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Rapid access to 6-bromo-5,7-dihydroxyphthalide 5-methyl ether by a $CuBr_2$-mediated multi-step reaction: concise total syntheses of hericenone J and 5′-deoxohericenone C (hericene A)

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ABSTRACT

A practical route to 6-bromo-5,7-dihydroxyphthalide 5-methyl ether, a versatile intermediate in the synthesis of hericenones and related bioactive polyphenols, was developed. The synthesis features a combination of tandem Michael addition-Claisen condensation and $CuBr_2$-mediated multi-step reactions. With this product in hand, total syntheses of hericenone J and 5′-deoxohericenone C (hericene A) were achieved.

1. Introduction

Development of efficient one-pot reactions with multi-functionalization remains a great challenge in organic synthesis.[1] In pharmaceutical and agrochemical synthesis, for example, simple, reliable, and cost-effective methods are highly desirable for the preparation of building blocks. For instance, 6-bromo-5,7-dihydroxyphthalide 5-methyl ether (**1a**) and its 4-methyl derivatives **1b** are potential precursors of bioactive polyphenols such as hericenones,[2] hericerin,[3] hericenes,[4] and mycophenolic acid[5] (Fig. 1). These molecules incorporate as a key feature a highly functionalized, penta- or hexasubstituted aromatic ring, which necessitates rigorous regiocontrol in their synthesis. Previous methods to obtain **1b** or mycophenolic acid include functionalization of resorcinols,[6] aromatization of 1,3-dioxocyclohexanes,[7] tandem Michael addition-Dieckmann cyclizations,[8] Diels–Alder reactions with appropriate dienes,[9] or aromatic annulation.[10] In contrast, **1a**, which is a key component of the hericenone skeleton, has yet to be synthesized, and only one total synthesis of hericenone A has been reported.[2b] Other members of the hericenone family have not been synthesized in spite of their attractive biological features, including stimulation of nerve growth factor (NGF) synthesis,[2c] suppression of endoplasmic reticulum (ER) stress-dependent cell death[2e] and inhibition of collagen-induced platelet aggregation.[2f] Herein, we wish to report a concise, four-step synthesis of **1a** from commercial reagents featuring a $CuBr_2$-mediated multi-step reaction, which culminated in the first total synthesis of hericenone J and hericene A (5′-deoxohericenone C).

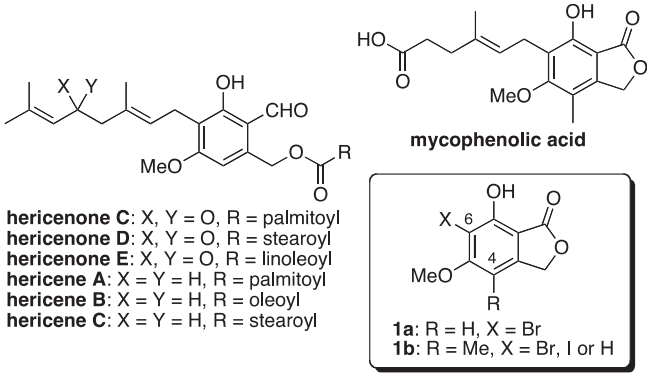

Fig. 1. Structures of bioactive polyphenols and their synthetic intermediates.

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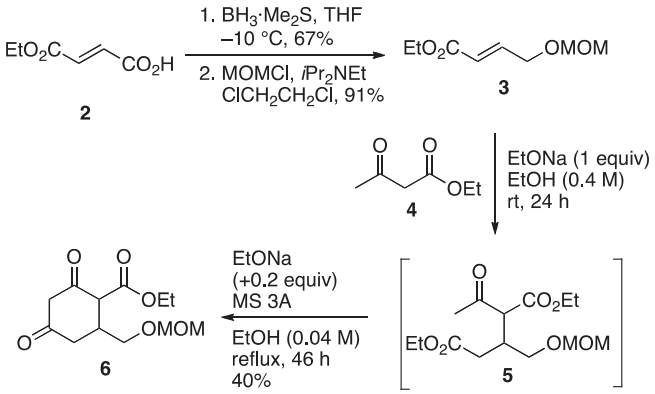
2. Results and discussion

2.1. Practical synthesis of 6-bromo-5,7-dihydroxyphthalide 5-methyl ether

The synthesis commenced with borane reduction of monoethyl fumarate (**2**) (Scheme 1).[11] The resultant alcohol was protected as its MOM ether to afford the Michael accepter **3**. A subsequent tandem Michael addition-Claisen condensation reaction was realized by mixing **3** (1 equiv), **4** (1.5 equiv), and NaOEt (1+0.2 equiv) in the appropriate order with careful control of temperature and concentrations.[12] Although the isolated yield of **6** was modest, its ready accessibility in gram quantities compelled us to investigate further transformations.



Scheme 1. Synthesis of cyclic 1,3-diketone **6**.

The next task was regioselective installation of the bromine and methoxy groups with concomitant aromatization. If the conventional method involving halogenated aromatization is conducted, more than three steps would be required to reach the target molecule. Indeed, treatment of **6** with Br_2/AcOH afforded highly crystalline 4,6-dibromo-5,7-dihydroxyphthalide (**7**) as the major product in 45% yield (Fig. 2), which would necessitate laborious regioselective methylation and debromination to access the phthalide **1a**. Therefore, we searched for more efficient conditions.

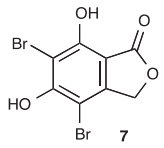
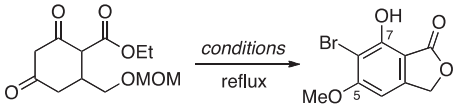


Fig. 2. Structure of **7**.

Inspired by previous work on the bromination of cyclic 1,3-diketones by $CuBr_2$,[13] we attempted the bromination of **6**. Interestingly, treatment of **6** with 6 equiv of $CuBr_2$ in MeOH successively induced multi-step reactions involving regioselective bromination, regioselective methoxylation, aromatization and lactonization, giving rise to the desired product **1a** in 31% yield (Table 1, entry 1). The structure of **1a** was unambiguously confirmed by NOE and HMBC experiments (Fig. 3). A byproduct, 4,6-dibromo-5,7-dihydroxyphthalide 5-methyl ether, was obtained in 28% yield in the 3 h reaction (entry 2). To avoid byproduct formation, the amount of $CuBr_2$ was reduced to 4.2 equiv, however the yield of **1a** decreased considerably and many byproducts appeared (entry 3). We suspected that this poor reproducibility arose from the higher solubility of $CuBr_2$ in MeOH, which induced non-selective overreactions, and

Table 1
$CuBr_2$-mediated multi-step reaction of **6**



Entry	Reagent[a] (equiv)	Solvent	Time (h)	Yield[b] (%)
1	$CuBr_2$ (6)	MeOH	1	31
2	$CuBr_2$ (6)	MeOH	3	25[c]
3	$CuBr_2$ (4.2)	MeOH	24	Trace
4	$CuBr_2$ (4.3)	$CHCl_3$/MeOH (2:1)	20	48
5	$CuBr_2$ (4.3)	$CHCl_3$/MeOH (2:1)	37	70
6[d]	NBS (2)	CCl_4 then HCl/MeOH		52[e]

[a] The number in parentheses refers to equivalents of the reagent.
[b] Isolated yield.
[c] 4,6-Dibromo-5,7-dihydroxyphthalide 5-methyl ether was obtained in 28% yield along with 25% of **1a**.
[d] Ketone **6** was treated with NBS in CCl_4 for 1 h. After concentration, the residue was dissolved in HCl/MeOH and refluxed for 21 h.
[e] Combined yield of 2:1 regioisomeric mixture of **1a** and its 7-methoxy isomer.

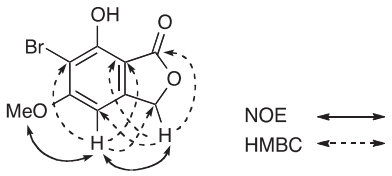
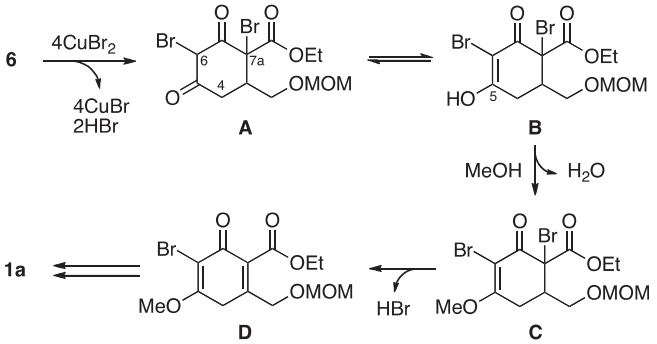


Fig. 3. NOE and HMBC correlations for **1a**.

accordingly, undertook a solvent screening. Remarkably, a heterogeneous system[14] consisting of 4.3 equiv of $CuBr_2$ in $CHCl_3$/MeOH (2:1) with an extended time reproducibly afforded the phthalide **1a** in good yield (entries 4 and 5). This result was superior to the NBS–HCl/MeOH system, where a 2:1 regioisomeric mixture of **1a** and its 7-methoxy isomer was produced (entry 6).

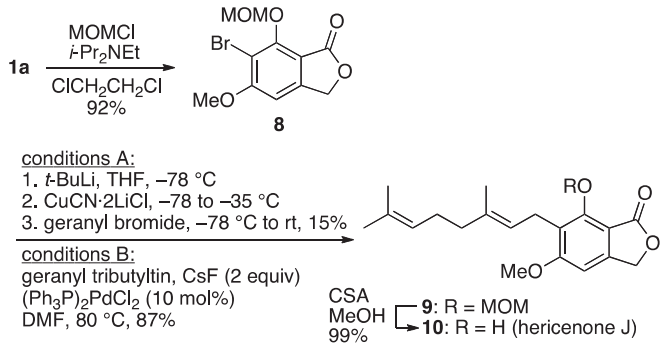
Scheme 2 shows one possible mechanism for the unprecedented $CuBr_2$-mediated one-pot multi-step reaction. In principle, 2 mol of $CuBr_2$ are necessary for one bromination of 1 mol of ketone,[13] and three possible bromination sites exist at C4, C6, and C7a. Among them, the most acidic C6-H and C7a-H hydrogens were replaced by bromine to give **A**, which is in equilibrium with its enol form **B**. Addition–elimination sequence of MeOH/H_2O then took place at the least hindered C5-position and produced the methoxylated enone **C**, which underwent elimination of HBr to give **D**. This was followed by aromatization and acid-catalyzed lactonization to afford **1a**. Although we were unsuccessful in isolating any of the reaction intermediates, this mechanism is most likely to explain the observed regiochemical outcome.



Scheme 2. Plausible reaction course leading to **1a**.

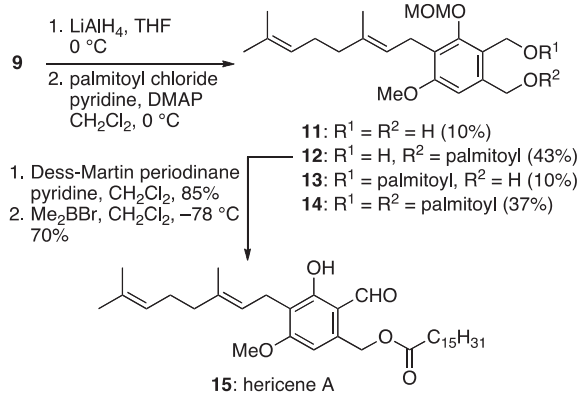
2.2. Total syntheses of hericenone J and hericene A

After establishing a practical route to **1a**, we turned our attention to the natural product synthesis with **1a**. Due to the synthetic and biological interest, hericene A[4] (5′-deoxohericenone C), the leading polyphenol of this family, was selected as the initial synthetic target. After protection of the phenolic hydroxy group as its MOM ether, aryl bromide **8** was treated with geranyl bromide via an arylcopper reagent[15] (Scheme 3, conditions A). However, the desired product **9** was obtained in only 15% yield, which was not improved by altering bases (*t*-BuLi, *n*-BuLi, and *i*-PrMgCl·LiCl[16]), copper reagents (CuCN·2LiCl and CuBr·Me_2S), additives (HMPA and DMPU), or temperature. Isolation of considerable amounts of byproducts lacking a MOM group indicated that the lactone carbonyl and two MOM oxygens contributed to chelation with metal cations, which hampered the desired halogen-metal exchange reaction. After many attempts, we found that coupling was successful under modified Stille conditions[17,18] in the presence of geranyl tributyltin[19] (2 equiv), $(Ph_3P)_2PdCl_2$ (10 mol %), and CsF (2 equiv) in 87% yield (Scheme 3, conditions B). Addition of CsF was crucial to obtain the product reproducibly.[20] This is a remarkable example of a successful Stille reaction of the electron-rich, bisortho-substituted aromatic bromide.[21] Acid-catalyzed removal of the MOM group in **9** furnished hericenone J (**10**), the spectra of which were identical to those of the natural product.[2e]



Scheme 3. Synthesis of hericenone J (**10**).

Synthesis of hericene A (**15**) was achieved as follows (Scheme 4). $LiAlH_4$ reduction of lactone **9** followed by acylation with palmitoyl chloride under precise conditions provided a mixture of acylation products **12**–**14**, all of which will be useful for SAR studies. After separation by silica gel chromatography, isomer **12** was subjected to Dess–Martin oxidation[22] and deprotection[23] to furnish hericene A (**15**).[4] In this case, Me_2BBr was superior to CSA for deprotection.[24] The biological activities of **15** and its analogs will be investigated in due course.



Scheme 4. Synthesis of hericene A.

3. Conclusion

In summary, we have achieved a concise synthesis of 6-bromo-5,7-dihydroxyphthalide 5-methyl ether (**1a**), a key synthetic intermediate of hericenones and related bioactive polyphenols, by a combination of tandem Michael addition-Claisen condensation and $CuBr_2$-mediated multi-step reactions. The current synthesis is straightforward, regioselective, and practical, and therefore, provides a new entry into the integrated synthesis that realizes multiple transformations in one-pot.[25] Furthermore, we succeeded in the first total syntheses of hericenone J and hericene A using **1a** as a common intermediate. We believe that the present investigation will become an important guideline for developing new efficient routes to polyfunctionalized bioactive polyphenols. Further studies to synthesize the natural hericenones and their analogs are currently underway in our laboratory.

4. Experimental section

4.1. General remarks

All reactions utilizing air- or moisture-sensitive reagents were performed under an atmosphere of argon. Commercially available dry solvents were used for DMF, $CHCl_3$, CH_2Cl_2, MeOH, and THF. Triethylamine and *i*-Pr_2NEt were distilled from CaH_2. DMAP was recrystallized from AcOEt. The commercially available LiCl was dried at 140 °C under vacuum overnight before use. Me_2BBr was prepared from BBr_3 and Me_4Sn[23] and stored as a 1.76 M dichloromethane solution in a refrigerator (−30 °C). Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel plates (60-F_{254}) that were analyzed by fluorescence upon 254 nm irradiation or by staining with *p*-anisaldeyde/AcOH/H_2SO_4/EtOH, $12MoO_3\cdot H_3PO_4$/EtOH, or $(NH_4)_6Mo_7O_{24}\cdot 4H_2O/H_2SO_4$. The products were purified by flash chromatography on silica gel (spherical, neutral, 40–50 μm) and, if necessary, were further purified by HPLC equipped with a pre-packed column using hexane/EtOAc as the eluent. NMR spectra were recorded with a 500 MHz (^{1}H: 500 MHz, ^{13}C: 125 MHz), a 400 MHz (^{1}H: 400 MHz, ^{13}C: 100 MHz), or a 300 MHz (^{1}H: 300 MHz, ^{13}C: 75 MHz) spectrometer and referenced to the solvent peak at 7.26 ppm (1H) and 77.16 ppm (^{13}C) for $CDCl_3$. Splitting patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Infrared spectra were recorded with an FT/IR spectrometer and reported as wavenumber (cm^{-1}). Low- and high-resolution mass spectra were measured by EI or FAB method.

*4.1.1. (E)-Ethyl 4-(methoxymethoxy)-2-butenoate (**3**).* To a solution of monoethyl fumarate (**2**) (25.0 g, 174 mmol) in THF (87 mL) was added a solution of $BH_3\cdot Me_2S$ (16.5 mL, 174 mmol) in THF (130 mL) dropwise over 2 h at −10 °C. The reaction mixture was gradually allowed to warm to room temperature and stirred for 18 h. The reaction was quenched by the dropwise addition of AcOH/H_2O (1:1, v/v, 5 mL) with stirring until no more gas evolution occurred. The mixture was concentrated and the residual slurry was treated with ice-cold saturated aqueous $NaHCO_3$ solution (80 mL). The resulting mixture was extracted with EtOAc (2×). The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution, dried over anhydrous $MgSO_4$ and concentrated to give (*E*)-ethyl 4-hydroxy-2-butenoate[11] (15.1 g, 116 mmol, 67%). To a solution of (*E*)-ethyl 4-hydroxy-2-butenoate (15.1 g, 116 mmol) in 1,2-dichloroethane (116 mL) were added *i*-Pr_2NEt (60.7 mL, 389 mmol) and MOMCl (10.6 mL, 140 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 70 h and quenched by the addition of saturated aqueous $NaHCO_3$ solution. The mixture was concentrated and the residue was extracted with hexane (2×). The combined organic layer was washed with 1 M aqueous HCl

solution, saturated aqueous $NaHCO_3$ solution, brine, dried over anhydrous $MgSO_4$, and concentrated to give MOM ether **3** (18.3 g, 105 mmol, 91%) as a brownish oil, which was used for the next reaction without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (dt, 1H, J=16, 4.0 Hz), 6.09 (dt, 1H, J=16, 2.0 Hz), 4.66 (s, 2H), 4.22 (dd, 2H, J=4.0, 2.0 Hz), 4.20 (q, 2H, J=7.2 Hz), 3.38 (s, 3H), 1.29 (t, 3H, J=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 144.0, 121.4, 96.2, 65.9, 60.5, 55.6, 14.4.

*4.1.2. Ethyl 2-((methoxymethoxy)methyl)-4,6-dioxocyclohexane carboxylate (**6**).* To a solution of MOM ether **3** (4.01 g, 23.0 mmol) and ethyl acetoacetate **4** (4.36 mL, 34.5 mmol) in EtOH (58 mL) was added NaOEt (1.0 M solution in EtOH, 23.0 mL, 23.0 mmol). The mixture was stirred at room temperature for 24 h. Upon addition of NaOEt (1 M solution in EtOH, 4.6 mL, 4.6 mmol), the reaction mixture was slowly poured into refluxing EtOH (518 mL) containing molecular sieves 3 Å (15 g) over a period of 12 h through a dropping funnel. After being stirred at reflux for 34 h, the reaction mixture was filtered through a pad of Celite. The filtrate was concentrated and treated with 1 M aqueous H_2SO_4 solution. The resulting mixture was extracted with EtOAc (2×). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc=2/1→1/1→1/2) to give diketone **6** (2.37 g, 9.17 mmol, 40%) as an amber solid. Data for **6** (diastereomeric mixture): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.47 (s, 2H, MOM), 4.26 (q, 1H, J=7.0 Hz, OEt), 4.26 (q, 1H, J=7.0 Hz, OEt), 3.64–3.55 (m, 4H, H1, H5, H8), 3.39 (dt, 1H, J=18, 1.8 Hz, H5), 3.27 (s, 3H, MOM), 2.86 (br dd, 1H, J=16, 6.0 Hz, H3), 2.79 (m, 1H, H2), 2.62 (ddt, 1H, J=16, 4.0, 1.6 Hz, H3), 1.30 (t, 3H, J=7.0 Hz, OEt); FT-IR (KBr) 2981, 2828, 1742, 1599, 1467, 1447, 1408, 1371, 1316, 1259, 1182 cm^{-1}; MS (EI, 70 eV) m/z (%) 227 (M^+−OMe, 17), 213 (7), 183 (100), 137 (55), 113 (19), 95 (22), 85 (13); HRMS (EI): m/z calcd for $C_{11}H_{15}O_5$ $[M-OMe]^+$ 227.0919, found: 227.0919.

*4.1.3. 6-Bromo-7-hydroxy-5-methoxyisobenzofuran-1(3H)-one (**1a**).* To a refluxing suspension of $CuBr_2$ (3.46 g, 15.5 mmol) in $CHCl_3$ (24 mL) was added dropwise a solution of diketone **6** (930 mg, 3.60 mmol) in MeOH (12 mL). The mixture was stirred at reflux for 37 h and the precipitate formed was removed by filtration through a pad of Celite. The filtrate was concentrated and treated with hexane/EtOAc (1:2) and 1 M aqueous HCl solution. The organic layer was separated and the aqueous layer was extracted with hexane/EtOAc (1:2) (3×). The combined organic layer was washed with H_2O, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc=2/1→1/1) to give phthalide **1a** (650 mg, 2.51 mmol, 70%) as a tan solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (s, 1H, H4), 5.26 (s, 2H, H3), 3.98 (s, 3H, OMe); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 163.2, 154.3, 147.4, 105.3, 98.8, 97.2, 70.5, 57.2; FT-IR (KBr) 3395, 1751, 1618, 1480, 1467, 1458, 1438 cm^{-1}; MS (EI, 70 eV) m/z (%) 260 (M^+, 89), 258 (M^+, 94), 231 (96), 229 (100); HRMS (EI): m/z calcd for $C_9H_7{}^{79}BrO_4$: 257.9528, $C_9H_7{}^{81}BrO_4$: 259.9508, found: 257.9530, 259.9503, respectively. Anal. Calcd for $C_9H_7BrO_4$: C, 41.73; H, 2.72. Found: C, 41.52; H, 2.72.

*4.1.4. 6-Bromo-5-methoxy-7-(methoxymethoxy)isobenzofuran-1(3H)-one (**8**).* To a solution of phthalide **1a** (954 mg, 3.68 mmol) in 1,2-dichloroethane (10 mL) were added i-Pr_2NEt (1.92 mL, 11.0 mmol) and MOMCl (419 mL, 5.52 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 13 h before it was quenched by the addition of saturated aqueous $NaHCO_3$ solution. The mixture was extracted with hexane/EtOAc (1:1) (3×), and the combined organic layer was washed with saturated aqueous NH_4Cl solution, brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was washed with hexane (3×) by decantation and dried in vacuo to give analytically pure MOM ether **8** (1.03 g, 3.38 mmol, 92%) as a tan solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71 (s, 1H, H4), 5.52 (s, 2H, MOM), 5.19 (s, 2H, H3), 4.00 (s, 3H, MOM), 3.67 (s, 3H, OMe); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 162.4, 154.8, 149.6, 110.6, 108.0, 101.2, 99.9, 68.7, 58.5, 57.2; FT-IR (KBr) 3023, 2967, 2947, 1750, 1599, 1459, 1432 cm^{-1}; MS (EI, 70 eV) m/z (%) 304 (M^+, 22), 302 (M^+, 21), 273 (64), 271 (76), 244 (100), 242 (94); HRMS (EI): m/z calcd for $C_{11}H_{11}{}^{79}BrO_5$: 301.9790, $C_{11}H_{11}{}^{81}BrO_5$: 303.9771, found: 301.9788, 303.9765, respectively. Anal. Calcd for $C_{11}H_{11}BrO_5$: C, 43.59; H, 3.66. Found: C, 43.80; H, 3.69.

4.1.5. Geranyl bromide. To a solution of geraniol (5.00 g, 32.4 mmol) and CBr_4 (21.5 g, 64.8 mmol) in benzene (100 mL) was added PPh_3 (17.0 g, 64.8 mmol) by portions over 15 min at 0 °C. The mixture was stirred at 0 °C for 3 h before it was diluted with hexane (150 mL). The precipitate was removed by filtration through a pad of Celite and the filtrate was concentrated. Hexane (50 mL) was added to the residue and the precipitate was again removed by filtration. After the filtrate was concentrated, the residue was distilled under reduced pressure to give geranyl bromide (6.71 g, 30.9 mmol, 95%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53 (m, 1H), 5.07 (m, 1H), 4.02 (d, 2H, J=8.4 Hz), 2.06–2.11 (m, 4H), 1.73 (s, 3H), 1.68 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5, 131.9, 123.5, 120.5, 39.5, 29.6, 26.2, 25.7, 17.7, 16.0. This product is commercially available and the ^{1}H and ^{13}C NMR spectra are consistent with those of the authentic sample.

4.1.6. Geranyl tributyltin. To a solution of geraniol (5.03 g, 32.6 mmol) in THF (60 mL) was added n-BuLi (1.6 M solution in hexane, 20.0 mL, 32.4 mmol) at −78 °C. The mixture was stirred for 20 min followed by the addition of MsCl (2.56 mL, 32.4 mmol). The mixture was stirred at −78 °C for 40 min followed by the addition of n-Bu_3SnLi (0.54 M solution in THF) [prepared from i-Pr_2NH (5.01 mL, 35.7 mmol), n-BuLi (1.6 M solution in hexane, 20.0 mL, 32.4 mmol), and Bu_3SnH (9.44 g, 32.4 mmol) in THF (60 mL) at 0 °C]. The resulting mixture was stirred at −78 °C for 2.5 h and allowed to warm to room temperature. The stirring was continued for 20 h before the mixture was quenched with H_2O. The resulting mixture was extracted with hexane (3×), and the organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel (hexane/Et_3N=100/1) to give geranyl tributyltin (8.97 g, 21.0 mmol, 64%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.32 (br td, 1H, J=8.8, 1.2 Hz), 5.10 (br tt, J=7.2, 1.4 Hz, 1H), 2.08–1.95 (m, 4H), 1.68 (s, 3H), 1.66 (d, 2H, J=9.2 Hz), 1.60 (s, 3H), 1.57 (s, 3H), 1.53–1.44 (m, 6H), 1.34–1.25 (m, 6H), 0.89 (t, 9H, J=7.6 Hz), 0.85–0.81 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.3, 129.3, 124.8, 123.0, 40.0, 29.4, 27.6, 27.2, 25.9, 17.8, 15.8, 13.9, 10.7, 9.5; FT-IR (neat) 2957, 2924, 2871, 2854, 1455, 1376 cm^{-1}; MS (FAB): m/z calcd for $C_{22}H_{44}Sn$ $[M-nBu]^+$ 371, found: 371.

*4.1.7. (E)-6-(3,7-Dimethylocta-2,6-dienyl)-5-methoxy-7-(methoxymethoxy)isobenzofuran-1(3H)-one (**9**). Conditions* A: To a solution of aryl bromide **8** (50.0 mg, 0.165 mmol) in THF (1 mL) was added t-BuLi (1.59 M in pentane, 218 μL, 0.347 mmol) at −78 °C. The mixture was stirred at −78 °C for 20 min followed by the addition of CuCN·2LiCl in THF (1 mL) [prepared by vigorously stirring CuCN (44.3 mg, 0.495 mmol) and LiCl (42.0 mg, 0.990 mmol) in THF for 18 h]. The suspension was gradually warmed to −35 °C, at which point copper reagent almost dissolved. The reaction mixture was again cooled to −78 °C followed by the addition of geranyl bromide (107 mg, 0.495 mmol) and HMPA (144 μL, 0.825 mmol) in THF (1 mL). The resulting dark purple solution was gradually warmed to room temperature over a period of 10 h before it was quenched by the addition of saturated aqueous NH_4Cl solution. The mixture was extracted with EtOAc (2×), and the combined organic layer was

washed with brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc=4/1→1/1) to give **9** (9.0 mg, 0.025 mmol, 15%).

Conditions B: Aryl bromide **8** (358 mg, 1.18 mmol), geranyl tributyltin (1.00 g, 2.36 mmol), $(Ph_3P)_2PdCl_2$ (84.0 mg, 0.120 mmol), and CsF (359 mg, 2.36 mmol) were dissolved in DMF (5.9 mL). The solution was warmed to 80 °C and stirred for 13 h. The insoluble materials were removed by filtration through a pad of Celite and successively washed with diethyl ether. The filtrate was treated with saturated aqueous KF solution and stirred at room temperature for 1 h. The mixture was extracted with diethyl ether (3×), and the combined organic layer was dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc=3/1) to give the coupling product **9** (370 mg, 1.03 mmol, 87%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (s, 1H, H4), 5.39 (s, 2H, MOM), 5.17 (s, 2H, H3), 5.15 (m, 1H, H2′), 5.05 (m, 1H, H6′), 3.90 (s, 3H, MOM), 3.58 (s, 3H, OMe), 3.45 (d, 2H, J=6.8 Hz, H1′), 2.04 (m, 2H, H5′), 1.95 (m, 2H, H4′), 1.77 (s, 3H, C3′-Me), 1.64 (s, 3H, C7′-Me), 1.57 (s, 3H, C7′-Me); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 164.3, 155.0, 148.7, 135.7, 131.4, 124.6, 124.4, 121.9, 109.3, 101.1, 99.1, 68.8, 57.9, 56.2, 39.8, 26.7, 25.8, 23.0, 17.8, 16.3; FT-IR (KBr) 3124, 2925, 2844, 1736, 1698, 1607, 1467, 1432, 1403, 1376 cm^{-1}; MS (EI, 70 eV) m/z (%) 360 (M^+, 5), 315 (54), 261 (40), 259 (20), 247 (28); HRMS (EI): m/z calcd for $C_{21}H_{28}O_5$: 360.1937, found: 360.1935.

*4.1.8. (E)-6-(3,7-Dimethylocta-2,6-dienyl)-7-hydroxy-5-methoxyisobenzofuran-1(3H)-one (hericenone J, **10**).* To a solution of **9** (10.6 mg, 0.0294 mmol) in MeOH (1 mL) was added CSA (1.4 mg, 0.0059 mmol). The mixture was stirred at room temperature for 6 days before it was quenched by the addition of Et_3N (1 mL). The reaction mixture was concentrated and the residue was purified by flash column chromatography on silica gel (hexane/EtOAc=5/1) to give hercenone J (**10**) (9.2 mg, 0.029 mmol, 99%) as a colorless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 6.48 (s, 1H), 5.21 (s, 1H) 5.17 (t, 1H, J=7.2 Hz), 5.04 (t, 1H, J=6.8 Hz), 3.88 (s, 3H), 3.34 (d, 2H, J=7.2 Hz), 2.03 (m, 2H), 1.95 (t, 2H, J=7.6 Hz), 1.76 (s, 3H), 1.63 (s, 3H), 1.56 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9 (C1), 164.9 (C5), 154.5 (C7), 146.1 (C3a), 135.9 (C3′), 131.3 (C7′), 124.4 (C6′), 121.3 (C2′), 116.9 (C6), 104.2 (C7a), 96.2 (C4), 70.5 (C3), 56.2 (OMe), 39.9 (C4′), 26.7 (C5′), 25.7 (C8′), 21.6 (C1′), 17.7 (C7′-Me), 16.2 (C3′-Me); FT-IR (KBr) 3427, 3002, 2979, 2920, 2859, 1736, 1698, 1619, 1492, 1467, 1449, 1349 cm^{-1}; MS (EI, 70 eV) m/z (%) 316 (M^+, 8), 236 (28), 194 (57), 193 (100), 176 (24), 145 (24); HRMS (EI): m/z calcd for $C_{19}H_{24}O_4$: 316.1675, found: 316.1676.

*4.1.9. (E)-4-(3,7-Dimethylocta-2,6-dienyl)-2-(hydroxymethyl)-5-methoxy-3-(methoxymethoxy)benzyl palmitate (**11**).* To a solution of phthalide **9** (50.0 mg, 0.139 mmol) in THF (2.8 mL) was added $LiAlH_4$ (16.6 mg, 0.437 mmol) at 0 °C. The mixture was stirred at 0 °C for 30 min before it was quenched by the addition of H_2O and 1 M aqueous NaOH solution. The resulting mixture was extracted with EtOAc (3×), and the combined organic layer was washed with 1 M aqueous HCl solution, brine, dried over anhydrous $MgSO_4$, and concentrated to give diol **11** (53.8 mg). The diol **11** (26.0 mg, 0.0713 mmol) was dissolved in CH_2Cl_2 (1.5 mL) followed by the addition of pyridine (27 μL, 0.33 mmol), DMAP (0.8 mg, 0.007 mmol), and palmitoyl chloride (11 μL, 0.036 mmol) at 0 °C. The mixture was stirred at 0 °C for 1 h and 11 μL (0.036 mmol) each of palmitoyl chloride was added twice at the intervals of 1 h with stirring at 0 °C. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution and extracted with EtOAc (3×). The combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc=15/1→6/1→3/1→1/2 containing 5% MeOH) to give esters **12** (18.3 mg, 0.0304 mmol, 43% for two steps), **13** (4.1 mg, 0.0068 mmol, 10% for two steps), **14** (22.5 mg, 0.0267 mmol, 37% in two steps), and the recovery of diol **11** (2.7 mg, 0.0074 mmol, 10%). Data for **11**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (s, 1H), 5.10–5.13 (m, 2H), 5.03–5.06 (m, 2H), 4.93 (s, 2H), 4.71 (d, 4H, J=8.8 Hz), 3.84 (s, 3H), 3.62 (s, 3H), 3.33 (d, 2H, J=6.4 Hz), 1.94–2.08 (m, 4H), 1.75 (s, 3H), 1.64 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 158.3, 156.1, 140.1, 135.2, 131.4, 125.4, 124.3, 122.9, 122.6, 108.5, 100.4, 64.5, 57.5, 56.6, 55.7, 39.7, 26.7, 25.7, 23.6, 17.7, 16.3; FT-IR (KBr) 3311, 3235, 2926, 2855, 1604, 1577, 1458, 1400 cm^{-1}; MS (EI, 70 eV) m/z (%) 364 (M^+, 2), 302 (49), 259 (30), 233 (100), 219 (65), 197 (96), 162 (26); HRMS (EI): m/z calcd for $C_{21}H_{32}O_5$: 364.2250, found: 364.2252. Data for **12**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (s, 1H), 5.25 (s, 2H), 5.11 (m, 1H), 5.04 (m, 1H), 4.98 (s, 2H), 4.65 (d, 2H, J=6.8 Hz), 3.83 (s, 3H), 3.63 (s, 3H), 3.33 (d, 2H, J=6.4 Hz), 3.07 (t, 1H, J=6.8 Hz, OH), 2.34 (t, 2H, J=7.2 Hz), 2.08–1.95 (m, 4H), 1.75 (s, 3H), 1.64 (s, 3H), 1.60 (m, 2H), 1.57 (s, 3H), 1.25 (m, 24H), 0.88 (t, 3H, J=6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 158.3, 156.4, 135.4, 134.3, 131.5, 126.4, 124.3, 123.9, 122.6, 108.9, 100.4, 64.2, 57.6, 56.2, 55.8, 39.8, 34.5, 32.1, 29.8, 29.6, 29.5, 29.4, 29.3, 29.2, 26.7, 25.8, 25.1, 24.9, 23.8, 22.8, 17.8, 16.4, 14.3; FT-IR (KBr) 3460, 2954, 2917, 2849, 1740, 1604, 1578, 1467, 1395 cm^{-1}. Data for **13**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 1H), 5.27 (s, 2H), 5.13 (m, 1H), 5.04 (m, 1H), 4.94 (s, 2H), 4.71 (d, 2H, J=6.4 Hz), 3.85 (s, 3H), 3.58 (s, 3H), 3.36 (d, 2H, J=6.4 Hz), 2.29 (t, 2H, J=7.6 Hz), 2.08–1.94 (m, 4H), 1.75 (s, 3H), 1.64 (s, 3H), 1.60 (m, 2H), 1.57 (s, 3H), 1.26 (m, 24H), 0.88 (t, 3H, J=6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 159.2, 156.4, 140.2, 135.4, 131.5, 124.4, 123.5, 122.7, 119.3, 107.5, 100.9, 63.2, 59.1, 57.8, 55.8, 39.8, 34.5, 32.1, 29.83, 29.79, 29.7, 29.6, 29.5, 29.4, 29.3, 26.7, 25.8, 25.0, 23.7, 22.8, 17.8, 16.3, 14.3; FT-IR (KBr) 3444, 2917, 2848, 1739, 1708, 1604, 1578, 1463, 1427, 1403, 1384 cm^{-1}. Data for **14**: colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (s, 1H), 5.23 (s, 2H), 5.14 (s, 2H), 5.14 (m, 1H), 5.04 (m, 1H), 4.93 (s, 2H), 3.83 (s, 3H), 3.57 (s, 3H), 3.36 (d, 2H, J=6.8 Hz), 2.37–2.26 (m, 4H), 2.05–1.95 (m, 4H), 1.74 (s, 3H), 1.64 (s, 3H), 1.60 (m, 4H), 1.57 (s, 3H), 1.26 (m, 48H), 0.88 (t, 6H, J=6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 173.7, 159.1, 156.5, 135.4, 131.5, 124.5, 124.4, 122.7, 120.6, 108.6, 101.0, 64.1, 58.9, 57.8, 55.9, 39.9, 34.6, 34.6, 32.2, 29.9, 29.7, 29.6, 29.5, 29.4, 26.8, 25.9, 25.2, 23.8, 22.9, 17.9, 16.4, 14.4; FT-IR (KBr) 2955, 2917, 2849, 1734, 1604, 1578, 1467, 1403 cm^{-1}.

*4.1.10. (E)-4-(3,7-Dimethylocta-2,6-dienyl)-2-formyl-3-hydroxy-5-methoxybenzyl palmitate (hericene A, **15**).* To a solution of alcohol **12** (25.6 mg, 0.0425 mmol) in CH_2Cl_2 (3.2 mL) were added pyridine (17.0 μL, 0.210 mmol) and Dess–Martin periodinane (26.7 mg, 0.0630 mmol). The reaction mixture was stirred at room temperature for 3 h before it was quenched by the addition of saturated aqueous $Na_2S_2O_3$ solution and saturated aqueous $NaHCO_3$ solution. The mixture was stirred for 30 min and extracted with EtOAc (2×). The combined organic layer was washed brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc=10/1) to give aldehyde (21.6 mg, 0.0360 mmol, 85%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 1H), 6.83 (s, 1H), 5.52 (s, 2H), 5.11 (m, 1H), 5.03 (m, 1H), 5.02 (s, 2H), 3.90 (s, 3H), 3.56 (s, 3H), 3.36 (d, 2H, J=6.4 Hz), 2.41 (t, 2H, J=7.6 Hz), 2.07–1.97 (m, 4H), 1.76 (s, 3H), 1.68 (m, 2H), 1.64 (s, 3H), 1.57 (s, 3H), 1.25 (m, 24H), 0.88 (t, 3H, J=7.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.5, 173.4, 162.9, 161.3, 139.2, 136.0, 131.6, 124.3, 123.3, 122.0, 121.1, 106.0, 101.7, 64.4, 58.2, 55.9, 39.8, 34.6, 32.1, 29.83, 29.80, 29.76, 29.6, 29.5, 29.5, 29.4, 26.7, 25.8, 25.2, 23.1, 22.8, 17.8, 16.4, 14.3; FT-IR (KBr) 2925, 2854, 1742, 1680, 1598, 1566, 1465, 1377, 1289, 1218, 1160, 1116, 1048 cm^{-1}; HRMS (FAB): m/z calcd for $C_{37}H_{61}O_6$ $[M+H]^+$ 601.4468, found 601.4476.

To a solution of the above aldehyde (7.0 mg, 0.012 mmol) in CH_2Cl_2 (2 mL) was added Me_2BBr (1.76 M in CH_2Cl_2, 11 μL, 0.019 mmol) at −78 °C. The mixture was stirred at −78 °C for 1.2 h

before it was quenched by the addition of saturated aqueous $NaHCO_3$. The mixture was extracted with EtOAc (3×), and the combined organic layer was washed with brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc=20/1→10/1) to give hericene A (**15**) (4.7 mg, 8.4 μmol, 70%) and the recovery of aldehyde (1.9 mg, 3.2 μmol, 26%). Data for **15**: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.37 (s, 1H, OH), 10.10 (s, 1H, CHO), 6.52 (s, 1H, H6), 5.32 (s, 2H, C1–CH_2), 5.16 (br t, 1H, J=7.2 Hz, H2′), 5.05 (br t, 1H, J=7.0 Hz, H6′), 3.91 (s, 3H, OMe), 3.33 (br d, 2H, J=7.2 Hz, H1′), 2.33 (t, 2H, J=7.2 Hz, H2″), 2.03 (m, 1H, H5′), 1.96 (m, 1H, H4′), 1.76 (br s, 3H, H10′), 1.63 (br s, 3H, H8′), 1.61 (m, 2H, H3″), 1.57 (br s, 3H, H9′), 1.25 (m, 26H), 0.88 (t, 3H, J=7.2 Hz, H16″). ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.3 (C8), 173.4 (C1″), 163.6 (C5), 163.0 (C3), 138.5 (C1), 135.9 (C7′), 131.4 (C3′), 124.5 (C6′), 121.3 (C2′), 118.2 (C4), 113.0 (C2), 105.7 (C6), 63.1 (C7), 56.0 (C9), 39.9 (C4′), 34.4 (C2″), 32.1 (C3″), 29.84, 29.81, 29.79, 29.73, 29.59, 29.51, 29.38, 29.26, 26.8 (C5′), 25.8 (C8′), 25.0, 22.8, 21.5 (C1′), 17.8 (C9′), 16.3 (C10′), 14.3 (C16″); FT-IR (film) 2923, 2855, 1741, 1637, 1622, 1578, 1498, 1466, 1410, 1377, 1344, 1311, 1286, 1253, 1223, 1172, 1150, 1122, 1017 cm^{-1}; HRMS (FAB): m/z calcd for $C_{35}H_{57}O_5$ $[M+H]^+$ 557.4206, found: 557.4244.

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Supplementary data

^{1}H and ^{13}C NMR spectra for all new synthetic compounds and comparisons of the NMR data for synthetic compounds and natural products. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.09.104.

References and notes

1. Bard, A. J. *Integrated Chemical Synthesis*; Wiley: New York, NY, 1994.
2. (a) Kawagishi, H.; Ando, M.; Mizuno, T. *Tetrahedron Lett.* **1990**, *31*, 373–376; (b) Rao, A. V. R.; Reddy, R. G. *Tetrahedron Lett.* **1992**, *33*, 4061–4064; (c) Kawagishi, H.; Ando, M.; Sakamoto, H.; Yoshida, S.; Ojima, F.; Ishiguro, Y.; Ukai, N.; Furukawa, S. *Tetrahedron Lett.* **1991**, *32*, 4561–4564; (d) Kawagishi, H.; Ando, M.; Sakamoto, H.; Yoshida, S.; Ojima, F.; Ishiguro, Y.; Ukai, N.; Furukawa, S. *Phytochemistry* **1992**, *32*, 175–178; (e) Ueda, K.; Tsujimori, M.; Kodani, S.; Chiba, A.; Kubo, M.; Masuno, K.; Sekiya, A.; Nagai, K.; Kawagishi, H. *Bioorg. Med. Chem. Lett.* **2008**, *16*, 9467–9470; (f) Mori, K.; Kikuchi, H.; Obara, Y.; Iwashita, M.; Azumi, Y.; Kinugasa, S.; Inatomi, S.; Oshima, Y.; Nakahata, N. *Phytomedicine* **2010**, *17*, 1082–1085.
3. Kimura, Y.; Nishibe, M.; Nakajima, H.; Hamasaki, T.; Shimada, A.; Tuneda, A.; Shigematsu, N. *Agric. Biol. Chem.* **1991**, *55*, 2673–2674.
4. Arnone, A.; Cardillo, R.; Nasini, G.; Vajna de Pava, O. *J. Nat. Prod.* **1994**, *57*, 602–606.
5. For a review on mycophenolic acid: Bentley, R. *Chem. Rev.* **2000**, *100*, 3801–3825.
6. (a) Kobayashi, K.; Shimizu, H.; Itoh, M.; Suginome, H. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2435–2437; (b) Makara, G. M.; Anderson, W. K. *J. Org. Chem.* **1995**, *60*, 5717–5718; (c) Lee, Y.; Fujiwara, Y.; Ujita, K.; Nagatomo, M.; Ohta, H.; Shimizu, I. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1437–1443; (d) Patterson, J. W. *J. Org. Chem.* **1995**, *60*, 4542–4548.
7. (a) Canonica, L.; Rindone, B.; Santaniello, E.; Scolastico, C. *Tetrahedron* **1972**, *28*, 4395–4404; (b) Plé, P. A.; Hamon, A.; Jones, G. *Tetrahedron* **1997**, *53*, 3395–3400.
8. Covarrubias-Zúñiga, A.; González-Lucas, A. *Tetrahedron Lett.* **1998**, *39*, 2881–2882.
9. (a) Birch, A. J.; Wright, J. J. *Aust. J. Chem.* **1969**, *22*, 2635–2644; (b) Watanabe, M.; Tsukazaki, M.; Hamada, Y.; Iwao, M.; Furukawa, S. *Chem. Pharm. Bull.* **1989**, *37*, 2948–2951; (c) de la Cruz, R. A.; Talamás, F. X.; Vázquez, A.; Muchowski, J. M. *Can. J. Chem.* **1997**, *75*, 641–645; (d) Nelson, P. H.; Carr, S. F.; Devens, B. H.; Eugui, E. M.; Franco, F.; Gonzalez, C.; Hawley, R. C.; Loughhead, D. G.; Milan, D. J.; Papp, E.; Patterson, J. W.; Rouhafza, S.; Sjogren, E. B.; Smith, D. B.; Stephenson, R. A.; Talamas, F. X.; Waltos, A.-M.; Weikert, R. J.; Wu, J. C. *J. Med. Chem.* **1996**, *39*, 4181–4196.
10. Danheiser, R. L.; Gee, S. K.; Perez, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 806–810.
11. Kende, A. S.; Fludzinski, P. *Org. Synth.* **1986**, *64*, 221–223.
12. When a 0.3 M ethanol solution of **3** (1 equiv) and ethyl acetoacetate **4** (1 equiv) was refluxed together in the presence of NaOEt (1 equiv), the expected cyclic ketone **6** was obtained in only 18% yield. Careful analysis of the crude mixture indicated that self-condensation of **3** took precedence over intermolecular Michael addition. Thus, a mixture of **3** (1 equiv), **4** (1.5 equiv) and NaOEt (1 equiv) was first stirred at room temperature for 24 h to induce intermolecular Michael addition. After addition of another aliquot of NaOEt (0.2 equiv), the mixture was added to refluxing EtOH over a period of 12 h (final concentration: 0.03 M) and stirred at reflux an additional 34 h. In this manner, the yield of **6** was doubly improved.
13. Cleaver, L.; Croft, J. A.; Ritchie, E.; Taylor, W. C. *Aust. J. Chem.* **1976**, *29*, 1989–2001.
14. King, L. C.; Ostrum, G. K. *J. Org. Chem.* **1964**, *29*, 3459–3461.
15. Related examples: (a) Saimoto, H.; Ohrai, S.; Sashiwa, H.; Shigemasa, Y.; Hirama, T. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2727–2734; (b) Falck, J. R.; Reddy, K. K.; Chandrasekhar, S. *Tetrahedron Lett.* **1997**, *38*, 5245–5248; (c) Treadwell, E. M.; Cermak, S. C.; Wiemer, D. F. *J. Org. Chem.* **1999**, *64*, 8718–8723.
16. Krasovskiy, A.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 3333–3336.
17. Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508–524.
18. Related examples: (a) Takemura, S.; Hirayama, A.; Tokunaga, J.; Kawamura, F.; Inagaki, K.; Hashimoto, K.; Nakata, M. *Tetrahedron Lett.* **1999**, *40*, 7501–7505; (b) Jung, Y.-S.; Joe, B.-Y.; Seong, C.-M.; Park, N.-S. *Bull. Korean Chem. Soc.* **2000**, *21*, 463–464; (c) Takaoka, S.; Nakade, K.; Fukuyama, Y. *Tetrahedron Lett.* **2002**, *43*, 6919–6923.
19. Weigand, S.; Brückner, R. *Synthesis* **1996**, 475–482.
20. Littke, A. F.; Schwarz, L.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 6343–6348.
21. For systematic study of the Stille reactions of the hindered, electron-rich phenol triflates and organostannanes: Saá, J. M.; Martorell, G.; García-Raso, A. *J. Org. Chem.* **1992**, *57*, 678–685.
22. Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277–7287.
23. Guindon, Y.; Yoakim, C.; Morton, H. E. *J. Org. Chem.* **1984**, *49*, 3912–3920.
24. When CSA was used for deprotection, less than 50% yield of the desired product was obtained, together with polar unknown byproducts.
25. Suga, S.; Yamada, D.; Yoshida, J. *Chem. Lett.* **2010**, *39*, 404–406.