

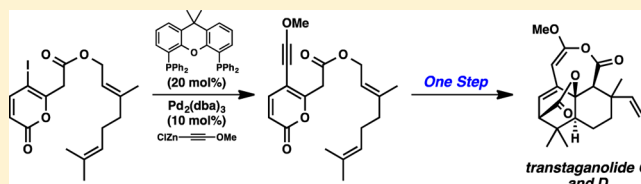
The Total Syntheses of Basiliolide C, epi-Basiliolide C, and Protecting-Group-Free Total Syntheses of Transtaganolides C and D

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Supporting Information

ABSTRACT: The total syntheses of basiliolide C and previously unreported epi-basiliolide C are achieved by an Ireland–Claisen/Diels–Alder cascade. The development of a palladium catalyzed cross-coupling of methoxy alkynyl zinc reagents allows for the protecting-group-free syntheses of transtaganolides C and D. Syntheses of transtaganolides C and D are accomplished in a single operation to generate three rings, two all-carbon quaternary centers, and four tertiary stereocenters from a monocyclic, achiral precursor.



INTRODUCTION

Indigenous to the Mediterranean, plants of the genus *Thapsia* have been recognized to possess valuable therapeutic properties since the birth of western medicine.¹ In modern times, their bioactivity has been attributed to major metabolite thapsigargin (1), a potent histamine releaser² and nontetradecanoylphorbol acetate (TPA) type tumor promoter³ (Figure 1). More importantly, thapsigargin (1) is a powerful sacroplasmatic-endoplasmatic reticulum Ca^{2+} -ATPase (SERCA-ATPase) inhibitor,⁴ for which it has been widely utilized as a biochemical tool.⁵ Further investigations of the chemical components of

Thapsia sp. have elucidated the existence of several additional SERCA-ATPase inhibiting metabolites, the transtaganolides (2–5) and the basiliolides (6 and 8).⁶ These natural products (2–6 and 8) bear characteristically different structural cores and are believed to act by different modes of action to that of thapsigargin (1).^{7,8}

Owing to the novel structures and bioactivity of the transtaganolides and basiliolides (2–9), several research groups have undertaken programs targeting the syntheses of these metabolites, which in turn have led to several biosynthetic hypotheses.⁹ Moreover, the oxabicyclo[2.2.2]octene core (ABD tricycle) of 4–9 and the caged ABEF tetracycle of 2 and 3 with two all-carbon quaternary stereocenters at C4 and C8 comprise novel frameworks that present a considerable challenge for total synthesis.

In our reports¹⁰ on the syntheses of the transtaganolides (2–5) and the basiliolides (6–9) we employ a concise strategy featuring an Ireland–Claisen rearrangement, Diels–Alder cycloaddition cascade (ICR/DA) followed by formal [5 + 2] annulation. With this general approach, we achieved the syntheses of transtaganolides C and D (4 and 5), basiliolide B and epi-basiliolide B (6 and 7),¹¹ and the enantioselective syntheses of transtaganolides A–D (2–5).¹² Herein, we present syntheses of the remaining members of this natural product family, basiliolide C and epi-basiliolide C (8 and 9), as well as the co-isolated basiliopyrone¹³ (10) (Figure 2a),¹⁴ which was recently synthesized by Sterner and co-workers in 12 steps (longest linear sequence) from commercially available material.¹⁵ Furthermore, improved conditions for our [5 + 2] annulation reaction, which avoid stoichiometric palladium and superstoichiometric organostannane through the use of organozinc reagents, are reported. Finally, utilization of these

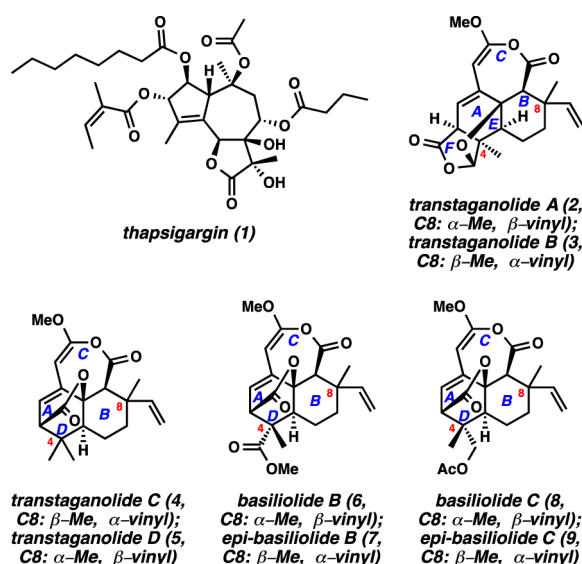


Figure 1. Metabolites (1–6 and 8) isolated from plants of the genus *Thapsia*. C8 epimers of basiliolide B and C (6 and 8), epi-basiliolide B and C (7 and 9), have not yet been isolated as natural products.

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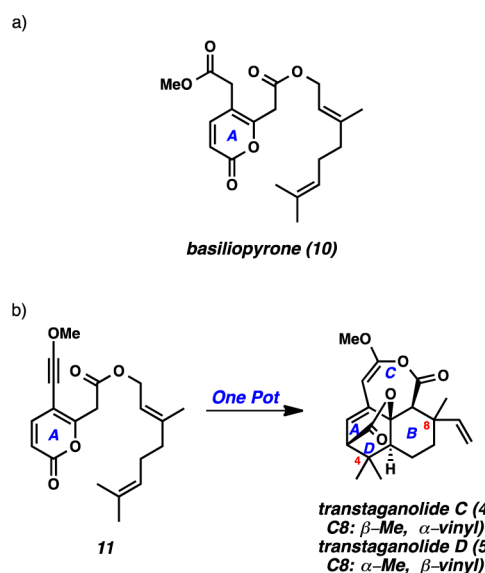


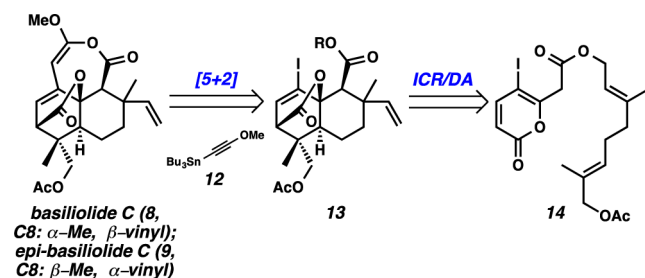
Figure 2. (a) Basiliopyrone (10). (b) One-pot synthesis of transtaganolides C and D (4 and 5) from pyrone ester 11.

developments enables a one-pot synthesis of transtaganolides C and D (4 and 5) from a simple monocyclic pyrone ester 11 (Figure 2b).

RESULTS AND DISCUSSION

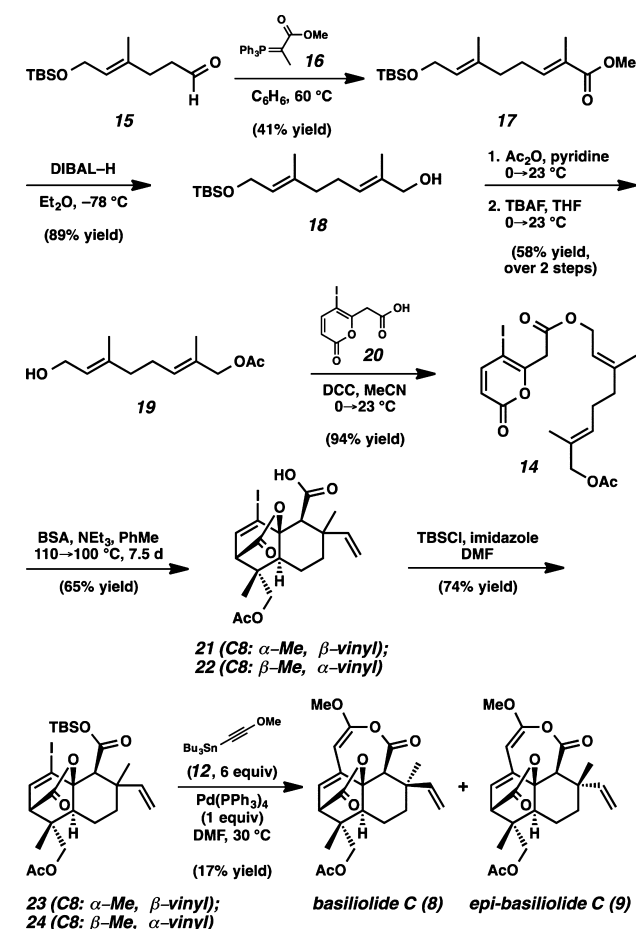
We envisioned that basiliolide C (8) and epi-basiliolide C (9) could retro-synthetically derive from pyrone ester 14 using our ICR/DA cascade and formal [5 + 2] annulation sequence (Scheme 1).

Scheme 1. Retrosynthetic Analysis of Basiliolide C and epi-Basiliolide C (8 and 9)



The total synthesis commenced with the treatment of known γ,δ -unsaturated aldehyde 15,¹⁶ with triphenylphosphonium ylide 16, to give the enoate 17 (Scheme 2). Subsequent reduction of α,β -unsaturated ester 17 with DIBAL-H afforded allylic alcohol 18 in 89% yield. Following protecting group manipulations (18 $\rightarrow$ 19), DCC coupling of alcohol 19 with pyrone acid 20¹¹ efficiently generated the ICR/DA cascade substrate 14. Submission of pyrone ester 14 to our ICR/DA protocol proved successful, affording tricycles 21 and 22 in 65% combined yield and as a 1:2 mixture of C8 diastereomers, respectively. Only two diastereomers, 21 and 22, are formed in the reaction resulting from a diastereoselective Diels–Alder cycloaddition, where diastereoselectivity is dictated by the C7 ester formed in the Ireland–Claisen rearrangement.^{10b,11,12} Protection of tricycles 21 and 22 gave silyl esters 23 and 24 in 74% yield. Completion of the synthesis was achieved via a palladium promoted formal [5 + 2] annulation of tricycles 23

Scheme 2. Forward Synthesis of Basiliolide C and epi-Basiliolide C (8 and 9)



and 24 with stannylmethoxy acetylide 12 to form basiliolide C (8) and previously unreported epi-basiliolide C (9) respectively, albeit in low yield (17% yield).

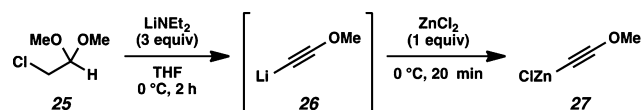
As exemplified by the syntheses of basiliolide C and epi-basiliolide C (8 and 9), the key formal [5 + 2] annulation which builds the ketene-acetal containing the seven-member C-ring is inefficient, a trend observed in our reported syntheses of basiliolide B, epi-basiliolide B (6 and 7, 18% yield), and transtaganolides A–D (2–5, 35% yield for 2 and 3, and 31% for 4 and 5).^{11,12} Furthermore, these transformations require stoichiometric palladium and superstoichiometric quantities of the organostannane. To date, similar cross-coupling reactions of organostannanes have not been accomplished on substrates of such complexity, and few examples are known that utilize stannyl oxy-acetylides.¹⁷ Therefore, we sought to improve the efficiency of this challenging cross-coupling, through improved yield, reduced catalyst loading, and reduction or elimination of equivalents of stannane utilized.

In 1992, Himbert and Löffler reported a palladium-catalyzed cross-coupling of zinc alkoxy acetylides to simple aryl iodides.¹⁸ Inspired by this precedent, we began investigations of palladium cross-coupling reactions of a zinc alkoxy acetylide to form the C-ring.

Synthesis of the precedented zinc alkoxy acetylide (27)¹¹ proceeded via known treatment of 1,1-dimethoxy-2-chloroacetaldehyde (25) with 3 equiv of lithium diethyl amide to form the putative lithium acetylide 26,¹⁹ which is then trapped as the zinc acetylide 27 by the addition of anhydrous zinc

chloride (Scheme 3). The methoxyethynyl zinc chloride (27) was stored at 0 °C as the crude solution and always used within hours of preparation.²⁰

Scheme 3. Synthesis of Methoxyethynyl Zinc Chloride (27)



As a model system, Pd-catalyzed coupling of organozinc 27 to iodo-cyclohexene (28)²¹ was evaluated (Table 1). Initially,

Table 1. Ligand Screen for the Cross-Coupling of Methoxyethynyl Zinc Chloride (27) and Iodo-cyclohexene (28)

entry	ligand	conversion (%) ^c	yield of 30 (%) ^c
1 ^a	PPh ₃ ^b	47	5
2	Bipy	54	0
3	H ₂ PHOX	46	10
4	BINAP	40	6
5	dpp-benzene	13	6
6	dppe	0	0
7	dppp	22	7
8	dppb	100	13
9	dppf	100	17

^aUtilized *n*-BuLi reduction of 10 mol % Pd(II) source [Cl₂Pd(Ph₃)₂], to generate catalyst as described by Himbert and Löffler. ^bLigand loading was 50 mol %. ^cDetermined by GC using a tridecane internal standard.

we investigated a variety of bidentate ligands, as well as those conditions described by Himbert and Löffler. Spontaneous hydration of the cross-coupled product 29 on workup yielded methyl ester 30, which could be quantified to determine the overall yield of the process. We found, the conditions reported by Himbert and Löffler (entry 1) did not extend readily from aryl iodides to vinyl iodides such as iodo-cyclohexene (28). The use of an N,N-ligand, bipyridine (Table 1, entry 2), as well as a P,N-ligand, H₂PHOX (entry 3), resulted in approximately 50% consumption of the vinyl iodide 28 giving a 0% or 10% yield of the product 30, respectively. This large discrepancy between

substrate 28 conversion and the calculated yield of 30 is general and attributed to the rapid decomposition of the cross-coupled product 29 under the reaction conditions. Among the diphosphines tested, BINAP (entry 4) gave 40% conversion of iodo-cyclohexene (28) but, unfortunately, provided the product 30 in a mere 6% yield. Dppe (entry 6) was found to provide no reactivity, whereas dpp-benzene (entry 5) and dppp (entry 7) gave minimal conversions (13% and 22% respectively) and poor yields (6% and 7% respectively). Lastly dppb (entry 8) and dppf (entry 9) gave the highest yields (13% and 17% respectively) and 100% conversion of iodo-cyclohexene (28). Although the yields were quite low, we were delighted to have found conditions that employ substoichiometric quantities of palladium for this challenging cross-coupling reaction.

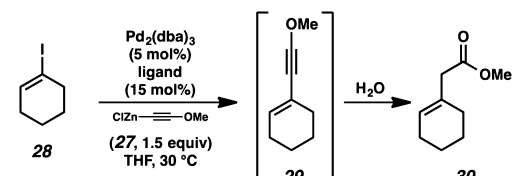
In our reported cross-coupling reactions of organostannanes, as well as the studies reported by others, the major decomposition pathway was Heck polymerization of the alkoxy alkynyl moiety.¹⁸ We posited that the nonproductive polymerization pathway led to degradation of the metal methoxy acetylide (i.e., 12 or 27), degradation of the intermediate enyne (e.g., 29), and degradation of the catalyst. We reasoned that these nonproductive pathways necessitated stoichiometric quantities of palladium in our [5 + 2] annulation. Thus, we were pleased to find dppb and dppf (Table 1, entries 8 and 9 respectively) could accomplish the coupling of organozinc 27 to iodide 28 utilizing substoichiometric quantities of palladium.

The superior reactivity demonstrated by both dppb and dppf were attributed to their relatively large bite angles (98° and 96° bite angles respectively).²² It has been shown that bidentate ligands with large bite angles are poor catalysts for ethylene carbonylative polymerization reactions,²³ which require an inner-sphere *cis*-geometry of monomers. We therefore envisioned that *trans*-chelating ligands could improve the efficiency of our reaction through the attenuation of acetylide polymerization, the putative catalyst and substrate decomposition pathway. Thus, we were eager to investigate Xantphos (Table 2, entries 9–12) within our reaction manifold, because of its large bite angle (111°) and demonstrated propensity for *trans*-chelation.^{22,23}

We probed this hypothesis through cross-coupling reactions of methoxyethynyl zinc chloride (27) and iodo-cyclohexene (28, Table 2), tabulating the conversion and yield as a function of time for dppb (Table 2, entries 1–4), dppf (entries 5–8), and Xantphos (entries 9–12). Consistent with our hypothesis, dppb and dppf (entries 1–4 and 5–8 respectively) with similar bite angles of 98° and 96° gave similar yields, 35% and 31% respectively. Xantphos (entries 9–12) with a considerably larger bite angle of 111°, provided the product in 48% yield. Furthermore, for all three ligand-catalyst frameworks we could observe product decomposition by the end of the 4 h window that the reactions were monitored, suggesting polymerization was possibly still a competing pathway.

Having found Xantphos optimal for achieving cross-coupling of acetylide 27 to vinyl iodide 28, we moved from the model iodide 28 to the tricyclic transtaganolide core 31. Unfortunately, our procedure did not readily translate to the more complex vinyl iodide (31) utilized in the total synthesis (Scheme 4a). Under these conditions we observed minimal substrate consumption and no noticeable product formation; surprisingly, use of stoichiometric palladium loading led to trace product formation. We attribute this poor reactivity to the demanding steric environment of the substrate when compared

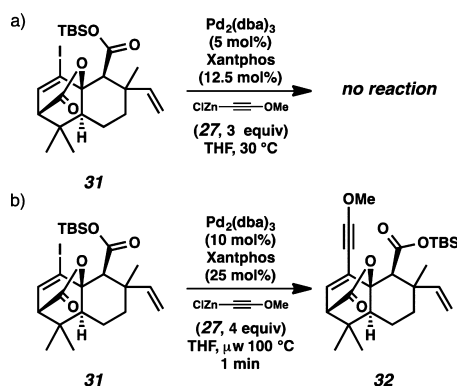
Table 2. Comparing dppb, dppf, and Xantphos, as Ligands for Catalyzing the Cross-Coupling of Methoxyethynyl Zinc Chloride (27) and Iodocyclohexene (28) as a Function of Time



entry	ligand	rxn time	conversion (%) ^a	yield of 30 (%) ^a
1		15 min	21	3
2	Ph ₂ P-CH ₂ -CH ₂ -CH ₂ -PPh ₂	1 h	78	35
3	dppb	2.5 h	94	29
4		4 h	100	26
5		15 min	46	3
6		1 h	81	30
7		2.5 h	98	31
8	dppf	4 h	100	29
9		15 min	59	40
10		1 h	87	48
11		2.5 h	91	39
12	Xantphos	4 h	96	44

^aDetermined by GC using a tridecane internal standard.

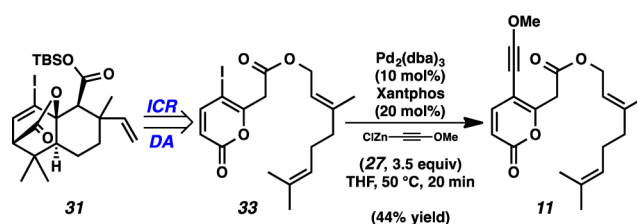
Scheme 4. (a) Cross-Coupling of Tricycle 31 Using the Palladium Xantphos Catalytic Conditions Developed on Model Cross-Couplings to Iodo-cyclohexene (28); (b) Cross-Coupling of Tricycle 31 Facilitated by Microwave Irradiation



to the simple cyclohexene 28 utilized in the model studies. In an effort to overcome the putative kinetic barrier, we explored heating of the reaction mixture. Ultimately, we found that microwave heating (100 °C) for short durations (<1 min) led to observable product formation (32, Scheme 4b). However, because of the rapid rate of product 32 decomposition at 100 °C, as well as the very short reaction time, the coupling could not be scaled and had poor reproducibility.

With no clear means to overcome the steric congestion of 31, we reevaluated our retrosynthetic analysis noting that, prior to the ICR/DA cascade, pyrone ester 33 bears a heteroaromatic iodine far more accessible for cross-coupling (Scheme 5). To our delight, Pd catalyzed cross-coupling of ICR/DA precursor 33 and methoxyacetylide 27 proceeded smoothly in 44% yield. Furthermore, we were pleased to find that the eneyne 11 could

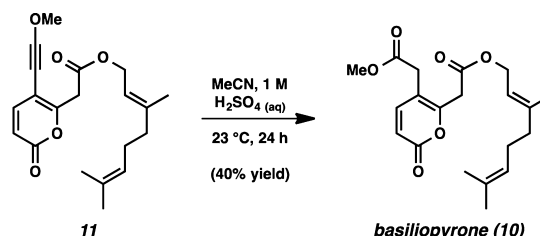
Scheme 5. Successful Negishi Cross-Coupling of ICR/DA Substrate 33



be purified by silica column chromatography without hydration or decomposition.

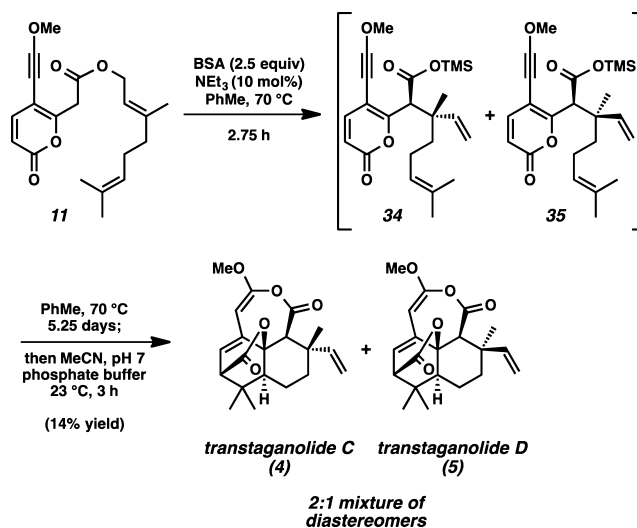
If desired, the cross-coupled product 11 could be hydrated by treatment with aqueous sulfuric acid in acetonitrile to cleanly furnish basiliopyrone (10) in 40% yield (Scheme 6). The total synthesis of basiliopyrone (10) required seven steps (longest linear sequence) from commercially available material.

Scheme 6. Acid Catalyzed Hydration of 11 Allows for the Formation of Basiliopyrone (10)



Finally, minor modification of our reported ICR/DA cascade conditions allowed direct access to transtaganolides C and D (4 and 5) in a single step from the alkynyl pyrone ester 11 in 14% yield and as a 2:1 mixture of diastereomers (Scheme 7). Because of the thermal instability of the substrate (11) the cascade was performed at a lower temperature than our standard conditions (70 °C) and in a nitrogen filled glovebox to ensure the absolute exclusion of adventitious water. Furthermore, the Ireland–Claisen step of the cascade proceeded smoothly, but the Ireland–Claisen products (34 and 35) were

Scheme 7. A One-Pot Synthesis of Transtaganolides C and D (4 and 5) from Alkynyl Pyrone 11



found to be unstable and prone to decomposition. Nevertheless, we were satisfied to observe the successful [4 + 2] cycloaddition of a substrate (**34** or **35**) bearing an electron-donating methoxy alkynyl moiety on the pyrone ring (subsequently, all prior pyrone Diels–Alder cycloadditions had required electron-withdrawing substituents). While low yielding, this one-pot procedure forms three rings, two all-carbon quaternary centers, and four tertiary stereocenters from a simple monocyclic, achiral precursor (**11**). Finally, the success of this cascade process further implicates the Ireland–Claisen/Diels–Alder sequence as a potential biosynthetic route.

CONCLUSION

In conclusion, basiliolide C and epi-basiliolide C (**8** and **9**) have been prepared by an ICR/DA cascade. We have improved our previously disclosed [5 + 2] annulation of methoxy acetyl stannane **12**, by obviating the need for organotin reagents and developing a complementary Negishi cross-coupling of methoxy acetylide **27**. This methodology, which employs catalytic quantities of a Xantphos palladium complex, was used to furnish the alkynyl pyrone ester **11**. The cross-coupled product **11** could be hydrated to furnish basiliopyrone (**10**) or, to our delight, transformed in a single step cascade process to transtaganolides C and D (**4** and **5**).

EXPERIMENTAL SECTION

Methyl (2E,6E)-8-((tert-Butyldimethylsilyloxy)-2,6-dimethylocta-2,6-dienoate (17). To a 23 °C solution of aldehyde **15** (1.39 g, 5.74 mmol) in benzene (57 mL, 0.1 M) was added ylide **16** (2.92 g, 8.38 mmol). The reaction was stirred at 60 °C for 6 h. The reaction flask was then cooled to ambient temperature. The crude mixture was poured directly onto a short pad of silica and subsequently flushed with ether (150 mL). Solvent was removed by rotary evaporation. The crude oil was redissolved in CH₂Cl₂ (50 mL) and then dry loaded onto silica (5 g). Purification by column chromatography (EtOAc in hexanes 1% → 1.5% on silica) yielded 722 mg (41% yield) of **17** as a clear oil and a single diastereomer; ¹H NMR (300 MHz, CDCl₃) δ 6.72 (tq, *J* = 7.3, 1.5 Hz, 1H), 5.31 (tq, *J* = 6.3, 1.3 Hz, 1H), 4.18 (dd, *J* = 6.3, 0.8 Hz, 2H), 3.71 (s, 3H), 2.34–2.23 (m, 2H), 2.16–2.06 (m, 2H), 1.82 (s, 3H), 1.62 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 168.7, 142.0, 135.8, 127.8, 125.3, 60.3, 51.8, 38.1, 27.0, 26.1, 18.5, 16.5, 12.5, –5.0; FTIR (Neat Film NaCl) 2952, 2930, 2896, 2857, 1717, 1672, 1651, 1472, 1463, 1436, 1387, 1361, 1259, 1218, 1193, 1124, 1107, 1065, 1006, 939, 837, 814, 776, 744 cm^{–1}; HRMS (ESI) *m/z* calcd for C₁₇H₃₂O₃SiNH₄ [M + NH₄]⁺: 330.2459, found 330.2468.

(2E,6E)-8-((tert-Butyldimethylsilyloxy)-2,6-dimethylocta-2,6-dien-1-ol (18). To a –78 °C solution of **17** (722 mg, 2.31 mmol) in Et₂O (23 mL, 0.1 M) was added neat DIBAL-H (1.03 mL, 5.78 mmol) in a dropwise fashion. The reaction mixture was then stirred for 45 min at –78 °C before being carefully quenched by the dropwise addition of a saturated solution of Rochelle's salt (6 mL) over a period of 5 min. The reaction mixture was then removed from the cold bath and allowed to warm to ambient temperature while being vigorously stirred for another 2 h. The aqueous phase was extracted with Et₂O (4 × 10 mL), and the organics were combined, washed with saturated brine (40 mL), and then dried over MgSO₄. Solvent was removed by rotary evaporation, and purification by column chromatography (EtOAc in hexanes 3.5% → 15% on silica) resulted in the isolation of 587 mg (89% yield) of **18** as a clear oil; ¹H NMR (300 MHz, CDCl₃) δ 5.37 (tq, *J* = 7.0, 1.3 Hz, 1H), 5.29 (tq, *J* = 6.3, 1.3 Hz, 1H), 4.18 (dd, *J* = 6.4, 0.8 Hz, 2H), 3.97 (s, 2H), 2.22–2.08 (m, 2H), 2.09–1.98 (m, 2H), 1.65 (s, 3H), 1.61 (s, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 136.6, 135.1, 125.8, 124.7, 69.0, 60.4, 39.2, 26.1, 25.9, 18.6, 16.4, 13.8, –4.9; FTIR (Neat Film NaCl) 3346, 2955, 2929, 2857, 1671, 1472, 1463, 1407, 1385, 1361, 1255, 1111,

1094, 1066, 1006, 939, 836, 814, 776 cm^{–1}; HRMS (ESI) *m/z* calcd for C₁₆H₃₂O₂SiNa [M + Na]⁺: 307.2064, found 307.2052.

(2E,6E)-8-Hydroxy-2,6-dimethylocta-2,6-dien-1-yl Acetate (19). To a 0 °C solution of **18** (585 mg, 2.06 mmol) in pyridine (2 mL, 1 M) was added acetic anhydride (390 μL, 4.11 mmol). The reaction was allowed to warm to 23 °C and stirred for 3.5 h. At this time the reaction mixture was diluted with Et₂O (15 mL) and washed with saturated NaHCO₃ solution (3 × 10 mL), saturated CuSO₄ solution (3 × 10 mL), and brine (10 mL). The organic fraction was dried with MgSO₄, and the solvent was removed by rotary evaporation. Purification by column chromatography (2.5% EtOAc in hexanes on silica) yielded 423 mg (63% yield) of the acetate protected product **SI-1** as a clear oil; ¹H NMR (300 MHz, CDCl₃) δ 5.43 (tq, *J* = 7.0, 1.3 Hz, 1H), 5.30 (tq, *J* = 6.3, 1.3 Hz, 1H), 4.43 (s, 2H), 4.18 (dq, *J* = 6.3, 0.9 Hz, 2H), 2.23–2.09 (m, 2H), 2.06–1.99 (m, 5H), 1.64 (s, 3H), 1.61 (s, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 171.1, 136.4, 130.3, 129.4, 124.9, 70.4, 60.4, 39.0, 26.1, 21.1, 18.6, 16.5, 14.1, –4.9; FTIR (Neat Film NaCl) 2954, 2930, 2886, 2857, 1744, 1671, 1472, 1462, 1445, 1377, 1360, 1249, 1230, 1111, 1065, 1024, 836, 776 cm^{–1}; HRMS (APCI) *m/z* calcd for C₁₈H₃₄O₃SiNa [M + Na]⁺: 349.2169, found 349.2180.

Cleavage of the silyl protecting group could be accomplished by the addition of 1 M TBAF solution in THF (1.95 mL, 1.94 mmol) to a 0 °C solution of the previously isolated acetate protected product **SI-1** (423 mg, 1.30 mmol) in THF (6.5 mL, 0.2 M). The reaction was allowed to warm to 23 °C and then was stirred for an additional hour, prior to quenching with saturated NH₄Cl (5 mL). The aqueous phase was extracted with Et₂O (3 × 5 mL), and the organics were combined, washed with brine (15 mL), and dried over MgSO₄. Solvent was removed by rotary evaporation, and purification by column chromatography (EtOAc in hexanes 10% → 20% on silica) resulted in the isolation of 253 mg (92% yield) of **19** as a clear oil; ¹H NMR (300 MHz, CDCl₃) δ 5.44–5.30 (m, 2H), 4.39 (s, 2H), 4.08 (d, *J* = 6.8 Hz, 2H), 2.19–1.97 (m, 7H), 1.61 (s, 3H), 1.60 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.1, 138.5, 130.2, 129.1, 124.0, 70.2, 59.2, 38.8, 25.9, 21.0, 16.8, 14.0; FTIR (Neat Film NaCl) 3423, 2975, 2923, 2879, 1738, 1671, 1442, 1378, 1232, 1090, 1022, 844 cm^{–1}; HRMS (ESI) *m/z* calcd for C₁₇H₃₀O₃Na [M + Na]⁺: 235.1305, found 235.1300.

(2E,6E)-8-Acetoxy-3,7-dimethylocta-2,6-dien-1-yl 2-(5-Iodo-2-oxo-2H-pyran-6-yl)acetate (14). To a 0 °C solution of **19** (254 mg, 1.20 mmol) and pyrone acid **20** (403 mg, 1.44 mmol) in MeCN (12 mL, 0.1 M) was added DCC (297 mg, 1.44 mmol). The reaction was allowed to warm to 23 °C and stirred for 1 h. The crude reaction mixture was then flushed through a short pad of Celite with additional MeCN (15 mL) to remove the insoluble urea byproduct. Solvent was removed by rotary evaporation and purification by column chromatography (EtOAc in hexanes 5% → 15% on silica) resulting in the isolation of 531 mg (94% yield) of iodo pyrone ester **14** as a yellow oil; ¹H NMR (300 MHz, CDCl₃) δ 7.45 (d, *J* = 9.7 Hz, 1H), 6.06 (d, *J* = 9.7 Hz, 1H), 5.45–5.38 (m, 1H), 5.33 (tq, *J* = 7.1, 1.3 Hz, 1H), 4.66 (d, *J* = 7.2 Hz, 2H), 4.43 (s, 2H), 3.77 (s, 2H), 2.24–2.02 (m, 7H), 1.70 (s, 3H), 1.64 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.1, 166.8, 160.5, 158.0, 151.3, 142.8, 130.6, 128.8, 118.0, 116.3, 70.8, 70.3, 62.7, 42.7, 38.9, 26.0, 21.2, 16.7, 14.1; FTIR (Neat Film NaCl) 2973, 2933, 2854, 1732, 1607, 1546, 1443, 1376, 1357, 1345, 1230, 1167, 1133, 1063, 1016, 959, 865, 821 cm^{–1}; HRMS (ESI) *m/z* calcd for C₁₉H₂₃IO₆Na [M + Na]⁺: 497.0432, found 497.0428.

1-(Acetoxymethyl)-4-iodo-1,6-dimethyl-10-oxo-6-vinyl-1,5,6,7,8a-hexahydro-2H-4a,2-(epoxymethano)naphthalene-5-carboxylic Acid (21 and 22). To a 23 °C solution of **14** (385 mg, 0.812 mmol) in toluene (4 mL, 0.2 M) in a 250 mL sealed tube were added *N,O*-bis(trimethylsilyl)acetamide (BSA) (397 μL, 1.62 mmol) and triethylamine (11.3 μL, 0.0812 mmol). The reaction was heated to 110 °C and stirred for 20 min. The solution was then cooled to 23 °C and diluted with toluene (200 mL, 0.004 M), leaving ample headspace in the sealed tube to allow for solvent expansion. The reaction mixture was then heated to 100 °C for 7.5 d or until complete as determined by ¹H NMR. The reaction mixture was then cooled to 23 °C, a 1% aqueous solution of AcOH was added (10 mL), and the reaction was stirred for an additional 2 min. The reaction was washed with an

additional 1% aqueous solution of AcOH (3×10 mL), and the aqueous phases were combined and backextracted with EtOAc (3×30 mL), while making sure the pH of the aqueous phase remained acidic. The organics were combined and dried over Na_2SO_4 , and solvent was removed by rotary evaporation. Purification by column chromatography (EtOAc in hexanes with 0.1% AcOH, 17% $\rightarrow$ 25% on silica) gave desired tricycles **21** and **22** with a coeluting impurity (<5% by ^1H NMR). Subsequent recrystallization from heptane and EtOAc gave 249 mg (65% yield) of pure **21** and **22** as white solids and a 1:2 mixture of the respective diastereomers (**21** and **22**).

Minor Diastereomer 21. ^1H NMR (300 MHz, CDCl_3) δ 6.91 (d, J = 6.7 Hz, 1H), 6.34 (dd, J = 17.4, 11.0 Hz, 1H), 5.17–4.96 (m, 2H), 3.86–3.61 (m, 2H), 3.20 (d, J = 6.8 Hz, 1H), 2.95 (s, 1H), 2.09 (s, 3H), 2.00–1.37 (m, 5H), 1.37 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.2, 170.9, 169.7, 140.5, 139.2, 113.5, 98.5, 84.2, 70.0, 60.6, 52.6, 44.1, 40.3, 40.1, 38.6, 29.9, 20.9, 19.5, 18.3.

Major Diastereomer 22. ^1H NMR (300 MHz, CDCl_3) δ 6.91 (d, J = 6.7 Hz, 1H), 6.01 (dd, J = 17.4, 10.7 Hz, 1H), 5.17–4.96 (m, 2H), 3.86–3.61 (m, 2H), 3.21 (d, J = 6.7 Hz, 1H), 3.01 (s, 1H), 2.09 (s, 3H), 2.00–1.37 (m, 5H), 1.30 (s, 3H), 1.13 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 174.1, 170.9, 169.8, 148.0, 138.9, 111.5, 98.9, 84.1, 70.0, 59.2, 52.5, 44.0, 40.1, 39.9, 39.5, 38.1, 20.9, 19.5, 18.3.

FTIR (Neat Film NaCl) 3084, 2977, 2665, 2253, 1733, 1638, 1465, 1438, 1414, 1394, 1379, 1337, 1315, 1229, 1172, 1120, 1041, 967, 913, 876, 839, 795, 735 cm^{-1} ; HRMS (Multimode-ESI/APCI) m/z calcd for $\text{C}_{19}\text{H}_{24}\text{IO}_6$ [$\text{M} + \text{H}$] $^+$: 475.0612, found 475.0608.

tert-Butyldimethylsilyl 1-(Acetoxymethyl)-4-iodo-1,6-dimethyl-10-oxo-6-vinyl-1,5,6,7,8,8a-hexahydro-2H-4a,2-(epoxymethano)naphthalene-5-carboxylate (23 and 24). To a 23 $^\circ\text{C}$ solution of **21** and **22** (115 mg, 0.243 mmol) in DMF (1.2 mL, 0.2 M) were added sequentially imidazole (99.4 mg, 1.46 mmol) and TBSCl (147 mg, 0.973 mmol). The reaction was stirred for 1 h at 23 $^\circ\text{C}$ and then quenched by the addition of saturated brine (4 mL). The resulting aqueous phase was extracted with a 50% solution of EtOAc in hexanes (3×4 mL), the organics were combined, washed with brine (6 mL), and dried with Na_2SO_4 . Solvent was removed by rotary evaporation, and purification by column chromatography (EtOAc in hexanes 10% $\rightarrow$ 20% on silica) gave 106 mg (74% yield) of **23** and **24** as white solids and a 1:2 mixture of the respected diastereomers (**23** and **24**).

Minor Diastereomer 23. ^1H NMR (300 MHz, CDCl_3) δ 6.87 (d, J = 6.7 Hz, 1H), 6.36 (dd, J = 17.4, 11.0 Hz, 1H), 5.19–4.88 (m, 2H), 3.80–3.63 (m, 2H), 3.14 (d, J = 6.8 Hz, 1H), 2.85 (s, 1H), 2.07 (s, 3H), 1.91–1.19 (m, 8H), 1.10 (s, 3H), 0.88 (s, 9H), 0.27 (s, 3H), 0.26 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.7, 169.7, 169.1, 141.0, 138.9, 113.2, 99.2, 84.3, 70.0, 61.8, 52.8, 44.4, 40.5, 39.6, 39.2, 29.8, 25.5, 21.1, 20.91, 19.5, 17.6, –4.8, –4.8.

Major Diastereomer 24. ^1H NMR (300 MHz, CDCl_3) δ 6.87 (d, J = 6.7 Hz, 1H), 6.01 (dd, J = 17.4, 10.6 Hz, 1H), 5.19–4.88 (m, 2H), 3.80–3.63 (m, 2H), 3.16 (d, J = 6.8 Hz, 1H), 2.94 (s, 1H), 2.07 (s, 3H), 1.91–1.19 (m, 8H), 1.10 (s, 3H), 0.88 (s, 9H), 0.27 (s, 3H), 0.24 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.7, 169.7, 168.9, 149.0, 138.7, 110.8, 99.6, 84.2, 70.0, 60.4, 52.6, 44.3, 40.3, 40.2, 38.5, 25.6, 21.1, 20.9, 19.52, 18.1, 17.6, –4.7, –4.8.

FTIR (Neat Film NaCl) 2951, 2930, 2896, 2858, 1760, 1745, 1716, 1472, 1464, 1413, 1393, 1378, 1364, 1341, 1283, 1250, 1229, 1194, 1173, 1042, 1021, 1007, 984, 968, 939, 930, 915, 885, 843, 828, 790, 733 cm^{-1} ; HRMS (Multimode-ESI/APCI) m/z calcd for $\text{C}_{25}\text{H}_{38}\text{IO}_6\text{Si}$ [$\text{M} + \text{H}$] $^+$: 589.1477, found 589.1496.

Basililide C (8) and epi-Basililide C (9). In a nitrogen filled glovebox, to a solution of **23** and **24** (13 mg, 0.022 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (28 mg, 0.0242 mmol) in DMF (220 μL , 0.1 M) was added tributyl(2-methoxyethynyl)stannane (**12**) (29 mg, 0.088 mmol). The reaction was stirred at 30 $^\circ\text{C}$ for 15 h at which point another equivalent of stannane **12** was added (7.5 mg, 0.022 mmol). The reaction was stirred for an additional 5 h, and then additional stannane **12** was added (7.5 mg, 0.022 mmol). After another 4 h of stirring at 30 $^\circ\text{C}$ (a total reaction time of 24 h) the reaction was filtered through cotton washing with MeCN in order to remove $\text{Pd}(\text{PPh}_3)_4$. The filtrate was further diluted with MeCN (making a total reaction

volume of 8 mL), and the reaction solution was removed from the glovebox. pH 7 phosphate buffer (150 μL) was added to the crude reaction solution, and it was then stirred at 23 $^\circ\text{C}$ for 6 h. MeCN was then removed by passing a stream of air over the reaction vessel (rotary evaporation could not be accomplished without bumping the liquid). The remaining liquid was diluted with 25% saturated brine solution in water (350 μL), and the aqueous phase was extracted with EtOAc (4×750 μL). The organics were pooled, dried over Na_2SO_4 , and concentrated by rotary evaporation. The crude oil was purified by normal phase HPLC (33% EtOAc in hexanes) to yield 0.51 mg (6% yield) of basililide C (**8**) and 0.97 mg (11% yield) of epi-basililide C (**9**). The spectroscopic data obtained from synthetic **9** match those published from natural sources.^{6b}

Basililide C (8). ^1H NMR (500 MHz, CDCl_3) δ 7.00 (dd, J = 17.7, 11.1 Hz, 1H), 6.05 (dd, J = 6.5, 1.2 Hz, 1H), 5.16 (dd, J = 11.1, 1.4 Hz, 1H), 5.06 (dd, J = 17.7, 1.2 Hz, 1H), 5.00 (d, J = 1.4 Hz, 1H), 3.73 (s, 3H), 3.73 (d, J = 10.8 Hz, 1H), 3.69 (d, J = 10.8 Hz, 1H), 3.29 (d, J = 6.5 Hz, 1H), 3.14 (s, 1H), 2.08 (s, 3H), 1.93 (dt, J = 13.5, 3.4 Hz, 1H), 1.75 (qd, J = 13.5, 3.0 Hz, 1H), 1.64–1.50 (m, 1H), 1.41 (td, J = 13.5, 3.0 Hz, 1H), 1.32–1.24 (m, 1H), 1.23 (s, 3H), 1.12 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.0, 170.7, 162.4, 157.0, 142.7, 138.6, 123.0, 112.5, 87.0, 79.2, 70.6, 56.6, 53.4, 49.8, 44.8, 40.3, 38.6, 37.1, 28.7, 21.2, 20.9, 19.8; FTIR (Neat Film NaCl) 3083, 2942, 2873, 2851, 1766, 1745, 1620, 1464, 1444, 1378, 1334, 1262, 1233, 1199, 1178, 1108, 1038, 1010, 994, 955, 914, 831, 733 cm^{-1} ; HRMS (Multimode-ESI/APCI) m/z calcd for $\text{C}_{22}\text{H}_{27}\text{O}_7$ [$\text{M} + \text{H}$] $^+$: 403.1751, found 403.1736.

epi-Basililide C (9). ^1H NMR (500 MHz, CDCl_3) δ 6.04 (dd, J = 6.5, 1.3 Hz, 1H), 5.80 (dd, J = 17.4, 10.8 Hz, 1H), 5.11–5.03 (m, 2H), 4.98 (d, J = 1.3 Hz, 1H), 3.72 (q, J = 10.8 Hz, 2H), 3.72 (s, 3H), 3.29 (d, J = 6.5 Hz, 1H), 3.23 (s, 1H), 2.09 (s, 3H), 1.84–1.72 (m, 1H), 1.70–1.62 (m, 2H), 1.61 (s, 3H), 1.50–1.41 (m, 1H), 1.26 (dd, J = 13.1, 4.9 Hz, 1H), 1.16 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.0, 170.8, 162.1, 157.0, 146.3, 138.9, 122.7, 113.2, 87.0, 79.0, 70.6, 56.5, 50.7, 49.7, 44.5, 38.6, 38.3, 37.0, 20.9, 20.7, 19.9, 19.3; FTIR (Neat Film NaCl) 2931, 1763, 1742, 1666, 1619, 1442, 1377, 1335, 1228, 1195, 1178, 1113, 1038, 1021, 999, 970, 952, 914, 830, 732 cm^{-1} ; HRMS (Multimode-ESI/APCI) m/z calcd for $\text{C}_{22}\text{H}_{27}\text{O}_7$ [$\text{M} + \text{H}$] $^+$: 403.1751, found 403.1744.

Methoxyethynyl Zinc Chloride (27). In a nitrogen glovebox, to a 0 $^\circ\text{C}$ solution of HNiEt_2 (807 μL , 7.8 mmol) in THF (4.25 mL) was added a 2.5 M solution of *n*-BuLi in hexanes (2.72 mL, 6.8 mmol). The reaction was stirred for 25 min at 0 $^\circ\text{C}$ at which point 1,1-dimethoxy-2-chloro-acetaldehyde (**25**) was added (228 μL , 2.0 mmol). The reaction was stirred at 0 $^\circ\text{C}$, and the formation of white precipitate was observed. After 2 h of stirring at 0 $^\circ\text{C}$, anhydrous zinc chloride was added (300 mg, 2.2 mmol), and the reaction was stirred for another 15 min at 0 $^\circ\text{C}$ or until all the zinc chloride had dissolved. The resulting 0.25 M solution of methoxyethynyl zinc chloride (**27**) in THF was kept at 0 $^\circ\text{C}$, in the glovebox, and used, as is, within hours of its generation.

Methyl 2-(Cyclohex-1-en-1-yl)acetate (30). General Procedure: In a nitrogen filled glovebox were combined $\text{Pd}_2(\text{dba})_3$ (1.4 mg, 1.5 μmol), Xantphos (2.6 mg, 4.5 μmol), and THF (180 μL) in a glass vial. The reaction mixture was stirred for 30 min at 30 $^\circ\text{C}$. Then a 1 M solution of known iodo-cyclohexene²¹ (**28**) in THF (30 μL , 0.030 mmol), internal standard tridecane (6 μL , 0.025 mmol), and freshly made 0.05 M methoxyethynyl zinc chloride (**27**) solution (90 μL , 0.045 mmol) were added sequentially, and the solution was stirred at 30 $^\circ\text{C}$. Aliquots (5 μL) were taken from the reaction solution at 15 min, 1 h, 2.5 h, and 4.5 h. Aliquots were diluted with ether, pushed through a short pad of silica, and then injected on GC for analysis. Yields of methyl ester **30** and consumption of vinyl iodide **28** were then quantified. All spectral data for **30** match the literature.²⁴

(E)-3,7-Dimethylocta-2,6-dien-1-yl 2-(5-(methoxyethynyl)-2-oxo-2H-pyran-6-yl)acetate (11). In a nitrogen filled glovebox, a solution of $\text{Pd}_2(\text{dba})_3$ (18.8 mg, 0.0205 mmol) and Xantphos (23.8 mg, 0.0411 mmol) in THF (900 μL) was stirred at 40 $^\circ\text{C}$ for 25 min. Following the catalyst prestir, **33** (85.6 mg, 0.206 mmol) was added as a solution in THF (350 μL) with internal standard diphenylether (37.1

mg, 0.218 mmol). This was subsequently followed by the addition of a freshly generated 0.25 M solution of methoxyethyl zinc chloride (**27**) (2.9 mL, 0.719 mmol). The resulting 0.05 M reaction solution was heated to 50 °C and stirred for 20 min. The reaction mixture was then immediately removed from heat, diluted with 0 °C THF (12 mL), removed from the glovebox, and flushed through a short pad of silica eluting with a 30% solution of Et₂O in hexanes (150 mL). Solvent was then removed by rotary evaporation and purified by column chromatography (EtOAc in a 50% solution of CH₂Cl₂ in hexanes 1% → 2% on silica) to give 31 mg (44% isolated yield, 61% SFC yield) of **11** as a reddish, yellow oil; ¹H NMR (500 MHz, CDCl₃) δ 7.23 (d, *J* = 9.6 Hz, 1H), 6.20 (d, *J* = 9.6 Hz, 1H), 5.32 (tq, *J* = 7.1, 1.3 Hz, 1H), 5.08–5.04 (m, 1H), 4.65 (d, *J* = 7.2 Hz, 2H), 3.96 (s, 3H), 3.71 (s, 2H), 2.13–1.98 (m, 4H), 1.69 (s, 3H), 1.67 (s, 3H), 1.59 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 167.6, 160.8, 159.9, 146.8, 143.2, 132.0, 123.8, 117.8, 114.5, 104.4, 103.5, 66.4, 62.6, 39.6, 38.8, 31.8, 26.4, 25.8, 17.8, 16.6; FTIR (Neat Film NaCl) 2926, 2856, 2271, 1742, 1634, 1548, 1446, 1418, 1377, 1347, 1318, 1294, 1238, 1208, 1167, 1134, 1064, 1040, 969, 895, 870, 826 cm⁻¹; HRMS (Multimode-ESI/APCI) *m/z* calcd for C₂₀H₂₅O₅ [*M* + *H*]⁺: 345.1697, found 345.1701.

Basiliopyrone (10). To a 23 °C solution of **11** (19 mg, 0.055 mmol) in MeCN (2 mL) was added a 1 M solution of H₂SO₄ in water (500 μL). The reaction mixture was then stirred at 23 °C for 24 h. After the reaction had gone to completion, the mixture was slowly quenched with a saturated solution of NaHCO₃ (5 mL), such that the reaction mixture was no longer acidic. The solution was then extracted with EtOAc (4 × 8 mL). The organics were combined and sequentially washed with saturated NaHCO₃ solution (25 mL), saturated brine solution (25 mL), and then once again with saturated NaHCO₃ solution (25 mL), and saturated brine solution (25 mL). The organics were then dried over Na₂SO₄, and solvent was removed by rotary evaporation. Purification by column chromatography (EtOAc in hexanes 10% → 25% on silica) yielded 8.1 mg (40% yield) of basiliopyrone (**10**) as a pale yellow oil. The spectroscopic data obtained from synthetic **10** match those published from natural sources;¹⁴ ¹H NMR (300 MHz, CDCl₃) δ 7.27 (d, *J* = 9.9 Hz, 1H), 6.27 (d, *J* = 9.5 Hz, 1H), 5.31 (tq, *J* = 7.2, 1.3 Hz, 1H), 5.10–5.04 (m, 1H), 4.64 (d, *J* = 7.2 Hz, 2H), 3.71 (s, 3H), 3.59 (s, 2H), 3.35 (s, 2H), 2.16–1.98 (m, 4H), 1.69 (s, 3H), 1.68 (s, 3H), 1.60 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 170.3, 167.5, 161.3, 155.8, 146.4, 143.4, 132.0, 123.9, 117.8, 115.3, 111.1, 62.9, 52.5, 39.7, 37.7, 34.9, 26.5, 25.8, 17.8, 16.7; FTIR (Neat Film NaCl) 2954, 2924, 2857, 1738, 1650, 1557, 1437, 1378, 1347, 1302, 1241, 1166, 1103, 1070, 975, 951, 872, 829 cm⁻¹; HRMS (Multimode-ESI/APCI) *m/z* calcd for C₂₀H₂₆O₆ [*M* + *H*]⁺: 363.1802, found 363.1792.

Transtaganolides C (4) and D (5). To ensure the absolute purity of **11** (10 mg, 0.029 mmol), directly following its isolation, the substrate (**11**) was submitted to ¹H NMR in C₆D₆, and upon confirmation of its purity, the solvent was pumped off in the antichamber of a nitrogen filled glovebox. This limited the possibility of substrate **11** decomposition as well as removed any deleterious, residual water. While the NMR solvent was removed in the antichamber, in the nitrogen filled glovebox, the reaction glassware was silylated by the addition of BSA (20 μL), triethylamine (0.41 μL), and PhMe (5 mL). This solution was heated to 70 °C and stirred for 30 min. The solution was then cooled to ambient temperature and then discarded. The reaction vessel was then rinsed with PhMe (3 × 1 mL). Once all C₆D₆ was removed from the substrate **11**, **11** (10 mg, 0.029 mmol) was transferred to the previously silylated reaction vessel with PhMe (600 μL, 0.05M). To this solution was then added BSA (17.8 μL, 0.073 mmol) and triethylamine (0.041 μL, 0.0029 mmol). The reaction solution was heated to 70 °C and stirred for 2.75 h, at which point the Ireland–Claisen rearrangement had gone to completion. The reaction was then cooled to ambient temperature and diluted with PhMe (9.2 mL, 0.003M) that had been doped with excess BSA (12.25 μL, PhMe/BSA = 1 mL/1.25 μL). The reaction mixture was then reheated to 70 °C and stirred for 5 d and 6 h. The reaction mixture was cooled to ambient temperature and removed from the nitrogen filled glovebox. The solution was concentrated by

rotary evaporation, and to the crude reaction residue was added MeCN (8 mL) and pH 7 phosphate buffer (100 μL). This solution was stirred at 23 °C for 3 h to allow for silyl cleavage and cyclization to the desired natural products (**4** and **5**). MeCN was then removed by passing a stream of air over the solution (rotary evaporation could not be accomplished without bumping the crude reaction mixture), and the remaining aqueous solution was further diluted with water (800 μL) and saturated brine (200 μL). The aqueous solution was then extracted with EtOAc (5 × 1 mL). The organics were pooled, dried over Na₂SO₄, and then concentrated by rotary evaporation. The crude oil was purified by normal phase HPLC (30% EtOAc in hexanes) to yield 0.90 mg (9% yield) of transtaganolide C (**4**) and 0.46 mg (5% yield) of transtaganolide D (**5**). The spectroscopic data obtained from synthetic **4** and **5** match those published from natural sources.^{6a,11}

Transtaganolide C (4). ¹H NMR (500 MHz, CDCl₃) δ 6.07 (dd, *J* = 1.5, 6.5 Hz, 1H), 5.80 (dd, *J* = 11.0, 17.5 Hz, 1H), 5.07 (d, *J* = 17.5 Hz, 1H), 5.03 (d, *J* = 11.0 Hz, 1H), 5.00 (d, *J* = 1.5 Hz, 1H), 3.71 (s, 3H), 3.23 (s, 1H), 3.06 (d, *J* = 6.5 Hz, 1H), 1.71–1.63 (m, 3H), 1.60 (s, 3H), 1.48–1.39 (m, 1H), 1.34–1.27 (m, 1H), 1.08 (s, 3H), 0.97 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 171.8, 162.3, 156.7, 146.5, 138.0, 123.6, 112.8, 87.3, 79.3, 56.3, 53.8, 50.6, 48.1, 38.4, 38.3, 33.3, 29.9, 24.8, 19.9, 19.2; FTIR (Neat Film NaCl) 2965, 2928, 2872, 1791, 1761, 1668, 1619, 1456, 1334, 1267, 1233, 1178, 1115, 970, 954, 828 cm⁻¹; HRMS (Multimode-ESI/APCI) *m/z* calcd for C₂₀H₂₅O₅ [*M* + *H*]⁺: 345.1697, found 345.1703.

Transtaganolide D (5). ¹H NMR (500 MHz, CDCl₃) δ 7.00 (dd, *J* = 11.0, 17.5 Hz, 1H), 6.09 (dd, *J* = 1.0, 6.5 Hz, 1H), 5.15 (dd, *J* = 1.0, 11.0 Hz, 1H), 5.05 (dd, *J* = 1.0, 17.5 Hz, 1H), 5.02 (d, *J* = 1.0 Hz, 1H), 3.73 (s, 3H), 3.13 (s, 1H), 3.06 (d, *J* = 6.5 Hz, 1H), 1.91 (dt, *J* = 3.5, 13.5 Hz, 1H), 1.64 (quint, *J* = 3.0, 13.5 Hz, 1H), 1.59–1.56 (m, 1H), 1.39 (dt, *J* = 3.5, 13.5 Hz, 1H), 1.33 (dd, *J* = 4.5, 13.5 Hz, 1H), 1.22 (s, 3H), 1.04 (s, 3H), 0.97 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 171.7, 162.6, 156.7, 142.9, 137.7, 123.9, 112.1, 87.3, 79.4, 56.3, 54.0, 53.3, 48.4, 40.5, 38.4, 33.3, 29.9, 28.5, 24.8, 20.5; FTIR (Neat Film NaCl) 2964, 2929, 2872, 1764, 1760, 1738, 1667, 1620, 1467, 1334, 1267, 1235, 1195, 1177, 1106, 1009, 954, 827 cm⁻¹; HRMS (Multimode-ESI/APCI) *m/z* calcd for C₂₀H₂₅O₅ [*M* + *H*]⁺: 345.1697, found 345.1698.

■ ASSOCIATED CONTENT

● Supporting Information

Experimental procedures, biological assays, HPLC data, and relevant spectra (¹H NMR, ¹³C NMR, and IR). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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