace[e]
6	Tf_2O, Et_3N, CH_2Cl_2, 0 °C, 1 h	5%
7	Tf_2O, Et_3N, CH_2Cl_2, 0–40 °C, 30 min	10%
8	Tf_2O, Et_3N, toluene, 0–60 °C, 30 min	23%
9	Tf_2O, Et_3N, toluene, 0 °C, 1 h	60%
10	Tf_2O, Et_3N, toluene, –78–0 °C, 2 h	92%

[a]The general procedures were followed. [b]Isolated yields (%) after silica gel flash column chromatography. [c]No reaction. [d]Decompositionof 34. [e]Observed in LC-MS.

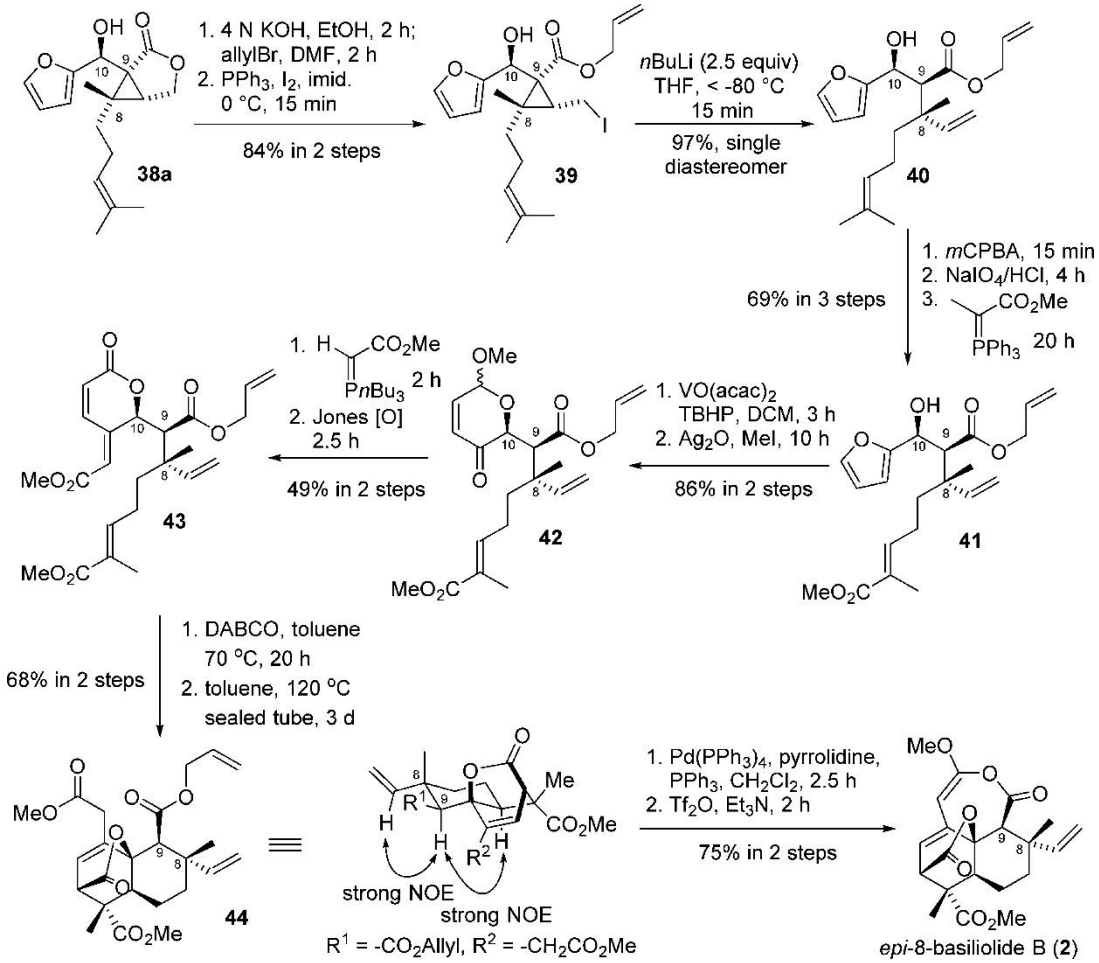
5. Diastereoselective Synthesis of *epi*-8-Basiliolide B (2).

ased on the conclusion of the above DFT calculations, theselectivity of protonation at C9 of the enolate generated *in situ*from the cyclopropane ring-opening reaction is controlled by the chelation effects of the lithium ion(s) rather than by the con*fi*guration at C8. Therefore, we decided to employ this strategy for the total synthesis of *epi*-8-basiliolide B (2). As shown in Scheme 8, oxidative coupling between furan-2-carboxaldehyde and diazoacetate (35) (prepared from nerol)[32] followed by intramolecular cyclopropanation provided 37 in good yield. Reduction of the ketone moiety of 37 at lowtemperature resulted in a single diastereoisomer, which is either38a or 38b. However, attempts to determine its structure via X-ay crystallography failed. Judging by conformational analysis,37 could, to minimize the dipole moment,[33] adopt the more stable conformation 37M-anti, in which the two carbonyls are *anti* to one another. DFT results con*fi*rmed that the *anti*-conformation is 1.3 kcal/mol lower in free energy than the *syn*conformation (Figure S2). The optimized geometry of 37M- anti was shown in Scheme 8. Hydride could be preferentially delivered from the less hindered α-face leading to 38a. The relative con*fi*gurations of 38a were con*fi*rmed by the 2D NMR studies of the DA product (44, Scheme 9) after several transformation steps.

Scheme 8. Synthesis of 38a and the Conformational Analysis for the Reduction of 37



Scheme 9. Synthesis of (±) epi-8-Basiliolide B (2)



With 38a in hand, its lactone moiety was converted to the allyl ester and iodide of 39 by the same procedures used for thepreparation of 13. Cyclopropane ring opening via lithium− halogen exchange afforded 40 as a single diastereoisomer in good yield. The relative configuration of 40 was assigned basedon the results of the above conformational analysis. Oxidative cleavage of the alkene in 40, followed by olefination, afforded 41 in good yield. Achmatowicz rearrangement[21] of 41 gave the corresponding lactol, which was then methylated and provided 42 as a mixture of lactol diastereoisomers. After olefination with methyl 2-(tri-*n*-butylphosphoranylidene) acetate,[24] Jones oxidation[25] of the methyl acetal to the lactone afforded the 2*H*- pyran-2,5-dione moiety of 43. Alkene migration with DABCO[26] followed by intramolecular DA cycloaddition afforded 44, which was characterized unambiguously with 2D NMR studies. This result confirmed the proposed relative configurations of 38a and 40. Finally, deprotection of the allyl ester followed by intramolecular *O*-acylation with Tf_2O in toluene completed the total synthesis of *epi*-8-basilolide B (2). The ^{1}H and ^{13}C NMR spectra of this natural product derivative were identical to those reported by Stoltz et al.[9c]

CONCLUSION

In summary, the diastereoselective total syntheses of (±)-basiliolide B (1) and (±)-*epi*-8-basiliolide B (2) havebeen achieved. The stereogenic centers at C8 and C9 were established stereoselectively using a cyclopropane ring-openingstrategy. Theoretical studies reveal that protonation at C9 ofthe enolate generated *in situ* from the cyclopropane ring opening is controlled selectively by the lithium chelate of the C10-hydroxyl regardless of the stereochemistry at C8. The synthesis features a 2-pyrone DA cycloaddition for constructionof the decalin core with the lactone bridge (ABD-ring system), and a bioinspired intramolecular *O*-acylation reaction for establishing the unprecedented 7-methoxy-4,5-dihydro-3*H*- oxepin-2-one, the C-ring, supporting the hypothesis that the *seco* acid derivatives are the biosynthetic precursors of the basiliolides and transtaganolides. This synthetic route is effcient and practical (5.7% in 17 steps from geranyl for 1 and 3.9% in 17 steps from neryl diazoacetate for 2), which canbe carried out on a scale of grams to decagrams for the *seco* acidderivative and a scale of hundreds of milligram for the biomimetic intramolecular *O*-acylation with good overall yieldsand precise control of stereochemistry. Currently, we are utilizing our synthetic strategy to synthesize other members of the basiliolide/transtaganolide family and their structural analogues for biological assays.

EXPERIMENTAL SECTION

General Information for Computational Methods.

All the calculations were carried out with the Gaussian 09 package.[34] geometries were optimized at M06/6-31G(d,p).[35] Frequency calculations at the same level of theory at the optimized geometries con*fi*rmed the stationary points as minima (zero imaginary frequencies) or transition state (one imaginary frequency) and provided thermal corrections at 298.15 K. Solvent effects were modeled with single-point energy calculations at 6-311++G(3df,3pd), using the SMD solvation model (solvent = tetrahydrofuran).[36] Geometries are illustrated using CYLView.[37]

General Information for Synthesis.

Unless otherwise noted, all air and water sensitive reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions. All the chemicals were purchased commercially and used without further purification. Anhydrous THF and toluene were distilled from sodium- benzophenone, and dichloromethane was distilled from calcium hydride. Yields were determined chromatographically, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates (60F-254) that were analyzed by staining with $KMnO_4$ solution (200 mL of H_2O of 1.5 g of$KMnO_4$, 10 g of K_2CO_3, and 1.25 mL of 10% aqueous NaOH),*fl*uorescence following 254 nm irradiation, or staining with anisaldehyde (450 mL of 95% EtOH, 25 mL of conc. H_2SO_4, 15mL of AcOH, and 25 mL of anisaldehyde). Silica gel (60, particle size 0.040−0.063 mm) was used for *fl*ash chromatography. NMR spectra were recorded at 300 MHz (^{1}H: 300 MHz, ^{13}C: 75 MHz), 400 MH (^{1}H: 400 MHz, ^{13}C: 100 MHz), and 500 MHz (^{1}H: 500 MHz, ^{13}C: 125 MHz). The following abbreviations were for multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. High-resolution mass spectra were obtained from a MALDI-TOF mass spectrometer. Crystallographic data were obtained from a single crystalX-ray di*ff*ractometer. All the IR spectra were obtained using an FT-IRspectrometer.

Experimental Details.

(E)-3,7-Dimethylocta-2,6-dien-1-yl 2- diazo-3-(furan-2-yl)-3-oxopropanoate (4).

Freshly distilled 2-fur- aldehyde (8.20 mL, 99.0 mmol), DBU (2.69 mL, 18.0 mmol), and IBX(37.8 g, 135 mmol) were added to a stirred solution of 3[11] (20.0 g, 90.0 mmol) in DMSO (400 mL) at 0 °C. The resulting solution was allowed to warm to room temperature and stirred for 5 h. The reactionwas quenched by addition of a saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with Et_2O (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, then *fi*ltered, and concentrated under reduced pressure. Silica gel *fl*ashcolumn chromatography of the residue gave a yellow oil (18.5 g, 65%)as the product. 4: R_f = 0.50 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, 1H, *J* = 0.9 Hz), 7.52 (d, 1H, *J* = 3.3 Hz,), 6.56 (dd, 1H, *J* = 3.7 Hz, 1.7 Hz), 5.39 (td, 1H, *J* = 7.1 Hz, 1.2 Hz), 5.09 (td, 1H, *J* = 6.9 Hz, 1.4 Hz), 4.80 (d, 1H, *J* = 7.1 Hz), 2.12 (m, 2H), 2.07 (m, 2H), 1.74 (s, 3H), 1.69 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 160.9, 150.5, 145.9, 143.3, 131.8, 123.6, 119.3, 117.7, 112.2, 74.7, 62.4, 39.4, 26.3, 25.5, 17.6, 16.5; IR (KBr) 2966, 2916, 2856, 2127, 1720, 1317, 1267, 960, 752 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{17}H_{20}N_2NaO_4$: 339.1321; found: 339.1313.

1-(Furan-2-carbonyl)-6-methyl-6-(4-methylpent-3-en-1-yl)-3- oxabicyclo[3.1.0]hexan-2-one (5).

A solution of 4 (16 g, 50.6 mmol) in toluene (50 mL) was added over 16−20 h by syringe pump to a solution of $Cu(TBS)_2$[13] (2.11 g, 5.06 mmol) in toluene (200 mL) at 80 °C. After TLC showed complete consumption of the startingmaterial, the reaction was cooled to room temperature and concentrated under reduced pressure. Silica gel *fl*ash column chromatography of the residue a*ff*orded a yellow oil

(10.8 g, 74%)as the product (single diastereoisomer). 5: R_f = 0.35 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, 1H, *J* = 1.0 Hz), 7.43 (d, 1H, *J* = 3.3 Hz), 6.62 (dd, 1H, *J* = 3.6 Hz, 1.6 Hz), 4.95 (tt, 1H, *J* = 7.1 Hz, 1.2 Hz), 4.50 (dd, 1H, *J* = 10.0 Hz, 5.6 Hz), 4.36 (dd, 1H, *J* = 9.9 Hz, 0.5 Hz) 2.72 (d, 1H, *J* = 4.9 Hz), 2.02 (m, 2H), 1.63 (s, 3H), 1.51 (s, 3H), 1.46 (m, 1H), 1.38 (s, 3H), 1.05 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.7, 170.6, 152.1, 147.6, 132.5, 122.6, 122.0, 112.6, 65.2, 46.8, 35.0, 34.8, 32.3, 25.5, 24.9, 17.4, 12.6; IR (KBr) 2968, 2914, 2856, 1762, 1659, 1464, 1312 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{17}H_{20}NaO_4$: 311.1259; found: 311.1257.

1-(Furan-2-yl(hydroxy)methyl)-6-methyl-6-(4-methylpent-3-en- 1-yl)-3-oxabicyclo[3.1.0]hexan-2-one (6). $NaBH_4$ (3.13 g, 82.8 mmol) was added to a stirred solution of 5 (19.9 g, 69.0 mmol) in MeOH (250 mL) at −78 °C. The resulting solution was allowed to warm up to −20 °C over 4 h. After TLC showed consumption of the starting material, the reaction was quenched by addition of a saturatedaqueous $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (×3) and the combined organic extracts were washed with brine, dried over $MgSO_4$, and *fi*ltered and concentrated under reduced pressure. Silica gel *fl*ash column chromatography of the residue gave acolorless oil (14.0 g, dr =10:1, 77%) as the product. 6 (major diastereoisomer): R_f = 0.38 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, 1H, *J* = 0.8 Hz), 6.35 (dd, 1H, *J* =3.2 Hz, 1.8 Hz), 6.32 (d, 1H, *J* = 3.2 Hz), 5.12 (tt, 1H, *J* = 7.1 Hz, 1.2 Hz), 4.71 (d, 1H, *J* = 10.3 Hz), 4.46 (d, 1H, *J* = 11.0 Hz), 4.36 (dd, 1H, *J* = 9.9 Hz, 5.3 Hz) 4.17 (d, 1H, *J* = 9.7 Hz), 2.37 (m, 1H), 2.20 (m, 1H), 2.02 (d, 1H, *J* = 5.1 Hz), 1.70 (s, 3H), 1.66 (s, 3H), 1.58 (m, 2H), 1.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.1, 155.4, 141.9, 132.4, 123.3, 110.5, 106.5, 66.2, 66.0, 40.1, 35.7, 32.9, 29.7, 25.6, 24.7, 17.6, 12.9; IR (KBr) 2966, 2914, 2858, 1743, 1367, 1004 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{17}H_{22}NaO_4$: 313.1416; found: 313.1409.

6-(2-(3,3-Dimethyloxiran-2-yl)ethyl)-1-(furan-2-yl(hydroxy)-methyl)-6-methyl-3-oxabicyclo[3.1.0]hexan-2-one (45).

m-CPBA (3.74 g, 15.2 mmol, 70%) was added in portions to a stirred solution of 6 (4.0 g, 13.8 mmol) in CH_2Cl_2 (75 mL) at 0 °C. After stirring at 0 °C for 15 min, TLC showed the complete consumption of the startingmaterial. The mixture was flltered, and the residue was washed with hexanes (×3) and ice-cooled CH_2Cl_2 (×3). The *fi*ltrate was quenched with saturated $Na_2S_2O_3$ and $NaHCO_3$. The aqueous phase was extracted with EtOAc (×3), and the organic extracts were washed withwater and brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was puri*fi*ed by silica gel *fl*ashcolumn chromatography to give a yellow oil (3.97 g, 94%) as the product. 45: R_f = 0.50 (silica gel, hexanes/EtOAc = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, 1H, *J* = 0.8 Hz, 1.2 Hz), 6.40−6.22 (m, 2H), 4.71 (d, *J* = 5.0 Hz, 1H), 4.42−4.28 (m, 1H), 4.17 (dd, *J* = 10.0, 5.5 Hz, 1H), 2.73 (ddd, *J* = 11.4, 7.0, 4.2 Hz, 1H), 2.07 (dd, *J* = 4.7, 3.3 Hz, 1H), 2.05−1.85 (m, 1H), 1.85−1.56 (m, 3H), 1.32 (s, 3H), 1.31 (d, *J* = 1.4 Hz, 3H), 1.22 (d, *J* = 5.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 154.9, 142.0, 141.9, 110.5, 110.4, 106.6, 66.3, 66.1, 65.9, 65.7, 64.0, 63.7, 59.0, 58.5, 40.2, 39.9, 32.9, 32.8, 32.5, 32.3, 29.3, 25.6, 25.2, 24.8, 18.8, 18.7, 12.9, 12.8; IR (KBr) 3490, 2965, 2927, 2882, 1744, 1378, 1005, 884, 753, 599

cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{17}H_{22}NaO_5$: 329.1365; found: 329.1359.

(1R,5R,6R)-6-(2-(1,3-Dioxolan-2-yl)ethyl)-1-((S)-furan-2-yl-(hydroxy)methyl)-6-methyl-3-oxabicyclo[3.1.0]hexan-2-one (7).

$NaIO_4$ (3.32 g, 15.5 mmol) was added to a stirred solution of 45(3.97 g, 12.9 mmol) in THF/H_2O (THF: H_2O = 2:1, 75 mL) at 0 °C and was followed by addition of 1 N aqueous HCl to adjust the pH to 3. After stirring at 0 °C for 4 h, TLC showed the consumption of the starting material. The mixture was *fi*ltered, the residue was washed with EtOAc (×3), and the *fi*ltrate was quenched with saturated $NaHCO_3$. The aqueous phase was extracted with EtOAc (×3), and thecombined organic extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was puri*fi*ed by silica gel flash column chromatography to givea yellow oil (2.97 g) as the crude product. Ethylene glycol (1.39 g, 22.4mmol) and PPTS (28.1 mg, 0.112 mmol) were added to a stirred solution of the crude product in benzene (50 mL) at 100 °C. TLC showed the consumption of the starting material after the water kept collecting for 20 min in a Dean−Stark apparatus. Then the reaction was quenched by saturated $NaHCO_3$. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine and then dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by silicagel *fl*ash column chromatography to give a yellow oil (2.59 g, 75%) asthe product. 7: R_f = 0.42 (silica gel, hexanes/EtOAc = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 1.0 Hz, 1H), 6.35 (dd, *J* = 3.3, 1.8 Hz, 1H), 6.33 (d, *J* = 3.3 Hz, 1H), 4.93 (t, *J* = 4.3 Hz, 1H), 4.75 (s, 1H), 4.37 (dd, *J* = 9.9, 5.3 Hz, 1H), 4.17 (d, *J* = 9.9 Hz, 1H), 4.02− 3.93 (m, 2H), 3.91−3.83 (m, 2H), 2.15−2.07 (m, 1H), 2.06 (d, *J* = 5.0Hz, 1H), 1.95−1.86 (m, 1H), 1.77 (ddd, *J* = 14.2, 11.8, 5.3 Hz, 1H), 1.67−1.59 (m, 1H), 1.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.0, 155.3, 141.9, 110.5, 106.5, 103.7, 66.2, 65.9, 64.9, 64.9, 40.2 32.9, 30.1, 29.4, 29.1, 12.9; IR (KBr) 3480, 2965, 2887, 1751, 1368, 1144, 1022, 943, 884, 753, 599 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{16}H_{20}NaO_6$: 331.1158; found: 331.1150.

Benzyl-2-(2-(1,3-dioxolan-2-yl)ethyl)-1-(furan-2-yl(hydroxy)-methyl)-3-(hydroxymethyl)-2-methylcyclopropane-1-carboxylate (8).

4 N KOH (200 mg in 0.9 mL H_2O, 3.57 mmol) was added to a stirred solution of compound 7 (1.0 g, 3.24 mmol) in EtOH (15 mL). After stirring for 2 h at 90 °C, TLC showed complete consumption ofthe starting material. Then the solution was concentrated under reduced pressure to a*ff*ord a yellow solid as the crude product. Benzylbromide (0.83 g, 4.86 mmol) was added to a stirred solution of the above crude product in DMF (15 mL). After stirring at room temperature for 2 h, TLC showed that the starting material had been consumed. The reaction was quenched by ice. The aqueous phase wasextracted with Et_2O (×3), and the combined organic extracts were washed with brine and then dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was puri*fi*ed by silicagel *fl*ash column chromatography to give a yellow oil (1.28 g, 95%) asthe product. 8: R_f = 0.21 (silica gel, hexanes/EtOAc = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.32 (m, 3H), 7.29 (dd, *J* = 1.7, 0.7 Hz, 1H), 7.27−7.23 (m, 2H), 6.28 (dd, J = 3.2, 1.8 Hz, 1H), 6.22 (d, *J* = 3.3 Hz, 1H), 5.10 (s, 2H), 4.90 (t, *J* = 4.4 Hz, 1H), 4.45 (s,

1H), 3.99−3.94 (m, 2H), 3.90−3.82 (m, 4H), 2.01−2.04 (m, 1H), 1.93−1.88 (m, 1H), 1.81−1.75 (m, 1H), 1.72−1.64 (m, 1H), 1.43 (t, *J* = 3.6 Hz, 1H), 1.09 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 154.8, 141.9, 134.8, 128.7, 128.7, 128.6, 110.3, 106.2, 104.2, 71.6, 67.3, 64.9, 64.9, 59.4, 42.4, 36.9, 30.8, 30.7, 30.2, 29.7, 15.0. IR (KBr) 3466, 2958, 2925, 2889, 1723, 1499, 1456, 1409, 1385, 1337, 1276, 1187, 1145, 1118, 1068, 1016, 944, 884, 862, 817, 749, 698 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{23}H_{28}NaO_7$: 439.1733; found: 439.1737.

6-(2-(1,3-Dioxolan-2-yl)ethyl)-1-(furan-2-carbonyl)-6-methyl-3- oxabicyclo[3.1.0]hexan-2-one (10).

BX (2.82 g, 10.1 mmol) was added to a stirred solution of 7 (2.59 g, 8.4 mmol) in DMSO (40 mL).After stirring at room temperature for 20 h, TLC showed that the starting material was consumed, and the reaction was quenched with saturated $NaHCO_3$. The aqueous phase was extracted with Et_2O (×3), and the combined organic extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by silica gel flash column chromatography to give a colorless oil (2.32 g, 90%) as the product. 10: R_f = 0.40 (silica gel, hexanes/EtOAc = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 1.0 Hz, 1H), 7.40 (d, *J* = 3.6 Hz, 1H), 6.60 (dd, *J* = 3.6, 1.6 Hz, 1H), 4.71 (t, *J* = 4.6 Hz, 1H), 4.49 (dd, *J* = 10.0, 5.5 Hz, 1H), 4.18 (d, *J* = 10.0 Hz, 1H), 3.89−3.83 (m, 2H), 3.80−3.74 (m, 2H), 2.71 (d, *J* = 5.3 Hz, 1H), 1.81−1.60 (m, 3H), 1.56 (ddd, *J* = 14.0, 11.1, 4.8 Hz, 1H), 1.35 (s, 3H), 1.16 (ddd, *J* = 13.7, 11.3, 5.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.6, 170.5, 151.9, 147.7, 122.0, 112.6, 103.4, 65.3, 64.9, 64.8, 47.0, 34.4, 32.3, 30.7, 29.0, 12.6; IR (KBr) 2963, 2889, 1761, 1662, 1564, 1464, 1313, 1184, 1029, 884, 772, 593 cm^{-1}; HRMS(ESI/[M + H]$^+$) calcd for $C_{16}H_{19}O_6$: 307.1182; found: 307.1174.

Benzyl 2-(2-(1,3-Dioxolan-2-yl)ethyl)-1-(furan-2-carbonyl)-3-(hy- droxymethyl)-2-methylcyclopropane-1-carboxylate (46).

4 N KOH (0.51 g in 2.3 mL H_2O, 9.1 mmol) was added to a stirred solution of 10 (2.32 g, 7.6 mmol) in EtOH (35 mL). After stirring for 2 h at 90°C, TLC showed that the starting material had been consumed. The solution was concentrated under reduced pressure to afford the crude product as a yellow solid. Benzyl bromide (1.95 g, 11.4 mmol) was added to a stirred solution of the above crude product in DMF (35 mL). After stirring at room temperature for 2 h, TLC showed the consumption of the starting material. The reaction was quenched withice. The aqueous phase was extracted with Et_2O (×3), and the combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel flash column chromatography to givea yellow oil (2.81 g, 89%) as the product. 46: R_f = 0.31 (silica gel, hexanes/EtOAc = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* =0.9 Hz, 1H), 7.26−7.21 (m, 4H), 7.08 (dd, *J* = 6.4, 2.9 Hz, 2H), 6.46 (dd, *J* = 3.6, 1.7 Hz, 1H), 5.12 (d, *J* = 12.3 Hz, 1H), 5.00 (d, *J* = 12.3 Hz, 1H), 4.73 (t, *J* = 4.7 Hz, 1H), 3.87 (tdd, *J* = 7.5, 5.8, 2.0 Hz, 4H), 3.81−3.74 (m, 2H), 2.20 (t, *J* = 7.6 Hz, 1H), 1.77 (s, 1H), 1.74−1.67 (m, 2H), 1.59−1.54 (m, 1H), 1.51 (s, 3H), 1.16−1.06 (m, 1H); ^{13}CNMR (125 MHz, $CDCl_3$) δ 181.9, 168.2, 152.8, 146.4, 135.3, 128.4, 128.2, 128.0, 118.1, 112.3, 104.2, 66.9, 64.9, 64.8, 58.3, 45.5, 35.7, 35.5, 31.6, 30.8, 12.8; IR (KBr)

3468, 2960, 2888, 1733, 1669, 1568, 1465, 1391, 1290, 1192, 1112, 1020, 884, 739, 698 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{23}H_{26}NaO_7$: 437.1576; found: 437.1569.

Benzyl 2-(2-(1,3-Dioxolan-2-yl)ethyl)-1-(furan-2-carbonyl)-3-(io-domethyl)-2-methylcyclopropane-1-carboxylate (11)

Iodine (5.15 g, 20.3 mmol) was added in portions to a stirred solution of 46 (2.81 g, 6.8 mmol), imidazole (1.38 g, 20.3 mmol), and PPh_3 (5.32 g, 20.3 mmol) in THF (30 mL) at 0 °C. After stirring at 0 °C for 10 min, TLC showed the consumption of the starting material. The reaction was quenched by saturated $Na_2S_2O_3$. The aqueous phase was extractedwith EtOAc (×3), and the combined organic extracts were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was pur*if*ied by silica gel flash column chromatography to give a colorless oil (3.21 g, 90%) as the product. 11: R_f = 0.50 (silica gel, hexanes/EtOAc = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 1.0 Hz, 1H), 7.26−7.20 (m, 3H), 7.14 (d, *J* = 3.5 Hz, 1H), 7.03 (dd, *J* = 7.3, 2.1 Hz, 2H), 6.46 (dd, *J* = 3.6, 1.6 Hz, 1H), 5.15 (d, *J* = 12.4 Hz, 1H), 4.95 (d, *J* = 12.4 Hz, 1H), 4.69 (t, *J* = 4.7 Hz, 1H), 3.88−3.82 (m, 2H), 3.79−3.72 (m, 2H), 3.43 (dd, *J* = 10.2, 6.7 Hz, 1H), 3.38 (t, *J* = 10.1 Hz, 1H), 2.50 (dd, *J* = 9.9, 6.7 Hz, 1H), 1.78−1.63 (m, 2H), 1.56 (s, 3H), 1.52−1.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.5, 167.3, 152.9, 146.1, 135.1, 128.3, 128.0, 127.9, 117.3, 112.4, 103.8, 66.8, 64.8, 64.8, 48.4, 38.1, 36.5, 31.0, 30.7, 10.9, −0.7; IR (KBr) 2957, 2916, 1730, 1672, 1568, 1465, 1389, 1262, 1209, 1145, 1024, 939, 884, 764, 749, 607 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{23}H_{25}NaIO_6$: 547.0594; found:547.0587.

Benzyl 3-(2-(1,3-Dioxolan-2-yl)ethyl)-2-(furan-2-carbonyl)-3- methylpent-4-enoate (I2).

AIBN (41 mg, 0.25 mmol) and *n*- Bu_3SnH (291 mg, 1.0 mmol) were added to a stirred solution of 11 (262.2 mg, 0.5 mmol) in toluene (2.5 mL). With ultrasonic desecration and argon charging, TLC showed the complete consumption of the starting material after stirring at 80 °C for 2 h.The reaction was quenched by a saturated aqueous KF. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was pur*if*ied by silica gel *fl*ash column chromatography to give a colorless oil (185.3 mg, 93%, dr = 5.8:1) as the product. 12: R_f = 0.42 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 1.0 Hz, 1H), 7.34−7.24 (m, 5H), 7.21 (d, *J* = 3.6 Hz, 1H), 6.51 (dd, *J* = 3.6, 1.7 Hz, 1H), 6.05 (dd, *J* = 17.5, 10.8 Hz, 1H), 5.10 (dt, *J* = 24.0, 12.6 Hz, 3H), 4.99 (d, *J* = 18.2 Hz, 1H), 4.76 (t, *J* = 4.7 Hz, 1H), 4.34 (s, 1H), 3.94−3.85 (m, 2H), 3.85−3.76 (m, 2H), 1.74−1.66 (m, 2H), 1.64−1.53 (m, 2H), 1.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.4, 167.4, 152.9, 146.6, 142.9, 135.5, 128.4, 128.2, 128.1, 118.0, 114.1, 112.6, 104.5, 66.7, 64.8, 64.8, 61.1, 42.9, 32.8, 28.7, 19.7; IR (KBr) 3455, 2922, 2850, 1742, 1674, 1566, 1464, 1267, 1141, 1044, 921, 883, 739, 699 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{23}H_{26}NaO_6$: 421.1627; found: 421.1621.

Allyl(1-(Furan-2-yl(hydroxy)methyl)-3-(hydroxymethyl)-2-meth-yl-2-(4-methylpent-3-en-1-yl) cyclopropane-1-carboxylate (47).

4 NKOH (2.12 g, 37.9 mmol) was added to a stirred solution of 6 (10.0 g,34.5 mmol) in EtOH (150 mL). After stirring for 2 h at 90 °C, TLC showed the consumption of the starting material. The solution was concentrated under reduced pressure to afford a yellow solid as the crude product. Allyl bromide (4.50 mL, 51.8 mmol) was added to a stirred solution of this yellow solid in DMF (150 mL). After stirring for 2 h at room temperature, TLC showed the consumption of the starting material, and the reaction was quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with Et_2O (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, then *fi*ltered, and concentrated under reduced pressure. Silica gel flash column chromatography of theresidue gave a colorless oil (11.8 g, 98%) as the product. 47: R_f = 0.31(silica gel, hexanes/EtOAc = 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ7.35 (d, 1H, J = 0.8 Hz), 6.32 (dd, 1H, J = 3.2 Hz, 1.8 Hz), 6.31 (d, 1H, J = 3.3 Hz), 5.83 (ddt, 1H, J = 17.2 Hz, 10.4 Hz, 6.1 Hz), 5.30 (dq, 1H, J = 17.4 Hz, 1.3 Hz), 5.26 (dd, 1H, J = 10.3 Hz, 1.0 Hz), 5.12(tt, 1H, J = 8.2 Hz, 1.3 Hz), 4.59 (m, 2H), 4.44 (d, 1H, J = 10.4 Hz), 3.92 (dd, 1H, J = 11.6 Hz, 6.7 Hz), 3.84 (dd, 1H, J = 12.0 Hz, 9.2 Hz),3.75 (d, 1H, J = 10.6 Hz), 2.30 (m, 1H), 2.12 (m, 1H), 2.05 (bs, 1H), 1.90 (dq, 1H, J = 14.2 Hz, 4.9 Hz), 1.70 (s, 3H), 1.64 (s, 3H), 1.55 (m,1H), 1.44 (dd, 1H, J = 9.2 Hz, 6.8 Hz), 1.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 155.0, 141.9, 132.1, 131.3, 123.7, 119.7, 110.3,106.2, 71.7, 66.0, 59.5, 42.2, 37.2, 36.2, 31.0, 25.6, 25.2, 17.6, 15.1; IR(KBr) 2961, 2916, 2848, 1734, 1716, 1697, 1016 cm^{-1}; HRMS (ESI/ $[M + Na]^+$) calcd for $C_{20}H_{28}NaO_5$: 371.1834; found: 371.1829.

Allyl(1-(Furan-2-yl(hydroxy)methyl)-3-(iodomethyl)-2-methyl-2-(4-methylpent-3-en-1-yl) cyclopropane-1-carboxylate (13).

Iodine (8.48 g, 33.4 mmol) was added in portions to a stirred solution of compound 47 (9.69 g, 27.8 mmol), imidazole (2.27 g, 33.4 mmol), and PPh_3 (8.76 g, 33.4 mmol) in THF (100 mL) at 0 °C. After stirringat 0 °C for 15 min, TLC showed the reaction to be complete. The reaction was quenched by addition of a saturated aqueous $Na_2S_2O_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$,then filtered, and concentrated under reduced pressure. Silica gel flashcolumn chromatography of the residue gave a colorless oil (10.8 g, 85%) as the product. 13: R_f = 0.60 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, 1H, J = 0.9 Hz), 6.31 (dd, 1H,J = 3.2 Hz, 1.9 Hz), 6.26 (d, 1H, J = 3.2 Hz), 5.81 (ddt, 1H, J = 17.1Hz, 10.5 Hz, 6.1 Hz), 5.27 (dd, 1H, J = 12.4 Hz, 1.2 Hz), 5.23 (dd, 1H, J = 5.5 Hz, 1.3 Hz), 5.12 (tt, 1H, J = 7.1 Hz, 1.2 Hz), 4.58 (m, 2H), 4.39 (d, 1H, J = 10.9 Hz), 3.98 (d, 1H, J = 10.9 Hz), 3.61 (m, 2H), 2.35 (m, 1H), 2.20 (m, 1H), 1.88 (m, 1H), 1.70 (s, 3H), 1.68 (m, 1H), 1.66 (s, 3H),1.56 (m, 1H), 1.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 155.0, 142.0, 132.1, 131.3, 123.9, 119.6, 110.2, 106.2, 71.1, 65.8, 44.5, 38.7, 36.3, 33.2, 25.7, 25.4, 17.7, 12.9, 2.9; IR (KBr) 2966, 2926, 2858, 1730, 1695, 1144, 734 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{20}H_{27}NaIO_4$: 481.0852; found: 481.0844.

Allyl(2-(Furan-2-yl(hydroxy)methyl)-3,7-dimethyl-3-vinyloct-6-enoate (16).

n-BuLi (25.0 mL of a 2.4 M solution in hexanes, 60.0 mmol) was added dropwise to a stirred solution of 13 (10.9 g, 24.0 mmol) in THF (100 mL) at < −80 °C in a liquid nitrogen/ethanol cooling bath. After stirring for 15 min, TLC showed the starting material had been consumed and the reaction was quenched by slow addition of a saturated aqueous NH_4Cl solution (50 mL). After warming to room temperature, the aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, *fi*ltered, and concentrated under reduced pressure. Silica gel *fl*ash column chromatography of the residue gave acolorless oil (7.74 g, 97%) as the product, a single diastereoisomer. 16:R_f = 0.50 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, 1H, J = 1.0 Hz), 6.28 (dd, 1H, J = 3.2 Hz, 1.9 Hz), 6.23 (d, 1H, J = 3.2 Hz), 6.07 (dd, 1H, J = 17.6 Hz, 10.8 Hz), 5.70 (ddt, 1H, J = 17.2 Hz, 10.4 Hz, 5.9 Hz), 5.24 (m, 2H), 5.16 (m, 2H), 5.09 (dd, 1H, J = 10.1 Hz, 3.8 Hz), 5.03 (tt, 1H, J = 7.1 Hz, 1.3 Hz), 4.37 (m, 2H), 3.14 (d, 1H, J = 10.1 Hz), 2.54 (d, 1H, J = 3.8 Hz), 1.91 (m, 2H), 1.66 (s, 3H), 1.57 (s, 3H), 1.50 (m, 1H), 1.38 (m, 1H), 1.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 154.1, 146.6, 142.3, 131.8, 131.6, 124.2, 118.5, 114.4, 110.0, 107.5, 67.8, 65.0, 59.3, 41.9, 40.1, 25.6, 22.3, 17.6, 17.6; IR (KBr) 2968, 2924, 1732, 1152, 1011, 989, 921, 737 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{20}H_{28}NaO_4$: 355.1885; found: 355.1879.

Allyl(2S,3R)-3-(2-(3,3-Dimethyloxiran-2-yl)ethyl)-2-((S)-furan-2-yl(hydroxy)methyl)-3-methylpent-4-enoate (48).

mCPBA (5.72 g, 23.2 mmol, 70%) was added in portions to a stirred solution of 16 (7.01 g, 21.1 mmol) in CH2Cl2 (100 mL) at 0 °C. After stirring at 0 °C for 15 min, TLC showed the starting material was consumed. The mixture was filtered and washed with hexanes (×2). The filtrate was quenched by addition of a saturated aqueous NaSO solution and a saturated aqueous NaHCO3 solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over MgSO4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (6.32 g, 86%) as the product. 48: Rf = 0.50 (silica gel, hexanes/EtOAc = 3:1); 1H NMR (500 MHz, CDCl) δ 7.36 (d, 1H, J = 1.0 Hz), 6.28 (dd, 1H, J = 3.2 Hz, 1.8 Hz), 6.23 (d, 1H, J = 3.2 Hz), 6.03 (m, 1H), 5.71 (m, 1H), 5.23 (m, 2H), 5.17 (m, 2H), 5.09 (d, 1H, J = 9.9 Hz), 4.38 (m, 2H), 3.13 (d, 1H, J = 10.0 Hz), 2.65 (t, 1H, J = 6.1 Hz), 2.45 (dd, 1H, J = 13.0 Hz, 3.9 Hz), 1.61 (m, 2H), 1.48 (m, 2H), 1.31 (s, 3H), 1.29 (s, 3H), 1.24 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 171.1, 171.0, 154.3, 145.8, 142.3, 131.8, 118.6, 114.6, 114.5, 110.1, 107.5, 67.8, 67.6, 65.1, 65.1, 64.5, 64.3, 59.5, 59.1, 58.3, 41.6, 41.6, 36.3, 24.8, 23.6, 18.7, 18.4, 18.2; IR (KBr) 2964, 2927, 2881, 1732, 1151, 1009, 991, 921, 738 cm−1; HRMS (ESI/[M + Na]+) calcd for C20H28NaO5: 371.1834; found: 371.1829.

8-Allyl 1-Methyl (E)-7-(Furan-2-yl(hydroxy)methyl)-2,6-dimethyl- 6-vinyloct-2-enedioate (17).

NaIO4 (4.64 g, 21.7 mmol) was added to a stirred solution of 48 (6.32 g, 18.1 mmol) in THF/H2O (THF: H2O = 2:1, 120 mL) at 0 °C and was followed by 1 N aqueous HCl (5 mL). After stirring at 0 °C for 4 h, TLC showed the starting material had been consumed. The reaction was quenched by addition of a

saturated aqueous NaHCO3 solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na2SO4, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (5.00 g) as the product, which was dissolved in CH2Cl2 (80 mL) and then treated with methyl 2-(triphenylphosphoranylidene)propanoate (7.56 g, 21.7 mmol). After stirring for 20 h at room temperature, TLC showed the starting material had been consumed. The reaction was quenched by addition of a saturated aqueous NH4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over MgSO4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (5.52 g, 81% for two steps) as the product (E-isomer only). 17: Rf = 0.55 (silica gel, hexanes/EtOAc = 3:1); 1H NMR (400 MHz, CDCl3) δ 7.36 (d, 1H, J = 1.0 Hz), 6.68 (td, 1H, J = 7.4 Hz, 1.3 Hz), 6.28 (dd, 1H, J = 3.2 Hz, 1.9 Hz), 6.24 (d, 1H, J = 3.2 Hz), 6.05 (dd, 1H, J = 17.6 Hz, 10.8 Hz), 5.69 (ddt, 1H, J = 17.1 Hz, 10.4 Hz, 5.9 Hz), 5.26 (m, 2H), 5.17 (m, 2H), 5.09 (dd, 1H, J = 10.0 Hz, 4.1 Hz), 4.37 (m, 2H), 3.73 (s, 3H), 3.14 (d, 1H, J = 10.0 Hz), 2.43 (d, 1H, J = 4.1 Hz), 2.13 (m, 2H), 1.81 (s, 3H), 1.62 (m, 1H), 1.51 (m, 1H), 1.34 (s, 3H); 13C NMR (100 MHz, CDCl3) δ 171.0, 168.6, 154.0, 145.7, 142.4, 142.1, 131.7, 127.6, 118.7, 114.8, 110.1, 107.6, 67.7, 65.1, 59.2, 51.7, 41.8, 38.4, 23.2, 18.0, 12.4; IR (KBr) 2972, 2951, 2881, 1714, 1647, 1282, 1249, 1151, 1010, 991, 921, 740 cm–1; HRMS (ESI/[M + Na]+) calcd for C21H28NaO6: 399.1784; found: 399.1776.

8-Allyl 1-Methyl (E)-7-(6-Hydroxy-3-oxo-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2-enedioate (18).

$VO(acac)_2$ (0.199 g,0.750 mmol) was added to a stirred solution of 17 (5.65 g, 15.0 mmol)and TBHP (3.27 mL, 18.0 mmol, ~5.5 M in *n*-decane) in CH_2Cl_2 (60 mL) at 0 °C. The resulting solution was allowed to warm up to room temperature. After stirring for 3 h at room temperature, TLC showed complete consumption of the starting material. The reaction wasquenched by addition of a saturated aqueous $Na_2S_2O_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, *fi*ltered, and concentrated under reduced pressure. Silica gel flash columnchromatography of the residue gave a yellow oil (5.59 g, 95%) as the product (a mixture of lactol diastereoisomers). 18: R_f = 0.19 (silica gel,hexanes/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.87 (dd,0.3H, J = 10.2 Hz, 1.2 Hz), 6.81 (dd, 0.7H, J = 10.3 Hz, 3.4 Hz), 6.72 (m, 1H), 6.11 (dd, 0.3H, J = 10.2 Hz, 1.6 Hz), 6.05 (d, 0.7H, J = 10.2 Hz), 5.96 (m, 1H), 5.90 (dd, 1H, J = 17.5 Hz, 10.9 Hz), 5.63 (m, 1H), 5.37 (m, 1H), 5.26 (m, 1H), 5.07 (m, 3H), 4.66 (m, 1H), 4.57 (m, 1H), 3.87 (d, 0.3H, J = 8.0 Hz), 3.73 (s, 3H), 3.51 (d, 0.7H, J = 5.4 Hz), 2.97 (d, 0.7H, J = 8.0 Hz), 2.94 (d, 0.3H, J = 8.7 Hz), 2.11 (m, 2H), 1.80 (s, 3H), 1.71 (m, 2H), 1.21 (s, 2.1H), 1.19 (s, 0.9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.2, 194.6, 171.4, 171.3, 168.9, 168.8, 147.9, 147.2, 145.3, 145.3, 145. 0, 144.0, 143.6, 143.1, 142.9, 142. 7, 140.4, 132.1, 132.1, 129.0, 128.4, 127.4, 127.3, 118.8, 118.7, 113.9, 113.5, 91.9, 87.9, 78.5, 73.8, 65.5, 65.4, 53.2, 52.8, 51.7, 41.6, 41.5, 38.2, 38.0, 23.6, 21.1, 20.7, 12.3; IR (KBr) 2951, 2881, 1703, 1647, 1284, 1253, 1163, 1033, 993, 923 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{21}H_{28}NaO_7$: 415.1733;

found: 415.1729.

5-Allyl1-Methyl1,6-Dimethyl-4,10-dioxo-6-vinyloctahydro-2H-4a,2-(epoxymethano)naphthalene-1,5-dicarboxylate (19).

Jones reagent (2.59 mL, 7.5 mmol, 2.9 M) was added dropwise to a stirred solution of 18 (0.59 g, 1.5 mmol) in Me_2CO (30 mL) at 0 °C. After stirring at 0 °C for 30 min, TLC showed the consumption of the starting material, and the reaction was quenched by adding *i*-PrOH slowly at 0 °C. The mixture was filtered through a pad of Celite and washed with Et_2O. The filtrate was washed with brine (×2). The organic layer was dried over $MgSO_4$ and filtered. Concentration of the solution gave the crude product, which was used directly in the next step without further purification. To a stirred solution of the crude product in *t*-BuOH (10 mL) was added *c*Hex_2NMe (65 µL, 0.3 mmol) at room temperature. After 24 h of stirring at room temperature, TLC showed consumption of the starting material. Silica gel (ca. 1.5 g) was added to the reaction mixture which was then concentrated. Silica gel flash column chromatography of the residue gave a white powder (352 mg, 60% for two steps) as the product (single diastereoisomer). 19: R_f = 0.60 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (dd, 1H, *J* = 17.5 Hz, 11.0 Hz), 5.87 (ddt, 1H, *J* = 16.2 Hz, 11.1 Hz, 5.7 Hz), 5.32 (dd, 1H, *J* = 17.1 Hz, 1.4 Hz), 5.22 (dd, 1H, *J* = 10.4 Hz, 1.0 Hz), 5.10 (d, 1H, *J* = 11.0 Hz), 5.03 (d, 1H, *J* = 17.6 Hz), 4.56 (dd, 2H, *J* = 5.6 Hz, 1.1 Hz), 3.76 (s, 3H), 3.13 (t, 1H, *J* = 2.8 Hz), 3.02 (s, 1H), 2.71–2.53 (m, 3H), 1.95 (dt, 1H, *J* = 13.8 Hz, 3.3 Hz), 1.81 (qd, 1H, *J* = 13.3 Hz, 3.1 Hz), 1.48 (dt, 1H, *J* = 13.6 Hz, 3.2 Hz), 1.36 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.3, 174.2, 170.5, 169.0, 141.1, 131.8, 118.5, 112.9, 86.9, 65.4, 53.2, 52.5, 46.6, 46.1, 43.2, 38.6, 38.4, 35.8, 29.8, 21.3, 20.1; IR (KBr) 3085, 2959, 2928, 2876, 1768, 1731, 1648, 1416, 1233, 1161, 1011, 963, 919, 748 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{21}H_{26}NaO_7$: 413.1576; found: 413.1571.

5-Allyl1-Methyl1,6-Dimethyl-10-oxo-4-(((trifluoromethyl)sulfonyl)oxy)-6-vinyl-1,5,6,7,8,8a-hexahydro-2H-4a,2-(epoxymethano)naphthalene-1,5-dicarboxylate (23)

KHMDS (0.38 mL, 0.38 mmol, 1 mol/L in THF) was added dropwise to a stirred solution of 19 (100 mg, 0.26 mmol) in THF (1 mL) at 0 °C. After stirring at 0 °C for 60 min, a solution of $PhNTf_2$ (185.8 mg, 0.52 mmol) in THF (0.5 mL) was added, and the reaction was stirred at 0 °C for 30 min and then allowed to warm to room temperature for 2 h. TLC showed the starting material had been consumed. The reaction was quenched by addition of water. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (13.6 mg, 10%) as the product. 23: R_f = 0.40 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.39 (dd, *J* = 17.5, 11.0 Hz, 1H), 6.31 (d, *J* = 7.1 Hz, 1H), 5.90 (ddt, *J* = 16.5, 10.5, 5.9 Hz, 1H), 5.34 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.24 (dd, *J* = 10.4, 1.0 Hz, 1H), 5.10 (d, *J* = 11.1 Hz, 1H), 5.01 (d, *J* = 17.5 Hz, 1H), 4.65 (dd, *J* = 13.1, 6.0 Hz, 1H), 4.57 (dd, *J* = 13.1, 5.9 Hz, 1H), 3.71 (s, 2H), 2.75 (s, 1H), 2.55 (dd, *J* = 11.4, 5.8 Hz, 1H), 2.04 (dd, *J* = 10.1, 3.7 Hz, 1H), 1.75–1.57 (m, 4H), 1.34 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5, 168.8, 168.3, 149.2, 140.8, 131.6, 118.9, 118.4(q, J_{CF} = 312 Hz), 117.2, 112.8, 82.2, 65.8,

53.6, 52.9, 48.9, 48.3, 45.8, 38.9, 38.5, 30.0, 26.9, 20.7; IR (KBr) 2924, 2851, 1771, 1733, 1674, 1429, 1214, 1138, 974, 853, 740, 602 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{22}H_{25}F_3NaO_9S$: 545.1069; found: 545.1065.

5-Allyl1-Methyl4-(2-Methoxy-2-oxoethyl)-1,6-dimethyl-10-oxo-6-vinyl-1,5,6,7,8,8a-hexahydro-2H-4a,2-(epoxymethano)naph- thalene-1,5-dicarboxylate (26a).

Methyl 2-(*n*-butylphosphoranylidene)propanoate (357 mg, 1.3 mmol) was added to a stirred solution of 19 (100 mg, 0.26 mmol) in mesitylene (2 mL). After stirring at 180 °C for 24 h, TLC showed consumption of the starting material was complete, and the reaction was cooled to room temperature and quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (5.8 mg, 5%) as the product. **26a**: R_f = 0.25 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (dd, 1H, *J* = 17.6 Hz, 11.0 Hz), 6.29 (d, 1H, *J* = 6.3 Hz), 5.89 (ddt, 1H, *J* = 16.3 Hz, 11.5 Hz, 5.8 Hz), 5.34 (dd, 1H, *J* = 15.8 Hz, 1.4 Hz), 5.23 (dd, 1H, *J* = 9.3 Hz, 1.1 Hz), 5.07 (dd, 1H, *J* = 11.0 Hz, 0.9 Hz), 4.99 (dd, 1H, *J* = 16.5 Hz, 1.0 Hz), 4.60 (m, 2H), 3.69 (s, 3H), 3.68 (s, 3H), 3.58 (d, 1H, *J* = 6.3 Hz), 3.20 (q, 2H, *J* = 16.9 Hz), 2.93 (s, 1H), 2.57 (dd, 1H, *J* = 12.2 Hz, 5.1 Hz), 1.95 (td, 1H, *J* = 13.5 Hz, 2.9 Hz), 1.66 (m, 3H), 1.30 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 171.0, 170.8, 169.5, 141.9, 139.3, 131.4, 130.3, 119.0, 112.4, 84.1, 65.4, 55.4, 52.6, 52.2, 49.6, 48.1, 45.0, 39.1, 39.0, 36.3, 29.6, 21.1, 20.8; IR (KBr) 2953, 1732, 1647, 1435, 1261, 1153, 1105, 958 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{24}H_{30}NaO_8$: 469.1838; found: 469.1834.

8-Allyl1-Methyl(E)-7-(6-Methoxy-3-oxo-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2-enedioate (27).

Ag_2O (8.83 g, 38.1 mmol) and CH_3I (3.95 mL, 63.5 mmol) were added to a stirred solution of 18 (5.00 g, 12.7 mmol) in Me_2CO (60 mL). After stirring at 50 °C for 10 h, TLC revealed the consumption of the starting material. The reaction was quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (4.75 g, 92%) as the product (a mixture of lactol diastereoisomers). 27: R_f = 0.47 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (dd, 0.8H, *J* = 10.2 Hz, 1.2 Hz), 6.76 (dd, 0.2H, *J* = 10.2 Hz, 3.5 Hz), 6.70 (m, 1H), 6.11 (dd, 0.8H, *J* = 10.2 Hz, 1.9 Hz), 5.96 (m, 2.2H), 5.38 (m, 1H), 5.25 (m, 2H), 5.12 (m, 1H), 5.04 (m, 1H), 4.68 (m, 1H), 4.59 (m, 1H), 4.52 (dd, 1H, *J* = 9.7 Hz, 1.4 Hz), 3.73 (s, 3H), 3.55 (s, 0.6H), 3.54 (s, 2.4H), 3.00 (d, 0.2H, *J* = 7.4 Hz), 2.96 (d, 0.8H, *J* = 9.7 Hz), 2.15 (m, 2H), 1.81 (s, 3H), 1.65 (m, 2H), 1.24 (s, 0.6H), 1.21 (s, 2.4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 171.2, 168.6, 146.6, 144.2, 142.5, 142.3, 142.2, 132.1, 132.0, 129.3, 127.5, 118.9, 113.1, 98.7, 78.4, 65.5, 65.4, 57.1, 52.9, 51.7, 41.3, 38.3, 23.5, 20.5, 12.4; IR (KBr) 2972, 2951, 1713, 1647, 1166, 1043, 995, 925, 739 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{22}H_{30}NaO_7$: 429.1889; found:

429.1882.

8-Allyl1-Methyl(E)-7-(E)-6-Methoxy-3-(2-methoxy-2-oxoethyli-dene)-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2-ene-dioate (28a).

Methyl 2-(*n*-butylphosphoranylidene)propanoate (24) (6.75 g, 24.6 mmol) was added to a stirred solution of 27 (2.00 g, 4.92 mmol) in toluene (50 mL). After stirring at 100 °C for 1.5 h, TLC showed consumption of the starting material was complete, and then the reaction was cooled to room temperature and quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (1.48 g, 65%) as the product (a mixture of lactol diastereoisomers). 28a: R_f = 0.50 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, 0.2H, *J* = 11.5 Hz), 7.51 (d, 0.8H, *J* = 10.5 Hz), 6.72 (m, 1H), 5.92 (m, 3H), 5.65 (s, 1H), 5.32 (m, 1H), 5.20 (m, 2H), 5.07 (m, 2H), 4.56 (m, 2H), 4.45 (m, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.51 (s, 2.4H), 3.42 (s, 0.6H), 3.24 (d, 0.8H, *J* = 8.2 Hz), 2.94 (d, 0.2H, *J* = 9.7 Hz), 2.15 (m, 2H), 1.82 (s, 3H), 1.73 (m, 1H), 1.57 (m, 1H), 1.33 (s, 0.6H), 1.24 (s, 2.4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 171.2, 168.6, 165.9, 165.9, 146.6, 146.5, 144.4, 144.0, 142.3, 142.2, 131.7, 131.6, 131.4, 131.0, 127.5, 125.9, 119.3, 119.2, 115.5, 115.3, 113.6, 113.5, 97.8, 94.5, 73.7, 65.3, 65.3, 57.6, 56.9, 55.3, 51.6, 51.3, 42.4, 42.0, 38.0, 37.8, 23.6, 23.5, 20.3, 12.3; IR (KBr) 2951, 1719, 1647, 1248, 1175, 1151, 1047, 993 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{25}H_{34}NaO_8$: 485.2151; found: 485.2146.

8-Allyl1-Methyl(E)-7-((E)-3-(2-(tert-Butoxy)-2-oxoethylidene)-6-methoxy-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2- enedioate (28b).

tert-Butyl 2-(*n*-butylphosphoranylidene)propanoate (24) (5.84 g, 18.5 mmol) was added to a stirred solution of 27 (1.50 g, 3.69 mmol) in toluene (50 mL). After stirring at 100 °C for 1.5 h, TLC showed consumption of the starting material, and the reaction was cooled to room temperature and quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (1.11 g, 60%) as the product (a mixture of lactol diastereoisomers). 28b: R_f = 0.55 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, 0.2H, *J* = 10.5 Hz), 7.50 (d, 0.8H, *J* = 10.5 Hz), 6.72 (m, 1H), 5.91 (m, 3H), 5.57 (s, 1H), 5.34 (m, 1H), 5.20 (m, 2H), 5.05 (m, 2H), 4.57 (m, 2H), 4.42 (m, 1H), 3.73 (s, 3H), 3.49 (s, 2.4H), 3.42 (s, 0.6H), 3.22 (d, 0.8H, *J* = 8.7 Hz), 2.93 (d, 0.2H, *J* = 10.0 Hz), 2.14 (m, 2H), 1.81 (s, 3H), 1.75 (m, 1H), 1.57 (m, 1H), 1.46 (s, 9H), 1.32 (s, 0.6H), 1.24 (s, 2.4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4, 168.6, 165.0, 145.2, 144.4, 144.0, 142.4, 142.3, 131.6, 131.5, 130.8, 127.4, 126.1, 126.0, 119.3, 117.6, 113.4, 97.9, 94.7, 80.6, 73.7, 65.3, 57.3, 56.9, 51.7, 42.3, 37.9, 28.1, 23.6, 20.3, 12.4; IR (KBr) 2978, 2951, 1713, 1647, 1251, 1145, 1049, 989 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{28}H_{40}NaO_8$:

527.2621; found: 527.2613.

8-Allyl1-Methyl(E)-7-(E)-3-(2-Methoxy-2-oxoethylidene)-6-oxo-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2-enedioate (29a).

Jones reagent (17.9 mL, 52.0 mmol, 2.9 M) was added dropwise to a stirred solution of 28a (1.20 g, 2.60 mmol) in Me_2CO (50 mL) at 0 °C. After stirring for 2.5 h at 0 °C, TLC showed complete consumption of starting material and the reaction was quenched by adding *i*-PrOH (30 mL) slowly at 0 °C. The mixture was then filtered through a pad of Celite and washed with EtOAc (×3). The filtrate was quenched by addition of a saturated aqueous $NaHCO_3$ solution, and the aqueous phase was extracted with EtOAc (×3). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (0.871 g, 75%) as the product. 29a: R_f = 0.40 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, 1H, *J* = 10.1 Hz), 6.68 (td, 1H, *J* = 7.4 Hz, 1.2 Hz), 6.15 (dd, 1H, *J* = 10.1 Hz, 1.6 Hz), 5.84 (m, 2H), 5.77 (dd, 1H, *J* = 17.6 Hz, 10.9 Hz), 5.31 (m, 2H), 5.24 (m, 2H), 5.10 (d, 1H, *J* = 17.5 Hz), 4.57 (q, 1H, *J* = 6.2 Hz), 4.45 (q, 1H, *J* = 6.2 Hz), 3.76 (s, 3H), 3.73 (s, 3H), 3.03 (d, 1H, *J* = 10.7 Hz), 2.09 (m, 2H), 1.80 (s, 3H), 1.68 (m, 1H), 1.53 (m, 1H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 168.5, 164.6, 160. 7, 143.5, 142.0, 141.7, 137.6, 131.2, 127.8, 123.2, 121.7, 119.7, 114.9, 80.2, 65.6, 60.5, 51.9, 51.6, 42.0, 37.6, 23.3, 19.9, 12.3; IR (KBr) 2953, 1732, 1715, 1647, 1437, 1260, 1171, 1111 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{24}H_{30}NaO_8$: 469.1838; found: 469.1833.

8-Allyl1-Methyl(E)-7-(E)-3-(2-(tert-Butoxy)-2-oxoethylidene)-6-oxo-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2-ene-dioate (29b).

Jones reagent (16.4 mL of a 2.9 M solution, 47.6 mmol) was added dropwise to a stirred solution of 28b (1.20 g, 2.38 mmol) in Me_2CO (50 mL) at 0 °C. After 2.5 h of stirring at 0 °C, TLC showed consumption of starting material and the reaction was quenched by addition of *i*-PrOH (30 mL) slowly at 0 °C. The mixture was then filtered through a pad of Celite and washed with EtOAc (×3). The filtrate was quenched by addition of a saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (0.872 g, 75%) as the product. 29b: R_f = 0.27 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, 1H, *J* = 10.1 Hz), 6.68 (t, 1H, *J* = 7.4 Hz), 6.11 (dd, 1H, *J* = 10.1 Hz, 1.1 Hz), 5.81 (m, 3H), 5.27 (m, 4H), 5.09 (d, 1H, *J* = 17.5 Hz), 4.57 (q, 1H, *J* = 6.0 Hz), 4.45 (q, 1H, *J* = 6.2 Hz), 3.73 (s, 3H), 3.03 (d, 1H, *J* = 10.8 Hz), 2.09 (m, 2H), 1.80 (s, 3H), 1.68 (m, 1H), 1.53 (m, 1H), 1.48 (s, 9H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 168.5, 163.5, 160.9, 143.6, 141.8, 140.6, 137.8, 131.3, 127.8, 124.2, 122.6, 119.7, 114.9, 81.9, 80.3, 65.6, 60.5, 51.6, 41.9, 37.6, 28.1, 23.4, 19.9, 12.3; IR (KBr) 2980, 2951, 1732, 1713, 1640, 1369, 1267, 1148, 1109, 738 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{27}H_{36}NaO_8$: 511.2308; found: 511.2300.

8-Allyl1-Methyl(E)-7-(5-(2-Methoxy-2-oxoethyl)-2-oxo-2H-pyran-6-yl)-2,6-dimethyl-6-vinyloct-2-enedioate (30a).

DABCO (0.528 g, 4.70 mmol) was added to a stirred solution of 29a (2.10 g, 4.70 mmol) in toluene (25 mL). After stirring for 17 h at 70 °C, TLC showed consumption of the starting material was complete. The reaction was then quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (1.88 g, 90%) as the product. 30a: R_f = 0.20 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, 1H, *J* = 9.6 Hz), 6.70 (td, 1H, *J* = 7.3 Hz, 1.1 Hz), 6.23 (d, 1H, *J* = 9.5 Hz), 5.86 (m, 2H), 5.28 (dd, 1H, *J* = 16.0 Hz, 1.3 Hz), 5.22 (dd, 1H, *J* = 9.5 Hz, 1.0 Hz), 5.11 (d, 1H, *J* = 10.9 Hz), 5.06 (d, 1H, *J* = 17.4 Hz), 4.60 (d, 2H, *J* = 5.6 Hz), 3.73 (s, 3H), 3.71 (s, 3H), 3.69 (s, 1H), 3.34 (s, 2H), 2.09 (m, 2H), 1.85 (m, 1H), 1.81 (s, 3H), 1.64 (m, 1H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 168.5, 167.4, 160.8, 158.2, 146.5, 141.9, 141.8, 131.4, 127.7, 118.6, 115.3, 114.8, 111.1, 65.8, 55.3, 52.4, 51.7, 43.9, 38.0, 35.2, 23.5, 19.5, 12.3; IR (KBr) 2953, 1732, 1715, 1643, 1548, 1435, 1260, 1169, 1103, 1005, 924 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{24}H_{30}NaO_8$: 469.1838; found: 469.1830.

8-Allyl1-Methyl(E)-7-(5-(2-(tert-Butoxy)-2-oxoethyl)-2-oxo-2H-pyran-6-yl)-2,6-dimethyl-6-vinyloct-2-enedioate (30b)

DABCO (0.505 g, 4.50 mmol) was added to a stirred solution of 29b (1.10 g, 2.25 mmol) in toluene (25 mL). The resulting solution was allowed to warm up to 70 °C and stirred for 17 h. The reaction was quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (0.879 g, 80%) as the product and recovered starting material (0.164 g, 15%). 30b: R_f = 0.20 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, 1H, *J* = 9.5 Hz), 6.69 (td, 1H, *J* = 7.4 Hz, 1.3 Hz), 6.20 (d, 1H, *J* = 9.5 Hz), 5.86 (m, 2H), 5.26 (dd, 1H, *J* = 17.1 Hz, 1.4 Hz), 5.20 (dd, 1H, *J* = 10.5 Hz, 1.2 Hz), 5.09 (d, 1H, *J* = 11.09 Hz), 5.04 (d, 1H, *J* = 17.3 Hz), 4.57 (dd, 2H, *J* = 5.5 Hz, 1.0 Hz), 3.71 (s, 3H), 3.69 (s, 1H), 3.22 (s, 2H), 2.07 (m, 2H), 1.83(m, 1H), 1.78 (s, 3H), 1.64 (m, 1H), 1.42 (s, 9H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 168.5, 167.6, 160.9, 157.8, 146.6, 142.0, 141.8, 131.4, 127.7, 118.6, 115.2, 114.6, 111.7, 82.1, 65.8, 55.1, 51.6, 43.9, 38.0, 36.6, 27.9, 23.6, 19.5, 12.3; IR (KBr) 2962, 1730, 1719, 1647, 1259, 1149, 1101, 1016, 800 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{27}H_{36}NaO_8$: 511.2308; found: 511.2300.

5-Allyl1-Methyl4-(2-Methoxy-2-oxoethyl)-1,6-dimethyl-10-oxo-6-vinyl-1,5,6,7,8,8a-hexahydro-2H-4a,2-(epoxymethano)naph-thalene-1,5-dicarboxylate (26a).

A solution of 30a (1.10 g, 2.46 mmol) in toluene (30 mL) was heated under reflux in a sealed tube for 3 days. After TLC showed consumption of the starting material, the reaction was cooled to room temperature and concentrated under reduced pressure. Silica gel flash column chromatography of the

residue afforded a yellow oil (979 mg, 89%) as the product (single diastereoisomer). 26a: R_f = 0.25 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (dd, 1H, *J* = 17.6 Hz, 11.0 Hz), 6.29 (d, 1H, *J* = 6.3 Hz), 5.89 (ddt, 1H, *J* = 16.3 Hz, 11.5 Hz, 5.8 Hz), 5.34 (dd, 1H, *J* = 15.8 Hz, 1.4 Hz), 5.23 (dd, 1H, *J* = 9.3 Hz, 1.1 Hz), 5.07 (dd, 1H, *J* = 11.0 Hz, 0.9 Hz), 4.99 (dd, 1H, *J* = 16.5 Hz, 1.0 Hz), 4.60 (m, 2H), 3.69 (s, 3H), 3.68 (s, 3H), 3.58 (d, 1H, *J* = 6.3 Hz), 3.20 (q, 2H, *J* = 16.9 Hz), 2.93 (s, 1H), 2.57 (dd, 1H, *J* = 12.2 Hz, 5.1 Hz), 1.95 (td, 1H, *J* = 13.5 Hz, 2.9 Hz), 1.66 (m, 3H), 1.30 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 171.0, 170.8, 169.5, 141.9, 139.3, 131.4, 130.3, 119.0, 112.4, 84.1, 65.4, 55.4, 52.6, 52.2, 49.6, 48.1, 45.0, 39.1, 39.0, 36.3, 29.6, 21.1, 20.8; IR (KBr) 2953, 1732, 1647, 1435, 1261, 1153, 1105, 958 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{24}H_{30}NaO_8$: 469.1838; found: 469.1834.

5-Allyl1-Methyl4-(2-(tert-Butoxy)-2-oxoethyl)-1,6-dimethyl-10-oxo-6-vinyl-1,5,6,7,8,8a-hexahydro-2H-4a,2-(epoxymethano)naphthalene-1,5-dicarboxylate (26b)

A solution of 30b (200 mg, 0.409 mmol) in toluene (10 mL) was heated under reflux in a sealed tube for 3 days. After TLC showed consumption of the starting material, the reaction was cooled to room temperature and concentrated under reduced pressure. Silica gel flash column chromatography of the residue afforded a yellow oil (170 mg, 85%) as the product (single diastereoisomer). 26b: R_f = 0.25 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 (dd, 1H, *J* = 17.6 Hz, 11.0 Hz), 6.28 (d, 1H, *J* = 6.3 Hz), 5.89 (ddt, 1H, *J* = 16.3 Hz, 10.6 Hz, 5.7 Hz), 5.35 (dd, 1H, *J* = 17.2 Hz, 1.4 Hz), 5.23 (dd, 1H, *J* = 10.4 Hz, 1.1 Hz), 5.07 (d, 1H, *J* = 11.1 Hz), 4.99 (d, 1H, *J* = 17.6 Hz), 4.61 (m, 2H), 3.68 (s, 3H), 3.57 (d, 1H, *J* = 6.3 Hz), 3.10 (q, 2H, *J* = 16.6 Hz), 3.00 (s, 1H), 2.57 (dd, 1H, *J* = 12.1 Hz, 5.3 Hz), 1.95 (dt, 1H, *J* = 13.4 Hz, 3.2 Hz), 1.66 (m, 3H), 1.46 (s, 9H), 1.30 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 171.2, 169.6, 141.9, 139.9, 131.6, 129.8, 118.9, 112.4, 84.2, 81.6, 65.3, 55.2, 52.5, 49.5, 47.9, 45.1, 39.6, 39.2, 38.9, 38.1, 29.6, 27.9, 21.4, 20.9; IR (KBr) 2953, 1732, 1647, 1435, 1261, 1153, 1105, 958 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{27}H_{36}NaO_8$: 511.2308; found: 511.2301.

4-(Carboxymethyl)-1-(methoxycarbonyl)-1,6-dimethyl-10-oxo-6-vinyl-1,5,6,7,8,8a-hexahydro-2H-4a,2-(epoxymethano)naphthalene-5-carboxylic Acid (31)

PPh_3 (24 mg, 0.09 mmol), pyrrolidine (45 µL, 0.54 mmol), and $Pd(PPh_3)_4$ (52 mg, 0.045 mmol) were added to a stirred solution of 26b (0.22 g, 0.45 mmol) in CH_2Cl_2 (5 mL) at 0 °C. After 2.5 h of stirring at 0 °C, TLC showed consumption of starting material, and the reaction was quenched by addition of an aqueous HCl (2 mL, 0.5M) solution. The aqueous phase was extracted with EtOAc (10 mL × 3), and the combined organic extracts were washed with a saturated aqueous $NaHCO_3$ solution (5 mL × 3). The organic extracts were discarded, and the aqueous phase was acidified to pH = 1. Then the aqueous phase was extracted with EtOAc (15 mL × 3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, then filtered, and concentrated to give a yellow oil as the crude product which was dissolved in HCO_2H (5 mL) and stirred for 10 h. The solution was concentrated under reduced pressure to afford the product as a white foam (159 mg, 90% for two steps), which was used directly in the next step without further purification. 31: ^{1}H NMR (500 MHz, CD_3OD) δ 6.51 (dd, 1H, *J* = 17.6 Hz, 11.1 Hz),

6.32 (d, 1H, *J* = 6.3 Hz), 5.01 (d, 1H, *J* = 8.4 Hz), 4.98 (d, 1H, *J* = 1.6 Hz), 3.63 (s, 3H), 3.49 (d, 1H, *J* = 6.3 Hz), 3.34 (dd, 1H, *J* = 17.0 Hz, 1.0 Hz), 3.23 (d, 1H, *J* = 17.0 Hz), 2.98 (s, 1H), 2.64 (dd, 1H, *J* = 11.3 Hz, 6.2 Hz), 1.96 (dt, 1H, *J* = 13.4 Hz, 3.2 Hz), 1.66 (m, 2H), 1.55 (m, 1H), 1.27 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 176.83, 173.92, 173.56, 143.72, 141.90, 130.76, 112.47, 86.34, 56.25, 53.11, 51.05, 49.37, 46.28, 39.93, 39.88, 37.22, 30.52, 22.12, 21.67; HRMS (ESI/[M + Na]$^+$) calcd for $C_{20}H_{24}NaO_8$: 415.1369; found: 415.1363.

Methyl8,13-Dimethyl-3,9,11-trioxo-8-vinyl-2,3,5,6,7,-8,8a,9,11,12-decahydro-2,5-methanobenzo[c]pyrano[2,3-d]-oxepine-13-carboxylate (32)

EDCI (30.0 mg, 0.153 mmol) in CH_2Cl_2 (1 mL) was added dropwise to a stirred solution of 31 (50.0 mg, 0.127 mmol) in CH_2Cl_2 (3 mL) at 0 °C, and then DMAP (1.5 mg, 0.0127 mmol) was added after 5 min. The resulting solution was allowed to warm up to room temperature and stirred for 2 h, then EDCI (30.0 mg, 0.153 mmol) was added in one portion, and the reaction solution was stirred for another 2 h. Silica gel flash column chromatography of the reaction solution gave a white powder (33.3 mg, 70%). 32: R_f = 0.16 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (dd, 1H, *J* = 17.7 Hz, 11.1 Hz), 6.06 (s, 1H), 5.21 (d, 1H, *J* = 11.1 Hz), 5.08 (d, 1H, *J* = 17.8 Hz), 3.80 (s, 3H), 3.04 (t, 1H, *J* = 2.7 Hz), 2.94 (s, 1H), 2.72 (s, 2H), 2.65 (dd, 1H, *J* = 12.9 Hz, 5.2 Hz), 2.03 (dt, 1H, *J* = 13.8 Hz, 3.1 Hz), 1.85 (qd, 1H, *J* = 13.4 Hz, 3.1 Hz),1.67 (m, 1H), 1.44 (m, 1H), 1.34 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 169.8, 161.9, 159.0, 150.3, 140.3, 117.7, 113.2, 79.5, 57.6, 53.2, 46.7, 44.9, 41.4, 39.3, 38.0, 28.9, 28.7, 21.5, 20.5; IR (KBr) 2955, 2922, 2851, 1803, 1734, 1225, 972 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{20}H_{22}NaO_7$: 397.1263; found: 397.1257.

4-(2-Methoxy-2-oxoethyl)-1-(methoxycarbonyl)-1,6-dimethyl-10-oxo-6-vinyl-1,5,6,7,8,8a-hexahydro-2H-4a,2-(epoxymethano)naph-thalene-5-carboxylic Acid(34).

PPh_3 (87 mg, 0.332 mmol), pyrrolidine (163 µL, 1.99 mmol), and $Pd(PPh_3)_4$ (192 mg, 0.166 mmol) were added to a stirred solution of 26a (0.74 g, 1.66 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After 30 min of stirring at 0 °C, TLC showed consumption of starting material, and the reaction was quenched by addition of aqueous HCl (10 mL, 0.5 M) solution. The aqueous phase was extracted with EtOAc (30 mL × 3), and the combined organic extracts were washed with a saturated aqueous $NaHCO_3$ solution (30 mL × 3). The organic extracts were discarded, and the aqueous phase was acidified to pH = 1. Then the aqueous phase was extracted with EtOAc (15 mL × 3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated to give an off-white amorphous solid as the product (645 mg, 96%). 34: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.44 (dd, 1H, *J* = 17.5 Hz, 11.0 Hz), 6.35 (d, 1H, *J* = 6.3 Hz), 5.17 (d, 1H, *J* = 11.0 Hz), 5.11 (d, 1H, *J* = 17.4 Hz), 3.70 (s, 3H), 3.69 (s, 3H), 3.64 (d, 1H, *J* = 6.3 Hz), 3.42 (d, 1H, *J* = 17.0 Hz), 3.23 (d, 1H, *J* = 17.0 Hz), 3.03 (s, 1H), 2.66 (dd, 1H, *J* = 12.0 Hz, 5.6 Hz), 1.94 (td, 1H, *J* = 13.7 Hz, 3.2 Hz), 1.75 (m, 2H), 1.63 (dt, 1H, *J* = 13.2 Hz, 3.7 Hz), 1.34 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.09, 173.64, 170.79, 170.68, 141.13, 139.28, 130.18, 113.26, 84.34, 55.52, 52.57, 52.15, 49.44, 47.95, 44.70, 38.82, 38.65, 36.10, 29.11, 21.02, 20.55; HRMS (ESI/[M + Na]$^+$) calcd for

$C_{21}H_{26}NaO_8$: 429.1525; found: 429.1520.

(±)-Basiliolide B (1).

TEA (0.60 mL, 4.31 mmol) and Tf_2O (0.29 mL, 1.72 mmol) were added dropwise to a stirred solution of 34 (350 mg, 0.86 mmol) in toluene (5 mL) at −78 °C. After 10 min of stirring at −78 °C, the mixture was gradually warmed to 0 °C and stirred for a further 10 min. Silica gel flash column chromatography (with TEA protection of the gel, 0.5 mL of TEA added) of the reaction solution gave a white powder (307 mg, 92%) as the natural product. The spectroscopic data obtained from our synthesis match those published by Appendino/Sterner (2) and Stoltz. (9c) Basiliolide B (1): R_f = 0.13 (silica gel, hexanes/EtOAc = 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (dd, 1H, *J* = 17.7 Hz, 11.1 Hz), 6.08 (dd, 1H, *J* = 6.3 Hz, 1.1 Hz), 5.16 (d, 1H, *J* = 11.2 Hz), 5.07 (dd, 1H, *J* = 17.7 Hz, 0.8 Hz), 4.97 (d, 1H, *J* = 1.2 Hz), 3.73 (s, 3H), 3.72 (s, 3H), 3.67 (d, 1H, *J* = 6.3 Hz), 3.18 (s, 1H), 2.30 (dd, 1H, *J* = 12.3 Hz, 5.5 Hz), 1.96 (dt, 1H, *J* = 13.4 Hz, 3.3 Hz), 1.75 (m, 1H), 1.67 (m, 1H), 1.52 (td, 1H, *J* = 13.1 Hz, 3.3 Hz), 1.31 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 170.1, 162.4, 156.7, 142.7, 139.2, 123.5, 112.2, 87.0, 79.1, 56.3, 53.2, 52.8, 50.0, 44.8, 44.7, 40.1, 38.4, 28.6, 20.9, 20.8; IR (KBr) 2953, 1764, 1732, 1667, 1618, 1458, 1442, 1335, 1263, 1107, 959, 908 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{21}H_{24}NaO_7$: 411.1420; found: 411.1421.

(Z)-3,7-Dimethylocta-2,6-dien-1-yl2-Diazoacetate(35).

K_2CO_3 (66.3 g, 480.0 mmol) and 2-bromoacetyl bromide (36.3 g, 180.0 mmol) were sequentially added dropwise to a stirred solution of nerol (18.5 g, 120.0 mmol) in CH_2Cl_2 (480 mL) at 0 °C. After 10 min of stirring at 0 °C, TLC showed consumption of starting material, and the reaction was quenched by addition of water. The aqueous phase was extracted with Et_2O (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, and then filtered. Concentration of the solution gave the crude product, which was used directly in the next step without further purification. 4-Methyl-*N*′-tosylbenzenesulfonohydrazide (TsNHNHTs) (53.1 g, 156.0 mmol) and DBU (54.8 g, 360.0 mmol) were sequentially added dropwise to a stirred solution of the crude product in THF (480 mL) at 0 °C. After 10 min stirring at 0 °C, TLC showed consumption of starting material, and the reaction was quenched by saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (17.3 g, 65% for two steps) as the product. 35: R_f = 0.60 (silica gel, hexanes/EtOAc = 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (t, *J* = 7.2 Hz, 1H), 5.10 (tt, *J* = 6.9, 1.3 Hz, 1H), 4.74 (s, 1H), 4.66 (d, *J* = 7.3 Hz, 2H), 2.16–2.04 (m, 4H), 1.77 (d, *J* = 1.0 Hz, 3H), 1.69 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 132.2, 123.5, 119.1, 77.2, 61.4, 46.1, 32.2, 26.6, 25.6, 23.5, 17.6; IR (KBr) 3123, 2969, 2931, 2860, 2109, 1696, 1445, 1389, 1363, 1338, 1237, 1179, 999, 831, 741, 469 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{12}H_{18}N_2NaO_2$: 245.1266; found: 245.1263.

(Z)-3,7-Dimethylocta-2,6-dien-1-yl 2-Diazo-3-(furan-2-yl)-3-oxo-propanoate (36).

Freshly distilled 2-furaldehyde (7.1 mL, 85.8 mmol), DBU (2.33 mL, 15.6 mmol), and IBX (32.8 g, 117 mmol) were added to a stirred solution of 35 (17.3 g, 78.0 mmol) in DMSO (400 mL) at 0 °C. The resulting solution was allowed to warm up to room temperature and stirred for 5 h. The reaction was quenched by addition of a saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with Et_2O (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and then concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (16.12 g, 65%) as the product. 36: R_f = 0.45 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.52 (d, *J* = 3.6 Hz, 1H), 6.56 (dd, *J* = 3.6, 1.6 Hz, 1H), 5.40 (t, *J* = 7.3 Hz, 1H), 5.10 (td, *J* = 7.0, 1.2 Hz, 1H), 4.76 (d, *J* = 7.3 Hz, 2H), 2.16 (dd, *J* = 11.4, 4.7 Hz, 2H), 2.09 (dd, *J* = 14.1, 7.1 Hz, 2H), 1.78 (s, 3H), 1.69 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 160.9, 150.5, 146.0, 143.6, 132.3, 123.4, 119.5, 118.6, 112.3, 77.2, 62.2, 32.2, 26.6, 25.7, 23.5, 17.6; IR (KBr) 2968, 2929, 2857, 2130, 1719, 1324, 1268, 962, 753 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{17}H_{20}N_2NaO_4$: 339.1321; found: 339.1315.

1-(Furan-2-carbonyl)-6-methyl-6-(4-methylpent-3-en-1-yl)-3-oxabicyclo[3.1.0]hexan-2-one (37).

A solution of compound 36 (16.12 g, 50.6 mmol) in toluene (50 mL) was added over 16–20 h via a syringe pump to a solution of $Cu(TBS)_2$ (13) (2.11 g, 5.06 mmol) in toluene (200 mL) at 80 °C. After TLC confirmed consumption of the starting material, the reaction was cooled to room temperature and concentrated under reduced pressure. Silica gel flash column chromatography of the residue afforded a yellow oil (10.23 g, 70%) as the product. 37 (single diastereoisomer): R_f = 0.25 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 1.0 Hz, 1H), 7.48 (d, *J* = 3.6 Hz, 1H), 6.61 (dd, *J* = 3.6, 1.6 Hz, 1H), 5.15 (tt, *J* = 7.2, 1.2 Hz, 1H), 4.47 (dd, *J* = 10.0, 5.7 Hz, 1H), 4.21 (d, *J* = 10.0 Hz, 1H), 2.72 (d, *J* = 5.6 Hz, 1H), 2.35–2.24 (m, 1H), 2.24–2.13 (m, 1H), 1.75–1.66 (m, 1H), 1.70(s, 3H), 1.63 (s, 3H), 1.50–1.57 (m, 1H), 1.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 170.6, 152.1, 147.6, 132.9, 122.8, 121.9, 112.6, 65.3, 46.9, 35.2, 33.8, 29.8, 25.7, 24.7, 18.5, 17.6; IR (KBr) 2968, 2917, 2857, 1758, 1654, 1463, 1388, 1324 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{17}H_{20}NaO_4$: 311.1259; found: 311.1256.

1-(Furan-2-yl(hydroxy)methyl)-6-methyl-6-(4-methylpent-3-en-1-yl)-3-oxabicyclo[3.1.0]hexan-2-one (38a).

$NaBH_4$ (1.61 g, 42.5 mmol) was added to a stirred solution of 37 (10.23, 35.4 mmol) in MeOH (150 mL) at −78 °C. The resulting solution was allowed to warm up to −20 °C over 4 h. After TLC showed consumption of the starting material, the reaction was quenched by addition of a saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (7.72 g, 75%) as the product. 38a (single diastereoisomer): R_f = 0.50 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 0.9 Hz, 1H), 6.34 (dt, *J* = 7.9, 2.6 Hz, 2H), 5.13 (tt, *J* = 7.3, 1.3 Hz, 1H), 4.69 (d, *J* = 11.1 Hz, 1H), 4.35 (dd, *J* = 10.5, 4.6 Hz, 2H), 4.19 (d, *J* = 9.9 Hz, 1H), 2.30–2.09 (m, 2H), 2.07 (d, *J* = 5.0 Hz, 1H), 1.69 (s, 3H),

1.62 (s, 3H), 1.60–1.47 (m, 1H), 1.46–1.40 (m, 1H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 155.2, 141.9, 132.6, 123.2, 110.5, 106.5, 66.3, 66.3, 40.2, 34.7, 30.2, 29.9, 25.7, 25.1, 19.2, 17.6; IR (KBr) 3509, 2969, 2914, 2864, 1744, 1371, 1004 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{17}H_{22}NaO_4$: 313.1416; found: 313.1425.

Allyl1-(Furan-2-yl(hydroxy)methyl)-3-(hydroxymethyl)-2-methyl-2-(4-methylpent-3-en-1yl)cyclopropane-1-carboxylate (49).

4 N KOH (1.63 g, 29.2 mmol) was added to a stirred solution of compound 38a (7.72 g, 26.5 mmol) in EtOH (120 mL). After stirring for 2 h at 90 °C, TLC showed the consumption of the starting material. The solution was concentrated under reduced pressure to afford a yellow solid as the crude product. Allyl bromide (3.50 mL, 39.8 mmol) was added to a stirred solution of this yellow solid in DMF (120 mL). After stirring for 2 h at room temperature, TLC showed the consumption of the starting material. The reaction was quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with Et_2O (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (8.77 g, 95%) as the product. 49: R_f = 0.40 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H), 6.36–6.28 (m, 2H), 5.81 (ddt, *J* = 16.6, 10.3, 6.2 Hz, 1H), 5.33–5.21 (m, 2H), 5.04 (tt, *J* = 7.2, 1.3 Hz, 1H), 4.57 (dd, *J* = 6.2, 1.0 Hz, 2H), 4.39 (d, *J* = 10.9 Hz, 1H), 3.99 (ddd, *J* = 12.0, 9.8, 6.6 Hz, 1H), 3.92–3.84 (m, 1H), 3.79 (d, *J* = 10.9 Hz, 1H), 2.13 (dd, *J* = 9.7, 3.7 Hz, 1H), 2.10–1.95 (m, 2H), 1.68 (s, 3H), 1.68 (s, 3H), 1.60 (s, 3H), 1.55 (ddd, *J* = 14.1, 11.0, 5.2 Hz, 1H), 1.48–1.43 (m, 1H), 1.47 (s, 3H), 1.35 (ddd, *J* = 14.0, 11.1, 5.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 154.9, 141.9, 132.1, 131.2, 123.5, 119.9, 110.3, 106.2, 72.2, 66.1, 59.4, 41.5, 39.0, 32.0, 31.6, 25.7, 24.9, 20.1, 17.6; IR (KBr) 3446, 2967, 2931, 1729, 1702, 1487, 1084, 1016, 1003 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{20}H_{28}NaO_5$: 371.1834; found: 371.1829.

Allyl(1-(Furan-2-yl(hydroxy)methyl)-3-(iodomethyl)-2-methyl-2-(4-methylpent-3-en-1-yl)cyclopropane-1-carboxylate (39).

Iodine (7.67 g, 30.2 mmol) was added in portions to a stirred solution of compound 49 (8.77 g, 25.2 mmol), imidazole (2.06 g, 30.2 mmol), and PPh_3 (7.92 g, 30.2 mmol) in THF (100 mL) at 0 °C. After stirring at 0 °C for 15 min, TLC showed that consumption of the starting material was complete. The reaction was quenched by addition of a saturated aqueous $Na_2S_2O_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (10.16 g, 88%) as the product. 39: R_f = 0.50 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 0.8 Hz, 1H), 6.32 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.27 (d, *J* = 3.2 Hz, 1H), 5.80 (ddt, *J* = 16.6, 10.4, 6.1 Hz, 1H), 5.24 (ddd, *J* = 10.6, 8.3, 1.0 Hz, 2H), 5.06 (t, *J* = 7.2 Hz, 1H), 4.56 (d, *J* = 6.1 Hz, 2H), 4.33 (d, *J* = 11.4 Hz, 1H), 4.04 (d, *J* = 11.4 Hz, 1H), 3.71 (t, *J* = 10.1 Hz, 1H), 3.64 (dd, *J* = 10.2, 5.9 Hz, 1H), 2.24 (ddd, *J* = 18.8, 12.5, 6.1 Hz, 1H), 2.03–1.94 (m, 1H), 1.74–1.70 (m, 1H), 1.69 (s, 3H), 1.65 (dd, *J*

= 10.3, 3.8 Hz, 1H), 1.62 (s, 3H), 1.53–1.46 (m, 1H), 1.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 155.1, 141.7, 131.9, 131.2, 123.7, 119.7, 110.2, 106.1, 71.7, 65.8, 43.2, 41.4, 33.9, 29.8, 25.6, 24.7, 20.3, 17.6, 2.0; IR (KBr) 3446, 2960, 2910, 2855, 1733, 1699, 1140, 732 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{20}H_{27}NaIO_4$: 481.0852; found: 481.0855.

Allyl 2-(Furan-2-yl(hydroxy)methyl)-3,7-dimethyl-3-vinyloct-6-enoate (40).

n-BuLi (23.1 mL, 55.5 mmol, 2.4 M) was added dropwise at < –80 °C to a stirred solution of 39 (10.16 g, 22.2 mmol) in THF (100 mL) in a liquid nitrogen/ethanol cooling bath. After stirring for 15 min, TLC showed the consumption of the starting material. The reaction was quenched by slow addition of a saturated aqueous NH_4Cl solution (50 mL). After warming to room temperature, the aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (7.16 g, 97%) as the product (single diastereoisomer). 40: R_f = 0.40 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 1.3 Hz, 1H), 6.28 (dd, *J* = 3.1, 1.8 Hz, 1H), 6.23 (d, *J* = 3.2 Hz, 1H), 6.11 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.72 (ddt, *J* = 16.4, 10.5, 5.9 Hz, 1H), 5.21 (d, *J* = 1.4 Hz, 1H), 5.17 (dd, *J* = 7.6, 1.2 Hz, 1H), 5.16–5.11 (m, 2H), 5.11–5.09 (m, 1H), 5.07 (d, *J* = 4.2 Hz, 1H), 5.06 (d, *J* = 1.3 Hz, 1H), 4.40–4.30 (m, 2H), 3.04 (d, *J* = 10.0 Hz, 1H), 2.03 (d, *J* = 5.9 Hz, 1H), 2.00–1.87 (m, 2H), 1.82–1.74 (m, 1H), 1.68 (s, 3H), 1.59 (s, 3H), 1.46 (dt, *J* = 12.7, 3.5 Hz, 1H), 1.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 154.8, 144.3, 142.2, 131.9, 131.4, 124.5, 118.4, 113.6, 110.2, 107.2, 67.8, 64.9, 59.7, 41.9, 39.3, 25.7, 22.7, 20.3, 17.6; IR (KBr) 3500, 2970, 2926, 1733, 1152, 1010, 990, 921, 738 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{20}H_{28}NaO_4$: 355.1885; found: 355.1889.

Allyl3-(2-(3,3-Dimethyloxiran-2-yl)ethyl)-2-(furan-2-yl(hydroxy)-methyl)-3-methylpent-4-enoate (50).

m-CPBA (2.71 g, 11.0 mmol, 70%) was added in portions to a stirred solution of 40 (3.32 g, 10.0 mmol) in CH_2Cl_2 (50 mL) at 0 °C. After stirring at 0 °C for 15 min, TLC confirmed the consumption of the starting material, and the mixture was filtered and washed with hexanes (×2). The filtrate was quenched by addition of a saturated aqueous $Na_2S_2O_3$ solution and a saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (2.96 g, 85%) as the product. 50: R_f = 0.20 (silica gel, hexanes/EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.31 (m, 1H), 6.29 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.23 (d, *J* = 3.2 Hz, 1H), 6.06 (ddd, *J* = 17.6, 10.9, 1.7 Hz, 1H), 5.71 (tt, *J* = 16.3, 5.9 Hz, 1H), 5.23–5.11 (m, 3H), 5.08 (ddd, *J* = 12.8, 7.5, 4.2 Hz, 2H), 4.41–4.28 (m, 2H), 3.05 (d, *J* = 10.1 Hz, 1H), 2.68 (t, *J* = 6.6 Hz, 1H), 2.14–2.03 (m, 1H), 2.03–1.94 (m, 1H), 1.94–1.63 (m, 1H), 1.60–1.53 (m, 1H), 1.53–1.38 (m, 2H), 1.28 (s, 3H), 1.25 (s, 3H), 1.25 (d, *J* = 2.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 154.7, 143.8, 143.8, 142.2, 131.9, 118.4, 113.9, 110.2, 107.2, 107.2, 67.7, 67.7, 64.9, 64.6, 64.5, 59.6, 59.5, 58.4, 58.3, 41.8, 41.7, 35.9, 35.5, 24.9, 23.9, 23.8, 20.0, 19.9, 18.6, 18.6; IR (KBr) 3438, 2966, 2930, 1733, 1152, 1010, 991, 922,

740 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{20}H_{28}NaO_5$: 371.1834; found: 371.1828.

8-Allyl 1-Methyl 7-(Furan-2-yl(hydroxy)methyl)-2,6-dimethyl-6-vinyloct-2-ene Dioate (41).

$NaIO_4$ (2.18 g, 10.2 mmol) was added to a stirred solution of 50 (2.96 g, 8.5 mmol) in THF/H_2O (THF/H_2O = 2:1, 45 mL) at 0 °C, and this was followed by dropwise addition of 1 N aqueous HCl to adjust the pH to 3. After stirring at 0 °C for 4 h, TLC showed the consumption of the starting material. The reaction was quenched by addition of a saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil as the product, which was dissolved in CH_2Cl_2 (40 mL) and then treated with methyl 2-(triphenylphosphoranylidene)propanoate (3.55 g, 10.2 mmol). After stirring for 20 h at room temperature, TLC showed the consumption of the starting material, and the reaction was quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (2.59 g, 81% two steps) as the product (*E*-isomer only). 41: R_f = 0.40 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 1.0 Hz, 1H), 6.73 (td, *J* = 7.4, 1.2 Hz, 1H), 6.28 (dd, *J* = 3.1, 1.8 Hz, 1H), 6.22 (d, *J* = 3.1 Hz, 1H), 6.08 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.70 (ddt, *J* = 16.4, 10.4, 5.9 Hz, 1H), 5.19 (dd, *J* = 18.4, 2.5 Hz, 2H), 5.14 (s, 1H), 5.09 (d, *J* = 9.8 Hz, 1H), 5.06 (dd, *J* = 5.5, 4.5 Hz, 1H), 4.40–4.27 (m, 2H), 3.72 (s, 3H), 3.04 (d, *J* = 10.0 Hz, 1H), 2.14 (ddd, *J* = 17.8, 12.7, 7.3 Hz, 2H), 2.08 (d, *J* = 5.7 Hz, 1H), 1.96–1.87 (m, 1H), 1.81 (s, 3H), 1.60–1.52 (m, 1H), 1.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 168.6, 154.8, 143.7, 142.4, 142.2, 131.9, 127.4, 118.4, 113.9, 110.1, 107.2, 67.7, 64.9, 59.6, 51.5, 41.9, 38.0, 23.6, 19.9, 12.2; IR (KBr) 3481, 2951, 1714, 1699, 1647, 1639, 1284, 1250, 1152, 1010, 991, 922, 741 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{21}H_{28}NaO_6$: 399.1784; found: 399.1787.

8-Allyl 1-Methyl (E)-7-(6-Hydroxy-3-oxo-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2-enedioate (51)

$VO(acac)_2$ (91 mg, 0.345 mmol) was added to a stirred solution of 41 (2.59 g, 6.89 mmol) and TBHP (1.50 mL, 8.27 mmol, ~5.5 M in decane) in CH_2Cl_2 (30 mL) at 0 °C. The resulting solution was allowed to warm to room temperature. After stirring for 3 h, consumption of the starting material was shown by TLC, and the reaction was quenched by addition of a saturated aqueous $Na_2S_2O_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (2.57 g, 95%) as the product. 51 (a mixture of lactol diastereoisomers): R_f = 0.20 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.88 (dd, *J* = 10.2, 1.0 Hz, 0.3H), 6.82 (dd, *J* = 10.2, 3.3 Hz, 0.7H), 6.71 (t, *J* = 7.3 Hz, 1H), 6.10 (dd, *J* = 10.2, 1.6 Hz, 0.3H), 6.06–6.02 (m, 0.7H), 6.02–5.98 (m, 1H), 5.97–5.91 (m, 1H), 5.65 (dt, *J* = 8.4, 4.4 Hz, 1H), 5.42–5.31 (m, 1H), 5.24 (dd, *J* = 10.4, 1.1 Hz, 1H), 5.15–5.11 (m, 1H), 5.11–5.05 (m, 1H), 5.02–4.95 (m, 1H), 4.68–4.57 (m, 1H), 4.57–

4.48 (m, 1H), 4.01 (d, *J* = 8.3 Hz, 0.3H), 3.77 (d, *J* = 5.7 Hz, 0.7H), 3.72 (s, 3H), 2.88–2.83 (m, 1H), 2.10 (dt, *J* = 18.7, 9.9 Hz, 2H), 1.93–1.84 (m, 1H), 1.82 (s, 0.9H), 1.80 (s, 2.1H), 1.59–1.47 (m, 1H), 1.26 (s, 0.9H), 1.25 (s, 2.1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.2, 194.5, 171.4, 171.2, 168.8, 147.4, 143.7, 143.3, 143.2, 142.8, 142.8, 132.2, 132.1, 129.0, 127.3, 127.2, 118.5, 118.4, 113.6, 113.3, 92.1, 88.1, 87.9, 78.7, 73.7, 65.4, 65.3, 53.3, 53.0, 51.6, 41.8, 41.8, 38.2, 38.1, 23.7, 23.6, 19.5, 19.2, 12.2; IR (KBr) 3446, 2951, 2932, 1709, 1645, 1439, 1373, 1287, 1252, 1168, 1092, 1034, 922, 750 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{21}H_{28}NaO_7$: 415.1733; found: 415.1737.

8-Allyl1-Methyl(E)-7-(6-Methoxy-3-oxo-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2-enedioate (42).

Ag2O (3.03 g, 13.1 mmol) and CH3I (1.22 mL, 19.65 mmol) were added to a stirred solution of 51 (2.57 g, 6.55 mmol) in Me2CO (30 mL). After stirring at 50 °C for 10 h, TLC showed the consumption of the starting material. The reaction was quenched by addition of a saturated aqueous NH4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na2SO4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a colorless oil (2.40 g, 90%) as the product. 42 (a mixture of acetal diastereoisomers): Rf = 0.42 (silica gel, hexanes/EtOAc = 3:1); 1H NMR (400 MHz, CDCl3) δ 6.83 (dd, J = 10.2, 1.1 Hz, 0.2H), 6.76 (dd, J = 10.2, 3.4 Hz, 0.8H), 6.69 (td, J = 7.5, 1.4 Hz, 1H), 6.10 (dd, J = 10.2, 1.9 Hz, 1H), 6.06–5.91 (m, 2H), 5.41–5.32 (m, 1H), 5.26 (dd, J = 2.5, 1.1 Hz, 0.4H), 5.25–5.23 (m, 1.6H), 5.11–5.08 (m, 1H), 5.04 (ddd, J = 10.0, 4.8, 1.2 Hz, 1H), 4.66 (dt, J = 5.9, 1.3 Hz, 0.2H), 4.63 (ddd, J = 5.0, 3.2, 1.9 Hz, 0.8H), 4.56–4.49 (m, 2H), 3.72 (s, 3H), 3.58 (s, 0.6H), 3.57 (s, 2.4H), 2.88 (d, J = 9.2 Hz, 0.2H), 2.85 (d, J = 10.2 Hz, 0.8H), 2.21–2.00 (m, 2H), 1.85 (ddd, J = 13.4, 11.4, 5.7 Hz, 1H), 1.79 (d, J = 1.1 Hz, 3H), 1.50–1.40 (m, 1H), 1.28 (s, 2.4H), 1.26 (s, 0.6H); 13C NMR (100 MHz, CDCl3) δ 195.3, 194.7, 171.2, 168.6, 146.6, 143.6, 142.9, 142.5, 142.3, 142.2, 132.2, 132.1, 129.4, 127.5, 127.2, 118.6, 118.5, 113.7, 98.9, 94.8, 78.8, 74.2, 65.4, 65.3, 57.5, 56.9, 53.4, 53.2, 51.6, 41.8, 41.7, 38.4, 38.0, 29.7, 23.7, 23.6, 19.4, 12.3; IR (KBr) 3446, 2951, 2932, 1709, 1645, 1439, 1373, 1287, 1252, 1168, 1092, 1034, 922, 750 cm–1; HRMS (ESI/[M + Na]+) calcd for C22H30NaO7: 429.1889; found: 429.1883.

8-Allyl1-Methyl(E)-7-(E)-6-Methoxy-3-(2-methoxy-2-oxoethyli-dene)-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2-ene- dioate (52).

Methyl 2-(*n*-butylphosphoranylidene)propanoate (24) (3.38 g, 12.3 mmol) was added to a stirred solution of 42 (1.00 g, 2.46 mmol) in toluene (25 mL). After stirring at 100 °C for 2 h, TLC showed consumption of the starting material was complete, and the reaction was cooled to room temperature and quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (0.74 g, 65%) as the product. 52 (a mixture of acetal diastereoisomers): R_f = 0.50 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 10.5 Hz, 0.2H), 7.50 (dt, *J*

= 10.5, 1.3 Hz, 0.8H), 6.70 (td, *J* = 7.5, 1.4 Hz, 1H), 6.21–6.09 (m, 1H), 5.99 (ddd, *J* = 9.4, 5.7, 3.7 Hz, 1H), 5.84 (ddt, *J* = 16.5, 10.3, 6.1 Hz, 1H), 5.63 (s, 0.2H), 5.59 (s, 0.8H), 5.35–5.26 (m, 1H), 5.26–5.17 (m, 2H), 5.14–5.06 (m, 1H), 5.05 (t, *J* = 1.8 Hz, 1H), 4.86 (d, *J* = 10.0 Hz, 0.2H), 4.57 (d, *J* = 7.9 Hz, 0.8H), 4.52–4.32 (m, 2H), 3.73 (s, 0.6H), 3.72 (s, 2.4H), 3.70 (s, 3H), 3.52 (s, 2.4H), 3.44 (s, 0.2H), 3.28 (d, *J* = 7.9 Hz, 0.8H), 2.91 (d, *J* = 9.9 Hz, 0.2H), 2.17–2.01 (m, 2H), 1.87 (d, *J* = 1.2 Hz, 0.6H), 1.80 (d, *J* = 1.0 Hz, 2.4H), 1.78–1.71 (m, 1H), 1.46 (dt, *J* = 13.2, 3.6 Hz, 1H), 1.32 (s, 2.4H), 1.31 (s, 0.6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 168.5, 165.9, 146.0, 143.0, 142.2, 131.7, 131.1, 127.5, 125.6, 118.9, 116.1, 114.8, 97.4, 74.1, 65.2, 58.1, 56.8, 53.9, 51.6, 51.2, 42.9, 38.7, 23.6, 19.8, 12.2; IR (KBr) 2951, 2924, 1717, 1652, 1436, 1249, 1176, 1150, 1050, 995, 748 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{25}H_{34}NaO_8$: 485.2151; found: 485.2154.

8-Allyl1-Methyl(E)-7-(E)-3-(2-Methoxy-2-oxoethylidene)-6-oxo-3,6-dihydro-2H-pyran-2-yl)-2,6-dimethyl-6-vinyloct-2-enedioate (43).

Jones reagent (11.0 mL of a 2.9 M solution, 32.0 mmol) was added dropwise to a stirred solution of 52 (0.74 g, 1.60 mmol) in Me_2CO (35 mL) at 0 °C. After stirring for 2.5 h at 0 °C, TLC showed consumption of starting material, and the reaction was quenched by adding *i*-PrOH (20 mL) slowly at 0 °C. The mixture was then filtered through a pad of Celite and washed with EtOAc (×3). The filtrate was quenched by addition of a saturated aqueous $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over $MgSO_4$, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (536 mg, 75%) as the product. 43: R_f = 0.32 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 10.1 Hz, 1H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.16 (dd, *J* = 10.1, 1.4 Hz, 1H), 6.04 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.89–5.73 (m, 1H), 5.84(s, 1H), 5.30 (d, *J* = 12.8 Hz, 1H), 5.27–5.17 (m, 3H), 5.12 (d, *J* = 17.5 Hz, 1H), 4.45 (ddd, *J* = 45.7, 12.8, 6.2 Hz, 2H), 3.75 (s, 3H), 3.72 (s, 3H), 2.96 (d, *J* = 10.5 Hz, 1H), 2.19–1.97 (m, 2H), 1.83 (dd, *J* = 13.1, 5.8 Hz, 1H), 1.79 (s, 3H), 1.51 (td, *J* = 12.6, 4.6 Hz, 1H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 168.5, 164.6, 160.9, 142.6, 141.8, 141.8, 137.8, 131.2, 127.7, 123.0, 122.1, 119.7, 115.4, 80.4, 65.6, 60.9, 51.9, 51.7, 42.4, 37.8, 23.6, 20.4, 12.3; IR (KBr) 2953, 2928, 1733, 1647, 1437, 1266, 1170, 1111, 1060, 1008, 939, 840, 738, 704 cm^{-1}; HRMS (ESI/[M + Na]$^+$) calcd for $C_{24}H_{30}NaO_8$: 469.1838; found: 469.1833.

8-Allyl1-Methyl(E)-7-(5-(2-Methoxy-2-oxoethyl)-2-oxo-2H-pyran-6-yl)-2,6-dimethyl-6-vinyloct-2-enedioate (53).

DABCO (148 mg, 1.32 mmol) was added to a stirred solution of 43 (536 mg, 1.2 mmol) in toluene (6 mL). After stirring for 24 h at 70 °C, the reaction was quenched by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with EtOAc (×3), and the combined organic extracts were washed with brine, dried over Na_2SO_4, then filtered, and concentrated under reduced pressure. Silica gel flash column chromatography of the residue gave a yellow oil (456 mg, 85%) as the product and recovered starting material (53 mg, 10%) 53: R_f = 0.60 (silica gel, hexanes/EtOAc = 1:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 9.7 Hz, 1H), 6.68 (td, *J* = 7.4, 1.3 Hz, 1H), 6.25 (d, *J* = 9.5 Hz, 1H), 5.99 (dd, *J* =

17.5, 10.8 Hz, 1H), 5.84 (ddt, *J* = 16.1, 10.5, 5.7 Hz, 1H), 5.26 (ddd, *J* = 17.3, 2.9, 1.5 Hz, 1H), 5.21 (ddd, *J* = 10.8, 6.1, 4.8 Hz, 2H), 5.06 (d, *J* = 17.4 Hz, 1H), 4.63–4.50 (m, 2H), 3.72 (s, 3H), 3.70 (s, 3H), 3.67 (s, 1H), 3.37 (s, 2H), 2.13–2.00 (m, 2H), 1.79 (d, *J* = 0.9 Hz, 3H), 1.72–1.59 (m, 2H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 168.5, 167.3, 160.7, 157.6, 146.5, 142.6, 141.8, 131.5, 127.8, 118.6, 115.1, 115.0, 111.6, 65.8, 55.9, 52.4, 51.7, 43.7, 37.1, 35.2, 23.5, 19.8, 12.3; IR (KBr) 2987, 2927, 1733, 1645, 1552, 1436, 1267, 1171, 1106, 1045, 1000, 926, 829, 739, 704 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{24}H_{30}NaO_8$: 469.1838; found: 469.1834.

5-Allyl1-Methyl4-(2-Methoxy-2-oxoethyl)-1,6-dimethyl-10-oxo-6-vinyl-1,5,6,7,8,8a-hexahydro-2H-4a,2-(epoxymethano)naph- thalene-1,5-dicarboxylate (44).

A solution of 53 (200 mg, 0.448 mmol) in toluene (10 mL) was heated under reflux in a sealed tube for 3 days. After TLC showed consumption of the starting material, the reaction was cooled to room temperature and concentrated under reduced pressure. Silica gel flash column chromatography of the residue afforded a yellow oil (160 mg, 80%) as the product. 44 (single diastereoisomer): R_f = 0.18 (silica gel, hexanes/EtOAc = 3:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (d, *J* = 6.3 Hz, 1H), 5.96–5.78 (m, 2H), 5.33 (dd, *J* = 17.2, 1.5 Hz, 1H), 5.21 (dd, *J* = 10.4, 1.3 Hz, 1H), 5.02 (dd, *J* = 14.0, 5.9 Hz, 2H), 4.56 (dt, *J* = 5.8, 1.3 Hz, 2H), 3.68 (s, 3H), 3.67 (s, 3H), 3.59 (d, *J* = 6.3 Hz, 1H), 3.21 (dd, *J* = 10.9, 1.0 Hz, 1H), 2.98 (s, 1H), 2.59–2.49 (m, 1H), 1.75- 1.57 (m, 4H), 1.33 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 171.0, 170.9, 169.4, 148.3, 139.6, 131.6, 130.1, 118.8, 111.6, 84.0, 65.2, 53.6, 52.6, 52.2, 49.5, 48.0, 44.9, 39.6, 38.4, 36.4, 21.2, 20.6, 18.5; IR (KBr) 2953, 2851, 1761, 1733, 1647, 1436, 1389, 1260, 1224, 1165, 1106, 996, 966, 915, 791, 771 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{24}H_{30}NaO_8$: 469.1838; found: 469.1834.

epi-8-Basiliolide B (2)

PPh_3 (18.9 mg, 0.072 mmol), pyrrolidine (35 µL, 0.429 mmol), and Pd $(PPh_3)_4$ (42.3 mg, 0.036 mmol) were added to a stirred solution of 44 (160 mg, 0.358 mmol) in CH_2Cl_2 (4 mL) at 0 °C. After 2.5 h of stirring at 0 °C, TLC showed consumption of starting material, and the reaction was quenched by addition of an aqueous HCl (1 mL, 0.5 M) solution. The aqueous phase was extracted with EtOAc (10 mL × 3), and the combined organic extracts were washed with a saturated aqueous $NaHCO_3$ solution (5 mL × 3). The organic extracts were discarded, and the aqueous phase was extracted with EtOAc (15 mL × 3). The combined organic extracts were washed with brine, dried over $MgSO_4$, then filtered, and concentrated to give a yellow oil as the crude product, which was used directly in the next step without further purification. TEA (0.137 mL, 0.984 mmol) and Tf_2O (67 µL, 0.394 mmol) were added dropwise to a stirred solution of the crude product (80.0 mg, 0.197 mmol) in toluene (5 mL) at −78 °C. After 10 min of stirring at −78 °C, the mixture was gradually warmed to 0 °C and stirred for a further 10 min. Silica gel flash column chromatography (with 5% TEA protection of the gel) of the reaction solution gave a white powder (57.4 mg, 75% for two steps). The spectroscopic data obtained from our synthesis match those published by Stoltz. (9c) *epi*-8-basiliolide B (2): R_f = 0.21 (silica gel, hexanes/EtOAc = 2:1); IR (KBr)

3466, 2958, 2925, 2889, 1723, 1499, 1456, 1409, 1385, 1337, 1276, 1187, 1145, 1118, 1068, 1016, 944, 884, 862, 817, 749, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.07 (dd, *J* = 6.3, 1.2 Hz, 1H), 5.81 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.09 (d, *J* = 10.7 Hz, 1H), 5.06 (d, *J* = 17.5 Hz, 1H), 4.95 (d, *J* = 1.1 Hz, 1H), 3.71 (s, 3H), 3.70 (s, 3H), 3.67 (d, *J* = 6.3 Hz, 1H), 3.27 (s, 1H), 2.26 (dd, *J* = 6.8, 11.9 Hz, 1H), 1.80–1.67 (m, 4H), 1.61 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 1 75.1, 170.0, 162.0, 156.8, 146.3, 139.6, 123.2, 112.9, 87.0, 79.1, 56.3, 52.9, 50.6, 49.9, 44.7, 44.6, 38.5, 38.3, 21.0, 20.3, 19.3; IR (KBr) 2953, 2849, 1767, 1733, 1669, 1619, 1436, 1335, 1262, 1231, 1214, 1180, 1108, 960, 908, 833 cm^{-1}; HRMS (ESI/$[M + Na]^+$) calcd for $C_{21}H_{24}NaO_7$: 411.1420; found: 411.1422.

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Notes

The authors declare no competing financial interest.

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