Palladium-Catalyzed Reductive Coupling of Acid Chlorides with β-Stannyl Enones: Synthesis of 1,4-Diketones and Mechanistic Aspects

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The palladium-catalyzed coupling of acid chlorides with (*E*)-1,2-bis(tri-*n*-butylstannyl)ethene or β-stannyl enones gives butane-1,4-diones directly by reduction of the intermediate enedicarbonyl intermediate. The double bond conjugated with a single carbonyl group was not significantly reduced. The generality of the method is illustrated by two syntheses of the 1,4-diketone ipomeanine. By performing the reaction at lower temperatures, α,β-unsaturated 1,4-diketones can also be prepared. The reduction of the intermediate α,β-unsaturated 1,4-diketones probably proceeds by insertion of a palladium hydride, formed *in situ* by reaction of a Pd(II) complex with Bu_3SnCl, followed by hydrolysis of the intermediate palladium enolate.

Introduction

A variety of synthetic methods have been developed for the preparation of 1,4-diketones[1-5] because of their importance as intermediates for the synthesis of cyclopentenones and heterocyclic compounds such as furans, pyrroles, thiophenes, and pyridazines.[6,7] As a simple alternative to the known methods, we expected that the double coupling reaction of (*E*)-1,2-bis(tri-*n*-butylstannyl)-ethene (**1**) with acid chlorides in the presence of palladium catalysts would provide a direct entry to the required α,β-unsaturated 1,4-diketones, precursors of 1,4-diketones. The required palladium-catalyzed acylation of organostannanes by acid chlorides is one of the best known and more general Stille coupling reactions.[8,9] The corresponding reaction with alkenylstannanes gives rise to α,β-unsaturated ketones in moderate to good yields.[10,11] On the other hand, distannane **1** has been reported to afford either mono-[12] or dicoupled[13] derivatives with suitable electrophiles in the presence of palladium catalysts depending on the reaction conditions. On the basis of these precedents, we have developed a new method for the preparation of 1,4-diketones based on the palladium-catalyzed coupling of acid chlorides with (*E*)-1,2-bis(tri-*n*-butylstannyl)ethene (**1**)[14,15] or β-stannyl enones that proceeds by the reduction of the intermediate α,β-unsaturated-1,4-diketones under the reaction conditions.[16] In the context of this method, stannane **1** behaves as a synthetic equivalent for the ethane 1,2-dianion,[17] which can be either transformed in a single operation into a symmetrical 1,4-diketone or, in two steps, into unsymmetrical derivatives (Scheme 1). In this paper we report on the scope and limitations of this procedure for the synthesis of 1,4-diketones as well as some mechanistic work directed to determine the nature of the reductant formed under the reaction conditions.

Results and Discussion

Synthesis of 1,4-Diketones. The first experiments were carried out with stannane **1** and benzoyl chloride as the electrophile in the presence of $Pd(PPh_3)_4$ catalyst in 1,4-dioxane under reflux. Surprisingly, 1,4-diphenylbutane-1,4-dione (**2a**), isolated in 50% yield, was the only characterized product of the reaction with 0.5 equiv of **1** (Table 1). When the coupling reaction between benzoyl chloride and **1** (1 equiv) was performed for 20 min at 60

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Scheme 1

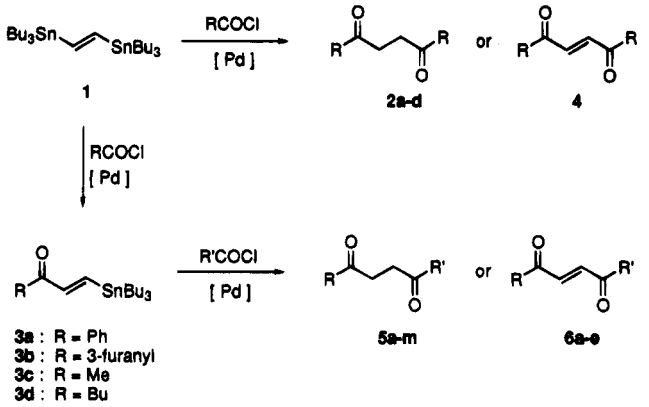


Table 1. Palladium-Catalyzed Coupling of Acid Chlorides RCOCl with Stannane 1

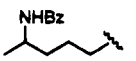
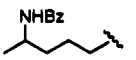
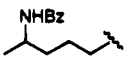
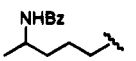
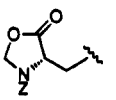
entry	R	reacn condns[a]	product	yield (%)
1	Ph	A	**2a**	50
2	Ph	B	**3a**	27
3	Ph	C	**4**	40
4	3-furanyl	A	**2b**	55
5	3-furanyl	B	**3b**	35
6	$Me_2C{=}CH^-$	A	**2c**	63
7	(*E*)-PhCH=CH$^-$	A	**2d**	25

[a] Key: (A) $Pd(PPh_3)_4$ (cat.), 1,4-dioxane, 100 °C, 23–30 h; (B) reaction run at 60 °C with 0.5 equiv of **1** for 0.3–2 h; (C) reaction run at 60 °C for 2–3 h.

°C, β-stannyl enone **3a** was isolated in low yield. Longer reaction times (2–3 h) at this temperature led to the formation of dienone **4** in 40% yield. Similarly, reaction of stannane **1** with 3-furoyl chloride in 1,4-dioxane under reflux with $Pd(PPh_3)_4$ as the catalyst gave diketone **2b** (Table 1, entry 4). Again, when the reaction of furoyl chloride and **1** (1 equiv) was allowed to proceed for 2 h at 60 °C, β-stannyl enone **3b** was obtained in 35% yield (Table 1, entry 5). 3,3-Dimethylacryloyl and cinnamoyl chlorides also led to the formation of symmetrical 1,4-diketones **2c** and **2d**, respectively (Table 1, entries 6 and 7). Although the yields were low to moderate due to some oligomerization, the crude reaction mixtures were quite clean. It is noteworthy that the double bond conjugated with a single carbonyl group was not reduced under the reaction conditions. The *E* stereochemistry of the α,β-unsaturated acid chloride was mantained in the coupled product **2d** (Table 1, entry 7).

The results of the synthesis of unsymmetrical 1,4-diketones by palladium-catalyzed coupling between β-stannyl enones and acid chlorides are summarized in Table 2. β-Stannyl enones **3a** and **3b** were prepared in low yield as described above by direct coupling of **1** and the acid chlorides in the presence of palladium(0) catalyst. Two other enone stannanes, **3c** and **3d**, were prepared by acylation of **1** in the presence of $AlCl_3$ according to a known procedure.[18] In several reactions (entries 2, 4, 8, 14, and 17) the α,β-unsaturated 1,4-diketones could also be isolated by performing the reaction at lower temperature (60 °C). The reaction proceeds satisfactorily in most cases. However, with the acid chloride derived from known (±)-5-(benzoylamino)hexanoic acid[19] the 1,4-diketones were obtained in 37–38% yield (entries 15, 16, and 18), probably due to the competing cyclization of the starting acid chloride to give the imide. A protected

Table 2. Palladium-Catalyzed Coupling of Acid Chlorides R'COCl with β-Stannyl Enones

entry	R'	R	Reaction conditions[a]	product	yield (%)
1	Me	Ph	A	**5a**	47
2	Me	Ph	B	**6a**	86
3	Me	3-furanyl	A	**5b**	100
4	Me	3-furanyl	B	**6b**	93
5	Me_3C	Ph	A	**5c**	87
6	Ph	Me	A	**5d**	70
7	Ph	Bu	A	**5e**	66
8	Ph	Bu	B	**6c**	56
9	3-furanyl	Me	A	**5b**	70
10	3-furanyl	Ph	A	**5f**	64
11	$Me_2C{=}CH$-	Me	A	**5g**	86
12	$Me_2C{=}CH$-	Ph	A	**5h**	97
13	(*E*)-PhC=CH-	Me	A	**5i**	52
14	(*E*)-PhC=CH-	Me	B	**6d**	36
15		Me	A	**5j**	37
16		Bu	A	**5k**	38
17		Bu	B	**6e**	50
18		Ph	A	**5l**	38
19		Me	A	**5m**	45

[a] Key: (A) $Pd(PPh_3)_4$ (cat.), 1,4-dioxane, 100 °C, 23–30 h; (B) reaction run at 60 °C for 2–3 h.

amino acid chloride derived from aspartic acid[20] gave the desired 1,4-diketone in 45% yield. Only in one instance (entry 13) could we observe in the crude reaction mixture traces of a product resulting from the reduction of the double bond conjugated with both a carbonyl and the phenyl group. The synthesis of ipomeanine (**5b**), a natural product detected in potatoes infected by *Ceratostomella fimbriata*,[21] illustrates the generality of the method (entries 3 and 9). The synthesis of this compound in a single step from readily available starting materials was carried out by coupling of either acetyl chloride with β-stannyl enone **3b** or 3-furoyl chloride with **3c**.[22]

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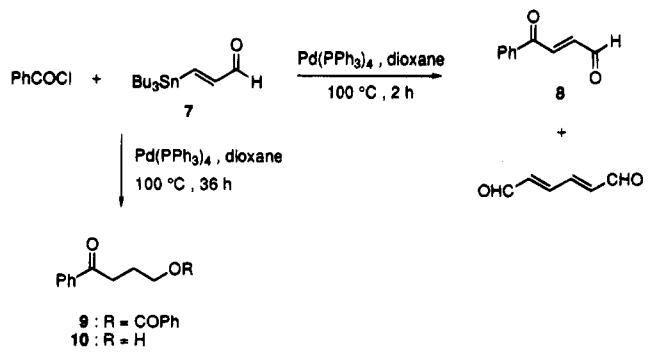
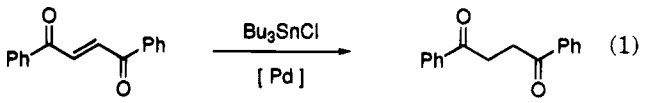
Scheme 2



For the extension of this method to the preparation of 4-oxo aldehydes, stannane **7** was prepared by hydrostannation of propargyl alcohol,[23] followed by oxidation with $BaMnO_4$.[24] Reaction of **7** with benzoyl chloride under the usual conditions gave the α,β-unsaturated keto aldehyde **8**[25] in 60% yield. Additionally, (*E*,*E*)-2,4-hexadienedial (muconaldehyde),[26] the product of homocoupling of the stannane, was isolated in 32% yield. When the reaction was allowed to proceed for longer times (36 h), the aldehyde was also reduced under the reaction conditions,[27] yielding keto ester **9** as the major product, albeit it was isolated in only 10% yield (Scheme 2). The structure of **9** was confirmed by its saponification to give known 4-hydroxy-1-phenyl-1-butanone (**10**).[28] However, this reduction of a carbonyl group is not general, since other aldehydes such as *p*-methoxybenzaldehyde and dodecanal were recovered unchanged when submitted to the reaction conditions. Cinnamaldehyde gave only 3-phenylpropanal in 30% yield after being heated in 1,4-dioxane under reflux with Bu_3SnCl and $Pd(PPh_3)_2Cl_2$ catalyst for 36 h.

Mechanistic Studies on the Reduction Step. The most remarkable aspect of the developed synthesis of 1,4-diketones is the facile reduction of the double bond of the intermediate α,β-unsaturated 1,4-diketone conjugated with both carbonyl groups.[29] Several unrelated reductions have also been observed in reactions catalyzed by palladium complexes.[30] Additionally, the conjugate reduction of α,β-unsaturated carbonyl compounds by Bu_3SnH and palladium catalysts has been reported.[31]

The Stille coupling reaction of tributylalkenylstannanes with acid chlorides yields Bu_3SnCl as a byproduct, which is less reactive that the tetraorganostannane in the transfer of an organic group to the electrophile.[8,32] However, 1,4-diketone **2a** was cleanly obtained in good yield when 1,4-diphenyl-2-butene-1,4-dione (**4**), the product of the double coupling between benzoyl chloride and stannane **1** under mild conditions, was heated with Bu_3SnCl in the presence of several palladium catalysts in 1,4-dioxane under refluxing conditions (eq 1). The best results were obtained with $Pd(PPh_3)_2Cl_2$ as the catalyst, although $Pd(PPh_3)_4$, $Pd(PPh_3)_2(PhCH_2)Cl$, $Pd(dppf)Cl_2$, $Pd(MeCN)_2Cl_2$, $Pd_2(dba)_4 + PPh_3$ (2–4 equiv), $Pd_2(dba)_4 + PCy_3$ (2 equiv)[33] gave similar results. However, $Pd_2(dba)_4$ in the absence of phosphines as the ligands was ineffective as a catalyst. Similarly, nickel complexes $Ni(PPh_3)_2Cl_2$ and $Ni(CO)_2(PPh_3)_2$ gave negative results.



Other tributyltin derivatives were not as effective as Bu_3SnCl for the reduction of **4**. With Bu_3SnF or Bu_3SnOMe no reduction was observed, while Bu_3SnI and Bu_3SnOTf gave only traces of 1,4-diketone **2a**. On the other hand, Bu_4Sn was as effective as Bu_3SnCl for the reduction of **4**. When the reduction of **4** to **2a** was performed with Bu_3SnCl (1–2 equiv) and $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ as the catalysts in $CDCl_3$ at 90 °C in a sealed tube, a mixture of 1- and 2-butenes (*cis* and *trans* isomers) was observed by ^1H NMR. After 12 h, the 1-butene was completely isomerized to a mixture of *cis*- and *trans*-2-butenes . Additionally, a stannane with a ^1H and ^{13}C NMR almost identical to that of Bu_2SnCl_2 was also observed as the only other product in the solution. GC–MS analysis of the reaction mixture showed the formation of Bu_2SnCl_2 and small amounts of the distannane $(Bu_3Sn)_2$ as the volatile products. We propose that the byproduct is Bu_2SnX_2 (X = Cl and/or OH) or a bridged oxide. Treatment of this product with aqueous HCl gives Bu_2SnCl_2. Almost clean conversion into Bu_2SnX_2 and butenes was also observed in $CDCl_3$ at 90 °C ($Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ as the catalysts). A cleaner conversion of Bu_3SnCl into Bu_2SnCl_2 was achieved when the reaction was allowed to proceed with a stoichiometric amount of palladium catalyst in the presence of excess LiCl. In none of these experiments was $BuSnX_3$ detected by ^1H or ^{13}C NMR analysis of the crude mixtures. The transformation of Bu_3SnCl into Bu_2SnX_2 and butenes suggests that the trialkyltin halide reacts with a palladium complex to give a butylpalladium intermediate, which undergoes β-hydride elimination to yield 1-butene and a palladium hydride. In agreement with this hypothesis, no reduction of **4** was observed with Me_3SnCl under the same reaction conditions. Furthermore, addition of Et_3N inhibits the reaction, probably by decomposition of the palladium hydride intermediate.

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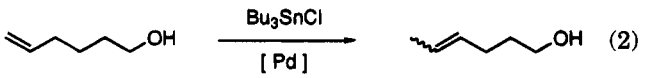
(33) dba = dibenzylideneacetone; dppf = 1,1′-bis(diphenylphosphino)ferrocene; PCy_3 = tricyclohexylphosphine.

With Bu_2SnCl_2, **4** was also converted into **2a**, although the reaction was rather slow in 1,4-dioxane under reflux. We have expected that a $BuSnX_3$ species would be a byproduct in this transformation. However, only Bu_2SnX_2 was observed by monitoring the reaction by ^1H and ^{13}C NMR. The product $BuSnX_3$ probably undergoes an exchange reaction[34] to give SnX_4 and the observed Bu_2SnX_2. This exchange is probably facilitated by a bridged oxide, since $BuSnCl_3$ did not undergo an exchange reaction under similar conditions.

The buildup of a palladium hydride from Bu_3SnCl is also supported by the almost quantitative isomerization of 5-hexenol to a *ca.* 3:1 mixture of *trans*- and *cis*-4-hexenols after 48 h at 55 °C in $CDCl_3$ (eq 2). No isomerization was observed in the absence of tin reagent or palladium catalyst.



(2)

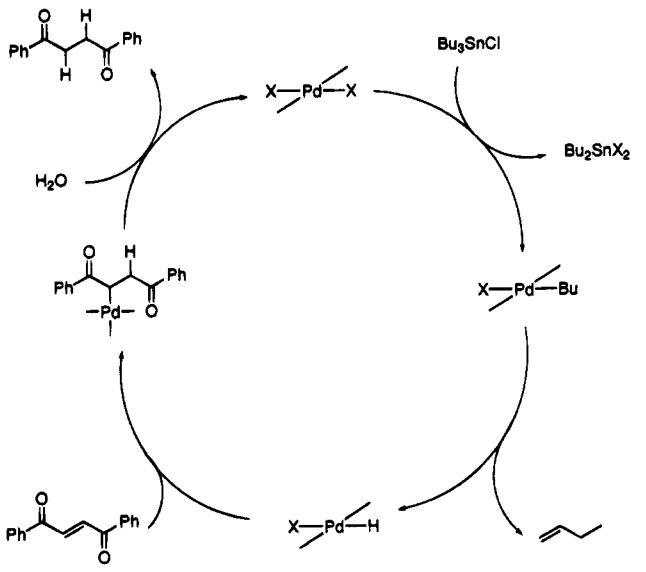
The palladium hydride formed from the chlorostannane under the reaction conditions probably undergoes insertion into the activated double bond of **4** to give a palladium enolate.[35] The intermediate, probably a carbon-bound palladium(II) enolate,[25] may undergo a transmetalation reaction with a second molecule of Bu_3SnCl to give an alkyl species, which, after β-hydride elimination and reductive elimination, would furnish the observed products. However, the above reduction experiments with substrate **4** involve only 1 equiv of tin reagent, while the transmetalation scheme requires 2 equiv of the chlorostannane. Alternatively, the second hydrogen needed for the reduction may proceed by hydrolysis of the palladium enolate intermediate by adventitious water. Consistent with this proposal, the reduction reaction proceeded very slowly when freshly dried 1,4-dioxane was used as the solvent. Furthermore, reaction of enedione **4** and Bu_3SnCl in the presence of 3 equiv of D_2O gave 1,4-diketone **2**-d_1 (50% deuterium).

All the above data are in agreement with the catalytic cycle shown in Scheme 3. In this scheme a Pd(II) catalyst undergoes transmetalation with Bu_3SnCl to give a butylpalladium species. β-Hydride elimination and insertion affords the carbon-bound palladium enolate. Hydrolysis of this intermediate yields the observed 1,4-diketone and Bu_2SnX_2 (X = Cl and/or OH) or a tin oxide. When a palladium(0) complex such as $Pd(PPh_3)_4$ was used, the active Pd(II) catalyst necessary for the reduction may be formed by oxidative addition to the stannane[36] or by other oxidative processes.

The cleavage of the Pd—C bond in the reduction step of the coupling reaction is probably promoted by HCl, formed by reaction of the acid chlorides with traces of water.

Other substrates with double or triple bonds activated by two electron-withdrawing groups are also reduced with Bu_3SnCl and palladium catalysts. Diethyl acetylenedicarboxylate reacts with Bu_3SnCl in the presence of $Pd(PPh_3)_4$ to give a 1:1 mixture of diethyl fumarate and diethyl succinate. Maleic anhydride was also reduced to succinic anhydride with Bu_3SnCl in the presence of the palladium catalyst. However, α,β-unsaturated ketones such as dibenzylideneacetone or carvone were recovered unchanged.

Scheme 3



Conclusions

The palladium-catalyzed coupling of acid chlorides with (*E*)-1,2-bis(tri-*n*-butylstannyl)ethene or β-stannyl enones affords butane-1,4-diones directly by reduction of the intermediate enedicarbonyl intermediate. The reaction is quite general, allowing for the general preparation of this type of compounds. However, lower yields were obtained with some sensitive acid chlorides. By performing the reaction at lower temperatures, the α,β-unsaturated 1,4-diketones could also be obtained. The reduction reaction appears to be promoted by a palladium hydride, formed *in situ* by reaction of a Pd(II) complex with Bu_3SnCl.

Experimental Section

Only the most significant IR absortions and the molecular ions and/or base peaks in the MS are given. Usual workup means drying with Na_2SO_4, evaporation, and flash column chromatography with the indicated eluent. All reactions were carried out under an atmosphere of Ar. 1,4-Dioxane routinely used for the synthesis of 1,4-diketones was distilled from Na and benzophenone and was stored under Ar over 4-Å molecular sieves. (*E*)-Bis(tri-*n*-butylstannyl)ethene (**1**) was prepared by using a known procedure.[37] (*E*)-4-(Tri-*n*-butylstannyl)-3-buten-2-one (**3c**) was prepared by acetylation of **1** according to the known procedure in 49 % yield as a pale yellow oil.[18] Stannane **7** was prepared according to a known procedure.[24] Acid chlorides of entries 15—18[19] and 19[20] were prepared from the corresponding carboxylic acids by standard procedures.

(*E*)-1-Phenyl-3-(tri-*n*-butylstannyl)-2-propen-1-one (3a). A mixture of benzoyl chloride (100 mg, 0.71 mmol), $Pd(PPh_3)_4$ (41 mg, 0.035 mmol), and stannane **1**

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(517 mg, 0.85 mmol) in 1,4-dioxane (5 mL) was heated at 60 °C for 20 min. The mixture was partitioned between EtOAc and aqueous $NaHCO_3$ (5%). The organic extract was stirred with a saturated aqueous KF solution for 5 min. After the usual workup, the residue was chromatographed (200:1 hexane–EtOAc) to give **3a** as a pale yellow oil (79 mg, 27%): IR (neat) 1665, 1600 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.94–7.90 (m, 2 H), 7.79 (d, J = 19.2 Hz, 1 H), 7.57–7.48 (m, 3 H), 7.29 (d, J = 19.4 Hz, 1 H), 1.67–0.87 (m, 27 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 189.57, 153.29, 141.35, 137.62, 132.47, 128.82, 128.41, 28.99, 27.20, 13.62, 9.73; MS m/z 421 (M^+, 1), 365 (100); HRMS calcd for $C_{21}H_{34}OSn$ m/z 421.1553, found m/z 421.1519.

(*E*)-1-(3-Furanyl)-3-(tri-*n*-butylstannyl)-2-propen-1-one (3b). A mixture of 3-furoyl chloride (341 mg, 2.62 mmol), $Pd(PPh_3)_4$ (150 mg, 0.13 mmol), and stannane **1** (1.58 g, 2.62 mmol) in 1,4-dioxane (5 mL) was heated at 60 °C for 2 h. The mixture was partitioned between EtOAc and aqueous $NaHCO_3$ (5%). The organic extract was stirred with a saturated aqueous KF solution for 5 min. After the usual workup, the residue was chromatographed (70:1 hexane–EtOAc) to give **3b** as a pale yellow oil (377 mg, 35%): IR (neat) 1660, 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.05 (t, J = 1.2 Hz, 1 H), 7.80 (d, J = 19.2 Hz, 1 H), 7.45 (t, J = 1.7 Hz, 1 H), 6.99 (d, J = 19.2 Hz, 1 H), 6.84 (dd, J = 1.9, 0.7 Hz, 1 H), 1.62–0.88 (m, 27 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 183.01, 151.33, 147.31, 144.08, 142.14, 127.55, 109.38, 28.79, 27.21, 13.62, 9.76; MS m/z 411 (M^+, 3), 355 (100); HRMS calcd for $C_{19}H_{32}O_2Sn$ m/z 411.1346, found m/z 411.1365.

(*E*)-1-(Tri-*n*-butylstannyl)-1-hepten-3-one (3d). This stannane was prepared by an extension of a known procedure:[18] To a solution of stannane **1** (3.50 g, 5.77 mmol) and pentanoyl chloride (685 μL, 696 mg, 5.77 mmol) in CH_2Cl_2 (21 mL) at −78 °C was added $AlCl_3$ (846 mg, 6.35 mmol). After being stirred for 10–15 min at −78 °C, the mixture was allowed to warm to 0 °C for 40–50 min. The reaction mixture was poured into a solution of KF (3.2 g) in H_2O (50 mL). After being stirred vigorously for 5 min, the mixture was extracted with CH_2Cl_2. After the usual workup, chromatography (150:1 hexane–EtOAc) gave **3d** as a pale yellow oil (2.20 g, 95%; average yield 75%): IR (neat) 1680, 1570 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.56 (d, J = 19.8 Hz, 1 H), 6.54 (d, J = 19.8 Hz, 1 H), 2.59 (t, J = 7.4 Hz, 2 H), 1.8–1.2 (m, 15 H), 1.02–0.86 (m, 18 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 199.54, 149.44, 145.73, 38.58, 28.97, 27.20, 26.48, 22.45, 13.86, 13.60, 9.65; MS m/z 401 (M^+, 1), 345 (100).

Synthesis of 1,4-Diketones: General Procedure. (a) Synthesis of Symmetrical 1,4-Diketones (Table 1). A mixture of acid chloride (1 mmol), stannane **1** (0.5 mmol), and $Pd(PPh_3)_4$ (0.05 mmol) in 1,4-dioxane (7 mL) was heated under reflux for 23–30 h. The progress of the reaction was followed by TLC. After being cooled to room temperature, the mixture was partitioned between EtOAc and aqueous $NaHCO_3$ (5%). The organic extract was washed with aqueous HCl (1.2 M), dried (Na_2SO_4), and evaporated. The residue was chromatographed to yield the 1,4-diketones. Treatment with aqueous HCl was omitted with the furanyl derivatives. **(b) Synthesis of Unsymmetrical 1,4-Diketones (Table 2).** A mixture of acid chloride (1 mmol), stannane **3a–3d** (1 mmol), and $Pd(PPh_3)_4$ (0.05 mmol) in 1,4-dioxane (7 mL) was heated under reflux for 23–30 h. Workup as above gave the 1,4-diketones. When the coupling reaction was carried out at 60 °C for 2–3 h, the α,β-unsaturated 1,4-diketones were isolated in the stated yields. These compounds decompose readily on standing. 1,4-Diketones **2a**,[1a] **4**,[38] **2b**,[39] **2c**,[5] **2d**,[1e] **5a**,[1f] **5b** (ipomeanine),[22a] **5c**,[40] **5g**,[5] **5h**,[41] **5i**,[38] and **6a**[42] are known compounds, and their physical and spectroscopic data (IR, ^1H NMR, and MS) agree with the reported values.

1-Phenyl-1,4-octanedione (5e). This derivative was obtained as an oil after chromatography (10:1 hexane–EtOAc): IR (KBr) 1715, 1690, 1600 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.99–7.96 (m, 2 H), 7.55–7.52 (m, 1H), 7.47–7.42 (m, 2 H), 3.27 (t, J = 6.3 Hz, 2 H), 2.85 (t, J = 6.3 Hz, 2 H), 2.52 (t, J = 7.4 Hz, 2 H), 1.61 (quintet, J = 7.5 Hz, 2 H), 1.34 (sextet, J = 7.5 Hz, 2 H), 0.92 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 209.65, 198.60, 136.65, 133.02, 128.48, 127.97, 42.64, 36.11, 32.31, 25.92, 22.28, 13.80; MS m/z (M^+ + 1, 6), 218 (M^+, 1), 105 (100); HRMS calcd for $C_{24}H_{18}O_2$ m/z 218.1309, found m/z 218.1304.

1-Phenyl-4-(3-furanyl)-1,4-butanedione (5f). This derivative was purified by chromatography (5:1 hexane–EtOAc): mp 110–111 °C; IR (Nujol) 1690, 1675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.13 (m, 1 H), 8.03–8.00 (m, 2 H), 7.60–7.44 (m, 4 H), 6.80 (dd, J = 1.9, 0.8 Hz, 1 H), 3.43 (t, J = 6.2, 2 H), 3.23 (t, J = 6.2 Hz, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 198.50, 193.39, 147.29, 144.15, 136.60, 133.19, 128.58, 128.07, 127.45, 108.59, 31.02, 32.26; MS m/z 228 (M^+, 11), 105 (100). Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.60; H, 5.29. Found: C, 73.89; H, 5.65.

(*E*)-1-(3-Furanyl)-2-pentene-1,4-dione (6b). This derivative was obtained after purification by chromatography (7:1 hexane–EtOAc) as a pale yellow solid contaminated with *ca.* 5% of **12** (ipomeanine): IR (KBr) 1715, 1675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.16 (m, 1 H), 7.50 (d, J = 1.7 Hz, 1 H), 7.32 (d, J = 15.7 Hz, 1 H), 7.10 (d, J = 15.7 Hz, 1 H), 6.87 (d, J = 1.9 Hz, 1 H), 2.41 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 197.50, 183.61, 148.41, 144.89, 137.29, 134.44, 128.12, 106.61, 29.19; EM m/z 165 (M^+, 3), 95 (100).

(*E*)-1-Phenyl-2-octene-1,4-dione (6c). This derivative was obtained as an oil after purification by chromatography (20:1 hexane–EtOAc): IR (neat) 1700, 1665 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.01–7.97 (m, 2 H), 7.73 (d, J = 15.6 Hz, 1 H), 7.62–7.59 (m, 1 H), 7.53–7.48 (m, 2 H), 7.13 (d, J =15.7 Hz, 1 H), 2.69 (t, J = 7.4 Hz, 2 H), 1.67 (quintet, J = 7.4 Hz, 2 H), 1.37 (sextet, J = 7.4 Hz, 2 H), 0.94 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$; DEPT) δ 200.18 (s), 190.35 (s), 137.91 (d), 136.88(s), 133.79 (d), 133.22 (d), 128.87 (d), 128.84 (d), 42.20 (t), 25.87 (t), 22.29 (t), 13.80 (q); MS m/z 216 (M^+, 6), 131 (100); HRMS calcd for $C_{14}H_{16}O_2$ m/z 216.1150, found m/z 216.1151.

(*E,E*)-7-Phenyl-3,6-heptadiene-2,5-dione (6d). This derivative was obtained after purification by chromatography (6:1 hexane–EtOAc) as a semisolid: IR (neat) 1710, 1680 (br) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 16.1 Hz, 1 H), 7.63–7.58 (m, 2 H), 7.46–7.41 (m, 3 H), 7.28 (d, J = 16.0 Hz, 1 H), 7.01 (br, 2 H), 2.41 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$; DEPT) δ 198.07 (s), 188.96 (s), 145.51 (d), 137.18 (d), 136.23 (d), 134.11 (s), 131.11

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(d), 129.02 (d), 128.60 (d), 124.70 (d), 28.59 (q); MS m/z 200 (M^+, 15), 103 (100).

(±)-9-(Benzoylamino)-2,5-decanedione (5j). This derivative was obtained after purification by chromatography (1:1.5 hexane–EtOAc): mp 91 °C; IR (KBr) 1705, 1635 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.82–7.75 (m, 2 H), 7.53–7.37 (m, 3 H), 6.13 (d, J = 8.5 Hz, 1 H), 4.18 (m, 1 H), 2.76–2.60 (m, 4 H), 2.58–2.40 (m, 2 H), 2.18 (s, 3 H), 1.80–1.47 (m, 4 H), 1.24 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 209.35, 207.21, 166.93, 134.92, 131.25, 128.48, 126.87, 45.58, 42.16, 36.95, 36.02 (2C), 29.88, 21.05, 20.15; MS m/z 290 (M^++1, 17), 289 (M^+, 1), 195 (100). Anal. Calcd for $C_{14}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.65; H, 8.15; N, 5.06.

(±)-2-(Benzoylamino)tridecane-5,8-dione (5k). This derivative was obtained after purification by chromatography (3:1 hexane–EtOAc): mp 87–89 °C; IR (KBr) 1700, 1635 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80–7.77 (m, 2 H), 7.48–7.39 (m, 3 H), 6.17 (d, J = 7.8 Hz, 1 H), 4.18 (septet, J = 7.0 Hz, 1 H), 2.70–2.61 (m, 4 H), 2.56–2.49 (m, 4 H), 1.71–1.65 (m, 2 H), 1.59–1.51 (m, 4 H), 1.35–1.27 (m, 2 H), 1.24 (d, J = 6.6 Hz, 3 H), 0.90 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 209.77, 209.49, 166.95, 134.93, 131.23, 128.46, 126.67, 45.61, 42.50, 42.21, 36.04, 35.98, 35.94, 25.96, 22.29, 21.06, 20.17, 13.79; MS m/z 331 (M^+, 0.3), 105 (100). Anal. Calcd for $C_{20}H_{29}O_3$: C, 72.47; H, 8.82; N, 4.23. Found: C, 72.15; H, 9.20; N, 4.50.

(±)-8-(Benzoylamino)-1-phenyl-1,4-nonanedione (5l). This derivative was obtained after purification by chromatography (3:1 hexane–EtOAc): mp 135–136 °C; IR (KBr) 1710, 1695 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.99–7.94 (m, 2 H), 7.81–7.76 (m, 2 H), 7.60–7.33 (m, 6 H), 6.27 (d, J = 8.0 Hz, 1 H), 4.18 (m, 1 H), 3.27 (m, 2 H), 2.86–2.79 (m, 2 H), 2.63–2.55 (m, 2 H), 1.78–1.50 (m, 4 H), 1.24 (d, J = 6.6 Hz, 3 H); ^{13}C RMN (50 MHz, $CDCl_3$) δ 209.39, 198.63, 166.94, 136.66, 134.92, 133.11, 131.15, 128.54, 128.47, 128.00, 126.86, 45.61, 42.29, 36.13, 35.98, 32.38, 21.01, 20.18; MS m/z 353 (M^+ + 2, 6), 352 (M^+ + 1, 23), 351 (M^+, 2), 105 (100). Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.18; H, 7.17; N, 3.98. Found: C, 74.85; H, 6.93; N, 4.31.

(±)-(*E*)-2-(Benzoylamino)-7-tridecene-6,9-dione (6e). This derivative was obtained after purification by chromatography (3:1 hexane–EtOAc): mp 110–112 °C; IR (KBr) 1680, 1635 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.79–7.76 (m, 2 H), 7.45–7.40 (m, 3 H), 6.86 (m, 2 H), 6.02 (d, J = 7.6 Hz, 1 H), 4.23 (m, 1 H), 2.76–2.69 (m, 2 H), 2.63 (t, J = 7.3 Hz, 2 H), 1.78–1.71 (m, 2 H), 1.67–1.57 (m, 4 H), 1.38–1.31 (m, 2 H), 1.26 (d, J = 6.6 Hz, 3 H), 0.92 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 200.62, 200.38, 166.97, 136.47, 136.11, 134.82, 131.36, 128.55, 126.82, 45.33, 41.34, 40.90, 36.15, 25.79, 22.22, 21.04, 19.91, 13.76; MS m/z 330 (M^+ + 1, 0.4), 105 (100). Anal. Calcd for $C_{20}H_{27}O_3$: C, 72.91; H, 8.26; N, 4.25. Found: C, 72.77; H, 8.50; N, 4.15.

(S)-4-(2,5-Dioxohexyl)-3-(benzyloxycarbonyl)-5-oxazolidinone (5m). This derivative was obtained after purification by chromatography (1:1 hexane–EtOAc): mp 67–69 °C; IR (KBr) 1805, 1720 (br) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.37 (s, 5 H), 5.50 (br s, 1 H), 5.30 (dd, J = 3.9, 1.4 Hz, 1 H), 5.25 (AB system, part A, d, J = 12.1 Hz, 1 H), 5.10 (AB system, part B, d, J = 12.1 Hz, 1 H), 4.27 (t, J = 3.0 Hz, 1 H), 3.45 (br s, 1H), 3.10 (dd, J = 18.6, 3.1 Hz, 1 H), 2.75–2.55 (m, 4 H), 2.15 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 206.22, 205.99, 172.02, 152.57, 135.48, 128.68, 128.56, 128.25, 78.47, 67.87, 50.88, 42.27 (br), 36.81, 35.73, 29.64. Anal. Calcd for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.74; N, 4.20. Found: C, 60.97; H, 5.82; N, 4.29.

(*E*)-1-Phenyl-4-oxo-2-butenal (8). A mixture of benzoyl chloride (36 mg, 0.29 mmol), 3-(tri-*n*-butylstannyl)-2-propenal (**7**)[24] (100 mg, 0.29 mmol), and $Pd(PPh_3)_4$ (0.05 mmol) in 1,4-dioxane (6 mL) was heated under reflux conditions for 2 h. After the mixture was cooled to room temperature, the solvent was evaporated. The residue was chromatographed (3:2 hexane–EtOAc) to yield **8** (25 mg, 65%) with physical and spectroscopic data in agreement with the reported values.[25] Additionally, muconaldehyde (5 mg, 32%) was also isolated. Muconaldehyde showed a ^1H NMR spectrum identical with the reported values.[43]

4-Hydroxy-1-phenyl-1-butanone (10). A mixture of benzoyl chloride (100 mg, 0.81 mmol) , 3-(tri-*n*-butylstannyl)-2-propenal (**7**) (230 mg, 0.63 mmol), and $Pd(PPh_3)_4$ (0.05 mmol) in 1,4-dioxane (6 mL) was heated under reflux conditions for 36 h. After the mixture was cooled to room temperature, the solvent was evaporated. The residue was chromatographed (4:1 hexane–EtOAc) to yield **9** as an orange oil (15 mg, 10%): ^1H NMR (200 MHz, $CDCl_3$) δ 8.09–8.00 (m, 4 H), 7.65–7.35 (m, 6 H), 4.44 (t , 2 H, J = 7.0 Hz), 3.16 (t, 2 H, J = 7.2 Hz), 2.26 (quint, 2 H, J = 7 Hz) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.87, 182.18, 136.75, 133.64, 133.10, 132.89, 129.51, 128.58, 128.31, 127.97, 64.26, 34.93, 23.30. Saponification of **9** (10 mg, 0.04 mmol) with KOH (2 M in MeOH, 1 mL) for 12 h at 23 °C gave **10** (4 mg, 66%) with physical and spectroscopic data in agreement with the reported values.[33]

Reduction Experiments: General Procedure. A mixture of tributylstannane (1 mmol), diketone **4** (1 mmol), and $Pd(PPh_3)_2Cl_2$ or $Pd(PPh_3)_4$ (0.05 mmol) in 1,4-dioxane (6 mL) was heated under reflux conditions for 8–48 h. After being cooled to room temperature, the solvent was evaporated. The residue was chromatographed to yield **2**. The product assigned structure Bu_2SnX_2 has a ^{13}C NMR spectrum similar to that of Bu_2SnCl_2: ^{13}C NMR (50 MHz, $CDCl_3$; DEPT) δ 26.85 (t), 26.54 (t), 26.26 (t), 13.44 (q). Authentic Bu_2SnCl_2 showed: ^{13}C NMR (50 MHz, $CDCl_3$; DEPT) δ 27.18 (t), 27.10 (t), 26.40 (t), 13.67 (q). GC–MS analysis of the reaction mixtures showed formation of Bu_2Cl_2 and $(Bu_3Sn)_2$, characterized by their molecular ions and by comparison with authentic samples.

1,4-Diphenyl-1,4-butanedione-2-*d*$_1$. A mixture of Bu_3SnCl (149 mg, 0.46 mmol), diketone **4** (108 mg, 0.46 mmol), D_2O (22 μL, 1.37 mmol), and $Pd(PPh_3)_2Cl_2$ (15 mg, 0.05 equiv) in 1,4-dioxane (6 mL) was heated under reflux conditions for 20 h. After being cooled to room temperature, the solvent was evaporated. The residue was chromatographed (4:1 hexane:EtOAc) to yield a 1:1 mixture of d_0 and d_1 isotopologs as a crystalline colorless solid (80 mg, 70%): ^1H NMR (200 MHz, $CDCl_3$) δ 8.09–8.00 (m, 4 H), 7.65–7.50 (m, 6 H), 3.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$; DEPT) δ 198.70 (s), 136.73 (s), 133.11 (d), 128.55 (s), 128.08 (s), 32.48 (t) (a low intensity signal at 32.2 (m) was assigned to the deuterated methylene); MS m/z 239 (M^+, 19), 105 (100).

Isomerization of 5-Hexenol (Eq 2). A mixture of 5-hexenol (100 mg, 1.0 mmol), Bu_3SnCl (325 mg, 218 mmol), and $Pd(PPh_3)Cl_2$ (35 mg, 0.05 mmol) in 1,4-

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dioxane (3 mL) was heated under reflux conditions for 3 h. After being cooled to room temperature, the mixture was filtered through Celite and chromatographed (5:1 hexane:EtOAc) to give a *ca.* 3:1 mixture of *trans*- and *cis*-4-hexenols (66 mg, 66%) with ^1H and ^{13}C NMR data in agreement with the reported values.[44] Longer reactions times led to the formation the above mixture of 4-hexenols contaminated with small amounts of hexanal.

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Supplementary Material Available: Copies of the ^1H and/or ^{13}C NMR spectra for compounds **3a**, **3b**, **3d**, **5e**, and **6b–6d** (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.